Photochemistry

International Edition: DOI: 10.1002/anie.201802891
German Edition: DOI: 10.1002/ange.201802891

Catalytic Asymmetric Dearomatization by Visible-Light-Activated [2+2] Photocycloaddition

Naifu Hu, Hoimin Jung, Yu Zheng, Juhyeong Lee, Lilu Zhang, Zakir Ullah, Xiulan Xie, Klaus Harms, Mu-Hyun Baik, and Eric Meggers**

Abstract: *A novel method for the catalytic asymmetric dearomatization by visible-light-activated [2+2] photocycloaddition with benzofurans and one example of a benzothiophene is reported, thereby providing chiral tricyclic structures with up to four stereocenters including quaternary stereocenters. The benzofurans and the benzothiophene are functionalized at the 2-position with a chelating N-acylpyrazole moiety which permits the coordination of a visible-light-activatable chiral-at-rhodium Lewis acid catalyst. Computational molecular modeling revealed the origin of the unusual regioselectivity and identified the heteroatom in the heterocycle to be key for the regiocontrol.*

Aromatic and heteroaromatic compounds are ubiquitous synthetic starting materials and many types of reactions have been developed for their functionalization and transformation. A recently emerging highly useful class of reactions are catalytic asymmetric dearomatizations (CADA reactions), a term coined by the group of You.[1–3] This synthetic methodology is highly appealing because it converts readily available aromatic moieties into enantioenriched three-dimensional cyclic molecules in a catalytic fashion, which is an important objective in contemporary organic synthesis.

Asymmetric cycloadditions enable straightforward access to complex architectures with multiple stereocenters in a single step and thereby generate structural complexity in a rapid and economical fashion.[4] Recently, the groups of Bach[5] and Yoon,[6] as well as ours,[6c,7] reported visible-light-activated catalytic asymmetric [2+2] photocycloadditions[8,9] which occur directly from an electronically excited substrate/catalyst complex without the involvement of charge separation. This chemistry is attractive because it employs visible light as an abundant and mild source of energy and at the same time circumvents drawbacks resulting from radical-ion intermediates which are typically generated in the course of photoredox processes.[10]

Herein we report the first application of visible-light-activated [2+2] photocycloadditions to catalytic asymmetric dearomatizations and we investigate the observed regioselectivity by computational modeling (Figure 1).[11,12]

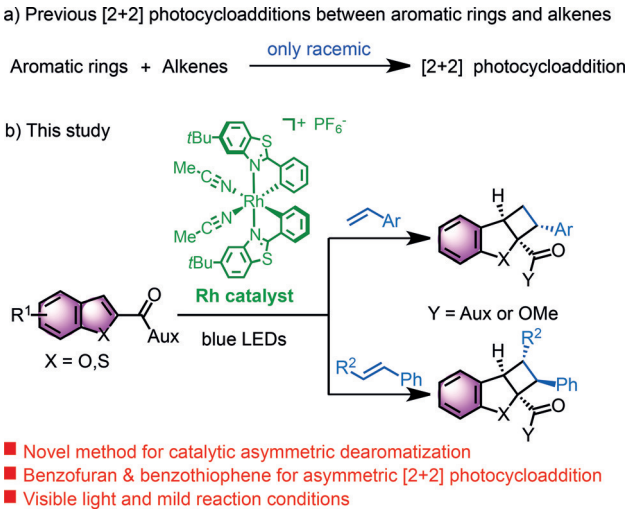
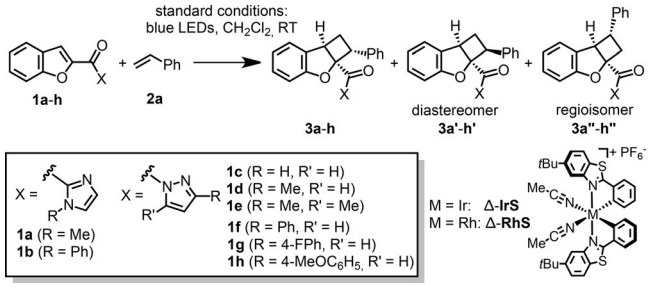


Figure 1. Catalytic asymmetric dearomatization by visible-light-activated [2+2] photocycloaddition reported in this study and its comparison with state of the art.

We started our study with benzofurans[13] functionalized at the 2-position with either 2-acylimidazole (**1a**,**b**) or *N*-acylpyrazole (**1c**–**h**) moieties for interacting with the photoactivatable chiral-at-metal rhodium catalyst Δ-**RhS**[14] (Table 1).[15,16] Initial experiments were disappointing. When 2-acyl imidazoles (**1a** or **1b**) and styrene (**2a**) were subjected to blue LEDs together with Δ-**RhS** (2 mol%), nearly no conversion occurred (entries 1 and 2). Gratifyingly, when **1c** was employed, 68% conversion was observed for the dearomative [2+2] photocycloaddition and the main product **3c** was formed with 97% *ee* together with the diastereomer **3c′** (5.4:1 d.r.) and regioisomer **3c″** (7.3:1 rr; entry 3). To our surprise, the main product features a head-to-tail regioselectivity in contrast to a tail-to-tail regioselectivity observed in related previous rhodium-catalyzed [2+2] photocycloadditions.[7] The substituents at the pyrazole have a profound effect on this reaction (entries 4–8). Best results were obtained with a Ph group at the 3-position of the pyrazole (**1f**), which gave complete conversion after 18 hours of irradiation and afforded the main product **3f** with 98% *ee*

[*] Dr. N. Hu, Y. Zheng, Dr. L. Zhang, Dr. X. Xie, Dr. K. Harms, Prof. Dr. E. Meggers
Fachbereich Chemie, Philipps-Universität Marburg
Hans-Meerwein-Strasse 4, 35043 Marburg (Germany)
E-mail: meggers@chemie.uni-marburg.de
H. Jung, J. Lee, Z. Ullah, Prof. Dr. M.-H. Baik
Department of Chemistry, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 34141 (Republic of Korea),
and
Center for Catalytic Hydrocarbon Functionalizations, Institute for Basic Science (IBS), Daejeon 34141 (Republic of Korea)
E-mail: mbaik2805@kaist.ac.kr
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.201802891.

Table 1: Initial experiments and optimization of conditions.



Entry	X	Reaction conditions[a]	Conv. [%][b]	d.r.[c]	rr[d]	*ee* [%][e]
1	**1a**	standard	< 5	–	–	–
2	**1b**	standard	< 5	–	–	–
3	**1c**	standard	68	5.4:1	7.3:1	97
4	**1d**	standard	89	4.7:1	4.3:1	98
5	**1e**	standard	< 5	–	–	–
6	**1f**	standard	100 (78)[f]	6.2:1	5.3:1	98[g]
7	**1g**	standard	98	6.1:1	5.0:1	98
8	**1h**	standard	100	5.9:1	4.3:1	82
9	**1f**	under air	98	5.7:1	4.7:1	97
10	**1f**	acetone as solvent	65	3.4:1	5.0:1	95
11	**1f**	THF as solvent	49	4.0:1	3.4:1	92
12[h]	**1f**	1.0 mol% Δ-**RhS**	100	6.1:1	5.1:1	98
13	**1f**	no light	0	–	–	–
14	**1f**	no catalyst	0	–	–	–
15	**1f**	2.0 mol% Δ-**IrS**	0	–	–	–

[a] Deviations from standard reaction conditions are shown. Standard conditions: Benzofuran **1a–h** (0.1 mmol), styrene **2a** (0.3 mmol), and 2.0 mol% Δ-**RhS** in CH_2Cl_2 (1 mL) were stirred at RT under N_2 for 18 h with blue LEDs (24 W) irradiation. [b] Conversion determined by ^{1}H NMR analysis of the crude reaction product. [c] The d.r. values were determined by ^{1}H NMR analysis of the crude reaction product. [d] The rr values were determined by ^{1}H NMR analysis of the crude reaction product. [e] The *ee* values were determined by HPLC analysis on chiral stationary phase. [f] Total yield of the isolated product **4a** with its regioisomer **4a″** (6.7:1 rr) after the conversion into the corresponding methyl esters. [g] The *ee* value was unchanged after converting the main product into the corresponding methyl ester. [h] Reaction time was 36 h.

together with the diastereomer **3f′** (6.2:1 d.r.) and regioisomer **3f″** (5.3:1 rr; entry 6). Because of the lability of the *N*-acylpyrazole moiety in this structural context, a prior conversion to its methyl ester allowed isolation of the main product together with its regioisomer in an overall yield of 78%. The reaction is quite robust and performs well under air (entry 9). However, the choice of solvent is important and the best results are obtained with CH_2Cl_2 (compare entries 6, 10, and 11). The catalyst loading can be reduced to 1 mol% with almost unchanged performance (entry 12). As a control, in the absence of either light or catalyst, no conversion was observed (entries 13 and 14). Likewise, the related iridium complex Δ-**IrS**[17] was not able to catalyze this reaction (entry 15).

With optimized reaction conditions in hand, we next investigated the scope with respect to the substituted styrenes and determined yields of the isolated products after conversion of the initial *N*-acylpyrazole products into their methyl esters (Figure 2). Overall, electron-withdrawing and electron-donating groups, as well as sterically bulky groups in the *para* and *meta* positions of the phenyl moiety are well

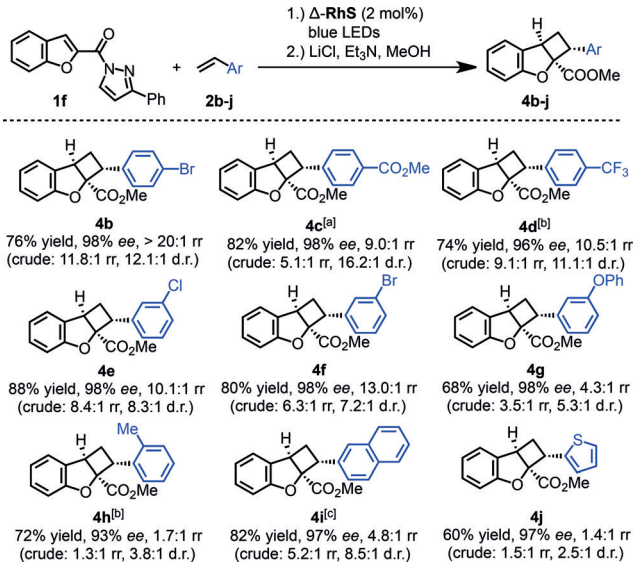


Figure 2. Substrate scope with respect to styrene derivatives. Yields of products, isolated as a combination of regioisomers, are provided. [a] 8 mol% catalyst and 48 h reaction time instead. [b] 4 mol% catalyst and 48 h reaction time instead. [c] The absolute configuration of a derivative of **4i** was determined by X-ray crystallography and all other products assigned by analogy.

tolerated. The dearomatization products **4b–g** were obtained with 96–98% *ee* and 68–88% yields as single diastereomers, but as regioisomeric mixtures (4.3:1 to > 20:1 rr). The phenyl moiety can also be replaced with a naphthyl (**4i**) or a thiophene moiety (**4j**). However, *ortho* substituents strongly affect the reactivity so that for 2-methylstyrene (**4h**) the catalyst loading was doubled to 4 mol% to obtain satisfactory results.

Generally, the reaction is expected to proceed as seen in previous rhodium catalyzed [2+2] photocycloadditions as summarized in Figure 3.[7,18] The catalytic cycle begins with the association of the *N*-acylpyrazole substrate (**^{1}1f**) with the chiral rhodium catalyst Δ-**RhS**. The reactant complex **^{1}A** absorbs blue light to reach its singlet excited state, **^{1}A***. After intersystem crossing (ISC) to form the triplet reactant complex **^{3}A**, it reacts with the alkene substrate to generate the 1,4-biradical intermediate **^{3}B**, which then recombines to

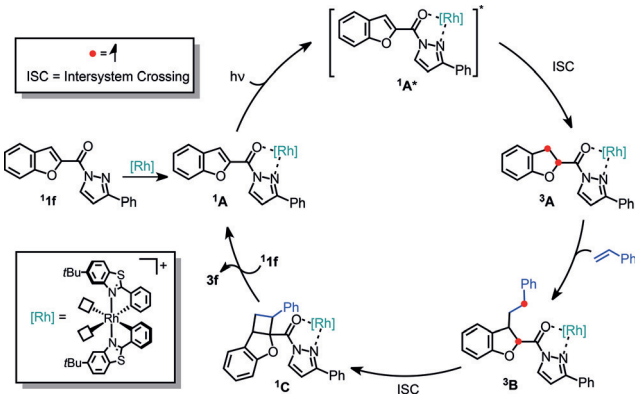


Figure 3. Proposed catalytic cycle.

form the desirable photocycloaddition product.[19] The subsequent release of **3 f** and coordination of a new equivalent of substrate completes the catalytic cycle. Our calculations confirm the location of the unpaired electrons across the ene moiety of the photoexcited ^{3}**A** as a 1,2-biradical species (indicated with red dots in Figure 3) which reacts with the alkene substrate in a stereocontrolled fashion. During this process, the enantioselectivity[20] is well-controlled by the chiral rhodium catalyst (see the Supporting Information for a structure of the transition state ^{3}**A-TS**) and the regioselectivity is probably determined by the stability of the 1,4-biradical intermediate, although other factors such as the rate of the backward reaction to the ground-state precursors have been determined to play an important role.[9b,21,22]

We sought to understand the origin of the unusual regioselectivity of this dearomatization using DFT calculations for the reaction with the catalyst Δ-**RhS**, substrate **1 f**, and styrene (Figure 4).[23] Once the substrate-bound rhodium complex ^{1}**A** is photoexcited and undergoes ISC into the triplet state to form the reactive ^{3}**A**, the styrene substrate can approach the 1,2-biradical from two possible faces. Since the formation of the benzyl radical is much more favorable than the generation of the methyl radical, we focused on identifying the transition state that couples the terminal carbon atom of styrene with one of the 1,2-biradical carbon atoms in the benzofuran fragment to afford a 1,4-biradical product. As illustrated in Figure 4 a, the head-to-tail addition (solid black line) has a barrier that is 2.0 kcal mol^{-1} lower in energy than the tail-to-tail addition (dashed, blue line). The thermodynamic stability of two analogous 1,4-biradical intermediates shows the same trend, as ^{3}**B** is 5.5 kcal mol^{-1} lower in free energy than ^{3}**B″**. To complete the cycloaddition, the 1,4-biradical species must undergo radical recombination and crossover to the singlet surface to produce ^{1}**C** and ^{1}**C″**, respectively. These processes will occur at the minimum energy crossing point (MECP), where the triplet and singlet surfaces cross.

The observation that styrene engages the 1,2-biradical with the terminal methylene moiety to generate a benzyl radical is plausible. However, the energy difference of 5.5 kcal mol^{-1} between the 1,4-biradical intermediates ^{3}**B** and ^{3}**B″** is not as easy to understand, but it is a key feature leading to the regioselectivity. To separate the impact of the chiral rhodium fragment from the intrinsic energy differences of the two possible intermediate isomers, we deleted the rhodium fragment and evaluated the relative energies of the two biradicals, labeled ^{3}**b** and ^{3}**b″**. Interestingly, our calculations indicate that ^{3}**b** is 6.2 kcal mol^{-1} lower in energy than ^{3}**b″**, as illustrated in Figure 4 b. An inspection of the underlying electronic structure reveals a simple reason for this energy difference (Figure 4 c). When the unpaired electron is placed at the benzylic C3-position, it is resonance-stabilized by the phenyl group. At the tertiary C2-position, however, the unpaired electron is stabilized by the neighboring carbonyl group and, more importantly, by the oxygen atom lone-pair orbital, shown in blue and red in Figure 4 c, respectively.[24] A more detailed energy decomposition is provided in the Supporting Information. Thus, the calculations suggest that the regiocontrol is based on an intrinsic electronic preference

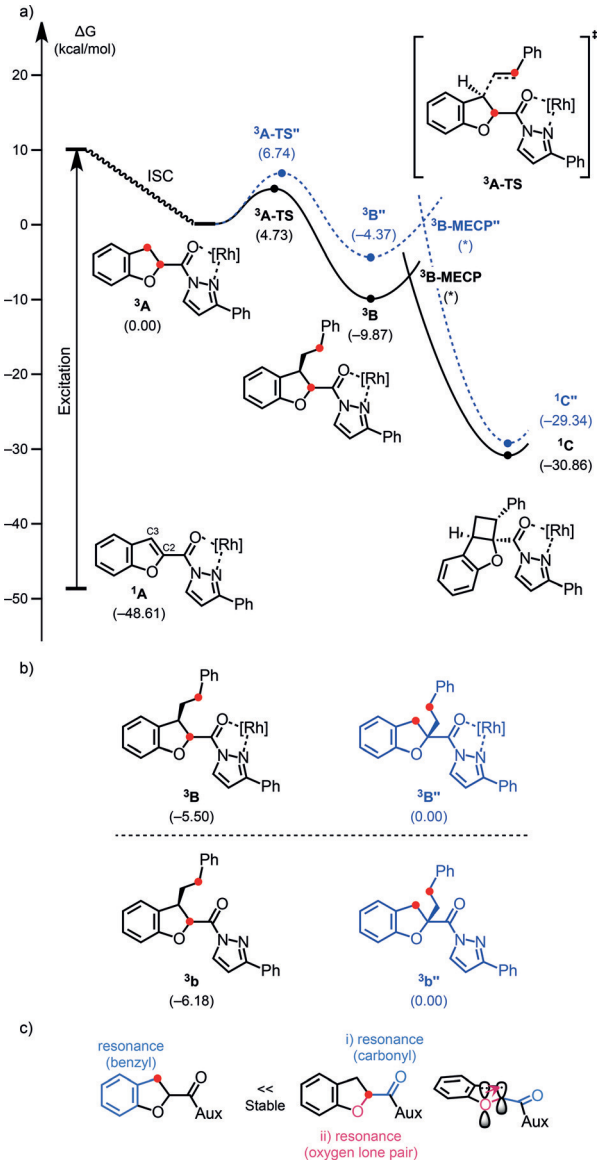


Figure 4. a) Gibbs free energy profile. b) Energy differences of two analogous 1,4-biradical intermediates. c) Schematic illustrations of the radical stabilizations.

of placing an unpaired electron of the 1,4-biradical intermediate at the tertiary carbon atom next to an oxo functionality.

Finally, we investigated reactions with internal alkenes that provide an additional stereocenter. To our delight, when (*E*)-β-methylstyrene (**5 a**) was tested with **1 f** and subsequently converted into its methyl ester, the dearomatization product **6 a** was obtained in 90 % yield and 99 % *ee* as a single diastereomer (> 20:1 d.r.) and as a single regioisomer (> 20:1 rr; Figure 5). With the geometrical isomer (*Z*)-β-methylstyrene (**5 a′**) the dearomatization product **6 a′** was formed as the main product instead, albeit with a low d.r. value of 1.8:1. Gratifyingly, when performed at −30 °C, only a single diastereomer was obtained (> 20:1 d.r.). This strong temperature dependence of the diastereoselectivity supports a mechanism via an intermediate, but a very short-lived 1,4-biradical

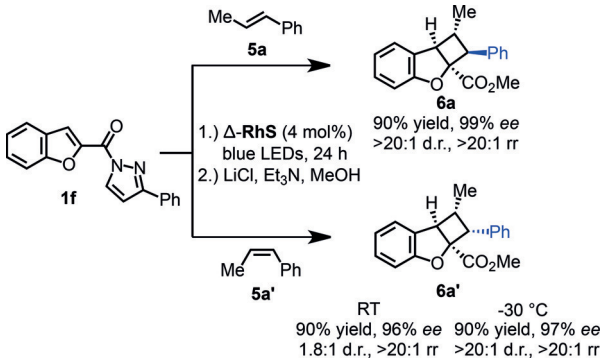


Figure 5. Asymmetric dearomatization with (*E*)- and (*Z*)-β-methylstyrene. For the reaction at −30 °C, 5 W blue LEDs were employed (see the Supporting Information for the setup) and reaction time was 60 h. The absolute configuration of a derivative of **6a** was determined by X-ray crystallography. The relative configuration of its diastereoisomer **6a′** was determined by NMR studies.

intermediate whereby the temperature affects the rotation around the single C–C bond before the radical recombination occurs, and thus conserves the memory of the radical conformation.[25]

Encouraged by these results, the substrate scope with internal *E*-configured alkenes was investigated (Figure 6). A variety of substituents at the benzene moiety of the benzofurans were well tolerated (**6b–g**) and the methyl group of (*E*)-β-methylstyrene could also be replaced by long-chain and functionalized alkyl groups without affecting the outcome (**6h,i**). All these dearomatization products were formed with high yields (80–93 %), excellent enantioselectivities (98–99 % *ee*) and virtually with complete diastereo- and regioselectivities, except for **6g** (16.7:1 d.r.). This catalytic asymmetric

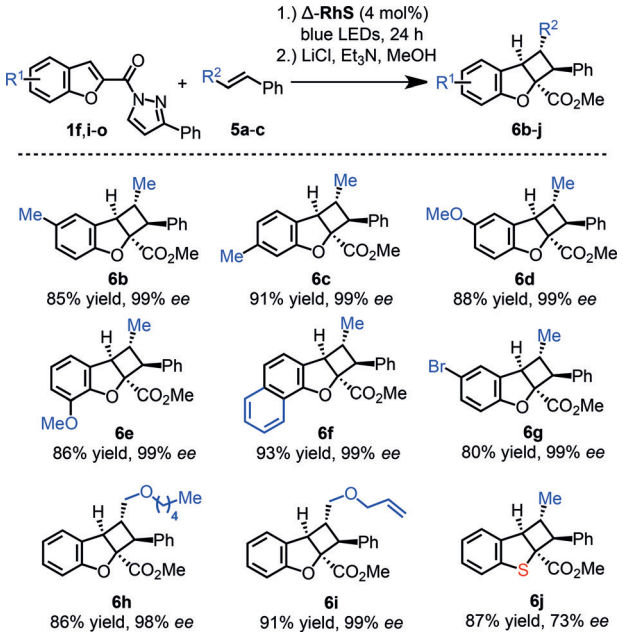


Figure 6. Substrate scope with respect to internal alkenes. The absolute configuration of a derivative of **6j** was determined by X-ray crystallography and all other compounds assigned by analogy.

dearomatization can also be applied to benzothiophene[26] to give the dearomatization product **6j** in 87 % yield with greater than 20:1 d.r. and greater than 20:1 rr, albeit with a diminished enantioselectivity (73 % *ee*).

In summary, we developed the first example of catalytic asymmetric dearomatizations by visible-light-activated [2+2] photocycloadditions and investigated the observed regioselectivity with computational molecular modeling. With internal alkene substrates, almost perfect head-to-tail regioselectivity was observed with the formation of a single diastereomer and a very high enantioselectivity for benzofuran substrates of 98–99 % *ee* to provide. The *N*-acylpyrazole moiety of the tricyclic structures with up to four stereocenters, including one quaternary stereocenter, can be easily further functionalized (see the Supporting Information for examples), thus indicating the potential synthetic value of this new methodology.[27]

Acknowledgements

Funding from the Deutsche Forschungsgemeinschaft (ME 1805/13-1) and the LOEWE Research Cluster SynChemBio of the Federal State of Hessen, Germany is gratefully acknowledged. This research was supported by the Institute for Basic Science (IBS-R10-D1) in Korea.

Conflict of interest

The authors declare no conflict of interest.

Keywords: asymmetric catalysis · cycloaddition · dearomatization · photochemistry · rhodium

How to cite: *Angew. Chem. Int. Ed.* **2018**, *57*, 6242–6246
Angew. Chem. **2018**, *130*, 6350–6354

[1] Reviews on catalytic asymmetric dearomatizations: a) C.-X. Zhuo, W. Zhang, S.-L. You, *Angew. Chem. Int. Ed.* **2012**, *51*, 12662–12686; *Angew. Chem.* **2012**, *124*, 12834–12858; b) C.-X. Zhuo, C. Zheng, S.-L. You, *Acc. Chem. Res.* **2014**, *47*, 2558–2573; c) W. Sun, G. Li, L. Hong, R. Wang, *Org. Biomol. Chem.* **2016**, *14*, 2164–2176; d) C. Zheng, S.-L. You, *Chem* **2016**, *1*, 830–857.

[2] W.-T. Wu, L. Zhang, S.-L. You, *Chem. Soc. Rev.* **2016**, *45*, 1570–1580.

[3] For a recent palladium-catalyzed asymmetric dearomative [3+2] cycloaddition with nitrobenzofurans, see: Q. Cheng, H.-J. Zhang, W.-J. Yue, S.-L. You, *Chem* **2017**, *3*, 428–436.

[4] a) J. D. Winkler, C. M. Bowen, F. Liotta, *Chem. Rev.* **1995**, *95*, 2003–2020; b) K. C. Nicolaou, S. A. Snyder, T. Montagnon, G. Vassilikogiannakis, *Angew. Chem. Int. Ed.* **2002**, *41*, 1668–1698; *Angew. Chem.* **2002**, *114*, 1742–1773.

[5] a) R. Alonso, T. Bach, *Angew. Chem. Int. Ed.* **2014**, *53*, 4368–4371; *Angew. Chem.* **2014**, *126*, 4457–4460; b) A. Tröster, R. Alonso, A. Bauer, T. Bach, *J. Am. Chem. Soc.* **2016**, *138*, 7808–7811.

[6] a) T. R. Blum, Z. D. Miller, D. M. Bates, I. A. Guzei, T. P. Yoon, *Science* **2016**, *354*, 1391–1395; b) Z. D. Miller, B. J. Lee, T. P. Yoon, *Angew. Chem. Int. Ed.* **2017**, *56*, 11891–11895; *Angew. Chem.* **2017**, *129*, 12053–12057; c) K. L. Skubi, J. B. Kidd, H.

Jung, L. A. Guzei, M.-H. Baik, T. P. Yoon, *J. Am. Chem. Soc.* **2017**, *139*, 17186 – 17192.
[7] X. Huang, T. R. Quinn, K. Harms, R. D. Webster, L. Zhang, O. Wiest, E. Meggers, *J. Am. Chem. Soc.* **2017**, *139*, 9120 – 9123.
[8] F. Müller, J. Mattay, *Chem. Rev.* **1993**, *93*, 99 – 117.
[9] a) Y. Xu, M. L. Conner, M. K. Brown, *Angew. Chem. Int. Ed.* **2015**, *54*, 11918 – 11928; *Angew. Chem.* **2015**, *127*, 12086 – 12097; b) S. Poplata, A. Tröster, Y.-Q. Zou, T. Bach, *Chem. Rev.* **2016**, *116*, 9748 – 9815.
[10] a) J. Mattay, *Synthesis* **1989**, 233 – 252; b) G. Pandey, *Top. Curr. Chem.* **1993**, *168*, 175 – 221; c) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322 – 5363.
[11] S. E. Reisman, M. E. Kieffer, H. Wang, *Asymmetric Dearomatization Reactions* (Ed.: S.-L. You), Wiley-VCH, Weinhiem, **2016**, p. 153 – 174.
[12] J. J. McCullough, *Chem. Rev.* **1987**, *87*, 811 – 860.
[13] For [2+2] photocycloadditions with benzofurans, see: a) C. H. Krauch, W. Metzner, G. O. Schenck, *Chem. Ber.* **1966**, *99*, 1723 – 1731; b) C. H. Krauch, S. Farid, *Chem. Ber.* **1967**, *100*, 1685 – 1695; c) K. Takamatsu, H.-S. Ryang, H. Sakurai, *J. Chem. Soc. Chem. Commun.* **1973**, 903 – 904; d) A. H. A. Tinnemans, D. C. Neckers, *J. Org. Chem.* **1977**, *42*, 2374 – 2377; e) J. H. M. Hill, S. T. Reid, *J. Chem. Soc. Chem. Commun.* **1983**, 501 – 502; f) M. Sakamoto, A. Kinbara, T. Yagi, T. Mino, K. Yamaguchi, T. Fujita, *Chem. Commun.* **2000**, 1201 – 1202; g) R. Sakamoto, T. Inada, S. Sakurai, K. Maruoka, *Org. Lett.* **2016**, *18*, 6252 – 6255.
[14] a) C. Wang, L.-A. Chen, H. Huo, X. Shen, K. Harms, L. Gong, E. Meggers, *Chem. Sci.* **2015**, *6*, 1094 – 1100; b) J. Ma, X. Shen, K. Harms, E. Meggers, *Dalton Trans.* **2016**, *45*, 8320 – 8323; c) J. Ma, X. Zhang, X. Huang, S. Luo, E. Meggers, *Nat. Protoc.* **2018**, *13*, 605 – 632.
[15] L. Zhang, E. Meggers, *Acc. Chem. Res.* **2017**, *50*, 320 – 330.
[16] For a novel design of a chiral-at-metal rhodium catalyst, see also: M. Carmona, R. Rodríguez, V. Passarelli, F. J. Lahoz, P. García-Orduña, D. Carmona, *J. Am. Chem. Soc.* **2018**, *140*, 912 – 915.
[17] H. Huo, X. Shen, C. Wang, L. Zhang, P. Röse, L.-A. Chen, K. Harms, M. Marsch, G. Hilt, E. Meggers, *Nature* **2014**, *515*, 100 – 103.
[18] X. Huang, X. Li, X. Xie, K. Harms, R. Riedel, E. Meggers, *Nat. Commun.* **2017**, *8*, 2245.
[19] S. Wilsey, L. González, M. A. Robb, K. N. Houk, *J. Am. Chem. Soc.* **2000**, *122*, 5866 – 5876.
[20] For computational studies, see: a) B. Tutkowski, E. Meggers, O. Wiest, *J. Am. Chem. Soc.* **2017**, *139*, 8062 – 8065; b) S. Chen, X. Huang, E. Meggers, K. N. Houk, *J. Am. Chem. Soc.* **2017**, *139*, 17902 – 17907; c) V. M. Fernandez-Alvarez, F. Maseras, *Org. Biomol. Chem.* **2017**, *15*, 8641 – 8647.
[21] D. I. Schuster, G. Lem, N. A. Kaprinidis, *Chem. Rev.* **1993**, *93*, 3 – 22.
[22] a) D. Andrew, D. J. Hastings, A. C. Weedon, *J. Am. Chem. Soc.* **1994**, *116*, 10870 – 10882; b) D. Andrew, A. C. Weedon, *J. Am. Chem. Soc.* **1995**, *117*, 5647 – 5663.
[23] For selected computational studies on the regioselectivity of [2+2] photocycloadditions between enones and substituted alkenes, see: a) J. L. Broeker, J. E. Eksterowicz, A. J. Belk, K. N. Houk, *J. Am. Chem. Soc.* **1995**, *117*, 1847 – 1848; b) E. García-Expósito, Á. Álvarez-Larena, V. Branchadell, R. M. Ortuño, *J. Org. Chem.* **2004**, *69*, 1120 – 1125; c) O. Yuka, S. Tetsuro, H. Kenji, S. Kenichi, *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1209 – 1215; d) F. De Proft, S. Fias, C. Van Alsenoy, P. Geerlings, *J. Phys. Chem. A* **2005**, *109*, 6335 – 6343; e) P. Jaque, A. Toro-Labbé, P. Geerlings, F. De Proft, *J. Phys. Chem. A* **2009**, *113*, 332 – 344.
[24] a) H. Zipse, *Top. Curr. Chem.* **2006**, *263*, 163 – 189; b) J. Hioe, H. Zipse, *Org. Biomol. Chem.* **2010**, *8*, 3609 – 3617.
[25] For conformational memory effects in 1,4-biradicals, see: A. G. Griesbeck, H. Mauder, S. Stadtmüller, *Acc. Chem. Res.* **1994**, *27*, 70 – 75.
[26] For [2+2] photocycloadditions with benzothiophenes, see: a) A. H. A. Tinnemans, D. C. Neckers, *J. Org. Chem.* **1978**, *43*, 2493 – 2500; b) D. Döpp, A. A. Hassan, G. Henkel, *Liebigs Ann.* **1996**, 697 – 700; c) B. Wex, B. R. Kaafarani, A. G. Oliver, J. A. Krause Bauer, D. C. Neckers, *J. Org. Chem.* **2003**, *68*, 8258 – 8260; d) M. Akita, S. - *y.* Mohri, M. Takahashi, K. Kobayashi, *Heterocycles* **2013**, 87, 1319 – 1326.
[27] The reaction can be scaled up to 1 mmol scale without a significant change in performance as demonstrated for the conversion **1f** + **5a** → **6a** (see the Supporting Information for details).

Manuscript received: March 9, 2018
Accepted manuscript online: April 6, 2018
Version of record online: April 2018, 27

