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Photocatalytic *S*-alkylation of sulfinamides: access to sulfoximines

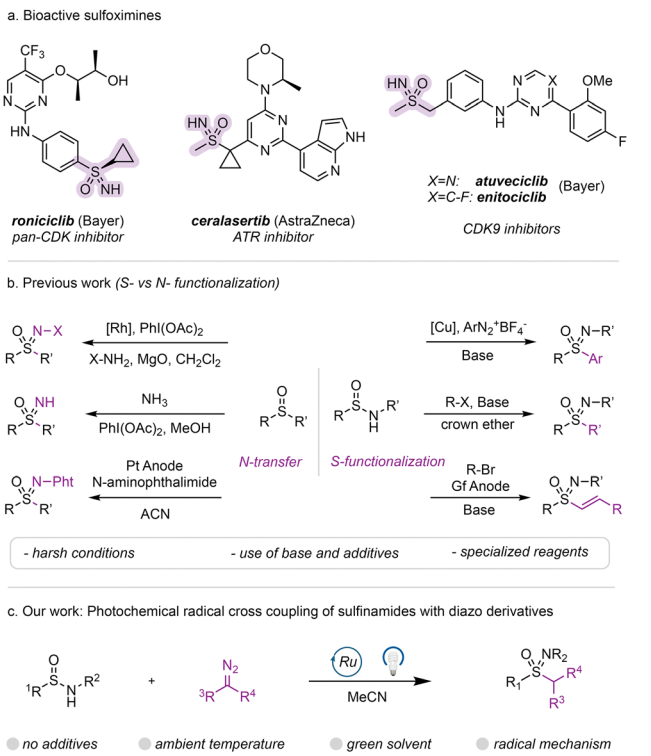
Ivan Sliusarevskyi,[a] Haripriyo Mondal[b] and Rene M. Koenigs *[ab]

We report a Ru-photocatalyzed *S*-alkylation of sulfinamides using diazo compounds under blue light. The reaction proceeds with high *S*/*N* selectivity, broad substrate scope, and mild conditions, furnishing sulfoximines that can be diversified through downstream chemical transformations.

Sulfoximines have emerged as valuable structural motifs in organic and medicinal chemistry due to their unique stereoelectronic features, including a stereogenic sulfur center and a compact, hydrophilic architecture.[1] These have found extensive applications in organic chemistry, as key intermediates, chiral auxiliaries, directing groups, and ligands in transition-metal catalysis, and additionally have notable applications in agrochemistry.[2] Furthermore, they have recently emerged as noteworthy structures in medicinal chemistry[3] since the discovery of BAY 1000394 (Scheme 1a), a sulfoximine-derived pan-CDK inhibitor developed by Bayer.[4] Given their broad utility, the development of efficient, practical, and sustainable synthetic routes to sulfoximines remains a compelling research objective.

Two general strategies are commonly employed for sulfoximine synthesis (Scheme 1b): (i) nitrogen transfer to sulfoxides followed by *N*-functionalization, and (ii) direct *S*-functionalization of sulfinamides.[5,6] Although the *N*-transfer strategy is operationally straightforward, it typically affords only unprotected N–H sulfoximines, or protected sulfoximines, thus requiring additional steps for *N*-functionalization, *e.g. via N*-alkylation or *N*-arylation reactions.[1i,7] In contrast, direct *S*-alkylation of sulfinamides represents a conceptually attractive alternative, providing direct access to fully substituted sulfoximines *via* C–S bond formation. However, achieving high *S*-selectivity remains challenging, as the sulfinamide nitrogen is generally more nucleophilic than sulfur, often leading to competing *N*-alkylation or over-alkylation.[8] Recent advances by Bolm,[6c–e] Maruoka,[6b,g] and Koenigs[9] have demonstrated that careful control of the *N*-protecting group can enable *S*-selective transformations, yet these approaches often require specialized reagents, stoichiometric oxidants, or sensitive organometallic intermediates, limiting their generality and practicality.[1i,10]

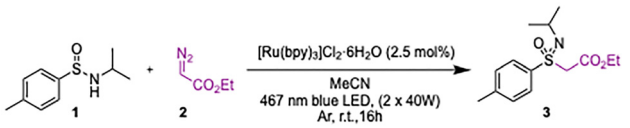
To address these limitations, we envisioned a visible-light-mediated approach to promote *S*-alkylation under mild and redox-neutral conditions (Scheme 1c). Photocatalytic activation of diazo compounds has recently emerged as a powerful strategy for generating reactive carbene or radical species capable of engaging in diverse C–H, C–C, and heteroatom functionalizations.[11,12]



Scheme 1 Sulfoximines in drugs, synthesis and *S*-alkylation reactions.

[a] *RWTH Aachen University, Institute of Organic Chemistry, Landoltweg 1, 52074, Aachen, Germany. E-mail: rene.koenigs@uni-bayreuth.de*
[b] *University of Bayreuth, Organic Chemistry II, Universitätsstraße 30, 95447, Bayreuth, Germany*

Table 1 Optimization of the reaction conditions[a]



Entry	Deviation from standard conditions	Yield[a] of **3a**
1	None	96 (92)[b]
2	Without light	Traces
3	Without photocatalyst	Traces
4	In a 370 nm purple LED	21
5	In air	24
6	Addition of 2 equiv. H_2O	27

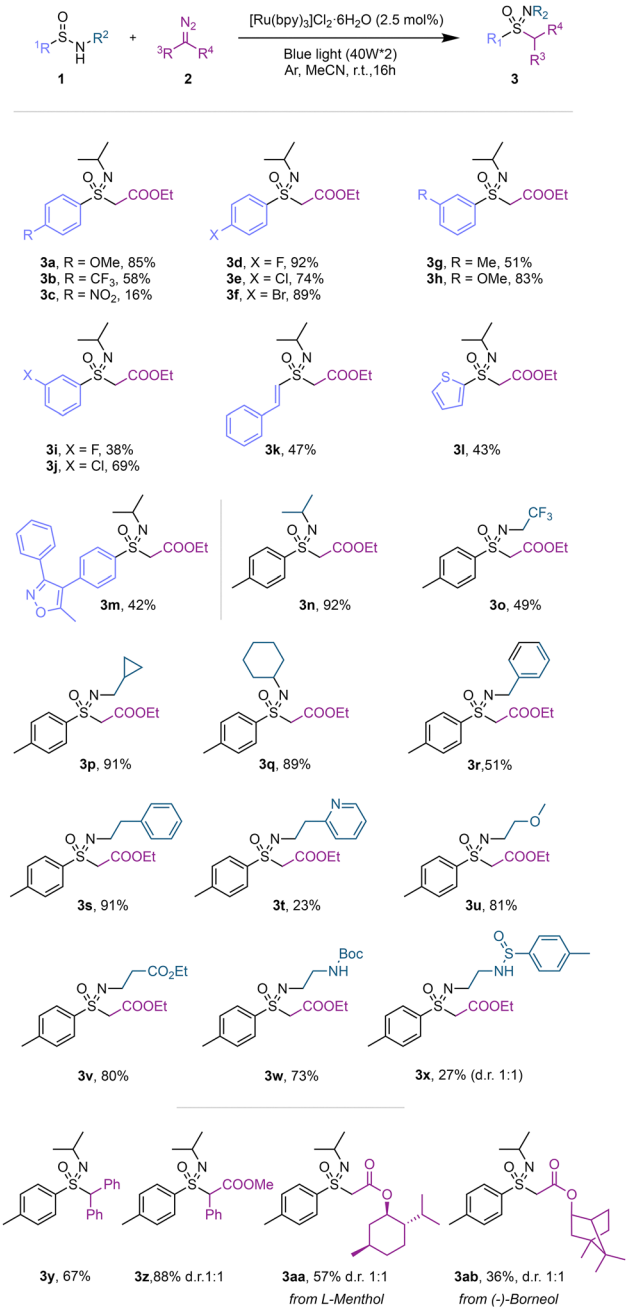
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (6.0 equiv.) and $[Ru(bpy)_3]Cl_2 \cdot 6H_2O$ (2.5 mol%) in MeCN (2.0 mL) under argon. ^1H NMR yields were calculated using 1,3,5-trimethoxybenzene as an internal standard. [b] Isolated yield.

Despite these advances, photocatalytic *S*-alkylation of sulfinamides using diazo compounds has not been reported. Herein, we disclose a photocatalytic *S*-alkylation reaction of sulfinamides with diazo compounds to access sulfoximines. The transformation proceeds with high *S*/*N* selectivity, and excellent functional-group tolerance, without requiring additives, bases, or oxidants. Mechanistic studies suggest a radical cross-coupling pathway rather than a carbene insertion process.

We began by examining the model reaction between sulfinamide **1a** and ethyl diazoacetate **2a** under visible-light irradiation. A comprehensive screening of photocatalysts, solvents, and reaction parameters identified $[Ru(bpy)_3]Cl_2 \cdot 6H_2O$ (2.5 mol%) in acetonitrile (0.1 M) under 467 nm irradiation for 16 h as the optimal conditions (see the SI for details, Tables S1–S4), providing sulfoximine **3a** in 92% yield (Table 1, entry 1). The reaction doesn't proceed in the absence of a photocatalyst or without blue light; asserting the importance of a photocatalytic reaction mechanism (entries 3 and 4). The reaction was also wavelength dependent, with 370 nm irradiation affording only 21% yield of **3a**. Other controls involving open air reaction and addition of water resulted in diminished yields (entries 5 and 6).

With the optimized conditions in hand, we explored the substrate scope of the transformation. A wide range of aryl, heteroaryl, and styrylic sulfinamides were compatible, affording the corresponding sulfoximines (**3a–3m**) in moderate to excellent yields. Electron-donating and electron-withdrawing substituents on the aryl ring were well tolerated, though para-nitro substitution led to a marked decrease in yield (**3c**, 16%), likely due to electronic deactivation. Substrates bearing heteroaromatic or styryl substituents underwent smooth conversion to the corresponding products (**3k–3m**) in good yields. In contrast, ortho-substituted aryl sulfinamides afforded only trace amounts of product, consistent with steric hindrance around the reactive sulfur center. Aliphatic sulfinamides were unreactive under the standard conditions (SI, Fig. S5).

Variation of the *N*-substituent on the sulfinamide further demonstrated the robustness of the protocol. Various substituents such as isopropyl, trifluoromethyl, phenyl, pyridyl, methoxy, ester, and Boc attached to the alkyl chain proved compatible with



Scheme 2 Substrates scope. Reaction conditions: **1a** (0.2 mmol), **2a** (6.0 equiv.) and $[Ru(bpy)_3]Cl_2 \cdot 6H_2O$ (2.5 mol%) in MeCN (2.0 mL) under argon.

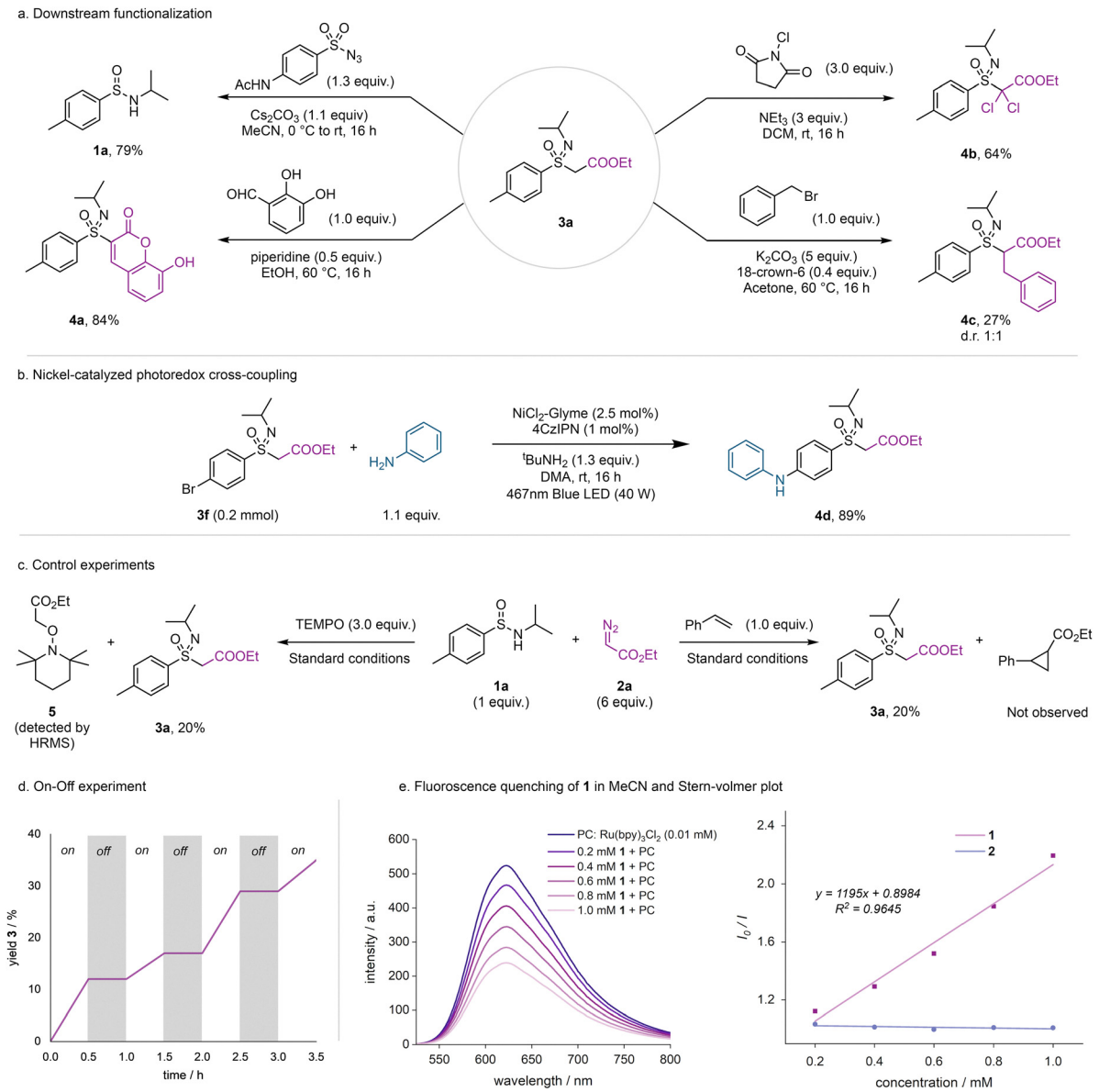
the reaction conditions giving the corresponding sulfoximines (**3n–3w**) in moderate to excellent yields (23–92%). The presence of a second sulfinamide in the side chain resulted in a decreased yield of 27% along with 1 : 1 diastereomers of the resulting sulfoximine **3x**. *N*-aryl and unprotected sulfinamides were largely unreactive under the optimized conditions (SI, Fig. S5).

The reaction also tolerated a variety of diazo compounds. Both donor/donor and donor/acceptor diazo compounds afforded the corresponding sulfoximines (**3y**, **z**) in high yield. Chiral diazo compounds derived from L-menthol and (−)-borneol gave a 1 : 1 mixture of diastereomers in moderate yield (Scheme 2).

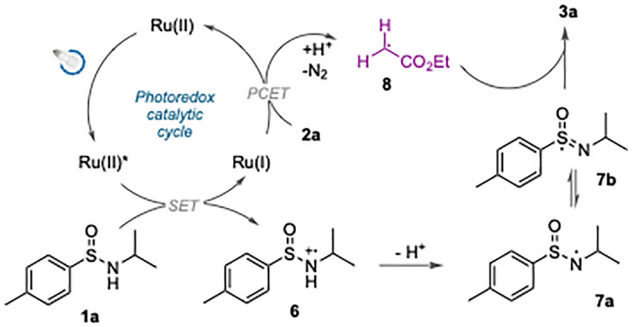
To demonstrate the synthetic utility of the obtained sulfoximines, several downstream transformations were performed (Scheme 3a). Treatment of **3a** with a sulfonyl azide resulted in a mild dealkylation reaction to regenerate the parent sulfinamide **1a** in 79% yield. Condensation of **3a** with 2-hydroxybenzaldehyde afforded coumarin derivative **4a**. α-Halogenation and α-alkylation proceeded smoothly to yield **4b** and **4c** in 64% and 27% yield, respectively. Furthermore, sulfoximine **3f** underwent a nickel-catalyzed photoredox-catalyzed cross-coupling to furnish the corresponding para-aminated product **4d** in 89% yield (Scheme 3b), underscoring the compatibility of the sulfoximine core in subsequent catalytic transformations.

We concluded our investigations with experimental studies on the reaction mechanism (Scheme 3c and d). When the reaction was performed using TEMPO as a radical quencher, the reaction resulted in a diminished yield of **3a** along with the TEMPO-adduct **5** suggesting the participation of radicals in the course of the reaction (Scheme 3c). A competition experiment with styrene resulted in sulfoximine formation without notable amounts of cyclopropane, which suggests that carbene intermediates are likely not involved. The on/off experiment shows that no reaction occurs in the absence of light (Scheme 3d). Additionally, the Stern–Volmer fluorescence quenching experiments demonstrated that only the sulfinamide **1a** efficiently quenches the excited state of the photocatalyst, while the diazo compound **2a** does not show quenching (Scheme 3e).

Based on these observations and literature precedents, we propose a plausible reaction mechanism (Scheme 4). Initially, the photoexcited state of the Ru(II) photocatalyst undergoes reductive quenching with sulfinamide **1a** to afford a Ru(I) species and



Scheme 3 Post-synthetic transformations and control experiments.



Scheme 4 Plausible reaction mechanism.

radical cation **6**. Deprotonation of **6** furnishes persistent *S*-centered radical **7b**, favored over its less stable isomer **7a**. Meanwhile, the reduced ground-state photocatalyst donates an electron to **2a** to complete the photocatalytic cycle, while simultaneously generating key radical intermediate **8** through a PCET process.[13] Radical cross-coupling between **7b** and **8** then furnishes the desired sulfoximine **3a**.

In summary, we have developed a visible-light-driven protocol for the formal *S*-alkylation of sulfinamides using diazo compounds. This protocol proceeds with excellent *S*/*N* selectivity under additive-free conditions, demonstrating broad substrate scope and functional-group tolerance. The resulting sulfoximines serve as versatile intermediates for further functionalization, enabling access to challenging sulfur–nitrogen architectures as well as cross-coupling chemistry.

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Conflicts of interest

There are no conflicts to declare.

Data availability

All experimental data, and detailed experimental procedures are available in the supplementary information (SI). Supplementary information is available. See DOI: https://doi.org/10.1039/d5cc06998j.

References

1 (*a*) M. Reggelin and C. Zur, *Synthesis*, 2000, 1–64; (*b*) U. Lücking, *Angew. Chem., Int. Ed.*, 2013, **52**, 9399–9408; (*c*) J. A. Sirvent and U. Luücking, *ChemMedChem*, 2017, **12**, 487–501; (*d*) M. Frings, C. Bolm, A. Blum and C. Gnamm, *Eur. J. Med. Chem.*, 2017, **126**, 225–245; (*e*) P. Mader and L. Kattner, *J. Med. Chem.*, 2020, **63**, 14243–14275; (*f*) Y. Han, K. Xing, J. Zhang, T. Tong, Y. Shi, H. Cao, H. Yu, Y. Zhang, D. Liu and L. Zhao, *Eur. J. Med. Chem.*, 2021, **209**, 112885–112907; (*g*) U. Lücking, *Chem. – Eur. J.*, 2022, **28**, e202201993; (*h*) H. J. Gais, *Eur. J. Org. Chem.*, 2024, e202301143; (*i*) J. J. Garrido-González, K. Medrano-Uribe, C. Rosso, H. Humbrías-Martín and L. Dell'Amico, *Chem. – Eur. J.*, 2024, **30**, e202401307.

2 (*a*) C. Sambiagio, D. Schönbauer, R. Blieck, T. Dao-Huy, G. Pototschnig, P. Schaaf, T. Wiesinger, M. F. Zia, J. Wencel-Delord, T. Besset, B. U. W. Maes and M. Schnürch, *Chem. Soc. Rev.*, 2018, **47**, 6603–6743; (*b*) Y. Zhu, M. R. Loso, G. B. Watson, T. C. Sparks, R. B. Rogers, J. X. Huang, B. C. Gerwick, J. M. Babcock, D. Kelley, V. B. Hegde, B. M. Nugent, J. M. Renga, I. Denholm, K. Gorman, G. J. DeBoer, J. Hasler, T. Meade and J. D. Thomas, *J. Agric. Food Chem.*, 2011, **59**, 2950–2957; (*c*) X. Yu, Y. Zhang, Y. Liu, Y. Li and Q. Wang, *J. Agric. Food Chem.*, 2019, **67**, 4224–4231; (*d*) Y. Zhu, M. R. Loso, B. M. Nugent, J. X. Huang and R. B. Rogers, WO/2008/057129A1, Dow AgroSciences LLC, Indianapolis, USA, 2008.

3 (*a*) Y. Han, K. Xing, J. Zhang, T. Tong, Y. Shi, H. Cao, H. Yu, Y. Zhang, D. Liu and L. Zhao, *Eur. J. Med. Chem.*, 2021, **209**, 112885; (*b*) P. Mäder and L. Kattner, *J. Med. Chem.*, 2020, **63**, 14243–14275.

4 G. Siemeister, U. Lücking, A. M. Wengner, P. Lienau, W. Steinke, C. Schatz, D. Mumberg and K. Ziegelbauer, *Mol. Cancer Ther.*, 2012, **11**, 2265–2273.

5 (*a*) H. Okamura and C. Bolm, *Org. Lett.*, 2004, **6**, 1305–1307; (*b*) P. Ghosh, B. Ganguly and S. Das, *Asian J. Org. Chem.*, 2020, **9**, 2035–2082; (*c*) M. Andresini, A. Tota, L. Degennaro, J. A. Bull and R. Luisi, *Chem. – Eur. J.*, 2021, **27**, 17293–17321; (*d*) R. Kowalczyk, A. J. F. Edmunds, R. G. Hall and C. Bolm, *Org. Lett.*, 2011, **13**, 768–771; (*e*) J. Miao, N. G. J. Richards and H. Ge, *Chem. Commun.*, 2014, **50**, 9687–9689; (*f*) M. Zenzola, R. Doran, L. Degennaro, R. Luisi and J. A. Bull, *Angew. Chem., Int. Ed.*, 2016, **51**, 7203–7207; (*g*) G. B. Craven, E. L. Briggs, C. M. Zammit, A. McDermott, S. Greed, D. P. Affron, C. Leinfellner, H. R. Cudmore, R. R. Tweedy, R. Luisi, J. A. Bull and A. Armstrong, *J. Org. Chem.*, 2021, **86**, 7403–7424; (*h*) P. M. Matos, W. Lewis, S. P. Argent, J. C. Moore and R. A. Stockman, *Org. Lett.*, 2020, **22**, 2776–2780.

6 (*a*) W. Zhang, Y. Ouyang, X. Zou and B. Gao, *Org. Chem. Front.*, 2025, **12**, 5252–5257; (*b*) Y. Aota, T. Kano and K. Maruoka, *Angew. Chem., Int. Ed.*, 2019, **58**, 17661–17665; (*c*) P. Shi, Y. Tu, D. Zhang, C. Wang, K.-N. Truong, K. Rissanen and C. Bolm, *Adv. Synth. Catal.*, 2021, **363**, 2552–2556; (*d*) P. Shi, Y. Tu, C. Wang, D. Ma and C. Bolm, *J. Org. Chem.*, 2022, **87**, 3817–3824; (*e*) D. Kong, M. M. Amer and C. Bolm, *Green Chem.*, 2022, **24**, 3125–3129; (*f*) X. Wu, W. Zhang, G. Sun, X. Zou, X. Sang, Y. He and B. Gao, *Nat. Commun.*, 2023, **14**, 5168–5178; (*g*) Y. Maeda, S. Hamada, Y. Aota, K. Otsubo, T. Kano and K. Maruoka, *J. Org. Chem.*, 2022, **87**, 3652–3660.

7 W. Zheng, X. Chen, F. Chen, Z. He and Q. Zeng, *Chem. Rec.*, 2021, **21**, 396–416.

8 M. C. Caserio and J. K. Kim, *J. Phys. Org. Chem.*, 2018, **31**, e3841.

9 (*a*) Y. Hussain, I. Sliusarevskyi, C. Empel, M. Rueping and R. M. Koenigs, *Chem. Commun.*, 2025, **61**, 11017–11020; (*b*) I. Sliusarevskyi, J. Diaz, S. Senapati, B. J. Ebel, N. J. Linnartz, I. M. Oppel, C. Empel, P. W. H. Chan and R. M. Koenigs, *Angew. Chem., Int. Ed.*, 2025, **64**, e202509870.

10 X. Zou, H. Wang and B. Gao, *Org. Lett.*, 2023, **25**, 7656–7660.

11 (*a*) J. Durka, J. Turkowska and D. Gryko, *ACS Sustainable Chem. Eng.*, 2021, **9**, 8895–8918; (*b*) C. Empel, C. Pei and R. M. Koenigs, *Chem. Commun.*, 2022, **58**, 2788–2798; (*c*) Z. Zhang and V. Gevorgyan, *Chem. Rev.*, 2024, **124**, 7214–7261; (*d*) Z.-Y. Xie and X. Xuan, *Chem. Commun.*, 2024, **60**, 2125–2136; (*e*) B. Cai and J. Xuan, *Chin. J. Org. Chem.*, 2021, **41**, 4565–4574.

12 (*a*) S. Zhu, F. Li, C. Empel, S. Jana, C. Pei and R. M. Koenigs, *Adv. Synth. Catal.*, 2022, **364**, 3149–3154; (*b*) S. Biswas, C. Empel, L. M. Sanchez-Palestino, H. Arman, R. M. Koenigs and M. P. Doyle, *Chem. Sci.*, 2024, **15**, 11065–11071; (*c*) B. G. Cai, C. Empel, S. Jana, J. Xuan and R. M. Koenigs, *ACS Catal.*, 2023, **13**, 11851–11856; (*d*) H. Zhou, G. Wang, C. Wang and J. Yang, *Org. Lett.*, 2022, **24**, 1530–1535; (*e*) J. Yang, S. Wang, Y. Han, Q. Dong, W. Ma and H. Zhou, *Chem. Commun.*, 2025, **61**, 1188–1191; (*f*) L. W. Ciszewski, J. Durka and D. Gryko, *Org. Lett.*, 2019, **21**, 7028–7032; (*g*) F. Li, C. Pei and R. M. Koenigs, *Angew. Chem., Int. Ed.*, 2022, **61**, e202111892; (*h*) C. Empel, S. Jana, L. W. Ciszewski, K. Zawada, C. Pei, D. Gryko and R. M. Koenigs, *Chem. – Eur. J.*, 2023, **29**, e202300214; (*i*) J. Tian, J. Ling, Y. Wang and L. Zhou, *Chem. Sci.*, 2025, **16**, 5701–5706; (*j*) S. Li and L. Zhou, *Org. Lett.*, 2024, **26**, 3294–3298; (*k*) W. Li, S. Li, C. Empel, R. M. Koenigs and L. Zhou, *Angew. Chem., Int. Ed.*, 2023, **62**, e202309947; (*l*) K. Orłowska, L. Łuczak, P. Krajewski, J. V. Santiago, K. Rybicka-Jasińska and D. Gryko, *Chem. Commun.*, 2023, **59**, 14649–14652; (*m*) K. Rybicka-Jasińska, W. Shan, K. Zawada, K. M. Kadish and D. Gryko, *J. Am. Chem. Soc.*, 2016, **138**, 15451–15458.

13 Y. Xie, Y.-P. Bao, X.-Y. Zhuo and J. Xuan, *Org. Lett.*, 2024, **26**, 1393–1398.

