Synthetic Methods

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Remote Hydroxylation through Radical Translocation and Polar Crossover**

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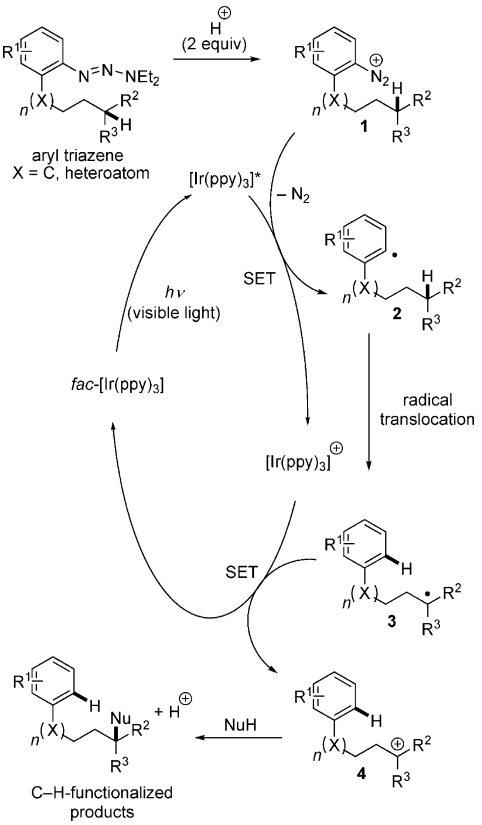
Abstract: *Mild conditions are reported for the hydroxylation of aliphatic C–H bonds through radical translocation, oxidation to carbocation, and nucleophilic trapping with H_2O. This remote functionalization employs fac-[Ir(ppy)$_3$] together with Tz^o sulfonate esters and sulfonamides to facilitate the site-selective replacement of relatively inert C–H bonds with the more synthetically useful C–OH group. The hydroxylation of a range of substrates and the methoxylation of two substrates through 1,6- and 1,7-hydrogen-atom transfer are demonstrated. In addition, a synthesis of the antidepressant fluoxetine using remote hydroxylation as a key step is presented.*

Despite recent advances,[1] the site-selective functionalization of unactivated aliphatic C–H bonds remains a significant challenge. The strategies employed for the functionalization of aliphatic C–H bonds largely fall into two categories: "innate" (hinging on the inherent reactivity of C–H bonds) and "guided" (C–H functionalization is "guided by external reagents or directing groups").[2]

Of the guided functionalization strategies, remote functionalization[3,4] involves the covalent attachment of a directing group to a substrate molecule. The directing groups may be armed with functionalities that 1) can be converted into an open-shell intermediate (for radical translocation),[3] 2) direct the inner sphere of a transition metal to a remote C–H bond,[4] and 3) direct a metal oxo species to a C–H bond for hydroxylation.[4]

An underexplored approach to the remote functionalization of aliphatic C–H bonds involves the transformation proposed in Scheme 1. We envisioned the formation of an electron-poor aryl radical **2** (R^1 and/or X = electron-withdrawing group) that abstracts a hydrogen atom from a remote sp^3-hybridized carbon atom to generate an alkyl radical **3** (a radical translocation event). Such translocations are often predictable and selective, proceeding with first-order rate constants of approximately 10^6–10^8 s^{-1}.[3i,o] The oxidation of an aryl radical (the calculated reduction potential, $E°$[Ar$^{\cdot}$/Ar$^+$], is around 2.0 V versus the saturated calomel electrode, SCE)[5] by single-electron transfer (SET) to generate an aryl cation is unlikely; the unproductive consumption of **2** is likely to involve hydrogen-atom transfer (HAT) from the solvent.[6] The alkyl radicals resulting from translocation can be oxidized by SET[7] and converted into carbocations **4** by mild oxidizing agents (the oxidation half potentials, E_{ox}, of tertiary/benzylic radicals are around 0–0.75 V, SCE).[7a] Such SET processes (**3**→**4**, Scheme 1) are likely to proceed near the diffusion limit.[7b] One can envision subsequent processes including elimination, nucleophilic attack, or rearrangement. While nature uses a similar strategy for the desaturation of fatty acids,[8] this approach has received scant attention from the synthetic community,[3j,k,n] and would serve as an example of a radical–polar crossover process that proceeds through radical translocation.[3j–l,n,9]



Scheme 1. A redox catalysis strategy for remote functionalization by radical translocation.

We recognized that a strategy such as the one depicted in Scheme 1 could be realized with the use of photoredox

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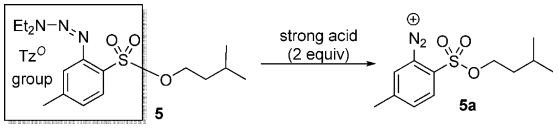
catalysis, which has recently proven instrumental in providing solutions to long-standing problems in organic synthesis.[10] We envisioned that a ground-state photocatalyst (*fac*-[Ir(ppy)$_3$]) could intercept a photon and undergo conversion to excited state [Ir(ppy)$_3$]* ($E°[Ir^{3+}*/Ir^{4+}] = -1.73$ V, SCE),[10c] which would donate an electron with diffusion-controlled efficiency[10i] to an arenediazonium **1** (the reduction half potential of **1**, $E_{red} = -0.1 - +0.5$ V, SCE)[11] to generate an aryl radical **2**, which would translocate to alkyl radical **3**. The oxidatively quenched photocatalyst ([Ir(ppy)$_3$]$^+$, $E°[Ir^{3+}/Ir^{4+}] = +0.77$ V, SCE)[10c] generated by SET from [Ir(ppy)$_3$]* to **1** would then accept an electron from the alkyl radical **3** to generate carbocation **4** and regenerate [Ir(ppy)$_3$]. Alternatively, SET from **3** to **1** to generate **4** and another radical **2** is a favorable process that gives rise to a chain reaction (rather than a catalytic process). Herein, we report a remote hydroxylation procedure (NuH = H_2O) inspired by Scheme 1.

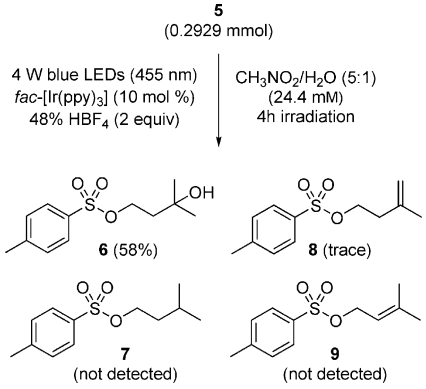
We identified the Tz^o group (Scheme 2) as an ideal starting point. Tz^{o}Cl-derived sulfonate esters and sulfonamides are effective substrates for remote desaturation that



Scheme 2. Isoamyl Tz^o ester.

proceeds along a pathway similar to the one in Scheme 1.[3n] Electron-deficient radicals derived from species such as this one are often reactive toward translocation to electron-rich aliphatic C–H bonds.[3m,n,12] Further, the tosylates resulting from remote functionalization would be readily manipulated. Thus, isoamyl alcohol was converted into Tz^o sulfonate ester **5** (Scheme 2), which was designated for feasibility and optimization studies for remote hydroxylation.

We employed Tz^o ester **5**, the photocatalyst *fac*-[Ir(ppy)$_3$], 48% HBF_4 (2 equiv, for the liberation of **5a** from **5**, Scheme 2),[13] H_2O, and CH_3NO_2 (Scheme 3). This mixture was degassed through three freeze-pump-thaw cycles in a round-bottom flask and then vigorously stirred and irradiated with blue LEDs (Supporting Information, Figure S1). The resulting mixture was irradiated for 4 h at 25 °C and afforded **6**, the desired product of hydroxylation at the tertiary position, in 58% yield. The ^{1}H NMR spectrum of the crude product mixture showed no evidence for the formation of either the reduction product **7** or desaturation product **9**, but small amounts of desaturation product **8**. 1,7-Hydrogen-atom transfers (HATs) such as this have been previously reported.[3n,o]



Scheme 3. Conversion of **5** into hydroxylation product **6**.

The optimization of this protocol and the establishment of the roles of the parameters listed in Scheme 3, including light, *fac*-[Ir(ppy)$_3$], acid, H_2O as co-solvent, and temperature, and a comparison to Baran's desaturation conditions[3n] are depicted in Table 1.[14] A decreased irradiation time resulted in decreased yields of **6**[14] (because of incomplete consumption of **5** as determined by TLC and NMR analyses). However, 18 h of irradiation resulted in the formation of **6** in 57% yield (Table 1, entry 1); **6** does not appear to degrade over prolonged periods of irradiation. When the loading of the photocatalyst was reduced (Table 1, entries 2–4), the yield of **6** dropped considerably, thus demonstrating the importance of *fac*-[Ir(ppy)$_3$]. The optimal catalyst loading was 10 mol%. Further increased loadings did not lead to an improved yield.[14] The omission of acid (Table 1, entry 5) resulted in the recovery of starting material **5**. Surprisingly, experiments run in the dark with 10 mol% *fac*-[Ir(ppy)$_3$] resulted in product yields of 40% and 50% when the reactions were stirred for 4 h and 18 h, respectively (Table 1, entries 6 and 7). The ground state $E°$ for *fac*-[Ir(ppy)$_3$] (+0.77 V, SCE)[10c] is higher than the E_{red} of **5a** (−0.12 V, SCE, see the Supporting Information) determined with cyclic voltammetry (CV). The difference of 890 mV for this electron transfer is not prohibitive, considering that the process is coupled to the irreversible loss of N_2. It is also possible that ground-state *fac*-[Ir(ppy)$_3$] serves as an initiator by transferring an electron to **1**, while SET from radical intermediates such as **3** to **1** is a propagation step in a chain reaction that accounts for product formation. The reduction of arenediazonium salts in the dark under conditions in which SET is even less favorable have been observed elsewhere, albeit at

Table 1: Optimization of reaction conditions.[a]

Entry	Deviation from conditions given in Scheme 3	Yield of **6** [%][b]
1	irradiation for 18 h	57
2	no *fac*-[Ir(ppy)$_3$]	11
3	*fac*-[Ir(ppy)$_3$] (1 mol%)	4
4	*fac*-[Ir(ppy)$_3$] (5 mol%)	12
5	no acid	0
6	light excluded, stirred for 4 h	40
7	light excluded	50
8	no freeze-pump-thaw	57
9	H_2O (20 equiv), irradiation for 4 h	trace
10	Baran's conditions, H_2O (2 mL) added	18
11	TEMPO (1 equiv)	31
12	reaction at 60 °C	40

[a] The reaction time was 18 h unless stated otherwise. [b] Yields of isolated products. Baran's conditions: TEMPO (1 equiv), TFA (2 equiv), at 60 °C for 1.5 h without irradiation.

lower efficiency,[15a–c] while the irreversible formation of alkyl radicals has been reported in a related context.[15d] Similarly, a ground-state Ru polypyridyl catalyzes the oxidative esterification of aldehydes without irradiation.[15e] We elected to irradiate future reactions with blue LEDs because of the improvement in yield, however, the reaction in the dark is a subject of ongoing investigation in our lab.

Product **6** was obtained in 57% yield without degassing the solvent, thus indicating that freeze-pump-thaw is not necessary (Table 1, entry 8). A decrease in the excess of H_2O that was used (Table 1, entry 9) resulted in the formation of trace quantities of **6**. Other photocatalysts ($[Ru(phen)_3]PF_6$, $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$, ethyl eosin, $[Ru(bpy)_3](PF_6)_2$)[16,17] afforded at most trace amounts of **6**, while solvent screens demonstrated that CH_3NO_2 was the optimal solvent.[14] The implementation of Baran's desaturation conditions[3n] with added H_2O (Table 1, entry 10) afforded only 18% of **6** and 30% of desaturation product **8**, thus demonstrating that this approach is less effective for hydroxylation. In addition, employment of the conditions summarized in entry 8 of Table 1, but in the presence of TEMPO (1 equiv) resulted in 31% of **6** and 40% of **8** (Table 1, entry 11). Finally, an experiment run at 60°C (Table 1, entry 12) gave **6** in 40% yield with traces of **8**, thus indicating that the elimination observed in entry 10 is not simply a result of higher temperature. Experiments run at lower temperature have also produced insight (Table 2, see below).

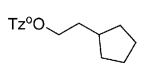
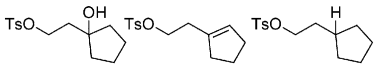
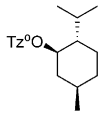
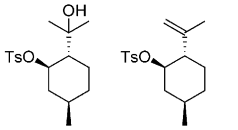
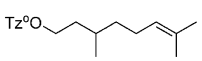
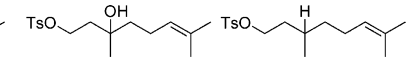
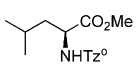
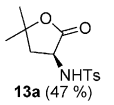
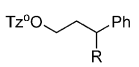
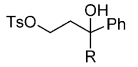
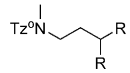
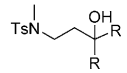
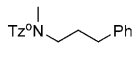
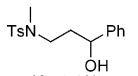
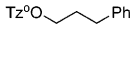
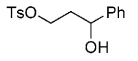
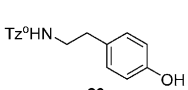
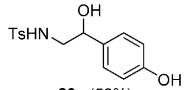
The divergence in behavior, favoring elimination in the presence of TEMPO, is not readily explained; Baran has proposed similar carbocationic intermediates.[3n] The present study and related desaturation work have produced no evidence for TEMPO adducts, however, Baran produced evidence of radical intermediates through deuteration studies.

To explore the substrate scope of this remote hydroxylation (Table 2), we employed conditions similar to the ones summarized in entry 8 of Table 1. Cyclopentylethanol derivative **10** produced alcohol **10a**, elimination product **10b**, and reduction product **10c** in 41%, 15%, and 4% yields, respectively (Table 2, entry 1). Conversion of **10** at 6°C (Table 2, entry 2) resulted in the slow consumption of the triazene of **10**, but an increase in the yield of **10a** (48%) after three days of irradiation. As we have never observed an arenediazonium salt in the ^{1}H NMR spectra of the crude reaction mixtures, we conclude that the HBF_4-promoted consumption of the triazene is the rate-determining step of this process and that intermediate arenediazonium ions are rapidly consumed. The consumption of **10** was prohibitively slow at lower temperatures.

Menthyl derivative **11** gave alcohol **11a** and elimination product **11b** in 31% and 22% yields, respectively (Table 2, entry 3). Substrate **12** afforded alcohol **12a** in 38% yield (Table 2, entry 4). The reaction of leucine derivative **13** gave lactone **13a** in 47% yield; the tertiary alcohol was not detected (Table 2, entry 5). Product **13a** is likely to arise from the intramolecular attack of the ester carbonyl group on the intermediate carbocation. Interestingly, **13** proceeded along the elimination pathway under TEMPO-promoted desaturation conditions.[3n] Benzylic C–H-bearing substrates **14**, **15**, and **17**–**20** (Table 2, entries 6, 7, 9–12, respectively) afforded the corresponding alcohol products in relatively high yields (41–63%) with none of the elimination or reduction products detected. Remote hydroxylation is also effective with Tz^o sulfonamides (**13**, **16**, **17**, **18**, and **20**, Table 2, entries 5, 8–10, and 12). Hydroxylations of secondary carbon atoms in benzylic positions were successful with both sulfonates and sulfonamides, transforming substrates **18**–**20** to the corresponding products in 52–56% yield (Table 2, entries 10–12). Entry 12 also shows a remote hydroxylation that proceeds by 1,6-HAT.

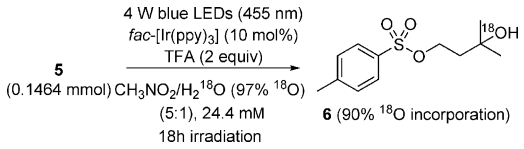
While our studies have not confirmed unambiguously that the remote hydroxylation proceeds according to Scheme 1 or a chain process involving SET from **3** to **1**, we provide evidence (Scheme 4) for a radical–polar crossover process (e.g. **3**→**4**, Scheme 1). Specifically, employment of $H_2{}^{18}O$ (97% ^{18}O) results in 90% incorporation of ^{18}O into **6**.

Table 2: Substrate scope.[a]

Entry	Substrate	Products (yield)
1	 **10**	 **10a** (41 %) **10b** (15 %) **10c** (4 %)
2[b]	**10**	**10a** (48 %)
3	 **11**	 **11a** (31 %) **11b** (22 %)
4	 **12**	 **12a** (38 %) **12c** (6 %)
5	 **13**	 **13a** (47 %)
6	 **14** (R=CH_3)	 **14a** (R=CH_3, 63 %)
7	**15** (R=Ph)	**15a** (R=Ph, 56 %)
8	 **16** (R=CH_3)	 **16a** (R=CH_3, 34 %)
9	**17** (R=Ph)	**17a** (R=Ph, 41 %)
10	 **18**	 **18a** (56%)
11	 **19**	 **19a** (52%)
12	 **20**	 **20a** (56%)

[a] Reaction conditions: substrate (0.2929 mmol), *fac*-$[Ir(ppy)_3]$ (10 mol%), CH_3NO_2 (10 mL), H_2O (2 mL), and 48% HBF_4 (2 equiv) were mixed and then irradiated for 18 h, unless stated otherwise. [b] Reaction was irradiated for 3 days at 6°C.

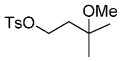
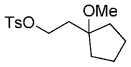
While our studies have not confirmed unambiguously that the remote hydroxylation proceeds according to Scheme 1 or a chain process involving SET from **3** to **1**, we provide evidence (Scheme 4) for a radical–polar crossover process (e.g. **3**→**4**, Scheme 1). Specifically, employment of $H_2{}^{18}O$ (97% ^{18}O) results in 90% incorporation of ^{18}O into **6**.



Scheme 4. ^{18}O-labeling study.

Finally, comparable methoxylations were possible with the replacement of H_2O by methanol (Table 3). The lower yields relative to hydroxylation are likely due to HAT from

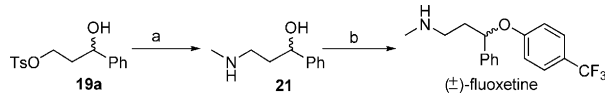
Table 3: Methoxylation.[a]

Entry	Substrate	Products (yield)
1	**5**	 **5d** (31 %)
2	**10**	 **10d** (27 %)

[a] Reaction conditions are the same as those described in Table 2, except for the replacement of H_2O with methanol.

methanol to radical intermediates. The reduction products isoamyl tosylate and **10c** were observed in these cases, while methanol has been used as hydrogen-atom donor for another process.[18] These results in addition to the observed elimination products and ^{18}O incorporation provide further evidence for carbocation intermediates. The hydroxylation by radical reaction with O_2 is, at best, a minor process.

In addition, we recognized the utility of hydroxylation product **19a** and converted it in two steps[19] into the antidepressant fluoxetine[20] (Scheme 5). This synthesis proceeds in only four steps from 3-phenyl-1-propanol.



Scheme 5. Synthesis of fluoxetine. a) 40% aqueous $MeNH_2$, THF, sealed flask, 65 °C, 3 h, 92%. b) 1. NaH, DMA, 0 °C to 95 °C, 1.5 h; 2. 4-chlorobenzotrifluoride, 105 °C, 2.5 h, 66%.

In summary, we have developed a remote hydroxylation that proceeds through radical translocation and oxidation to carbocation en route to alcohol products and demonstrated the utility of this method with the synthesis of fluoxetine. These transformations represent a step toward the development of a general radical–polar crossover methodology exploiting radical translocations and redox catalysis/initiation.

Keywords: C–H functionalization · hydroxylation · redox catalysis · remote functionalization · synthetic methods

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[1] a) T. Newhouse, P. S. Baran, *Angew. Chem. Int. Ed.* **2011**, *50*, 3362–3374; *Angew. Chem.* **2011**, *123*, 3422–3435; b) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115; *Angew. Chem.* **2009**, *121*, 5196–5217; c) M. C. White, *Science* **2012**, *335*, 807–809; d) A. A. Fokin, P. R. Schreiner, *Chem. Rev.* **2002**, *102*, 1551–1593; e) R. H. Crabtree, *J. Chem. Soc. Dalton Trans.* **2001**, 2437–2450; f) R. Jazzar, J. Hitce, A. Renaudat, J. Sofack-Kreutzer, O. Baudoin, *Chem. Eur. J.* **2010**, *16*, 2654–2672; g) Y. Ishii, S. Sakaguchi, T. Iwahama, *Adv. Synth. Catal.* **2001**, *343*, 393–427; h) R. Breslow, *Acc. Chem. Res.* **1980**, *13*, 170–177.

[2] T. Brückl, R. D. Baxter, Y. Ishihara, P. S. Baran, *Acc. Chem. Res.* **2012**, *45*, 826–839.

[3] a) A. W. Hofmann, *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 558–560; b) K. Löffler, C. Freytag, *Ber. Dtsch. Chem. Ges.* **1909**, *42*, 3427–3431; c) D. H. R. Barton, J. M. Beaton, L. E. Geller, M. M. Pechet, *J. Am. Chem. Soc.* **1960**, *82*, 2640–2641; d) D. H. R. Barton, J. M. Beaton, L. E. Geller, M. M. Pechet, *J. Am. Chem. Soc.* **1961**, *83*, 4076–4083; e) R. Breslow, S. W. Baldwin, *J. Am. Chem. Soc.* **1970**, *92*, 732–734; f) J. Brunckova, D. Crich, Q. Yao, *Tetrahedron Lett.* **1994**, *35*, 6619–6622; g) T. Cohen, K. W. Smith, M. D. Swerdloff, *J. Am. Chem. Soc.* **1971**, *93*, 4303–4304; h) V. Snieckus, J.-C. Cuevas, C. P. Sloan, H. Liu, D. P. Curran, *J. Am. Chem. Soc.* **1990**, *112*, 896–898; i) D. P. Curran, J. Xu, *J. Am. Chem. Soc.* **1996**, *118*, 3142–3147; j) G. Han, M. LaPorte, M. McIntosh, S. M. Weinreb, *J. Org. Chem.* **1996**, *61*, 9483–9493; k) G. Han, M. McIntosh, S. M. Weinreb, *Tetrahedron Lett.* **1994**, *35*, 5813–5816; l) J. A. Murphy, F. Rasheed, S. J. Roome, N. Lewis, *Chem. Commun.* **1996**, 737–738; m) K. Chen, J. M. Richter, P. S. Baran, *J. Am. Chem. Soc.* **2008**, *130*, 7247–7249; n) A.-F. Voica, A. Mendoza, W. R. Gutekunst, J. O. Fraga, P. S. Baran, *Nat. Chem.* **2012**, *4*, 629–635; o) M. Nechab, S. Mondal, M. Bertrand, *Chem. Eur. J.* **2014**, *20*, 16034–16059.

[4] a) B. D. Dangel, J. A. Johnson, D. Sames, *J. Am. Chem. Soc.* **2001**, *123*, 8149–8150; b) M. E. Harvey, D. G. Musaev, J. DuBois, *J. Am. Chem. Soc.* **2011**, *133*, 17207–17216; c) M. E. Harvey, J. L. Roizen, J. DuBois, *Acc. Chem. Res.* **2012**, *45*, 911–922; d) Z. Ren, F. Mo, G. Dong, *J. Am. Chem. Soc.* **2012**, *134*, 16991–16994; e) E. M. Simmons, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 17092; f) D.-H. Wang, M. Wasa, R. Giri, J.-Q. Yu, *J. Am. Chem. Soc.* **2008**, *130*, 7190; g) R. Giri, N. Maugel, B. M. Foxman, J.-Q. Yu, *Organometallics* **2008**, *27*, 1667–1670; h) J. A. Johnson, N. Li, D. Sames, *J. Am. Chem. Soc.* **2002**, *124*, 6900–6903; i) O. Baudoin, A. Herrbach, F. Guéritte, *Angew. Chem. Int. Ed.* **2003**, *42*, 5736–5740; *Angew. Chem.* **2003**, *115*, 5914–5918; j) E. Motti, M. Catellani, *Adv. Synth. Catal.* **2008**, *350*, 565–569; k) R. Breslow, Y. Huang, X. Zhang, J. Yang, *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 11156–11158; l) M. A. Bigi, S. A. Reed, M. C. White, *J. Am. Chem. Soc.* **2012**, *134*, 9721–9726; m) M. A. Bigi, S. A. Reed, M. C. White, *Nat. Chem.* **2011**, *3*, 218–222.

[5] M. Majek, A. J. von Wangelin, *Angew. Chem. Int. Ed.* **2015**, *54*, 2270–2274; *Angew. Chem.* **2015**, *127*, 2298–2302.

[6] J. C. Scaiano, L. C. Stewart, *J. Am. Chem. Soc.* **1983**, *105*, 3609–3614.

[7] a) D. D. M. Wayner, A. Houmam, *Acta Chem. Scand.* **1998**, *52*, 377–384; b) K. L. Rollick, J. K. Kochi, *J. Am. Chem. Soc.* **1982**, *104*, 1319–1330.

[8] a) J. Shanklin, E. B. Cahoon, *Annu. Rev. Plant Physiol. Plant Mol. Biol.* **1998**, *49*, 611–641; b) P. H. Buist, *Nat. Prod. Rep.* **2004**, *21*, 249–262.

[9] a) N. Bashir, J. A. Murphy, *Chem. Commun.* **2000**, 627–628; b) T. Koizumi, N. Bashir, A. R. Kennedy, J. A. Murphy, *J. Chem. Soc. Perkin Trans. 1* **1999**, 3637–3643; c) A. Martín, I. Perez-Martin, E. Suarez, *Org. Lett.* **2005**, *7*, 2027–2030; d) C. G.

Francisco, A. J. Herrera, E. Suarez, *J. Org. Chem.* **2003**, *68*, 1012 – 1017.
[10] a) M. Reckenthäler, A. G. Griesbeck, *Adv. Synth. Catal.* **2013**, *355*, 2727 – 2744; b) J. Hu, J. Wang, T. H. Nguyen, N. Zheng, *Beilstein J. Org. Chem.* **2013**, *9*, 1977 – 2001; c) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322 – 5363; d) D. P. Hari, B. König, *Angew. Chem. Int. Ed.* **2013**, *52*, 4734 – 4743; *Angew. Chem.* **2013**, *125*, 4832 – 4842; e) J. Xuan, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828 – 6838; *Angew. Chem.* **2012**, *124*, 6934 – 6944; f) J. W. Tucker, C. R. J. Stephenson, *J. Org. Chem.* **2012**, *77*, 1617 – 1622; g) F. Teplý, *Collect. Czech. Chem. Commun.* **2011**, *76*, 859 – 917; h) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102 – 113; i) H. Cano-Yelo, A. Deronzier, *J. Chem. Soc. Faraday Trans. 1* **1984**, *80*, 3011 – 3019.
[11] C. Galli, *Chem. Rev.* **1988**, *88*, 765 – 792.
[12] a) Z. Li, L. Song, C. Li, *J. Am. Chem. Soc.* **2013**, *135*, 4640 – 4643; b) L. R. Reddy, B. V. S. Reddy, E. J. Corey, *Org. Lett.* **2006**, *8*, 2819 – 2821.
[13] D. B. Kimball, M. M. Haley, *Angew. Chem. Int. Ed.* **2002**, *41*, 3338 – 3351; *Angew. Chem.* **2002**, *114*, 3484 – 3498.
[14] Additional optimization procedures are summarized in Table S1 in the Supporting Information.
[15] a) S. D. Verberne-Sutton, R. D. Quarels, X. Zhai, J. C. Garno, J. R. Ragains, *J. Am. Chem. Soc.* **2014**, *136*, 14438 – 14444; b) B. Sahoo, M. N. Hopkinson, F. Glorius, *J. Am. Chem. Soc.* **2013**, *135*, 5505 – 5508; c) D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc.* **2012**, *134*, 2958 – 2961; d) D. N. Primer, I. Karakaya, J. C. Tellis, G. A. Molander, *J. Am. Chem. Soc.* **2015**, *137*, 2195 – 2198; e) J. Zhao, C. Mück-Lichtenfeld, A. Studer, *Adv. Synth. Catal.* **2013**, *355*, 1098 – 1106.
[16] M. S. Lowry, J. I. Goldsmith, J. D. Slinker, R. Rohl, R. A. Pascal, Jr., G. G. Malliaras, S. Bernhard, *Chem. Mater.* **2005**, *17*, 5712 – 5719.
[17] Y. Bi, D. C. Neckers, *J. Photochem. Photobiol. A* **1993**, *74*, 221 – 230.
[18] S. Mizuta, S. Verhoog, K. M. Engle, T. Khotavivattana, M. O'Duill, K. Wheelhouse, G. Rassias, M. Médebielle, V. Gouverneur, *J. Am. Chem. Soc.* **2013**, *135*, 2505 – 2508.
[19] Y. Gao, K. B. Sharpless, *J. Org. Chem.* **1988**, *53*, 4081 – 4084.
[20] P. Benfield, R. C. Heel, S. P. Lewis, *Drugs* **1986**, *32*, 481 – 508.

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