Visible-Light-Induced Alkoxy Radicals Enable $\alpha$-C(sp$^3$)-H Bond Allylation

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HIGHLIGHTS
- 1,2-Hydrogen atom transfer (HAT) of alkoxy radical enables $\alpha$-C(sp$^3$)-H allylation
- $\alpha$-Carbonyl, $\alpha$-cyano, $\alpha$-trifluoromethyl, and benzylic C(sp$^3$)-H bonds are applicable
- Mechanistic and electron paramagnetic resonance (EPR) studies confirmed 1,2-HAT
- DFT calculations explained the methanol acceleration of alkoxy radical 1,2-HAT

R = carbonyl, CF$_3$, cyano, aryl; R' = allyl; phth = phthalimide

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Visible-Light-Induced Alkoxyl Radicals Enable $\alpha$-C(sp$^3$)-H Bond Allylation

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SUMMARY
The alkoxyl radical is an essential reactive intermediate in mechanistic studies and organic synthesis with hydrogen atom transfer (HAT) reactivity. However, compared with intramolecular 1,5-HAT or intermolecular HAT of alkoxyl radicals, the intramolecular 1,2-HAT reactivity has been limited to theoretical studies and rarely synthetically utilized. Here we report the first selective 1,2-HAT of alkoxyl radicals for $\alpha$-C(s$^3$)-H bond allylation of $\alpha$-carbonyl, $\alpha$-cyano, $\alpha$-trifluoromethyl, and benzyl N-alkoxylphthalimides. The mechanistic probing experiments, electron paramagnetic resonance (EPR) studies, and density functional theory (DFT) calculations confirmed the 1,2-HAT reactivity of alkoxyl radicals, and the use of protic solvents lowered the activation energy by up to 10.4 kcal/mol to facilitate the $\alpha$-C(s$^3$)-H allylation reaction.

INTRODUCTION
The selective inert C(sp$^3$)-H bond activation for new C-C bond formation is very desirable in organic synthesis (Chen et al., 2009; Lyons and Sanford, 2010; Frier et al., 2013; Gensch et al., 2016; Yi et al., 2017). The hydroxyl groups are ubiquitous in organic molecules, and the use of hydroxyl derivatives provides an effective tool to differentiate chemically indistinguishable C-H bonds (Holmes et al., 2018; Engle et al., 2012; Ren et al., 2012; Wappes et al., 2017; Espino et al., 2001; Simmons and Hartwig, 2012a; Chen et al., 2008, 2015; Karmel et al., 2018). The alkoxyl radical is an essential reactive intermediate in mechanistic studies and organic synthesis, and its highly reactive character enables unactivated C-H bond functionalization with the hydrogen atom transfer (HAT) reaction (Čeković, 2003, 2005; Hartung, 2001; Chiba and Chen, 2014; Lundgren et al., 2006; Salamone et al., 2011, 2012, 2013, 2014a, 2014b, 2016a, 2016b; Bietti and Salamone, 2014; Salamone and Bietti, 2015). When intramolecular $\delta$-C-H bonds are present within the molecule, the 1,5-HAT reaction of alkoxyl radicals preferentially occurs to abstract the $\delta$-C-H; otherwise, the intermolecular HAT reaction dominates (Scheme 1A) (Dorio and Houk, 1988; Robertson et al., 2001; Weavers, 2001; Burke et al., 1988; Petrovic et al., 2004; Zhu et al., 2009, 2015; Rueda-Becerril et al., 2011; Hu et al., 2018; Wu et al., 2018a, 2018b; Guan et al., 2018). In contrast, the intramolecular C-H abstraction at positions other than $\delta$-position by alkoxyl radicals has been less reported owing to the unfavorable transition states and high activation energies (Čeković, 2003, 2005; Hartung, 2001; Chiba and Chen, 2014). Currently, there are only a few reports on the 1,2-HAT reactivity of alkoxyl radicals in theoretical or biological studies, and the synthetic utilization of 1,2-HAT for new C-C bond formation remains elusive (Buszek et al., 2011; Elford and Roberts, 1996; Fernández-Ramos and Zgierski, 2002; Konya et al., 2000; Gilbert et al., 1976; Che et al., 2016, 2018). Here we report the first visible-light-induced $\alpha$-C(sp$^3$)-H allylation reaction enabled by the selective 1,2-HAT of alkoxyl radicals, which is facilitated by protic solvents and applicable to various $\alpha$-carbonyl, $\alpha$-cyano, $\alpha$-trifluoromethyl, and benzyl C(sp$^3$)-H bonds (Scheme 1B).

RESULTS AND DISCUSSION
Optimization of the Reaction Conditions
Our investigation was initiated by the serendipitous discovery with N-alkoxylphthalimide 1 as the alkoxyl radical precursor, which can be readily prepared from alcohols and are bench-stable (Scheme 2) (Zhu et al., 2009; Kim et al., 1998; Zhang et al., 2016, 2017; Wang et al., 2016; Ito et al., 2018; Han et al., 2019; Deng et al., 2019; Shi et al., 2019). Under the reaction conditions of fac-Ir(ppy)$_3$ and Hantzsch ester known to generate alkoxyl radicals (Zhang et al., 2016, 2017; Wang et al., 2016; Ito et al., 2018; Han et al., 2019; Deng et al., 2019; Shi et al., 2019), the ester-derived N-alkoxylphthalimide 1 gave no $\alpha$-C(sp$^3$)-H allylation adduct 3 with allyl sulfone 2 under blue LED irradiation. Instead, the $\alpha$-C(sp$^3$)-H allylation adduct 4 was observed in 41% yield, together with the hydrogenation adduct alcohol 5 in 52% yield (entry 1 in Table 1) (Zhang et al., 2016). These results were in sharp contrast with our previous observation on the reactivity of alkoxyl radicals under photocatalysis conditions (Zhang et al., 2016, 2017). We then tested the addition of
Acids or bases to the reaction and found the outcomes of the reaction were not significantly affected (entries 2–3). The further screen of different Hantzsch ester derivatives has little effect on the reaction (entries 4–6) (Chen et al., 2016). Significantly, the use of ethanol or methanol as solvents dramatically improved the \( \alpha\)-C(sp\(^3\))-H allylation adduct to 93%–97% yields (93% isolated yield, entries 7–8) and minimalized the hydrogenation adduct alcohol formations. The mixed protic solvents were also beneficial that the addition of methanol or water improved the reaction of dioxane from 41% to 52%–66% yields (entries 9–10) (see Tables S2 and S3).

Scheme 1. Selective C(sp\(^3\))-H Functionalization via Hydrogen Atom Transfer of Alkoxyl Radicals

(A) Alkoxyl radicals enable C(sp\(^3\))-H functionalization with intermolecular HAT, intramolecular 1,5-HAT (previous work) or 1,2-HAT (this work)

\[
\begin{align*}
R-O & \xrightarrow{\text{intermolecular HAT}} R-OH + R' \\
& \xrightarrow{\text{intramolecular HAT}} HO- \xrightarrow{1,5-HAT} HO-R'
\end{align*}
\]

(B) \( \alpha\)-C(sp\(^3\))-H functionalization via 1,2-HAT of alkoxyl radical by photoredox catalysis with Hantzsch ester (this work)

\[
\begin{align*}
\text{[Ir], blue LED, HE, MeOH} & \xrightarrow{\alpha\text{-C(sp}^3\text{)-H functionalization}} R = \text{carbonyl, aryl, cyano, CF}_3, \\
& \quad R' = \text{allyl} \\
\text{[Ir], HE, blue LED} & \xrightarrow{\text{alkoxyl radical 1,2-HAT reaction}} \uparrow \quad \text{C-C bond formation}
\end{align*}
\]

Scheme 2. 1,2-HAT Reaction of N-alkoxylphthalimide 1

\[
\begin{align*}
\text{fac-Ir(ppy)}_3 & \xrightarrow{\text{blue LED}} \text{Hantzsch ester} \\
\text{EtO}_2\text{C} & \xrightarrow{\text{Hantzsch ester}} \text{EtO}_2\text{C} \\
\text{CO}_2\text{Et} & \xrightarrow{\text{eq. 1}} \\
\end{align*}
\]
We next explored the scope of this 1,2-HAT reaction for other substrates (Scheme 3). The glycol-derived 6 without rings at the \( \alpha \)-C-H bonds afforded 7 in 89% yield, without the observation of the \( \alpha \)-C-H alkylation adducts. The benzyl ester 8 with the activated benzylic \( \alpha \)-C-H bonds gave the \( \alpha \)-C(sp\(^3\))-H allylation adduct 9 in 92% yield. The N-alkoxylphthalimides 10 and 12 provided 88% and 95% yields of \( \alpha \)-C-H allylation adducts, successfully, with the ketone or the free hydroxyl group unaffected. The N-alkoxylphthalimide 14 with the amide linkage provided the 1,2-HAT adduct 15 smoothly in 52% yield, together with 17% yield of hydrogenation adduct as the side product (See Figures S1–S26).

The 1,2-HAT reaction is also applicable to N-alkoxylphthalimides without the ester or amide linkages. The N-alkoxylphthalimide 16 with benzyl C(sp\(^3\))-H bonds gave the \( \alpha \)-C(sp\(^3\))-H allylation adduct in 66% yield (Scheme 3). The incorporation of electron-rich methoxyl group on the phenyl ring slightly improved the reaction to give 19 in 71% yield, whereas the electron-deficient fluorides decreased the reaction to give 21 in 52% yield. The \( \alpha \)- and \( \beta \)-substituted naphthalenes reacted nicely to give 23 and 25 in 68%–73% yields. The heterocyclic furans and thiophenes reacted to provide 27 and 29 in 71%–75% yields. The secondary-alcohol-derived N-alkoxylphthalimides 30 and 32 gave the corresponding tertiary homoallylic alcohols 31 and 33 in 51% and 53% yields, respectively (See Figures S27–S64).

This reaction is particularly valuable for the homoallylic alcohol synthesis when the corresponding aldehydes are inaccessible by the nucleophilic addition methods (Yamamoto and Asao, 1993; Yus et al., 2011). The cyano-substituted homoallylic alcohol 35 can be obtained from the stable N-alkoxylphthalimide 34 by 1,2-HAT reaction smoothly in 59% yield, and the corresponding formyl cyanide 36 is unstable and cannot be synthetically utilized (Scheme 4) (Lewis-Bevan et al., 1992). Similarly, the trifluoromethyl-substituted homoallylic alcohol 37 can be prepared from the stable N-alkoxylphthalimide 38 in 39% yield, whereas the trifluoromethyl aldehyde 39 is very unstable and volatile (Scheme 5) (Ishikawa et al., 1984; Loh and Li, 1999). We also tested a structurally complexed steroid derivative 40 with multiple tertiary and allylic C-H bonds, which are challenging substrates to differentiate the targeted \( \alpha \)-C-H bonds by intermolecular HAT reactions (Scheme 6) (Roberts, 1999; Chu and Rovis, 2018). Gratifyingly, the \( \alpha \)-C(sp\(^3\))-H alkylation adduct 41 was selectively obtained in 62% yield, leaving other six tertiary C-H and four allylic C-H bonds untouched (see Figures S65–S78).

**Mechanistic Investigations**

We next carried out mechanistic investigations (Scheme 7). The possible intermolecular hydrogen atom transfer pathway instead of the 1,2-HAT was first evaluated by crossover experiments (Schemes 7A and
Scheme 3. Substrate Scope of the 1,2-HAT Reactions
Reaction condition is in entry 8 in Table 1, and isolated yields are reported.
With N-alkoxylphthalimide 16 and a structurally similar alcohol 42, the reaction with allylsulfone 2 gave the exclusive homoallylic alcohol 17 from 16 in 69% yield, whereas the formation of 23 from 42 was not observed. This result together with the chemoselective $\alpha$-C(sp$^3$)-H allylation demonstrated in Scheme 6 excluded the intermolecular HAT reaction pathway. We then compared the 1,2-HAT with other potential reaction pathways of alkoxyl radicals in different N-alkoxylphthalimides (Scheme 7B). With benzyl alcohol-derived N-alkoxylphthalimide 43 bearing a pendant alkene at the $\delta$-position, the tetrahydrofuran 44 was obtained via the preferential 5-exo cyclization of alkoxyl radicals, whereas neither the $\alpha$-C(sp$^3$)-H allylation adduct nor the oxidized ketone adduct 45 was observed (Zlotorzynska and Sammis, 2011). With benzyl alcohol-derived N-alkoxylphthalimide 46 bearing activated $\delta$-C-H bonds, the $\alpha$-C(sp$^3$)-H allylation adduct 47 was observed in 36% yield, together with the $\delta$-C(sp$^3$)-H allylation adduct 48 in 15% yield (see Scheme S3 for details). These results confirmed the presence of alkoxyl radicals and suggested other alkoxyl radical reaction pathways may be favored over 1,2-HAT pathway in certain substrates (the KIE ($k_H/k_D$) with deuterated N-alkoxylphthalimide was measured to be 0.87, suggesting the cleavage of the C-H bond was not the rate-determining step, see Table S1, Scheme S2 and Simmons and Hartwig, 2012b) (see Figures S79–S96).

We further investigated the radical intermediates in the reaction by the electron paramagnetic resonance (EPR) measurements (EPR) using 5,5-dimethyl-pyrroline N-oxide (DMPO) 50 as the radical spin trap. Scheme 8 illustrates the EPR spectrum from the addition of DMPO to the reaction of N-alkoxylphthalimide 49 (see Schemes S11–S13). The spectrum can be fit as the admixture of a triplet of doublets ($a_H = 14.1$ G, $a_N = 9.6$ G) and a triplet of doublets ($a_H = 14.2$ G, $a_N = 19.7$ G) in dioxane. The first triplet of doublets is attributed to DMPO-trapped alkoxyl radical 51 (asterisk * signals in the left panel), and the second triplet of doublets is attributed to DMPO-trapped ketyl radical 52. However, only the ketyl radical trapping adduct 51 (right panel) could be observed in methanol. These results were consistent with the increased hydrogenation adduct from alkoxyl radicals in dioxane compared with in methanol, which indicated that the 1,2-HAT process of alkoxyl radicals to yield ketyl radicals was accelerated in methanol (the Stern-Volmer plots suggest the Hantzsch ester quenched the photoexcited fac-Ir(ppy)$_3$ more effectively than N-alkoxylphthalimides and allyl sulfones; see Schemes S4–S8 for details).

We then performed density functional theory (DFT) calculations to investigate the free energy profiles of the alkoxyl radical generation (Scheme 9A). From computational studies, the N-alkoxylphthalimide 1 first undergoes single electron reduction to generate the radical anion CP1. After protonation by the Hantzsch ester radical cation, the alkyl radical intermediate CP2 was formed with 5.8 kcal/mol endothermically (black line) (Azizi et al., 2015; McSkimming and Colbran, 2013; Zheng and You, 2012; Turovska et al., 2008; Zhu et al., 1999). The N-O bond was then homolytically cleaved to form the alkoxyl radical CP3 via the transition state TS1 with an activation energy of 18.8 kcal/mol. Alternatively, the radical anion CP1 may form the intermediate CP6 via the transition state TS3 with 39.5 kcal/mol of activation energy, and the following redox
fragmentation generates the ketoester CP7 (red line) (Qi and Chen, 2016). However, the prohibitively high 39.5 kcal/mol of activation energy of TS3 excludes it as the major reaction pathway, which is consistent with the experimental observation of the preferential formation of alkoxyl radicals in different substrates.

The methanol-assisted 1,2-HAT of alkoxyl radicals was next investigated by computational studies (Scheme 9B). The direct hydrogen atom transfer to form the ketyl radical CP5 was calculated to have 16.4 kcal/mol of activation energy in TS2. In contrast, the involvement of methanol dramatically affects the energy diagram with hydrogen bonds. With one molecule of methanol participation, a 3.5-kcal/mol decrease of activation energy can be obtained in TS5. Significantly, two methanol molecules reduce the activation energy by 10.4 kcal/mol to merely 6.0 kcal/mol in TS6 with multiple hydrogen bond formation, and three methanol molecules can lower the activation energy by 7.8 kcal/mol in TS7. From the computational studies mentioned above, the methanol facilitates the alkoxyl radical CP3 rearrangement to ketyl radical CP5 with hydrogen bonds, and an up to 10.4 kcal/mol decrease of activation energy can be obtained with the methanol assistance (the involvement of one methanol and one water molecule decreased the activation barrier to 6.9 kcal/mol; see Scheme S14. The α-C-H functionalization product distribution in different solvents is not only determined by the 1,2-HAT reactivity, but also affected by the alkoxyl radical generation) (see Tables S4, S5, S6, and S7).

With mechanistic experiments and DFT calculations mentioned above, we propose the reaction is initiated from the reductive quenching of the photoexcited Ir(III)* to Ir(II) by Hantzsch ester, and Ir(II) subsequently

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**Scheme 6. 1,2-HAT Reaction of N-alkoxylphthalimide 40**

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**Scheme 7. Mechanistic Investigations of the 1,2-HAT of Alkoxyl Radicals**

(A) The crossover experiment with N-alkoxylphthalimide 16 and alcohol 42. (B) The investigation of potential reaction pathways of alkoxyl radicals.
reduces the N-alkoxylphthalimides to the radical anion (Scheme 10). The radical anion undergoes proton transfer with Hantzsch ester radical cation and subsequent N-O bond cleavage to form the alkoxyl radical (Fukuzumi et al., 1983; Lackner et al., 2015; Pratsch et al., 2015; Taylor et al., 2018, and see Schemes S4–S10 for details). Two methanol molecules then assist the 1,2-HAT reaction with hydrogen bonds at the α-carbonyl, α-cyano, α-trifluoromethyl, or benzylic C(sp<sup>3</sup>)-H bonds to form ketyl radicals for new C-C bond formations (Poutsma, 2007; Nechab et al., 2014).

**Conclusions**

In conclusion, we have developed the first regioselective α-C(sp<sup>3</sup>)-H functionalization enabled by 1,2-HAT of alkoxyl radicals using photoredox catalysis. The 1,2-HAT of alkoxyl radicals was confirmed by various
Scheme 9. DFT Calculation of the 1,2-HAT of Alkoxyl Radicals
(A) The free energy profile of two reaction pathways of N-alkoxyphthalimides. (B) The free energy profile of methanol-assisted 1,2-HAT of alkoxyl radicals.
mechanistic investigations including EPR studies and was useful for the new C-C bond formation of \(\alpha\)-carboxyl, \(\alpha\)-cyano, \(\alpha\)-trifluoromethyl, and benzylic N-alkoxylphthalimides. The computational studies indicate the assistance of protic solvents significantly facilities the 1,2-HAT reaction of alkoxyl radicals for new C-C bond formations. Further investigations are ongoing to explore this new 1,2-HAT reactivity of alkoxyl radicals.

**Limitations of the Study**

The 1,2-HAT pathway is not always favored for alkoxyl radicals; other alkoxyl radical reaction pathways may complete over 1,2-HAT pathway in different substrates. The existence of the carbonyl intermediate cannot be completely excluded; however, it is not the main reaction pathway from the performed computational and experimental studies.

**METHODS**

All methods can be found in the accompanying Transparent Methods supplemental file.

**SUPPLEMENTAL INFORMATION**

Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.100755.

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**AUTHOR CONTRIBUTIONS**

J.Z., D.L., Y.L., and Y.C. designed the research, analyzed the data, and wrote the manuscript. J.Z., D.L., and Y.G. performed the experimental studies. S.L. performed the computational studies.

**DECLARATION OF INTERESTS**

The authors declare no competing interests.

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REFERENCES

Azizi, S., Ulrich, G., Guglielmino, M., le Calve, S., Haggin, J.P., Harriman, A., and Zessou, R. (2015). Photoinduced proton transfer promoted by peripheral subunits for some Hantzsch esters. J. Phys. Chem. A 119, 39–49.

Betti, M., and Salomone, M. (2014). Reaction pathways of alkoy radicals. The role of solvent effects on C–C bond fragmentation and hydrogen atom transfer reactions. Synlett 25, 1803–1816.

Burke, S.D., Silks, L.A., and Stickland, S.M.S. (1998). Remote functionalization and molecular modeling: observations relevant to the Barton and hypophoside reactions. Tetrahedron Lett. 29, 2761–2764.

Buszek, R.J., Sinha, A., and Francisco, J.S. (2011). The isomerization of methoxy radical: intramolecular hydrogen atom transfer mediated through acid catalysis. J. Am. Chem. Soc. 133, 2013–2015.

Čeković, Z. (2003). Reactions of α-carbon radicals generated by 1,5-hydrogen transfer to alkoy radicals. Tetrahedron 59, 8073–8090.

Čeković, Z. (2005). Reactions of carbon radicals generated by 1,5-transposition of reactive centers. J. Serb. Chem. Soc. 70, 287–318.

Che, C., Huang, Q., Zheng, H., and Zhu, G. (2016). Copper-catalyzed cascade annulation of unsaturated α-bromocarbonyls with enynals: a facile access to ketones from aldehydes. Chem. Sci. 7, 4134–4139.

Che, C., Qian, Z., Wu, M., Zhao, Y., and Zhu, G. (2018). Intermolecular oxidative radical addition to aromatic aldehydes: direct access to 1,4- and 1,5-diketones via silver-catalyzed ring-opening to aromatic aldehydes: direct access to 1,4- and 1,5-diketones via silver-catalyzed ring-opening acylation of cyclopropanols and cyclobutanols. J. Org. Chem. 82, 5665–5673.

Chen, K., Richter, J.J., and Baran, P.S. (2008). 1,3-Diol synthesis via controlled, radical-mediated C–H functionalization. J. Am. Chem. Soc. 130, 7247–7249.

Chen, X., Engle, K.M., Wang, D.H., and Yu, J.Q. (2009). Palladium(II)-catalyzed C–H activation/c–C cross-coupling reactions: versatility and practicality. Angew. Chem. Int. Ed. 48, 5094–5115.

Chen, Z., Wang, B., Zhang, J., Yu, W., Liu, Z., and Zhang, Y. (2015). Transition metal-catalyzed C–H bond functionalizations by the use of diverse directing groups. Org. Chem. Front. 2, 1107–1295.

Chen, W., Liu, Z., Tian, J., Li, J., Chen, X., and Li, G. (2016). Building congested ketone: substituted Hantzsch ester and nitrile as alkyllyation reagents in photoredox catalysis. J. Am. Chem. Soc. 138, 12312–12315.

Chiba, S., and Chen, H. (2014). sp2 C–H oxidation by remote α-radical shift with oxygen- and nitrogen-radicals: a recent update. Org. Biomol. Chem. 12, 4051–4060.

Chu, J.C.K., and Rovis, T. (2018). Complementary strategies for directed Csp3–H functionalization: a comparison of transition-metal-catalyzed activation, hydrogen atom transfer, and carbene/nitrile transfer. Angew. Chem. Int. Ed. 57, 62–101.

Deng, Y., Nguyen, M.D., Zou, Y., Houk, K.N., and Smith, A.B., III (2019). Generation of diethyl and divinylsiloxanes using photoredox catalysis: application in the total synthesis of the daneshsiropektallatone via radical relay chemistry. Org. Lett. 21, 1708–1712.

Dorigo, A.E., and Houk, K.N. (1988). The relationship between proximity and reactivity. An ab initio study of the flexibility of the OH–CH4 hydrogen abstraction transition state and a force-field model for the transition states of intramolecular hydrogen abstractions. J. Org. Chem. 53, 1650–1664.

Elford, P.E., and Roberts, B.P. (1996). EPR studies of the formation and transformation of isomeric radicals (C3H5SO). Rearrangement of the allyloxy radical in non-polar solvents involving a formal 1,2-hydrogen-atom shift promoted by alcohols. J. Chem. Soc. 2, 2247–2256.

Engle, K.M., Mei, T.S., Wasa, M., and Yu, J.Q. (2012). Weak coordination as a powerful means for developing broadly useful C–H functionalization reactions. Acc. Chem. Res. 45, 788–802.

Espino, C.G., Wehm, P.M., Chow, J., and Du Bois, J. (2001). Synthesis of 1,3-difunctionalized amine derivatives through selective C–H bond activation. J. Am. Chem. Soc. 123, 6935–6936.

Fernández-Ramos, A., and Zegers, M.Z. (2002). Theoretical study of the rate constants and kinetic isotope effects of the 1,2-hydrogen-atom shift of methoxyl and benzoxyl radicals assisted by water. J. Phys. Chem. A 106, 10578–10583.

Fukuzumi, S., Hironaka, K., and Tanaka, T. (1983). Photo reduction of alkyl halides by an NADH model compound. An electron-transfer chain mechanism. J. Am. Chem. Soc. 105, 4722–4727.

Gensch, T., Hopkinson, M.N., Glorius, F., and Wencel-Delord, J. (2016). Mild metal-catalyzed C–H activation: examples and concepts. Chem. Soc. Rev. 45, 2900–2936.

Gilbert, B.C., Holmes, R.G.G., Laue, H.A.H., and Lewis-Bevan, W., Gaston, R.D., Tyrrell, J., Stork, H., and Wencel-Delord, J. (2016). Reaction of singlet-excited 2,3-diazabicyclo[2.2.2]oct-2-ene and tert-butoxyl radicals with aryl-substituted benzozenulenes. J. Am. Chem. Soc. 122, 7518–7527.

Hackler, H.M., Quasdorf, K.W., Pratsch, G., and Overman, L.E. (2015). Fragment coupling and the construction of quaternary carbons using tertiary radicals generated from tert-alkyl N-alkoxyphthalimidy oxides by visible-light photocatalysis. J. Org. Chem. 80, 6012–6024.

Lewis-Bevan, W., Gaston, R.D., Tyrrell, J., Stork, W.D., and Salmon, G.L. (1992). Formyl cyanide: a stable species. Experimental and Theoretical studies. J. Am. Chem. Soc. 114, 1933–1938.

Loh, T.-P., and Li, X.-R. (1999). A simple and practical synthesis of α-tert-butylnatrium compounds in water. Tetrahedron 55, 5611–5622.

Lundgren, C.V., Koner, A.L., Tinkl, M., Pachol, U., and Nau, W.M. (2006). Reaction of singlet-excited 2,3-diazabicyclo[2.2.2]oct-2-ene and tert-butoxyl radicals with aryl-substituted benzozenulenes. J. Org. Chem. 71, 1977–1983.

Lyons, T.W., and Sanford, M.S. (2010). Palladium-catalyzed ligand-directed C–H functionalization reactions. Chem. Rev. 110, 1147–1169.

McSkimming, A., and Calborean, S.B. (2013). The coordination chemistry of organo-hydride donors: new prospects for efficient multi-electron reduction. Chem. Soc. Rev. 42, 5439–5488.

Nechab, M., and Mondal, S., Bertrand, M.P. (2014). 1,1-hydrogen-atom transfer (HAT) reactions in which n < 5: an updated inventory. Chem. Eur. J. 20, 16034–16059.

Petrovic, G., Saicic, L., Dosen-Micovic, L., and Čeković, Z. (2004). Stereoselective free radical
Hydrogen abstraction selectivity and the role of hydrogen bonding. J. Org. Chem. 79, 9009–9017.

Salamone, M., Amorati, R., Menichetti, S., Vigliancis, C., and Bietti, M. (2014a). Structural and medium effects on the reactions of the cumyloxy radical with intramolecular hydrogen bonded phenols. The interplay between hydrogen-bonding and acid-base interactions on the hydrogen atom transfer reactivity and selectivity. J. Org. Chem. 79, 6196–6205.

Salamone, M., Milan, M., DiLabio, G.A., and Bietti, M. (2014b). Absolute rate constants for hydrogen atom transfer from tertiary amides to the cumyloxy radical: evaluating the role of stereoelectronic effects. J. Org. Chem. 79, 7179–7184.

Salamone, M., Carbone, G., and Bietti, M. (2016a). Fine control over site and substrate selectivity in hydrogen atom transfer-mediated functionalization of aliphatic C-H bonds. J. Org. Chem. 81, 9269–9278.

Salamone, M., Mangiacapra, L., Carbone, G., and Bietti, M. (2016b). Hydrogen atom transfer from tertiary alkylamides to the cumyloxy radical. The role of substrate structure on alkali and alkaline metal ion induced C-H bond deactivation. Tetrahedron 72, 7757–7763.

Shi, J.-L., Wang, Z., Zhang, R., Wang, Y., and Wang, J. (2019). Visible-light-promoted ring-opening alkynylation, alkenylation, and allylation of cyclic hemiacetals through b-scission of alkoxyl radicals. Chem. Eur. J. 25, 8992–8995.

Simmons, E.M., and Hartwig, J.F. (2012a). Catalytic functionalization of unactivated sp3 C-H bonds via exo-directing groups: synthesis of chemically differentiated 1,2-diols. J. Am. Chem. Soc. 134, 16991–16994.

Simmons, E.M., and Hartwig, J.F. (2012b). On the role of substrate structure on alkali and alkaline metal hydride donors. Chem. Soc. Rev. 41, 6264–6267.

Singh, A.K., and Lei, A. (2017). Recent advances in radical C-H activation/radical cross-coupling. Chem. Rev. 117, 9016–9085.

Weavers, R.T. (2001). Laurenances: fenestranes with a twist. J. Org. Chem. 66, 6453–6461.
Supplemental Information

Visible-Light-Induced Alkoxy radicals Enable \( \alpha \)-C(sp\(^3\))-H Bond Allylation

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I. Spectra of New Compounds

Figure S1. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 1, related to Scheme 2.

Figure S2. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 1, related to Scheme 2.
Figure S3. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 4, related to Scheme 2.

Figure S4. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 4, related to Scheme 2.
Figure S5. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 5, related to Scheme 2.

Figure S6. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 5, related to Scheme 2.
Figure S7. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 6, related to Scheme 2.

Figure S8. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 6, related to Scheme 2.
**Figure S9.** $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 7, related to Scheme 2.

**Figure S10.** $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 7, related to Scheme 2.
Figure S11. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 8, related to Scheme 2.

Figure S12. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 8, related to Scheme 2.
Figure S13. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 9, related to Scheme 2.

Figure S14. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 9, related to Scheme 2.
Figure S15. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 10, related to Scheme 2.

Figure S16. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 10, related to Scheme 2.
Figure S17. $^1$H NMR (500 MHz, CDCl$3$) spectrum of compound 11, related to Scheme 2.

Figure S18. $^{13}$C NMR (126 MHz, CDCl$3$) spectrum of compound 11, related to Scheme 2.
Figure S19. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 12, related to Scheme 2.

Figure S20. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 12, related to Scheme 2.
Figure S21. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 13, related to Scheme 2.

Figure S22. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 13, related to Scheme 2.
Figure S23. $^1$H NMR (500 MHz, CDCl₃) spectrum of compound 14, related to Scheme 2.

Figure S24. $^{13}$C NMR (126 MHz, CDCl₃) spectrum of compound 14, related to Scheme 2.
Figure S25. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 15, related to Scheme 2.

Figure S26. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 15, related to Scheme 2.
Figure S27. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 16, related to Scheme 2.

Figure S28. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 16, related to Scheme 2.
Figure S29. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 17, related to Scheme 2.

Figure S30. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 17, related to Scheme 2.
Figure S31. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 18, related to Scheme 2.

Figure S32. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 18, related to Scheme 2.
Figure S33. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 19, related to Scheme 2.

Figure S34. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 19, related to Scheme 2.
Figure S35. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 20, related to Scheme 2.

Figure S36. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 20, related to Scheme 2.
Figure S37. $^{19}$F NMR (376 MHz, CDCl3) spectrum of compound 20, related to Scheme 2.
Figure S38. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 21, related to Scheme 2.

Figure S39. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 21, related to Scheme 2.
Figure S40. $^{19}$F NMR (376 MHz, CDCl₃) spectrum of compound 21, related to Scheme 2
Figure S41. $^1$H NMR (500 MHz, CDCl$3$) spectrum of compound 22, related to Scheme 2.

Figure S42. $^{13}$C NMR (126 MHz, CDCl$3$) spectrum of compound 22, related to Scheme 2.
Figure S43. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 23, related to Scheme 2.

Figure S44. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 23, related to Scheme 2.
Figure S45. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 24, related to Scheme 2.

Figure S46. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 24, related to Scheme 2.
Figure S47. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 25, related to Scheme 2.

Figure S48. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 25, related to Scheme 2.
Figure S49. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 26, related to Scheme 2.

Figure S50. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 26, related to Scheme 2.
Figure S51. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 27, related to Scheme 2.

Figure S52. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 27, related to Scheme 2.
Figure S53. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 28, related to Scheme 2.

Figure S54. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 28, related to Scheme 2.
Figure S55. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 29, related to Scheme 2.

Figure S56. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 29, related to Scheme 2.
Figure S57. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 30, related to Scheme 2.

Figure S58. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 30, related to Scheme 2.
Figure S59. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 31, related to Scheme 2.

Figure S60. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 31, related to Scheme 2.
Figure S61. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 32, related to Scheme 2.

Figure S62. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 32, related to Scheme 2.
Figure S63. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 33, related to Scheme 2.

Figure S64. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 33, related to Scheme 2.
Figure S65. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 34, related to Scheme 2.

Figure S66. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 34, related to Scheme 2.
Figure S67. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 35, related to Scheme 2.

Figure S68. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 36, related to Scheme 2.
Figure S69. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 37, related to Scheme 2.

Figure S70. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 37, related to Scheme 2.
Figure S71. $^{19}$F NMR (376 MHz, CDCl3) spectrum of compound 37, related to Scheme 2
Figure S72. 1H NMR (500 MHz, CDCl3) spectrum of compound 38, related to Scheme 2.

Figure S73. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 38, related to Scheme 2.
Figure S74. $^{19}\text{F NMR}$ (376 MHz, CDCl$_3$) spectrum of compound 38, related to Scheme 2.
Figure S75. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 40, related to Scheme 2.

Figure S76. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 40, related to Scheme 2.
Figure S77. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 41, related to Scheme 2.

Figure S78. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 41, related to Scheme 2.
Figure S79. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 43, related to Scheme 3.

Figure S80. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 43, related to Scheme 2.
Figure S81. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 44, related to Scheme 3.

Figure S82. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 44, related to Scheme 3.
Figure S83. $^1$H NMR (500 MHz, CDCl3) spectrum of compound 46, related to Scheme 3.

Figure S84. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound 46, related to Scheme 3.
Figure S85. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 47-ox, related to Scheme 3.

Figure S86. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 47-ox, related to Scheme 3.
Figure S87. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound 48-ox, related to Scheme 3.

Figure S88. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound 48-ox, related to Scheme 3.
Figure S89. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound D-1, related to Scheme 3.

Figure S90. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound D-1, related to Scheme 3.
Figure S91. $^1$H NMR (500 MHz, CDCl3) spectrum of compound A2, related to Scheme 2.

Figure S92. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound A2, related to Scheme 2.
Figure S93. $^1$H NMR (500 MHz, CDCl$_3$) spectrum of compound A5, related to Scheme 2.

Figure S94. $^{13}$C NMR (126 MHz, CDCl$_3$) spectrum of compound A5, related to Scheme 2.
Figure S95. $^1$H NMR (500 MHz, CDCl3) spectrum of compound A6, related to Scheme 3.

Figure S96. $^{13}$C NMR (126 MHz, CDCl3) spectrum of compound A6, related to Scheme 3.
II. Mechanistic Investigations

The Cross-Over Experiment

Scheme S1. The NMR spectra of the Cross-Over Experiment, Related to Scheme 3.

The allylation adduct 17 in 69% yield and no occurrence of 23 from crude NMR spectra.
KIE experiments

![Chemical reactions]

Table S1. The NMR Yield of the KIE Experiment, Related to Scheme 3.
Scheme S2. Deuterium labeling experiments, Related to Scheme 3.
The KIE value was calculated as \( K_H / K_D = 0.65 / 0.75 = 0.87 \), suggesting that the cleavage of the \( \alpha\)-C(sp\(^3\))-H bond was not the rate determining step.
1,2-HAT Competes with Other Alkoxy Radical Reaction Pathways

Scheme S3. 1,2-HAT Competes with 1,5-HAT, Related to Scheme 3.

| entry | conditions | conversion | NMR yield of 47 | NMR yield of 48 |
|-------|------------|------------|-----------------|-----------------|
| 1     | Entry 8, in table 1 | > 95 %     | 37 %            | 14 %            |
| 2     | Entry 1, in table 1 | > 95 %     | 28 %            | 53 %            |
Luminescence Quenching Experiments

Scheme S4. \( \text{fac-Ir(ppy)\textsubscript{3}} \) Emission Quenching by \( N \)-alkoxyphthalimide 1, Related to Scheme 6.

Scheme S5. \( \text{fac-Ir(ppy)\textsubscript{3}} \) Emission Quenching by Hantzsch Ester (HE), Related to Scheme 6.
Scheme S6. *fac*-Ir(ppy)$_3$ Emission Quenching by Allyl Sulfone 2, Related to Scheme 6.
Cyclic Voltammetry Data

Scheme S7. Cyclic Voltammogram of N-alkoxyphthalimide 1, Related to Scheme 6.

\[ E_{1/2}^{\text{red}} (1) = -1.37 \text{ V vs. SCE in CH}_3\text{CN} \]

Scheme S8. Cyclic Voltammogram of N-alkoxyphthalimide 16, Related to Scheme 6.

\[ E_{1/2}^{\text{red}} (1) = -1.40 \text{ V vs. SCE in CH}_3\text{CN} \]
The Quantum Yield Measurement

\[
\Phi = \frac{N_{\text{prod}}}{N_{\text{abs.-photon}}} = \frac{n_x}{n_p}
\]

Scheme S9. The Quantum Yield Measurement, Related to Scheme 6.
The quantum yield is calculated to be 1.96.
The On-Off-Light Experiments

Scheme S10. The On-off-light Experiments, Related to Scheme 6.
The results suggest the radical chain may exist, however the chain length is short.
Detailed Reaction Optimizations

![Chemical Reaction Diagram]

| entry | conditions | conversion | 4 yield (%) | 5 yield (%) |
|-------|------------|------------|-------------|-------------|
| 1     | HE, 1,4-dioxane | >95% | 41% | 52% |
| 2     | entry 1, 0.05 M | >95% | 36% | 60% |
| 3     | entry 1, 0.2 M | >95% | 49% | 48% |
| 4     | entry 1, CH$_3$CN | >95% | 37% | 56% |
| 5     | entry 1, DCM | >95% | 60% | 33% |
| 6     | entry 1, EtOH | >95% | 93% | 7% |
| 7     | entry 1, MeOH | >95% | 97% | <5% |
| 8     | entry 1, CHCl$_3$ | >95% | 66% | 25% |
| 9     | entry 7, 0.05 M | >95% | 89% | 11% |

*Reaction conditions: 1 (0.10 mmol, 1.0 equiv.), 2 (0.30 mmol, 3.0 equiv.), fac-Ir(ppy)$_3$ (0.001 mmol, 1%) and Hantzsch ester (0.15 mmol, 1.5 equiv.) in 1.0 mL solvent under nitrogen with 4 W blue LED irradiation at ambient temperature for 3 h, conversion was >95%, unless otherwise noted. *Conversion and yields were determined by $^1$H NMR analysis and isolated yields were in parentheses. *Hantzsch ester (HE)

Table S2. Detailed Reaction Optimizations, Related to Table 1.
The Effect of Water Addition for the Reaction

![Reaction Scheme]

| entry | conditions                  | conversion | 4 (%) | 5 (%) |
|-------|-----------------------------|------------|-------|-------|
| 1     | ultra dry MeOH              | >95%       | >95%  | <5%   |
| 2     | ultra dry MeOH : H₂O = 9:1  | >95%       | 93%   | <5%   |
| 3     | ultra dry MeOH : H₂O = 1:1  | >95%       | 89%   | 9%    |
| 4     | ultra dry 1,4-dioxane       | >95%       | 29%   | 67%   |
| 5     | ultra dry 1,4-dioxane : H₂O = 9:1 | >95% | 66% | 33% |
| 6     | ultra dry 1,4-dioxane : H₂O = 1:1 | >95% | 76% | 11% |

*aReaction conditions: 1 (0.10 mmol), 2 (0.30 mmol), HE (0.15 mmol) in 1.0 mL solvents under nitrogen with 4 W blue LED irradiation at ambient temperature.

*bConversions and yields were determined by ¹H NMR analysis.

Table S3. The Effect of Water Addition, Related to Table 1.
EPR studies

The ketyl radical addition adduct 52 was found in MeOH. Instrumental parameters: $\nu = 9.37$ GHz, modulation frequency = 100 kHz, modulation amplitude = 1.00 G, microwave power = 7.96 mW, conversion time = 58.59 ms, time constant = 0 ms, sweep time = 60 s. The hyperfine coupling constants determined after simulation correspond to an adduct DMPO-CH ($a_N = 14.9$ G and $a_{H\beta} = 21.1$ G, $g = 2.00538$). The simulated EPR signals were obtained by Xepr software.

![Scheme S11. EPR Spectrum of Spin Adducts in MeOH, Related to Scheme 4.](image)
The alkoxyl radical and the ketyl radical addition adducts 51 and 52 were found in dioxane. Instrumental parameters: $\nu = 9.37$ GHz, modulation frequency = 100 kHz, modulation amplitude = 1.00 G, microwave power = 0.50 mW, conversion time = 58.59 ms, time constant = 0 ms, sweep time = 60 s. The hyperfine coupling constants determined after simulation correspond to a mixture of adduct DMPO-OCH ($a_N = 14.1$ G and $a_{H\beta} = 9.6$ G, $g = 2.00585$) and adduct DMPO-CH ($a_N = 14.2$ G, and $a_{H\beta} = 19.7$ G, $g = 2.00573$). The asterisks peaks are assigned to the alkoxyl radical addition adduct 47. The simulated EPR signals were obtained by Xepr software.

Scheme S12. EPR Spectrum of Spin Adducts in Dioxane, Related to Scheme 4.
The alkyl radical addition adduct **43-adduct** was found. Instrumental parameters: $\nu = 9.37$ GHz, modulation frequency = 100 kHz, modulation amplitude = 1.00 G, microwave power = 7.96 mW, conversion time = 58.59 ms, time constant = 0 ms, sweep time = 60 s. The coupling constants of adduct DMPO-CH is $a_N = 14.3$ G and $a_{\text{HB}} = 20.1$ G.

![Scheme S13. EPR Spectrum of Spin Adduct in Dioxane, Related to Scheme 4.](image-url)
DFT Calculation

| Geometry | \( E_{(\text{elec-B3LYP})} \) \(^1\) | \( H_{(\text{corr-B3LYP})} \) \(^2\) | \( G_{(\text{corr-B3LYP})} \) \(^3\) | \( E_{(\text{solv-M11})} \) \(^4\) | IF \(^5\) |
|----------|-----------------|-----------------|-----------------|-----------------|-----------------|
| CP1      | -1203.234367    | 0.356076        | 0.279012        | -1203.054513    | -               |
| HE\(^+\) | -862.231455     | 0.330610        | 0.258334        | -862.095451     | -               |
| CP2      | -1203.749639    | 0.369532        | 0.291021        | -1203.493082    | -               |
| E\(^-\)  | -861.846557     | 0.316992        | 0.245785        | -861.647058     | -               |
| TS1      | -1203.725890    | 0.366709        | 0.287669        | -1203.459777    | -654.9          |
| CP3      | -690.707331     | 0.241721        | 0.184576        | -690.528852     | -               |
| CP4      | -513.047076     | 0.124823        | 0.083306        | -512.948779     | -               |
| TS2      | -690.660762     | 0.236711        | 0.179942        | -690.499607     | -2017.5         |
| CP5      | -690.748343     | 0.242768        | 0.186119        | -690.583403     | -               |
| TS3      | -1203.174837    | 0.352692        | 0.276452        | -1202.988998    | -338.5          |
| CP6      | -1203.206799    | 0.354285        | 0.277336        | -1203.016213    | -               |
| TS4      | -1203.198201    | 0.351380        | 0.275214        | -1202.994127    | -398.4          |
| CP7      | -690.167476     | 0.230970        | 0.174412        | -690.007959     | -               |
| CP8      | -513.070911     | 0.121791        | 0.079440        | -513.072304     | -               |
| MeOH     | -115.712204     | 0.055708        | 0.028753        | -115.704694     | -               |
| TS5      | -806.401221     | 0.294046        | 0.228819        | -806.230046     | -1206.9         |
| TS6      | -922.153016     | 0.352611        | 0.277625        | -921.965704     | -743.9          |
| TS7      | -1037.893693    | 0.410793        | 0.325078        | -1037.684964    | -752.6          |
| TS8      | -690.692319     | 0.240238        | 0.185178        | -690.522421     | -64.8           |
| CP9      | -690.700720     | 0.241164        | 0.185274        | -690.530673     | -               |
| TS9      | -690.690385     | 0.235426        | 0.179987        | -690.521347     | -1362.4         |
| CP10     | -690.718503     | 0.241179        | 0.183760        | -690.557158     | -               |

Table S4. B3LYP geometries for all the optimized compounds and transition states, Related to Scheme 5.

\(^1\)The electronic energy calculated by B3LYP in gas phase.
\(^2\)The thermal correction to enthalpy calculated by B3LYP in gas phase.
\(^3\)The thermal correction to Gibbs free energy calculated by B3LYP in gas phase.
\(^4\)The electronic energy calculated by M11 in methanol solvent.
\(^5\)The B3LYP calculated imaginary frequencies for the transition states.

Table S5. B3LYP and M11 absolute calculation energies, enthalpies, and free energies, Related to Scheme 5.

The Gibbs free energy profiles for the MeOH/H\(_2\)O-assisted 1,2-HAT reaction are shown in Scheme S14. The direct hydrogen atom transfer to form the ketyl radical...
CP5-1 was calculated to have 16.0 kcal/mol of activation barrier in TS2-1 (red line). With one molecule of H₂O assisted (blue line), the activation barrier of the hydrogen atom transfer transition state TS3-1 could be increased to be 16.2 kcal/mol. Significantly, one methanol and one H₂O molecules decrease the activation barrier to 6.9 kcal/mol in TS4-1 (black line), while two methanol and one H₂O molecules can lower the activation barrier to 9.4 kcal/mol in TS5-1 (purple line). The calculated results indicate that one methanol and one H₂O molecules decrease the activation barrier to merely 6.9 kcal/mol with multiple hydrogen bonds formation.

Scheme S14. Gibbs Free Energy Profiles for the MeOH/H₂O-assisted 1,2-HAT reaction, Related to Scheme 5.
| Geometry | $E_{(\text{elec-B3LYP})}^{1}$ | $H_{(\text{corr-B3LYP})}^{2}$ | $G_{(\text{corr-B3LYP})}^{3}$ | $E_{(\text{solv-M11})}^{4}$ | IF$^{5}$ |
|----------|--------------------------------|----------------------------|-----------------------------|-----------------------------|-----------|
| CP3-1    | -690.708645                   | 0.241817                  | 0.184734                    | -690.529933                 | -         |
| TS2-1    | -690.660762                   | 0.236711                  | 0.179942                    | -690.499607                 | -2017.5   |
| TS3-1    | -767.093055                   | 0.262944                  | 0.202253                    | -766.952305                 | -1363.3   |
| H$_2$O   | -76.407024                    | 0.024920                  | 0.002821                    | -76.433519                  | -         |
| TS4-1    | -882.849357                   | 0.322367                  | 0.252417                    | -882.693235                 | -746.6    |
| MeOH     | -115.712204                   | 0.055708                  | 0.028753                    | -115.704694                 | -         |
| TS5-1    | -998.589743                   | 0.380337                  | 0.299903                    | -998.412740                 | -748.4    |
| CP5-1    | -690.748343                   | 0.242768                  | 0.186119                    | -690.583403                 | -         |

Table S6 B3LYP and M11 absolute calculation energies, enthalpies, and free energies, Related to Scheme 5.

$^{1}$The electronic energy calculated by B3LYP in gas phase.
$^{2}$The thermal correction to enthalpy calculated by B3LYP in gas phase.
$^{3}$The thermal correction to Gibbs free energy calculated by B3LYP in gas phase.
$^{4}$The electronic energy calculated by M11 in methanol solvent.
$^{5}$The B3LYP calculated imaginary frequencies for the transition states.

Table S7. B3LYP geometries for all the optimized compounds and transition states, Related to Scheme 5.
III. Transparant Methods:

General Procedures

Unless otherwise noted, all reactions of substrates preparation were conducted in flame-dried glassware under a nitrogen atmosphere using anhydrous solvent passed through an activated alumina column (Innovative Technology). Commercially available anhydrous MeOH was treated by 4 Å MS. Commercially available reagents were used without further purification. Hantzsch ester (HE) was recrystallized from ethanol and 1,4-dioxane was distilled over sodium. Thin layer chromatography (TLC) was performed using Jiangyou TLC silica gel plates HSG F$_{254}$ and visualized using UV light, and potassium permanganate. Flash chromatography was performed on Lisure science EZ purification system using the Santai technologies silica gel cartridge. Preparative thin layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). Photochemical reactions were carried with 4.8 W blue LED (ZL-3036R) obtained from Beijing Jolly Lighting Engineering Co. Ltd. $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$, unless otherwise noted, on a Bruker AV-400 MHz or an Agilent 500 MHz spectrometer. Chemical shifts in $^1$H NMR spectra were reported in parts per million (ppm) on the δ scale from an internal standard of residual CDCl$_3$ (7.26 ppm). Data for $^1$H NMR were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in Hertz (Hz) and integration. Data for $^{13}$C NMR spectra were reported in terms of chemical shift in ppm from the central peak of CDCl$_3$ (77.16 ppm). IR spectra were recorded on a Thermo Scientific Nicolet 380 FT-IR spectrometer. MS experiments were performed on a Bruker maXis 4G instrument for HRMS-ESI, an Agilent 5973N instrument for EI-MS, and a Waters Micromass GCT Premier instrument for HRMS-EI. Cyclic Voltammetry was performed on a CH Instruments Electrochemical Workstation model CHI600E.
Synthesis of \(N\text{-alkoxypythalimide Precursors}\)

\[
\text{Scheme S15. Synthetic Procedure, Related to Scheme 2}
\]

To a solution of 4-methylbenzyl bromide (1.11 g, 6.0 mmol) and DBU (0.76 g, 5.0 mmol) in benzene (12 mL) was stirred for 15 min at room temperature. The reaction mixture was slowly added glycolic acid (0.38 g, 5.0 mmol) and refluxed for 6 hours. The resulting reaction mixture was extracted with 1 M aqueous HCl (2 x 20 mL). The organic layers were washed with brine, dried over anhydrous Na\(_2\)SO\(_4\), and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (20\% hexanes/EtOAc) to give A1 as a colorless oil.

\[
\text{Scheme S16. Synthetic Procedure, Related to Scheme 2}
\]

To a solution of 4-methoxy-\(N\)-phenethylaniline (0.68 g, 3.0 mmol), glycolic acid (0.19 g, 2.5 mmol) and 1-hydroxybenzotriazole (0.68 g, 5.0 mmol) in DCM (10 mL) was added dicyclohexylcarbodiimide (0.78 g, 3.8 mmol) at 0 °C. The resulting suspension was filtered and the filtrate was concentrated in vacuo. The crude product was purified by column chromatography on silica gel (20\% hexanes/EtOAc) to give A2 as a colorless oil.
Synthesis of N-alkoxyphthalimide substrates

Method A

Scheme S17. Synthetic Procedure, Related to Scheme 2
To a solution of the alcohol (10.0 mmol), PPh₃ (3.15 g, 12.0 mmol), and N-hydroxyphthalimide (1.96 g, 12.0 mmol) in THF (30 mL) was added diisopropyl azodicarboxylate (2.4 mL, 12.0 mmol) over 10 min at room temperature. The resulting mixture was stirred for 3-24 h, taken up in EtOAc (20 mL), and washed with saturated NaHCO₃ (3 x 20 mL) and brine (2 x 30 mL). The organic layers were dried over anhydrous Na₂SO₄, concentrated in vacuo, and subjected to flash chromatography to afford the N-alkoxyphthalimides.

Method B

Scheme S18. Synthetic Procedure, Related to Scheme 2
To a solution of N-alkoxyphthalimides (33 mmol) in 110 mL DCM was slowly added TFA (37.0 mL, 495 mmol) at 0 °C. The reaction mixture was stirred at room temperature under N₂ for 2 hours. The reaction was then concentrated and azeotroped with DCM to afford N-alkoxyphthalimides and the crude product was directly subjected to the next reaction without further purification.
Method C

Scheme S19. Synthetic Procedure, Related to Scheme 2
To a solution of N-alkoxyphthalimides (1.5 mmol), alcohol (1.0 mmol) and DMAP (61.1 mg, 0.5 mmol) in 10 mL DCM was added N,N'-dicyclohexylcarbodiimide (0.31 g, 1.5 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and continued stirring at 25 °C overnight. The resulting suspension was filtered and the filtrate was concentrated in vacuo. Purification by column chromatography afforded the N-alkoxyphthalimides.

Method D

Scheme S20. Synthetic Procedure, Related to Scheme 2
To a solution of the alcohol (10 mmol) and Et3N (2.2 mL, 16 mmol) in CH2Cl2 (30 mL) was added methanesulfonyl chloride (0.93 mL, 12 mmol) dropwise over 5 min at 0 °C. The reaction mixture was then allowed to warm to ambient temperature and stirred for 1 h. It was then washed with brine (3 x 30 mL). The organic layer was dried over Na2SO4, the solvent was removed by rotary evaporation to provide a yellow oil. The crude mesylate and directly mixed with N-hydroxyphthalimide (2.61 g, 16.0 mmol) and diisopropylethylamine (3.5 mL, 20 mmol) in DMF (20 mL). The resulting reaction mixture was stirred at 70 °C for 3 h and allowed to cool to room
temperature. The mixture was then taken up in Et₂O (50 mL), washed with sat. NaHCO₃ solution (3 x 25 mL), and brine (50 mL). It was then dried over Na₂SO₄, concentrated in vacuo, purified by column chromatography to afford the N-alkoxyphthalimides.

2-((1,3-dioxoisindolin-2-yl)oxy)acetic acid (A3). Following the general method B, the reaction of tert-butyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (9.12 g, 33.0 mmol) afforded N-alkoxyphthalimides A3 as a white solid (7.49 g, 100% yield) and the crude product was directly subjected to the next reaction without further purification.

2-((1,3-dioxoisindolin-2-yl)oxy)acetic acid (A4). Following the general method B, the reaction of tert-butyl 2-((1,3-dioxoisindolin-2-yl)oxy)propanoate (6.89 g, 23.6 mmol) afforded N-alkoxyphthalimides A4 as a white solid (5.54 g, 100% yield) and the crude product was directly subjected to the next reaction without further purification.

2,3-Dihydro-1H-inden-2-yl 2-((1,3-dioxoisindolin-2-yl)oxy)propanoate (1). Following the general method C, the reaction of 2-indanol (1.34 g, 10.0 mmol) afforded N-alkoxyphthalimides 1 as a white solid.
2-Methoxyethyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (6). Following the general method C, the reaction of 2-methoxyethanol (0.23 g, 3.0 mmol) afforded N-alkoxyphthalimides 6 as a white solid.

4-Methylbenzyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (8). Following the general method D, the reaction of A1 (0.62 g, 3.5 mmol) afforded N-alkoxyphthalimides 8 as a white solid.

2-Oxopropyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (10). Following the general method C, the reaction of hydroxyacetone (0.15 g, 1.0 mmol) afforded N-alkoxyphthalimides 10 as a white solid.

2-Hydroxyethyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (12). Following the general method C, the reaction of ethylene glycol (0.16 g, 2.5 mmol) and N-alkoxyphthalimides 12 (0.83 g, 3.8 mmol) afforded N-alkoxyphthalimides 12 as a white solid.
2-((1,3-Dioxoisooindolin-2-yl)oxy)-N-(4-methoxyphenyl)-N-phenethylacetamide (14). Following the general method A, the reaction of A2 (0.43 g, 1.5 mmol) afforded N-alkoxyphthalimides 14 as a white solid.

2-((4-Methylbenzyl)oxy)isoindoline-1,3-dione (16). Following the general method A, the reaction of 4-methylbenzyl alcohol (1.22 g, 10.0 mmol) afforded N-alkoxyphthalimides 16 as a white solid.

2-((4-Methoxybenzyl)oxy)isoindoline-1,3-dione (18). Following the general method A, the reaction of 4-methoxybenzyl alcohol (1.38 g, 10.0 mmol) afforded N-alkoxyphthalimides 18 as a white solid.

2-(4-fluorobenzyl)oxyisoindoline-1,3-dione (20). Following the general method A, the reaction of 4-fluorobenzyl alcohol (1.26 g, 10.0 mmol) afforded N-alkoxyphthalimides 20 as a white solid.
\textbf{2-(Naphthalen-2-ylmethoxy)isoindoline-1,3-dione (22).} Following the general method A, the reaction of 2-naphthalenemethanol (0.40 g, 2.6 mmol) afforded \( N \)-alkoxyphthalimides 22 as a white solid.

\textbf{2-(Naphthalen-1-ylmethoxy)isoindoline-1,3-dione (24).} Following the general method A, the reaction of 1-naphthalenemethanol (0.79 g, 5.0 mmol) afforded \( N \)-alkoxyphthalimides 24 as a white solid.

\textbf{2-(Furan-2-ylmethoxy)isoindoline-1,3-dione (26).} Following the general method A, the reaction of furfuryl alcohol (0.98 g, 10.0 mmol) afforded \( N \)-alkoxyphthalimides 26 as a white solid.

\textbf{2-(Thiophen-2-ylmethoxy)isoindoline-1,3-dione (28).} Following the general method A, the reaction of 2-thiophenemethanol (1.14 g, 10.0 mmol) afforded \( N \)-alkoxyphthalimides 28 as a white solid.
Benzyl 2-((1,3-dioxoisindolin-2-yl)oxy)propanoate (30). Following the general method A, the reaction of benzyl 2-hydroxypropanoate (0.53 g, 3.0 mmol) afforded N-alkoxyphthalimides 30 as a white solid.

2-(1-(thiophen-2-yl)ethoxy)isoindoline-1,3-dione (32). Following the general method A, the reaction of 1-(thiophen-2-yl)ethan-1-ol (1.28 g, 10.0 mmol) afforded N-alkoxyphthalimides 32 as a white solid.

Scheme S21. Synthetic Procedure, Related to Scheme 2

To a solution of the N-hydroxyphthalimide (1.63 g, 10.0 mmol) in DMF (10 mL) was added Et$_3$N (3.1 mL, 22.0 mmol) and bromoacetonitrile (1.44 g, 12.0 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred overnight. The mixture was then taken up in EtOAc (100 mL), washed with H$_2$O (3 x 30 mL), and brine (30 mL). It was then dried over Na$_2$SO$_4$, concentrated in vacuo, purified by column chromatography to afford 34 as a white solid.
(3S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-(6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (40). Following the general method C, the reaction of cholesterol (0.77 g, 2.0 mmol) afforded N-alkoxyphthalimides 40 as a white solid.

2-((1-Phenylpent-4-en-1-yl)oxy)isoindoline-1,3-dione (43). Following the general method A, the reaction of 1-phenylpent-4-en-1-ol (1.26 g, 8.0 mmol) afforded N-alkoxyphthalimides 43 as a white solid.

2-(2,2,2-trifluoroethoxy)isoindoline-1,3-dione(37). Following the general method D, the reaction of 2,2,2-trifluoroethan-1-ol (1.00 g, 10.0 mmol) afforded N-alkoxyphthalimides 37 as a white solid.
2-((2-(methoxymethyl)benzyl)oxy)isoindoline-1,3-dione. (46) Following the general method A, the reaction of (2-(methoxymethyl)phenyl)methanol (1.52 g, 10.0 mmol) afforded N-alkoxyphthalimides 46 as a white solid.
**Synthesis of Allyl Sulfones**

![Chemical Reaction](image)

**Scheme S22. Synthetic Procedure, Related to Scheme 2**

**Ethyl-2-((phenylsulfonyl)methyl)acrylate (2).** To a solution of B2 (1.99 g, 10.4 mmol) in dry methanol (25 mL) was added sodium phenylsulfinate (2.50 g, 15.2 mmol). After 2.5 h of reflux, the mixture was concentrated under reduced pressure, the obtained residue was dissolved in EtOAc and the mixture was washed with water, brine, dried with Na₂SO₄, filtered and the filtrate was evaporated and purified by chromatography (50% EtOAc/hexanes) to give 2 as a viscous oil.

**Benzyl-2-((phenylsulfonyl)methyl)acrylate (2-a).** Following the above procedure, the reaction of benzylacrylate (3.24 g, 20.0 mmol) afforded 2-a as a white solid.
Procedure for Allylation

standard procedure for allylation:

A solution of N-alkoxyphthalimides (0.1 mmol, 1.0 equiv.), allyl sulfone (0.3 mmol, 3.0 equiv.) and Hantzsch ester (38.0 or 76.0 mg, 0.15 or 0.3 mmol, 1.5 or 3.0 equiv.) was placed in a 5 mL clear-colored glass vial. After 1.0 mL MeOH (bubbled with nitrogen gas for 30 minutes to remove oxygen) was added, the vial was sealed and exposed to 4W blue LED at room temperature with stirring for appropriate hours. The reaction mixture was concentrated and purified directly by column chromatography to afford the allylation adduct.

*The heating effect from LED irradiation conditions above is minimal. With 6-12 hours irradiation, the increase of temperature is less than 5°C.

![Scheme S23. Synthetic Procedure, Related to Scheme 2](image)
1-(2,3-Dihydro-1H-inden-2-yl) 5-ethyl 2-hydroxy-2-methyl-4-methylenepentanedioate (4). Following the standard procedure, the reaction of N-alkoxyphthalimides 1 (35.1 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 3 h afforded target product 4 as a colorless oil.

1-Benzyl 5-(2-methoxyethyl) 4-hydroxy-2-methylenepentanedioate (7). Following the standard procedure, the reaction of N-alkoxyphthalimides 6 (27.9 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 3 h afforded target product 7 as a light yellow oil.

1-Ethyl 5-(4-methylbenzyl) 4-hydroxy-2-methylenepentanedioate (9). Following the standard procedure, the reaction of N-alkoxyphthalimides 8 (32.5 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 3 h afforded target product 9 as a light yellow oil.

1-Benzyl 5-(2-oxopropyl) (S)-4-hydroxy-2-methylenepentanedioate (11).
Following the standard procedure, the reaction of \( N \)-alkoxyphthalimides 10 (27.7 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 3 h afforded target product 11 as a light yellow oil.

\[
\begin{align*}
&\text{HO-} \quad \text{O-} \\
&\quad \text{OH} \\
&\quad \text{COOBn}
\end{align*}
\]

1-Benzyl 5-(2-hydroxyethyl) 4-hydroxy-2-methylenepentanedioate (13).

Following the standard procedure, the reaction of \( N \)-alkoxyphthalimides 12 (26.5 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 3 h afforded target product 13 as a light yellow oil.

\[
\begin{align*}
&\text{OMe} \\
&\text{N} \\
&\text{COOEt} \\
&\text{OH}
\end{align*}
\]

Ethyl 4-hydroxy-5-((4-methoxyphenyl)(phenethyl)amino)-2-methylene-5-oxopen-tanoate (15). Following the standard procedure, the reaction of \( N \)-alkoxyphthalimides 14 (43.0 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 3 h afforded target product 15 as a light yellow oil.

\[
\begin{align*}
&\text{COOEt} \\
&\text{OH}
\end{align*}
\]

Ethyl 4-hydroxy-2-methylene-4-(p-tolyl)butanoate (17). Following the standard procedure, the reaction of \( N \)-alkoxyphthalimides 16 (26.7 mg, 0.1 mmol), Hantzsch
ester (38.0 mg, 0.15 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 6 h afforded target product 17 as a light yellow oil.

**Benzyl 4-hydroxy-4-(4-methoxyphenyl)-2-methylenebutanoate (19).** Following the standard procedure, the reaction of $N$-alkoxyphthalimides 18 (28.3 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 6 h afforded target product 19 as a light yellow oil.

**Ethyl 4-(4-fluorophenyl)-4-hydroxy-2-methylenebutanoate (21).** Following the standard procedure, the reaction of $N$-alkoxyphthalimides 20 (27.1 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 3 h afforded target product 21 as a light yellow oil.

**Ethyl 4-hydroxy-2-methylene-4-(naphthalen-2-yl)butanoate (23).** Following the standard procedure, the reaction of $N$-alkoxyphthalimides 22 (30.3 mg, 0.1 mmol), Hantzsch ester (76.0 mg, 0.3 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 12 h afforded target product 23 as a light yellow oil.
Ethyl 4-hydroxy-2-methylene-4-(naphthalen-1-yl)butanoate (25). Following the standard procedure, the reaction of N-alkoxyphthalimides 24 (30.3 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 6 h afforded target product 25 as a light yellow oil.

Ethyl 4-(furan-2-yl)-4-hydroxy-2-methylenebutanoate (27). Following the standard procedure, the reaction of N-alkoxyphthalimides 26 (24.3 mg, 0.1 mmol), Hantzsch ester (76.0 mg, 0.3 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 12 h afforded target product 27 as a light yellow oil.

Ethyl 4-hydroxy-2-methylene-4-(thiophen-2-yl)butanoate (29). Following the standard procedure, the reaction of N-alkoxyphthalimides 28 (25.9 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2 (76.2 mg, 0.3 mmol) in 1 mL MeOH for 6 h afforded target product 29 as a light yellow oil.
Dibenzyl 2-hydroxy-2-methyl-4-methylenepentanedioate (31). Following the standard procedure, the reaction of \(N\)-alkoxyphthalimides 30 (32.5 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 3 h afforded target product 31 as a colourless oil.

\[
\text{Benzy1 4-hydroxy-2-methylene-4-(thiophen-2-yl)pentanoate (33). Following the standard procedure, the reaction of } N\text{-alkoxyphthalimides 32 (27.3 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 12 h afforded target product 33 as a colourless oil.}
\]

\[
\text{Benzy1 4-cyano-4-hydroxy-2-methylenebutanoate (35). Following the standard procedure, the reaction of } N\text{-alkoxyphthalimides 34 (20.2 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 6 h afforded target product 35 as a light yellow oil.}
\]

\[
\text{benzy1 5,5,5-trifluoro-4-hydroxy-2-methylenepentanoate (38). Following the standard procedure, the reaction of } N\text{-alkoxyphthalimides 37 (25.4 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 6 h afforded target product 38 as a colourless oil.}
\]
1-Benzyl 5-((3S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-(6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl) 4-hydroxy-2-methylenepentanedioate (41). Following the standard procedure, the reaction of N-alkoxyphthalimides 40 (58.9 mg, 0.1 mmol), Hantzsch ester (38.0 mg, 0.15 mmol) and allyl sulfone 2-a (94.8 mg, 0.3 mmol) in 1 mL MeOH for 12 h afforded target product 41 as a colourless oil.
**Procedure for the Cross-Over Experiment**

Following the standard procedure for allylations, the reaction of **16** (26.7 mg, 0.1 mmol), **42** (15.8 mg, 0.1 mmol) and allyl sulfone **2** (76.2 mg, 0.3 mmol) for 6 h.

\[
\begin{align*}
\text{16} & \quad + \quad \text{EtO}_2\text{C} - \text{SO}_2\text{Ph} \\
\text{42} & \quad \xrightarrow{\text{entry 8, in Table 1}} \quad \text{17, 69\% yield} \quad + \quad \text{23, not observed}
\end{align*}
\]

**Scheme S24. Cross-Over Experiment, Related to Scheme 3**
Procedure for the KIE experiments

A solution of $N$-alkoxyphthalimides 1/ D-1 (0.3 mmol, 1.0 equiv.), allyl sulfone 2 (0.9 mmol, 3.0 equiv.), Hantzsch ester (0.45 mmol, 1.5 equiv.) and 1,3,5-trimethoxybenzene (0.3 mmol, 1.0 equiv.) was placed in an 8 mL clear-colored glass vial. After 3.0 mL MeOH was added, the vial was sealed and exposed to 4W blue LED at room temperature with stirring. The reaction mixture was tested at different time points by $^1$H-NMR.

Scheme S25. KIE experiments, Related to Scheme 3.
Procedure for the 1,2-HAT Competes with Other Alkoxy Radical Reaction Pathways

Following the standard procedure without the addition of allyl sulfone, the reaction of 42 (29.5 mg, 0.1 mmol) and Hantzsch ester (0.30 mmol, 3.0 equiv.) in 1 mL 1,4-dioxane for 12 h.

Scheme S26. 1,2-HAT Competition Experiments, Related to Scheme 3.
Following the standard procedure, the reaction of 46 (29.7 mg, 0.1 mmol) and Hantzsch ester (0.30 mmol, 3.0 equiv.) in 1 mL MeOH for 6 h afforded an unseparable mixture of 47 and 48 as a colorless oil after flash chromatography (90\% hexanes : 10\% EtOAc). Then the mixture of X and X was dissolved in 2 mL DCM and treated with Dess-Martin Periodinane (0.2 mmol, 2.0 equiv.) at room temperature for 3 hours. The saturated Na$_2$S$_2$O$_3$ aqueous solution was then added to quench the reaction, after which the mixture was washed with brine, dried over Na$_2$SO$_4$, and concentrated in vacuo. The crude product was purified by preparative thin layer chromatography (75\% hexanes : 25\% EtOAc).

Scheme S27. 1,2-HAT Competition Experiments, Related to Scheme 3.
Procedure for the Luminescence Quenching Experiments

Emission intensities were recorded using Microplate Accessory 5JO-0139 spectrometer for all experiments. All fac-Ir(ppy)$_3$ solutions were excited at 320 nm and the emission intensity was collected at 518 nm. In a typical experiment, the 1,4-dioxane solution of fac-Ir(ppy)$_3$ (100 μM) was added the appropriate amount of quencher in a screw-top 1.0 cm quartz cuvette. After degassing with nitrogen for 10 min, the emission spectra of the samples were collected.

Procedure for the Cyclic Voltammetry

Cyclic Voltammetry was performed on a CH Instruments Electrochemical Workstation model CHI600E. A 0.001 M MeCN solution of the sample was prepared with 0.1 M Bu$_4$NPF$_6$ as the supporting electrolyte, using a glassy carbon working electrode, a Pt counter electrode, and a saturated calomel electrode reference electrode. Scan rate = 0.05 V/s, 2 sweep segments, a sample interval of 0.001 V.

Procedure for the Quantum Yield Measurement

$n_x$ is the amount of photochemical or photophysical events during irradiation, $n_p$ is the amount of photons absorbed by the reactant. $n_x$ was calculated by NMR analysis, $n_p$ was measured by Handy FZ-A Portable Radiometer/Photometer. 

$N$-alkoxyphthalimides 1 (0.10 mmol, 1.0 equiv.), allyl sulfone 2, fac-Ir(ppy)$_3$ (0.7 mg, 0.001 mmol, 0.01 equiv.) and Hantzsch eater (38.0 mg, 0.15 mmol, 1.5 equiv.) were placed in a 5 mL tube vial equipped with a magnetic stir bar. After 1.0 mL MeOH (treated by 4 Å MS) was added into the tube via a syringe, the reaction mixture was
exposed to blue LEDs at room temperature for 60 min and analyzed by $^1$H-NMR

**Produce for the On-Off-Light Experiments**

Following the standard procedure, to a solution of 1 (105.2 mg, 0.3 mmol), 2 (232.2 mg, 0.9 mmol), fac-Ir(ppy)$_3$ (1.9 mg, 0.003 mmol), and HE (113.8 mg, 0.45 mmol) in MeOH (3 mL). The reaction mixture was stirred at 25 °C using 4W blue LED with on-off-light. 500 μL of the reaction mixture aliquot was collected at different points and concentrated in vacuo. The $^1$H NMR analysis was calculated using 1,3,5-Trimethoxybenzene as the internal standard.

**Proceduce for EPR studies**

EPR experiments were performed on a Bruker E500 CW-EPR spectrometer at 298 K.
A solution of N-alkoxyphthalimides 45 (0.1 mmol, 1.0 equiv.), Hantzsch ester (38.0 mg, 0.15 mmol, 1.5 equiv.) and DMPO 46 (5,5-dimethyl-pyrroline N-oxide) (13 μL 0.12 mmol, 1.2 equiv.) was placed in a 5 mL clear-colored glass vial. After 1.0 mL MeOH or dioxane (bubbled with nitrogen gas for 30 seconds to remove oxygen) was added, the vial was sealed and exposed to 4W blue LED at room temperature with stirring for 45 min. The reaction mixture was diluted 10 times and transferred to a sealed melting point tube in the glove box. The EPR signals were subsequently tested.

**Computational methods for DFT caculations**

All DFT calculations were performed with the GAUSSIAN 09 series of programs. Density functional B3-LYP (Becke, 1993; Lee et al., 1988) with a standard 6-31G(d) basis set was used for geometry optimizations. Harmonic frequency calculations were
performed at all stationary points to confirm them as local minima or transition structures and to derive the thermochemical corrections for the enthalpies and free energies. The DFT method M11 functional was used to calculate the single point energies in methanol and 1,4-dioxane. (Peverati and Truhlar, 2011) The solvent effects were considered by single point calculations on the gas-phase stationary points with a continuum solvation model SMD. (Cossi et al., 1996; Cances et al., 1997; Barone et al., 1998; Marenich et al., 2009; Liu et al., 2018) The larger basis set 6-311+G(d) was used in the solvation single point calculations. The energies given in this report are the M11 calculated Gibbs free energies in methanol and 1,4-dioxane solvent.

Complete reference for Gaussian 09

Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adami, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; and Fox, D. J. Gaussian 09, revision D.01; Gaussian, Inc.: Wallingford, CT, 2013.
IV. Substrate And Product Characterizations

Characterizations of N-alkoxyphthalimide Precursors

4-Methylbenzyl 2-hydroxyacetate (A1).
Colorless oil (0.62 g, 57% yield): TLC Rf = 0.43 (EtOAc/hexanes = 1/5); ¹H NMR (400 MHz, CDCl₃) δ 7.26 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 5.19 (s, 2H), 4.18 (d, J = 5.3 Hz, 2H), 2.36 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 138.8, 132.2, 129.5, 128.8, 67.4, 60.8, 21.4.

2-Hydroxy-N-(4-methoxyphenyl)-N-phenethylacetamide (A2).
Colorless oil (0.43 g, 62% yield): TLC Rf = 0.27 (EtOAc/hexanes = 1/2); ¹H NMR (500 MHz, CDCl₃) δ 7.29 – 7.26 (m, 2H), 7.23 – 7.16 (m, 3H), 6.96 – 6.94 (m, 2H), 6.92 – 6.89 (m, 2H), 3.96 – 3.93 (m, 2H), 3.84 (s, 3H), 3.73 (d, J = 4.5 Hz, 2H), 3.39 (t, J = 4.5 Hz, 1H, -OH), 2.91 – 2.87 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 172.2, 159.8, 138.5, 132.3, 129.3, 129.0, 128.7, 126.6, 115.2, 60.7, 55.7, 51.4, 34.0; IR (KBr, thin film): 3436, 2933, 1655, 1512, 1386, 1250, 1030, 840, 743, 700 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C₁₇H₁₉NNaO₃ 308.1257, found 308.1258.
Characterizations of N-alkoxyphthalimide substrates

2,3-Dihydro-1H-inden-2-yl 2-((1,3-dioxoisindolin-2-yl)oxy)propanoate (1).
White solid (2.36 g, 67% yield): TLC Rf = 0.46 (EtOAc/hexanes = 1/3); 1H NMR (500 MHz, CDCl3) δ 7.80 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 7.20 – 7.14 (m, 4H), 5.62 – 5.58 (m, 1H), 4.84 (q, J = 6.8 Hz, 1H), 3.37 – 3.30 (m, 2H), 3.08 – 3.02 (m, 2H), 1.61 (d, J = 6.8 Hz, 3H); 13C NMR (125 MHz, CDCl3) δ 169.8, 163.3, 140.2, 140.2, 134.7, 128.9, 126.9, 124.7, 124.7, 123.8, 81.3, 76.8, 39.5, 39.4, 16.4; IR (KBr, thin film): 3073, 2943, 1792, 1737, 1467, 1375, 1188, 978, 747, 701 cm⁻¹; HRMS-ESI (m/z) [M+H⁺]: calcd. for C20H18NO5 352.1179, found 352.1188.

2-Methoxyethyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (6).
White solid (0.21 g, 27% yield): TLC Rf = 0.47 (EtOAc/hexanes = 1/4); 1H NMR (500 MHz, CDCl3) δ 7.85 (dd, J = 5.5, 3.1 Hz, 2H), 7.76 (dd, J = 5.5, 3.1 Hz, 2H), 4.87 (s, 2H), 4.36 – 4.34 (m, 2H), 3.63 – 3.61 (m, 2H), 3.35 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 167.1, 163.1, 134.8, 129.0, 123.9, 73.1, 70.1, 64.6, 59.1; IR (KBr, thin film): 2987, 1793, 1733, 1276, 1260, 1187, 1130, 1054, 764, 702 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C13H13NnaO6 302.0635, found 302.0642.
4-Methylbenzyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (8).

White solid (0.26 g, 24% yield over two steps): TLC Rf = 0.51 (EtOAc/hexanes = 1/4); 1H NMR (500 MHz, CDCl3) δ 7.84 (dd, J = 5.5, 3.1 Hz, 2H), 7.75 (dd, J = 5.5, 3.1 Hz, 2H), 7.25 (d, J = 7.8 Hz, 2H), 7.15 (d, J = 7.8 Hz, 2H), 5.19 (s, 2H), 4.84 (s, 2H), 2.34 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 166.9, 163.1, 138.7, 134.8, 132.0, 129.4, 129.0, 128.9, 123.9, 73.2, 67.4, 21.4; IR (KBr, thin film): 3032, 2946, 1755, 1732, 1466, 1378, 1187, 1054, 878, 700 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C18H15NNaO5 348.0842, found 348.0844.

2-Oxopropyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (10).

White solid (0.19 g, 68% yield): TLC Rf = 0.38 (EtOAc/hexanes = 1/1); 1H NMR (500 MHz, CDCl3) δ 7.86 (dd, J = 5.5, 3.1 Hz, 2H), 7.77 (dd, J = 5.5, 3.1 Hz, 2H), 4.96 (s, 2H), 4.79 (s, 2H), 2.17 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 200.2, 166.4, 163.1, 134.8, 128.9, 123.9, 72.9, 68.9, 26.1; IR (KBr, thin film): 3326, 2923, 1770, 1732, 1625, 1373, 1173, 1064, 877, 701 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C13H11NNaO6 300.0479, found 300.0484.

2-Hydroxyethyl 2-((1,3-dioxoisindolin-2-yl)oxy)acetate (12).

White solid (0.24 g, 24% yield): TLC Rf = 0.44 (EtOAc/hexanes = 1/1); 1H NMR (500 MHz, CDCl3) δ 7.86 (dd, J = 5.5, 3.1 Hz, 2H), 7.78 (dd, J = 5.5, 3.1 Hz, 2H),
4.86 (s, 2H), 4.35 – 4.33 (m, 2H), 3.89 – 3.87 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 167.5, 163.4, 135.0, 128.8, 124.0, 73.9, 67.6, 60.7; IR (KBr, thin film): 3505, 1732, 1375, 1276, 1187, 1082, 1050, 877, 750, 701 cm$^{-1}$; HRMS-ESI (m/z) [M+Na$^+$]: calcd. for C$_{12}$H$_{11}$NO$_6$ 288.0479, found 288.0478.

![Chemical Structure](image)

**2-((1,3-Dioxoisooindolin-2-yl)oxy)-N-(4-methoxyphenyl)-N-phenethyacetamide (14).**

White solid (0.46 g, 69% yield): TLC R$_f$ = 0.24 (EtOAc/hexanes = 1/2); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.82 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.73 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.24 (t, $J$ = 7.6 Hz, 2H), 7.19 – 7.12 (m, 5H), 6.91 (d, $J$ = 8.8 Hz, 2H), 4.51 (s, 2H), 3.91 – 3.88 (m, 2H), 3.83 (s, 3H), 2.91 – 2.88 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 165.8, 163.2, 159.6, 138.7, 134.6, 133.3, 129.5, 129.1, 129.0, 128.5, 126.4, 123.7, 115.2, 73.8, 55.6, 51.2, 33.7; IR (KBr, thin film): 3058, 2931, 1734, 1676, 1511, 1375, 1249, 1185, 877, 700 cm$^{-1}$; HRMS-ESI (m/z) [M+Na$^+$]: calcd. for C$_{25}$H$_{22}$N$_2$NaO$_5$ 453.1421, found 453.1423.

![Chemical Structure](image)

**2-((4-Methylbenzyl)oxy)isoindoline-1,3-dione (16).**

White solid (2.23 g, 83% yield): TLC R$_f$ = 0.43 (EtOAc/hexanes = 1/4); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.81 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.73 (dd, $J$ = 5.5, 3.1 Hz, 2H), 7.42 (d, $J$ = 8.0 Hz, 2H), 7.18 (d, $J$ = 8.0 Hz, 2H), 5.17 (s, 2H), 2.35 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 163.6, 139.4, 134.5, 130.8, 130.1, 129.4, 129.0, 123.6, 79.8, 21.5; IR (KBr, thin film): 3093, 1785, 1737, 1466, 1391, 1186, 1142, 975, 880, 699
cm\(^{-1}\); HRMS-ESI (m/z) [M+Na\(^+\): calcd. for C\(_{16}\)H\(_{13}\)NNaO\(_3\) 290.0788, found 290.0795.

\[
\begin{align*}
\text{MeO} & \quad \text{O} \quad \text{N} \quad \text{O} \\
& \quad \begin{array}{c}
\text{Ar} \\
\end{array}
\end{align*}
\]

**2-((4-Methoxybenzyl)oxy)isoindoline-1,3-dione (18).**
White solid (2.30 g, 81% yield): TLC R\(_f\) = 0.27 (EtOAc/hexanes = 1/4); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.80 (dd, \(J = 5.5, 3.1\) Hz, 2H), 7.72 (dd, \(J = 5.5, 3.1\) Hz, 2H), 7.47 – 7.44 (m, 2H), 6.90 – 6.87 (m, 2H), 5.15 (s, 2H), 3.80 (s, 3H); \(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 163.7, 160.6, 134.5, 131.8, 129.0, 126.0, 123.6, 114.1, 79.6, 55.4; IR (KBr, thin film): 2963, 1786, 1736, 1612, 1515, 1392, 1253, 1143, 879, 698 cm\(^{-1}\); HRMS-ESI (m/z) [M+Na\(^+\): calcd. for C\(_{16}\)H\(_{13}\)NNaO\(_3\) 306.0737, found 306.0744.

\[
\begin{align*}
& \quad \begin{array}{c}
\text{F} \\
\end{array}
\end{align*}
\]

**2-(4-fluorobenzyl)oxy)isoindoline-1,3-dione (20).**
White solid (0.85 g, 31% yield): TLC R\(_f\) = 0.57 (EtOAc/hexanes = 1/5); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.82 (dd, \(J = 5.5, 3.1\) Hz, 2H), 7.74 (dd, \(J = 5.5, 3.1\) Hz, 2H), 7.52 (dd, \(J = 8.6, 5.4\) Hz, 2H), 7.06 (t, \(J = 8.6\) Hz, 2H), 5.18 (s, 2H); \(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 164.5, 163.6, 162.5, 134.6, 132.1, 132.0, 129.8, 129.8, 128.9, 123.7, 115.8, 115.6, 79.1; \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -111.9 (m); IR (KBr, thin film): 3647, 3098, 1726, 1466, 1389, 1187, 1127, 975, 878, 696 cm\(^{-1}\); HRMS-ESI (m/z) [M+NH\(_4\)^+]: calcd. for C\(_{15}\)H\(_{14}\)FN\(_2\)O\(_3\) 289.0983, found 289.0987.

\[
\begin{align*}
& \quad \begin{array}{c}
\text{N} \\
\end{array}
\end{align*}
\]
2-(Naphthalen-2-ylmethoxy)isoindoline-1,3-dione (22).
White solid (1.33 g, 88% yield): TLC Rf = 0.42 (EtOAc/hexanes = 1/4); 1H NMR (500 MHz, CDCl3) δ 7.93 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.84 (dd, J = 6.5, 3.0 Hz, 2H), 7.79 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 – 7.70 (m, 3H), 7.52 – 7.46 (m, 2H), 5.38 (s, 2H); 13C NMR (125 MHz, CDCl3) δ 163.7, 134.6, 133.8, 133.1, 131.4, 129.5, 129.0, 128.6, 128.3, 127.9, 127.2, 126.8, 126.4, 123.6, 80.1; IR (KBr, thin film): 3093, 1739, 1466, 1383, 1275, 1261, 1139, 972, 750, 699 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C19H13NNaO3 326.0788, found 326.0793.

![Structure of 2-(Naphthalen-2-ylmethoxy)isoindoline-1,3-dione (22).]

2-(Naphthalen-1-ylmethoxy)isoindoline-1,3-dione (24).
White solid (0.83 g, 54% yield): TLC Rf = 0.36 (EtOAc/hexanes = 1/4); 1H NMR (500 MHz, CDCl3) δ 8.63 (dd, J = 8.5, 1.1 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.82 (dd, J = 5.5, 3.1 Hz, 2H), 7.72 (dd, J = 5.5, 3.1 Hz, 2H), 7.67 (ddd, J = 8.4, 6.8, 1.3 Hz, 1H), 7.61 (dd, J = 7.0, 1.1 Hz, 1H), 7.54 (ddd, J = 8.0, 6.8, 1.1 Hz, 1H), 7.43 (dd, J = 8.4, 6.8 Hz, 1H), 5.64 (s, 2H); 13C NMR (125 MHz, CDCl3) δ 163.7, 134.6, 133.8, 132.6, 130.7, 129.7, 129.6, 129.1, 128.6, 127.1, 126.3, 125.2, 124.6, 123.6, 78.2; IR (KBr, thin film): 3043, 2896, 1786, 1729, 1383, 1186, 1131, 971, 877, 699 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C19H13NNaO3 326.0788, found 326.0795.

![Structure of 2-(Naphthalen-1-ylmethoxy)isoindoline-1,3-dione (24).]

2-(Furan-2-ylmethoxy)isoindoline-1,3-dione (26).
White solid (0.70 g, 29% yield): TLC Rf = 0.50 (EtOAc/hexanes = 1/4); 1H NMR (500 MHz, CDCl3) δ 7.81 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 7.56 (dd, J = 8.4, 6.8 Hz, 1H), 7.52 (s, 1H), 5.62 (s, 2H); 13C NMR (125 MHz, CDCl3) δ 163.7, 134.6, 133.8, 132.6, 130.7, 129.7, 129.6, 129.1, 128.6, 127.1, 126.3, 125.2, 124.6, 123.6, 78.2; IR (KBr, thin film): 3043, 2896, 1786, 1729, 1383, 1186, 1131, 971, 877, 699 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C19H13NNaO3 326.0788, found 326.0795.

![Structure of 2-(Furan-2-ylmethoxy)isoindoline-1,3-dione (26).]
7.48 – 7.47 (m, 1H), 6.49 (dd, J = 3.3, 0.8 Hz, 1H), 6.35 (dd, J = 3.3, 1.8 Hz, 1H), 5.16 (s, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.4, 148.1, 144.6, 134.6, 128.9, 123.6, 113.3, 110.9, 70.4; IR (KBr, thin film): 3123, 1786, 1742, 1380, 1185, 1137, 976, 925, 759, 700 cm$^{-1}$; HRMS-ESI (m/z) [M+H$^+$]: calcd. for C$_{13}$H$_{10}$NO$_4$ 244.0604, found 244.0607.

![Chemical Structure](image)

2-(Thiophen-2-ylmethoxy)isoindoline-1,3-dione (28).

White solid (0.61 g, 23% yield): TLC $R_f$ = 0.49 (EtOAc/hexanes = 1/4); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.81 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 7.40 (dd, J = 5.1, 1.2 Hz, 1H), 7.20 – 7.19 (m, 1H), 6.99 (dd, J = 5.1, 3.5 Hz, 1H), 5.38 (s, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.6, 135.5, 134.6, 130.5, 129.0, 128.7, 127.2, 123.7, 73.1; IR (KBr, thin film): 3102, 3040, 1719, 1465, 1386, 1185, 1132, 1084, 875, 699 cm$^{-1}$; HRMS-ESI (m/z) [M+Na$^+$]: calcd. for C$_{13}$H$_{9}$NNaO$_3$S 282.0195, found 282.0202.

![Chemical Structure](image)

Benzyl 2-((1,3-dioxoisooindolin-2-yl)oxy)propanoate (30).

White solid (0.57 g, 38% yield): TLC $R_f$ = 0.35 (EtOAc/hexanes = 1/4); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.82 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 7.37 – 7.27 (m, 5H), 5.26 – 5.14 (m, 2H), 4.92 (q, J = 6.8 Hz, 1H), 1.66 (d, J = 6.8 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 169.7, 163.4, 135.2, 134.7, 129.0, 128.7, 128.6, 128.6, 123.8, 81.4, 67.5, 16.4; IR (KBr, thin film): 3446, 1734, 1620, 1384, 1187, 1080, 977, 877, 698, 664 cm$^{-1}$; HRMS-ESI (m/z) [M+H$^+$]: calcd. for C$_{18}$H$_{16}$NO$_5$ 326.1023, found 326.1021.
2-(1-(thiophen-2-yl)ethoxy)isoindoline-1,3-dione (32).
White solid (2.10 g, 77% yield): TLC Rf = 0.52 (EtOAc/hexanes = 1/4): 1H NMR (500 MHz, CDCl3) δ 7.78 (dd, J = 5.5, 3.1 Hz, 2H), 7.72 (dd, J = 5.5, 3.1 Hz, 2H), 7.35 (d, J = 5.0 Hz, 1H), 7.11 (d, J = 4.4 Hz, 1H), 6.93 (dd, J = 5.0, 3.6 Hz, 1H), 5.68 (q, J = 6.5 Hz, 1H), 1.85 (d, J = 6.5 Hz, 3H); 13C NMR (125 MHz, CDCl3) δ 163.8, 141.8, 134.5, 128.9, 127.9, 127.2, 126.7, 123.6, 80.0, 20.7; IR (KBr, thin film): 1789, 1831, 1466, 1373, 1186, 1128, 1081, 971, 878, 699 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C14H11NaO3S 296.0352, found 296.0357.

2-((1,3-Dioxoisindolin-2-yl)oxy)acetonitrile (34).
White solid (1.38 g, 68% yield): TLC Rf = 0.29 (EtOAc/hexanes = 1/2); 1H NMR (500 MHz, CDCl3) δ 7.90 (dd, J = 5.5, 3.1 Hz, 2H), 7.82 (dd, J = 5.5, 3.1 Hz, 2H), 4.96 (s, 2H); 13C NMR (125 MHz, CDCl3) δ 162.8, 135.3, 128.7, 124.3, 113.8, 62.0; IR (KBr, thin film): 2993, 1793, 1735, 1362, 1276, 1187, 1021, 876, 750, 701 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C10H6N2O3 225.0271, found 225.0278.
11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl
2-((1,3-dioxoisodolin-2-yl)oxy)acetate (40).

White solid (0.73 g, 62% yield): TLC R<sub>f</sub> = 0.48 (EtOAc/hexanes = 1/4): <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.86 (dd, <i>J</i> = 5.4, 3.1 Hz, 2H), 7.76 (dd, <i>J</i> = 5.4, 3.1 Hz, 2H), 5.37 (d, <i>J</i> = 4.2 Hz, 1H), 4.80 (s, 2H), 4.74 (ddt, <i>J</i> = 12.5, 8.0, 4.3 Hz, 1H), 2.36 (d, <i>J</i> = 7.8 Hz, 2H), 2.04 – 1.78 (m, 5H), 1.65 (ddd, <i>J</i> = 14.0, 8.7, 3.1 Hz, 1H), 1.49 (dtdd, <i>J</i> = 37.3, 16.2, 12.4, 10.3 Hz, 6H), 1.39 – 1.30 (m, 3H), 1.24 (ddd, <i>J</i> = 13.2, 9.8, 3.1 Hz, 1H), 1.20 – 1.03 (m, 7H), 1.03 – 0.94 (m, 6H), 0.91 (d, <i>J</i> = 6.5 Hz, 3H), 0.86 (dd, <i>J</i> = 6.6, 2.3 Hz, 6H), 0.67 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 166.5, 163.1, 139.3, 134.8, 129.0, 123.8, 123.2, 75.8, 73.3, 56.8, 56.3, 50.1, 42.4, 39.8, 39.7, 38.0, 37.0, 36.7, 36.3, 35.9, 32.0, 32.0, 28.4, 28.2, 27.7, 24.4, 24.0, 23.0, 22.7, 21.2, 19.4, 18.9, 12.0. IR (KBr, thin film): 3445, 2944, 1731, 1466, 1383, 1188, 1135, 1052, 877, 696 cm<sup>-1</sup>; HRMS-ESI (m/z) [M+Na]<sup>+</sup>: calcd. for C<sub>37</sub>H<sub>51</sub>NNaO<sub>5</sub> 612.3659, found 612.3665.

2-((1-Phenylpent-4-en-1-yl)oxy)isoindoline-1,3-dione (43).

White solid (1.53 g, 62% yield): TLC R<sub>f</sub> = 0.51 (EtOAc/hexanes = 1/4): <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.71 (dd, <i>J</i> = 5.3, 3.2 Hz, 2H), 7.66 (dd, <i>J</i> = 5.3, 3.2 Hz, 2H), 7.46 (d, <i>J</i> = 6.4 Hz, 2H), 7.31 (q, <i>J</i> = 5.9 Hz, 3H), 5.85 (ddt, <i>J</i> = 16.8, 10.2, 6.5 Hz, 1H), 5.34 (t, <i>J</i> = 6.9 Hz, 1H), 5.03 (dd, <i>J</i> = 26.7, 13.7 Hz, 2H), 2.29 (ddd, <i>J</i> = 13.1, 8.6, 6.7 Hz, 1H), 2.23 – 2.15 (m, 2H), 2.00 (dq, <i>J</i> = 14.8, 6.8 Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 163.8, 138.1, 137.5, 134.4, 129.1, 128.9, 128.4, 128.2, 123.4, 115.5, 88.7, 34.1, 29.9.
2-(2,2,2-trifluoroethoxy)isoindoline-1,3-dione (37).

White solid (1.64 g, 67% yield): TLC Rf = 0.53 (EtOAc/hexanes = 1/4); 1H NMR (500 MHz, CDCl3) δ 7.86 (dd, J = 5.5, 3.1 Hz, 2H), 7.78 (dd, J = 5.4, 3.1 Hz, 2H), 4.55 (q, J = 8.0 Hz, 2H). 13C NMR (126 MHz, CDCl3) δ 162.5, 134.9, 128.6, 123.9, 73.5, 73.2, 72.9, 72.7. 19F NMR (376 MHz, CDCl3) δ -73.94 (t, J = 8.0 Hz).

2-((2-(methoxymethyl)benzyl)oxy)isoindoline-1,3-dione (46).

White solid (1.40 g, 47% yield): TLC Rf = 0.43 (EtOAc/hexanes = 1/4); 1H NMR (500 MHz, CDCl3) δ 7.81 (dd, J = 5.5, 3.0 Hz, 2H), 7.73 (dd, J = 5.5, 3.1 Hz, 2H), 7.50 – 7.46 (m, 1H), 7.45 – 7.42 (m, 1H), 7.38 (td, J = 7.5, 1.3 Hz, 1H), 7.30 (td, J = 7.5, 1.4 Hz, 1H), 5.31 (s, 2H), 4.79 (s, 2H), 3.45 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 163.5 138.4 134.4, 131.9, 131.6 129.7 129.3, 128.9, 127.9, 123.6, 77.2 72.2, 58.4; IR (KBr, thin film): 1731, 1464, 1386, 1184, 1136, 1087, 928, 877, 753 cm⁻¹; HRMS-ESI (m/z) [M+NH4⁺]: calcd. for C17H16N2O4 315.1339, found 315.1339.
Characterization of Allyl Sulfones

**Ethyl-2-((phenylsulfonyl)methyl)acrylate (2).**

Viscous oil (1.94 g, 74% yield): TLC Rf = 0.50 (EtOAc/hexanes = 1/4); 1H NMR (400 MHz, CDCl3) δ 7.86 (d, J = 7.6 Hz, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.6 Hz, 2H), 6.51 (s, 1H), 5.92 (s, 1H), 4.17 (s, 2H), 4.01 (q, J = 7.2 Hz, 2H), 1.17 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 164.7, 138.4, 133.9, 133.3, 129.1, 129.0, 128.8, 61.5, 57.5, 14.0.

**Benzyl-2-((phenylsulfonyl)methyl)acrylate (2-a).**

White solid (1.3 g, 20% yield over three steps): TLC Rf = 0.49 (EtOAc/hexanes = 1/4); 1H NMR (400 MHz, CDCl3) δ 7.82 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 6.9 Hz, 1H), 7.46 (t, J = 7.9 Hz, 2H), 7.42 – 7.15 (m, 5H), 6.54 (s, 1H), 5.94 (s, 1H), 4.99 (s, 2H), 4.16 (s, 2H); 13C NMR (125 MHz, CDCl3) δ 164.7, 138.4, 135.4, 134.0, 133.9, 129.1, 129.0, 128.8, 128.7, 128.5, 128.3, 67.3, 57.6; IR (KBr, thin film) 2938, 1721, 1447, 1309, 1246, 1177, 1145, 1084, 967, 750, 689 cm⁻¹; HRMS-ESI (m/z) [M+H⁺]: calcd. for C17H17O4S 317.0841, found 317.0842.
Characterization of Allylation Product

1-(2,3-Dihydro-1H-inden-2-yl) 5-ethyl 2-hydroxy-2-methyl-4-methylenepentanedioate (4).

Colorless oil (29.5 mg, 93% yield) after flash chromatography (95% hexanes : 5% EtOAc): TLC Rf = 0.48 (EtOAc/hexanes = 1/4); 1H NMR (500 MHz, CDCl3) δ 7.24 – 7.18 (m, 4H), 6.22 (d, J = 1.5 Hz, 1H), 5.60 (d, J = 1.3 Hz, 1H), 5.60 – 5.50 (m, 1H), 4.17 (qd, J = 7.1, 5.6 Hz, 2H), 3.64 (s, 1H, -OH), 3.37 – 3.31 (m, 2H), 3.08 – 2.98 (m, 2H), 2.80 (dd, J = 14.0, 1.0 Hz, 1H), 2.64 (dd, J = 14.0, 1.0 Hz, 1H), 1.40 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); 13C NMR (125 MHz, CDCl3) δ 175.9, 167.9, 140.2, 140.2, 136.0, 128.9, 127.0, 127.0, 124.7, 74.3, 61.2, 41.8, 39.7, 39.5, 25.9, 14.2; IR (KBr, thin film): 3502, 2981, 1720, 1628, 1483, 1370, 1177, 1024, 965, 743 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C18H22NaO5 341.1359, found 341.1360.

1-Benzy1 5-(2-methoxyethyl) 4-hydroxy-2-methylenepentanedioate (7).

Light yellow oil (27.5 mg, 89% yield) after flash chromatography (95% DCM : 5% EtOAc): TLC Rf = 0.14 (EtOAc/DCM = 1/10); 1H NMR (500 MHz, CDCl3) δ 7.38 – 7.31 (m, 5H), 6.35 (d, J = 1.2 Hz, 1H), 5.77 (d, J = 1.2 Hz, 1H), 5.24 – 5.18 (m, 2H), 4.47 – 4.43 (m, 1H), 4.34 – 4.25 (m, 2H), 3.59 (t, J = 4.7 Hz, 2H), 3.36 (s, 3H), 3.03 (d, J = 6.5 Hz, 1H, -OH), 2.91 – 2.87 (m, 1H), 2.72 – 2.67 (m, 1H); 13C NMR (125 MHz, CDCl3) δ 174.3, 167.0, 135.9, 135.6, 129.1, 128.7, 128.4, 128.2, 70.3, 69.6,
66.9, 64.6, 59.1, 37.2; IR (KBr, thin film): 3492, 2930, 1720, 1630, 1456, 1272, 1140, 1039, 742, 699 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C₁₆H₂₀NaO₆ 331.1152, found 331.1158.

1-Ethyl 5-(4-methylbenzyl) 4-hydroxy-2-methylenepentanedioate (9).
Light yellow oil (26.8 mg, 92% yield) after preparative thin layer chromatography separation (75% hexanes : 12.5% acetone : 12.5% EtOAc): TLC Rₜ = 0.49 (DCM /acetone/hexanes = 1/1/6); ¹H NMR (500 MHz, CDCl₃) δ 7.25 (d, J = 7.8 Hz, 2H), 7.17 (d, J = 7.8 Hz, 2H), 6.24 (d, J = 1.3 Hz, 1H), 5.64 (d, J = 1.2 Hz, 1H), 5.19 – 5.12 (m, 2H), 4.44 – 4.40 (m, 1H), 4.20 (qd, J = 7.1, 2.4 Hz, 2H), 3.09 (d, J = 6.6 Hz, 1H, -OH), 2.87 – 2.83 (m, 1H), 2.67 – 2.62 (m, 1H), 2.36 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 174.2, 167.2, 138.6, 135.8, 132.3, 129.4, 128.7, 128.5, 69.8, 67.4, 61.2, 37.3, 21.3, 14.3; IR (KBr, thin film): 3487, 2981, 1716, 1632, 1447, 1206, 1148, 1098, 1031, 808 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C₁₆H₂₀NaO₆ 315.1203, found 315.1205.

1-Benzyl 5-(2-oxopropyl) (S)-4-hydroxy-2-methylenepentanedioate (11).
Light yellow oil (26.8 mg, 88% yield) after flash chromatography (95% DCM : 5% EtOAc): TLC Rₜ = 0.15 (EtOAc/DCM = 1/10); ¹H NMR (500 MHz, CDCl₃) δ 7.39 – 7.32 (m, 5H), 6.37 (d, J = 1.2 Hz, 1H), 5.82 (d, J = 1.1 Hz, 1H), 5.24 – 5.18 (m, 2H), 4.69 (d, J = 1.3 Hz, 2H), 4.56 – 4.52 (m, 1H), 3.06 (d, J = 6.4 Hz, 1H, -OH), 3.00 – 2.96 (m, 1H), 2.77 – 2.72 (m, 1H), 2.16 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 200.5, 173.5, 167.1, 135.9, 135.3, 129.6, 128.7, 128.4, 128.3, 69.7, 68.9, 67.0, 37.4, 26.2; IR
(KBr, thin film): 3473, 2929, 1719, 1423, 1274, 960, 742, 699 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C₁₆H₁₈NaO₆ 329.0996, found 329.0998.

1-Benzyl 5-(2-hydroxyethyl) 4-hydroxy-2-methylenepentanedioate (13).
Light yellow oil (27.9 mg, 95% yield) after flash chromatography (50% hexanes : 50% EtOAc): TLC Rf = 0.32 (EtOAc/hexanes = 2/1); ¹H NMR (500 MHz, CDCl₃) δ 7.38 – 7.33 (m, 5H), 6.36 (d, J = 1.3 Hz, 1H), 5.80 (d, J = 1.1 Hz, 1H), 5.21 (s, 2H), 4.44 (td, J = 6.5, 5.5 Hz, 1H), 4.35 – 4.30 (m, 1H), 4.21 – 4.17 (m, 1H), 3.79 (q, J = 4.9 Hz, 2H), 3.02 (d, J = 6.7 Hz, 1H, -OH), 2.87 – 2.79 (m, 2H), 2.32 (d, J = 5.9 Hz, 1H, -OH); ¹³C NMR (125 MHz, CDCl₃) δ 174.5, 167.3, 135.7, 135.1, 129.8, 128.8, 128.5, 128.3, 69.5, 67.6, 67.2, 60.9, 37.1; IR (KBr, thin film): 3400, 2954, 1719, 1632, 1455, 1210, 1145, 1083, 748, 699 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C₁₅H₁₈NaO₆ 317.0996, found 317.0996.

Ethyl 4-hydroxy-5-((4-methoxyphenyl)(phenethyl)amino)-2-methylene-5-oxopentanoate (15).
Light yellow oil (20.7 mg, 52% yield) after flash chromatography (70% hexanes : 30% EtOAc): TLC Rf = 0.29 (EtOAc/hexanes = 1/2); ¹H NMR (500 MHz, CDCl₃) δ 7.28 – 7.25 (m, 2H), 7.21 – 7.17 (m, 3H), 7.11 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 8.6 Hz, 2H), 6.20 (d, J = 1.5 Hz, 1H), 5.54 (d, J = 1.5 Hz, 1H), 4.25 – 4.21 (m, 1H), 4.11 – 4.04 (m, 2H), 4.02 – 3.98 (m, 1H), 3.84 (s, 3H), 3.78 – 3.73 (m, 1H), 3.31 (d, J = 9.3
Hz, 1H, -OH), 2.93 – 2.81 (m, 2H), 2.46 (dd, \(J = 13.9, 7.0\) Hz, 1H), 2.36 (dd, \(J = 13.9, 4.4\) Hz, 1H), 1.21 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 173.8, 166.8, 159.5, 138.7, 135.5, 133.6, 129.7, 129.0, 128.6, 128.4, 126.5, 115.0, 67.1, 60.8, 55.6, 52.0, 37.1, 33.8, 14.3; IR (KBr, thin film): 3417, 2934, 1714, 1650, 1512, 1455, 1249, 1145, 1029, 701 cm\(^{-1}\); HRMS-ESI (m/z) [M+Na\(^+\)]: calcd. for C\(_{23}\)H\(_{27}\)N\(_4\)O\(_5\) 420.1781, found 420.1786.

**Ethyl 4-hydroxy-2-methylene-4-(p-tolyl)butanoate (17).**

Light yellow oil (15.5 mg, 66% yield) after flash chromatography (90% hexanes : 10% acetone): TLC \(R_f = 0.36\) (EtOAc/hexanes = 1/3); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.25 (d, \(J = 7.8\) Hz, 2H), 7.15 (d, \(J = 7.8\) Hz, 2H), 6.24 (d, \(J = 1.5\) Hz, 1H), 5.60 (d, \(J = 1.3\) Hz, 1H), 4.86 (dt, \(J = 8.1, 3.7\) Hz, 1H), 4.23 (qd, \(J = 7.1, 1.0\) Hz, 2H), 2.80 – 2.76 (m, 1H), 2.69 – 2.65 (m, 1H), 2.54 (d, \(J = 3.5\) Hz, 1H, -OH), 2.34 (s, 3H), 1.32 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 167.8, 141.2, 137.4, 137.3, 129.2, 128.2, 125.8, 73.2, 61.2, 42.6, 21.3, 14.3; IR (KBr, thin film): 3486, 2981, 1713, 1631, 1370, 1305, 1192, 1144, 1028, 816 cm\(^{-1}\); HRMS-ESI (m/z) [M+Na\(^+\)]: calcd. for C\(_{14}\)H\(_{18}\)NaO\(_3\) 257.1148, found 257.1151.

**Benzyl 4-hydroxy-4-(4-methoxyphenyl)-2-methylenebutanoate (19).**

Light yellow oil (22.1 mg, 71% yield) after preparative thin layer chromatography separation (75% hexanes : 12.5% acetone : 12.5% DCM): TLC \(R_f = 0.30\) (DCM/acetone/hexanes = 1/1/6); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.38 – 7.33 (m, 5H), 7.27 – 7.24 (m, 2H), 6.87 – 6.84 (m, 2H), 6.28 (d, \(J = 1.4\) Hz, 1H), 5.62 (d, \(J = 1.2\) Hz,
1H), 5.21 (d, J = 3.2 Hz, 2H), 4.84 (dt, J = 8.0, 3.8 Hz, 1H), 3.79 (s, 3H), 2.79 – 2.75 (m, 1H), 2.72 – 2.67 (m, 1H), 2.43 (d, J = 3.3 Hz, 1H, -OH); 13C NMR (125 MHz, CDCl$_3$) δ 167.5, 159.2, 137.1, 136.2, 136.0, 128.7, 128.4, 128.3, 127.1, 113.9, 72.9, 66.9, 55.4, 42.6; IR (KBr, thin film): 3485, 2955, 1715, 1513, 1456, 1177, 1034, 832, 739, 698 cm$^{-1}$; HRMS-ESI (m/z) [M+Na$^+$]: calcd. for C$_{19}$H$_{20}$NaO$_4$ 335.1254, found 335.1258.

![Ethyl 4-(4-fluorophenyl)-4-hydroxy-2-methylenebutanoate (21).](image)

**Ethyl 4-(4-fluorophenyl)-4-hydroxy-2-methylenebutanoate (21).**

Light yellow oil (12.3 mg, 52% yield) after preparative thin layer chromatography separation (80% hexanes : 20% EtOAc): TLC R$_f$ = 0.52 (EtOAc/hexanes = 1/5); 1H NMR (500 MHz, CDCl$_3$) δ 7.36 – 7.30 (m, 2H), 7.06 – 6.99 (m, 2H), 6.23 (d, J = 1.5 Hz, 1H), 5.58 (q, J = 1.2 Hz, 1H), 4.88 (dd, J = 8.3, 4.0 Hz, 1H), 4.23 (qd, J = 7.1, 0.9 Hz, 2H), 2.81 (s, 1H), 2.76 (ddd, J = 13.9, 4.2, 1.1 Hz, 1H), 2.64 (ddd, J = 14.1, 8.4, 0.9 Hz, 1H), 1.32 (t, J = 7.2 Hz, 3H); 13C NMR (125 MHz, CDCl$_3$) δ 167.9, 163.2, 161.3, 139.8, 139.8, 137.1, 128.5, 127.5, 127.5, 115.4, 115.2, 72.7, 61.3, 42.8, 14.3; 19F NMR (376 MHz, CDCl$_3$) δ -115.4 (m); IR (KBr, thin film): 3081, 2955, 1730, 1574, 1451, 1189, 1065, 952, 750, 661 cm$^{-1}$; HRMS-ESI (m/z) [M-H$_2$O+H$^+$]: calcd. for C$_{13}$H$_{13}$FO$_2$ 221.0972, found 221.0976.

![Ethyl 4-hydroxy-2-methylene-4-(naphthalen-2-yl)butanoate (23).](image)

**Ethyl 4-hydroxy-2-methylene-4-(naphthalen-2-yl)butanoate (23).**

Light yellow oil (19.8 mg, 73% yield) after preparative thin layer chromatography separation (80% hexanes : 20% EtOAc): TLC R$_f$ = 0.36 (EtOAc/hexanes = 1/4); 1H
NMR (500 MHz, CDCl₃) δ 7.84 – 7.81 (m, 4H), 7.50 – 7.44 (m, 3H), 6.24 (d, J = 1.4 Hz, 1H), 5.61 (d, J = 1.2 Hz, 1H), 5.07 (dd, J = 8.4, 4.0 Hz, 1H), 4.23 (qd, J = 7.2, 1.1 Hz, 2H), 2.91 – 2.87 (m, 1H), 2.84 (s, 1H, -OH), 2.78 – 2.73 (m, 1H), 1.31 (t, J = 7.2 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 168.0, 141.5, 137.3, 133.4, 133.1, 128.4, 128.3, 128.1, 127.8, 126.2, 125.9, 124.5, 124.1, 73.5, 61.3, 42.7, 14.3; IR (KBr, thin film): 3464, 2981, 1710, 1630, 1321, 1142, 1028, 858, 819, 747 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C₁₇H₁₈NaO₃ 293.1148, found 293.1155.

**Ethyl 4-hydroxy-2-methylene-4-(naphthalen-1-yl)butanoate (25).**

Light yellow oil (18.3 mg, 68% yield) after preparative thin layer chromatography separation (80% hexanes : 20% EtOAc): TLC Rₚ = 0.39 (EtOAc/hexanes = 1/4); ¹H NMR (500 MHz, CDCl₃) δ 8.22 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.73 (d, J = 7.2 Hz, 1H), 7.56 – 7.53 (m, 1H), 7.50 – 7.47 (m, 2H), 6.31 (d, J = 1.4 Hz, 1H), 5.70 – 5.68 (m, 2H), 4.28 (qd, J = 7.1, 4.5 Hz, 2H), 3.09 – 3.06 (m, 1H), 2.77 (s, 1H, -OH), 2.68 – 2.64 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.9, 139.9, 137.5, 133.8, 130.3, 129.0, 128.6, 128.0, 126.2, 125.6, 123.2, 122.7, 69.7, 61.3, 42.3, 14.3; IR (KBr, thin film): 3472, 2981, 1708, 1630, 1512, 1325, 1144, 1028, 802, 779 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C₁₇H₁₈NaO₃ 293.1148, found 293.1152.

**Ethyl 4-(furan-2-yl)-4-hydroxy-2-methylenebutanoate (27).**

Light yellow oil (15.7 mg, 75% yield) after preparative thin layer chromatography
separation (75% hexanes : 12.5% acetone : 12.5% EtOAc): TLC Rf = 0.30 (EtOAc /acetone/hexanes = 1/1/6); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.37 (dd, \(J = 1.8, 0.8\) Hz, 1H), 6.32 (dd, \(J = 3.3, 1.8\) Hz, 1H), 6.26 – 6.25 (m, 2H), 5.64 (d, \(J = 1.2\) Hz, 1H), 4.91 (dt, \(J = 8.2, 4.9\) Hz, 1H), 4.23 (q, \(J = 7.1\) Hz, 2H), 2.92 – 2.88 (m, 1H), 2.86 – 2.81 (m, 1H), 2.65 (d, \(J = 5.0\) Hz, 1H, -OH), 1.31 (t, \(J = 7.1\) Hz, 4H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 167.7, 156.1, 142.1, 136.8, 128.4, 110.3, 106.3, 67.2, 61.3, 39.0, 14.3; IR (KBr, thin film): 3448, 2983, 1713, 1630, 1370, 1275, 1190, 1012, 949, 748 cm\(^{-1}\); HRMS-EI (m/z) [M\(^+\)]: calcd. for C\(_{11}\)H\(_{14}\)O\(_2\) 210.0892, found 210.0891.

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\text{Ethyl 4-hydroxy-2-methylene-4-(thiophen-2-yl)butanoate (29).}
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Light yellow oil (16.0 mg, 71% yield) after preparative thin layer chromatography separation (75% hexanes : 25% acetone): TLC Rf = 0.50 (acetone/hexanes = 1/3); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.23 (dd, \(J = 4.6, 1.7\) Hz, 1H), 6.97 – 6.95 (m, 2H), 6.26 (d, \(J = 1.4\) Hz, 1H), 5.65 (d, \(J = 1.2\) Hz, 1H), 5.15 (dd, \(J = 8.3, 4.5\) Hz, 1H), 4.23 (q, \(J = 7.1\) Hz, 2H), 2.91 – 2.84 (m, 2H), 2.82 – 2.78 (m, 1H), 1.32 (t, \(J = 7.1\) Hz, 3H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 167.7, 148.1, 136.8, 128.7, 126.8, 124.5, 123.7, 69.5, 61.3, 42.8, 14.3; IR (KBr, thin film): 3469, 2982, 2931, 1712, 1630, 1443, 1306, 1200, 1028, 700 cm\(^{-1}\); HRMS-ESI (m/z) [M+Na\(^+\)]: calcd. for C\(_{11}\)H\(_{14}\)NaO\(_3\)S 249.0556, found 249.0555.

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\text{Dibenzyl 2-hydroxy-2-methyl-4-methylenepentanedioate (31).}
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Colourless oil (17.9 mg, 51 % yield) after preparative thin layer chromatography separation (75% hexanes : 12.5% acetone : 12.5% EtOAc): TLC Rf = 0.68
(EtOAc/acetone/hexanes = 1/1/6); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.38 – 7.30 (m, 8H), 6.26 (d, $J = 1.3$ Hz, 1H), 5.65 – 5.60 (m, 1H), 5.19 – 5.04 (m, 4H), 3.58 (s, 1H), 2.88 (d, $J = 13.9$ Hz, 1H), 2.70 (d, $J = 13.9$ Hz, 1H), 1.46 (s, 3H); $\text{IR (KBr, thin film): } 3445, 2935, 1721, 1627, 1455, 1267, 1214, 962, 697 \text{ cm}^{-1}$; HRMS-ESI (m/z) [M+H$^+$]: calcd. for C$_{21}$H$_{23}$O$_5$ 355.1540, found 355.1538.

\[
\text{COO} \quad \text{Bn} \\
\text{OH} \\
\text{C} \quad \text{C} \quad \text{C} \\
\text{S} \quad \text{O} \\
\]

**Benzyl 4-hydroxy-2-methylene-4-(thiophen-2-yl)pentanoate (33).**

Colourless oil (14.4 mg, 53 % yield) after preparative thin layer chromatography separation (75% hexanes : 12.5% acetone : 12.5% EtOAc): TLC $R_f = 0.74$ (EtOAc/acetone/hexanes = 1/1/6); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.44 – 7.30 (m, 5H), 7.15 (dd, $J = 5.1$, 1.2 Hz, 1H), 6.92 (dd, $J = 5.1$, 3.5 Hz, 1H), 6.86 (dd, $J = 3.5$, 1.2 Hz, 1H), 6.27 (d, $J = 1.3$ Hz, 1H), 5.53 (d, $J = 1.1$ Hz, 1H), 5.18 (s, 2H), 3.83 (s, 1H), 2.91 (s, 2H), 1.61 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 168.8, 153.3, 136.1, 135.7, 130.2, 128.7, 128.5, 128.3, 126.8, 123.8, 122.4, 73.6, 67.2, 47.2, 30.6; IR (KBr, thin film): 3445, 3066, 2975, 1714, 1625, 1455, 1383, 1164, 750, 697 cm$^{-1}$; HRMS-ESI (m/z) [M+Na$^+$]: calcd. for C$_{17}$H$_{18}$NaO$_3$S 325.0869, found 325.0874.

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\text{COO} \quad \text{Bn} \\
\text{OH} \\
\text{C} \quad \text{C} \quad \text{C} \\
\text{S} \quad \text{O} \\
\]

**Benzyl 4-cyano-4-hydroxy-2-methylenebutanoate (35).**

Light yellow oil (13.7 mg, 59% yield) after preparative thin layer chromatography separation (75% hexanes : 12.5% acetone : 12.5% DCM): TLC $R_f = 0.27$ (DCM /acetone/hexanes = 1/1/6); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.40 – 7.36 (m, 5H), 6.48 (d, $J = 0.8$ Hz, 1H), 5.92 (d, $J = 1.0$ Hz, 1H), 5.24 (d, $J = 1.7$ Hz, 2H), 4.74 (td, $J = 6.8$, 1.3 Hz, 1H), 5.19 – 5.04 (m, 4H), 3.58 (s, 1H), 2.88 (d, $J = 13.9$ Hz, 1H), 2.70 (d, $J = 13.9$ Hz, 1H), 1.46 (s, 3H); $\text{IR (KBr, thin film): } 3445, 2935, 1721, 1627, 1455, 1267, 1214, 962, 697 \text{ cm}^{-1}$; HRMS-ESI (m/z) [M+Na$^+$]: calcd. for C$_{17}$H$_{18}$NaO$_3$S 325.0869, found 325.0874.
4.9 Hz, 1H), 3.86 (d, J = 6.9 Hz, 1H, -OH), 2.92 – 2.88 (m, 1H), 2.85 – 2.81 (m, 1H); 13C NMR (125 MHz, CDCl₃) δ 167.9, 135.3, 134.1, 131.8, 128.9, 128.8, 128.5, 118.9, 67.8, 61.4, 38.6; IR (KBr, thin film): 3456, 2924, 1713, 1456, 1304, 1148, 1074, 913, 743, 699 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C₁₅H₁₃NNaO₃ 254.0788, found 254.0784.

Benzy1 5,5,5-trifluoro-4-hydroxy-2-methylenepentanoate (38).

Colourless oil (10.9 mg, 39 % yield) after preparative thin layer chromatography separation (75% hexanes : 12.5% acetone : 12.5% EtOAc): TLC Rf = 0.63 (EtOAc /hexanes = 1/4); ¹H NMR (500 MHz, CDCl₃) δ 7.46 – 7.29 (m, 4H), 6.40 (s, 1H), 5.83 (s, 1H), 5.24 (s, 2H), 4.14 (th, J = 9.5, 3.3 Hz, 1H), 3.30 (d, J = 5.9 Hz, 1H), 2.79 (dd, J = 14.3, 2.8 Hz, 1H), 2.63 (dd, J = 14.4, 9.6 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 167.55, 135.34, 134.87, 130.03, 128.64, 128.46, 128.17, 70.25, 70.00, 69.80, 69.75, 69.50, 67.24, 33.38. ¹⁹F NMR (376 MHz, Chloroform-d) δ -79.78 (d, J = 6.5 Hz); IR (KBr, thin film): 3446, 1714, 1697, 1455, 1415, 1318, 1213, 1171, 1127, 696 cm⁻¹; HRMS-ESI (m/z) [M+NH₄⁺]: calcd. for C₁₃H₁₇F₃NO₃ 292.1155, found 292.1155.

1-Benzyl 5-((3S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-(6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl) 4-hydroxy-2-methylenepentanedioate (41).

Colourless oil (38.4 mg, 62 % yield) after flash chromatography separation (EtOAc/hexanes = 1/10): TLC Rf = 0.71 (EtOAc /acetone/hexanes = 1/1/6); ¹H NMR (500 MHz, CDCl₃) δ 7.41 – 7.31 (m, 4H), 6.35 (d, J = 1.3 Hz, 1H), 5.76 (t, J = 1.3 Hz, 1H),
1H), 5.42–5.34 (m, 1H), 5.27–5.16 (m, 2H), 4.68 (dq, J = 10.7, 6.0, 5.3 Hz, 1H), 4.38 (dd, J = 8.2, 4.3 Hz, 1H), 2.88 (dd, J = 14.4, 4.3 Hz, 1H), 2.64 (dd, J = 14.3, 8.2 Hz, 1H), 2.32 (t, J = 6.7 Hz, 2H), 2.04–1.94 (m, 2H), 1.85 (tdd, J = 13.0, 6.7, 3.4 Hz, 3H), 1.64–1.41 (m, 8H), 1.39–1.21 (m, 5H), 1.20–1.05 (m, 7H), 1.01 (s, 6H), 0.91 (d, J = 6.5 Hz, 3H), 0.86 (dd, J = 6.6, 2.4 Hz, 6H), 0.68 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 173.9, 166.9, 139.3, 135.9, 135.7, 129.0, 128.7, 128.4, 128.2, 123.2, 75.9, 69.5, 66.9, 56.8, 56.2, 50.1, 42.4, 39.8, 39.6, 38.1, 37.4, 37.0, 36.7, 36.3, 35.9, 32.0, 31.9, 28.4, 28.2, 27.8, 24.4, 23.9, 23.0, 22.7, 21.1, 19.4, 18.8, 12.0; IR (KBr, thin film): 3446, 2947, 2867, 1723, 1466, 1383, 1210, 1101, 749, 696 cm⁻¹; HRMS-ESI (m/z) [M+Na⁺]: calcd. for C40H58NaO5 641.4176, found 641.4180.

2-Methyl-5-phenyltetrahydrofuran (44).

Colorless oil (10.1 mg, 62 % yield) after flash chromatography (90% hexanes : 10% EtOAc): TLC Rf = 0.87 (EtOAc/hexanes = 1/9); 1H NMR (500 MHz, CDCl3) δ 8.36–8.23 (m, 5H), 6.05–5.86 (m, 1H), 5.39–5.14 (m, 1H), 3.39–3.28 (m, 1H), 3.17–3.07 (m, 1H), 2.90–2.82 (m, 1H), 2.64–2.59 (m, 1H), 2.34 (dd, J = 25.1, 6.1 Hz, 3H); 13C NMR (125 MHz, CDCl3) δ 144.1, 143.7, 128.4, 128.4, 127.3, 127.2, 126.0, 125.7, 81.2, 80.4, 76.1, 76.1, 35.7, 34.8, 34.4, 33.2, 21.7, 21.5.

Ethyl 4-(2-(methoxymethyl)phenyl)-2-methylene-4-oxobutanoate (47-ox).

Colorless oil (7.9 mg, 30 % yield): TLC Rf = 0.65 (EtOAc/hexane = 1/4); 1H NMR (500 MHz, CDCl3) δ 7.79 (d, J = 7.7 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 6.41 (s, 1H), 5.69 (s, 1H), 4.71 (s, 2H), 4.21 (q, J = 7.1 Hz, 2H), 3.94 (s, 2H), 3.43 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H); 13C NMR (126 MHz, CDCl3) δ 200.26, 166.39, 139.49, 135.97, 134.85, 131.88, 128.65, 128.54, 127.73,
126.94, 72.48, 61.03, 58.63, 44.26, 14.12. IR (KBr, thin film) 2982, 2930, 1716, 1685, 1312, 1198, 1146, 1100, 1026, 1003, 950, 760 cm\(^{-1}\); HRMS-ESI (m/z) [M+H\(^+\)]: calcd. for C\(_{15}\)H\(_{18}\)O\(_4\) 263.1278, found 263.1278.

Ethyl 4-(2-formylphenyl)-4-methoxy-2-methylenebutanoate (48-ox)

Colorless oil (2.6 mg, 10 % yield): TLC Rf = 0.68 (EtOAc/hexane = 1/4); \(^1\)H NMR (500 MHz, Chloroform-\(d\)) \(\delta\) 10.36 (s, 1H), 7.86 (d, \(J = 7.6\) Hz, 1H), 7.61 (d, \(J = 5.9\) Hz, 2H), 7.45 (t, \(J = 7.0\) Hz, 1H), 6.20 (s, 1H), 5.57 (s, 1H), 5.27 (dd, \(J = 8.1, 4.8\) Hz, 1H), 4.18 (q, \(J = 7.1\) Hz, 2H), 3.24 (s, 3H), 2.86 – 2.61 (m, 2H), 1.29 (t, \(J = 7.1\) Hz, 3H). \(^13\)C NMR (126 MHz, cdcl\(_3\)) \(\delta\) 192.52, 167.03, 144.41, 136.89, 133.98, 133.91, 131.74, 127.74, 127.22, 127.21, 78.45, 60.72, 57.17, 40.51, 14.17. IR (KBr, thin film) 2982 2933 1713 1693 1599 1310 1188 1144 1098 1027 763 cm\(^{-1}\); HRMS-ESI (m/z) [M+H\(^+\)]: calcd. for C\(_{15}\)H\(_{18}\)O\(_4\) 263.1278, found 263.1279.
V. References

Barone, V.; Cossi, M.; Tomasi, J. (1998) Geometry optimization of molecular structures in solution by the polarizable continuum model. J. Comput. Chem. 19, 404.

Becke, A. D. (1993) Density-functional thermochemistry. III. The role of exact exchange. J. Chem. Phys. 98, 5648.

Cances, E.; Mennucci, B.; Tomasi, J. (1997) A new integral equation formalism for the polarizable continuum model: Theoretical background and applications to isotropic and anisotropic dielectrics. J. Chem. Phys. 107, 3032.

Cossi, M.; Barone, V.; Cammi, R.; Tomasi, J. (1996) Ab initio study of solvated molecules: a new implementation of the polarizable continuum model. Chem. Phys. Lett. 255, 327.

Lee, C.; Yang, W.; Parr, R. G. (1988) Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. Phys. Rev. B: Condens. Matter Mater. Phys. 37, 785.

Liu, S.; Qi, X.; Qu, L.-B.; Bai, R. B.; Lan, Y. (2018) C–H bond cleavage occurring on a Rh(V) intermediate: a theoretical study of Rh-catalyzed arene azidation. Catal. Sci. Technol. 8, 1645.

Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. (2009) Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. J. Phys. Chem. B 113, 6378.

Peverati, R.; Truhlar, D. G. (2011) Improving the accuracy of hybrid meta-GGA density functionals by range separation. J. Phys. Chem. Lett. 2, 2810.