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Transition metal-catalyzed (remote) deconjugative isomerization of α,β-unsaturated carbonyls

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ABSTRACT

The seemingly counter-intuitive transition metal-catalyzed deconjugative isomerizations of α,β-unsaturated carbonyls offer novel perspectives within the context of remote functionalization strategies. This Digest provides an overview of the handful of examples that have been reported over the last two decades in this area.

Contents

Introduction

The transition metal-catalyzed remote functionalization of organic compounds by alkene isomerization along a hydrocarbon chain has gained impressive momentum during the last decades [1]. The identification of a suitable catalyst that triggers olefin migration combined with a sufficiently strong thermodynamic driving force are prerequisites for the successful development of such reactions. The nature and number of substituents on the starting alkene as well as its geometry strongly influence the feasibility of the transformation. Moreover, the design and/or outcome of certain processes is complicated by the fact that product selectivities are governed by either thermodynamic or kinetic factors [2]. Therefore, and perhaps not surprisingly, examples of transition metal-catalyzed remote functionalizations that are initiated by a thermodynamically disfavored deconjugation of α,β-unsaturated carbonyl compounds are much less documented. This digest, aims at providing an overview of the transition metal-(photo)catalyzed processes that have been reported during the last two decades for the deconjugative isomerization of α,β-unsaturated carbonyl derivatives. Given the limited number of examples, both short-

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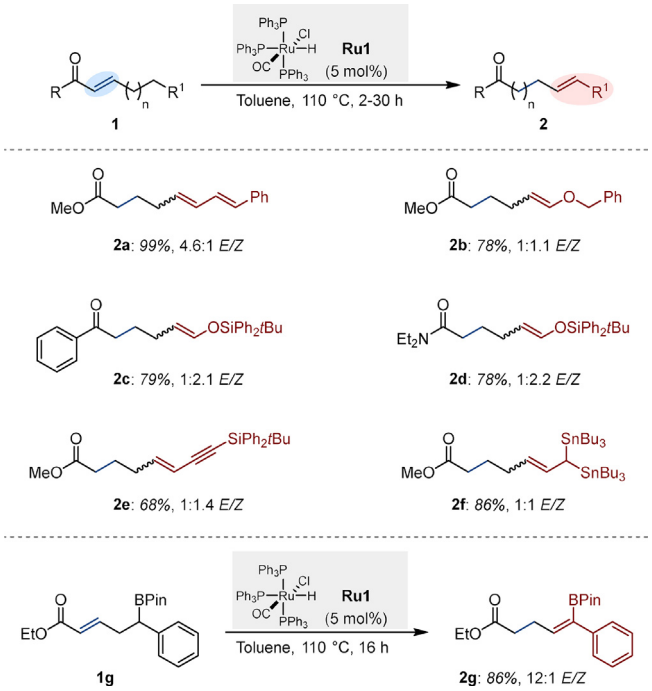

Fig. 1. Ru-catalyzed deconjugative isomerization of α,β-unsaturated carbonyls.

and long-range reactions are discussed. Photochemical transformations and protocols that rely on the use of strongly basic reagents fall outside of the scope of this brief account and will not be covered herein [3]. Examples of deconjugative isomerizing functionalizations of fatty acids/esters and polymeric materials will not be discussed either [4].

Ruthenium

In 2000, using Wilkinson's ruthenium hydride **Ru-1**, Mori and co-workers disclosed an efficient catalytic deconjugative isomerization of a series of α,β-unsaturated carbonyls (**1**) including conjugated ketones, esters and amides (Fig. 1) [5a]. This study was built on serendipitous observations made during the development of a Ru-catalyzed intramolecular enyne cyclization [5b]. Although certainly counter-intuitive from a thermodynamic point of view, the deconjugation was driven by functionalities such as vinyl arenes, alkyl ethers, silyl ethers, alkynes, or *gem*-bis-stannyl fragments. These were located up to three methylene units away from the β-carbon, which upon isomerization led to the formation of the corresponding 1,3-dienes (**2a**), vinyl ethers (**2b**), vinyl silyl ethers (**2c-d**), enynes (**2e**), and allyl bis-stannyl derivatives (**2f**) respectively. The products were isolated in high yield and with moderate *E/Z* selectivity. In the absence of mechanistic investigations, the reaction was reasonably proposed to proceed via iterative hydroruthenation/β-H elimination sequences. In 2020, Marek and coworkers developed a long-range Ru-catalyzed isomerization of ω-alkenylboronates for the selective preparation of vinylboronates. Their study included one example of deconjugative isomerization that afforded **2g** in excellent yield and with a particularly high *E/Z* ratio [6].

Within their program aimed at developing remote functionalizations based on alkene isomerization, Mazet and co-workers have reported several multimetallic catalytic systems that enable a rapid increase in molecular complexity of readily available starting materials [7]. A notable example combines a Ru-catalyzed deconjugation of α,β-unsaturated methyl ester **3** using **Ru1**, followed by an Os-catalyzed Sharpless asymmetric dihydroxylation (SAD) of the transiently generated vinyl arene [8]. A spontaneous lactonization between the methyl ester and the remote homobenzylic alcohol stereocenter led to the formation of the naturally occurring and biologically active lactone **4** in excellent diastereo- and enantioselectivity (*dr* > 20:1; >99:1 *er*) (Fig. 2).

Starting from non-conjugated dienes (**5**), the same group identified subtle reaction conditions for the controlled synthesis of 2,4-disubstituted-dienes (**6**) [9]. These kinetic products were obtained preferentially over the thermodynamically more stable linear isomers (**7**) by conducting the reaction at temperatures not exceeding 60 °C and in the presence of a catalytic combination of Wilkinson's ruthenium hydride **Ru1** and triphenylphosphine. As part of this study, the authors also disclosed an example where the experimentally supported hydroruthenation triggers the deconjugation of an α,β-conjugated ester and still permits to generate the targeted kinetic branched diene with excellent control of the stereoselectivity (**6**: *E/Z* > 20:1, 53% yield) (Fig. 3).

Palladium

In 2016, Lin et al. reported the long-range deconjugative isomerization of a broad range of α,β-unsaturated ketones, esters and amides using an in situ generated palladium hydride catalyst by activation of the air-stable complex **Pd1** [10]. Mechanistic studies served to establish that the initial hydropalladation is followed by a β-H elimination and that the sequence is repeated iteratively until the thermodynamically favorable refunctionalization of a primary or a secondary alcohol into the corresponding carbonyl terminates the process. Of particular note, the authors demonstrated that di-, tri- or even tetrasubstituted Cα=Cβ bonds were compatible with the reaction conditions. Moreover, although bidirectional, the isomerization can be sustained over 30 carbon atoms (**9g**). Overall, products were isolated in good to excellent yields and a broad functional group tolerance was disclosed (Fig. 4).

In the same study, the development of an enantioselective variant of the deconjugative isomerization enabled to install a poten-

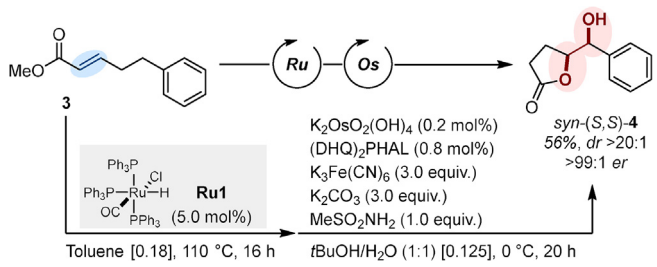

Fig. 2. Enantioselective access to γ-butyrolactone **4** by a [Ru/Os]-catalyzed deconjugative isomerization/SAD/lactonization sequence.

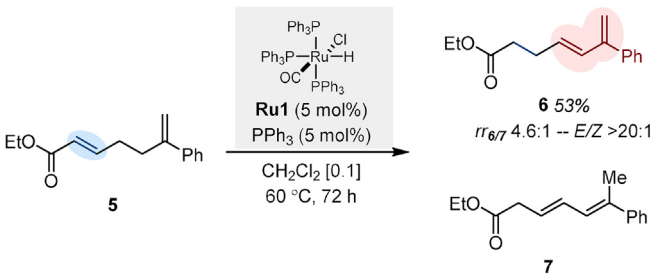

Fig. 3. Kinetically-controlled Ru-catalyzed deconjugative/reconjugative isomerization of an α,β-unsaturated ester into a 1,3-diene.

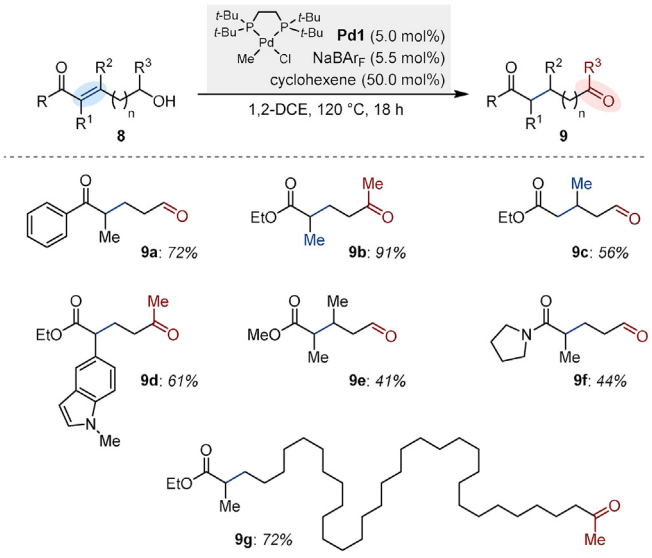

Fig. 4. Palladium-catalyzed long-range deconjugative Isomerization of highly substituted α,β-unsaturated carbonyl compounds.

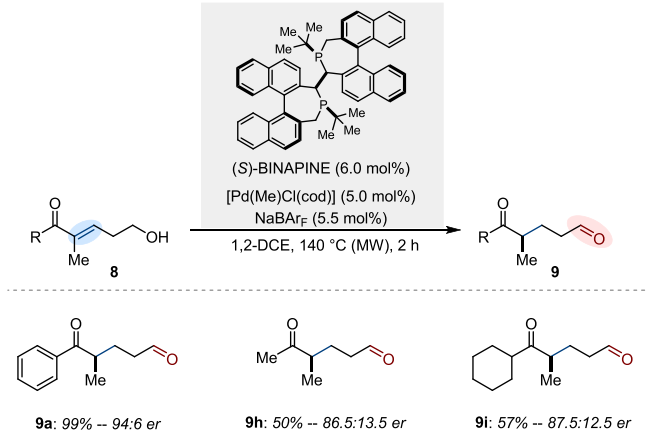

Fig. 5. Pd-catalyzed enantioselective deconjugative isomerization of α,β-unsaturated ketones.

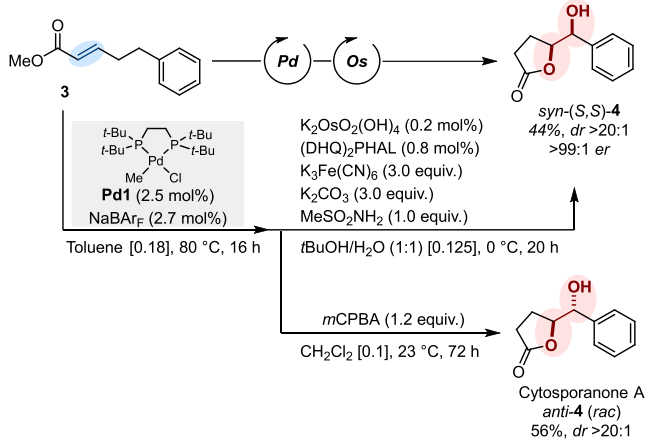

Fig. 6. Enantioselective access to γ-butyrolactone **4** by a [Pd/Os]-catalyzed deconjugative isomerization/SAD/lactonization sequence.

tially stereolabile alkyl tertiary center α to the initial carbonyl functionality was achieved by using (*S*)-BINAPINE as supporting chiral ligand. An enantiomeric ratio as high as 94:6 was obtained despite the issue associated with site-selective insertion of the [Pd-H] across a trisubstituted olefin and the bidirectional nature of the migration process as evidenced by experimental mechanistic investigations (Fig. 5).

In complement to the results obtained with Wilkinson's ruthenium hydride **Ru1** (*vide supra*), the Mazet group showed that access to vinyl arenes by deconjugation of α,β-unsaturated carbonyl derivatives could also be accomplished with their homemade palladium precatalyst **Pd1** [8]. The isomerization reaction was found to be reversible and under thermodynamic control, with preference for the formation of the styrenyl derivatives. To circumvent purification issues of the isomeric mixtures, selective functionalizations of the 1,2-vinyl arenes generated in situ were developed. These include a Cu-catalyzed β-borylation, an enantioselective Cu-catalyzed α-hydroboration, a Cu-catalyzed enantioselective α-hydroamination and finally an Os-catalyzed SAD followed by in situ lactonization. The latter is illustrated in Fig. 6 and shall be compared with Fig. 2.

Ye and co-workers designed an elegant Pd-catalyzed deconjugative isomerization of α,β-unsaturated ketones, esters and amides followed by an intramolecular cyclization engaging the transiently generated enamine in a C—H functionalization with a pendant heterocycle [11]. The method provides access to a broad array of N- and O-containing compounds (**12**), displays excellent functional group tolerance and enables the construction of quaternary centers. Its synthetic utility was established with the expedient syntheses of (±)-desbromoarborescidines A, B and C, natural products which display antiproliferative activity (Fig. 7). Notice-

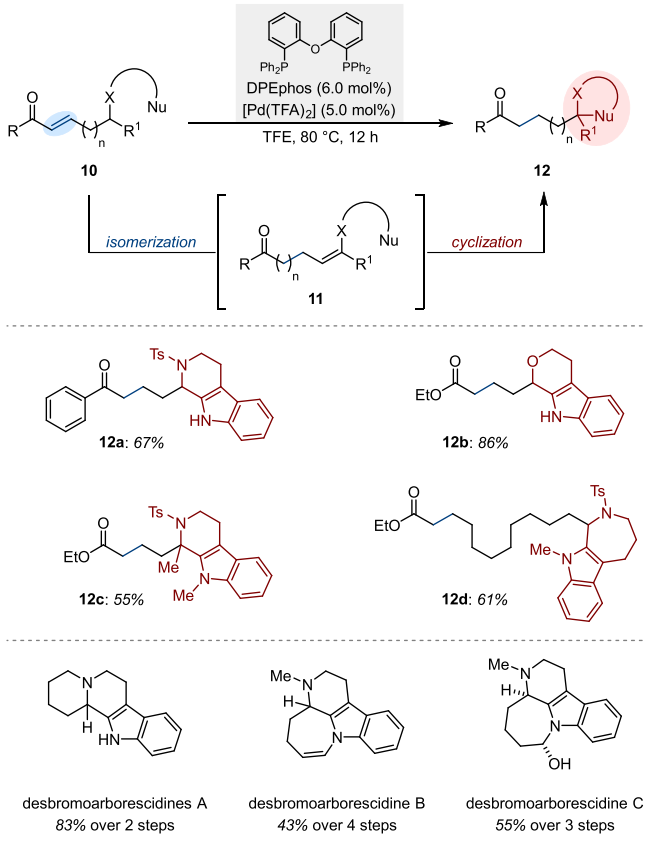

Fig. 7. Pd-catalyzed α amino C–H functionalization via isomerization of α,β-unsaturated carbonyls.

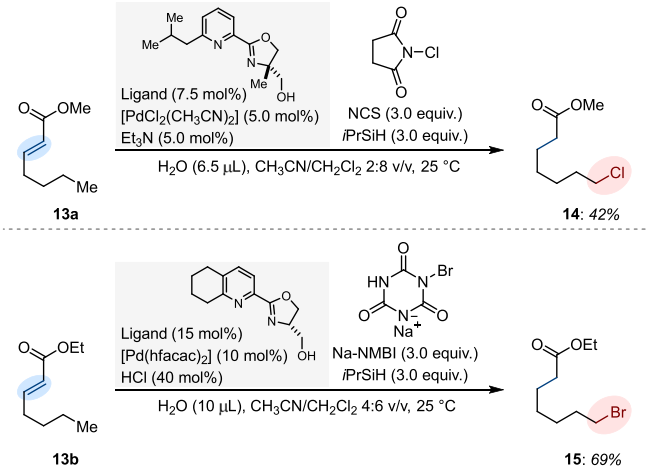

Fig. 8. Pd-catalyzed remote hydrohalogenation of alkenes initiated by deconjugative isomerization of α,β-unsaturated esters.

ably, the authors showed that the Pd catalyst intervenes in both steps of the sequence: (i) it is responsible for migrating the double bond towards enamine (**11**) formation by iterative migratory insertion/β-H elimination events in the isomerization step; (ii) it favors ring-closure by acting as a Lewis acid in the cyclization step.

Early this year, Liu and co-workers reported a broadly applicable Pd-catalyzed oxidative isomerization/ hydrohalogenation of alkenes affording linear alkyl halides with exquisite anti-Markovnikov selectivity [12]. The system is broadly applicable. Terminal alkenes and mixtures of internal alkenes can be employed indifferently leading to primary alkyl chlorides and bromides depending on the electrophilic source of halide employed. As part of an impressive substrate scope of nearly 75 examples, the authors disclosed the deconjugative isomerization/hydrochlorination of methyl-hept-2-enoate **13a** and deconjugative isomerization/hydrobromation of ethyl-hept-2-enoate **13b**, which delivered the corresponding primary alkyl halides **14** and **15** in 42% and 69% yield respectively (Fig. 8). Mechanistically, after migration of the

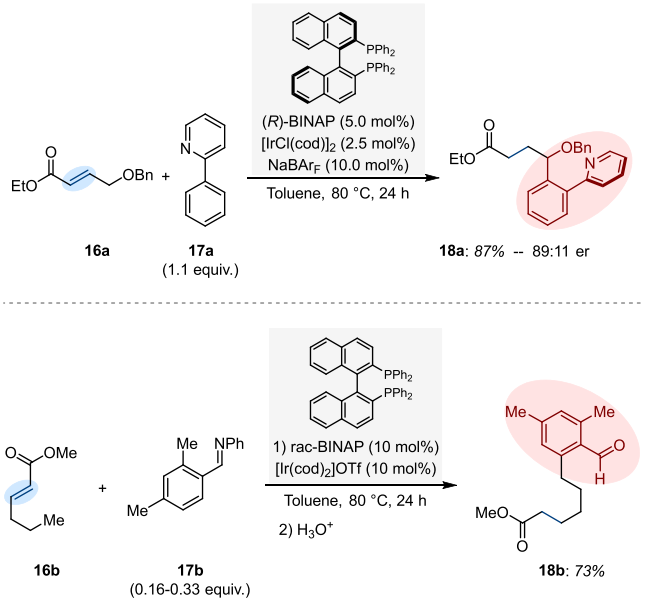

Fig. 9. Ir-catalyzed enantioselective hydroarylation of alkenyl ethers by deconjugative isomerization.

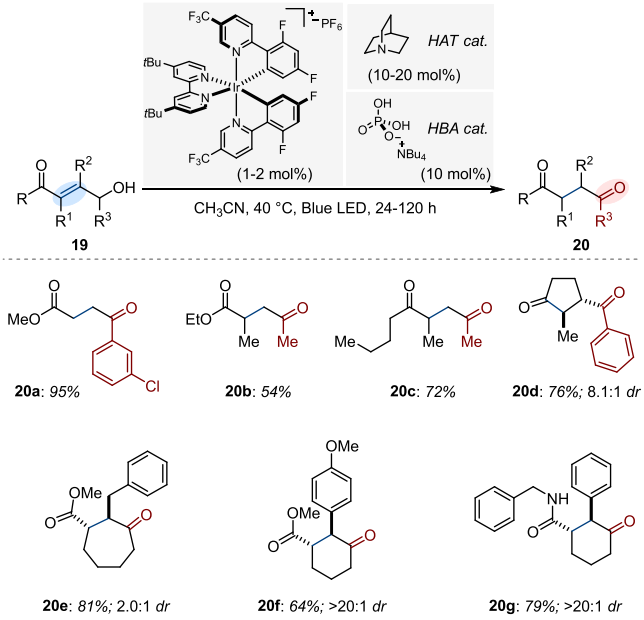

Fig. 10. Photoredox-catalyzed isomerization of highly substituted allylic alcohols by C–H bond activation.

C=C bond along the hydrocarbon chain by a Pd-H species to the terminal position, the system was proposed to involve oxidation of a 1° alkyl-Pd(II) intermediate into the corresponding 1° alkyl-Pd(IV)-X analog thus favoring reductive elimination over β-H elimination.

Iridium

In 2017, the Nishimura group reported a catalytic regio- and enantioselective hydroarylation of vinyl ethers affording secondary alkyl ethers with high levels of enantioselectivity [13]. The process is initiated by an Ir-catalyzed isomerization of alkenyl ethers; migration along the hydrocarbon chain is sustained by the presence of a chelating heteroaromatic unit (**17a**) in the arylation partner and enantiocontrol is ensured by an adequately selected chiral bisphosphine ligand. Among the various olefinic substrates investigated, the study features one α,β-unsaturated ester **16a**, which is deconjugated towards the formation of the final chiral secondary ether **18a** in excellent yield and relatively high enantiomeric ratio (**18**: 87% yield; 89:11 *er*) (Fig. 9). A related study was reported by Shibata and coworkers. Using benzylideneanilines such as **17b**, an Ir-catalyzed long-range deconjugative isomerization of α,β-unsaturated esters (**16b**) produces a primary alkyl iridium intermediate which undergoes hydroarylation to afford a variety of benzaldehyde derivatives after hydrolysis (**18b**) [14].

Huang, Yang and co-workers elaborated a 1-C catalytic deconjugative isomerization of highly substituted γ-hydroxy-α,β-unsaturated esters (**19**) that produces 1,4-keto-esters (**20**) in excellent yield (Fig. 10) [15]. The system consists in a subtle combination of an iridium photoredox catalyst, a hydrogen-atom-transfer catalyst (HAT) and a hydrogen-bond-acceptor catalyst (HBA). Not only it is compatible with cyclic and acyclic substrates with heavily substituted C=C bonds but the reaction conditions are readily transposed to γ-hydroxy-α,β-unsaturated ketones and amides. Representative examples of the products accessible by this method are displayed in Fig. 10. Based on a combined experimental and theoretical study, the authors propose that the radical cation of the HAT catalyst is generated following a SET with the photocatalyst. This species subsequently abstract a H atom from the HAB-activated hydroxyl substrate to eventually produce an allylic

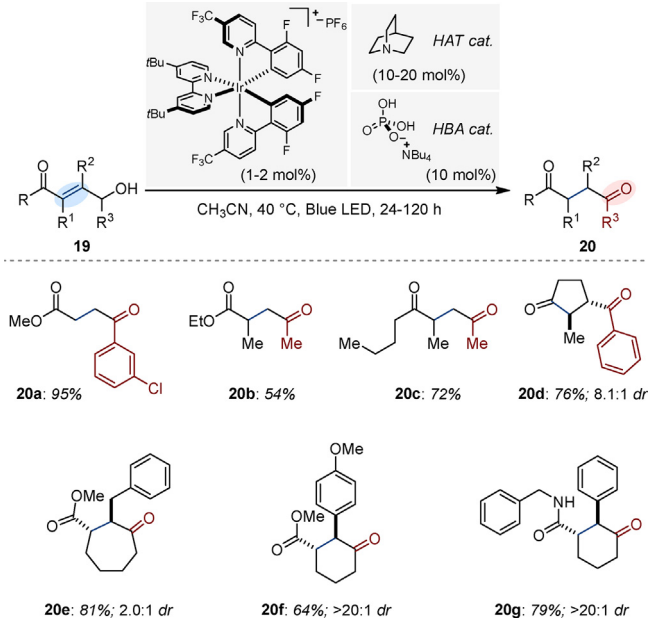

Fig. 11. Rh-catalyzed, remote hydroarylation of alkenes by long-range deconjugative isomerization.

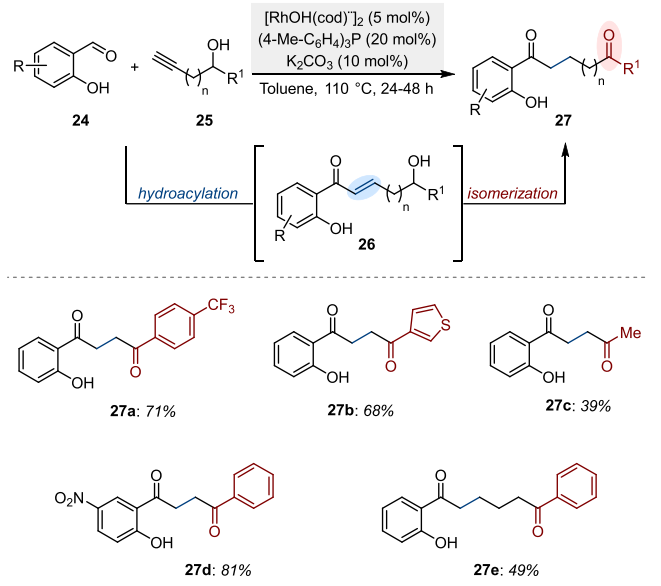

Fig. 12. Rh-catalyzed auto-tandem intermolecular hydroacylation/deconjugative isomerization.

alcohol radical. A second SET with a reduced form of the iridium photocatalyst, followed by protonation and tautomerization of the generated enol, affords the targeted dicarbonyl compound.

Rhodium and cobalt

In 2018, Borah and Shi developed a long-range Rh-catalyzed deconjugative hydroarylation of activated alkenes [16]. Key to the successful development of the deconjugative hydroarylation (rather than Michael addition) was the installation of a removable tertiary phosphine at the *N* atom of indole or indoline derivatives to direct C-H_7 activation by a (2,2′-biphenol)-rhodium precursor. Subsequent hydrometallation and sustained migration bring the rhodium shuttle to the sterically less crowded terminal position

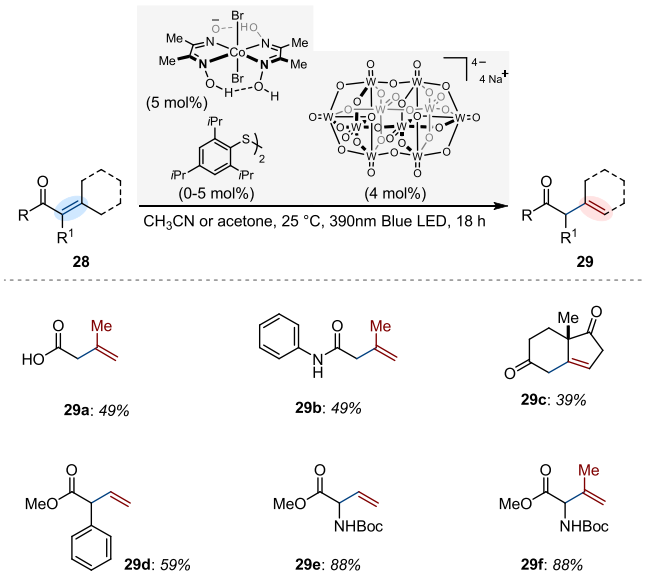

Fig. 13. Catalytic, *contra*-thermodynamic 1-C isomerization of α,β-unsaturated carbonyl compounds.

where reductive elimination delivers the linear product and regenerates the active Rh(I) catalyst (Fig. 11).

Starting from terminal alkynyl alcohols and salicylaldehyde derivatives, the Li group disclosed an auto-tandem Rh-catalyzed hydroacylation/deconjugative isomerization that provides access to a variety of 1,4-, 1,5- or 1,6-diketones (Fig. 12) [17]. The initial Rh-catalyzed intermolecular hydroacylation produces a transient α,β-unsaturated aryl ketone with a remote alcohol functionality. Isotopic labelling experiments support the in situ generation of a Rh-H intermediate, which is responsible for deconjugative isomerization by repeated migratory insertion/β-hydride elimination sequences. The protocol is applicable to a wide substrate scope, displays broad functional group tolerance and the dicarbonyl compounds are isolated in practical yield and excellent regioselectivity.

Wendlandt and co-workers recently disclosed a dual catalytic system for the contra-thermodynamic isomerization of internal alkenes to terminal alkenes under photochemical irradiation [18,19]. The optimized protocol, which combines catalytic quantities of decatungstate photocatalyst, cobaltoxime and 2,4,6-triisopropylbenzene disulfide, operates at room temperature under near-UV LED irradiation (390 nm) (Fig. 13). The reaction conditions have been extended to highly electron-deficient α,β-unsaturated acids (**28a**), amides (**28b**), ketones (**28c**), esters (**28d**) and dehydroamino acid derivatives (**28e-f**). The yields were usually moderate except for the latter substrate subclass. Experimental data are in support of a regiospecific bimolecular homolytic substitution mechanism proceeding via a key terminal σ-allyl-cobaltoxime (III) intermediate, itself generated by W-photocatalyzed abstraction of an allylic hydrogen atom and radical addition. Product formation is thought to occur via regiospecific bimolecular homolytic substitution (S_H2') of the allyl-cobaltoxime(III) by a H donor thiol intermediate or, alternatively, by a reduced state of the decatungstate catalyst.

Perspectives and conclusions

As testified by the examples discussed in this *Digest*, the transition metal-catalyzed deconjugative isomerization of α,β-unsaturated carbonyls bears the potential to expand significantly the scope of (remote) functionalization strategies. The dearth of enan-

tioselective transformations that rely on this approach as well as the lack of protocols using abundant, cheap and non-toxic first row transition metal catalysts will certainly stimulate future research efforts in this area.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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References

[1] (a) E. Larionov, H. Li, C. Mazet, Chem. Commun. 50 (2014) 9816–9826;
(b) A. Vasseur, J. Bruffaerts, I. Marek, Nat. Chem. 8 (2016) 209–219;
(c) H. Sommer, F. Juliá-Hernández, R. Martin, I. Marek, A.C.S. Cent, Sci. 4 (2018) 153–165;
(d) T. Kochi, S. Kanno, F. Kakiuchi, Tetrahedron Lett. 60 (2019) 150938;
(e) D. Janssen-Müller, B. Sahoo, S.-Z. Sun, R. Martin, Isr. J. Chem. 60 (2020) 195–206;
(f) S. Ghosh, S. Patel, I. Chatterjee, Chem. Commun. 57 (2021) 11110–11130;
(g) D. Fiorito, S. Scaringi, C. Mazet, Chem. Soc. Rev. 50 (2021) 1391–1406;
(h) I. Massad, R. Suresh, L. Segura, I. Marek, Nat. Synth. 1 (2022) 37–48.
[2] (a) J.J. Molloy, T. Morack, R. Gilmour, Angew. Chem. Int. Ed. 58 (2019) 13654–13664;
(b) S.L. Kraus, S.P. Ross, M.S. Sigman, Org. Lett. 23 (2021) 2505–2509.
[3] (a) Selected examples: (a) N.C. Yang, M.J. Jorgenson, Tetrahedron Lett. 5 1964 1203 1207.;
(b) R.R. Rando, W.E. Doering, J. Org. Chem. 33 (1968) 1671–1673;
(c) J.A. Barltrop, J. Wills, Tetrahedron Lett. 48 (1968) 4987–4990;
(d) J.L. Herrman, G.R. Kieczykowski, R.H. Schlessinger, Tetrahedron Lett. 26 (1973) 2433–2436;
(e) A. van Wageningen, P.C.M. van Noort, F.W.M. van der Wielen, H. Cerfontain, Synth. Commun. 4 (1974) 325–330;
(f) I.A. Skinner, A.C. Weedon, Tetrahedron Lett. 24 (1983) 4299–4302;
(g) S. Tsuboi, A. Kuroda, T. Masuda, A. Takeda, Chem. Lett. 13 (1984) 1541–1542;
(h) Y. Ikeda, H. Yamamoto, Tetrahedron Lett. 25 (1984) 5181–5182;
(i) O. Piva, R. Mortazei, F. Henin, J. Muzart, J.-P. Pete, J. Am. Chem. Soc. 112 (1990) 9263–9272;
(j) F. Bargiggia, O. Piva, Tetrahedron Asymmetry 14 (2003) 1819–1827;
(k) T. Bach, J.P. Hehn, Angew. Chem. Int. Ed. 50 (2011) 1000–1045;
(l) M. Vishe, R. Hrdina, A.I. Poblador-Bahamonde, C. Besnard, L. Guénée, T. Bürgi, J. Lacour, Chem. Sci. 6 (2015) 4923–4928;
(m) W.J. Jang, S.B. Song, S. Lee, S.Y. Yoo, Y.K. Chung, J. Huh, J. Yun, Org. Chem. Front. 7 (2020) 3427–3433;
(n) A.R. Choudhury, S. Mukherjee 49 (2020) 6755–6788;
(o) T. Morack, C. Onneken, H. Nakakohara, C. Mück-Lichtenfeld, R. Gilmour, ACS Catal. 11 (2021) (1937) 11929–11931.
[4] (a) C. Jimenez-Rodriguez, G.R. Eastham, D.J. Cole-Hamilton, Inorg. Chem. Commun. 8 (2005) 878–881;
(b) V. Goldbach, P. Roesle, S. Mecking, ACS Catal. 5 (2015) 5961–5972;
(c) Y. Liu, K. Dong, M. Beller, S. Mecking, ACS Catal. 8 (2018) 9232–9237;
(d) T. Yan, D. Guironnet, Macromolecules 53 (2020) 4338–4344.
[5] (a) H. Wakamatsu, M. Nishida, N. Adachi, M. Mori, J. Org. Chem. 65 (2000) 3966–3970;
(b) M. Nishida, N. Adachi, K. Onozuka, H. Matsumura, M. Mori, J. Org. Chem. 63 (1998) 9158–9159.
[6] G.-M. Ho, L. Segura, I. Marek, Chem. Sci. 11 (2020) 5944–5949.
[7] C. Romano, C. Mazet, J. Am. Chem. Soc. 140 (2018) 4743–4750.
[8] C. Romano, D. Fiorito, C. Mazet, J. Am. Chem. Soc. 141 (2019) 16983–16990.
[9] S. Scaringi, C. Mazet, ACS Catal. 11 (2021) 7970–7977.
[10] L. Lin, C. Romano, C. Mazet, J. Am. Chem. Soc. 138 (2016) 10344–10350.
[11] S.-J. Cheng, G. Wang, K. Liu, Z.-S. Ye, Org. Lett. 24 (2022) 864–868.
[12] X. Li, J. Jin, P. Chen, G. Liu, Nat. Chem. (2022), https://doi.org/10.1038/s41557-021-00869-x.
[13] Y. Ebe, M. Onoda, T. Nishimura, H. Yorimitsu, Angew. Chem. Int. Ed. 56 (2017) 5607–5611.
[14] K.H.N. Tang, K. Uchida, K. Nishihara, M. Ito, T. Shibata, Org. Lett. 24 (2022) 1313–1317.
[15] K. Guo, Z. Zhang, A. Li, Y. Li, J. Huang, Z. Yang, Angew. Chem. Int. Ed. 59 (2020) 11660–11668.
[16] A.J. Borah, Z. Shi, J. Am. Chem. Soc. 140 (2018) 6062–6066.
[17] G. You, Z.-X. Chang, J. Yan, C. Xia, F.-R. Li, H.-S. Li, Org. Chem. Front. 8 (2021) 39–45.
[18] G. Occhialini, V. Palani, A.E. Wendlandt, J. Am. Chem. Soc. 144 (2022) 145–152.
[19] For a similar study focused exclusively on alkenes, see: K. Zhao, R.R. Knowles, J. Am. Chem. Soc. 144 (2022) 137–144.