



Cite this: *Org. Biomol. Chem.*, 2021, **19**, 6781

Received 24th May 2021,

Accepted 14th July 2021

DOI: 10.1039/d1ob01002f

rsc.li/obc

## Photo-induced oxidative cleavage of C–C double bonds for the synthesis of biaryl methanone *via* $\text{CeCl}_3$ catalysis†

Pan Xie, \* Cheng Xue, Dongdong Du and SanShan Shi

A Ce-catalyzed strategy is developed to produce biaryl methanones *via* photooxidative cleavage of C–C double bonds at room temperature. This reaction is performed under air and demonstrates high activity as well as functional group tolerance. A synergistic Ce/ROH catalytic mechanism is also proposed based on the experimental observations. This protocol should be the first successful Ce-catalyzed photooxidation reaction of olefins with air as the oxidant, which would provide inspiration for the development of novel Ce-catalyzed photochemical synthesis processes.

Biaryl methanones are important chemicals that exist extensively in numerous natural products and biologically active compounds (Fig. 1).<sup>1</sup> Therefore, intense efforts have been devoted to the synthesis of these carbonyl-containing systems.<sup>2</sup> Among many types of synthesis methods, oxidative cleavage of olefins is a very attractive choice due to its atom economy.<sup>3</sup>

In the beginning,  $\text{O}_3$  and toxic  $\text{OsO}_4$  have been used in ozonolysis and Lemieux–Johnson oxidation reactions.<sup>4</sup> After that, hypervalent metals and peroxides were also used to cleave the C–C double bonds of olefins.<sup>5</sup> In these processes, stoichiometric amounts of oxidants are always desirable, so large amounts of waste could be produced as the reaction progresses.

Undoubtedly,  $\text{O}_2$  is the “greenest” oxidant because  $\text{H}_2\text{O}$  is the only by-product of the oxidation reaction.<sup>6</sup> Thus, increased attention has been gradually paid to the in-depth study of sustainable development. Mn, Fe, Cu and other metal catalysts are firstly used in the aerobic oxidation of olefins to biaryl methanone compounds.<sup>7</sup> Sometimes, organic radicals are suggested to behave like high-valence metals.<sup>8</sup> Therefore, Jiao and co-workers reported NHPI-catalysed cleavage of C–C

double bonds to biaryl methanones.<sup>9</sup> By just changing the solvent from DMA to HFIP, Luo and co-workers successfully performed this reaction at room temperature and attained similar results.<sup>10</sup> Besides, some heterogeneous catalytic processes were also developed. In 2019, Nam, Cho and their co-workers successfully used  $\text{Sono-BiVO}_4$  to realise the oxidative cleavage of C–C double bonds under light illumination.<sup>11</sup> Then, Das and co-workers developed an efficient aerobic oxidative strategy by using polymeric carbon nitrides (PCNs) as a heterogeneous photocatalyst.<sup>12</sup> In the last few years, heterogeneous photocatalysis has gained fast development in the field of oxidative cleavage of C–C double bonds, but in this area, the development of homogeneous catalysis was still relatively slow. In most cases, the utilization of  $\text{O}_2$  is necessary for getting good results, but it would induce many operational difficulties and increase experimental risks in most of the cases. Meanwhile, the cost and restricted availability of common photocatalysts also impeded their industrial applications. Therefore, further searching for cheap and readily available photocatalysts to develop more efficient oxidative strategies for the cleavage of C–C double bonds would be still highly desirable (Scheme 1).

Recently, rare earth complexes have started to become new choices because they are cheap and readily available.<sup>13</sup> As the

College of Chemistry and Chemistry Engineering, Shaanxi Key Laboratory of Chemistry Additives for Industry, Shaanxi University of Science & Technology, Xi'an 710021, China. E-mail: pan.xie@sust.edu.cn

† Electronic supplementary information (ESI) available: Experimental procedures and details, mechanistic and optimization results and NMR spectra. See DOI: 10.1039/d1ob01002f

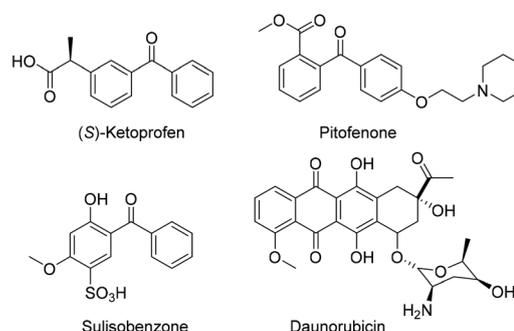
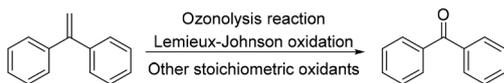


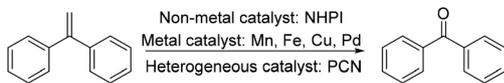
Fig. 1 Drug molecules containing a diaryl ketone motif.

## Traditional oxidation reactions



Drawbacks: Toxic oxidants, Poor atom-economy

## Molecular oxygen as the oxidant



Drawbacks: Expensive ligands or catalyst, High operation difficulty, Experimental risk

**Scheme 1** Present methodologies to produce biaryl methanones from olefins.

most abundant rare earth element, cerium complexes demonstrated unique luminescence properties because both the +3 and +4 oxidation states are accessible in certain Ce(III) compounds.<sup>14</sup> Thus, the applications of cerium compounds in organic transformations have attracted much attention in light-induced organic synthesis.<sup>15</sup> By using a Ce-promoted LMCT (ligand-to-metal charge transfer) process, a series of novel photo-mediated organic transformations have been developed in the past few years.<sup>16</sup> Lately, we realized the aqueous C–H aerobic oxidation protocol *via* a CeCl<sub>3</sub>-mediated photocatalytic process.<sup>17</sup> Inspired by this result, we hope to extend the CeCl<sub>3</sub>-mediated photocatalysis to the oxidative cleavage of C–C double bonds.

Initially, the photo-promoted aerobic oxidation of 1,1-diphenylethylene **1a** was selected as a model reaction and air was used as the oxidant (Table 1). The most commonly used cerium salts were first examined, and CeCl<sub>3</sub> demonstrated better catalytic activity to give benzophenone in 52% yield. Decreasing the catalyst loading made the result a little worse, so 10 mol% CeCl<sub>3</sub> was used as the catalyst for further examin-

**Table 1** Optimization of the reaction parameters<sup>a</sup>

Entry	[Ce]	ROH	Solvent	Yield <sup>b</sup> (%)
1	CeCl <sub>3</sub>	—	CH <sub>3</sub> CN	52
2	CeBr <sub>3</sub>	—	CH <sub>3</sub> CN	42
3 <sup>c</sup>	CeCl <sub>3</sub>	—	CH <sub>3</sub> CN	45
4	CeCl <sub>3</sub>	MeOH	CH <sub>3</sub> CN	60
5	CeCl <sub>3</sub>	EtOH	CH <sub>3</sub> CN	68
6	CeCl <sub>3</sub>	CCl <sub>3</sub> CH <sub>2</sub> OH	CH <sub>3</sub> CN	92
7	CeCl <sub>3</sub>	CCl <sub>3</sub> CH <sub>2</sub> OH	CCl <sub>3</sub> CH <sub>2</sub> OH	55
8	CeCl <sub>3</sub>	CCl <sub>3</sub> CH <sub>2</sub> OH	DMF	65
9	CeCl <sub>3</sub>	CCl <sub>3</sub> CH <sub>2</sub> OH	DMSO	60
10	CeCl <sub>3</sub>	CCl <sub>3</sub> CH <sub>2</sub> OH	THF	64
11	CeCl <sub>3</sub>	CCl <sub>3</sub> CH <sub>2</sub> OH	DCM	73

<sup>a</sup> **1a** (0.2 mmol), catalyst (10 mol%), solvent (1.0 mL), room temperature (25 °C), blue LED (4 W) and 40 h. <sup>b</sup> Isolated yield. <sup>c</sup> CeCl<sub>3</sub> (5 mol%).

ation. Previous work displayed that the addition of alcohols could improve the catalytic efficiency for Ce-promoted photochemical reactions.<sup>16a</sup> Thus, some commercially available alcohols were screened, and the results proved that TCE (trichloroethanol) was the best choice. After that, the effects of solvents were also examined. No matter what other solvents were used, inferior results were obtained.

With the optimized conditions in hand, the substrate scope of biaryl olefins was first investigated. As shown in Table 2, the reaction tolerated electron-donating groups such as methyl and alkoxy groups at the *ortho*-, *meta*-, and *para*-positions of the phenyl ring, providing the corresponding substituted ketones in good yields. The difference of reactivity between *ortho*- and *para*-methyl-substituted stilbene demonstrated a slight steric hindrance effect on this transformation. Furthermore, we found that substrates with electron-withdrawing groups such as F, Cl, and nitro groups at any position of the phenyl ring were effective under the standard conditions. In some cases, olefin polymerizations were observed, which

**Table 2** Substrate scope of biaryl olefins<sup>a</sup>

$\text{Ar}^1\text{C}(\text{Ar}^2)=\text{C} \xrightarrow[\text{Air, 25 }^\circ\text{C, 40 h}]{\text{CeCl}_3 (10 \text{ mol\%}), \text{TCE} (20 \text{ mol\%})} \text{Ar}^1\text{C}(\text{Ar}^2)=\text{O}$		

<sup>a</sup> **1a** (0.2 mmol), CeCl<sub>3</sub> (10 mol%), TCE (20 mol%), CH<sub>3</sub>CN (1.0 mL), room temperature (25 °C), blue LED (4 W) and 40 h; isolated yield. <sup>b</sup> Blue LED (2 W). <sup>c</sup> Blue LED (10 W).

may be the reason for lower yields. To expand the  $\pi$ -conjugated system, naphthyl- and biphenyl-substituted olefins (Table 2, **1o** and **1p**) were employed as substrates, and the corresponding products were generated in 40% and 88% yields, respectively. It is worth noting that the tolerance of some functional groups (methoxy, fluoride, chloride, dimethylamino, and nitro groups) in this protocol offered potential possibilities for further derivation. To our delight, some unusual substrates in the previous oxidative process of olefins, heterocycle derived biaryl olefins, were also found to be tolerated in this transformation, furnishing the corresponding products in good yields (Table 2, **2s–2u**, 70%–76%).

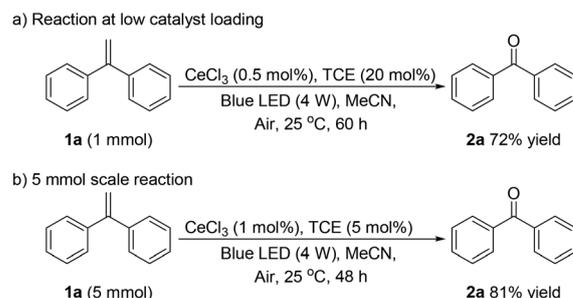
To further explore the synthesis potential of this process, some  $\alpha$ -methyl styrenes were subjected to this reaction under the optimized reaction conditions. To our delight, our photocatalysis strategy exhibited medium to good reactivity towards different styrenes. With either electron-donating or -withdrawing groups at any position of the phenyl ring, oxidative reactions ran efficiently and gave the corresponding ketones in good yields (Table 3, **4a–4g**). 2-(Prop-1-en-2-yl) naphthalene was also a suitable substrate, and good yield was obtained. However, inferior reactivity was observed when a pyridine substituted olefin was used, and only moderate yield was obtained (**4i–4j**), which may be due to the strong electron-withdrawing effect of the pyridine group. Next, we turned our interest to the reactions of terminal styrene. The results demonstrated that various *para*-substituted styrenes could successfully participate in this process, furnishing substituted benzaldehydes in good yields (Table 3, **4l–4q**).

Additionally, we found that the reaction could proceed smoothly, even if the catalyst loading was decreased to 0.5 mol%. By prolonging the reaction time, a satisfactory yield

was also obtained. Besides, the reaction is amenable for scaling up: using 1 mol% Ce catalyst, the model oxidation could be run with 5 mmol **1a** to provide the pure isolated product **2a** in 81% yield (Scheme 2).

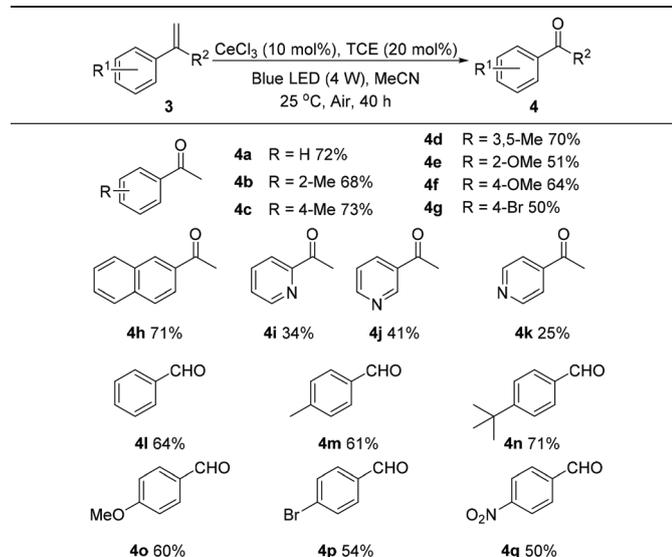
To shed light on the mechanism of our recommended protocol, some control and quenching experiments were carried out (Table 4). The obtained results revealed that light, Ce catalyst and air are necessary and exclusion of each one can lead to complete inhibition of the oxidation reaction. In addition, the target reaction was also inhibited by the traditional radical scavengers such as TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) and BHT (2,6-di-*tert*-butyl-4-methyl phenol), demonstrating a free-radical mechanism. Besides, the addition of  $\text{CuCl}_2$  led to a trace amount of the product, which proved the contribution of single-electron processes.<sup>18</sup> Finally, further addition of benzoquinone to the reaction mixture reduced the product yield. This observation confirmed the presence of superoxide radicals in the oxidation process.<sup>19</sup>

Next,  $\text{H}_2^{18}\text{O}$  was used instead of TCE to detect the actual source of oxygen in the ketone product. After the reaction was completed, no  $^{18}\text{O}$ -labelled ketone was observed. Finally, the reaction was carried out in the presence of  $^{18}\text{O}_2$  (1 atm) and the  $^{18}\text{O}$ -labelled product was generated in 70% yield. Both results demonstrated that the oxygen of the product was from



Scheme 2 The reaction practicability.

Table 3 Substrate scope of  $\alpha$ -methyl and terminal styrene<sup>a</sup>



<sup>a</sup> **1a** (0.2 mmol),  $\text{CeCl}_3$  (10 mol%), TCE (20 mol%),  $\text{CH}_3\text{CN}$  (1.0 mL), room temperature (25 °C), blue LED (4 W) and 40 h; isolated yield.

Table 4 Control and quenching experiments<sup>a</sup>

Entry	Additive	Yield (%)
1 <sup>b</sup>	—	No reaction
2 <sup>c</sup>	—	No reaction
3 <sup>d</sup>	—	No reaction
4	TEMPO (2.0 equiv.)	No reaction
5	BHT (2.0 equiv.)	No reaction
6	$\text{CuCl}_2$ (1.0 equiv.)	Trace
7	Benzoquinone (1.0 equiv.)	8%

<sup>a</sup> **1a** (0.2 mmol),  $\text{CeCl}_3$  (10 mol%), TCE (20 mol%),  $\text{CH}_3\text{CN}$  (1.0 mL), room temperature (25 °C), blue LED (4 W) and 40 h; isolated yield. <sup>b</sup>  $\text{N}_2$  atmosphere instead of air. <sup>c</sup> No light. <sup>d</sup> No catalyst.

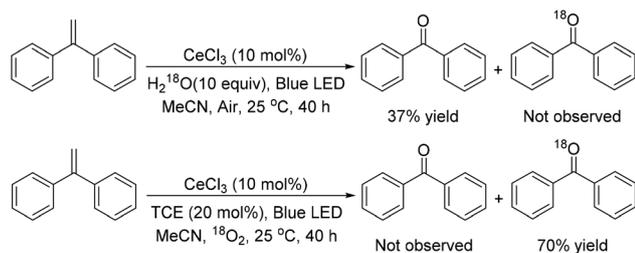
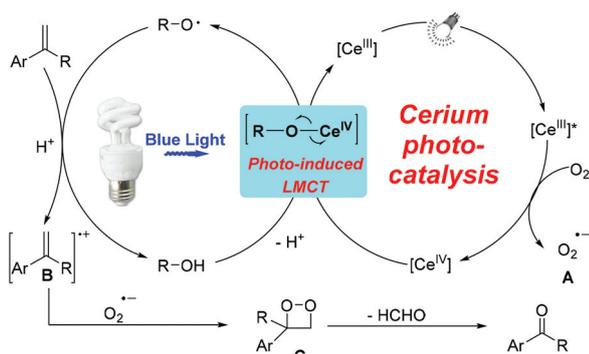
Scheme 3  $^{18}\text{O}$ -labeling experiment.

Fig. 2 Plausible mechanism for oxidation of olefins.

dioxygen in the air, rather than from  $\text{H}_2\text{O}$  or alcohols (Scheme 3).

According to the performed experiments and previous studies, a plausible electron transfer pathway was proposed (Fig. 2). Firstly, the  $\text{Ce}^{\text{III}}$  species would be photoexcited to its excited state, reducing  $\text{O}_2$  to a superoxide radical anion **A** along with the generation of a  $\text{Ce}^{\text{IV}}$  intermediate. By releasing the proton, the reaction of alcohol with the  $\text{Ce}^{\text{IV}}$  species and the following photoinduced LMCT would furnish the highly electrophilic alkoxy radicals.<sup>16a</sup> This radical would abstract an H atom from the olefin to give an olefin radical, which reacted with the proton to generate the radical cation intermediate **B**. Then, the [2 + 2] cycloaddition of an alkene radical cation with a superoxide radical anion would occur to give the dioxetane intermediate **C**. Finally, the corresponding carbonyl product could be afforded by the decomposition of **C** and formation of formaldehyde.<sup>20</sup>

## Conclusions

In summary, we have developed an efficient and operationally convenient method to produce ketone compounds *via* the oxidative cleavage of  $\text{C}=\text{C}$  bonds with air as the oxidant. The absence of toxic metal catalysts and over-stoichiometric oxidants are significant advantages of this economical and environmentally benign methodology. This Ce-catalyzed photo-induced oxidative strategy is more suitable for the oxidation of diaryl alkenes to produce biaryl methanones, giving a compe-

tent supplement to the existing reported catalytic systems. The application of this new protocol and further investigations on the mechanism are still ongoing in our laboratory.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

This work was financially supported by the Education Foundation of Shaanxi Province (No. 18JK0105).

## Notes and references

- (a) T. Ukita, Y. Nakamura, A. Kubo, Y. Yamamoto, Y. Moritani, K. Saruta, T. Higashijima, J. Kotera, M. Takagi, K. Kikkawa and K. Omori, *J. Med. Chem.*, 2001, **44**, 2204–2218; (b) M. Fukuda, R. Sekiya and R. Kuroda, *Angew. Chem., Int. Ed.*, 2008, **47**, 706–710; (c) H.-B. Yang, K. Ghosh, Y. Zhao, B. H. Northrop, M. M. Lyndon, D. C. Muddiman, H. S. White and P. J. Stang, *J. Am. Chem. Soc.*, 2008, **130**, 839–841; (d) H. Kim, S. M. So, C. P.-H. Yen, E. Vinhato, A. J. Lough, J.-I. Hong, H.-J. Kim and J. Chin, *Angew. Chem., Int. Ed.*, 2008, **47**, 8657–8660; (e) K. Albrecht and K. Yamamoto, *J. Am. Chem. Soc.*, 2009, **131**, 2244–2251; (f) S. K. Vooturi, C. M. Cheung, M. J. Rybak and S. M. Firestine, *J. Med. Chem.*, 2009, **52**, 5020–5031; (g) J. R. Luque-Ortega, P. Reuther, L. Rivas and C. Dardonville, *J. Med. Chem.*, 2010, **53**, 1788–1798.
- (a) G. A. Olah, *Friedel Crafts and Related Reaction, vol. III, Part I*, Interscience, New York, 1964; (b) J. Otera, *Modern carbonyl chemistry*, John Wiley & Sons, 2008; (c) L. Kollár, *Modern carbonylation methods*, John Wiley & Sons, 2008.
- (a) R. A. Sheldon and J. K. Kochi, *Metal Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, 1981; (b) C. J. Allpress and L. M. Berreau, *Coord. Chem. Rev.*, 2013, **257**, 3005–3029; (c) A. Rajagopalan, M. Lara and W. Kroutil, *Adv. Synth. Catal.*, 2013, **355**, 3321–3335.
- (a) R. Pappo, D. S. Allen, R. U. Lemieux and W. S. Johnson, *J. Org. Chem.*, 1956, **21**, 478–479; (b) V. Balzani, A. Credi and M. Venturi, *ChemSusChem*, 2008, **1**, 26–58.
- (a) S. Lai and D. G. Lee, *Synthesis*, 2001, 1645–1648; (b) S. R. Hart, D. C. Whitehead, B. R. Travis and B. Borhan, *Org. Biomol. Chem.*, 2011, **9**, 4741–4744; (c) B. R. Travis, R. S. Narayan and B. Borhan, *J. Am. Chem. Soc.*, 2002, **124**, 3824–3825; (d) W. B. Sheats, L. K. Olli, R. Stout, J. T. Lundeen, R. Justus and W. G. Nigh, *J. Org. Chem.*, 1979, **44**, 4075–4078; (e) T. E. Nielsen and M. Meldal, *Org. Lett.*, 2005, **7**, 2695–2698; (f) D. A. Chaudhari and R. A. Fernandes, *J. Org. Chem.*, 2016, **81**, 2113–2121; (g) K. Miyamoto, Y. Sei, K. Yamaguchi and M. Ochiai, *J. Am.*

- Chem. Soc.*, 2009, **131**, 1382–1383; (h) F. V. Singh, H. M. S. Milagre, M. N. Eberlin and H. A. Stefani, *Tetrahedron Lett.*, 2009, **50**, 2312–2316.
- 6 (a) J. H. Clark, *Green Chem.*, 1999, **1**, 1; (b) W. Schilling, D. Riemer, Y. Zhang, N. Hatami and S. Das, *ACS Catal.*, 2018, **8**, 5425–5430.
- 7 (a) T. Amaya and H. Fujimoto, *Tetrahedron Lett.*, 2018, **59**, 2657–2660; (b) Q. Tang, Y. Wang, J. Zhang, R. Qiao, X. Xie, Y. Wang and Y. Yang, *Appl. Organomet. Chem.*, 2016, **30**, 435–440; (c) J.-J. Liu, Y. Liang, H.-S. Wang and Y.-T. Pan, *Synlett*, 2015, 2024–2028; (d) A. Wang and H. Jiang, *J. Org. Chem.*, 2010, **75**, 2321–2326.
- 8 (a) Y. Ishii, S. Sakaguchi and T. Iwahama, *Adv. Synth. Catal.*, 2001, **343**, 393–427; (b) F. Recupero and C. Punta, *Chem. Rev.*, 2007, **107**, 3800–3842; (c) J. Luo and J. Zhang, *J. Org. Chem.*, 2016, **81**, 9131–9137; (d) M. Bietti, O. Lanzalunga, A. Lapi, T. Martin, M. Mazzonna, M. Polin and M. Salamone, *J. Org. Chem.*, 2017, **82**, 5761–5768; (e) L. Vanoye, M. Abdelaal, K. Grundhauser, B. Guicheret, P. Fongarland, C. D. Bellefon and A. Favre-Réguillon, *Org. Lett.*, 2019, **21**, 10134–10138.
- 9 R. Lin, F. Chen and N. Jiao, *Org. Lett.*, 2012, **14**, 4158–4161.
- 10 Z. Zhang, W. Chen and J. Luo, *Tetrahedron Lett.*, 2020, **61**, 152527–152531.
- 11 S. S. Han, J. Y. Park, H. S. Hwang, H. R. Choe, K. M. Nam and J. Cho, *ChemSusChem*, 2019, **12**, 3018–3022.
- 12 Y. Zhang, N. S. Langeb, N. Hatamib, E. Rongec, W. Schillingb, C. Joossc and S. Das, *Green Chem.*, 2020, **22**, 4516–4522.
- 13 (a) K. Suzuki, F. Tang, Y. Kikukawa, K. Yamaguchi and N. Mizuno, *Angew. Chem., Int. Ed.*, 2014, **53**, 5356–5360; (b) H. Yin, P. J. Carroll, J. M. Anna and E. J. Schelter, *J. Am. Chem. Soc.*, 2015, **137**, 9234–9237; (c) H. Yin, P. J. Carroll, B. C. Manor, J. M. Anna and E. J. Schelter, *J. Am. Chem. Soc.*, 2016, **138**, 5984–5993; (d) H. Yin, Y. Jin, J. E. Hertzog, K. C. Mullane, P. J. Carroll, B. C. Manor, J. M. Anna and E. J. Schelter, *J. Am. Chem. Soc.*, 2016, **138**, 16266–16273; (e) J.-J. Guo, A. Hu, Y. Chen, J. Sun, H. Tang and Z. Zuo, *Angew. Chem., Int. Ed.*, 2016, **55**, 15319–15322; (f) A. Hu, J.-J. Guo, H. Pan, H. Tang, Z. Gao and Z. Zuo, *J. Am. Chem. Soc.*, 2018, **140**, 1612–1616; (g) T. C. Jenks, M. D. Bailey, J. Hovey, S. Fernando, G. Basnayake, M. E. Cross, W. Li and M. J. Allen, *Chem. Sci.*, 2018, **9**, 1273–1278; (h) Y. Qiao, D.-C. Sergentu, H. Yin, A. V. Zabula, T. Cheisson, A. McSkimming, B. C. Manor, P. J. Carrol, J. M. Anna, J. Autschbach and E. J. Schelter, *J. Am. Chem. Soc.*, 2018, **140**, 4588–4595.
- 14 S. Cotton, *Lanthanide and Actinide Chemistry*, John Wiley and Sons, West Sussex, U.K., 2006, pp. 61–77.
- 15 Y. Qiao and E. J. Schelter, *Acc. Chem. Res.*, 2018, **51**, 2926–2936.
- 16 (a) A. Hu, J.-J. Guo, H. Pan and Z. Zuo, *Science*, 2018, **361**, 668–677; (b) J. Schwarz and B. König, *Chem. Commun.*, 2019, **55**, 486–488; (c) Q. An, Z. Wang, Y. Chen, X. Wang, K. Zhang, H. Pan, W. Liu and Z. Zuo, *J. Am. Chem. Soc.*, 2020, **142**, 6216–6226.
- 17 P. Xie, C. Xue, S. Shi and D. Du, *ChemSusChem*, 2021, **14**, 2689–2693.
- 18 (a) W. Huang, B.-C. Ma, H. Lu, R. Li, L. Wang, K. Landfester and K. A. I. Zhang, *ACS Catal.*, 2017, **7**, 5438–5442; (b) Y. Zhang, D. Riemer, W. Schilling, J. Kollmann and S. Das, *ACS Catal.*, 2018, **8**, 6659–6664; (c) J. Kollmann, Y. Zhang, W. Schilling, T. Zhang, D. Riemer and S. Das, *Green Chem.*, 2019, **21**, 1916–1920; (d) W. Schilling, Y. Zhang, D. Riemer and S. Das, *Chem. – Eur. J.*, 2020, **26**, 390–395.
- 19 (a) Y. Zhang, W. Schilling and S. Das, *ChemSusChem*, 2019, **12**, 2898–2910; (b) W. Schilling, Y. Zhang, P. K. Sahoo, S. K. Sarkar, S. Gandhi, H. W. Roesky and S. Das, *Green Chem.*, 2021, **23**, 379–387; (c) P. Xie, C. Xue, D. Du and S. Shi, *Org. Chem. Front.*, 2021, **8**, 3427–3433.
- 20 A. Frimer, *Chem. Rev.*, 1979, **79**, 359–387.