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One-Pot Photo-Mediated Giese Reaction/Friedel-Crafts Hydroxyalkylation/Oxidative Aromatization to Access Naphthalene Derivatives from Toluenes and Enones

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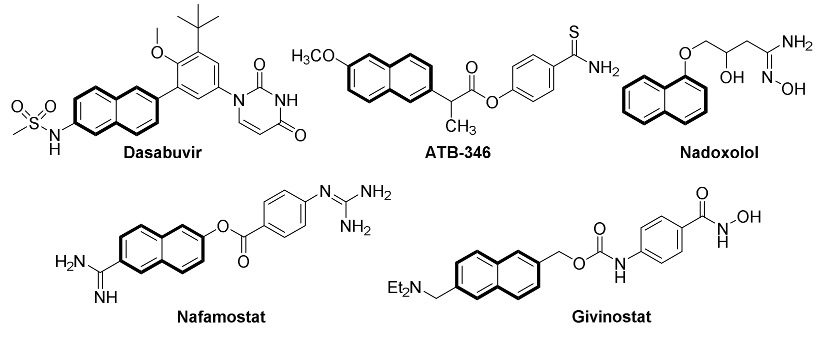
ABSTRACT: Value-added chemicals, γ-aryl ketones and naphthalenes, were conveniently synthesized from readily available toluenes and enones through the synergistic combination of photoredox and Lewis acid catalysis. The direct synthesis of γ-aryl ketones represents a rare example of Giese reactions between benzylic C(sp^3)–H and enones that avoids the use of prefunctionalized metallic nucleophiles. Naphthalene derivatives were accessed through a one-pot Giese reaction/Friedel-Crafts hydroxyalkylation/oxidative aromatization sequential transformation.

KEYWORDS: C–H activation; photocatalysis; Lewis acid catalysis; γ-aryl ketone; naphthalene

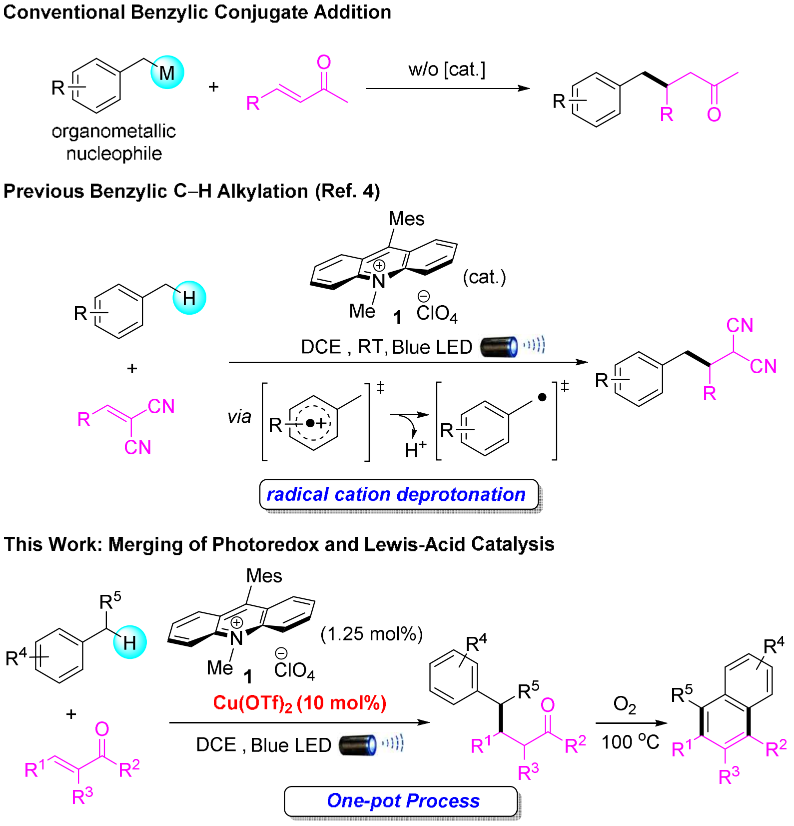
Introduction

Naphthalenes are important and ubiquitous structural motifs in many important pharmaceutical drugs (Scheme 1), and have also received much attention in material science.[1] However, most of the naphthalene building blocks for complex molecule synthesis were introduced by pre-functionalized naphthalene moieties (e.g. halogenated naphthalene, naphthalenol, etc). Synthetic methodologies towards the preparation of naphthalene scaffolds from readily available and inexpensive chemical feedstocks have been less explored and are highly desirable. Current strategies for the synthesis of naphthalene derivatives are mainly limited to annulation or cycloaddition of benzene derivatives.[2]



Scheme 1. Drugs Containing the Naphthalene Core

Visible-light-mediated photoredox catalysis has attracted increasing attention over the past decade because of its unique reactivity patterns, high efficiency, and mild reaction conditions.[3] Our group has recently disclosed a direct benzylic C(sp^3)–H alkylation using only acridinium organo-catalyst **1** under visible-light mediation via a radical cation deprotonation pathway without using any base additive (Scheme 2).[4] However, an efficient transformation requires the use of very strong Michael acceptor methylene-malononitriles, to generate a radical adduct that is oxidative enough to oxidize the reduced photoredox catalyst **1'** to regenerate catalyst **1**. Mild electron-deficient alkenes such as unsaturated ketones, that deliver important synthetic building blocks, γ-aryl ketones, gave sluggish reactivity in the presence of only photocatalyst **1** (less than 2% conversion after 24 hours, Table 1, entry 1). Conventional methods for the benzylic conjugate addition to unsaturated ketones involve the use of various benzyl metallic species, which will introduce undesired by-products as waste. The catalytic activation of benzylic C(sp^3)–H bonds as latent nucleophilic handles thus represents a green and sustainable process. However, efficient conjugate additions of benzylic C(sp^3)–H to electron deficient alkenes *via* benzyl radical intermediates, falling into Giese reactions,[5] are normally limited to strong electron-deficient alkenes (bearing two electron-withdrawing substituents).[6] To the best of our knowledge, there is only a single report on the addition of toluene-type compounds to enones via a radical process, which proceeded with poor reactivity (27% yield, 87% conversion).[6c] We envisioned that adding a Lewis acid catalyst might significantly enhance the electrophilicity of the unsaturated ketone for an efficient radical addition,[7] and also increase the oxidative ability of the radical adduct to turn over the catalytic cycle. We herein disclosed an efficient synthesis of γ-aryl ketones from benzylic C(sp^3)–H and unsaturated ketones through the synergistic combination of photoredox and Lewis acid catalysis,[3d,8] which can further undergo Friedel-Crafts hydroxyalkylation and oxidative aromatization to access useful naphthalene derivatives in a one-pot fashion (Scheme 2). The addition of Lewis acid catalyst was essential in enone activation to achieve an efficient Giese reaction as well as to promote the subsequent Friedel-Crafts hydroxyalkylation.

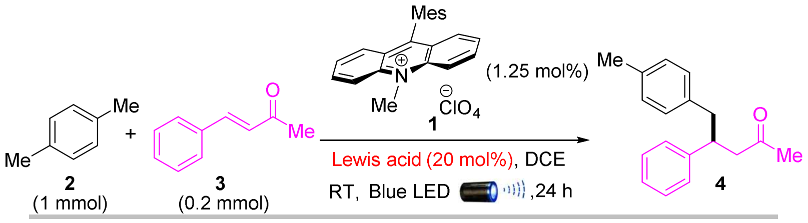


Scheme 2. Benzylic Conjugate Addition

Results and Discussion

p-Xylene **2** and benzylideneacetone **3** were chosen as model substrates to investigate the effectiveness of a variety of Lewis acid catalysts (20 mol%) on the Giese reaction in the presence of photocatalyst **1** (Table 1). Some common Lewis acids including $AlCl_3$, $BF_3{\cdot}OEt_2$, $SnCl_4$, CuI, and CuI_2 were ineffective (entries 2 to 6). Gratifyingly, the use of cationic transition-metal triflates (entries 7 to 10) produced desired product **4** at ambient conditions, among which, $Cu(OTf)_2$ was dramatically effective, giving **4** in 77% isolated yield (entry 10). The catalyst loading of $Cu(OTf)_2$ can be decreased to 10 mol% with similar efficiency (entry 11). However, further reducing catalyst loading to 5 mol% resulted in decreased conversion (entry 12).

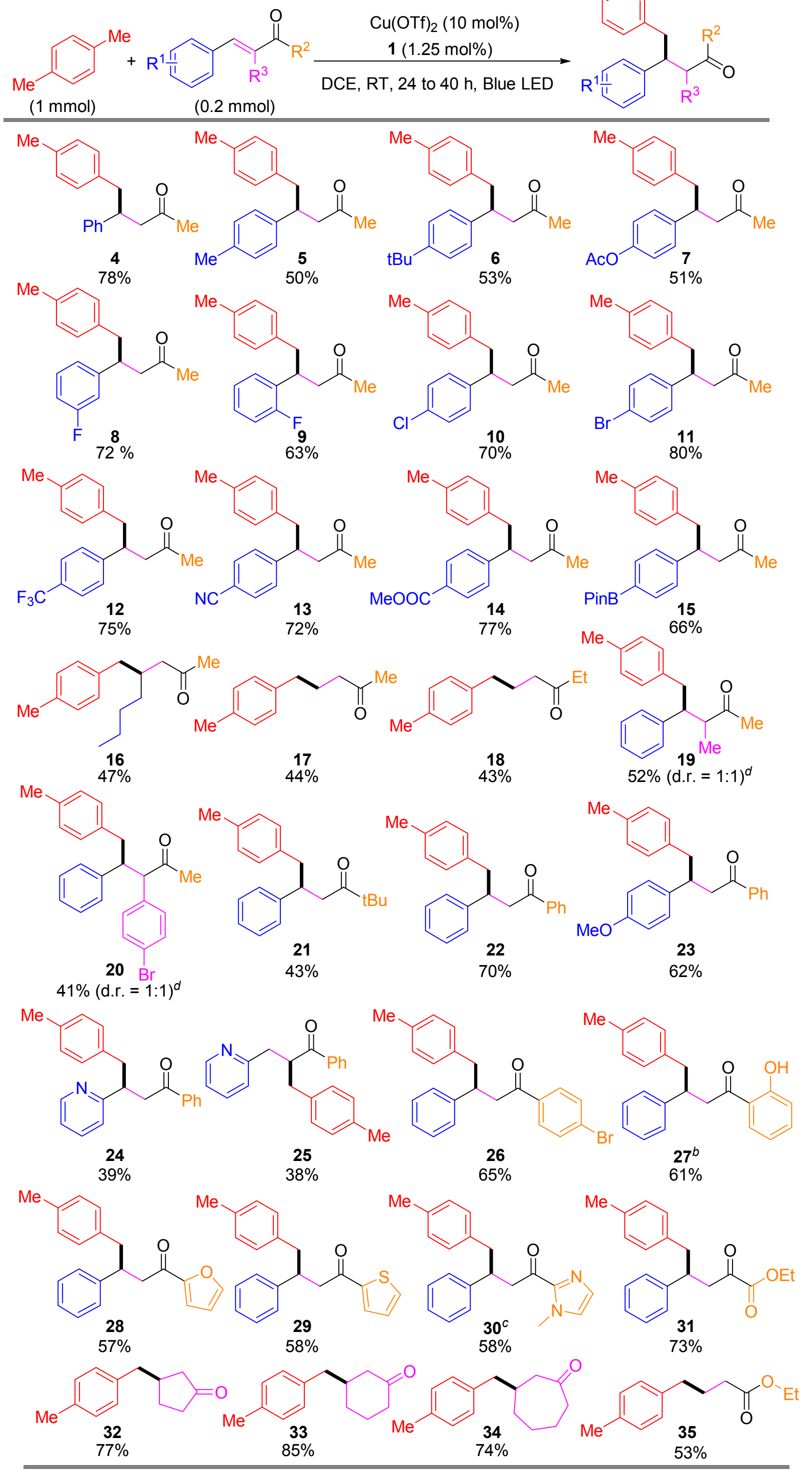
Table 1. Evaluation of Various Lewis Acid Catalysts



entry	Lewis acid	yield (%)[a]	entry	Lewis acid	yield (%)[a]
1	no	trace	2	$AlCl_3$	trace
3	BF_3•Et_2O	trace	4	$SnCl_4$	trace
5	CuI	trace	6	CuI_2	trace
7	$Zn(OTf)_2$	18%	8	$Sc(OTf)_3$	25%
9	$Yb(OTf)_3$	33%	10	$Cu(OTf)_2$	77%
11[b]	$Cu(OTf)_2$	78%	12[c]	$Cu(OTf)_2$	44%

[a]Isolated yields. [b]Using 10 mol% of $Cu(OTf)_2$. [c]Using 5 mol% of $Cu(OTf)_2$.

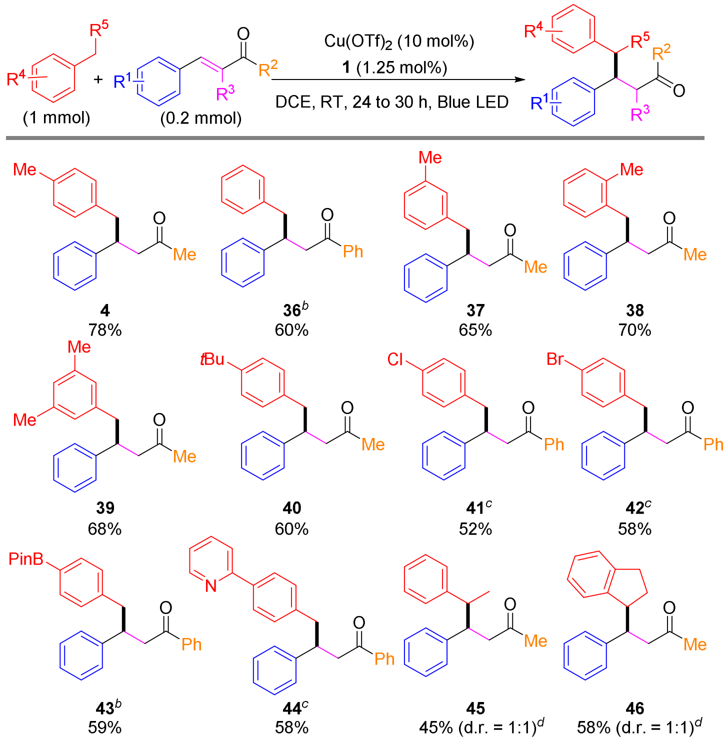
Adopting the optimal conditions (Table 1, entry 11), we sought to evaluate the generality of enone substrates for benzylic conjugate addition using p-xylene as the benzylic substrate (Scheme 3). Experiments probing the scope of benzylideneacetone revealed that substrates possessing either electron-rich (**5-7**) or electron-deficient arenes (**8-14**) proceeded well to afford 1,4-addition products in moderate to good yields. Functional groups such as acetate (**7**), halogen (**8-11**), trifluoromethyl (**12**), cyanide (**13**), ester (**14**), and boronate ester (**15**) were well tolerated. The β-alkylated enone participated in the Giese reaction to afford product **16** in moderate yield. Moreover, simple vinyl ketones such as methyl and ethyl vinyl ketones could be employed to obtain the benzylic addition products **17** and **18**. Trisubstituted benzylideneacetones were readily accommodated to deliver the desired products (**19** and **20**). The change of methyl ketone to sterically demanding *tert*-butyl ketone was feasible (**21**). Chalcone-type substrates could also participate efficiently in this coupling (**22-30**). Notably, when employing enone bearing a β-substituted pyridine moiety, both β and α-addition products (**24** and **25**) were isolated in similar yields. Importantly, aryl ketone substrates with an additional Lewis basic atom that can bind to the Lewis acid catalyst more effectively as bidentate substrates, such as phenol (**27**), furan (**28**), thiofuran (**29**) and imidazole (**30**), were suitable candidates. This provides an opportunity to develop a chiral Lewis acid catalyst system using chiral ligand to achieve an asymmetric conjugate addition starting with readily available benzylic $C(sp^3)$–H bonds, considering that the racemic transformation is diminished in the absence of the Lewis acid catalyst.[8,9] The 2-oxoester substrate which could be another type of bidentate substrates for Lewis acid, proceeded well to afford product **31** in good yield. Furthermore, the coupling reactions proceeded quite efficiently with various cyclic enones bearing different ring sizes (**32** to **34**). In addition to enones, unsaturated esters such as ethyl acrylate could be employed in this protocol to deliver the benzylic conjugate addition product **35** in moderate yield.



[a]Isolated yields, diastereoselectivity based on the analysis of ^{1}H NMR spectra of the crude reaction mixture. [b]Reaction conducted at 80 °C. [c]Reaction conducted at 60 °C. [d]Diastereomeric ratios were determined by analysis of ^{1}H NMR spectra of the crude mixture.

Scheme 3. Scope of Enones for the Benzylic Conjugate Addition[a]

The scope of benzylic substrates for the Giese reaction was subsequently explored. As shown in Scheme 4, all electron-neutral (**36**), electron-rich (**37-40**), and electron-poor (**41** and **42**) toluene moieties underwent effective coupling in the presence of the dual catalysts under blue LED irradiation. The steric ortho-methyl substituent did not hinder the reaction process (**38**). Incorporation of a boronate ester (**43**) or a pyridine (**44**) substituent on toluene was also feasible. In addition to toluene, ethylbenzene and indane were all suitable candidates and the reactions proceeded smoothly to deliver the desired products in good yields (**45** and **46**). This photoredox induced coupling represents a rare case of effective Giese reactions between benzylic C(sp^3)–H bonds and enone substrates.

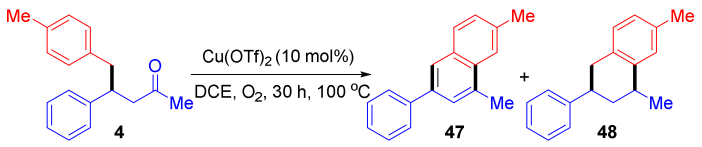


^{a}Isolated yields, diastereoselectivity based on the analysis of ^{1}H NMR spectra of the crude reaction mixture. ^{b}Reaction conducted at 60 °C. ^{c}Reaction conducted at 80 °C. ^{d}Diastereomeric ratios were determined by analysis of ^{1}H NMR spectra of the crude mixture.

Scheme 4. Scope of Benzylic C–H Partners for the Giese Reaction[a]

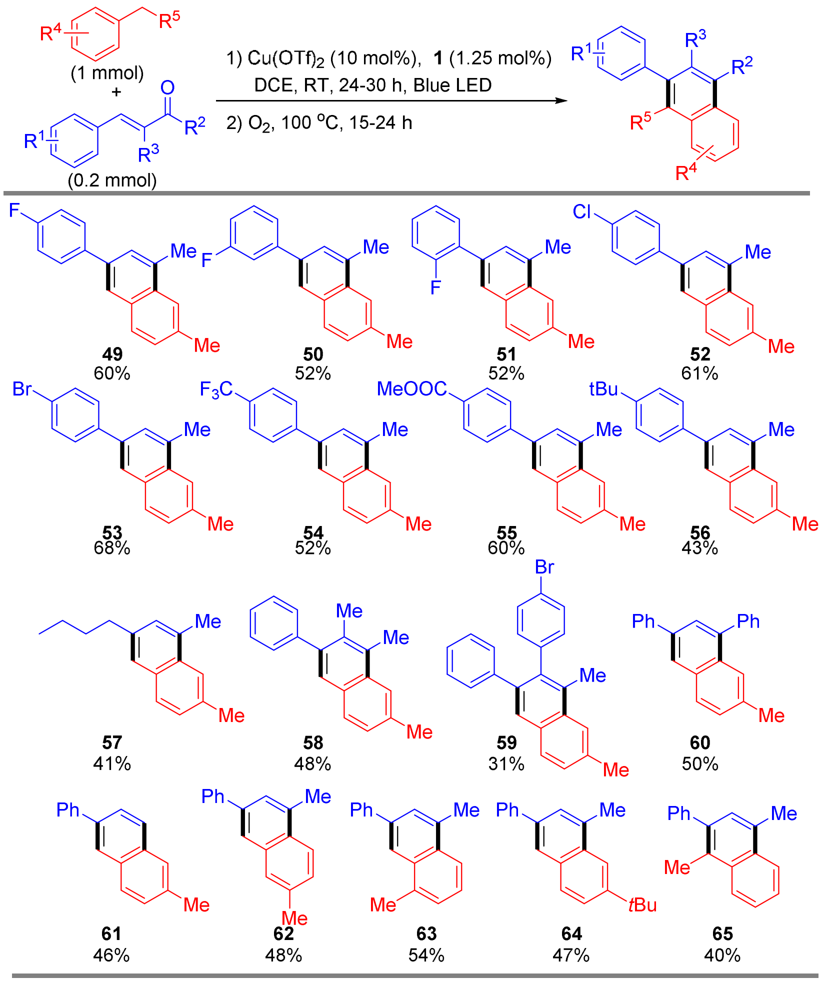
In the midst of Giese reaction optimization, naphthalene **47** was detected when reaction temperature was elevated to 70 °C. We proposed that this compound may be derived from $Cu(OTf)_2$-catalyzed Friedel-Crafts hydroxyalkylation of coupling product **4** followed by oxidative aromatization. The cascade transformation was thus investigated attempting to access naphthalene products in high yields. Pleasingly, naphthalene **47** was cleanly generated from methyl ketone **4** in the presence of a catalytic amount of $Cu(OTf)_2$ at 100 °C under O_2 atmosphere (Table 2, entry 1). At 70 °C the conversion was significantly lower (entry 2). No reaction occurred without Lewis acid catalyst $Cu(OTf)_2$ (entry 3). O_2 was essential for this transformation, as a significant amount of tetralin by-product **48** was generated in the absence of O_2 (entry 4). Previous reports have demonstrated that the Friedel-Crafts hydroxyalkylation product 1,2-dihydronaphthalene would undergo disproportionation to produce tetraline and naphthalene at elevated temperature in the absence of external oxidants.[10] Other oxidant such as $K_2S_2O_8$ was inferior to O_2 which resulted in lower yield of naphthalene **47** together with a small amount of by-product **48** (entry 5).

Table 2. Evaluation of Lewis Acid-Promoted Friedel-Crafts Hydroxyalkylation/Oxidative Aromatization Cascade



entry	modifications	yield of **47** (%)	yield of **48** (%)
1	no	80	0
2	70 °C instead of 100 °C, no O_2	17	0
3	no Cu $(OTf)_2$	0	0
4	no O_2	58	35
5	$K_2S_2O_8$ instead of O_2	68	15

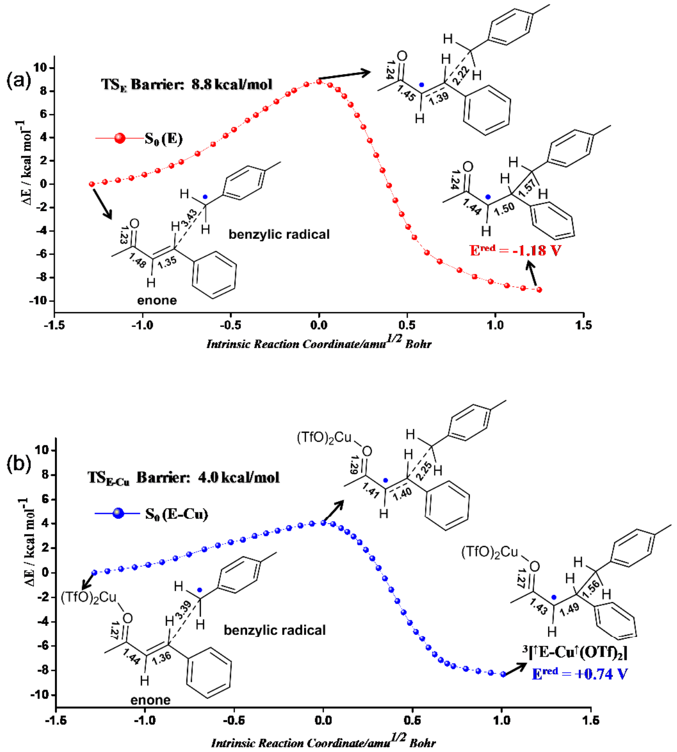
With both optimized conditions for the Giese reaction and cascade Friedel-Crafts hydroxyalkylation/oxidative aromatization in hand, we then attempted the one-pot generation of naphthalene compounds directly from readily available toluenes and enones (Scheme 5). We were pleased to isolate the desired naphthalene **47** in 58% yield in a one-pot process using p-xylene **2** and benzylideneacetone **3** as the starting compounds. The impact of substitution on the enone was evaluated with various aryl rings with para, meta, or ortho substituents (**49-51**), exhibiting electron-withdrawing (**49-55**) or electron-donating properties (**56**), which were well tolerated to deliver the naphthalenes in good yields. The alkyl substituted enone could participate well in the one-pot naphthalene synthesis (**57**). Introduction of additional alkyl or aryl substituent on the alkene moiety of enones yielded naphthalene products in moderate yield (**58** and **59**). Chalcones could be applied to this one-port three-step transformation as well (**60**). Notably, the sequential transformations proceeded smoothly using α,β-unsaturated aldehydes to deliver naphthalene product **61** in moderate yield. The scope for the toluene moiety was subsequently investigated. Derivatives with para, meta, or ortho methyl substituents proceeded well (**47**, **62** and **63**). Changing para-derivative to steric demanding tert-butyl group was feasible (**64**). Ethylbenzene was also a suitable candidate (**65**). In summary, this one-pot protocol demonstrated that selective functionalization of naphthalene at any desired position C1-C8 is possible with the proper choice of starting toluenes and enones.



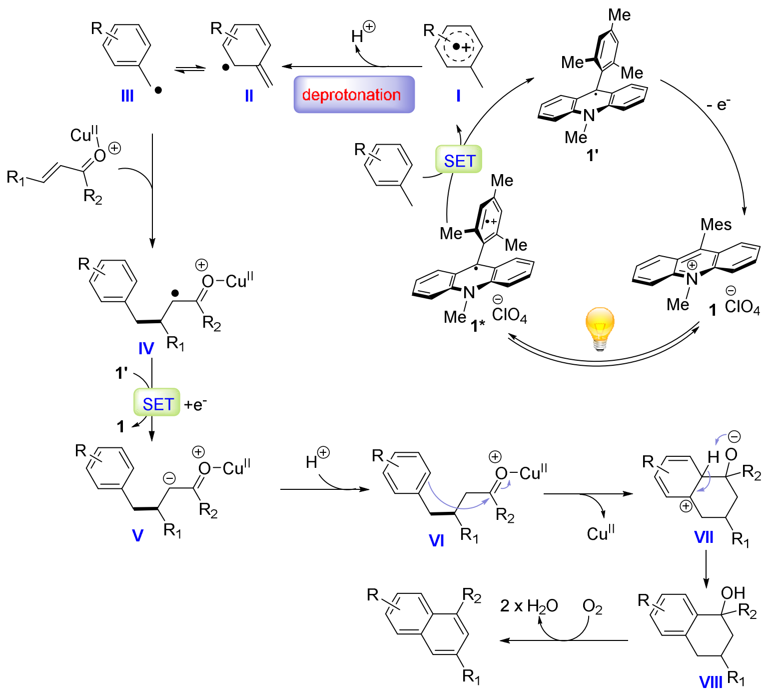
^{a}Isolated yields for one-pot two-step transformations.

Scheme 5. One-Pot Three-Step Synthesis of Naphthalenes[a]

Several control experiments were performed to gain further insights of the dual catalyst-promoted Giese reaction.[11] First, no alkylation products were detected in the presence of radical scavenger TEMPO, suggesting that a radical process was involved. Moreover, as indicated by the luminescence quenching experiments, p-xylene could quench the excited state of acridinium **1***, whereas enones gave negligible quenching. The energy barrier for benzylic radical addition to enones was significantly lower in the presence of $Cu(OTf)_2$ Lewis acid as demonstrated by DFT calculations (4.0 kcal/mol vs 8.8 kcal/mol, Scheme 6). In addition, the reductive potential changes drastically upon the formation of Lewis acid adduct. As estimated by DFT calculation, radical adducts without Lewis acid (E^{red} = -1.18 V vs SCE) and with $Cu(OTf)_2$ Lewis acid (E^{red} = +0.74 V vs SCE) suggest that only the Lewis acid adduct can oxidize the reduced catalyst **1'** ($E^{ox}_{1/2}$ = -0.57 V vs SCE in MeCN). Deuterium-labelling experiments (Supporting Information, Figure S4) revealed that the proton source could be derived from either the toluene substrate or active protons in the solvent. The intermolecular competition experiment established that the magnitude of the kinetic isotopic effect (KIE) given by k_H/k_D was 2.8 (Supporting Information, Figure S7), indicating that the deprotonation might be involved in the rate-limiting step. A tentative mechanistic pathway was proposed in light of all the experimental data (Scheme 7). As supported by the luminescence study, visible-light irradiation of the $[Acr^+\text{-}Mes]ClO_4$ photocatalyst **1** to its excited state **1*** ($E^{red*}_{1/2}$ = +2.06 V vs SCE in MeCN) oxidizes the toluene-type substrate to its radical cation **I**. Then subsequent deprotonation of **I** delivers radical **II**, which is in equilibrium with the more stable benzylic radical **III**. Nucleophilic addition of radical **III** to the Cu(II) Lewis acid-activated enone will furnish Lewis acid alkyl radical adduct **IV**, which is capable of oxidizing the reduced form of acridinium catalyst **1'** to regenerate ground state catalyst **1**. Protonation of intermediate **V** produces the Giese reaction product **VI**. The deuterium-labeling experiments shown that the anion intermediate **V** would abstract a proton from the reaction mixture. Upon heating, compound **VI** can further undergo an intramolecular Friedel-Crafts hydroxyalkylation assisted by $Cu(OTf)_2$ catalyst to afford **VIII**. The final oxidative aromatization in the presence of O_2 will accomplish the synthesis of naphthalene product.



Scheme 6. Calculated Energy Barriers of Radical Addition and Reductive Potentials of Radical Adducts (a) without Lewis Acid; (b) in the Presence of Cu(OTf)$_2$ Lewis Acid. Atomic Distances Denoted in Ångström



Scheme 7. Plausible Mechanism for the One-Pot Synthesis of Naphthalenes

Conclusion

Overall, we have developed a convenient direct synthesis of γ-aryl ketones and naphthalenes from readily available toluenes and enones by the synergistic combination of photoredox and Lewis acid-catalysis, featuring atom- and step-economical synthesis. The effective radical addition represents a rare successful example of Giese reactions between toluenes and enones, without the need of strong Michael acceptors. The unprecedented one-pot photo-induced Giese reaction/Friedel-Crafts hydroxyalkylation/oxidative aromatization provides an easy method to access naphthalenes with selective functionalization at any desired position from inexpensive feedstocks. The Cu(OTf)$_2$ Lewis acid catalyst plays a dual role in this sequential transformation to enable an efficient Giese reaction and to promote the subsequent Friedel-Crafts hydroxyalkylation.

Supporting information

Detailed experimental procedures, characterization data, copies of ^{1}H NMR and ^{13}C NMR spectra of final products are reported in the Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org/.

Acknowledgements

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References

[1] a) Jiang, W.; Li, Y.; Wang, Z.-H. Tailor-Made Rylene Arrays for High Performance n-Channel Semiconductors. *Acc. Chem. Res.* **2014**, *47*, 3135-3147. b) Watson, M. D.; Fechtenkötter, A.; Müllen, K. Big Is Beautiful–"Aromaticity" Revisited from the Viewpoint of Macromolecular and Supramolecular Benzene Chemistry. *Chem. Rev.* **2001**, *101*, 1267-1300.

[2] For selected recent examples, see: a) Manojveer, S.; Balamurugan, R. Synthesis of Naphthalene Derivatives from ortho-Alkynylacetophenone Derivatives via Tandem in Situ Incorporation of Acetal and Intramolecular Heteroalkyne Metathesis/Annulation. *Org. Lett.* **2014**, *16*, 1712-1715. b) Zhu, S.-F.; Xiao, Y.-L.; Guo, Z.-J.; Jiang, H.-F. Iron-Catalyzed Benzannulation Reactions of 2-Alkylbenzaldehydes and Alkynes Leading to Naphthalene Derivatives. *Org. Lett.* **2013**, *15*, 898-901. c) Chen, Z.-W.; Zeng, W.; Jiang, H.-F.; Liu, L.-X.

Cu(II)-Catalyzed Synthesis of Naphthalene-1,3-Diamine Derivatives from Haloalkynes and Amines. *Org. Lett.* **2012**, *14*, 5385-5387. d) Feng, C.; Loh, T.-P. Palladium-Catalyzed Bisolefination of C−C Triple Bonds: A Facile Method for the Synthesis of Naphthalene Derivatives. *J. Am. Chem. Soc.* **2010**, *132*, 17710-17712.

[3] For selected reviews, see: a) Twilton, J.; Le, C.; Zhang, P.; Shaw, M. H.; Evans, R. W.; MacMillan, D. W. C. The Merger of Transition Metal and Photocatalysis. *Nat. Rev. Chem.* **2017**, *1*, 0052. b) Romero, N. A.; Nicewicz, D. A. Organic Photoredox Catalysis. *Chem. Rev.* **2016**, *116*, 10075-10166. c) Ravelli, D.; Protti, S.; Fagnoni, M. Carbon–Carbon Bond Forming Reactions via Photogenerated Intermediates. *Chem. Rev.* **2016**, *116*, 9850-9913. d) Skubi, K. L.; Blum, T. R.; Yoon, T. P. Dual Catalysis Strategies in Photochemical Synthesis. *Chem. Rev.* **2016**, *116*, 10035-10074. e) Murphy, J. J.; Melchiorre, P. Organic Chemistry: Light Opens Pathways for Nickel Catalysis. *Nature* **2015**, *524*, 297-298. f) Meggers, E. Asymmetric Catalysis Activated by Visible Light. *Chem. Commun*. **2015**, *51*, 3290-3301. g) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev.* **2013**, *113*, 5322-5363. h) Xuan, J.; Xiao, W.-J. Visible-Light Photoredox Catalysis. *Angew. Chem. Int. Ed.* **2012**, *51*, 6828-6838. i) Narayanam, J. M. R.; Stephenson, C. R. J. Visible Light Photoredox Catalysis: Applications in Organic Synthesis. *Chem. Soc. Rev.* **2011**, *40*, 102-113.

[4] Zhou, R.; Liu, H.-W; Tao, H.-R.; Yu, X.-J.; Wu, J. Metal-Free Direct Alkylation of Unfunctionalized Allylic/Benzylic sp^3 C–H Bonds via Photoredox Induced Radical Cation Deprotonation. *Chem. Sci.* **2017**, *8*, 4654-4659.

[5] a) Giese, B. Formation of CC Bonds by Addition of Free Radicals to Alkenes. *Angew. Chem. Int. Ed.* **1983**, *22*, 753-764. b) Ryu, I.; Uehara, S.; Hirao, H.; Fukuyama, T. Tin-Free Giese Reaction and the Related Radical Carbonylation Using Alkyl Iodides and Cyanoborohydrides. *Org. Lett.* **2008**, *10*, 1005-1008.

[6] a) Kamijo, S.; Takao, G.; Kamijo, K.; Tsuno, T.; Ishiguro, K.; Murafuji, T. Alkylation of Nonacidic C(sp^3)–H Bonds by Photoinduced Catalytic Michael-Type Radical Addition. *Org. Lett.* **2016**, *18*, 4912-4915. b) Bonassi, F.; Ravelli, D.; Protti, S.; Fagnoni, M. Decatungstate Photocatalyzed Acylations and Alkylations in Flow via Hydrogen Atom Transfer. *Adv. Synth. Catal.* **2015**, *357*, 3687-3695. c) Qrareya, H.; Ravelli, D.; Fagnoni, M.; Albini, A. Decatungstate Photocatalyzed Benzylation of Alkenes with Alkylaromatics. *Adv. Synth. Catal.* **2013**, *355*, 2891-2899. d) Ueda, M.; Kondoh, E.; Ito, Y.; Shono, H.; Kakiuchi, M.; Ichii, Y.; Kimura, T.; Miyoshi, T.; Naito, T.; Miyata*,* O. Benzyl Radical Addition Reaction Through the Homolytic Cleavage of A Benzylic C–H bond. *Org. Biomol. Chem.* **2011**, *9*, 2062-2064. e) Cermenati, L.; Fagnoni, M.; Albini, A. TiO_2-Photocatalyzed Reactions of Some Benzylic Donors. *Can. J. Chem.* **2003**, *81*, 560-566. f) Mella, M.; Fagnoni, M.; Albini, A. Benzyl Radicals from Toluene by Photosensitization with Naphthalene-1,4-dicarbonitrile – Benzylation and Hydroxymethylation of Unsaturated Compounds. *Eur. J. Org. Chem.* **1999**, 2137-2142.

[7] a) Sibi, M. P.; Jasperse, C. P.; Ji, J.-G. Lewis Acid-Mediated Intermolecular β-Selective Radical Additions to *N*-Enoyloxazolidinones. *J. Am. Chem. Soc.* **1995**, *117*, 10779-10780. b) Sibi, M. P.; Ji, J.-G. Participation of Organotin Lewis Acids in Radical Reactions: Manipulation of Rotamer Population in *N*-Enoyloxazolidinones. *J. Am. Chem. Soc.* **1996**, *118*, 3063-3064. c) Sibi, M. P.; Ji, J.-G.; Sausker, J. B.; Jasperse, C. P. Free Radical-

Mediated Intermolecular Conjugate Additions. Effect of the Lewis Acid, Chiral Auxiliary, and Additives on Diastereoselectivity. *J. Am. Chem. Soc.* **1999**, *121*, 7517-7526. d) Sibi, M. P.; Porter, N. A. Enantioselective Free Radical Reactions. *Acc. Chem. Res.* **1999**, *32*, 163-171. e) Sibi, M. P.; Manyem, S.; Zimmerman, J. Enantioselective Radical Processes. *Chem. Rev.* **2003**, *103*, 3263-3295. f) Sibi, M. P.; Petrovic, G.; Zimmerman, J. Enantioselective Radical Addition/Trapping Reactions with α, β-Disubstituted Unsaturated Imides. Synthesis of anti-Propionate Aldols. *J. Am. Chem. Soc.* **2005**, *127*, 2390-2391. g) Sibi, M. P.; Yang, Y-H.; Lee, S. Tin-Free Enantioselective Radical Reactions Using Silanes. *Org. Lett.* **2008**, *10*, 5349-5352.

[8] a) Yoon, T. P. Photochemical Stereocontrol Using Tandem Photoredox–Chiral Lewis Acid Catalysis. *Acc. Chem. Res.* **2016**, *49*, 2307-2315. b) Amador, A. G.; Sherbrook, E. M.; Yoon, T. P. Enantioselective Photocatalytic [3 + 2] Cycloadditions of Aryl Cyclopropyl Ketones. *J. Am. Chem. Soc.* **2016**, *138*, 4722-4725. c) Huo, H.-H.; Harms, K.; Meggers, E. Catalytic, Enantioselective Addition of Alkyl Radicals to Alkenes via Visible-Light-Activated Photoredox Catalysis with a Chiral Rhodium Complex. *J. Am. Chem. Soc.* **2016**, *138*, 6936-6939. d) Espelt, L. R.; McPherson, I. S.; Wiensch, E. M.; Yoon, T. P. Enantioselective Conjugate Additions of α-Amino Radicals via Cooperative Photoredox and Lewis Acid Catalysis. *J. Am. Chem. Soc*. **2015**, *137*, 2452-2455. e) Du, J.; Skubi, K. L.; Schultz, D. M.; Yoon, T. P. A Dual-Catalysis Approach to Enantioselective [2 + 2] Photocycloadditions Using Visible Light. *Science* **2014**, *344*, 392-396. f) Zhu, S.-Q.; Rueping, M. Merging Visible-Light Photoredox and Lewis Acid Catalysis for the Functionalization and Arylation of Glycine Derivatives and Peptides. *Chem. Commun.* **2012**, *48*, 11960-11962. g) Ischay, M. A.; Anzovino, M. E.; Du, J.; Yoon, T. P. Efficient Visible Light Photocatalysis of [2+2]

Enone Cycloadditions. *J. Am. Chem. Soc*. **2008**, *130*, 12886-12887. h) Tutkowski, B.; Meggers, E.; Wiest, O. Understanding Rate Acceleration and Stereoinduction of an Asymmetric Giese Reaction Mediated by a Chiral Rhodium Catalyst. *J. Am. Chem. Soc*. **2017**, *139*, 8062-8065.

[9] For selected recent literatures on chiral copper Lewis acid catalysts, see: a) Rodríguez-Fernández, M.; Yan, X.-C.; Collados, J. F.; White, P. B.; Harutyunyan, S. R. Lewis Acid Enabled Copper-Catalyzed Asymmetric Synthesis of Chiral β-Substituted Amides. *J. Am. Chem. Soc.* **2017**, *139*, 14224-14231. b) Jumde, R. P.; Lanza, F.; Veenstra, M. J.; Harutyunyan, S. R. Catalytic Asymmetric Addition of Grignard Reagents to Alkenyl-Substituted Aromatic N-heterocycles. *Science* **2016**, *352*, 433-437. c) Guo, C.; Song, J.; Luo, S.-W.; Gong, L.-Z. Enantioselective Oxidative Cross-Coupling Reaction of 3-Indolylmethyl C−H Bonds with 1,3-Dicarbonyls Using a Chiral Lewis Acid-Bonded Nucleophile to Control Stereochemistry. *Angew. Chem. Int. Ed*. **2010**, *49*, 5558-5562; d) Ishihara, K.; Fushimi, M. Catalytic Enantioselective [2 + 4] and [2 + 2] Cycloaddition Reactions with Propiolamides. *J. Am. Chem. Soc*. **2008**, *130*, 7532-7533.

[10] Franz, J.; Camaioni, D. M; Beishline, R. R.; Dalling, D. K. Products, Radical Intermediates, and Hydrogen Atom Production in the Thermal Decomposition of 1,2-Dihydronaphthalene. *J. Org. Chem.* **1984**, *49*, 3563-3570.

[11] See the Supporting Information for details on the control experiments, luminescence quenching studies, CV tests, and DFT calculations.

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