ACS Catalysis

Letter

Cite This: ACS Catal. 2019, 9, 2400−2406

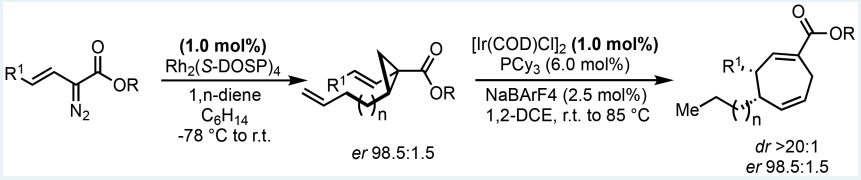
pubs.acs.org/acscatalysis

A Tandem Iridium-Catalyzed "Chain-Walking"/Cope Rearrangement Sequence

Heiko Sommer, Tal Weissbrod, and Ilan Marek*

Schulich Faculty of Chemistry, Technion—Israel Institute of Technology, Technion City, Haifa, 32000, Israel

Supporting Information



ABSTRACT: An iridium-catalyzed tandem olefin migration/Cope rearrangement of alkenyl ω-ene cyclopropanes is reported. By this means, a variety of complex annulenes are obtained as single diastereomers starting from cyclopropyl ester derived from simple 1,ω-dienes and alkenyldiazo compounds. Long-range olefin migration over up to 10 positions could be realized and coupled with an efficient Cope rearrangement to yield valuable scaffolds. Various functional groups are well-tolerated, giving rise to densely functionalized products. Furthermore, the present methodology could be successfully extended to yield bicyclic cycloheptenones starting from readily available alkenyl cyclopropanols via a Kulinkovich reaction.

KEYWORDS: *chain-walking, remote functionalization, iridium catalysis, Cope rearrangement, alkenyl cyclopropane*

Transition-metal-catalyzed C−H activation has received considerable attention in the context of remote functionalization. This methodology has the power to transform abundant starting materials into valuable, functionalized scaffolds at a nonreactive site (Scheme 1a).[1−4] In contrast to directed remote functionalization (Scheme 1b),[5−9] metal-walk functionalization allows for the transformation of positions distal to the initiating site (Scheme 1c).[10−14] From the initial processes utilizing stoichiometric zirconium,[15−20] protocols relying on palladium,[13,21−25] ruthenium,[26,27] nickel,[28,29] or cobalt[30,31] catalysis have been developed and applied in various C−C- and C−X-bond forming processes, respectively.[12−14]

Continuing our efforts to combine transition-metal-catalyzed chain-walking processes with subsequent remote functionalization,[13,19,20,25] we decided to explore the possibility to intercept an intermediately formed olefin in a rearrangement process. Merging our long-standing interest in cyclopropane chemistry[32−37] with transition-metal-catalyzed "chain-walking", the dialkenylcyclopropane rearrangement was deemed as an ideal testing ground. This well-studied process has found countless applications in complex molecule synthesis and developed into a useful tool for the synthesis of (bicyclo)heptadienes.[38,39] This ubiquitous motif forms the core of numerous classes of natural products and has inspired many elegant synthetic approaches (Scheme 2).[40−44]

At the outset of our study, several challenges had to be met. In order to achieve high diastereoselectivity in the key Cope rearrangement, excellent control over double-bond geometry during the metal-walk had to be ensured. It should be noted that commonly employed catalytic systems for long-range olefin isomerization/remote functionalization generally lack this important attribute. As chain-walking processes can proceed via different mechanisms, control over olefin geometry is determined by the mode of action of the catalyst employed.[45] Because of their simplicity, the majority of utilized catalytic systems follow a sequence of hydrometalation/β-hydride-elimination events to achieve the metal-walk. Typically under these conditions olefin geometry is solely based on kinetic control and fails to provide sufficient levels of selectivity.

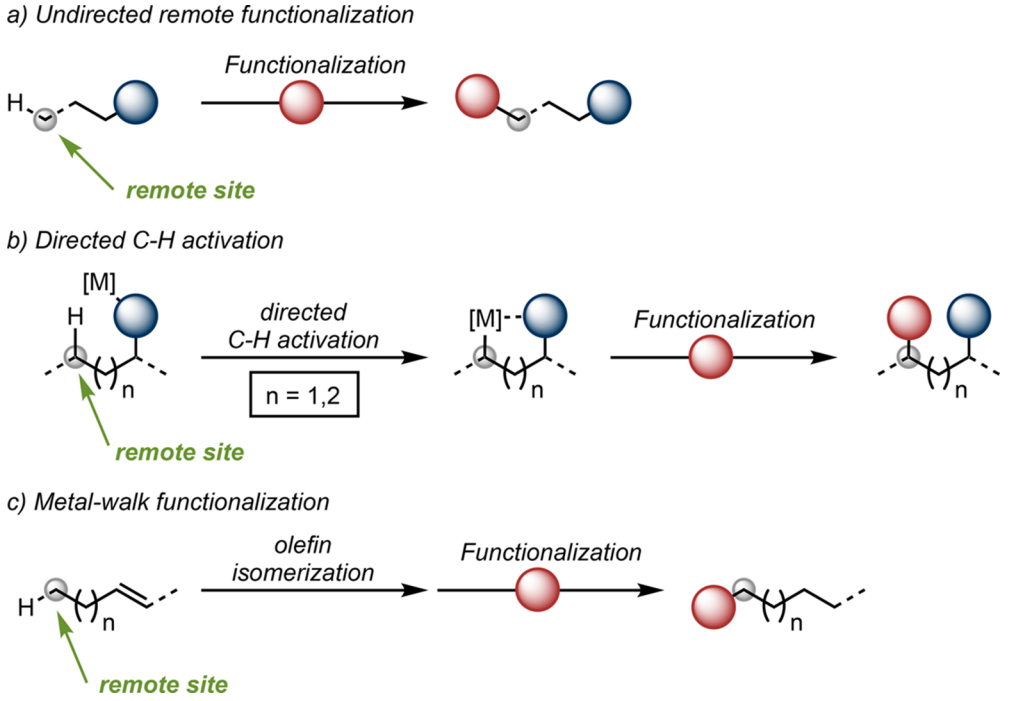
To address these shortcomings, studies have focused on the development of catalysts that affect olefin migration via allylic activation (Scheme 3a). Interestingly, only a limited number of examples achieving this goal have been reported solely utilizing zirconium,[15−20,46] ruthenium,[26,47] or iridium catalysts, respectively.[48−55] Because of their robustness, ease of preparation, and functional group tolerance, we decided to study the utility of cationic bis-phosphine iridium complexes. These have been shown to promote medium-range olefin isomerizations of silyl ethers with excellent levels of control of olefin geometry (Scheme 3b).[54] Related iridium complexes have been successfully employed in single-positional isomerization of allylic alcohols into the corresponding carbonyl derivatives which can be directly used in cross-coupling reactions (Scheme 3c),[56,57] and in a one-carbon isomerization followed by a Claisen rearrangement (Scheme 3d).[53] Additionally the resulting high *trans*-selectivity has been exploited in an enantioselective allylboration of aldehydes.[58]

Based on this 1,3-allylic migration mechanism, we envisioned to perform an Ir-catalyzed migration of a remote double bond of various functionalized ω-ene alkenylcyclopropanes as an efficient

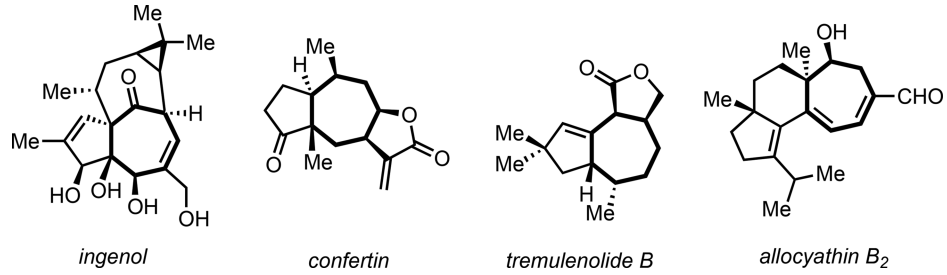
Received: January 10, 2019
Revised: January 30, 2019
Published: February 5, 2019

DOI: 10.1021/acscatal.9b00118
ACS Catal. 2019, 9, 2400−2406

Scheme 1. Potential Strategies for C−H Functionalization



Scheme 2. Cycloheptane-Containing Annulene Natural Products



access to stereodefined dialkenylcyclopropanes en route to diversely functionalized cycloheptadiene structures (Scheme 3e).

With the goal of developing an experimentally user-friendly protocol, we decided to prepare the catalyst in situ by simply mixing commercially available $[Ir(COD)Cl]_2$, PCy_3 and $NaBArF_4$ without recurring to the semihydrogenation reaction of the supporting COD-ligand prior to the catalytic reaction.[59] Under these conditions, the obtained $[Ir(PCy_3)_3]BArF_4$ complex exerted excellent activity even at room temperature. At the outset, we turned our attention toward styrenyl ω-ene cyclopropanes, easily accessible through the rhodium-catalyzed decomposition of the respective alkenyl diazoester with various 1,ω-dienes.[60,61]

To our delight, olefin isomerizations over up to four positions with subsequent Cope rearrangement occurred rapidly upon heating to 85 °C with only 1.0 mol % of Ir-dimer complex (Table 1, entries 1−3). Extending the chain-length required slightly increased catalyst loading (2.5 mol % of Ir-dimer complex) but still furnished the products in moderate to good yields with isomerizations over up to 10 positions (Table 1, entries 4,5).[62] It should be noted that separation of the product from small amounts of remaining internal olefin isomers proved to be challenging and was only achieved after reduction of the ester functionality (Table 1, entry 5). The relative stereochemistry of **2a** was determined by comparison with reported data.[61]

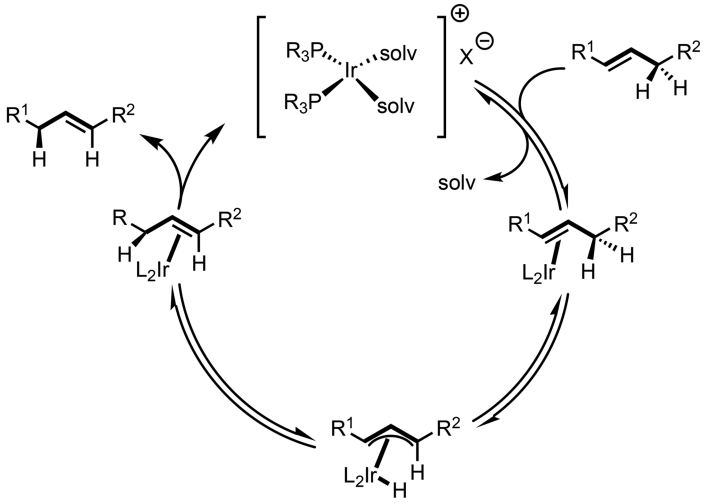
It should be highlighted that the present methodology allowed for the synthesis of enantioenriched cycloheptadiene **2a** in only two catalytic steps utilizing only minute amounts of catalyst (Scheme 4).

Having established a protocol for the long-range olefin isomerization/Cope rearrangement for styrenylcyclopropanes, we examined the scope of various olefinic counterparts with 1,5-hexadiene- and 1,7-octadiene-derived alkenylcyclopropanes (Table 2). To this end, a variety of alkenyldiazo derivatives were synthesized following established procedures and subsequently transformed in the rhodium-catalyzed cyclopropanation reaction (see Supporting Information). Various annulenes were obtained in moderate to good yields with excellent diastereocontrol. Simple cyclopentyl- and cyclohexyl-annelated compounds (Table 2, entries 1−4) could be accessed in good yield with as low as 1.0 mol % of catalyst loading. However, incorporating Lewis-basic groups (i.e., ketones or ethers) necessitated the utilization of slightly increased catalyst loading (2.5 mol % of Ir-dimer complex, Table 2, entries 5−11). Nevertheless, the corresponding annulenes were obtained in good yields including benzofuranes (Table 2, entries 7, 8) or cyclic ketones (Table 2, entries 5, 6, and 9). As reported by Davies, upon Cope rearrangement of benzofurane **2l** and **2m**, the dearomatized products were obtained.[63,64] Even quaternary carbon stereocenters could be efficiently installed, giving rise to densely functionalized

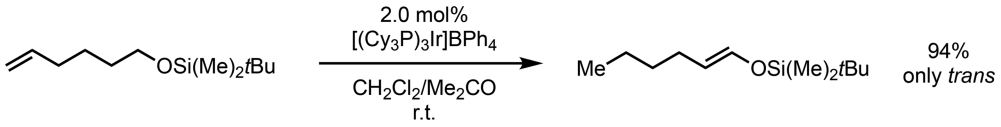
DOI: 10.1021/acscatal.9b00118
ACS Catal. 2019, 9, 2400−2406

Scheme 3. Iridium-Catalyzed Olefin Isomerization and Novel Application in Tandem Process

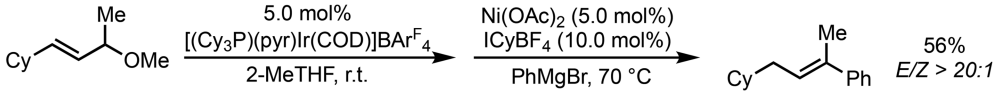
a) Iridium-catalyzed olefin isomerization via allylic activation pathway



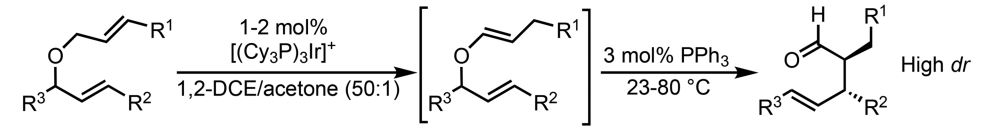
b) RajanBabu and coworkers - olefin migration to form silyl enol ethers (2009)



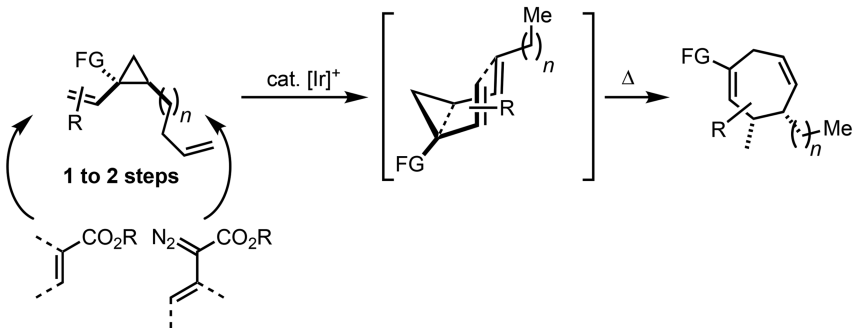
c) Mazet and coworkers - enol ether formation and nickel-catalyzed cross coupling (2018)



d) Nelson and coworkers - One-carbon isomerization followed by a Claisen rearrangement (2003)



e) Our design - tandem iridium-catalyzed olefin migration/Cope rearrangement

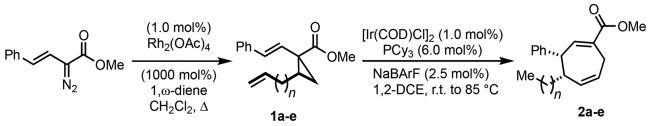


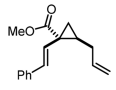
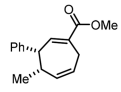
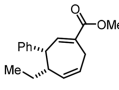
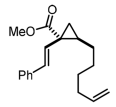
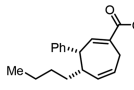
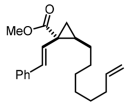
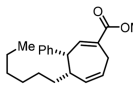
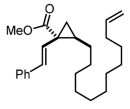
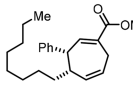
scaffolds (Table 2, entries 5, 6). Interestingly, without the quaternary carbon center, isomerization of the newly formed olefin into conjugation with the ketone was observed (Table 2, entry 9). It should be noted that in this case only the *syn*-isomer underwent the crucial Cope rearrangement. The corresponding *anti*-isomer merely furnished a mixture of internal olefins, advocating the existence of an iridium-catalyzed olefin equilibration. Finally, challenging sulfonyl-piperidine derived annulenes were obtained in good yield (Table 2, entries 10, 11) after prolonged heating (48 h).

In order to expand the utility of the present methodology, we then turned our attention toward the synthesis of bicyclic cycloheptenones. As the required starting materials are not accessible by the above-presented sequence, a complementary approach was envisioned. The utilization of a Kulinkovich reaction[65,66] would provide a straightforward access to simple alkenyl cyclopropanols which can subsequently be transformed into valuable ketoannulenes.[67] Utilizing a modified Kulinkovich procedure,[68] the thus-obtained cyclopropanols were exposed to the

DOI: 10.1021/acscatal.9b00118
ACS Catal. 2019, 9, 2400−2406

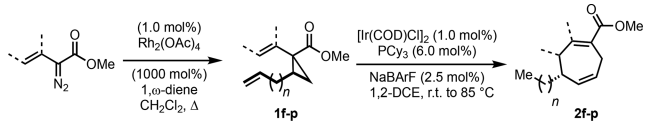
Table 1. Iridium-Catalyzed Olefin Migration/Cope Rearrangement of ω-Ene Styrenyl Cyclopropanes[a]

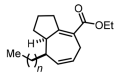
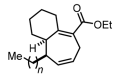
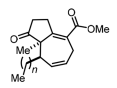
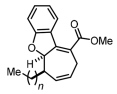
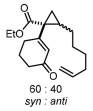
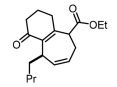
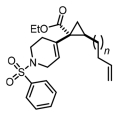
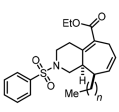


No	Alkenyl-CP		Product		Yield[b] (dr)
1	**1a** *n=0*			**2a**	82% (>20:1)
2	**1b** *n=1*			**2b**	74% (>20 : 1)
3	**1c** *n=3*			**2c**	80% (>20 : 1)
4	**1d** *n=5*			**2d**	79%[c] (>20 : 1)
5	**1e** *n=9*			**2e**	52%[c,d] (>20 : 1)

[a]Reaction conditions: ω-ene alkenylcyclopropane (0.5 mmol), $[Ir(COD)Cl]_2$ (1.0 mol %), PCy_3 (6.0 mol %), $NaBArF_4$ (2.5 mol %), 1,2-DCE (1.0 mL), 85 °C. [b]Yield of isolated products after purification by flash chromatography. [c]$[Ir(COD)Cl]_2$ (2.5 mol %), PCy_3 (15.0 mol %), $NaBArF_4$ (6.25 mol %). [d]Isolated after DIBAL-H reduction: DIBAL-H (250 mol %), THF (0.1M), −78 °C to room temperature.

Table 2. Scope of Different ω-Ene Alkenylcyclopropanes in the Iridium-Catalyzed Tandem Olefinmigration/Cope Rearrangement[a]



No	Alkenyl-CP		Product		Yield [%][b] (dr)
1	**1f** *n=1*			**2f** *n=1*	70 (>20:1)
2	***1g*** *n=3*			**2g** *n=3*	88 (> 20 : 1)
3	**1h** *n=1*			**2h** *n=1*	58 (> 20 : 1)
4	**1i** *n=3*			**2i** *n=3*	52 (>20 : 1)
5	**1j** *n=1*			**2j** *n=1*	87 (>20 : 1)[c]
6	**1k** *n=3*			**2k** *n=3*	55 (>20 : 1)[c]
7	**1l** *n=1*			**2l** *n=1*	73 (> 20 : 1)[c]
8	**1m** *n=3*			**2m** *n=3*	78 (>20 : 1)[c]
9	**1n** *n=3*	 60 : 40 *syn : anti*		**2n** *n=3*	59[c,d] (>20 : 1)
10	**1o** *n=1*			**2o** *n=1*	51 (>20 : 1)[c,e]
11	**1p** *n=3*			**2p** *n=3*	75 (>20 : 1)[c]

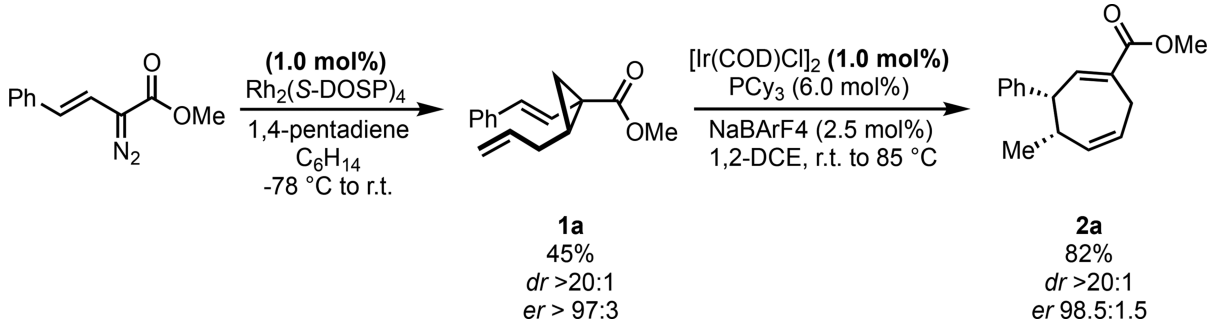
[a]Reaction conditions: ω-ene alkenylcyclopropane (0.25−0.5 mmol), $[Ir(COD)Cl]_2$ (1.0 mol %), PCy_3 (6.0 mol %), $NaBArF_4$ (2.5 mol %), 1,2-DCE (0.5M), 85 °C. [b]Yield of isolated products after purification by flash chromatography. [c]$[Ir(COD)Cl]_2$ (2.5 mol %), PCy_3 (15.0 mol %), $NaBArF_4$ (6.25 mol %). [d]Starting material as 60:40 mixture of *syn*/*anti* isomers, yield based on *syn*-isomer [e]Isolated after DIBAL-H reduction: DIBAL-H (250 mol %), THF (0.1M), −78 °C to room temperature.

optimized reaction conditions after silylation of the hydroxy group (Table 3).

Facile cyclic enol ether formation was observed in the presence of only 1.0 mol % of Ir-dimer complex and subsequent mild desilylation delivered the products in good yield (Table 3, entries 1−4). Annulated cycloheptenones comprising cyclohexane and cyclopentane cores with different tether lengths were again well-tolerated. All bicyclic cycloheptenones (**2q−2t**) were again formed as a single diastereomer, advocating the perfect control over the double-bond geometry. Interestingly, during the deprotection step, we could observe in two cases (Table 3, entries 1 and 3) partial isomerization of the olefin into the corresponding α,β-unsaturated ketones. The sensitive α′-position at the ring-junction remained unchanged under these conditions.

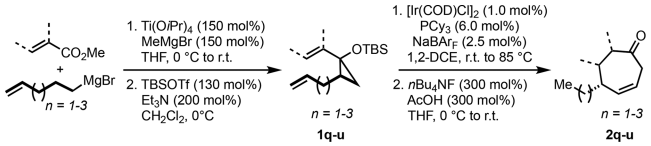
Herein we report a facile protocol for the synthesis of valuable annulenes starting from simple olefinic precursors obtained in one or two catalytic steps. In the presence of a highly reactive,

Scheme 4. Efficient Enantioselective Synthesis of Enantioenriched 2a



DOI: 10.1021/acscatal.9b00118
ACS Catal. 2019, 9, 2400−2406

Table 3. Iridium-Catalyzed Olefin Migration/Cope Rearrangement of Alkenyl Cyclopropanol Ethers[a]



No	Alkenyl-CP	Product		Yield[b] (dr)
1	**1q** *n=1*		**2q** *n=1*  57 : 43	61[c] (>20 : 1)
2	**1r** *n=2*		**2r** *n=2* 	63 (>20 : 1)
3	**1s** *n=3*		**2s** *n=3*  **2s'** *n=3*	41 (α,β) (>20 : 1) 34 (β,γ) (>20 : 1)
4	**1t** *n=3*		**2t** *n=3* 	77 (>20 : 1)

[a]Reaction conditions: ω-Ene alkenylcyclopropanol derivative (0.5 mmol), $[Ir(COD)Cl]_2$ (1.0 mol %), PCy_3 (6.0 mol %), $NaBArF_4$ (2.5 mol %), 1,2-DCE (1.0 mL), 85 °C. [b]Yield of isolated product after purification by flash chromatography. [c]Inseparable mixture of olefin isomers.

cationic iridium catalyst, a tandem olefin migration/Cope rearrangement of intermediately formed dialkenyl cyclopropanes could be realized. This functional-group tolerant procedure smoothly delivers bicyclic cycloheptadiene esters and cycloheptenones in moderate to good yield as single stereoisomers. The obtained complex scaffolds comprise quaternary stereocenters, heteroaromatic systems or cyclic amine motifs, present in numerous biologically active compounds. Studies to extend the scope of this useful tandem sequence and to obtain insights into the mechanistic underlying are ongoing.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.9b00118.

Details of experimental procedures, instrumentation used, ^1H and ^{13}CNMR spectra of all new compounds, HPLC traces of racemic and enantiomerically pure compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: chilanm@technion.ac.il.

ORCID

Ilan Marek: 0000-0001-9154-2320

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

H.S. acknowledges the Max Planck Society for a Minerva Fellowship. Ms G. Hong is acknowledged for preliminary studies on substrate preparation. I.M. is holder of the Sir Michael and Lady Sobell Academic Chair. This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement no. 786976 "Selective Functionalization of saturated Hydrocarbons".

■ REFERENCES

(1) Chen, H.; Schlecht, S.; Semple, T. C.; Hartwig, J. F. Thermal, Catalytic, Regiospecific Functionalization of Alkanes. *Science* **2000**, *287*, 1995−1997.

(2) Davies, H. M. L.; Manning, J. R. Catalytic C−H functionalization by metal carbenoid and nitrenoid insertion. *Nature* **2008**, *451*, 417−424.

(3) He, J.; Hamann, L. G.; Davies, H. M. L.; Beckwith, R. E. J. Late-stage C−H functionalization of complex alkaloids and drug molecules via intermolecular rhodium-carbenoid insertion. *Nat. Commun.* **2015**, *6*, 5943.

(4) Liao, K.; Negretti, S.; Musaev, D. G.; Bacsa, J.; Davies, H. M. L. Site-selective and stereoselective functionalization of unactivated C−H bonds. *Nature* **2016**, *533*, 230−234.

(5) Godula, K.; Sames, D. C-H Bond Functionalization in Complex Organic Synthesis. *Science* **2006**, *312*, 67−72.

(6) Brückl, T.; Baxter, R. D.; Ishihara, Y.; Baran, P. S. Innate and Guided C−H Functionalization Logic. *Acc. Chem. Res.* **2012**, *45*, 826−839.

(7) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. Weak Coordination as a Powerful Means for Developing Broadly Useful C−H Functionalization Reactions. *Acc. Chem. Res.* **2012**, *45*, 788−802.

(8) Hartwig, J. F. Catalyst-Controlled Site-Selective Bond Activation. *Acc. Chem. Res.* **2017**, *50*, 549−555.

(9) Yang, Y.-F.; Hong, X.; Yu, J.-Q.; Houk, K. N. Experimental−Computational Synergy for Selective Pd(II)-Catalyzed C−H Activation of Aryl and Alkyl Groups. *Acc. Chem. Res.* **2017**, *50*, 2853−2860.

(10) Breslow, R. Biomimetic control of chemical selectivity. *Acc. Chem. Res.* **1980**, *13*, 170−177.

(11) Schwarz, H. Remote functionalization of C-H and C-C bonds by "naked" transition-metal ions (Cosi Fan Tutte). *Acc. Chem. Res.* **1989**, *22*, 282−287.

(12) Franzoni, I.; Mazet, C. Recent trends in Pd-catalyzed remote functionalization of carbonyl compounds. *Org. Biomol. Chem.* **2014**, *12*, 233−241.

(13) Vasseur, A.; Bruffaerts, J.; Marek, I. Remote functionalization through alkene isomerization. *Nat. Chem.* **2016**, *8*, 209−219.

(14) Sommer, H.; Juliá-Hernández, F.; Martin, R.; Marek, I. Walking Metals for Remote Functionalization. *ACS Cent. Sci.* **2018**, *4*, 153−165.

(15) Chinkov, N.; Majumdar, S.; Marek, I. New Approach to the Stereoselective Synthesis of Metalated Dienes via an Isomerization−Elimination Sequence. *J. Am. Chem. Soc.* **2002**, *124*, 10282−10283.

(16) Chinkov, N.; Majumdar, S.; Marek, I. Stereoselective Preparation of Dienyl Zirconocene Complexes via a Tandem Allylic C−H Bond Activation-Elimination Sequence. *J. Am. Chem. Soc.* **2003**, *125*, 13258−13264.

(17) Marek, I.; Chinkov, N.; Levin, A. A Zirconium Promenade - An Efficient Tool in Organic Synthesis. *Synlett* **2006**, *2006*, 0501−0514.

(18) Chinkov, N.; Levin, A.; Marek, I. Unsaturated Fatty Alcohol Derivatives as a Source of Substituted Allylzirconocene. *Angew. Chem., Int. Ed.* **2006**, *45*, 465−468.

(19) Masarwa, A.; Didier, D.; Zabrodski, T.; Schinkel, M.; Ackermann, L.; Marek, I. Merging allylic carbon-hydrogen and selective carbon-carbon bond activation. *Nature* **2014**, *505*, 199−203.

(20) Vasseur, A.; Perrin, L.; Eisenstein, O.; Marek, I. Remote functionalization of hydrocarbons with reversibility enhanced stereocontrol. *Chem. Sci.* **2015**, *6*, 2770−2776.

(21) Mei, T.-S.; Patel, H. H.; Sigman, M. S. Enantioselective construction of remote quaternary stereocentres. *Nature* **2014**, *508*, 340−344.

(22) Hamasaki, T.; Aoyama, Y.; Kawasaki, J.; Kakiuchi, F.; Kochi, T. Chain Walking as a Strategy for Carbon-Carbon Bond Formation at

DOI: 10.1021/acscatal.9b00118
ACS Catal. 2019, 9, 2400−2406

Unreactive Sites in Organic Synthesis: Catalytic Cycloisomerization of Various 1,n-Dienes. *J. Am. Chem. Soc.* **2015**, *137*, 16163−16171.
(23) Dupuy, S.; Zhang, K.-F.; Goutierre, A.-S.; Baudoin, O. Terminal-Selective Functionalization of Alkyl Chains by Regioconvergent Cross-Coupling. *Angew. Chem., Int. Ed.* **2016**, *55*, 14793−14797.
(24) Lin, L.; Romano, C.; Mazet, C. Palladium-Catalyzed Long-Range Deconjugative Isomerization of Highly Substituted α,β-Unsaturated Carbonyl Compounds. *J. Am. Chem. Soc.* **2016**, *138*, 10344−10350.
(25) Singh, S.; Bruffaerts, J.; Vasseur, A.; Marek, I. A unique Pd-catalysed Heck arylation as a remote trigger for cyclopropane selective ring-opening. *Nat. Commun.* **2017**, *8*, 14200.
(26) Grotjahn, D. B.; Larsen, C. R.; Gustafson, J. L.; Nair, R.; Sharma, A. Extensive Isomerization of Alkenes Using a Bifunctional Catalyst: An Alkene Zipper. *J. Am. Chem. Soc.* **2007**, *129*, 9592−9593.
(27) Wakamatsu, H.; Nishida, M.; Adachi, N.; Mori, M. Isomerization Reaction of Olefin Using RuClH(CO)(PPh3)3. *J. Org. Chem.* **2000**, *65*, 3966−3970.
(28) Gaydou, M.; Moragas, T.; Juliá-Hernández, F.; Martin, R. Site-Selective Catalytic Carboxylation of Unsaturated Hydrocarbons with CO2 and Water. *J. Am. Chem. Soc.* **2017**, *139*, 12161−12164.
(29) He, Y.; Cai, Y.; Zhu, S. Mild and Regioselective Benzylic C−H Functionalization: Ni-Catalyzed Reductive Arylation of Remote and Proximal Olefins. *J. Am. Chem. Soc.* **2017**, *139*, 1061−1064.
(30) Obligacion, J. V.; Chirik, P. J. Bis(imino)pyridine Cobalt-Catalyzed Alkene Isomerization−Hydroboration: A Strategy for Remote Hydrofunctionalization with Terminal Selectivity. *J. Am. Chem. Soc.* **2013**, *135*, 19107−19110.
(31) Scheuermann, M. L.; Johnson, E. J.; Chirik, P. J. Alkene Isomerization−Hydroboration Promoted by Phosphine-Ligated Cobalt Catalysts. *Org. Lett.* **2015**, *17*, 2716−2719.
(32) Marek, I.; Simaan, S.; Masarwa, A. Enantiomerically Enriched Cyclopropene Derivatives: Versatile Building Blocks in Asymmetric Synthesis. *Angew. Chem., Int. Ed.* **2007**, *46*, 7364−7376.
(33) Simaan, M.; Delaye, P.-O.; Shi, M.; Marek, I. Cyclopropene Derivatives as Precursors to Enantioenriched Cyclopropanols and n-Butenals Possessing Quaternary Carbon Stereocenters. *Angew. Chem., Int. Ed.* **2015**, *54*, 12345−12348.
(34) Müller, D. S.; Marek, I. Copper mediated carbometalation reactions. *Chem. Soc. Rev.* **2016**, *45*, 4552−4566.
(35) Dian, L.; Müller, D. S.; Marek, I. Asymmetric Copper-Catalyzed Carbomagnesiation of Cyclopropenes. *Angew. Chem., Int. Ed.* **2017**, *56*, 6783−6787.
(36) Dian, L.; Marek, I. Asymmetric Preparation of Polysubstituted Cyclopropanes Based on Direct Functionalization of Achiral Three-Membered Carbocycles. *Chem. Rev.* **2018**, *118*, 8415−8434.
(37) Sommer, H.; Marek, I. Diastereo- and enantioselective copper catalyzed hydroallylation of disubstituted cyclopropenes. *Chem. Sci.* **2018**, *9*, 6503−6508.
(38) Hudlicky, T.; Fan, R.; Reed, J. W.; Gadamasetti, K. G. In *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 1992; Vol. *42*.
(39) Krüger, S.; Gaich, T. Recent applications of the divinylcyclopropane−cycloheptadiene rearrangement in organic synthesis. *Beilstein J. Org. Chem.* **2014**, *10*, 163−193.
(40) Wender, P. A.; Eissenstat, M. A.; Filosa, M. P. A general methodology for pseudoguaiane synthesis: total synthesis of (.+-.)-damsinic acid and (.+-.)-confertin. *J. Am. Chem. Soc.* **1979**, *101*, 2196−2198.
(41) Habeck, T.; Wolff, C.; Tochtermann, W. An approach to the tremulane skeleton: Synthesis of (±)-8a-epi-tremulenolide B. *Tetrahedron Lett.* **1995**, *36*, 2041−2044.
(42) Davies, H. M. L.; Doan, B. D. Asymmetric synthesis of the tremulane skeleton by a tandem cyclopropanation/cope rearrangement. *Tetrahedron Lett.* **1996**, *37*, 3967−3970.
(43) Takeda, K.; Nakane, D.; Takeda, M. Synthesis of the Tricyclic Skeleton of Cyathins Using Brook Rearrangement-Mediated [3 + 4] Annulation. *Org. Lett.* **2000**, *2*, 1903−1905.
(44) McKerrall, S. J.; Jørgensen, L.; Kuttruff, C. A.; Ungeheuer, F.; Baran, P. S. Development of a Concise Synthesis of (+)-Ingenol. *J. Am. Chem. Soc.* **2014**, *136*, 5799−5810.
(45) Biswas, S. Mechanistic Understanding of Transition-Metal-Catalyzed Olefin Isomerization: Metal-Hydride Insertion-Elimination vs. π-Allyl Pathways. *Comments Inorg. Chem.* **2015**, *35*, 300−330.
(46) Prosenc, M.-H.; Brintzinger, H.-H. Zirconium−Alkyl Isomerizations in Zirconocene-Catalyzed Olefin Polymerization: A Density Functional Study. *Organometallics* **1997**, *16*, 3889−3894.
(47) Miura, T.; Nakahashi, J.; Zhou, W.; Shiratori, Y.; Stewart, S. G.; Murakami, M. Enantioselective Synthesis of anti-1,2-Oxaborinan-3-enes from Aldehydes and 1,1-Di(boryl)alk-3-enes Using Ruthenium and Chiral Phosphoric Acid Catalysts. *J. Am. Chem. Soc.* **2017**, *139*, 10903−10908.
(48) Matsuda, I.; Kato, T.; Sato, S.; Izumi, Y. Regiocontrolled synthesis of allylsilanes by means of rhodium(I) or iridium(I) catalyzed isomerization of olefins. *Tetrahedron Lett.* **1986**, *27*, 5747−5750.
(49) Moriya, T.; Suzuki, A.; Miyaura, N. A stereoselective preparation of γ-alkoxyallylboronates via catalytic isomerization of pinacol [(E)-3-alkoxy-1-propenyl]boronates. *Tetrahedron Lett.* **1995**, *36*, 1887−1888.
(50) Ohmura, T.; Yamamoto, Y.; Miyaura, N. A stereoselective isomerization of allyl silyl ethers to (E)- or (Z)-silyl enol ethers using cationic iridium complexes. *Chem. Commun.* **1998**, 1337−1338.
(51) Ohmura, T.; Yamamoto, Y.; Miyaura, N. Stereoselective Synthesis of Silyl Enol Ethers via the Iridium-Catalyzed Isomerization of Allyl Silyl Ethers. *Organometallics* **1999**, *18*, 413−416.
(52) Yamamoto, Y.; Miyairi, T.; Ohmura, T.; Miyaura, N. Synthesis of Chiral Esters of (E)-3-(Silyloxy)-2-propenylboronic Acid via the Iridium-Catalyzed Isomerization of the Double Bond. *J. Org. Chem.* **1999**, *64*, 296−298.
(53) Nelson, S. G.; Bungard, C. J.; Wang, K. Catalyzed Olefin Isomerization Leading to Highly Stereoselective Claisen Rearrangements of Aliphatic Allyl Vinyl Ethers. *J. Am. Chem. Soc.* **2003**, *125*, 13000−13001.
(54) Lim, H. J.; Smith, C. R.; RajanBabu, T. V. Facile Pd(II)- and Ni(II)-Catalyzed Isomerization of Terminal Alkenes into 2-Alkenes. *J. Org. Chem.* **2009**, *74*, 4565−4572.
(55) Li, H.; Mazet, C. Catalyst-Directed Diastereoselective Isomerization of Allylic Alcohols for the Stereoselective Construction of C(20) in Steroid Side Chains: Scope and Topological Diversification. *J. Am. Chem. Soc.* **2015**, *137*, 10720−10727.
(56) Li, H.; Mazet, C. Iridium-Catalyzed Selective Isomerization of Primary Allylic Alcohols. *Acc. Chem. Res.* **2016**, *49*, 1232−1241.
(57) Romano, C.; Mazet, C. Multicatalytic Stereoselective Synthesis of Highly Substituted Alkenes by Sequential Isomerization/Cross-Coupling Reactions. *J. Am. Chem. Soc.* **2018**, *140*, 4743−4750.
(58) Miura, T.; Nishida, Y.; Morimoto, M.; Murakami, M. Enantioselective Synthesis of Anti Homoallylic Alcohols from Terminal Alkynes and Aldehydes Based on Concomitant Use of a Cationic Iridium Complex and a Chiral Phosphoric Acid. *J. Am. Chem. Soc.* **2013**, *135*, 11497−11500.
(59) Baudry, D.; Ephritikhine, M.; Felkin, H. Isomerisation of allyl ethers catalysed by the cationic iridium complex [Ir(cyclo-octa-1,5-diene)(PMePh2)2]PF6. A highly stereoselective route to trans-propenyl ethers. *J. Chem. Soc., Chem. Commun.* **1978**, 694−695.
(60) Davies, H. M. L. Tandem cyclopropanation/cope rearrangement: a general method for the construction of seven-membered rings. *Tetrahedron* **1993**, *49*, 5203−5223.
(61) Davies, H. M. L.; Stafford, D. G.; Doan, B. D.; Houser, J. H. Tandem Asymmetric Cyclopropanation/Cope Rearrangement. A Highly Diastereoselective and Enantioselective Method for the Construction of 1,4-Cycloheptadienes. *J. Am. Chem. Soc.* **1998**, *120*, 3326−3331.
(62) In our study we focused on the utilization of 1,ω−dienes as commercially available dienes comprising internal olefins can only be obtained as isomeric mixtures. We found that cis-olefins fail to undergo the projected iridium-catalyzed "chain-walking"; therefore, mixed dienes containing terminal and internal olefins were not employed.

DOI: 10.1021/acscatal.9b00118
ACS Catal. 2019, 9, 2400−2406

(63) Olson, J. P.; Davies, H. M. L. Asymmetric [4 + 3] Cycloadditions between Benzofuranyldiazoacetates and Dienes: Formal Synthesis of (+)-Frondosin B. *Org. Lett.* **2008**, *10*, 573−576.
(64) Olson, J. P.; Davies, H. M. L. Asymmetric [4 + 3] Cycloadditions between Benzofuranyldiazoacetates and Dienes: Formal Synthesis of (+)-Frondosin B. *Org. Lett.* **2010**, *12*, 1144−1144.
(65) Lee, J.; Kim, H.; Cha, J. K. A New Variant of the Kulinkovich Hydroxycyclopropanation. Reductive Coupling of Carboxylic Esters with Terminal Olefins. *J. Am. Chem. Soc.* **1996**, *118*, 4198−4199.
(66) Kulinkovich, O. G.; Kananovich, D. G. Advanced Procedure for the Preparation of cis-1,2-Dialkylcyclopropanols − Modified Ate Complex Mechanism for Titanium-Mediated Cyclopropanation of Carboxylic Esters with Grignard Reagents. *Eur. J. Org. Chem.* **2007**, *2007*, 2121−2132.
(67) Lee, J.; Kim, H.; Cha, J. K. Diastereoselective Synthesis of cis-1,2-Dialkenylcyclopropanols and Subsequent Oxy-Cope Rearrangement. *J. Am. Chem. Soc.* **1995**, *117*, 9919−9920.
(68) Sethofer, S. G.; Staben, S. T.; Hung, O. Y.; Toste, F. D. Au(I)-Catalyzed Ring Expanding Cycloisomerizations: Total Synthesis of Ventricosene. *Org. Lett.* **2008**, *10*, 4315−4318.

DOI: 10.1021/acscatal.9b00118
ACS Catal. 2019, 9, 2400−2406