JOC The Journal of Organic Chemistry

Article

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Room-Temperature Coupling/Decarboxylation Reaction of α-Oxocarboxylates with α-Bromoketones: Solvent-Controlled Regioselectivity for 1,2- and 1,3-Diketones

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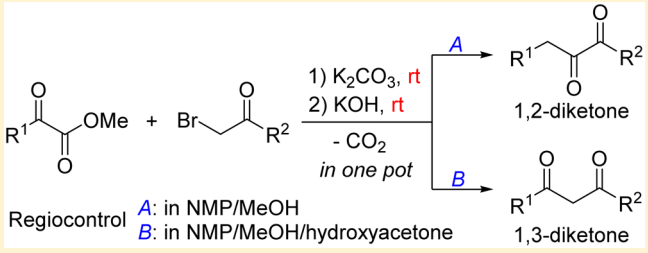
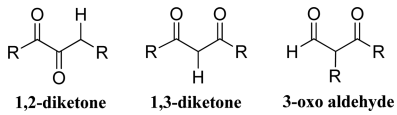
Supporting Information

ABSTRACT: A transition-metal-free and room-temperature coupling/decarboxylation reaction between α-oxocarboxylates and α-bromoketones is reported herein. It represents the first mild and regioselective synthesis of either 1,2- or 1,3-diketones from the same starting materials. Notably, the regioselectivity is simply controlled by solvents. The preliminary experimental data and DFT calculations suggest sequential Darzens-type coupling, alkaline hydrolysis, KOH-promoted oxirane opening and decarboxylation in one pot. This method is efficient for the synthesis of α,β-epoxy-γ-butyrolactone and curcuminoids.



INTRODUCTION

1,2-Diketone and 1,3-diketone are both important and versatile synthetic precursors, bioactive molecules, and functional materials.[1,2] The main synthetic methods for the preparation of 1,2-diketones include the oxidation of benzoins,[3] epoxides,[4] and alkynes[5] and the coupling of α-oxo acid chlorides with organostannanes[6] as well as acid chlorides with trimethylsilyl cyanohydrins.[7] A recent interesting method is the selective C−C bond cleavage of 1,3-diketones.[8] 1,3-Diketones can be synthesized by the oxidation of aldol products,[9] the coupling of two carbonyl compounds through hard enolate strategy (classical Claisen condensation),[10] soft enolate strategy,[11] and organo-[12] and transition-metal catalysis,[13] the rearrangement of γ-acyloxyl enones triggered by bis(iodozincio)methane,[14] and the palladium-catalyzed carbonylative α-arylation of ketones with aryl iodides using carbon monoxide.[15] However, these protocols for both diketones start from different materials and suffer from the multistep preparation of starting materials, the use of specific catalysts or toxic or expensive reagents, and/or harsh reaction conditions. Moreover, a regioselective protocol for the preparation of both regioisomers is not yet available.



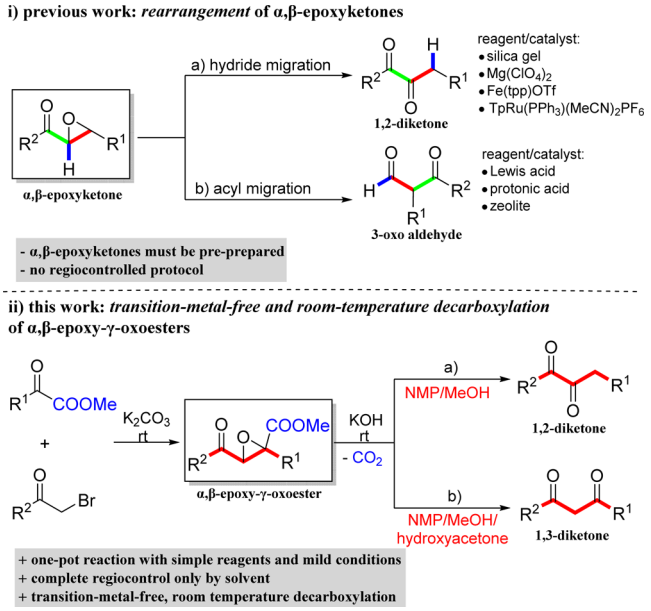
1,2-Diketone and its regioisomer 3-oxo aldehyde can be obtained by the rearrangement of α,β-epoxy ketones under different conditions through either acyl or hydride migrations, respectively.[16] The acyl migration is generally more favored and may be promoted by Lewis acids,[17] protonic acids,[17a] and zeolites[18] to afford 3-oxo aldehydes. On the other hand, the hydride migration is less favored and in the presence of $Mg(ClO_4)_2$,[19] silica gel,[20] or catalzyed by Fe(tpp)OTf (tpp = tetraphenylporphyrin)[21] and $TpRu(PPh_3)(MeCN)_2PF_6$ (Tp = tris(1-pyrazolyl)borate)[22] generates 1,2-diketones. These reactions suffer from pre-preparation of α,β-epoxy ketones, limited substrate scope, precious complex catalysts, and in some cases, harsh conditions. It should be noted that none of them can regioselectively provide either isomer (Scheme 1, i).

Stable and easily prepared α-oxocarboxylic acids have recently emerged as an attractive acyl synthon for transition-metal (TM)-catalyzed decarboxylative coupling reactions.[23] A TM-free version between potassium α-oxocarboxylates and α-bromoketones at 150 °C to generate 1,3-diketones has also been discovered.[24] The DFT calculations suggested a unique coupling/decarboxylation pathway. Particularly noteworthy is that the energy barrier for decarboxylation is much lower than in TM-catalyzed decarboxylations. However, high temperature is still needed because the generation of the key intermediate involves the thermolysis of an α-bromoketone, which has a very high energy barrier. Herein, a room-temperature coupling/decarboxylation reaction between methyl α-oxocarboxylates and α-bromoketones to give not only 1,3- but also 1,2-diketones in a completely regioselective manner is reported (Scheme 1, ii). The unique advantages of this reaction include simple reagents, mild conditions, and a solvent-controlled

Received: October 25, 2016
Published: January 4, 2017

DOI: 10.1021/acs.joc.6b02575
J. Org. Chem. 2017, 82, 1403−1411

Scheme 1. Synthetic Protocols for Dicarbonyl Compounds from Epoxides

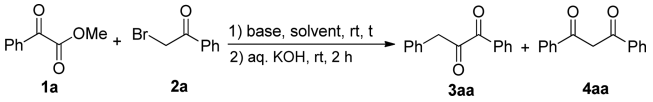


regioselectivity. This represents the first mild and regiocontrollable protocol to permit the synthesis of either 1,2- or 1,3-diketones. The key intermediates for this reaction are *α,β*-epoxy-*γ*-oxoesters, which can also be formed diastereoselectively. This reaction is applicable for the synthesis of *α,β*-epoxy-*γ*-butyrolactone and curcuminoids.

RESULTS AND DISCUSSION

Optimization of Reaction Conditions. A model coupling reaction between methyl 2-oxo-2-phenylacetate (**1a**) and 2-bromo-1-phenylethanone (**2a**) in the presence of 2.0 equiv of K_2CO_3 in *N*-methyl-2-pyrrolidone (NMP) at room temperature for 24 h, followed by the addition of 300 μL of a 4 N aqueous KOH solution and continuous stirring at room temperature for another 2 h, was conducted for the initial optimization. The ^{1}H NMR analysis of the isolated product unexpectedly revealed a mixture of 1,3-diphenylpropane-1,2-dione (**3aa**) and 1,3-diphenylpropane-1,3-dione (**4aa**) in a ratio of 11:9. The total yield was 36% (Table 1, entry 1). The addition of the KOH solution over a period of 0.5 h improved the yield to 63%, although the selectivity remained unchanged (Table 1, entry 2). Other bases (i.e., Na_2CO_3, EtONa, Et_3N, DBU, and pyridine) and solvents (i.e., CH_3CN, DMSO, CH_2Cl_2, and toluene) significantly decreased the yield (for details, see the Supporting Information). However, the reaction in MeOH was much faster, and the starting materials vanished in 2 h. Interestingly, **3aa** was obtained almost as a single product but in less than 15% yield (Table 1, entry 3). These results indicated that MeOH not only dramatically accelerates the coupling of **1a** and **2a** but also controls a perfect regioselectivity for **3aa**. Therefore, a mixed solvent of NMP/MeOH (1:1, v/v) was eventually selected to promote the formation of **3aa** in 91% yield (Table 1, entry 4). The use of EtOH instead of MeOH resulted in 84% yield, but with a much lower ratio of 3:1 (Table 1, entry 5). Lowering the concentration of aqueous KOH abruptly decreased the yield to less than 10% (Table 1, entry 6). More interestingly, the use of hydroxyacetone completely reversed the selectivity and

Table 1. Optimization for Selective Synthesis of 1,2- and 1,3-Diketones[a]



entry	solvent	ratio (**3aa**/**4aa**)[b]	total yield[c] (%)
1[d,e]	NMP (1.0 mL)	11/9	36
2[d]	NMP (1.0 mL)	11/9	63
3	MeOH (1.0 mL)	>99/1	<15
4	NMP/MeOH (0.5/0.5 mL)	>99/1	**91**
5	NMP/EtOH (0.5/0.5 mL)	3/1	84
6[f]	NMP/MeOH (0.5/0.5 mL)	>99/1	<10
7	NMP/hydroxyacetone (0.5/0.5 mL)	<1/99	<10
8	NMP/MeOH/hydroxyacetone (1 mL/100 μL/25 μL)	<1/99	63
9[g]	NMP/MeOH/hydroxyacetone (1 mL/100 μL/25 μL)	<1/99	**78**

[a]The reaction was carried out with **1a** (0.25 mmol), **2a** (0.325 mmol), and K_2CO_3 (0.50 mmol) in solvent at room temperature for 2 h (*t*), followed by the addition of 300 μL of 4 N KOH over a period of 0.5 h, and continued stirring for another 1.5 h. [b]Determined by ^{1}H NMR analysis. [c]Isolated yield. [d]*t* = 24 h. [e]300 μL of 4 N KOH was added by one time. [f]2 N KOH was used. [g]*t* = 4 h.

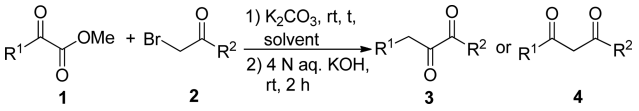
provided **4aa** as a single product, yet the reaction was sluggish and the yield of **4aa** was very low (Table 1, entry 7). To balance the reaction kinetics and selectivity, MeOH and hydroxyacetone were both added, and their amounts were carefully tuned. It was found that the reaction in the mixed solvent of 1 mL of NMP, 100 μL of MeOH, and 25 μL of hydroxyacetone could deliver **4aa** in 63% yield (Table 1, entry 8). Extending the time of the coupling step to 4 h resulted in an optimal yield of 78% (Table 1, entry 9).

Substrate Scope. A series of methyl *α*-oxocarboxylates **1** and *α*-bromoketones **2** were subjected to reaction under the two optimized conditions, respectively. As summarized in Table 2, both 1,2- and 1,3-diketones (**3** and **4**) were obtained in moderate to good yields. 1,3-Diketones **4** were produced in relatively lower yields than 1,2-diketones **3**. The best yields were 94% for **3ca** and 85% for **4fj** (entries 3 and 27). The steric hindrance on the *α*-oxocarboxylate side showed a much greater impact than on the *α*-bromoketone side. When R^1 was the *o*-methylphenyl group, the first coupling reaction did not occur whatever base was used. When R^2 was the *o*-methoxyphenyl group, **3ad** was obtained in a low yield of 32% (entry 14). The substrates containing heteroaryls were suitable, and the corresponding diketones containing 2-thienyl, 3-thienyl, and 2-furyl groups were all obtained in good yields (entries 9, 10, 20, 21, 26, and 27). Notably, the *α,β*-unsaturated substrate was also compatible. 1,3-Diketone **4al** was isolated in 63% yield, but the yield of 1,2-diketone **3al** was only 30% (entry 22). Aliphatic oxocarboxylate **1k** gave 1,3-diketone **4ka** in 67% yield, whereas the decomposition occurred under the conditions for the synthesis of 1,2-dikeones (entry 11).

Mechanism Studies and DFT Calculations. Following the coupling reaction process in NMP with TLC revealed the emergence of two new spots rather than the diketone products before addition of KOH. The major spot was determined by the X-ray diffraction analysis to be *trans*-methyl 3-benzoyl-2-phenyloxirane-2-carboxylate (*trans*-**5aa**),[15] a Darzens-type product[26] (eq 1a and Figure S2, left). The minor spot was found to be *cis*-**5aa** by using ^{1}H NMR and HRMS in

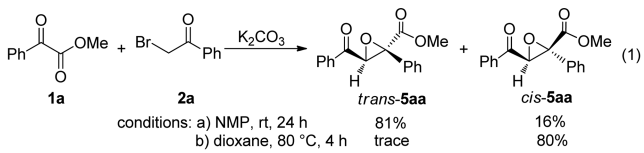
DOI: 10.1021/acs.joc.6b02575
J. Org. Chem. 2017, 82, 1403−1411

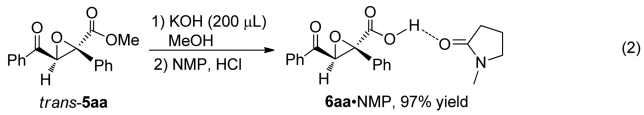
Table 2. Substrate Scope for the Synthesis of 1,2- and 1,3-Diketones[a]

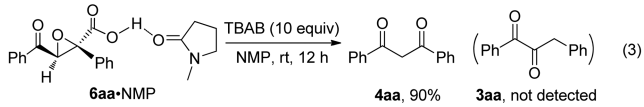


entry	R^1	R^2	3 (yield, %)[b,d]	4 (yield, %)[c,d]
1	Ph	Ph	**3aa** (91)	**4aa** (78)
2	*p*-MeC_6H_4	Ph	**3ba** (90)	**4ba** (45)
3	*m*-MeC_6H_4	Ph	**3ca** (94)	**4ca** (63)
4	*p*-$MeOC_6H_4$	Ph	**3da** (63)	**4da** (40)
5	*p*-BrC_6H_4	Ph	**3ea** (48)	**4ea** (70)
6	*p*-FC_6H_4	Ph	**3fa** (80)	**4fa** (62)
7	2-naphthyl	Ph	**3ga** (65)	**4ga** (68)
8	biphenyl	Ph	**3ha** (85)	**4ha** (70)
9	2-thienyl	Ph	**3ia** (64)	**4ia** (61)
10	3-thienyl	Ph	**3ja** (61)	**4ja** (61)
11	cyclohexyl	Ph	**3ka** (trace)	**4ka** (67)
12	Ph	*p*-$MeOC_6H_4$	**3ab** (58)	**4ab** (50)
13	Ph	*m*-$MeOC_6H_4$	**3ac** (76)	**4ac** (65)
14	Ph	*o*-$MeOC_6H_4$	**3ad** (32)	**4ad** (56)
15	Ph	benzo[*d*][1,3]dioxol-5-yl	**3ae** (45)	**4ae** (63)
16	Ph	*p*-BrC_6H_4	**3af**[25] (86)	**4af** (68)
17	Ph	*p*-FC_6H_4	**3ag** (70)	**4ag** (66)
18	Ph	*p*-$CF_3C_6H_4$	**3ah** (64)	**4ah** (60)
19	Ph	2-naphthyl	**3ai** (81)	**4ai** (70)
20	Ph	2-thienyl	**3aj** (90)	**4aj** (80)
21	Ph	2-furyl	**3ak** (86)	**4ak** (75)
22	Ph	PhCH=CH–	**3al** (30)	**4al** (63)
23	*p*-BrC_6H_4	*p*-BrC_6H_4	**3ef** (63)	**4ef** (60)
24	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	**3db** (52)	**4db** (42)
25	*p*-MeC_6H_4	*p*-BrC_6H_4	**3bf** (70)	**4bf** (55)
26	2-thienyl	2-thienyl	**3ij** (71)	**4ij** (70)
27	*p*-FC_6H_4	2-thienyl	**3fj** (81)	**4fj** (85)

[a]The reactions were carried out with **1** (0.25 mmol), **2** (0.325 mmol), and K_2CO_3 (0.50 mmol) in a solvent at room temperature for 2 h (for **3**) or 4 h (for **4**), followed by the addition of 300 μL of 4 N KOH over a period of 0.5 h, and continued stirring for another 1.5 h. [b]Solvent: NMP/MeOH (0.5/0.5 mL). [c]Solvent: NMP/MeOH/hydroxyacetone (1.0 mL/100 μL/25 μL). [d]Isolated yield.







comparison with *trans*-**5aa**. The yields of the two diastereomers were 81% and 16%, respectively. Interestingly, the coupling conducted in dioxane at 80 °C for 4 h delivered *cis*-**5aa** almost as a single diastereomer in 80% yield (eq 1b). Thus, this mild Darzens-type coupling offers a highly efficient protocol to access synthetically challenging α,β-epoxy-γ-oxoesters **5** in both diastereomeric forms.

The treatment of *cis*-**5aa** with KOH under the standard conditions delivered 1,2- and 1,3-diketones in yields similar to those from *trans*-**5aa** (see the SI), indicating that the regioselectivity was not derived from these two diastereomeric intermediates. Then the hydrolysis of **5aa** by the dropwise addition of 300 μL of KOH in MeOH was carefully monitored. Compound **5aa** disappeared after the addition of 200 μL of KOH, and highly polar substances were produced, suggesting that **5aa** was completely hydrolyzed into an organic salt. The reaction mixture would stay unchanged if no more KOH was added. The addition of the remaining 100 μL of KOH gave a small amount of 1,2-diketone **3aa** (Table 1, entry 3). The hydrolyzed intermediate in its acid form was fortunately obtained as a white solid, **6aa**·NMP,[27] which was stabilized by NMP through hydrogen bonding as resolved by the single-crystal analysis (eq 2 and Figure S2).[25] It needs to be pointed out that, without KOH, **6aa**·NMP only decarboxylated in NMP at a high temperature of 150 °C and gave a small amount of 1,3-diketone **4aa** as the single product, which followed the traditional decarboxylation-triggered ring opening pathway (Darens type).[28] These results indicated the most possible sequence of the current reaction is hydrolysis, oxirane opening, and then decarboxylation.[29]

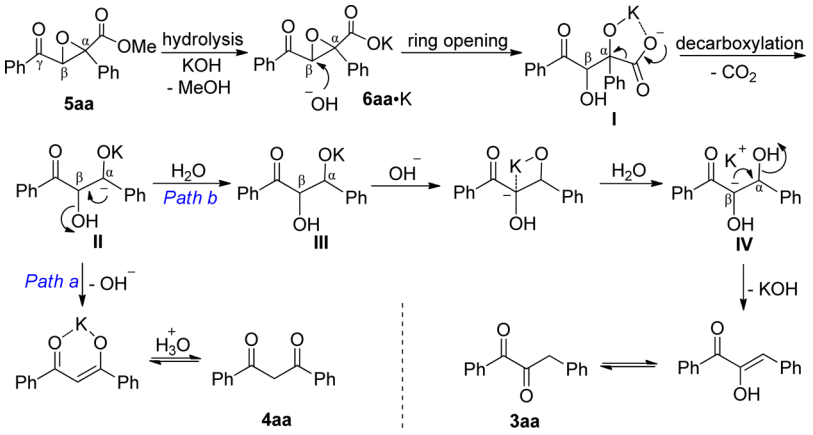
To verify the ring-opening step, tetrabutylammonium bromide (TBAB), a neutral nucleophile, was tested instead of the basic nucleophile KOH. Stirring **6aa**·NMP with TBAB at room temperature for 12 h afforded 1,3-diketone **4aa** in 90% yield as a single product (eq 3). Therefore, it is reasonable to conclude that KOH sequentially plays three roles in this reaction: (1) as a base to hydrolyze the ester, (2) as a nucleophile to open the oxirane ring, and (3) as a base to switch the production from 1,3- to 1,2-diketones.

Density functional theory (DFT) calculations were then performed to elucidate the possible pathways for the oxirane opening by hydroxide and the decarboxylation of **6aa**·K. They suggest that two pathways (a and b) having similar activation free energies (29.0 and 28.2 kcal/mol) produce 1,2- and 1,3-diketone, respectively (for details, see the SI). The activation free energy of path b is 0.8 kcal/mol lower than that of path a, indicating the slightly higher selectivity for the 1,2-diketone product. This bias is so small in NMP that the regioselectivity is only 11/9 (**3aa**/**4aa**, Table 1, entry 1).

On the basis of the above experiment results and DFT calculations, a tentative mechanism is shown in Scheme 2. Compound **5aa** is first hydrolyzed in aqueous KOH to form the corresponding carboxylate **6aa**·K. Then the hydroxide ion acts as a nucleophile to attack the oxirane ring on the β carbon and the ring is opened to form the intermediate **I**, which is an analogue of the previously proposed key intermediate.[24] Therefore, the decarboxylation takes place very easily at room temperature to generate the carbanion **II**. The elimination of the β-hydroxy group will give the β-hydroxy chalcone derivative, which is protonated and isomerizes into 1,3-diketone **4aa** (path a). However, **II** is also prone to rapid protonation by water to form the intermediate **III** (path b) because of the poor leaving ability of the hydroxy group. In a strong alkaline environment, **III** is deprotonated by hydroxide again on the more acidic β carbon and protonated by water on the α oxygen to generate the carbanion **IV**, which is more stable than **II** due to the stabilization by the vicinal acyl group. Finally, the elimination of KOH affords α-hydroxy chalcone, which is the

DOI: 10.1021/acs.joc.6b02575
J. Org. Chem. 2017, 82, 1403−1411

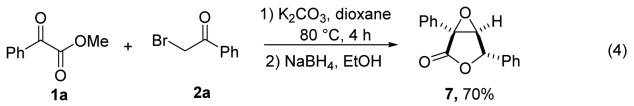
Scheme 2. Proposed Mechanism



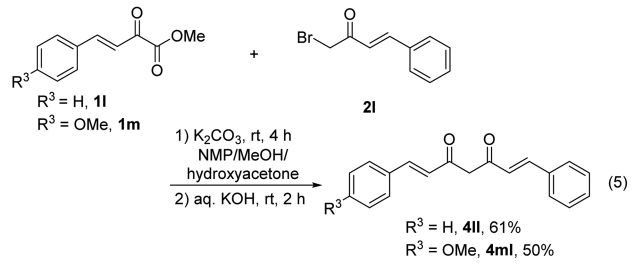
isomer of 1,2-diketone **3aa**. Although the regioselectivity caused by MeOH and hydroxyacetone is still unclear at this time and needs further investigation, the system basicity and kinetics should be taken into consideration. MeOH may kinetically favor the formation of the more stable intermediate **IV** in path b, while acidic hydroxyacetone may retard the generation of **IV** by subtly lowering the system pH.

Synthetic Applications. To showcase the usefulness and simple practicability of the current method, the syntheses of two kinds of synthetically difficult molecules are demonstrated. *α,β*-Epoxy-*γ*-butyrolactone is an important skeleton found in many bioactive natural products.[30] The concise and convenient methods to obtain these compounds are highly desirable and demanding.[31] Herein, the reaction mixture of **1a** and **2a** in dioxane was directly subjected to the $NaBH_4$ reduction at room temperature for 0.5 h, providing *α,β*-epoxy-*γ*-butyrolactone **7** in 70% yield (eq 4). Compound **7** was previously synthesized in three steps in a total yield of 61%.[32]

one-pot synthesis of α,β-epoxy-γ-butyrolactone:



synthesis of curcuminoid analogues:



Curcuminoids possess antiinflammatory, antioxidant, antiarthritic, and antitumor bioactivities, but efficient synthetic methodologies are very limited.[33] To date, the prevailing synthetic protocol was developed as early as in 1964.[34] In this approach, acetylacetone is first protected with boron trioxide and then condensed with benzaldehyde. The final dissociation of the boron complex in a slightly acidic environment provides the corresponding curcuminoid. The drawbacks are obvious, including a multistep process and especially the inaccessibility to pure unsymmetrical curcuminoids. By utilizing the method described herein, the reactions of *α,β*-unsaturated methyl *α*-oxocarboxylate **1l** and **1m** with *α,β*-unsaturated *α*-bromoketone **2l** produced the symmetrical curcuminoid analogue **4ll** and unsymmetrical curcuminoid analogue **4ml** in 61% and 50% yield in one pot, respectively (eq 5). It provides a very convenient and efficient protocol to synthesize curcuminoids, especially the unsymmetrical ones.

CONCLUSIONS

In conclusion, the first regioselective synthesis of 1,2- and 1,3-diketones is developed by using easily prepared methyl *α*-oxocarboxylates and *α*-bromoketones as the starting materials. This coupling/decarboxylation reaction is mild enough to conduct at room temperature, and the excellent regioselectivity is simply controlled by methanol and hydroxyacetone. The key intermediate is isolated and identified to be an *α,β*-epoxy-*γ*-oxoester after the first coupling step, which can also be obtained diastereoselectively in different solvents. The mechanism study as well as DFT calculations suggest a sequential process consisting of a very mild Darzens-type reaction, an alkaline hydrolysis, a KOH-promoted oxirane opening, and a transition-metal-free decarboxylation. The very convenient one-pot syntheses of *α,β*-epoxy-*γ*-butyrolactone and curcuminoid analogues highlight the synthetic usefulness of the current protocol.

EXPERIMENTAL SECTION

General Procedure for the Preparation of 1,2-Diketones 3. A flame-dried Schlenk tube with a magnetic stirring bar was charged with methyl *α*-oxocarboxylate **1** (0.25 mmol), *α*-bromoketone **2** (0.325 mmol), and K_2CO_3 (0.50 mmol). The system was evacuated and backfilled with N_2 twice, and NMP/MeOH (0.5/0.5 mL) was injected. The reaction was allowed to stir at room temperature for 2 h. Then 300 *μ*L of 4 N aq KOH solution was added over a period of 0.5 h and the reaction continued for another 1.5 h. The reaction mixture was neutralized to pH 7 with 2 N HCl and extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4. After the volatile solvent was evaporated, the residue was purified by column chromatography on silica gel (100−200 mesh) using ethyl acetate (EA)/petroleum ether (PE) as the eluent to afford the corresponding 1,2-diketone **3**.

*1,3-Diphenylpropane-1,2-dione (**3aa**).*[3] Eluted with EA/PE = 1/10. Yellow oil, 51.0 mg, 91% yield. Enol/ketone = 1.3:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.20 (s, 2H, ketone form), 6.40 (s, 1.3H, enol form), 7.27 (d, J = 7.6 Hz, 2H, ketone form), 7.30−7.35 (m, 3H, ketone form), 7.38−7.40 (m, 3.9H, enol form), 7.42−7.46 (m, 2H + 1.3H), 7.49−7.53 (m, 2H, ketone form), 7.58−7.63 (m, 1H + 1.3H), 7.73−7.75 (m, 2.6H, enol form), 7.82−7.84 (m, 2.6H, enol form),

DOI: 10.1021/acs.joc.6b02575
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7.88−7.90 (m, 2H, ketone form). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.6, 119.6, 127.6, 128.5, 128.7, 128.89, 128.95, 129.1, 129.2, 130.0, 130.3, 130.5, 131.8, 132.2, 132.3, 134.3, 134.7, 136.1, 147.0, 192.2, 193.6, 199.3.

*1-Phenyl-3-(p-tolyl)propane-1,2-dione (**3ba**).* Eluted with EA/PE = 1/10. Yellow oil for enol/ketone mixture and a white solid for enol form recrystallized from PE. 53.5 mg, 90% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 3H), 6.38 (s, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.34 (s, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.72 (d, J = 8.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 120.0, 128.5, 129.2, 129.5, 130.6, 131.5, 132.1, 136.2, 139.3, 146.6, 193.6.

*1-Phenyl-3-(m-tolyl)propane-1,2-dione (**3ca**).* Eluted with EA/PE = 1/10. Yellow oil for enol/ketone mixture and a white solid for enol form recrystallized from PE. 56.0 mg, 90% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3H), 6.37 (s, 1H), 7.14 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.37 (s, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.59−7.66 (m, 3H), 7.72−7.74 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 119.9, 127.7, 128.5, 128.7, 129.2, 129.9, 131.2, 132.2, 134.2, 136.1, 138.3, 146.9, 193.7. HRMS (ESI$^+$): calcd for $C_{16}H_{15}O_2$ $[M + H]^+$ 239.1072, found 239.1066.

*3-(4-Methoxyphenyl)-1-phenylpropane-1,2-dione (**3da**).*[20] Eluted with EA/PE = 1/5. Yellow oil for enol/ketone mixture and a light yellow solid for enol form recrystallized from PE. 40.0 mg, 63% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3H), 6.38 (s, 1H), 6.92 (d, J = 9.2 Hz, 2H), 7.32 (d, J = 1.6 Hz, 1H), 7.49 (t, J = 7.4 Hz, 2H), 7.57−7.61 (m, 1H), 7.70−7.72 (m, 2H), 7.79 (d, J = 9.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4, 114.2, 120.0, 127.1, 128.5, 129.2, 132.0, 132.3, 136.4, 145.9, 160.2, 193.4.

*3-(4-Bromophenyl)-1-phenylpropane-1,2-dione (**3ea**).* Eluted with EA/PE = 1/10. Yellow oil for enol/ketone mixture and a white solid for enol form recrystallized from PE. 36.0 mg, 48% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.32 (s, 1H), 7.43 (s, 1H), 7.49−7.53 (m, 4H), 7.62 (t, J = 7.6 Hz, 1H), 7.69 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.1, 123.0, 128.6, 129.2, 131.9, 132.4, 133.2, 135.8, 147.3, 193.4.

*3-(4-Fluorophenyl)-1-phenylpropane-1,2-dione (**3fa**).* Eluted with EA/PE = 1/10. Yellow oil for enol/ketone mixture and a light yellow solid for enol form recrystallized from PE. 48.5 mg, 80% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.36 (s, 1H), 7.04−7.11 (m, 2H), 7.38 (s, 1H), 7.49−7.53 (m, 2H), 7.59−7.63 (m, 1H), 7.71−7.74 (m, 2H), 7.80−7.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 115.8 (d, J = 21.5 Hz), 118.5 (d, J = 0.9 Hz), 128.6, 129.2, 130.5 (d, J = 3.3 Hz), 132.3 (d, J = 9.3 Hz), 132.5, 136.0, 146.6 (d, J = 2.5 Hz), 162.8 (d, J = 248.9 Hz), 193.5.

*3-(Naphthalen-2-yl)-1-phenylpropane-1,2-dione (**3ga**).* Eluted with EA/PE = 1/5. Yellow solid for enol/ketone mixture and a light yellow solid for enol form recrystallized from PE. 44.5 mg, 65% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.57 (s, 1H), 7.48−7.55 (m, 5H), 7.63 (t, J = 7.2 Hz, 1H), 7.77−7.87 (m, 5H), 7.95 (d, J = 8.4 Hz, 1H), 8.32 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 119.8, 126.5, 127.0, 127.7, 127.8, 128.2, 128.6, 128.7, 129.3, 130.5, 131.9, 132.3, 133.4, 133.5, 136.1, 147.3, 193.6.

*3-[(1,1′-Biphenyl)-4-yl]-1-phenylpropane-1,2-dione (**3ha**).* Eluted with EA/PE = 1/5. Yellow solid for enol/ketone mixture, a light yellow solid for enol form recrystallized from PE/DCM. 63.5 mg, 85% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.45 (s, 1H), 7.37 (t, J = 7.2 Hz, 1H), 7.44−7.48 (m, 3H), 7.52 (t, J = 7.6 Hz, 2H), 7.60−7.66 (m, 5H), 7.76 (d, J = 7.2 Hz, 2H), 7.91 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 119.3, 127.2, 127.3, 127.8, 128.6, 129.0, 129.3, 131.0, 132.3, 133.4, 136.1, 140.5, 141.5, 147.1, 193.5.

*1-Phenyl-3-(thiophene-2-yl)propane-1,2-dione (**3ia**).* Eluted with EA/PE = 1/5. Light brown solid for enol/ketone mixture, as well as a light brown solid for enol form recrystallized from PE. 37.0 mg, 64% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.74 (s, 1H), 7.09−7.11 (m, 1H), 7.35 (d, J = 3.6 Hz, 1H), 7.38 (s, 1H), 7.49−7.53 (m, 3H), 7.59−7.63 (m, 1H), 7.71−7.73 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 113.8, 127.6, 128.6, 129.1, 130.1, 130.6, 132.3, 136.0, 137.3, 145.1, 192.1.

*1-Phenyl-3-(thiophene-3-yl)propane-1,2-dione (**3ja**).* Eluted with EA/PE = 1/5. Yellow oil for enol/ketone mixture, and a milky white solid for enol form recrystallized from PE. 35.0 mg, 61% yield. Enol form. Mp: 90−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.48 (s, 1H), 7.28 (s, 1H), 7.32−7.34 (m, 1H), 7.44 (d, J = 5.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.72 (d, J = 7.6 Hz, 2H), 7.88 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 113.9, 125.6, 128.0, 128.6, 129.1, 129.2, 132.2, 135.4, 136.1, 146.2, 193.2.

*1-(4-Methoxyphenyl)-3-phenylpropane-1,2-dione (**3ab**).*[20] Eluted with EA/PE = 1/5. Yellow oil, 37.0 mg, 58% yield. Enol/ketone = 0.5:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3H, ketone form), 3.91 (s, 1.5H, enol form), 4.18 (s, 2H, ketone form), 6.40 (s, 0.5H, enol form), 6.90 (d, J = 8.8 Hz, 2H, ketone form), 7.00 (d, J = 8.4 Hz, 1H, enol form), 7.25−7.27 (m, 2 + 1H), 7.30−7.34 (m, 2H + 0.5H), 7.38−7.41 (m, 1 + 0.5H), 7.78 (d, J = 8.8 Hz, 1H, enol form), 7.83 (d, J = 8.0 Hz, 1H, enol form), 7.89 (d, J = 8.8 Hz, 2H, ketone form). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.7, 55.68, 55.73, 113.9, 114.3, 118.5, 125.2, 127.5, 128.3, 128.7, 129.0, 130.0, 130.4, 131.0, 131.7, 132.1, 132.9, 134.5, 147.0, 163.2, 164.9, 190.6, 192.3, 199.9.

*1-(3-Methoxyphenyl)-3-phenylpropane-1,2-dione (**3ac**).* Eluted with EA/PE = 1/5. Yellow oil, 48.0 mg, 76% yield. Enol/ketone = 2:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3H, ketone form), 3.87 (s, 6H, enol form), 4.19 (s, 2H, ketone form), 6.44 (s, 2H, enol form), 7.13−7.16 (m, 4H), 7.24−7.29 (m, 3H), 7.30−7.35 (m, 8H), 7.38−7.44 (m, 10H), 7.82 (d, J = 7.2 Hz, 4H, enol form). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.7, 55.57, 55.62, 113.5, 114.0, 118.4, 119.6, 121.7, 121.8, 123.4, 127.6, 128.7, 129.0, 129.1, 129.6, 129.9, 130.0, 130.6, 131.8, 133.4, 134.3, 137.3, 146.9, 159.6, 159.9, 192.2, 193.4, 199.4.

*1-(Benzo[d][1,3]dioxol-5-yl)-3-phenylpropane-1,2-dione (**3ae**).* Eluted with EA/PE = 1/5. Yellow oil for enol/ketone mixture and a light yellow solid for ketone form recrystallized from PE. 30.0 mg, 45% yield. Ketone form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.16 (s, 2H), 6.05 (s, 2H), 6.81 (d, J = 8.4 Hz, 1H), 7.24−7.26 (m, 3H), 7.30−7.34 (m, 2H), 7.39 (s, 1H), 7.47 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.8, 101.3, 107.4, 108.0, 125.9, 126.6, 127.2, 128.0, 129.0, 131.0, 147.5, 152.4, 189.4, 198.7.

*1-(4-Bromophenyl)-3-phenylpropane-1,2-dione (**3af**).* Eluted with EA/PE = 1/10. Yellow oil for enol/ketone mixture and a light yellow solid for enol form recrystallized from PE. 65.0 mg, 86% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.34 (s, 1H), 7.31−7.35 (m, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 119.9, 127.2, 128.8, 129.2, 130.6, 130.8, 131.9, 134.1, 134.8, 146.8, 192.6.

*1-(4-Fluorophenyl)-3-phenylpropane-1,2-dione (**3ag**).* Eluted with EA/PE = 1/10. Yellow oil for enol/ketone mixture and a white solid for enol form recrystallized from PE. 42.5 mg, 70% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.36 (s, 1H), 7.20 (t, J = 8.4 Hz, 2H), 7.31−7.34 (m, 2H), 7.40 (t, J = 7.6 Hz, 2H), 7.76−7.83 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$):, δ = 115.8 (d, J = 21.8 Hz), 119.6, 128.8, 129.1, 130.5, 131.8 (d, J = 8.9 Hz), 132.2 (d, J = 3.2 Hz), 134.2, 146.9, 165.3 (d, J = 252.4 Hz), 192.3.

*3-Phenyl-1-(4-(trifluoromethyl)phenyl)propane-1,2-dione (**3ah**).* Eluted with EA/PE = 1/10. Yellow oil for enol/ketone mixture and a white solid for enol form recrystallized from PE. 46.5 mg, 64% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.32 (s, 1H), 7.30 (s, 1H), 7.33−7.39 (m, 1H), 7.41 (t, J = 7.4 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H), 7.82−7.84 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 120.7, 125.6 (q, J = 3.7 Hz), 128.8, 129.4, 129.5, 130.7, 133.9, 139.4, 146.8, 192.6.

*1-(Naphthalen-2-yl)-3-phenylpropane-1,2-dione (**3ai**).* Eluted with EA/PE = 1/5. Yellow oil for enol/ketone mixture and a light yellow solid for enol form recrystallized from PE. 55.0 mg, 81% yield. Enol form. Mp: 95−98 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.49 (s, 1H), 7.33−7.35 (m, 1H), 7.39−7.45 (m, 3H), 7.60−7.64 (m, 2H), 7.80−7.85 (m, 3H), 7.93−7.98 (m, 3H), 8.28 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 119.8, 125.4, 127.2, 128.0, 128.4, 128.6, 128.8, 129.0, 129.3, 130.3, 130.6, 132.3, 133.3, 134.3, 135.1, 147.2, 193.6.

DOI: 10.1021/acs.joc.6b02575
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*3-Phenyl-1-(thiophene-2-yl)propane-1,2-dione (**3aj**).* Eluted with EA/PE = 1/5. Yellow oil. 51.5 mg, 90% yield. Enol/ketone = 0.25:1. ^{1}H NMR (400 MHz, $CDCl_3$):δ = 4.23 (s, 2H, ketone form), 6.77 (s, 0.25H, enol form), 7.12−7.15 (m, 1H, ketone form), 7.18−7.20 (m, 0.25H, enol form), 7.25−7.28 (m, 2H + 0.5H), 7.31−7.35 (m, 2H + 0.5H), 7.41 (t, J = 7.7 HZ, 1H, ketone form) 7.71 (dd, J = 5.2 Hz, 1.2 Hz, 0.25H, enol form), 7.77 (dd, J = 4.8 Hz, 1,2 Hz, 1H, ketone form), 7.84 (dd, J = 3.6 Hz, 0.8 Hz, 0.25H, enol form), 7.86 (d, J = 8.0 Hz, 0.5H, enol form), 8.05 (dd, J = 3.6 Hz, 0.8 Hz, 1H, ketone form). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.2, 117.3, 127.4, 128.0, 128.72, 128.74, 128.87, 128.91, 130.0, 130.5, 132.4, 133.7, 133.9, 134.3, 137.4, 137.6, 137.7, 139.3, 146.8, 181.0, 183.9, 197.5.

*1-(Furan-2-yl)-3-phenylpropane-1,2-dione (**3ak**).* Eluted with EA/PE = 1/5. Yellow solid for enol/ketone mixture. 46.0 mg, 86% yield. Enol/ketone = 0.75:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.23 (s, 2H, ketone form), 6.58 (d, J = 2.0 Hz, 1H, ketone form), 6.63 (d, J = 1.6 Hz, 0.75H, enol form), 7.16 (s, 0.75H, enol form), 7.25−7.29 (m, 2 + 0.75H), 7.32−7.35 (m, 2H + 0.75H), 7.40−7.44 (m, 1 + 1.5H), 7.48 (s, 0.75H, enol form), 7.63 (d, J = 3.6 HZ, 1H, ketone form), 7.73 (brs, 1 + 0.75H), 7.91 (d, J = 7.6 Hz, 1.5H, enol form). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.0, 112.5, 113.0, 117.1, 120.5, 125.1, 127.3, 128.6, 128.7, 128.8, 129.9, 130.7, 132.1, 134.4, 145.9, 147.0, 148.8, 149.4, 150.7, 175.9, 177.4, 196.8.

*1,3-Bis(4-methoxyphenyl)propane-1,2-dione (**3db**).*[20] Eluted with EA/PE = 1/4. Yellow oil for enol/ketone mixture and a light yellow solid for enol form recrystalled from PE/DCM. 37.0 mg, 52% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3H), 3.90 (s, 3H), 6.38 (s, 1H), 6.92 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 7.33 (s, 1H), 7.75 (d, J = 8.8 Hz, 2H), 7.79 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5, 55.7, 113.8, 114.2, 118.9, 127.3, 128.7, 131.5, 132.1, 145.9, 160.0, 163.0, 192.1.

*1,3-Bis(4-bromophenyl)propane-1,2-dione (**3ef**).* Eluted with EA/PE = 1/10. Light yellow solid, 60.0 mg, 63% yield. Enol/ketone = 1.6:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.15 (s, 2H, ketone form), 6.27 (s, 1.6H, enol form), 7.13 (d, J = 8.0 Hz, 2H, ketone form), 7.35 (s, 1.6H, enol form), 7.46 (d, J = 8.4 Hz, 2H, ketone form), 7.52 (d, J = 8.4 Hz, 3.2H, enol form), 7.59−7.61 (m, 2H + 3.2H), 7.65−7.69 (m, 6.4H, enol form), 7.80 (d, J = 8.4 Hz, 2H, ketone form). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.7 (ketone form), 110.2, 118.3 (enol form), 121.9, 123.3, 127.4, 130.6, 130.7, 130.8, 130.9, 131.7, 131.8, 131.95, 131.98, 132.2, 132.4, 133.0, 134.6, 147.1, 190.1, 192.3, 198.0.

*1-(4-Bromophenyl)-3-(p-tolyl)propane-1,2-dione (**3bf**).* Eluted with EA/PE = 1/10. Yellow oil for enol/ketone mixture and a white solid for enol form recrystallized from PE/DCM. 55.0 mg, 70% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 3H), 6.32 (s, 1H), 7.20 (d, J = 7.6 Hz, 2H), 7.25 (s, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 120.2, 127.0, 129.6, 130.6, 130.7, 131.3, 131.8, 134.9, 139.6, 146.4, 192.4.

*1,3-Di(thiophene-2-yl)propane-1,2-dione (**3ij**).* Eluted with EA/PE = 1/4. Brown solid for enol/ketone mixture as well as a brown solid for enol form recrystallized from PE/DCM. 42.0 mg, 71% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11−7.13 (m, 2H), 7.20 (t, J = 4.2 Hz, 1H), 7.36 (s, 1H), 7.42 (d, J = 3.2 Hz, 1H), 7.52 (d, J = 5.2 Hz, 1H), 7.72 (d, J = 5.2 Hz, 1H), 7.82 (d, J = 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.7, 127.6, 128.1, 129.9, 130.6, 133.4, 133.5, 137.3, 139.2, 144.9, 182.4.

*3-(4-Fluorophenyl)-1-(thiophene-2-yl)propane-1,2-dione (**3fj**).* Eluted with EA/PE = 1/5. Yellow oil for enol/ketone mixture and a yellow solid for ketone form recrystallized from PE/DCM. 49.5 mg, 80% yield. Enol form. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.21 (s, 2H), 7.05 (t, J = 8.8 Hz, 2H), 7.17 (t, J = 4.4 Hz, 1H), 7.22−7.25 (m, 2H), 7.80 (d, J = 4.8 Hz, 1H), 8.07 (d, J = 4.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.4, 115.9 (d, J = 21.4 Hz), 128.1 (d, J = 3.2 Hz), 128.8, 131.6 (d, J = 8.0 Hz), 137.5, 137.6, 138.0, 162.3 (d, J = 244.6 Hz), 180.8, 197.3.

General Procedure for the Preparation of 1,2-Diketones 4. A flame-dried Schlenk tube with a magnetic stirring bar was charged with methyl α-oxocarboxylate **1** (0.25 mmol), α-bromoketone **2** (0.325 mmol), and K_2CO_3 (0.50 mmol). The system was evacuated and backfilled with N_2 twice, and NMP/MeOH/hydroxyacetone (1.0 mL/100 μL/25 μL) was injected. The reaction was allowed to stir at room temperature for 4 h. Then 300 μL of 4 N aq KOH solution was added over a period of 0.5 h and the reaction continued for another 1.5 h. The reaction mixture was neutralized to pH 7 with 2 N HCl and extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4. After the volatile solvent was evaporated, the residue was purified by column chromatography on silica gel (100−200 mesh) using EA/PE as the eluent to afford the corresponding 1,3-diketone **4**.

*1,3-Diphenylpropane-1,3-dione (**4aa**).*[24] Eluted with EA/PE = 1/10. White solid, 43.5 mg, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.87 (s, 1H), 7.50 (t, J = 7.2 Hz, 4H), 7.56 (t, J = 7.2 Hz, 2H), 8.00 (d, J = 7.6 Hz, 4H), 16.88 (s, 1H).

*1-Phenyl-3-(p-tolyl)propane-1,3-dione (**4ba**).*[35] Eluted with EA/PE = 1/10. White solid, 27.0 mg, 45% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3H), 6.84 (s, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.49 (t, J = 7.4 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.99 (d, J = 7.6 Hz, 2H), 16.93 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 93.0, 127.2, 127.4, 128.8, 129.5, 132.4, 133.0, 135.7, 143.4, 185.3, 186.2.

*1-Phenyl-3-(m-tolyl)propane-1,3-dione (**4ca**).*[35] Eluted with EA/PE = 1/10. Light brown oil, 37.5 mg, 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3H), 6.86 (s, 1H), 7.37−7.39 (m, 2H), 7.48−7.52 (m, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.78−7.81 (m, 2H), 8.00 (d, J = 7.6 Hz, 2H), 16.90 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 93.3, 124.5, 127.3, 127.9, 128.7, 128.8, 132.6, 133.4, 135.66, 135.72, 138.6, 185.8, 186.2.

*1-(4-Methoxyphenyl)-3-phenylpropane-1,3-dione (**4da** and **4ab**).*[24] Eluted with EA/PE = 1/5. White solid, **4da**, 25.5 mg, 40% yield. **4ab**, 32.0 mg, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (s, 3H), 6.80 (s, 1H), 6.99 (d, J = 8.4 Hz, 2H), 7.49 (t, J = 7.4 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.97−8.00 (m, 4H), 17.00 (s, 1H).

*1-(4-Bromophenyl)-3-phenylpropane-1,3-dione (**4ea** and **4af**).*[24] Eluted with EA/PE = 1/10. White solid, **4ea**, 53.0 mg, 70% yield. **4af**, 51.5 mg, 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.82 (s, 1H), 7.50 (t, J = 7.4 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 8.0 Hz, 2H), 7.98 (d, J = 7.6 Hz, 2H), 16.82 (s, 1H).

*1-(4-Fluorophenyl)-3-phenylpropane-1,3-dione (**4fa** and **4ag**).*[35] Eluted with EA/PE = 1/10. White solid, **4fa**, 37.5 mg, 70% yield. **4ag**, 35.5 mg, 66% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.80 (s, 1H), 7.17 (t, J = 8.6 Hz, 2H), 7.49 (t, J = 7.4 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.97−8.03 (m, 4H), 16.86 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 93.0, 116.0 (d, J = 21.8 Hz), 127.3, 128.9, 129.8 (d, J = 9.1 Hz), 132.1 (d, J = 3,1 Hz), 132.7, 135.4, 165.6 (d, J = 252.3 Hz), 185.3.

*1-(Naphthalen-2-yl)-3-phenylpropane-1,3-dione (**4ga** and **4ai**).*[36] Eluted with EA/PE = 1/5. White solid, **4ga**, 46.5 mg, 68% yield; **4ai**, 48.0 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (s, 1H), 7.50−7.62 (m, 5H), 7.88−8.05 (m, 6H), 8.55 (s, 1H), 16.98 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 93.6, 123.4, 127.0, 127.4, 127.9, 128.3, 128.5, 128.6, 128.9, 129.5, 132.6, 132.88, 132.90, 135.5, 135.7, 185.7, 185.9.

*1-[(1,1′-Biphenyl)-4-yl]-3-phenylpropane-1,3-dione (**4ha**).*[36] Eluted with EA/PE = 1/5. Milky white solid, 52.5 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.91 (s, 1H), 7.41 (t, J = 7.4 Hz, 1H), 7.50 (q, J = 7.6 Hz, 4H), 7.57 (t, J = 7.2 Hz, 1H), 7.66 (d, J = 7.2 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 8.02 (d, J = 6.8 Hz, 2H), 8.08 (d, J = 8.4 Hz, 2H), 16.93 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 93.3, 127.3, 127.4, 127.5, 127.9, 128.3, 128.8, 129.1, 132.6, 134.4, 135.8, 140.1, 145.4, 185.4, 185.9.

*1-Phenyl-3-(thiophene-2-yl)propane-1,3-dione (**4ia** and **4aj**).*[24] Eluted with EA/PE = 1/5. Yellow solid, **4ia**, 35.0 mg, 61% yield; **4aj**, 46.0 mg, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.69 (s, 1H), 7.18 (t, J = 4.0 Hz, 1H), 7.49 (t, J = 7.2 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.65 (d, J = 5.2 Hz, 1H), 7.82 (d, J = 3.6 Hz, 1H), 7.95 (d, J = 7.6 Hz, 2H), 16.31 (s, 1H).

*1-Phenyl-3-(thiophene-3-yl)propane-1,3-dione (**4ja**).* Eluted with EA/PE = 1/5. Yellow solid, 35.0 mg, 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68 (s, 1H), 7.39 (m, 1H), 7.49 (t, J = 7.4 Hz, 2H),

DOI: 10.1021/acs.joc.6b02575
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7.54−7.58 (m, 2H), 7.96 (d, J = 7.6 Hz, 2H), 8.12 (s, 1H), 16.61 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 93.9, 126.1, 126.8, 127.2, 128.8, 130.1, 132.5, 135.5, 139.6, 181.3, 185.1. HRMS (ESI$^+$): calcd for $C_{13}H_{10}O_2SNa$ $[M + Na]^+$ 253.0299, found 253.0302.

*1-Cyclohexyl-3-phenylpropane-1,3-dione (**4ka**).*[37] Eluted with EA/PE = 1/10. Light brown oil, 38.5 mg, 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22−1.95 (m, 10H), 2.32 (tt, J = 10.8 Hz, 3.2 Hz, 1H), 6.18 (s, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.52 (t, J = 7.2 Hz, 1H), 7.88 (d, J = 7.2 Hz, 2H), 16.31 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.9, 26.0, 29.8, 47.5, 94.6, 127.1, 128.7, 132.3, 135.4, 184.4, 200.0.

*1-(3-Methoxyphenyl)-3-phenylpropane-1,3-dione (**4ac**).*[24] Eluted with EA/PE = 1/5. White solid, 41.0 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (s, 3H), 6.85 (s, 1H), 7.10 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.48−7.58 (m, 5H), 7.99 (d, J = 7.6 Hz, 2H), 16.86 (s, 1H).

*1-(2-Methoxyphenyl)-3-phenylpropane-1,3-dione (**4ad**).*[24] Eluted with EA/PE = 1/5. White solid, 35.5 mg, 56% yield. Enol/ketone = 91:9. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.97 (s, 3H), 7.01 (d, J = 8.4 Hz, 1H), 7.08 (t, J = 7.2 Hz, 1H), 7.14 (s, 1H), 7.46−7.56 (m, 4H), 7.93−7.98 (m, 3H), 16.85 (s, 1H).

*1-(Benzo[d][1,3]dioxol-5-yl)-3-phenylpropane-1,3-dione (**4ae**).*[24] Eluted with EA/PE = 1/5. White solid, 42.0 mg, 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.07 (s, 2H), 6.75 (s, 1H), 6.90 (d, J = 8.0 Hz, 1H), 7.48−7.50 (m, 3H), 7.55 (t, J = 7.2 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 7.6 Hz, 2H), 16.92 (s, 1H).

*1-Phenyl-3-(4-(trifluoromethyl)phenyl)propane-1,3-dione (**4ah**).*[24] Eluted with EA/PE = 1/10. White solid, 44.5 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88 (s, 1H), 7.51 (t, J = 7.2 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.75 (d, J = 8.0 Hz, 2H), 8.00 (d, J = 7.6 Hz, 2H), 8.09 (d, J = 8.0 Hz, 2H), 16.75 (s, 1H).

*1-(Furan-2-yl)-3-phenylpropane-1,3-dione (**4ak**).*[38] Eluted with EA/PE = 1/5. Light brown solid, 40.0 mg, 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.57−6.58 (m, 1H), 6.76 (s, 1H), 7.23−7.24 (m, 1H), 7.46 (t, J = 7.2 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.60 (s, 1H), 7.95 (d, J = 7.6 Hz, 2H), 16.19 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 92.8, 112.8, 115.9, 127.1, 128.8, 132.5, 134.8, 146.2, 151.1, 177.8, 182.5.

*(E)-1,5-Diphenylpent-4-ene-1,3-dione (**4al**):*[24] Eluted with EA/PE = 1/10. Bright yellow solid, 39.5 mg, 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.36 (s, 1H), 6.66 (d, J = 16.0 Hz, 1H), 7.38−7.43 (m, 3 H), 7.49 (t, J = 7.6 Hz, 2H), 7.54−7.58 (m, 3H), 7.70 (d, J = 16.0 Hz, 1H), 7.96 (d, J = 7.6 Hz, 2H), 16.16 (s, 1H).

*1,3-Bis(4-bromophenyl)propane-1,3-dione (**4ef**).*[24] Eluted with EA/PE = 1/10. White solid, 57.0 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.77 (s, 1H), 7.63 (d, J = 8.4 Hz, 4H), 7.85 (d, J = 8.4 Hz, 4H), 16.75 (s, 1H).

*1,3-Bis(4-methoxyphenyl)propane-1,3-dione (**4db**).*[24] Eluted with EA/PE = 1/4. White solid, 30 mg, 42% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (s, 6H), 6.74 (s, 1H), 6.98 (d, J = 8.8 Hz, 4H), 7.96 (d, J = 8.4 Hz, 4H), 17.14 (s, 1H).

*1-(4-Bromophenyl)-3-(p-tolyl)propane-1,3-dione (**4bf**).*[39] Eluted with EA/PE = 1/10. White solid, 43.5 mg, 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44 (s, 3H), 6.79 (s, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.0 Hz, 2H), 16.88 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 92.8, 127.3, 127.4, 128.7, 129.6, 132.1, 132.7, 134.6, 143.7, 184.1, 186.3.

*1,3-Di(thiophene-2-yl)propane-1,3-dione (**4ij**).*[24] Eluted with EA/PE = 1/4. Bright yellow solid, 41.0 mg, 70% yield. Enol/ketone = 82:18. ^{1}H NMR (400 MHz, $CDCl_3$): δ= 6.54 (s, 1H), 7.16 (br, 2H), 7.61 (d, J = 4.4 Hz, 2H), 7.77 (br, 2H), 16.20 (s, 1H).

*1-(4-Fluorophenyl)-3-(thiophene-2-yl)propane-1,3-dione (**4fj**).* Eluted with EA/PE = 1/5. Milky white solid, 53.0 mg, 85% yield. Mp: 100−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.62 (s, 1H), 7.13−7.17 (m, 3H), 7.63 (d, J = 4.8 Hz, 1H), 7.79 (t, J = 3.6 Hz, 1H), 7.93−7.95 (m, 2H), 16.36 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 92.9, 116.0 (d, J = 21.8 Hz), 128.5, 129.4 (d, J = 9.1 Hz), 130.5, 130.9 (d, J = 3.1 Hz), 132.8, 142.0, 165.4 (d, J = 252.2 Hz), 180.2, 182.7. HRMS (ESI$^+$): calcd for $C_{13}H_9FO_2SNa$ $[M + Na]^+$ 271.0205, found 271.0204.

Isolation of Coupling Intermediate 5aa (Method a). A flame-dried schlenck tube with a magnetic stirring bar was charged with methyl 2-oxo-2-phenylacetate **1a** (0.25 mmol), 2-bromo-1-phenylethanone **2a** (0.325 mmol), and K_2CO_3 (0.50 mmol), the system was evacuated twice and backfilled with N_2, and NMP (1.0 mL) was added. The reaction was allowed to stir at room temperature for 24 h. Water was then added, and the mixture was extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4. After the volatile solvent was evaporated, the residue was purified by column chromatography on silica gel (100−200 mesh) using EA/PE (up to 1/3) as the eluent to afford *trans*-**5aa** in 81% yield and *cis*-**5aa** in 16% yield with a *trans*/*cis* ratio of 5.1:1.

Isolation of Coupling Intermediate 5aa (Method b). A flame-dried Schlenk tube with a magnetic stirring bar was charged with methyl 2-oxo-2-phenylacetate **1a** (0.25 mmol), 2-bromo-1-phenylethanone **2** (0.325 mmol), and K_2CO_3 (0.50 mmol), the system was evacuated twice and then backfilled with N_2, and 1,4-dioxane (1.0 mL) was added. The reaction was allowed to stir at 80 °C for 4 h. Water was then added, and the mixture was extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4. After the volatile solvent was evaporated, the residue was purified by column chromatography on silica gel (100−200 mesh) using EA/PE (up to 1/3) as the eluent to afford *cis*-**5aa** in 80% yield and a trace amount of *trans*-**5aa**.

*Methyl 3-Benzoyl-2-phenyloxirane-2-carboxylate (trans-**5aa**).* White solid. Mp: 40−44 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3H), 4.81 (s, 1H), 7.20−7.23 (m, 3H), 7.38−7.45 (m, 4H), 7.54−7.58 (m, 1H), 7.84−7.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 53.6, 63.2, 63.3, 127.8, 128.1, 128.3, 128.9, 129.0, 129.9, 134.1, 135.1, 168.4, 190.5. HRMS (ESI$^+$): calcd for $C_{17}H_{14}O_4Na$ $[M + Na]^+$ 305.0790, found 305.0795.

*Methyl 3-Benzoyl-2-phenyloxirane-2-carboxylate (cis-**5aa**).*[40] Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.70 (s, 3H), 4.31 (s, 1H), 7.43−7.46 (m, 3H), 7.51 (t, J = 7.6 Hz, 2H), 7.61−7.65 (m, 3H), 8.01 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 53.0, 64.4, 65.3, 126.3, 128.6, 128.96, 129.02, 129.6, 133.4, 134.3, 135.5, 166.6, 191.3. HRMS (ESI$^+$): calcd for $C_{17}H_{14}O_4Na$ $[M + Na]^+$ 305.0790, found 305.0782.

Isolation of 6aa·NMP. A flame-dried Schlenk tube with a magnetic stirring bar was charged with methyl 3-benzoyl-2-phenyloxirane-2-carboxylate (*trans*-**5aa**, 0.25 mmol) and methanol. Then 200 μL of 4 N aq KOH solution was added over a period of 15 min and the reaction continued for another 15 min at room temperature. NMP (1.25 mmol, 120 μL) was added. The mixture was neutralized to pH 7 with 2 N HCl and extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4. After the volatile solvent was evaporated, the residue was dissolved in a minimum amount of ethyl acetate. A white solid was precipitated out by the addition of petroleum ether as *trans*- and *cis*-**6aa**·NMP in 97% yield. The structure of (*trans*-**6aa**)·NMP was determined by X-ray diffraction analysis.

*3-Benzoyl-2-phenyloxirane-2-carboxylic Acid·NMP (**6aa·NMP**).* White solid. 89 mg, 97% yield. *trans*/*cis* = 2.5:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02 (q, J = 7.6 Hz, 2 + 0.8H), 2.45 (t, J = 8.0 Hz, 2 + 0.8H), 2.85 (s, 3 + 1.2H), 3.40 (t, J = 7.2 Hz, 2 + 0.8H), 4.36 (s, 1H, *trans*), 4.84 (s, 0.4H, *cis*), 6.35 (brs, 1 + 0.4H), 7.19−7.21 (m, 3H, *trans*), 7.41−7.45 (m, 4 + 1.2H), 7.50 (t, J = 7.8 Hz, 0.8H, *cis*), 7.56 (t, J = 7.4 Hz, 1H, *trans*), 7.62 (t, J = 7.2 Hz, 0.4H, *cis*), 7.69−7.70 (m, 0.8H, *cis*), 7.88 (d, J = 7.6 Hz, 2H, *trans*), 8.00 (d, J = 7.6 Hz, 0.8H, *cis*).

One-Pot Synthesis of α,β-Epoxy-γ-butyrolactones 7. A flame-dried Schlenk tube with a magnetic stirring bar was charged with methyl 2-oxo-2-phenylacetate **1a** (0.25 mmol), 2-bromo-1-phenylethanone **2a** (0.325 mmol), K_2CO_3 (0.50 mmol), and 1,4-dioxane (1.0 mL). The reaction was stirred at 80 °C for 4 h in an oil bath under an N_2 atmosphere. After the mixture was cooled to room temperature, EtOH (1 mL) and $NaBH_4$ (0.075 mmol, 3 mg) were added under an N_2 atmosphere. The resulting mixture was stirred at room temperature for 30 min. After the volatile solvent was evaporated, the residue was purified by column chromatography on silica gel (100−200 mesh)

DOI: 10.1021/acs.joc.6b02575
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using EA/PE (up to 1/10) as the eluent to afford the corresponding 1,4-diphenyl-3,6-dioxabicyclo[3.1.0]hexan-2-one **7** in 70% yield.

1,4-Diphenyl-3,6-dioxabicyclo[3.1.0]hexan-2-one (7).[32] Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.22 (s, 1H), 5.60 (s, 1H), 7.34 (d, J = 6.8 Hz, 2H), 7.43-7.45 (m, 6H), 7.56-7.57 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.4, 67.7, 79.3, 126.2, 127.1, 128.3, 128.8, 129.5, 129.6, 129.8, 134.7, 170.4. HRMS (ESI$^+$): calcd for $C_{16}H_{12}O_3Na$ $[M + Na]^+$ 275.0684, found 275.0677.

Synthesis of Curcuminoid Analogues 4ll and 4ml. A flame-dried Schlenk tube with a magnetic stirring bar was charged with methyl α-oxocarboxylate **1** (0.25 mmol), α-bromoketone **2** (0.325 mmol), and K_2CO_3 (0.50 mmol). The system was evacuated and backfilled with N_2 twice, and NMP/MeOH/hydroxyacetone (1.0 mL/100 μL/25 μL) was injected. The reaction was allowed to stir at room temperature for 4 h. Then 300 μL of 4 N aq KOH solution was added over a period of 0.5 h and the reaction continued for another 1.5 h. The reaction mixture was neutralized to pH 7 with 2 N HCl and extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4. After the volatile solvent was evaporated, the residue was purified by column chromatography on silica gel (100–200 mesh) using EA/PE as the eluent to afford the corresponding 1,3-diketone **4**.

(1E,6E)-1,7-Diphenylhepta-1,6-diene-3,5-dione (4ll).[41] Eluted with EA/PE = 1/10. Bright yellow solid, 42.0 mg, 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.86 (s, 1H), 6.64 (d, J = 16.0 Hz, 2H), 7.39–7.41 (m, 6H), 7.56–7.58 (m, 4H), 7.68 (d, J = 15.6 Hz, 2H), 15.92 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 102.0, 124.2, 128.3, 129.1, 130.3, 135.1, 140.8, 183.4.

(1E,6E)-1-(4-Methoxyphenyl)-7-phenylhepta-1,6-diene-3,5-dione (4ml). Eluted with EA/PE = 1/5. Bright yellow solid, 38.0 mg, 50% yield. Mp: 128–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 3H), 5.82 (s, 1H), 6.52 (d, J = 15.6 Hz, 1H), 6.62 (d, J = 16.0 Hz, 1H), 6.92 (d, J = 8.4 Hz, 2H), 7.38–7.40 (m, 3H), 7.51–7.57 (m, 4H), 7.65 (dd, J = 15.6, 3.6 Hz, 2H), 16.00 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.6, 101.8, 114.5, 121.9, 124.2, 127.8, 128.2, 129.0, 130.0, 130.1, 135.2, 140.3, 140.7, 161.5, 182.3, 184.5. HRMS (ESI$^+$): calcd for $C_{20}H_{18}O_3Na$ $[M + Na]^+$ 329.1154, found 329.1150.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02575.

Optimization and mechanistic experiments, computational data, crystallographic data, and ^{1}H and ^{13}C NMR spectral data of all compounds (PDF)

X-ray data for compound **3af** (CIF)

X-ray data for compound *trans*-**5aa** (CIF)

X-ray data for compound *trans*-**6aa**·NMP (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the grants from the NSFC (Nos. 21172159, 21321061, and 21372266) and the NCET-13-0384.

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DOI: 10.1021/acs.joc.6b02575
J. Org. Chem. 2017, 82, 1403−1411