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Manganese-Catalyzed Ring-Opening Coupling Reactions of Cyclopropanols with Enones

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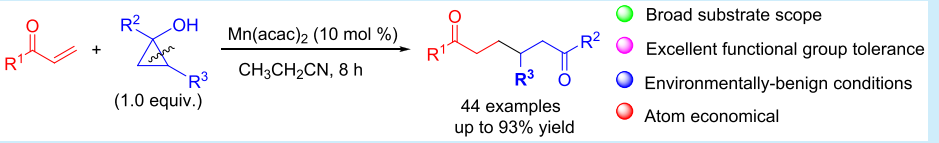
Supporting Information

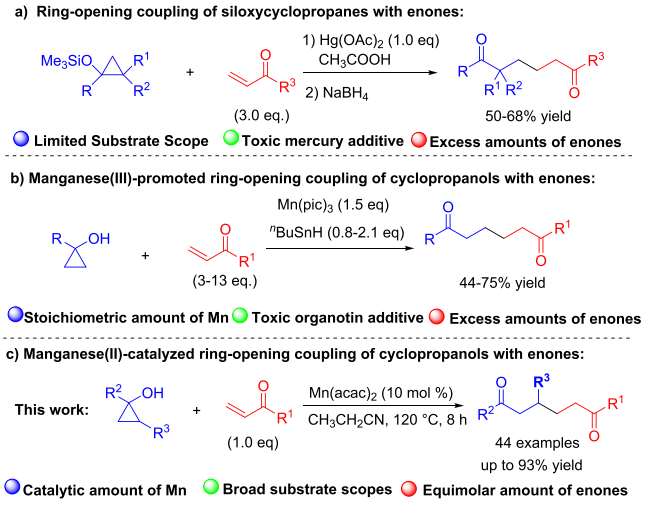


ABSTRACT: A manganese-catalyzed ring-opening coupling reaction of cyclopropanols with enones for the facile and efficient preparation of 1,6-diketones is described. A wide array of synthetically important 1,6-diketones bearing manifold functional groups are obtained with up to 93% yield. These reactions feature broad substrate scopes, environmentally benign conditions, inexpensive catalyst, and operational simplicity.

1,6-Diketones are privileged and pivotal building blocks in the construction of biologically and pharmaceutically important five- and six-membered carbocyclic and heterocyclic compounds.[1] In contrast to their structural analogues such as 1,4- and 1,5-diketones which could be easily and efficiently prepared through dozens of methods,[2] the synthetic strategies to access 1,6-diketones are considered to be more challenging and less developed.[3] The generally applicable methods leading to 1,6-diketones include transition-metal-catalyzed hydration of alkynes,[4] Wacker-type oxyfunctionalization of terminal alkenes,[5] oxidative ring-opening cleavage of cyclohexanone, cyclohexenes and vicinal diols,[6] and reductive homocoupling of enones.[7] However, most of the above-mentioned methods suffer from limitations including relatively harsh reaction conditions, nonreadily available starting materials, limited substrate scopes that always gave rise to symmetrical 1,6-diketones, as well as other limitations in terms of selectivity and efficiency. Unsymmetrical 1,6-diketones bearing a broad array of functional groups are recognized as more attractive synthetic targets in comparison with their symmetrical analogues in view of their versatile utilities in modern synthetic chemistry. In the past few decades, the carbon−carbon bond-forming reaction of β-carbonyl nucleophiles (generated through copper-, mercury-, or silver-promoted electrophilic ring opening of siloxycyclopropanes)[8] or β-carbonyl radicals (generated via manganese-promoted ring opening of cyclopropanol derivatives)[9] with electrophilic enones has emerged as an efficacious and useful reaction platform for the preparation of unsymmetrical 1,6-diketones.

Nevertheless, the pioneering examples to furnish unsymmetrical 1,6-diketones via the reaction of β-carbonyl nucleophiles/or radicals with enones as demonstrated by Giese[8c] and Narasaka[9] suffered from relative limitations in terms of the employment of more than a stoichiometric amount of heavy metal reagents such as mercury acetate (Scheme 1a) or radical initiators such as tributylhydrido tin (Scheme 1b), the need of an excess amount of enones, as well as the selectivity issue attributed to the inevitable formation of homocoupling products. In this regard, the quest for catalytic

Scheme 1. Ring-Opening Coupling of Cyclopropanol Derivatives with Enones to Access 1,6-Diketones



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protocols for the practical and selective preparation of unsymmetrical 1,6-diketones under operationally simple and environmentally benign conditions remains an unmet challenge for synthetic chemists.

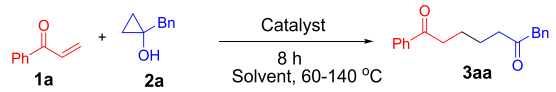
In the past few years, cyclopropanols prepared through Kulinkovich reaction[10] have been widely employed as surrogates of homoenolates or β-keto radicals for the preparation of β-functionalized ketones or aldehydes, as evidenced by several significant breakthroughs achieved by the groups of Narasaka,[9] Chiba,[11] Dai,[12] Cha,[13] Zhu,[14] Walsh,[15] Li,[16] Kananovich,[17] Ma,[18] Wang,[19] Chen,[20] Orellana,[21] and many others.[22] Our group has also demonstrated a silver-catalyzed oxidative fluorination of cyclopropanols to yield β-fluorinated ketones.[23] Enlightened by those seminal works, we herein demonstrated a highly selective and efficient manganese-catalyzed ring-opening coupling reaction of cyclopropanols with equimolar amounts of enones, giving rise to a broad range of synthetically valuable unsymmetrical 1,6-diketones bearing various functional groups in an atom-economical and environmentally benign manner without resorting to substrate prefunctionalization and toxic metal reagents (Scheme 1c).

Our investigation commenced by examining the model reaction of 1-benzylcyclopropan-1-ol (**2a**) with phenyl vinyl ketone (**1a**) to optimize the reaction conditions.

The reaction was performed at 60 °C using acetonitrile as the solvent. Unsurprisingly, the desired 1,6-diketone (**3aa**) was not obtained in the absence of catalyst (Table 1, entry 1). Meanwhile, a number of transition-metal catalysts such as $CoBr_2$, $Pd(OAc)_2$, $RhCl(PPh_3)_3$, and $NiCl_2$ etc., proved to be noneffective for the above transformation (Table 1, entries 2–9). It is worth noting that in the presence of $InCl_3$, $FeCl_3$, and $Fe(OTf)_3$ the reaction proceeded to give the desired product, albeit in moderate yields (Table 1, entries 10–12). Subsequently, a number of manganese catalysts were examined, and it was observed that $Mn(OAc)_3$, $Mn(acac)_3$, $MnBr_2$, and $Mn(OAc)_2$ were inferior to the reactivity (Table 1, entries 13–16). To our delight, $Mn(acac)_2$ could efficiently promote the reaction to forge **3aa** in 66% yield. Upon the elevation of the reaction temperature, a dramatic increase of the product yields was observed (Table 1, entries 17–20). The optimal result was obtained when $Mn(acac)_2$ was employed as a catalyst and propiononitrile bearing a higher boiling point than acetonitrile was used as a solvent at 120 °C (Table 1, entry 20).

With the optimal reaction conditions in hand, we started to investigate the substrate scope with respect to enones, and the results were summarized in Scheme 2.

Table 1. Optimization of Reaction Conditions[a]

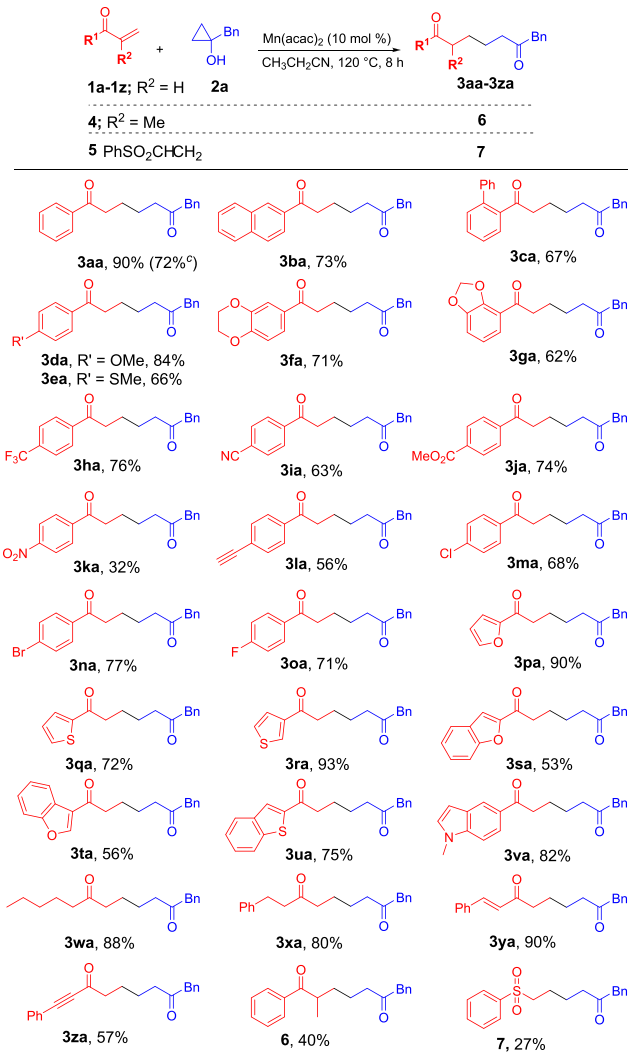


1a 2a 3aa

entry	catalyst	solvent	temp (°C)	yield[b] (%)
1	-	CH_3CN	60	0
2	$CoBr_2$	CH_3CN	60	0
3	$Co(OAc)_2$	CH_3CN	60	0
4	$Fe(acac)_3$	CH_3CN	60	0
5	$PdCl_2$	CH_3CN	60	<5%
6	$Pd(OAc)_2$	CH_3CN	60	0
7	$NiCl_2$	CH_3CN	60	0
8	$[Rh(C_5Me_5)_2]_2$	CH_3CN	60	0
9	$RhCl(PPh_3)_3$	CH_3CN	60	0
10	$InCl_3$	CH_3CN	60	30
11	$FeCl_3$	CH_3CN	60	53
12	$Fe(OTf)_3$	CH_3CN	60	45
13	$MnBr_2$	CH_3CN	60	<5%
14	$Mn(OAc)_2$	CH_3CN	60	<5%
15	$Mn(OAc)_3$	CH_3CN	60	0
16	$Mn(acac)_3$	CH_3CN	60	0
17	$Mn(acac)_2$	CH_3CN	60	66
18	$Mn(acac)_2$	C_2H_5CN	80	70
19	$Mn(acac)_2$	C_2H_5CN	100	88
20	$Mn(acac)_2$	C_2H_5CN	120	90
21	$Mn(acac)_2$	C_2H_5CN	140	88

[a]Unless otherwise noted, all reactions were performed with **1a** (0.5 mmol), **2a** (0.5 mmol), catalyst (10 mol %), and solvent (2 mL), for 8 h. [b]Isolated yields.

Scheme 2. Substrate Scope of Enones[a,b]



[a]Unless otherwise noted, all reactions were performed with **1a**–**1z**, **4** or **5** (0.5 mmol), **2a** (0.5 mmol), $Mn(acac)_2$ (10 mol %), and CH_3CH_2CN (2 mL), for 8 h. [b]Isolated yields. [c]The reaction was performed on a 3.4 mmol scale, with **1a** (0.45 g, 3.4 mmol), **2a** (0.5 g, 3.4 mmol), $Mn(acac)_2$ (0.34 mmol), and CH_3CH_2CN (35 mL).

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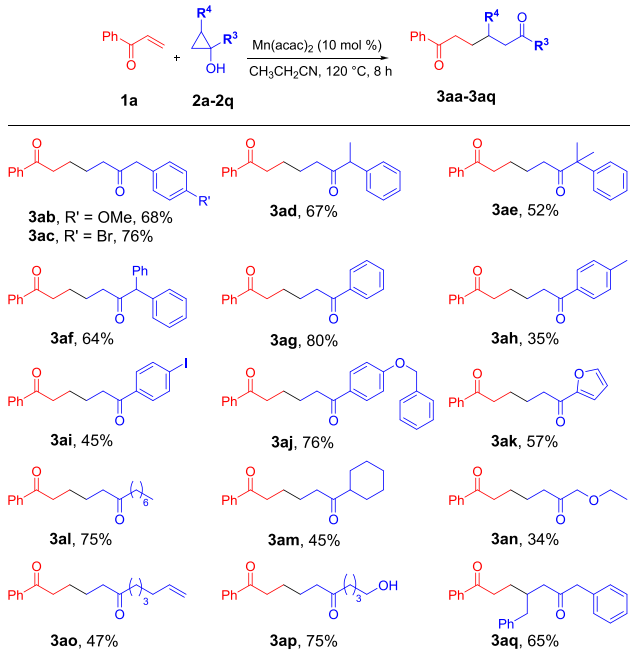
In general, enones bearing either electron-donating groups (**1a**−**1g**) or electron-withdrawing substituents (**1h**−**1k**) were viable substrates that could react with 1-benzylcyclopropan-1-ol (**2a**) smoothly to give the desired products (**3aa**−**3ja**) in moderate to good yields. It is notable that a diverse range of synthetically crucial functional groups such as $-CF_3$, −CN, $-CO_2Me$, $-NO_2$, and alkyne moiety were well tolerated in standard reaction conditions and remained intact. Notably, halide-substituted 1,6-diketones **3ma** and **3na** were also attained in good yields, rendering them amenable for further functionalization through cross-coupling reactions. Gratifyingly, a diverse array of heterocyclic-substituted enones were well-adapted to the reaction with **2a** to furnish the desired 1,6-diketones (**3pa**−**3va**) in 53−93% yields. Importantly, aliphatic enones were eligible substrates to give **3wa** and **3xa** in excellent yields, respectively. Unsaturated alkene and alkyne substituents did not result in a deleterious effect on the reaction, thus giving **3ya** and **3za** in synthetically useful yields. It was notable that *α*-methyl-substituted enone **4** could also react with **2a** smoothly to give the coupling product **6**, albeit with a slight decrease of the product yield. In addition, the *α*,*β*-unsaturated sulfone **6** proved to be a feasible coupling partner of **2a** to forge the desired product **7** in 27% yield. Remarkably, in all cases, equimolar amounts of enones were adequate to produce the 1,6-diketones in satisfying yields in an atom-economical manner. Gratifyingly, a large-scale reaction of **1a** of **2a** proved to be practical and efficient, forging **3aa** in 72% yield.

Next, the substrate scope of cyclopropanols was also investigated, and the results were summarized in Scheme 3.

Scheme 3. Substrate Scope of Cyclopropanols[a,b]

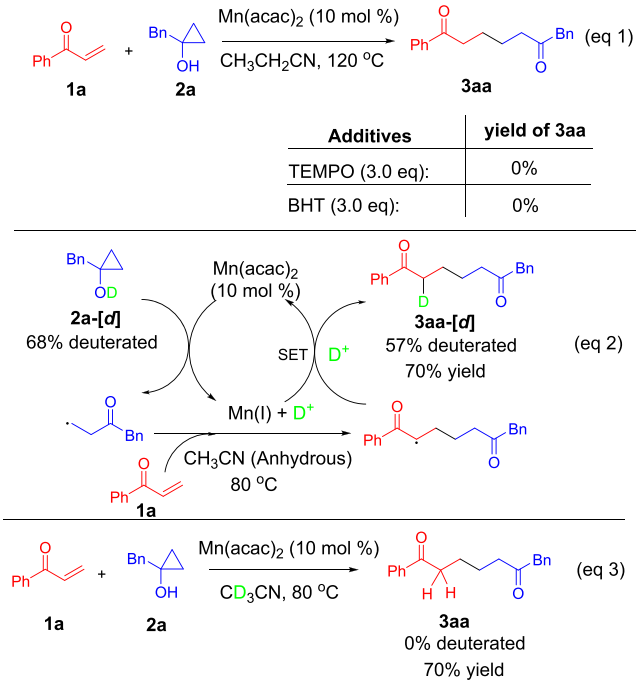


[a]Unless otherwise noted, all reactions were performed with **1a** (0.5 mmol), **2a**−**2q** (0.5 mmol), catalyst (10 mol %), and solvent (2 mL), for 8 h. [b]Isolated yields.

Initially, a broad range of benzyl-substituted cyclopropanols were examined. To our delight, the substituents on the phenyl ring and benzylic position did not lead to an obvious negative effect on the reaction efficiency, giving **3ab**−**3af** in moderate to good yields. Next, a plethora of phenyl-substituted cyclopropanols proved to be viable in this reaction to furnish the desired products **3ag**−**3aj** in synthetically useful yields. Also noteworthy was the excellent compatibility of furan-containing cyclopropanol, affording **3ak** in 57% yields. Gratifyingly, aliphatic-substituted cyclopropanols uneventfully participate in the transformation to provide **3al**−**3an** with good yields and selectivities. Notably, the presence of relatively sensitive functional groups such as an alkene moiety and hydroxyl group did not attenuate the reaction efficiency, thus giving rise to synthetically useful products **3ao** and **3ap** in one step without resorting to the protection and deprotection steps. It is notable that the trisubstituted cyclopropanol (**2q**) also proved to be a suitable substrate for this transformation, affording **3aq** in 65% yield.

To shed more light on the mechanism of the aforementioned transformations, a series of control experiments were conducted. The reaction of **1a** with **2a** in the presence of radical scavengers such as 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) under optimized conditions was completely suppressed, implicating a plausible radical pathway (Scheme 4, eq 1). Importantly, the

Scheme 4. Control Experiments



reaction of deuterium-labeled cyclopropanol **2a**-[*d*] (68% deuterated) with **1a** led to the formation of 1,6-diketone **3aa**-[*d*] (57% deuterated), which was probably formed through the addition of a *β*-carbonyl radical to enone followed by an ensuing D-abstraction (Scheme 4, eq 2). The ring-opening coupling reaction carried out in deuterated acetonitrile led to no deuterium-substituted product, thus ruling out the possibility of solvent as the deuterium source (Scheme 4, eq 3).

A plausible radical reaction pathway was proposed to rationalize the above observations, as depicted in Figure 1. Initially, the reaction of $Mn(acac)_2$ with cyclopropanol **2a** gives a Mn(I) species and an O-centered radical species (**I**) through proton-coupled electron transfer (PCET),[24] wherein the

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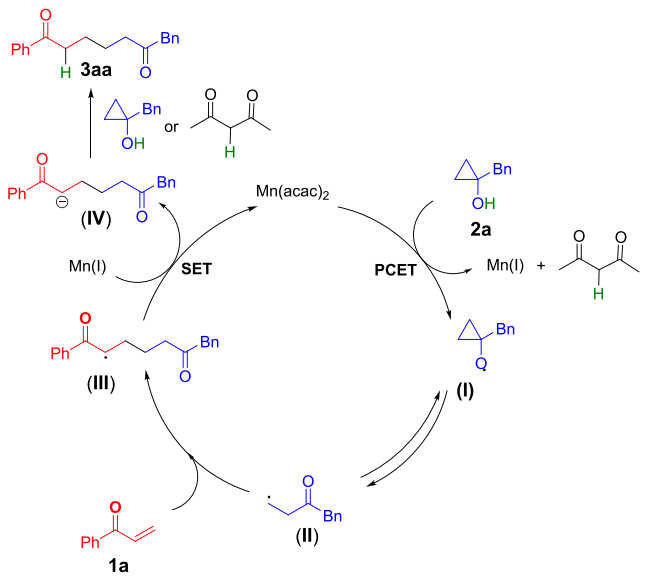

Figure 1. Plausible mechanism of the ring-opening coupling reactions.

proton transfers to the acetylacetonate anion to generate acetylacetone. Subsequently, the O-centered radical species undergoes ring-opening isomerization to generate a C-centered radical species (**II**), which is then intercepted by enone to furnish the radical intermediate (**III**). Next, the radical intermediate (**III**) is converted into an anion species (**IV**) via single electron transfer along with the regeneration of the $Mn(acac)_2$ to complete the catalytic cycle. Finally, the protonation of the anion intermediate (**IV**) by **2a** or acetylacetone occurs to afford the desired 1,6-diketone product.

In summary, we have developed an efficient and robust manganese-catalyzed ring-opening coupling reaction of cyclopropanols with enones. This transformation exhibits broad substrate scopes, excellent tolerance to diverse functional groups, and environmentally benign reaction conditions. Preliminary mechanistic studies enable a radical-mediated pathway. This novel synthetic strategy may open up a brand new avenue for the delivery of synthetically important unsymmetrical 1,6-diketone derivatives, which are versatile building blocks toward a variety of natural products and pharmaceuticals.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b01703.

Experimental details, analytical data, and ^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Brown, H. C.; Racherla, U. S.; Singh, S. M. *Synthesis* **1984**, *1984*, 922−924. (b) Nishinaga, A.; Rindo, K.; Matsuura, T. *Synthesis* **1986**, *1986*, 1038−1041. (c) Saikia, A.; Chetia, A.; Bora, U.; Boruah, R. C. *Synlett* **2003**, *10*, 1506−1508.

(2) (a) O'Neill, E. T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol *1*, p 448, p 452. (b) Hassner, A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol *1*, p 542. (c) Panek, J. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol *1*, p 558. (d) Solladie, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol *6*, p 159. (e) Linderman, R. J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. *1*, p 738. (f) Varvounis, G. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. *2*, p 923. (g) Fan, W.-Q.; Katritzky, A. R. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. *4*, p 91. (h) Page, P. C. B.; McFarland, H. L.; Millar, A. P. In *Comprehensive Organic Functional Group Transformation*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Pergamon Press: Oxford, 1995; Vol. *1*, p 254. (i) Vallée, Y.; Bulpin, A. In *Comprehensive Organic Functional Group Transformation*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Pergamon Press: Oxford, 1995; Vol. *4*, pp 255, 287. (j) Che, C.; Qian, Z.; Wu, M.; Zhao, Y.; Zhu, G. *J. Org. Chem.* **2018**, *83*, 5665−5673.

(3) (a) Katritzky, A. R.; Huang, Z. Z.; Fang, Y. F.; Prakash, I. *J. Org. Chem.* **1999**, *64*, 2124−2126. (b) Balskus, E. P.; Mendez-Andino, J.; Arbit, R. M.; Paquette, L. A. *J. Org. Chem.* **2001**, *66*, 6695−6704. (c) Dekker, J.; Martins, F. J. C.; Kruger, J. A. *Tetrahedron Lett.* **1975**, *16*, 2489−2490. (d) Maekawa, H.; Nakano, K.; Hirashima, T.; Nishiguchi, I. *Chem. Lett.* **1991**, *20*, 1661−1664. (e) Ryu, I.; Ikebe, M.; Sonoda, N.; Yamato, S.-y.; Yamamura, G.-h.; Komatsu, M. *Tetrahedron Lett.* **2000**, *41*, 5689−5692. (f) Watanabe, S.; Suga, K.; Fujita, T.; Takahashi, Y. *Can. J. Chem.* **1972**, *50*, 2786−2787. (g) van Leusen, A. M.; Oosterwijk, R.; van Echten, E.; van Leusen, D. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 50−53.

(4) Xu, Y.; Hu, X. B.; Shao, J.; Yang, G. Q.; Wu, Y. T.; Zhang, Z. B. *Green Chem.* **2015**, *17*, 532−537.

(5) (a) Mitsudome, T.; Umetani, T.; Nosaka, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 481−485. (b) Yokota, T.; Sakakura, A.; Tani, M.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2002**, *43*, 8887−8891.

(6) (a) Kasun, Z. A.; Geary, L. M.; Krische, M. J. *Chem. Commun.* **2014**, *50*, 7545−7547. (b) Miyamoto, K.; Sei, Y.; Yamaguchi, K.; Ochiai, M. *J. Am. Chem. Soc.* **2009**, *131*, 1382−1383. (c) Fujiwara, T.; Tsuruta, Y.; Arizono, K.; Takeda, T. *Synlett* **1997**, *1997*, 962−964. (d) Lee, J. C.; Ku, C. H. *Synlett* **2002**, 1679−1680. (e) Murayama, E.; Sato, T. *Tetrahedron Lett.* **1977**, *18*, 4079−4082.

(7) (a) Theocharis, C. R. *The Chemistry of Enones. Chapter 22. Dimerization and polymerization of enones in the fluid and solid states*; John Wiley & Sons Ltd., 1989. (b) Pons, J. M.; Santelli, M. *Tetrahedron Lett.* **1988**, *29*, 3679−3682. (c) Taniguchi, Y.; Nakahashi,

DOI: 10.1021/acs.orglett.9b01703
Org. Lett. XXXX, XXX, XXX−XXX

M.; Kuno, T.; Tsuno, M.; Makioka, Y.; Takaki, K.; Fujiwara, Y. *Tetrahedron Lett.* **1994**, *35*, 4111−4114. (d) Di Vona, M. L.; Rosnati, V. *Chem. Inform.* **1993**. (e) Wang, C. C.; Lin, P. S.; Cheng, C. H. *Tetrahedron Lett.* **2004**, *45*, 6203−6206.

(8) (a) Ryu, I.; Matsumoto, K.; Kameyana, Y.; Ando, M.; Kusumoto, N.; Ogawa, A.; Kambe, N.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1993**, *115*, 12330−12339. (b) Giese, B.; Horler, H.; Zwick, W. *Tetrahedron Lett.* **1982**, *23*, 931−934. (c) Giese, B.; Horler, H. *Tetrahedron* **1985**, *41*, 4025−4037. (d) Ryu, I.; Ando, M.; Ogawa, A.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1983**, *105*, 7192−7194.

(9) Iwasawa, N.; Hayakawa, S.; Funahashi, M.; Isobe, K.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 819−827.

(10) (a) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2789−2834. (b) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597−2632. (c) Kulinkovich, O. G. *Russ. Chem. Bull.* **2004**, *53*, 1065−1086. (d) Wolan, A.; Six, Y. *Tetrahedron* **2010**, *66*, 15−61. (e) Epstein, O. L.; Lee, S.; Cha, J. K. *Angew. Chem., Int. Ed.* **2006**, *45*, 4988−4991. (f) Lee, H. G.; Lysenko, I.; Cha, J. K. *Angew. Chem., Int. Ed.* **2007**, *46*, 3326−3328. (g) Racouchot, S.; Sylvestre, I.; Ollivier, J.; Kozyrkov, Y. Y.; Pukin, A.; Kulinkovich, O. G.; Salaün, J. *Eur. J. Org. Chem.* **2002**, *2002*, 2160−2176.

(11) Wang, Y. F.; Chiba, S. *J. Am. Chem. Soc.* **2009**, *131*, 12570−12572.

(12) (a) Li, Y.; Ye, Z.; Bellman, T. M.; Chi, T.; Dai, M. *Org. Lett.* **2015**, *17*, 2186−2189. (b) Ye, Z.; Dai, M. *Org. Lett.* **2015**, *17*, 2190−2193. (c) Ye, Z.; Gettys, K. E.; Shen, X.; Dai, M. *Org. Lett.* **2015**, *17*, 6074−6077. (d) Davis, D. C.; Walker, K. L.; Hu, C.; Zare, R. N.; Waymouth, R. M.; Dai, M. J. *J. Am. Chem. Soc.* **2016**, *138*, 10693−10699. (e) Ye, Z.; Cai, X.; Li, J.; Dai, M. J. *ACS Catal.* **2018**, *8*, 5907−5914.

(13) (a) Parida, B. B.; Das, P. P.; Niocel, M.; Cha, J. K. *Org. Lett.* **2013**, *15*, 1780−1783. (b) Murali, R. V. N. S.; Rao, N. N.; Cha, J. K. *Org. Lett.* **2015**, *17*, 3854−3856. (c) Rao, N. N.; Parida, B. B.; Cha, J. K. *Org. Lett.* **2014**, *16*, 6208−6211. (d) Ydhyam, S.; Cha, J. K. *Org. Lett.* **2015**, *17*, 5820−5823.

(14) (a) Zhao, H. J.; Fan, X. F.; Yu, J. J.; Zhu, C. *J. Am. Chem. Soc.* **2015**, *137*, 3490−3493. (b) Fan, X.; Zhao, H.; Yu, J.; Bao, X.; Zhu, C. *Org. Chem. Front.* **2016**, *3*, 227−232. For similar examples using cyclobutanols to access γ-functionalized Ketones, see: (c) Ren, R.; Wu, Z.; Xu, Y.; Zhu, C. *Angew. Chem., Int. Ed.* **2016**, *55*, 2866−2869. (d) Ren, R.; Zhao, H.; Huan, L.; Zhu, C. *Angew. Chem., Int. Ed.* **2015**, *54*, 12692−12696. (e) Wang, D. P.; Ren, R. G.; Zhu, C. *J. Org. Chem.* **2016**, *81*, 8043−8049.

(15) Cheng, K.; Walsh, P. J. *Org. Lett.* **2013**, *15*, 2298−2301.

(16) (a) Zhou, X. K.; Yu, S. J.; Kong, L. H.; Li, X. W. *ACS Catal.* **2016**, *6*, 647−651. (b) Zhou, X. K.; Yu, S. J.; Qi, Z. S.; Kong, L. H.; Li, X. W. *J. Org. Chem.* **2016**, *81*, 4869−4875.

(17) (a) Konik, Y. A.; Elek, G. Z.; Kaabel, S.; Järving, I.; Lopp, M.; Kananovich, D. G. *Org. Biomol. Chem.* **2017**, *15*, 8334−8340. (b) Kananovich, D. G.; Konik, Y. A.; Zubrytski, D. M.; Järving, I.; Lopp, M. *Chem. Commun.* **2015**, *51*, 8349−8352.

(18) Wu, P. L.; Jia, M. Q.; Lin, W. L.; Ma, S. M. *Org. Lett.* **2018**, *20*, 554−557.

(19) Zhang, H.; Wu, G. J.; Yi, H.; Sun, T.; Wang, B.; Zhang, Y.; Dong, G. B.; Wang, J. B. *Angew. Chem., Int. Ed.* **2017**, *56*, 3945−3950.

(20) Jia, K. F.; Zhang, F. Y.; Huang, H. C.; Chen, Y. Y. *J. Am. Chem. Soc.* **2016**, *138*, 1514−1517.

(21) (a) Nithiy, N.; Orellana, A. *Org. Lett.* **2014**, *16*, 5854−5857. (b) Rosa, D.; Orellana, A. *Org. Lett.* **2011**, *13*, 110−113. (c) Rosa, D.; Orellana, A. *Chem. Commun.* **2013**, *49*, 5420−5422. (d) Nikolaev, A.; Legault, C. Y.; Zhang, M. H.; Orellana, A. *Org. Lett.* **2018**, *20*, 796−799.

(22) (a) Jiao, J.; Nguyen, L. X.; Patterson, D. R.; Flowers, R. A. *Org. Lett.* **2007**, *9*, 1323−1326. (b) Ilangovan, A.; Saravanakumar, S.; Malayappasamy, S. *Org. Lett.* **2013**, *15*, 4968−4971. (c) Wang, S.; Guo, L.-N.; Wang, H.; Duan, X.-H. *Org. Lett.* **2015**, *17*, 4798−4801. (d) Liu, H.; Fu, Z.; Gao, S.; Huang, Y.; Lin, A. J.; Yao, H. Q. *Adv. Synth. Catal.* **2018**, *360*, 3171−3175. (e) Huang, F.-Q.; Xie, J.; Sun, J.-G.; Wang, Y.-W.; Dong, X.; Qi, L.-W.; Zhang, B. *Org. Lett.* **2016**, *18*, 684−687. (f) Lu, S.-C.; Li, H.-S.; Xu, S.; Duan, G.-Y. *Org. Biomol. Chem.* **2017**, *15*, 324−327. (g) Feng, Y.-S.; Shu, Y.-J.; Cao, P.; Xu, T.; Xu, H.-J. *Org. Biomol. Chem.* **2017**, *15*, 3590−3593. (h) He, X.-P.; Shu, Y.-J.; Dai, J.-J.; Zhang, W.-M.; Feng, Y.-S.; Xu, H.-J. *Org. Biomol. Chem.* **2015**, *13*, 7159−7163. (i) Wang, C.-Y.; Song, R.-J.; Xie, Y.-X.; Li, J.-H. *Synthesis* **2016**, *48*, 223−230.

(23) Ren, S. C.; Feng, C.; Loh, T.-P. *Org. Biomol. Chem.* **2015**, *13*, 5105−5109.

(24) For selected reviews on PCET, see: (a) Huynh, M. H. V.; Meyer, T. *Chem. Rev.* **2007**, *107*, 5004−5064. (b) Hammes-Schiffer, S. *Acc. Chem. Res.* **2001**, *34*, 273−281.

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