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Novikov, Roman

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UNIVERSITE DE GENEVE FACULTE DES SCIENCES
Section de chimie et biochimie
Département de chimie organique Professeur Jérôme Lacour

Enantioselective Epoxidation of Prochiral Alkenes Catalyzed by Axially Chiral Biaryl Iminium Salts

THESE

présentée à la Faculté des sciences de l'Université de Genève
pour obtenir le grade de Docteur ès sciences, mention chimie

par

Roman Novikov

de

Saint-Pétersbourg (Russie)

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La Faculté des sciences, sur le préavis de Messieurs J. LACOUR, professeur ordinaire et directeur de thèse (Département de chimie organique), A. ALEXAKIS, professeur ordinaire (Département de chimie organique), A. BERKESSEL (Universität zu Köln, Institut für Organische Chemie, Köln, Deutschland), autorise l'impression de la présente thèse, sans exprimer d'opinion sur les propositions qui y sont énoncées.

Genève, le 23 novembre 2009

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Les résultats rapportés dans ce manuscrit ont été obtenus dans le cadre d'un travail de thèse réalisé au sein du laboratoire du Prof. Jérôme Lacour, dans le département de Chimie Organique de l'Université de Genève, du 1er Octobre 2005 au 19 Novembre 2009.

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Abbreviations

br. s: broad singlet
s: singlet
d: doublet
dd: doublet of doublets
t: triplet
q: quartet
sept: septet
m: multiplet
hv: light
TLC: thin layer chromatography
CD: circular dichroism
R_f: retardation factor
cat.: catalytic amount
equiv.: equivalent
conv.: conversion
Mp: melting point
ppm: part per million
ee: enantiomeric excess
Conf.: configuration
r.t.: room temperature
DMSO: dimethylsulfoxide
DCM: dichloromethane
MeOH: methanol
Et_2O: diethyl ether
EtOAc: ethyl acetate
THF: tetrahydrofuran
MeCN: acetonitrile
DMF: *N*,*N*-dimethylformamide
DIPEA: *N*,*N*-diisopropylethylamine
Dibal-H: diisobutylaluminium hydride
PCC: pyridinium chlorochromate
Me: methyl
Et: ethyl
i-Bu: *iso*-butyl
i-Pr: *iso*-propyl
t-Bu: *tert*-butyl
Cy: cyclohexyl
Ph: phenyl
NBS: *N*-bromosuccinimide
AIBN: 2,2′-azobisisobutyronitrile
Py: pyridine

Units

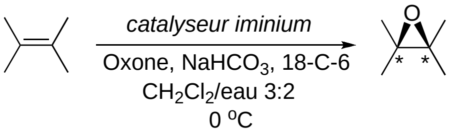
^{o}C: degree Celsius
K: Kelvin
cal: calories
mL: milliliter
μl: microliter
mol: mole
mmol: millimole
M: molarity
g: gram
mg: milligram
min: minute
h: hour
Å: argstrom

Symbols

δ: chemical shift
J: coupling constant
t_R: retention time
l: length
$\Delta G^{\neq}$: free energy of activation
λ: wave length
Hz: Hertz

Résumé

L’objectif des travaux de cette thèse a été de développer la réaction d’époxydation énantiosélective d’oléfines (Equation 1) catalysée par des sels d’iminium rigides et configurationellement stables au type **2**-**5** (Figure 1).



(1)

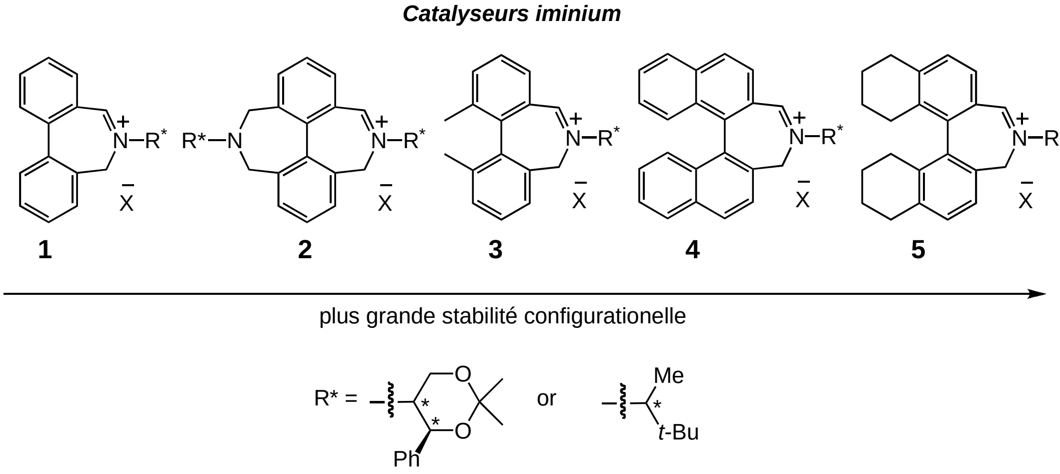
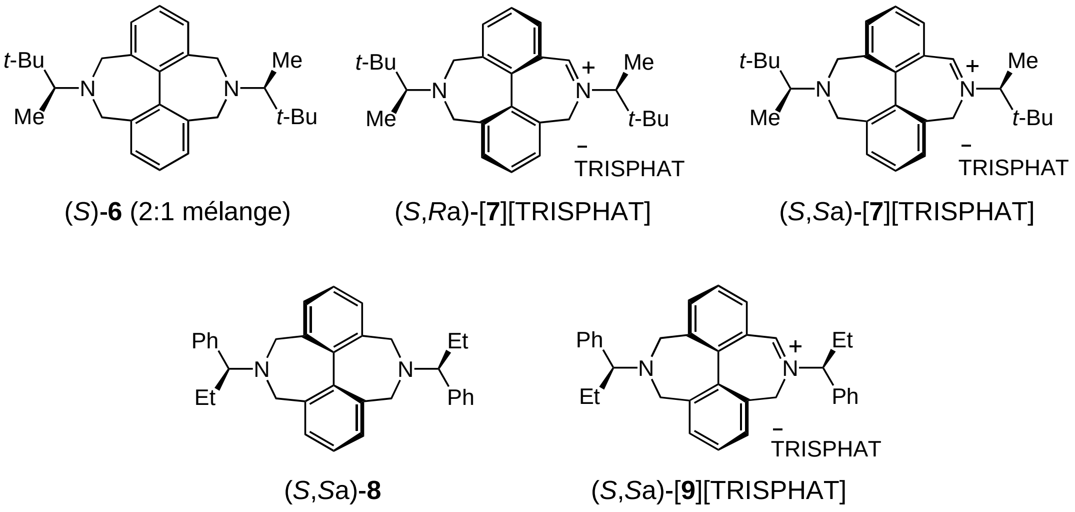


Figure 1. Catalyseurs biarylazépinium pour l’epoxydation énantioselective d’alcènes.

Depuis la premiere publication de Bohé *et al.* en 1993,[1] l’époxydation énantiosélective d’alcènes catalysée par des sels d’iminiums a reçu un intérêt croissant de la part de la communauté chimique. Malgré les nombreuses publications et le grand nombre de catalyseurs rapportés, seuls quelques exemples ont permis d’atteindre des niveaux d’induction asymétrique réellement satisfaisants. Parmi ceux-ci, la famille des diarylazépiniums est apparue comme la plus prometteuse dans le contexte de l’époxydation énantiosélective d’alcènes.[2-4] Dans la majorité des cas, le catalyseur comprend deux éléments stéréogenes : la chiralité axiale du fragment biaryle, elle-même souvent complétée par un ou plusieurs centres de chiralité portés par le fragment exocyclique dérivé d’amines primaires énantiopures. Le catalyseur **1**, de type biphenylazépinium, a été décrit indépendamment par Page[5, 6] et Lacour[7, 8] comme une molécule configurationellement labile (*tropos*). En effet, la rotation des noyaux aromatiques autour de l’axe de chiralité C(sp^2)-C(sp^2) est rapide à température ambiante. La configuration absolue de l’époxyde obtenu est alors essentiellement contrôlée par la chiralité de l’amine exocyclique. Le cas des composés de type **2** (azépines DBB) dont le fragment biphényle est doublement ponté a été étudié précédemment au sein de notre laboratoire.[9] Ces molécules sont synthétisées en deux étapes à partir du pyrène. La présence du second cycle à sept chaînons accolé confère une rigidité accrue au fragment biphenyle (molécules *atropos*), cependant la configuration des époxydes finaux est toujours contrôlée par l'amine chirale et non pas par la chiralité axiale du fragment biaryle stable. Les travaux décrits dans ce manuscrit ont permis de montrer que, dans le cadre de l'époxydation énantiosélective d'alcènes prochiraux, un mélange 2:1 des diastéréoisomères d'azépines DBB (*S*,*S*a)-**6** et (*S*,*R*a)-**6** (notés *S*-**6**) fournit essentiellement les mêmes résultats que les sels diastéréoisomériquement purs de TRISPHAT (*S*,*R*a)-[**7**][TRISPHAT] et (*S*,*S*a)-[**7**][TRISPHAT]. De plus, la DBB azépine (*S*,*S*a)-**8** (Figure 2) est globalement moins active que le sel de TRISPHAT correspondant ((*S*,*S*a)-[**9**][TRISPHAT]). Ce problème peut être contourné en traitant le composé (*S*,*S*a)-**8** avec de la NBS avant l'ajout des autres réactifs : le sel d'azépinium (*S*,*S*a)-[**8**][Br], formé *in situ*, fournit des résultats très similaires au composé (*S*,*S*a)-[**9**][TRISPHAT] (jusqu'à 95 % *ee* dans le cas du 1-phenyl-3,4-dihydronaphtalene). Ainsi les sels d'azépiniums ont pu être formés *in situ* dans les études suivantes.



(*S*)-**6** (2:1 mélange) (*S*,*R*a)-[**7**][TRISPHAT] (*S*,*S*a)-[**7**][TRISPHAT]

(*S*,*S*a)-**8** (*S*,*S*a)-[**9**][TRISPHAT]

Figure 2.

Les dérivés azépiniums de type **4**, comportant un fragment binaphtyle configurationellement stable, d'abord introduit par Aggarwal[10] en 1996 puis utilisés par Page[2] et Lacour,[4] sont actuellement la meilleure famille de catalyseurs pour l'époxydation en termes de réactivité et d'énantiosélectivité (jusqu'à 95 % *ee* dans le cas du 1-phenyl-3,4-dihydronaphtalene). Contrairement aux catalyseurs **1** et **2**, la configuration de l'époxyde obtenu à l'aide des composés de type **4** est déterminée par la configuration du fragment binaphtyle et non pas par celle du fragment provenant de l'amine chirale. L'hypothèse de travail suivie pendant ces travaux a été que la différence de comportement observée pouvait être la résultante de différences d’angles dièdre Θ et F̣mesurés respectivement à l’intérieur et à l’extérieur du cycle à sept chainons contenant l’atome d’azote (Figure 3).

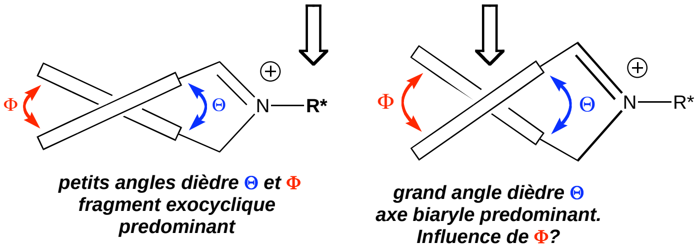


Figure 3. Influence sur la stéréochimie du produit des angles dièdre Θ et F̣mesurés respectivement à l’intérieur et à l’extérieur du cycle à sept chainons).

Nous avons supposé que de faibles valeurs de l’angle dièdre Θ entre les deux noyaux aromatiques (40-45°) rendraient l’influence de la chiralité du fragment exocyclique prédominante alors que de grandes valeurs (Θ > 53°) rendraient la chiralité axiale du fragment biaryle prédominante pour le contrôle de la stéréochimie de l’époxyde obtenu.

En vue de confirmer cette hypothèse, deux catalyseurs, comprenant un fragment biaryle configurationellement stable, mais dont l’angle dièdre Θ serait légèrement supérieur et inférieur à celui d’un dérivé azépinium de type **2** ont été préparés. Les études rapportées dans la littérature nous ont menés à penser que des composés de types **3** et **5** seraient des candidats idéaux. La synthèse des azépines **10** et **12**, précurseurs des sels d’azépinium **3**, **4** et **5** est présentée Schéma 1. Les azépines comportant un fragment 6,6’-dimethylbiphenyle, précurseurs des sels **3**, ont été obtenues en huit étapes à partir d’acide 2-amino-3-méthoxybenzoïque commercial. Les binaphtylazépines **11** ont été obtenues en quatre étapes à partir de (*R*)-BINOL énantiopur. Enfin, les azépines comportant un fragment 5,5’,6,6’,7,7’,8,8’-octahydronaphtalène ont été synthétisées en six étapes également à partir du (*R*)-BINOL. Les azépines **10** à **12** sont de configuration axiale *R*a et portent en tant qu’auxilaire chiral supplémentaire diverses amines chirales. Les analyses par diffraction des rayons X des composés **10b**, **11b**·HCl et **12b**·HCl ont permis de montrer que l’angle dièdre Φ augmente effectivement de manière sensible de **10** à **11** puis de **11** à **12** (de 57,5° à 67,0°) alors que l’angle Θ n’est que peu modifié.

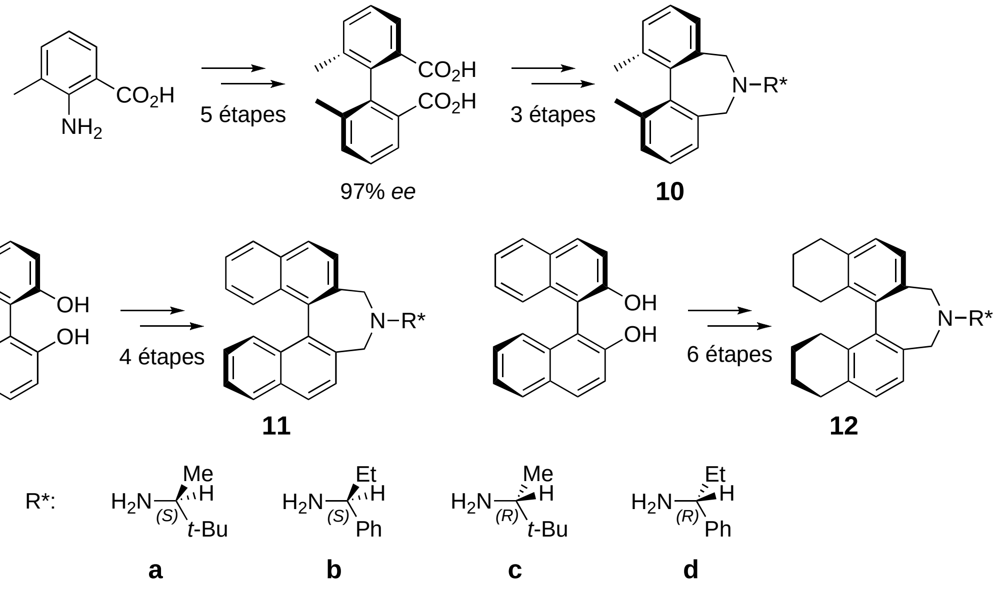
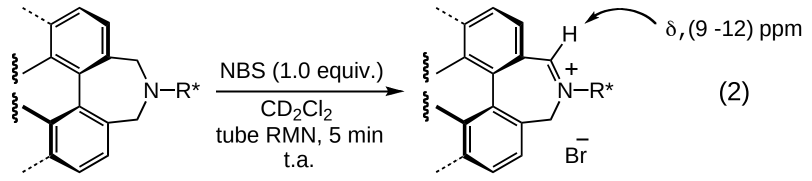


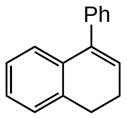
Schéma 1. Synthèse des azépines **11** et **12**.

Les sels d'iminiums, utilisés en tant que catalyseurs pour l'époxydation d'oléfines, sont généralement synthétisés par l'oxydation d'amines tertiaires. Les méthodes traditionnellement employées sont basées sur des combinaisons de I_2/KOAc/EtOH ou NBS/AIBN/CCl_4. Il a été récemment montré dans notre groupe que la combinaison de NBS et de $CHCl_3$ était plus efficace. Les travaux de cette thèse ont démontré (suivi par RMN ^{1}H) que l'utilisation de NBS dans le CH_2Cl_2 permet d'obtenir l'iminium correspondant à partir d'une azépine encore plus rapidement (moins de cinq minutes). Les solutions de sels d'azépinium bromure obtenues peuvent être directement utilisées pour l'époxydation énantiosélective d'alcènes.

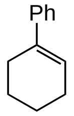


(2)

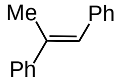
Pour cette étude, des conditions standard d'époxydation (5 mol% d'azépine + 5 mol% de NBS, Oxone® /CH_2Cl_2/$NaHCO_3$/18-Crown-6/H_2O) ont été utilisées pour l'époxydation des trois alcènes trisubstitués commerciaux (Figure 4). Certains résultats sont reportés dans le Tableau 1 : l'excès énantiomérique des époxydes obtenus augmente en passant de **3** à **4** puis de **4** à **5**. De manière générale, les catalyseurs de type **5** sont les plus sélectifs.



S1



S2



S3

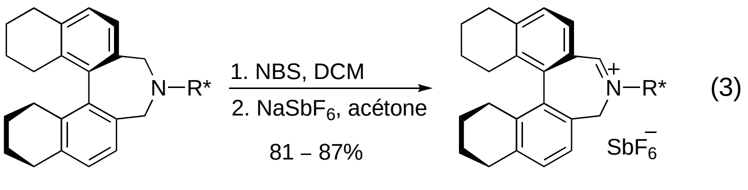
Figure 4. Alcènes trisubstitués prochiraux.

Tableau 1 Epoxydation des oléfines **S1**, **S2, S3** avec [**3c**][Br], [**4c**][Br] et [**5c**][Br] comme catalyseurs. Excès énantiomériques (%).[a]

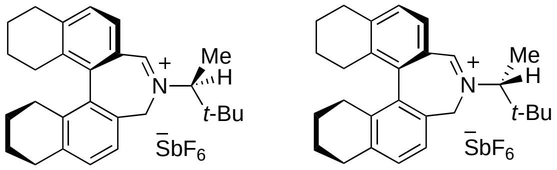
Alkene	[**3c**][Br]	[**4c**][Br]	[**5c**][Br]	[**5c**][BPh_4]	Configuration
S1	57	85	92	91	(+)-(1*R*,2*S*)
S2	67	75	83	81	(-)-(1*S*,2*S*)
S3	44	54	67	72	(-)-(1*S*,2*S*)

[a] Conditions: substrat (0.2 mmol), 5 mol % de catalyseur, 2.5 mol % 18-C-6, 1.1 eq Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 2 heurs, 0 °C. Moyenne de deux expériences. Excès énantiomériques déterminés par CSP-GC (**S2**, Chiraldex Hydrodex *b*-3P) ou CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, l 230 nm). La configuration indiquée est celle de l'époxyde obtenu.

Les résultats obtenus avec **5** sont, à quelques exceptions près, très similaires à ceux obtenus avec des sels isolés de tétraphénylborate (Tableau 1), un contre-ion communément utilisé dans cette chimie d'epoxydation. Cependant, une décomposition rapide de l'anion tétraphényl borate en milieu oxydant à été montrée. Cette réaction parasite, générant du biphenyle, conduit très rapidement à la dégradation du catalyseur dans les conditions réactionnelles, diminuant ainsi notablement la conversion dans le cas de substrats peu activés. Le contre-ion hexafluoroantimoine fut donc choisi comme alternative du fait de son poids moléculaire relativement faible et de sa grande stabilité chimique. Les sels de type [**5**][SbF_6] ont été synthétisés en deux étapes par métathèse d'ions des sels de bromure obtenus par l'oxydation des azépines **12** (Equation 3).



Ces sels ont montré une forte activité catalytique et une grande stabilité dans les conditions réactionnelles. Il a de plus été observé que (*R*a,*S*)-[**5a**][SbF_6] est plus réactif que l'épimère (*R*a,*R*)-[**5c**][SbF_6] ; ce dernier étant cependant plus sélectif (89 contre 92 *% ee* dans le cas du 1-phenylcyclohexène) (Figure 5).



Le plus réactif
(*R*a,*S*)-[**5a**][SbF_6]

Le plus sélectif
(*R*a,*R*)-[**5c**][SbF_6]

Figure 5.

Pour la suite du projet il a donc été décidé d'employer le sel (*R*a,*R*)-[**5c**][SbF_6] donnant les meilleurs résultats en termes d'énantiosélectivité ; la diminution de réactivité pouvant être simplement compensée en augmentant soit le temps de réaction soit la charge catalytique.

L'étape suivante fut de déterminer quels types d'oléfines donnent de bons résultats avec le catalyseur choisi et de rationnaliser les sélectivités obtenues. A l'aide d'alcènes « classiques » ou commerciaux, il a été observé que les oléfines trisubstituées donnent les meilleures énantiosélectivités avec (*R*a,*S*)-[**5a**][SbF_6], surtout dans le cas de doubles liaisons de configuration (*E*). Le groupe R peut être aryle (idéalement riche en électrons) ou alkyle (idéalement encombré) et le groupe R' ne doit pas être un hydrogène (Figure 6).

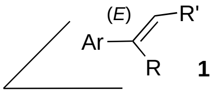


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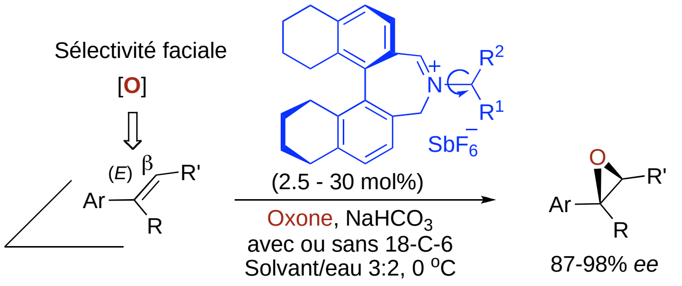
Figure 6.

Pour ces substrats, les produits d'époxydation en conditions biphasiques (CH_2Cl_2/eau) furent obtenus avec de bons rendements et un excès énantiomérique entre 87 et 98 %. Pour les substrats peu réactifs, le catalyseur (*R*a,*S*)-[**5a**][SbF_6] a été utilisé, une légère diminution de la sélectivité étant cependant obtenue.

Il a aussi été montré que dans le cas des alcools allyliques trisubstitués et encombrés, l'époxydation reste fortement énantiosélective. Deux types de conditions biphasiques ont été utilisées : le système classique MeCN/H_2O et le système CH_2Cl_2/H_2O, ce dernier permettant d'obtenir les meilleures énatiosélectivités pour les substrats activés. Dans les autres cas, l'utilisation du catalyseur plus actif (*R*a,*S*)-[**5a**][SbF_6], pour surmonter les faibles réactivités, entraîne une forte baisse de l'énantiosélectivité (jusqu'à 16 %). Dans le cas des substrats peu réactifs dans les conditions CH_2Cl_2/H_2O, le système MeCN/H_2O est alors apparu comme une meilleure alternative: des conversions complètes étant obtenues avec seulement une très légère perte en termes d'excès énantiomériques (2 à 3 %). Dans les cas de substrats activés, le système CH_2Cl_2/H_2O est le plus adapté alors que pour des substrats désactivés, le système classique $MeCN/H_2O$ est plus approprié.

Les configurations absolues des époxydes obtenus pouvant être déduits de la littérature, il est apparu intéressant de rationaliser les effets de la stéréochimie du catalyseur sur celle du produit final (Figure 7).



R': petit groupe comme CH_3, CH_2OH, CH_2OMe, CH_2 cyclique
R: Ar, Alkyl (encombré)

Figure 7. Sélectivité faciale.

Dans tous les cas, les produits obtenus proviennent de l'insertion de l'atome d'oxygène sur la même face des alcènes prochiraux étudiés : la face *Si* du carbone β des alcènes et la face *Re* des alcools allyliques (toujours la face supérieure, Figure 7; la différence de nomenclature provenant d'une inversion suivant les règles CIP due à la présence de l'atome d'oxygène). En appliquant ce modèle, la configuration absolue de l'époxyde obtenu peut être prédite avec de fortes certitudes.

Enfin, les populations de rotamères des sels (*R*a,*S*)-[**5a**][SbF_6] et (*R*a,*R*)-[**5c**][SbF_6] ont été étudiées par RMN en température variable pour expliquer leurs sélectivités très similaires mais leurs réactivités différentes. Par une série d'expériences NOESY à -80 °C, il a été montré que (*R*a,*R*)-[**5c**][SbF_6] existe en solution sous forme de deux rotamères, la conformation *antipériplanaire* étant majoritaire (*anti*/*syn* 85 :15 à 193 K) ; alors que (*R*a,*S*)-[**5a**][SbF_6] existe uniquement sous forme *synpériplanaire* (Figure 8).

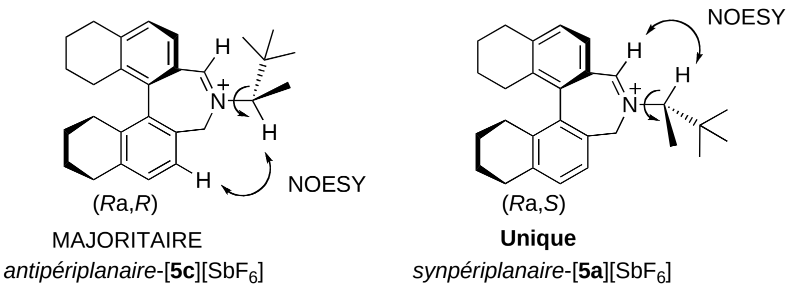


Figure 8. Rotamère majoritaire et unique de (*R*a,*R*)-[**5c**][SbF_6] et (*R*a,*S*)-[**5a**][SbF_6] respectivement.

Cette différence fondamentale dans les populations de conformères peut expliquer aussi bien la différence de réactivité entre les deux espèces que le manque de différence dans les sélectivités respectives. En effet, l'agencement majoritairement *antipériplanaire* de (*R*a,*R*)-[**5c**][SbF_6] et uniquement *synpériplanaire* de (*R*a,*S*)-[**5a**][SbF_6] conduit à une situation où le groupe *tert*-butyle se trouve toujours sur la face *Si* (derrière le plan, Figure 8). Ainsi la face la plus encombrée de l'espèce iminium est toujours la même quelque soit la configuration de l'auxiliaire chiral exocyclique. L'arrangement de la chaine latérale renforce ainsi l'approche préférentielle de l'ion peroxymonosulfate sur le cycle *R*a-iminium, générant ainsi des espèces oxaziridinium de configuration R_C,R_N; confirmant de fait les calculs de Washington et Houk[11] et les résultats expérimentaux de Závada[12] *et al*. De plus, le fait que (*R*a,*S*)-[**5a**][SbF_6] ne soit présent que sous la forme d'un unique rotamère peut expliquer la réactivité plus forte observée pour (*R*a,*R*)-[**5c**][SbF_6] (Figure 9).

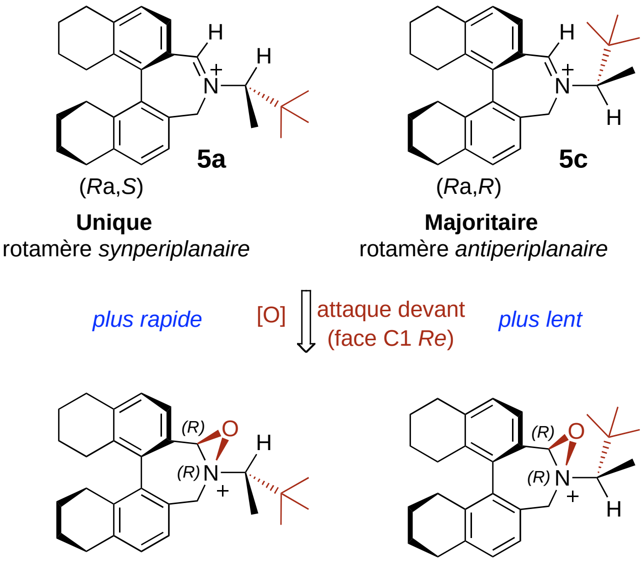


Figure 9. Importance des populations de rotamères sur le manque d'influence du fragment exocyclique R* sur la stéréochimie obtenue et sur la réactivité observée.

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7. Experimental part 103

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1. Genaral Introduction

1.1 Chirality

The term *chirality* is derived from the Greek word for hand, χειρ-(cheir) and the word *chiral* is used to describe any object that is non-superposable on its mirror image. This term was coined by Lord Kelvin in 1904 during his Baltimore Lectures on Molecular Dynamics and the Wave of Theory of Ligth then he sad: “*I call any geometrical figure, or group of points, chiral, and say it has chirality, if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself.*” Human hands are probably the most known example of chirality: the left hand is a non-superposable mirror image of the right hand, and no matter how these hands are oriented, it is impossible for all the major features of both hands to coincide.

Then we use this term in the context of chemistry, chirality usually refers to molecules. If two mirror images of a molecule cannot be superposed onto each other the molecule is chiral. A molecule is *achiral* (not chiral) if and only if it has an axis of improper rotation; that is, an n-fold rotation (rotation by 360°/n) followed by a reflection in the plane perpendicular to this axis that maps the molecule onto itself. Basically all molecules, which contain a plane of symmetry, are not chiral. It should be mention that most of organic molecules around us are chiral.

In 1874 the Dutch chemist Jacobus Henricus van't Hoff[1] and the French chemist Joseph Le Bel[2] independently discovered the tetrahedral arrangement of the groups or atoms bound to carbon and this epoch-making discovery had the crucial effect on the evolution of chirality and stereochemistry. They postulated that the carbon atom with four different substituents attached to it is chiral and the molecule with such stereogenic element must be chiral as well and should exist in two forms which are called enantiomers E and E* (Figure 1-1).

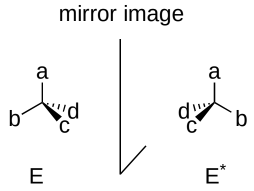


Figure 1-1. Representation of the enantiomers resulting form the different arrangement around a carbon atom invoked by van’t Hoff and Le Bel.

In terms of physical properties, enantiomers behave normaly identically. In the absence of other chiral molecules or objects they have for example identical NMR or IR spectra. However, they have different chiroptical properties and, for instance, they rotate plane-polarized light differently. Each enantiomer will rotate the plane of plane-polarized light with the same α value but one clockwise and the other counterclockwise. Molecules with this property are said to be optically active. It was first observed by Jean-Baptiste Biot in 1815 and in 1848 Louis Pasteur deduced that this phenomenon has a molecular basis. This difference of physical behavior observed for enantiomers is of importance because these compounds can have completely different chemical and biological properties. Many biologically active molecules are chiral and usually present in nature just in one enantiomeric form, including, for example, the naturally occurring L-amino acids and D-sugars. It is quite rare that both forms of chiral molecules are present in nature.

Enzymes, which are chiral macromolecules, often distinguish the two enantiomers of a chiral substrate. Imagine an enzyme as having a glove-like cavity that binds a substrate. If this glove is right-handed, then one enantiomer will fit inside and be bound, whereas the other enantiomer will have a poor fit and is unlikely to bind. This is the reason why two enantiomers of a chiral compound often taste and smell differently and have different effects as drugs. These effects reflect the chirality inherent to biological systems.

D-form amino acids tend to taste sweet, whereas L-forms are usually tasteless. Carvone (Figure 1-2), natural terpene which presents the oils from seeds of caraway (*Carum carvi*) and dill forms two mirror image forms or enantiomers: *S*-(+)-carvone smells like caraway. Its mirror image, *R*-(–)-carvone, smells like spearmint.

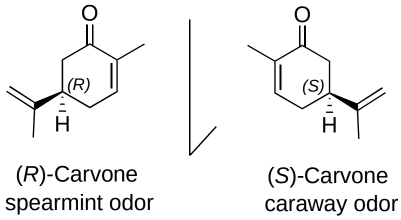
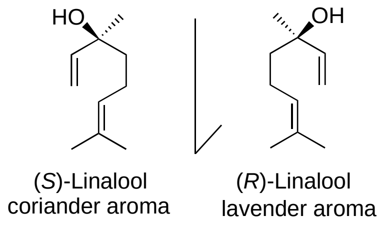


Figure 1-2. Enantiomers of terpene Carvone.

Another classical example is Linalool (Figure 1-3), a naturally-occurring terpene alcohol, found in many flowers and spice plants. Both enantiomeric forms are found in nature: (*S*)-(+)-linalool is found, for example, as a major constituent of the essential oils of coriander seed, palmarosa, and sweet orange flowers and coriander order. (*R*)-(-)-linalool is present in lavender, laurel, and sweet basil among others and smells like lavender.



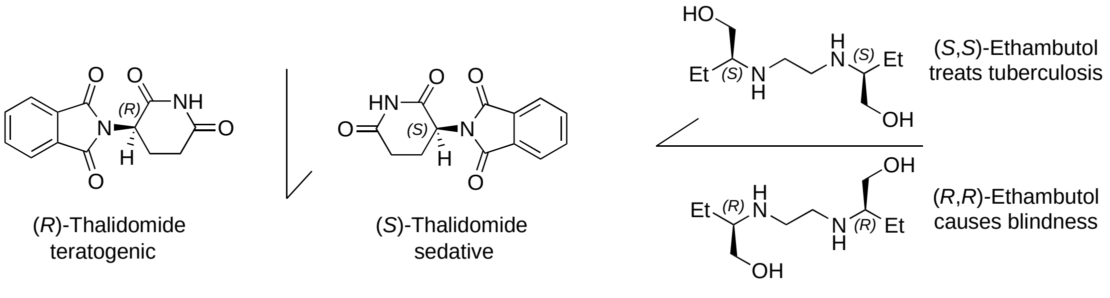
(*S*)-Linalool
coriander aroma

(*R*)-Linalool
lavender aroma

Figure 1-3. Enantiomers of Linalool.

In the field of pharmaceutical molecules, the concepts of chirality and enantiopurity have been found to the crucial. Essentially all chiral drugs must be prepared now as single enantiomer due to potential side-effects from the other enantiomer. The two enantiomers can be recognized differently by cells and have therefore completely different biological behavior. The most known example is Thalidomide, a drug discovered by German pharmaceutical company Grünenthal in the middle of last century. It was sold in Europe between 1957 and 1961 as a sedative agent for pregnant woman. However, only one (*S*) enantiomer is effective against morning sickness, whereas the other is teratogenic and causes birth defects (Figure 1-4). In this particular case, administering just one of the enantiomers to a pregnant patient does not help, as the two enantiomers are readily interconverted *in vivo*. Thus, if a person is given either enantiomer, both the (*R*) and (*S*) isomers will eventually be present in the patient's serum. Due to this fact more than 10,000 children in 46 countries were born with deformities such as phocomelia.

Another example is Ethambutol, a bacteriostatic antimycobacterial drug prescribed to treat tuberculosis. Only one enantiomer is used for this propose, the other causes blindness.



(*R*)-Thalidomide
teratogenic

(*S*)-Thalidomide
sedative

(*S*,*S*)-Ethambutol
treats tuberculosis

(*R*,*R*)-Ethambutol
causes blindness

Figure 1-4. Both enantiomers of Thalidomide and Ethambutol and their respective physiological effects.

There are plenty of other examples of chemical compounds, which exist as a mixture of enantiomers, and each enantiomer has different biological properties. Due to this fact it is important to be able to produce each of the two forms pure.

There are several strategies for artificially producing specific enantiomers, either by separation or synthesis.

One method is to produce a 1:1 mixture called racemic, and then separate the enantiomers. Historically, it was the first method used to achieve enantioenriched molecule, however, this limits the theoretical maximum yield to 50%. Modern chiral stationary phases, such as chromatographic columns filled with natural chiral compounds, are particularly effective for the enantioseparation of chiral substrates. Separation can be achieved by crystallization, but this requires a fairly high enantiomeric excess to begin with and the development of a reliable method is not always trivial.

Asymmetric synthesis is the second tool to reach this goal. One may (i) start from natural sources (chiral pool), (ii) utilize a chiral auxiliary attached to the substrate, or (iii) use an external reagent or a catalyst to introduce the chirality. During the last few decades, asymmetric synthesis and asymmetric catalysis have received a lot of attention. Yet, this field remains as one of the most challenging and pursued domain of organic chemistry.

1.2 Stereoselective catalysts. General remarks

Catalysis is the process in which the rate of a chemical reaction is either increased or decreased by means of a chemical substance known as a catalyst. In a general sense, anything that increases the rate of a process is a "catalyst", a term derived from Greek καταλύειν, meaning "to annul," or "to untie," or "to pick up." The phrase *catalysed processes* was created by the Swedish chemist Jöns Jakob Berzelius in 1836 to describe reactions that are accelerated by substances that remain unchanged after the reaction.[3]

"A catalyst is a substance that promotes a chemical reaction with no net participation in it; it is neither consumed nor replenished" (J. J. Berzelius, **1836**).

Due to increasing demand for non racemic compounds in both industrial and academic laboratories many efforts have been devoted to the developement of enantioselective processes using enantiopure moieties as chiral catalysts. Catalylic transformations provide the best “atom economy” because the stoichiometric introduction and removal of the (chiral) ancillary is avoided, or at least minimized.[4, 5] Nowadays, catalytic processes are classified in three groups that are reactions catalyzed by (i) transition metals, (ii) enzymes and (iii) organocatalysts. Since the 1970’s most efforts in this area of catalytic asymmetric synthesis have focused on the design and synthesis of reactive organometallic complexes or the use of enzymes as stereoselective catalysts. A less studied although equally intriguing field is the use of organic molecules to catalyze reactions and induce chirality into the products. This topic, so-called stereoselective organocatalysis, has received considerable attention in the last few years.[6-9]

Typically, organic catalysts require a higher loading (or amount of catalyst per unit amount of reactant) than transition metal-based catalysts, but these catalysts are usually commercially available in bulk, helping to reduce costs. In the early 2000s, organocatalysts were considered "new generation" and are competitive to traditional metal-containing catalysts.[9]

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2. Enantioselective synthesis of epoxides *via* asymmetric epoxidation reactions. General aspects

Epoxides, especially in optically active form, are highly useful intermediates and building blocks in synthetic organic chemistry, quite often used for the synthesis of biological active compounds. Moreover, epoxides are frequent structures in natural products,[1-3] often related to their biological activity,[4] and believed to be a key intermediates in the biosynthesis of many polyether-containing natural products such as Brevetoxin B (Figure 2-1).[4, 5]

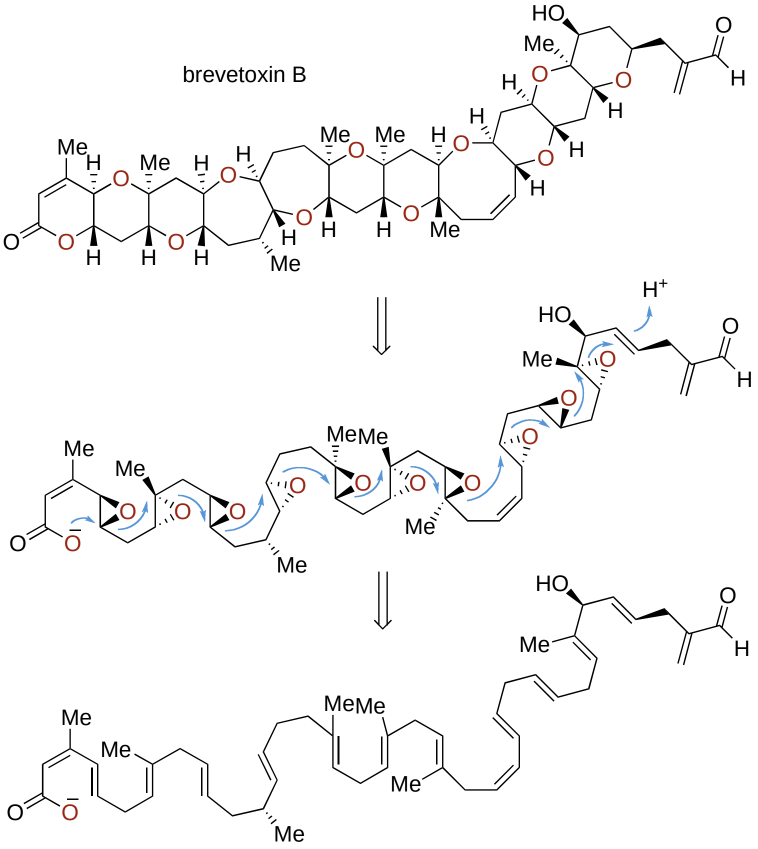

Figure 2-1. Biosynthetic pathway of Brevetoxin B.

The first example of epoxide formation from alkenes was described 100 years ago in 1909 by the polish chemist Nikolaus Prileschajew.[6] Reaction of alkenes with peracid-containing reagents such as *m*CPBA is today known as the Prileschajew reaction, a reaction that still remains one of the standard methods for the synthesis of epoxides. Since the transformation of olefins to epoxides was discovered, many attempts have been made to develop an enantioselective variant of this reaction. Despite very extensive studies over the last few decades, just a few effective and reliable systems have been developed for preparation of nonracemic epoxides, and asymmetric epoxidation of alkenes has been proven to be one of the most powerful approaches. Most strategies based on transition metal catalysis such as the Katsuki-Sharpless epoxidation of allylic alcohols with chiral titanium catalyst,[7] vanadium-catalyzed epoxidation of allylic[8-10] and homoallylic alcohols[11, 12] mainly developed by Yamamoto and the Katsuki-Jacobsen protocol with Mn(salen) catalysts for unfunctionalized olefins (Figure 2-2).[13-16]

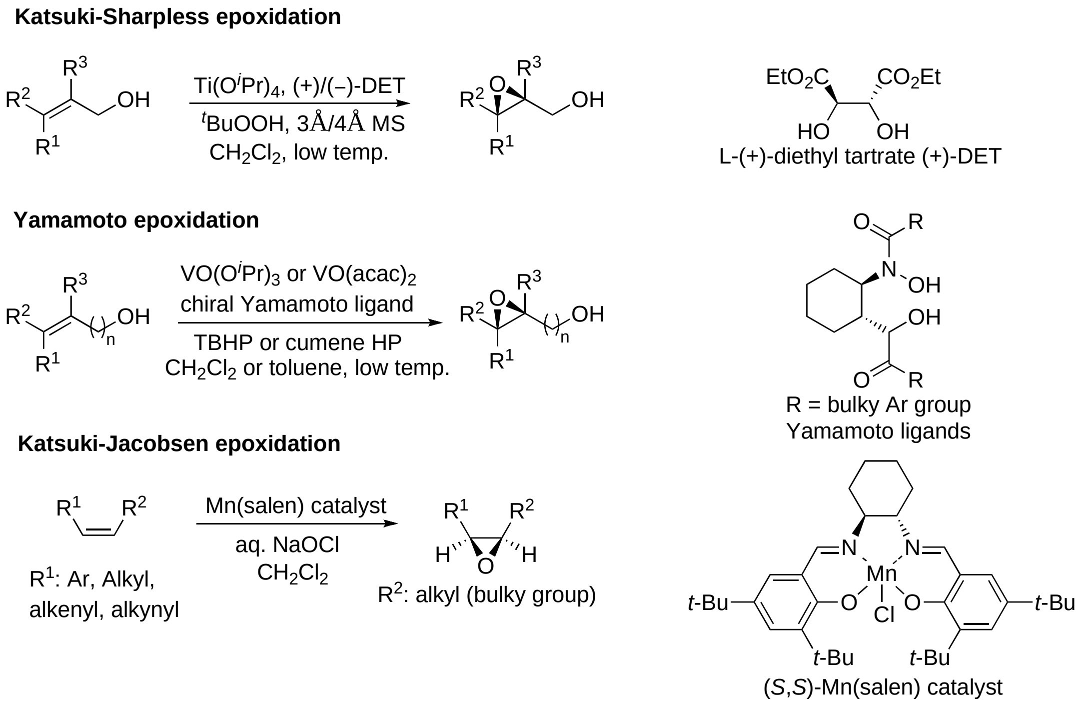

Figure 2-2. General methods for catalytic electrophilic epoxidations.

These epoxidation methods are applicable to several olefin classes; however, they do not encompass the enantioselective epoxidation of electron-deficient alkenes. For the epoxidation of substrates such as enones, enoates or quinones, nucleophilic oxidants such as alkaline solutions of hydroperoxides, hydrogen peroxide or hyperhalites are often applied. Existing technologies for the enantioselective epoxidation of olefines[17] *via* LUMO-lowering activation have been founded upon the Weitz-Scheffer reaction,[18] wherein a nucleophilic chiral peroxide adds to an enone or enal (Figure 2-3). This strategy of hydroperoxide delivery *via* a homogeneous chiral metal complex has been adopted and developed by Enders[19, 20] in a stoichiometric manner and in catalytic approach by Jackson[21, 22] and Shibasaki.[23, 24]

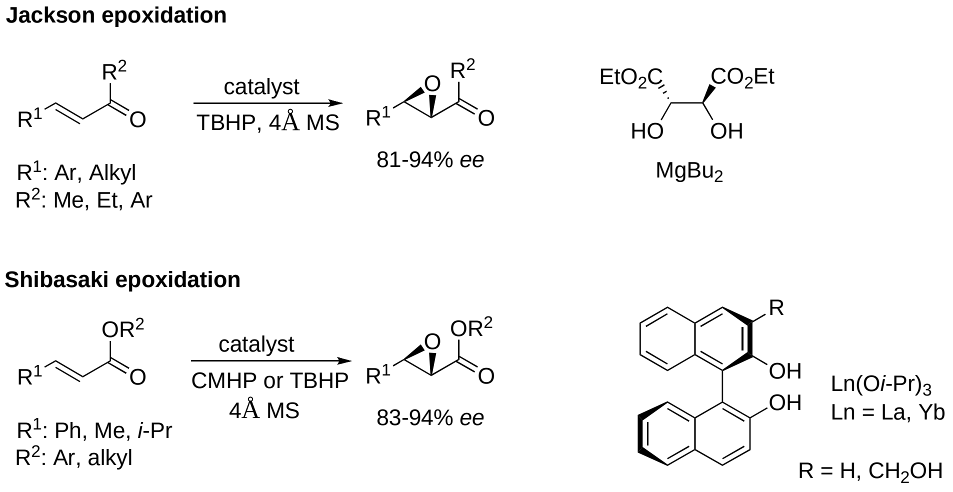

Figure 2-3. Several general methods for catalytic nucleophilic epoxidations.

Alternative methods for the preparation of enantiomerically pure epoxides include, inter alia, enzymatic transformations, the addition of chiral sulfur ylides to aldehydes (asymmetric versions of the Corey-Chaykovsky reaction),[25] and asymmetric epoxidation of enones catalized by peptides or peptide-based molecules.[26-29] Peptide-promoted epoxidation of olefins are of course organocatalitic procedures that have received significant attention during the last two decades.

The first example of an organocatalytic epoxidation of α,β-unsaturated ketones catalyzed by polyamino acids was described in 1980 by Juliá et al. (Juliá-Colonna epoxidation (Figure 2-4).[30, 31] Their reaction system compromised an aqueous alkaline hydrogen peroxide, the enone in a water-immiscible solvent (e.g., toluene or dichloromethane), and the polyamino acid which is insoluble both in water and the organic solvent and thus forms a third phase.

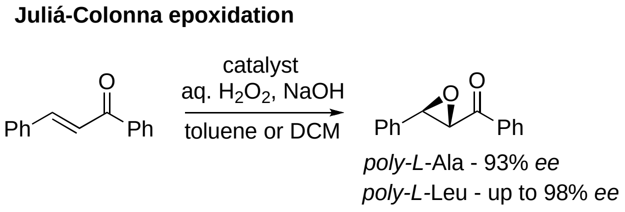

Figure 2-4. Juliá-Colonna epoxidation reaction of chalcone.

In the subsequent years, several modifications and improvements of the Juliá-Colonna procedure have been introduced mainly by Roberts and co-workers,[32, 33] who performed the reaction in the absence of water leading to a significant increase of the rate of epoxidation,[34] and Berkessel et al. who discovered the dominant role of the peptide helicity in this reaction.[35] The reaction is expecially effective using poly-L-leucine as a catalyst.

Alternatively, asymmetric Weitz-Scheffer epoxidation reaction under phase-transpher conditions has been utilized to transport reactive oxo-species to olefine substrates. In fact, asymmetric Weitz-Scheffer epoxidations with chiral phase-transpher catalysts (PTCs) belong to the earliest examples of asymmetric catalysis in general: in 1978, Wynberg and co-workers reported the asymmetric epoxidation of chalcones **1a,b** (Figure 2-5) using chiral quaternary ammonium salts derived from quinine and quinidine. Using the benzylquininium chloride **3** as the PTC up to 54% *ee* of epoxide **2a** were achieved.[36-38]

Major breakthroughts in the phase-transfer catalyzed epoxidation of chalcones **1** resulted from work by Corey (PTC **4**),[39] Lygo (PTC **4**),[40, 41] Arai, Shioiri (TPC **5**),[42] Maruoka (TPC **6**)[43] and recently by Berkessel on enantioselective epoxidation of 2-methylnaphthoquinone (Vitamine K_3) mediated by *Cinchona* alkaloid PTCs.[44] Enantioselectivities up to 97% *ee* were achieved in chalcone epoxidation using PTC **4** to **6**.

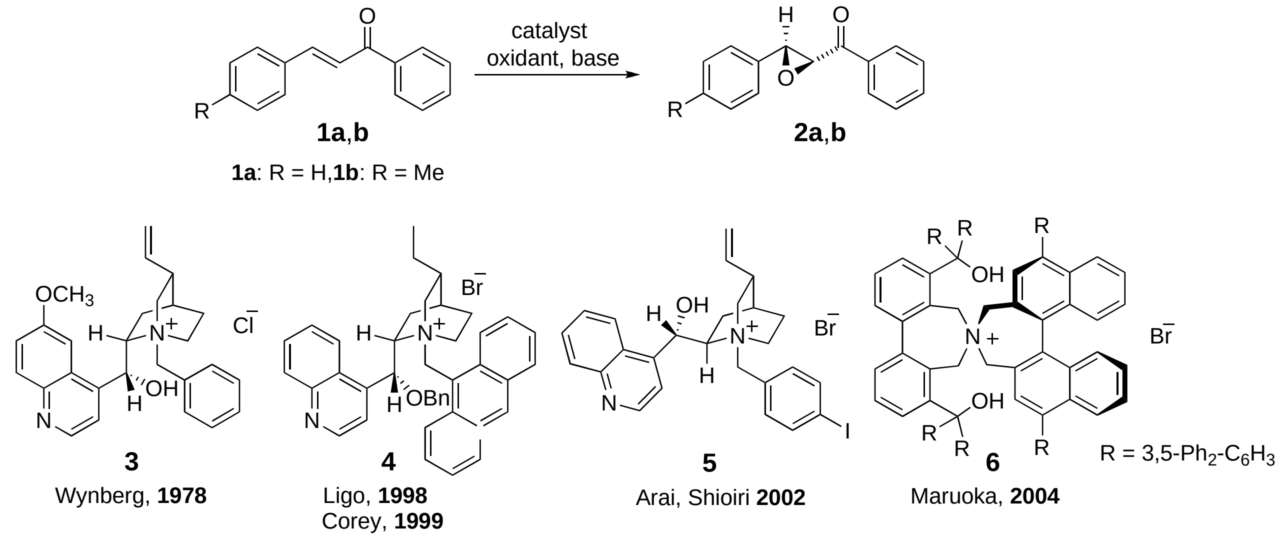

Figure 2-5. Asymmetric epoxidation of chalcone derivatives using phase-transfer catalysts.

Most recently, Jørgensen and co-workers have demonstrated the first asymmetric organocatalytic epoxidation of α,β-unsaturated aldehydes using iminium catalysis (Figure 2-6).[45] In these elegant studies, a variety of enals rapidly underwent asymmetric epoxidation using hydrogen peroxide as the stoichiometric oxidant in the presence of a proline-derived catalyst **7**. Later, MacMillan's group demonstrated the use of chiral imidazolidinone salt **8** as iminium activation catalyst for the asymmetric epoxidation of α,β-unsaturated aldehydes using hypervalent iodine reagents as oxidants (Figure 2-6).[46]

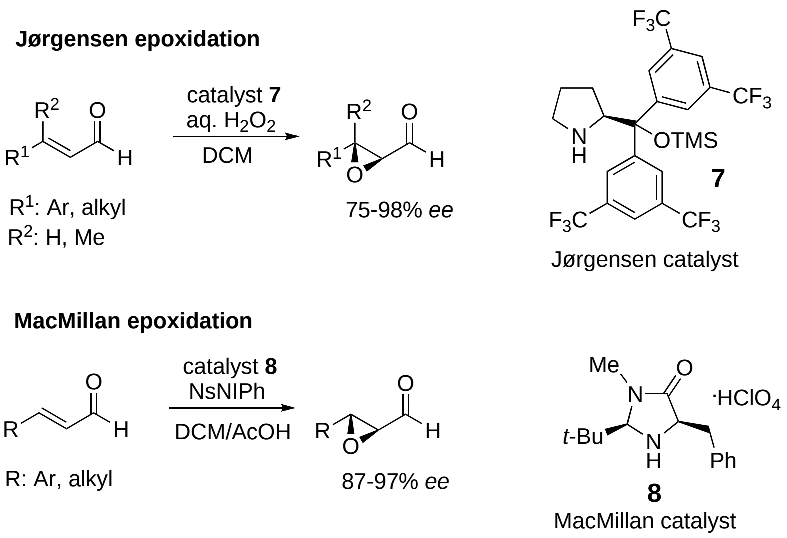

Figure 2-6. Asymmetric epoxidation of α,β-unsaturated aldehydes.

In these studies iminium catalyst was generated *in situ* by condensation of α,β-unsaturated aldehydes with secondary amines.

More recently, List's group reported enantioselective epoxidation of cyclic enones[47] and α,β-unsaturated aldehydes using secondary ammonium TRIP salts (Figure 2-7). They have found that bis(3,5-bis(trifluoromethyl)benzyl)-ammonium derivative affords good to excellent yields (60–95%) and levels of enantioselectivity (*ee* 84–96%) with aromatic and aliphatic unsaturated aldehydes.[48] Again, the reaction proceeds through the formation of quaternary iminium ion intermediates associated with enantiopure TRIP phosphate anion.

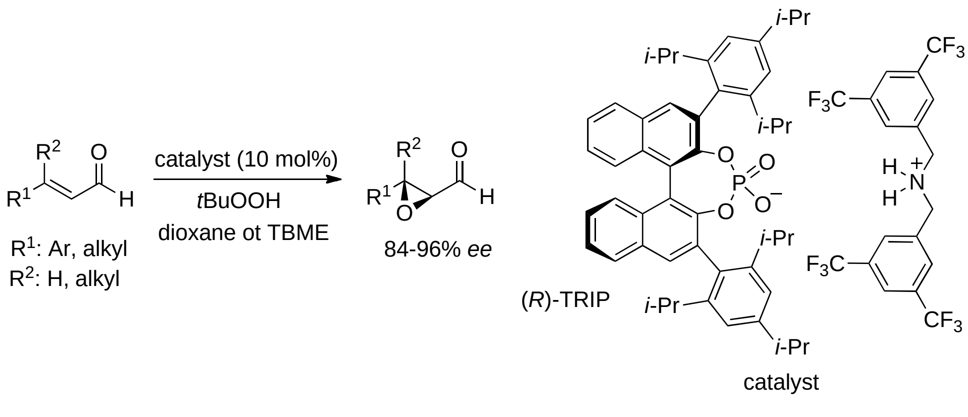

Figure 2-7. Enantioselective epoxidation of α,β-unsaturated aldehydes via “Asymmetric Counteranion-Directed Catalysis”.

These transient species undergo nucleophilic additions of *tert*-butyl hydroperoxide, the facial selectivity being controlled by the anionic enantiopure counterion (Figure 2-8).

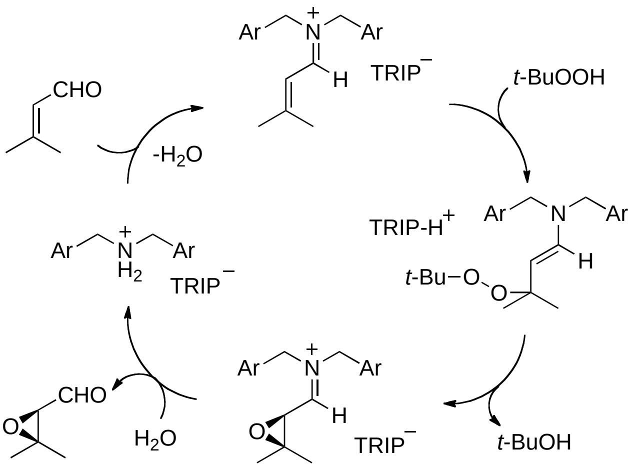

Figure 2-8. Enantioselective epoxidation of α,β-unsaturated aldehydes described by List and co-workers. Proposed catalytic cycle.

It is also well known that isolated iminium salts can effectively used for enantioselective epoxidation of olefins. Organocatalytic epoxidation of alkenes mediated by chiral iminium salts, ketones, secondary amines and ammonium salts will be discussed in the next chapter.

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3. Organocatalytic Oxidation. Asymmetric Epoxidation of Olefins Catalyzed by Chiral Ketones, Iminium Salts, Secondary amines or Ammonium salts

Despite many successful results obtained in enantioselective epoxidation of olefins using organometallic catalysts, much efforts have been devoted to the development of organocatalytic systems that would afford metal-free procedures, such as asymmetric epoxidation mediated by chiral ketones and iminium salts.[1] In this field, three-membered ring heterocycles such as dioxiranes,[2, 3] oxaziridines,[4] ammonium and oxaziridinium salts[2] have been shown to be effective oxidation agents. Significant progress has been made toward the epoxidation of various types of olefins, particularly unfunctionalized *trans*- and trisubstituted alkenes, which has been a long-standing challenge.

3.1 Chiral Ketone-Catalyzed Epoxidation

3.1.1 Early ketones

Ketone-catalyzed epoxidation of alkenes is one of the most studied organocatalytic process. Isotopic labeling studies performed by Curci and co-workers in 1979 showed that using Oxone® ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$) as a stoichiometric oxidant, dioxirane species were generated *in situ* form ketones *via* Craigee intermediate (Figure 3-1).[5, 6]

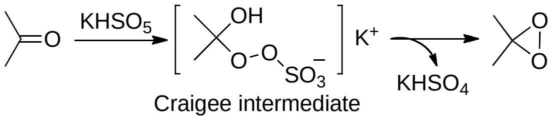
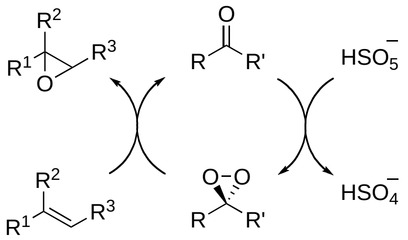


Figure 3-1. Formation of dimethyldioxirane from acetone by oxidation with Oxone® triple salt *via* Craigee intermediate.

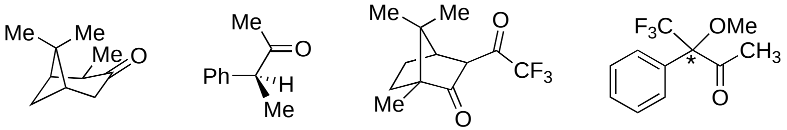
They discovered that dioxirane formed *in situ* is a perfect oxidant for olefins and leads to fast epoxide formation. In principle, only a catalytic amount of ketone should be need for dioxirane formation since the ketone is regenerated upon epoxidation of the olefin (Figure 3-1), and asymmetric epoxidation could also be possible with a chiral ketone catalyst.

The first example of enantioselective ketone promoted epoxidation of alkenes was described in 1984 by Curci and co-workers as well. Asymmetric epoxidation of 1-methylcyclohexene and *trans*-β-methylstyrene with (+)-isopinocamphone **9** and (*S*)-(+)-3-phenylbutan-2-one **10** as catalyst in a biphasic mixture of CH_2Cl_2/water (pH 7-

8) was reported (Figure 3-2).[7] These ketones provided good yields but very poor enantioselectivities were obtained (max 12.5% *ee*).



Scheme 3-1. Ketone-catalyzed epoxidation of olefines.



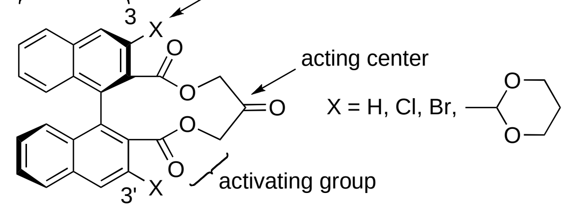
9 **10** **11** **12**

Figure 3-2. Curci's chiral ketone catalysts.

Then in 1995, two ketone catalysts containing electron-withdrawing trifluoromethyl groups (**11** and **12**) were reported by the same group.[8] These ketones were much more active than **9** and **10**, but again only modest levels of asymmetric induction were obtained (20% *ee* for *trans*-2-octene with (*S*)-**12** catalyst). Moreover, a very high amount of ketones (up to 1.2 equiv.) was required to achieve full conversion of substrate.

3.1.2 C_2-Symmetric binaphthyl-based and related ketones

In 1996, Yang and co-workers reported a series of elegant binaphthyllene-derived chiral ketones **13** (Figure 3-3).[9-11]



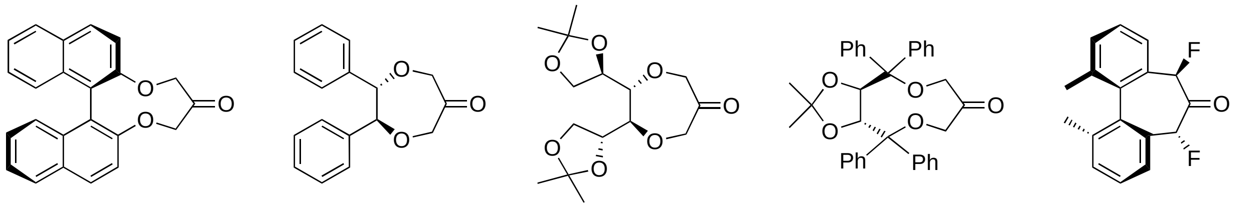
13

Figure 3-3. Yang's 11-membered ring C_2-symmetric ketone catalysts.

The catalysts relied on a rigid symmetric structure lying on a C_2 axis. C_2 symmetry was intended to simplify the stereochemical analysis, and a remote binaphthylene unit

was used as the chiral control element instead of substituents at the α carbon of the carbonyl, thus eliminating possible racemization of stereogenic centers and steric hindrance at the α carbon. The unhindered carbonyl plus electron-withdrawing esters at the α carbon made ketones **13** very active catalysts. When the simplest catalyst was used (X = H), moderate to good enantiomeric excesses were obtained on *trans*-disubstituted and trisubstituted alkenes (up to 87% *ee* for *trans*-stilbene derivatives).[11] The X-ray structure of ketone **13** (X = H) showed that hydrogen on carbons 3 and 3´ to be closest to the reacting center among all the atoms of the binaphthylene unit, and likely to be the steric sensor for the epoxidation.[9, 10] Various substituents were subsequently introduced in place of hydrogens at the 3 and 3´ positions (few selected examples are shown in Figure 3-3). It was found that an appropriate size is required as two small (X = H) or too big (X = I) groups leads to a decrease in enantioselectivity; the best balance being for instance a chloride or a bromide. Up to 95% *ee* was obtained for some *trans*-stilbene derivatives with catalyst **13** containing ketal group (this catalyst was found to be the most reactive as well).[9]
Despite the fact that catalysts of type **13** was found to be effective for enantioselective epoxidation of some *trans*-stilbene derivatives, very strong substrate dependence was found in terms of reactivity and enantioselectivity; terminal or cyclic olefines gave for instance very low *ee* values.

In 1997, Song and co-workers described the use of ether-linked C_2-symmetric ketones **14** and **15** (Figure 3-4).[12, 13] These ketones showed both lower reactivity and enantioselectivity (max. 59% *ee* for *trans*-olefines) when compare to ketones **13**, possibly due to the weaker electron-withdrawing ability of the ether as compared to the ester.



14
Song, **1997**
max. 29% *ee*
(*trans*-β-methylstyrene)

15
Song, **1997**
max. 59% *ee*
(*trans*-stilbene)

16
Adam, **1997**
max. 38% *ee*
(*trans*-stilbene)

17
Adam, **1997**
max. 81% *ee*
(*trans*-α-phenylstilbene)

18
Denmark, **2002**
max. 94% *ee*
(*trans*-stilbene)

Figure 3-4. C_2-symmetric ketone catalysts.

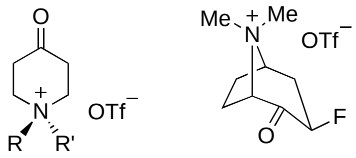
In the same year, Adam also reported the synthesis of two ether-linked C_2-symmetric ketones **16** and **17**, which are derived form mannitol and (+)-tartaric acid, respectively

(Figure 3-4).[14] Up to 81% *ee* was obtained with these catalysts.

A few years letter in 1999 and 2002 Denmark reported asymmetric epoxidation using 7-membered C_2-symmetric carbocyclic biaryl ketones **18** (one example is presented in Figure 3-4)[15, 16]. Considering that stereogenic control elements closer to the reacting center could further increase the stereodifferentiation in the epoxidation as compared to 11-membered ketone **13**. Introduction of two fluorine atoms at the α positions to the carbonyl fonction was found to be crucial for obtaining highly reactive catalysts. A variety of *trans*-alkenes can be epoxidized with good to high enantioselectivity (up to 94% *ee* for *trans*-stilbene).

3.1.3 Ammonium Ketones

In 1995, Denmark and co-workers reported that 4-oxopiperidinium salt **19** (Figure 3-5) is an effective catalyst for epoxidation. The electron-withdrawing ammonium ion not only inductively activates the carbonyl but also acts as phase transfer agent, thus allowing efficient partition of the ketone and its dioxirane between the organic and aqueous phases.[17] The partitioning ability between two phases can be controlled by the choice of alkyl groups on the nitrogen atom. Based on this study, a range of chiral ketones bearing ammonium ions was synthesized. Tropinone-based rigid ammonium ketone **20** was found to be the most reactive and one of the most selective from this type of catalysts. Thus epoxidation of *trans*-stilbene with 10 mol% of this ketone provided the epoxide in 79% isolated yield and 58% *ee*.[16, 18]

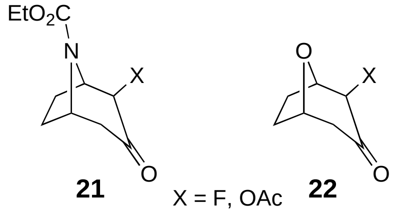


19 **20**

Figure 3-5.

3.1.4 Armstrong's bicyclo[3.2.1]octan-3-one and related catalysts

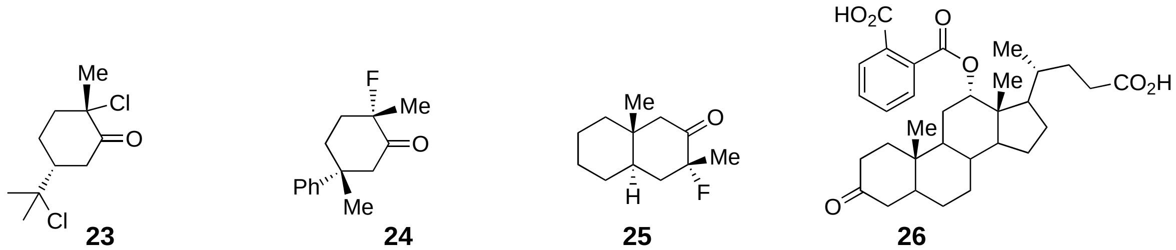
In 1998, Armstrong described tropinone-based ketone **21** (Figure 3-6), structurally similar to **20**.[19, 20] A variety of alkenes could be epoxidazed with up to 83% *ee*. Further studies showed that replacing the fluorine of **21** with an acetate and/or replacing the bridgehead nitrogen with an oxygen (ketone **22**) increased the enantioselectivity of the epoxidation reaction.[20-22] Up to 98% *ee*$_{\text{max}}$ was obtained for phenylstilbene with catalyst **22** (X = OAc).



21 **22**

Figure 3-6. Selected Armstrong's ketones for enantioselective olefin epoxidation.

Over the last decade, many other groups have entered the field by proposing novel structures and geometries for ketone moieties. The most recent reported catalysts are displayed on Figure 3-7 along with the highest enantiomeric excess values obtained with them and the nature of the alkene used in the reaction.



23
Yang, **1998**
max. 88.9% *ee*
((*E*)-3,3′-dimethylphenylpropene)

24
Solladié-Cavallo, **2001**
max. 90% *ee*
(*trans*-stilbene)

25
Solladié-Cavallo, **2004**
max. 86% *ee*
(*trans*-stilbene)

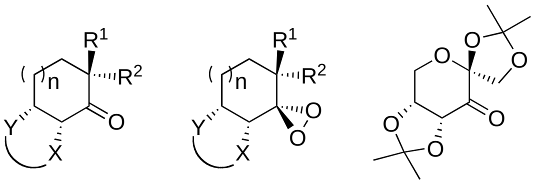
26
Bortolini, **2001**
max. 98% *ee*
(*trans*-stilbene)

Figure 3-7. Chiral ketones for asymmetric epoxidation of olefins: Yang (**23**[23]), Solladié-Cavallo (**24**[24], **25**[25]) and Bortolini (**26**[26]) systems.

One can notice that all catalysts described so far were efficient only for the epoxidation of *trans*-stilbene or it derivatives. Terminal mono- and 1,2-disubstituted olefins among with trisubstituted alkenes provided quite moderate results in terms both reactivity and enantioselectivity. More over, no model existed to allow chemists to predict epoxide formation with defined absolute configuration and in high enantiomeric purity. The breaking studies in ketone-catalyzed epoxidation results were made by Y. Shi and collaborators.

3.1.5 Shi's epoxidation

In 1996, Yian Shi and co-workers reported a highly enantioselective epoxidation of *trans*- di- and trisubstituted alkenes using a fructose-derived ketone **27** (Figure 3-8).[27] This compound can be readily obtained *via* a two-steps synthesis (ketalization and oxidation) from D-fructose.



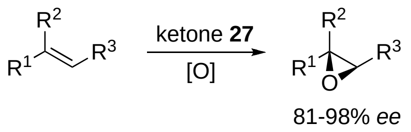
27

Figure 3-8. Shi's designed ketones.

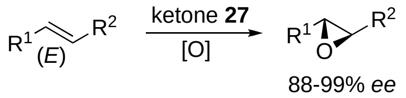
It belongs to a class of ketones designed on the basis of the following general considerations: (1) the stereogenic control elements are placed close to the reacting carbonyl to enhance the stereochemical interaction between substrate and catalyst; (2) fused ring(s) and/or a quaternary center α to the carbonyl group is used to minimize the potential epimerization of the stereogenic center; (3) the approach of an olefin to the reacting dioxirane is directed by sterically blocking one face or by a C_2- or pseudo-C_2-symmetric element; (4) the carbonyl is inductively activated by the introduction of electron-withdrawing substituents.[27, 28]

These efficient ketone-mediated reactions need often to be carefully monitored as moving a few tenths of a unit away form a 7.5 – 8 pH region may lead to a rapid decomposition of the hydrogenpersulfate oxidant in basic conditions (pH > 8). While, on the contrary, if lower pH conditions (pH < 7.5) are used during the course of the reaction, then a fast decomposition of the ketone is observed *via* Baeyer-Villiger like oxidation pathway.[17] However, if enantioselectivities are excellent with ketone **27** working in this range of pH leads essentially to poor conversions (< 10%) so that an excess amount of ketone "catalyst" is needed (up to 3.0 equiv.).[27] Interestingly, when conducted at pH 10.5, very high *ee*'s were still observed with good conversions (> 80%) and the quantity of ketone catalysts can be reduced to 20-30 mol% as the catalyst is reactive enough to compete with the Oxone® autodecomposition usually seen at such high pH.[28]

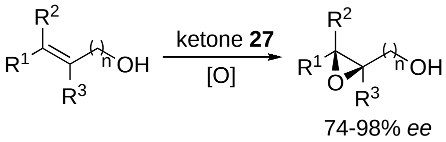
High enantioselectivities can be obtained for a very wide range of unfunctionalized *trans*- di- and trisubstituted alkenes (Equations 3-1 and 3-2).[28] Allylic, homoallylic and bishomoallylic alcohols are effective substrates as well (Equation 3-3).[29] The epoxidation of conjugated dienes (Equation 3-4) [30] and enynes (Equation 3-5)[31, 32] can be accomplished with high *ee* values to obtain vinyl epoxides and propargyl epoxides. A variety of silyl enol ethers and esters were also studied.[33-36] The epoxides of silyl enol ethers rearrange to give α-hydroxyl ketone under reaction conditions. Finally, ketone catalyst **27** was successfully applied for the desymmetrization and kinetic resolution of 1,4-cyclohexadienes (Equations 3-6).[37]



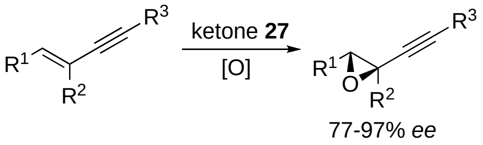
(3-1)



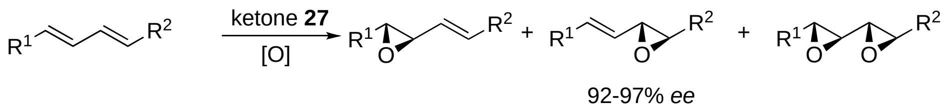
(3-2)



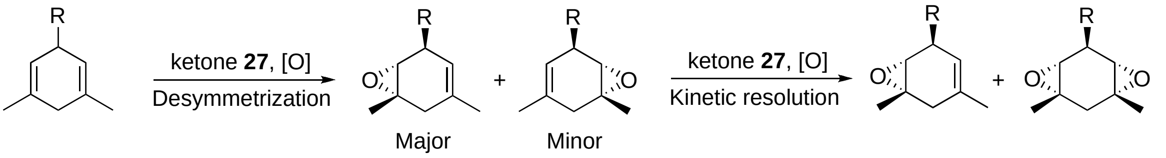
(3-3)



(3-4)

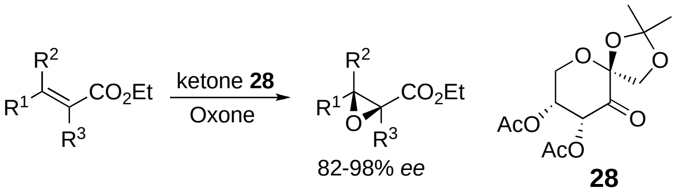


(3-5)



(3-6)

The enantioselective epoxidation of α,β-unsaturated esters can be done as well using dioxirane mediated epoxidation chemistry. Ketone **28**, a readily available acetate analogue of **27**, was found to be both active and highly enantioselective (up to 98% *ee*) for the epoxidation of α,β-unsaturated esters (Equation 3-7).



Equation 3-7. Asymmetric epoxidation of α,β-unsaturated esters promoted by ketone **28**.

Thus far, only *trans*- di- and trisubstituted olefins have effectively been epoxidazed with high *ee*'s. Ketone **27** gave poor enantioselectivities for *cis*-alkenes, styrenes and other alkenes. Efforts were made to develop ketone catalysts for other type of olefins and the solution to this long challenging problem was found a few years later. In 2000, glucose-derived ketone **29a** was reported by Shi and co-workers to be a highly enantioselective catalyst for the epoxidation of *cis*-olefins and terminal alkenes (Figure 3-9).[38, 39] Later investigation has shown that ketone **30** (prepared in 13 steps from quinic acid with 1.1% overall yield), a carbocyclic analogue of **29**, gives slightly better *ee*'s for styrenes (89-93% *ee*).[40] Unfortunately, such long step synthesis precludes its practical use.

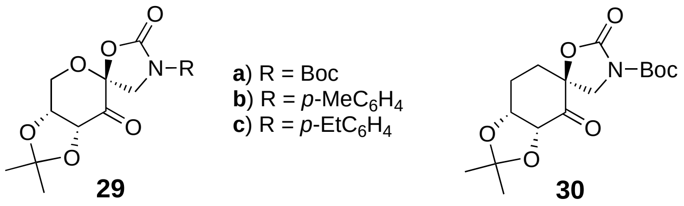
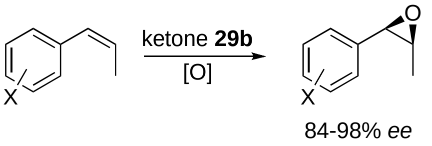
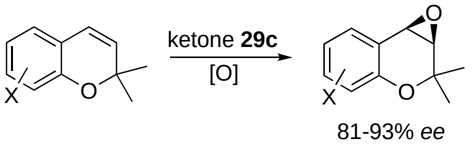


Figure 3-9. Shi's oxazolidinone-containing ketones.

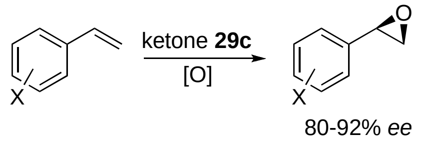
Studies have shown that ketones of type **29** can give high *ee* values for olefins such conjugated aromatic *cis*-olefins (Equation 3-8),[41] chromenes (Equation 3-9),[42] styrenes (Equation 3-10), [43] conjugated *cis*-enynes (Equation 3-11)[44] and *cis*-dienes (Equation 3-12),[45] certain trisubstituted and tetrasubstituted olefins (Equations 3-13 and 3-14).[46-48]



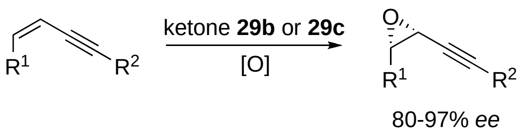
(3-8)



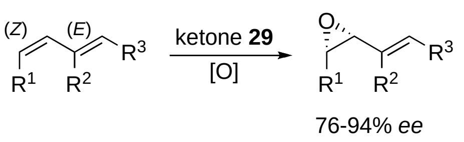
(3-9)



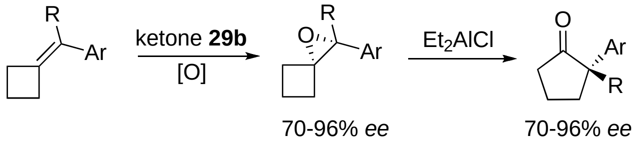
(3-10)



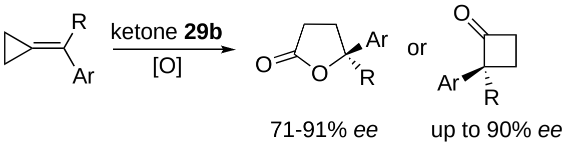
(3-11)



(3-12)



(3-13)



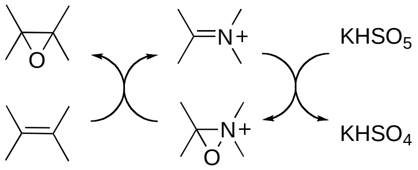
(3-14)

It should be mentioned that all reactions performed both with ketones **27**, **28** and **29** were stereospecific meaning that, for example, *cis*-olefins yielded only *cis*-epoxides with no isomerization under the reaction conditions. In general, reactions required high catalyst loading 20-30 mol% and precise control of pH during the epoxidation process.

3.2 Chiral Iminium-Catalyzed Epoxidation

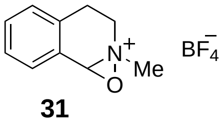
3.2.1 Introduction

Oxaziridinium ions, usually generated *in situ* by the oxidation of iminium salts, are attractive alternatives to the commonly used dioxiranes. These organic salts are effective oxygen transfer reagents towards nucleophilic substrates[49-52] and electron-rich unfunctionalized olefins in particular. Moreover, the propensity of iminium ions to react with Oxone® to generate the oxaziridinium species renders the development of catalytic processes possible (Scheme 3-2).[53, 54]



Scheme 3-2. Catalytic cycle for iminium-catalyzed epoxidation.

In 1987, Hanquet and co-workers described the synthesis of an oxaziridinium salt **31** by either (i) the oxidation of an *N*-methyl isoquinolinium fluoroborate salt **32** with *p*-nitrobenzoyl peroxide or (ii) the methylation of its corresponding oxaziridine with trimethyloxonium fluoroborate (Figure 3-10).[55, 56]



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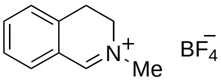


32

Figure 3-10. Hanquet's isolated oxaziridinium **31** and iminium **32** salts.

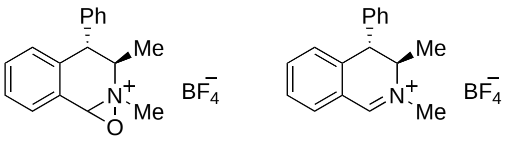
A year later, in 1988, they reported that oxaziridinium salt **31** can efficiently epoxidize various olefins.[57] Later studies showed that the epoxidation can be in fact carried out with *in situ* generated oxaziridinium salt **31** using a catalytic amount of its corresponding iminium salt **32** and Oxone®-NaHCO$_3$ in MeCN/water[54] or *m*CPBA/NaHCO$_3$[53] in dichloromethane. The proposed reaction pathway for this iminium-catalized epoxidation is shown in Scheme 3-2.

Since this pioneering study, many attempts have been made to develop an asymmetric version of this reaction.

3.2.2 Chiral cyclic iminium salts

3.2.2.1 Dihydroisoquinoline-based iminium salts

1n 1993, Bohé and co-workers reported the first study on the asymmetric epoxidation of alkenes with enantiomerically pure oxaziridinium salt **33** (Figure 3-11).[58, 59] A dihydroisoquinolinium moiety, structurally similar to **31**, was synthesized in five steps starting form benzaldehyde and aminoalcohol (1*S*,2*R*)-(+)-norephedrine. It was isolated in pure form and fully characterized by X-ray diffraction. To our knowledge this remains the only X-ray structure of a reactive oxaziridinium species.



33 **34**

Figure 3-11. Bohé's isolated oxaziridinium **33** and iminium **34** salts used in asymmetric epoxidation of olefines.

Several olefins were effectively epoxidized with either isolated or *in situ* generated oxaziridinium **33**. For example, epoxidation of *trans*-stilbene with the *in situ* formed oxaziridinium salt using a catalytic amount (5 mol%) of iminium salt **34** and Oxone®-NaHCO$_3$ in MeCN/water gave 80-90% conversion and 35% *ee*. The reaction conditions (solvent, temperature) were later optimized and the mechanism was furthermore studied.[53, 58] It was observed that the epoxidation process proceeds much faster in polar solvents than in nonpolar conditions, suggesting that the transition state of such a reaction has a strong polar character.

In 1998, Page and co-workers described a series of dihydroisoquinoline related iminium salt catalysts with tetraphenylborate as counterion easily synthesized from a chiral primary amine (Figure 3-12).[60, 61] These types of catalyst, containing chiral element outside the dihydroisoquinoline ring, have an advantage compare to salts previously descried by Bohé because the exocyclic appendage can be easily modified. Based on this strategy, up to 97% *ee* was obtained with catalyst **35** in asymmetric epoxidation of 2,2-dimethyl-6-cyanochromene.[62]

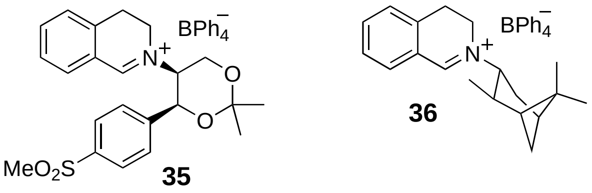


Figure 3-12. Selected examples of dihydroisoquinoline type iminium salts described by Page and co-workers for asymmetric epoxidation of alkenes.

3.2.2.2 Binaphthylazepinium-based iminium salts

In 1996, Aggarwal and co-workers reported axially chiral, configurationally stable, binaphthyl-derived iminium catalyst **37** (Figure 3-13); this compound being particularly efficient for the epoxidation of 1-phenylcyclohexene (71% *ee*).[63]

In 2004, Page modified the core structure of catalyst **37** by introducing an additional stereogenic element outside of the seven-membered ring.[64, 65] L-(+)-acetonamine[1] was found to be one of the best exocyclic auxiliary for this type of iminium catalyst. Thus catalyst **38** gave good to excellent *ee*'s for a set of substrates (up to 95% *ee* for 1-phenyl-3,4-dihydronaphthalene).

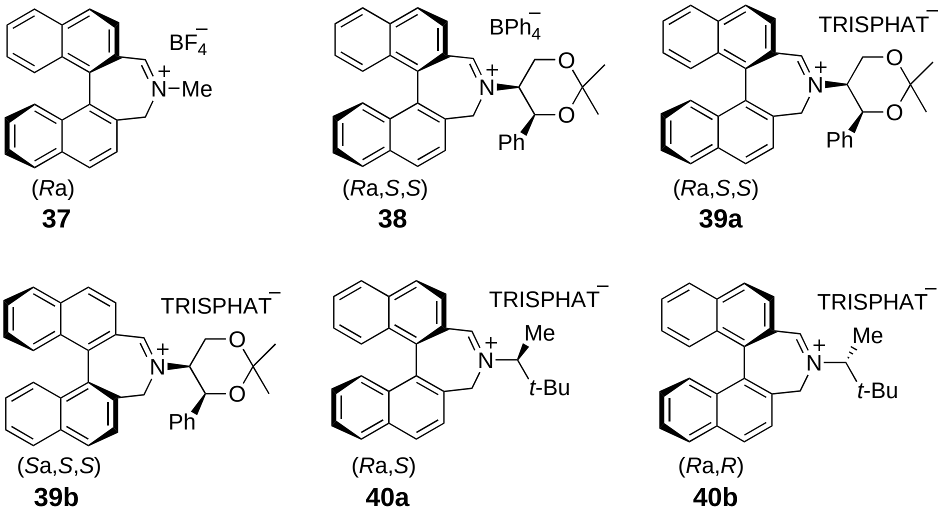


Figure 3-13. Configurationally stable Binaphthyl-based iminium salts.

Recently, Lacour and co-workers described a range of catalysts (**39** to **40**) structurally similar to iminium salt **38** with TRISPHAT as the counterion instead of tetraphenylborate (Figure 3-13).[66, 67] Interesting results were observed with these catalysts. Thus, iminium salts **39a** and **39b**, having the same exocyclic chiral

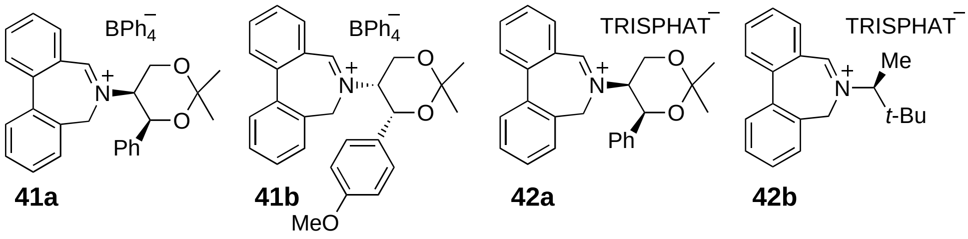
---

[1] L-(+)-acetonamine corresponds to (4*S*,5*S*)-5-amino-2,2-dimethyl-4-phenyl-1,3-dioxane.

appendage but opposite binaphthyl configuration, gave epoxides of opposite configuration;[67] the catalysts **40a** and **40b**, having the same binaphthyl configuration and opposite configuration on the *N*-substituent, gave epoxides with same absolute configuration.[66] This result suggested that the binaphthyl framework than the exocyclic appendage is more effective in inducting chirality in the epoxidation process. However, both the conversion and the level of asymmetric induction for the epoxidation process was affected by “matched/mismatched” configurations of the binaphtyl core and the *N*-auxiliary.[64-67]

3.2.2.3 Biphenylazepinium-based iminium salts

In 2002, a series of novel biphenylazepinium salt catalysts (**41** and **42**) was reported independently by the group of Page[68, 69] and Lacour (Figure 3-14).[70, 71] Unlike rigid binaphthylene derivatives of type **37-39**, compounds **40** and **42** possess a biphenyl skeleton, which is chiral but configurationally labile at room temperature. Literature precedents (*vide infra*) have shown that a biphenyl core of this type exists as two atropisomeric (*R*a and *S*a) conformations that interconvert freely in solution simply by rotation around the stereogenic axis. In both systems **41** and **42**, the cationic iminium moiety was associated with lipophilic BPh$_4$ and TRISPHAT anions. The lipophilicity of these anions keeps the iminium salt in organic solvent layers, which can be beneficial to enantioselectivities.[66, 67, 70, 71] Up to 80% *ee* was obtained for the epoxidation of 1-phenyl-3,4-dihydronaphthalene with **42b**. In general, conformationally labile biphenylazepinium salt catalysts were less effective in terms of asymmetric transfer than their configurationally stable binaphthyl type analogues.

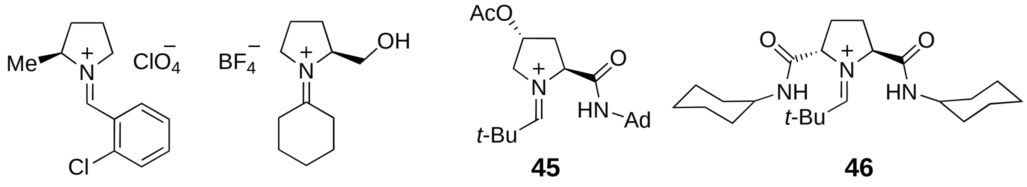


41a **41b** **42a** **42b**

Figure 3-14. Biphenylazepinium-based iminium salts described by Page (**41**) and Lacour (**42**).

3.2.3 Chiral acyclic iminium salts

Most iminium salts used in asymmetric epoxidation are cyclic; however several acyclic derivatives have also been investigated. Several examples are presented in Figure 3-15. Most of these salts derived from intermolecular condensation between a chiral pyrrolidine moiety and a carbonyl compound.[72-75] Asymmetric epoxidation can be performed with either isolated[73-75] of *in situ* generated catalysts.[72] In both cases, decent levels of stereoselective induction were obtained using these cations (65% $ee_{\max}$ form *trans*-stilbene with catalyst **46**[72]). Quite high catalyst loading is required (10 mol% for **44**,[73] 100 mol% for **43**,[74] between 20 and 50 mol% for **45**[72]), probably due to their facile hydrolysis under the aqueous conditions.



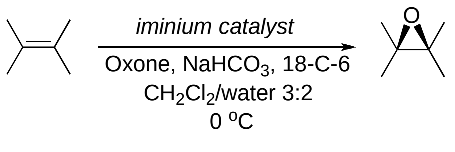
43 **44** **45** **46**

Figure 3-15. Acyclic iminium salts described by Armstrong (**43**), Komatsu (**44**) and Yang (**45** and **46**).

3.2.4 Gain in enantioselectivity in iminium-catalyzed epoxidation reaction by solvent and temperature modifications

Historically, the iminium promoted epoxidation reactions are performed in mixtures of MeCN and water. MeCN/water combination is often good for all reagents; most of the lipophilic alkenes as well as the polar iminium salts have good solubility in acetonitrile.

In our group, biphasic CH_2Cl_2/water (3:2, pH ~8) conditions were extensively used in iminium-catalyzed epoxidation processes (Equation 3-15).[70, 71]



(3-15)

Traditionally in Lacour's group, cationic iminium core is associated with lipophilic TRISPHAT anion. In fact, the lipophilicity of TRISPHAT anion confers to its salt an affinity for organic solvents and, once dissolved, the ion pairs do not partition in aqueous layer. Consequently, a tight containment of the reagents it two liquid phases occurs; the iminium salt in the organic layer and Oxone® in the aqueous layer. Addition of catalytic amount of 18-Crown-6 (2.5 mol%) as a phase-transfer reagent is strictly required to establish a transport mechanism of $KHSO_5$/$KHSO_4$ between aqueous and organic phases and permit the oxidation in CH_2Cl_2 of the iminium cation into the reactive oxaziridinium form (Figure 3-16).

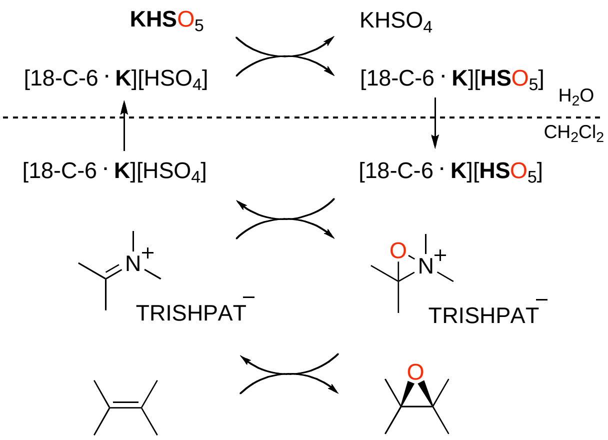


Figure 3-16. Double catalytic cycle in iminium-catalyzed epoxidation of alkenes under biphasic CH_2Cl_2/water conditions.

Slightly better results were obtained using this conditions in which oxidation occurs presumably only in dichloromethane phase.

Page and co-workers observed that a lower temperature can lead to increase in the enantioselectivity of the epoxidation reaction.[76]

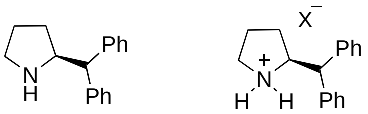
Because of the aqueous reaction conditions (water is required for Oxone® solubility), the lowest temperature that the epoxidation can be performed at is about -8 °C since the solvent system freezes under that temperature (acetonitrile/water system). Recently, Page introduced nonaqueous conditions for iminium salt-mediated asymmetric epoxidation using, an organic solvent-soluble oxidant tetraphenylphosphonium monoperoxysulfate (TPPP), which is synthesized by treating Oxone® with tetraphenylphosphonium chloride.[62] With this reagent, epoxidation reactions can be done in different solvents at much lower temperatures (up to -40 °C) and an increase in enantioselectivity can usually be.[62, 76]

In the biphasic CH_2Cl_2/water/18-C-6 protocol, the presence of 4.0 equiv of $NaHCO_3$ (1.0 M) and 1.1 equiv of Oxone® (0.27 M) saturated the aqueous phase which lowers the freezing point, and the experiments can be performed at -5 °C as a lower limit. However, for practical reasons, most experiments were carried out at 0 °C; all reagents being soluble in both phases.

Both solvent systems described above have some advantages and disadvantages. The epoxidation reactions under MeCN/water conditions proceed faster than with CH_2Cl_2 as solvent, however a relatively high amount of epoxide-opening products (diols) is usually observed.[77, 78] Biphasic CH_2Cl_2/water conditions were found to be suitable for the synthesis of very acid sensitive epoxides.

3.3 Chiral amine or ammonium salt catalyzed epoxidation

Following the work of Yang's group, while studying the *in situ* formation of an iminium salt with the appropriate combination of a carbonyl and a chiral amine partner,[72] Aggarwal and co-workers discovered that epoxidation reaction could proceed in the presence of the amine alone, and an asymmetric induction was obtained when a chiral amine such as **47** was used (Figure 3-17).[79, 80]



47 **48**

X = HSO_5^-, KSO_4^-

Figure 3-17.

Later it was found that the HCl salt of **47** was even more efficient than the free amine in terms of both reactivity and enantioselectivity. By trying to recover the catalyst at the end of the reaction performed at room temperature, the amine was fully oxidized to its *N*-oxide derivative. However, the oxidation product was found not to be catalytically active and unable to promote the epoxidation reaction. By performing the same reaction at lower temperature (-10 ^{o}C), the epoxidation occurs and the amine can be recovered. It was discovered that the reaction of amine with Oxone® led to the formation of salt **48** which contains a mixture of the potassium peroxymonosulphate and sulfate anions. Performing the epoxidation reaction with complex **48**, results identical to that with **47** were obtained indicating that compound **48** was the effective epoxidation moiety.[81]

Armstrong later highlighted the reason why complex **48** is more reactive than Oxone® itself; the ammonium counterion acting possibly as a phase-transfer catalyst.[82]

Aggarwal proposed a new model of activation involving an hydrogen bonding between HSO_5^- and the ammonium (Figure 3-18).

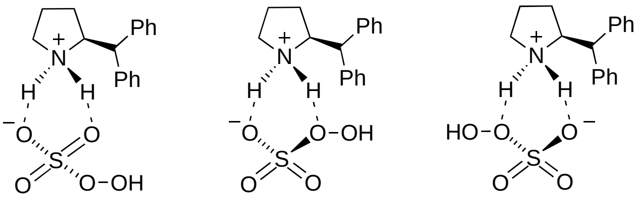


Figure 3-18. Possible interactions between a pyrrilidine-derived ammonium salt and HSO_5^- anion.

Similarly, Yang and co-workers observed that amines themselves can drive epoxidation reaction under slightly acidic conditions.[78] Cyclic secondary amines were found to be better catalysts than acyclic amines (primary or secondary) in terms of activity. Moreover, introducing electron-withdrawing (O, F) atoms at the β-position of the amine group increased reactivity of such catalysts. The Yang group reported a series of chiral amines structurally similar to Aggarwal catalysts as well, having different substitution fragments. The most selective catalyst of this type was **49** (61% ee_{max} for 1-phenylcyclohexene), containing a fluorine atom at the stereogenic center. According to the author's proposal, the presence of electronegative atom could stabilize the positively charged ammonium salts through favorable charge-dipole interactions or mild hydrogen bond formation with ammonium proton (Figure 3-19).

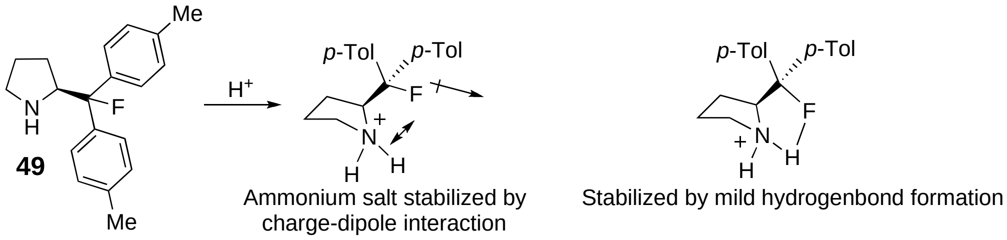
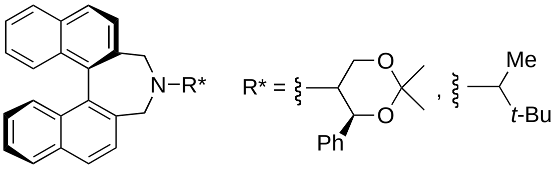


Figure 3-19. Effect of fluorine atom on stability of the ammonium salt.

The slightly acidic conditions used obviate the need to use an ammonium salt which are actual catalysts that mediate the epoxidation with the dual role of (1) phase-transfer catalyst and (2) Oxone® activator.

So far for all mentioned pyrrolidine-based catalysts for alkene epoxidation, no-stable iminium analogues can be found (due to their rapid hydrolysis). Recently, Lacour and co-workers showed that azepine derived tertiary amines of type **50** can also promote epoxidation reactions (Figure 3-20).[66, 67] These tertiary amines can be used directly as catalysts as well as their corresponding iminium salts (*vide supra*) as catalysts; however isolated azepinium iminium salts have shown better reactivity and enantioselectivity than their corresponding saturated azepine analogues.



50

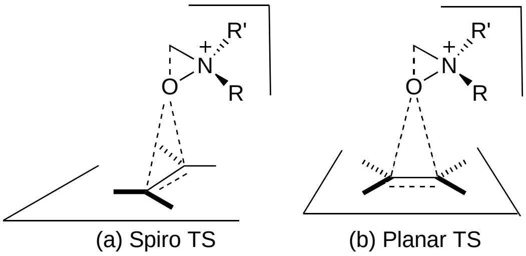
Figure 3-20.

3.4 Transition states and the origin of the stereoselectivity in epoxidation reactions catalyzed by chiral ketones and iminium salts

Enantioselective epoxidation of alkenes by chiral dioxiranes and oxaziridinium salts is known to be a stereospecific process; the *trans*- and *cis*-olefins lead to a *trans*- and *cis*-epoxides respectively. The epoxidation reactions of non-particularly activated alkenes by electrophilic oxygen atom transfer reagents are assumed to be S_N2-type displacements[83] and are usually rationalized in terms of two energetically preferred transition states (TS):

(1) a *spiro* transition state (Figure 3-21, a)

(2) a *planar* transition state (Figure 3-21, b)



(a) Spiro TS (b) Planar TS

Figure 3-21. Two possible transition states: (a) spiro TS and (b) planar TS.

In a planar TS, the electrophilic oxygen containing fragment of the reagent and the forming epoxide lays within the plane (as in the classic Bartlett's "butterfly" arrangement for the TS of the epoxidation by peracids). In the spiro TS, the electrophilic containing core of the reagent and the developing epoxide are reciprocally perpendicular. Theoretical studies performed by Houk and co-workers revealed that the spiro TS is preferred over the planar TS in the dioxirane mediated epoxidation reactions. High level computational studies then allowed to show a preference for the asynchronous spiro TS in the epoxidation promoted by oxaziridines and for a synchronous TS in the dioxirane and performic acid catalyzed reactions.[84, 85] The terms synchronous and asynchronous describe equal or unequal C-O bond formation respectively in the TS. Concerning epoxidation mediated by iminium salts **34** and **37**, Houk proposed, based on B3LYP/6-31G calculations, that reactions with these catalysts proceed rather *via* spiro and synchronous TS.[86]

The spiro TS is the favored one possibly due to the stabilizing interaction between the oxygen nonbonding orbital and the alkene π^* orbital, which is not feasible geometrically in the planar TS.[84, 85, 87, 88]

3.5 Conclusion

To conclude, the asymmetric epoxidation of olefins catalyzed by chiral ketones and iminium salts has been intensively studied over the past two decades. However, the development of highly enantioselective catalysts has proven to be challenging. A variety of chiral ketones and iminium salts have been investigated in various groups, and significant progresses have been made in this area. Chiral ketones have been shown to be very effective catalysts for the asymmetric epoxidation of alkenes with a wide substrate scope. High enantioselectivities were obtained for *trans*- and trisubstituted olefins, and a number of *cis*-olefins as well as certain terminal and tetrasubstituted alkenes. The epoxidation transition state model has been thoroughly studied, allowing rationalization and prediction of the stereochemical outcome with a reasonable level of confidence.

Chiral iminium salts have been shown to be effective catalysts as well. In some cases, for very reactive substrates, catalyst loading can be very low (up to 2.5 mol%) making these moieties attractive candidates for practical applications. So far, the best results were obtained using rigid binaphthylazepinium salts. However, despite the extensive work in this field there was no model to predict an epoxide formation in high enantiomeric purity and defined absolute configuration. The stability of iminium salts under the reaction conditions was rather untested and still an unsolved issue. Understanding the factors responsible for their stability or instability would help in the design of more robust catalysts with possibly lower catalyst loading. Further understanding of the reaction transition states and factors governing the stereochemical control would also certainly facilitate the development of more effective catalysts.

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4. Enantioselective epoxidation of alkenes using axially chiral iminium salts as catalysts

4.1 Enantioselective olefin epoxidation using doubly bridged biphenyl azepines and azepinium salts as catalysts

4.1.1 Preamble

As it was described in the previous section, quite a few successful iminium promoted enantioselective epoxidation reactions have been reported, many of them using biarylazepinium salts as catalysts. Typical structures are biphenyl **51**[1-6] and binaphthyl **52**[2, 5, 7-9] iminium salts (Figure 4-1). Further to the stereogenic biaryl element, most of these chiral salts bear an exocyclic chiral appendage R* derived from enantiopure amines.

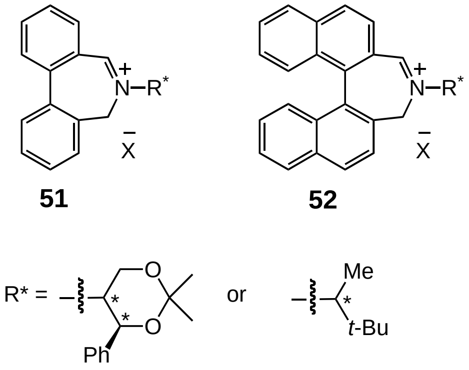


Figure 4-1. Biphenyl **51** and binaphthyl **52** iminium catalysts and typical chiral exocyclic appendages R* derived from L-acetonamine or 3,3-dimethylbutyl-2-amine.

Interestingly, in configurationally labile compound **51** (*tropos*), the stereocontrol over the reaction is provided by the exocyclic chiral auxiliary whereas for configurationally stable compounds **52** (*atporos*), the origin of the stereocontroling element is exactly the opposite. In this case, the *atropos* binaphthyl core has an overwhelming stereogenic influence. The enantioselectivity of the epoxidation reaction is solely controlled by the configuration of the binaphthyl moiety and not by the exocyclic appendage.[5, 8-10] Essentially similar *ee* values are obtained in the reaction of prochiral olefins in the presence of diastereomeric iminium salts that differ only by the configuration of the exocyclic auxiliary, and this in favor of epoxides of identical absolute configurations.

Recently, in search for alternatives to the classical *tropos* biphenyl and *atropos* binaphthyl moieties, a series of iminium salts derived from *atropos* enantiopure diastereomeric doubly bridged biphenyl (DBB) azepines were prepared in our group and tested as organocatalysts in the asymmetric epoxidation of prochiral alkenes, and atropisomeric DBB iminium salts (*S*,*R*a)-[**53**][TRISPHAT] and (*S*,*S*a)-[**53**][TRISPHAT] in particular (Figure 4-2).[11]

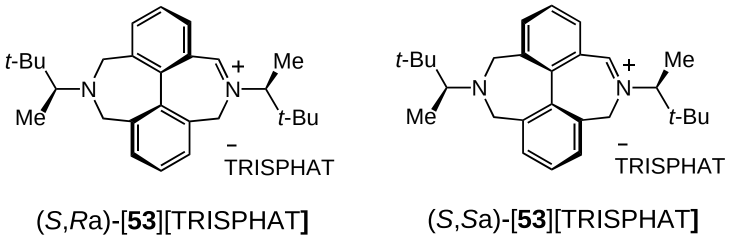
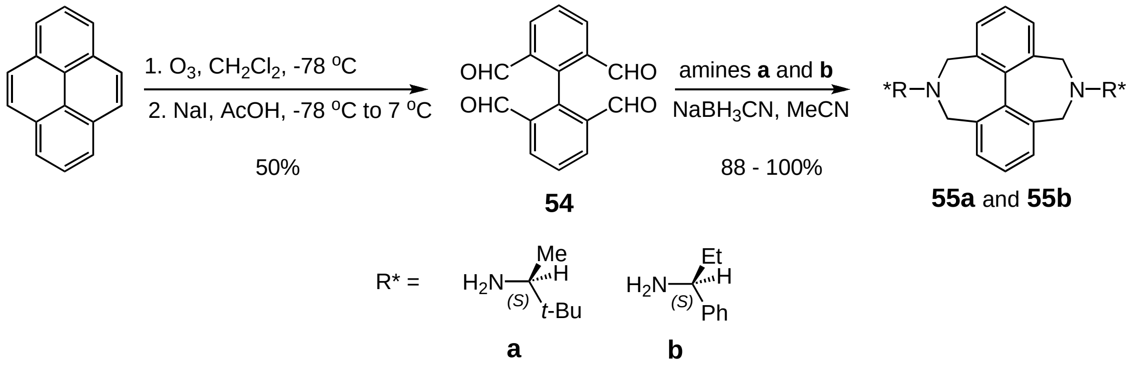


Figure 4-2.

The synthesis of doubly bridged biphenyl azepines (DBBA), precursors to the corresponding DBB iminium salts, was realized in two steps as described previously by Jérôme Vachon, a former PhD member of the group (Scheme 4-1).[11]



Scheme 4-1. Synthesis of DBB azepines **55a** and **55b**.

After the ozonolysis of pyrene (O_3, then NaI, AcOH) giving biphenyl-2,2′,6,6′-tetracarbaldehyde **54** (50%), reductive amination in the presence of (*S*)-configurated amines **a** and **b**, $NaBH_3CN$ in MeCN afforded compounds **55a** (quantitative) and **55b** (88 %) as kinetic mixtures of the desired (*S*,*R*a) and (*S*,*S*a) atropisomers.[11]

In sharp contrast with the *atropos* binaphthyl series (*vide supra*), the enantioselectivity of the epoxidation reaction is controlled by the configuration of the exocyclic appendage rather than that of the biaryl moiety. Somewhat different *ee* values were obtained in the reaction of prochiral olefins in the presence of diastereomeric (*S*,*R*a)-[**53**][TRISPHAT] and (*S*,*S*a)-[**53**][TRISPHAT], however always in favor of epoxides of identical absolute configurations – the differences being assigned to moderate “matched/mismatched” effects.

In that study, it was also shown that the central DBB core can also strongly enhance the stereochemical outcome of epoxidation reactions when the chiral exocyclic auxiliary fails to provide an effective stereoinduction by itself (as in the *tropos* biphenyl series). It was particularly evident in the reactions performed with *atropos* DBB (*S*,*S*a)-[**56**][TRISPHAT] and *tropos* (*S*)-[**57**][TRISPHAT] (Figure 4-3) derived from "less effective" (*S*)-1-phenylpropylamine for which much better enantioselectivity could be achieved with DBB (*S*,*S*a)-[**56**][TRISPHAT] over (*S*)-biphenyl [**57**][TRISPHAT] (*ee* up to 85% *vs*. 35% with 1-phenyl-3,4-dihydronaphthalene as substrate).

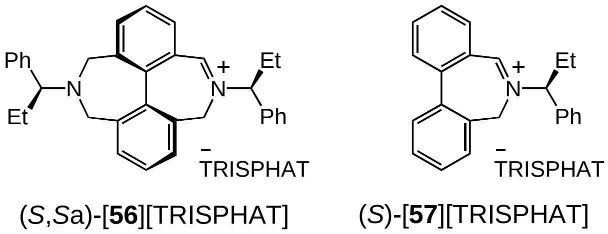


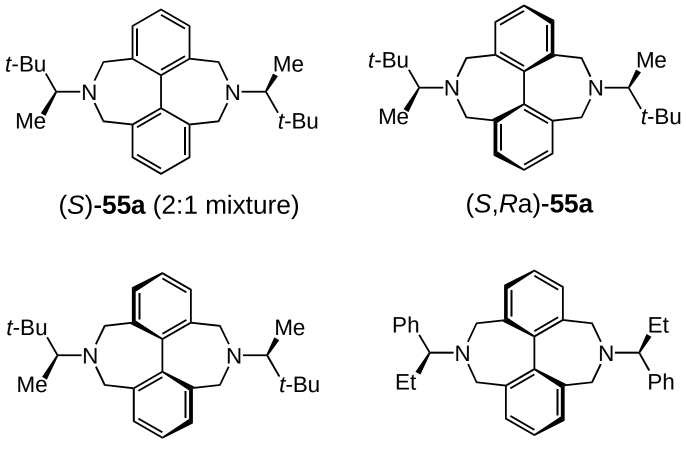
Figure 4-3.

Recently it has been demonstrated that the saturated azepines precursors to the iminium salts **51** and **52** are essentially as effective catalysts for the enantioselective epoxidation of alkenes than their unsaturated derivatives.[5, 10] As such, in these PhD studies we wondered whether DBB azepines **55a** and **55b** (Figure 4-4) would behave similarly and display also effective enantioselective oxidation abilities. Moreover, as the reactions of (*S*,*R*a)-[**53**][TRISPHAT] and (*S*,*S*a)-[**53**][TRISPHAT] gave virtually the same results, we wondered if the diastereomeric mixture of (*S*,*R*a)-**55a** and (*S*,*S*a)-**55a** (ratio 2:1 in favor of (*S*,*R*a)), namely (*S*)-**55a** would be as effective a catalyst as the separated diastereomers; this allowing to avoid a rather tedious separation (*S*,*R*a)-**55a** and (*S*,*S*a)-**55a**.

4.1.2 Results and discussion

*4.1.2.1 Epoxidation reactions with DBB azepines **55a** prepared from (S)-3,3-dimethylbutyl-2-amine*

To test this idea, one set of epoxidation conditions (Oxone®/CH_2Cl_2/$NaHCO_3$/18-Crown-6/H_2O) and three different commercially available prochiral trisubstituted unfunctionalized alkenes (**S1**-**S3**, Figure 4-5) were selected for the study. The results are reported in Tables 4-1 and 4-2.



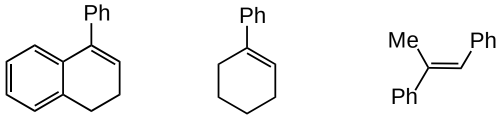
(*S*)-**55a** (2:1 mixture)

(*S*,*R*a)-**55a**

(*S*,*S*a)-**55a**

(*S*,*S*a)-**55b**

Figure 4-4.



S1 **S2** **S3**

Figure 4-5. Prochiral trisubstituted alkenes.

Table 4-1. Enantioselective epoxidation of olefine **S1** using catalyst (*S*)-**55a** (mixture of diastereomers), and pure (*S*,*R*a)-**55a** and (*S*,*S*a)-**55a**.[a]

alkene	(*S*)-**55a** (mixture)			Amine (*S*,*R*a)-**55a** (reference)			Amine (*S*,*S*a)-**55a** (reference)		
	ee [b]	Conv.	Conf.	*ee* [b]	Conv.	Conf.	*ee* [b]	Conv.	Conf.
S1	75	98	(+)-(1*R*,2*S*)	77	55	(+)-(1*R*,2*S*)	79	69	(+)-(1*R*,2*S*)

[a] Conditions: substrate (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 /H_2O (3:2), 2 hours, 0 °C. Average of at least two runs; [b] The enantiomeric excesses were determined by CSP-HPLC (Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, λ 230 nm); the conversions using an internal standard (naphthalene).

Significantly, amine **55a** behave as an effective catalyst for the enantioselective epoxidation of unfunctionalized olefins. Initial screening (Table 4-1) was performed with alkene **S1** as a substrate and, as catalysts, the simple-to-use mixture of atropisomers (*S*)-**55a** or the separated diastereomers (*S*,*R*a)-**55a** and (*S*,*S*a)-**55a**. As expected, it revealed very similar results for the three catalyst combinations. Whereas the enantioselectivity was slightly lower for the atropisomeric mixture (*ee* 75 vs. 77-79%), the conversion was quite better.

Table 4-2. Enantioselective epoxidation of olefins **S1**-**S3** using diastereomeric mixture of amine (*S*)-**55a**; (*S*,*R*a)-[**53][**TRISPHAT] and (*S*,*S*a)-[**53][**TRISPHAT] used as references.[a]

alkene	(*S*)-**55a** (mixture)			(*S*,*R*a)-[**53][**TRISPHAT] (reference[11])			(*S*,*S*a)-[**53][**TRISPHAT] (reference[11])		
	ee [b]	Conv.	Conf.	*ee* [b]	Conv.	Conf.	*ee* [b]	Conv.	Conf.
S1	75	98	(+)-(1*R*,2*S*)	76	80	(+)-(1*R*,2*S*)	49	76	(+)-(1*R*,2*S*)
S2	71	82	(–)-(1*S*,2*S*)	76	56	(–)-(1*S*,2*S*)	– [c]	– [c]	– [c]
S3	45	46	(–)-(1*S*,2*S*)	59	61	(–)-(1*S*,2*S*)	41	75	(–)-(1*S*,2*S*)

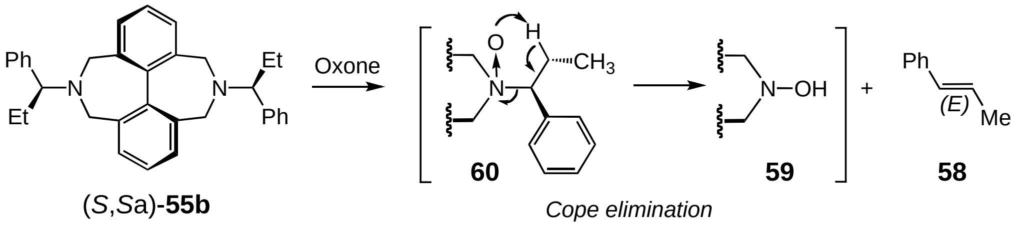
[a] Conditions: substrate (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 /H_2O (3:2), 2 hours, 0 °C. Average of at least two runs; [b] The enantiomeric excesses were determined by CSP-GC (**S2**, Chiraldex Hydrodex β-3P) or CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, λ 230 nm); the conversions using an internal standard (naphthalene); [c] experiment not performed.

With that result in hand, further reactions were performed with trivial mixture (*S*)-**55a** exclusively and compared to that of separated iminium salts (*S*,*R*a)-[**53**][TRISPHAT] and (*S*,*S*a)-[**53**][TRISPHAT] (Table 4-2). In terms of conversions, results were often better for the simple amine; enantiomeric excesses being alternatively at the higher or lower ends of the “matched/mismatched” scale. On one hand, for olefin **S1**, an *ee* value of 75% was obtained that fits well with that obtained with matched catalyst (*S*,*R*a)-[**53**][TRISPHAT] (*ee* 76%). On the other hand, for olefin **S3**, the enantioselectivity reached only 45%, barely above the value (41%) obtained with the mismatched catalyst (*S*,*S*a)-[**53**][TRISPHAT]. In any case, non-racemic epoxides of analogous absolute configurations were detected in the reactions with amine **55a** and iminium salts of (*S*,*R*a)-[**53**][TRISPHAT] and (*S*,*S*a)-[**53**][TRISPHAT].

4.1.2.2 (Lack of) Epoxidation reactions with DBB azepines prepared from (S)-1-phenylpropylamine

Having confirmed with **55a** that DBB azepines can be indeed as effective catalysts as their iminium derivatives for the enantioselective epoxidation of alkenes **S1**-**S3**, an extension of this chemistry to DBB (*S*,*S*a)-**55b** was looked for. However, in this case and to our surprise, no conversion could be detected (^{1}H NMR, GC-MS) in reactions performed in the presence of catalytic amounts of amine (*S*,*S*a)-**55b** (Table 4-3). Whereas the olefinic substrates remained unchanged in the crude reaction mixtures, diamine (*S*,*S*a)-**55b** seemed to decompose. It was then our analysis that, under the reaction conditions, the particular DDB azepine (*S*,*S*a)-**55b** was transformed into an unreactive material. Care was thus taken to treat, in the absence of any olefin, (*S*,*S*a)-**55b** (5 mol%) with Oxone® (1.1 equiv.), $NaHCO_3$ (4.0 equiv.) in CH_2Cl_2 /H_2O at 0 °C to identify the negative reaction pathway (Scheme 4-2). ^1H NMR spectroscopic analysis of the crude reaction mixture revealed the presence of unreacted diamine (*S*,*S*a)-**55b** along with some unexpected (*E*)-1-phenylpropene **58**[1] and an unknown reaction compound **59**.

At this stage, only a Cope elimination pathway can put forward to rationalize the formation of the conjugated olefin **58** that is obviously linked to the presence of the 1-phenylpropanyl side chains of (*S*,*S*a)-**55b**. It is our proposal that, under the reaction conditions, DBB (*S*,*S*a)-**55b** is oxidized to a tertiary N-oxide derivative **60**. The oxygen atom then subsequently reacts intramolecularly with a β-hydrogen atom of the exocyclic side chain to yield olefin **58**; compound **59** being possibly the resulting hydroxyl amine or a derivative of it.



Scheme 4-2.

In any case, no trace of iminium ion of type **56** can be observed in the crude reaction mixture of the above mentioned reaction; the presence of iminium ions being easy to monitor by the appearance (or not) of singlet signals between 8-12 ppm in ^1H NMR spectroscopy. To confirm this fact, the NMR experiment was performed in conditions similar to that of a standard reaction used to make iminium salts: (*S*,*S*a)-**55b** was treated with a stoichiometric amount of NBS in CD_2Cl_2 for 5 minutes and, as expected from

---

[1] This product was subsequently isolated in pure state by simple filtration of the crude reaction mixture through silica gel plug eluted with *n*-pentane.

previous studies,[5] such a signal at 11.4 ppm appeared predominantly on the ^{1}H NMR spectrum.

Table 4-3. Enantioselective epoxidation of olefins **S1**-**S3** using (*S*,*S*a)-**55b** or (*S*,*S*a)-**55b** + NBS; (*S*,*S*a)-[**56**][TRISPHAT] used as reference.[a]

alkene	Amine (*S*,*S*a)-**55b** [a]			(*S*,*S*a)-**55b** + 5 mol% NBS [b]			(*S*,*S*a)-[**56**][TRISPHAT] (reference[11])		
	ee [c]	Conv.	Conf.	*ee* [c]	Conv.	Conf.	*ee* [c]	Conv.	Conf.
S1	-	0	-	84	96	(–)-(1*S*,2*R*)	85	60	(–)-(1*S*,2*R*)
S2	-	0	-	73	85-94	(+)-(1*R*,2*R*)	71	82	(+)-(1*R*,2*R*)
S3	-	0	-	41	33-43	(+)-(1*R*,2*R*)	55	51	(+)-(1*R*,2*R*)

[a] Conditions: substrate (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 /H_2O (3:2), 2 hours, 0 °C. Average of at least two runs; [b] 5 mol% of (*S*,*S*a)-**55b** + 5 mol% of NBS in CH_2Cl_2 added after 5 min to water (2:3 ratio to CH_2Cl_2), 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, 2 hours, 0 °C. Average of at least two runs; [c] The enantiomeric excesses were determined by CSP-GC (**S2**, Chiraldex Hydrodex β–3P) or CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C , λ 230 nm); the conversions using an internal standard (naphthalene).

As such, epoxidation of alkenes **S1**-**S3** can be performed with (*S*,*S*a)-**55b** as precatalyst if care is taken to treat the DBB amine with NBS prior to the addition of other reagents and substrates. The results are summarized in Table 4-3. Not too surprisingly, virtually identical results are obtained using the mixture of (*S*,*S*a)-**55b** and NBS (5 mol% each) instead of isolated iminium ion (*S*,*S*a)-[**56**][TRISPHAT]; only in the case of olefin **S3** are the enantioselectivity and conversions lower if starting from the DBB azepine reagent directly.

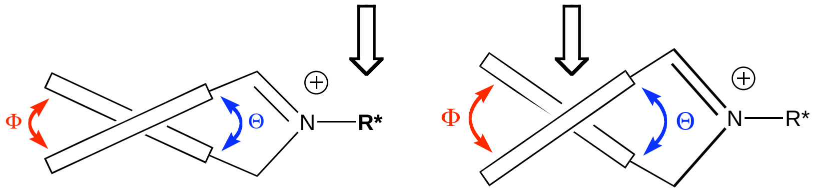
4.1.3 Conclusion

To conclude, the 2:1 mixture of atropisomeric DBB azepines (*S*,*R*a)-**55a** and (*S*,*S*a)-**55a** performs essentially as well as the separated diastereomers or the derived iminium salts (*S*,*R*a)-[**53**][TRISPHAT] and (*S*,*S*a)-[**53**][TRISPHAT] as catalysts for the enantioselective epoxidation of some prochiral olefins. As using the DBB azepine mixture requires less synthetic and purification steps than the preparation of the diastereomerically pure iminium salts, it is therefore advantageous to use the trivial mixture for synthetic applications.

4.2 Enantioselective olefin epoxidation using axially chiral biaryl azepinium salts as catalysts. Rapid *in situ* screening and origin of the stereocontrol

4.2.1 Preamble

Based on this and previous observations for the stereocontrol of the iminium-catalized epoxidation reaction, there was thus a clear dichotomy between the catalytic behaviour of *tropos* biphenyl compounds **51** and *atropos* double bridged biphenyl compounds on one side and binaphthyl derivatives **52** on the other. To our knowledge, no explanation had been so far given to account for this difference. Minimally, one could consider that the chemical nature of the biaryls at play – biphenyl *vs*. binaphthyl – is the determining factor in the sense of the enantioselective induction. However, a declaration of the presence of two extra aromatic groups was falling short of any rational explanation. For us, it was clear that other parameters could well influence the reaction – and the dihedral angle θ around the central bond joining the aromatic rings in particular (Figure 4-6). It is indeed known that such a parameter can be crucial on the level of asymmetric induction obtained in enantioselective catalytic reactions.[12, 13] In the present case, we wondered if a low dihedral angle value at the junction of the rings (θ ~ 40-45 °) would entice a stronger (dominant) influence of chiral exocyclic appendage R* whereas higher values (θ ~ 53 ° and higher) would lead to the predominance of the biaryl element for the stereocontrol of the epoxidation reaction; this predominance of the axial over the centered chirality resulting also possibly in higher enantiomeric excesses values for the epoxides.



smaller Θ and Φ angles
exocyclic appendage
predominant

larger Θ angle
biaryl axis predominant.
Influence of Φ?

Figure 4-6. Stereochemical influence as a function of θ and Φ dihedral angles (measured inside and outside the N-containing seven membered-ring respectively).

To test this hypothesis, it was decided to synthesize two rigid, configurationally stable biphenyl systems for which the θ dihedral angle would be similar to that of the binaphthyl derivatives with, ideally, (slightly) lower and higher dihedral angle values, respectively than of compounds of type **52**. In the first instance, lower level of enantioselectivity ought to be reached with a possible influence of the chiral exocyclic appendage whereas, in the second case, higher levels of stereoinduction should be observed with the biaryl system acting solely for the stereocontrol. Alternatively, this analysis performed with θ values could be performed with the “external” dihedral angle Φ. However and unfortunately, at the start of the study, little structural information was found in the literature on biaryl azepines or azepinium salts to help us in the selection of the catalyst skeletons. In fact, an extensive search of the Cambridge Structural database revealed only 35 structures of seven-membered ring biaryl azepine derivatives with very little structural overlap between the compounds. A precise determination of the nature of the θ angle in this family of compounds was therefore impossible to achieve from literature precedents. Nevertheless, an analysis of the data revealed that some of these compounds could be grouped into sub-families from which some trends could be inferred. These moieties (**61**-**69**) are detailed in the Figure 4-7; the CSD refcodes corresponding to the structures are detailed in the caption text and the dihedral angle(s) θ (and Φ) mentioned on the drawing.

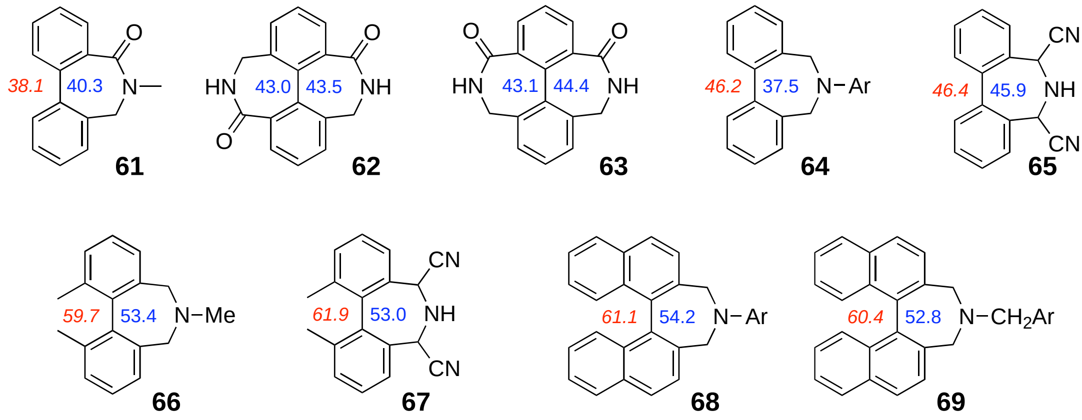
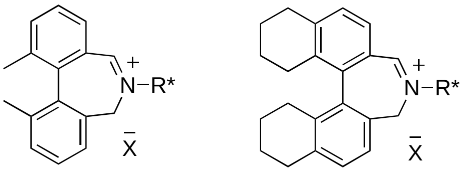


Figure 4-7. Biaryl azepine derivatives and dihedral angles θ (blue) and Φ (red, italic): **61** (HMBAZO), **62** (GEMQOE), **63** (GEMQUK), **64** (GAVKET), **65** (WIPJAG), **66** (NUBGOG), **67** (WIPJIO), **68** (XEBNIB), **69** (HOVGII).

Clearly, two groups could be discerned based on θ values. On one hand, biphenyl and doubly-bridged biphenyl moieties (**61** to **65**) presented rather low dihedral angle values (θ ≤ 45.9°) whereas, on the other hand, quite higher values (θ > 52°) were observed for dimethylbiphenyl and binaphthyl derivatives. Unfortunately, very little difference was noticed between the θ values of latter two classes of compounds (**66** to **69**). This observation was rather disappointing. However, a closer investigation of the second sub-family revealed rather large differences between the θ and Φ dihedral angles measured inside and outside the N-containing seven membered-ring respectively (see Figure 4-7). Considering that (i) the Φ (rather than θ) ought to be more sensitive to the nature of the substituents positioned at the 6,6′-position of the biphenyl and (ii) Φ values mentioned on Figure 4-7 might not be representative of the derivatives of study, we decided to investigate dimethylbiphenyl azepinium cations of type **70** as catalysts and verify if a reactivity difference could be found with **52** in the context of the epoxidation chemistry. Furthermore, taking into account the possible importance of Φ, we considered that the second system of study ought to be a 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl azepinium cation of type **71** (Figure 4-8); strong repulsion between the hydrogenated rings leading possibly to higher Φ values than systems **52** and **70** and hence a better selectivity in the epoxidation reactions.

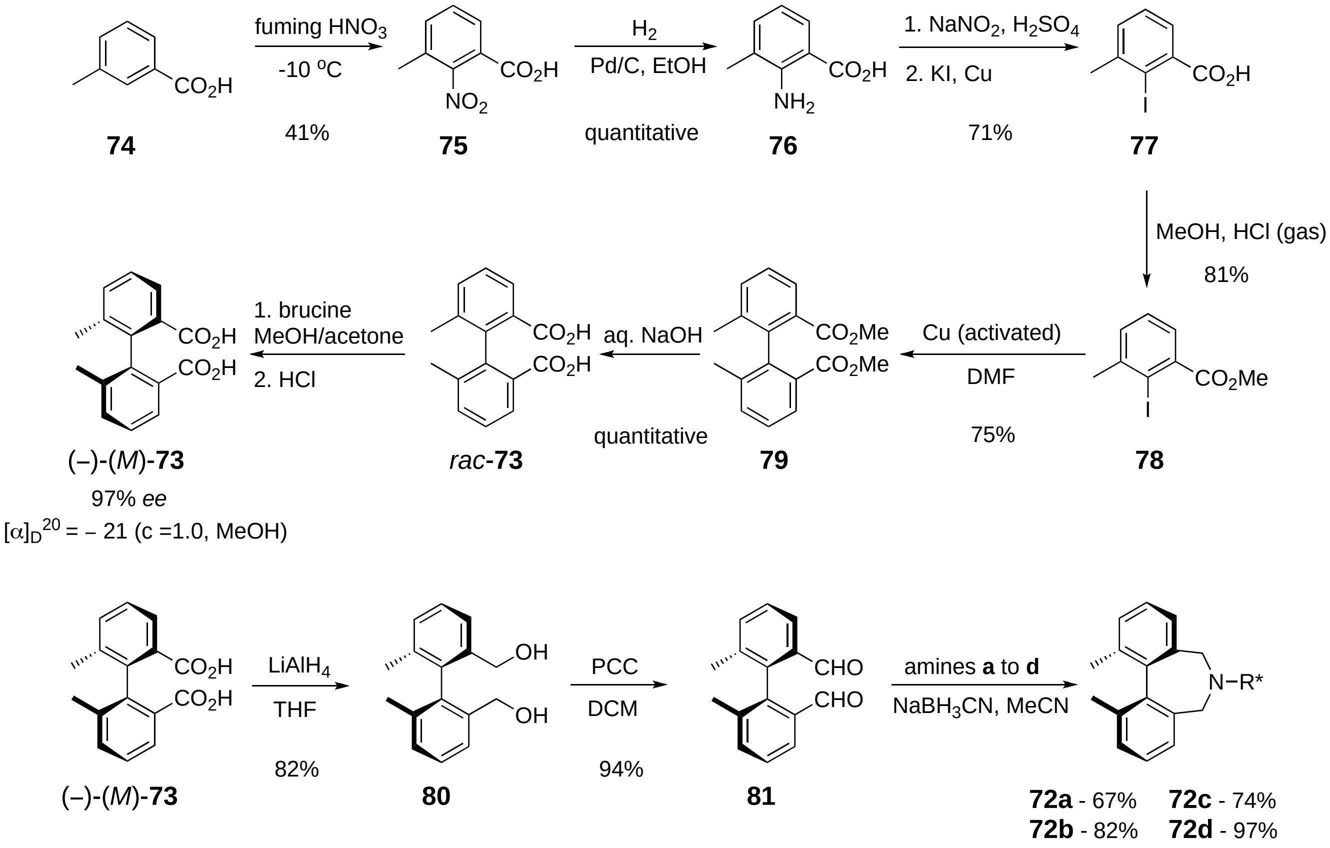


70 **71**

Figure 4-8.

4.2.2 Synthesis of 6,6′-dimethylbiphenylazepines 72a to 72d

The synthesis of the 6,6′-dimethylbiphenylazepine amines (**72a** to **72d**), precursors to catalysts of type **70**, was realized in three steps starting from highly enantioenriched (-)-(*M*)-6,6′-dimethylbiphenyl-2,2′-dicarboxylic acid **73** (Scheme 4-3). This acid, the key intermediate of the synthesis, was prepared in 7 steps starting from commercially available 3-methylbenzoic acid **74** according to the Suda's protocol.[14] Reaction **74** with freshly prepared fuming nitric acid at -10 ^{o}C provided a mixture of nitrated isomers. Fortunately, poor solubility of the desired 3-methyl-2-nitrobenzoic acid **75** in cooled fuming nitric acid facilitated the separation of **75** from undesirable isomers by a simple filtration. Reduction of **75** by molecular hydrogen under Pd/C (10 mol%) in ethanol provided 2-amino-3-methylbenzoic acid **76** in quantitative yield. The Sandmeyer reaction with **76** gave 2-iodo-3-methylbenzoic acid **77** (71%) which was treated with methanol under acidic conditions to form methyl 2-iodo-3-methylbenzoate **78** (81%).



Scheme 4-3. Synthesis of azepines **72a** to **72d**.

The Ullmann coupling of **78** at the presence of activated copper powder[15] in DMF at reflux resulted in the clean formation of dimethyl 6,6'-dimethylbiphenyl-2,2'-dicaboxylate **79** in good yield (75%). Saponification of **79** gave the desired 6,6′-dimethylbiphenyl-2,2′-dicarboxylic acid in racemic form. The resolution of enantiomers was realized using brucine as a resolving agent. The enantiomeric purity (97% *ee*) of the desired (-)-(*M*)-**73** was determined by HPLC analysis of the corresponding dimethyl ester, prepared by treatment of **73** with methanol in HCl. The absolute configuration of the product was determined by comparison of its optical rotation with that reported in the literature. Reduction of (-)-(*M*)-6,6′-dimethylbiphenyl-2,2′-dicarboxylic acid with lithium aluminium hydride gave the corresponding diol (**80**, 82%)[16] which was oxidized to the desire dialdehyde **81** with excellent yield (94%) following an already reported protocol.[17]

Reductive amination in the presence of enantiopure amines **a** to **d** (Figure 4-9) using $NaBH_3CN$ in MeCN provided the desired compounds **72a** to **72d** in decent to good yields (67-97%). Diastereomeric **72a** / **72c** and **72b** / **72d** were obtained as single enantiomers after purification; no trace of stereoisomeric entities being evidenced in the ^{1}H NMR analysis.

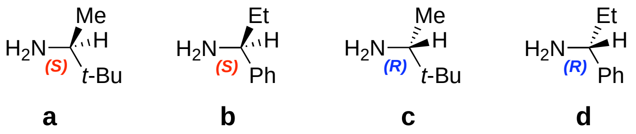
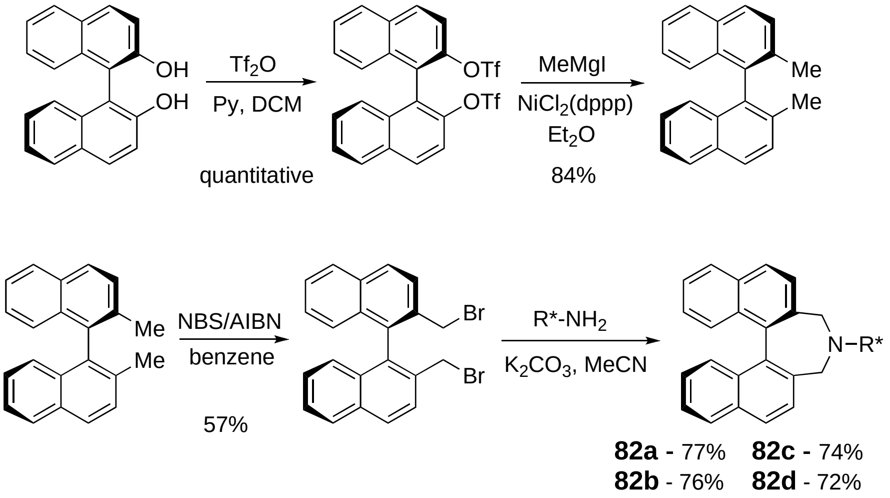


Figure 4-9. Selected optically pure commercially available amines for the formation of diastereomeric biphenyl and binaphthyl azepines.

4.2.3 Synthesis of binaphthyl azepines 82a to 82d

The four step synthesis of the binaphthyl azepines **82a** to **82d** was previously reported using as starting material (*R*a)-2,2′-bis(bromomethyl)-1,1′-binaphthyl.[5] Two novel binaphthyl azepines **82b** and **82d** were prepared following a procedure similar to the one described above and this in 76% and 72% yield, respectively (Scheme 4-4).



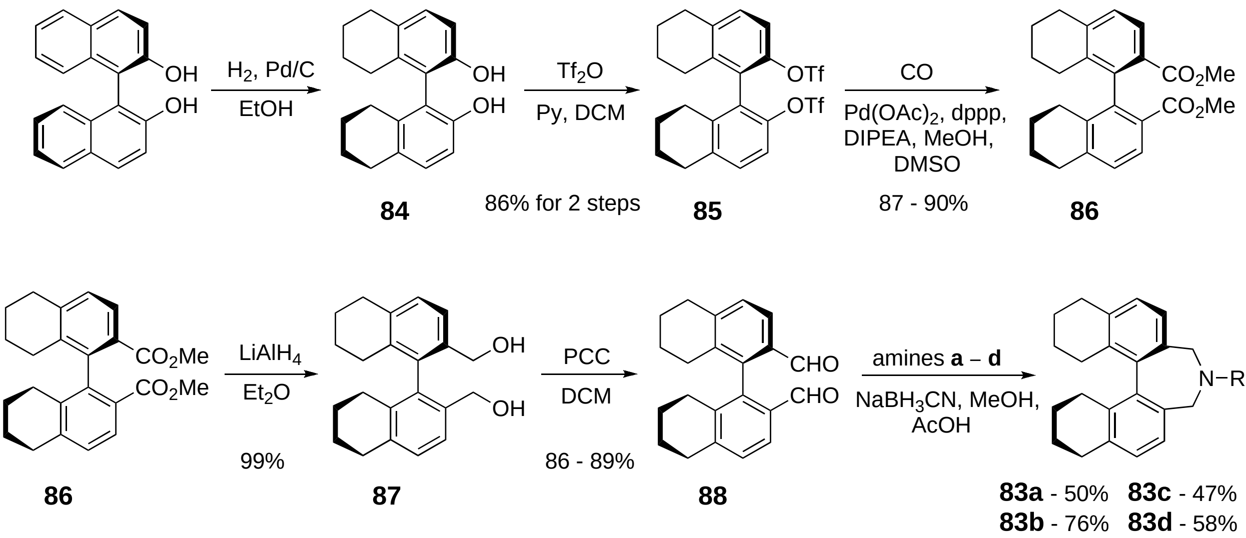
Scheme 4-4. Synthesis of azepines **82a** to **82d**.

4.2.4 Synthesis of 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl azepines 83a to 83d

The four novel 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl azepines **83a**, **83b**, **83c** and **83d**, precursors to catalysts of type **71**, were prepared in six steps starting from commercially available enantiopure (*R*a)-BINOL (Scheme 4-5).

Catalytic hydrogenation of (*R*a)-BINOL (Pd/C, EtOH) and subsequent recrystallization from *n*-heptane provided (*R*a)-2,2′-dihydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl **84** in more than 99% enantiomeric purity.[18] This compound was then treated with triflic anhydride (CH_2Cl_2, pyridine, 0 °C) to form the (*R*a)-2,2′-

ditrifluoromethanesulfonyloxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl **85** in 86% isolated yield.



Scheme 4-5. Synthesis of azepines **83a** to **83d**.

Palladium-mediated carbonylation of the bistriflate ($Pd(OAc)_2$, dppp, (i-Pr)$_2$NEt, MeOH, DMSO) provided the known 2,2′-bis(carbomethoxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl **86** in good yield[2] (87-90%).[19] The reduction with lithium aluminum hydride in diethyl ether gave the desired bisdiol **87** in almost quantitative yield. The subsequent oxidation (PCC, CH_2Cl_2) proceeded smoothly and afforded pure bisaldehyde **88** in 86-89% yield which was the starting material for the synthesis of all four octahydrobinaphthyl azepines **83a**, **83b**, **83c** and **83d**.[3] The derivatives were subjected to the reductive amination procedure used for the synthesis of azepines **72a** to **72d** (amines **a** to **d** (2.0 equiv.), **88** (1.0 equiv.), $NaBH_3CN$ (4.0 equiv.), MeCN). Surprisingly, this protocol was not successful. After 24 h, only a moderate conversion of starting aldehyde was observed. Nevertheless, using a slightly modified protocol (amines **a** to **d** (1.1 equiv.), **88** (1.0 equiv.), $NaBH_3CN$ (2.0 equiv.), MeOH, catalytical amount of glacial AcOH), azepines **83a** to **83d** were provided in moderate to decent yields (47-76%).

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[2] The key factor in this reaction to obtain a good yield of the diester and avoid formation of the monoinsertion product it is essential to use strict anhydrous solvents and reagents. The CO pressure must be held at 2-2.5 bar (constantly) during the whole reaction time. For further details see the experimental part.

[3] Each step can be done in a multigram scale. Based on this procedure more then 5g of dialdehyde **84** was synthesized in one pot as colorless needles (Mp = 130.8 – 131.7 °C).

4.2.5 X-ray analysis of 72b, 82b·HCl, 83b·HCl and 83d

Finally, for four azepine derivatives (or their hydrogen chloride salts), monocrystals were obtained and their structural X-ray analyses were performed.[4] The ORTEP views of **72b**, **82b**·HCl, **83b**·HCl, and **83d** are reported in Figure 4-10 along with θ and Φ values.

Interestingly, assuming little structural perturbation from the protonation and quite opposite to the Cambridge Structural database situation, rather strong differences were observed for θ and Φ in the three biaryl series. As it could be expected, the 6,6′-dimethylbiphenyl azepine **72b** presented the lowest dihedral angle values. Comparison with **82b**·HCl to **83b**·HCl indicated that this θ angle change only moderately, whereas a strong variation of the Φ angle could be noticed with values increasing from 57.5° to 61.0° and 67.0° respectively. Diastereomeric structures **83b**·HCl and **83d** are also remarkably similar. With that information in hands, the catalysts behavior was studied.

4.2.6 Iminium salts formation

Traditionally the iminium catalysts are prepared prior to the epoxidation step by, for instance, the oxidation of their tertiary amine precursors. Oxidation of tertiary amines to iminium salts is indeed feasible and literature precedents have indicated that a mixture of I_2 and KOAc is a useful oxidative combination for that transformation.[1, 21] However, this protocol leads to many by-products and is not appropriate for compounds containing several amine functional groups, and DBB azepines in particular. To overcome this problem, milder reaction conditions were developed (NBS, AIBN (10 mol%), CCl_4, 25 °C).[22] This protocol is indeed more selective than I_2/KOAc. However, the oxidation occurs quite slowly. In our group, it was found that the process can be greatly accelerated (20 min *vs.* hours) by performing the reaction without AIBN and using chloroform as solvent instead of carbon tetrachloride.[5, 6] The bromide counterion of the iminium salts was then exchanged to more lipophilic anions of TRISPHAT type in a second series of experiments.

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[4] All the seven-membered rings adopt a twist-boat conformation with a pseudo twofold axis passing through the N atom and show minimum ΔC_2 values of 0.021, 0.011, 0.001 and 0.041 for compound **72b**, **82b**·HCl, **83b**·HCl and **83d** respectively. For an article describing ΔC_2 values, see: [20] M. Nardelli, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1983**, *39*, 1141-1142.

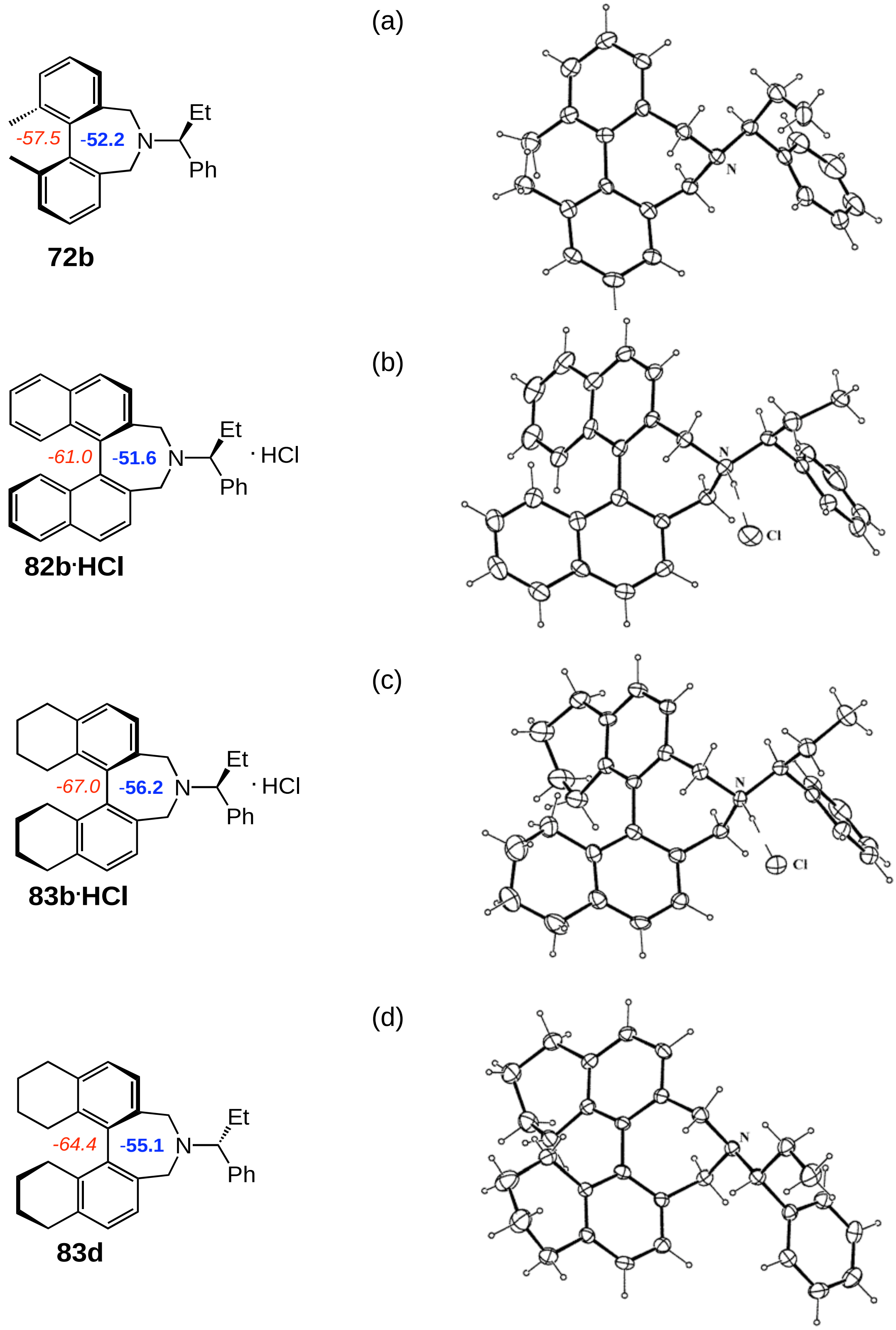
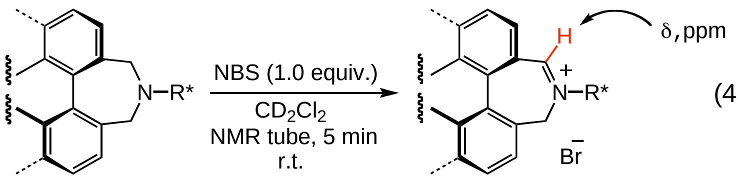


Figure 4-10. Chemical structures and ORTEP views of (a) **72b**, (b) salt **82b**·HCl, (c) salt **83b**·HCl and (d) **83d**. Ellipsoids are presented at the 50% probability level. Dihedral angles θ (blue, bond) and Φ (red, italic) are indicated with a mean value of uncertainty of 0.5°.

More recently, during our studies on the epoxidation of olefins using DBB azepines and azepinium salts as catalysts we have shown that the transformation of azepine to azepinium salts can be even simplified if the oxidation reaction is performed in dichloromethane instead of chloroform (NBS 1.0 equiv., 5 min).

Based on such an observation, we wondered about the necessity of isolating the iminium salts altogether and whether the bromide precursors generated *in situ* could not be used directly as catalysts. It was thus decided to test this hypothesis with all azepines **72a** to **72d**, **82a** to **82d** and **83a** to **83d** – and then compare the reactivity of one of the systems with that of a classical, isolated, iminium salt.

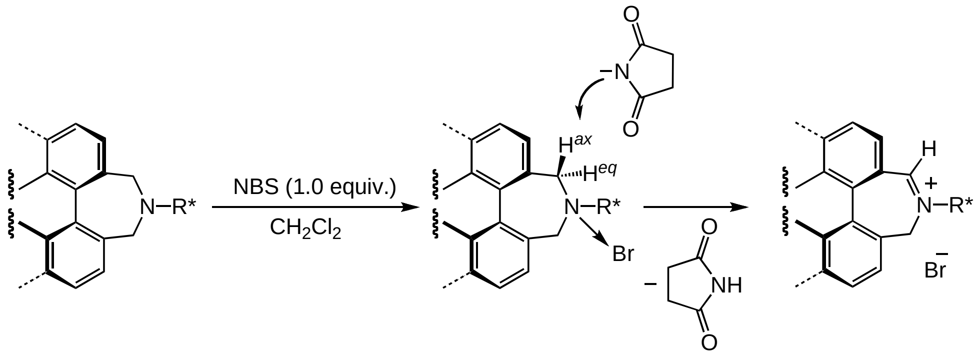
To check on the new skeletons the validity of the amine to iminium ion transformation, NMR tube experiments were performed in conditions similar to that of flask reactions (NBS (1.0 equiv.), CD_2Cl_2, see next section). ^{1}H NMR spectra of the crude reaction mixtures indicated the clean conversion of the azepine moieties to the corresponding iminium bromide salts (Equation 4-1, Table 4-4). The formation of the unsaturated species [**52a**][Br] to [**52d**][Br], [**70a**][Br] to [**70d**][Br], [**71a**][Br] to [**71d**][Br] was particularly easily to monitor in the 10 to 12 ppm region as singlet signals corresponding to the C*H*=N$^+$ proton appears (e.g. Figure 4-11).



(4-1)

The oxidation proceeded smoothly with either commercial, yellowish (due to the traces of molecular bromine) NBS or purified (colorless) NBS, obtained by recrystallization from water. This observation strongly suggests that the mechanism of this oxidation is not radical and involves a simple N-Br bond formation followed by an elimination to form the iminium salt (Scheme 4-6).

Globally, higher frequencies were observed for the chemical shifts of the iminium protons of the derivatives **52** and the lowest values for the derivatives of **71**; derivatives of amines **c** and **d** presenting the lowest and highest frequencies in each series respectively (Table 4-4).



Scheme 4-6. Proposed mechanism for the oxidation of tertiary azepines to their iminium salts.

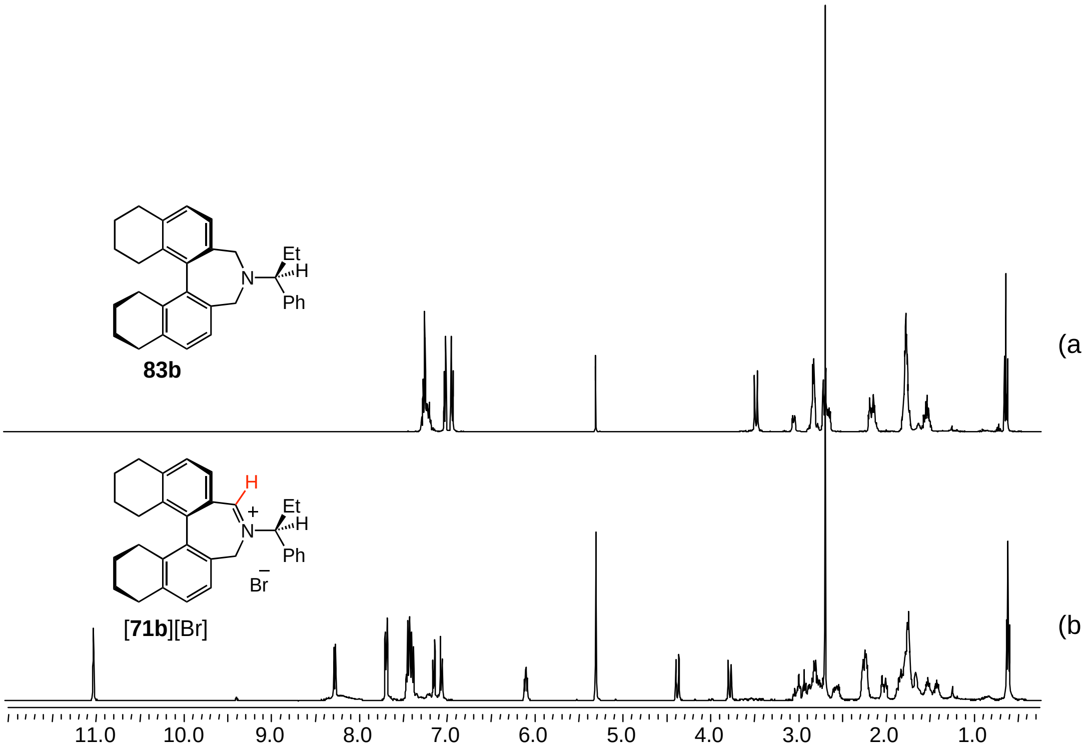
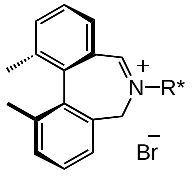
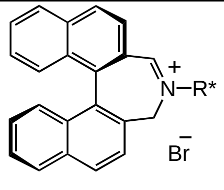
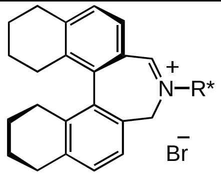


Figure 4-11. ^{1}H-NMR spectra (CD_2Cl_2, 400 MHz) of (a) **83b** and (b) *in situ* generated [**71b**][Br].

Table 4-4. *In situ* formation of iminium salts.[a] Chemical shifts of the C*H*=N$^+$ proton (^{1}H-NMR)

Iminium salt		Iminium salt		Iminium salt	
	δ, ppm		δ, ppm		δ, ppm
[**70a**][Br]	10.98	[**52a**][Br]	11.21	[**71a**][Br]	10.79
[**70b**][Br]	10.87	[**52b**][Br]	10.47	[**71b**][Br]	11.00
[**70c**][Br]	10.42	[**52c**][Br]	11.57	[**71c**][Br]	10.25
[**70d**][Br]	11.31	[**52d**][Br]	11.54	[**71d**][Br]	10.99

[a] Conditions: 0.2 mmol of azepine, 0.2 mmol of NBS in 0.5 mL of CD_2Cl_2, 5 min, 400 MHz. Chemical shifts are given relative to Me_4Si with the solvent resonance used as the internal standard (CD_2Cl_2 δ = 5.32 ppm).

4.2.7 Enantioselective epoxidation reaction of olefins using in situ formed iminium salts

Having established the feasibility of the *in-situ* oxidation of the various biarylazepines to the corresponding iminium salts, we decided to use these species directly for our study on the influence the dihedral angle of the biaryl moieties onto the enantioselectivity of the epoxidation reaction.

One set of epoxidation conditions (5 mol% catalyst, Oxone®/CH_2Cl_2/$NaHCO_3$/18-Crown-6/H_2O) and three different prochiral tri-substituted unfunctionalized alkenes were selected for the study (Figure 4-5) – these alkenes being chosen for their proven record of performing well in iminium-catalyzed epoxidation reactions (*vide supra*). The biphasic CH_2Cl_2/H_2O protocol, which has been detailed previously, is easy to run and usually allows the ready isolation of the epoxides after the oxidation reaction. To perform the reaction with the *in-situ* bromide catalysts derived from **72a** to **72d**, **82a** to **82d** and from **83a** to **83d**, the only modification to the protocol was the separated treatment of the azepines with NBS (CH_2Cl_2, 5 min) and the addition of the resulting solution to a mixture of the other reagents. The results for the various experiments are reported in Tables 4-5, 4-6, 4-7 and 4-8. Only the enantiomeric excesses are reported as the purpose of this study was essentially the evaluation of the sense of induction of the enantioselective transformation and the global asymmetric efficiency of the catalysts.[5] Information about the reactivity will be given later in the course of the study. Importantly, all iminium salts from [**52a**][Br] to [**52d**][Br], [**70a**][Br] to [**70d**][Br], [**71a**][Br] to [**71d**][Br] behaved as catalysts under this set of conditions. As catalysts of type **70** have in general been less effective than that of type **52** and **71**, data in Tables 4-5 to 4-8 are indicated with the catalysts positioned in the following order **70** → **52** → **71**, from left to right.

Table 4-5. Epoxidation of olefins **S1**, **S2, S3** using catalysts (*R*a,*S*)-[**70a**][Br], [**52a**][Br], [**71a**][Br]. Enantiomeric excesses (%).[a]

Alkene	[**70a**][Br]	[**52a**][Br]	[**71a**][Br]	Configuration
S1	75	80	87	(+)-(1*R*,2*S*)
S2	78	67	82	(-)-(1*S*,2*S*)
S3	60	46	63	(-)-(1*S*,2*S*)

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[5] The resulting epoxides were not isolated at this stage of the studies. The enantiomeric excesses were determined CSP-GC or CSP-HPLC analysis of the crude reaction mixtures.

[a] Conditions: substrate (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 2 hours, 0 °C. Average of at least two runs. The enantiomeric excesses were determined by CSP-GC (**S2**, Chiraldex Hydrodex β-3P) or CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, λ 230 nm). The configuration indicated is that of the resulting epoxide.

Table 4-6. Epoxidation of olefins **S1**, **S2, S3** using catalysts (*R*a,*R*)-[**70c**][Br], [**52c**][Br], [**71c**][Br]. Enantiomeric excesses (%).[a]

Alkene	[**70c**][Br]	[**52c**][Br]	[**71c**][Br]	Configuration
S1	57	85	92	(+)-(1*R*,2*S*)
S2	67	75	83	(-)-(1*S*,2*S*)
S3	44	54	67	(-)-(1*S*,2*S*)

[a] Conditions: substrate (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 2 hours, 0 °C. Average of at least two runs. The enantiomeric excesses were determined by CSP-GC (**S2**, Chiraldex Hydrodex β-3P) or CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, λ 230 nm). The configuration indicated is that of the resulting epoxide.

Table 4-7. Epoxidation of olefins **S1**, **S2, S3** using catalysts (*R*a,*S*)-[**70b**][Br], [**52b**][Br], [**71b**][Br]. Enantiomeric excesses (%).[a]

Alkene	[**70b**][Br]	[**52b**][Br]	[**71b**][Br]	Configuration
S1	68	76	82-88 [b]	(+)-(1*R*,2*S*)
S2	63	59	72	(-)-(1*S*,2*S*)
S3	58	42	61	(-)-(1*S*,2*S*)

[a] Conditions: substrate (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2) , 2 hours, 0 °C. Average of at least two runs. The enantiomeric excesses were determined by CSP-GC (**S2**, Chiraldex Hydrodex β-3P) or CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, λ 230 nm). The configuration indicated is that of the resulting epoxide. [b] In the particular case of the epoxidation of 1-phenyl-3,4-dihydronaphthalene with salt [**71b**][Br], and contrary to the other reactions, a large deviation in the enantiomeric excess values was observed while performing multiple runs of the reactions. Rather than indicate an average, we have decided to put the range of the *ee* values observed.

Table 4-8. Epoxidation of olefins **S1**, **S2, S3** using catalysts (*R*a,*R*)-[**70d**][Br], [**52d**][Br], [**71d**][Br]. Enantiomeric excesses (%).[a]

Alkene	[**70d**][Br]	[**52d**][Br]	[**71d**][Br]	Configuration
S1	85	91	88	(+)-(1*R*,2*S*)
S2	77	69	69	(-)-(1*S*,2*S*)
S3	53	34	57	(-)-(1*S*,2*S*)

[a] Conditions: substrate (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 2 hours, 0 °C. Average of at least two runs. The enantiomeric excesses were determined by CSP-GC (**S2**, Chiraldex Hydrodex β-3P) or CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, λ 230 nm). The configuration indicated is that of the resulting epoxide.

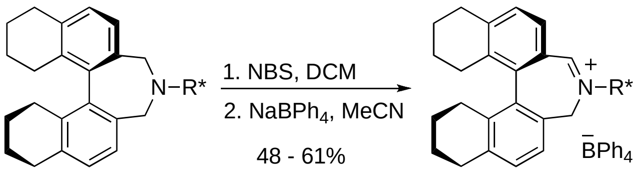
If one compares the selectivity of the diastereomeric catalysts derived from 3,3-dimethylbutyl-2-amine together – that is [**70a**][Br] with [**70c**][Br]**,** [**52a**][Br] with [**52c**][Br] and [**71a**][Br] with [**71c**][Br], some definite trends can be observed. First, the levels of stereoinduction in the (*R*a,*S*) and (*R*a,*R*) series are different. For catalysts [**70a**][Br] and [**70c**][Br] much better *ee* values were observed with (*R*a,*S*)-configurated catalyst [**70a**][Br] (Tables 4-5, 4-6). For diastereomeric series [**52a**][Br] and [**52c**][Br], [**71a**][Br] and [**71c**][Br], it is the opposite as better *ee* values were found with (*R*a,*R*)-configurated catalysts. This indicates a sensitivity of the reaction to the global stereoisomeric environment of the catalysts. However, importantly, an identical sense of induction was obtained for the epoxides in all experiments. These results indicate that the two new types of biphenyl frameworks are, like in the binaphthyl series, more influential as chiral auxiliaries than the exocyclic appendage derived from 3,3-dimethylbutyl-2-amine. In fact, the configuration of the epoxides remains the same while using catalysts with opposite absolute configuration at the chiral exocyclic appendage.

That said, divergences in the outcome can still be found for the diastereomeric catalysts and rather strong differences between the *ee* values of reactions performed with [**70a**][Br] and [**70c**][Br] were observed (e.g. for alkene **S3** the catalyst [**70a**][Br] provided epoxide formation with 60% *ee*, then catalyst [**70c**][Br] with 44% *ee*) This difference is attenuated in the reactions of catalysts [**52a**][Br] and [**52c**][Br] (for substrate **S3** the catalysts [**52a**][Br] and [**52c**][Br] gave epoxide with 46% *ee* and 54% *ee* respectively) and becomes minimal with [**71a**][Br] and [**71c**][Br] (alkene **S3**, 63% *ee* observed with catalyst [**71a**][Br] and 67% *ee* with catalyst [**71c**][Br]). These results probably indicates that the H_8-binaphthyl skeleton has a stronger stereochemical influence than the binaphthyl and 6,6'-dimethylbiphenyl structures respectively.

Now if one compares together the selectivity of the other diastereomeric catalysts derived from 1-phenylpropylamine, that is [**70b**][Br] with [**70d**][Br], [**52b**][Br] with [**52d**][Br] and [**71b**][Br] with [**71d**][Br], the same kind of observations can be made. Again the levels of stereoinduction in the (*R*a,*S*) and (*R*a,*R*) series can be different, but in this case the (*R*a,*R*)-configurated catalysts are most effective in terms of enantioselectivity than the (*R*a,*S*)-series. The configuration of the epoxides is again controlled by the axial stereogenic element of the iminium salts and it does not change with an inversion of the configuration of the exocyclic appendage.

From these studies, one can conclude that larger twist angles around the biaryl axes lead indeed to the predominance of the axially chiral stereogenic element over the exocyclic centred one; the chemistry of iminiums **70** and **71** confirming the observations made previously for the binaphthyl series **52**. Furthermore, if one assumes that the crystallographic trends observed for the amine and ammoniums species (*vide supra*), hold for iminium salts as well, then one can draw a correlation between the enantioselectivity of the process and the dihedral angle Φ of the biaryl systems. It can be clearly seen on the results of the epoxidation reactions of [**70c**][Br], [**52c**][Br] and [**71c**][Br]. Moving from the *a priori* smallest dihedral angle to the biggest, from [**70c**][Br] to [**71c**][Br] *via* [**52c**][Br], one can see an increase of the enantioselectivity for all substrates. For the other catalysts, this correlation can also be found for alkene **S1**. For olefins **S2** and **S3**, the situation is different as the two biphenyl series (**70** and **71**) are more selective than the binaphthyl one – the difference between the iminiums **70** and **71** remaining although modest. Globally, the best results in terms of enantioselectivity have been achieved with the catalysts derived from the H_8-binaphthyl skeleton.

However, although interesting, these results were obtained with a "new" untested protocol of epoxidation using *in situ* generated bromide iminium salts. Care was thus taken to compare this outcome with that of more classical isolated salts. We selected for the comparison study commercially available tetraphenylborate as lipophilic counterion, extensively and routinely used in the enantioselective epoxidation reactions catalyzed by iminium salts. The synthesis of the four derived isolated iminium salts [**71a**][BPh_4] to [**71d**][BPh_4] was realized in two steps starting from the azepines **83a – 83d** (Equation 4-2).



83a to **83d**

[**71a**][BPh_4] to [**71d**][BPh_4]

(4-2)

Treatment of tertiary amines **83a** to **83d** with NBS in dichloromethane provided a rapid and clean formation of the desired iminium salts [**71a**][Br] to [**71d**][Br] in 5 minutes. Subsequent anion exchange metathesis in acetonitrile with sodium tetraphenylborate and trituration/recrystallization in EtOH gave catalysts [**71a**][BPh_4] to [**71d**][BPh_4] in appropriate yields (48-61%) for two steps.

The epoxidation reactions were performed under the same reaction conditions and the novel salts behaved unsurprisingly as catalysts. The results are given in Tables 4-9 and 4-10.

Table 4-9. Epoxidation of olefins **S1**, **S2, S3** using catalysts [**71a**][Br], [**71a**][BPh_4], [**71c**][Br], [**71c**][BPh_4]. Enantiomeric excesses (%).[a]

Alkene	[**71a**][Br]	[**71a**][BPh_4]	[**71c**][Br]	[**71c**][BPh_4]	Configuration
S1	87	87	92	91	(+)-(1*R*,2*S*)
S2	82	80	83	81	(-)-(1*S*,2*S*)
S3	63	67	67	72	(-)-(1*S*,2*S*)

[a] Conditions: substrates (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 2 hours, 0 °C. Average of at least two runs. The enantiomeric excesses were determined by CSP-GC (**S2**, Chiraldex Hydrodex β-3P) or CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, λ 230 nm). The configuration indicated is that of the resulting epoxide.

Table 4-10. Enantioselective epoxidation of olefins **S1**, **S2, S3** using catalysts [**71b**][Br], [**71b**][BPh_4], [**71d**][Br], [**71d**][BPh_4]. Enantiomeric excesses (%).[a]

Alkene	[**71b**][Br]	[**71b**][BPh_4]	[**71d**][Br]	[**71d**][BPh_4]	Configuration
S1	82-88 [b]	88	88	94	(+)-(1*R*,2*S*)
S2	72	67	69	68	(-)-(1*S*,2*S*)
S3	61	77	57	68	(-)-(1*S*,2*S*)

[a] Conditions: substrate (0.2 mmol), 5 mol% of catalyst, 2.5 mol% 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 2 hours, 0 °C. Average of at least two runs. The enantiomeric excesses were determined by CSP-GC (**S2**, Chiraldex Hydrodex β-3P) or CSP-HPLC (**S1** and **S3**, Chiralcel OD-H, *n*-Hexane/*i*-PrOH 95:5, 0.5 mL·min^{-1}, 23 °C, λ 230 nm). The configuration indicated is that of the resulting epoxide. [b] In the particular case of the epoxidation of 1-phenyl-3,4-dihydronaphthalene with salt [**71b**][Br], and contrary to the other reactions, a large deviation in the enantiomeric excess values was observed while performing multiple runs of the reactions. Rather than indicate an average, we have decided to put the range of the *ee* values observed.

For catalysts [**71a**][Br] and [**71a**][BPh_4], [**71c**][Br] and [**71c**][BPh_4], little difference in the enantioselectivity of the epoxidation reaction is observed (Table 4-9). For alkenes **S1** and **S2** the *ee* values are either identical or slightly lower, while for substrate **S3** the values are always better by 4 - 5% with the isolated salt. If one compares [**71a**][BPh_4] with [**71c**][BPh_4], the trends determined for the bromides salts are perfectly applicable.

Surprisingly, for [**71b**][Br] and [**71b**][BPh_4], [**71d**][Br] and [**71d**][BPh_4], the situation is different (Table 4-10). Substantial variations in *ee* values can be noticed in all direct comparison of the bromide and BPh_4 salts. The stronger counterion effect is observed for alkene **S3**. This ionic interplay was something that had not been observed previously in our group or others in this field of epoxidation chemistry and an issue that we decided to study later (see paragraph below). Nevertheless, the global trends determined for the bromide salts remained with the tetraphenylborate counterion – just the selectivity can be better with the more lipophilic counterion (to the exception of olefin **S2**).

4.2.8 Conclusion

At this stage of our studies we have described two new classes of biaryl azepinium salts that behave as effective catalysts for the enantioselective epoxidation of prochiral olefins. We have been able to show that the origin of the predominance of the axially chiral stereogenic element is to be found in the dihedral angle values for the biaryl twist – and the external angle Φ in particular. The larger angle, the better for the asymmetric transfer. We have further used an oxidation protocol that allows a rapid assay for the enantioselective efficiency by *in situ* oxidation of tertiary amine precursors to bromide iminium salts.

4.3 Enantioselective epoxidation of olefins using 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl derived azepinium catalysts

4.3.1 Optimisation of the catalyst structure. On importance of the counterion

As just mentioned, a rather strong difference in behaviour was noticed in the reactions of salts [**71b**][Br] and [**71b**][BPh_4], [**71d**][Br] and [**71d**][BPh_4]. This led to careful analysis of all reactions performed with tetraphenylborate salts.

Analysing again the epoxidation reactions with isolated catalysts [**71a**][BPh_4] and [**71c**][BPh_4], a somewhat puzzling observation was made: for all substrates **S1**-**S3**, biphenyl was detected in reaction mixtures. This observation was completely astonishing at first view. We thus decided to characterize this effect better and looked more closely at what was happening with tetraphenylborate salts in order to explain the biphenyl formation during the epoxidation process. First, a study of the enantioselectivity of the epoxidation of 1-phenylcyclohexene as a function of catalyst loading was performed using salt [**71a**][BPh_4]. The results are reported in Table 4-11. The stereoinduction is greatly affected by the amount of active salt in the medium and, to a bit of our surprise, the larger the amount of catalyst the lower the selectivity.

This unusual observation was difficult to rationalize at first glance. One possible explanation was, at low amount of catalyst, the occurrence of a degradation generating a more selective catalyst *in situ*. Care was then taken to fully characterize the result of these reactions and those performed with the largest amount of catalysts in particular.

Table 4-11. Epoxidation of 1-phenylcyclohexene using catalyst [**71a**][BPh_4]. [a]

Catalyst, mol%	*ee* [b], %	Conv.[c], %
1.0	90	80
2.5	90	90
5	80	> 99
10	66	> 99

[a] Conditions: 1-phenylcyclohexene (0.2 mmol), naphthalene (0.2 mmol), catalyst (*x* mol%), 2.5 mol% of 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 2 hours, 0 °C. Average of at least two runs. [b] Determined by CSP-GC (Chiraldex Hydrodex β-3P). [c] Determined by GC analysis of crude reaction mixture using naphthalene as an internal standard.

Relatively high amounts of biphenyl could be identified in the GC-MS analyses of the reaction mixtures, a compound that was furthermore isolated in pure form from the crudes. Different hypotheses could then account for this observation as biphenyl might (i) be an impurity brought in solution along with the starting alkene, (ii) result from degradation and aromatization under the reaction conditions of *in-situ* formed 1-phenylcyclohexene oxide or (iii) be derived from tetraphenylborate anion by an oxidative decomposition pathway.[23]

To distinguish these hypotheses, a few tests were performed. First of all, the purity of 1-phenylcyclohexene (commercial, 98 %) was checked by GC-MS and no trace of biphenyl could be found. Then, 1-phenylcyclohexene was submitted to the epoxidation procedure with bromide salts as catalysts (*eg* [**71a**][Br]); no biphenyl was observed rendering unlikely the existence of a pathway from 1-phenylcyclohexene oxide to biphenyl. Finally, [**71a**][BPh_4] (5 mol%) was treated under the reaction conditions in the absence of alkene and, after two hours of vigorous stirring at 0 °C and work up of the biphasic mixture, an ^{1}H-NMR analysis was performed which revealed a complete disappearance of the tetraphenylborate species and only signals of biphenyl were found.

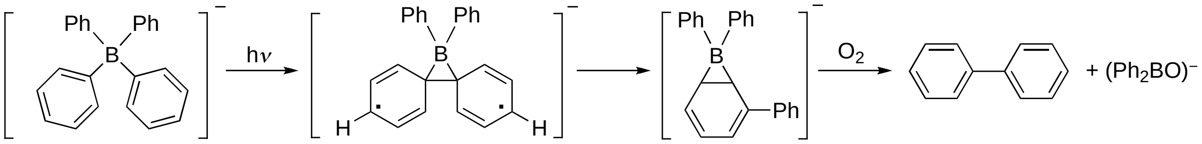
Clearly, under the oxidative reaction conditions,[23] the lipophilic counterion undergoes a decomposition to form biphenyl as by-product. This process is of particular importance as it modifies profoundly the solubility and/or the partition ability of the [iminium / oxaziridinium] species in the two-layer situation of the reaction conditions. The epoxidation, which is most probably occurring in the organic layer exclusively when the lipophilic anion is intact,[24] might now occur at the interface of the heterogeneous solvent mixture or even in the aqueous phase upon degradation. This explanation perfectly fits with our observation that the amount of biphenyl, formed in this process, was found to be dependant from the amount of the used catalyst: the higher is the catalyst loading the more quantity of biphenyl was observed in reaction mixtures.

In the literature we have found that the biphenyl formation from tetraphenylborate moiety is in fact a known and well studied process. It has been shown for a long time that tetraarylborates and tetraphenylborate in particular are easily oxidized compounds. In 1959, Geske reported the electrochemical oxidation of tetraphenylborate gives biphenyl in good yield.[25] He also proved, based on labeling studies, that biphenyl formation is an intramolecular process: the two phenyl group of the biphenyl are formed by electrochemical oxidation come form the same borate and the bond linking the benzene rings is formed between the carbons that had been bound to boron.[26] A few years later, Williams and his co-workers studied the photolysis of tetraarylborates and found that irradiation of tetraphenylborate in protic solvents containing dissolved oxygen led to biphenyl and diphenylborinic acid.[27, 28] Very similar results were obtained by Schuster and Wilkey performing photolysis of tetraphenylborate in oxygen-saturated acetonitrile or THF solutions.[23] (Equation 4-3).

$$M^+(BPh_4)^- \xrightarrow[\text{MeCN, } O_2]{h\nu} \text{Ph-Ph} + (Ph_2BO)^- M^+ \qquad (4\text{-}3)$$

$$M^+ = \text{Na, K, } R_4N^+$$

This process is quite general and the results do not depend on the identity of M^+. Based on extensive studies, a radical mechanism of this transformation was again proposed (Scheme 4-7).

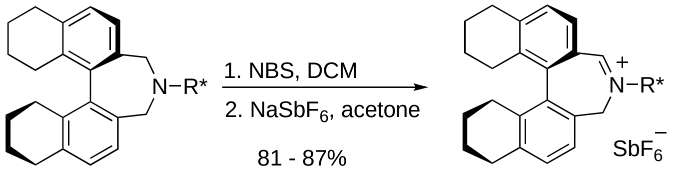


Scheme 4-7. Schuster and Wilkey proposed mechanism of biphenyl formation.

Probably, in our reaction conditions using Oxone as a strong oxidant, the same or very similar transformation takes place.

In view of these results, a search for a stable and reliable alternative to BPh_4 was started and that of a “light” counterion rather than a “heavy” TRISPHAT.

Hexafluorophosphate was first evaluated as an alternative. The PF_6 iminium salts of cations **71a** and **71c** were easily prepared in pure form by ion exchange metathesis from the corresponding bromide salts (~70% yield for two steps). However, to our big surprise, these salts were stable only in the solid state. ^{19}F and ^{31}P-NMR spectroscopic analysis of the salts revealed a hydrolysis of the counterion already in CD_2Cl_2 only; the signals of the cations remaining however unchanged in ^1H and ^{13}C-NMR spectroscopy. Hexafluoroantimonate, which was studied next, was found to be suitable for the catalysis work (*vide infra*). The synthesis of catalysts [**71a**][SbF_6] and [**71c**][SbF_6] was performed in two steps following a general and highly-reproducible procedure (Equation 4-4). Treatment of azepines **83a** and **83c** with *N*-bromosuccinimide (NBS) in dichloromethane provided a fast and clean formation of the desired iminium bromide salts in 5 minutes (*vide supra*). Subsequent anion metathesis in acetone with sodium hexafluoroantimonate (5 min) and trituration in EtOH provided the pure catalysts (*R*a,*S*)-[**71a**][SbF_6] and (*R*a,*R*)-[**71c**][SbF_6] in good yield for two steps (81-87%).



83a to **83d**

[**71a**][SbF_6], [**71c**][SbF_6]

(4-4)

The first task at hand was the verification that different loading of salts [**71a**][SbF_6] and [**71c**][SbF_6] would afford non-racemic epoxides with identical levels of enantiomeric excesses. To test this hypothesis, 1-phenylcyclohexene was used again as substrate along with the following reaction conditions that are suitable for even very sensitive epoxides (Oxone®/$NaHCO_3$/18-Crown-6/CH_2Cl_2/H_2O/0 °C). The results are summarized in Table 4-12.

Table 4-12. Asymmetric epoxidation of 1-phenylcyclohexene with SbF_6 salts. Catalyst loading influence.[a]

Catalyst, mol%	[**71a**][SbF_6]		[**71c**][SbF_6]	
	ee [b], %	Conv.[c], %	*ee* [b], %	Conv.[c], %
2.5	89	97	92	60
5.0	89	> 99	92	66
10	89	> 99	92	68

[a] Conditions: 1-phenylcyclohexene (0.2 mmol), naphthalene (0.2 mmol), 2.5 mol% of 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 /H_2O (3:2), 2h, 0 °C. Average of at least two runs. [b] Determined by CSP-GC (Chiraldex Hydrodex β-3P). In all cases, the absolute configuration of 1-phenylcyclohexene oxide is (–)-(1*S*,2*S*). [c] Determined by GC analysis of crude reaction mixture using naphthalene as an internal standard.

The reactions were performed with 2.5, 5.0 and 10 mol% of [**71a**][SbF_6] and [**71c**][SbF_6] to afford (–)-(1*S*,2*S*)-1-phenylcyclohexene oxide with, as desired, invariable 89 and 92% *ee* respectively. Clearly, catalyst [**71a**][SbF_6] is more reactive than [**71c**][SbF_6] and it can be used in the epoxidation reaction in amounts as low as 2.5 mol% without significant lost of activity (97% conversion in 2h). Under the same conditions, only a 60% conversion to the desired epoxide is reached with [**71c**][SbF_6] albeit with a better enantiomeric excess of 92% that remains constant with larger amount of **71c**. While [**71a**][SbF_6] is the most reactive, [**71c**][SbF_6] is the most selective. It was also noted that the epoxidation reaction was very clean and no traces of ring opening by-products were detected by GC-MS analysis of reaction mixtures. The pure epoxide was obtained by simple filtration through a silica gel plug necessarily buffered though with triethylamine.

Finally with a range of isolated iminium salts in hands in order to show the importance of counterion associated to cationic iminium species and to check the role of the anionic part on the global stability of catalyst, few test experiments were performed. The results are summarised in Table 4-13.

Table 4-13. Asymmetric epoxidation of 1-phenylcyclohexene with [**71a**][X] salts. Catalysts stability as a function of counterion.

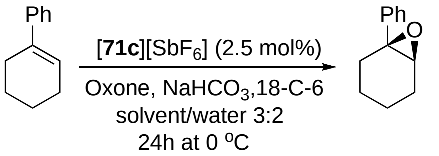
Entry	[**71a**][BPh_4]		[**71a**][PF_6]		[**71a**][SbF_6]	
	ee [c], %	Conv.[d], %	*ee* [c], %	Conv.[d], %	*ee* [c], %	Conv.[d], %
1 [a]	80	> 99	88	> 99	89	> 99
2 [b]	–	0	88	94	89	> 99

[a] Conditions: catalyst (5 mol%), 1-phenylcyclohexene (0.2 mmol), naphthalene (0.2 mmol), 2.5 mol% of 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 /H_2O (1.2 mL/0.8 mL), 2h, 0 °C. One pot addition of all reagents. Average of two runs. [b] Conditions: catalyst (5 mol%), 2.5 mol% of 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 /H_2O (0.7 mL/0.8 mL), 30 min, 0 °C. Then addition of 1-phenylcyclohexene (0.2 mmol) and naphthalene (0.2 mmol) in CH_2Cl_2 (0.5 mL) and stirring for 2h at 0 °C. Average of two runs. [c] Determined by CSP-GC (Chiraldex Hydrodex β-3P). In all cases, the absolute configuration of 1-phenylcyclohexene oxide is (–)-(1*S*,2*S*). [d] Determined by GC analysis of crude reaction mixture using naphthalene as an internal standard.

First [**71a**][BPh_4] (5 mol%) was treated under conditions similar to the reaction in the absence of alkene, and after two hours of vigorous stirring at 0 ^{o}C the 1-phenylcyclohexene was added and the resulting mixture was stirred for another two hours at 0 ^{o}C. To our surprise no 1-phenylcyclohexene oxide formation was observed in GC, GC-MS analyses of crude reaction mixtures. These results strongly suggested that in the first two hours of our experiment the catalyst is completely decomposed and the species, which we previously observed in ^{1}H-NMR of such reaction mixtures, are not catalytically active. Care was taken to see the relative rate of the degradation process. For doing this, the first part of the experiment was decreased: instead of stirring the catalyst without alkene for two hours we performed the stirring for one hour and a half, one hour, and finally for thirty minutes. Even after thirty minutes of stirring the catalyst fully decomposed and lost its catalytical properties (Table 13, entry 2). Exactly the same experiments were performed with catalyst [**71a**][PF_6] and [**71a**][SbF_6]. One can clearly see, in the case of PF_6 catalyst, no lost in enantioselectivity and a slight loss in reactivity (94% conv. *vs.* >99% conv.) as compared to a classical experiment realized with all reagents mixed together. The catalyst [**71a**][SbF_6] showed the best stability properties. No loss both in enantioselectivity and reactivity was found after a pre-stirring of 30 min. before adding the substrate. In view of these observations, the negative counterion of the iminium salts has to be chosen wisely to provide robust catalysts. While the hexafluoroantimonate anion [SbF_6^-] is optimal for reliable results, one has to be careful of using tetraphenylborate [BPh_4^-] salts.

Finally, we decided to use for our further studies the most selective salt [**71c**][SbF_6] (92% *ee vs.* 89% *ee* with [**71a**][SbF_6] using 1-phenylcyclohexene as substrate) as its reactivity is addressable by increasing either reaction time or catalyst loading.

Care was also taken to check other solvents that dichloromethane for the enantioselective epoxidation reaction (Equation 4-5). The results are summarized in Table 4-14.



(4-5)

Table 4-14. Enantioselective epoxidation of 1-phenylcyclohexene with [**71c**][SbF_6] as catalyst. Solvent effect. [a]

solvent	*ee* [b], %	Conv.[c], %
CH_2Cl_2	92	> 99
$ClCH_2CH_2Cl$	90	> 99
MeCN	86	> 99

[a] Conditions: 1-phenylcyclohexene (0.2 mmol), catalyst (2.5 mol%), 2.5 mol% of 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, solvent /H_2O (3:2), 2h, 0 °C. Average of at least two runs. [b] Determined by CSP-GC (Chiraldex Hydrodex β-3P). In all cases, the absolute configuration of 1-phenylcyclohexene oxide is (–)-(1*S*,2*S*). [c] Determined by GC, GC-MS analysis of crude reaction mixture.

Both 1,2-dichloroethane and acetonitrile can be successfully used in such process.[6] In all cases only 2.5 mol% of [**71c**][SbF_6] is required to achieve full and clean conversion

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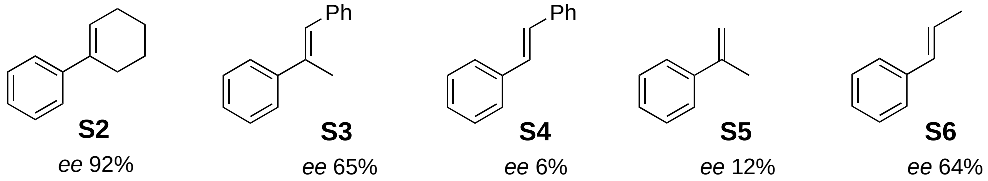
[6] These solvents were selected for the studies due to the good solubility of SbF_6 iminium salts in these solvents. Our catalysts are not soluble in $CHCl_3$ or CCl_4. In general we observed that [**71a**][SbF_6] is more soluble in organic solvents than its diastereomeric [**71c**][SbF_6] salt.

of 1-phenylcyclohexene to 1-phenylcyclohexene oxide, however the best enantioselectivity was observed using dichloromethane as a solvent.

4.3.2 Asymmetric epoxidation of unfunctionalized alkenes using [71c][SbF$_6$] salt as catalyst

4.3.2.1 Initial substrate screen

The epoxidation was then performed with a few simple commercially-available substrates (Figure 4-12) looking for leads that would indicate which olefins are best for this asymmetric catalyzed process.



S2 *ee* 92%
S3 *ee* 65%
S4 *ee* 6%
S5 *ee* 12%
S6 *ee* 64%

Figure 4-12. Tested commercial alkenes.

Whereas the epoxidation was highly disappointing with *trans*-stilbene **S4** and α-methylstyrene **S5** (6% and 12% *ee* respectively), much higher selectivity was obtained with *trans*-β-methylstyrene (**S6**, 64% *ee*) and, as already mentioned, 1-phenylcyclohexene (**S2**, 92% *ee*). In view of these results and considering that one aromatic group is beneficial (as in **S2**), we reasoned that the second aromatic group on **S4** was too large for the chiral pocket of the catalyst and that a methyl or a methylene group at the same *trans*-β-position was however favorable; these smaller substituents being actually needed for high selectivity (in comparison with **S5**). Looking at the larger enantiomeric excess of **S2** over **S6**, we reasoned that the presence of a third α-substituent next to aromatic group was also beneficial. This was tested with *trans*-α-methylstilbene **S3** which afforded its epoxide with a 65% *ee* value, quite better than that of **S4** (6% *ee*); the moderate *ee* value being the result of antagonistic effects of the favorable α-Me and unfavorable β-phenyl substituents.

All considered, any alkene of type **89** corresponding to the general formula displayed in Figure 4-13 should lead to high enantiomeric excesses in the enantioselective epoxidation catalyzed by salt [**71c**][SbF$_6$]; the size of the α-substituent compatible with the process remaining to be determined in the course of the study.

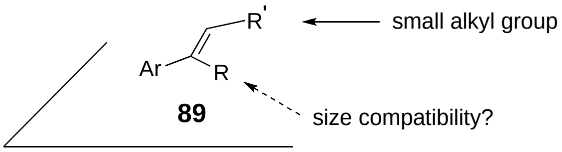
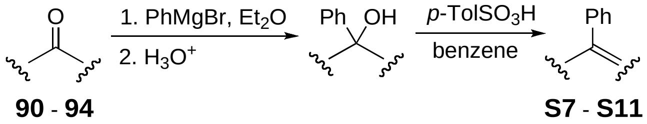


Figure 4-13. Proposed model type of alkenes giving epoxides with high enantiomeric excesses.

4.3.2.2 Extended substrate screen

4.3.2.2.1 Synthesis of trisubstituted alkenes of type 89

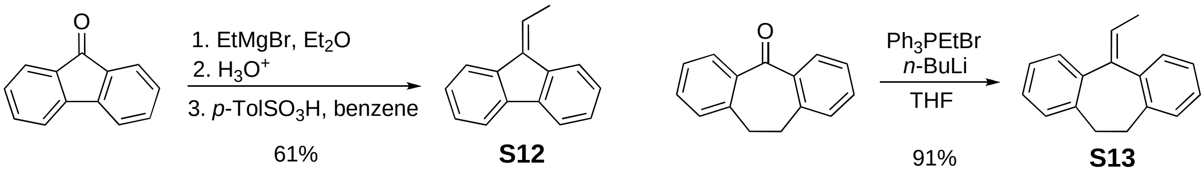
To test this hypothesis, a range of substrates was prepared. The synthesis of alkenes **S7** to **S11** was performed in two steps starting from commercially available ketones (Scheme 4-8).



Scheme 4-8. Synthesis of alkenes **S7** to **S11**.

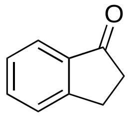
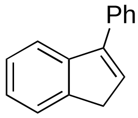
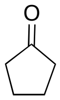
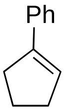
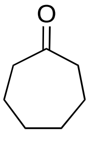
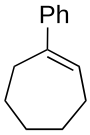
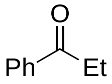
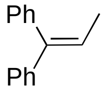
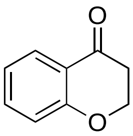
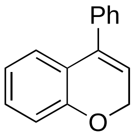
Reactions of phenylmagnesium bromide with ketones **90-94** in diethyl ether at 0 ^{o}C proceeded smoothly and provided clean formation of the corresponding tertiary alcohols which were used in the next step without further purification. Subsequent dehydratation with *p*-toluenesulfonic acid gave the desired alkenes, which were isolated in pure form by simple vacuum distillation (Table 4-15).

Following a similar procedure 9-Ethylidenefluorene (**S12**) was prepared starting from 9-fluorenone in 61% yield.[29] 5-Ethylidene-l0,11-dihydro-5H-dibenzo[*a*,*d*]cycloheptene (**S13**) was however synthesized from dibenzosuberone[30] by Wittig reaction in 91% yield (Scheme 4-9).

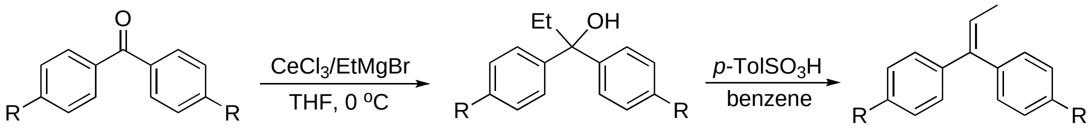


Scheme 4-9. Synthesis of olefins **S12** and **S13**.

Table 4-15. Synthesis of trisubstituted alkenes **S8** to **S11**.

Starting ketone		Alkene		Isolated yield, %
	**90**		**S7**	67
	**91**		**S8**	75
	**92**		**S9**	82
	**93**		**S10**	77
	**94**		**S11**	82

In order to check the possible influence of electronic effects on epoxidation process, a range of trisubstituted alkenes derived from commercial benzophenones were prepared containing electron rich (**S14** and **S15**) and electron withdrawing (**S16** and **S17**) groups (Scheme 4-10, Table 4-16).



95 to **98** **99** to **102** **S14** to **S17**

Scheme 4-10. Synthesis of alkenes **S15** to **S18**.

It is known that addition of *Grignard* and alkyllithium reagents to ketones and benzophenones in particular give the desired adducts of nucleophilic addition along with competitive reduction products due to the β-hydride transfer of alkyl groups. Recently, the addition of stoichiometric or an excess amount of $CeCl_3$,[31-33] LiCl,[34-36] $LiClO_4$,[37] $FeCl_2$,[38, 39] and $LnCl_3 \cdot 2LiCl$[40] with *Grignard* reagents or using catalytic amount of $ZnCl_2$[41] have afforded smooth alkylations and minimum side products formation.

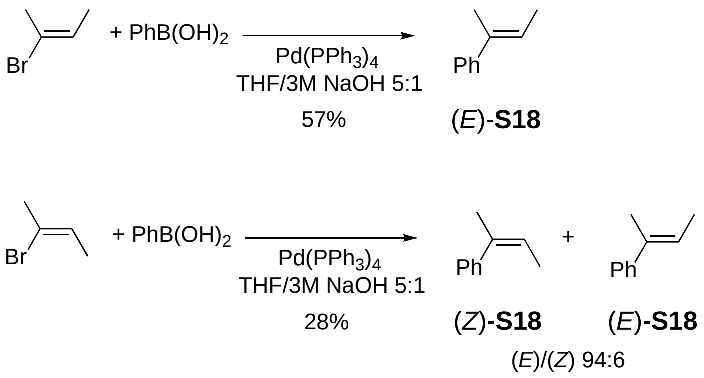
Table 4-16. Synthesis of tertiary benzylic alcohols **99** – **102** and trisubstituted aryl alkenes **S14** – **S17**

R	Substituted benzophenone	Tertiary alcohol	Yield, %	Alkene	Yield, %
-Me	**95**	**99**	96	**S14**	89
-OMe	**96**	**100**	89	**S15**	99
-F	**97**	**101**	78	**S16**	98
-Cl	**98**	**102**	45	**S17**	96

Anhydrous $CeCl_3$ prepared by Dimitrov's method[42] was chosen for the synthesis of alkenes **S14** to **S17** since cerium (III) chloride is known to be one of the best additive for activation of ketones in reactions with nucleophiles.

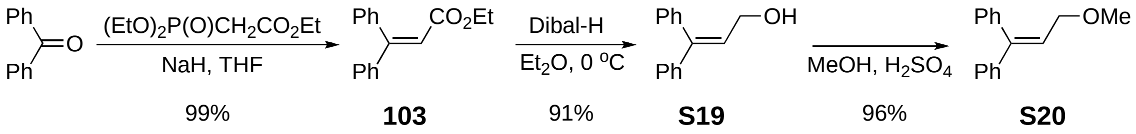
In case of electron rich benzophenones (**95** and **96**) the starting carbonyl compound was activated towards nucleophilic addition of ethylmagnesium bromide by precomplexation with stoichiometric amount of $CeCl_3$ in THF for 1h. As expected, reaction of Grignard reagent with such Lewis acid activated complexes gave fast (30 min at 0 ^{o}C) and clean formation of the desire tertiary alcohols (**99** and **100**) in excellent yields. In case of benzophenones containing electron-withdrawing groups (**97**, **98**) the nucleophilicity of EtMgBr was decreased by its reaction with $CeCl_3$ in THF. Addition of ketone to this mixture provided good (78% for **101**) and decent (45% for **102**) yields of alkylated products. Finally, dehydratation of tertiary alcohols **99** – **102** gave the corresponding trisubstituted aryl alkenes **S14** to **S17**.

Taking in consideration the importance of the double bond configuration in almost all known asymmetric epoxidation reactions, diastereomeric (*E*) and (*Z*)-1-Methyl-1-phenylpropenes ((*E*)-**S18** and (*Z*)-**S18**) were synthesised starting from commercial vinyl bromides and phenylboronic acid (Scheme 4-11).[43] Reaction of (*E*)-1-bromo-1-methylpropene with phenylboronic acid provided clean formation of the desire (*E*)-**S18** olefin in 57% yield, whereas Suzuki reaction starting form (*Z*)-1-bromo-1-methylpropene gave poor yield of (*Z*)-**S18** and only in 94% purity. Around 6% of (*E*)-**S18** were detected in GC-MS analysis of the product. All attempts to get isomerically pure (*Z*)-**S18** failed even using semi-preparative GC (in collaboration with Firmenich) due to extreme volatility of these olefins.



Scheme 4-11. Synthesis of alkenes (*E*)-**S18** and (*Z*)-**S18**.

Finally, 3,3-diphenylprop-2-en-1-ol **S19** and its methyl ether **S20** were prepared in two and three steps respectively (Scheme 4-12). Horner-Wadsworth-Emmons reaction of benzophenone with triethylphosphonoacetate in THF at reflux gave the desire α,β-unsaturated ester **103** in almost quantitative yield.[44] Selective 1,2-reduction of **103** with Dibal-H at 0 °C provided clean formation of allylic alcohol **S19** in 91% yield[45] which was treated with methanol in the presence of catalytic amount of concentrated sulfuric acid to obtain **S20** in nearly perfect yield (96%).



Scheme 4-12. Synthesis of allylic alcohol **S19** and ether **S20**.

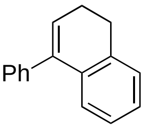
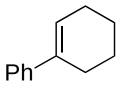
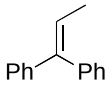
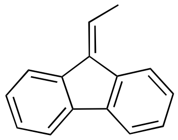
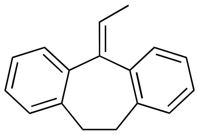
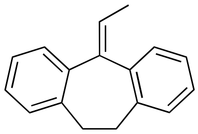
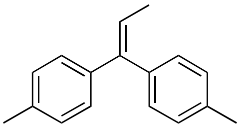
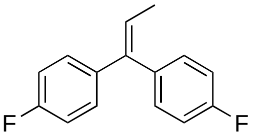
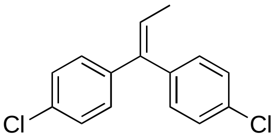
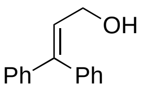
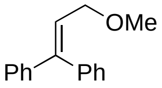
4.3.2.2.1 Enantioselective epoxidation of alkenes of type 89

Having prepared all required substrates, their asymmetric epoxidation using [**71c**][SbF_6] as catalyst was studied. The results are reported in Tables 4-17, 4-18 and 4-19.

It should be first mentioned that for all the alkenes, experiments with different catalyst loading (mol%) led, as for 1-phenylcyclohexene, to constant levels of asymmetric induction.

For **S2**, full conversion to the desired epoxide was obtained after 24h at 0 °C with just 2.5 mol% of [**71c**][SbF_6]. 1-Phenyl-3,4-dihydronaphthalene **S1**, another classical substrate, was very reactive as well. The resulting epoxide was isolated in 83% yield and 91% *ee* which can be enantioenriched (98% *ee*) by single recrystallization from *n*-hexane. An unexpected observation was made during the study of this alkene: if, at the

Table 4-17. Asymmetric epoxidation of various alkenes mediated by catalyst [**71c**][SbF_6].[a]

Substrate		Catalyst, (mol%)	Time, h	Yield [d] (conversion, %)	*ee*, %	Configuration [i]
	**S1**	2.5	24	83 (> 97 [c])	91 [f] (98 [j])	(+)-(1*R*,2*S*)
		2.5	24 [k]	(> 97 [c])	97 [f] (> 99 [j])	(+)-(1*R*,2*S*)
		2.5	72	97 (> 97 [c])	97 [f] (> 99 [j])	(+)-(1*R*,2*S*)
	**S2**	2.5	24	85 (> 99 [b])	92 [e]	(–)-(1*S*,2*S*)
	**S10**	5	48	95 (> 99 [b])	90 [g]	(–)-(*S*)
	**S12**	10	24	94 (> 99 [b])	90 [f]	(–)-(*S*)
	**S13**	20	91	67 (75 [b])	98 [f]	(+)
	**S13**	10 [h]	66 [h]	85 [h] (> 99 [h])	93 [h]	(+)
	**S14**	5	24	67 (> 99 [b])	94 [f]	(–)
	**S16**	10	43	87 (> 99 [b])	91 [f]	(–)
	**S17**	10	47	84 (> 99 [b])	91 [f]	(–)
	**S19**	20	48	80 (> 97 [c])	88 [f]	(–)-(*S*)
	**S20**	20	24	76 (93 [b])	87 [f]	(–)

[a] Conditions: substrate (0.2 mmol), catalyst (*x* mol%), 2.5 mol% of 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 0 °C. [b] Determined by GC-MS (HP-5MS) analysis of crude reaction mixture. [c] Determined by ^1H NMR analysis of crude reaction mixture (400 MHz). [d] Isolated yields of pure epoxides. [e] Determined by CSP-GC (Chiraldex Hydrodex β-3P). [f] Determined by CSP-HPLC (see experimental part). [g] Determined by ^1H NMR spectroscopy in the presence of (+)-Eu(hfc)$_3$. [h] Results obtained with catalyst [**71a**][SbF_6]. [i] The absolute configuration of major enantiomers was determined by comparison of optical rotation with that reported in the literature. [j] After single recrystallization from *n*-hexane. [k] After 24 h of vigorous stirring (full conversion) the reaction mixture was kept without stirring for 15 h and then work up was performed with subsequent purification of the epoxide.

end of the reaction, the crude mixture is kept overnight (15h) without any stirring than, after work up, the 1-phenyl-3,4-dihydronaphthylene oxide is isolated in 97% *ee*. Moreover, if the reaction time is increased from 24 h to 72 h, the enantiomeric excess of the resulting epoxide increases again from 91% *ee* to 97% *ee* as well! So far, we do not have reasonable explanation of this phenomena. It might be possible that a crystallization of the product occurs out of the reaction mixture when a longer reaction time is provided which would lead to epoxide with higher enantiomeric excess. Alternative explanation is a very selective background decomposition of one enantiomer (in this case (1*S*,2*R*)).

Similar results to **S1** and **S2** were obtained with 1,1-diphenylprop-1-ene **S10** (90% *ee*); the system being however slightly less reactive. Interestingly, moving from this substrate to the analogous allylic alcohol (**S19**, 88% *ee*) and 1,1-diphenyl-3-methoxypropene (**S20**, 87% *ee*) only very small decreases in enantioselectivities were measured. The reactivity was however much lower as 5 mol% and 20 mol% of catalyst [**71c**][SbF_6] were required to achieve full conversion with **S10** and **S19** respectively under the same reaction time.

This difference in reactivity may be explained by the electron withdrawing effect of the hydroxyl moiety that renders the double bound of allylic alcohol less electrophilic and also possibly by a less favorable partition of the olefin in the biphasic CH_2Cl_2 / water layers. The 1^{st} hypothesis seems to be correct as allylic alcohol **S19** and its methyl ether **S20** have quite similar reactivity.

Then, a range of substrates structurally analogous to **S10** were studied bearing either electron withdrawing (F, Cl: **S16** and **S17** respectively) or electron donating (Me, OMe: **S14** and **S15** respectively) groups at the *para*-positions. In case of **S16** and **S17**, essentially the same level of asymmetric induction was observed than for **S10** (*ee* 91% *vs.* 90% *ee),* whereas electronically-rich alkene **S14** led to an increase in the enantiomeric excess value (94% *ee*). If only a moderate impact was seen on the selectivity, it was not the case on the reactivity. While only 5 mol% of catalyst was required to achieve full conversion after 48 h at 0 °C with **S10**, its electron rich analogue **S14** reacted in half the time for the same catalyst loading. Electron poor derivatives **S16** and **S17** required however quite more of the catalyst as full conversion was observed only after 2 days with 10 mol% of [**71c**][SbF_6].

In the case of very electron rich alkene **S15** the reactivity was even better then for **S14**; just 2.5 mol% of catalyst being needed to achieve full conversion.

Unfortunately the resulting epoxide was very unstable and all our attempts for its isolation failed. The same unlucky results were obtained with epoxides derived from olefins **S7** and **S11**. Both substrates were very reactive, but again their corresponding epoxides are very unstable. Due to this fact, the enantiomeric excesses in these epoxidation reactions were not determined.

We then turned our attention to **S12** and **S13**, cyclic analogues of **S10** derived from 9*H*-fluoren-9-one and dibenzosuberone respectively. Whereas all carbons are virtually coplanar in **S12**[29], it is not the case for **S13**. The central cycloheptadiene ring of **S13** adopts a bent conformation intermediate between boat and chair forms and the aromatic groups adjacent to the double bond are twisted by 45 and 65° out of the plane of the alkene.[46-48] Despite this very large difference, both **S12** and **S13** afforded the corresponding epoxides in high to very high enantiomeric purity (90% and 98% *ee* respectively). The reaction with **S13** was however much slower than others as, with 20 mol% of catalyst and 4 days, the isolated epoxide was obtained in only 67% yield (75% conversion).[7] In view of this result, **S13** was treated with the more active catalyst [**71a**][SbF_6]. As expected, the reaction was faster and only required 10 mol% of iminium salt to yield the epoxide in 85% yield and still a decent 93% *ee* after ca. 3 days.

The impact of the olefin geometry was also tested using the *E* and *Z* geometrical isomers of 1-methyl-1-phenylpropene **S18** (Table 4-18). If the reaction could be performed with an essentially pure *E* isomer (>99%), that of the *Z* isomer was conducted with a sample only 95% pure in the *cis* form. In the first case, (*E*)-**S18** was epoxidized using just 2.5 mol% of catalyst [**71c**][SbF_6] in 48 h and 90% *ee*, whereas (*Z*)-**S18** afforded its epoxide in only 76 % *ee*. Moreover, the *Z* isomer was less reactive; 5 mol% of catalyst being required to achieve full conversion after 48 h.

Finally, after these largely successful examples, two other 1-phenyl-cycloalkenes, namely the 5- and 7-membered ring **S8** and **S9**, were tested in epoxidation reaction (Table 4-19). Only 2.5 mol% of [**71c**][SbF_6] was required to achieve full and clean conversion of olefins to the corresponding epoxides that were isolated in good yields (85-92%) albeit lower enantiomeric excesses (72 and 83% *ee* respectively). The results are compared to that of alkene **S2.**

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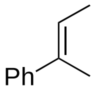
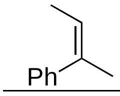
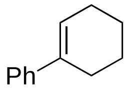
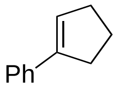
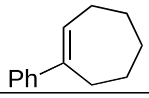
[7] The slower kinetics are possibly the result of the increased hindrance around the double bond generated by the twisted phenyl groups.

Table 4-18. Effect of double bond geometry on asymmetric epoxidation of **S18** with catalyst [**71c**][SbF_6].[a]

Substrate		Catalyst, (mol%)	Time, h	Yield[c]) (conversion,[b] %)	*ee*,[d] %	Configuration[e]
	(*E*)-**S18**	2.5	48	91 (> 99)	90	(−)-(1*S*,2*S*)
	(*Z*)-**S18** [f]	5	48	93[f] (> 99)	76 [f]	– [f]

[a] Conditions: substrate (0.2 mmol), catalyst (*x* mol%), 2.5 mol% of 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 24 h, 0 °C. [b] Determined by GC-MS (HP-5MS) analysis of crude reaction mixture. [c] Isolated yields. [d] Determined by CSP-GC (Chiraldex Hydrodex *β*-3P). [e] The absolute configuration of major enantiomers was determined by comparison of optical rotation with that reported in the literature. [f] A 94:6 mixture of (*Z*)-**S18** and (*E*)-**S18** was used. Due to the stereospecificity of the reaction and the occurrence of a minor diastereomeric epoxide, the optical rotation was not measured.

Table 4-19. Ring size effect on the epoxidation of few cycloalkenes with catalyst [**71c**][SbF_6]. [a]

Substrate		Yield[c]) (conversion, [b]%)	*ee*, %	Configuration [f]
	**S2**	85 (> 99)	92 [d]	(−)-(1*S*,2*S*)
	**S8**	85(> 99)	72 [e]	(−)-(1*S*,2*S*)
	**S9**	92 (> 99)	83 [d]	(−)

[a] Conditions: substrate (0.2 mmol), catalyst (2.5 mol%), 2.5 mol% of 18-C-6, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, CH_2Cl_2 / H_2O (3:2), 24 h, 0 °C. [b] Determined by GC-MS (HP-5MS) analysis of crude reaction mixture. [c] Isolated yields. [d] Determined by CSP-GC (Chiraldex Hydrodex *β*-3P). [e] Determined by CSP-HPLC (OD-H column). [f] The absolute configuration of major enantiomers was determined by comparison of optical rotation with that reported in the literature.

4.3.3 Validity of the alkene model hypothesis and absolute sense of stereoinduction

Clearly, at this stage, the alkene model type proposed earlier for double bonds that would provide high levels of enantioselectivity in reactions catalyzed by [**71c**][SbF_6] is a working model. From all alkenes in Table 4-17, the 2nd lowest *ee* value is 88% - and this corresponds to **S19** that might react differently in the biphasic catalytic system due to the presence of hydroxyl group. Slightly lower enantiomeric excess for **S20** compare to **S10** and **S19** (87% *ee vs*. 90% *ee* and 88% *ee* for **S10** and **S19** respectively) might be explained by the larger steric effects of CH_2OMe group compare to CH_2OH and Me fragments. Having at the *trans*-β-position from the aromatic group a small alkyl moiety R' of type CH_3, CH_2OH or CH_2 (cyclic) is something favorable. The group at the α-position R can be possibly quite large and even twisted out of the plane of the double bond as in **S13**.

If (*E*)-**S18** also fits the model, it is however not the case for the (*Z*) isomer. For that substrate, the β-methyl group is positioned in a quadrant usually occupied by an H-atom only and this most probably leads to an unsatisfactory interaction with the iminium catalyst and hence the lower enantioselectivity (Figure 4-14). The exact reasons why 1-phenylcyclopentene **S8** and 1-phenylcycloheptene **S9** lead to lower *ee* values remain undetermined for the moment, the different conformations of the three rings systems play possibly a role.

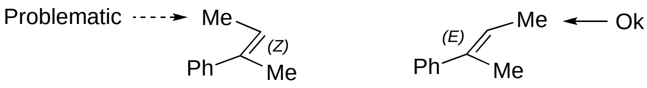


Figure 4-14. Different recognition of *E* and *Z* isomers.

Finally, the stereochemical outcome was analyzed for the reactions providing epoxides of known absolute configuration and the results are summarized in Figure 4-15. All the major enantiomers produced come from the addition of the O-atom onto the same prochiral face of the alkene; the top face in the geometrical description provided on Figure 4-15. For substrates **S1**, **S2**, **S3**, **S8**, **S10**, **S12** and (*E*)-**S18**, it is the *Si* face of the β-carbon of the alkene. For **S19**, due to the presence of the oxygen at the allylic position which changes the priority sequence in the CIP rule, it is the *Re* face. It is then highly probable that compounds **S9**, **S13**, **S14**, **S16**, **S17** and **S20** have reacted in a similar fashion.

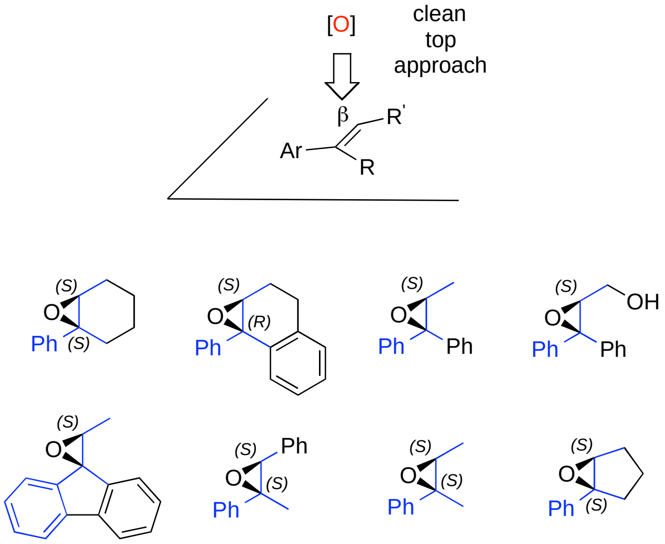


Figure 4-15. Facial selectivity.

4.3.4 Conclusion

At this stage of the studies, we have looked for an optimal chiral iminium cation / achiral anion combination and found that the counterion, associated to cationic iminium part has to be chosen rather carefully. The stability of the anion under reaction conditions is crucial to provide robust and reliable catalysts. This is something that has not been observed before in this particular field of iminium-catalyzed epoxidation chemistry. We have also created a general model to predict with certainty high selectivity in the formation of non-racemic epoxides of defined absolute configuration.

4.4 Enantioselective epoxidation of allylic alcohols using 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl derived azepinium catalysts

Encouraged by the previous results, we decided to extend the range of substrates which could be epoxidized under similar reaction conditions. Allylic alcohols were chosen for further studies. Epoxides derived from allylic alcohols are known to be useful precursors and building blocks in synthetic organic chemistry. To our knowledge, so far no examples of highly enantioselective iminium promoted epoxidation of allylic alcohols have been reported.

4.4.1 Synthesis of allylic alcohols of type 104

A range of allylic alcohols of type **104** was synthesised to be tested in asymmetric epoxidation reactions (Figure 4-16).

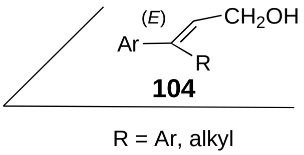
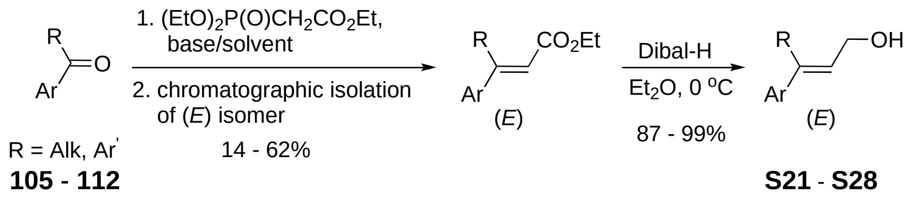


Figure 4-16.

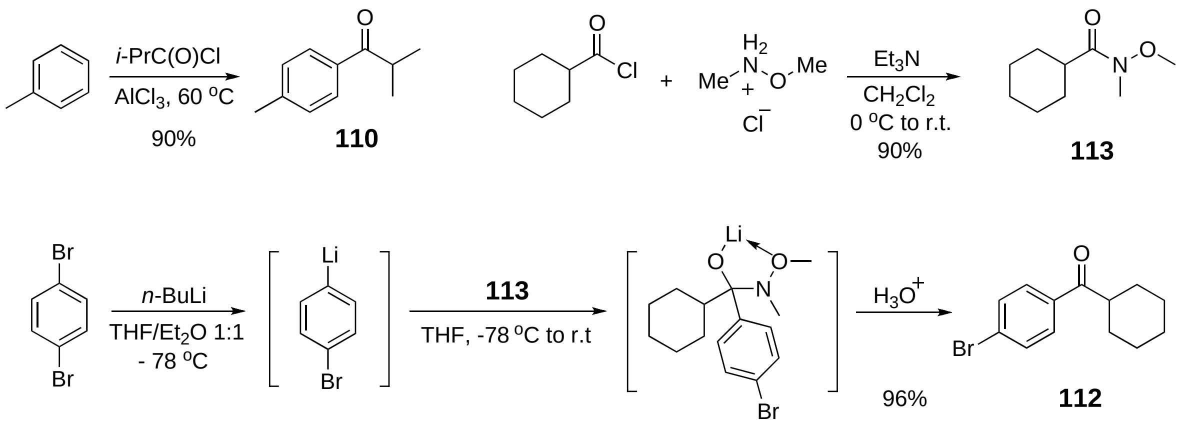
Based on our previous observations made (*vide supra*), these allylic alcohols were chosen to be trisubstituted with a (*E*) configuration for the double bond. The group R at the α-position can be aryl or alkyl and possibly very sterically demanding.

The synthesis of allylic alcohols **S21** to **S28** was performed in two steps starting from aromatic ketones (Scheme 4-13, Table 4-20).



Scheme 4-13. Synthesis of allylic alcohols **S21** to **S28**.

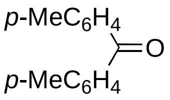
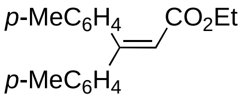
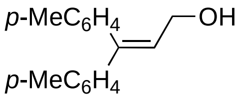
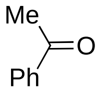
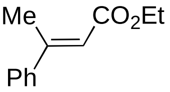
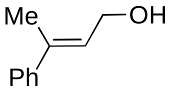
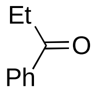
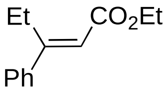
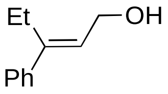
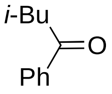
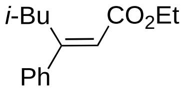
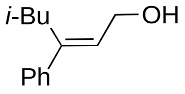
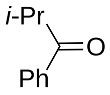
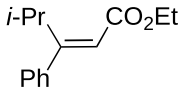
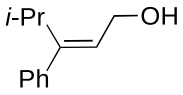
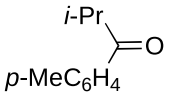
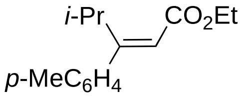
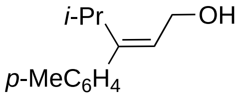
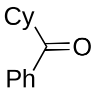
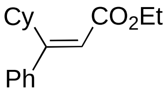
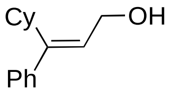
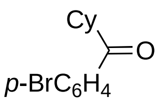
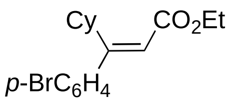
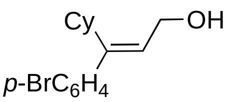
All starting carbonyl compounds were commercially available except ketones **110** and **112** which were easily prepared in the one step protocol detailed in Scheme 4-14. *Iso*propyl-*p*-tolylketone **110** was obtained by Friedel-Crafts acylation of toluene with *iso*butyryl chloride and sublimated $AlCl_3$ in good yield (90%).[49] Cyclohexyl-4-bromophenylketone was synthesized starting from 1,4-dibromobenzene. Reaction of 1,4-dibromobenzene with *n*-BuLi (1.0 equiv.) in THF/Et_2O at -78 °C provided clean monobromide lithium exchange[50]; the resulting 4-bromophenyllithium was then treated *in situ* with Weinreb amide **113**[51]. Hydrolysis of the Li complex gave the desired product **112** in 96% yield.



Scheme 4-14. Synthesis of ketones **105** and **107**.

The synthesis of the α,β-unsaturated esters, precursors to the allylic alcohols, was realized by Horner-Wadsworth-Emmons reactions of carbonyl compounds **105** to **112** with thiethylphosphonoacetate. Two sets of reaction conditions were explored to generate the resonance-stabilized carbanion: NaH/THF and *n*-BuLi/Hexane. NaH/THF system was found to be suitable for the synthesis of non or moderately hindered esters. In general, the reaction was clean but full conversion of the starting material was never achieved. The second reaction system, *n*-BuLi/hexane, was better for the preparation of bulky α,β-unsaturated esters. Full conversion of the starting ketones was obtained. The desired (*E*)-isomers were isolated in all cases in pure form after careful column chromatography on silica gel. The first eluted isomer was always the (*E*). The poor yields in products can be explained by the difficult separation of the (*E*) isomers from the starting material and the (*Z*) isomer. It should be mentioned that in all cases the (*E*) configuration of the double bond was confirmed by NOESY experiments despite the fact that most of the synthesised α,β-unsaturated esters are known compounds. Having prepared all esters, allylic alcohols **S21** to **S28** were easily synthesised by Dibal-H reduction in diethyl ether at 0 °C in good to excellent yields (87 – 99%).

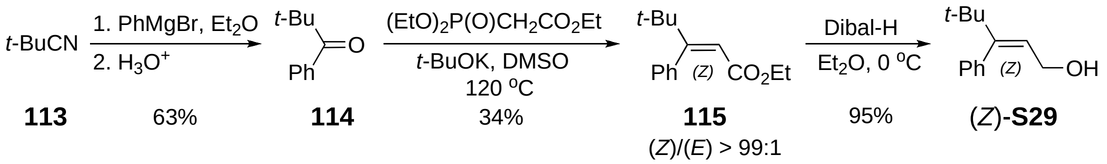
Table 4-20. Synthesis of α,β-unsaturated esters and allylic alcohols **S21** to **S28**.

Starting ketone		Base/solvent	(*E*)–α,β-unsaturated ester	*E*/*Z* ratio[a]	Yield,[b] %	Allylic alcohol		Yield, %
	**105**	*n*-BuLi/Hexane		–	62		**S21**	99
	**106**	NaH/THF		7:1	50		**S22**	91
	**107**	NaH/THF		3:2	28		**S23**	98
	**108**	*n*-BuLi/Hexane		2:3	28		**S24**	99
	**109**	NaH/THF		1:1	14		**S25**	99
	**110**	*n*-BuLi/Hexane		1:1	26		**S26**	92
	**111**	*n*-BuLi/Hexane		2:3	34		**S27**	87
	**112**	*n*-BuLi/ Hexane:THF (6:1)		2:3	28		**S28**	93

[a] Ratio of (*E*)/(*Z*) isomers of α,β-unsaturated esters was determined by GC-MS (HP-5MS) analysis of crude reaction mixture.
[b] Isolated yield of (*E*)-isomer after column chromatography separation (always first eluted fraction).

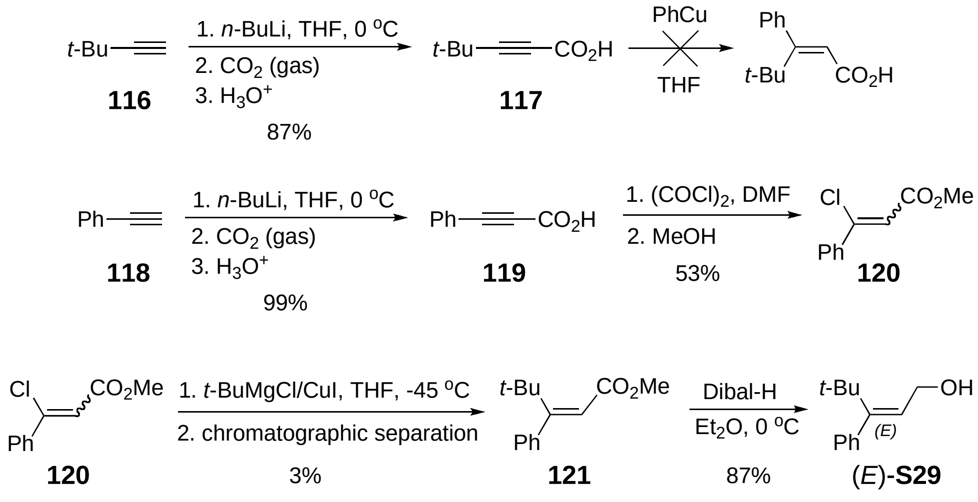
The synthesis of extremely bulky allylic alcohols (*E*)-**S29** and (*Z*)-**S29** was performed slightly differently. It is described in Schemes 4-15 and 4-16 respectively.

The (*Z*)-**S29** was made in three steps starting from *tert*-butyl cyanide. Reaction of pivalonitrile **113** with phenylmagnesium bromide and subsequent hydrolysis of the imine magnesium salt provided *tert*-butylphenyl ketone **114** in good yield.[52] Horner-Wadsworth-Emmons reaction of **114** with thiethylphosphonoacetate under previously used conditions (*n*-BuLi/hexane) gave inseparable mixture of products. Moving to another base/solvent combination (*t*-BuOK/DMSO), the desired α,β-unsaturated carbonyl compound **115** was obtained with an exclusively (*Z*) configuration of the double bond. Selective Dibal-H reduction of **115** provided pure (*Z*)-**S29** in perfect (95%) yield.



Scheme 4-15. Synthesis of (*Z*)-**S29**.

The synthesis of (*E*)-**S29** was found to be more difficult. First, 4,4-dimethyl-2-pentynoic acid **117** was obtained from commercial *tert*-butylacetylene **116**. Performing the reaction of acid **117** with freshly prepared PhCu in THF at -45 °C we expected to obtain *syn*-1,4-addition of phenylcopper to the triple bound.[53, 54] Unfortunately, the main product of this synthesis was biphenyl. Small amounts of phenol and the starting material were also detected.

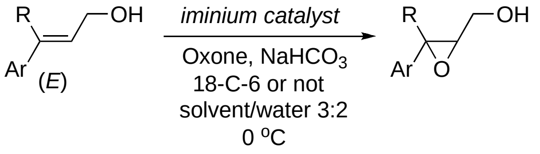


Scheme 4-16. Synthesis of (*E*)-**S29**.

Our second strategy based on exploring phenylacetylene **118** as a starting material. Reaction of **118** with *n*-BuLi (1.0 equiv) in THF at 0 °C gave a fast H-Li exchange in 30 min. The obtained lithium-phenylacetylene was treated with carbon dioxide to provide phenylacetylene carboxylic acid **119** in almost quantitative yield. Reaction of **119** with oxalyl chloride/DMF and dry methanol gave 3-chloro-α,β-unsaturated esters **120** as inseparable mixture of (*E*)/(*Z*) isomers (70/30 ratio). Reaction of **120** with *tert*-butylmagnesium chloride in the presence of CuI in THF at -45 °C gave a very complicated mixture of products. Around thirty signals were observed on the GC-MS spectrum of the crude reaction mixture. However, the peaks of the desired products were presented. After three precise column chromatography separations, the required (*E*)-isomer of **121** was isolated in 3% yield. After reduction of **121** under standard conditions (Dibal-H, Et_2O, 0 °C) the (*E*)-**S29** was obtained.

4.4.2 Enantioselective epoxidation of allylic alcohols with [71a][SbF$_6$] and [71c][SbF$_6$]

Having prepared the desired range of substrates, their asymmetric epoxidation was studied (Equation 4-6). The results are reported in Tables 4-21, 4-22, 4-23 and 4-24.



(4-6)

In Table 4-21 results are compared to that of alkene **S19** (entry 1). We have previously shown that 3,3-diphenylprop-2-en-1-ol (**S19**) can be successfully epoxidized under our biphasic dichloromethane/water conditions to the corresponding epoxide in good yield and enantioselectivity. However, the reaction was quite slow and required 20 mol% of catalyst as mentioned previously. Such slow kinetics could be assigned to (i) the electron-withdrawing effect of the hydroxyl group that renders the double bound of allylic alcohol less nucleophilic and also to (ii) a possibly less favorable partition of the allylic alcohol in the biphasic CH_2Cl_2 / water layers. To test this hypothesis, compound **S21**, structurally similar to that **S19** and containing two electron-donating methyl groups in *para*-position of phenyl rings was prepared. As expected, the increasing nucleophilicity of the double bound significantly accelerated the epoxidation process; less catalyst [**71c**][SbF_6] (10 mol% for **S21** *vs*. 20 mol% for **S19** respectively) was required to get full conversion of **S21** to the product in less amount of time (Table 4-21, entries 1 and 2). The reaction was clean as judged by GC-MS and ^{1}H NMR of crude reaction mixture, but unfortunately we were not able to isolate the epoxide in analytically pure form due to its very acid sensitive nature. In spite of this fact, the enantioselectivity of the “crude” product was determined to be 88% *ee* proving again the lack of sensitivity of the asymmetric induction of our process to electronic effects.

Then, a range of compounds containing different R alkyl groups (**S22** to **S28**) were studied (see equation 6) to test the steric effect of R on both the enantioselectivity and reactivity.

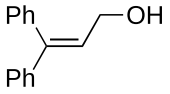
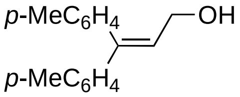
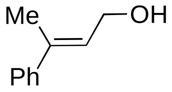
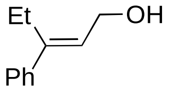
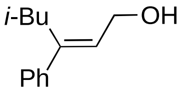
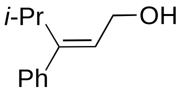
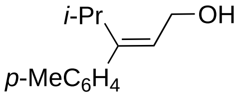
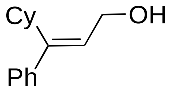
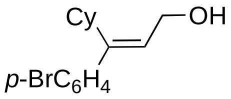
Unexpected and disappointing results were obtained with allylic alcohol **S22** containing Me as R group (entry 3 in Table 4-21). Only 10 mol% of [**71c**][SbF_6] was needed to obtain full conversion of the substrate. However, in this particular case, the reaction was very capricious; the desired epoxide was detected in the ^{1}H NMR of reaction mixture, but it was not possible to separate our product from other derivatives. We could not even determine the enantiomeric excess of the epoxide in the crude mixture.

Moving to more hindered substrates **S23** and **S24**, better results were found. For both allylic alcohols, full and clean conversion of staring materials to their corresponding epoxides was observed. The products were isolated in pure form in good yields and enantioselectivities. A higher asymmetric induction in case of **S24** compared to **S23** (90% *ee vs*. 87% *ee*) was observed which might be explained by the larger steric hindrance of isobutyl group relatively to an ethyl. Moreover, moving to more bulky substrates **S25** and **S27** the enantioselectivities were even better; 95% *ee* and 98% *ee* obtained for epoxides derived from **S25** and **S27** respectively (entries 6a and 8a). Clearly the level of asymmetric induction depends from the bulk of R group; the bulkier the group, the better the enantioselectivity.

In general the reaction was clean, no post-decomposition or racemisation of the products takes place under the reaction conditions. For example, increasing the reaction time in the epoxidation reaction of **S23** from 24 h to 48 h (full conversion is obtained in 24 h) did not yield any variation in the enantiomeric excess of the desired epoxide which was isolated in similar yield.

However, whereas enantioselectivity levels were increasing from non-hindered substrates to bulky compounds, reactivity significantly dropped. Only 80% conversion of **S25** was obtained under CH_2Cl_2/water reaction conditions in 24 h. Increasing reaction time from 24 h to 48 h or longer did not have any effect, the conversion remaining the same.

Table 4-21. Asymmetric epoxidation of various allylic alcohols mediated by catalyst [**71c**][SbF_6] (***the most selective*** catalyst).

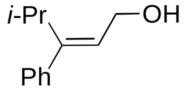
Entry	Substrate	Solvent	Catalyst, mol%	Time, h	Yield,[e] (conversion, %)	*ee*,[f] %	Configuration [h]
1	 **S19**	CH_2Cl_2 [a]	20	48	80 (> 97 [c])	88	(−)-(*S*)
2	 **S21**	CH_2Cl_2 [a]	10	24	(> 99 [d])	88	–
3	 **S22**	CH_2Cl_2 [a]	10	24	(> 99 [d])	n.d.	–
4	 **S23**	CH_2Cl_2 [a]	20	24	84 (> 99 [d])	87	(+)
5a	 **S24**	CH_2Cl_2 [a]	20	24	69 (> 99 [d])	90	(+)
5b		MeCN [b]	20	24	73 (> 99 [d])	91	(+)
6a	 **S25**	CH_2Cl_2 [a]	20	24	65 (80 [d])	95	(+)
6b		MeCN [b]	25	24	79 (98 [d])	95	(+)
7a	 **S26**	CH_2Cl_2 [a]	20	24	63 (85 [d])	95	(+)
7b		MeCN [b]	20	24	84 (> 99 [d])	95	(+)
8a	 **S27**	CH_2Cl_2 [a]	10	24	65 (75 [d])	98 (> 99 [g])	(+)-(2*S*,3*S*)
8b		MeCN [b]	30	24	80 (> 99 [d])	96 (> 99 [g])	(+)-(2*S*,3*S*)
9a	 **S28**	CH_2Cl_2 [a]	20	24	37 (75 [d])	95	(+)
9b		MeCN [b]	30	24	77 (98 [d])	94	(+)

[a] Conditions: substrate (0.2 mmol), catalyst (*x* mol%), 2.5 mol% of **18-C-6**, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **CH_2Cl_2** / H_2O (3:2), 0 °C. [b] Conditions: substrate (0.2 mmol), catalyst (*x* mol%), 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **MeCN** / H_2O (3:2), 0 °C. [c] Determined by ^1H NMR analysis of crude reaction mixture (400 MHz). [d] Determined by GC-MS (HP-5MS) analysis of crude reaction mixture. [e] Isolated yields of pure epoxides. [f] Determined by CSP-HPLC (see experimental part). [g] After single recrystallization from *n*-hexane/*i*-PrOH. [h] The absolute configuration of major enantiomers was determined by comparison of optical rotation with that reported in the literature.

Moreover, we could not increase the catalyst loading due to a limited solubility of [**71c**][SbF_6] in dichloromethane. At this stage, we decided to change the solvent from dichloromethane to acetonitrile. The results on the epoxidation of **S25** under novel conditions are presented in Table 4-22.

MeCN is a good solvent for iminium mediated epoxidation processes; both the alkenes and iminium salts usually have good solubility in it, and more importantly the epoxidation reactions are known to proceed faster in acetonitrile/water system compared to the dichloromethane/water one. As expected changing the solvent increased the reactivity. 95% and 80% conversion values were observed for the reactions using MeCN and DCM as solvents respectively (same catalyst loading, same other conditions). Finally, and importantly, we found that performing the reaction in MeCN/water system no 18-C-6 required. Exactly the same results were obtained with and without 18-C-6.

Table 4-22. Asymmetric epoxidation of 4-methyl-3-phenylprop-2-en-1-ola (**S25**) mediated by catalyst [**71c**][SbF_6].

Substrate		Solvent	Catalyst, mol%	Additive	Time, h	Conversion, [d]%	*ee*, [e] %	Optical rotation
	**S25**	CH_2Cl_2 [a]	20	18-C-6	24	80	95	(+)
		MeCN [b]	20	18-C-6	24	95	94	(+)
		MeCN [c]	20	–	24	95	94	(+)
		MeCN [c]	25	–	24	98	95	(+)

[a] Conditions: substrate (0.2 mmol), catalyst (20 mol%), 2.5 mol% of **18-C-6**, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **CH_2Cl_2** / H_2O (3:2), 0 °C. [b] Conditions: substrate (0.2 mmol), catalyst (20 mol%), 2.5 mol% of **18-C-6**, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **MeCN** / H_2O (3:2), 0 °C. [c] Conditions: substrate (0.2 mmol), catalyst (*x* mol%), **without 18-C-6**, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **MeCN** / H_2O (3:2), 0 °C. [d] Determined by GC-MS (HP-5MS) analysis of crude reaction mixture. [e] Determined by CSP-HPLC.

If under biphasic CH_2Cl_2/water conditions is necessarily needed 18-C-6 as a phase-transfer reagent, its presence in three-phasic MeCN/water system is nor required. It should be mentioned that the acetonitrile/water (3:2) system is not monophasic as one might expect but rather triphasic (Figure 4-17).

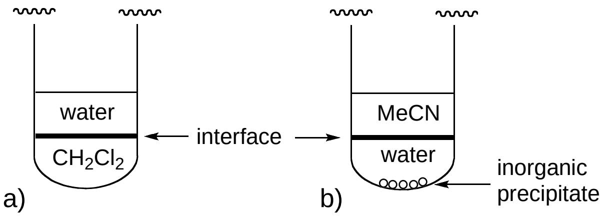


Figure 4-17. Solvent systems used in asymmetric epoxidation of alkenes; a) biphasic dichloromethane/water (3:2), b) classical acetonitrile/water (3:2).

Two liquid layers and one inorganic precipitate can be clearly seen even from the beginning of the reaction. Most probably, the solubility of acetonitrile in water helps to drive the reaction and the mixing of the various components between the phases.

Another astonishing observation is that the enantioselectivity values obtained in the different solvent systems are essentially the same. At this stage, it is not clear in which phase the epoxidation reaction actually proceeds. Most probably, the epoxidation process takes place at an interface. This might explain the global lack of difference obtained with both solvent systems.

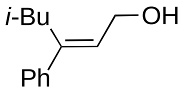
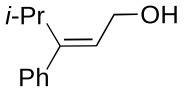
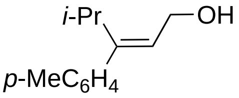
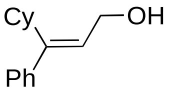
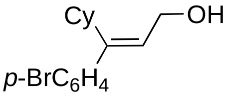
In view of these results, the asymmetric epoxidation of allylic alcohols **S24 – S28** was performed with catalyst [**71c**][SbF_6] under the new set of conditions (Table 4-21, entries 5 to 9). The reaction proceeds faster in the acetonitrile/water system (entries 7a and 7b respectively). Full conversion of **S25** - **S28** to their corresponding epoxides being achieved even for bulky trisubstituted allylic alcohols like **S28**. As for **S25**, non or very small (1-2%) decrease in enantioselectivities were detected with MeCN as a solvent. In all cases, the epoxides have the same absolute configuration whether formed in CH_2Cl_2/water or MeCN/water systems.

At this stage we have shown that highly enantioselective epoxidation of hindered trisubstituted allylic alcohols catalysed by iminium salts is feasible as well. However, relatively high amount of catalyst (up to 30 mol%) was required to reach full conversion. Considering the results obtained for alkenes **S2** and **S13** with catalysts [**71a**][SbF_6] and [**71c**][SbF_6], the use of the most reactive catalyst [**71a**][SbF_6] for the asymmetric epoxidation of poor reactive hindered substrates **S24 – S28** was decided. The results are presented in Table 4-23. To our surprise, strong matched/mismatched behaviour between diastereomeric catalyst [**71a**][SbF_6] and [**71c**][SbF_6] was observed for this type of substrates both in terms of reactivity and selectivity.

One can clearly see that in all cases and even for electron poor substrate **S28**, a much lower catalyst loading is required to drive the reaction to completion under CH_2Cl_2/water conditions. Only 10 mol% of [**71a**][SbF_6] was enough to reach full conversion. In case of electron rich alkene **S26** the amount of catalyst can be decreased up to 5 mol%.

The levels of asymmetric induction observed with catalyst [**71a**][SbF_6] were much lower then for [**71c**][SbF_6]. If the epoxidation of allylic alcohol **S26** promoted by

Table 4-23. Asymmetric epoxidation of various allylic alcohols mediated by catalyst [**71a**][SbF_6] (***the most reactive*** catalyst).

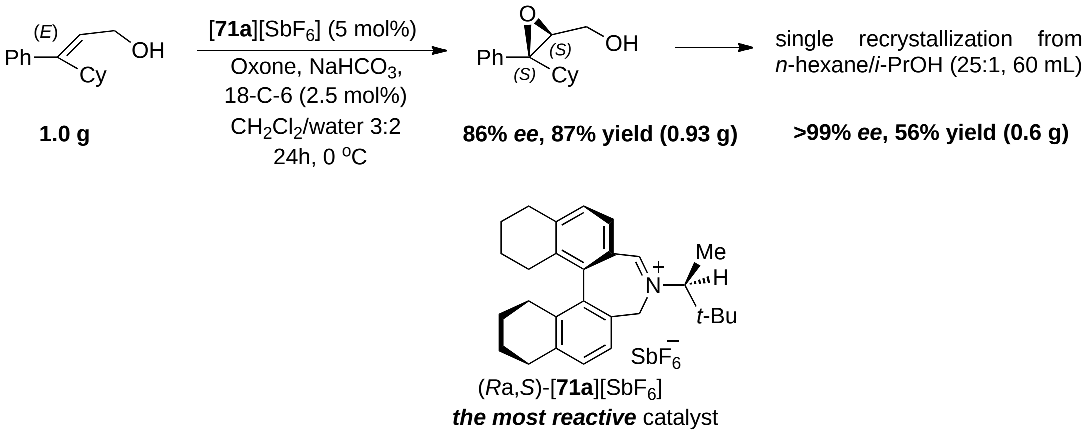
Entry	Substrate		Solvent	Catalyst, mol%	Time, h	Yield,[d] (conversion, [c]%)	*ee*, [e] %	Configuration [g]
1		**S24**	CH_2Cl_2 [a]	10	24	61 (> 99)	80	(+)
2		**S25**	CH_2Cl_2 [a]	10	24	86 (> 99)	85	(+)
3		**S26**	CH_2Cl_2 [a]	5	24	86 (> 99)	88	(+)
4a		**S27**	CH_2Cl_2 [a]	10	24	81 (> 99)	85 (96 [f])	(+)-(2*S*,3*S*)
4b			MeCN [b]	10	24	80 (> 99)	84 (96 [f])	(+)-(2*S*,3*S*)
5		**S28**	CH_2Cl_2 [a]	10	24	82 (> 99)	79	(+)

[a] Conditions: substrate (0.2 mmol), catalyst (*x* mol%), 2.5 mol% of **18-C-6**, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **CH_2Cl_2** / H_2O (3:2), 0 °C. [b] Conditions: substrate (0.2 mmol), catalyst (10 mol%), 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **MeCN** / H_2O (3:2), 0 °C. [c] Determined by GC-MS (HP-5MS) analysis of crude reaction mixture. [d] Isolated yields of pure epoxides. [e] Determined by CSP-HPLC (see experimental part). [f] After single recrystallization from *n*-hexane/*i*-PrOH. [g] The absolute configuration of major enantiomers was determined by comparison of optical rotation with that reported in the literature.

catalyst [**71c**][SbF_6] afford a 95% *ee* value (Table 4-21, entry 6a), only 88% *ee* was observed with catalyst [**71a**][SbF_6] under the same reaction conditions (Table 4-23, entry 3). In case of compounds **S24**, **S25** and **S27** the difference is even stronger (10% *ee* for **S24**, **S25** and 13% *ee* for **S27**) and became the strongest for **S28** (16% *ee* difference).

Practical issues. For the epoxidation of allylic alcohol **S27** under our CH_2Cl_2/water conditions (Table 4-23, entry 4a) using the [**71a**][SbF_6] iminium catalyst we decided to scale up our reaction in order to provide an example of a preparative-scale process (Scheme 4-17). Previously the epoxidation reaction of **S27** (0.2 mmol, 41 mg) using 5 mol% of iminium catalyst after 24 hours led to a clean and full conversion of the allylic alcohol to the epoxide (81% yield, 85% *ee*). Performing now the epoxidation reaction with 1.0 g (4.63 mmol) of substrate **S27** (scale up in 23 times), the desired epoxide was isolated with the same enantiomeric purity (86% *ee*) and slightly better yield (87%).

After a careful single recrystallization from *n*-hexane/*i*-PrOH (25:1) the product was obtained in enantiopure form (>99 % *ee*).

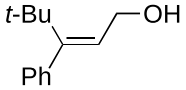
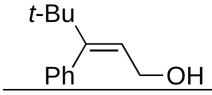


Scheme 4-17.

If the level of asymmetric induction observed in enantioselective epoxidation of allylic alcohols strongly depends from the bulk of R group *cis* to CH_2OH moiety, we might expect even higher *ee* values moving from compound **S27** (R = Cy) to extremely hindered allylic alcohol **S29** (R = *t*-Bu). Considering the fact that the *tert*-butyl group is one of the bulkiest group known, we have prepared both (*E*) and (*Z*) isomers of **S29**. In this particular case a very strong steric effect of *tert*-butyl group might change the reactivity of the isomers and their asymmetric discrimination with the iminium catalysts. If only sterics play a role then one would expect (*Z*)-**S29** rather than (*E*)-**S29** to yield high enantioselectivity due to a larger influence of the *t*-Bu group over the Ph; if electronic factors take place then the situation should be the opposite. The results on asymmetric epoxidation of (*E*)-**S29** and (*Z*)-**S29** are presented in Table 4-24.

Unfortunately, both isomers (*E*)-**S29** and (*Z*)-**S29** have shown very poor reactivity; only 5% and 1% conversion was obtained after 24 h with 30 mol% of [**71c**][SbF_6] under MeCN/water conditions for (*E*) and (*Z*) isomers respectively! Enantiomeric excess of the epoxide derived from (*E*)-**S29** was determined as 68% by CSP-GC analysis of concentrated crude reaction mixture.

Table 4-24. Asymmetric epoxidation of (*E*)-**S29** and (*Z*)-**S29** mediated by catalyst [**71c**][SbF_6].[a]

Substrate		Catalyst (mol%)	Time, h	Conversion,[b] %	*ee*,[c] %
	(*E*)-**S29**	30	24	5	68
	(*Z*)-**S29**	30	24	1	n.d.

[a] Conditions: substrate (0.2 mmol), catalyst (30 mol%), 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **MeCN** / H_2O (3:2), 24 h, 0 °C. [b] Determined by GC-MS (HP-5MS) analysis of crude reaction mixture.
[c] Determined by CSP-GC (Chiraldex Hydrodex *β*-3P).

To conclude, catalyst [**71c**][SbF_6] is good for the highly enantioselective epoxidation of hindered allylic alcohols, but when steric shielding becomes overwhelming, almost no reactivity and moderate levels of asymmetric induction is observed.

The best enantiomeric excess (98% *ee*) in the asymmetric epoxidation of allylic alcohols was achieved with substrate **S27**. Based of the fact that the configuration of the epoxide derived from this allylic alcohol is known, the stereochemical outcome can be predicted and generalised. As previously observed for the simple alkenes (*vide supra*), the major enantiomer produced (2*S*,3*S*) come from a top attack (*Re* face) of the O-atom onto the double bond of the allylic alcohol (Figure 4-18). For the others substrates probably the same *Re* approach takes place.

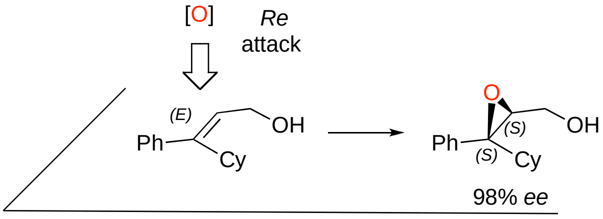


Figure 4-18. Clear *Re*-face selectivity.

4.4.3 Conclusion

Highly enantioselective iminium catalysed epoxidation of hindered allylic alcohols have been developed. The reaction is stereospecific. The general model for the asymmetric epoxidation of prochiral trisubstituted alkenes developed previously can be applied to these substrates as well. The level of asymmetric induction obtained with compounds **99** was found to be a function of steric size of R group; the highest values being obtained for bulky substrates. Two sets of reaction conditions can be used. Our extensively used dichloromethane/water system is suitable for reactive substrates whereas the classical acetonitrile/water system is better for poorly reactive and hindered allylic alcohols. In both cases the resulting epoxides can be isolated in good yields and very importantly with essentially the same enantiomeric excesses.

Strong matched/mismatched behaviour between catalyst [**71a**][SbF_6] and [**71c**][SbF_6] were observed for this class of substrates.

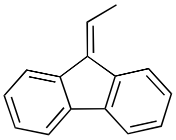
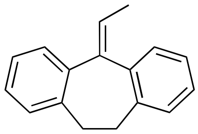
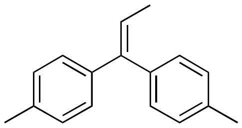
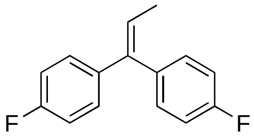
4.5 Comparison of the Enantioselective epoxidation of few prochiral alkenes promoted by catalyst [71c][SbF_6] under acetonitrile/water and dichloromethane/water reaction conditions

During our studies on the enantioselective epoxidation of trisubstituted allylic alcohols we have found very small differences in the asymmetric induction obtained under dichloromethane/water and acetonitrile/water conditions. However, in acetonitrile as a solvent reactions proceed faster in spite of the fact that the reaction mixture is triphasic. In view of these observations we decided to perform a few more test experiments on the epoxidation of simple alkenes **S12** to **S14** and **S16** under acetonitrile/water (3:2) conditions. The results obtained using dichloromethane/water and acetonitrile/water systems are presented together in the Table 4-25 for comparison.

9-Ethylidenefluorene (**S12**) was shown to be poorly soluble in the standard amount of acetonitrile (500 μL for 0.2 mmol of substrate) used for epoxidation process. Due to this fact, the acetonitrile/water ratio was changed from 3:2 to 5:2. Under both dichloromethane/water (3:2) and acetonitrile/water (5:2) reaction condition, the same amount of catalyst [**71c**][SbF_6] (10 mol%) was required to achieve full conversion of **S12** to the epoxide, but the isolated yield of the product was better using CH_2Cl_2 as a solvent (94% *vs*. 77%). Moreover, performing reaction in acetonitrile led to a lowering the enantiomeric excess compared to that obtained in dichloromethane (85% *ee vs*. 90% *ee* respectively). For the other alkenes **S13**, **S14** and **S16** reactions proceeded much faster in acetonitrile/water (3:2) compared to our previously used dichloromethane/water (3:2) conditions. Full conversion of **S13** was archieved with 20 mol% of the catalyst in 2 days, whereas only 75% conv. was obtained with the same catalyst loading in almost 4 days under dichloromethane/water conditions. The resulting epoxide was isolated in perfect yield and with excellent enantioselectivity (96% *ee*).

Asymmetric epoxidation of electron rich (**S14**) and electron deficient (**S16**) substrates can be successfully performed under acetonitrile/water conditions as well. In all cases, less amount of catalyst are needed to obtain clean and full conversion after the same

Table 4-25. Asymmetric epoxidation of alkenes **S12** to **S14** and **S16** mediated by catalyst [**71c**][SbF_6]. Comparison of two sets of reaction conditions.

Substrate		Solvent	Catalyst, (mol%)	Time, h	Yield [e] (conversion,[d] %)	*ee*,[f] %	Configuration [g]
	**S12**	CH_2Cl_2 [a]	10	24	94 (> 99)	90	(–)-(*S*)
		MeCN [b]	10	24	77 (> 99)	85	(–)-(*S*)
	**S13**	CH_2Cl_2 [a]	20	91	67 (75)	98	(+)
		MeCN [c]	20	48	94 (> 99)	96	(+)
	**S14**	CH_2Cl_2 [a]	5	24	67 (> 99)	94	(–)
		MeCN [c]	2.5	24	82 (> 99)	91	(–)
	**S16**	CH_2Cl_2 [a]	10	43	87 (> 99)	91	(–)
		MeCN [c]	5 (10)	48 (24)	89 (> 99)	89	(–)

[a] Conditions: substrate (0.2 mmol), catalyst (*x* mol%), 2.5 mol% of **18-C-6**, 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **CH_2Cl_2** / H_2O (3:2), 0 °C. [b] Conditions: substrate (0.2 mmol), catalyst (10 mol%), 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **MeCN** / H_2O (**5:2**), 0 °C. [c] Conditions: substrate (0.2 mmol), catalyst (*x* mol%), 1.1 equiv. Oxone®, 4.0 equiv. $NaHCO_3$, **MeCN** / H_2O (**3:2**), 0 °C. [d] Determined by GC-MS (HP-5MS) analysis of crude reaction mixture. [e] Isolated yields of pure epoxides. [f] Determined by CSP-HPLC (see experimental part). [g] The absolute configuration of major enantiomers was determined by comparison of optical rotation with that reported in the literature.

reaction time compare to one required in dichloromethane/water system. However, the enantiomeric excesses were always better using dichloromethane as a solvent. In all cases, the absolute configuration of the produced epoxides was the same under two sets of reaction conditions.

4.5.1 Conclusion

Two sets of reaction conditions were compared for the enantioselective epoxidation of simple trisubstituted alkenes. Classical acetonitrile/water system have shown good results in terms reactivity: reaction proceeds much faster and required less amount of catalyst. However, in terms of enantioselectivity slightly better results (2-3% *ee*) were obtained using our dichloromethane/water (3:2) system. Under both sets of reaction conditions the desired epoxides can be easily isolated in good to excellent yields and the same absolute configuration. The results perfectly fit with the observations made in enantioselective epoxidation of allylic alcohols described previously.

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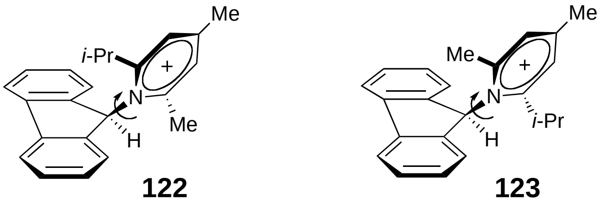
5. Slow rotation around the $N^+(sp^2)$–$C(sp^3)$ bond and importance of the resulting rotameric situation

Atropisomerism around $N^+(sp^2)$–$C(sp^3)$ bonds has been known for almost thirty years and well exemplified by the work of Balaban and co-workers with the synthesis of various *N*-(9-fluorenyl)-pyridinium salts and their isolation when asymmetrically substituted (*e.g.* pyridinium **122** and **123**, Figure 5-1).[1-4]



122 **123**

Figure 5-1. Isolated *N*-(9-fluorenyl)-pyridinium atropisomers.

More recently, the dynamic conformational isomerism of *N*-Alkyl acridinium cations **124** was studied in our group (Figure 5-2).[5] It was shown that the introduction of bulky substituents at the nitrogen atom of the acridinium ring leads to a restricted rotation around the $N^+(sp^2)$–$C(sp^3)$ bond. For various acridinium moieties, rotation barriers were determined in the range of 11.8 to 18.1 kcal/mol depending on the size of the alkyl group attached to the acridinium fragment. The bulkier the exocyclic appendage attached to nitrogen atom, the higher the rotation barrier. For instance, a rotation barier of ~20.1 kcal/mol was measured for the 3,3-dimethylbutyl-2-amine derivative.

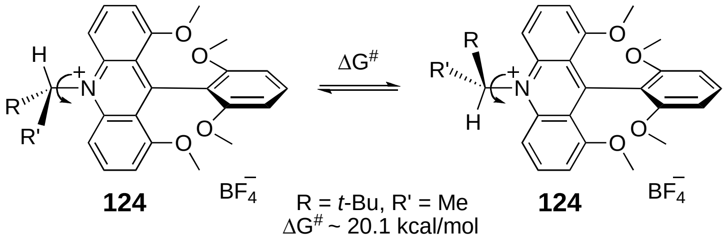
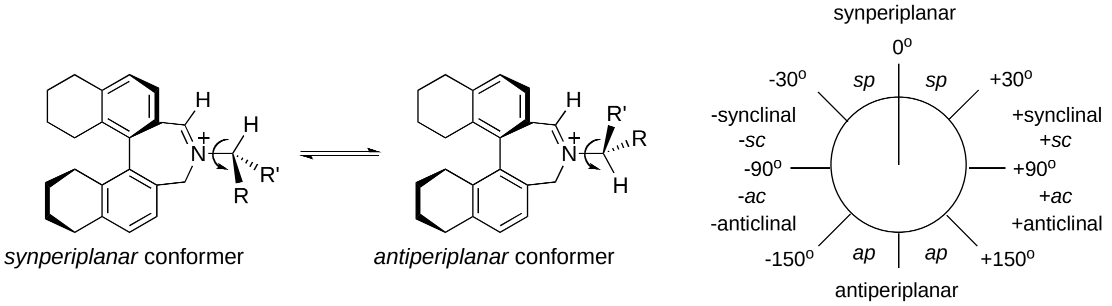


Figure 5-2. Dynamic conformational isomerism in acridinium cations **124**.

In view of these results, it was possible that a hindered rotation around the $N^+(sp^2)$–$C(sp^3)$ bond that links the azepinium core to the chiral appendage would also occur for salts [**71a**][SbF_6] and [**71c**][SbF_6].[6] Care was thus taken to characterize the diarylazepinium cations by variable temperature (VT) NMR in a search for atropisomeric *anti*- and *synperiplanar* conformations (Figure 5-3).



synperiplanar conformer

antiperiplanar conformer

Figure 5-3. *Syn*- and *antiperiplanar* conformers of iminium salts **71**. General IUPAC nomenclature of atropisomers.

While the ^{1}H NMR analysis of [**71c**][SbF_6] in CD_2Cl_2 displayed sharp signals at 298 K, a gradual decrease of the temperature led to a broadening of all signals (with a coalescence around 243 K) before them becoming sharp again at 193 K (Figure 5-4). Then, two sets of signals appeared indicative of the existence indeed of two atropisomeric conformers and of their slow interconversion on the NMR time scale at 193 K. The signal of the iminium proton at δ 8.6 ppm was particularly useful to monitor. If one considers that the NMR coalescence is reached at 243 K, then an approximate energy barrier in the range of 11-12 kcal.mol^{-1} can be estimated.[1] An atropisomeric enrichment was also observed between the *anti*- and *synperiplanar* conformers and a 85:15 ratio was measured by integration of the respective signals.

In ^{13}C NMR spectroscopy, an analogous behavior was observed although with a broadening of some of the signals appearing already at 298 K; these enlargements disappearing at 193 K along with the splitting of all carbon signals (for spectrum see appendix).

The determination of the conformations of the major and minor atropisomer in solution was realized by a NOESY experiment at 193 K. In the case of the minor conformer, a strong cross-peak was observed between the signal of the iminium proton ($H^{1'}$, δ 8.68 ppm) and that of the hydrogen α to *t*-Bu group (δ 4.09 ppm, Figure 23) whereas, for the major atropisomer, a weak cross-peak was only observed for the analogous signals. For that major isomer, a strong cross-peak was nevertheless seen

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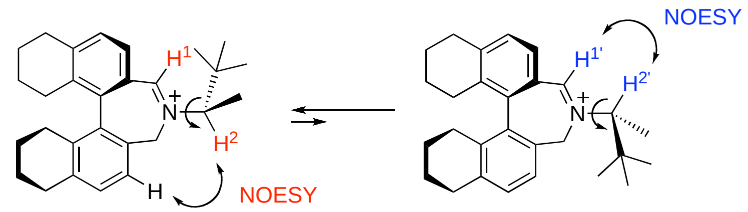
[1] The relationship $\Delta G^‡ = RT_c\,(22.96 + \ln\,(T_c\,/\,\Delta\nu))$ was used to determine the activation energy, $\Delta G^‡$, from the coalescence temperature, T_c (243 K), and the frequency separation of the peaks of the iminium protons, $\Delta\nu$ (115.1 Hz at 193 K).

between the H^2 signal and that of the *ortho*-aromatic proton next to the CH_2N group. It strongly points towards *syn*- and *antiperiplanar* conformations for the minor and major conformers respectively (Figure 5-5).



antiperiplanar-**71c**
MAJOR

synperiplanar-**71c**
minor

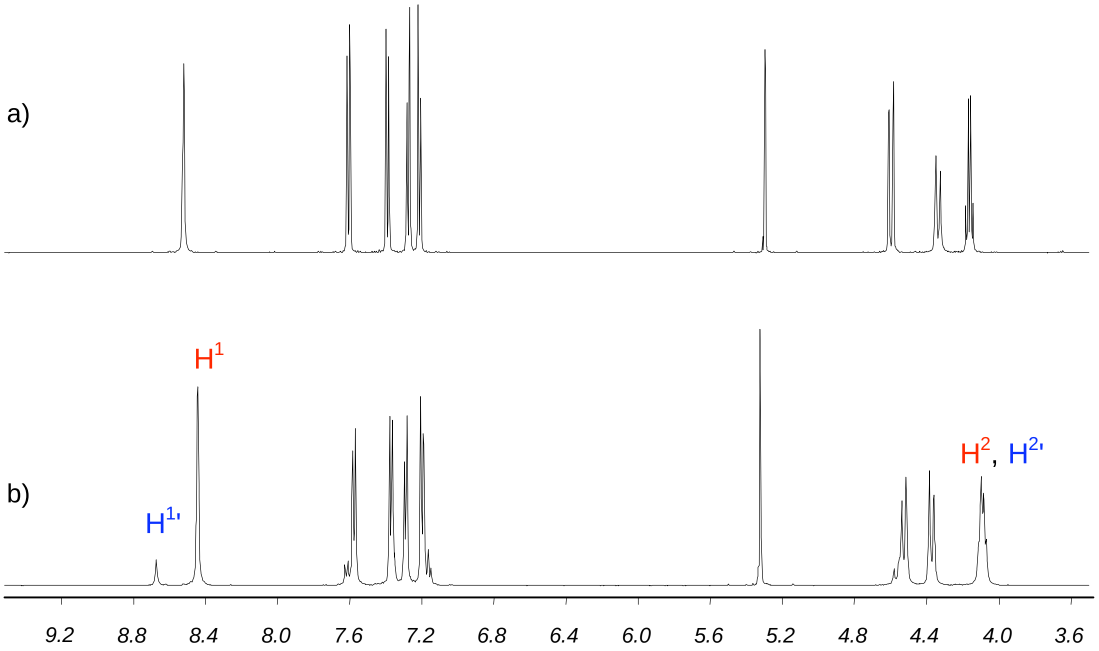


Figure 5-4. ^1H NMR (δ 9.3-3.6 ppm, CD_2Cl_2, 500 MHz) of [**71c**][SbF_6] at (a) 298 K (25 °C) and (b) 193 K (-80 °C).

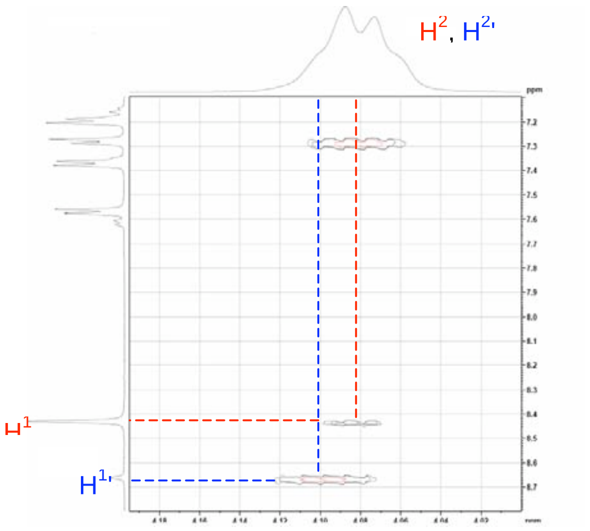


Figure 5-5. NOESY experiment (CD_2Cl_2, 500 MHz) of [**71c**][SbF_6] at 193 K (-80 °C).

Monocrystals of compound [**71c**][SbF_6] were obtained and an X-Ray structural analysis was performed. The ORTEP view is reported in Figure 5-6. Clearly, in the solid state, the *antiperiplanar* conformer is the preferred atropisomer as well.[2]

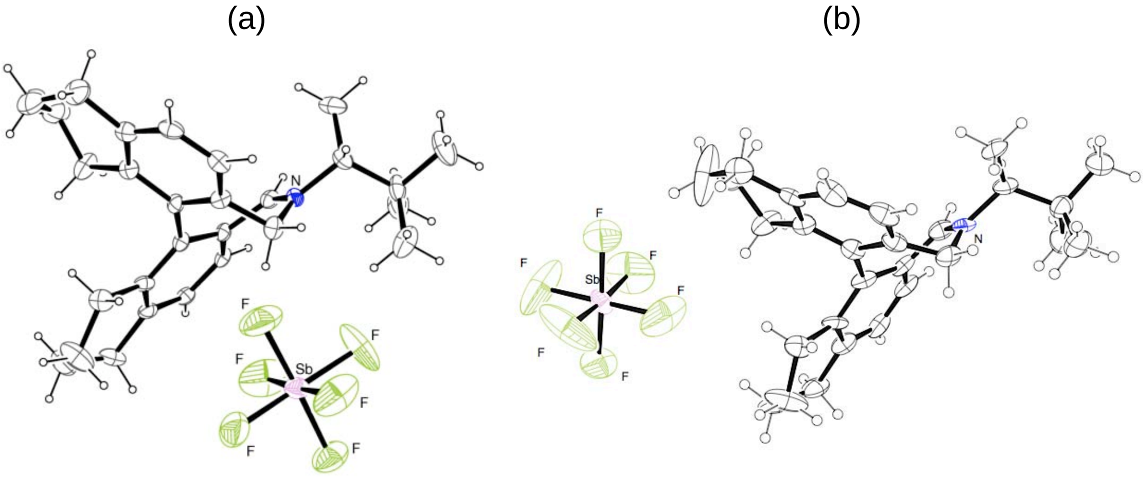


Figure 5-6. Ortep views of (a) [**71c**][SbF_6] (*most selective* catalyst) and (b) [**71a**][SbF_6] (*most reactive* catalyst). Ellipsoids are presented at (a) 50 % and (b) 40% probability levels.

Interestingly, for catalyst [**71a**][SbF_6], a totally different situation was observed (Figure 5-7). At 193 K, ^1H and ^{13}C NMR analyses revealed a lone set of signals indicating the presence of a single conformer (>98%). A NOESY experiment was performed at low temperature (193 K) and a strong cross-peak was observed between the signal of the iminium proton ($H^{1'}$, δ 8.62 ppm) and that of the hydrogen α to *t*-Bu group (δ 4.05 ppm). Then, only a *synperiplanar* geometry can account for the spectrum of the unique atropisomer of **71a**. The reason for this change in the preferred atropisomeric population between **71a** and **71c** is unclear at the moment.

Finally, X-ray quality crystals of salt [**71a**][SbF_6] were obtained by slow evaporation of CH_2Cl_2/hexane mixture and low-temperature structural analysis revealed that in the solid state this compound exists as *synperiplanar* conformer. The ORTEP view is presented in Figure 5-6.

However, this dichotomy in the atropisomeric situation is important as it is a possible reason for (i) the "lack" of observed stereochemical influence from the exocyclic auxiliary and (ii) the higher reactivity of diastereomer **71a** over **71c** during the course

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[2] For this compound, the θ and Φ angle values are –58.8° and –61.2° respectively. These θ and Φ angles are quite larger and lower respectively than that reported for saturated analogues of type **83** (mean average, –55.5° and –65.7° respectively). However, it is difficult to draw a conclusion as the azepines previously studied by X-ray crystallography were derived from the 1-phenylpropylamine and not from 3,3-dimethylbutyl-2-amine.

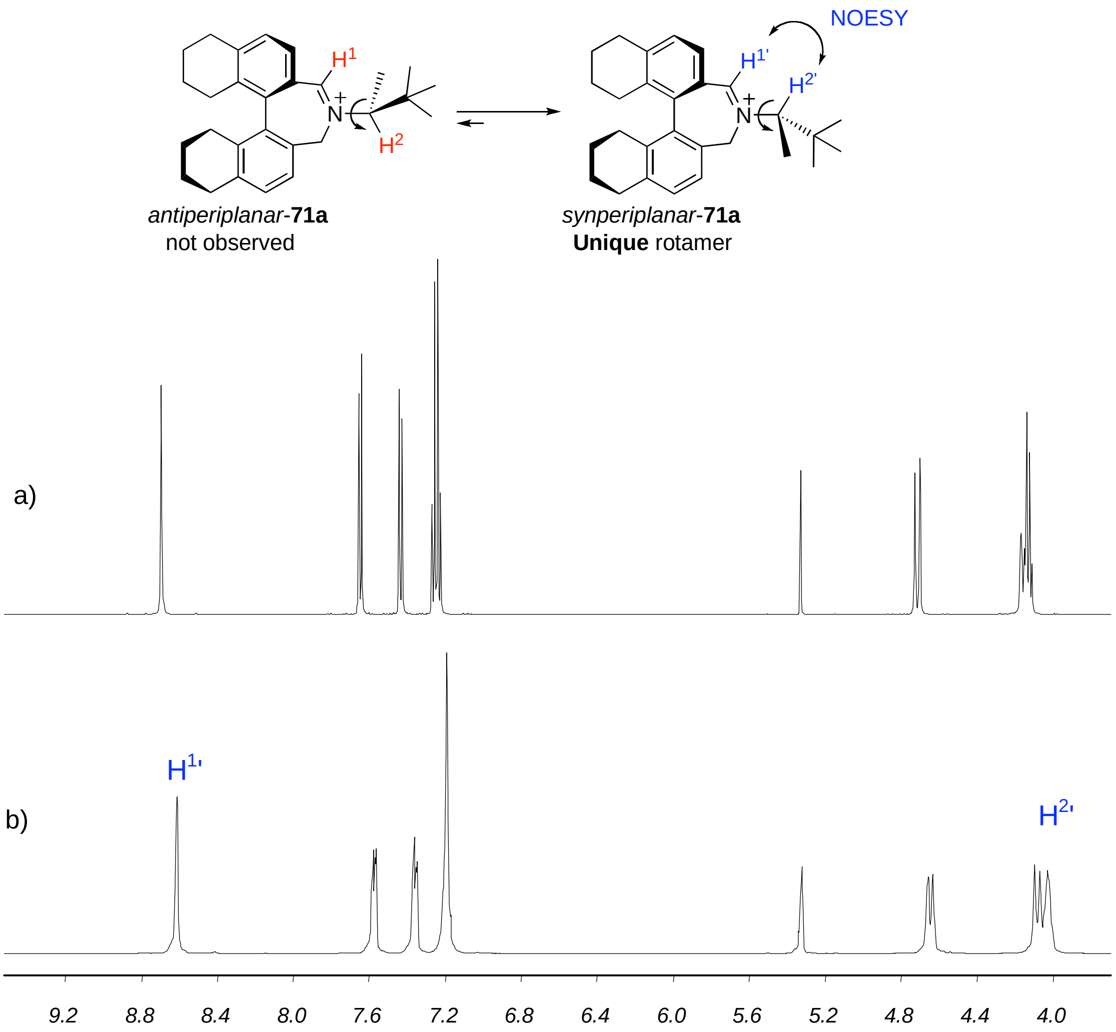

Figure 5-7. ^1H NMR (δ 9.2-3.6 ppm, CD_2Cl_2, 500 MHz) of [**71a**][SbF_6] at (a) 298 K (25 °C) and (b) 193 K (-80 °C).

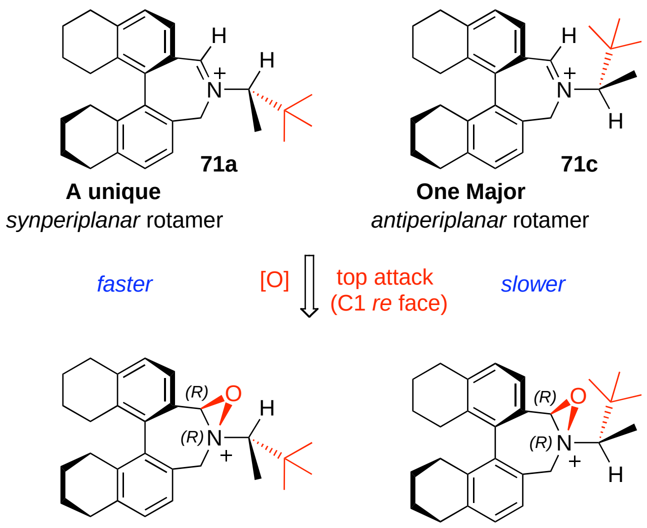

Figure 5-8. Importance of the rotameric situation for the "lack" of stereochemical influence of the R* appendage.

of the studies (*vide supra*). Indeed, the fact that **71a** and **71c** are exclusively and predominantly *synperiplanar* and *antiperiplanar* respectively, creates a situation in which the bulky *t*-butyl side chain of the chiral auxiliary is always positioned on the bottom (*si* face, C1 atom) of the iminium ion irrespective of the diastereomeric situation. As such, iminium ions **71a** and **71c** react with the same sense of stereoinduction and little influence from the chiral auxiliary.

This geometrical arrangement of the side chain furthermore reinforces the natural preference for a top face attack of the peroxymonosulfate anion on the (*R*a)-iminium species to generate oxaziridinium rings of R_C,R_N configuration in accordance to the calculations from Washington and Houk[7] and the experimental results from Závada[8] and collaborators (Figure 5-8).

Finally, in the case of **71a**, the fact that the atropisomeric situation is shifted towards a single rotamer may also entice a faster reaction of this diastereomer with the peroxymonosulfate anion than with **71c** for which the mixed *antiperiplanar* / *synperiplanar* population retards possibly the formation of the R_C,R_N oxaziridinium species. In the *antiperiplanar* conformation the double bond of the iminium ion is also more strongly shielded by the alkyl group on the exocyclic group (and the Me in particular) than the *synperiplanar* conformation.

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6. General Conclusion

In chapter 4 (paragraph 4.1.2) we have presented already known D_2-symmetric amines, namely the “Double Bridged Biphenyl Azepines” (DBBA). DBBA and their corresponding iminium salts were previously prepared and studied in our group. During this thesis, we have continued studies on the use of these compounds as catalysts in amine/iminium promoted epoxidation reactions. We have shown that a diastereomeric mixture of DBB azepines provides essentially the same results than the isolated diastereomers. In accordance with previous results, the configuration of formed epoxides was proven to be controlled by the configuration of the exocyclic appendage and not by the configuration of the biaryl framework. During this project we observed that iminium salts formed *in situ* can be used as catalysts as well as isolated analogues. Up to 85% *ee* and 98% conv. were achieved using such catalysts.

In the paragraphs 4.2 and 4.3, we have described two novel classes of rigid biaryl azepinium salts that behave as catalysts for the enantioselective epoxidation of prochiral alkenes. We have been able to show that the origin of the predominance of this time, the axially chiral biaryl stereogenic element is to be found in the dihedral angle values for the biaryl twist – and the external dihedral angle Φ in particular. The larger angle, the better the asymmetric transfer. In general, 5,5′,6,6′,7,7′,8,8′-octahydrobinaphthyl derived azepinium salts have shown the best asymmetric induction in iminium promoted asymmetric epoxidation reactions. We have further used an oxidation protocol that allows a rapid assay for the enantioselective efficiency by *in situ* oxidation tertiary amine precursors to bromide iminium salts.

We have also observed that the counterion, associated to cationic iminium part has to be chosen wisely. The stability of the counterion under epoxidation reaction conditions is crucial to provide robust catalyst performance. If view of these results we have looked for an optimal chiral iminium cation / achiral anion combination and found that the hexafluoroantimonate to be optimal counterion for reliable results. One has to be careful with other anions and with tetraphenylborate in particular. We have also created a general model to predict with certainty high selectivity (up to 98% *ee*) in the formation of non-racemic epoxides of defined absolute configuration.

In the paragraph 4.4, we described the synthesis of hindered trisubstituted allylic alcohols and their highly enantioselective (87% - 98% *ee*) iminium-catalyzed epoxidation. Two sets of reaction conditions were used: the biphasic CH_2Cl_2/water 3:2 and the MeCN/water 3:2 system. We observed that enantioselectivities obtained under both conditions were nearly the same or very similar. However, in terms of reactivity MeCN/water 3:2 system provided better results. The model, previously developed for simple olefins (*Si* face attack of the oxidant) can be successfully applied to the allylic alcohols as well; the absolute configuration of the formed epoxides can be predicted with a high probability level (*Re* face approach of the oxidant due to the presence of the oxygen at the allylic position which changes the priority sequence in the CIP rule).

In chapter 5, we reported that the so far unexplained "lack" of stereochemical control from the chiral exocyclic appendage in this type of catalysts is due to the existence of atropisomers around the N(sp^2)-C(sp^3) bond that links the azepinium core to the exocyclic stereocenter.

7. Experimental part

General Remarks: NMR spectra were recorded on Bruker AMX-300, AMX-400 and DRX-500 MHz at room temperature (25 °C) unless otherwise stated. ^{1}H-NMR: chemical shifts are given in ppm relative to Me_4Si with the solvent resonance used as the internal standard ($CDCl_3$ δ 7.26 ppm; CD_2Cl_2 δ 5.32 ppm, DMSO-d_6 δ 2.50 ppm). ^{13}C-NMR (75 MHz, 100 MHz, 125 MHz): chemical shifts were given in ppm relative to Me_4Si, with the solvent resonance used as the internal standard ($CDCl_3$ δ 77.16 ppm; DMSO-d_6 δ 39.52 ppm; CD_2Cl_2 δ 54.0 ppm). ^{19}F-NMR (282 MHz): chemical shifts were given in ppm to C_6F_6 as the standard (δ -164.9 ppm). Assignments may have been achieved using COSY, DEPT-135, HSQC and NOESY experiments. IR spectra were recorded with a Perkin-Elmer 1650 FT-IR and a Perkin-Elmer FT-IR Spectrum 100 spectrometer using a diamond ATR Golden Gate sampling. Melting points (Mp) were measured in open capillary tubes on a Büchi B-540 melting point apparatus and were uncorrected. Electrospray mass spectra (MS-ES) were obtained on a Finnigan SSQ 7000 spectrometer and MS-EI spectra were obtained on a Varian CH4 or SM1 spectrometer; ionizing voltage 70eV and 40eV; *m*/z (intensity in %) by the Department of Mass Spectroscopy of the University of Geneva. Optical rotations were measured on a JASCO P-1030 polarimeter in a thermostated 10.0 cm long microcell with high pressure lamp of sodium and are reported as follows: $[\alpha]^t_D$ (c (g/100 ml), solvent). HPLC analyses were performed on an Agilent 1100 apparatus (binary pump, autosampler, column thermostat and diode array detector using Chiralcel OD-H, OJ and OJ-H (0.46 x 25 cm) columns. Chiral stationary phase (CSP) chromatography was performed on a Hewlett Packard 6890 GC chromatograph using a Hydrodex-β column (25 m × 0.25 mm, H_2, 40 Psi). GC-Mass analysis was performed on a Hewlett Packard 6890 apparatus using a HP-5MS column (30 m × 0.25 mm, He 1.0 ml/min). X-ray diffraction analysis was performed at the “Laboratoire de Cristallographie aux rayons X, Service de Resolution Structurale par Diffraction des Rayons X” by Dr. G. Bernardinelli and Dr. Céline Besnard. Elemental analyses were performed at the Laboratory of elemental analysis of ETH Zürich.

Commercial reagents were purchased from Aldrich, Fluka, Acros or TCI and used without further purification, unless otherwise noted. Flash chromatography was performed using silica gel 60 (230–400 mesh ASTM) from Fluka.

Typical Biphasic Enantioselective Epoxidation Procedure with *in situ* Prepared Catalysts

In a 5 ml flask equipped with a magnetic stirring bar, $NaHCO_3$ (67 mg, 0.80 mmol, 4.0 equiv.) was added to 800 µL of water. Oxone® (132 mg, 0.21 mmol, 1.0 equiv.) was then added and the solution stirred for few minutes until effervescence subsided. 500 µL of a 0.4 mol/L solution of the alkene (0.20 mmol, 1.0 equiv.) and naphthalene (0.20 mmol, 1.0 equiv., internal reference) in CH_2Cl_2 was added and the resulting biphasic mixture was cooled to 0 °C with an ice-bath. The catalyst was prepared by mixing the azepine precursor and NBS (10.0 µmol each, 5 mol%) in CH_2Cl_2 (500 µL) for five minutes. The resulting solution was added, followed by a solution of 18-crown-6 (1.0 mg, 5.0 µmol, 2.5 mol%) in CH_2Cl_2 (200 µL). After 5 minutes at 0 °C without any stirring, the reaction mixture was then vigorously stirred (*very important*!) at that temperature for 2h.

Typical enantioselective epoxidation procedure with isolated iminium salts under CH_2Cl_2/water conditions

All reactions were performed in a standard test-tube equipped with a magnetic stirring bar. $NaHCO_3$ (67 mg, 0.80 mmol, 4.0 equiv.) was dissolved in 800 µL of water. Oxone® (132 mg, 0.21 mmol, 1.1 equiv.) was then added as a solid in one portion and the solution stirred for few minutes until effervescence subsided. 500 µL of a 0.4 mol/L solution of an alkene (0.20 mmol, 1.0 equiv.) in CH_2Cl_2 was added and the resulting biphasic mixture was cooled to 0 °C with a cryostat bath. A catalyst was added in CH_2Cl_2 (500 µL) in one pot followed by a solution of 18-C-6 (1.0 mg, 5.0 µmol, 2.5 mol%) in CH_2Cl_2 (200 µL) and the resulting mixture was then vigorously stirred (*very important*!) at 0 °C. After the indicated amount of time, the reaction mixture was diluted with dichloromethane (10 mL), water (10 mL) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, concentrated under vacuum and purified.

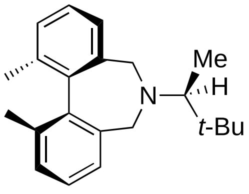
Typical enantioselective epoxidation procedure with isolated iminium salts under MeCN/water conditions

The reaction procedure is similar to the CH_2Cl_2/water protocol with small modifications. All reactions were performed in a standard test-tube equipped with a magnetic stirring bar. $NaHCO_3$ (67 mg, 0.80 mmol, 4.0 equiv.) was dissolved in 800 µL of water. Oxone® (132 mg, 0.21 mmol, 1.1 equiv.) was then added as a solid in one portion and the solution stirred for few minutes until effervescence subsided. 500 µL of a 0.4 mol/L solution of an alkene (0.20 mmol, 1.0 equiv.) in MeCN was added (after the addition was done the mixture became triphasic: precipitation of inorganic material was observed and the liquid layer separated in two phases) with the aid of MeCN (200 µL) which was used to rinse the walls of the flask, and the resulting mixture was cooled to 0 °C with a cryostat bath. A catalyst was added as a solution in MeCN (500 µL) in one pot. After few minutes without any stirring the resulting triphasic mixture was then vigorously stirred (*very important*!) at 0 °C. After the indicated amount of time, the reaction mixture was diluted with dichloromethane (20 mL), water (10 mL) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, concentrated under vacuum and purified.

General procedure for the synthesis of 6,6´-dimethylbiphenyl-derived azepine amines (72a to 72d)

To a solution of (*R*a)-6,6'-dimethyl-1,1'-biphenyl-2,2'-dicarboxaldehyde (100 mg, 0.42 mmol, 1.0 equiv) in MeCN (5 mL) the corresponding enantiopure amine (**a** to **d**, 2.0 equiv) was added. After 15 min of stirring $NaBH_3CN$ (106 mg, 1.68 mmol, 4.0 equiv) was added to the reaction mixture and the resulting colorless solution was stirred for 23h at room temperature. The reaction mixture was quenched by addition of AcOH (0.24 mL, 10.0 equiv), stirred for 10 min, then diluted with MeOH (1 mL) and DCM (30 mL). The resulting solution was washed with 2M aqueous solution of NaOH (30 mL): The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (2 × 25 mL). Combined organic layers were washed with brine (25 mL), dried ($MgSO_4$), filtered, concentrated *in vacuo* and purified.

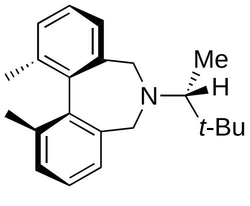
(*R*a)-6,7-Dihydro-5*H*-6-[(*R*)-3,3-dimethylbutan-2-yl]-1,11-dimethyldibenz[*c*,*e*]azepine (72a)



(*R*a,*S*)

Purified by flash chromatography on silica gel (Et_2O/pentane 1:10). Yield – 67%. Colorless viscous oil. **R$_f$** = 0.69 (silica gel, Et_2O/*n*-hexane 1:10). **[α]$_D^{20}$** = + 37.8 (c = 1.0, $CHCl_3$). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.90 (s, 9H, *t*-Bu), 1.04 (d, 3H, CH_3, *J* = 7.3 Hz), 2.14 (s, 6H, CH_3), 2.43 (q, 1H, CH-N, *J* = 7.0 Hz), 3.29 (d, 2H, Ar-CH_2-N, *J* = 12.4 Hz), 3.52 (d, 2H, Ar-CH_2-N, *J* = 12.4 Hz), 7.1 – 7.29 (m, 6H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 11.8, 20.1, 27.3, 37.1, 54.4, 68.7, 127.4, 127.8, 129.3, 135.9, 137.5, 139.0 ppm. **IR** (neat): 2949 (s), 2865 (m), 1458 (m), 1370 (w), 1117 (m), 785 (w), 751 (w) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 308.5 [M+1] (67), 224.4 (100), 207.4 (48), 192.4, (76). **HRMS-ESI** (+): Calculated for $C_{22}H_{30}N^+$ ($[M+H]^+$) 308.2372, found 308.2380.

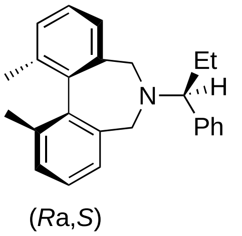
(*R*a)-6,7-Dihydro-5*H*-6-[(*R*)-3,3-dimethylbutan-2-yl]-1,11-dimethyldibenz[*c*,*e*]azepine (72c)



(*R*a,*R*)

Purified by flash chromatography on silica gel (Et_2O/pentane 1:10). Yield - 74%. Colorless viscous oil. **R$_f$** = 0.44 (silica gel, Et_2O/*n*-hexane 1:10). **[α]$_D^{20}$** = + 20.1 (c = 1.0, $CHCl_3$). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 0.79 (d, 3H, CH_3, *J* = 7.1 Hz), 0.92 (s, 9H, *t*-Bu), 2.19 (s, 6H, CH_3), 2.67 (q, 1H, CH-N, *J* = 7.2 Hz), 3.32 (s, 4H, Ar-CH_2-N), 7.08 – 7.17 (m, 2H, $C^{ar}H$), 7.18 – 7.29 (m, 4H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 11.6, 20.0, 27.3, 37.3, 55.6, 69.2, 125.8, 127.5, 129.0, 135.5, 137.3, 138.5 ppm. **IR** (neat): 2953 (m), 2866 (m), 1455 (m), 1377 (w), 1358 (w), 1110 (m), 786 (w), 748 (w) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 308.3 [M+1] (30.5), 224.3 (100), 207.3 (30.5), 192.1 (56). **HRMS-ESI** (+): Calculated for $C_{22}H_{30}N^+$ ($[M+H]^+$) 308.2372, found 308.2382.

(*R*a)-6,7-Dihydro-5*H*-1,11-dimethyl-6-[(*S*)-1-phenylpropyl]dibenz[*c*,*e*]azepine (72b)

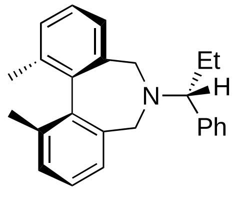


(*R*a,*S*)

Purified by preparative TLC (silica gel, Et_2O/pentane 2:3). Yield - 82 %. White solid, **Mp** = 96.5 – 98.5 °C. **R$_f$** = 0.52 (silica gel, Et_2O/pentane 2:3). **[α]$_D^{20}$** = – 51.5 (c = 1.0, $CHCl_3$). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.66 (t, 3H, CH_3, *J* = 7.4 Hz), 1.72 – 1.87 (m, 1H, CH_2), 2.13 – 2.22 (m, 7H, CH_3, CH_2), 2.8 (d, 2H, Ar-CH_2-

N, *J* = 12.6 Hz), 3.1 (dd, 1H, CH-N, *J* = 9.5 Hz, 3.7 Hz), 3.57 (d, 2H, Ar-CH_2-N, *J* = 12.6 Hz), 7.0 – 7.08 (m, 2H, $C^{ar}H$), 7.18 – 7.32 (m, 9H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 10.5, 20.1, 28.1, 53.0, 68.9, 126.7, 127.3, 127.6, 128.6, 129.1, 129.8, 135.8, 136.2, 139.2, 143.7 ppm. **IR** (neat): 3021 (w), 2962 (w), 2920 (w), 2876 (w), 1595 (w), 1451 (w), 1377 (w), 1134 (w), 760 (m), 748 (m), 705 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 342.1 [M+1] (43), 224.4 (100), 207.4 (23), 192.4 (43). **HRMS-ESI** (+): Calculated for $C_{25}H_{28}N^+$ ($[M+H]^+$) 342.2221, found 342.2222.

(*R*a)-6,7-Dihydro-5*H*-1,11-dimethyl-6-[(*R*)-1-phenylpropyl]dibenz[*c,e*]azepine (72d)



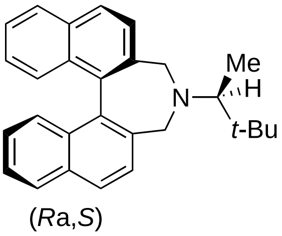
(*R*a,*R*)

Purified by preparative TLC (silica gel, Et_2O/pentane 2:3). Pale yellow viscous oil. Yield – 97%. **R_f** = 0.69 (silica gel, Et_2O/pentane 2:3). **$[\alpha]_D^{20}$** = + 26.8 (c = 1.0, $CHCl_3$). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.58 (t, 3H, CH_3, *J* = 7.3 Hz), 1.52 – 1.69 (m, 1H, CH_2), 1.8 – 1.94 (m, 1H, CH_2), 2.17 (s, 6H, CH_3), 2.82 (d, 2H, Ar-CH_2-N, *J* = 12.1 Hz), 3.23 (dd, 1H, CH-N, *J* = 9.3 Hz, 3.8 Hz), 3.58 (d, 2H, Ar-CH_2-N, *J* = 12.1 Hz), 7.02 – 7.1 (m, 2H, $C^{ar}H$), 7.22 – 7.31 (m, 5H, $C^{ar}H$), 7.32 – 7.42 (m, 4H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 10.4, 20.1, 27.6, 53.3, 68.6, 127.0, 127.3, 127.5, 128.7, 129.3, 129.8, 135.8, 136.2, 139.1, 144.5 ppm. **IR** (neat) : 3024 (w), 2961 (w), 2929 (w), 2874 (w), 1490 (w), 1452 (m), 1377 (w), 770 (m), 748 (s), 701 (s) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 342.3 [M+1] (56), 224.3 (100), 207.3 (25.5), 192.1 (46). **HRMS-ESI** (+): Calculated for $C_{25}H_{28}N^+$ ($[M+H]^+$) 342.2221, found 342.2229.

General procedure for the synthesis of binaphthyl-derived azepine amines (82a to 82d)

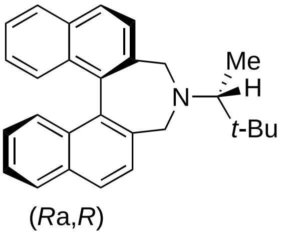
In a 25 mL round bottom flask containing a solution of enantiopure amine (**a** to **d**) (0.818 mmol, 1.2 equiv) in acetonitrile (10 mL) was added (*R*a)-2,2′-bis(bromomethyl)-1,1′-binaphthyl (300 mg, 0.682 mmol, 1.0 equiv) and potassium carbonate (376 mg, 2.73 mmol, 4.0 equiv). The mixture was heated at reflux for ca. 5 hours (monitoring by thin layer chromatography (TLC)), allowed to cool down to room temperature and filtered though a Celite plug washed with CH_2Cl_2. Evaporation of the solvent under reduced pressure gave the crude product which was purified by column chromatography.

(*R*a)-4,5-Dihydro-3*H*-4-[(*S*)-3,3-dimethylbutan-2-yl]dinaphth[2,1-*c*:1´,2´-*e*]azepine[1] (82a)



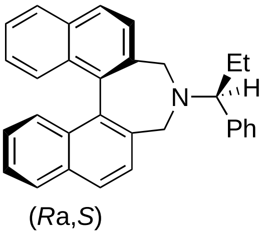
Purified by column chromatography on silica gel, eluting with Et_2O/*n*-hexane (1:10). Yield 77% (199 mg). Amorphous yellow powder. **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.95 (s, 9H, *t*-Bu), 1.1 (d, 3H, CH_3, J = 7.1 Hz), 2.50 (q, 1H, CH, J = 7.0 Hz), 3.47 (d, 2H, Ar-CH_2-N, J = 12.1 Hz), 3.74 (d, 2H, Ar-CH_2-N, J = 12.4 Hz), 7.18 – 7.26 (m, 2H, $C^{ar}H$), 7.34 (d, 2H, $C^{ar}H$, J = 8.3 Hz), 7.40 – 7.47 (m, 2H, $C^{ar}H$), 7.58 (d, 2H, $C^{ar}H$, J = 8.3 Hz), 7.94 (d, 2H, $C^{ar}H$, J = 8.1 Hz), 7.95 (d, 2H, $C^{ar}H$, J = 8.3 Hz) ppm.

(*R*a)-4,5-Dihydro-3*H*-4-[(*R*)-3,3-dimethylbutan-2-yl]dinaphth[2,1-*c*:1´,2´-*e*]azepine [1] (82c)



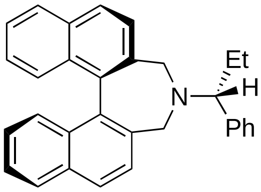
Purified by column chromatography on silica gel, eluting with Et_2O/*n*-hexane (1:10). Yield 74% (193 mg). Amorphous yellow powder. **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.83 (d, 3H, CH_3, J = 7.3 Hz), 0.97 (s, 9H, *t*-Bu), 2.84 (q, 1H, CH, J = 7.2 Hz), 3.48 (d, 2H, Ar-CH_2-N, J = 12.1 Hz), 3.59 (d, 2H, Ar-CH_2-N, J = 12.1 Hz), 7.21 – 7.29 (m, 2H, $C^{ar}H$), 7.40 – 7.49 (m, 4H, $C^{ar}H$), 7.57 (d, 2H, $C^{ar}H$, J = 8.3 Hz), 7.95 (d, 2H, $C^{ar}H$, J = 7.8 Hz), 7.96 (d, 2H, $C^{ar}H$, J = 8.1 Hz) ppm.

(*R*a)-4,5-Dihydro-3*H*-4-[(*S*)-1-phenylpropyl]dinaphth[2,1-*c*:1´,2´-*e*]azepine (82b)



Purified by column chromatography on silica gel eluting with Et_2O/ *n*-hexane (2:3). Yield 76% (214 mg). Amorphous pale yellow solid. **R_f** = 0.42 (silica gel, Et_2O/Hexane 2:3). **$[\alpha]_D^{20}$** = –352.3 (c = 1.0, $CHCl_3$). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.73 (t, 3H, CH_3, J = 7.3 Hz), 1.82 – 1.99 (m, 1H, CH_2), 2.2 – 2.33 (m, 1H, CH_2), 3.04 (d, 2H, Ar-CH_2-N, J = 12.6 Hz), 3.28 (dd, 1H, CH-N, J = 9.4 Hz, 3.9 Hz), 3.81 (d, 2H, Ar-CH_2-N, J = 12.6 Hz), 7.2 – 7.33 (m, 7H, $C^{ar}H$), 7.39 – 7.52 (m, 6H, $C^{ar}H$), 7.88 – 7.99 (m, 4H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 10.7, 28.2, 53.2, 69.5, 125.8, 126.1, 127.4, 127.8, 128.1, 128.6, 128.7, 128.8, 129.1, 131.8, 133.6, 134.9, 135.6, 143.6 ppm. **IR** (neat): 3051 (w), 2959 (w), 2873 (w), 1594 (w), 1508 (w), 1490 (w), 1452 (w), 1341 (w), 816 (s), 750 (m), 702 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 414.3 [M+1] (59), 296.5 (100), 294.5 (37), 281.3 (42), 279.5 (58), 267.5 (28). **HRMS-ESI** (+): Calculated for $C_{31}H_{28}N^+$ ($[M+H]^+$) 414.2216, found 414.2223.

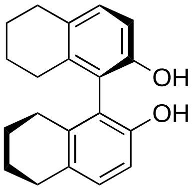
(*R*a)-4,5-Dihydro-3*H*-4-[(*R*)-1-phenylpropyl]dinaphth[2,1-*c*:1´,2´-*e*]azepine (82d)



(*R*a,*R*)

Purified by gradient column chromatography on silica gel eluting with Et_2O/*n*-hexane (1:10 – 2:3). Yield 72% (204 mg). Amorphous white solid. $\mathbf{R_f}$ = 0.53 (silica gel, Et_2O/Hexane 2:3). $[\alpha]_D^{20}$ = – 172.2 (c = 1.0, $CHCl_3$). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.6 (t, 3H, CH_3, *J* = 7.4 Hz), 1.61 – 1.76 (m, 1H, CH_2), 1.88 – 2.1 (m, 1H, CH_2), 3.07 (d, 2H, Ar-CH_2-N, *J* = 12.2 Hz), 3.32 (dd, 1H, CH-N, *J* = 9.4 Hz, 3.8 Hz), 3.82 (d, 2H, Ar-CH_2-N, *J* = 12.2 Hz), 7.25 – 7.38 (m, 3H, $C^{ar}H$), 7.4 – 7.6 (m, 10H, $C^{ar}H$), 8.0 (d, 4H, $C^{ar}H$, *J* = 8.1 Hz) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 10.5, 27.7, 53.6, 69.3, 125.9, 126.1, 127.4, 127.8, 128.4, 128.6, 128.7, 128.8, 129.2, 131.8, 133.6, 134.9, 135.6, 144.4 ppm. **IR** (neat): 3032 (w), 2964 (w), 2924 (w), 2872 (w), 1595 (w), 1508 (w), 1454 (w), 1357 (w), 817 (s), 755 (m), 699 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 414.5 [M+1] (73), 296.5 (100), 294.5 (38), 279.5 (46), 266.5 (19). **HRMS-ESI** (+): Calculated for $C_{31}H_{28}N^+$ ($[M+H]^+$) 414.2216, found 414.2219.

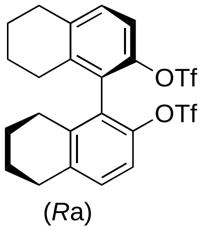
(*R*a)-5,5′,6,6′,7,7′,8,8′-Octahydro-1,1′-binaphthyl-2,2′-diol[2] (84)



(*R*a)

(*R*a)-H_8-BINOL was synthesis in a multigram scale (>25 g) following procedure describey by A. Börner and co-workers[2] as a white solid in quantitative yield and >99% *ee.* $[\alpha]_D^{20}$ = + 74.8 (c = 1.0, THF) [lit.(Aldrich) $[\alpha]_D^{20}$ = + 75 (c = 1.0, THF) for > 99% *ee* product). The compound can be recrystallised form *n*-heptane to provide white cotton-like crystals with Mp = 163.2 – 164.1 °C (decomp).

(*R*a)-2,2'-bis(trifluoromethanesulfonate)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl (85)

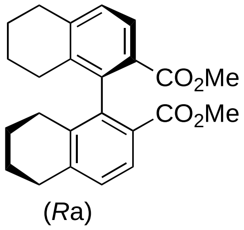


The title compound was prepared following a procedure for triflation of BINOL.[3]

The synthesis was performed in a dry two-neck flask (100 mL) equipped with a magnetic stirring bar and an additional funnel under nitrogen atmosphere. (*R*a)-H_8-BINOL (10.2 mmol, 3.0 g, 1.0 equiv) and freshly distilled under KOH pyridine (25.5 mmol, 2.1 mL, 2.5 equiv) were dissolved in dry dichloromethane (30 mL) and the solution was cooled down to 0 °C with an ice bath. Trifluoromethanesulfonic anhydride (Tf_2O) (22.5 mmol, 3.8 mL, 2.2 equiv) was added dropwise to the solution via additional funnel at 0 °C and the resulting orange mixture was stirred at room temperature for 1h (TLC monitoring). ~1M HCl (50 mL) and dichloromethane (20 mL) were added and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with 10% aqueous solution of $NaHCO_3$ (50 mL), brine (50 mL) and dried under Na_2SO_4. Evaporation of the solvent under reduced pressure provided crude product, which was recrystallised form *n*-hexane. Yield 87% (4.95 g). Colourless rhombic crystals. Mp = 120.7 – 121.5 °C. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 1.62 – 1.90 (m, 8H), 2.19 – 2.50 (m, 4H), 2.77 – 2.93 (m, 4H), 7.15 (d, 2H, $C^{ar}H$, *J* = 8.6 Hz), 7.22 (d, 2H, $C^{ar}H$, *J* = 8.6 Hz) ppm.

The procedure can be easily scaled up on a multigram scale.

(*R*a)-Dimethy-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl-2,2'-dicarboxylate[4] (86)



A dried Schlenk tube for high-pressure reactions containing a magnetic stir bar was charged with $Pd(OAc)_2$ (0.59 mmol, 133 mg, 15 mol%), dppp (0.59 mmol, 244 mg, 15 mol%) and powdered (*R*a)-2,2'-bis(trifluoromethanesulfonate)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl (3.94 mmol, 2.20 g, 1.0 equiv). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with nitrogen (this sequence was repeated three times). Dry MeOH (197 mmol, 8 mL, 50 equiv), Hünig's base (17.33 mmol, 3 mL, 4.4 equiv) and DMSO (20 mL), were added through the septum *via* syringe and the resulting orange-red mixture was stirred for few minutes. The rubber septum was very fast changed to a monometer under strong stream of nitrogen. The system was carefully flashed with CO under the stirring for two minutes, filled with CO until 1.5 bar and the pressure was dropped to almost 0 bar (this procedure was repeated five times to fully fill the system with CO and remove nitrogen and traces of air form the solution). During this sequence the mixture became dark. The CO pressure in the Schlenk tube was increased to 2 bar and the sealed system was putted into a pre-heated oil bath at 80 °C. The resulting mixture was stirred under ~2-2.5 bar (constantly) at 80 ^{o}C for three days until complete consumption of all starting material. The reaction was allowed to cool to room temperature and, after releasing the pressure, the system was purged with nitrogen. Water (100 mL) and EtOAc (50 mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with brine (50 mL) and dried over anhydrous $MgSO_4$. The filtered solution was concentrated *in vacuo* and purified by column chromatography on silica gel (EtOAc/*n*-hexane 1:5) to afford a white solid (1.3 g, 87 %). Mp = 103.5 – 104.3 ^{o}C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.58 – 1.80 (m, 8H), 1.92 – 2.25 (m, 4H), 2.76 – 2.95 (m, 4H), 3.56 (s, 6H, 2 × CH_3), 7.12 (d, 2H, C^{ar}H, *J* = 8.1 Hz), 7.75 (d, 2H, C^{ar}H, *J* = 7.8 Hz) ppm.

Important notes:

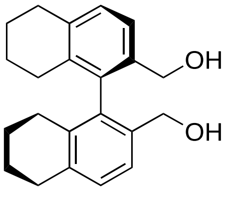
All liquid components in this reaction have to be dry. Anhydrous MeOH was prepared by refluxing overnight under Mg scobs with iodine and used immidiately. DMSO was stirred at 140 ^{o}C with CaH_2 under nitrogen atmosphere for several hours, then distiled in vacuum and stored overnight under activated molecular seaves 3 and 4Å. Dry diisopropylethylamine (Hünig’s base) was obtained after refluxing under CaH_2 for few hours, subsequent distilation in nitrogen atmosphere and keeping under activated molecular seaves 3 and 4Å for overnight.

During all reaction time the CO pressure must be keeped constantly at 2-2.5 bar to obtaine exclusively diester formation. Low CO pressure and(or) using non-anhydrous solvents significantly decrease the yield in this reaction.

The synthesis can be easily scaled up on a multigram scale.

Reaction on 8 g of starting bistriflate

(*R*a)-5,5′,6,6′,7,7′,8,8′-Octahydro-1,1′-binaphthyl-2,2′-dimethanol (87)



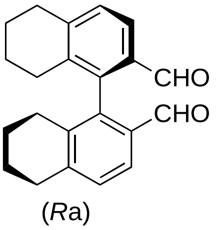
(*R*a)

To a suspension of $LiAlH_4$ (6.66 mmol, 0.25 g, 2.0 equiv) in dry diethyl ether (30 mL) (*R*a)-2,2'-bis(carbomethyl)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl was added as a solid by small portions at 0 °C. After the addition, the resulting mixture was stirred at room temperature for 0.5 h, refluxed for 0.5 h and recooled to 0 °C. Water (20 mL) was added carefully via an additional funnel and concentrated HCl was added until the mixture became homogeneous. Diethyl ether (20 mL) was added and the resulting two-phase mixture was separated. The aqueous layer was extracted with ether (2 × 20 mL). The combined organic layers were washed with 10% aqueous solution of $NaHCO_3$ (30 mL), brine (30 mL) and dried under $MgSO_4$. Evaporation of the solvent under reduced pressure provided pure product as a white amorphous solid. 1.06 g (99%).

$[\alpha]_D^{20}$ = + 39.1 (c = 1.0, MeOH). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.6 – 1.8 (m, 8H, CH_2), 1.95 – 2.15 (m, 4H, CH_2), 2.75 – 2.85 (m, 4H, CH_2), 2.88 (s, 2H, OH), 4.06 (d, 2H, CH_2-OH, J = 11.1 Hz), 4.24 (d, 2H, CH_2-OH, J = 11.1 Hz), 7.12 (d, 2H, $C^{ar}H$, J = 7.8 Hz), 7.25 (d, 2H, $C^{ar}H$**,** J = 7.3 Hz) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 22.9, 23.4, 27.9, 30.1, 63.2, 127.3, 129.0, 134.9, 135.7, 137.7, 138.3 ppm. **IR** (neat): 3268 (broad, m), 2924 (m), 2856 (m), 1595 (w), 1434 (m), 1006 (m), 816 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 345.3 $[M+Na]^+$ (25), 305.3 (24), 287.3 (53), 275.3 (100), 259.3

(20), 245.5 (29), 233.3 (60), 205.3 (10). **HRMS-ESI** (+): Calculated for $C_{22}H_{26}O_2Na$ ($[M+Na]^+$) 345.1825, found 345.1834.

(*R*a)-5,5′,6,6′,7,7′,8,8′-Octahydro-1,1′-binaphthyl-2,2′-dicarboxaldehyde (88)



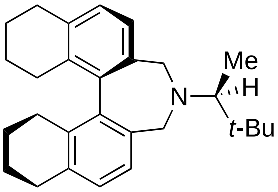
A round-bottomed flask (100 mL), equipped with a magnetic stirring bar, containing PCC (9.6 mmol, 2.06 g, 3.0 equiv) was charged with dry CH_2Cl_2 (15 mL). A solution of substrate (3.2 mmol, 1.03 g, 1.0 equiv) in CH_2Cl_2 (15 mL) was added to the resulting suspension in one portion. The resulting dark mixture was vigorously stirred for 3h at ambient temperature, then diethyl ether (30 mL) was added. The mixture was stirred for 10 minutes, filtered through silica gel plug topped with a layer of Celite, which was then washed with ether. The filtrate was concentrated under reduced pressure to provide a green solid. Subsequent purification by column chromatography on silica gel (EtOAc/*n*-hexane 1:5) gave pure product as a colorless solid (86-89%). **Mp** = 129.5 – 131 °C. The compound can be recrystallised from *n*-hexane to provided colorless needles with **Mp** = 130.8 – 131.7 °C. **R$_f$** = 0.36 (silica gel, EtOAc/*n*-hexane 1:5). **$[\alpha]_D^{20}$** = + 50.6 (c = 1.0, MeOH).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.6 – 1.9 (m, 8H, CH_2), 2.05 – 2.25 (m, 4H, CH_2), 2.85 – 3.0 (m, 4H, CH_2), 7.28 (d, 2H, $C^{ar}H$, J = 8.1 Hz), 7.81 (d, 2H, $C^{ar}H$, J = 7.8 Hz), 9.5 (s, 2H, CHO) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 22.4, 23.0, 27.6, 30.7, 125.2, 129.9, 132.4, 136.2, 140.8, 145.3, 191.6 ppm. **IR** (neat): 2938 (w), 2855 (w), 2832 (w), 2744 (w), 1689 (s), 1582 (s), 1230 (m), 814 (m), 759 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 318 [M^+] (100), 299 (25), 289 (28), 283 (52), 272 (27). **HRMS-ESI** (+): Calculated for $C_{22}H_{23}O_2^+$ ($[M+H]^+$) 319.1692, found 319.1700. **Elemental analysis**: requires C, 82.99; H, 6.96; O, 10.05 %. $C_{22}H_{22}O_2$. Found: C, 82.90; H, 7.04; O, 10.07 %.

General procedure for the synthesis of 5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-derived azepine amines (83a to 83d)

To a suspension of (*R*a)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-dicarboxaldehyde **88** (100 mg, 0.314 mmol, 1.0 equiv) in MeOH (4 mL) the corresponding enantiopure amine (**a** to **d**, 1.1 equiv) was added. After few minutes of stirring, $NaBH_3CN$ (40 mg, 0.628 mmol, 2.0 equiv) and glacial acetic acid (2 drops) were added to the reaction mixture and the resulting colorless solution was stirred for 1 day at ambient temperature. The reaction mixture was quenched by addition of an aqueous solution of NaOH (1M, 25 mL). Diethyl ether (25 mL) was added and the resulting two-phase mixture separated. The aqueous phase was extracted with ether (2 × 15 mL). The combined organic layers were washed with brine (25 mL), dried ($MgSO_4$), filtered, concentrated *in vacuo* and purified by preparative TLC on silica gel plates (20 × 20 cm, 2 mm, EtOAc/*n*-hexane 1:5).

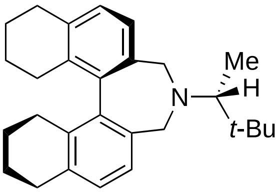
(*R*a)-4,5,8,9,10,11,12,13,14,15-Decahydro-3*H*-4-[(*S*)-3,3-dimethylbutan-2-yl]dinaphth[2,1-*c*:1′,2′-*e*]azepine (83a)



(*R*a,*S*)

Yield 50% (61 mg). Amorphous colorless solid **R_f** = 0.78 (silica gel, EtOAc/*n*-hexane 1:5). **$[\alpha]_D^{20}$** = – 63.3 (c = 1.0, $CHCl_3$). **NMR ^{1}H** (CD_2Cl_2, 500 MHz): δ = 0.87 (s, 9H, *t*-Bu), 1.0 (d, 3H, CH_3, *J* = 6.9 Hz), 1.45 – 1.6 (m, 2H, CH_2), 1.7 – 1.84 (m, 6H, CH_2), 2.08 – 2.17 (m, 2H, CH_2), 2.37 (q, 1H, CH-N, *J* = 6.9 Hz), 2.6 – 2.69 (m, 2H, CH_2), 2.74 – 2.89 (m, 4H, CH_2), 3.21 (d, 2H, Ar-CH_2-N, *J* = 12.3 Hz), 3.42 (d, 2H, Ar-CH_2-N, *J* = 12.3 Hz), 7.03 (s, 4H, $C^{ar}H$) ppm. **NMR ^{13}C** (CD_2Cl_2, 125 MHz): δ = 11.9, 23.4, 23.6, 27.3, 28.3, 30.0, 37.1, 54.2, 68.5, 127.0, 128.7, 134.5, 135.5, 136.6, 138.7 ppm. **IR** (neat): 2931 (w), 2858 (w), 1459 (w), 1349 (w), 1113 (w), 830 (w) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 388.5 [M+1] (61), 304.3 (87), 302.5 (15), 287.3 (66), 274.3 (37), 272.3 (62), 259.3 (70), 247.3 (100), 245.5 (96), 233.3 (31). **HRMS-ESI** (+): Calculated for $C_{28}H_{38}N^+$ ($[M+H]^+$) 388.2998, found 388.2988.

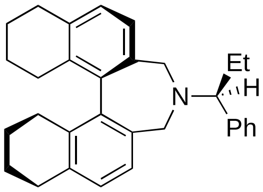
(*R*a)-4,5,8,9,10,11,12,13,14,15-Decahydro-3*H*-4-[(*R*)-3,3-dimethylbutan-2-yl]dinaphth[2,1-*c*:1′,2′-*e*]azepine (83c)



(*R*a,*R*)

Yield 47% (57 mg). Amorphous colorless solid. **R_f** = 0.71 (silica gel, EtOAc/*n*-hexane 1:5). **$[\alpha]_D^{20}$** = – 65.2 (c = 1.0, $CHCl_3$). **^{1}H NMR** (CD_2Cl_2, 500 MHz): δ = 0.76 (d, 3H, CH_3, *J* = 7.3 Hz), 0.88 (s, 9H, *t*-Bu), 1.51 – 1.59 (m, 2H, CH_2), 1.71 – 1.84 (m, 6H, CH_2), 2.12 – 2.22 (m, 2H, CH_2), 2.6 – 2.72 (m, 3H), 2.75 - 2.89 (m, 4H), 3.2 (d, 2H, Ar-CH_2-N, *J* = 12.2 Hz), 3.25 (d, 2H, Ar-CH_2-N, *J* = 12.2 Hz), 7.0 (d, 2H, $C^{ar}H$, *J* = 7.6 Hz), 7.03 (d, 2H, $C^{ar}H$, *J* = 7.6 Hz) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 11.6, 23.3, 23.4, 27.3, 28.1, 29.9, 37.4, 55.5, 69.5, 125.7, 128.5, 134.6, 135.5, 136.6, 138.4 ppm. **IR** (neat): 2925 (m), 2859 (w), 1452 (w), 1376 (w), 1356 (w), 1109 (w), 834 (w) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 388.5 [M+1] (100), 304.3 (78), 289.3 (49), 287.3 (38), 274.3 (11), 272.3 (21), 259.3 (23), 247.3 (36), 245 (35). **HRMS-ESI** (+): Calculated for $C_{28}H_{38}N^+$ ($[M+H]^+$) 388.2998, found 388.2998.

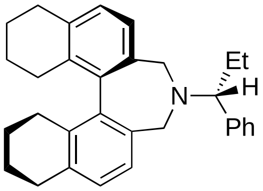
(*R*a)-4,5,8,9,10,11,12,13,14,15-Decahydro-3*H*-4-[(*S*)-1-phenylpropyl]dinaphth[2,1-*c*:1´,2´-*e*]azepine (83b)



(*R*a,*S*)

Yield 76% (100 mg). Amorphous colorless solid. **R_f** = 0.46 (silica gel, EtOAc/*n*-hexane 1:5). **$[\alpha]_D^{20}$** = – 128.5 (c = 1.0, $CHCl_3$). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.63 (t, 3H, CH_3, *J* = 7.2 Hz), 1.45 – 1.6 (m, 2H, CH_2), 1.65 – 1.85 (m, 7H, CH_2), 2.07 – 2.23 (m, 3H, CH_2), 2.6 – 2.95 (m, 8H, CH_2), 3.05 (dd, 1H, CH-N, *J* = 9.4 Hz, *J* = 3.0 Hz), 3.48 (d, 2H, Ar-CH_2-N, *J* = 12.4 Hz), 6.94 (d, 2H, C^{ar}H, *J* = 7.6 Hz), 7.02 (d, 2H, C^{ar}H, *J* = 7.6 Hz), 7.1 – 7.35 (m, 5H, C^{ar}H) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 10.4, 23.3, 23.4, 28.2, 28.3, 30.0, 52.7, 68.7, 126.4, 127.2, 128.3, 128.5, 129.1, 132.9, 135.9, 137.2, 138.9, 143.9 ppm. **IR** (neat): 2929 (m), 2858 (w), 1599 (w), 1450 (w), 1333 (w), 1094 (w), 815 (m), 701 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 422.3 [M+1] (99), 304.3 (100), 302.3 (25), 289.3 (41), 287.3 (30), 272.3 (13), 259.3 (15), 247 (18), 245.3 (21). **HRMS-ESI** (+): Calculated for $C_{31}H_{36}N^+$ ($[M+H]^+$) 422.2842, found 422.2855.

(*R*a)-4,5,8,9,10,11,12,13,14,15-Decahydro-3*H*-4-[(*R*)-1-phenylpropyl]dinaphth[2,1-*c*:1´,2´-*e*]azepine (83d)



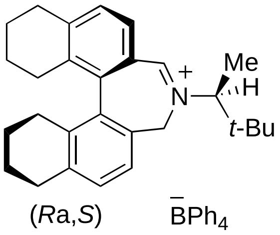
(*R*a,*R*)

After purification by preparative TLC the product was precipitated from MeOH. Yield 58%. Colorless solid, **Mp** = 174.5 – 180 ^{o}C. **R_f** = 0.55 (silica gel, EtOAc/*n*-hexane 1:5). **$[\alpha]_D^{20}$** = – 27.9 (c = 1.0, $CHCl_3$). **^{1}H NMR** (CD_2Cl_2, 500 MHz): δ = 0.55 (t, 3H, CH_3, *J* = 7.4 Hz), 1.45 – 1.67 (m, 3H, CH_2), 1.71 – 1.9 (m, 7H, CH_2), 2.12 – 2.23 (m, 2H, CH_2), 2.62 – 2.71 (m, 2H, CH_2), 2.73 (d, 2H, Ar-CH_2-N, *J* = 12.3 Hz), 2.77 – 2.9 (m, 4H, CH_2), 3.13 (dd, 1H, CH-N, *J* = 9.5 Hz, J = 3.8 Hz), 3.48 (d, 2H, Ar-CH_2-N, *J* = 12.3 Hz), 6.95 (d, 2H, C^{ar}H, *J* = 7.6 Hz), 7.05 (d, 2H, C^{ar}H, *J* = 7.6 Hz), 7.21 – 7.27 (m, 1H, C^{ar}H), 7.3 – 7.39 (m, 4H, C^{ar}H) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 10.5, 23.4, 23.5, 27.6, 28.3, 30.0, 53.1, 68.6, 126.7, 127.2, 128.3, 128.7, 129.3, 132.8, 136.1, 137.3, 138.9, 144.7 ppm. **IR** (neat): 2926 (m), 2860 (w), 1599 (w), 1454 (m), 1351 (w), 1328 (w), 1096 (w), 816 (m), 700 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 422.5 [M+1] (90), 304.3 (100), 289.3 (44), 287.3 (27), 259.3 (13), 247.3 (16). **HRMS-ESI** (+): Calculated for $C_{31}H_{36}N^+$ ($[M+H]^+$) 422.2842, found 422.2852.

General procedure for the synthesis of the 5,5′,6,6′,7,7′,8,8′-Octahydro-1,1′-binaphthyl-derived azepinium BPh_4 salts ([71a][BPh_4] to [71d][BPh_4])

To a solution of substrate in CH_2Cl_2 (5 mL for 200 mg of starting tertiary amine) NBS (1.0 equiv) was added by small portions (exothermic reaction). The resulting deep yellow solution was stirred for 5 min at ambient temperature. A solution of sodium tetraphenylborate (1.0 equiv in 2 mL of MeCN) was added in one portion, and the resulting mixture was stirred for 5 min. The suspension was diluted with CH_2Cl_2 (15 mL), washed twice with water (2 × 15 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was purified by trituration/recrystallization from ethanol. The resulting salts were dried in high vacuum at 80 °C.

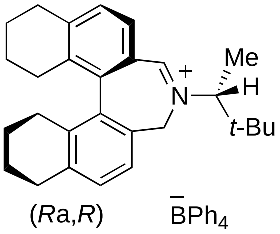
(*R*a)-4-[(*R*)-3,3-dimethylbutan-2-yl]-8,9,10,11,12,13,14,15-octahydro-3*H*-dinaphth[2,1-*c*:1´,2´-*e*]azepinium tetraphenylborate ([71a][BPh_4])



361 mg of desire product was prepared starting from 361 mg of substrate. Recrystallized from ethanol. Yield 48%. Yellow amorphous solid. **$[\alpha]_D^{20}$** = – 406.1 (c = 1.0, CH_2Cl_2). **^{1}H NMR** (DMSO-*d*$_6$, 500 MHz): δ = 1.0 (s, 9H, *t*-Bu), 1.34 – 1.45 (m, 1H), 1.49 (d, 3H, CH_3, *J* = 6.6 Hz), 1.51 – 1.6 (m, 1H), 1.65 – 1.89 (m, 6H), 1.91 – 2.01 (m, 1H), 2.24 – 2.34 (m, 1H), 2.53 – 2.63 (m, 1H), 2.69 – 3.08 (m, 5H), 4.13 (q, 1H, CH-N, *J* = 6.6), 4.34 (d, 1H, Ar-C*H*H-N, *J* = 13.4 Hz), 4.85 (d, 1H, Ar-CH*H*-N, *J* = 13.4 Hz), 6.78 (t, 4H, $C^{ar}H$, *para* in BPh_4, *J* = 7.2 Hz), 6.91 (t, 8H, $C^{ar}H$, *ortho* in BPh_4, *J* = 7.4 Hz), 7.14 – 7.22 (m, 8H, $C^{ar}H$, *meta* in BPh_4), 7.25 (d, 1H, $C^{ar}H$, *J* = 7.9 Hz), 7.46 (d, 1H, $C^{ar}H$, *J* = 8 Hz), 7.49 (d, 1H, $C^{ar}H$, *J* = 7.9 Hz), 7.74 (d, 1H, $C^{ar}H$, *J* = 8 Hz), 9.23 (s, 1H, *H*C=N) ppm. **^{13}C NMR** (DMSO-*d*$_6$, 125 MHz): δ = 13.0 (CH_3), 21.4 (CH_2), 21.72 (CH_2), 21.73 (CH_2), 21.9 (CH_2), 26.4 (CH_3), 27.2 (CH_2), 27.3 (CH_2), 28.8 (CH_2), 29.4 (CH_2), 35.5 (C quat.), 52.3 (Ar-CH_2-N), 76.7 (CH-N), 121.5 (CH), 125.2 (CH), 126.0 (CH), 126.2 (C quat.), 128.8 (CH), 129.1 (CH), 129.5 (CH), 134.1 (C quat.), 135.3 (C quat.), 135.5 (CH), 136.6 (C quat.), 138.5 (C quat.), 138.9 (C quat.), 139.9 (C quat.), 145.4 (C quat.), 163.3 (4 x C quat., q, *J* = 49 Hz, C-B *ipso* in BPh_4), 170.1 (H*C*=N) ppm. **IR** (neat): 3055 (w), 2935 (w), 1621 (w), 1577 (w), 1478 (w), 1426 (w), 1382 (w), 1308 (w), 1246 (w), 1121 (w), 844 (w), 731 (m), 702 (m)

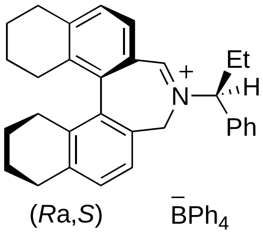
cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 386.5 [$C_{28}H_{36}N^+$] (100), 302.1 (36). **MS-ES** (-) *m/z* (rel intensity): 320.3 [M+1] (30), 319.3 [BPh_4^-] (100), 318.3 [M-1] (27). **HRMS-ESI** (+): Calculated for $C_{28}H_{36}N$ 386.2842, found 386.2835. **Elemental analysis**: requires C, 88.49; H, 8.00; N, 1.98 %. $C_{52}H_{56}NB$. Found: C, 88.31; H, 8.08; N, 2.00 %.

(*R*a)-4-[(*R*)-3,3-dimethylbutan-2-yl]-8,9,10,11,12,13,14,15-octahydro-3*H*-dinaphth[2,1-*c*:1´,2´-*e*]azepinium tetraphenylborate ([71c][BPh$_4$])



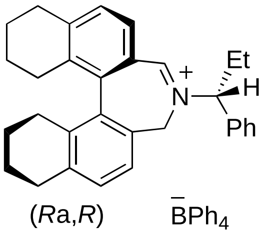
210 mg of desire product was prepared starting from 202 mg of substrate. Refluxed in ethanol for purification. Yield 57%. Shiny amorphous yellow solid. **[α]$_D^{20}$** = – 482.5 (c = 1.0, CH_2Cl_2). **^{1}H NMR** (DMSO-*d$_6$*, 500 MHz): δ = 0.98 (s, 9H, *t*-Bu), 1.22 – 1.44 (m, 4H), 1.48 – 1.6 (m, 1H), 1.64 – 2.2 (m, 7H), 2.24 – 2.35 (m, 1H), 2.57 – 2.67 (m, 1H), 2.71 – 3.1 (m, 5H), 4.33 – 4.55 (m, 2H, Ar-C*H*H-N, CH-N), 4.91 (d, 1H, Ar-CH*H*-N, *J* = 13.2 Hz), 6.78 (t, 4H, C^{ar}H, *para* in BPh_4, *J* = 7.2 Hz), 6.92 (t, 8H, C^{ar}H, *ortho* in BPh_4, *J* = 7.4 Hz), 7.14 – 7.23 (m, 8H, C^{ar}H, *meta* in BPh_4), 7.27 (d, 1H, C^{ar}H, *J* = 7.9 Hz), 7.49 (d, 1H, C^{ar}H, *J* = 8.2 Hz), 7.53 (d, 1H, C^{ar}H, *J* = 7.9 Hz), 7.76 (d, 1H, C^{ar}H, *J* = 8.2 Hz), 9.25 (s, 1H, *H*C=N) ppm. **^{13}C NMR** (DMSO-*d$_6$*, 125 MHz): δ = 15.9 (CH_3), 21.4 (CH_2), 21.6 (CH_2), 21.7 (CH_2), 21.9(CH_2), 26.1 (CH_3), 27.2 (CH_2), 27.3 (CH_2), 28.7 (CH_2), 29.4 (CH_2), 35.7 (C quat.), 59.5, 74.9, 59.5 (Ar-CH_2-N), 74.9 (CH-N), 121.4 (CH), 125.2 (CH), 126.6 (C quat.), 128.7 (CH), 129.4 (CH), 129.6 (CH), 133.4 (C quat.), 135.1 (C quat.), 135.5 (CH), 137.0 (C quat.), 138.4 (C quat.), 139.1 (C quat.), 139.9 (C quat.), 145.5 (C quat.), 163.3 (4 x C quat., q, *J* = 49 Hz, C-B *ipso* in BPh_4), 168.5 (H*C*=N) ppm. **IR** (neat): 3055 (w), 2936 (w), 1620 (w), 1576 (w), 1478 (w), 1426 (w), 1310 (w), 1247 (w), 1118 (w), 844 (w), 731 (m), 701 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 386.4 [$C_{28}H_{36}N^+$] (100), 302.4 (45). **MS-ES** (-) *m/z* (rel intensity): 320.4 [M+1] (31), 319.3 [BPh_4^-] (100), 318.1 [M-1] (29). **HRMS-ESI** (+): Calculated for $C_{28}H_{36}N$ 386.2842, found 386.2841. **Elemental analysis**: requires C, 88.49; H, 8.00; N, 1.98 %. $C_{52}H_{56}NB$. Found: C, 88.33; H, 8.05; N, 2.02 %.

(*R*a)- 8,9,10,11,12,13,14,15-Octahydro-3*H*-4-[(*S*)-1-phenylpropyl]dinaphth[2,1-*c*:1´,2´-*e*]azepinium tetraphenylborate ([71b][BPh$_4$])



545 mg of desire compound was prepared starting from 509 mg of substrate. Recrystallized from ethanol. Yield 61%. Pale amorphous yellow solid. **[α]$_D$^{20}** = – 426.4 (c = 1.0, CH_2Cl_2). **^{1}H NMR** (DMSO-*d*$_6$, 500 MHz): δ = 0.62 (t, 3H, CH_3, *J* = 7.1 Hz), 1.3 – 1.41 (m, 1H), 1.44 – 1.55 (m, 1H), 1.61 – 1.87 (m, 6H), 1.9 – 2.02 (m, 1H), 2.17 – 2.4 (m, 3H), 2.54 – 2.64 (m, 1H), 2.66 – 3.08 (m, 5H), 4.07 (d, 1H, Ar-C*H*H-N, *J* = 13.7 Hz), 4.68 (d, 1H, Ar-CH*H*-N, *J* = 13.7 Hz), 5.36 (t, 1H, CH-N, *J* = 7.6 Hz), 6.78 (t, 4H, $C^{ar}H$, *para* in BPh_4, *J* = 7.2 Hz), 6.92 (t, 8H, $C^{ar}H$, *ortho* in BPh_4, *J* = 7.4 Hz), 7.09 (d, 1H, $C^{ar}H$, *J* = 7.9 Hz), 7.14 (d, 1H, $C^{ar}H$, *J* = 7.9 Hz), 7.17 – 7.27 (m, 8H, $C^{ar}H$, *meta* in BPh_4), 7.39 – 7.46 (m, 3H, $C^{ar}H$), 7.49 (d, 1H, $C^{ar}H$, *J* = 8.0 Hz), 7.53 – 7.63 (m, 2H, $C^{ar}H$), 7.88 (d, 1H, $C^{ar}H$, *J* = 8.0 Hz), 9.56 (s, 1H, *H*C=N) ppm. **^{13}C NMR** (DMSO-*d*$_6$, 125 MHz): δ = 10.0 (CH_3), 21.3 (CH_2), 21.7 (CH_2), 21.9 (CH_2), 23.6 (CH_2), 27.1 (CH_2), 27.2 (CH_2), 28.7 (CH_2), 29.5 (CH_2), 53.5 (Ar-CH_2-N), 76.4 (CH-N), 121.5 (CH), 125.2 (CH), 125.4 (CH), 126.2 (C quat.), 128.3 (CH), 128.8 (CH), 129.0 (CH), 129.3 (CH), 129.4 (CH), 129.8 (CH), 133.5 (C quat.), 134.6 (C quat.), 135.0 (C quat.), 135.5 (CH), 136.6 (C quat.), 138.6 (C quat.), 138.7 (C quat.), 140.2 (C quat.), 145.8 (C quat.), 163.3 (4 x C quat., q, *J* = 49 Hz, C-B *ipso* in BPh_4), 167.7 (H*C*=N) ppm. **IR** (neat): 3055 (w), 2936 (w), 1633 (w), 1579 (w), 1478 (w), 1454 (w), 1429 (w), 1307 (w), 1246 (w), 1134 (w), 848 (w), 731 (m), 702 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 420.3 [$C_{31}H_{34}N^+$] (100), 302.3 (57), 275.3 (21). **MS-ES** (-) *m/z* (rel intensity): 320.5 [M+1] (33), 319.5 [BPh_4^-] (100), 318.5 [M-1] (30). **HRMS-ESI** (+): Calculated for $C_{31}H_{34}N$ 420.2685, found 420.2693. **Elemental analysis**: requires C, 89.29; H, 7.36; N, 1.89 %. $C_{55}H_{54}NB$. Found: C, 88.29; H, 7.50; N, 1.96 % for $C_{55}H_{54}NB$ 0.5 H_2O.

(*R*a)- 8,9,10,11,12,13,14,15-Octahydro-3*H*-4-[(*R*)-1-phenylpropyl]dinaphth[2,1-*c*:1´,2´-*e*]azepinium tetraphenylborate ([71d][BPh$_4$])



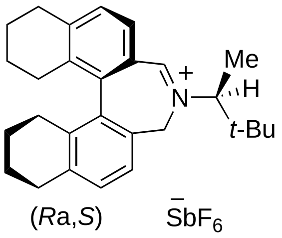
432 mg of desire product was prepared starting from 432 mg of substrate. Recrystallized from ethanol. Yield 48%. Shiny amorphous colorless solid. **[α]$_D$^{20}** = – 369.7 (c = 1.0, CH_2Cl_2). **NMR ^{1}H** (DMSO-*d*$_6$, 500 MHz): δ = 0.85 (t, 3H, CH_3, *J* = 7.2 Hz), 1.3 – 1.42 (m, 1H), 1.46 – 1.57 (m, 1H), 1.6 – 1.87 (m, 6H),

1.89 – 1.99 (m, 1H), 2.2 – 2.4 (m, 3H), 2.53 – 2.81 (m, 4H), 2.86 – 3.08 (m, 2H), 4.15 (d, 1H, Ar-C*H*H-N, *J* = 13.5 Hz), 4.66 (d, 1H, Ar-CH*H*-N, *J* = 13.5 Hz), 5.31 (t, 1H, CH-N, *J* = 7.6 Hz), 6.46 (d, 1H, $C^{ar}H$), 6.79 (t, 4H, $C^{ar}H$, *para* in BPh_4, *J* = 7.2 Hz), 6.92 (t, 8H, $C^{ar}H$, *ortho* in BPh_4, *J* = 7.4 Hz), 7.15 – 7.25 (m, 8H, $C^{ar}H$, *meta* in BPh_4), 7.39 – 7.47 (m, 3H, $C^{ar}H$), 7.49 (d, 1H, $C^{ar}H$, *J* = 7.9 Hz), 7.52 – 7.59 (m, 2H, $C^{ar}H$), 7.87 (d, 1H, $C^{ar}H$, *J* = 7.9 Hz), 9.53 (s, 1H, *H*C=N) ppm. **NMR ^{13}C** (DMSO-d_6, 125 MHz): δ = 10.1 (CH_3), 21.3 (CH_2), 21.6 (CH_2), 21.7 (CH_2), 21.9 (CH_2), 23.8 (CH_2), 27.1 (CH_2), 27.3 (CH_2), 28.7 (CH_2), 29.4 (CH_2), 53.0 (Ar-CH_2-N), 75.2 (CH-N), 121.5 (CH), 124.8 (CH), 125.2 (CH), 126.3 (C quat.), 128.6 (CH), 128.8 (CH), 128.9 (CH), 129.2 (CH), 129.5 (CH), 129.6 (CH), 133.6 (C quat.), 134.3 (C quat.), 134.5 (C quat.), 135.5 (CH), 136.5 (C quat.), 138.6 (C quat.), 138.7 (C quat.), 140.2 (C quat.), 145.7 (C quat.), 163.3 (4 x C quat., q, *J* = 49 Hz, C-B *ipso* in BPh_4), 167.7 (H*C*=N) ppm. **IR** (neat): 3055 (w), 2931 (w), 1626 (w), 1579 (w), 1454 (w), 1423 (w), 1305 (w), 1246 (w), 1137 (w), 848 (w), 733 (m), 701 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 420.1 [$C_{31}H_{34}N^+$] (100), 302.3 (60), 275.3 (64). **MS-ES** (-) *m/z* (rel intensity): 320.5 [M+1] (34), 319.5 [BPh_4^-] (100), 318.5 [M-1] (29). **HRMS-ESI** (+): Calculated for $C_{31}H_{34}N$ 420.2685, found 420.2672. Elemental analysis: requires C, 89.29; H, 7.36; N, 1.89 %. $C_{55}H_{54}NB$. Found: C, 89.03; H, 7.47; N, 1.90 %.

General procedure for the synthesis of 5,5′,6,6′,7,7′,8,8′-Octahydro-1,1′-binaphthyl-derived azepinium SbF_6 salts ([71a][SbF_6] and [71c][SbF_6])

To a solution of substrate in CH_2Cl_2 (2 mL for 100 mg of starting tertiary amine), NBS (1.0 equiv) was added by small portions (exothermic reaction). The resulting deep yellow solution was stirred for 5 min at ambient temperature. A solution of sodium hexafluoroantimonate (1.0 equiv in 1.0 mL of acetone) was added in one portion, and the resulting mixture was stirred for 5 min. The suspension was diluted with CH_2Cl_2 (15 mL), water (15 mL) and the resulting two-phase mixture separated. The aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated in vacuum. The crude product was purified by trituration from ethanol. The resulting salts were filtered, washed with a small amount of ethanol, diethyl ether, *n*-pentane and dried in high vacuum at 70 °C for at least one day.

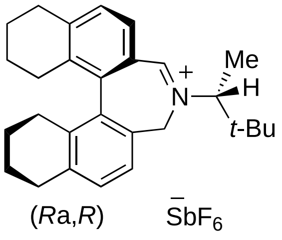
(*R*a)-4-[(*S*)-3,3-dimethylbutan-2-yl]-8,9,10,11,12,13,14,15-octahydro-3*H*-dinaphth[2,1-*c*:1´,2´-*e*]azepinium hexafluoroantimonate ([71a][SbF$_6$])



106 mg (66% yield) of the desired product was prepared starting from 100 mg of substrate. Yield 81% (211 mg) starting from 163 mg of substrate. White amorphous solid. **[α]$_D^{20}$** = – 502.9 (c = 0.5, CH$_2$Cl$_2$). **^{1}H NMR** (CD$_2$Cl$_2$, 500 MHz): δ = 1.08 (s, 9H, *t*-Bu), 1.4 -1.52 (m, 1H), 1.57 (d, 3H, CH$_3$, *J* = 6.9 Hz), 1.59 – 1.69 (m, 1H), 1.73 – 1.96 (m, 6H), 1.98 – 2.07 (m, 1H), 2.32 – 2.42 (m, 1H), 2.56 – 2.65 (m, 1H), 2.75 – 3.11 (m, 5H), 4.07 – 4.22 (m, 2H, CH-N, Ar-C*H*H-N), 4.71 (dd, 1H, Ar-CH*H*-N, *J* = 13.2 Hz, *J* = 0.9 Hz), 7.22 (d, 1H, C^{ar}H, *J* = 7.9 Hz), 7.25 (d, 1H, C^{ar}H, *J* = 7.9 Hz), 7.42 (d, 1H, C^{ar}H, *J* = 7.9 Hz), 7.63 (d, 1H, C^{ar}H, *J* = 7.9 Hz), 8.68 (s, 1H, *H*C=N) ppm. **^{13}C NMR** (CD$_2$Cl$_2$, 125 MHz): δ = 14.3 (CH$_3$), 22.3 (CH$_2$), 22.7 (CH$_2$), 22.8 (CH$_2$), 27.0 (C(*C*H$_3$)$_3$), 28.3 (CH$_2$), 30.0 (CH$_2$), 30.8 (CH$_2$), 36.6 (*C*(CH$_3$)$_3$), 54.8 (Ar-CH$_2$-N, broad), 78.9 (CH-N), 125.8 (CH), 126.1 (C quat.), 129.9 (CH), 130.0 (CH), 130.8 (CH), 134.4 (C quat.), 134.7 (C quat.), 138.8 (C quat.), 140.3 (C quat.), 141.1 (C quat.), 141.5 (C quat.), 148.2 (C quat.), 169.4 (H*C*=N) ppm. Two signals of CH$_2$ group are missing. **IR** (neat): 2943 (w), 2868 (w), 1625 (m), 1576 (w), 1445 (w), 1372 (w), 1310 (w), 1245 (w), 1222 (w), 1124 (w), 1101 (w), 835 (w), 820 (w), 653 (s) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 386.1 [C$_{28}$H$_{36}$N$^+$] (100), 302.1 (90). **MS-ES** (-) *m/z* (rel intensity): 236.8 [^{123}SbF$_6^-$] (80), 234.9 [^{121}SbF$_6^-$] (100), 217.9 [^{123}SbF$_5^-$] (11) , 215.9 [^{121}SbF$_5^-$] (15), 198.8 [^{123}SbF$_4^-$] (32), 196.6 [^{121}SbF$_4^-$] (42). **HRMS-ESI** (+): Calculated for C$_{28}$H$_{36}$N 386.2842, found 386.2823.

Elemental analysis: requires C, 54.04; H, 5.83; N, 2.25; F, 18.32 %. C$_{28}$H$_{36}$NF$_6$Sb. Found: C, 54.12; H, 5.85; N, 2.23; F, 18.09 %.

(*R*a)-4-[(*R*)-3,3-dimethylbutan-2-yl]-8,9,10,11,12,13,14,15-octahydro-3*H*-dinaphth[2,1-*c*:1´,2´-*e*]azepinium hexafluoroantimonate ([71c][SbF$_6$])

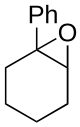


108 mg (67% yield) of the desired product was prepared starting from 100 mg of substrate. Yield 87% (400 mg) starting from 286 mg of substrate. White amorphous solid. **[α]$_D^{20}$** = – 573.1 (c = 0.5, CH$_2$Cl$_2$). **^{1}H NMR** (CD$_2$Cl$_2$, 500 MHz): δ = 1.05 (s, 9H, *t*-Bu), 1.44 (d, 3H, CH$_3$, *J* = 6.9 Hz), 1.45 – 1.51 (m, 1H), 1.55 – 1.66 (m, 1H), 1.73 – 1.96 (m, 6H), 1.99 – 2.08 (m, 1H), 2.31 – 2.41 (m, 1H), 2.56 - 2.67

(m, 1H), 2.75 – 3.12 (m, 5H), 4.17 (q, 1H, CH-N, J = 7.0 Hz), 4.35 (d, 1H, Ar-C*H*H-N, *J* = 13.1 Hz), 4.61 (dd, 1H, Ar-CH*H*-N, *J* = 13.1 Hz, *J* = 0.9 Hz), 7.26 (d, 1H, $C^{ar}H$, *J* = 7.8 Hz), 7.32 (d, 1H, $C^{ar}H$, *J* = 7.8 Hz), 7.44 (d, 1H, $C^{ar}H$, *J* = 7.9 Hz), 7.66 (d, 1H, $C^{ar}H$, *J* = 7.9 Hz), 8.58 (s, 1H, *H*C=N) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 16.7 (CH_3), 22.3 (CH_2), 22.7 (CH_2), 22.8 (CH_2), 26.9 ($C(CH_3)_3$), 28.3 (CH_2), 28.4 (CH_2), 30.0 (CH_2), 30.9 (CH_2), 36.7 ($C(CH_3)_3$), 60.6 (Ar-CH_2-N, broad), 78.1 (CH-N), 125.5 (CH), 126.6, 129.9 (CH), 130.0 (CH), 130.8 (CH), 134.2 (C quat.), 134.4 (C quat.), 139.0 (C quat.), 140.3 (C quat.), 141.3 (C quat.), 141.7 (C quat.), 148.4 (C quat.), 168.0 (H*C*=N) ppm. One signal of CH_2 group is missing. **IR** (neat): 2940 (w), 2863 (w), 1628 (m), 1577 (w), 1445 (w), 1372 (w), 1336 (w), 1307 (w), 1243 (w), 1221 (w), 1091 (w), 835 (w), 820 (w), 650 (s) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 386.3 [$C_{28}H_{36}N^+$] (89), 302.1 (100). **MS-ES** (-) *m/z* (rel intensity): 236.8 [$^{123}SbF_6^-$] (80), 234.9 [$^{121}SbF_6^-$] (100), 217.9 [$^{123}SbF_5^-$] (8) , 215.9[$^{121}SbF_5^-$] (11), 198.9 [$^{123}SbF_4^-$] (30), 196.6 [$^{121}SbF_4^-$] (40). **HRMS-ESI** (+): Calculated for $C_{28}H_{36}N$ 386.2842, found 386.2831. **Elemental analysis**: requires C, 54.04; H, 5.83; N, 2.25; F, 18.32 %. $C_{28}H_{36}NF_6Sb$. Found: C, 54.17; H, 5.81; N, 2.25; F, 18.26 %.

Data for epoxides derived from unfunctionalized alkenes and allylic alcohols

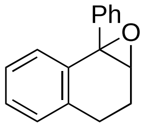
(–)-(1*S*,2*S*)-1-Phenylcyclohex-1-ene oxide[5]



Starting from 31.6 mg of 1-phenylcyclohexene, 29.6 mg (85% isolated yield) of the resulting epoxide was prepared as a colorless oil. Purification – filtration through silica gel plug eluted with pentane/Et_2O/Et_3N - 100:4:1. **$[\alpha]_D^{25}$** = – 58.8 (c = 1.0, $CHCl_3$, 92% *ee*). [lit.[5] $[\alpha]_D^{35}$ = – 75.5 (c = 0.7, $CHCl_3$) for > 99 % *ee* epoxide with absolute configuration (1*S*,2*S*)]. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.24 – 1.7 (m, 4H), 1.94 – 2.2 (m, 3H), 2.25 – 2.37 (m, 1H), 3.10 (s, 1H, CH), 7.24- 7.43 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 19.9 (CH_2), 20.2 (CH_2), 24.8 (CH_2), 29.0 (CH_2), 60.3 (C quat.), 62.1 (CH), 125.4 (CH), 127.3 (CH), 128.4 (CH), 142.6 (C quat.) ppm.

CSP-GC separation: Chiraldex Hydrodex β-3P column: T_{inj} = 250 °C, P = 0.842 bar, 80 °C for 5 min, then gradient 5°C/min up to 180 °C, hold at 180 °C for 5 min); t_R (major) = 20.13 min, t_R (minor) = 20.32 min.

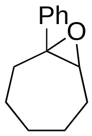
(+)-(1*R*,2*S*)-1-Phenyl-3,4-dihydronaphthalene oxide[6]



Starting from 41.2 mg of 1-phenyl-3,4-dihydronaphthylene, 37 mg (83% isolated yield) of the desired epoxide was prepared as a white solid. Purification – column chromatography on silica gel, eluent pentane/Et_2O/Et_3N - 100:4:1. Single recrystallization from *n*-hexane provided product with 98% *ee*. White crystals, **Mp** = 132.5 – 133.3 °C [lit.[6] 124 – 126 °C]. **$[\alpha]_D^{25}$** = + 53.0 (c = 1.0, $CHCl_3$, 98 % *ee* product). [lit.[6] $[\alpha]_D^{25}$ = – 42.75 (c = 0.95, $CHCl_3$, for 95.2 % *ee* epoxide with absolute configuration (1*S*,2*R*)]. **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 1.97 – 2.10 (m, 1H), 2.41 – 2.51 (m, 1H), 2.69 (dd, 1H, *J* = 15.4 Hz, 5.6 Hz), 2.82-2.96 (m, 1H), 3.59 (d, 1H, CH, *J* = 3.3 Hz), 6.94 (dd, 1H, $C^{ar}H$, *J* = 7.8 Hz, 1.0 Hz), 7.02 – 7.10 (m, 1H, $C^{ar}H$), 7.16 (d, 1H, $C^{ar}H$, *J* = 7.3 Hz), 7.22 (td, 1H, $C^{ar}H$, *J* = 7.4 Hz, *J* = 1.2 Hz), 7.34 – 7.50 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 22.6 (CH_2), 25.9 (CH_2), 60.9 (C quat.), 63.5 (CH), 126.3 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 128.6 (CH), 129.0 (CH), 130.1 (CH), 135.5 (C quat.), 137.9 (C quat.), 139.3 (C quat.) ppm.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 95/5 %, 0.5 mL/min, 23 °C, λ = 230 nm); t_R (minor) = 10.58 min, t_R (major) = 15.40 min.

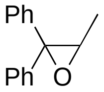
(–)-1-Phenylcyclohept-1-ene oxide[7]



Starting from 34.4 mg of 1-phenylcycloheptene, 34.6 mg (92% isolated yield) of the resulting epoxide was prepared as a pale yellow oil. Purification – filtration through silica gel plug eluted with pentane/Et_2O/Et_3N - 100:4:1. **$[\alpha]_D^{25}$** = – 59.8 (c = 1.0, $CHCl_3$, 83% *ee*). **^{1}H NMR** (CD_2Cl_2, 300 MHz): δ = 1.5 - 1.8 (m, 6H), 1.9 -2.16 (m, 3H), 2.35 – 2.5 (m, 1H), 3.0 (dd, 1H, *J* = 6.3 Hz, *J* = 3.3 Hz), 7.2 – 7.4 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 75 MHz): δ = 25.2 (CH_2), 25.8 (CH_2), 30.1 (CH_2), 31.9 (CH_2), 34.1 (CH_2), 63.5 (CH), 66.0 (C quat.), 125.7 (CH), 127.5 (CH), 128.7 (CH), 144.6 (C quat.) ppm.

CSP-GC separation: Chiraldex Hydrodex β-3P column: T_{inj} = 250 °C, P = 0.842 bar, 80 °C for 5 min, then gradient 1°C/min up to 180 °C, hold at 180 °C for 5 min); t_R (major) = 60.01 min, t_R (minor) = 60.83 min.

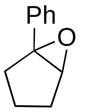
(–)-(*S*)-1,1-Diphenylprop-1-ene oxide[8]



Starting from 38.8 mg of 1,1-diphenylpropene, 40 mg (95 % isolated yield) of the desired epoxide was prepared as a colorless oil. Purification – filtration through silica gel plug eluted with pentane/Et_2O – 25:1. **$[\alpha]_D^{25}$** = **–** 39.9 (c = 1.0, EtOH, 90% *ee*). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 1.15 (d, 3H, CH_3, *J* = 5.6 Hz), 3.47 (q, 1H, CH, *J* = 5.6 Hz), 7.21 – 7.42 (m, 10 H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 15.8 (CH_3), 62.8 (CH), 66.4 (C quat.), 127.4 (CH), 128.0 (CH), 128.1 (CH), 128.7 (CH), 128.8 (CH), 138.2 (C quat.), 141.9 (C quat.) ppm. One $C^{ar}H$ signal is missing due to overlap with other signals.

The enantiomeric excess was determined by ^{1}H-NMR analysis using Eu(hfc)$_3$ as a shift reagent.

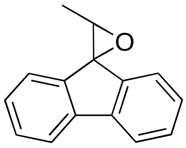
(–)-(1*S*,2*S*)-1-Phenylcyclopent-1-ene oxide[8]



Starting from 28.8 mg of 1-phenylcyclopentene, 27.4 mg (85% isolated yield) of the resulting epoxide was prepared as a colorless oil. Purification – filtration through silica gel plug, eluted with pentane/Et_2O/Et_3N - 100:4:1. **$[\alpha]_D^{20}$** = **–** 47.8 (c = 1.02, $CHCl_3$, 72% *ee*). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.57 – 1.85 (m, 3H), 2.06 – 2.26 (m, 3H), 3.57 (m, 1H, CH), 7.27 – 7.42 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 19.5 (CH_2), 28.2 5 (CH_2), 29.0 5 (CH_2), 66.6 (CH), 67.0 (C quat.), 126.0 (CH), 127.7 (CH), 128.4 (CH), 138.1 (C quat.) ppm.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 99.9/0.1 %, 0.5 mL/min, 23 °C, λ = 210 nm); t_R (major) = 39.49 min, t_R (minor) = 48.39 min.

(–)-(*S*)-9-Ethylidenefluorene oxide[9]

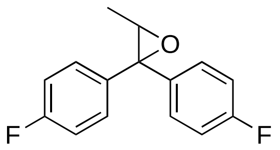


Starting from 38.4 mg of 9-ethylidenefluorene, 39 mg (94 % isolated yield) of the resulting epoxide was prepared as a colorless oil. Purification – preparative TLC on silica gel, eluent *n*-Hexane/Et_2O/Et_3N - 100:4:1. **$[\alpha]_D^{20}$** = **–** 38.7 (c = 1.0, $CHCl_3$, 90% *ee*) [lit.[9] $[\alpha]_D^{23}$ = – 44.2 (c = 1.57, $CDCl_3$) for 95 % *ee* epoxide with absolute configuration (*S*)]. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.7 (d, 3H, CH_3, *J* = 5.3 Hz), 3.87 (q, 1H, CH, *J* = 5.3 Hz), 7.22– 7.48 (m, 6H, $C^{ar}H$), 7.72 (d, 1H, $C^{ar}H$, *J* = 7.6 Hz), 7.76 (d, 1H, $C^{ar}H$, *J* = 7.6 Hz) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 14.8 (CH_3), 62.1

(CH), 66.8 (C quat.), 120.2 (CH), 120.6 (CH), 121.5 (CH), 124.6 (CH), 127.2 (CH), 127.7 (CH), 129.1 (CH), 129.2 (CH), 139.8 (C quat.), 140.4 (C quat.), 141.9 (C quat.), 142.7 (C quat.) ppm.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 95:5 %, 0.5 mL/min, 23 °C, λ = 210 nm); t_R (minor) = 18.70 min, t_R (major) = 20.02 min.

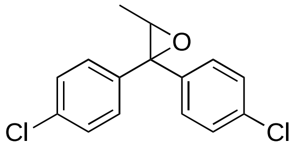
(–)-1,1-Di(4-fluorophenyl)prop-1-ene oxide



Starting from 46 mg of substrate 42.6 mg (87 % isolated yield) of the resulting epoxide was prepared as a colorless oil. Purification – preparative TLC on silica gel, eluent *n*-Hexane/EtOAc - 10:1. **R$_f$** = 0.61 (silica gel, EtOAc/*n*-hexane 1:10). **[α]$_D^{25}$** = – 19.1 (c = 1.0, CH_2Cl_2, 91% *ee*). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 1.14 (d, 3H, CH_3, J = 5.3 Hz), 3.45 (q, 1H, CH, J = 5.3 Hz), 6.95 – 7.13 (m, 4H, $C^{ar}H$), 7.22 – 7.40 (m, 4H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 15.7 (CH_3), 63.0 (CH), 65.5 (C quat.), 115.61 (d, CH, $^2J_{C\text{-}F}$ = 21.9 Hz), 115.64 (d, CH, $^2J_{C\text{-}F}$ = 21.9 Hz), 129.2 (d, CH, $^3J_{C\text{-}F}$ = 8.2 Hz), 130.4 (d, CH, $^3J_{C\text{-}F}$ = 8.2 Hz), 133.9 (d, C quat., $^4J_{C\text{-}F}$ = 2.7 Hz), 137.7 (d, C quat., $^4J_{C\text{-}F}$ = 3.6 Hz), 162.80 (d, C quat., $^1J_{C\text{-}F}$ = 244 Hz), 162.85 (d, C quat., $^1J_{C\text{-}F}$ = 245 Hz) ppm. **^{19}F NMR** (CD_2Cl_2, 282 MHz): δ = - 117.4, - 117.6 pm. **IR** (neat): 2998 (w), 1606 (m), 1509 (s), 1444 (w), 1419 (w), 1373 (w), 1327 (w), 1221 (s), 1156 (m), 832 (s), 614 (m) cm$^-$1. **MS-EI** (*m/z*, %): 246 (18) [M$^+$], 245 (24) [M-1], 203 (19), 202 (90), 201 (100), 200 (19). **HRMS-EI** (*m/z*): Calculated for $C_{15}H_{12}OF_2$ $[M]^+$ 246.0856, found $[M]^+$ 246.0843. Due to overlapping with the 13C-isotope of the M-H fragment, the measured mass of the molecular ion is very low. Therefore the mass of the M-H ion was also measured. Calculated for $C_{15}H_{12}OF_2$ $[M\text{-}H]^+$ 245.0778, found $[M\text{-}H]^+$ 245.0780. **Elemental analysis**: requires C, 73.16; H, 4.91; O, 6.50; F, 15.43 %. $C_{15}H_{12}OF_2$. Found: C, 73.11; H. 5.07; F, 15.48 %.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 99.5/0.5 %, 0.5 mL/min, 23 °C, λ = 210 nm); t_R (minor) = 10.95 min, t_R (major) = 11.82 min.

(–)-1,1-Di(4-chlorophenyl)prop-1-ene oxide

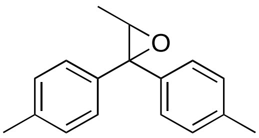


Starting from 52.6 mg of substrate 47 mg (84 % isolated yield) of the resulting epoxide was prepared as a colorless oil. Purification – preparative TLC on silica gel, eluent *n*-

Hexane/EtOAc/Et_3N- 100:10:1. **R_f** = 0.6 (silica gel, EtOAc/*n*-hexane 1:10). **$[\alpha]_D^{25}$** = **–** 22.2 (c = 1.0, $CHCl_3$, 91% *ee*). **^{1}H NMR** (CD_2Cl_2, 300 MHz): δ = 1.15 (d, 3H, CH_3, *J* = 5.4 Hz), 3.45 (quartet, 1H, CH, *J* = 5.4 Hz), 7.20 – 7.42 (m, 8H, C^{ar}H) ppm. **^{13}C NMR** (CD_2Cl_2, 75 MHz): δ = 15.7 (CH_3), 63.1 (CH), 65.5 (C quat.), 128.8 (CH), 128.9 (CH), 129.0 (CH), 130.2 (CH), 134.1 (C quat.), 134.2 (C quat.), 136.3 (C quat.), 140.0 (C quat.) ppm. **IR** (neat): 2996 (w), 2927 (w), 1598 (w), 1489 (m), 1454 (w), 1398 (w), 1090 (m), 1012 (m), 817 (s), 779 (m) cm^{-1}. **MS-EI** (*m/z,* %): 280 (10) [M^+], 279 (12) [M^+], 278 (16) [M^+], 277 (15), 236 (33), 235 (16), 234 (48), 201 (42), 200 (19), 199 (100), 163 (25). **HRMS-EI** (*m/z*): Calculated for $C_{15}H_{12}OCl_2$ $[M]^+$ 278.0265, , found $[M]^+$ 278.0248. **Elemental analysis**: requires C, 64.54; H, 4.33; O, 5.73, Cl, 25.40 %. $C_{15}H_{12}OCl_2$. Found: C, 64.70; H, 4.43; O, 5.83; Cl, 25.28 %.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 99.5/0.5 %, 0.5 mL/min, 23 °C, λ = 230 nm); t_R (minor) = 11.7 min, t_R (major) = 12.64 min.

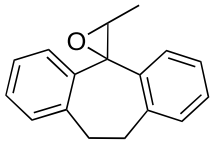
(–)-1,1-Di(4-methylphenyl)prop-1-ene oxide



Starting from 44.4 mg of substrate 32 mg (67 % isolated yield) of the resulting epoxide was prepared as a colourless viscous oil. Purification – preparative TLC on silica gel, eluent *n*-Hexane/EtOAc/Et_3N- 100:4:1. **R_f** = 0.42 (silica gel, eluent *n*-Hexane/EtOAc/Et_3N- 100:4:1). **$[\alpha]_D^{25}$** = **–** 24.2 (c = 1.0, $CHCl_3$, 94% *ee*). **^{1}H NMR** (DMSO-d_6, 300 MHz): δ = 1.06 (d, 3H, CH_3, *J* = 5.3 Hz), 2.26 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 3.48 (quartet, 1H, CH, *J* = 5.3 Hz), 7.07 – 7.25 (m, 8H, C^{ar}H) ppm. **^{13}C NMR** (DMSO-d_6, 75 MHz): δ = 15.3 (CH_3), 20.6 (CH_3), 20.7 (CH_3), 61.2 (CH), 65.3 (C quat.), 126.7 (CH), 127.7 (CH), 128.71 (CH), 128.73 (CH), 134.7 (C quat.), 136.6 (C quat.), 136.8 (C quat.), 138.3 (C quat.) ppm. **IR** (neat): 2963 (w), 2923 (w), 1513 (w), 1447 (w), 1372 (w), 1330 (w), 1108 (w), 1018 (w), 811 (m), 780 (m) cm^{-1}. **MS-ES (+)** *m/z* (rel intensity): 239.3 [M+1] (100), 223.3 (37), 147.3 (19). **HRMS-EI** (*m/z*): Calculated for $C_{17}H_{18}O$ $[M]^+$ 238.1358, , found $[M]^+$ 238.1354. **Elemental analysis:** requires C, 85.67; H, 7.61; O, 6.71 %. $C_{17}H_{18}O$. Found: C, 85.41; H, 7.76; O, 6.93 %.

CSP-HPLC separation: Chiracel OJ column, *n*-Hexane/*i*-PrOH 95:5 %, 0.7 mL/min, 23 °C, λ = 210 nm); t_R (minor) = 12.76 min, t_R (major) = 26.72 min.

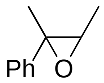
(+)-5-Ethylidene-10,11-dihydro-5H-dibenzo[*a*,*d*]-cycloheptene oxide



Starting from 44 mg of substrate 31 mg of the resulting epoxide was prepared as a white solid. Purification – preparative TLC on silica gel, eluent *n*-Hexane/Et_2O/Et_3N 100:2:1. **R_f** = 0.42 (silica gel, *n*-Hexane/Et_2O/Et_3N 100:2:1). **Mp** = 70.4 – 71.2 °C. **$[\alpha]_D^{25}$** = + 66.5 (c = 1.0, $CHCl_3$, 98% *ee*). **^{1}H NMR** (DMSO-d_6, 300 MHz): δ = 1.0 (d, 3H, CH_3, *J* = 5.3 Hz), 2.80 – 3.0 (m, 2H), 3.19 (quartet, 1H, CH, *J* = 5.3 Hz), 3.21 – 3.44 (m, 2H), 7.07 – 7.45 (m, 8H, $C^{ar}H$) ppm. **^{13}C NMR** (DMSO-d_6, 75 MHz): δ = 13.9 (CH_3), 31.2 (CH_2), 32.1 (CH_2), 63.3 (CH), 63.5 (C quat.), 123.2 (CH), 125.4 (CH), 125.7 (CH), 126.0 (CH), 127.5 (CH), 127.7 (CH), 128.6 (CH), 129.4 (CH), 136.8 (C quat.), 137.6 (C quat.), 138.6 (C quat.), 139.0 (C quat.) ppm. **IR** (neat): 2958 (w), 2933 (w), 2893 (w), 1485 (w), 1442 (w), 1176 (w), 1023 (w), 746 (m) cm^{-1}. **MS-EI** (*m/z*, %): 236 (63) [M^+], 235 (93) [M-1], 193 (17), 192 (72), 191 (100), 190 (30), 189 (43), 165 (32). **HRMS-EI** (*m/z*): Calculated for $C_{17}H_{15}O$ $[M]^+$ 236.1201, found $[M]^+$ 236.1183. Due to overlapping with the 13C-isotope of the M-H fragment, the measured mass of the molecular ion is very low. Therefore the mass of the M-H ion was also measured. Calculated for $C_{17}H_{15}O$ $[M-H]^+$ 235.1123, found $[M-H]^+$ 235.1121. **Elemental analysis**: requires C, 86.41; H, 6.82; O, 6.77 %. $C_{17}H_{16}O$. Found: C, 86.26; H, 6.98; O, 6.71 %.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 95/5 %, 0.5 mL/min, 23 °C, λ = 210 nm), t_R (minor) = 8.5 min, t_R (major) = 11.13 min.

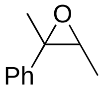
(–)-(2*S*,3*S*)-*trans*-2,3-Dimethyl-2-phenyloxirane[6]



Starting from 26.4 mg of (*E*)-1-methyl-1-phenylpropene, 26.9 mg (91% yield) of the resulting epoxide was prepared as a pale yellow oil. Purification – filtration through silica gel plug eluted with pentane/Et_2O - 25:1. **$[\alpha]_D^{25}$** = – 15.9 (c = 1.0, $CHCl_3$, 90% *ee*) [lit.[10] $[\alpha]_D^{25}$ = – 16.0 (c = 1.0, $CHCl_3$) for >99 % *ee* epoxide with absolute configuration (2*S*,3*S*)]. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.43 (d, 3H, CH_3, *J* = 5.6 Hz), 1.66 (s, 3H, CH_3), 2.95 (q, 1H, CH, *J* = 5.6 Hz), 7.23 – 7.37 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 14.6 (CH_3), 17.5 (CH_3), 60.5 (C quat.), 62.7 (CH), 125.2 (CH), 127.3 (CH), 128.4 (CH), 143.2 (C quat.) ppm.

CSP-GC separation: Chiraldex Hydrodex β-3P column: T_{inj} = 250 °C, P = 0.842 bar, 80 °C for 5 min, then gradient 1°C/min up to 180 °C, hold at 180 °C for 5 min); t_R (minor) = 16.78 min, t_R (major) = 17.04 min.

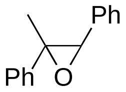
cis-2,3-Dimethyl-2-phenyloxirane[10]



Starting from 26.4 mg of (*Z*)-1-methyl-1-phenylpropene (95% purity), 27.5 mg (93% yield) of the resulting epoxide was prepared as a pale yellow oil. Purification – filtration through silica gel plug eluted with pentane/Et_2O - 25:1. **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 0.94 (d, 3H, CH_3, *J* = 5.3 Hz), 1.61 (s, 3H, CH_3), 3.14 (q, 1H, CH, *J* = 5.3 Hz), 7.23 - 7.38 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 100 MHz): δ = 14.8 (CH_3), 24.8 (CH_3), 61.6 (CH), 62.9 (C quat.), 127.1 (CH), 127.6 (CH), 128.5 (CH), 140.5 (C quat.) ppm.

CSP-GC separation: Chiraldex Hydrodex β-3P column: T_{inj} = 250 °C, P = 0.842 bar, 80 °C for 5 min, then gradient 1°C/min up to 180 °C, hold at 180 °C for 5 min); t_R (major) = 11.48 min, t_R (minor) = 12.45 min. The resulting epoxide containes ~5 % of trance isomer (GC-MS analysis), due to this fact we did not measured it optical rotation.

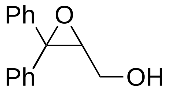
(–)-(1*S*,2*S*)-*trans*-2-Methyl-2,3-biphenyloxirane (*trans*-(〈-methyl)-stilbene oxide)



Starting from 38.8 mg of *trans*-α-methylstilbene, 39.4 mg (94% yield) of the resulting epoxide was prepared as a pale yellow oil. Purification – column chromatography on silica gel eluting with pentane /Et_2O - 25:1. **$[\alpha]_D^{25}$** = – 74.9 (c = 1.0, EtOH, 65% *ee*). [lit. [2] $[\alpha]_D^{25}$ = + 113.9 (c = 0.9, EtOH, for 95.5 % *ee* product with absolute configuration (1*R*,2*R*)]. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.47 (s, 3H, CH_3), 3.98 (s, 1H, CH), 7.28 – 7.50 (m, 10H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 100 MHz): δ = 16.8 (CH_3), 63.2 (CH), 67.3 (C quat.), 125.3 (CH), 126.6 (CH), 127.7 (CH), 127.8 (CH), 128.3 (CH), 128.6 (CH), 136.1 (C quat.), 142.4 (C quat.) ppm.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 95:5 %, 0.5 mL/min, 23 °C, λ = 230 nm); t_R (major) = 10.13 min, t_R (minor) = 21.24 min.

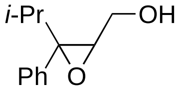
(–)-(*S*)-3,3-Diphenyloxiranemethanol[11]



Starting from 42 mg of 3,3-diphenylprop-2-en-1-ola, 36 mg (80 % isolated yield) of the resulting epoxide was prepared as a yellow viscous oil. Purification – preparative TLC on silica gel, eluent *n*-Hexane/EtOAc- 3:2. **$[\alpha]_D^{25}$** = – 16.6 (c = 0.5, $CHCl_3$, 88% *ee*) [lit.[11] $[\alpha]_D^{25}$ = + 33.8 (c = 0.42, $CHCl_3$) for 94 % *ee* epoxide with absolute configuration (*R*)]. **^{1}H NMR** (CD_2Cl_2, 300 MHz): δ = 1.96 (bs, 1H, OH), 3.3 – 3.42 (m, 1H), 3.55 – 3.72 (m, 2H), 7.25 – 7.45 (m, 10H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 75 MHz): δ = 62.6 (CH_2), 66.2 (CH), 66.5 (C quat.), 127.4 (CH), 128.3 (CH), 128.4 (CH), 128.5 (CH), 128.8 (CH), 128.9 (CH), 137.6 (C quat.), 141.0 (C quat.) ppm.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 95/5 %, 0.5 mL/min, 23 °C, λ = 210 nm); t_R (major) = 35.09 min, t_R (minor) = 40.47 min.

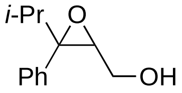
(+)-*trans*-3-Isopropyl-3-phenyloxiranemethanol



Purification – preparative TLC on silica gel, eluent *n*-Hexane/EtOAc/Et_3N- 60:40:1. **R_f** = 0.53 (silica gel, *n*-Hexane/EtOAc 3:2). colourless viscous oil. **$[\alpha]_D^{25}$** = + 33.0 (c = 1.0, $CHCl_3$, 95% *ee*). **^{1}H NMR** (CD_2Cl_2, 500 MHz): δ = 0.91 (d, 3H, CH_3, *J* = 6.6 Hz), 0.99 (d, 3H, CH_3, *J* = 7.0 Hz), 1.83 (sept. 1H, CH, *J* = 7.0 Hz), 2.50 (br. s, 1H, OH), 3.12 (dd, 1H, C*H*-O, *J* = 6.6 Hz, 4.4 Hz), 3.85 (dd, 1H, -C*H*H-, *J* = 12.0 Hz, 6.6 Hz), 4.02 (dd, 1H, -CH*H*-, *J* = 12.0 Hz, 4.4 Hz), 7.26 – 7.35 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 18.4 (CH_3), 19.8 (CH_3), 31.9 (CH of *i*-Pr), 61.1 (CH_2), 65.2 (*C*H-O), 69.9 (C quat.), 127.9 (CH), 128.0 (CH), 128.7 (CH), 138.7 (C quat.) ppm. **IR** (neat): 3415 (br. w), 2967 (w), 2934 (w), 2875 (w), 1497 (w), 1462 (w), 1447 (w), 1386 (w), 1365 (w), 1030 (m), 905 (w), 760 (m), 701 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity, 40 eV): 191 $[M-H]^+$ (12), 161 (7), 149 (12), 131 (76), 117 (100), 105 (45), 91 (68), 77 (41). **HRMS-EI**: Calculated for $C_{12}H_{16}O_2$ $[M]^+$ 192.1150, found 192.1129.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 90:10 %, 0.8 mL/min, 23 °C, λ = 210 nm); t_R (major) = 9.84 min, t_R (minor) = 16.92 min.

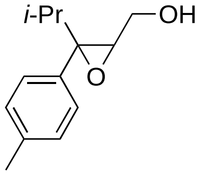
(+)-*cis*-3-Isopropyl-3-phenyloxiranemethanol



Colourless viscous oil. $\mathbf{R_f}$ = 0.43 (silica gel, *n*-Hexane/EtOAc 3:2). Due to the low conversion (~ 20 %) the product was not isolated. **^{1}H NMR** (CD_2Cl_2, 500 MHz): δ = 0.89 (d, 3H, CH_3, *J* = 7.0 Hz), 0.94 (d, 3H, CH_3, *J* = 7.0 Hz), 1.90 (sept. 1H, CH, *J* = 7.0 Hz), 1.99 (br s, 1H, OH), 3.07 (dd, 1H, -C*H*H-, *J* = 12.0 Hz, 7.0 Hz), 3.28 (dd, 1H, CH-O, *J* = 7.0 Hz, 3.9 Hz), 3.46 (dd, 1H, -CH*H*-, *J* = 12.0 Hz, 3.9 Hz), 7.21 – 7.38 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 17.8 (CH_3), 19.0 (CH_3), 35.6 (CH of *i*-Pr), 62.8 (CH_2), 63.1 (*C*H-O), 69.6 (C quat.), 127.9 (CH), 128.2 (CH), 128.4 (CH), 137.3 (C quat.) ppm. **IR** (neat): 3402 (br. w), 2965 (w), 2934 (w), 2875 (w), 1496 (w), 1446 (w), 1385 (w), 1366 (w), 1070 (w), 1028 (m), 904 (w), 759 (m), 701 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 191 $[M-H]^+$ (15), 161 (9), 149 (18), 131 (90), 117 (100), 105 (46), 91 (51), 77 (44). **HRMS-EI**: Calculated for $C_{12}H_{16}O_2$ $[M]^+$ 192.1150, found 192.1134.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 95:5 %, 0.5 mL/min, 23 °C, λ = 210 nm); t_R (minor) = 16.55 min, t_R (major) = 17.76 min.

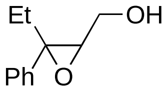
(+)-*trans*-3-Isopropyl-3-(4'-methylphenyl)oxiranemethanol



Purification – preparative TLC on silica gel, eluent *n*-Hexane/EtOAc/Et_3N - 60:40:1. $\mathbf{R_f}$ = 0.53 (silica gel, *n*-Hexane/EtOAc 3:2). Pale yellow viscous oil. $[\alpha]_D^{25}$ = + 25.9 (c = 1.0, $CHCl_3$, 95% *ee*). **^{1}H NMR** ($CDCl_3$, 500 MHz): δ = 0.93 (d, 3H, CH_3, *J* = 6.6 Hz), 0.99 (d, 3H, CH_3, *J* = 7.3 Hz), 1.82 (sept., 1H, CH, *J* = 7.0 Hz), 1.91 (br. s, 1H, OH), 2.34 (s, 3H, CH_3), 3.17 (dd, 1H, CH-O, *J* = 6.6 Hz, 4.4 Hz), 3.89 (dd, 1H, -C*H*H-, *J* = 12.1 Hz, 7.0 Hz), 4.03 (dd, 1H, -CH*H*-, *J* = 12.1 Hz, 4.6 Hz), 7.12 (d, 2H, $C^{ar}H$, *J* = 7.9 Hz), 7.20 (d, 2H, $C^{ar}H$, *J* = 7.9 Hz) ppm. **^{13}C NMR** ($CDCl_3$, 125 MHz): δ = 18.2 (CH_3 of *i*-Pr), 19.7 (CH_3 of *i*-Pr), 21.3 (CH_3), 31.5 (CH of *i*-Pr), 60.8 (CH_2), 64.7 (*C*H-O), 69.8 (C quat.), 128.1 (CH), 128.4 (CH), 135.0 (C quat.), 137.3 (C quat.) ppm. **IR** (neat): 3416 (br. w), 2966 (w), 2874 (w), 1516 (w), 1459 (w), 1385 (w), 1365 (w), 1031 (m), 905 (w), 815 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity, 40 eV): 205 $[M-H]^+$ (10), 191 (31), 163 (15), 145 (66), 131 (100), 105 (80), 91 (69). **HRMS-EI**: Calculated for $C_{13}H_{17}O_2$ $[M-H]^+$ 205.1226, found 205.1229.

CSP-HPLC separation: Chiracel OJ column, *n*-Hexane/*i*-PrOH 90:10 %, 1.0 mL/min, 23 °C, λ = 210 nm); t_R (major) = 8.59 min, t_R (minor) = 13.27 min.

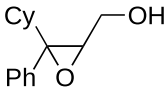
(+)-*trans*-3-Ethyl-3-phenyloxiranemethanol



Purification – preparative TLC on silica gel, eluent *n*-Hexane/EtOAc 3:2. $\mathbf{R_f}$ = 0.45. Pale yellow oil. $\mathbf{[\alpha]_D^{25}}$ = + 5.3 (c = 1.0, $CHCl_3$, 87% *ee*). **^{1}H NMR** ($CDCl_3$, 500 MHz): δ = 0.94 (t, 3H, CH_3, *J* = 7.4 Hz), 1.74 – 1.84 (m, 1H, -C*H*H-CH_3), 1.87 (dd, 1H, OH, *J* = 6.9 Hz, 5.0 Hz), 2.08 – 2.18 (m, 1H, -C*H*H-CH_3), 3.12 (dd, 1H, CH-O, *J* = 6.4 Hz, 4.2 Hz), 3.80 – 3.90 (m, 1H, -C*H*H-OH), 3.94 – 4.04 (m, 1H, -CH*H*-OH), 7.26 – 7.37 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 125 MHz): δ = 9.6 (CH_3), 24.7 (-*C*H_2-CH_3), 61.2 (-*C*H_2-OH), 65.9 (C quat.), 66.0 (CH-O), 126.1 (CH), 127.6 (CH), 128.5 (CH), 140.3 (C quat.) ppm. **IR** (neat): 3399 (br. w), 2975 (w), 2938 (w), 2878 (w), 1496 (w), 1449 (w), 1379 (w), 1303 (w), 1030 (m), 888 (w), 761 (m), 698 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity, 40 eV): 177 $[M-H]^+$ (9), 160 (9), 147 (14), 131 (50), 117 (100), 105 (39), 91 (83), 77 (50). **HRMS-EI**: Calculated for $C_{11}H_{13}O_2$ $[M-H]^+$ 117.0917, found 117.0916.

CSP-HPLC separation: Chiracel OJ column, *n*-Hexane/*i*-PrOH 90:10 %, 1.0 mL/min, 23 °C, λ = 210 nm); t_R (major) = 7.51 min, t_R (minor) = 9.23 min.

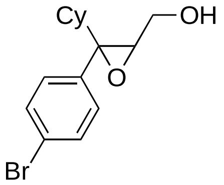
(+)-*trans*-3-Cyclohexyl-3-phenyloxiranemethanol



Purification - preparative TLC on silica gel, eluent *n*-Hexane/EtOAc/Et_3N- 60:40:1. $\mathbf{R_f}$ = 0.53 (silica gel, *n*-Hexane/EtOAc 3:2). White solid, **Mp** = 153.8-155 °C (recrystallized from *n*-hexane/*i*-PrOH, 96% *ee*). $\mathbf{[\alpha]_D^{25}}$ = + 42.0 (c = 1.0, $CHCl_3$, 96% *ee*). [Lit.[12] $[\alpha]_D^{20}$ = + 42.0 (1g/100 mL, $CHCl_3$) for 97% epoxide with absolute configuration (2*S*,3*S*)). **^{1}H NMR** ($CDCl_3$, 500 MHz): δ = 0.83 – 1.03 (m, 2H), 1.07 – 1.30 (m, 3H), 1.49 (tt, 1H, CH of Cy ring, *J* = 12.3 Hz, 3.1 Hz), 1.55 – 1.63 (m, 1H), 1.65 – 1.79 (m, 3H), 1.84 – 1.93 (m, 1H), 2.0 (br m, 1H, OH), 3.17 (dd, 1H, CH-O, *J* = 6.6 Hz, 4.4 Hz), 3.91 (dd, 1H, -C*H*H-OH, *J* = 12.1 Hz, 6.8 Hz), 4.03 (dd, 1H, -CH*H*-OH, *J* = 12.1 Hz, 4.4 Hz), 7.26 – 7.34 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 125 MHz): δ = 26.0 (CH_2), 26.1 (CH_2), 26.4 (CH_2), 28.7 (CH_2), 30.1 (CH_2), 42.0 (CH of Cy), 60.8 (CH_2-OH), 64.3 (CH-O), 69.4 (C quat.), 127.6 (CH), 127.7 (CH), 128.0 (CH), 138.9 (C quat.) ppm. **IR** (neat): 3427 (m), 2928 (m), 2855 (w), 1495 (w), 1460 (w), 1446 (w), 1297 (w), 1279 (w), 1029 (m), 885 (w), 770 (m), 722 (w), 707 (m), 653 (w) cm^{-1}. **MS-EI** *m/z* (rel intensity, 40 eV): 231 [M-H]$^+$ (36), 187 (17), 131 (100), 105 (79), 91 (89), 55 (41). **HRMS-EI**: Calculated for $C_{15}O_{20}O_2$ [M]$^+$ 232.1446, found 232.1463.

CSP-HPLC separation: Chiracel OJ column, *n*-Hexane/*i*-PrOH 90:10 %, 1.0 mL/min, 23 ^{o}C, λ = 210 nm); t_R (major) = 6.10 min, t_R (minor) = 11.14 min.

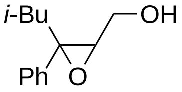
(+)-*trans*- 3-(4-Bromophenyl)-3-cyclohexyloxiranemethanol



Purification - preparative TLC on silica gel, eluent *n*-Hexane/EtOAc/Et$_3$N- 60:40:1. **R$_f$** = 0.4 (silica gel, *n*-Hexane/EtOAc 3:2). Pale yellow tar. **[α]$_D$^{25}** = + 26.1 (c = 1.0, CHCl$_3$, 79% *ee*). **^{1}H NMR** (CDCl$_3$, 500 MHz): δ = 0.75 – 1.38 (m, 6H), 1.47 (tt, 1H, CH of Cy, *J* = 12.3 Hz, 2.8 Hz), 1.53 – 1.93 (m, 7H), 3.11 (dd, 1H, CH-O, *J* = 6.6 Hz, 4.7 Hz), 3.8 – 4.08 (m, 2H, -C*H*$_2$-OH), 7.17 (d, 2H, C^{ar}H, *J* = 8.2 Hz), 7.44 (d, 2H, C^{ar}H, *J* = 8.5 Hz) ppm. **^{13}C NMR** (CDCl$_3$, 125 MHz): δ = 26.0 (CH$_2$), 26.1 (CH$_2$), 26.4 (CH$_2$), 28.6 (CH$_2$), 30.1 (CH$_2$), 41.8 (CH of Cy), 60.6 (CH$_2$-OH), 64.2 (CH-O), 68.8 (C quat.), 121.7 (C quat.), 129.7 (CH), 130.9 (CH), 137.9 (C quat.) ppm. **IR** (neat): 3405 (br. w), 2927 (m), 2853 (m), 1592 (w), 1490 (w), 1451 (w), 1027 (w), 1011 (m), 884 (w), 825 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 312 [M]$^+$ (13), 310 [M]$^+$ (13), 253 (28), 251 (33), 211 (76), 209 (70), 169 (97), 141 (36), 129 (72), 81 (96), 55 (100). **HRMS-EI**: Calculated for $C_{15}H_{19}O_2Br$ [M]$^+$ 310.0568, found 310.0552.

CSP-HPLC separation: Chiracel OJ-H column, *n*-Hexane/*i*-PrOH 95:5 %, 1.0 mL/min, 23 ^{o}C, λ = 210 nm); t_R (major) = 7.76 min, t_R (minor) = 10.75 min.

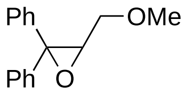
(+)-*trans*-3-Isobutyl-3-phenyloxiranemethanol



Purification – preparative TLC on silica gel, eluent *n*-Hexane/EtOAc/Et$_3$N- 60:40:1. **R$_f$** = 0.65. Pale yellow oil. **[α]$_D$^{25}** = + 20.4 (c = 1.0, CHCl$_3$, 92% *ee*). **^{1}H NMR** (CDCl$_3$, 300 MHz): δ = 0.87 (d, 3H, CH$_3$, *J* = 6.0 Hz), 0.89 (d, 3H, CH$_3$, *J* = 6.0 Hz), 1.45 – 1.73 (m, 3H), 2.18 (dd, 1H, *i*-Pr-C*H*H-, *J* = 13.9 Hz, 5.2 Hz), 2.98 (dd, 1H, CH-O, *J* = 6.6 Hz, 4.3 Hz), 3.77 – 3.89 (m, 1H, -C*H*H-OH), 3.92 – 4.04 (m, 1H, -CH*H*-OH), 7.22 – 7.40 (m, 5H, C^{ar}H) ppm. **^{13}C NMR** (CD$_2$Cl$_2$, 125 MHz): δ = 22.5 (CH$_3$), 23.7 (CH$_3$), 25.9 (CH of *i*-Pr), 40.2 (*i*-Pr-*C*H$_2$-), 61.6 (-*C*H$_2$-OH), 64.7 (C quat.), 65.1 (CH-O), 126.4 (CH), 127.8 (CH), 128.8 (CH), 141.7 (C quat.) ppm. **MS-EI** *m/z* (rel intensity): 205 [M-H]$^+$ (16), 176 (9), 163 (12), 147 (36), 131 (100), 105 (78), 91 (95), 77 (76). **IR** (neat): 3398 (w), 2955 (w), 2870 (w), 1496 (w), 1465 (w), 1450 (w), 1368 (w), 1294 (w), 1033 (m), 761 (w), 698 (m) cm^{-1}. **HRMS-EI**: Calculated for $C_{13}H_{18}O_2$ [M]$^+$ 206.1307, found 206.1293.

CSP-HPLC separation: Chiracel OJ-H column, *n*-Hexane/*i*-PrOH 90:10 %, 1.0 mL/min, 23 °C, λ = 210 nm); t_R (mijor) = 8.09 min, t_R (minor) = 9.34 min.

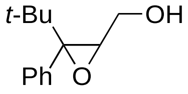
1,1-Diphenyl-3-methoxyprop-2-ene oxide



Purification – preparative TLC on silica gel, eluent *n*-Hexane/EtOAc/Et$_3$N- 80:20:1. **R$_f$** = 0.57. Pale yellow oil. **[α]$_D^{25}$** = –28.6 (c = 1.0, CHCl$_3$, 87% *ee*). **^{1}H NMR** (CDCl$_3$, 300 MHz): δ = 3.16 (dd, 1H, -C*H*H-OMe, *J* = 11.1 Hz, 6.2 Hz), 3.33 (s, 3H, CH$_3$), 3.45 (dd, 1H, -CH*H*-OMe, *J* = 11.1 Hz, 4.2 Hz), 3.61 (dd, 1H, CH-O, *J* = 5.8 Hz, 4.6 Hz), 7.20 – 7.50 (m, 10H, C^{ar}H) ppm. **^{13}C NMR** (CDCl$_3$, 75 MHz): δ = 59.3 (CH$_3$), 64.3 (CH), 65.2 (C quat.), 71.8 (CH$_2$), 127.0 (CH), 128.0 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 137.0 (C quat.), 140.4 (C quat.) ppm. **IR** (neat): 3061 (w), 3029 (w), 2984 (w), 2928 (w), 2821 (w), 1495 (w), 1448 (m), 1122 (m), 1088 (m), 764 (m), 753 (m), 696 (s) cm^{-1}. **MS-EI** *m/z* (rel intensity): 240 [M]$^+$ (4), 208 (37), 195 (11), 165 (100), 105 (28), 77 (24). **HRMS-EI**: Calculated for $C_{16}H_{16}O_2$ [M]$^+$ 240.1141, found 240.1150.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 99:1 %, 0.5 mL/min, 23 °C, λ = 210 nm); t_R (minor) = 16.04 min, t_R (major) = 17.43 min.

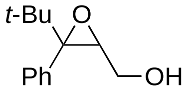
trans-3-*tert*-Butyl-3-phenyloxiranemethanol



White solid. **Mp** = 72.5 – 73.5 °C. **^{1}H NMR** (CD$_2$Cl$_2$, 500 MHz): δ = 0.99 (s, 9H, *t*-Bu), 2.01 (br. s, 1H, OH), 3.0 (dd, 1H, CH-O, *J* = 6.6 Hz, 3.2 Hz), 4.05 (dd, 1H, -C*H*H-OH, *J* = 12.3 Hz, 6.9 Hz), 4.11 (dd, 1H, -CH*H*-OH), *J* = 12.3 Hz, 3.2 Hz), 7.21 – 7.35 (m, 5H, C^{ar}H) ppm. **^{13}C NMR** (CD$_2$Cl$_2$, 125 MHz): δ = 28.8 (CH$_3$), 34.6 (C quat.), 61.8 (CH$_2$), 67.4 (CH), 71.7 (C quat.), 127.5 (CH), 127.8 (CH), 128.4 (CH), 142.7 (C quat.) ppm. **IR** (neat): 3442 (m), 2955 (w), 2910 (w), 2872 (w), 1495 (w), 1480 (w), 1448 (w), 1395 (w), 1366 (w), 1044 (m), 1029 (m), 907 (m), 890 (m), 757 (m), 709 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 205 [M-H]$^+$ (14), 175 (4), 161 (15), 149 (11), 131 (100), 120 (33), 115 (28), 105 (36), 91 (72), 77 (29). **HRMS-EI**: Calculated for $C_{13}H_{17}O_2$ [M-H]$^+$ 205.1229, found 205.1228.

CSP-HPLC separation: Chiracel OD-H column, *n*-Hexane/*i*-PrOH 90:10 %, 1.0 mL/min, 23 ^oC, λ = 210 nm); t_R = 6.64 min, 15.85 min.

cis-3-*tert*-Butyl-3-phenyloxiranemethanol

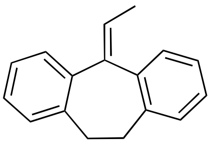


Colorless oil. **^{1}H NMR** (CD_2Cl_2, 500 MHz): δ = 0.95 (s, 9H, *t*-Bu), 1.65 (br. s, 1H, OH), 2.96 (dd, 1H, -C*H*H-OH, *J* = 12.0 Hz, 6.9 Hz), 3.40 (dd, 1H, CH-O, *J* = 6.9 Hz, 3.4 Hz), 3.43 – 3.50 (m, 1H, -CH*H*-OH), 7.09 – 7.41 (m, 5H, C^{ar}H) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 26.6 (CH_3), 34.8 (C quat.), 60.3 (CH), 63.5 (CH_2), 71.0 (C quat.), 127.3 (CH), 127.8 (CH), 128.5 (CH), 129.9 (CH), 137.5 (C quat.) ppm. **IR** (neat): 3398 (br., w), 2958 (w), 2872 (w), 1481 (w), 1463 (w), 1393 (w), 1363 (w), 1040 (m), 1028 (m), 753 (m), 703 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 205 [M-H]$^+$ (13), 175 (4), 149 (13), 131 (100), 105 (62), 91 (26), 77 (25), 57 (16). **HRMS-ESI** (+): Calculated for $C_{13}H_{18}O_2Na$ [M+Na]$^+$ 229.1199, found 229.1189.

CSP-HPLC separation: Chiracel OJ-H column, *n*-Hexane/*i*-PrOH 90:10 %, 1.0 mL/min, 23 ^oC, λ = 210 nm); t_R = 5.93 min, 8.84 min.

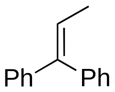
Data for substrates used in enantioselective epoxidation reactions: alkenes and allylic alcohols

5-Ethylidene-10,11-dihydro-5H-dibenzo[*a,d*]-cycloheptene[13]



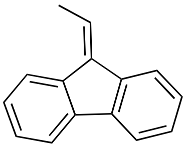
Colorless viscous oil. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.75 (d, 3H, CH_3, *J* = 6.8 Hz), 2.5 – 3.8 (br m, 4H, benzylic), 5.96 (q, 1H, CH vinyl, *J* = 6.8 Hz), 7.05- 7.40 (m, 8H, C^{ar}H) ppm.

1,1-Diphenylprop-1-ene[14]



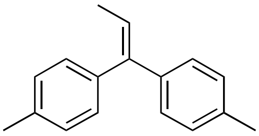
Colorless solid. **Mp** = 45.8 – 47.8 ^oC (lit. 45 – 47 ^oC [14]). **^{1}H NMR** (CD_2Cl_2, 400 MHz): δ = 1.73 (d, 3H, CH_3, *J* = 7.0 Hz), 6.16 (q, 1H, CH vinyl, *J* = 7.0 Hz), 7.1 – 7.4 (m, 10H, C^{ar}H) ppm.

9-Ethylidenefluorene[15]



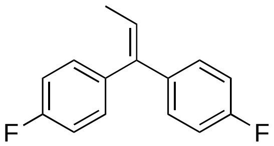
Colorless solid. **Mp** = 93 – 97 °C (lit. 76.5 – 78 °C [15], 103 - 104 °C [16], 52 – 54 °C [17]). **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 2.41 (d, 3H, CH_3, *J* = 7.6 Hz), 6.87 (q, 1H, vinyl, *J* = 7.6 Hz), 7.25- 7.75 (m, 4H, $C^{ar}H$), 7.62 - 7.81 (m, 3H, $C^{ar}H$), 7.90 (d, 1H, $C^{ar}H$, *J* = 7.3 Hz) ppm.

1,1-Bis(4-methylphenyl)prop-1-ene[18]



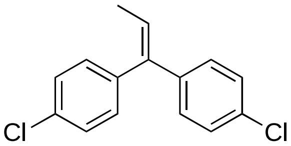
Colorless oil. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.75 (d, 3H, CH_3, *J* = 7.1 Hz), 2.32 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 6.10 (q, 1H, CH vinyl, *J* = 7.1 Hz), 7.03 – 7.14 (m, 6H, $C^{ar}H$), 7.17 (d, 2H, $C^{ar}H$, *J* = 7.6 Hz) ppm.

1,1-Bis(4-flourophenyl)prop-1-ene



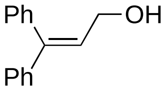
Cream colored solid. **Mp** = 43.2 – 44.2 °C (lit. 43 - 44 °C) **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 1.74 (d, 3H, CH_3, *J* = 7.1 Hz), 6.10 (q, 1H, CH vinyl, *J* = 7.1 Hz), 6.88 – 7.21 (m, 8H, $C^{ar}H$) ppm. **^{19}F NMR** ($CDCl_3$, 282 MHz), δ = - 118.6, -119.3 ppm. Reference: C_6D_6 δ = -164.9 ppm.

1,1-Bis(4-chlorophenyl)prop-1-ene[18]



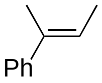
White solid. **Mp** = 63.8 – 64.5 °C (lit. 63.5 – 64 °C [18]). **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 1.75 (d, 3H, CH_3, *J* = 7.0 Hz), 6.16 (q, 1H, CH vinyl, *J* = 7.0 Hz), 7.04 – 7.16 (m, 4H, $C^{ar}H$), 7.19 – 7.25 (m, 2H, $C^{ar}H$), 7.31 – 7.40 (m, 2H, $C^{ar}H$) ppm.

3,3-Diphenylprop-2-en-1-ol[19]



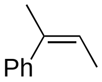
White solid. **Mp** = 62.8 – 63.5 °C (lit. 53 – 56 °C [19]). **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 1.57 (bs, 1H, OH), 4.33 (d, 2H, CH_2, *J* = 6.8 Hz), 6.36 (t, 1H, CH vinyl, *J* = 6.8 Hz), 7.24 – 7.53 (m, 10H, $C^{ar}H$) ppm.

(*E*)-2-Phenylbut-2-ene[20]



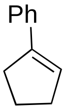
Colorless liquid. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.82 (dq, 3H, CH_3, *J* = 6.8 Hz, 0.7 Hz), 2.05 (d, 3H, CH_3, *J* = 1.3 Hz), 5.87 (qq, 1H, CH vinyl, *J* = 6.8 Hz, 1.3 Hz), 7.2 – 7.45 (m, 5H, $C^{ar}H$) ppm.

(*Z*)-2-Phenylbut-2-ene[20]



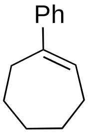
Colorless liquid. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.61 (dq, 3H, CH_3, *J* = 6.9 Hz, 0.7 Hz), 2.04 (q, 3H, CH_3, *J* = 1.3 Hz), 5.58 (qq, 1H, CH vinyl, *J* = 6.9 Hz, 1.3 Hz), 7.15 – 7.40 (m, 5H, $C^{ar}H$) ppm.

1-Phenylcyclopentene[21]



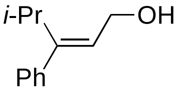
Colorless liquid. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.95 – 2.10 (m, 2H), 2.50 – 2.60 (m, 2H), 2.70 – 2.80 (m, 2H), 6.20 (t, 1H, CH vinyl, *J* = 2.0 Hz), 7.20 – 7.35 (m, 3H, $C^{ar}H$), 7.45 (d, 2H, $C^{ar}H$, *J* = 7.4 Hz) ppm.

1-Phenylcycloheptene[22]



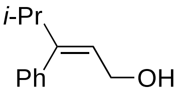
Colorless liquid. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.55 – 1.70 (m, 4H), 1.80 – 1.90 (m, 2H), 2.25 – 2.35 (m, 2H), 2.57 – 2.68 (m, 2H), 6.10 (t, 1H, CH vinyl, *J* = 6.8 Hz), 7.15 – 7.35 (m, 5H, $C^{ar}H$) ppm.

(*E*)-4-Methyl-3-phenylpent-2-en-1-ol[23]



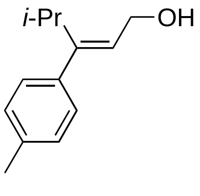
Colorless oil. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 1.03 (d, 6H, 2 × CH_3, *J* = 7.0 Hz), 1.29 (br m, 1H, OH), 3.01 (sept, 1H, CH, *J* = 7.0 Hz), 4.34 (dd, 2H, CH_2, *J* = 6.5 Hz, 5.3 Hz), 5.46 (t, 1H, CH vinyl, *J* = 6.8 Hz), 7.11 – 7.31 (m, 5H, $C^{ar}H$) ppm.

(*Z*)-4-Methyl-3-phenylpent-2-en-1-ol[23]



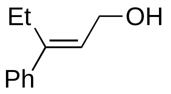
Colorless oil. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 1.0 (d, 6H, 2 × CH_3, *J* = 6.9 Hz), 1.14 (br m, 1H, OH), 2.55 (sept, 1H, CH, *J* = 6.9 Hz), 3.85 – 3.97 (m, 2H, CH_2), 5.60 (td, 1H, CH vinyl, *J* = 6.9 Hz, 1.2 Hz), 6.98 – 7.07 (m, 2H, $C^{ar}H$), 7.17 – 7.33 (m, 3H, $C^{ar}H$) ppm.

(*E*)-4-Methyl-3-(4-methylphenyl)pent-2-en-1-ol[23]



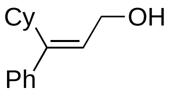
Colorless oil. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 1.05 (d, 6H, 2 × CH_3, *J* = 7.1 Hz), 1.30 (t, 1H, OH, *J* = 5.4 Hz), 2.35 (s, 3H, CH_3), 3.02 (sept., 1H, CH, *J* = 7.1 Hz), 4.35 (dd, 2H, CH_2, *J* = 6.6 Hz, 5.4 Hz), 5.47 (t, 1H, CH vinyl, *J* = 6.6 Hz), 7.03 – 7.14 (m, 4H, $C^{ar}H$) ppm.

(E)-3-Phenylpent-2-en-1-ol[24]



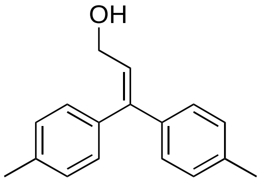
Colorless oil. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 0.93 (t, 3H, CH_3, *J* = 7.5 Hz), 1.27 (br. s, 1H, OH), 2.48 (q, 2H, CH_2, *J* = 7.5 Hz), 4.29 (dd, 2H, CH_2-OH, *J* = 6.3 Hz, 4.3 Hz), 5.77 (t, 1H, CH vinyl, *J* = 6.8 Hz), 7.14 – 7.36 (m, 5H, $C^{ar}H$) ppm.

(*E*)-3-Cyclohexyl-3-phenylprop-2-en-1-ol[19]



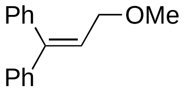
Colorless viscous oil.**^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.19 – 1.39 (m, 6H), 1.56 – 1.80 (m, 5H), 2.55 – 2.68 (m, 1H), 4.36 (dd, 2H, CH_2-OH, *J* = 6.3 Hz, 5.3 Hz), 5.46 (t, 1H, CH vinyl, *J* = 6.8 Hz), 7.12 – 7.18 (m, 2H, $C^{ar}H$), 7.22 – 7.32 (m, 3H, $C^{ar}H$) ppm.

3,3-Di(4-methylphenyl)prop-2-en-1-ol[25]



White solid.**Mp** = 68 **–** 69.5 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ = 1.36 (t, 1H, OH, *J* = 5.5 Hz), 2.34 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 4.22 (dd, 2H, CH_2-OH, *J* = 6.8 Hz, 5.5 Hz), 6.18 (t, 1H, CH vinyl, *J* = 6.8 Hz), 7.02 – 7.21 (m, 8H, $C^{ar}H$) ppm.

1,1-Diphenyl-3-methoxyprop-1-ene

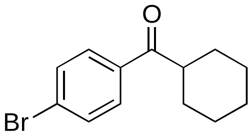


A solution of 3,3-diphenylprop-2-en-1-ola (1.9 mmol, 400 mg) in MeOH (15 mL) with 2 drops of concentrated sulfuric acid was refluxed for 15h. The reaction mixture was allowed to cool down to room temperature, then 40 mL of water and 20 mL of diethyl ether were added and the layers were separated. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phases were washed with $NaHCO_3$ (10 % aqueous solution, 15 mL), brine (15 mL), dried under sodium sulfate and filtered. Evaporation of the solvent under reduced pressure gave 411 mg (96%) of pure product as a pale yellow oil.

^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 3.28 (s, 3H, CH_3), 3.96 (d, 2H, CH_2, *J* = 6.6 Hz), 6.19 (t, 1H, CH vinyl, *J* = 6.6 Hz), 7.14 – 7.19 (m, 2H, $C^{ar}H$), 7.22 – 7.42 (m, 8H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 58.3 (CH_3), 70.7 (CH_2), 126.5 (CH vinyl), 128.01 (CH), 128.03 (CH), 128.1 (CH), 128.7 (CH), 128.72 (CH), 130.3 (CH), 139.9 (C quat.), 142.6 (C quat.), 145.0 (C quat.) ppm. **IR** (neat): 3056 (w), 3027 (w), 2981 (w), 2923 (w), 2818 (w), 1599 (w), 1576 (w), 1493 (w), 1444 (w), 1378 (w), 1114 (m), 1086 (m), 757 (m), 695 (s) cm^{-1}. **MS-EI** *m/z* (rel intensity): 224 $[M]^+$ (42), 193 (40), 192 (100), 165 (34), 115 (61), 77 (26).

HRMS-EI Calculated for $C_{16}H_{16}O$ $[M]^+$ 224.1193, found 224.1201.

4-Bromophenylcyclohexyl ketone



The synthesis was preformed in a three neck flask, equipped with an additional funnel, low-temperature thermometer and a magnetic stirring bar under nitrogen atmosphere. To a cooled (–78 °C) stirred solution of 1,4-dibromobenzene (40.94 mmol, 9.66 g, 1.0 equiv.) in dry THF/Et_2O (1:1, 110 mL, 110 mL) *n*-BuLi (40.94 mmol, 26 mL, 1.6 M solution in hexane, 1.0 equiv.) was added dropwise via additional funnel over 35 min.[26] The resulting cloudy mixture was stirred at low temperature for an additional 1h, then a solution of *N*-methoxy-*N*-methylcyclohexanecarboxamide[27] (40.94 mmol, 7.0 g, 1.0 equiv.) in dry THF (40 mL) was added slowly over 30 min. at –78 °C. The resulting clean colorless solution was slowly warmed to room temperature and stirred overnight. Diethyl ether (50 mL) and ~2N HCl (100 mL) were added to the reaction mixture and the layers were separated. The aqueous phase was extracted with Et_2O (2 × 60 mL). The combined organic extracts were washed with saturated aqueous solution of $NaHCO_3$ (100 mL), brine (100 mL), dried under Na_2SO_4, filtered and concentrated in vacuum. High vacuum (<10^{-2} mbar) distillation of the crude product (pale yellow solid) usingKügelrohr technique provided 10.48 g (96%) of a pure product as a white solid. The compound can be recrystallised from minimum amount of MeOH to obtain white crystals (6.7 g, 61%). **Mp** = 78.8 – 79.5 °C (lit. 77 – 79 °C).

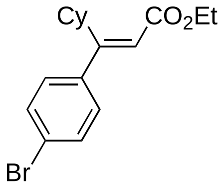
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.17 – 1.56 (m, 5H), 1.67 – 1.95 (m, 5H), 3.12 – 3.25 (m, 1H, CH), 7.59 (d, 2H, $C^{ar}H$, *J* = 8.8 Hz), 7.80 (d, 2H, $C^{ar}H$, *J* = 8.6 Hz) ppm. **^{13}C**

NMR ($CDCl_3$, 100 MHz): δ = 25.9 (CH_2), 26.0 (CH_2), 29.5 (CH_2), 45.7 (CH of Cy), 127.9 (C quat.), 130.0 (CH), 132.0 (CH), 135.1 (C quat.), 202.9 (C=O) ppm. **IR** (neat): 2925 (m), 2854 (m), 1679 (m), 1582 (m), 1566 (w) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 269.1 $[M]^+$ (31), 267.1 $[M]^+$ (30), 187.1 (90), 185.1 (100), 171.1 (56), 169.3 (52). **HRMS-ESI (+)**: Calculated for $C_{13}H_{16}OBr$ $[M+H]^+$ 267.0379, found 267.0392.

(*E*), (*Z*)-Ethyl-3-(4-bromophenyl)-3-cyclohexylacrylates

The reaction was preformed in a three neck flask equipped with a condenser, additional funnel and a magnetic stirring bar under nitrogen atmosphere. *n*-BuLi (22.5 mmol, 14 mL, 1.6 M in hexane, 1.5 equiv.) was added slowly over 25 min to a stirred solution of triethylphosphonoacetate (22.5 mmol, 4.5 mL, 1.5 equiv.) in dry *n*-hexane (50 mL) at 0 °C. The resulting suspension was stirred at 0 °C for another 30 min, then a solution of 4-bromophenylcyclohexyl ketone (15 mmol, 4.0 g,1.0 equiv.) in dry THF/*n*-hexane (2:1, 45 mL) was added rapidly in 10 min at 0 °C. The resulting mixture was heated at reflux for 22 h. GC-MS analysis of an aliquot of the reaction mixture, quenched into ether/water, indicated that complete consumption of the 4-bromophenylcyclohexyl ketone starting material and clean conversion to (*E*), (*Z*)-ethyl-3-(4'-bromophenyl)-3-cyclohexylacrylates had occurred. The reaction mixture was quenched by addition of a saturated aqueous solution of NH_4Cl (100 mL) and EtOAc (50 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with water (100 mL), brine (100 mL), dried under Na_2SO_4, filtered and concentrated in vacuum. The resulting residue was purified by careful column chromatography on silica gel (*n*-hexane/EtOAc 10:1) to provide (*E*)-ethyl-3-(4'-bromophenyl)-3-cyclohexylacrylate (first eluted fraction, 1.4 g, 28%) as a pale yellow oil and (*Z*)-ethyl-3-(4'-bromophenyl)-3-cyclohexylacrylate (second eluted fraction, 2.51 g, 50%) as a colorless oil. The configurations of double bonds were determined by NOESY experiments.

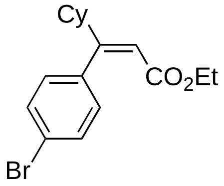
(*E*)-Ethyl-3-(4-bromophenyl)-3-cyclohexylacrylate



R_f = 0.72 (silica gel, *n*-hexane/EtOAc 10:1). **^{1}H NMR** ($CDCl_3$, 500 MHz): δ = 1.0 – 1.25 (m, 3H), 1.30 (t, 3H, CH_3, *J* = 7.1 Hz), 1.32 – 1.44 (m, 2H), 1.60 – 1.77 (m, 5H), 3.72 (tt, 1H, CH, *J* = 12.1 Hz, 3.0 Hz), 4.19 (q, 2H, CH_2, *J* = 7.1 Hz), 5.64 (s, 1H, CH vinyl), 7.04

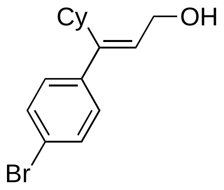
(d, 2H, C*ar*H, *J* = 8.5 Hz), 7.44 (d, 2H, C*ar*H, *J* = 8.5 Hz) ppm. **^{13}C NMR** ($CDCl_3$, 125 MHz): δ = 14.4 (CH_3), 26.0 (CH_2), 26.5 (CH_2), 31.7 (CH_2), 40.5 (CH of Cy), 60.1 (CH_2 of OEt), 119.1 (CH vinyl), 121.7 (C qaut.), 129.4 (CH), 131.0 (CH), 140.4 (C quat.), 165.5 (C quat.), 166.2 (C qaut.) ppm. **IR** (neat): 2980 (w), 2925 (m), 2853 (w), 1713 (m), 1627 (m), 1586 (w), 1485 (m), 1448 (w), 1270 (m), 1228 (w), 1159 (s), 827 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 339.0 [M+H]$^+$ (52), 337.0 [M+H]$^+$ (53), 293.0 (100), 291.0 (97), 212.1 (72). **HRMS-ESI** (+): Calculated for $C_{17}H_{22}O_2Br$ [M+H]$^+$ 337.0797, found 337.0787.

(*Z*)-Ethyl-3-(4-bromophenyl)-3-cyclohexylacrylate



R$_f$ = 0.54 (silica gel, *n*-hexane/EtOAc 10:1). **^{1}H NMR** ($CDCl_3$, 500 MHz): δ = 1.08 (t, 3H, CH_3, *J* = 7.1 Hz), 1.10 – 1.31 (m, 5H), 1.61 – 1.84 (m, 5H), 2.15 – 2.25 (m, 1H, CH of Cy), 3.97 (q, 2H, CH_2 *J* = 7.1 Hz), 5.83 (d, 1H, CH vinyl, *J* = 1.0 Hz), 6.96 (d, 2H, C*ar*H, *J* = 8.5 Hz), 7.46 (d, 2H, C*ar*H, *J* = 8.2 Hz) ppm. **^{13}C NMR** ($CDCl_3$, 125 MHz): δ = 14.1 (CH_3), 26.1 (CH_2), 26.5 (CH_2), 31.7 (CH_2), 47.4 (CH of Cy), 60.0 (CH_2 of OEt), 116.6 (CH vinyl), 121.4 (C quat.), 129.1 (CH), 131.0 (CH), 139.5 (C quat.), 163.5 (C quat.), 166.4 (C quat.) ppm. **IR** (neat): 2979 (w), 2926 (m), 2853 (w), 1723 (m), 1706 (m), 1637 (m), 1588 (w), 1486 (w), 1448 (w), 1267 (m), 1218 (m), 1157 (s), 829 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 339.0 [M+H]$^+$ (67), 337.0 [M+H]$^+$ (65), 293.0 (98), 291.0 (100), 212.1 (80). **HRMS-ESI** (+): Calculated for $C_{17}H_{22}O_2Br$ [M+H]$^+$ 337.0797, found 337.0782.

(*E*)-3-(4-Bromophehyl)-3-cyclohexylprop-2-en-1-ol

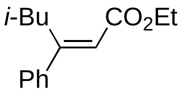


The synthesis was performed in a two neck flask, equipped with an additional funnel and a magnetic stirring bar under nitrogen atmosphere. A solution of (*E*)-ethyl-3-(4'-bromophenyl)-3-cyclohexylacrylate (3.56 mmol, 1.2 g, 1.0 equiv.) in dry diethyl ether (30 mL) was cooled to 0 °C with an ice bath and DIBAL-H (7.83 mmol, 6.5 mL, 1.2 M solution in toluene, 2.2 equiv.) was added slowly over 15 min. The resulting mixture was allowed to warm to room temperature and stirred for 30 min, then recooled to 0 °C and quenched by slow addition of water (10 mL). ~2N HCl (25 mL) and EtOAc (25 mL) were added and the layers were separated. The aqueous phase was extracted with EtOAc (2 × 15 mL). The combined organic phases were washed with an aqueous $NaHCO_3$ (25 mL), brine (25 mL), dried (Na_2SO_4), filtered and concentrated. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc 3:2, $\mathbf{R_f}$ = 0.57) gave pure product (0.98 g, 93%) as a colorless very viscous oil which crystallized after few days of standing at room temperature. **Mp** = 69.6 – 70.2 °C. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ = 0.98 – 1.11 (m, 1H), 1.15 – 1.36 (m, 4H), 1.42 (s, 1H, OH), 1.56 – 1.78 (m, 5H), 2.53 – 2.65 (m, 1H, CH of Cy), 4.34 (dd, 2H, C*H*$_2$-OH, *J* = 6.3 Hz, 3.3 Hz), 5.44 (t, 1H, CH vinyl, *J* = 6.7 Hz), 7.02 (d, 2H, CH_2, *J* = 8.5 Hz), 7.40 (d, 2H, CH_2, *J* = 8.2 Hz) ppm. **^{13}C NMR** ($CDCl_3$, 125 MHz): δ = 26.0 (CH_2), 26.7 (CH_2), 32.2 (CH_2), 40.8 (CH of Cy), 59.0 (CH_2-OH), 120.8 (C quat.), 128.1 (CH vinyl), 130.2 (CH), 130.8 (CH), 141.8 (C quat.), 148.6 (C quat.) ppm. **IR** (neat): 3307 (br, w), 2925 (m), 2851 (m), 1646 (w), 1586 (w), 1485 (m), 1448 (w), 1009 (m), 823 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 296 $[M]^+$ (11), 294 $[M]^+$ (16), 252 (19), 213 (85), 169 (40), 141 (62), 115 (96), 83 (77), 55 (100). **HRMS-EI**: Calculated for $C_{15}H_{17}OBr$ $[M-2H]^+$ 292.0463, found 292.0463. **Elemental analysis**: requires C, 61.03; H, 6.49 %.$C_{15}H_{19}OBr$. Found: C, 61.13; H, 6.39 %.

(*E*), (*Z*)-Ethyl-5-methyl-3-phenylhex-2-enoates

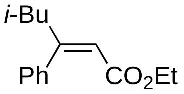
The reaction was preformed in a three neck flask (250 mL) equipped with a condenser, additional funnel and a magnetic stirring bar under nitrogen atmosphere. *n*-BuLi (46.4 mmol, 29 mL, 1.6 M in hexane, 1.5 equiv.) was added slowly to a stirred solution of triethylphosphonoacetate (46.4 mmol, 9.2 mL, 1.5 equiv.) in dry *n*-hexane (80 mL) at 0 °C. The resulting suspension was stirred at 0 °C for another 30 min, then isovalerophenone (30.9 mmol, 5.2 mL, 1.0 equiv.) was added as a neat in one pot at 0 °C. The resulting mixture was heated at reflux for 35 h. GC-MS analysis of an aliquot of the reaction mixture, quenched into ether/water, indicated that complete consumption of the isovalerophenone starting material and clean conversion to (*E*), (*Z*)-ethyl-5-methyl-3-phenylhex-2-enoates had occurred. The reaction mixture was quenched by addition of a saturated aqueous solution of NH_4Cl (150 mL) and EtOAc (60 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 60 mL). The combined organic phases were washed with water (100 mL), brine (100 mL), dried under Na_2SO_4, filtered and concentrated in vacuum. The resulting residue was purified by careful column chromatography on silica gel (*n*-hexane/EtOAc 20:1) to provide (*E*)-ethyl-5-methyl-3-phenylhex-2-enoate (first eluted fraction, 2.03 g, 28%) as a colorless oil and (*Z*)-ethyl-5-methyl-3-phenylhex-2-enoate (second eluted fraction, 3.8 g, 53%) as a colorless oil. The configurations of double bonds were determined by NOESY experiments.

(*E*)-Ethyl-5-methyl-3-phenylhex-2-enoate[28]



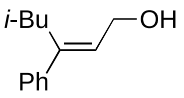
R$_f$ = 0.6 (silica gel, *n*-hexane/EtOAc 10:1). **^{1}H NMR** ($CDCl_3$, 300 MHz): δ = 0.87 (d, 6H, 2 × CH_3 of *i*-Pr, *J* = 6.7 Hz), 1.31 (t, 3H, CH_3 of –OEt, *J* = 7.1 Hz), 1.57 – 1.73 (m, 1H, CH of *i*-Pr), 3.07 (d, 2H, CH_2, *J* = 7.3 Hz), 4.20 (q, 2H, CH_2 of –OEt, *J* = 7.1 Hz), 6.0 (s, 1H, CH vinyl), 7.30 – 7.45 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 125 MHz): δ = 14.5 (CH_3 of –OEt), 22.5 (CH_3 of *i*-Pr), 28.0 (CH of *i*-Pr), 39.0 (CH_2), 59.9 (CH_2 of –OEt), 118.8 (CH vinyl), 126.9 (CH), 128.6 (CH), 128.8 (CH), 141.9 (C quat.), 160.2 (C quat.), 166.8 (C quat.) ppm. **IR** (neat): 2958 (w), 2870 (w), 1713 (m), 1623 (m), 1576 (w), 1493 (w), 1464 (w), 1446 (w), 1368 (w), 1154 (s), 1048 (m), 876 (w), 764 (m), 695 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 232 $[M]^+$ (94), 217 (41), 187 (55), 171 (55), 145 (86), 118 (52), 115 (100), 91 (43), 77 (33). **HRMS-EI**: Calculated for $C_{15}H_{20}O_2$ $[M]^+$ 232.1463, found 232.1462.

(*Z*)-Ethyl-5-methyl-3-phenylhex-2-enoate[28]



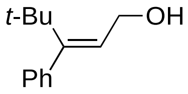
R$_f$ = 0.44 (silica gel, *n*-hexane/EtOAc 10:1). **^{1}H NMR** ($CDCl_3$, 500 MHz): δ = 0.88 (d, 6H, 2 × CH_3 of *i*-Pr, *J* = 6.6 Hz), 1.07 (t, 3H, CH_3 of –OEt, *J* = 7.1 Hz), 1.53 – 1.63 (m, 1H, CH of *i*-Pr), 2.32 (dd, 2H, CH_2, *J* = 7.2 Hz, 1.3 Hz), 3.98 (q, 2H, CH_2 of –OEt, *J* = 7.1 Hz), 5.86 (t, 1H, CH vinyl, *J* = 1.0 Hz), 7.13 (m, 2H, $C^{ar}H$), 7.27 – 7.37 (m, 3H, $C^{ar}H$) ppm. **^{13}C NMR** ($CDCl_3$, 125 MHz): δ = 14.1 (CH_3 of –OEt), 22.4 (CH_3 of *i*-Pr), 26.0 (CH of *i*-Pr), 50.1 (CH_2), 59.5 (CH_2 of –OEt), 118.5 (CH vinyl), 127.3 (CH), 127.7 (CH), 127.9 (CH), 140.2 (C quat.), 158.8 (C quat.), 166.1 (C quat.) ppm. **IR** (neat): 2956 (w), 2929 (w), 2870 (w), 1725 (m), 1707 (m), 1637 (w), 1494 (w), 1464 (w), 1443 (w), 1369 (w), 1223 (m), 1155 (m), 1061 (m), 697 (m) cm^{-1}. **MS-ES** (+) *m/z* (rel intensity): 233.4 $[M+H]^+$ (25), 187.3 (100). **HRMS-ESI** (+): Calculated for $C_{15}H_{20}O_2Na$ $[M+Na]^+$ 255.1355, found 255.1360.

(*E*)-5-Methyl-3-phenylhex-2-en-1-ol



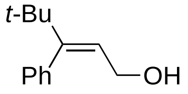
The synthesis was performed in a two neck flask, equipped with an additional funnel and a magnetic stirring bar under nitrogen atmosphere. A solution of (*E*)-ethyl-5-methyl-3-phenylhex-2-enoate (8.62 mmol, 2.0 g, 1.0 equiv.) in dry diethyl ether (60 mL) was cooled to 0 ^oC with an ice bath and DIBAL-H (18.96 mmol, 15.8 mL, 1.2 M solution in toluene, 2.2 equiv.) was added slowly over 15 min. The resulting mixture was stirred for 30 min, at 0 ^oC and quenched by slow addition of water (10 mL). ~2N HCl (60 mL) and EtOAc (30 mL) were added and the layers were separated. The aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic phases were washed with water (60 mL), an aqueous $NaHCO_3$ (60 mL), brine (60 mL), dried (Na_2SO_4), filtered and concentrated in vacuum. The yellow residue was filtered through silica gel plug eluting with EtOAc. Concentration in vacuum provided pure product (1.62 g, 99%) as a clean colorless oil. **^{1}H NMR** (CD_2Cl_2, 500 MHz): δ = 0.84 (d, 6H, 2 × CH_3, *J* = 6.6 Hz), 1.43 (br. s, 1H, OH), 1.49 – 1.59 (m, 1H, CH of *i*-Pr), 2.42 (d, 2H, CH_2, *J* = 7.2 Hz), 4.31 (d, 2H, CH_2-OH, *J* = 6.6 Hz), 5.86 (t, 1H, CH vinyl, *J* = 6.8 Hz), 7.22 – 7.39 (m, 5H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 22.6 (CH_3), 27.7 (CH of *i*-Pr), 39.3 (CH_2), 60.3 (CH_2-OH), 127.1 (CH), 127.6 (CH), 128.8 (CH), 129.0 (CH), 142.8 (C quat.), 143.3 (C quat.) ppm. **IR** (neat): 3315 (br. w), 2953 (w), 2867 (w), 1643 (w), 1599 (w), 1493 (w), 1463 (w), 1444 (w), 1366 (w), 1010 (m), 764 (m), 696 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 190 $[M]^+$ (25), 133 (100), 115 (40), 91 (50), 77 (37), 55(23). **HRMS-EI**: Calculated for $C_{13}H_{18}O$ $[M]^+$ 190.1355, found 190.1358.

(*E*)-4,4-Dimethyl-3-phenylpent-2-en-1-ol[29]



Colorless oil. **^{1}H NMR** (CD_2Cl_2, 300 MHz): δ = 1.13 (s, 9H, *t*-Bu), 1.54 (t, 1H, OH, *J* = 5.5 Hz), 4.46 (t, 2H, CH_2, *J* = 5.8 Hz), 5.29 (t, 1H, CH vinyl, *J* = 6.1 Hz), 7.03 – 7.13 (m, 2H, $C^{ar}H$), 7.16 – 7.33 (m, 3H, $C^{ar}H$) ppm.

(*Z*)-4,4-Dimethyl-3-phenylpent-2-en-1-ol



The compound was prepared according the same procedure used for the synthesis of (*E*)-5-methyl-3-phenylhex-2-en-1-ola.

White solid, **Mp** = 37 – 39 ^oC. **^{1}H NMR** (CD_2Cl_2, 500 MHz): δ = 1.08 (s, 9H, *t*-Bu), 1.23 (br.s, 1H, OH), 3.68 (d, 2H, CH_2, *J* = 6.6 Hz), 5.75 (t, 1H, CH vinyl, *J* = 6.6 Hz), 6.99 – 7.05 (m, 2H, $C^{ar}H$), 7.24 – 7.35 (m, 3H, $C^{ar}H$) ppm. **^{13}C NMR** (CD_2Cl_2, 125 MHz): δ = 29.8 (CH_3), 36.3 (C quat.), 61.2 (CH_2), 124.2 (CH vinyl), 127.0

(CH), 128.1 (CH), 130.0 (CH), 140.1 (C quat.), 153.6 (C quat.) ppm. **IR** (neat): 3341 (br. w), 2953 (m), 2934 (w), 2867 (w), 1646 (w), 1600 (w), 1574 (w), 1480 (w), 1386 (w), 1358 (w), 1023 (m), 978 (m), 769 (w), 706 (m) cm^{-1}. **MS-EI** *m/z* (rel intensity): 190 $[M]^+$ (29), 157 (27), 146 (37), 133 (93), 115 (60), 91 (67), 77 (52), 57 (100). **HRMS-EI**: Calculated for $C_{13}H_{18}O$ $[M]^+$ 190.1355, found 190.1358.

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A.1 GC-MS analysis of alkenes and their corresponding epoxides

Conditions: Column HP-5MS, 60 °C hold for 5 min, then progression 10 °C/min up to 320 °C, hold at 320 °C for 5 min. Constant flow 1 ml/min. $T_{inj.}$ = 250 °C

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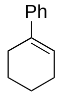
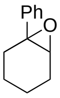
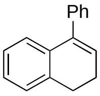
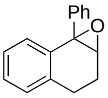
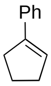
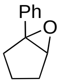
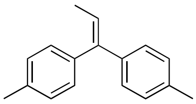
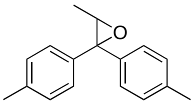
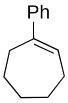
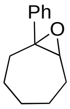
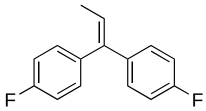
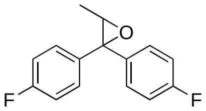
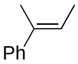
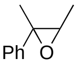
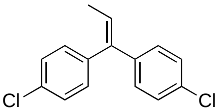
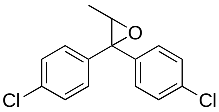
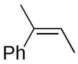
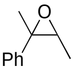
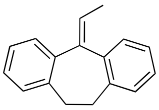
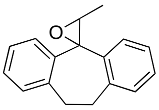
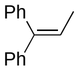
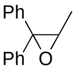
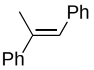
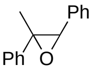
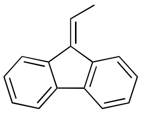
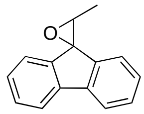
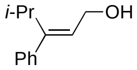
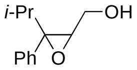
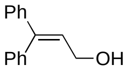
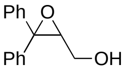
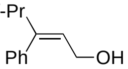
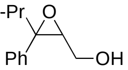
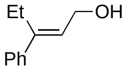
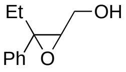
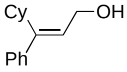
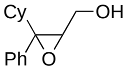
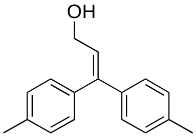
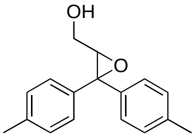
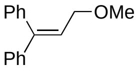
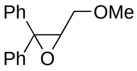
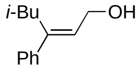
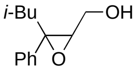
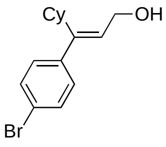
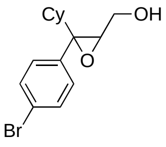
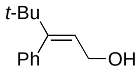
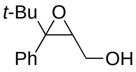
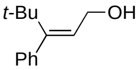
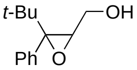
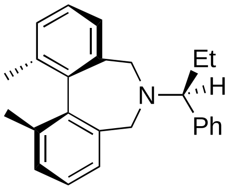
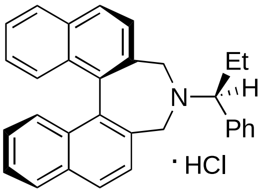
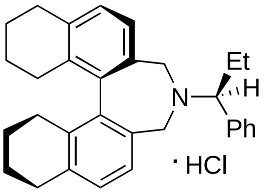
	15.16		15.78		20.25		–
	15.16		14.52		20.00		–
	16.24		17.39		17.57		18.15
	10.68		11.49		20.01		22.45
	8.84		10.50		20.78		21.33
	17.63		18.35		18.99		18.85
	21.18		–		15.75		16.78
	20.61		–		15.22		16.21
	15.51		16.04		20.24		21.08
	22.70		–		19.92		20.33
	17.09		17.47		23.37		24.01
	15.74		16.85		16.45		17.71

A.2 Crystallographic data

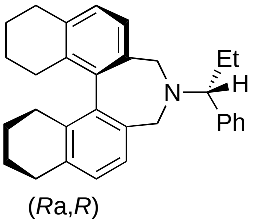
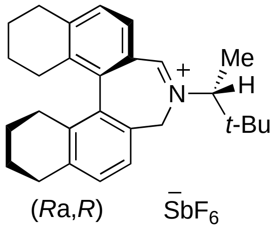
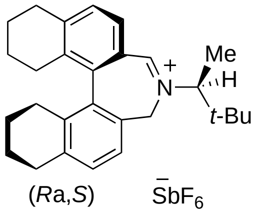
Summary of crystal data, intensity measurement and structure refinement for:

Compound	**72b**	**82b·HCl**	**83b·HCl**
Chemical structure			
	(*Ra*,*S*)	(*Ra*,*S*)	(*Ra*,*S*)
Brutto formula	$C_{25}H_{27}N$	$(C_{31}H_{29}N)^+Cl^-$ (CH_2Cl_2)	$(C_{31}H_{36}N)^+Cl^-$ (CH_2Cl_2)
Molecular weight	341.5	535.0	543.1
Solvent	hexane	CH_2Cl_2/hexane	CH_2Cl_2/hexane
Crystal size (mm)	0.11 x 0.19 x 0.24	0.14 x 0.23 x 0.25	0.110 x 0.336 x 0.406
Crystal system	monoclinic	monoclinic	monoclinic
Space group	$C\,2$	$P\,2_1$	$P\,2_1$
a (Å)	21.6071(15)	9.4639(9)	9.0889(8)
b (Å)	7.2501(6)	11.2349(6)	11.6892(6)
c (Å)	12.9562(11)	13.3132(12)	14.2112(12)
α (°)	90	90	90
β (°)	98.425(9)	102.973(11)	97.361(10)
γ (°)	90	90	90
V ($Å^3$)	2007.7(3)	1379.4(2)	1497.4(2)
Z	4	2	2
D_x $gr.cm^{-3}$	1.130	1.288	1.204
μ(Mo (Kα)) mm^{-1}	0.065	0.354	0.327
Tmin, Tmax	0.9867, 0.9934	0.9176, 0.9550	0.9067, 0.9655
No. measured reflc.	13863	19095	19068
No. independent reflc.	4332	5756	5828
No. observed reflc.	2435	4045	4156
Criterion for observed	$\|Fo\| > 4\sigma(Fo)$	$\|Fo\| > 4\sigma(Fo)$	$\|Fo\| > 4\sigma(Fo)$
Refinement (on F)	Full matrix	Full matrix	Full matrix
No. parameters	234	351	385
Weighting scheme *p* [a]	0.00015	0.00015	0.00025
Maximum Δ/σ	0.000024	0.00018	0.00022
Max. and min. $\Delta\rho$ (e.$Å^3$)	-0.27, 0.31	-0.61, 0.68	-0.32, 0.30
Flack parameter x	Fixed at 0,0	0.00(8)	-0.02(7)
S [b] (all data)	1.50(2)	1.73(3)	1.59(2)
R [c], ωR [d]	0.039, 0.036	0.041, 0.038	0.034, 0.034

[a] $\omega = 1/[\sigma^2(F_o) + p(F_o)^2]$; [b] $S = [\Sigma\{((F_o-F_c)/\sigma(F_o))^2\}/(N_{ref}-N_{var})]^{1/2}$

[c] $R = \Sigma||F_o| - |F_o||/\Sigma|F_o|$; [d] $\omega R = [\Sigma(\omega|F_o|-|F_c|)^2/\Sigma|F_o|^2]^{1/2}$

Summary of crystal data, intensity measurement and structure refinement for:

Compound	**83d**	**[71c][SbF$_6$]**	**[71a][SbF$_6$]**
Chemical structure			
Brutto formula	$C_{31}H_{35}N$	$(C_{28}H_{36}N)(SbF_6)$	$(C_{28}H_{36}N)(SbF_6)$
Molecular weight	421.7	622.4	622.4
Solvent	hexane	CH_2Cl_2/hexane	CH_2Cl_2/hexane
Crystal size (mm)	0.14 x 0.20 x 0.23	0.21 x 0.23 x 0.31	0.2 x 0.2 x 0.4
Crystal system	orthorhombic	orthorhombic	Monoclinic f)
Space group	$P\ 2_12_12_1$	$P\ 2_12_12_1$	$P\ 2_1$ f)
a (Å)	8.5829(4)	10.6995(5)	10.898(4)
b (Å)	15.1810(9)	15.0173(11)	15.245(2)
c (Å)	18.1570(10)	16.9203	16.219(3)
α (°)	90	90	90
β (°)	90	90	90.12(1)
γ (°)	90	90	90
V (Å^3)	2365.8(2)	2718.7(3)	2694.6
Z	4	4	4
D_x gr.cm^{-3}	1.181	1.520	1.525
μ(Mo (Kα)) mm^{-1}	0.067	1.073	1.08
Tmin, Tmax	0.9861, 0.9917	0.7976, 0.8377	No absorption correction (twinning)
No. measured reflc.	28195	35941	21116
No. independent reflc.	5151	5851	12147
No. observed reflc.	3034	4674	9145
Criterion for observed	$\vert Fo\vert > 4\sigma(Fo)$	$\vert Fo\vert > 3\sigma(Fo)$	$\vert Fo\vert > 2\sigma(Fo)$
Refinement	Full matrix on F	Full matrix on F	Full matrix on F^2
No. parameters	289	326	772
Weighting scheme *p* a)	0.0003	0.0002	2.54,2.86,0.771 e)
Maximum Δ/σ	0.000098	0.00004	0.003
Max. and min. Δρ (e.Å^3)	-0.39, 0.58	-1.08, 0.94	-1.13,0.90
Flack parameter x	Fixed at 0.0	-0.03(3)	See f)
S b) (all data)	1.33(2)	1.90(3)	0.90
R c), ωR d)	0.036, 0.036	0.034, 0.034	0.043,0.084

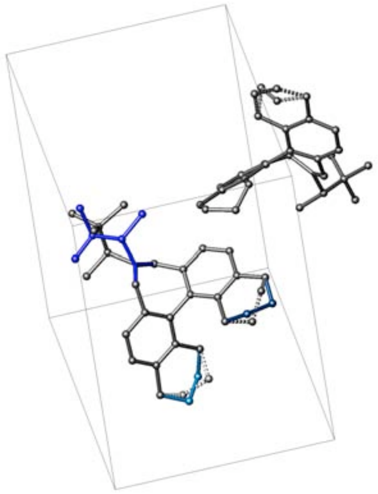
a) $\omega = 1/[\sigma^2(F_o) + p(F_o)^2]$; b) $S = [\Sigma\{((F_o-F_c)/\sigma(F_o))^2\}/(N_{ref}-N_{var})]^{1/2}$

c) $R = \Sigma\vert\,\vert F_o\vert - \vert F_o\vert\,\vert/\Sigma\vert F_o\vert$; d) $\omega R = [\Sigma(\omega\vert F_o\vert - \vert F_c\vert)^2/\Sigma\vert F_o\vert^2]^{1/2}$

e) ω = 1.0/[A0*T0(x) +A1*T1(x) ··· + An-1]*Tn-1(x)] where Ai are the Chebychev coefficients listed and x = *F* /*F*max

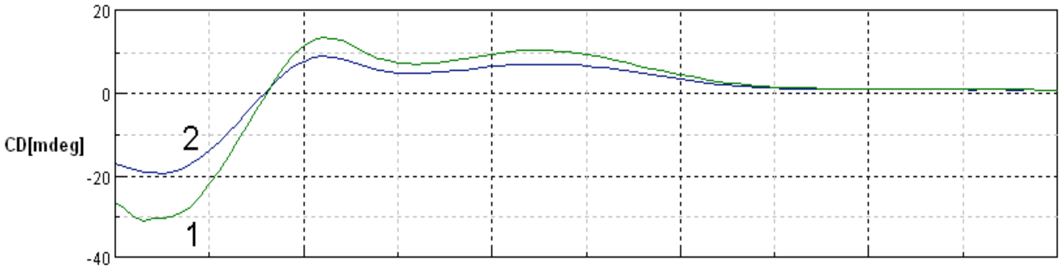
f) The crystal structure is almost orthorhombic with space group $P\ 2_12_12_1$ but some reflections violates the glide plane extinctions and orthorhombic models were unsatisfactory. The symmetry was therefore lowered to $P2_1$. Twinning corresponding to a two-fold rotation of the crystal around the a-axis was applied. This twinning law is compatible with an enantiopure compound. Four different domains were included : the non-twinned part , its inversion twin , the 2-fold twin and its inversion twin. The final twin fractions refined to 0.69(2),0.03(2),0.22(2) and 0.06(2). The low fraction of both inversion twins confirmed the enantiopurity of the compound which was further assessed by performing a CD spectrum on the measured crystal.

For one of the two molecules present in the asymmetric unit, the difference Fourier map showed peaks corresponding to a 2-fold rotation of the molecule along an axis passing through N. This two-fold disorder was included in the model. (Picture 1)

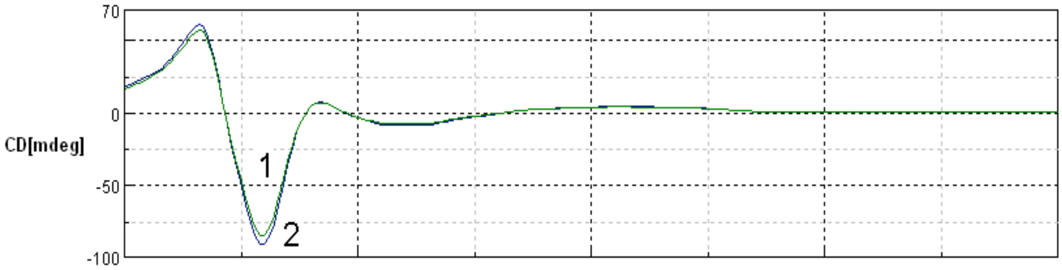


Picture of the asymmetric unit of [71a][SbF$_6$].
In blue are shown the disordered parts that correspond to a two-fold rotation of the molecule. The torsion angles of the terminal cycles of the molecules are still not perfectly described by this model, this may be due to some flipping of the cycle.

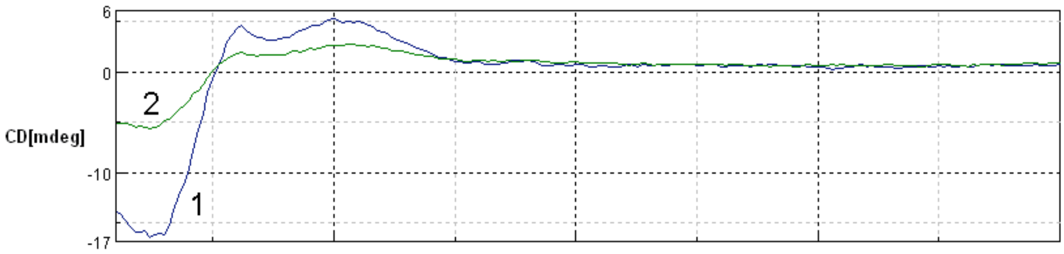
Circular dichroism (CD) analysis of the pure compounds and their corresponding crystals which were used for the X-ray structure determination



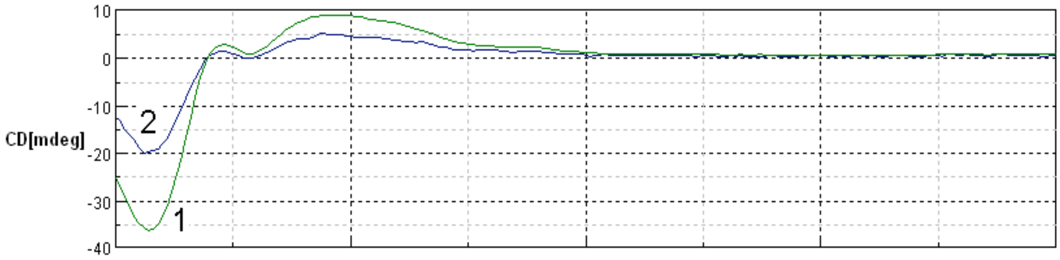
1. CD spectrum of **72b** (MeOH, 1 × 10^{-5} M) (green line)
2. CD spectrum of the crystal used in the X-ray structural analysis of **72b** (MeOH solution) (blue line)



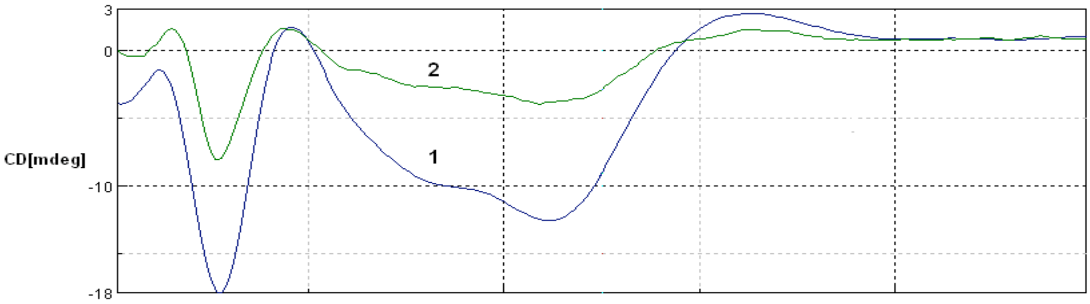
1.CD spectrum of **82b·HCl** (MeOH, 1 × 10^{-6} M) (green line)
2.CD spectrum of the crystal used in the X-ray structural analysis of **82b·HCl** (MeOH solution) (blue line)



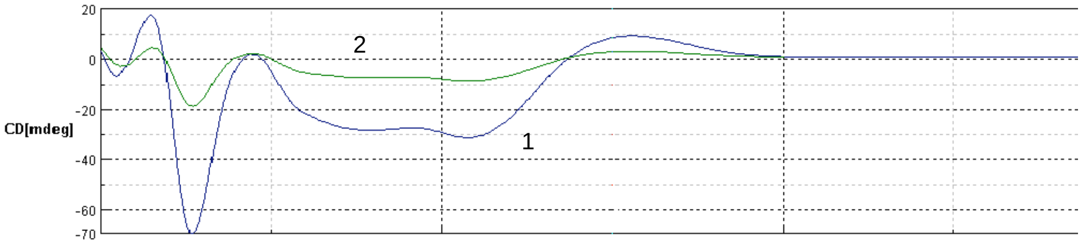
1.CD spectrum of **83b·HCl** (*i*-PrOH, 1 × 10^{-5} M) (blue line)
2.CD spectrum of the crystal used in the X-ray structural analysis of **83b·HCl** (*i*-PrOH solution) (green line)



1.CD spectrum of **83d** (*n*-hexane, 1 × 10^{-5} M) (green line)
2.CD spectrum of the crystal used in the X-ray structural analysis of **83d** (*n*-hexane solution) (blue line)

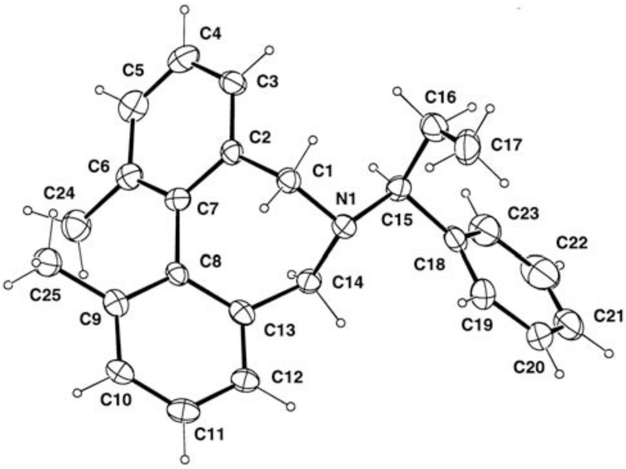


1.CD spectrum of **[71c][SbF$_6$]** (MeCN, 5 × 10^{-4} M) (blue line)
2.CD spectrum of the crystal used in the X-ray structural analysis of **[71c][SbF$_6$]** (MeCN solution) (green line)



1.CD spectrum of **[71a][SbF$_6$]** (MeCN, 5 × 10^{-4} M) (blue line)
2.CD spectrum of the crystal used in the X-ray structural analysis of **[71a][SbF$_6$]** (MeCN solution) (green line)

A.2.1 Compound 72b



Bond Distances (Angstroms)

N1-C1	1.484(6)	N1-C14	1.495(6)
N1-C15	1.473(6)	C1-C2	1.517(6)
C2-C3	1.382(7)	C2-C7	1.421(8)
C3-C4	1.383(6)	C4-C5	1.390(9)
C5-C6	1.402(8)	C6-C7	1.400(6)
C6-C24	1.512(8)	C7-C8	1.511(7)
C8-C9	1.416(7)	C8-C13	1.408(7)
C9-C10	1.390(7)	C9-C25	1.504(7)
C10-C11	1.387(7)	C11-C12	1.400(8)
C12-C13	1.389(7)	C13-C14	1.514(7)
C15-C16	1.544(9)	C15-C18	1.512(8)
C16-C17	1.497(7)	C18-C19	1.397(7)
C18-C23	1.391(8)	C19-C20	1.403(8)
C20-C21	1.39(1)	C21-C22	1.35(1)
C22-C23	1.374(9)		

Bond Angles (degrees)

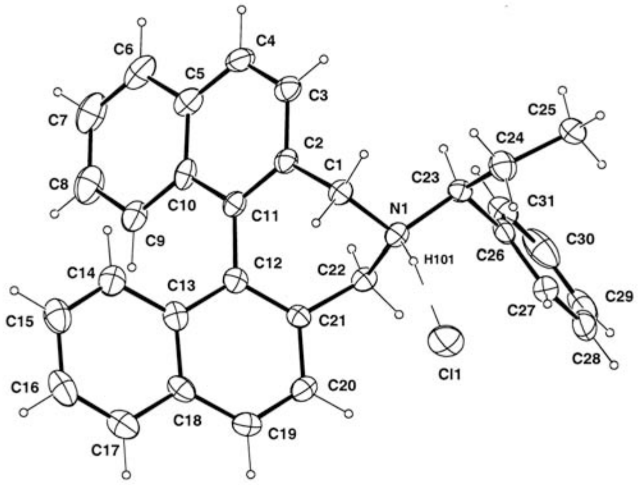
C1-N1-C14	109.9(4)	C1-N1-C15	115.1(3)

C14-N1-C15	108.7(4)	N1-C1-C2	115.1(4)
C1-C2-C3	121.6(5)	C1-C2-C7	118.6(4)
C3-C2-C7	119.7(4)	C2-C3-C4	121.2(5)
C3-C4-C5	118.9(5)	C4-C5-C6	121.8(4)
C5-C6-C7	118.6(5)	C5-C6-C24	118.5(4)
C7-C6-C24	122.7(5)	C2-C7-C6	119.5(5)
C2-C7-C8	117.3(4)	C6-C7-C8	123.1(5)
C7-C8-C9	122.7(4)	C7-C8-C13	117.6(4)
C9-C8-C13	119.6(5)	C8-C9-C10	118.7(5)
C8-C9-C25	123.6(5)	C10-C9-C25	117.6(5)
C9-C10-C11	121.8(5)	C10-C11-C12	119.4(5)
C11-C12-C13	120.1(5)	C8-C13-C12	120.3(5)
C8-C13-C14	120.4(4)	C12-C13-C14	119.3(4)
N1-C14-C13	113.1(4)	N1-C15-C16	112.7(4)
N1-C15-C18	111.0(4)	C16-C15-C18	110.2(4)
C15-C16-C17	115.3(5)	C15-C18-C19	121.5(5)
C15-C18-C23	120.5(4)	C19-C18-C23	117.9(5)
C18-C19-C20	119.5(5)	C19-C20-C21	120.6(5)
C20-C21-C22	119.3(6)	C21-C22-C23	120.9(7)
C18-C23-C22	121.8(5)		

Dihedral Angles (degrees)

C14-N1-C1-C2	-48.0(5)	C15-N1-C1-C2	75.2(5)
C1-N1-C14-C13	-41.2(5)	C15-N1-C14-C13	-168.1(4)
C1-N1-C15-C16	51.9(5)	C1-N1-C15-C18	176.1(4)
C14-N1-C15-C16	175.7(4)	C14-N1-C15-C18	-60.1(4)
N1-C1-C2-C3	-103.5(6)	N1-C1-C2-C7	74.1(6)
C1-C2-C3-C4	175.6(5)	C7-C2-C3-C4	-1.9(8)
C1-C2-C7-C6	-173.4(5)	C1-C2-C7-C8	5.4(7)
C3-C2-C7-C6	4.2(7)	C3-C2-C7-C8	-177.0(5)
C2-C3-C4-C5	-1.2(8)	C3-C4-C5-C6	2.2(8)
C4-C5-C6-C7	.1(8)	C4-C5-C6-C24	-176.3(5)
C5-C6-C7-C2	-3.2(8)	C5-C6-C7-C8	178.0(5)
C24-C6-C7-C2	172.9(5)	C24-C6-C7-C8	-5.8(8)
C2-C7-C8-C9	123.7(5)	C2-C7-C8-C13	-52.2(7)
C6-C7-C8-C9	-57.5(7)	C6-C7-C8-C13	126.6(5)
C7-C8-C9-C10	-179.6(5)	C7-C8-C9-C25	-3.9(8)
C13-C8-C9-C10	-3.7(8)	C13-C8-C9-C25	172.0(5)
C7-C8-C13-C12	177.9(5)	C7-C8-C13-C14	-1.4(7)
C9-C8-C13-C12	1.8(8)	C9-C8-C13-C14	-177.5(5)
C8-C9-C10-C11	2.2(8)	C25-C9-C10-C11	-173.8(5)
C9-C10-C11-C12	1.2(8)	C10-C11-C12-C13	-3.1(8)
C11-C12-C13-C8	1.6(8)	C11-C12-C13-C14	-179.1(5)
C8-C13-C14-N1	75.9(5)	C12-C13-C14-N1	-103.5(5)
N1-C15-C16-C17	55.2(6)	C18-C15-C16-C17	-69.4(6)
N1-C15-C18-C19	-40.8(7)	N1-C15-C18-C23	142.6(5)
C16-C15-C18-C19	84.8(6)	C16-C15-C18-C23	-91.8(6)
C15-C18-C19-C20	-174.7(6)	C23-C18-C19-C20	2.0(9)
C15-C18-C23-C22	175.2(6)	C19-C18-C23-C22	-1.5(9)
C18-C19-C20-C21	0(1)	C19-C20-C21-C22	-1(1)
C20-C21-C22-C23	2(1)	C21-C22-C23-C18	0(1)

A.2.2 Compound 82b·HCl



Bond Distances (Angstroms)

N1-C1	1.515(6)	N1-C22	1.520(5)
N1-C23	1.528(6)	C1-C2	1.523(5)
C2-C3	1.408(7)	C2-C11	1.394(6)
C3-C4	1.361(6)	C4-C5	1.419(7)
C5-C6	1.418(6)	C5-C10	1.413(7)
C6-C7	1.358(7)	C7-C8	1.402(9)
C8-C9	1.373(6)	C9-C10	1.429(6)
C10-C11	1.445(5)	C11-C12	1.485(7)
C12-C13	1.441(6)	C12-C21	1.385(6)
C13-C14	1.419(7)	C13-C18	1.426(7)
C14-C15	1.373(8)	C15-C16	1.411(8)
C16-C17	1.370(7)	C17-C18	1.431(7)
C18-C19	1.421(7)	C19-C20	1.355(7)
C20-C21	1.422(7)	C21-C22	1.504(6)
C23-C24	1.532(5)	C23-C26	1.520(6)
C24-C25	1.530(7)	C26-C27	1.400(6)
C26-C31	1.392(6)	C27-C28	1.372(8)
C28-C29	1.380(8)	C29-C30	1.395(9)
C30-C31	1.380(7)	Cl1a-C1a	1.87(2)
Cl2a-C1a	1.66(1)	C1b-Cl2b	1.73(3)
C1b-Cl1b	1.81(4)		

Bond Angles (degrees)

C1-N1-C22	111.1(3)	C1-N1-C23	113.2(4)
C22-N1-C23	113.7(3)	N1-C1-C2	112.4(3)
C1-C2-C3	119.7(4)	C1-C2-C11	119.6(4)
C3-C2-C11	120.7(4)	C2-C3-C4	120.8(4)
C3-C4-C5	120.9(5)	C4-C5-C6	121.1(5)
C4-C5-C10	119.3(4)	C6-C5-C10	119.6(4)
C5-C6-C7	120.6(5)	C6-C7-C8	120.0(4)
C7-C8-C9	121.8(5)	C8-C9-C10	119.2(5)
C5-C10-C9	118.9(4)	C5-C10-C11	119.4(4)
C9-C10-C11	121.7(4)	C2-C11-C10	118.8(4)
C2-C11-C12	118.3(4)	C10-C11-C12	122.7(4)

C11-C12-C13	123.1(4)	C11-C12-C21	117.9(4)
C13-C12-C21	118.8(4)	C12-C13-C14	122.5(4)
C12-C13-C18	119.3(4)	C14-C13-C18	118.1(4)
C13-C14-C15	121.0(5)	C14-C15-C16	120.7(5)
C15-C16-C17	120.4(5)	C16-C17-C18	120.0(5)
C13-C18-C17	119.8(4)	C13-C18-C19	119.4(4)
C17-C18-C19	120.8(4)	C18-C19-C20	120.5(5)
C19-C20-C21	120.9(4)	C12-C21-C20	120.9(4)
C12-C21-C22	120.6(4)	C20-C21-C22	118.4(4)
N1-C22-C21	110.9(3)	N1-C23-C24	110.0(3)
N1-C23-C26	110.3(4)	C24-C23-C26	113.6(3)
C23-C24-C25	113.2(4)	C23-C26-C27	121.6(4)
C23-C26-C31	119.6(4)	C27-C26-C31	118.9(4)
C26-C27-C28	120.3(4)	C27-C28-C29	121.0(5)
C28-C29-C30	119.0(6)	C29-C30-C31	120.5(5)
C26-C31-C30	120.3(5)	Cl1a-C1a-Cl2a	109.4(8)
Cl2b-C1b-Cl1b	110(2)		

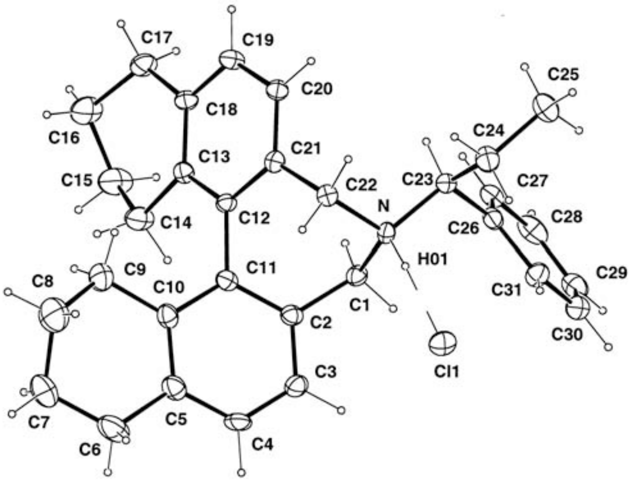
Dihedral Angles (degrees)

C22-N1-C1-C2	-41.3(5)	C23-N1-C1-C2	88.2(4)
C1-N1-C22-C21	-46.0(4)	C23-N1-C22-C21	175.1(3)
C1-N1-C23-C24	68.9(4)	C1-N1-C23-C26	-165.0(3)
C22-N1-C23-C24	-163.0(4)	C22-N1-C23-C26	-36.9(4)
N1-C1-C2-C3	-106.0(4)	N1-C1-C2-C11	74.8(5)
C1-C2-C3-C4	179.3(4)	C11-C2-C3-C4	-1.6(7)
C1-C2-C11-C10	-177.2(4)	C1-C2-C11-C12	-.8(6)
C3-C2-C11-C10	3.7(6)	C3-C2-C11-C12	180.0(4)
C2-C3-C4-C5	-1.3(7)	C3-C4-C5-C6	-178.2(5)
C3-C4-C5-C10	1.9(7)	C4-C5-C6-C7	179.2(5)
C10-C5-C6-C7	-.9(8)	C4-C5-C10-C9	-178.3(4)
C4-C5-C10-C11	.3(7)	C6-C5-C10-C9	1.8(7)
C6-C5-C10-C11	-179.7(4)	C5-C6-C7-C8	-.7(8)
C6-C7-C8-C9	1.4(8)	C7-C8-C9-C10	-.4(8)
C8-C9-C10-C5	-1.1(7)	C8-C9-C10-C11	-179.7(5)
C5-C10-C11-C2	-3.0(6)	C5-C10-C11-C12	-179.2(4)
C9-C10-C11-C2	175.5(4)	C9-C10-C11-C12	-.6(7)
C2-C11-C12-C13	122.9(4)	C2-C11-C12-C21	-51.6(5)
C10-C11-C12-C13	-61.0(6)	C10-C11-C12-C21	124.6(4)
C11-C12-C13-C14	-3.4(6)	C11-C12-C13-C18	-179.0(3)
C21-C12-C13-C14	171.1(4)	C21-C12-C13-C18	-4.6(5)
C11-C12-C21-C20	179.2(3)	C11-C12-C21-C22	.4(5)
C13-C12-C21-C20	4.4(5)	C13-C12-C21-C22	-174.3(3)
C12-C13-C14-C15	177.2(4)	C18-C13-C14-C15	-1.5(6)
C12-C13-C18-C17	178.5(4)	C12-C13-C18-C19	1.6(6)
C14-C13-C18-C17	2.6(6)	C14-C13-C18-C19	-174.2(4)
C13-C14-C15-C16	.3(6)	C14-C15-C16-C17	-.3(7)
C15-C16-C17-C18	1.5(6)	C16-C17-C18-C13	-2.7(6)
C16-C17-C18-C19	174.1(4)	C13-C18-C19-C20	1.6(6)
C17-C18-C19-C20	175.2(4)	C18-C19-C20-C21	-1.8(6)
C19-C20-C21-C12	-1.3(6)	C19-C20-C21-C22	177.6(3)
C12-C21-C22-N1	76.2(4)	C20-C21-C22-N1	-102.6(4)
N1-C23-C24-C25	171.7(4)	C26-C23-C24-C25	47.5(6)
N1-C23-C26-C27	-71.6(5)	N1-C23-C26-C31	108.6(5)
C24-C23-C26-C27	52.4(6)	C24-C23-C26-C31	-127.4(5)
C23-C26-C27-C28	179.4(4)	C31-C26-C27-C28	-.8(7)
C23-C26-C31-C30	178.2(5)	C27-C26-C31-C30	2.0(7)
C26-C27-C28-C29	-.6(8)	C27-C28-C29-C30	.8(9)
C28-C29-C30-C31	.5(9)	C29-C30-C31-C26	-1.9(9)

Hydrogen bonds

N1-H101	0.82(6) Å	N1...Cl1	3.008(4) Å
H101...Cl1	2.20(6) Å	N1-H101...Cl1	172(6) Å

A.2.3 Compound 83b·HCl



Bond Distances (Angstroms)

N-C1	1.526(4)	N-C22	1.520(5)
N-C23	1.529(5)	C1-C2	1.501(5)
C2-C3	1.383(5)	C2-C11	1.402(5)
C3-C4	1.380(6)	C4-C5	1.394(6)
C5-C6	1.516(6)	C5-C10	1.407(6)
C6-C7	1.494(7)	C7-C8	1.529(8)
C8-C9	1.494(7)	C9-C10	1.505(6)
C10-C11	1.416(5)	C11-C12	1.502(5)
C12-C13	1.410(5)	C12-C21	1.400(5)
C13-C14	1.524(5)	C13-C18	1.398(5)
C14-C15	1.522(6)	C15-C16	1.495(7)
C16-C17	1.511(6)	C17-C18	1.512(5)
C18-C19	1.395(5)	C19-C20	1.384(5)
C20-C21	1.389(5)	C21-C22	1.509(5)
C23-C24	1.533(5)	C23-C26	1.517(5)
C24-C25	1.524(6)	C26-C27	1.394(5)
C26-C31	1.398(6)	C27-C28	1.381(6)
C28-C29	1.376(6)	C29-C30	1.384(5)
C30-C31	1.379(6)		

Bond Angles (degrees)

C1-N-C22	111.0(2)	C1-N-C23	113.2(3)
C22-N-C23	112.6(3)	N-C1-C2	111.8(3)
C1-C2-C3	119.8(3)	C1-C2-C11	120.3(3)
C3-C2-C11	119.8(4)	C2-C3-C4	120.4(4)
C3-C4-C5	120.9(4)	C4-C5-C6	118.9(4)
C4-C5-C10	119.9(4)	C6-C5-C10	121.3(4)
C5-C6-C7	114.3(4)	C6-C7-C8	110.9(4)
C7-C8-C9	110.8(4)	C8-C9-C10	114.3(4)
C5-C10-C9	120.6(3)	C5-C10-C11	118.5(3)
C9-C10-C11	120.8(4)	C2-C11-C10	120.3(4)
C2-C11-C12	116.7(3)	C10-C11-C12	122.8(3)

C11-C12-C13	123.2(3)	C11-C12-C21	116.9(3)
C13-C12-C21	119.7(3)	C12-C13-C14	120.0(3)
C12-C13-C18	119.7(3)	C14-C13-C18	120.2(3)
C13-C14-C15	113.4(3)	C14-C15-C16	111.7(4)
C15-C16-C17	109.9(3)	C16-C17-C18	114.5(3)
C13-C18-C17	121.8(3)	C13-C18-C19	119.1(3)
C17-C18-C19	119.1(3)	C18-C19-C20	121.5(3)
C19-C20-C21	119.4(3)	C12-C21-C20	120.2(3)
C12-C21-C22	120.1(3)	C20-C21-C22	119.6(3)
N-C22-C21	112.1(3)	N-C23-C24	110.3(3)
N-C23-C26	109.9(3)	C24-C23-C26	112.7(3)
C23-C24-C25	112.3(3)	C23-C26-C27	120.3(3)
C23-C26-C31	121.3(3)	C27-C26-C31	118.3(3)
C26-C27-C28	120.4(4)	C27-C28-C29	120.9(4)
C28-C29-C30	119.2(4)	C29-C30-C31	120.6(4)
C26-C31-C30	120.5(3)		

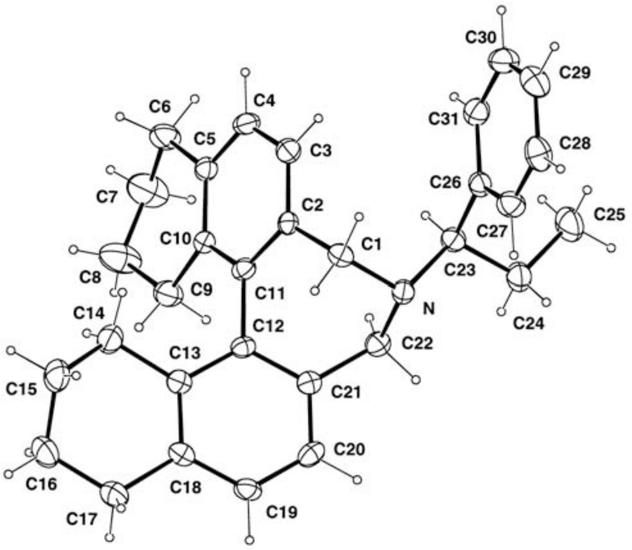
Dihedral Angles (degrees)

C22-N-C1-C2	-44.0(4)	C23-N-C1-C2	-171.7(3)
C1-N-C22-C21	-44.0(4)	C23-N-C22-C21	84.0(3)
C1-N-C23-C24	-163.3(3)	C1-N-C23-C26	-38.4(4)
C22-N-C23-C24	69.8(3)	C22-N-C23-C26	-165.3(3)
N-C1-C2-C3	-102.0(4)	N-C1-C2-C11	74.5(4)
C1-C2-C3-C4	175.0(3)	C11-C2-C3-C4	-1.5(6)
C1-C2-C11-C10	-171.6(3)	C1-C2-C11-C12	2.7(5)
C3-C2-C11-C10	4.9(5)	C3-C2-C11-C12	179.2(3)
C2-C3-C4-C5	-2.5(6)	C3-C4-C5-C6	-175.1(4)
C3-C4-C5-C10	3.2(6)	C4-C5-C6-C7	-169.5(4)
C10-C5-C6-C7	12.3(5)	C4-C5-C10-C9	-175.7(3)
C4-C5-C10-C11	.2(5)	C6-C5-C10-C9	2.5(5)
C6-C5-C10-C11	178.4(3)	C5-C6-C7-C8	-43.4(5)
C6-C7-C8-C9	61.7(5)	C7-C8-C9-C10	-46.9(5)
C8-C9-C10-C5	15.6(5)	C8-C9-C10-C11	-160.2(4)
C5-C10-C11-C2	-4.2(5)	C5-C10-C11-C12	-178.1(3)
C9-C10-C11-C2	171.7(3)	C9-C10-C11-C12	-2.2(5)
C2-C11-C12-C13	118.8(4)	C2-C11-C12-C21	-56.2(5)
C10-C11-C12-C13	-67.0(5)	C10-C11-C12-C21	117.9(4)
C11-C12-C13-C14	-4.1(6)	C11-C12-C13-C18	180.0(4)
C21-C12-C13-C14	170.8(4)	C21-C12-C13-C18	-5.1(6)
C11-C12-C21-C20	-179.9(3)	C11-C12-C21-C22	3.6(5)
C13-C12-C21-C20	4.8(5)	C13-C12-C21-C22	-171.6(3)
C12-C13-C14-C15	-162.0(4)	C18-C13-C14-C15	13.9(5)
C12-C13-C18-C17	178.2(4)	C12-C13-C18-C19	.8(6)
C14-C13-C18-C17	2.4(6)	C14-C13-C18-C19	-175.0(4)
C13-C14-C15-C16	-46.4(5)	C14-C15-C16-C17	62.3(5)
C15-C16-C17-C18	-45.2(5)	C16-C17-C18-C13	13.6(5)
C16-C17-C18-C19	-169.0(4)	C13-C18-C19-C20	3.8(6)
C17-C18-C19-C20	-173.7(4)	C18-C19-C20-C21	-4.0(6)
C19-C20-C21-C12	-.3(5)	C19-C20-C21-C22	176.2(3)
C12-C21-C22-N	73.9(4)	C20-C21-C22-N	-102.7(4)
N-C23-C24-C25	-177.8(3)	C26-C23-C24-C25	59.0(4)
N-C23-C26-C27	109.0(4)	N-C23-C26-C31	-70.2(4)
C24-C23-C26-C27	-127.6(4)	C24-C23-C26-C31	53.3(5)
C23-C26-C27-C28	-177.5(4)	C31-C26-C27-C28	1.7(6)
C23-C26-C31-C30	177.4(4)	C27-C26-C31-C30	-1.7(6)
C26-C27-C28-C29	-.1(6)	C27-C28-C29-C30	-1.5(6)
C28-C29-C30-C31	1.4(6)	C29-C30-C31-C26	.2(6)

Hydrogen bond

N-H01	0.96(4) Å	N...Cl1	3.020(3) Å
H01...Cl1	2.06(5) Å	N-H01...Cl1	175(4) Å

A.2.4 Compound 83d



Bond Distances (Angstroms)

N-C1	1.490(5)	N-C22	1.499(5)
N-C23	1.482(5)	C1-C2	1.520(5)
C2-C3	1.389(5)	C2-C11	1.401(5)
C3-C4	1.387(5)	C4-C5	1.391(5)
C5-C6	1.526(5)	C5-C10	1.398(5)
C6-C7	1.513(7)	C7-C8	1.474(8)
C8-C9	1.497(6)	C9-C10	1.525(5)
C10-C11	1.423(5)	C11-C12	1.504(5)
C12-C13	1.419(6)	C12-C21	1.394(5)
C13-C14	1.519(6)	C13-C18	1.402(5)
C14-C15	1.527(6)	C15-C16	1.515(7)
C16-C17	1.511(6)	C17-C18	1.529(6)
C18-C19	1.391(5)	C19-C20	1.389(6)
C20-C21	1.395(6)	C21-C22	1.512(6)
C23-C24	1.541(6)	C23-C26	1.527(5)
C24-C25	1.524(6)	C26-C27	1.392(5)
C26-C31	1.392(6)	C27-C28	1.384(6)
C28-C29	1.388(6)	C29-C30	1.384(6)
C30-C31	1.388(6)		

Bond Angles (degrees)

C1-N-C22	110.6(3)	C1-N-C23	111.6(3)
C22-N-C23	109.5(3)	N-C1-C2	113.3(3)
C1-C2-C3	120.9(3)	C1-C2-C11	119.0(3)
C3-C2-C11	119.8(3)	C2-C3-C4	120.1(3)
C3-C4-C5	121.1(4)	C4-C5-C6	118.7(3)
C4-C5-C10	119.8(3)	C6-C5-C10	121.5(3)

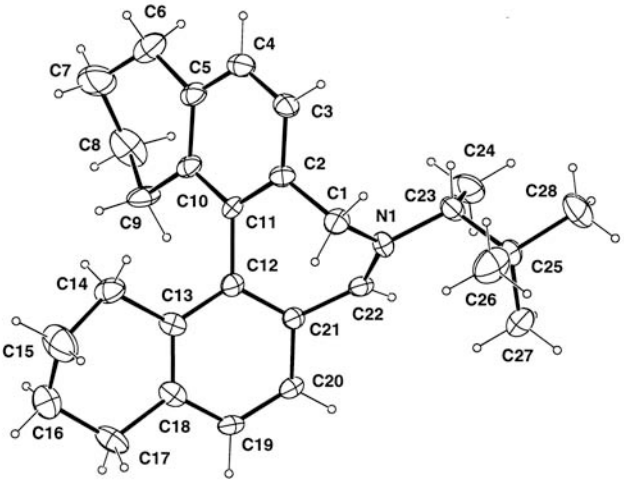
C5-C6-C7	113.6(4)	C6-C7-C8	112.4(4)
C7-C8-C9	114.9(4)	C8-C9-C10	114.8(4)
C5-C10-C9	120.2(3)	C5-C10-C11	119.0(3)
C9-C10-C11	120.4(3)	C2-C11-C10	119.9(3)
C2-C11-C12	117.4(3)	C10-C11-C12	122.6(3)
C11-C12-C13	122.1(3)	C11-C12-C21	117.4(4)
C13-C12-C21	120.2(3)	C12-C13-C14	120.0(3)
C12-C13-C18	119.4(3)	C14-C13-C18	120.4(4)
C13-C14-C15	112.7(4)	C14-C15-C16	109.6(4)
C15-C16-C17	110.8(4)	C16-C17-C18	114.1(4)
C13-C18-C17	121.7(3)	C13-C18-C19	119.1(4)
C17-C18-C19	119.1(4)	C18-C19-C20	121.4(4)
C19-C20-C21	120.1(4)	C12-C21-C20	119.4(4)
C12-C21-C22	120.1(3)	C20-C21-C22	120.4(3)
N-C22-C21	113.9(3)	N-C23-C24	112.2(3)
N-C23-C26	111.8(3)	C24-C23-C26	109.3(3)
C23-C24-C25	113.1(4)	C23-C26-C27	121.6(4)
C23-C26-C31	120.5(3)	C27-C26-C31	117.8(4)
C26-C27-C28	120.8(4)	C27-C28-C29	120.5(4)
C28-C29-C30	119.7(4)	C29-C30-C31	119.2(4)
C26-C31-C30	121.9(4)		

Dihedral Angles (degrees)

C22-N-C1-C2	-50.9(4)	C23-N-C1-C2	71.3(4)
C1-N-C22-C21	-37.0(4)	C23-N-C22-C21	-160.4(3)
C1-N-C23-C24	179.3(3)	C1-N-C23-C26	56.1(4)
C22-N-C23-C24	-57.9(4)	C22-N-C23-C26	178.8(3)
N-C1-C2-C3	-101.4(4)	N-C1-C2-C11	72.1(5)
C1-C2-C3-C4	171.7(4)	C11-C2-C3-C4	-1.7(6)
C1-C2-C11-C10	-167.9(4)	C1-C2-C11-C12	9.4(5)
C3-C2-C11-C10	5.7(6)	C3-C2-C11-C12	-177.1(4)
C2-C3-C4-C5	-2.9(6)	C3-C4-C5-C6	-175.9(4)
C3-C4-C5-C10	3.4(6)	C4-C5-C6-C7	157.9(4)
C10-C5-C6-C7	-21.4(6)	C4-C5-C10-C9	-172.5(4)
C4-C5-C10-C11	.6(6)	C6-C5-C10-C9	6.8(6)
C6-C5-C10-C11	179.9(4)	C5-C6-C7-C8	44.4(5)
C6-C7-C8-C9	-55.0(6)	C7-C8-C9-C10	39.6(6)
C8-C9-C10-C5	-15.2(6)	C8-C9-C10-C11	171.8(4)
C5-C10-C11-C2	-5.1(6)	C5-C10-C11-C12	177.8(4)
C9-C10-C11-C2	168.0(4)	C9-C10-C11-C12	-9.1(6)
C2-C11-C12-C13	118.5(4)	C2-C11-C12-C21	-55.1(5)
C10-C11-C12-C13	-64.4(5)	C10-C11-C12-C21	122.0(4)
C11-C12-C13-C14	-4.6(5)	C11-C12-C13-C18	179.5(3)
C21-C12-C13-C14	168.9(3)	C21-C12-C13-C18	-7.0(5)
C11-C12-C21-C20	179.4(3)	C11-C12-C21-C22	-1.9(5)
C13-C12-C21-C20	5.6(5)	C13-C12-C21-C22	-175.6(3)
C12-C13-C14-C15	-158.3(3)	C18-C13-C14-C15	17.6(5)
C12-C13-C18-C17	-179.1(3)	C12-C13-C18-C19	3.7(5)
C14-C13-C18-C17	5.0(5)	C14-C13-C18-C19	-172.2(3)
C13-C14-C15-C16	-51.4(4)	C14-C15-C16-C17	64.0(4)
C15-C16-C17-C18	-41.3(5)	C16-C17-C18-C13	7.2(5)
C16-C17-C18-C19	-175.7(4)	C13-C18-C19-C20	1.0(6)
C17-C18-C19-C20	-176.2(3)	C18-C19-C20-C21	-2.5(6)
C19-C20-C21-C12	-.9(5)	C19-C20-C21-C22	-179.7(3)
C12-C21-C22-N	74.4(4)	C20-C21-C22-N	-106.8(4)
N-C23-C24-C25	177.0(3)	C26-C23-C24-C25	-58.3(4)
N-C23-C26-C27	53.1(5)	N-C23-C26-C31	-129.8(4)
C24-C23-C26-C27	-71.8(5)	C24-C23-C26-C31	105.3(4)

C23-C26-C27-C28	176.5(4)	C31-C26-C27-C28	-.7(6)
C23-C26-C31-C30	-176.4(4)	C27-C26-C31-C30	.8(6)
C26-C27-C28-C29	.3(7)	C27-C28-C29-C30	.1(7)
C28-C29-C30-C31	.1(7)	C29-C30-C31-C26	-.5(7)

A.2.5 Compound [71c][SbF$_6$]



Bond Distances (Angstroms)

N1-C1	1.495(7)	N1-C22	1.294(8)
N1-C23	1.508(7)	C1-C2	1.506(8)
C2-C3	1.390(8)	C2-C11	1.406(8)
C3-C4	1.370(9)	C4-C5	1.392(9)
C5-C6	1.502(9)	C5-C10	1.421(8)
C6-C7	1.43(1)	C7-C8	1.60(1)
C8-C9	1.51(1)	C9-C10	1.503(8)
C10-C11	1.413(8)	C11-C12	1.506(7)
C12-C13	1.410(8)	C12-C21	1.413(7)
C13-C14	1.527(8)	C13-C18	1.387(8)
C14-C15	1.54(1)	C15-C16	1.47(1)
C16-C17	1.49(1)	C17-C18	1.516(8)
C18-C19	1.403(8)	C19-C20	1.396(8)
C20-C21	1.403(8)	C21-C22	1.445(8)
C23-C24	1.524(9)	C23-C25	1.562(9)
C25-C26	1.57(1)	C25-C27	1.509(9)
C25-C28	1.54(1)	Sb-F1	1.843(6)
Sb-F2	1.879(5)	Sb-F3	1.868(5)
Sb-F4	1.854(5)	Sb-F5	1.859(6)
Sb-F6	1.838(6)		

Bond Angles (degrees)

C1-N1-C22	120.6(5)	C1-N1-C23	116.6(5)
C22-N1-C23	122.3(5)	N1-C1-C2	106.6(4)
C1-C2-C3	121.1(5)	C1-C2-C11	117.5(5)
C3-C2-C11	120.8(5)	C2-C3-C4	119.7(5)
C3-C4-C5	121.3(5)	C4-C5-C6	119.1(5)
C4-C5-C10	120.2(5)	C6-C5-C10	120.7(5)
C5-C6-C7	115.9(6)	C6-C7-C8	109.4(6)
C7-C8-C9	105.4(6)	C8-C9-C10	113.0(5)

C5-C10-C9	119.7(5)	C5-C10-C11	118.2(5)
C9-C10-C11	121.9(5)	C2-C11-C10	119.6(5)
C2-C11-C12	118.0(5)	C10-C11-C12	122.1(5)
C11-C12-C13	122.4(5)	C11-C12-C21	118.2(5)
C13-C12-C21	119.3(5)	C12-C13-C14	119.8(5)
C12-C13-C18	119.9(5)	C14-C13-C18	120.2(5)
C13-C14-C15	112.3(6)	C14-C15-C16	113.1(7)
C15-C16-C17	110.7(6)	C16-C17-C18	114.2(6)
C13-C18-C17	122.3(5)	C13-C18-C19	120.1(5)
C17-C18-C19	117.6(5)	C18-C19-C20	120.7(5)
C19-C20-C21	119.1(5)	C12-C21-C20	120.0(5)
C12-C21-C22	124.3(5)	C20-C21-C22	115.7(5)
N1-C22-C21	123.4(5)	N1-C23-C24	110.6(5)
N1-C23-C25	110.6(5)	C24-C23-C25	114.7(5)
C23-C25-C26	109.3(5)	C23-C25-C27	113.0(6)
C23-C25-C28	107.0(5)	C26-C25-C27	107.5(5)
C26-C25-C28	109.0(6)	C27-C25-C28	110.9(6)
F1-Sb-F2	176.0(3)	F1-Sb-F3	91.5(3)
F1-Sb-F4	93.3(3)	F1-Sb-F5	88.9(3)
F1-Sb-F6	90.4(4)	F2-Sb-F3	89.3(2)
F2-Sb-F4	90.6(3)	F2-Sb-F5	90.5(3)
F2-Sb-F6	85.6(4)	F3-Sb-F4	89.0(2)
F3-Sb-F5	177.5(2)	F3-Sb-F6	91.7(3)
F4-Sb-F5	88.5(2)	F4-Sb-F6	176.2(3)
F5-Sb-F6	90.8(3)		

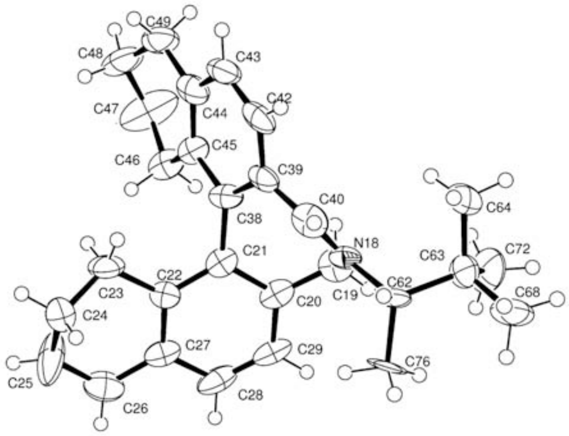
Dihedral Angles (degrees)

C22-N1-C1-C2	-69.1(6)	C23-N1-C1-C2	103.0(5)
C1-N1-C22-C21	-5.1(8)	C23-N1-C22-C21	-176.7(5)
C1-N1-C23-C24	-134.4(5)	C1-N1-C23-C25	97.5(6)
C22-N1-C23-C24	37.6(7)	C22-N1-C23-C25	-90.6(6)
N1-C1-C2-C3	-101.8(6)	N1-C1-C2-C11	69.8(6)
C1-C2-C3-C4	171.2(5)	C11-C2-C3-C4	-.1(8)
C1-C2-C11-C10	-167.5(5)	C1-C2-C11-C12	7.0(7)
C3-C2-C11-C10	4.2(8)	C3-C2-C11-C12	178.7(5)
C2-C3-C4-C5	-3.1(9)	C3-C4-C5-C6	-174.9(5)
C3-C4-C5-C10	2.3(9)	C4-C5-C6-C7	-173.4(6)
C10-C5-C6-C7	9.5(9)	C4-C5-C10-C9	-173.2(5)
C4-C5-C10-C11	1.8(8)	C6-C5-C10-C9	3.9(8)
C6-C5-C10-C11	178.9(5)	C5-C6-C7-C8	-44.8(8)
C6-C7-C8-C9	67.8(7)	C7-C8-C9-C10	-54.7(7)
C8-C9-C10-C5	21.8(8)	C8-C9-C10-C11	-153.0(6)
C5-C10-C11-C2	-4.9(8)	C5-C10-C11-C12	-179.2(5)
C9-C10-C11-C2	170.0(5)	C9-C10-C11-C12	-4.3(8)
C2-C11-C12-C13	124.4(6)	C2-C11-C12-C21	-58.8(7)
C10-C11-C12-C13	-61.2(8)	C10-C11-C12-C21	115.6(6)
C11-C12-C13-C14	-11.7(8)	C11-C12-C13-C18	171.6(5)
C21-C12-C13-C14	171.5(5)	C21-C12-C13-C18	-5.2(8)
C11-C12-C21-C20	-166.5(5)	C11-C12-C21-C22	16.9(8)
C13-C12-C21-C20	10.4(8)	C13-C12-C21-C22	-166.2(5)
C12-C13-C14-C15	-162.4(6)	C18-C13-C14-C15	14.3(8)
C12-C13-C18-C17	176.1(5)	C12-C13-C18-C19	-2.4(9)
C14-C13-C18-C17	-.6(9)	C14-C13-C18-C19	-179.2(5)
C13-C14-C15-C16	-44.8(9)	C14-C15-C16-C17	61.2(9)
C15-C16-C17-C18	-45.5(8)	C16-C17-C18-C13	16.1(9)
C16-C17-C18-C19	-165.2(6)	C13-C18-C19-C20	5.1(9)
C17-C18-C19-C20	-173.6(5)	C18-C19-C20-C21	.1(8)
C19-C20-C21-C12	-7.8(8)	C19-C20-C21-C22	169.0(5)
C12-C21-C22-N1	38.3(9)	C20-C21-C22-N1	-138.4(6)
N1-C23-C25-C26	-58.0(7)	N1-C23-C25-C27	61.6(7)

N1-C23-C25-C28	-176.0(5)	C24-C23-C25-C26	176.1(5)
C24-C23-C25-C27	-64.2(7)	C24-C23-C25-C28	58.2(7)

A.2.6 Compound [71a][SbF$_6$]

(Distances and bond angles taken from the non-disordered position of the molecule)



Bond Distances (Angstroms)

N18-C19	1.457(12)	N18-C40	1.292(11)
N18-C62	1.523(11)	C19-C20	1.473(14
C20-C21	1.435(11)	C20-C29	1.399(13)
C21-C22	1.422(12)	C21-C38	1.501(12)
C22-C23	1.519(13)	C22-C27	1.389(11)
C23-C24	1.485(14)	C24-C25	1.495(16)
C25-C26	1.42(2)	C26-C27	1.478(13)
C27-C28	1.409(14)	C28-C29	1.370(14)
C38-C39	1.413(12)	C38-C45	1.427(11)
C39-C40	1.425(13)	C39-C42	1.376(12)
C42-C43	1.392(15)	C43-C44	1.390(13)
C44-C45	1.409(12)	C44-C49	1.491(14)
C45-C46	1.490(13)	C46-C47	1.499(15)
C47-C48	1.448(19)	C48-C49	1.474(16)
C62-C63	1.555(12)	C62-C76	1.499(14)
C63-C64	1.569(18)	C63-C68	1.519(15)
C63-C72	1.530(15)		

Bond Angles (degrees)

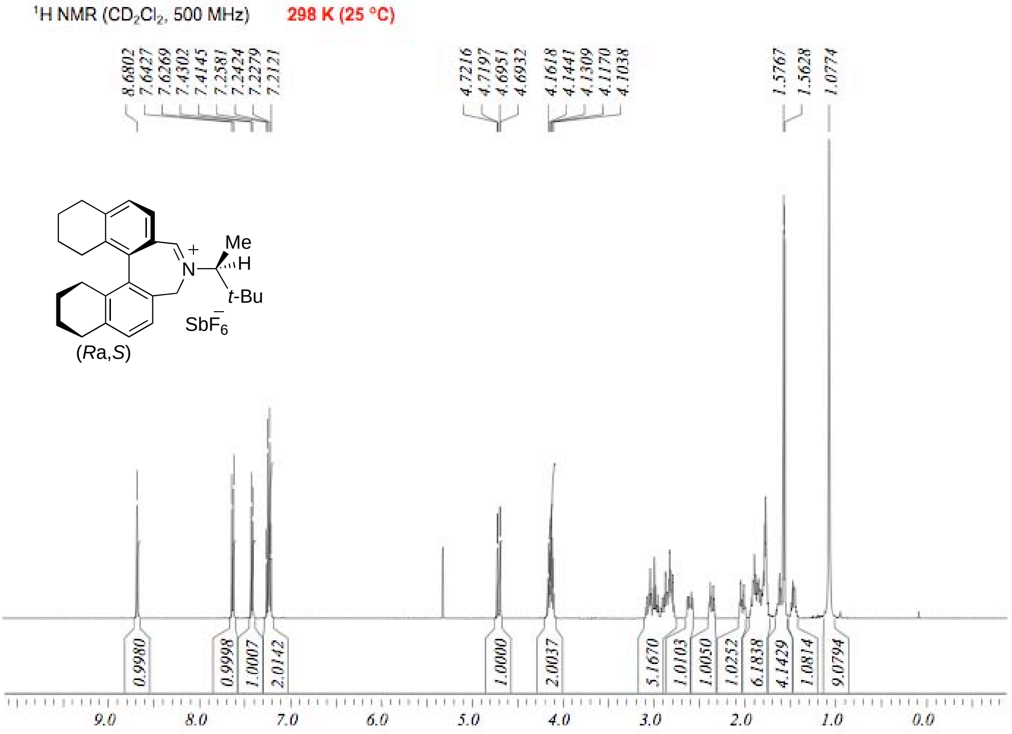
C19-N18-C40	122.6(7)	C19-N18-C62	121.2(7)
C40-N18-C62	116.0(7)	N18-C19-C20	110.8(7)
C19-C20-C21	118.0(8)	C19-C20-C29	123.2(8)
C21-C20-C29	118.4(8)	C20-C21-C22	119.2(7)
C20-C21-C38	118.4(7)	C22-C21-C38	122.3(7)
C21-C22-C23	120.0(7)	C21-C22-C27	120.9(7)
C23-C22-C27	119.0(7)	C22-C23-C24	112.7(8)
C23-C24-C25	108.0(10)	C24-C25-C26	117.0(11)

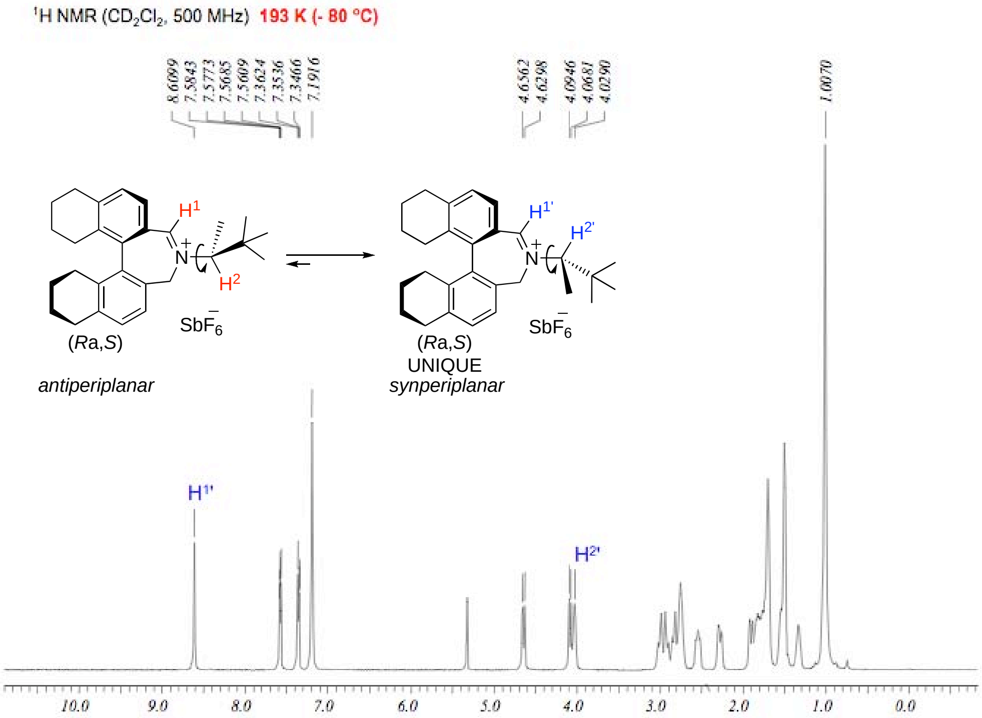
C25-C26-C27	116.7(9)	C22-C27-C26	120.8(8)
C22-C27-C28	117.8(8)	C26-C27-C28	121.4(8)
C27-C28-C29	122.9(9)	C20-C29-C28	120.3(9)
C21-C38-C39	120.6(7)	C21-C38-C45	120.6(7)
C39-C38-C45	118.8(8)	C38-C39-C40	122.4(8)
C38-C39-C42	120.2(8)	C40-C39-C42	117.3(8)
N18-C40-C39	124.4(8)	C39-C42-C43	121.5(8)
C42-C43-C44	118.1(8)	C43-C44-C45	122.6(8)
C43-C44-C49	116.5(8)	C45-C44-C49	120.9(8)
C38-C45-C44	117.7(8)	C38-C45-C46	120.7(7)
C44-C45-C46	121.4(7)	C45-C46-C47	112.8(9)
C46-C47-C48	116.5(11)	C47-C48-C49	112.5(10)
C44-C49-C48	115.6(8)	N18-C62-C63	113.8(7)
N18-C62-C76	109.3(7)	C63-C62-C76	115.0(8)
C62-C63-C64	108.0(8)	C62-C63-C68	110.2(9)
C62-C63-C72	113.3(9)	C64-C63-C68	110.6(10)
C64-C63-C72	106.7(10)	C68-C63-C72	108.1(10)

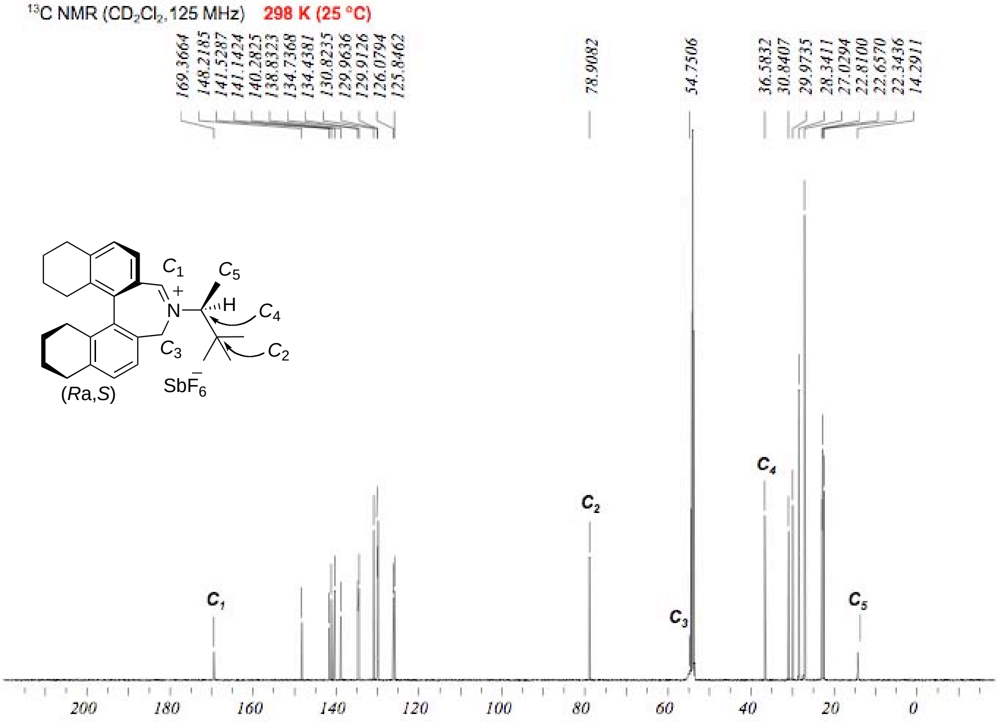
Dihedral Angles (degrees)

C40-N18-C19-C20	-65.4(10)	C62-N18-C19-C20	109.2(8)
C19-N18-C40-C39	-7.5(13)	C62-N18-C40-C39	177.7(8)
C19-N18-C62-C63	83.2(9)	C9-N18-C62-C76	-46.9(11)
C40-N18-C62-C63	-102.0(9)	C40-N18-C62-C76	128.0(9)
N18-C19-C20-C21	62.5(10)	N18-C19-C20-C29	-110.6(9)
C19-C20-C21-C22	165.4(7)	C9-C20-C21-C38	11.1(11)
C29-C20-C21-C22	8.0(11)	C29-C20-C21-C38	-175.5(7)
C19-C20-C29-C28	169.1(9)	C21-C20-C29-C28	-4.0(13)
C20-C21-C22-C23	167.7(8)	C20-C21-C22-C27	-7.4(12)
C38-C21-C22-C23	-8.6(12)	C38-C21-C22-C27	176.2(7)
C20-C21-C38-C39	-57.1(10)	C27-C22-C23-C24	25.2(11)
C20-C21-C38-C45	123.2(8)	C22-C21-C38-C39	119.3(8)
C22-C21-C38-C45	-60.4(10)	C21-C22-C23-C24	-150.1(8)
C21-C22-C27-C26	-178.9(8)	C21-C22-C27-C28	2.5(12)
C23-C22-C27-C26	5.9(12)	C23-C22-C27-C28	-172.7(8)
C22-C23-C24-C25	-53.1(13)	C23-C24-C25-C26	55.6(18)
C24-C25-C26-C27	-26(2)	C25-C26-C27-C22	-5.9(16)
C25-C26-C27-C28	172.6(12)	C22-C27-C28-C29	1.8(13)
C26-C27-C28-C29	-176.8(9)	C27-C28-C29-C20	-1.0(14)
C21-C38-C39-C40	13.4(11)	C21-C38-C39-C42	-167.5(8)
C45-C38-C39-C40	-166.9(7)	C45-C38-C39-C42	12.2(11)
C21-C38-C45-C44	172.3(7)	C21-C38-C45-C46	-12.6(10)
C39-C38-C45-C44	-7.5(10)	C39-C38-C45-C46	167.7(7)
C38-C39-C40-N18	40.3(13)	C42-C39-C40-N18	-138.8(9)
C38-C39-C42-C43	-10.1(13)	C40-C39-C42-C43	169.0(8)
C39-C42-C43-C44	3.1(13)	C42-C43-C44-C45	1.6(12)
C42-C43-C44-C49	-177.8(8)	C43-C44-C45-C38	0.7(11)
C43-C44-C45-C46	-174.4(8)	C49-C44-C45-C38	-179.9(7)
C49-C44-C45-C46	5.0(12)	C43-C44-C49-C48	-170.4(8)
C45-C44-C49-C48	10.2(12)	C38-C45-C46-C47	-166.5(9)
C44-C45-C46-C47	8.5(12)	C45-C46-C47-C48	-38.7(15)
C46-C47-C48-C49	54.5(16)	C47-C48-C49-C44	-38.6(13)
N18-C62-C63-C64	54.2(11)	N18-C62-C63-C68	175.1(9)
N18-C62-C63-C72	-63.7(10)	C76-C62-C63-C64	-178.6(10)
C76-C62-C63-C68	-57.7(11)	C76-C62-C63-C72	63.4(12)

A.3 NMR data for [71a][SbF_6] and [71c][SbF_6] iminium salts



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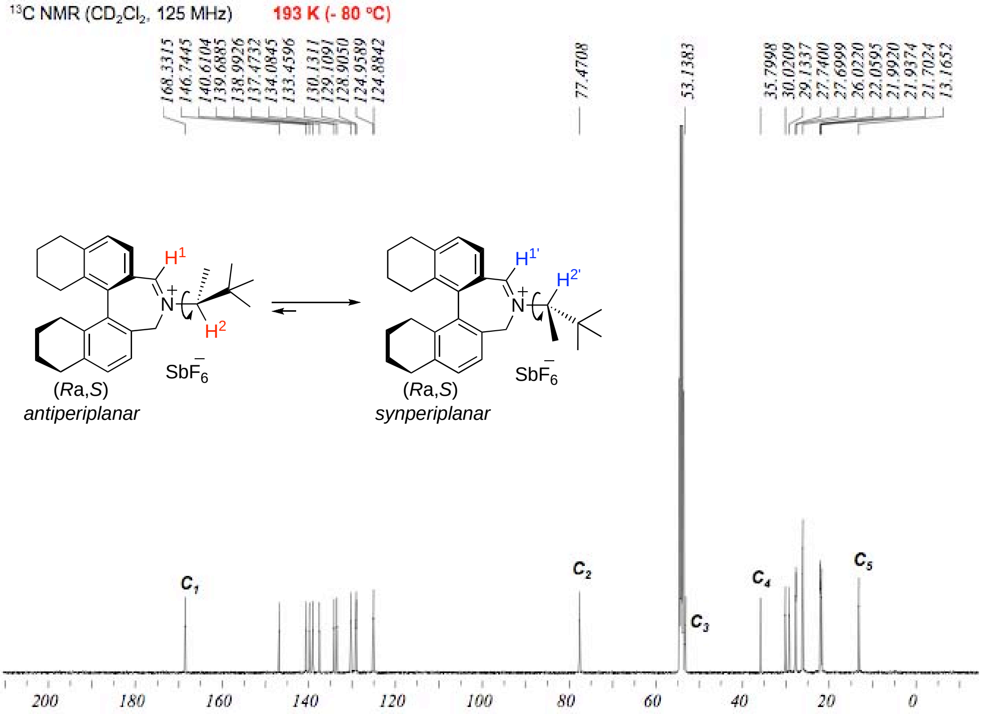
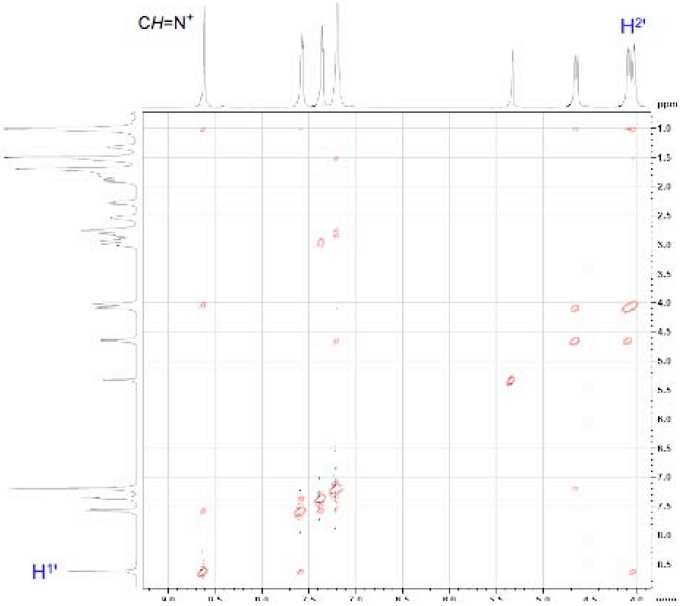
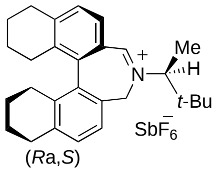
148.2185
141.5287
141.1424
140.2825
138.8323
134.7368
134.4381
130.8235
129.9636
129.9126
126.0794
125.8462
78.9082
54.7506
36.5832
30.8407
29.9735
28.3411
27.0294
22.8100
22.6570
22.3436
14.2911
C1
C5
+
N
H
C4
C3
C2
SbF6
(Ra,S)
C1
C2
C3
C4
C5
200
180
160
140
120
100
80
60
40
20
0

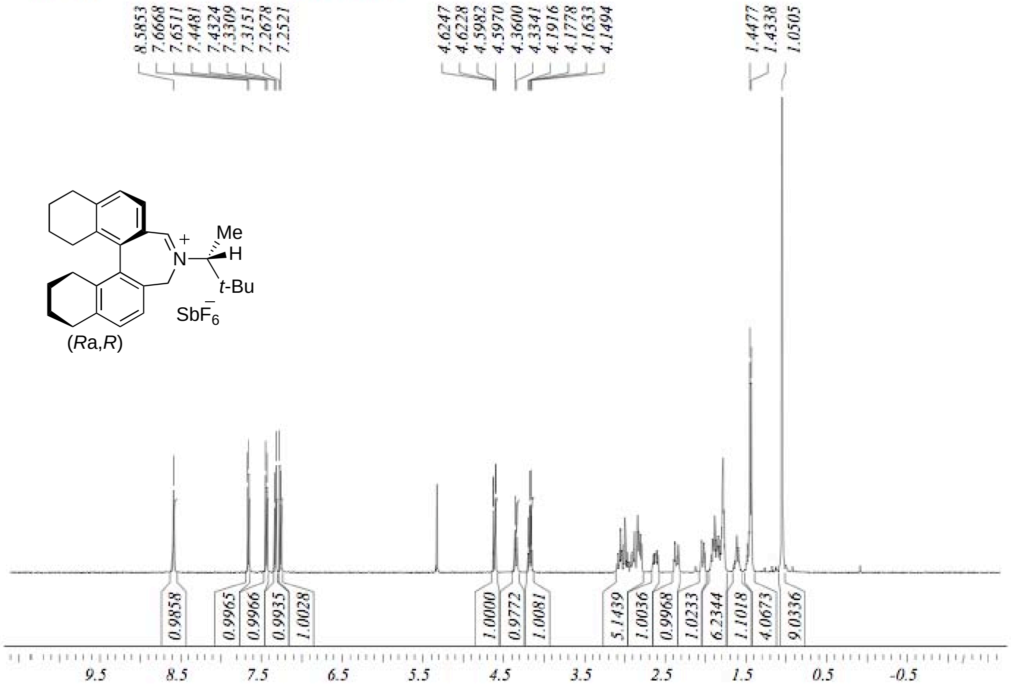

13C NMR (CD2Cl2, 125 MHz) 193 K (- 80 °C)
168.3315
146.7445
140.6104
139.6885
138.9926
137.4732
134.0845
133.4596
130.1311
129.1091
128.9050
124.9589
124.8842
77.4708
53.1383
35.7998
30.0209
29.1337
27.7400
27.6999
26.0220
22.0595
21.9920
21.9374
21.7024
13.1652
H1
N+
H2
SbF6
(Ra,S)
antiperiplanar
H1'
H2'
N+
SbF6
(Ra,S)
synperiplanar
C1
C2
C3
C4
C5
200
180
160
140
120
100
80
60
40
20
0

NOESY experiment (CD_2Cl_2, 500 MHz) at - 80 °C

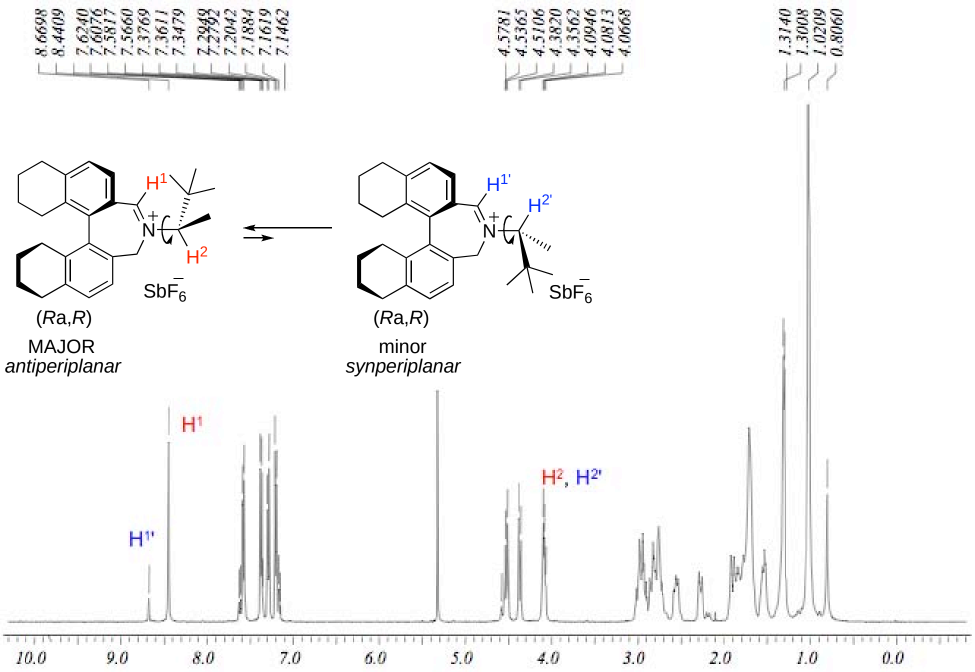




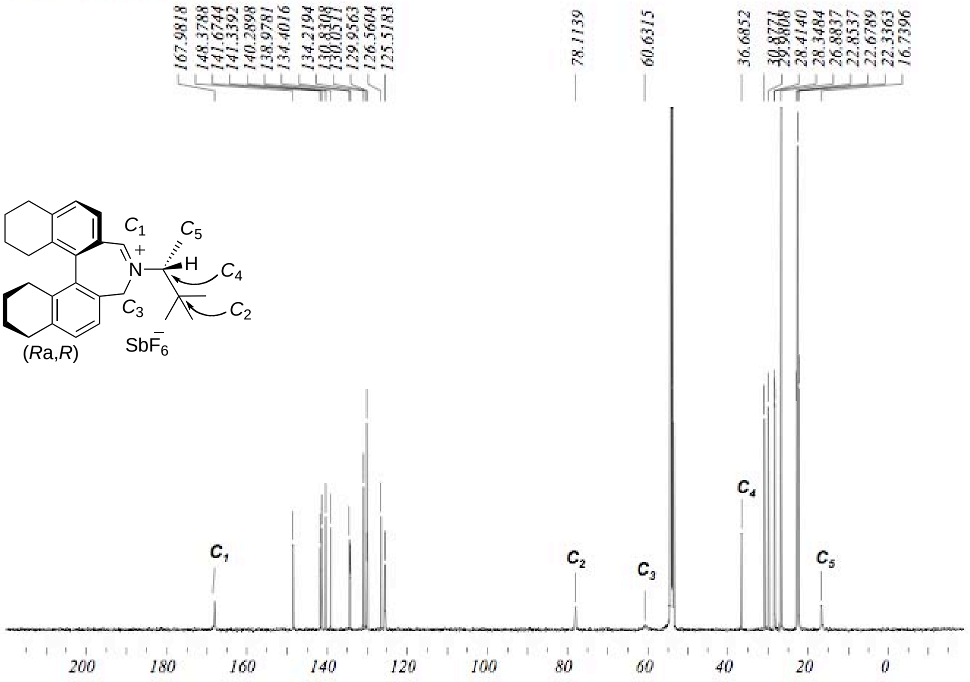
¹H NMR (CD_2Cl_2, 500 MHz) 298 K (25 °C)



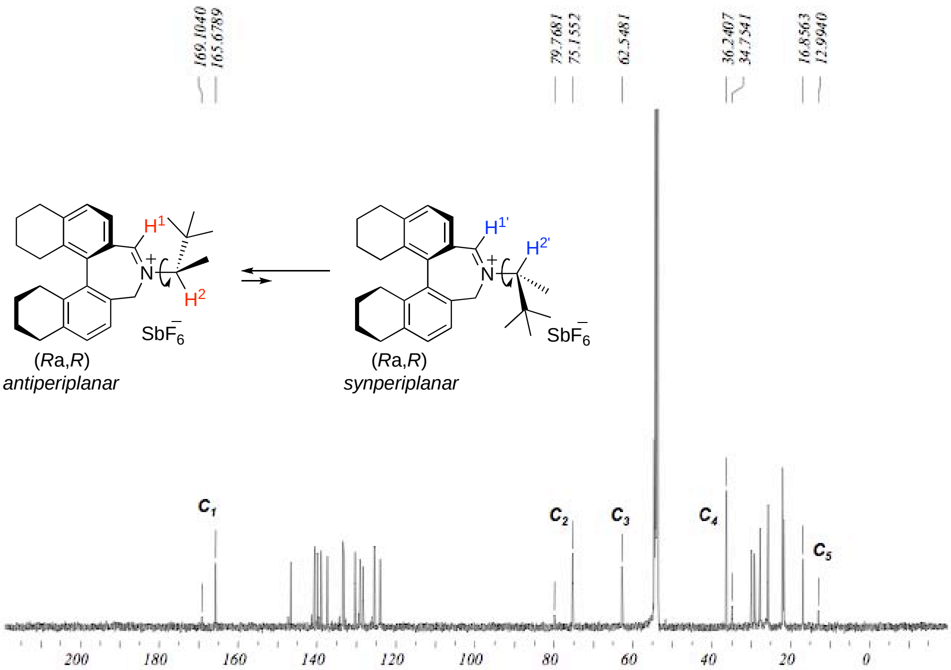
^{1}H NMR (CD_2Cl_2, 500 MHz) **193 K (- 80 °C)**



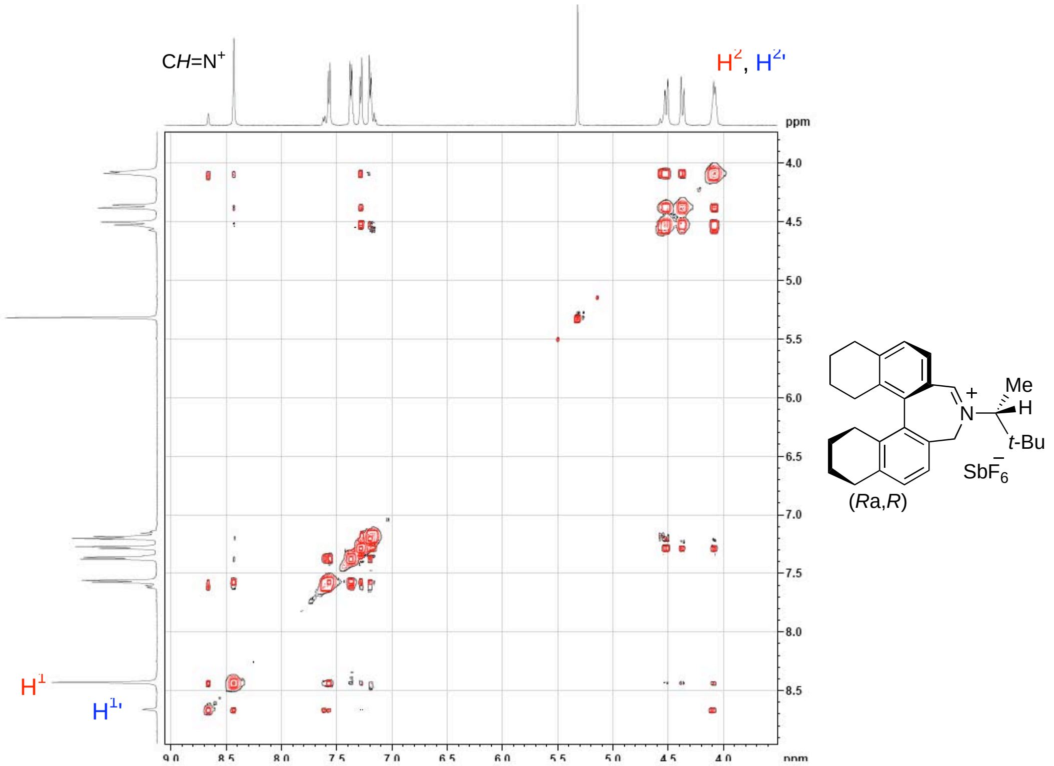
^{13}C NMR (CD_2Cl_2,125 MHz) **298 K (25 °C)**



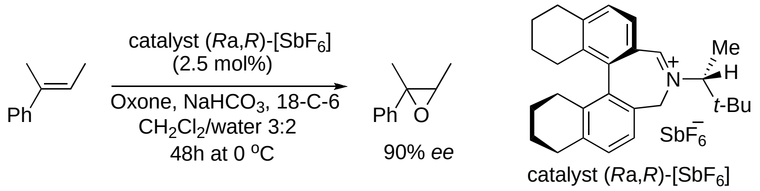
^{13}C NMR (CD_2Cl_2, 125 MHz) 193 K (- 80 °C)

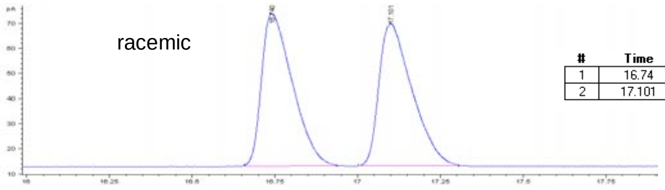


NOESY experiment (CD_2Cl_2, 500 MHz) at - 80 °C

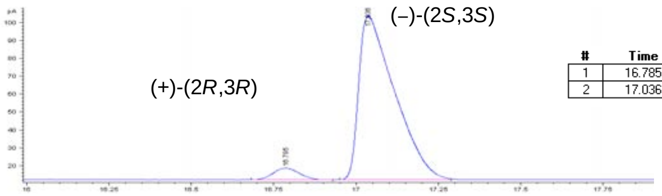


A.4 CSP-HPLC and CSP-GC data for epoxides



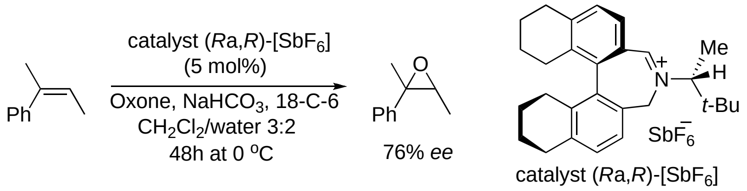


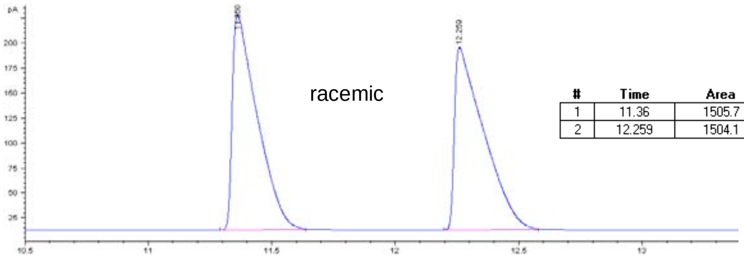
#	Time	Area	Height	Width	Symmetry
1	16.74	395.9	60.9	0.0902	0.452
2	17.101	394.3	56.9	0.0953	0.509



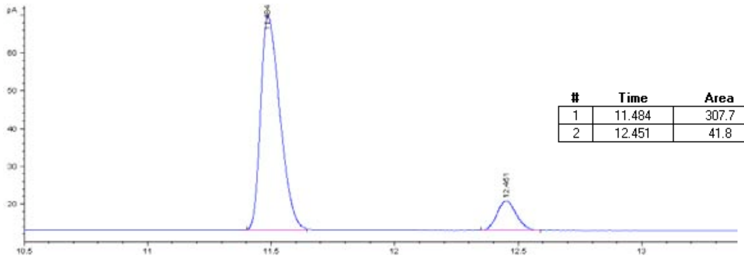
#	Time	Area	Height	Width	Symmetry
1	16.785	36.3	6.5	0.0862	0.902
2	17.036	693.1	91.5	0.1035	0.338

CSP-GC: Chiraldex Hydrodex β -3P: T_{inj} = 250 °C, P = 0.842 bar, 80 °C for 5 min, then gradient up to 180 °C 1 °C/min, hold at 180 °C for 5 min



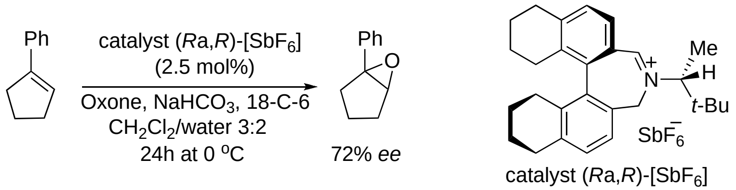


#	Time	Area	Height	Width	Symmetry
1	11.36	1505.7	214.7	0.0954	0.245
2	12.259	1504.1	182.1	0.1076	0.192

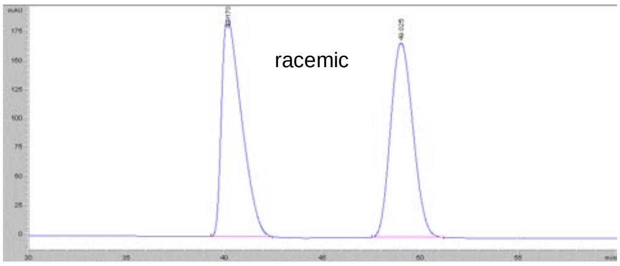


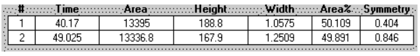
#	Time	Area	Height	Width	Symmetry
1	11.484	307.7	56.8	0.0776	0.566
2	12.451	41.8	7.8	0.0784	0.929

CSP-GC: Chiraldex Hydrodex β-3P: T_{inj} = 250 °C, P = 0.842 bar, 80 °C for 5 min, then gradient up to 180 °C 1 °C/min, hold at 180 °C for 5 min

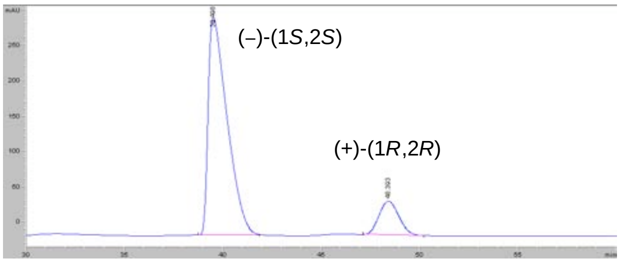


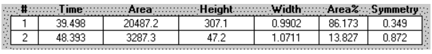
catalyst (*R*a,*R*)-[SbF$_6$]





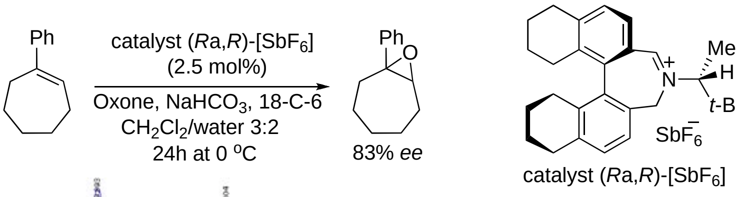
#	Time	Area	Height	Width	Area%	Symmetry
1	40.17	13395	188.8	1.0575	50.109	0.404
2	49.025	13336.8	167.9	1.2509	49.891	0.846



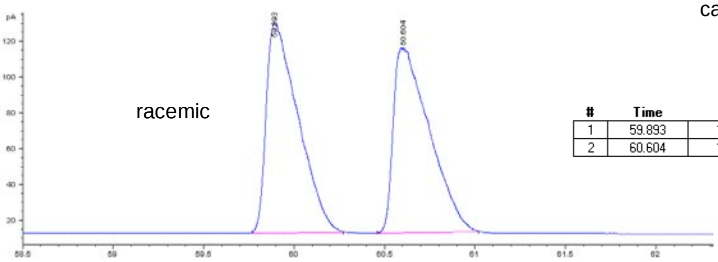


#	Time	Area	Height	Width	Area%	Symmetry
1	39.498	20487.2	307.1	0.9902	86.173	0.349
2	48.393	3287.3	47.2	1.0711	13.827	0.872

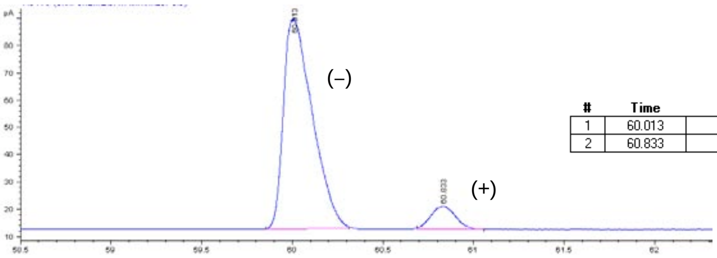
CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 99.9/0.1 %, 0.5 ml/min, 23 ^{o}C, λ = 210 nm



catalyst (*R*a,*R*)-[SbF$_6$]

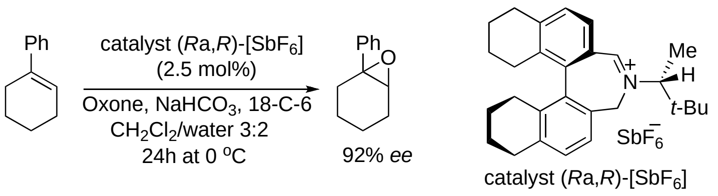


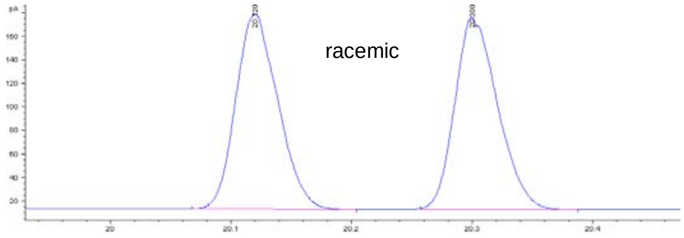
#	Time	Area	Height	Width	Symmetry
1	59.893	1441.2	117.3	0.1513	0.334
2	60.604	1436.7	103.3	0.1702	0.337

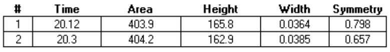


#	Time	Area	Height	Width	Symmetry
1	60.013	852.3	76.6	0.1347	0.557
2	60.833	78.5	8.4	0.1223	0.947

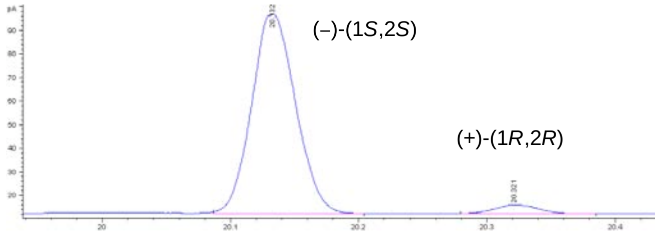
CSP-GC: Chiraldex Hydrodex β-3P: T$_{inj}$ = 250 ^{o}C, P = 0.842 bar, 80 ^{o}C for 5 min, then gradient up to 180 ^{o}C 1 ^{o}C/min, hold at 180 ^{o}C for 5 min

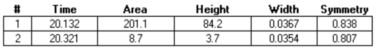






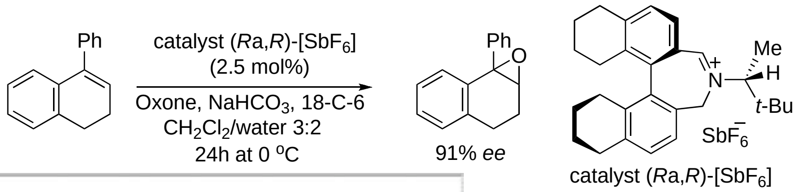
#	Time	Area	Height	Width	Symmetry
1	20.12	403.9	165.8	0.0364	0.798
2	20.3	404.2	162.9	0.0385	0.657

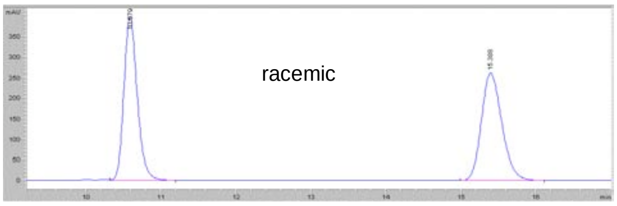


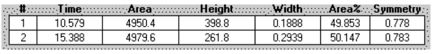


#	Time	Area	Height	Width	Symmetry
1	20.132	201.1	84.2	0.0367	0.838
2	20.321	8.7	3.7	0.0354	0.807

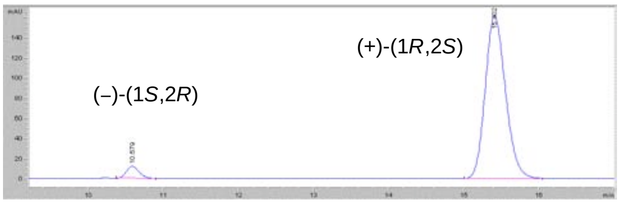
CSP-GC (Chiraldex Hydrodex β-3P), T_{inj} 250 °C, P = 0.842 bar;
Conditions: 80 °C for 5 min, then progression to 180 °C gradient 5 °C/min, then 180 °C for 5 min.

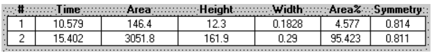




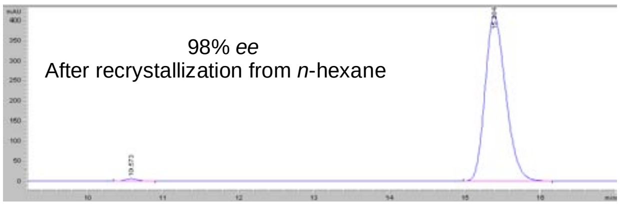


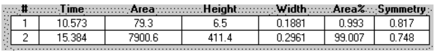
#	Time	Area	Height	Width	Area%	Symmetry
1	10.579	4950.4	398.8	0.1888	49.853	0.778
2	15.388	4979.6	261.8	0.2939	50.147	0.783





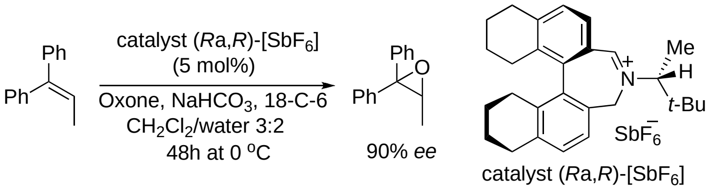
#	Time	Area	Height	Width	Area%	Symmetry
1	10.579	146.4	12.3	0.1828	4.577	0.814
2	15.402	3051.8	161.9	0.29	95.423	0.811

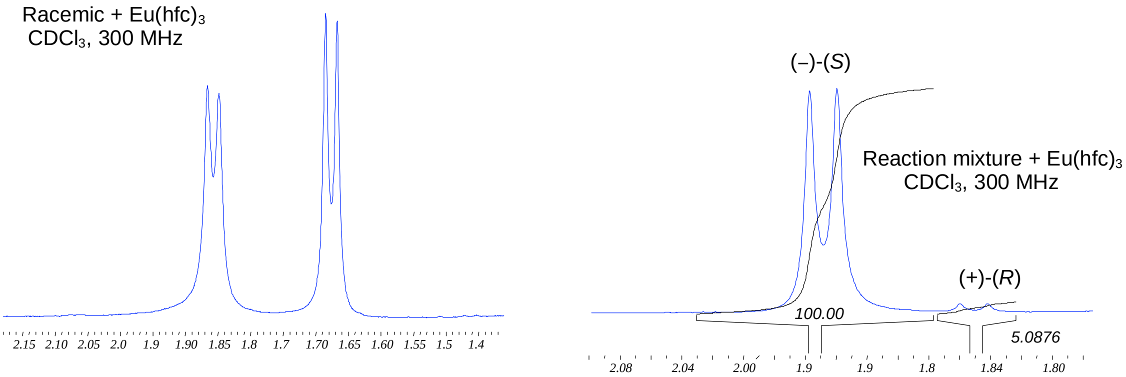


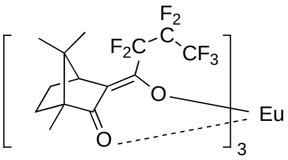


#	Time	Area	Height	Width	Area%	Symmetry
1	10.573	79.3	6.5	0.1881	0.993	0.817
2	15.384	7900.6	411.4	0.2961	99.007	0.748

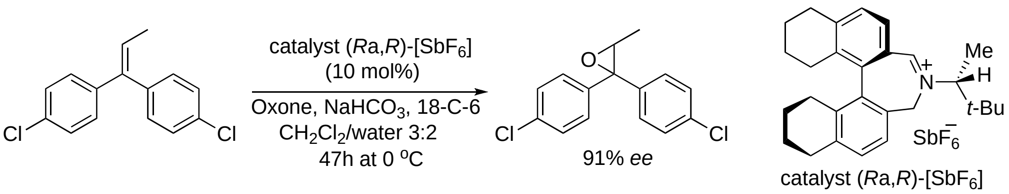
CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 95/5 %, 0.5 ml/min, 23 °C, λ = 230 nm

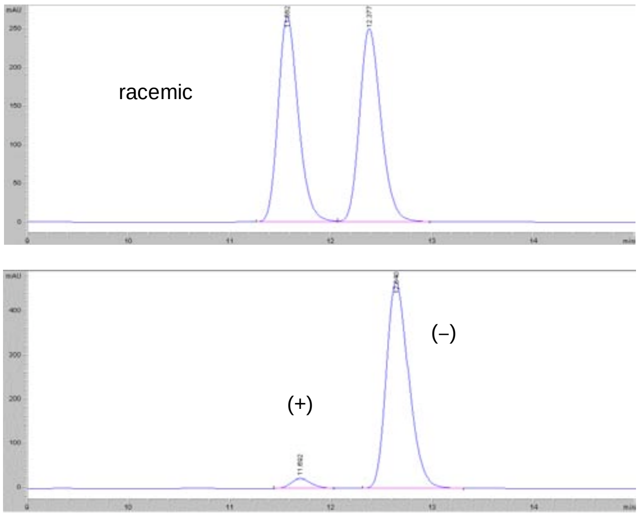


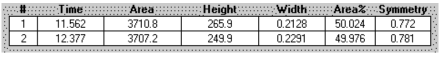




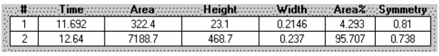
Eu(hfc)$_3$





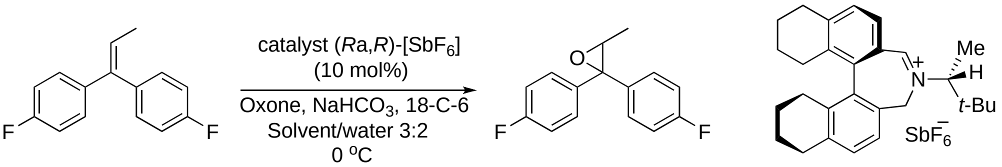


#	Time	Area	Height	Width	Area%	Symmetry
1	11.562	3710.8	265.9	0.2128	50.024	0.772
2	12.377	3707.2	249.9	0.2291	49.976	0.781

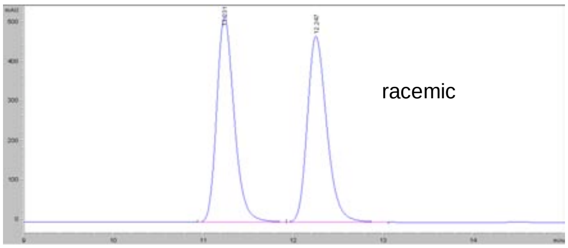


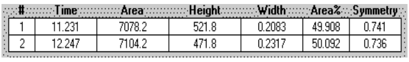
#	Time	Area	Height	Width	Area%	Symmetry
1	11.692	322.4	23.1	0.2146	4.293	0.81
2	12.64	7188.7	468.7	0.237	95.707	0.738

CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 99.5/0.5 %, 0.5 ml/min, 23 °C, λ = 210 nm

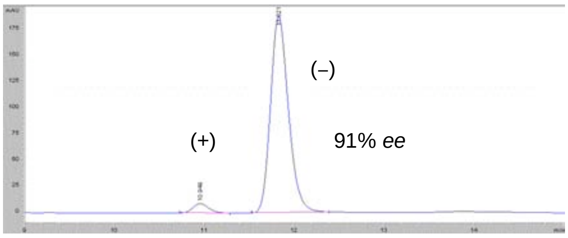


catalyst (*R*a,*R*)-[SbF$_6$]

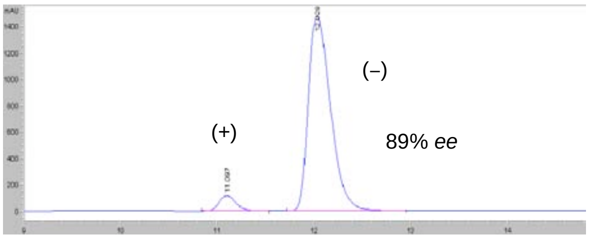




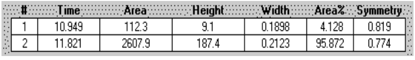
#	Time	Area	Height	Width	Area%	Symmetry
1	11.231	7078.2	521.8	0.2083	49.908	0.741
2	12.247	7104.2	471.8	0.2317	50.092	0.736



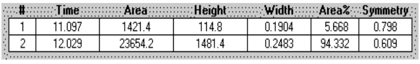
CH$_2$Cl$_2$/water 3:2, 18-C-6, 43h at 0 °C



MeCN/water 3:2, without 18-C-6, 24h at 0 °C

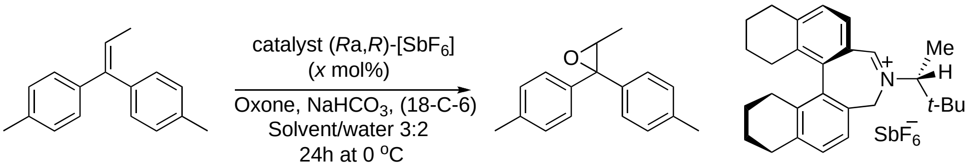


#	Time	Area	Height	Width	Area%	Symmetry
1	10.949	112.3	9.1	0.1898	4.128	0.819
2	11.821	2607.9	187.4	0.2123	95.872	0.774

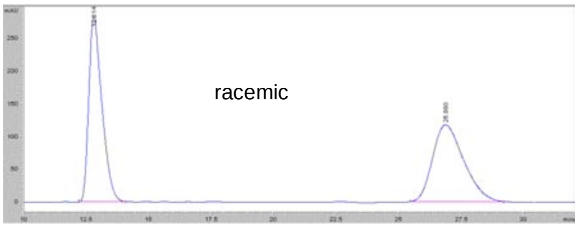


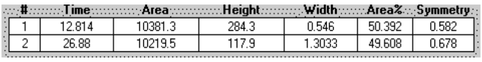
#	Time	Area	Height	Width	Area%	Symmetry
1	11.097	1421.4	114.8	0.1904	5.668	0.798
2	12.029	23654.2	1481.4	0.2483	94.332	0.609

CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 99.5/0.5 %, 0.5 ml/min, 23 °C, λ = 210 nm

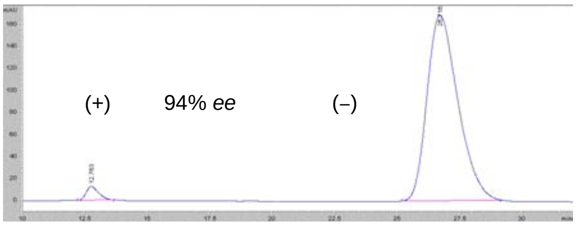


catalyst (*R*a,*R*)-[SbF$_6$]



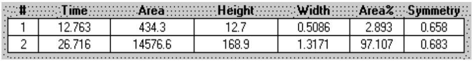


#	Time	Area	Height	Width	Area%	Symmetry
1	12.814	10381.3	284.3	0.546	50.392	0.582
2	26.88	10219.5	117.9	1.3033	49.608	0.678

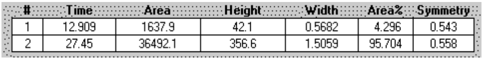


CH$_2$Cl$_2$/water 3:2, 5 mol% of catalyst; 18-C-6

MeCN/water 3:2, 2.5 mol% of catalyst,
without 18-C-6

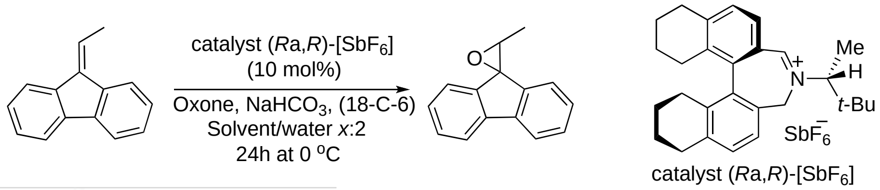


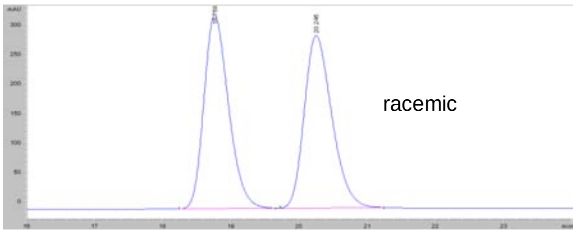
#	Time	Area	Height	Width	Area%	Symmetry
1	12.763	434.3	12.7	0.5086	2.893	0.658
2	26.716	14576.6	168.9	1.3171	97.107	0.683

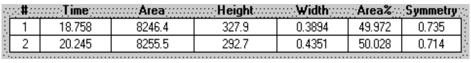


#	Time	Area	Height	Width	Area%	Symmetry
1	12.909	1637.9	42.1	0.5682	4.296	0.543
2	27.45	36492.1	356.6	1.5059	95.704	0.558

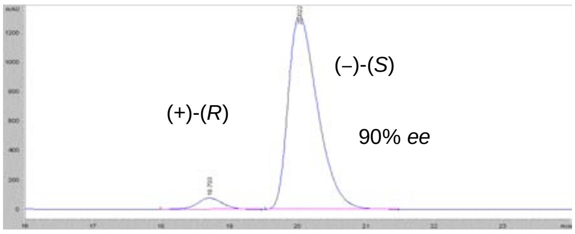
CSP-HPLC: OJ column, *n*-Hexane/*i*-PrOH 95/5 %, 0.7 ml/min, 23 °C, λ = 210 nm

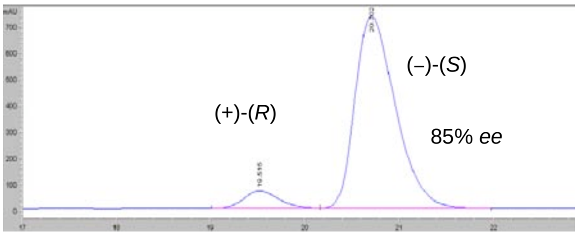






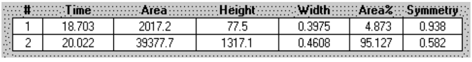
#	Time	Area	Height	Width	Area%	Symmetry
1	18.758	8246.4	327.9	0.3894	49.972	0.735
2	20.245	8255.5	292.7	0.4351	50.028	0.714



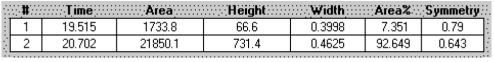


CH$_2$Cl$_2$/water 3:2, 18-C-6

MeCN/water 5:2, without 18-C-6

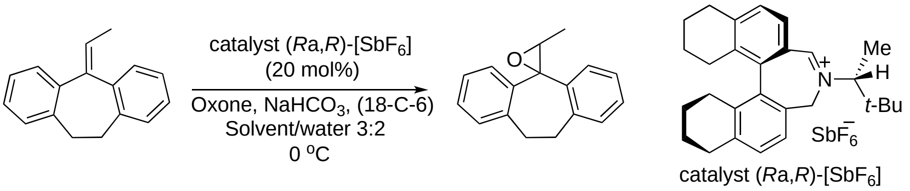


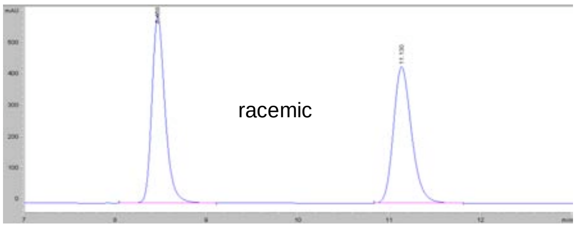
#	Time	Area	Height	Width	Area%	Symmetry
1	18.703	2017.2	77.5	0.3975	4.873	0.938
2	20.022	39377.7	1317.1	0.4608	95.127	0.582

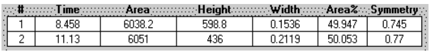


#	Time	Area	Height	Width	Area%	Symmetry
1	19.515	1733.8	66.6	0.3998	7.351	0.79
2	20.702	21850.1	731.4	0.4625	92.649	0.643

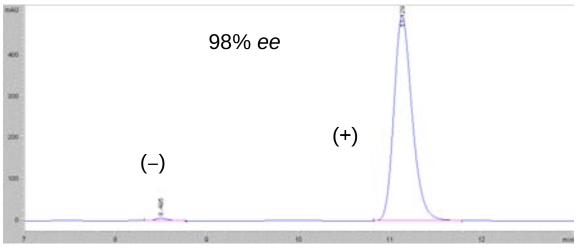
CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 95/5 %, 0.5 ml/min, 23 °C, λ = 210 nm

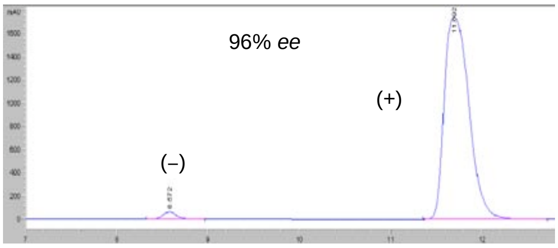






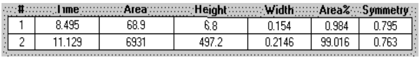
#	Time	Area	Height	Width	Area%	Symmetry
1	8.458	6038.2	598.8	0.1536	49.947	0.745
2	11.13	6051	436	0.2119	50.053	0.77



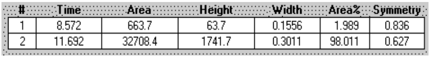


CH$_2$Cl$_2$/water 3:2, 18-C-6, 91h at 0 °C

MeCN/water 3:2, without 18-C-6, 48h at 0 °C

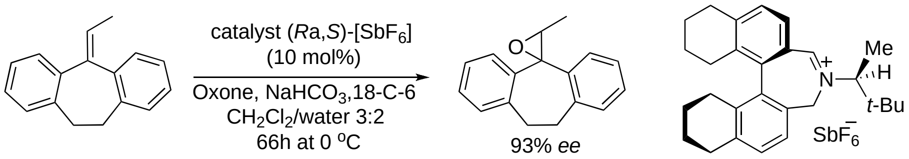


#	Time	Area	Height	Width	Area%	Symmetry
1	8.495	68.9	6.8	0.154	0.984	0.795
2	11.129	6931	497.2	0.2146	99.016	0.763

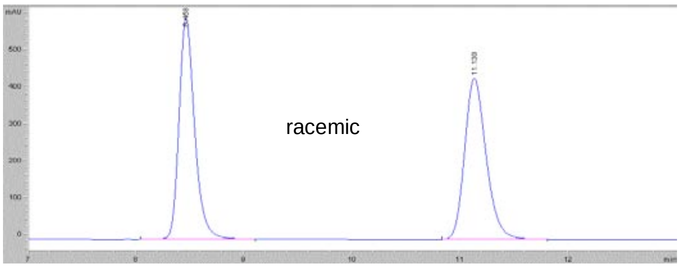


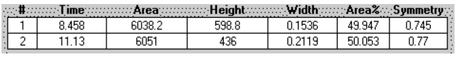
#	Time	Area	Height	Width	Area%	Symmetry
1	8.572	663.7	63.7	0.1556	1.989	0.836
2	11.692	32708.4	1741.7	0.3011	98.011	0.627

CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 95/5 %, 0.5 ml/min, 23 °C, λ = 210 nm

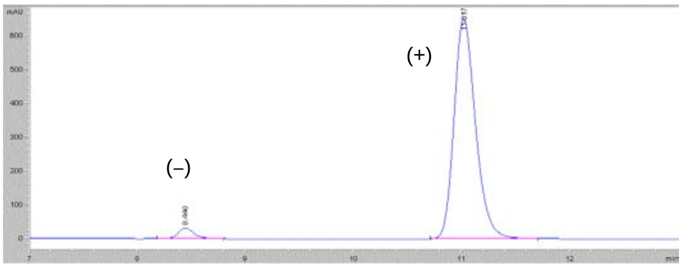


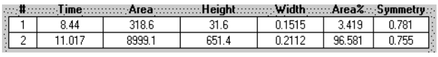
catalyst (*R*a,*S*)-[SbF$_6$]
most reactive





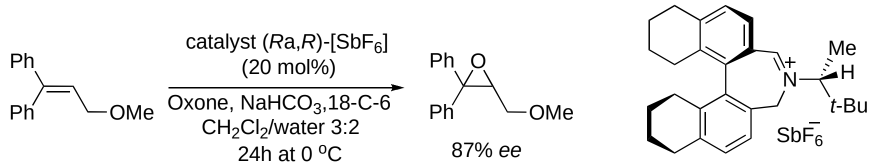
#	Time	Area	Height	Width	Area%	Symmetry
1	8.458	6038.2	598.8	0.1536	49.947	0.745
2	11.13	6051	436	0.2119	50.053	0.77



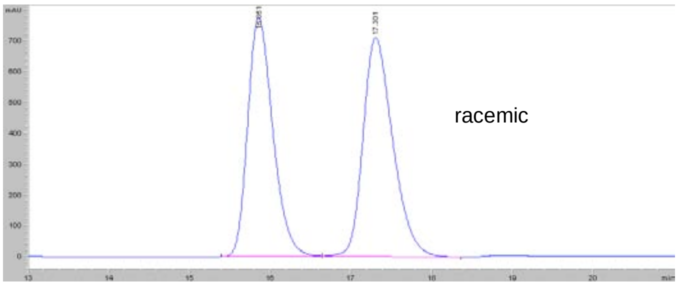


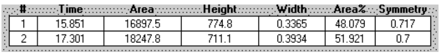
#	Time	Area	Height	Width	Area%	Symmetry
1	8.44	318.6	31.6	0.1515	3.419	0.781
2	11.017	8999.1	651.4	0.2112	96.581	0.755

CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 95/5 %, 0.5 ml/min, 23 ^{o}C, λ = 210 nm

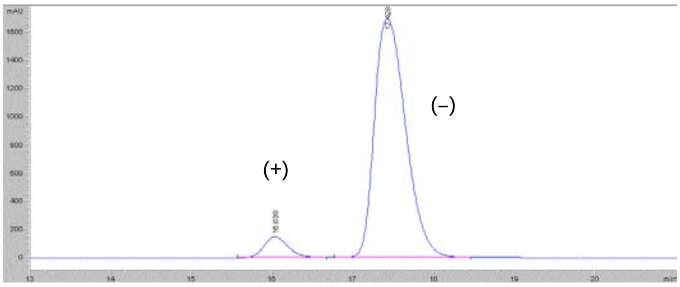


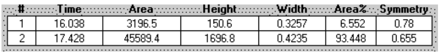
catalyst (*R*a,*R*)-[SbF$_6$]





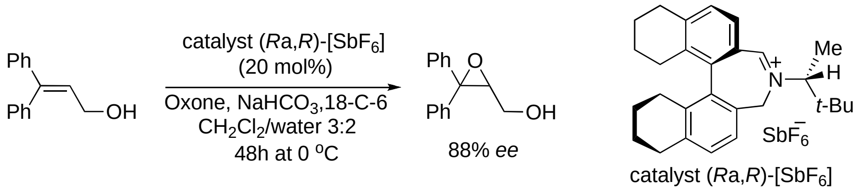
#	Time	Area	Height	Width	Area%	Symmetry
1	15.851	16897.5	774.8	0.3365	48.079	0.717
2	17.301	18247.8	711.1	0.3934	51.921	0.7

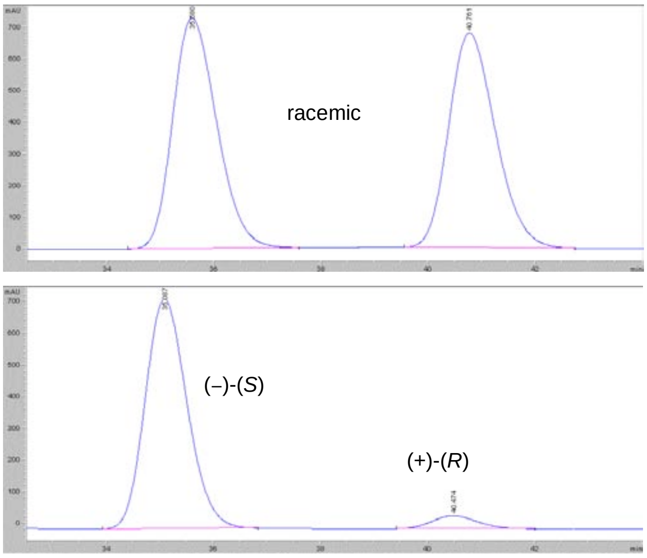




#	Time	Area	Height	Width	Area%	Symmetry
1	16.038	3196.5	150.6	0.3257	6.552	0.78
2	17.428	45589.4	1696.8	0.4235	93.448	0.655

CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 99/1 %, 0.5 ml/min, 23 ^{o}C, λ = 210 nm

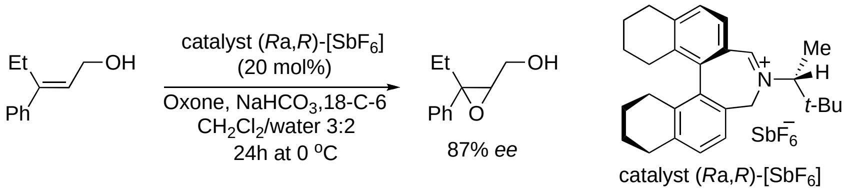


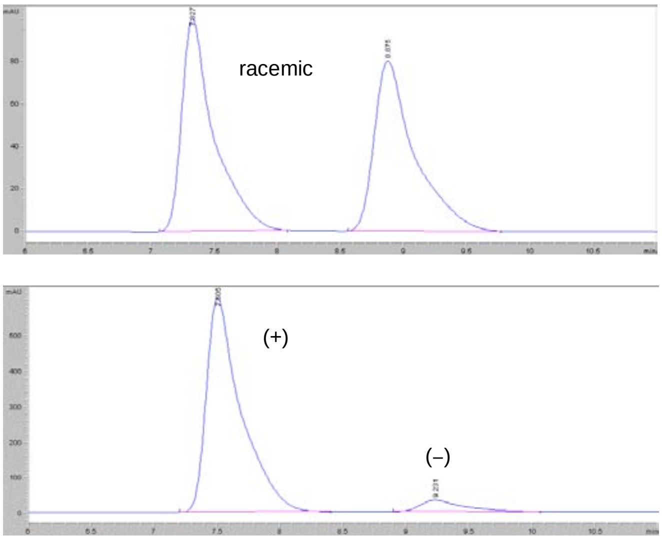


#	Time	Area	Height	Width	Area%	Symmetry
1	35.58	41649.9	727.7	0.8958	50.272	0.749
2	40.761	41198.8	677	0.95	49.728	0.765

#	Time	Area	Height	Width	Area%	Symmetry
1	35.087	39452.2	723.7	0.848	94.275	0.821
2	40.474	2395.7	41	0.9001	5.725	0.854

CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 95/5 %, 0.5 ml/min, 23 °C, λ = 210 nm

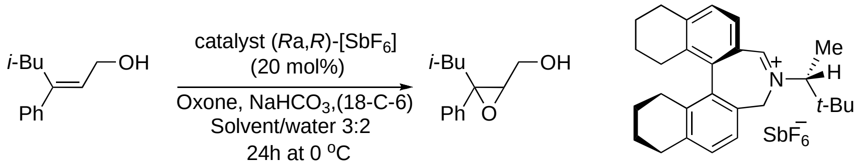




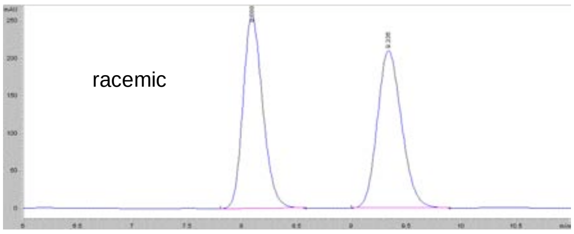
#	Time	Area	Height	Width	Area%	Symmetry
1	7.327	1794.8	100.9	0.2536	50.128	0.458
2	8.875	1785.6	80.5	0.3168	49.872	0.471

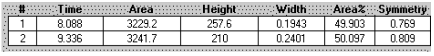
#	Time	Area	Height	Width	Area%	Symmetry
1	7.505	11510.5	601.8	0.2731	93.772	0.445
2	9.231	764.5	32.7	0.3363	6.228	0.49

CSP-HPLC: OJ column, *n*-Hexane/*i*-PrOH 90/10 %, 1.0 ml/min, 23 °C, λ = 210 nm

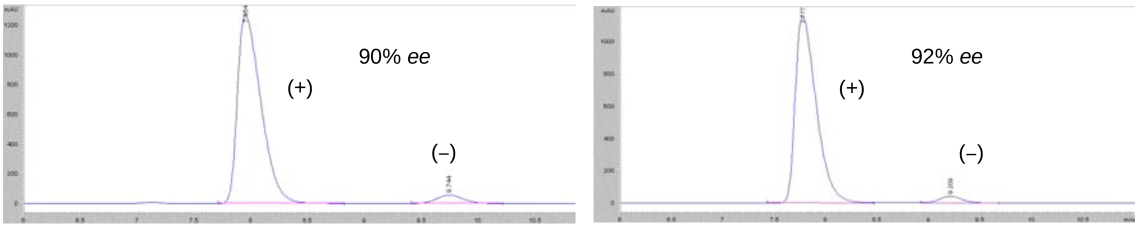


catalyst (*R*a,*R*)-[SbF$_6$]



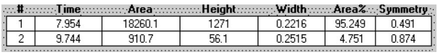


#	Time	Area	Height	Width	Area%	Symmetry
1	8.088	3229.2	257.6	0.1943	49.903	0.769
2	9.336	3241.7	210	0.2401	50.097	0.809

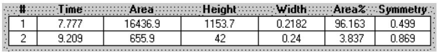


CH$_2$Cl$_2$/water 3:2, 18-C-6

MeCN/water 3:2, without 18-C-6

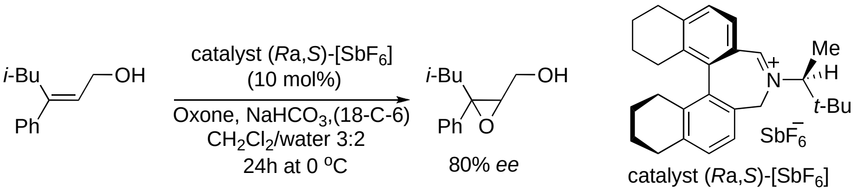


#	Time	Area	Height	Width	Area%	Symmetry
1	7.954	18260.1	1271	0.2216	95.249	0.491
2	9.744	910.7	56.1	0.2515	4.751	0.874

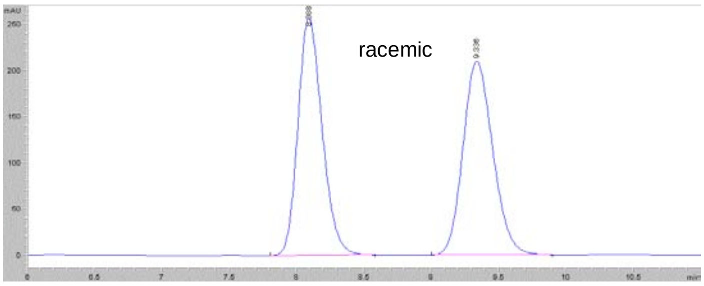


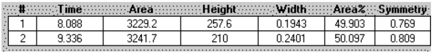
#	Time	Area	Height	Width	Area%	Symmetry
1	7.777	16436.9	1153.7	0.2182	96.163	0.499
2	9.209	655.9	42	0.24	3.837	0.869

CSP-HPLC: OJ-H column, *n*-Hexane/*i*-PrOH 90/10 %, 1.0 ml/min, 23 °C, λ = 210 nm

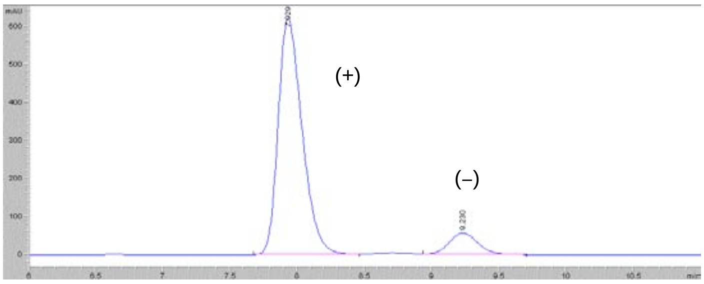


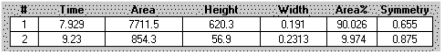
catalyst (*R*a,*S*)-[SbF$_6$]
most reactive





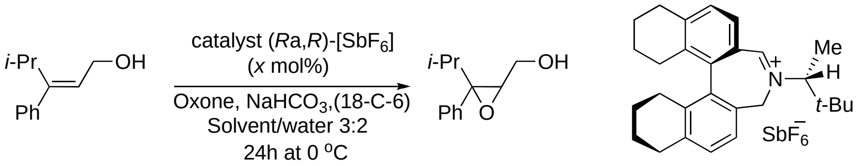
#	Time	Area	Height	Width	Area%	Symmetry
1	8.088	3229.2	257.6	0.1943	49.903	0.769
2	9.336	3241.7	210	0.2401	50.097	0.809



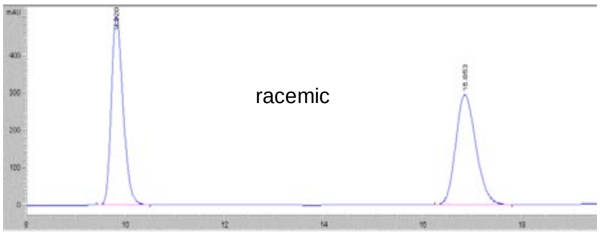


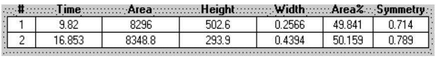
#	Time	Area	Height	Width	Area%	Symmetry
1	7.929	7711.5	620.3	0.191	90.026	0.655
2	9.23	854.3	56.9	0.2313	9.974	0.875

CSP-HPLC: OJ-H column, *n*-Hexane/*i*-PrOH 90/10 %, 1.0 ml/min, 23 °C, λ = 210 nm

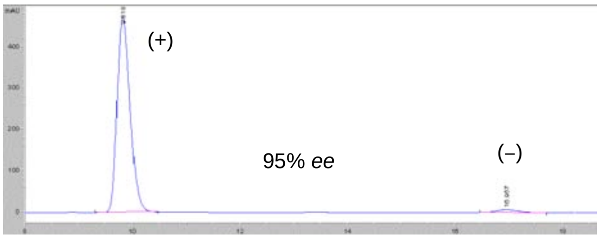


catalyst (Ra,R)-[SbF_6]

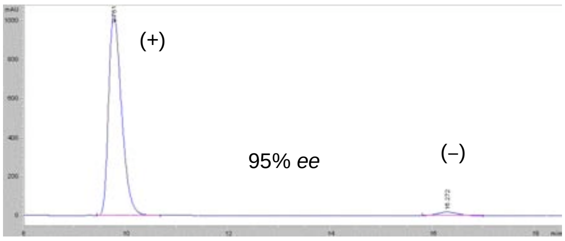




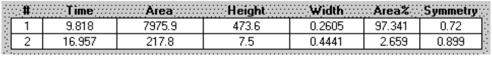
#	Time	Area	Height	Width	Area%	Symmetry
1	9.82	8296	502.6	0.2566	49.841	0.714
2	16.853	8348.8	293.9	0.4394	50.159	0.789



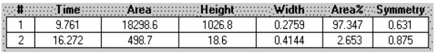
CH$_2$Cl$_2$/water 3:2, 20 mol% of catalyst, 18-C-6



MeCN/water 3:2, 25 mol% of catalyst,
without 18-C-6

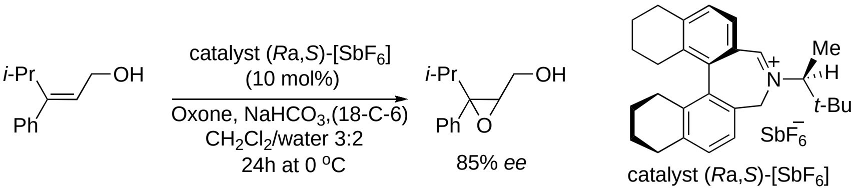


#	Time	Area	Height	Width	Area%	Symmetry
1	9.818	7975.9	473.6	0.2605	97.341	0.72
2	16.957	217.8	7.5	0.4441	2.659	0.899

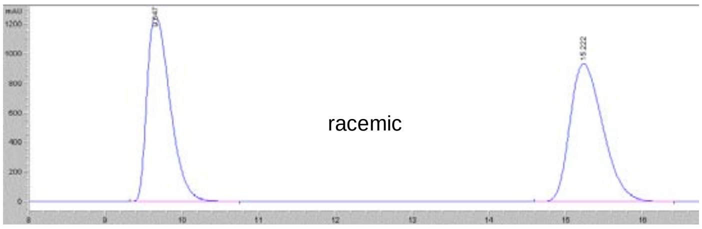


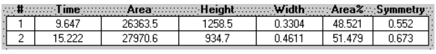
#	Time	Area	Height	Width	Area%	Symmetry
1	9.761	18298.6	1026.8	0.2759	97.347	0.631
2	16.272	498.7	18.6	0.4144	2.653	0.875

CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 90/10 %, 0.8 ml/min, 23 °C, λ = 210 nm

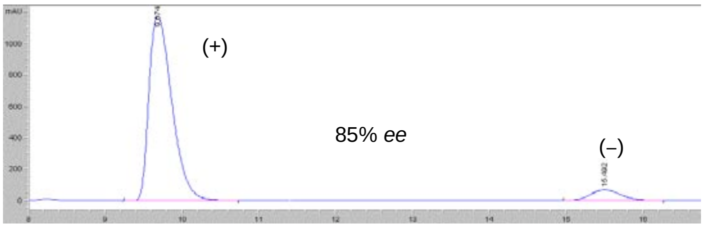


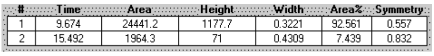
catalyst (Ra,S)-[SbF_6]
most reactive





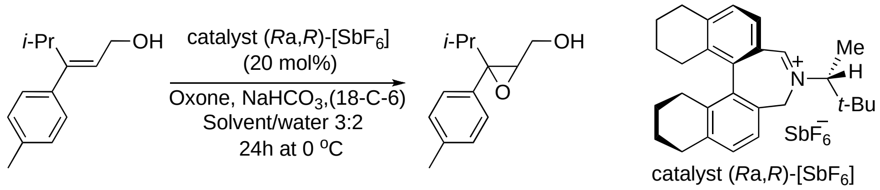
#	Time	Area	Height	Width	Area%	Symmetry
1	9.647	26363.5	1258.5	0.3304	48.521	0.552
2	15.222	27970.6	934.7	0.4611	51.479	0.673



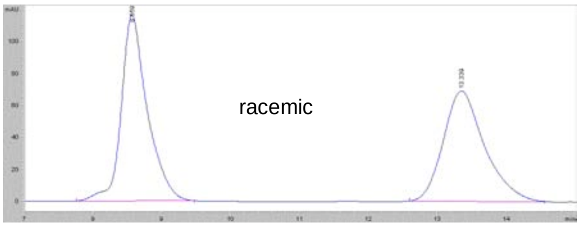


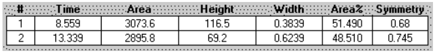
#	Time	Area	Height	Width	Area%	Symmetry
1	9.674	24441.2	1177.7	0.3221	92.561	0.557
2	15.492	1964.3	71	0.4309	7.439	0.832

CSP-HPLC: OD-H column, *n*-Hexane/*i*-PrOH 90/10 %, 0.8 ml/min, 23 °C, λ = 210 nm

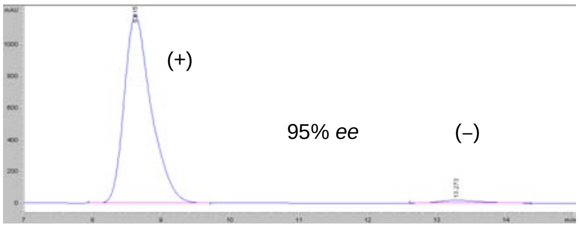


catalyst (*R*a,*R*)-[SbF$_6$]

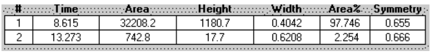




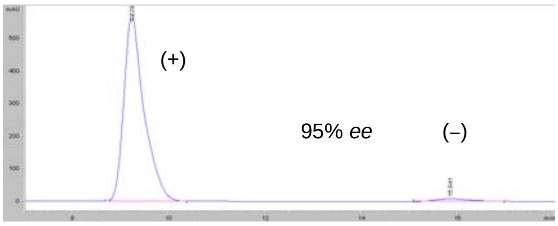
#	Time	Area	Height	Width	Area%	Symmetry
1	8.559	3073.6	116.5	0.3839	51.490	0.68
2	13.339	2895.8	69.2	0.6239	48.510	0.745



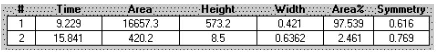
CH$_2$Cl$_2$/water 3:2, 18-C-6



#	Time	Area	Height	Width	Area%	Symmetry
1	8.615	32208.2	1180.7	0.4042	97.746	0.655
2	13.273	742.8	17.7	0.6208	2.254	0.666

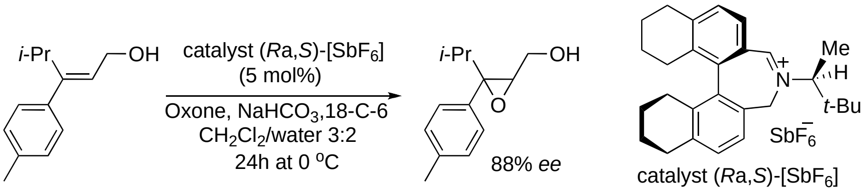


MeCN/water 3:2, without 18-C-6

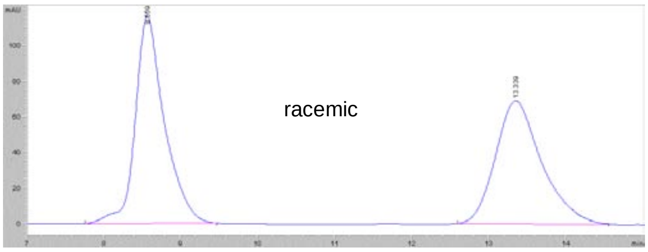


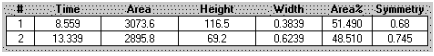
#	Time	Area	Height	Width	Area%	Symmetry
1	9.229	16657.3	573.2	0.421	97.539	0.616
2	15.841	420.2	8.5	0.6362	2.461	0.769

CSP-HPLC: OJ column, *n*-Hexane/*i*-PrOH 90/10 %, 1.0 ml/min, 23 °C, λ = 210 nm

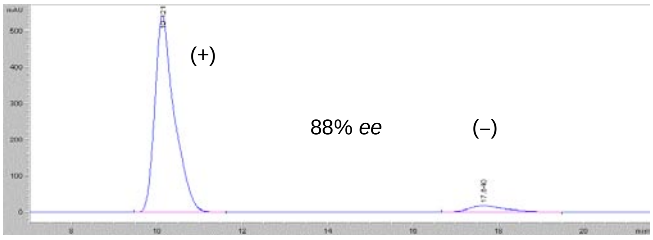


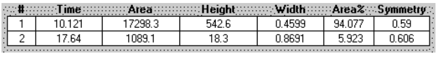
catalyst (*R*a,*S*)-[SbF$_6$]
most reactive





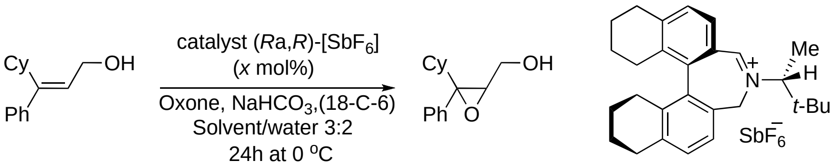
#	Time	Area	Height	Width	Area%	Symmetry
1	8.559	3073.6	116.5	0.3839	51.490	0.68
2	13.339	2895.8	69.2	0.6239	48.510	0.745



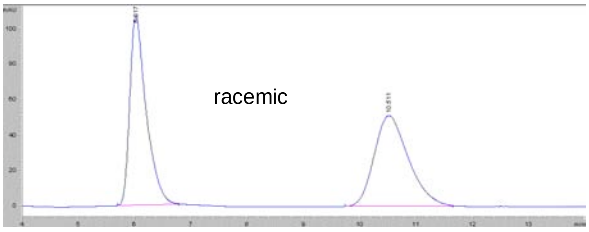


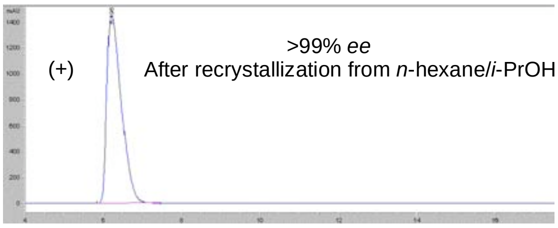
#	Time	Area	Height	Width	Area%	Symmetry
1	10.121	17298.3	542.6	0.4599	94.077	0.59
2	17.64	1089.1	18.3	0.8691	5.923	0.606

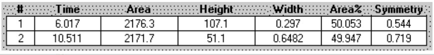
CSP-HPLC: OJ column, *n*-Hexane/*i*-PrOH 90/10 %, 1.0 ml/min, 23 °C, λ = 210 nm



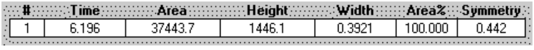
catalyst (*Ra*,*R*)-[SbF_6]



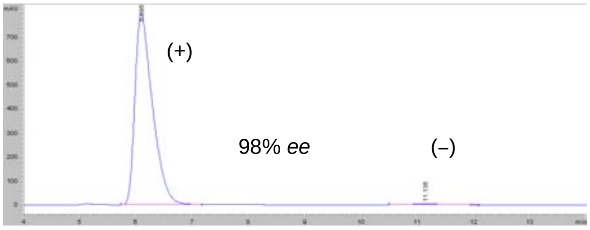


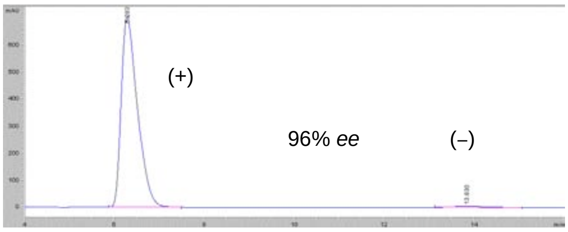


#	Time	Area	Height	Width	Area%	Symmetry
1	6.017	2176.3	107.1	0.297	50.053	0.544
2	10.511	2171.7	51.1	0.6482	49.947	0.719



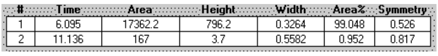
#	Time	Area	Height	Width	Area%	Symmetry
1	6.196	37443.7	1446.1	0.3921	100.000	0.442



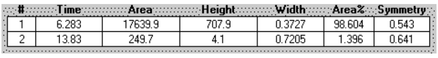


CH_2Cl_2/water 3:2, 20 mol% of catalyst, 18-C-6

MeCN/water 3:2, 30 mol% of catalyst,
without 18-C-6

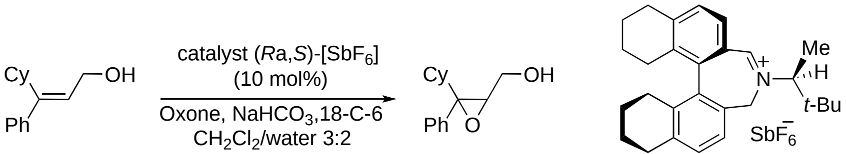


#	Time	Area	Height	Width	Area%	Symmetry
1	6.095	17362.2	796.2	0.3264	99.048	0.526
2	11.136	167	3.7	0.5582	0.952	0.817



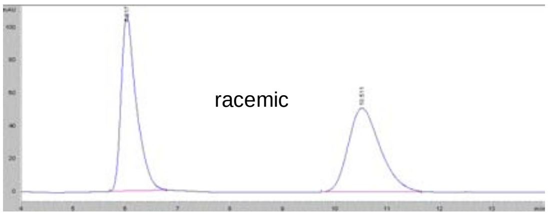
#	Time	Area	Height	Width	Area%	Symmetry
1	6.283	17639.9	707.9	0.3727	98.604	0.543
2	13.83	249.7	4.1	0.7205	1.396	0.641

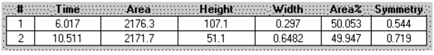
CSP-HPLC: OJ column, *n*-Hexane/*i*-PrOH 90/10 %, 1.0 ml/min, 23 °C, λ = 210 nm



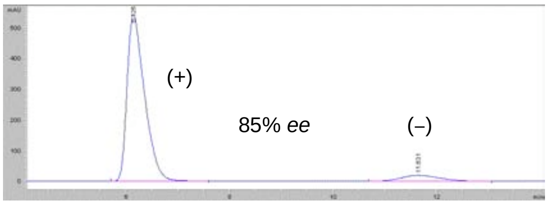
85% *ee*

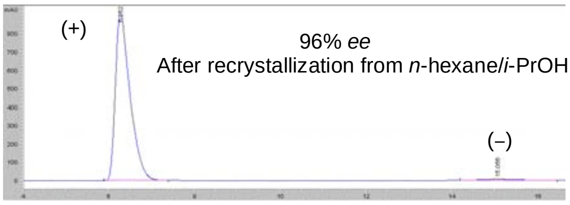
catalyst (*Ra*,*S*)-[SbF_6]
most reactive

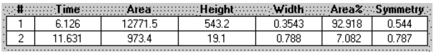




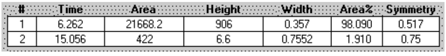
#	Time	Area	Height	Width	Area%	Symmetry
1	6.017	2176.3	107.1	0.297	50.053	0.544
2	10.511	2171.7	51.1	0.6482	49.947	0.719





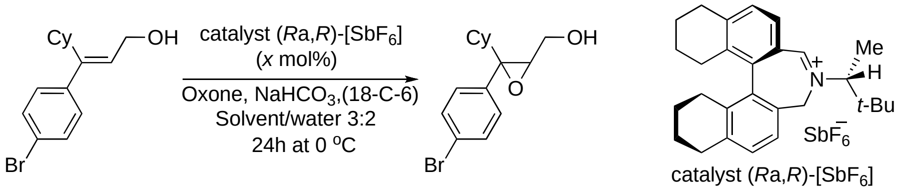


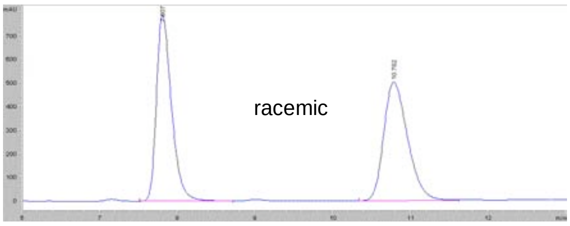
#	Time	Area	Height	Width	Area%	Symmetry
1	6.126	12771.5	543.2	0.3543	92.918	0.544
2	11.631	973.4	19.1	0.788	7.082	0.787

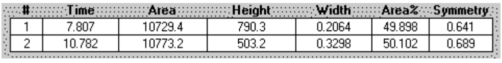


#	Time	Area	Height	Width	Area%	Symmetry
1	6.262	21668.2	906	0.357	98.090	0.517
2	15.056	422	6.6	0.7552	1.910	0.75

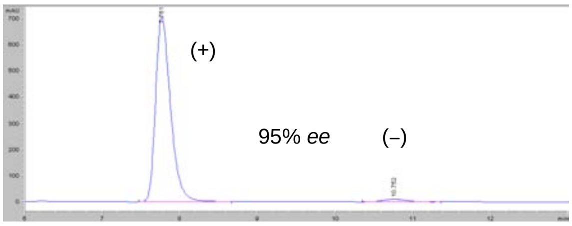
CSP-HPLC: OJ column, *n*-Hexane/*i*-PrOH 90/10 %, 1.0 ml/min, 23 °C, λ = 210 nm

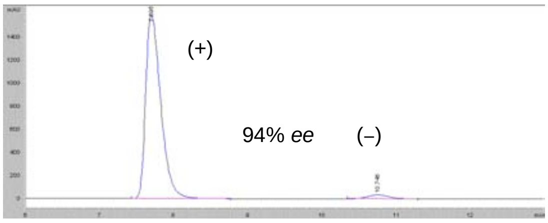




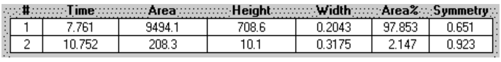


#	Time	Area	Height	Width	Area%	Symmetry
1	7.807	10729.4	790.3	0.2064	49.898	0.641
2	10.782	10773.2	503.2	0.3298	50.102	0.689



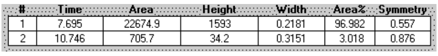


CH_2Cl_2/water 3:2, 20 mol% of catalyst, 18-C-6



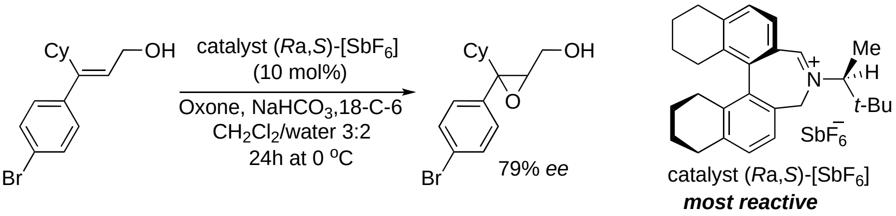
#	Time	Area	Height	Width	Area%	Symmetry
1	7.761	9494.1	708.6	0.2043	97.853	0.651
2	10.752	208.3	10.1	0.3175	2.147	0.923

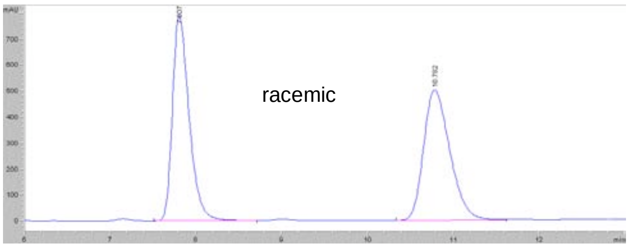
MeCN/water 3:2, 30 mol% of catalyst,
without 18-C-6

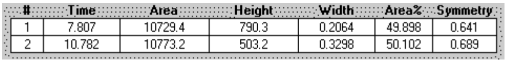


#	Time	Area	Height	Width	Area%	Symmetry
1	7.695	22674.9	1593	0.2181	96.982	0.557
2	10.746	705.7	34.2	0.3151	3.018	0.876

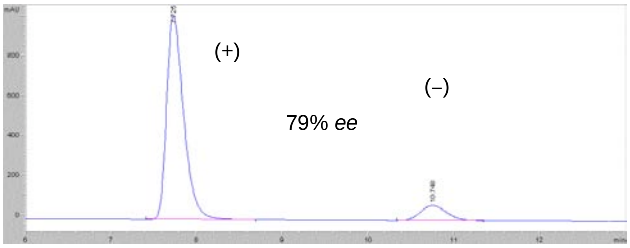
CSP-HPLC: OJ-H column, *n*-Hexane/*i*-PrOH 95/5 %, 1.0 ml/min, 23 ^{o}C, λ = 210 nm

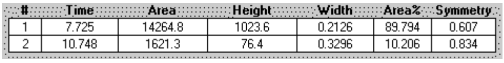






#	Time	Area	Height	Width	Area%	Symmetry
1	7.807	10729.4	790.3	0.2064	49.898	0.641
2	10.782	10773.2	503.2	0.3298	50.102	0.689





#	Time	Area	Height	Width	Area%	Symmetry
1	7.725	14264.8	1023.6	0.2126	89.794	0.607
2	10.748	1621.3	76.4	0.3296	10.206	0.834

CSP-HPLC: OJ-H column, *n*-Hexane/*i*-PrOH 95/5 %, 1.0 ml/min, 23 ^{o}C, λ = 210 nm