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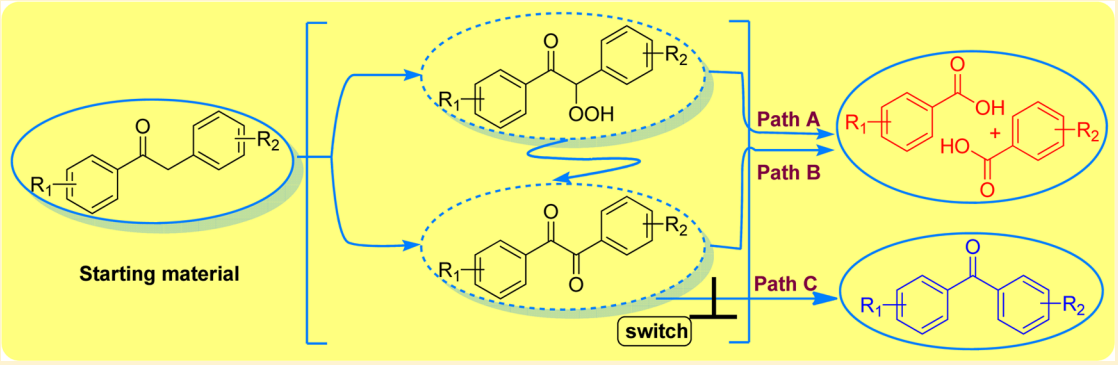
Chemoselective Transformation of Diarylethanones to Arylmethanoic Acids and Diarylmethanones and Mechanistic Insights

Xing Wang, Rui-Xi Chen, Zeng-Feng Wei, Chen-Yang Zhang, Hai-Yang Tu,* and Ai-Dong Zhang*

Key Laboratory of Pesticide & Chemical Biology of the Ministry of Education, College of Chemistry, Central China Normal University, Wuhan 430079, P. R. China

Supporting Information



ABSTRACT: The chemoselective transformation of diarylethanones via either aerobic oxidative cleavage to give arylmethanoic acids or tandem aerobic oxidation/benzilic acid rearrangement/decarboxylation to give diarylmethanones has been developed. The transformation is controllable and applicable to a broad spectrum of substrates and affords the desired products in good to excellent yields. Mechanistic insights with control reactions, ^{1}H NMR tracking, and single-crystal X-ray diffraction reveal a complex mechanistic network in which two common intermediates, α-ketohydroperoxide and diarylethanedione, and three plausible pathways are proposed and verified. These pathways are interlinked and can be switched reasonably by changing the reaction conditions. This method enables scalable synthesis and access to a number of valuable compounds, including vitamin B_3, diphenic acid, and the nonsteroidal anti-inflammatory drug ketoprofen. The present protocol represents a step forward in exploiting complex mechanistic networks to control reaction pathways, achieving divergent syntheses from the same class of starting materials.

INTRODUCTION

Arylmethanoic acids and diarylmethanones are important substructural units that have been found in a number of natural products[1] and synthetic compounds of agrochemical and pharmaceutical value.[2] Significant efforts have been devoted to the development of various approaches to access these two types of valuable compounds and their derivatives. For the synthesis of arylmethanoic acids, conventional oxidation of aldehydes and primary alcohols[3] or hydrolysis of acid derivatives and nitriles[4] can be used. New synthetic strategies have been developed recently, including the carboxylation of stoichiometric organometallic reagents[5] or aryl halides[6] with carbon dioxide as well as the oxidative cleavage of vicinal diols[7] or 1,3-dicarbonyl compounds[8] (Scheme 1, left). On the other hand, diarylmethanones can be obtained either by conventional Friedel−Crafts acylation of aryl rings with acid halides or acid anhydrides[9] or by catalytic cross-coupling of organometallic reagents with electrophiles[10] or CO[11] or even by the catalytic cross-coupling reactions of aryl halides with aldehydes/aldehyde derivatives[12] or aryl methyl ketones[13] (Scheme 1, right). Although these methods are generally efficient for the syntheses of arylmethanoic acids and diarylmethanones, the need for unstable organometallic reagents or costly and toxic oxidants in most cases limits to some extent the application of these appealing transformations. Therefore, there is a need to develop alternative methods to synthesize these two types of compounds. On the basis of the structural patterns of the starting materials and products, it can be seen that with the exception of the methods of carboxylation with CO_2, the syntheses in these reported methods are achieved through either intermolecular splicing or intramolecular splitting of reactants with diverse structural patterns. Since carbonyl is involved in these reactions, they might share some common characteristics. It was anticipated that using the same class of materials to synthesize the two distinct types of compounds via similar approaches would be possible and worthy of exploration.

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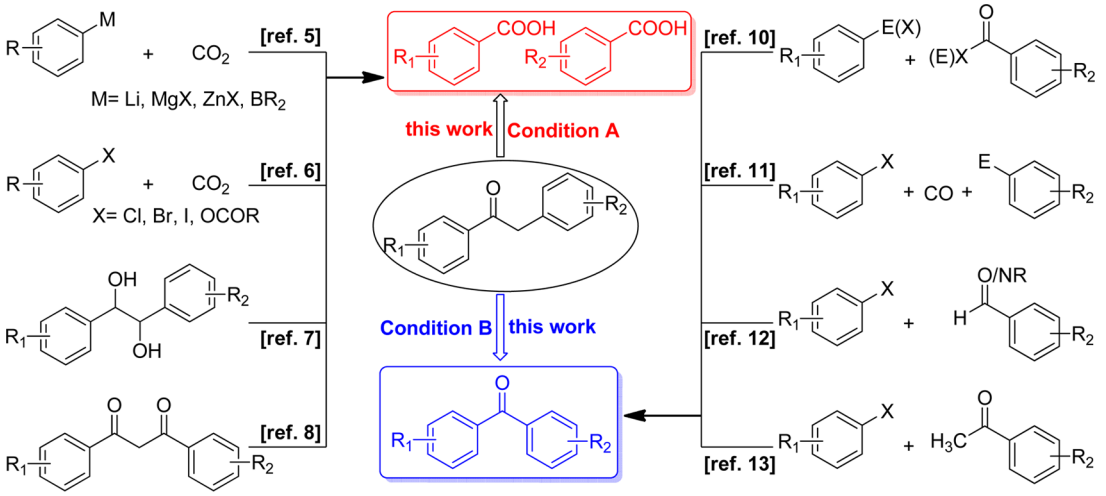
Scheme 1. Reported Approaches for the Syntheses of Arylmethanoic Acids and Diarylmethanones and Our Method



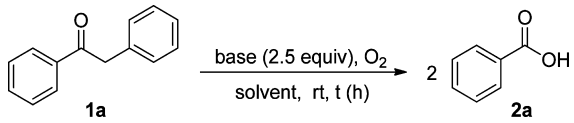
In our previous studies, we have realized an oxygen-switchable chemoselective approach for the synthesis of two distinct types of compounds, diarylmethanes and diarylmethanones, from the same types of starting materials, acetophenones and aryl halides, in which a common intermediate, diarylethanone, is shared in different pathways in the reactions.[13,14] Diarylethanones can easily be obtained by α-arylation of acetophenones with aryl halides[15] and have been used as versatile synthons for a large variety of organic molecules.[13,14,16] Making use of diarylethanones as the raw materials for syntheses of arylmethanoic acids and diarylmethanones would lead to valuable and straightforward methods because oxidative cleavage and oxidative shortening of carbon chains are all known mechanisms.[17] However, to the best of our knowledge, the oxidative cleavage of diarylethanones to give arylmethanoic acids has not been systematically investigated,[18] and there is only one elegant example of the synthesis of diarylmethanones by oxidative removal of methylene from diarylethanones with the assistance of toluidine imine formation.[19] On the basis of these facts, we explored the feasibility for chemoselective transformation of diarylethanones for the divergent syntheses of arylmethanoic acids and diarylmethanones.

In this article, we report the results of this investigation of the reactions and mechanisms. The work began with screening for the optimal reaction conditions using the reaction of diphenylethanone to give benzoic acid or diphenylmethanone as the model reactions, which was followed by substrate scope expansions. To gain insights into the mechanisms, control reactions, ^{1}H NMR tracking, and single-crystal X-ray diffraction of the key intermediate were performed, and a complex mechanistic network was proposed that involves three plausible pathways and two common intermediates, α-ketohydroperoxide and diarylethanedione, for the transformation to arylmethanoic acids and diarylmethanones chemoselectively. The gram-scale production of benzoic acid and access to vitamin B_3, diphenic acid, and ketoprofen, a nonsteroidal anti-inflammatory drug, were demonstrated as well using the established method.

RESULTS AND DISCUSSION

To evaluate the feasibility of the aerobic oxidative cleavage to give arylmethanoic acids, diphenylethanone (**1a**) was selected as the model substrate, and various variables such as bases, solvents, and temperature were systematically examined.

Table 1. Optimization of the Conditions for the Transformation of Diphenylethanone to Benzoic Acid[a]



entry	base	solvent	t (h)	yield (%)
1	Cs_2CO_3	DMF	12	69 (52)[b]
2	K_2CO_3	DMF	24	50
3	$K_3PO_4{\cdot}3H_2O$	DMF	6	67
4	NaOH	DMF	3	69
5	KOH	DMF	21	69
6	NaO*t*Bu	DMF	3	39
7	NaOMe	DMF	3	31
8	DABCO	DMF	24	0
9	Cs_2CO_3	DMSO	24	28
10	Cs_2CO_3	THF	24	25
11	Cs_2CO_3	1,4-dioxane	24	14
12	Cs_2CO_3	toluene	24	0
13	Cs_2CO_3	CH_3CN	24	61
14	Cs_2CO_3	NMP	24	67
15	Cs_2CO_3	DMI	24	93 (67/0)[c]
16	KOH powder	DMI	3	92

[a]Reactions were conducted with **1a** (1.5 mmol) in solvent (10 mL) at ambient temperature under an O_2 atmosphere for 3–24 h. [b]The yield in parentheses was obtained when the mixture was stirred at 150 °C for 3 h. [c]The yields in parentheses were obtained for the reactions using air as the oxidant or run under an argon atmosphere for 24 h.

The selected results are summarized in Table 1. To our delight, the desired product benzoic acid (**2a**) was obtained in 69% yield when the reaction was carried out in the presence of 2.5 equiv of Cs_2CO_3 in DMF at ambient temperature under an O_2 atmosphere for 12 h (Table 1, entry 1), without the need for transition-metal catalysis as was necessary for most of the reported oxidative cleavage reactions.[20] The effects of the base nature (Table S1) and loading (Table S2 and Table S3, entry 23) on the yield were also examined. Some bases, including K_2CO_3, sodium alkoxides, and tertiary amines, gave low product yields (Table 1, entries 2 and 6–8), while others, such as $K_3PO_4{\cdot}3H_2O$, NaOH, and sheet KOH, gave results comparable to that with Cs_2CO_3 but with much short reaction times (Table 1, entries 3–5). The solvent seemed to have a

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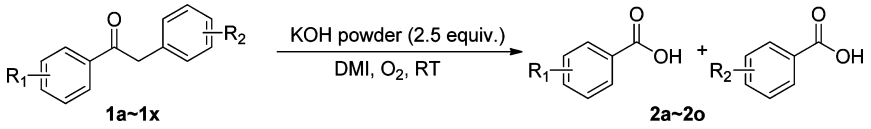
Table 2. Substrate Scope for the Synthesis of Arylmethanoic Acids[a]



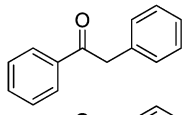
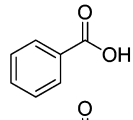
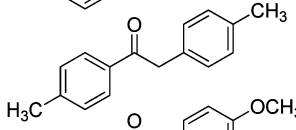
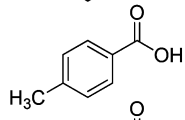
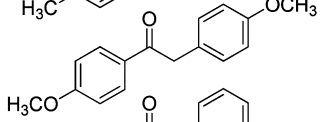
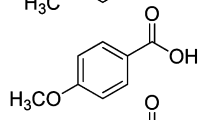
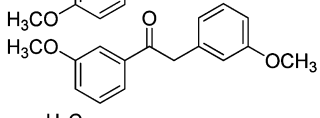
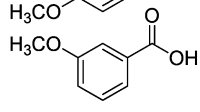
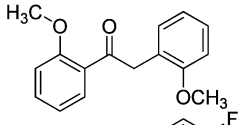
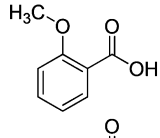
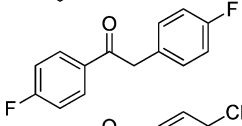
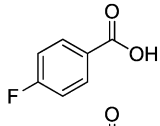
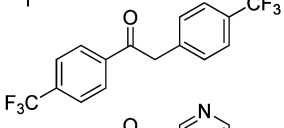
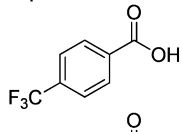
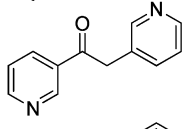
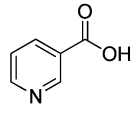
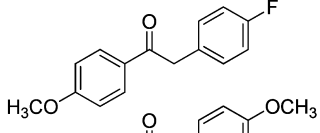
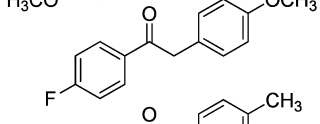
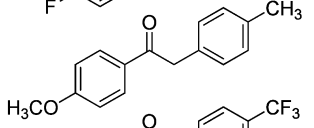
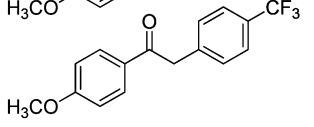
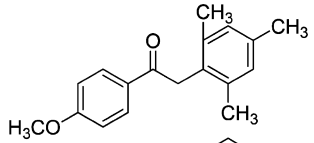
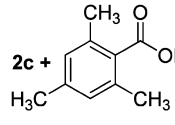
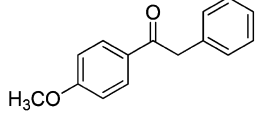
entry	substrate		product		yield (%)
1		1a		2a	94
2		1b		2b	81
3		1c		2c	87
4		1d		2d	66
5		1e		2e	40
6		1f		2f	64
7		1g		2g	74
8		1h		2h	90
9		1i	**2c + 2f**		96 (**2c**) + 95 (**2f**)
10		1j	**2c + 2f**		96 (**2c**) + 94 (**2f**)
11		1k	**2b + 2c**		93 (**2b**) + 97 (**2c**)
12		1l	**2c + 2g**		93 (**2c**) + 90 (**2g**)
13		1m	**2c +** 	**2i**	63 (**2c**) + 62 (**2i**)
14		1n	**2a + 2c**		79 (**2a**) + 80 (**2c**)

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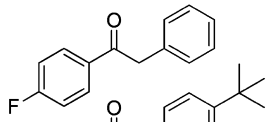
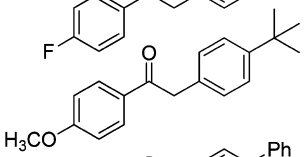
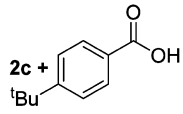
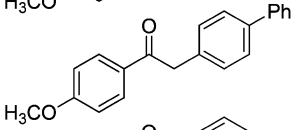
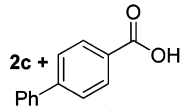
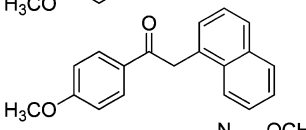
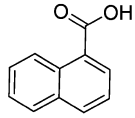
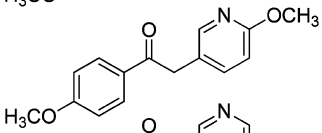
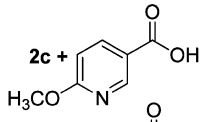
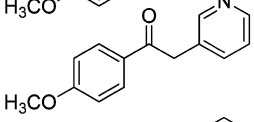
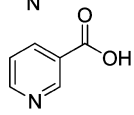
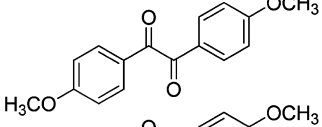
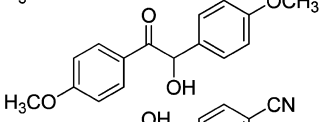
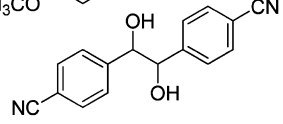
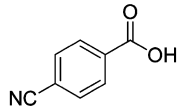
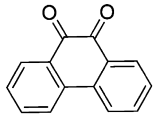
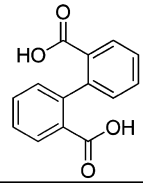
Table 2. continued

entry	substrate		product		yield (%)
15		1o	**2a + 2f**		76 (**2a**) + 75 (**2f**)
16		1p	**2c** + 	**2j**	79 (**2c**) + 77 (**2j**)
17		1q	**2c** + 	**2k**	91 (**2c**) + 90 (**2k**)
18		1r	**2c** + 	**2l**	92 (**2c**) + 92 (**2l**)
19		1s	**2c** + 	**2m**	78 (**2c**) + 76 (**2m**)
20		1t	**2c** + 	**2h**	92 (**2c**) + 92 (**2h**)
21		1u	**2c**		73
22		1v	**2c**		87
23		1w		**2n**	58
24		1x		**2o**	92

[a]Conditions: diarylethanone (0.5 mmol) under the optimal conditions using 5 mL of DMI.

larger influence, with dimethylimidazolidinone (DMI) being superior to DMF, NMP, CH_3CN, etc., affording the desired product **2a** in 93% yield (Table 1, entries 1 and 9−15, and Table S3). When O_2 was replaced with air or argon, the desired product **2a** was obtained in only 67% or 0% yield, respectively (Table 1, entry 15), indicating that O_2 is essential for the transformation. Interestingly, the yield was raised considerably to 92% when powdered KOH instead of KOH flakes (69%) was used, and the reaction time decreased dramatically to 3 h versus 21 h (Table 1, entries 5 and 16). However, when the temperature raised to 150 °C, **2a** was obtained only in 52% yield (Table 1, entry 1) along with the byproduct diphenylmethanone in 11% yield. This minor byproduct formally resulted from oxidative shortening of the carbon chain of diphenylethanone. After screening, the optimal reaction conditions were established to be KOH powder (2.5 equiv) in DMI at ambient temperature under an O_2 atmosphere.

With the optimized reaction conditions in hand, we next explored the substrate scope in the transformation of diarylethanones to arylmethanoic acids, and the results are presented in Table 2. Notably, a wide range of symmetrical and unsymmetrical diarylethanones were able to undergo oxidative cleavage to give the corresponding arylmethanoic acids in good to excellent yields. Little electronic effect was observed, as the diarylethanones bearing electron-withdrawing or electron-donating groups gave the products in comparable yields (Table 2, entries 2, 3, 6, and7). The influence of steric hindrance on the yield was significant; for example, 2,2′-, 3,3′-, and 4,4′-dimethoxy-substituted (**1c−e**) and 3,6-dimethyl-substituted (**1m**) diarylethanones afforded the corresponding products in 40, 66, 87, and 62% yield, respectively (Table 2, entries 3−5 and 13). Unsymmetrical diarylethanones were oxidatively cleaved to give two different acids in yields generally much higher than those for symmetrical ones (Table 2, entries 9−12 vs entries 2, 3, 6, and 7). In addition, diarylethanone derivatives such as bis(4-methoxyphenyl)ethanedione (**1u**), 4,4′-dimethoxybenzoin (**1v**), and 1,2-bis(4-cyanophenyl)-ethane-1,2-diol (**1w**) were also able to give the corresponding

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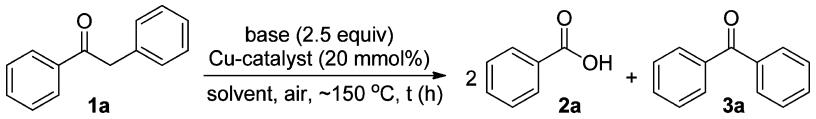
J. Org. Chem. 2016, 81, 238−249

Table 3. Optimization of the Conditions for the Transformation of Diphenylethanone to Diphenylmethanone[a]



entry	base	solvent	catalyst	t (h)	yields of **2a**/**3a** (%)
1	Cs_2CO_3	DMF	none	12	42/30
2	Cs_2CO_3	DMF	CuCl	10	3/48
3	Cs_2CO_3	DMF	CuCl/1,10-Phen	6	11/30
4	Cs_2CO_3	DMF	$Cu(OAc)_2$	7	17/30
5	Cs_2CO_3	DMF	$Cu(OTf)_2$	10	11/52
6	Cs_2CO_3	DMF	CuO	12	17/53
7	Cs_2CO_3	DMI	CuO	24	36/11
8	Cs_2CO_3	DMSO	CuO	18	22/26
9	K_3PO_4	DMF	CuO	34	42/trace
10	KOH	DMF	CuO	6	31/30
11	NaO*t*Bu	DMF	CuO	12	0/41
12	DBU	DMF	CuO	9	0/7
13	Cs_2CO_3	DMF	CuO (5)	12	14/59
14[b]	NaO*t*Bu	DMF	CuO (5)/Ag_2O (2.5)	3	8/67

[a]Reactions were conducted with **1a** (1.5 mmol) in the solvent (10 mL) at 150 °C under an air atmosphere for 3−24 h. [b]Under an O_2 atmosphere.

arylmethanoic acids in satisfactory yields of 58−87% under the optimized conditions (Table 2, entries 21−23). More importantly, heteroarylethanones such as bis(pyrid-3-yl)ethanone (**1h**), 1-(4-methoxyphenyl)-2-(6-methoxypyrid-3-yl)ethanone (**1s**), and 1-(4-methoxyphenyl)-2-(pyrid-3-yl)ethanone (**1t**) were suitable substrates, affording the corresponding nicotinic acids **2h, 2m**, and **2h** in yields of 90, 76, and 92%, respectively (Table 2, entries 8, 19, and 20). It is worth mentioning that this method affords an alternative efficient approach for the synthesis of nicotinic acid under mild reaction conditions. Reported methods for the synthesis of nicotinic acid usually use 3-methylpyridine as the raw material and are performed under harsh conditions such as high temperature and the presence of strong acid and oxidant.[21] Nicotinic acid, known as vitamin B_3, is widely used as a clinical drug for reducing plasma cholesterol level in patients with hypercholesterolemia.[22] Interestingly, when phenanthrene-9,10-dione (**1x**) was subjected to the standard conditions, oxidative ring opening occurred to give diphenic acid (**2p**), a very useful compound for the modular assembly of metal−organic frameworks (MOFs) with special properties,[23] in 92% yield (Table 1, entry 24).

As previously mentioned in the optimization of conditions for the transformation of diphenylethanone to benzoic acid, a minor byproduct, diphenylmethanone, was observed in 11% yield when the temperature was elevated to 150 °C (Table 1, entry 1). This is interesting because formally it is a product resulting from oxidative shortening of the carbon chain of diphenylethanone. One recent work that used 1.2 equiv of toluidine to assist the synthesis of diarylmethanones from diarylethanones at 140 °C in DMSO was reported.[19] This finding in our synthesis attracted us to develop a direct method without the use of toluidine. As a result, we started to screen reaction conditions for the chemoselective transformation of diphenylethanone (**1a**) to diphenylmethanone (**3a**), and selected results are shown in Table 3. Air was first used as the oxidant to switch the reaction to the formation of **3a**. As expected, the yield of **3a** increased to 30% when **1a** was treated with 2.5 equiv of Cs_2CO_3 in DMF under an air atmosphere at 150 °C for 12 h (Table 3, entry 1). The occurrence of benzoic acid as a byproduct was dramatically suppressed by the addition of 20 mol % CuCl catalyst (Table 3, entry 2), suggesting that the copper salt promotes the reaction. However, an attempt to introduce 1,10-phenanthroline as a ligand for the CuCl catalyst reduced the yield to 30% (Table 3, entry 2), although it was effective in promoting the copper-catalyzed decarboxylation in a literature report.[24] Thus, various copper catalysts along with other metal salts were investigated, and it was found that the use of CuO as the catalyst enabled the transformation of **1a** to **3a** in much higher yields (Table 3, entries 2−6, and Table S4). When DMF was replaced with another solvent such as DMI or DMSO, the reaction could not achieve comparable yields (Table 3, entries 7 and 8, and Table S5). Among the tested bases, Cs_2CO_3 was superior to K_3PO_4, KOH, NaO*t*Bu, and DBU, whereas the use of DABCO and NaOAc gave diphenylethanedione instead of **3a** as the final product (Table 3, entries 9−12, and Table S6). Reducing catalyst loading from 20 mol % to 5 mol % led to an increase in the yield (Table 3, entry 13, and Table S7). The combination of 5 mol % CuO and 2.5 mol % Ag_2O in the presence of 2.5 equiv of NaO*t*Bu under an O_2 atmosphere for 3 h gave the desired product **3a** in 67% yield (Table 3, entry 14, and Table S8). It is noted that a catalytic amount of NaO*t*Bu, for example 20 mol %, delivered only diphenylethanedione instead of the expected diphenylmethanone (Table S8, entry 7). After screening, the optimal reaction conditions were as follows: 5 mol % CuO, 2.5 mol % Ag_2O, and 2.5 equiv of NaO*t*Bu in DMF at 150 °C under an O_2 atmosphere.

The reaction conditions were applied to the transformation of an array of diarylethanones to diarylmethanones, and the results are shown in Table 4. Diarylethanones, either symmetric or unsymmetric, could give the corresponding diarylmethanones in acceptable yields (Table 4, entries 1−4), although it was observed that minor arylmethanoic acid byproducts resulted in some cases. Pyridyl-containing diarylmethanone **3e** was obtained in 80% yield (Table 4, entry 5). In addition, diarylethanone derivatives, including bis(4-methoxyphenyl)-ethanedione (**1u**), 4,4′-dimethoxybenzoin (**1v**), 1,2,3-triphenylpropane-1,3-dione (**1y**), and 1,2,2-tris(4-methoxyphenyl)-ethanone (**1z**), could also be converted to the desired products in yields of 75, 58, 83, and 96%, respectively (Table 4, entries 6−9).

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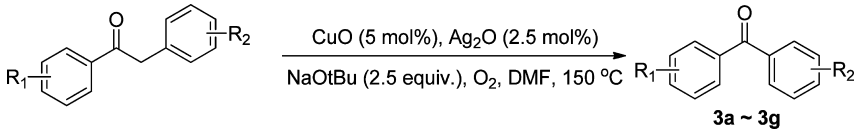
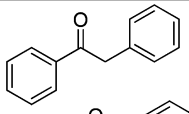
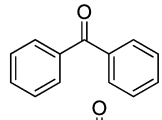
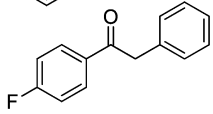
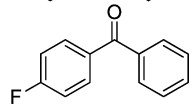
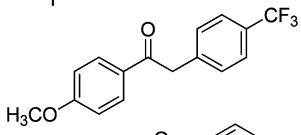
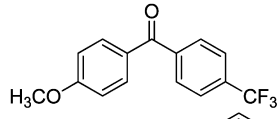
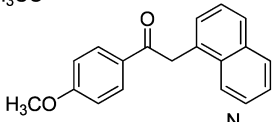
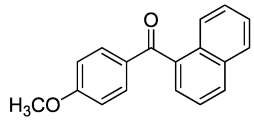
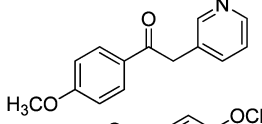
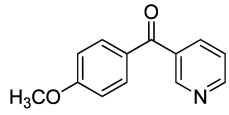
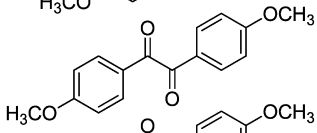
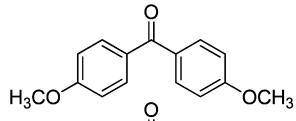
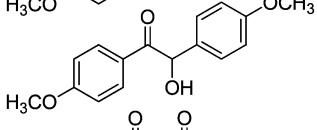
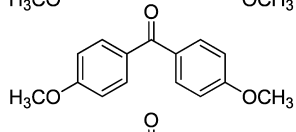
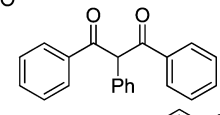
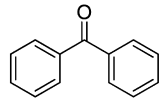
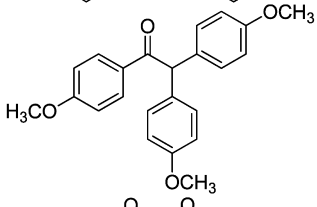
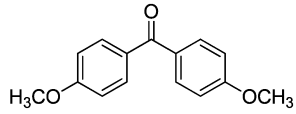
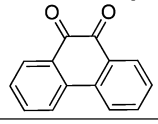
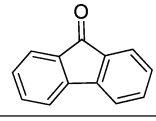
Table 4. Substrate Scope for the Synthesis of Diarylmethanones[a]



entry	substrate		product		yield (%)
1		1a		3a	72
2		1o		3b	50
3		1l		3c	68
4		1r		3d	69
5		1t		3e	80
6		1u		3f	75
7		1v		3f	58
8		1y		3a	83
9		1z		3f	96
10		1x		3g	78

[a]Conditions: Diarylethanone (0.5 mmol) under the optimal conditions with 5 mL of DMF.

Furthermore, phenanthrene-9,10-dione (**1x**) was able to undergo ring contraction to produce 9*H*-fluoren-9-one (**3g**) in 78% yield (Table 4, entry 10).

To demonstrate the scalability and practicability of the developed method, a 20-fold scale-up production of benzoic acid (**2a**) from diphenylethanone (**1a**) was carried out, resulting a yield of 90% (Scheme S1), which is comparable to that in the substrate scope expansion experiments (Table 2, entry 1). On the other hand, an unreported diphenylethanone derivative, 1-phenyl-2-(3-vinylphenyl)ethanone (**1hh**), was synthesized and used for the transformation to phenyl(3-vinylphenyl)-methanone (**3h**) in 78% yield. Compound **3h** is a key precursor in the synthesis of the nonsteroidal anti-inflammatory drug ketoprofen,[25] and on the basis of the present results, a three-step procedure can be established for the synthesis of ketoprofen in 51% overall yield (Scheme 2),[26] an improvement over the reported methods.[27]

The transformation of diarylethanones to arylmethanoic acids and diarylmethanones by varying the reaction conditions must be a chemoselective process, and the underlying mechanisms are worthy of exploration. A series of control reactions were first carried out, including two condition experiments and four speculated intermediates as raw materials transforming to benzoic acid and diphenylmethanone, respectively. The results are shown in Scheme S2 and Scheme 3. It was found that oxygen is essential, as replacing O_2 with an argon atmosphere

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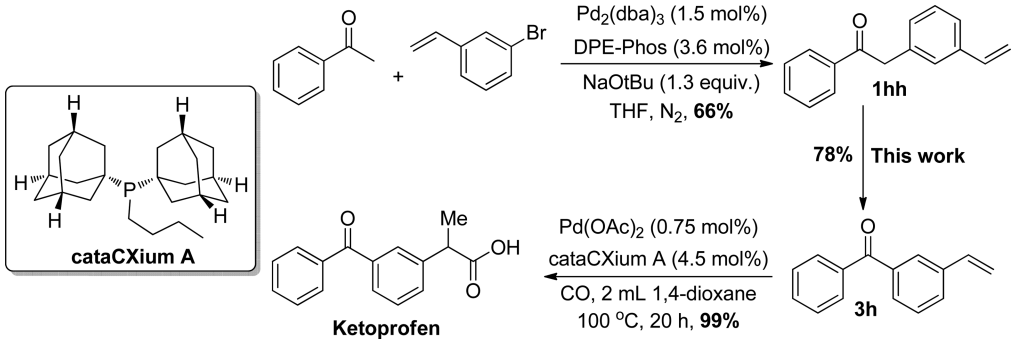
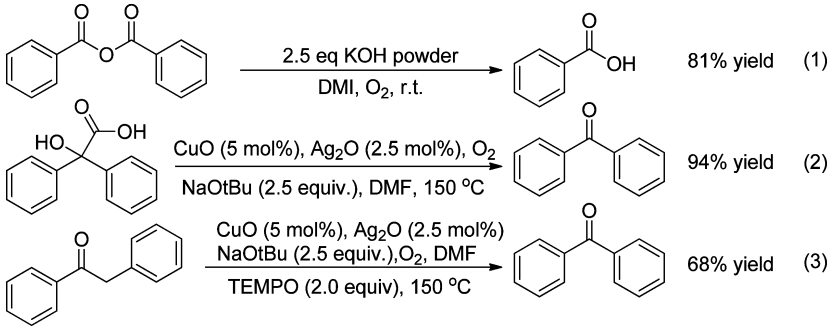
Scheme 2. Synthesis of Ketoprofen Using the Developed Method



Scheme 3. Control Reactions To Explore the Mechanism



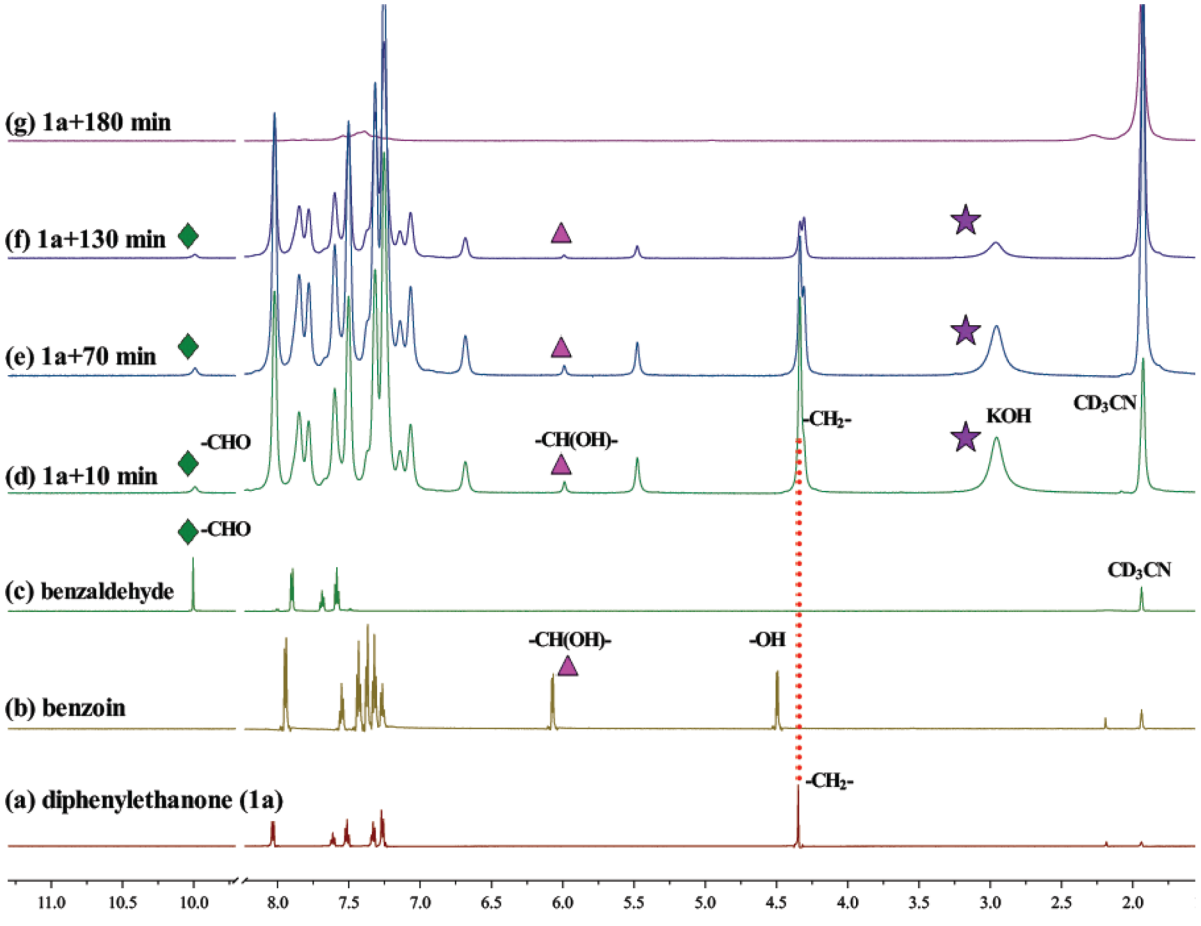


Figure 1. ^{1}H NMR spectra of the control compounds and the reaction mixture in the transformation of **1a** to benzoate measured at the indicated time points (600 MHz, CD_3CN, 298 ± 0.5 K).

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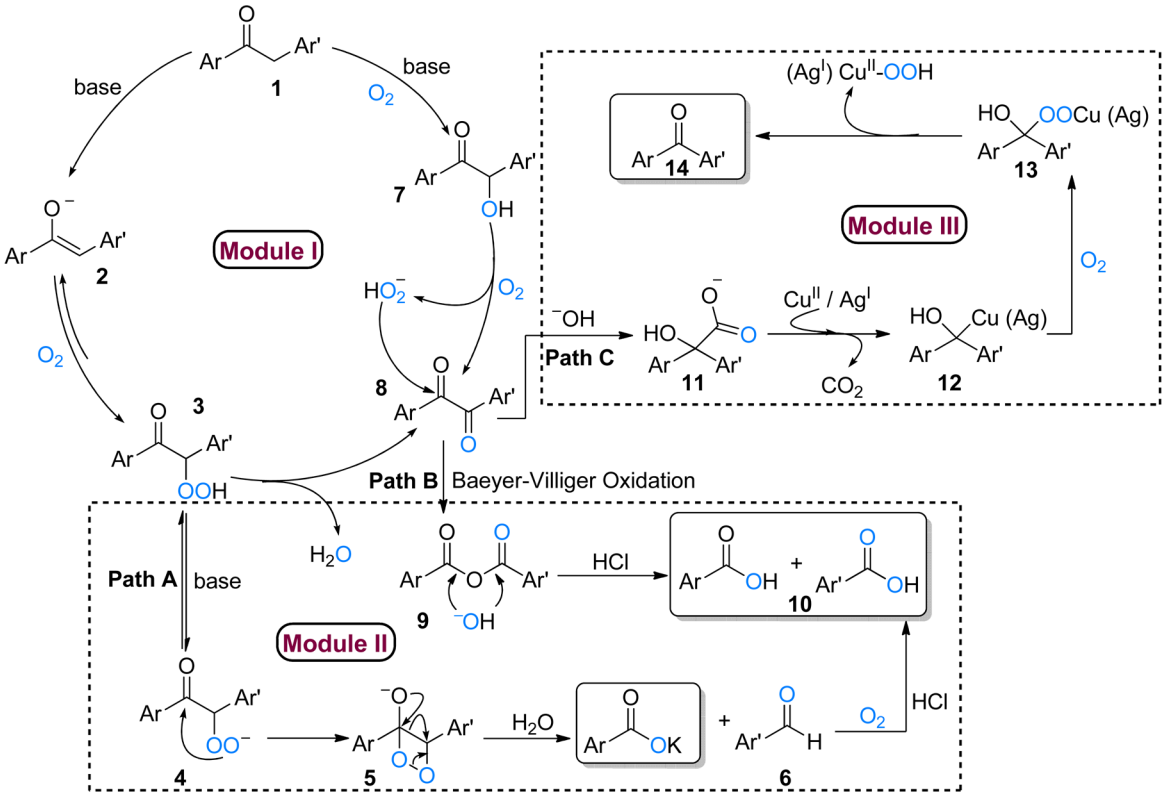
Scheme 4. Proposed Mechanism for the Chemoselective Transformations



shut down both transformations completely (Scheme S2, eq 1). Two possible intermediates, including benzoin and diphenylethanedione, whose analogues were used in the preceding transformations (Tables 2 and 4), were subjected to the two types of reaction conditions and gave benzoic acid and diphenylmethanone in good yields (Scheme S2, eqs 2 and 3). Other two possible intermediates that may appear in different pathways, benzoic anhydride and benzilic acid, were also treated with the two types of conditions to give benzoic acid and diphenylmethanone in yields of 81 and 94%, respectively (Scheme 3, eqs 1 and 2). When 2.0 equiv of 2,2,6,6-tetramethyl-1-piperidin-1-oxyl (TEMPO), a radical scavenger, was added to the reaction shown in Table 4, entry 1, the yield of diphenylmethanone was reduced by only 4% (Scheme 3, eq 3), suggesting the exclusion of a possible radical reaction in the process, which was demonstrated to be involved in a similar transformation of diphenylethanone to diphenylmethanone with slightly different conditions.[19]

Next, the reaction of **1a** (0.15 mmol) with KOH (0.38 mmol) in CD_3CN was monitored over time with ^1H NMR spectroscopy, and the results are presented in Figure 1. The control compounds **1a** (curve a), benzoin (curve b), and benzaldehyde (curve c) have their characteristic signals at 4.36, 6.01, and 10.02 ppm for $-CH_2-$, $-CH(OH)-$, and $-CHO$, respectively. As the reaction progressed and **1a** was consumed, the signal intensity of $-CH_2-$ decreased continuously, whereas the characteristic peaks of $-CH(OH)-$ and $-CHO$ appeared at first, increased over 70 min, and then disappeared over time. The results of ^1H NMR monitoring indicate that at least two possible intermediates, benzoin and benzaldehyde, are involved in the oxidative cleavage of diphenylethanone to give benzoic acid. To verify the involvement of benzaldehyde, it was subjected to the standard conditions, and a 61% yield of benzoic acid was indeed obtained (Scheme S2, eq 4).

Taken together, the control experiments and ^1H NMR monitoring suggest five possible intermediates in total. When these results are combined with results from the relevant literature, an overall mechanism can be proposed that consists of three modules (I, II, and III) as shown in Scheme 4. Module I is a common process for the transformation of diarylethanone **1** either to α-ketohydroperoxide **3** via enolization/oxidization[8c,28] or to diarylethanedione **8** via α-hydroxylation[29]/dehydrogenation;[30] **3** and **8** are common intermediates for the subsequent transformations, and the dehydration of **3** to give **8** is also possible.[31] In module II, path A, **3** undergoes cyclization/decomposition to form benzoate[13a,32] and benzaldehyde **6**, which can be oxidized and acidified to give benzoic acid **10**; in path B, diarylethanedione **8** undergoes Baeyer–Villiger oxidation[33] to give benzoic anhydride **9**, which is hydrolyzed and acidified to form benzoic acid **10**. In module III (path C), diarylethanedione **8** undergoes benzilic acid rearrangement[34] to give benzilate **11**, which decarboxylates to afford the active copper or silver species **12**, followed by oxidation to form diphenylmethanone **14**.[35]

The overall mechanism has the following supporting facts: (i) parts of the mechanism have been revealed in a number of previous reports, as shown in the above description; (ii) control experiments indicated the presence of four key intermediates, including benzoin **7**, diarylethanedione **8**, benzoic anhydride **9**, and benzilate **11**; (iii) ^1H NMR monitoring of the reaction of diphenylethanone to give benzoic acid showed the appearance and disappearance of benzaldehyde **6** and benzoin **7**. These obtained results enable us to outline this complex mechanistic network in the chemoselective transformation of diarylethanones to arylmethanoic acids and diarylmethanones.

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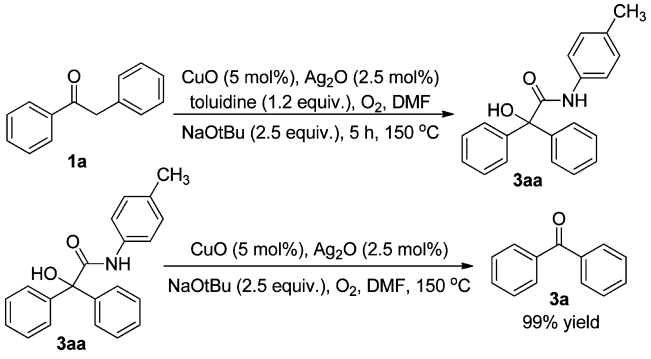
J. Org. Chem. 2016, 81, 238–249

Some other points need to be clarified here: (i) ^{1}H NMR monitoring revealed the presence of benzaldehyde **6**, which for the first time verifies the process experimentally from **1** to **10** via **6** in path A. (ii) In the transformation of **8** to **10**, the participation of hydroperoxide anion is not indispensable because in the control experiment (Scheme S2, eq 3) and the substrate scope expansion (Table 2, entry 21) diarylethanedione **8** was converted smoothly to arylmethanoic acid **10** under our conditions. This result is in sharp contrast with the recent reports[30a,36] suggesting the existence of another possible intermediate, 2-dioxyethanone (oxoxide), in the Baeyer–Villiger oxidation of α-diketones to carboxylic acids in the early reports.[37] (iii) With the switch of the reaction conditions, transformation of diarylethanones to arylmethanoic acids and diarylmethanones can be chemoselectively controlled.

In a previous work, Maiti and co-workers reported a plausible mechanism in which the benzilic acid rearrangement is involved in path C in the presence of toluidine, but no experimental evidence was given.[19] To validate the benzilic acid rearrangement, toluidine was added to the reaction mixture for the transformation of diphenylethanone to diphenylmethanone in path C. Fortunately, the key intermediate 2-hydroxy-2,2-diphenyl-*N*-(*p*-tolyl)acetamide (**3aa**) was captured, and its structure was confirmed by NMR spectroscopy and single-crystal X-ray diffraction (Figure S1; CCDC registry number CCDC-1432275). More interestingly, this intermediate can be smoothly converted to diphenylmethanone in 99% yield (Scheme 5), providing further experimental evidence for the benzilic acid rearrangement process.

Scheme 5. Validation of the Benzilic Acid Rearrangement in Path C



CONCLUSIONS

We have successfully realized the chemoselective transformation of diarylethanones to arylmethanoic acids and diarylmethanones by controlling the reaction conditions. The conversion to arylmethanoic acids was accomplished efficiently at room temperature without the use of a metal catalyst or toxic or costly oxidant; the transformation to diarylmethanones has the merits of low catalyst loadings and substrate diversity. Large-scale preparation using a model reaction and the application to the syntheses of vitamin B_3, diphenic acid, and the drug ketoprofen were also achieved, demonstrating the feasibility and efficiency of the developed protocol. The results from control reactions, ^{1}H NMR tracking, and single-crystal X-ray diffraction suggested a complex mechanistic network and provided convincing hints that enabled us to outline a plausible mechanism in detail. The overall mechanism involves three modules with module I shared by modules II and III. Moreover, five key intermediates were determined, among which two in module I are common that give rise to branches as paths A and B in module II and path C in module III. The findings in exploration of this complex mechanistic network may provide feasible strategies to manipulate the reaction pathways for the divergent synthesis from the same class of starting materials with some modifications of the reaction conditions.

EXPERIMENTAL SECTION

General Information. ^{1}H NMR spectra were recorded with a 400/600 MHz spectrometer. Chemical shifts (δ) are reported in parts per million quoted relative to internal tetramethylsilane (internal standard, 0.0 ppm) and DMSO-d_6 (δ = 2.5 ppm); coupling constants (J) are given in hertz. ^{13}C{^{1}H} NMR spectra were recorded with the same spectrometer operating at 100/150 MHz with complete proton decoupling (internal standard: $CDCl_3$, 77.0 ppm; DMSO-d_6, 39.5 ppm). Splitting patterns were assigned as s = singlet, d = doublet, t = triplet, dd = doublet of doublets, dt = doublet of triplets, q = quartet, etc. Crystallographic data for compound **3aa** were collected on a diffractometer equipped with a CCD detector. Reagents **1a**, **1o**, **1u**, **1v**, and **1x** were purchased from commercial suppliers, and others were prepared according to literature procedures. All of the reactions were carried out on a 0.50 mmol scale unless otherwise mentioned. All of the reactions were monitored by TLC analysis on silica-gel-coated plates. Flash column chromatography was performed using 200–300 mesh silica gel.

General Procedure for the Synthesis of Diarylethanone Raw Materials 1.[38] The representative procedure is exemplified using the synthesis of compound **1hh**. An oven-dried Schlenk tube was charged with a magnetic stir bar, $Pd_2(dba)_3$ (27.47 mg, 0.03 mmol, 1.5 mol %), DPE-Phos (38.78 mg, 0.072 mmol, 3.6 mol %), and NaO*t*Bu (250 mg, 2.6 mmol). The Schlenk tube was evacuated and filled with argon. Anhydrous and degassed THF (5 mL) was added, followed by 1-bromo-3-vinylbenzene (366.10 mg, 2 mmol) and acetophenone (240 mg, 2 mmol). The resulting mixture was heated under an argon atmosphere at 70 °C for 3 h and then cooled to room temperature. Water (10 mL) was added, and the mixture was extracted with diethyl ether (3 × 30 mL). The organic layers were combined and dried over anhydrous Na_2SO_4. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel using a 25:1 petroleum ether/ethyl acetate mixture to afford compound **1hh** as a pale-yellow oil (290 mg, 66%). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 8.01 (d, J = 12.0 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.27–7.31 (m, 3H), 7.15 (d, J = 6.0 Hz, 1H), 6.68 (dd, J_1 = 12.0, J_2 = 12.0 Hz, 1H), 5.73 (d, J = 18.0 Hz, 1H), 5.23 (d, J = 12.0 Hz, 1H), 4.27 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 197.5, 137.9, 136.6, 136.5, 134.7, 133.2, 128.9, 128.8, 128.6, 128.5, 127.4, 124.7, 114.1, 45.3. MS: m/z = 222 $[M]^+$. Anal. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.36; H, 6.27.

General Procedure for the Synthesis of Raw Material 1z.[39] Dry degassed DMF (10 mL) was added to an oven-dried reaction flask charged with $Pd(OAc)_2$ (22.42 mg, 0.10 mmol), Cs_2CO_3 (1.95g, 5.99 mmol), PPh_3 (104.79 mg, 0.4 mmol), 4-methoxyacetophenone (300 mg, 2 mmol), and 1-bromo-4-methoxybenzene (747 mg, 4.0 mmol) under an argon atmosphere at room temperature. The resultant stirred suspension was heated to 153 °C for 4 h. After the mixture was cooled, 20 mL of 1.4 M HCl was added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with saturated aqueous NH_4Cl (3 × 100 mL), dried over anhydrous Na_2SO_4, and evaporated in vacuo to give a residue that was purified by flash chromatography on silica gel using a 20:2 petroleum ether/ethyl acetate mixture as the eluent to give compound **1z** as a yellow oil (594 mg, 82%; CAS no. 61161-13-5).

General Procedure for the Synthesis of 1,2-Diol Raw Material 1w.[30b] To a solution of 4-formylbenzonitrile (2 mmol) in methanol (5 mL) was added aluminum powder (108 mg, 4 mmol) at 0 °C, followed by the immediate addition of KOH (1.01 g, 18 mmol) under vigorous stirring. Upon completion of the reaction (TLC), the

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resulting slurry was filtered with diatomaceous earth and washed with methanol. The filtrate was acidized with 5% aqueous HCl solution and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using a 20:5 petroleum ether/ethyl acetate mixture as the eluent to give 1,2-*vic*-diol **1w** as a yellow solid (0.36 g, 68%; CAS no. 113365-36-9).

Procedure for the 20-Fold-Scale Preparation of Benzoic Acid. DMI (68 mL) was added to a Schlenk tube charged with KOH powder (1.43 g, 25.48 mmol) and diphenylethanone (**1a**) (2.0 g, 10.19 mmol) at room temperature. The resulting mixture was stirred at ambient temperature under an O_2 atmosphere, and the reaction progress was monitored by TLC. Upon completion of the reaction, the mixture was acidified to pH 2−3 by the addition of 1.4 M HCl aqueous solution. The aqueous layer was extracted with Et_2O (3 × 100 mL), and the organic extracts were combined, washed with brine (3 × 100 mL), dried with anhydrous Na_2SO_4, and concentrated in vacuo to give a residue. The residue was purified by column chromatography on silica gel using a 20:3 petroleum ether/ethyl acetate mixture as the eluent to give benzoic acid as a needle-shaped crystal (2.24 g, 90%).

General Procedure for the Synthesis of 2-Hydroxy-2,2-diphenyl-*N*-(*p*-tolyl)acetamide (3aa). DMF (5 mL) was added to a Schlenk tube charged with NaO*t*Bu (0.12 g, 1.25 mmol), CuO (2.0 mg, 0.025 mmol), Ag_2O (3.0 mg, 0.013 mmol), toluidine (64.3 mg, 0.06 mmol), and diphenylethanone (98.1 mg, 0.5 mmol) at room temperature. The resulting mixture was stirred at 150 °C under an O_2 atmosphere for 5 h. The mixture was acidified to pH 3−4 by the addition of 1.4 M HCl aqueous solution. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), and the organic extracts were combined, washed with brine (3 × 100 mL), dried with anhydrous Na_2SO_4, and concentrated in vacuo to give a residue. The residue was purified by column chromatography on silica gel using a 20:3 petroleum ether/ethyl acetate mixture as the eluent to give the product **3aa**[40] as a white flocculent solid (58 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 8.42 (s, 1H), 7.46−7.48 (m, 4H), 7.41 (d, J = 12.0 Hz, 2H), 7.33−7.37 (m, 6H), 7.11 (d, J = 12.0 Hz, 2H), 3.73 (s, 1H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 170.9, 142.6, 134.6, 134.4, 129.5, 128.4, 128.3, 127.5, 119.7, 81.8, 20.9. MS: m/z = 317 $[M]^+$.

General Procedure for the Synthesis of Arylmethanoic Acids. DMI (5 mL) was added to a Schlenk tube charged with KOH powder (70.1 mg, 1.25 mmol) and the diarylethanone (0.5 mmol) at room temperature. The resulting mixture was stirred at ambient temperature under an O_2 atmosphere, and the reaction progress was monitored by TLC. Upon completion of the reaction, the mixture was acidified to pH 2−3 by the addition of 1.4 M HCl aqueous solution. The aqueous layer was extracted with Et_2O (3 × 20 mL), and the organic extracts were combined, washed with brine (3 × 100 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo to give a residue. The residue was purified by column chromatography on silica gel using a petroleum ether/ethyl acetate mixture as the eluent to give the product. All of the as-synthesized arylmethanoic acids are shown in Table 2.

General Procedure for the Synthesis of Diarylmethanones. DMF (5 mL) was added to a Schlenk tube charged with NaO*t*Bu (0.12 g, 1.25 mmol), CuO (2.0 mg, 0.025 mmol), Ag_2O (3.0 mg, 0.013 mmol), and the diarylethanone (0.5 mmol) at room temperature. The resulting mixture was stirred at 150 °C under an O_2 atmosphere, and the reaction progress was monitored by TLC. Upon completion of the reaction, the mixture was acidified to pH 3−4 by the addition of 1.4 M HCl aqueous solution. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), and the organic extracts were combined, washed with brine (3 × 100 mL), dried with anhydrous Na_2SO_4, and concentrated in vacuo to give a residue. The residue was purified by column chromatography on silica gel using a petroleum ether/ethyl acetate mixture as the eluent to give the product. All of the as-synthesized diarylmethanones are shown in Table 4.

*Benzoic Acid (**2a**).*[30b] The product was obtained as a white crystalline solid (122 mg, 94%; 48 mg, 79%; and 46 mg, 76% from the substrates **1a**, **1n**, and **1o**, respectively). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 12.33 (s, 1H), 8.13 (d, J = 8.0 Hz, 2H), 7.60 (t, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): δ 172.6, 133.8, 130.2, 129.3, 128.4. MS: m/z = 122 $[M]^+$.

*4-Methylbenzoic Acid (**2b**).*[30b] The product was obtained as a white solid (110 mg, 81% and 63 mg, 93% from the substrates **1b** and **1k**, respectively). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 12.38 (s, 1H), 8.01 (d, J = 12.0 Hz, 4H), 7.27 (d, J = 6.0 Hz, 4H), 2.42 (s, 5H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 172.6, 144.6, 130.2, 129.2, 126.6, 21.7. MS: m/z = 136 $[M]^+$.

*4-Methoxybenzoic Acid (**2c**).*[30b] The product was obtained as a white solid (130 mg, 87%; 67 mg, 96%; 67 mg, 96%; 74 mg, 97%; 71 mg, 93%; 48 mg, 63%; 61 mg, 80%; 60 mg, 79%; 69 mg, 91%; 70 mg, 92%; 60 mg, 78%; 70 mg, 92%; 110 mg, 73%; and 130 mg, 87% from the substrates **1c**, **1i**−**n**, and **1p**−**v**, respectively). ^{1}H NMR (600 MHz, DMSO-d_6, ppm): δ 12.64 (s, 1H), 7.90 (d, J = 6.0 Hz, 2H), 7.00 (d, J = 12.0 Hz, 2H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, ppm): δ 167.1, 162.9, 131.4, 123.0, 113.8, 55.4. MS: m/z = 152 $[M]^+$.

*3-Methoxybenzoic Acid (**2d**).*[30a] White solid, 66% yield (100 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 12.43 (s, 1H), 7.73 (d, J = 12.0 Hz, 1H), 7.63 (s, 1H), 7.39 (t, J = 12.0 Hz, 1H), 7.16 (dd, J_1 = 6.0, J_2 = 2.4 Hz, 1H), 3.87 (s, 4H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 172.3, 159.6, 130.5, 129.5, 122.7, 120.5, 114.3, 55.4. MS: m/z = 152 $[M]^+$.

*2-(Methylperoxy)benzoic Acid (**2e**).*[5b] White solid, 40% yield (60 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 10.93 (s, 1H), 8.17 (d, J = 6.0 Hz, 1H), 7.58 (t, J = 6.0 Hz, 1H), 7.13 (t, J = 6.0 Hz, 1H), 7.07 (d, J = 6.0 Hz, 1H), 4.08 (s, 4H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 165.7, 158.1, 135.0, 133.6, 122.0, 117.4, 111.6, 56.57. MS: m/z = 152 $[M]^+$.

*4-Fluorobenzoic Acid (**2f**).*[30b] The product was obtained as a white solid (90 mg, 64%; 67 mg, 95%; 66 mg, 94%; 53 mg, 75%, from the substrates **1f**, **1i**, **1j**, and **1o**, respectively). ^{1}H NMR (600 MHz, DMSO-d_6, ppm): δ 13.06 (s, 1H), 7.99−8.01 (m, 2H), 7.31 (t, J = 8.7 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, ppm): δ 166.4, 165.8, 164.1, 132.2, 132.1, 127.4, 115.7, 115.6. MS: m/z = 140 $[M]^+$.

*4-(Trifluoromethyl)benzoic Acid (**2g**).*[30b] The product was obtained as a white solid (140 mg, 74%; 86 mg, 90%, from the substrates **1g** and **1l**, respectively). ^{1}H NMR (600 MHz, DMSO-d_6, ppm): δ 13.49 (s, 1H), 8.13 (d, J = 12.0 Hz, 2H), 7.87 (d, J = 12.0 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, ppm): δ 166.3, 134.6, 132.8, 132.6, 132.4, 132.2, 130.1, 126.5, 125.6, 125.6, 124.7, 122.9, 121.1. MS: m/z = 190 $[M]^+$.

*Nicotinic Acid (**2h**).*[6b] Upon completion of the reaction using the preceding conditions, the resulting mixture was basicified with $NaHCO_3$ solution and then washed with CH_2Cl_2 three times. The water phase was acidified with 1.4 M HCl and extracted with CH_2Cl_2 three times. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to deliver nicotinic acid as a white solid (67 mg, 90% and 57 mg, 92%, for the substrates **1h** and **1t**, respectively). ^{1}H NMR (600 MHz, DMSO-d_6, ppm): δ 10.45 (s, 1H), 9.13 (s, 1H), 8.94 (d, J = 6.0 Hz, 1H), 8.60 (d, J = 12.0 Hz, 1H), 7.86 (t, J = 12.0 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, ppm): δ 163.9, 147.3, 144.7, 142.6, 128.8, 126.2. MS: m/z = 123 $[M]^+$.

*2,4,6-Trimethylbenzoic Acid (**2i**).*[5c] White solid, 62% yield (51 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 10.54 (s, 1H), 6.89 (s, 2H), 2.42 (s, 6H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 175.7, 140.1, 136.1, 129.2, 128.8, 21.1, 20.3. MS: m/z = 164 $[M]^+$.

*4-(tert-Butyl)benzoic Acid (**2j**).*[5c] White solid, 77% yield (69 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 8.05 (d, J = 6.0 Hz, 2H), 7.50 (d, J = 6.0 Hz, 2H), 1.36 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 172.1, 157.5, 130.1, 126.5, 125.5, 35.2, 31.1. MS: m/z = 178 $[M]^+$.

*4-Phenylbenzoic Acid (**2k**).*[5c] White solid, 90% yield (89 mg). ^{1}H NMR (600 MHz, DMSO-d_6, ppm): δ 13.01 (s, 1H), 8.02 (d, J = 12.0 Hz, 2H), 7.80 (d, J = 12.0 Hz, 2H), 7.73 (d, J = 6.0 Hz, 2H), 7.50 (t, J = 6.0 Hz, 2H), 7.42 (t, J = 6.0 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, ppm): δ 167.2, 144.3, 139.0, 130.0, 129.6, 129.1, 128.3, 127.0, 126.8. MS: m/z = 198 $[M]^+$.

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J. Org. Chem. 2016, 81, 238−249

*1-Naphthoic Acid (**2l**).*[6c] White solid, 92% yield (79 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 12.57 (s, 1H), 9.10 (d, J = 6.0 Hz, 1H), 8.43 (d, J = 12.0 Hz, 1H), 8.10 (d, J = 6.0 Hz, 1H), 7.92 (d, J = 6.0 Hz, 1H), 7.67 (t, J = 6.0 Hz, 1H), 7.57 (dd, J_1 = 12.0, J_2 = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 173.3, 134.6, 133.9, 131.8, 131.6, 128.7, 128.1, 126.3, 125.9, 125.5, 124.5. MS: m/z = 172 [M]$^+$.

*6-Methoxynicotinic Acid (**2m**).*[41] The synthesis followed the procedure for the synthesis of nicotinic acid and gave the desired product in 76% yield (58 mg) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.90 (d, J = 4.0 Hz, 1H), 8.17 (dd, J_1 = 2.0, J_2 = 2.4 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 4.01 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): δ 170.4, 167.1, 150.7, 139.8, 118.7, 110.8, 54.2. MS: m/z = 153 [M]$^+$.

*4-Cyanobenzoic Acid (**2n**).*[30b] White solid, 58% yield (86 mg). ^{1}H NMR (400 MHz, DMSO-d_6, ppm): δ 13.51 (s, 1H), 8.06 (d, J = 8.0 Hz, 2H), 7.95 (d, J = 8.0 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, ppm): δ 165.6, 134.5, 132.4, 129.6, 117.9, 114.8. MS: m/z = 147 [M]$^+$.

*1,1′-Biphenyl-2,2′-dicarboxylic Acid (**2o**).*[36] White solid, 92% yield (110 mg). ^{1}H NMR (600 MHz, DMSO-d_6, ppm): δ 12.47 (s, 1H), 7.88 (d, J = 6.0 Hz, 2H), 7.54 (t, J = 12.0 Hz, 2H), 7.43 (t, J = 12.0 Hz, 2H), 7.15 (d, J = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, ppm): δ 167.9, 143.0, 131.0, 130.4, 129.5, 126.9. MS: m/z = 242 [M]$^+$.

*Diphenylmethanone (**3a**).*[13] The product was obtained as a pale-yellow oil (65 mg, 72% and 25 mg, 83% from the substrates **1a** and **1y**, respectively). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.81 (d, J = 4.0 Hz, 4H), 7.59 (t, J = 8.0 Hz, 2H), 7.48 (t, J = 8.0 Hz, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): δ 196.7, 137.5, 132.4, 130.0, 128.2. MS: m/z = 182 [M]$^+$.

*(4-Fluorophenyl)(phenyl)methanone (**3b**).*[13] Pale-yellow oil, 50% yield (50 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 7.84 (m, J = 6.0 Hz, 2H), 7.77 (d, J = 6.0 Hz, 2H), 7.59 (t, J = 12.0 Hz, 1H), 7.48 (t, J = 6.0 Hz, 2H), 7.15 (t, J = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 195.2, 166.1, 164.4, 137.4, 133.7, 132.6, 132.5, 132.4, 129.8, 128.3, 115.4, 115.3. MS: m/z = 200 [M]$^+$.

*(4-Methoxyphenyl)(4-(trifluoromethyl)phenyl)methanone (**3c**).*[42] White solid, 68% yield (95 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 7.84 (m, 4H), 7.75 (d, J = 6.0 Hz, 2H), 6.98 (d, J = 6.0 Hz, 2H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 194.3, 163.7, 141.4, 133.3, 133.1, 132.6, 132.5, 130.2, 129.8, 129.3, 127.2, 125.2, 125.2, 124.60, 122.8, 119.9, 114.5, 113.8, 55.5. MS: m/z = 280 [M]$^+$.

*(4-Methoxyphenyl)(naphthalen-1-yl)methanone (**3d**).*[42] Colorless oil, 69% yield (90 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 7.98 (dd, J_1 = 12.0, J_2 = 6.0 Hz, 2H), 7.90 (d, J = 12.0 Hz, 1H), 7.85 (d, J = 6.0, 2H), 7.56−7.44 (m, 4H), 6.92 (d, J = 12.0 Hz, 2H), 3.85 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 196.7, 163.7, 136.9, 133.6, 132.7, 131.0, 130.8, 130.6, 128.3, 126.9, 126.8, 126.3, 125.6, 124.4, 113.6, 55.47. MS: m/z = 262 [M]$^+$.

*(4-Methoxyphenyl)(pyridin-3-yl)methanone (**3e**).*[43] White solid, 80% yield (85 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 8.96 (s, 1H), 8.80 (d, J = 6.0 Hz, 1H), 8.08 (d, J = 12.0 Hz, 1H), 7.84 (d, J = 12.0 Hz, 2H), 7.45 (t, J = 6.0 Hz, 1H), 7.00 (d, J = 6.0 Hz, 2H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 193.4, 163.7, 152.3, 150.4, 137.0, 133.8, 132.5, 129.3, 123.3, 113.8, 55.5. MS: m/z = 213 [M]$^+$.

*Bis(4-methoxyphenyl)methanone (**3f**).*[13] The product was obtained as a white crystalline solid (90 mg, 75%; 70 mg, 58%; and 116 mg, 96% from the substrates **1u**, **1v**, and **1z**, respectively). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.79 (d, J = 8.0 Hz, 4H), 6.96 (d, J = 8.0 Hz, 4H), 3.87 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): δ 194.4, 162.7, 132.1, 130.6, 113.4, 55.4. MS: m/z = 242 [M]$^+$.

*9H-Fluoren-9-one (**3g**).*[19] Yellow solid, 78% yield (70 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 7.65 (d, J = 6.0 Hz, 2H), 7.53−7.45 (m, 4H), 7.28 (dd, J_1 = 12.0, J_2 = 6.0 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 193.9, 144.4, 134.6, 134.1, 129.0, 124.3, 120.3. MS: m/z = 180 [M]$^+$.

*Phenyl(3-vinylphenyl)methanone (**3h**).*[13] Pale-yellow oil, 78% yield (70 mg). ^{1}H NMR (600 MHz, $CDCl_3$, ppm): δ 7.86−7.79 (m, 3H), 7.66 (d, J = 6.0 Hz, 1H), 7.63 (d, J = 6.0 Hz, 1H), 7.60 (t, J = 12.0 Hz, 1H), 7.49 (t, J = 12.0 Hz, 2H), 7.42−7.45 (m, 1H), 6.76 (dd, J_1 = 10.8, J_2 = 10.8 Hz, 1H), 5.82 (d, J = 18.0 Hz, 1H), 5.33 (d, J = 12.0 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, ppm): δ 196.6, 137.9, 137.7, 137.4, 135.9, 132.5, 130.0, 129.9, 129.4, 128.4, 128.3, 127.7, 115.3. MS: m/z = 208 [M]$^+$.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02506.

Additional data for optimization of the reaction conditions, large-scale production, and control reactions and copies of the ^{1}H NMR and ^{13}C{^{1}H} NMR spectra for **3aa**, **1hh**, and all of the synthesized target compounds (PDF)

Single-crystal X-ray diffraction data for **3aa** (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: adzhang@mail.ccnu.edu.cn.

*E-mail: haiytu@mail.ccnu.edu.cn. Tel: +86-027-67867635. Fax: +86-027-67867141.

Notes

The authors declare no competing financial interest.

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