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Perchloric Acid Catalyzed Homogeneous and Heterogeneous Addition of β-Dicarbonyl Compounds to Alcohols and Alkenes and Investigation of the Mechanism

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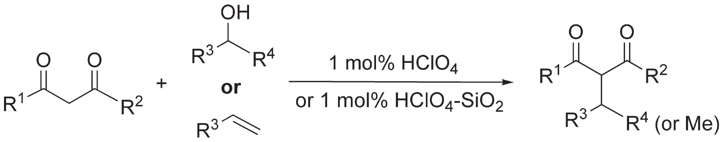

The direct addition of various β-dicarbonyl compounds to a series of secondary alcohols and alkenes has been achieved using 1 mol % perchloric acid ($HClO_4$) as the catalyst. The $HClO_4$-catalyzed reactions could be conveniently conducted in commercial solvent and gave moderate to excellent yields. Moreover, the silica gel-supported $HClO_4$ could also catalyze the heterogeneous addition for a series of substrates with similar or even higher yields in comparison with the homogeneous ones. The supported catalyst could be readily recovered and reused for four runs. Furthermore, the mechanism of the $HClO_4$-catalyzed addition of the β-diketone to alcohol was investigated, and an S_N1 mechanism was proved unambiguously for the first time through a series of experiments. The discrimination of catalytic abilities among different Brønsted acids was also rationalized by DFT calculations.

Introduction

The construction of C−C bonds is always one of the central themes in organic synthesis.[1] Because of the call of "green chemistry",[2] the direct reaction of alcohols (ROH) and active methylenes (R'-CH_2-R'') has attracted much attention in recent years because only H_2O is generated as the side product and the preparation of the active intermediates, such as organometallic compounds and halides or a related species, is not required. Although the advantages of enhancing atom efficiency and avoiding waste are realized, the successful examples of such "green" transformation are limited due to the low reactivity of alcohols toward the nucleophiles.[3] Recently, some Lewis acidic metal catalysts such as $InCl_3$,[4] $InBr_3$,[5] $FeCl_3$,[6] $Bi(OTf)_3$,[7] and $Ln(OTf)_3$ (Ln = La, Yb, Sc, Hf)[8] have been described as effective catalysts for the addition of β-dicarbonyl compounds to allylic and benzylic alcohols. Besides, Brønsted acids, such as H-montmorillonite,[9]

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[1] (a) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992. (b) *Current Trends in Organic Synthesis*; Scolastico, C., Nicotra, F., Eds.; Plenum: New York, 1999.

[2] (a) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University, Press: New York, 1988. (b) Matlack, A. S. *Introduction to Green Chemistry*; Marcel Dekker Inc.: New York, 2001. (c) Lancester, M. *Green Chemistry: An Introductory Text*; Royal Society of Chemistry: Cambridge, 2002. (d) Clark, J. H.; Macquarrie, D. *Handbook of Green Chemistry & Technology*; Blackwell Publishers: Oxford, 2002.

[3] Guillena, G.; Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2358.

[4] Yasuda, M.; Somyo, T.; Baba, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 793.

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[6] (a) Kischel, J.; Mertins, K.; Michalik, D.; Zapf, A.; Beller, M. *Adv. Synth. Catal.* **2007**, *349*, 865. (b) Yuan, Y.; Shi, Z.; Feng, X.; Liu, X. *Appl. Organomet. Chem.* **2007**, *21*, 958. (c) Jana, U.; Biswas, S.; Maiti, S. *Tetrahedron Lett.* **2007**, *48*, 4065.

[7] Rueping, M.; Nachtsheim, B. J.; Kuenkel, A. *Org. Lett.* **2007**, *9*, 825.

[8] (a) Noji, M.; Konno, Y.; Ishii, K. *J. Org. Chem.* **2007**, *72*, 5161. (b) Huang, W.; Wang, J.; Shen, Q.; Zhou, X. *Tetrahedron Lett.* **2007**, *48*, 3969.

[9] (a) Motokura, K.; Fujita, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2605. (b) Motokura, K.; Nakagiri, N.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Org. Chem.* **2007**, *72*, 6006.

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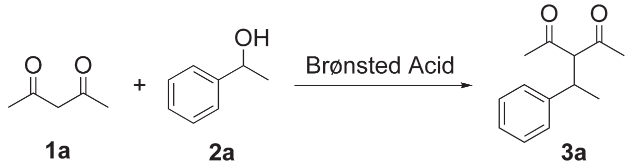
"dodecylbenzenesulfonic acid,[10] *p*-toluenesulfonic acid,[11,12] triflic acid,[12]" and 12-phosphotungstic acid,[13] have been found to be the effective catalysts for the addition of β-diketones to secondary alcohols in recent years.

Although remarkable progress has been made in the Lewis acid or Brønsted acid catalyzed addition of β-dicarbonyl compounds to alcohols, few investigations of the reaction mechanism have been conducted and no single process has been established. Recently, we have successfully applied a perchloric ruthenium complex to the addition of β-diketones to secondary alcohols and alkenes.[14] Further mechanistic investigation of this Lewis acid catalyzed addition has revealed that the ruthenium complex reacts first with the β-diketone to form a stable β-diketone chelate ruthenium complex and concomitantly yields an equivalent of perchloric acid, which proved to be the true catalyst for the addition reaction. From this preliminary study, we became interested in the addition of β-dicarbonyl compounds to alcohols and alkenes catalyzed directly by $HClO_4$ and the reaction mechanism of the Brønsted acid catalyzed addition. Herein, we report our results of the efficient homogeneous and heterogeneous addition of β-dicarbonyl compounds to alcohols and alkenes catalyzed by perchloric acid ($HClO_4$) and the silica gel supported perchloric acid ($HClO_4-SiO_2$), as well as the investigation of the reaction mechanism through experimental and theoretical studies.

Results and Discussion

$HClO_4$-Catalyzed Reactions. In the screening of effective catalysts and reaction conditions, we chose acetylacetone (**1a**) and 1-phenylethanol (**2a**) as the substrates for model reaction. It can be seen from Table 1 that some usual Brønsted acids such as HCl, HBF_4, HNO_3, CF_3CO_2H, and CH_3CO_2H were all ineffective for the reaction of **1a** and **2a**, except that H_2SO_4 gave 9% yield after 17 h (Table 1, entries 1−6). TfOH and $HClO_4$ proved to be effective catalysts for the addition of **1a** to **2a** to generate **3a**, and $HClO_4$ gave the higher yield (Table 1, entries 7 and 8). In this $HClO_4$-catalyzed addition, only 1 mol % catalyst loading was needed compared with 5 mol % TfOH in the early report.[12] The reactions of **1a** and **2a** catalyzed by $HClO_4$ could be conveniently conducted in air in the absence of solvent or in commercial grade solvents such as toluene, 1,2-dichloroethane (DCE) or $CHCl_3$; the reaction in toluene gave the best result (Table 1, entries 8−12). When the temperature was increased or decreased, the yields were affected negatively after the same reaction time (Table 1, entries 13 and 14). Moreover, this reaction also proceeded smoothly when only 0.4 mol % $HClO_4$ was used (Table 1, entry15). Interestingly, the best result (88% yield) was obtained when 2 equiv of **2a** relative to **1a** were used, although better reaction results are observed when excess molar of **1a** are used in most related reports[8−12] (Table 1, entry 16). If the reaction time was shortened, the reactions gave worse yields (Table 1, entries 17 and 18).

TABLE 1. Reactions of 1a and 2a Using Brønsted Acids As Catalysts under Various Conditions[a]



entry	acid	solvent	temp (°C)	yield (%)[b]
1	HCl	toluene	70	0
2	HBF_4	toluene	70	0
3	HNO_3	toluene	70	0
4	CF_3CO_2H	toluene	70	0
5	CH_3CO_2H	toluene	70	0
6	H_2SO_4	toluene	70	9
7	TfOH	toluene	70	74
8	$HClO_4$	toluene	70	83
9	$HClO_4$	DCE	70	73
10	$HClO_4$	$CHCl_3$	70	70
11	$HClO_4$	1,4-dioxane	70	0
12	$HClO_4$	solvent-free	70	76
13	$HClO_4$	solvent-free	60	57
14	$HClO_4$	solvent-free	80	68
15[c]	$HClO_4$	toluene	70	63
16	$HClO_4$	toluene	70	88
17	$HClO_4$	toluene	70	74[d]
18	$HClO_4$	toluene	70	80[e]

[a] Reaction conditions: acid (0.01 mmol), **1a** (1.5 mmol), **2a** (1.0 mmol), 17 h, 2.0 mL of solvent was added where noted. [b] Based on **2a** except for entry 16 where 1.0 mmol of **1a** and 2.0 mmol of **2a** were used. [c] 0.004 mmol of $HClO_4$ was used. [d] The reaction time was 6 h. [e] The reaction time was 12 h.

Subsequently, the addition of β-diketones to various alcohols was examined in commercial grade toluene at 70 °C, using 1 mol % $HClO_4$ as the catalyst (Table 2). The reactions of β-diketones **1a**−**c** with benzylic alcohols **2a**−**e** were all highly effective, giving products in excellent yields (Table 2, entries 1−5, 10, 12−14). Note that when 1-(4-nitrophenyl)ethanol with a strong electron-withdrawing group on the aromatic ring was used to react with **1a** and **1c**, no addition product (with **1a**) or only trace product (with **1c**) was observed. Acetylacetone **1a** also reacted with 1-(2-naphthyl)ethanol **2f** smoothly to give **3f** in moderate (65%) yield, and this yield could not be enhanced even when the reaction time was prolonged (Table 2, entry 6). The reactions of β-diketones and diphenylmethanol **2g** also afforded the products in excellent to good yields (Table 2, entries 7 and 15). In the allylation of **1a** with allylic alcohol **2h**, product **3h** was obtained with 75% yield after 70 h, although only 59% yield was observed after 17 h (Table 2, entry 8). Moreover, the allylations of **1a** and **1c** with allylic alcohol **2i** proceeded smoothly, although the yields of the products **3i** and **3p** were a little lower than those using benzylic alcohols (Table 2, entries 9 and 16). Note that the identity of **3p** has been confirmed from X-ray crystallography analysis (Supporting Information).[15] The reaction of **1c** and *exo*-norborneol **2j** produced **3q** in 98% yield but needed a prolonged reaction time due to the rigid structure of **2j** (Table 2, entry 17). When the sterically hindered cyclic diketone **1d** was used in the reaction with **2g**, product **3r** with a quaternary carbon atom

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(10) Shirakawa, S.; Kobayashi, S. *Org. Lett.* **2007**, *9*, 311.

(11) (a) Sanz, R.; Martínez, A.; Miguel, D.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Adv. Synth. Catal.* **2006**, *348*, 1841. (b) Sanz, R.; Miguel, D.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Org. Lett.* **2007**, *9*, 727.

(12) Sanz, R.; Miguel, D.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Org. Lett.* **2007**, *9*, 2027.

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(14) Liu, P. N.; Zhou, Z. Y.; Lau, C. P. *Chem.—Eur. J.* **2007**, *13*, 8610.

(15) See Supporting Information.

TABLE 2. Reactions of Various β-Dicarbonyl Compounds and Alcohols Catalyzed by $HClO_4$[a]

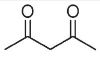
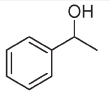
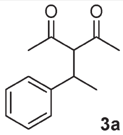
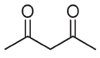
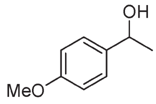
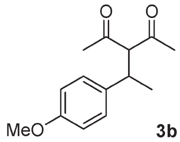
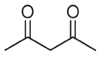
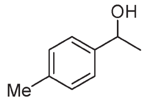
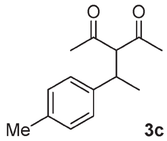
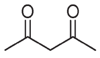
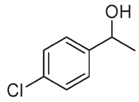
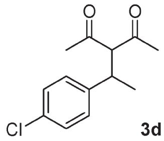
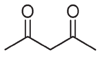
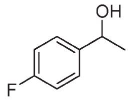
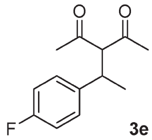
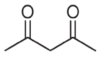
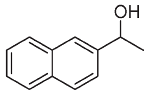
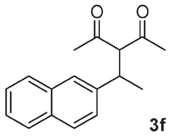
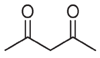
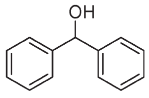
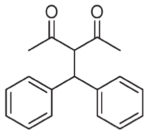
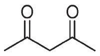
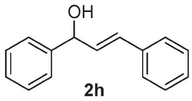
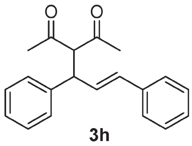
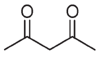
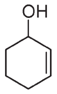
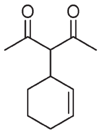
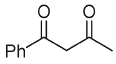
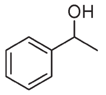
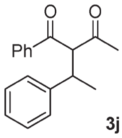
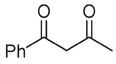
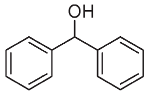
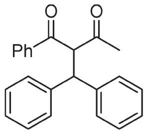
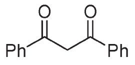
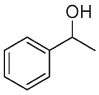
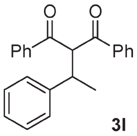
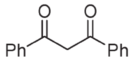
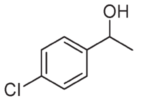
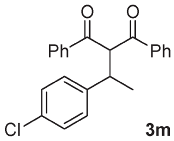
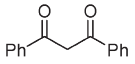
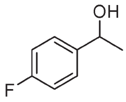
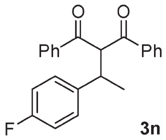
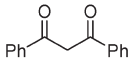
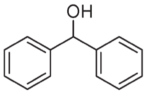
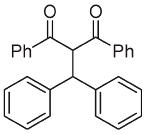
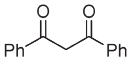
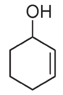
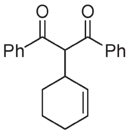
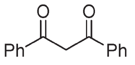
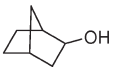
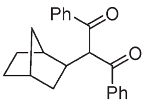
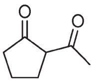
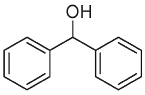
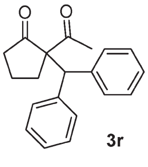
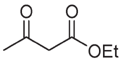
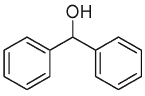
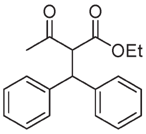
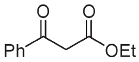
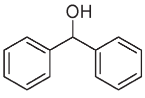
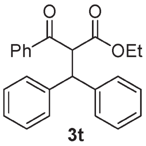
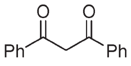
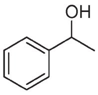
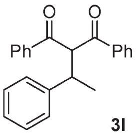
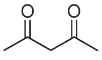
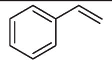
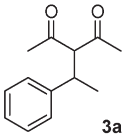
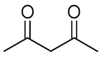
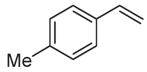
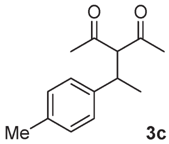
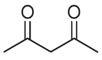
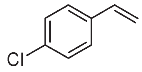
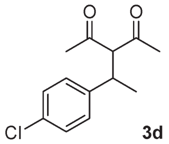
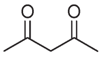
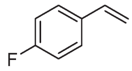
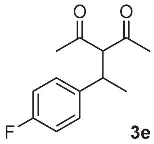
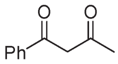
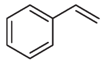
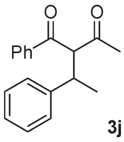
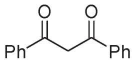
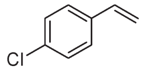
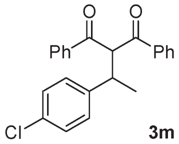
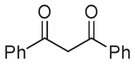
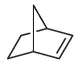
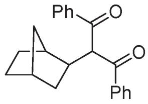
entry	dicarbonyl compound	alcohol	product	yield (%)[b]
1	 **1a**	 **2a**	 **3a**	88
2	 **1a**	 **2b**	 **3b**	83
3	 **1a**	 **2c**	 **3c**	81
4	 **1a**	 **2d**	 **3d**	70
5	 **1a**	 **2e**	 **3e**	96
6	 **1a**	 **2f**	 **3f**	65
7[c,d]	 **1a**	 **2g**	 **3g**	98
8[d]	 **1a**	 **2h**	 **3h**	75
9	 **1a**	 **2i**	 **3i**	73
10	 **1b**	 **2a**	 **3j**	98 (1:0.8)[e]
11	 **1b**	 **2g**	 **3k**	96

TABLE 2. Continued

entry	dicarbonyl compound	alcohol	product	yield (%)[b]
12	 **1c**	 **2a**	 **3l**	95
13	 **1c**	 **2d**	 **3m**	98
14	 **1c**	 **2e**	 **3n**	86
15	 **1c**	 **2g**	 **3o**	77
16	 **1c**	 **2i**	 **3p**	68
17[c,d]	 **1c**	 **2j**	 **3q**	98
18[f]	 **1d**	 **2g**	 **3r**	96
19	 **1e**	 **2g**	 **3s**	82
20	 **1f**	 **2g**	 **3t**	99
21[g]	 **1c**	 **2a**	 **3l**	89

[a] Reaction conditions: $HClO_4$ (0.01 mmol), β-dicarbonyl compound (1.0 mmol), alcohol (2.0 mmol), toluene (2 mL), 70 °C, 17 h unless noted. [b] Based on β-dicarbonyl compounds used. [c] 2 mL of DCE was used as the solvent. [d] The reaction time was 70 h. [e] The diastereomer ratio was determined by ^{1}H NMR. [f] 0.03 mmol of $HClO_4$ was used. [g] 20 mmol of alcohol and 10 mmol of β-diketone were used

TABLE 3. Addition of Various β-Diketones to Alkenes Catalyzed by $HClO_4$[a]

entry	diketone	alkene	product	yield (%)[b]
1[c]	 **1a**	 **4a**	 **3a**	71
2	 **1a**	 **4b**	 **3c**	58
3	 **1a**	 **4c**	 **3d**	76
4	 **1a**	 **4d**	 **3e**	79
5	 **1b**	 **4a**	 **3j**	57 (1:0.8)[d]
6	 **1c**	 **4c**	 **3m**	56
7[e]	 **1c**	 **4e**	 **3q**	80

[a] Reaction conditions: $HClO_4$ (0.01 mmol), β-diketone (1.0 mmol), alkene (2.0 mmol), toluene (2 mL), 70 °C, 20 h, unless noted. [b] Based on β-diketone used. [c] The reaction was performed at 80 °C. [d] The diastereomer ratio was determined by ^1H NMR. [e] The reaction was performed in 2 mL of CH_3NO_2 with 5 mol % $HClO_4$.

at C2 of the five-membered ring was obtained in 96% yield, using 3 mol % $HClO_4$ as the catalyst (Table 2, entry18). In an expansion of the substrates, β-keto esters **1e** and **1f** were used in reaction with diphenylmethanol **2g**, and products **3s** and **3t** were obtained successfully in high yields (Table 2, entries 19 and 20). However, the $HClO_4$-catalyzed addition of β-diester to secondary alcohols was not successful under the present reaction conditions, nor was the addition of β-diketones to primary alcohols. By increasing the reaction scale to 10 mmol of **1c** and 20 mmol of **2a**, 2.92 g (89% yield) of product was isolated, thereby demonstrating the applicability of this $HClO_4$-catalyzed reaction in organic compound preparation (Table 2, entry 21).

The addition of β-dicarbonyl compounds to olefins, which yields alkylated dicarbonyls, is considered to be a highly atom-economical process.[16] Several cases of palladium-catalyzed intramolecular[17] and intermolecular addition[18] of β-dicarbonyl compounds to olefins have been described. Li and coworkers have employed silver triflate or combinations of silver and gold salts as catalysts for the addition of β-dicarbonyl compounds to styrenes, dienes, trienes, and cyclic enol ethers.[19] Recently, H-montmorillonite,[9] $Bi(OTf)_3$,[20] $FeCl_3$,[21] $Cu(OTf)_2$,[22] and phosphotungstic acid[23] were also reported to be effective to catalyze the addition of β-diketones to

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[16] (a) Trost, B. M. *Science* **1991**, *254*, 1471. (b) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259. (c) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695.

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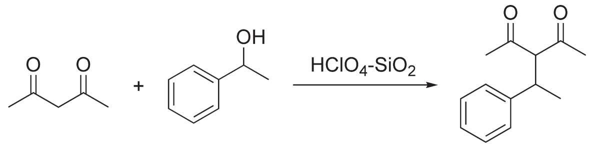
alkenes. At this stage, we were curious to see whether $HClO_4$ was also active in catalytic addition of acetylacetone to styrene (**4a**) and yielded the same product **3a**.

With 1 mol % $HClO_4$ as catalyst, various diketones **1a**−**c** reacted with styrenes **4a**−**d** and 2-norbornene **4e** in toluene at 70 °C to yield the corresponding addition products in moderate yields (Table 3). Compared with the corresponding addition of β-diketones to alcohols, the yields were generally lower and probably result from side reaction forming dimer or oligomers.

$HClO_4$−SiO_2 Catalyzed Reactions. On the demanding of "green chemistry", catalyst immobilization has attracted lots of attention in the past decades, because heterogeneous catalysis provides for easy separation of the products from the catalysts without tedious experimental workup. Moreover, it enables the efficient recovery of the catalysts and allows for the potential adaptation of the immobilized catalysts in continuous flow-type processes.[24] In recent years, a series of reactions were studied using silica gel supported perchloric acid ($HClO_4$−SiO_2) as the catalyst.[25]

To expand the versatility of $HClO_4$-catalyzed addition of β-diketones to alcohols, we tried the heterogeneous addition of β-diketones to alcohols and styrene in the presence of $HClO_4$−SiO_2 (containing 1 mol % $HClO_4$). We were gratified to find that the addition proceeds smoothly and displays even better reaction result than the homogeneous reaction with the acid. As shown in Table 4, immobilized catalysts **A**, **B**, and **C**, prepared respectively by simple absorption of $HClO_4$ onto 100−200 mesh, 200−300 mesh, or H-type silica gel, demonstrated similar reactivity for the reaction of **1a** and **2a** in toluene, and catalyst **B** gave the best yield (94%; Table 4, entries 1−3). Further optimization of the reaction conditions showed that the solvent-free reaction afforded even better result (96% yield) than the reaction in toluene (Table 4, entries 2 and 4). Recycling of the supported catalyst **B** was readily achieved by simple filtration and it could be used for four runs (Table 4, entries 4−7). However, if the ratio of **1a** to **2a** is changed from 1:2 to 2:1, both the product yield and recyclability of the catalyst diminished (Table 4, entries 8−11). This heterogeneous reaction is a rather nice case of green chemistry with the advantages of recyclable catalyst, solvent-free conditions, and only water as the byproduct.

TABLE 4. Reactions of 1a and 2a Using $HClO_4$−SiO_2 as Catalysts under Various Conditions[a]



entry	$HClO_4$−SiO_2	solvent	**1a**:**2a**	run	yield (%)[b]
1	**A**	toluene	1:2	1	93
2	**B**	toluene	1:2	1	94
3	**C**	toluene	1:2	1	92
4	**B**	neat	1:2	1	96
5	**B**	neat	1:2	2	92
6	**B**	neat	1:2	3	79
7	**B**	neat	1:2	4	70
8	**B**	neat	2:1	1	92
9	**B**	neat	2:1	2	91
10	**B**	neat	2:1	3	73
11	**B**	neat	2:1	4	0

[a] Reaction conditions: $HClO_4$−SiO_2 (containing 0.01 mmol $HClO_4$), **1a** (1.0 mmol), **2a** (2.0 mmol) as **1a**:**2a** = 1:2 or **1a** (2.0 mmol), **2a** (1.0 mmol) as **1a**:**2a** = 2:1, 70 °C, 17 h, 2.0 mL of solvent were added if noted. [b] Isolated yields based on **1a** as **1a**:**2a** = 1:2 or based on **2a** as **1a**:**2a** = 2:1.

Following the successes recorded above, we applied $HClO_4$−SiO_2 **B** to the heterogeneous addition of a range of β-dicarbonyl compounds to various alcohols and styrene under solvent-free conditions at 70 °C; the results are listed in Table 5. In the benzylation of β-diketones **1a**−**c** with benzylic alcohols **2a**−**d**, the reactions generating **3a** and **3c** provided better product yields while the other reactions listed led to similar or slightly worse yields compared with those from the homogeneous reactions (Table 5, entries 1−4, 7, 9, and 10). When the solid substrates were used, in some cases a small amount of solvent was needed to dissolve the reagents (Table 5, entries 5, 6, 8, 11, 12, and 14). The reaction of **1a** with 1-(2-naphthyl)ethanol **2f** gave much higher yield (93%) than the homogeneous reaction (65%) with 3 mol % catalyst loading (Table 5, entry 5). The addition of **1a**−**c** to diphenylmethanol **2g** also generated the products in excellent yields (Table 5, entries 6, 8, and 11). The sterically hindered cyclic diketone **1d** afforded the product **3r** in moderate yield with **2g** and 3 mol % $HClO_4$−SiO_2 **B** (Table 5, entry 12). When the substrates expanded to include β-keto esters **1e** and **1f**, the reactions also gave the products **3s** and **3t** smoothly in 85% and 98% yields, respectively (Table 5, entries 13 and 14). Moreover, the $HClO_4$−SiO_2 catalyzed addition of diketone **1a** to styrene **4a** gave 63% isolated yield (Table 5, entry 15).

Mechanism. The mechanism of addition of β-diketones to alcohols and alkenes catalyzed by Brønsted acids is generally thought to involve the formation of a carbocation intermediate and subsequent S_N1 attack on the β-dicarbonyl compound to yield the addition product.[2,12−14] However, no detailed experimental investigation on the mechanism of Brønsted acid catalyzed reaction has been reported in recent times. As the first stage of our mechanistic study, we performed the reaction of diketone **1c** and chiral alcohol (*S*)-**2a** (99% ee) in the presence of 1 mol % $HClO_4$ in toluene at 70 °C. After 17 h, the product **3l**, which could be analyzed by HPLC on chiral OJ-H column, was obtained as a racemate (Scheme 1). Such racemization has been regarded as the main proof for the S_N1 mechanism proposal in the early reports.[2,7,14]

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TABLE 5. Reactions of Various Alcohols and β-Dicarbonyl Compounds Catalyzed by $HClO_4$–SiO_2 B[a]

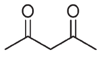
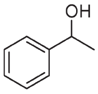
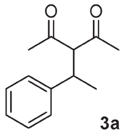
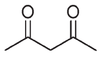
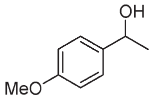
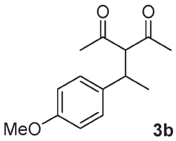
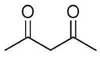
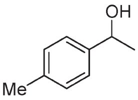
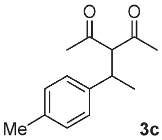
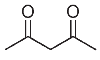
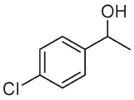
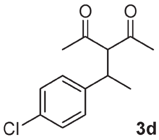
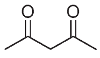
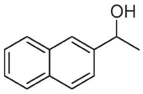
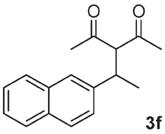
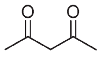
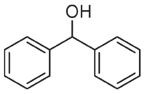
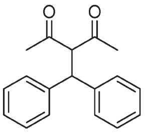
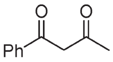
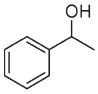
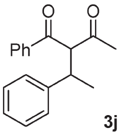
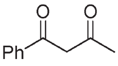
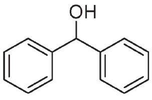
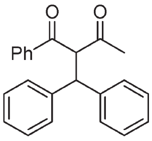
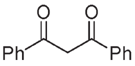
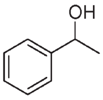
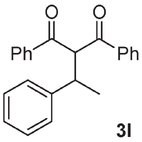
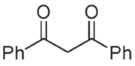
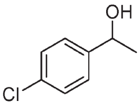
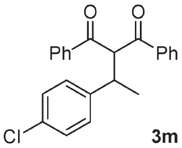
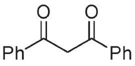
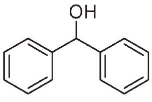
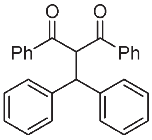
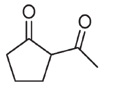
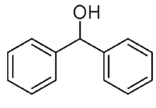
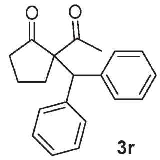
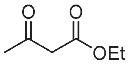
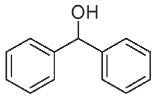
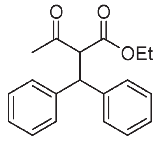
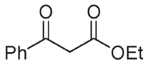
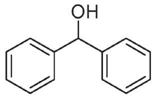
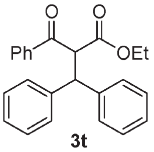
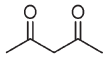
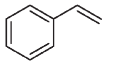
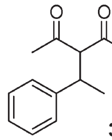
entry	dicarbonyl compound	alcohol	product	yield (%)[b]
1	 **1a**	 **2a**	 **3a**	96
2	 **1a**	 **2b**	 **3b**	82
3	 **1a**	 **2c**	 **3c**	92
4	 **1a**	 **2d**	 **3d**	57
5[c,d]	 **1a**	 **2f**	 **3f**	93
6[c,e,f]	 **1a**	 **2g**	 **3g**	95
7	 **1b**	 **2a**	 **3j**	97 (1:0.8)[g]
8[c]	 **1b**	 **2g**	 **3k**	99
9	 **1c**	 **2a**	 **3l**	95
10	 **1c**	 **2d**	 **3m**	88
11[c]	 **1c**	 **2g**	 **3o**	99

TABLE 5. Continued

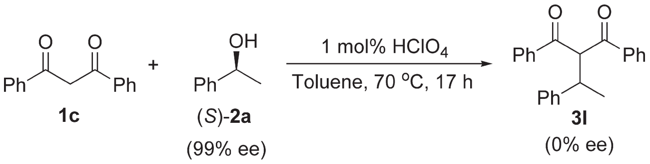
entry	dicarbonyl compound	alcohol	product	yield (%)[b]
12[c,d]	 **1d**	 **2g**	 **3r**	61
13[d]	 **1e**	 **2g**	 **3s**	85
14[c,d]	 **1f**	 **2g**	 **3t**	98
15[h]	 **1a**	 **4a**	 **3a**	63

[a]Reaction conditions: $HClO_4-SiO_2$ **B** (20 mg, containing 0.01 mmol $HClO_4$), *β*-diketone (1.0 mmol), alcohol (2.0 mmol), solvent-free, 70 °C, 17 h unless noted. [b]Based on *β*-diketone used. [c]Toluene (2 mL) was used as the solvent. [d]$HClO_4-SiO_2$ **B** (60 mg, containing 0.03 mmol $HClO_4$) was used. [e]DCE (2 mL) was used as the solvent. [f]The reaction time was 70 h. [g]The diastereomer ratio was determined by ^{1}H NMR. [h]The reaction was performed at 80 °C.

We suspected that the racemization of chiral alcohol likely occurred before the reaction of the alcohol with the *β*-diketone. To gain experimental evidence for the racemization of chiral alcohol, the same reaction of (*S*)-**2a** (99% ee) and **1c** with 1 mol % $HClO_4$ catalyst was carried out in toluene at 70 °C. HPLC analysis of the reaction mixture showed that the ee value of (*S*)-**2a** had decreased to 65% ee after 10 min, at which point only trace of **3l** could be detected. On heating a solution of (*S*)-**2a** (99% ee) in toluene to 70 °C in the presence of 1 mol % $HClO_4$, (*S*)-**2a** became achiral (< 5% ee) in 30 min. This demonstrates that (*S*)-**2a** racemizes before its reaction with **1c**, and one can not judge the process to be S_N1 or S_N2 just on the observation of racemic **3l** at the completion of the reaction.

The observed racemization of chiral alcohol in the $HClO_4$-catalyzed reaction argues that S_N2 mechanisms cannot be dismissed. In the early studies, the change of the cationic S_N1 mechanism to a concerted S_N2 mechanism has been reported for 1-phenylethyl substrates as the carbocation becomes less stable.[26] Recently, a concerted, eight-membered-ring transition structure was proposed for the addition of alcohol/amine to the alkene with TfOH as a catalyst.[27] Moreover, Brønsted acid oriented reactions, especially chiral Brønsted acid catalyzed asymmetric reactions, have attracted great attention in recent years.[28] In these transformations, a hydrogen bond is formed between the donor site of the acid catalyst and the acceptor site of the electrophile, and it is critical in achieving high reaction selectivity.[29] We were curious to see whether $HClO_4$ could also donate the proton to OH of the alcohol to form a hydrogen bond, which might assist an S_N2 reaction with the *β*-diketone. So, we carried out the DFT calculations on the $HClO_4$-catalyzed reaction of **1a** with **2a** through an S_N2 mechanism and found that the energy profiles seemed reasonable because the barrier of the S_N2 process was only 26.5 kcal/mol (the relative free

SCHEME 1. Reaction of (*S*)-2a and Diketone 1c with 1 mol % $HClO_4$ as the Catalyst



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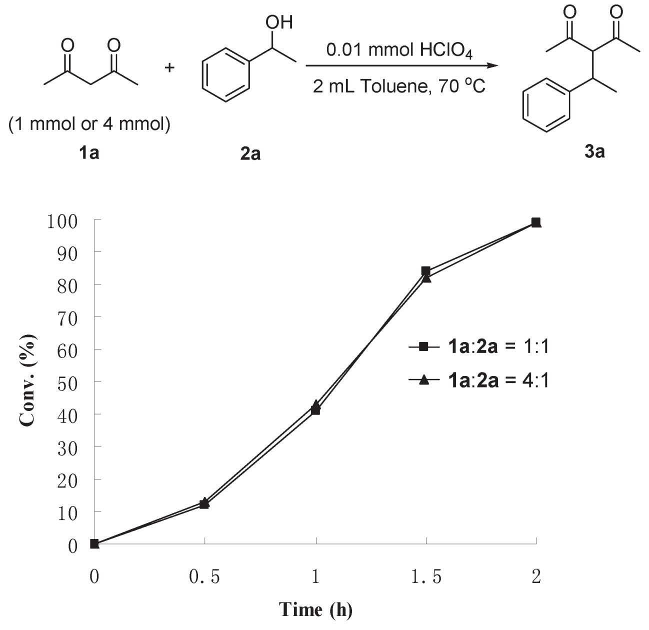

FIGURE 1. Conversion of **1a** into **3a** (based on **2a**) versus time plots of $HClO_4$-catalyzed reaction of **1a** and **2a** with 1:1 and 4:1 ratios.

energy, ΔG) and further lowered in calculations that included the solvation effect of toluene.[15]

The rate of addition is in direct proportion to the concentration of **1a** in an S_N2 mechanism and independent of it in an S_N1 mechanism. To further clarify the mechanism of the $HClO_4$-catalyzed addition of β-diketone to the alcohol, we carried out two parallel $HClO_4$-catalyzed reactions of **1a** and **2a** under identical reaction conditions, with one containing 1 equiv of **1a** and the other containing 4 equiv of **1a**. The conversions at different times were measured, and the results showed that the reactions proceeded with the same reaction rates (Figure 1). This observation demonstrates that the concentration of **1a** does not affect the reaction rate and that the reaction proceeds by an S_N1 mechanism.

It is known that acids can act as promoters for conversion of alcohols to symmetrical ethers.[12,14,30] In the reaction of **1a** and **2a** with 1 mol % $HClO_4$ as the catalyst, we noticed that the symmetric ether *meso*- and (±)-Ph(CH_3)CH-O-CH-(CH_3)Ph (**5**) was generated rapidly and consumed later with the formation of the addition product **3a**. For example, in the reaction of **1a** (1 mmol) and **2a** (1 mmol), ^{1}H NMR analysis at different reaction times showed **2a**:**5**:**3a** ratios of 0.83:6.7:1 (0.5 h), 0.12:1.31:1 (1 h), 0.02:0.17:1 (1.5 h), and 0:0:1 (2 h). Subsequent etherification of (*S*)-**2a** with 1 mol % $HClO_4$ as catalyst in toluene at 70 °C was complete in 40 min, and ^{1}H NMR analysis of the reaction mixture at 10 min showed the ratio of (*R*,*S*)-**5** to (*S*,*S*)-**5** to be 1:1, while **2a** still possessed 75% ee. This result is unambiguous in demanding that carbocation **6** is formed in the etherification reaction of (*S*)-1-phenylethanol through an S_N1 process (Scheme 3). Nucleophilic attack of chiral (*S*)-**2a** on another (*S*)-**2a** should generate (*R*,*S*)-**5** as the main product in the S_N2 reaction, whereas attack of chiral (*S*)-**2a** ($>75\%$ ee) to both faces of cation **6** would afford the equal amount of (*R*,*S*)-**5** and (*S*,*S*)-**5** in an S_N1 process.

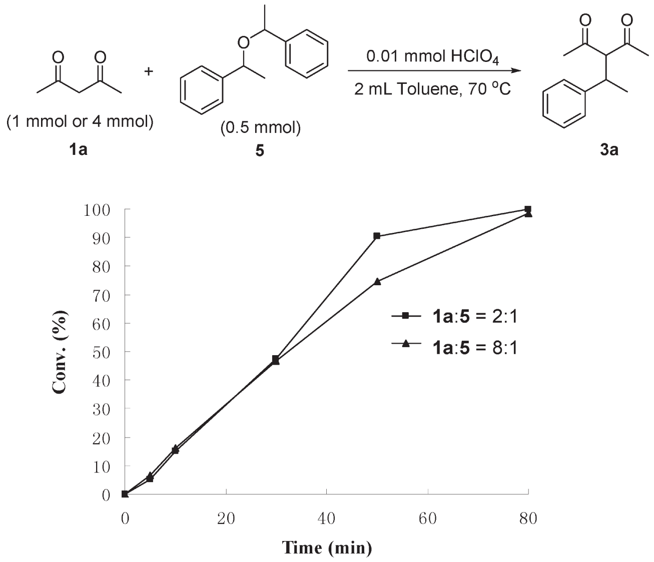

FIGURE 2. Conversion of **1a** into **3a** (based on **5**) versus time plots of $HClO_4$-catalyzed reaction of **1a** and **5** with 2:1 and 8:1 ratios.

Subsequently, two parallel $HClO_4$-catalyzed reactions of **1a** with *meso*- and (±)-ether **5** (**1a**:**5** = 2:1 and 8:1) were carried out under identical reaction conditions, except the 4-fold change in ratio of **1a** to **5**. The conversion of **1a** into **3a** at different reaction times was measured, and the results showed that the concentration of **1a** had no obvious effect on the reaction rate (Figure 2). This result also proves that the reaction of **1a** and **5** is by an S_N1 mechanism involving carbocation intermediate **6** because the rate of addition is in direct proportion to the concentration of **1a** in an S_N2 mechanism but independent of it in an S_N1 mechanism. Moreover, we analyzed product **3l** from **1c** and (*S*)-**2a** (99% ee) at 10 min, when (*S*)-**2a** still possessed 65% ee; $<2\%$ ee was observed for **3l** (Scheme 2). This result is also consistent with the S_N1 mechanism for the $HClO_4$-catalyzed reaction of **1c** and (*S*)-**2a**, because the reaction of **1c** with chiral (*S*)-**2a** ($>65\%$ ee) should give **3l** in $>65\%$ ee at 10 min in an S_N2 mechanism but with 0% ee in an S_N1 mechanism.

On the basis of the observations, we are prompted to propose the S_N1 mechanism of Scheme 3 (using acetylacetone **1a** and 1-phenylethanol **2a** as examples) for the addition of β-diketones to the secondary alcohols. The perchloric acid protonates the alcohol and carbocation intermediate **6** would rapidly be generated by loss of water. Intermediate **6** would then attack an alcohol molecule to give the symmetric *meso*- and (±)-ether **5** or undergo electrophilic attack at the α-carbon of the β-diketone to give the addition product, with regeneration of a proton. Note that the β-diketone might be preferentially in an enol tautomeric form in the nonpolar solvent (toluene) at higher temperature (70 °C).[31] Through the series of experiments described above, we have proved that the various reactions involve in the conversion, including **2a** and **1a** to **3a**, **2a** and **2a** to **5**, **5** and **1a** to **3a**, all proceed via S_N1 mechanisms. Although the mechanism discovered here is similar to those formerly proposed,[2,13,14] it is the first

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[30] Diaz, D. D.; Martín, V. S. *Tetrahedron Lett.* **2000**, *41*, 9993.

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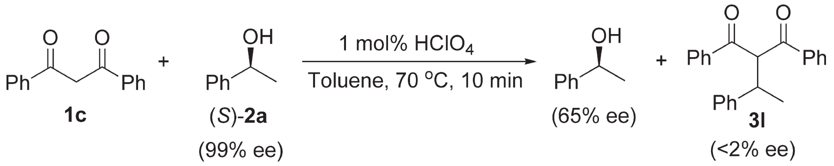
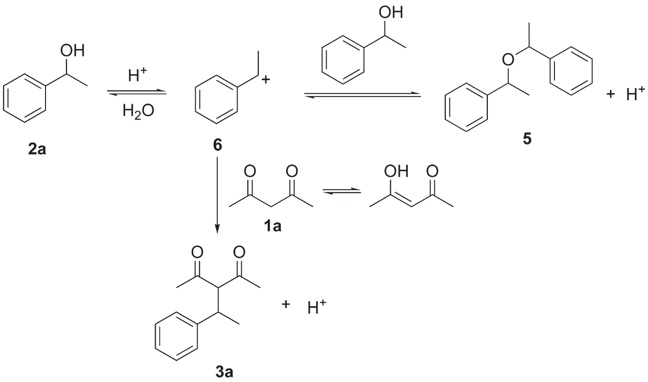
SCHEME 2. Reaction of (*S*)-2a and Diketone 1c with 1 mol % $HClO_4$ as Catalyst



SCHEME 3. Proposed Mechanism of the $HClO_4$-Catalyzed Addition of β-Diketones to Alcohols



unambiguous proof of an S_N1 mechanism for the addition of β-diketones to alcohols by experiments that include kinetic studies and racemization experiments. Note that in this $HClO_4$-catalyzed addition, the substitution of carbocations into the toluene ring have not been observed in the substrate scope we investigated. Moreover, with the mechanism established as S_N1, the reaction of allylic alcohols **2h** and **2i** must proceed via the delocalized allylic cation and the products were formed with the probability to capture at both C1 and C3.

To understand the discrimination of the catalytic abilities among various Brønsted acids, we carried out DFT calculations on the effect of different acids in carbocation formation. As shown in Scheme 4, the relative free energy ($\Delta G_{\text{toluene}}$) at 25 °C for the formation of carbocation **6** with $HClO_4$ in toluene is 32.7 kcal/mol (eq 1),[15] and corresponding $\Delta G_{\text{toluene}}$ with TfOH and H_2SO_4 in toluene are 33.0 and 40.2 kcal/mol (eqs 2 and 3), respectively. The calculations suggest that $HClO_4$ and TfOH are more powerful in facilitating generation of carbocation **6** in comparison with H_2SO_4. The calculations are also consistent with the experiment in that $HClO_4$ and TfOH are effective catalysts and H_2SO_4 exhibits only a very low reactivity in the addition of β-diketone to the alcohol (Table 1, entries 6−8). At the same time, compared with TfOH, a slightly smaller energy difference between reactants and carbocation intermediate for $HClO_4$ is consistent with the higher yield obtained with it as the catalyst (Table 1, entries 7 and 8). Our calculated free energies in gas phase at 70 °C are smaller than those at room temperature (see Table 3 in Supporting Information). This result is consistent with the experimental fact that the reactions carried out at higher temperature proceed more smoothly than those at room temperature.

To investigate whether a carbocation intermediate is also generated in the $HClO_4$-catalyzed addition of β-diketones to styrenes,[27] we performed two parallel reactions of **1a** and **4a** in 1:1 and 4:1 ratios, with 1 mol % $HClO_4$ as the catalyst. The yields of the product **3a** after 2 h in the two reactions were 42% and 43%, respectively, demonstrating that the concentration of **1a** has no effect on the reaction rate and that the addition of **1a** to **4a** also proceeds through a carbocation intermediate. So, a mechanism very similar to the addition of β-diketones to alcohols is proposed as operative for the $HClO_4$-catalyzed addition of β-diketones to styrenes (Scheme 5, using **1a** and **4a** as examples). Again, the crucial species is the carbocation intermediate **6**; it attacks the β-diketone (or in enol form) to yield the addition product or reacts with styrene to yield dimer and higher oligomers as byproduct,[32] which might result in the observed relatively low yield for the reactions of β-diketones with styrene.

Conclusion

In summary, very cheap $HClO_4$ (1 mol %) has been used for the first time as an effective catalyst for the direct addition of various β-dicarbonyl compounds to a series of sluggish alcohols or alkenes. The metal-free reactions gave out moderate to excellent yields with water as the only byproduct. Moreover, silica-gel-supported $HClO_4$ has also been successfully applied to give a solvent-free catalytic addition as an environmentally benign protocol. The supported catalyst could be readily recovered and reused for 4 runs. For a series of substrates, the heterogeneous catalytic reactions provided similar or better results in comparison with the homogeneous ones. Furthermore, the mechanism of the $HClO_4$-catalyzed addition of the β-diketone to alcohol was investigated in detail, and an S_N1 mechanism was unambiguously established for the first time. The catalytic abilities of different Brønsted acids was investigated through DFT calculations and $HClO_4$ was found to be the stronger promoter for the generation of the carbocation intermediate than TfOH and H_2SO_4.

Experimental Section

General. 1-(4-Methylphenyl)ethanol **2c**, 1-(4-chlorophenyl)-ethanol **2d**, 1-(4-fluororophenyl) ethanol **2e**, and 1,3-diphenyl-2-propenol **2h** were prepared by reduction of the corresponding ketone precursors with $NaBH_4$ in methanol. Chemical shifts (δ, ppm) in the ^1H spectra were recorded using TMS as internal standard. Chemical shifts in $^{13}C\{^1H\}$ NMR spectra were internally referenced to $CHCl_3$ (δ = 77.0 ppm). The silica gel was dried at 110 °C for 2 h before loading with $HClO_4$.

Typical Procedure A for the Reaction of β-Dicarbonyl Compound with Alcohol (or Styrene) Catalyzed by $HClO_4$. β-Dicarbonyl compound (1.0 mmol) and alcohol (or styrene, 2.0 mmol) were combined in 2 mL of toluene, and $HClO_4$ (1 μL, 60%,

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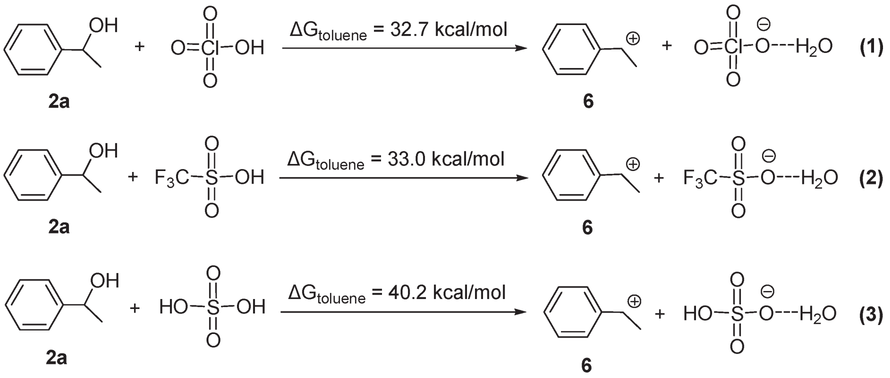
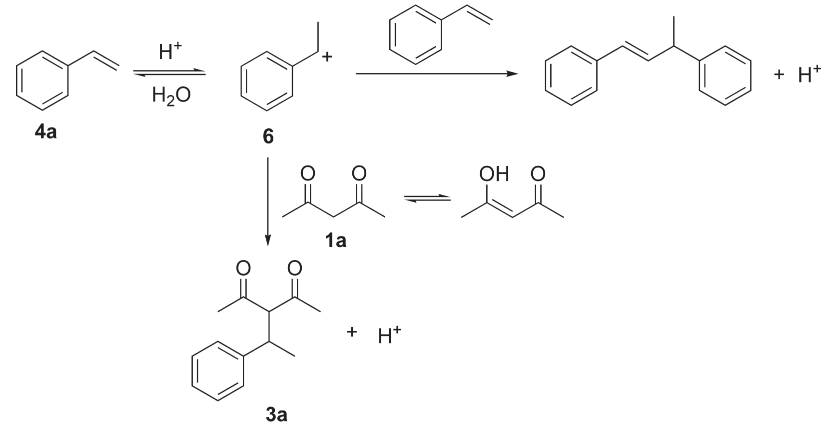
SCHEME 4. Computed Relative Free Energies (kcal/mol) for the Formation of Carbocation 6 from 1a with $HClO_4$, TfOH, or H_2SO_4 as the Catalysts in Toluene (see Table 3 in Supporting Information)



SCHEME 5. Proposed Mechanism of the $HClO_4$-Catalyzed Addition of β-Diketone to Styrene



0.01 mmol) was added. The mixture was stirred at 70 °C and monitored by TLC or ^1H NMR. When maximum conversion was reached, the solvent was removed under reduced pressure, and the residue was flash column chromatographed over silica gel to give the product.

Preparation of Silica Gel Supported Perchloric Acid ($HClO_4-SiO_2$).[25c]. To a suspension of silica gel (10.00 g) in Et_2O (35 mL) was added 70% aqueous solution of $HClO_4$ (0.75 g, 5.0 mmol), and the mixture was stirred magnetically for 30 min at room temperature. The Et_2O was removed under reduced pressure, and the residue was dried at 110 °C for 2 h to afford $HClO_4-SiO_2$ (0.5 mmol g^{-1}) as a white powder.

Typical Procedure B for the Reaction of β-Dicarbonyl Compound with Alcohol (Or Styrene) Catalyzed by $HClO_4-SiO_2$ and the Recycling Reactions. A mixture of the β-dicarbonyl compound (1.0 mmol), alcohol (or alkene, 2.0 mmol), and $HClO_4-SiO_2$ (20 mg, containing 0.01 mmol $HClO_4$) was combined and stirred vigorously at 70 °C (2 mL of toluene or DCE was added to dissolve the solid substrates as noted in entries 5, 6, 8, 11, 12, and 14 in Table 5). The reaction was monitored by TLC. After the completion of the reaction, CH_2Cl_2 (1 mL) was added, and the mixture was stirred for 1 min. Then the reactor was centrifuged (2000 rpm) for 1−2 min, and the solution was removed by syringe. The catalyst was then washed with CH_2Cl_2 (1 mL) twice, and the solution was removed; a new reaction could be conducted by adding the new batch of β-dicarbonyl compound (1.0 mmol) and alcohol (or alkene, 2.0 mmol) to the recovered catalyst. The solution containing the product was passed through a silica gel flash column to afford the product.

3-(1-Phenylethyl)pentane-2,4-dione (3a)[12]. The compound was prepared from **1a** (0.100 g, 1.0 mmol) and **2a** (0.244 g, 2.0 mmol). Following typical procedure A, 0.180 g (88% yield) of product was obtained after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B, 0.196 g (96% yield) of product was obtained after column chromatography. Mp: 42−44 °C (lit. 43−45 °C);[12] ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (d, J = 6.8 Hz, 3H), 1.83 (s, 3H), 2.27 (s, 3H), 3.57−3.62 (m, 1H), 4.04 (d, J = 11.2 Hz, 1H), 7.18−7.22 (m, 3H), 7.27−7.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 29.6, 29.7, 40.3, 76.5, 126.8, 127.1, 128.7, 142.9, 203.2, 203.3; MS (ESI) m/z (%) 227.03 (M + Na^+, 100), 205.02.

3-[1-(4-Methoxyphenyl)ethyl]pentane-2,4-dione (3b)[8a]. The compound was prepared from **1a** (0.100 g, 1.0 mmol) and **2b** (0.304 g, 2.0 mmol). Following typical procedure A, 0.194 g (83% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B, 0.192 g (82% yield) of product was obtained after column chromatography. Mp: 54−55 °C (lit. 52−53 °C);[8a] ^1H NMR (400 MHz, $CDCl_3$) δ 1.18 (d, J = 6.8 Hz, 3H), 1.84 (s, 3H), 2.26 (s, 3H), 3.51−3.59 (m, 1H), 3.77 (s, 3H), 3.99 (d, J = 11.2 Hz, 1H), 6.83 (d, J = 6.8 Hz, 2H), 7.10 (d, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 29.5, 29.7, 39.5, 55.0, 114.0, 128.1, 134.8, 158.2, 203.3, 203.4; MS (ESI) m/z (%) 257.11 (M + Na^+, 100), 135.02.

3-[1-(4-Tolylethyl)]pentane-2,4-dione (3c)[14]. The compound was prepared from **1a** (0.100 g, 1.0 mmol) and **2c** (0.272 g, 2.0 mmol). Following typical procedure A, 0.176 g (81% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B, 0.201 g (92% yield) of product was obtained after column chromatography. Mp: 55−56 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (d, J = 6.8 Hz, 3H), 1.84 (s, 3H), 2.26 (s, 3H), 3.00 (s, 3H), 3.53−3.58 (m, 1H), 4.02 (d, J = 11.2 Hz, 1H), 7.06−7.11 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.8, 29.6, 39.9, 76.6, 127.0, 129.3, 136.3, 139.8, 203.4; MS (ESI) m/z (%) 241.07 (M + Na$^+$, 100).

3-[1-(4-Chlorophenyl)ethyl]pentane-2,4-dione (3d)[12]**.** The compound was prepared from **1a** (0.100 g, 1.0 mmol) and **2d** (0.312 g, 2.0 mmol). Following typical procedure A, 0.167 g (70% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B, 0.136 g (57% yield) of product was obtained after column chromatography. Mp: 77−79 °C (lit. 77−79 °C);[12] ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.19 (d, J = 7.2 Hz, 3H), 1.87 (s, 3H), 2.26 (s, 3H), 3.55−3.63 (m, 1H), 3.98 (d, J = 11.6 Hz, 1H), 7.14 (dd, J_1 = 6.4 Hz, J_2 = 2.0 Hz, 2H), 7.26 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.5, 29.5, 29.6, 39.5, 76.3, 128.5, 128.7, 132.4, 141.5, 202.7, 202.8; MS (ESI) m/z (%) 261.05 (M + Na$^+$, 100).

3-[1-(4-Fluorophenyl)ethyl]pentane-2,4-dione (3e)[14]**.** The compound was prepared from **1a** (0.100 g, 1.0 mmol) and **2e** (0.280 g, 2.0 mmol). Following typical procedure A, 0.231 g (96% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v). Mp: 57−58 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.20 (d, J = 6.9 Hz, 3H), 1.86 (s, 3H), 2.26 (s, 3H), 3.58−3.63 (m, 1H), 4.01 (d, J = 11.3 Hz, 1H), 6.96−7.00 (m, 2H), 7.15−7.19 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.7, 29.5, 29.7, 39.5, 76.6, 115.4, 115.6, 128.6, 128.7, 138.7, 160.3, 162.7, 202.9, 203.1; MS (ESI) m/z (%) 245.10.

3-[1-(2-Naphthalenyl)ethyl]pentane-2,4-dione (3f)[14]**.** The compound was prepared from **1a** (0.100 g, 1.0 mmol) and **2f** (0.344 g, 2.0 mmol). Following typical procedure A, 0.165 g (65% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B (2 mL of toluene was added and 3 mol % catalyst was used), 0.236 g (93% yield) of product was obtained after column chromatography. Mp: 86−88 °C (lit. 86−88 °C);[14] ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.27 (d, J = 6.7 Hz, 3H), 1.81 (s, 3H), 2.28 (s, 3H), 3.74−3.79 (m, 1H), 4.17 (d, J = 11.3 Hz, 1H), 7.31−7.34 (m, 1H), 7.41−7.43 (m, 2H), 7.62 (s, 1H), 7.76−7.78 (m, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.7, 29.6, 40.3, 76.3, 125.2, 125.6, 125.8, 126.1, 127.5, 127.6, 128.5, 132.3, 133.3, 140.4, 203.2; MS (ESI) m/z (%) 277.09 (M + Na$^+$, 100), 155.01.

3-(Diphenylmethyl)pentane-2,4-dione (3g)[6b]**.** The compound was prepared from **1a** (0.100 g, 1.0 mmol) and **2g** (0.368 g, 2 mmol). Following typical procedure A (2 mL of DCE was used instead of toluene), 0.260 g (98% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B (2 mL of DCE was added), 0.253 g (95% yield) of product was obtained after column chromatography. Mp: 117−118 °C (lit. 115−117 °C);[6b] ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.00 (s, 6H), 4.75 (d, J = 12.0 Hz, 1H), 4.82 (d, J = 12.0 Hz, 1H), 7.16−7.19 (m, 2H), 7.26−7.27 (m, 8H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 29.5, 51.0, 74.2, 126.8, 127.6, 128.7, 141.1, 202.7; MS (ESI) m/z (%) 289.12 (M + Na$^+$, 100).

3-(1,3-Diphenyl-2-propenyl)pentane-2,4-dione (3h)[14]**.** The compound was prepared from **1a** (0.100 g, 1.0 mmol) and **2h** (0.420 g, 2.0 mmol). Following typical procedure A, 0.172 g (75% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v). Mp: 85−87 °C (lit. 85−87 °C);[14] ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.85 (s, 3H), 2.17 (s, 3H), 4.27 (d, J = 2.4 Hz, 2H), 6.09−6.15 (m, 1H), 6.35 (d, J = 15.6 Hz, 1H), 7.12−7.26 (m, 10H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 29.7, 30.0, 49.1, 74.5, 126.3, 127.2, 127.7, 127.9, 128.5, 128.9, 129.2, 131.6, 136.5, 140.0, 202.7, 202.8; MS (ESI) m/z (%) 315.14 (M + Na$^+$, 84), 193.11 (100).

3-(2-Cyclohexen-1-yl)pentane-2,4-dione (3i)[14]**.** The compound was prepared from **1a** (0.100 g, 1 mmol) and **2i** (0.196 g, 2.0 mmol). Following typical procedure A, 0.131 g (73% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v). Mp: 94−96 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.19−1.22 (m, 1H), 1.57−1.59 (m, 1H), 1.68−1.74 (m, 2H), 1.98−2.00 (m, 2H), 2.18 (s, 3H), 2.20 (s, 3H), 3.00−3.04 (m, 1H), 3.61(d, J = 10.6 Hz, 1H), 5.38 (t, J_1 = 10.2 Hz, J_2 = 2.4 Hz, 1H), 5.75−5.80 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.4, 24.7, 26.4, 29.4, 29.9, 35.4, 74.5, 126.9, 129.7, 203.5, 203.7; MS (ESI) m/z (%) 203.02 (M + Na$^+$, 100).

2-(1-Phenylethyl)-1-phenylbutane-1,3-dione (3j)[14]**.** The compound was prepared from **1b** (0.162 g, 1.0 mmol) and **2a** (0.244 g, 2.0 mmol) following typical procedure A, 0.260 g (98% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B, 0.258 g (97% yield) of product was obtained after column chromatography. **Diastereomer with lower polarity:** Mp: 83−85 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.22 (d, J = 6.9 Hz, 3H), 1.91 (s, 3H), 3.85−3.91 (m, 1H), 4.92 (d, J = 10.9 Hz, 1H), 7.20−7.22 (m, 1H), 7.28−7.32 (m, 4H), 7.47−7.52 (m, 2H), 7.60−7.61 (m, 1H), 8.08−8.10 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 21.5, 27.9, 40.9, 70.8, 126.9, 127.4, 128.8, 133.8, 137.2, 143.2, 195.1, 203.1; MS (ESI) m/z (%) 289.20 (M + Na$^+$, 100), 163.10. **Diastereomer with higher polarity:** Mp: 84−86 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.31(d, J = 7.0 Hz, 3H), 2.24 (s, 3H), 3.82−3.87 (m, 1H), 4.82 (d, J = 11.0 Hz, 1H), 7.06−7.08 (m, 1H), 7.14−7.20 (m, 4H), 7.33−7.37 (m, 2H), 7.47−7.49 (m, 1H) 7.77−7.80 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.2, 27.5, 40.3, 71.5, 126.6, 127.3, 128.4, 128.6, 133.4, 137.0, 143.4, 195.2, 203.7; MS (ESI) m/z (%) 289.11 (M + Na$^+$, 100), 163.15.

2-Diphenylmethyl-1-phenylbutane-1,3-dione (3k)[33]**.** The compound was prepared from **1b** (0.162 g, 1.0 mmol) and **2g** (0.368 g, 2.0 mmol). Following typical procedure A, 0.315 g (96% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B (2 mL of toluene was added), 0.324 g (99% yield) of product was obtained after column chromatography. Mp: 150−152 °C (lit. 149.8−150.7 °C);[33] ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.04 (s, 3H), 5.10 (d, J = 12.0 Hz, 1H), 5.61 (d, J = 12.0 Hz, 1H), 7.02−7.11 (m, 3H), 7.13−7.18 (m, 3H), 7.28−7.37 (m, 6H), 7.44−7.56 (m, 1H), 7.93−7.95 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 27.7, 51.4, 68.8, 126.6, 127.1, 127.6, 128.1, 128.6, 128.7, 128.9, 133.6, 136.9, 141.2, 141.6, 194.2, 202.9; MS (MALDI) m/z (%) 351.13 (M + Na$^+$, 100).

1,3-Diphenyl-2-(1-phenylethyl)propane-1,3-dione (3l)[14]**.** The compound was prepared from **1c** (0.224 g, 1.0 mmol) and **2a** (0.244 g, 2.0 mmol). Following typical procedure A, 0.312 g (95% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B, 0.312 g (95% yield) of product was obtained after column chromatography. Mp: 129−131 °C (lit. 129−131 °C);[14] ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.34 (d, J = 6.8 Hz, 3H), 4.06−4.10 (m, 1H), 5.60 (d, J = 10.0 Hz, 1H), 7.08−7.10 (m, 1H), 7.16−7.19 (m, 2H), 7.25−7.30 (m, 4H), 7.40−7.43 (m, 3H), 7.44−7.56 (m, 1H), 7.73−7.75 (m, 2H), 8.03−8.05 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.1, 41.1, 64.6, 126.5, 127.6, 128.3, 128.4, 128.7, 128.8, 133.0, 133.5, 136.8, 137.1, 143.7, 194.5, 194.9; MS (ESI) m/z (%) 351.16 (M + Na$^+$, 100), 329.46. HPLC analysis: Chiralcel OJ-H column, 2-propanol/hexane = 5:95 (1.0 mL/min), t_1 = 24.8 min, t_2 = 33.0 min.

2-(1-(4-Chlorophenyl)ethyl)-1,3-diphenylpropane-1,3-dione (3m)[14]**.** The compound was prepared from **1c** (0.224 g, 1.0 mmol) and **2d** (0.312 g, 2.0 mmol). Following typical procedure A, 0.355 g (98% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B, 0.319 g (88% yield) of product was obtained after column chromatography. Mp: 107−109 °C (lit.107−109 °C);[14] ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.31 (d, J = 7.2 Hz, 3H), 4.02−4.10 (m, 1H), 5.53 (d, J = 10.0 Hz, 1H), 7.13−7.21 (m, 4H), 7.29−7.33 (m, 2H), 7.42−7.48 (m, 3H), 7.55−7.59 (m, 1H), 7.73−7.76 (m, 2H), 8.02−8.05 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.1, 40.5,

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64.4, 128.3, 128.4, 128.6, 128.8, 129.0, 132.1, 133.1, 133.6, 136.6, 136.9, 142.3, 194.3, 194.6; MS (ESI) *m*/*z* (%) 385.11 (M + Na$^+$, 79%), 225.10 (100%).

1,3-Diphenyl-2-[1-(4-fluorophenyl)ethyl]propane-1,3-dione (3n)[14]. The compound was prepared from **1c** (0.224 g, 1.0 mmol) and **2e** (0.280 g, 2.0 mmol). Following typical procedure A, 0.298 g (86% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v). Mp: 110−112 °C (lit. 110−112 °C);[14] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (d, J = 7.0 Hz, 3H), 4.06−4.14 (m, 1H), 5.66 (d, J = 10.0 Hz, 1H), 6.81−6.86 (m, 2H), 7.23−7.28 (m, 4H), 7.39−7.43 (m, 3H), 7.51−7.53 (m, 1H), 7.77 (d, 2H), 8.06 (d, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 40.4, 64.4, 114.8, 115.1, 128.3, 128.4, 128.6, 128.7, 129.1, 129.2, 133.1, 133.5, 136.6, 136.9, 139.3, 160.0, 162.5, 194.4, 194.6; MS (ESI) *m*/*z* (%) 369.13 [M + Na]$^+$.

1,3-Diphenyl-2-(diphenylmethyl)propane-1,3-dione (3o)[33]. The compound was prepared from **1c** (0.224 g, 1.0 mmol) and **2g** (0.368 g, 2 mmol). Following typical procedure A, 0.300 g (77% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B (2 mL of toluene was added), 0.386 g (99% yield) of product was obtained after column chromatography. Mp: 232−234 °C (lit. 228.6−230.2 °C);[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.25 (d, J = 11.6 Hz, 1H), 6.27 (d, J = 11.6 Hz, 1H), 6.96−7.00 (m, 2H), 7.05−7.16 (m, 4H), 7.24−7.26 (m, 4H), 7.30−7.34 (m, 4H), 7.44−7.46 (m, 2H), 7.82−7.84 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.4, 62.4, 126.6, 128.3, 128.4, 128.5, 128.6, 133.2, 137.0, 141.7, 194.0; MS (ESI) *m*/*z* (%) 413.16 (M + Na$^+$, 100).

1,3-Diphenyl-2-(2-cyclohexen-1-yl)propane-1,3-dione (3p)[14]. The compound was prepared from **1c** (0.224 g, 1.0 mmol) and **2i** (0.196 g, 2.0 mmol). Following typical procedure A, 0.207 g (68% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v). Mp: 96−98 °C (lit. 96−98 °C);[14] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37−1.41 (m, 1H), 1.57−1.59 (m, 1H), 1.70−1.79 (m, 2H), 1.98−2.00 (m, 2H), 3.48−3.50 (m, 1H), 5.32 (d, J = 10.0 Hz, 1H), 5.52 (dd, J_1 = 10.2 Hz, J_2 = 2.1 Hz, 1H), 5.70−5.73 (m, 1H), 7.39−7.50 (m, 4H), 7.52−7.54 (m, 2H), 7.98−8.01 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 25.0, 27.3, 37.1, 62.2, 128.4, 128.6, 128.7, 129.2, 133.3, 133.4, 136.9, 137.1, 194.7, 195.1; MS (ESI) *m*/*z* (%) 327.14 (M + Na$^+$, 100), 225.10.

1,3-Diphenylpropane-2-(bicyclo[2.2.1]heptan-2-yl)-1,3-dione (3q)[22]. The compound was prepared from **1c** (0.224 g, 1.0 mmol) and **2j** (0.224 g, 2.0 mmol). Following typical procedure A (2 mL of DCE was used instead of toluene), 0.312 g (98% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v). Mp: 119−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18−1.19 (m, 1H), 1.21−1.22 (m, 2H), 1.27−1.34 (m, 1H), 1.43−1.50 (m, 3H), 1.60−1.64 (m, 1H), 1.94 (s, 1H), 2.24 (s, 1H), 2.69−2.75 (m, 1H), 5.01 (d, J = 11.2 Hz, 1H), 7.37−7.39 (m, 2H), 7.40−7.44 (m, 3H), 7.58−7.59 (m, 1H), 7.92−7.95 (m, 2H), 8.03−8.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 29.9, 35.8, 36.5, 37.1, 39.4, 43.5, 63.9, 128.5, 128.7, 133.1, 133.3, 136.9, 137.0, 195.0, 195.7; MS (ESI) *m*/*z* (%) 341.16 (M + Na$^+$, 32%), 319.18 (M+H$^+$, 37%), 225.10 (100%).

2-Acetyl-2-benzhydrylcyclopentanone (3r). The compound was prepared from **1d** (0.126 g, 1.0 mmol) and **2g** (0.368 g, 2.0 mmol). Following typical procedure A (3 mol % catalyst was used), 0.280 g (96% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B (2 mL of toluene was added and 3 mol % catalyst was used), 0.178 g (61% yield) of product was obtained after column chromatography. Mp: 156−158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31−1.40 (m, 1H), 1.63−1.76 (m, 2H), 2.05−2.22 (m, 5H), 3.12−3.17 (m, 1H), 5.34 (s, 1H), 7.00−7.02 (m, 2H), 7.16−7.30 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 25.9, 27.4, 38.9, 55.1, 74.3, 126.9, 128.3, 128.8, 128.9, 129.8, 140.4, 202.6, 215.2; HRMS (+ESI) calcd for $C_{20}H_{20}O_2^+$: 292.1458, found 292.1460 [M]$^+$.

Ethyl-2-diphenylmethyl-3-oxobutanoate (3s).[34]**.** The compound was prepared from **1e** (0.130 g, 1.0 mmol) and **2g** (0.368 g, 2.0 mmol). Following typical procedure A, 0.243 g (82% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B (3 mol % catalyst was used), 0.252 g (85% yield) of product was obtained after column chromatography. Mp: 88−90 °C (lit. 89−91 °C);[34] ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, J = 7.2 Hz, 3H), 2.09 (s, 3H), 3.97 (q, J_1 = 14.0 Hz, J_2 = 7.2 Hz, 2H), 4.53 (d, J = 12.4 Hz, 1H), 4.76 (d, J = 12.4 Hz, 1H), 7.14−7.15 (m, 2H), 7.16−7.30 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 30.0, 50.8, 61.4, 65.1, 126.8, 126.9, 127.7, 127.8, 128.6, 128.8, 141.2, 141.5, 167.6, 201.7; MS (MALDI,) *m*/*z* (%) 319.07 (M + Na$^+$, 100).

Ethyl-2-benzhydryl-3-oxo-3-phenylpropanoate (3t)[33]. The compound was prepared from **1f** (0.192 g, 1.0 mmol) and **2g** (0.368 g, 2.0 mmol). Following typical procedure A, 0.354 g (99% yield) of product after column chromatography (eluent = petroleum ether/acetone, 20:1 v/v); following typical procedure B (2 mL of toluene was added and 3 mol % catalyst was used), 0.351 g (98% yield) of product was obtained after column chromatography. Mp: 138−140 °C (lit. 141.9−143.1 °C);[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3H), 3.87−3.96 (m, 2H), 5.07(d, J = 11.6 Hz, 1H), 5.41(d, J = 11.6 Hz, 1H), 7.03−7.06 (m, 1H), 7.07−7.45 (m, 7H), 7.53−7.57 (m, 5H), 8.00−8.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 50.8, 59.4, 61.6, 126.5, 126.8, 127.7, 128.5, 128.6, 128.7, 133.6, 136.6, 141.7, 167.7, 192.8; MS (MALDI) *m*/*z* (%) 381.17 (M + Na$^+$, 100).

Computational Details. Molecular geometries of the model complexes were optimized without constraints via DFT calculations using the Becke3LYP (B3LYP)[35] functional. Frequency calculations at the same level of theory have also been performed to identify all stationary points as minima (zero imaginary frequencies) to provide free energies at 298.15 K that include entropic contributions by taking into account the vibrational, rotational, and translational motions of the species under consideration. The effective core potentials (ECPs) of Hay and Wadt with double-ζ valence basis sets (LanL2DZ)[36] were used to describe Cl and S. Polarization functions were also added for

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Cl (ζ_d = 0.640) and S (ζ_d = 0.503).[37] The 6-311G(d,p) Pople basis set was used for water molecule and the O atom of acid that were connected to the water molecule.[38] The 6-31G basis set was used for all the other atoms.[39] The solvent effect was examined by performing single-point self-consistent reaction field (SCRF) calculations based on the polarizable continuum model (PCM)[40] for the gas-phase optimized species. Toluene was used as the solvent, corresponding to the experimental conditions, and the atomic radii used for the PCM calculations were specified using the BONDI keyword. All of the DFT calculations were performed with the Gaussian 03 package.[41]

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Supporting Information Available: The crystal data of **3p**, ^{1}H spectra of all products **3a-t** and ^{13}C NMR spectra of new compound **3r**, and the computation details can be found in the Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.