Regio- and Stereoselective Electrochemical Alkylation of Morita–Baylis–Hillman Adducts

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ABSTRACT: Electrosynthesis is effectively employed in a general regio- and stereoselective alkylation of Morita–Baylis–Hillman compounds. The exposition of N-acyloxyphthalimides (redox-active esters) to galvanostatic electroreductive conditions, following the sacrificial-anode strategy, is proved an efficient and practical method to access densely functionalized cinnamate and oxindole derivatives. High yields (up to 80%) and wide functional group tolerance characterized the methodology. A tentative mechanistic sketch is proposed based on dedicated control experiments.

Morita–Baylis–Hillman (MBH) adducts (1) are arguably referred to as “privileged scaffolds” within the synthetic community, due to their ease of preparation, ready diversification and faceted reactivity. In recent years, S$_2$ or S$_2$' substitution reactions on MBH compounds has faced high interest with a variety of ionic-based nucleophiles, as well as their transformation in reactive dipolar species. These led to the development of a large number of uncatalyzed or Lewis-based catalyzed protocols, targeting, among others, functionalized methacrylates, cinnamates, azine heterocycles, and indole derivatives. On the contrary, the rapidly expanding radical chemistry scenario has scarcely permeated the functionalization of MBH adducts. Here, some elegant examples have recently been disclosed under metal- or photocatalytic regimes with a focus on specific classes of stabilized alkyl radicals (Scheme 1a). Protocols displaying a wide scope of simple and functionalized radicals are much more narrow in number, with notable shortcomings related to the employment of stoichiometric organic reductants or poor stereochemical outcomes.

Our current research interest toward the implementation of site-selective radical-based transformations prompted us to envision eChem as a valuable direct toolbox for the functionalization of MBH adducts 1 with “green electrons.”

To realize such a strategy, we deemed a general, cheap, easy to prepare, and broadly applicable class of radical precursors to be necessarily employed. N-Acloyxyphthalimides (redox-active esters, RAE, 2), prepared in one step from inexpensive N-hydroxyphthalimide and ubiquitous carboxylic acids, represent a class of benchmark radical precursors. RAEs have been extensively employed in metal- or photoassisted and (to a lower extent) electrochemical generation of radicals under reductive conditions. Among others, C–H functionalizations and cross-coupling processes were primary targeted, whereas

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Scheme 1. Previous Methodologies for the Radical Alkylation of MBH Acetates and Present eChem Protocol

“NPhth: phthalimide.”
the use of RAEs on eChem derivatizations of olefins have faced less attention. In particular, the condensation of RAEs 2 and MBH acetates 1 is unprecedented (Scheme 1b), posing some important questions toward the overall chemo- and regioselectivity of the process. In this report, we disclose a highly stereoselective (the E-isomers were exclusively isolated), electroreductive strategy for the regioselective $S_2^2$ radical alkylation of MBH adducts 1 with RAEs 2. The protocol targets the formation of $\alpha$-substituted $\alpha\beta$-unsaturated esters or ketones 3, under mild and organic reductant-free conditions. It is worth mentioning that alternative synthetic methodologies for the installation of alkyl (i.e., methyl) groups at the $\beta$-position of the MBH acceptors requires the utilization of harmful organometallic reagents such as trialkyl-Al and trialkyl-Ln compounds. Our investigation started by subjecting MBH acetate 1a and RAE 2a (1 equiv) to a constant current electrolysis of 10 mA. A graphite (C) cathode and a Zn sacrificial anode were used as electrodes with tetraethylammonium tetrafluoroborate (TEABF$_4$, 1 equiv) as the supporting electrolyte in DMF (Table 1, entry 1). Encouragingly, the desired product 3aa was always found to be >20:1.

| entry | electrolyte (equiv) | anode (+) cathode (-) | $i$ (mA) | yield (%) |
|-------|---------------------|-----------------------|---------|-----------|
| 1'    | TEABF$_4$ (1)       | Zn(+)C(−)             | 10      | 25        |
| 2'    | TEABF$_4$ (2)       | Zn(+)C(−)             | 10      | 38        |
| 3'    | TEABF$_4$ (2)       | Zn(+)C(−)             | 10      | 59        |
| 4'    | TEABF$_4$ (2)       | Zn(+)C(−)             | 4       | 67        |
| 5'    | TEABF$_4$ (2)       | Zn(+)C(−)             | 2       | 79        |
| 6'    | TEABF$_4$ (2)       | Zn(+)C(−)             | 4       | 65        |
| 7'    | LiBF$_4$ (2)        | Zn(+)C(−)             | 4       | 66        |
| 8'    | TEABF$_4$ (2)       | Zn(+)RVC(−)           | 4       | 65        |
| 9'    | TEABF$_4$ (2)       | Zn(+)Ni$^{2+}$ (−)    | 4       | 54        |
| 10'   | TEABF$_4$ (2)       | Mg(+)C(−)             | 4       | 54        |
| 11'   | TEABF$_4$ (2)       | Ni(+)C(−)             | 4       | 50        |
| 12'   | TEABF$_4$ (2)       | C(+)C(−)              | 4       | 34        |

*Reaction conditions, unless otherwise noted: 1a (0.15 mmol), 2a (0.30 mmol), electrolyte (0.15 or 0.30 mmol), dry DMF (3 mL), CCE (10, 4, or 2 mA; 2 F/mol$_{\text{RAE}}$), rt. $E/Z$ ratios were determined via $^1$H NMR spectroscopy on the reaction crude mixtures and were always found to be >20:1. Isolated yields after flash chromatography.

Isolated in 25% yield as a single E isomer, along with 5% of the reduction–deacetylation product 1a'. Exclusive $S_2^2$ radical trapping was recorded, and no over-reduced product 3aa' was detected. The high $E$ selectivity of cinnamates 3 means the present eChem approach is a desirable and complementary alternative to the poorly stereoselective photocatalytic strategy, aiming at similar tasks (vide infra). Moreover, the use of a nontoxic and inexpensive sacrificial anode (Zn) circumvents the use of organic reductants whose cost and separation from the reaction mixture might be burdensome.

In order to optimize the reaction conditions, the equivalents of both the electrolyte (2 equiv, entry 2, 38% yield) and of 2a (2 equiv, entry 3, 59% yield) were beneficially increased. Next, we reasoned that a slower generation of the radical species, as the result of a lower current, could be beneficial in avoiding radical–radical homocoupling and other undesired side reactions. Interestingly, by lowering the current value from 10 to 4 mA (entry 4, 67% yield) and further to 2 mA (entry 5, 79% yield) a significant increase in reaction efficiency was recorded (with 2 mA current, the formation of 1a was completely suppressed). On the other hand, salts such as tetrabutylammonium hexafluorophosphate (TBAPF$_6$, entry 6) and LiBF$_4$ (entry 7) behaved similarly to TEABF$_4$. Cathodes different from graphite, such as RVC (reticulated vitreous carbon, entry 8) and Ni foam (entry 9), and sacrificial anodes such as Mg and Ni (entries 10 and 11), delivered 3aa in comparable or lower yields with respect to the optimal set (entry 5). To demonstrate the superiority of the strategy based on the sacrificial anode, an attempt using Hantzsch ester 4 as the terminal reductant and two graphite (C) electrodes was performed (entry 12). Here, product 3a was isolated in low yield (34%) along with 22% of reduced byproduct 1a'.

Having established the optimal reaction conditions (Table 1, entry 5), the generality of the electrochemical alkylation was tested (Scheme 2) on different MBH acetates (or carbonates) 1 (or 5). Cinnamates 3, having both electron-withdrawing ($3b$–$3d$, $3g$) and electron-donating ($3e$, $3f$) substituents at the para or ortho position of the benzene ring, were productively formed (61–77% yield). Naphthalene (1h) and heteroarenes (thiophene 1i and quinoline 1j) on the MBH acceptor were also well tolerated, although in the case of 1j a complete reduction of the C–C double bond occurred, resulting in saturated compound 3ja' as the sole product (64%). Pleasingly, MBH acetate 1k, derived from an aliphatic aldehyde (i.e., hydrocinnamaldehyde) was proved to be productive ($3k$, 62% yield) and product 3ia, having a conjugated diene moiety, could also be formed in synthetically useful 57% yield. It is worth mentioning that radical-sensitive moieties such as benzylic (1m) and propargylic esters (1n) were adequately tolerated in the present eChem alkylation process (yield: 76% and 74%, respectively). Finally, the protocol was not limited to ester-like MBH adducts; as a matter of fact, when methyl ketone 1o was subjected to the optimal conditions the desired $\alpha$-alkylated enone 3oa was isolated in synthetically useful amounts (76% yield).

Additionally, the electrochemical alkylation protocol was extended to MBH carbonates derived from N-methylsuccinimides (5a,b) in the presence of RAEs 2a and 2c. Delightfully, the corresponding oxindoles 6 were isolated with high diastereoselectivity (>20:1) and useful yields (51–66%) as a result of an alkylation–reduction sequence. To the best of our knowledge, this protocol represents the first example of $S_2^2$-type radical alkylations of oxindole-based MBH acceptors. The exclusive isolation of the fully reduced compounds 6 and 3ja' might be rationalized in term of lower reduction potential of $\alpha\beta$-unsaturated esters featuring conjugated highly electron-deficient moieties. Over-reductive SET processes and hydrogen abstraction of the resulting radical anions could lead to “zinc-enolate” intermediates that will smoothly undergo protonation during the aqueous reaction quenching.
Next, we examined the adaptability of the disclosed strategy to different radical precursors. Methyl (2b), primary (2c), secondary (2d and 2f), and tertiary (2e) alkyl radicals were all installed regio- and stereoselectively at MBH acetate 1a, highlighting the generality of the methodology (3ab−af, 49−80% yield). As a rule of thumb, the higher the substitution (hence, the stability) of the radical the higher the yield observed. Tolerance toward an unprotected indole group was also ascertained (3ag, 61% yield). Pleasingly, amino acid derived RAEs (Boc-Ala) and (Boc-Pro) as well as dehydrocholic acid derived 2j generated competent alkyl radicals for the alkylation of 1a (3ah-aj, 66−75% yield). This demonstrates the possibility to employ naturally occurring acids as precursors of functionalized radicals as well as developing bioconjugation protocols via a late-stage eChem approach. The millimole scale reaction on the model substrates 1a and 2a was also effectively carried out, delivering the desired 3aa in 83% isolated yield.

To gain mechanistic insights into the formation of byproduct 1a', voltammetric experiments on 1a were then carried out (see the Supporting Information). Unfortunately, no clear evidence for a reductive event was recorded, suggesting that 1a' could result from successive reactive steps. However, a control experiment run on 1a in the absence of 2a (optimal reaction conditions) furnished 1a' in 18% yield, along with poor recovery of unreacted 1a (34%, decomposition to unidentified byproducts, Scheme 3a). This result rules out an exclusive RAE-mediated formation of 1' from 1 and proves MBH acceptors 1 are not inert toward reductive conditions, rendering a judicious choice of the reaction parameters pivotal for their productive employment in electroreductive processes.

Finally, our attention was caught by the stereochemical discrepancy between our protocol (E/Z > 20:1) and previously reported photochemical radical alkylations of MBH derivatives.
To prove a possible photomediated isomerization of the final cinnamyl C–C double bond, we subjected (E)-3aa (E/Z > 20:1) to visible-light irradiation in the presence of a common triplet-emitter Ir-based photosensitizer [Ir(dF(CF3)ppy)2(dtbbpy)]PF6 (1 mol %, Scheme 3b). Interestingly, 3aa was recovered in 95% yield as a 1:1.7 E/Z mixture, showing the intrinsic unsuitability of some photocatalytic methodologies aiming at the stereoselective formation of α-substituted cinnamates.19

Mechanistically, the eChem cycle depicted in Scheme 4 is tentatively proposed. This starts with the cathodic fragmenta-

![Diagram of proposed mechanistic profile](image_url)

**Scheme 4. Proposed Mechanistic Profile**

- **Path a**: Formation of CO2 phthalimide anion, and the desired cyclohexyl radical. This event is in accordance with cyclo-
- **Path b**: Voltagmetry experiments run on 2a, showing a clear irreversible cathodic event at −1.57 V vs ferrocene (−1.15 V vs Ag/AgCl). The possible involvement of the MBH adduct into cathodic reduction was judged unlikely due to the absence of reductive signals on the collected voltametric spectra in the same reductive windows of 2a (see the Supporting Information).

In conclusion, we have developed a novel photoelectrochemical alklylation of MBH adducts with redox-active esters as radical precursors. Under galvanostatic conditions and employing a sacrificial anode, a wide range of α-substituted α,β-unsaturated esters or ketones were formed chemo- and stereoselectively (E/Z ratio >20:1). Extension of the protocol to iatin-derived MBH carbonates resulted in the formation of substituted oxindoles following an alkylation—reduction sequence. Control experiments and mechanistic proposals completed the present investigation.

**ASSOCIATED CONTENT**

**Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.2c01529.

Additional screening of reaction conditions, detailed experimental procedures, characterization data, CV experiments and NMR spectra (PDF)

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**Notes**

The authors declare no competing financial interest.

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**REFERENCES**

1. (a) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. Recent Advances in the Baylis–Hillman Reaction and Applications. Chem. Rev. 2003, 103, 811–892. (b) Masson, G.; Housseman, C.; Zhu, J. The Enantioselective Morita–Baylis–Hillman Reaction and Its Aza Counterpart. Angew. Chem., Int. Ed. 2007, 46, 4614–4628. (c) Basavaiah, D.; Reddy, B. S.; Badsara, S. S. Recent Contributions from the Baylis–Hillman Reaction to Organic Chemistry. Chem. Rev. 2010, 110, 5447–5674.

2. (a) For selected reviews, see: Liu, T. Y.; Xie, M.; Chen, Y.-C. Organocatalytic asymmetric transformations of modified Morita–Baylis–Hillman adducts. Chem. Soc. Rev. 2012, 41, 4101–4112. (b) Basavaiah, D.; Naganaboina, R. T. The Baylis–Hillman reaction: a new continent in organic chemistry – our philosophy, vision and over three decades of research. New J. Chem. 2018, 42, 14036–14066. (c) List, B.; Grossman, O. The Morita-Baylis-Hillman reaction. Synfacts 2019, 15, 295. (d) Calcatelli, A.; Cherubini-Cella, A.; Carletti, E.; Company, X. Unconventional Transformations of Morita–Baylis–Hillman Adducts. Synthesis 2020, 52, 2922–2939.

3. (a) Zhong, N.-J.; Wang, Y.-Z.; Cheng, L.; Wang, D.; Liu, L. Recent advances in the annulation of Morita–Baylis–Hillman adducts. Org. Biomol. Chem. 2018, 16, 5214–5227. (b) Jia, R.-L.; Liu, Q.-L.; Yang, L.-W.; Deng, S.; Song, Y. [6 + 3] Annulations of Morita–Baylis–Hillman carbonates and dicyanoheptafulvene. Org. Biomol. Chem. 2021, 19, 9867–9871.
(4) Kaye, P. T. Applications of the Morita–Baylis–Hillman reaction in the synthesis of heterocyclic systems. *Adv. Heterocycl. Chem.* 2019, 127, 101–152.

(5) For a selection of S₄,2-type metal and photocatalyzed radical additions, see: (a) Paria, S.; Carletti, E.; Marcon, M.; Cherubini-Celli, A.; Mazzanti, A.; Rancan, M.; Dell’Amico, L.; Bonchi, M.; Companyó, X. Light-triggered catalytic asymmetric allylic benzylation with photogenerated C-nucleophiles. *J. Org. Chem.* 2020, 85, 4463–4474.

(6) (a) Yadav, A. K.; Sharma, A. K.; Singh, K. N. Visible light enabled trichloromethylation of Baylis–Hillman acetates: stereo-selective synthesis of trisubstituted alkenes. *Org. Chem. Front.* 2019, 6, 989–993. (b) Dai, X.; Cheng, D.; Guan, B.; Mao, W.; Xu, X.; Li, X. The Coupling of Tertiary Amines with Acrylate Derivatives via Visible-Light Photoredox Catalysis. *J. Org. Chem.* 2014, 79, 7212–7219.

(7) (a) Ye, H.; Ye, Q.; Cheng, D.; Li, X.; Xu, X. The coupling reaction of α-silylaminos with Baylis-Hillman adducts by visible light photoredox catalysis. *Tetrahedron Lett.* 2021, 65, 152746. (b) Lebagy, C.; De Schutter, C.; Legay, R.; Pfund, E.; Lequeux, V. Radical Allylation: E-Selective Radical Conjugate Addition—Elimination Reaction from Morita–Baylis–Hillman Adducts. *Synlett* 2018, 46–50. (c) Mandal, S. K.; Paria, M.; Roy, S. C. Titanocene(III) Chloride Mediated Radical-Induced addition to Baylis-Hillman adducts: synthesis of (E)- and (Z)-Trisubstituted alkenes and p-Methylene/Arylidene β-Lactones. *J. Org. Chem.* 2008, 73, 3832–3837.

(8) (a) Ye, H.; Ye, Q.; Cheng, D.; Li, X.; Xu, X. The coupling of potassium organotrifluoroborates with Baylis-Hillman derivatives via visible-light photoredox catalysis. *Tetrahedron Lett.* 2018, 59, 2046–2049. (b) Ye, H.; Zhao, H.; Ren, S.; Ye, H.; Cheng, D.; Li, X.; Xu, X. The coupling of alkylboronic acids and esters with Baylis–Hillman derivatives by Lewis base/photoredox dual catalysis. *Tetrahedron Lett.* 2019, 60, 1302–1305.

(9) (a) Liu, Y.; Battaglioni, S.; Lombardi, L.; Menichetti, A.; Valenti, G.; Montalit, M.; Bandini, M. Visible-Light Photoredox Catalyzed Dehydrogenative Synthesis of Aliphatic Carboxylates from Styrenes. *Org. Lett.* 2021, 23, 4441–4446. (b) Battaglioni, S.; Bertuzzi, G.; Pedrazzani, R.; Benetti, J.; Valenti, G.; Montalit, M.; Monari, M.; Bandini, M. Visible-Light-Assisted Synthesis of Aliphatic Trifluoromethylation via Dual Acrinum/Co Catalysis. *Adv. Synth. Catal.* 2022, 364, 720–725. (c) Lombardi, L.; KovaÁın, A.; Mantovani, S.; Bertuzzi, G.; Favaretto, L.; Bettini, C.; Palermo, V.; Melucci, M.; Bandini, M. Visible-light assisted covalent surface functionalization of reduced graphene oxide nanosheets with alyl azene sulfones. *Chem.—Eur. J.* 2022, No. e202200333.

(10) (a) Horn, E. J.; Rosen, B. R.; Baran, P. S. Synthetic Organic Electrochemistry: An Enabling and Innately Sustainable Method. *ACS Cent. Sci.* 2016, 2, 302–308. (b) Yan, M.; Kawamata, Y.; Baran, P. S. Synthetic organic electrochemical methods since 2000: on the verge of a renaissance. *Chem. Rev.* 2017, 117, 13230–13319. (c) Wiebe, A.; Gieshoff, T.; Mühle, S.; Rodrigo, E.; Zirbes, M.; Waldvogel, S. R. Electrifying organic synthesis. *Angew. Chem., Int. Ed.* 2018, 57, 5949–5961. (d) Kingston, C.; Palkowitz, M. D.; Takahira, Y.; Vantourout, J. C.; Peters, B. Y.; Kawamata, Y.; Baran, P. S. A Survival Guide for the “Electro-curious.” *Acc. Chem. Res.* 2020, 53, 72–83. (e) Skatisky, A.; Lundberg, H.; KärkiÁ, M. D. Organic electrolysisc: applications in complex molecule synthesis. *ChemElectroChem.* 2019, 6, 4067–4092.

(11) (a) Rafiee, M.; Mayer, M. N.; Punchihewa, B. T.; MumaÁ, M. R. Constant potential and constant current electrolysis: an introduction and comparison of different techniques for organic electrochemistry. *J. Org. Chem.* 2021, 86, 15866–15874. (b) McKenzie, E. C. R.; Hosseini, S. C. T.; Couto Petro, A. G.; Rudman, K. K.; G erroll, B. H. R.; Mubarak, M. S.; Baker, L. A.; Little, R. D. Versatile tools for understanding electrosynthetic mechanisms. *Chem. Rev.* 2022, 122, 3292–3353.

(12) (a) For metal-catalyzed relevant examples, see: Qian, T.; Cornella, J.; Li, C.; Malins, L. R.; Edwards, J. T.; Kawamata, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S. A general alkyl-allyl cross-coupling enabled by redox-active esters and alkylene reagents. *Science* 2016, 352, 801–805. (b) Huihui, K. M. M.; Caputo, J. A.; Melchor, Z.; Olivas, A. M.; Spiewak, A. M.; Johnson, K. A.; DiBenedetto, T. A.; Kim, S.; Ackerman, L. K. G.; Weix, D. J. Decarboxylative cross-electrophile coupling of N-hydroxyphthalimide esters with aryliodides. *J. Am. Chem. Soc.* 2016, 138, 5016–5019.

(13) (a) Lu, J.; Wang, Y.; McCallum, T.; Fu, N. Harnessing Radical Chemistry via Electrochemical Transition Metal Catalysis. *Science* 2020, 373, 101796.

(14) (a) For a selection of examples, see: Li, H.; Breen, C. P.; Seo, H.; Jamison, T. F.; Fang, Y. Q.; Bio, M. M. Ni-Catalyzed electrochemical decarboxylative C–C coupling in batch and continuous flow. *Org. Lett.* 2018, 20, 1338–1341. (b) Liu, Y.; Xue, L.; Shi, B.; Bu, F.; Wang, D.; Lu, L.; Shi, R.; Le, A. Catalyst-free electrochemical decarboxylative cross-coupling of N-hydroxphthalimide esters with bromoalkenes. *Angew. Chem., Int. Ed.* 2017, 56, 11901–11905. (c) Lu, X.-G.; Zhou, C.-J.; Lin, E.; Han, X.-L.; Zhang, S.-S.; Li, Q.; Wang, H. Decarboxylative Negishi coupling of redox-active aliphatic esters by cobalt catalysis. *Angew. Chem., Int. Ed.* 2018, 57, 13096–13100 For photocatalyzed relevant examples, see: (f) Okada, K.; Okamoto, K.; Morita, N.; Okubo, K.; Oda, M. Photosensitized decarboxylative Michael addition through N-(acyl)phthalimides via an electron-transfer mechanism. *J. Am. Chem. Soc.* 1991, 113, 9401–9402. (g) Cheng, W.-M.; Shang, R.; Fu, Y. Photoredox/Bronsted Acid Co-Catalysis enabling decarboxylative coupling of amino acid and peptide redox-active esters with N-heteroarenes. *ACS Catal.* 2017, 7, 907–911. (h) Mao, R.; Frey, A.; Balon, J.; Hu, X. Decarboxylative C(sp³)−N cross-coupling via synergetic photoredox and copper catalysis. *Nat. Catal.* 2018, 1, 120–126.

(15) (a) Chen, X.; Luo, X.; Peng, X.; Guo, J.; Zai, J.; Wang, P. Catalyst-free decarboxylation of carboxylic acids and deoxygenation of...
alcohols by electro-induced radical formation. Chem.—Eur. J. 2020, 26, 3226−3230. (b) Claraz, A.; Allain, C.; Masson, G. Electro-reductive cross-coupling of trifluoromethyl alkenes and redox active esters for the synthesis of gem-difluoroalkenes. Chem.—Eur. J. 2022, 28, No. e202103337.

(16) (a) Ranu, B. C.; Chattopadhyay, K.; Jana, R. Chemo-, regio- and stereoselective addition of triorganoindium reagents to acetates of Baylis−Hillman adducts: a new strategy for the synthesis of (E)- and (Z)-trisubstituted alkenes. Tetrahedron Lett. 2007, 48, 3847−3850. (b) Novak, A.; Calhorda, M. J.; Costa, P. J.; Woodward, S. Mapping the mechanism of nickel-ferrophite catalysed methylation of Baylis−Hillman-derived S2O2Cl2 electrophiles. Eur. J. Org. Chem. 2009, 2009, 898−903.

(17) eChem experiments were carried out on a commercially available ElectraSyn 2.0 (undivided cell).

(18) (a) For selected reviews comparing photo- and electrochemical protocols, see: Verschueren, R. H.; De Borggraeve, W. M. Electrochemistry and photoredox catalysis: a comparative Evaluation in Organic synthesis. Molecules 2019, 24, 2122. (b) Liu, J.; Lu, L.; Wood, D.; Lin, S. New redox strategies in organic synthesis by means of electrochemistry and photochemistry. ACS Scent. Sci. 2020, 6, 1317−1340. (c) Tay, N. E. S.; Lehnher, D.; Rovis, T. Photons or electrons? A critical comparison of electrochemistry and photoredox catalysis for organic synthesis. Chem. Rev. 2022, 122, 2487−2649.

(19) Corpas, J.; Mauleón, P.; Arrayás, R. G.; Carretero, J. C. E/Z Photoisomerization of Olefins as an emergent strategy for the control of stereodivergence in catalysis. Adv. Synth. Catal. 2022, 364, 1348−1370.