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Zinc-Mediated Chain Extension Reaction of 1,3-Diketones to 1,4-Diketones and Diastereoselective Synthesis of *trans*-1,2-Disubstituted Cyclopropanols

Song Xue,* Le-Zhen Li, Yong-Kang Liu, and Qing-Xiang Guo

Department of Chemistry, University of Science and Technology of China, Hefei 230026, People's Republic of China

xuesong@ustc.edu.cn

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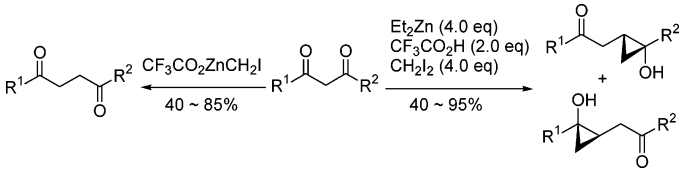

A variety of 1,3-diketones can be efficiently converted into the corresponding 1,4-diketones and trans-1,2-disubstituted cyclopropanols by using organozinc species in one-pot reactions. It was found that 2.3 equiv of $CF_3CO_2ZnCH_2I$ was effective to give the corresponding chain-extended products in 44−85% yields, while a mixture of organozinc species formed from 4.0 equiv of Et_2Zn, 2.0 equiv of CF_3CO_2H, and 4.0 equiv of CH_2I_2 resulted in the formation of *trans*-1,2-disubstituted cyclopropanols with quite good yields and diastereoselectivity.

Introduction

1,4-Diketones are important and valuable precursors for the synthesis of substituted cyclopentenones,[1,2] such as jasmones, rethorolones, cuparenones, and prostaglandins, and of five-membered heterocyclic compounds,[3] such as furans, pyrroles, thiophenes, and pyridazines. A variety of synthetic methods have been developed for the preparation of 1,4-diketones.[4−6] These methods are efficient for the synthesis of 1,4-diketones, but most of them follow lengthy procedures, require multistep preparation of a special reagent, and utilize expensive transition-metal complexes. Therefore, an simple and efficient methodology for the synthesis of 1,4-diketones from facile materials is of great interest. Here, we wish to report our preliminary results regarding zinc-mediated conversion of 1,3-diketones to 1,4-diketones under mild reaction conditions.

In 1997, Zercher reported an operationally simple approach to the chain extension of β-keto esters using the zinc reagent $EtZnCH_2I$.[7] This reaction system could be extended to β-keto amides[8] and β-keto phosphonates.[9] However, the reaction of acyclic β-diketones, such as 2,4-pentanedione, with $EtZnCH_2I$ resulted in no observable reaction.[7a] Very recently, free-radical-

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promoted ring expansion and chain extension of 1,3-diketones to give the corresponding 1,4-diketones was reported.[10] To the best of our knowledge, examples of preparing 1,4-diketones from 1,3-diketones have not been described using zinc reagents. Our interest in CF_3COOH enhancing the reactivity of zinc reagents prompted us to verify the possibility of the zinc-mediated synthesis of 1,4-diketones from 1,3-diketones.[11]

Results and Discussion

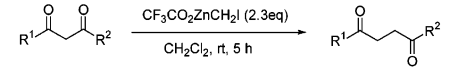
As the zinc species $CF_3CO_2ZnCH_2I$ shows high activity in the cyclopropanation of olefins,[12] our initial efforts were directed at the application of $CF_3CO_2ZnCH_2I$ to commercially available 2,4-pentanedione. According to this procedure,[12b] 1 equiv of diethylzinc was combined with 1 equiv of trifloroacetic acid to form CF_3CO_2ZnEt, which was then reacted with 1 equiv of methylene iodide to generate the cyclopropanation reagent $CF_3CO_2ZnCH_2I$. It is fortunate to find that the chain-extended product 2,5-hexanedione was detected by GC-MS analysis when 2,4-pentanedione was added to the in situ generated zinc species. To obtain the isolated yield, a high-boiling-point substrate was used in this reaction. Treatment of 6-phenyl-2,4-hexanedione with 2.3 equiv of $CF_3CO_2ZnCH_2I$ at room temperature for 5 h provided the chain-extended product **2a** in 44% yield. Although unreacted starting material was observed at this stoichiometry of zinc reagent, prolonging the reaction time resulted in no obvious effect on the reaction yield. A variety of 1,3-diketones were then allowed to react with the zinc species; these results are summarized in Table 1. Both aromatic and aliphatic 1,3-diketones can be employed as starting materials. Aromatic 1,3-diketones provided the corresponding chain-extended products in good isolated yields. Substitution of an electron-donating group on the aromatic ring gave a higher yield than that of an electron-withdrawing group on the aromatic ring. More hindered 1,3-diketones were less efficient and gave moderate yields. Although $CF_3CO_2ZnCH_2I$ was found to accelerate the cyclopropanation reaction of olefins dramatically compared to the Furukawa reagent $EtZnCH_2I$, the 1,3-diketone which contained an electron-deficient alkene underwent selective chain extension in preference to cyclopropanation of the olefin under the standard reaction conditions. This zinc-mediated process to synthesize symmetrical and unsymmetrical 1,4-diketones holds many distinct advantages over the previously reported methods. The most obvious advantages are no lengthy procedures and no requirement of multistep preparation of a special reagent, especially avoiding utilizing expensive transition-metal complexes.

The chain extension reaction worked very well for simple acyclic and aromatic 1,3-diketones, especially for aromatic 1,3-diketones. However, no reaction was observed when α-substituted β-diketone was submitted to this reaction. For example, 2-methyl-1-phenylbutane-1,3-dione gave no reaction under the typical reaction conditions (entry 17, Table 1).

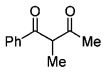
On the basis of the work of Zercher,[7] a plausible mechanism for the reaction is shown in Scheme 1. The first step of the reaction is formation of the enolate **3**, which consumes 1 equiv of $CF_3CO_2ZnCH_2I$. Enolate **3** then undergoes cyclopropanation with a second equivalent of the zinc species to give the cyclopropyl intermediate **4**, followed by cleavage to give the intermediate **5** or **6**, and the reaction is then quenched by saturated aqueous NH_4Cl to provide the chain-extended product **2**. The chain extension reaction proceeded smoothly under these reaction conditions. The reason may be that ionization of the electron-deficient CF_3CO_2 group creates a vacant coordination site on the zinc, permitting coordination of the iodine that results in activation of the methylene group toward reaction with enolate, resulting in the efficient formation of intermediate **4**.[12b]

In the process of the chain extension reaction of 1,3-diketone to 1,4-diketone, when the amount of $CF_3CO_2ZnCH_2I$ was increased to over 2.3 equiv, the desired product yield decreased, and a new polar compound was found. For example, exposure of 1-phenylbutane-1,3-dione to 3.3 equiv of $CF_3CO_2ZnCH_2I$ gave the desired product **2c** in 55% yield, along with a 31% yield of a new polar compound. This compound was determined to be **7a** by NMR and HRMS spectra. The relative stereochem-

TABLE 1. Chain Extension of 1,3-Diketones to 1,4-Diketones



1 2

entry	R^1	R^2	product	yield[a],%
1	$C_6H_5CH_2CH_2$	Me	**2a**	44
2[b]	CH_3CH_2	CH_3CH_2	**2b**	45
3	C_6H_5	Me	**2c**	66 (41)[c]
4	C_6H_5	$CH_3CH_2CH_2$	**2d**	51
5	C_6H_5	Bu^t	**2e**	40
6	*p*-$MeOC_6H_5$	Me	**2f**	78
7[b]	*p*-$MeOC_6H_5$	$CH_3CH_2CH_2$	**2g**	50
8	*p*-ClC_6H_5	Me	**2h**	57
9	*p*-ClC_6H_5	CH_3CH_2	**2i**	54
10	*trans*-C_6H_5CH=CH	Me	**2j**	66
11	*trans*-C_6H_5CH=CH	C_6H_5	**2k**	85
12	C_6H_5	C_6H_5	**2l**	78
13	*p*-ClC_6H_5	C_6H_5	**2m**	59
14	*p*-$MeOC_6H_5$	C_6H_5	**2n**	82
15	2-Naphthyl	Me	**2o**	65
16	2-Thienyl	Me	**2p**	62
17				NR[d]

[a] Isolated yields. [b] Performed at 0 °C for 5 h. [c] Performed with 2.0 equiv of $CF_3CO_2ZnCH_2I$. [d] NR = no reaction.

SCHEME 1. Plausible Mechanism of the Chain Extension Reaction

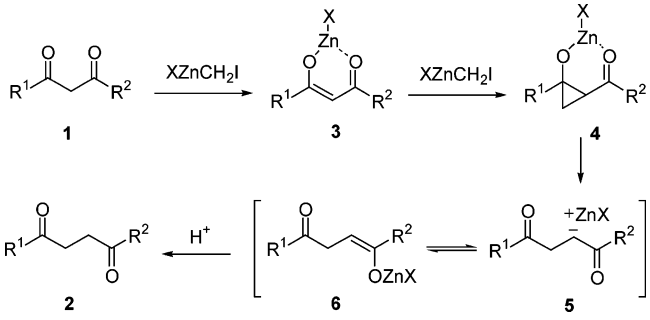


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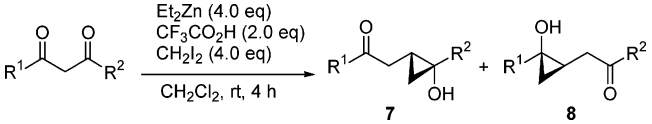
TABLE 2. Diastereoselective Synthesis of Trans-1,2-Disubstituted Cyclopropanols



entry	R^1	R^2	product **7** (yield,[a] %)	product **8** (yield,[a] %)
1	C_6H_5	Me	**7a** (93)	**8a** (0)
2	*p*-$MeOC_6H_5$	Me	**7b** (95)	**8b** (0)
3	*p*-ClC_6H_5	Me	**7c** (70)	**8c** (14)
4	*p*-ClC_6H_5	CH_3CH_2	**7d** (41)	**8d** (25)
5	C_6H_5	$CH_3CH_2CH_2$	**7e** (45)	**8e** (12)
6	*p*-$MeOC_6H_5$	$CH_3CH_2CH_2$	**7f** (94)	**8f** (0)
7	C_6H_5	C_6H_5	**7g** (61)	
8	*p*-$MeOC_6H_5$	C_6H_5	**7h** (73)	**8h** (<3)
9	*p*-ClC_6H_5	C_6H_5	**7i** (18)	**8i** (47)
10	2-thienyl	Me	**7j** (60)	**8j** (0)
11	$C_6H_5CH_2CH_2$	Me	**7k** (43)	**8k** (20)
12	CH_3CH_2	CH_3CH_2	**7l** (61)	
13	Me	Me	**7m** (65)	

[a] Isolated yields.

istry of methyl and alkyl substituents of the cyclopropanol **7a** was absolutely trans, which was firmly established by NOESY studies.[13] The completely diastereoselective synthesis of the 1,2-disubstituted cyclopropanol **7a** may be due to the zinc enolate intermediate **6** proceeding through carbonyl oxygen complexation to zinc to form a seven-membered-ring transition state, and then enolate **6** undergoes cyclopropanation with a third equivalent of the zinc species to give the cyclopropyl alcohol intermediate. Cyclopropanols are valuable in synthetic practice as useful intermediates[14] and as important substances capable of possessing different kinds of biological activity.[15] Therefore, we attempted to develop a new methodology to synthesize trans-1,2-disubstituted cyclopropanols from 1,3-diketones.

Through an effort to optimize the reaction conditions, it is found that a mixture of zinc species formed from 4.0 equiv of Et_2Zn, 2.0 equiv of CF_3CO_2H, and 4.0 equiv of CH_2I_2 resulted in its clean and efficient conversion to compound **7a** in 93% yield at room temperature for 4 h.[16] The substituents on the benzene ring have a remarkable effect on the reaction. These can be seen from Table 2; the substrate with an electron-donating group on the aromatic ring gave the desired product **7b** in excellent yield. When the substrate contained an electron-withdrawing group on its aromatic ring, its regioselective isomer **8** was obtained, but still maintaining absolute diastereoselectivity. For example, 1-(4-chlorophenyl)butane-1,3-dione, which has an electron-withdrawing group on the aromatic ring, provided the product **7c** in 70% yield along with isomer **8c** in 14% yield. The two isomers **7c** and **8c** were easily assigned on the basis of ^1H NMR spectra, since proton signals of the methyl group (R^2) were singlets at δ 1.50 and 2.23, respectively. At the same time, the steric hindrance effect has an obvious influence on the yield and regioselectivity as well. When the R^2 group varied from a methyl to an ethyl group, the yield of isomer **8d** increased to 25%, but that of cyclopropanol **7d** decreased obviously (entries 3 and 4, Table 2). A propyl group resulted in a dramatic loss of yield (entries 1 and 5, Table 2). These results suggest that the yield of isomer **8** increased, but the combined yields of **7** and **8** decreased, when R^2 was a bulky group. It is notable that even when R^2 was a propyl group, a substrate with an electron-donating group on the aromatic ring could afford the sole product **7f** in 94% yield. For aliphatic 1,3-diketones, the corresponding cyclopropanols were obtained in moderate yields.

Conclusions

In summary, we have identified a simple and efficient synthetic methodology for the synthesis of 1,4-diketones and 1,2-disubstituted cyclopropanols from 1,3-diketones by using organozinc reagents in a one-pot reaction. The chain-extended 1,4-diketone products were obtained in moderate to good yields. Excess amounts of zinc species gave cyclopropanols with good yields and diastereoselectivity. Although the reaction worked well for α-unsubstituted β-diketones, no reaction was observed for acyclic α-substituted β-diketones. Efforts are underway to define more clearly the scope and synthetic utility of this chain extension reaction.

Experimental Section

General Procedure for the Preparation of 1,4-Diketones from 1,3-Diketones using Organozinc Reagents. A 50 mL round-bottom flask was equipped with a stir bar and charged with freshly distilled methylene chloride (4 mL), and diethylzinc (70 μL, 0.69 mmol) was added via syringe under nitrogen. The solution was cooled in an ice bath, and trifluoroacetic acid (54 μL, 0.69 mmol) was then dropped very slowly into the reaction mixture via syringe. After the mixture was stirred for 30 min, CH_2I_2 (58 μL, 0.69 mmol) was added dropwise via syringe under nitrogen. After an additional 30 min of stirring at 0 °C, the 1,3-diketone (0.3 mmol) was added as quickly as possible, and the ice bath was removed. The reaction mixture was stirred for 5 h at room temperature. The solution was quenched by saturated aqueous ammonium chloride solution and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine and then dried over anhydrous magnesium sulfate, filtered, and concentrated on the rotary evaporator. The desired product was isolated by silica gel chromatography with petroleum ether/EtOAc (20:1−5:1).

1-Phenylheptane-1,4-dione (2d). Light yellow oil (51% yield). ^1H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.91 (d, J = 7.2 Hz, 2H), 7.49 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.2 Hz, 2H), 3.21(t, J = 6.6 Hz, 2H), 2.78 (t, J = 6.6 Hz, 2H), 2.44 (t, J = 7.2 Hz, 2H), 1.59 (m, 2H), 0.87 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 209.8, 198.8, 136.8, 133.2, 128.7, 128.1, 45.0, 36.3, 32.4, 17.4, 13.9. IR (neat; cm^{-1}): ν 3062, 2962, 2933, 2875, 1714, 1686, 1359, 746, 690. HRMS (EI): calcd for $C_{13}H_{16}O_2$ (M^+), 204.1150; found, 204.1159.

1-(4-Methoxyphenyl)heptane-1,4-dione (2g). The title compound was prepared according to the general procedure, except that the reaction mixture was stirred for 5 h at 0 °C and then purified by chromatography on silica gel (10:1 petroleum ether/EtOAc) to give a light yellow solid (50% yield). Mp: 39−40 °C. ^1H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.90 (d, J = 8.9 Hz, 2H), 6.85 (d, J = 8.9 Hz, 2H), 3.80 (s, 3H), 3.17 (t, J = 6.3 Hz, 2H), 2.76 (t, J = 6.3 Hz, 2H), 2.44 (t, J = 7.5 Hz, 2H), 1.58 (dt, J = 7.5 Hz, 2H), 0.86 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 210.0, 197.3, 163.6, 130.4, 129.9, 113.8, 55.6, 45.0, 36.4, 32.1, 17.4, 13.9. IR (neat; cm^{-1}): ν 2961, 1713, 1677, 1600, 1259, 1169, 1025, 834. HRMS (EI): calcd for $C_{14}H_{18}O_3$ (M^+), 234.1256; found, 234.1252.

(13) See the Supporting Information for details.

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(16) Treatment of 4.0 equiv of $CF_3CO_2ZnCH_2I$ with 1-phenylbutane-1,3-dione gave **7a** in 63% yield along with a 31% yield of the chain-extended product **2c**.

1-(4-Chlorophenyl)hexane-1,4-dione (2i). White solid (54% yield). Mp: 86−87 °C. ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.86 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), 3.18 (t, J = 6.6 Hz, 2H), 2.79 (t, J = 6.6 Hz, 2H), 2.48 (q, J = 7.2 Hz, 2H), 1.02 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 210.1, 197.6, 139.7, 135.1, 129.6, 129.0, 36.2, 35.9, 32.5, 7.9. IR (neat; cm^{-1}): υ 2981, 2939, 1708, 1671, 1588, 1089, 848, 799. HRMS (EI): calcd for $C_{12}H_{13}O_2Cl$ (M^+), 224.0604; found, 224.0605.

(*E*)-1,6-Diphenylhex-5-ene-1,4-dione (2k). White solid (85% yield). Mp: 109−111 °C. ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.95 (d, J = 6.9, 2H), 7.49 (d, J = 16.2 Hz, 1H), 7.51−7.32 (m, 9H), 6.79 (d, J = 16.2 Hz, 1H), 3.34 (t, J = 6.6 Hz, 2H), 3.10 (t, J = 6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 198.8, 143.0, 136.8, 134.6, 133.3, 129.1, 128.7, 128.5, 128.3, 126.26, 33.6, 32.7. IR (neat; cm^{-1}): υ 2903, 1686, 1615, 1098, 750, 689. HRMS (EI): calcd for $C_{18}H_{16}O_2$ (M^+), 264.1150; found, 264.1143.

1-Naphthalen-2-ylpentane-1,4-dione (2o). Light yellow solid (65% yield). Mp: 82−84 °C. ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 8.45 (s, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.81 (m, 2H), 7.48 (m, 2H), 3.36 (t, J = 6.0 Hz, 2H), 2.88 (t, J = 6.0 Hz, 2H), 2.22 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 207.6, 198.6, 135.8, 134.1, 132.7, 129.9, 129.7, 128.6, 128.6, 127.9, 126.9, 123.9, 37.3, 32.6, 30.3. IR (neat; cm^{-1}): υ 3058, 1713, 1677, 1408, 1306, 1125, 819, 757. HRMS (EI) calcd for $C_{15}H_{14}O_2$ (M^+), 226.0994; found, 226.0995.

1-Thiophen-2-ylpentane-1,4-dione (2p). Oil (62% yield). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.76 (dd, J = 3.8, 0.9 Hz, 1H), 7.63 (dd, J = 4.9, 0.9 Hz, 1H), 7.13 (dd, J = 4.9, 3.8 Hz, 1H), 3.22 (t, J = 6.5 Hz, 2H), 2.88 (t, J = 6.5 Hz, 2H), 2.24 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 207.1, 191.6, 143.8, 133.6, 132.1, 128.2, 37.1, 33.1, 30.1. IR (neat; cm^{-1}): υ 2921, 2253, 1717, 1665, 1416. HRMS (EI): calcd for $C_9H_{10}O_2S$ (M^+), 182.0402; found, 182.0394.

General Procedure for the Synthesis of Trans-1,2-Disubstituted Cyclopropanols from 1,3-Diketones Using Organozinc Reagents. A 50 mL round-bottom flask was equipped with a stir bar and charged with freshly distilled methylene chloride (4 mL), and diethylzinc (120 μL, 1.20 mmol) was added via syringe under nitrogen. The solution was cooled in an ice bath, and trifluoroacetic acid (47 μL, 0.6 mmol) was then dropped very slowly into the reaction mixture via syringe. After it was stirred for 30 min, diiodomethane (98 μL, 1.20 mmol) was added dropwise via syringe under nitrogen. After an additional 30 min of stirring at 0 °C, the 1,3-diketone (0.3 mmol) was added as quickly as possible, and the ice bath was removed. The reaction mixture was stirred for 4 h at room temperature until TLC indicated complete consumption of the starting 1,3-diketone. The solution was quenched by saturated aqueous ammonium chloride solution at 0 °C and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine and then dried over anhydrous magnesium sulfate, filtered, and concentrated on the rotary evaporator. The desired product was isolated by silica gel chromatography with petroleum ether/EtOAc (15:1−5:1).

2-(2-Hydroxy-2-methylcyclopropyl)-1-phenylethanone (7a). Light yellow oil (93% yield). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.98 (d, J = 7.4 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.4 Hz, 2H), 3.55 (dd, J = 17.2, 5.1 Hz, 1H), 3.85 (dd, J = 17.2, 9.0 Hz, 1H), 2.45 (br s, 1H), 1.50 (s, 3H), 1.25−0.97 (m, 1H), 0.76 (dd, J = 9.1, 5.8 Hz, 1H), 0.56 (dd, J = 5.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 201.6, 137.0, 133.3, 128.8, 128.3, 54.7, 38.0, 25.9, 20.7, 19.9. IR (neat; cm^{-1}): υ 3428, 1681, 1264, 1215, 753. HRMS (EI): calcd for $C_{12}H_{14}O_2$ (M^+), 190.0994; found, 190.0988.

2-(2-Hydroxy-2-methylcyclopropyl)-1-(4-methoxyphenyl)-ethanone (7b). Light yellow oil (95% yield). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.91 (d, J = 9.6 Hz, 2H), 6.88 (d, J = 9.6 Hz, 2H), 3.80 (s, 3H), 3.49 (dd, J = 16.8, 4.9 Hz, 1H), 2.66 (dd, J = 16.8, 9.1 Hz, 1H), 1.41 (s, 3H), 0.88 (m, 1H), 0.68 (dd, J = 9.0, 5.7 Hz, 1H), 0.49 (t, J = 5.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 200.3, 163.7, 130.7, 129.9, 113.9, 55.6, 54.6, 37.5, 25.8, 20.9, 19.9. IR (neat; cm^{-1}): υ 3441, 1667, 1260, 1025. HRMS (EI): calcd for $C_{13}H_{16}O_3$ (M^+), 220.1099; found, 220.1105.

1-(4-Chlorophenyl)-2-(2-hydroxy-2-methylcyclopropyl)ethanone (7c). Light yellow oil (70% yield). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.92 (d, J = 6.6 Hz, 2H), 7.45 (d, J = 6.6 Hz, 2H), 3.46 (dd, J = 17.4, 5.1 Hz, 1H), 2.85 (dd, J = 17.4, 9.0 Hz, 1H), 2.23 (br s, 1H), 1.50 (s, 3H), 0.99 (m, 1H), 0.75 (dd, J = 9.0, 5.7 Hz, 1H), 0.55 (t, J = 5.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 200.2, 139.8, 135.3, 129.7, 129.1, 54.7, 38.0, 25.8. 20.5, 19.9. IR (neat; cm^{-1}): υ 3425, 1714, 1221, 1092. HRMS (EI): calcd for $C_{12}H_{13}O_2Cl$ (M^+), 224.0604; found, 224.0608.

1-[2-(4-Chlorophenyl)-2-hydroxycyclopropyl]propan-2-one (8c). Light yellow oil (14% yield). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.32−7.26 (m, 4H), 3.03 (dd, J = 17.2, 5.1 Hz, 1H), 3.00 (br s, 1H), 2.51 (dd, J = 17.2, 8.7 Hz, 1H), 2.22 (s, 3H), 1.31 (m, 2H), 0.95 (dd, J = 5.7, 5.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 210.0, 143.0, 132.5, 128.5, 126.5, 58.2, 42.8, 30.3, 23.3, 22.3. IR (neat; cm^{-1}): υ 3411, 1707, 1092, 1012. HRMS (EI): calcd for $C_{12}H_{13}O_2Cl$ (M^+), 224.0604; found, 224.0609.

1-(4-Chlorophenyl)-2-(2-ethyl-2-hydroxycyclopropyl)ethanone (7d). Light yellow oil (41% yield). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.93 (d, J = 9.0 Hz, 2H), 7.45 (d, J = 9.0 Hz, 2H), 3.48 (dd, J = 17.1, 5.1 Hz, 1H), 2.85 (dd, J = 17.1, 8.8 Hz, 1H), 2.35 (br s, 1H), 1.67−1.56 (m, 2H), 1.05 (m, 3H), 0.76 (dd, J = 9.1, 5.6 Hz, 1H), 0.52 (t, J = 5.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 200.3, 139.8, 135.3, 129.8, 129.1, 59.1, 37.9, 32.2, 19.7, 18.9, 9.7. IR (neat; cm^{-1}): υ 3429, 1714, 1173, 1092. HRMS (EI): calcd for $C_{13}H_{15}O_2Cl$ (M^+), 238.0761; found, 238.0757.

1-[2-(4-Chlorophenyl)-2-hydroxycyclopropyl]butan-2-one (8d). Light yellow oil (25% yield). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.32−7.25 (m, 4H), 3.18 (br,s, 1H), 3.11 (dd, J = 16.8, 4.8 Hz, 1H), 2.48 (m, 3H), 1.27 (m, 2H), 1.07 (t, J = 7.6 Hz, 3H), 0.98 (t, J = 6.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 212.9, 143.2, 132.3, 129.0, 128.4, 58.1, 41.6, 36.4, 23.6, 22.5, 7.6. IR (neat; cm^{-1}): υ 3440, 2972, 2938, 1709, 1684, 1589, 1092. HRMS (EI): calcd for $C_{13}H_{15}O_2Cl$ (M^+), 238.0761; found, 238.0762.

1-(4-Chlorophenyl)-2-(2-hydroxy-2-phenylcyclopropyl)ethanone (7i). Light yellow oil (18% yield). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.96 (dd, J = 8.7, 1.8 Hz, 2H), 7.46−7.23 (m, 7H), 3.66 (dd, J = 17.4, 5.1 Hz, 1H), 3.04 (dd, J = 17.4, 9.0 Hz, 1H), 2.93 (br s, 1H), 1.35 (dd, J = 9.6, 5.7 Hz, 1H), 1.04 (t, J = 6.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 199.8, 144.2, 139.9, 135.1, 129.7, 129.0, 128.4, 126.8 125.2, 58.9, 37.7, 23.2, 22.1. IR (neat; cm^{-1}): υ 3426, 1681. HRMS (EI): calcd for $C_{17}H_{15}O_2Cl$ (M^+), 286.0761; found, 286.0759.

2-[2-(4-Chlorophenyl)-2-hydroxycyclopropyl]-1-phenylethanone (8i). Light yellow solid (47% yield). Mp: 71−73 °C. ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 7.92 (d, J = 8.4 Hz, 2H), 7.54 (t, J = 8.4 Hz, 1H), 7.41 (t, J = 8.4 Hz, 2H), 7.30−7.18 (m, 4H), 3.70 (dd, J = 17.1, 4.8 Hz, 1H), 3.12 (br s, 1H), 2.90 (dd, J = 17.1, 9.3 Hz, 1H), 1.46−1.40 (m, 1H), 1.24 (dd, J = 9.3, 5.7 Hz, 1H), 1.00 (t, J = 6.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 201.3, 143.2, 136.7, 133.6, 132.4, 128.8, 128.5, 128.4, 126.7, 58.4, 37.8, 23.6, 22.5. IR (neat; cm^{-1}): υ 3449, 1680, 1343, 1279, 1092, 1008. HRMS (EI): calcd for $C_{17}H_{15}O_2Cl$ (M^+), 286.0761; found, 286.0764.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for products **2a**−**c**,**e**,**f**,**h**,**j**,**l**−**n**, **7a**,**e**, **8e**, **7f**−**h**,**j**,**k**, **8k**, and **7l**,**m**. This material is available free of charge via the Internet at http://pubs.acs.org.

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