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Base-Controlled Selective Conversion of Michael Adducts of Malonates with Enones in the Presence of Iodine

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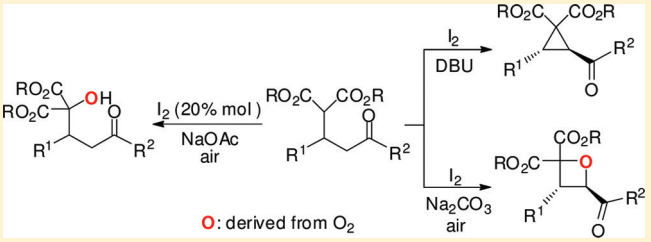
Supporting Information

ABSTRACT: An efficient base-controlled selective conversion of the Michael adducts of malonates with enones in the presence of iodine is reported. Highly functionalized cyclopropane, oxetane, and α-hydroxylmalonate derivatives are obtained selectively using DBU, Na_2CO_3, and NaOAc as the base, respectively. O_2 was identified to be crucial to the formation of oxetane and α-hydroxylmalonate derivatives.



INTRODUCTION

Highly strained cyclic compounds such as cyclopropanes and oxetanes are important molecular architectures of a large number of biologically and medicinally relevant substances.[1] Moreover, the rigid scaffolds can undergo a variety of ring-opening reactions to generate new molecular skeletons.[2] Their unique reactivity and structural properties have led chemists to develop different methodologies for preparation of such strained cycles. Compared to the diverse ways to construct the cyclopropane skeleton,[1g,i,3] fewer methods have been explored in the synthesis of oxetane derivatives due mainly to Dunitz−Schumaker strain.[4] Oxetane rings can be prepared via intramolecular nucleophilic substitution reactions.[1d,2d,5] The Paternò−Büchi (PB) reaction is a versatile method for the construction of oxetane ring systems.[2b,6] A new oxidative cyclization of Michael adducts with iodosobenzene and tetrabutylammonium iodide to oxetanes was reported recently.[7]

α-Hydroxymalonates and their equivalents are valuable class of compounds utilized in organic transformation. The direct introduction of a hydroxyl group at the α-position of malonates has been developed using stoichiometric amounts of oxidants such as CAN,[8] *N*-sulfonyloxaziridine derivatives,[9] and dimethyldioxirane.[10] Oxygenation of α-substituted malonates has also been achieved under oxygen atmosphere with CsF or Cs_2CO_3 as base[11] or with a catalytic amount of a transition-metal reagent.[12]

We now present an interesting base-controlled selective conversion of Michael adducts of malonates with enones to cyclopropane, oxetane, and α-hydroxymalonate derivatives, respectively, in the presence of I_2.

The Michael reaction is generally regarded as one of the most efficient carbon−carbon bond-forming reactions. Furthermore, the Michael adducts afford synthetically useful building blocks in organic synthesis as a result of their possessing various functional groups for further elaboration. On the other hand, I_2 as an inexpensive and efficient reagent has been used extensively in organic transformation.[13] Recently, it was reported that I_2 mediated an oxidative addition reaction of aldehydes with dimedone or 1,3-indandione to selectively afford spiro dihydrofuran or cyclopropane derivatives.[14] Inspired by their results,[14] we attempted to construct the cyclopropane and dihydrofuran structure selectively from the Michael adducts of malonates with enones in the presence of I_2 under basic condition.

RESULTS AND DISCUSSION

An initial examination was carried out using the Michael adduct of diethyl malonate with chalcone (**1a**) as a substrate (Table 1). In the presence of I_2, **1a** was treated with different bases in EtOH at 35 °C. The results summarized in Table 1 showed that no dihydrofuran derivative was obtained as expected in all cases. Under most of the organic bases such as DMAP, DBU, piperidine, morpholine, Et_3N, DABCO, pyridine (except *N*-methylimidazole), NaOH, and NaOt-Bu, *trans*-cyclopropane **2a** was isolated as the main or single product (Table 1, entries 1−7 and 11−14). When Na_2CO_3 or $NaHCO_3$ was used as the base, it was surprising that compound **3a**,[7] which contains an oxetane framework involving *trans*-orientation of both phenyl and benzoyl groups, was a major product (Table 1, entries 9 and 10). More interestingly, the employment of NaOAc resulted in the formation of undesired α-hydroxymalonate **4a** as the dominating product (Table 1, entry 15). It should be noted that more oxetane **3a** was generated while further prolonging the reaction time (Table 1, entry 16 vs 15). Herein, the I_2/NaOAc system was discovered to be a novel system to realize the direct α-hydroxylation of malonates.

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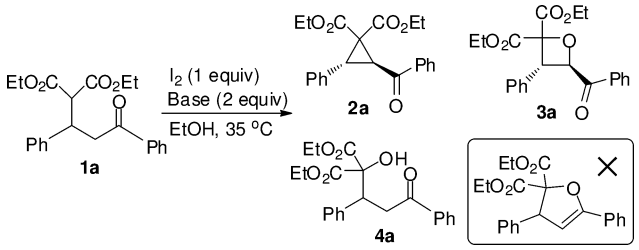
Table 1. Conversion of the Michael Adduct of Diethyl Malonate with Chalcone (1a) in the Presence of I_2 with Different Bases[a]



			yield[b]		
entry	base	time (h)	**2a** (%)	**3a** (%)	**4a** (%)
1	DMAP	36	87	tr	tr
2	DBU	3	91	0	tr
3	piperidine	24	84	tr	6
4	morpholine	36	71	tr	7
5	TEA	48	19	0	0
6	DABCO	48	53	0	0
7	pyridine	48	9	0	0
8	*N*-methylimidazole	48	27	4	52
9	Na_2CO_3	48	tr	85	0
10	$NaHCO_3$	48	tr	67	10
11	NaOH	6	41	0	0
12	NaOH	24	31	0	0
13	NaOt-Bu	6	49	0	0
14	NaOt-Bu	24	35	0	0
15	NaOAc	20	0	10	61
16	NaOAc	48	0	43	39

[a]All reactions were performed with 0.5 mmol of **1a**, 0.5 mmol of I_2, and 1.0 mmol of base in 5 mL of EtOH at 35 °C for the designated time. [b]Isolated yield based on substrate **1a**; tr = trace.

It is significant that the chemoselective conversion of **1a** to **2a**, **3a**, or **4a** in the presence of I_2 is controlled by the base (Table 1, entries 2, 9, and 15). As is known to all, selective synthesis is a formidable challenge in organic synthesis, especially controlled highly selective synthesis derived from the same starting materials.[15] Encouraged by these interesting results, we further optimized the reaction conditions using DBU, Na_2CO_3, and NaOAc as the base, respectively (Table 2).

The influence of molar ratio of **1a**:I_2:base on the reaction was first investigated (Table 2, entries 1−4). Although 3 equiv of DBU gave the best yield of **3a** (92%), 2 equiv of DBU was enough to give nearly identical yield (91%). For this reason, the better molar ratio of **1a**:I_2:DBU for the formation of cyclopropane **2a** was determined to be 1:1:2 (Table 2, entry 2, condition A). For the generation of oxetane **3a**, if it was formed through iodination and then substitution by H_2O in the solvent, 2 equiv of I_2 would be required. Instead, 1 equiv of I_2 and 2 equiv of Na_2CO_3 was found to be sufficient to provide the highest yield of **3a** (85%, Table 2, entry 2, condition B). As for the preparation of α-hydroxymalonate **4a**, 1 equiv of I_2 and 1 equiv of NaOAc was enough to give the highest yield (79%, Table 2, entry 1, condition C). When the amount of NaOAc was increased to 2−4 equiv, more oxetane derivative was generated (Table 2, entries 2, 3, and 4, condition C).

Our further optimizing efforts were shifted to the examination of the range of solvents compatible with the three kinds of selective reactions (Table 2, entries 5−12). For the conversion of **1a** to **2a**, the solvent had no dramatic influence on the reaction. EtOH was chosen as the best solvent (Table 2, entry 2, condition A) because the use of a protic solvent seemed to give a little higher yield than with other solvents. Comparatively, it was another case for the preparation of oxetane **3a** and α-hydroxymalonate **4a**. Although 85% yield of **3a** in EtOH was acceptable, the reaction sustained a long time (48 h). Finally, DMF was deemed the optimal solvent for the formation of oxetane **3a** in 91% yield (Table 2, entry 7, condition B). For the production of **4a**, the selectivity and yield were higher by performing the reaction in ether solvent, rather than in protic solvent or dipolar solvent from which more oxetane **3a** was generated. Eventually, THF was chosen as the optimal solvent in which **4a** could be isolated with the best yield (88%, Table 2, entry 12, condition C).

Most puzzling of all was that the conversion of **1a** to **4a** and **3a** only needed 1 equiv of NaOAc and 1 equiv of I_2, respectively. If it was just a simple iodination-substitution process, the conversion of **1a** to **4a** would need 2 equiv of NaOAc and conversion to **3a** would need 2 equiv of I_2. Therefore, a major aim of ours was to achieve a better insight into the mechanism of the selected conversion.

The α-iodomalonate **5a** was found to be a key intermediate, which could be isolated under I_2/NaOAc and I_2/Na_2CO_3 conditions. However, under I_2/DBU condition, **5a** could not be observed because the subsequent intramolecular S_N2 reaction to form **2a** was very fast. For the reaction of **1a** with I_2/NaOAc in THF, it could be observed clearly that **5a** converted into **4a** gradually until the complete conversion along with the extension of reaction time (Table 3, entries 2 and 3). However, under nitrogen atmosphere, only α-iodomalonate **5a** was obtained in 59% yield (Table 3, entry 1). This proved that the O_2 took a crucial role in the reaction. The oxygen atom of the hydroxyl in **4a** may be derived from O_2 but not the water in solvent. Therefore, we further decreased the quantity of I_2. To our surprise, the reaction proceeded well even using 0.2 equiv of I_2 under air condition (Table 3, entry 4). Moreover, under anhydrous condition and O_2 atmosphere, **4a** was also obtained in high yield with a catalytic amount of I_2 (96%, Table 3, entry 6). It should be noted that I_2 also played an essential role in the reaction because the absence of I_2 resulted in no conversion under similar conditions. Comparatively, for the conversion of **1a** to **3a** under Na_2CO_3 condition, a catalytic amount of I_2 was insufficient. The reaction of **1a** with 0.2 equiv of I_2 and 2 equiv of Na_2CO_3 in DMF for 48 h gave only 30% of **3a**.

When **5a** was treated with 1 equiv of DBU, 1 equiv of Na_2CO_3, and 0.2 equiv of NaOAc, respectively, **2a**, **3a**, and **4a** could be formed in 96%, 95%, and 97% yields selectively (Table 4, entries 1, 7, and 9). However, under nitrogen atmosphere only a trace of **3a** and **4a** was observed on TLC (Table 4, entries 2 and 8). A catalytic amount of Na_2CO_3 could not realize the total conversion of **5a** to **3a** (Table 4, entry 6), which was different from the formation of **4a**. To further confirm the oxygen atom source in product **3a** and **4a**, the reaction of **5a** with 0.2 equiv of NaOAc was performed in dry THF under O_2 condition with addition of 5 Å molecular sieves for 22 h; **4a** also could be obtained in 95% yield (Table 4, entry 3). This revealed that the oxygen atom was derived from O_2 but not the water in solvent. It was further proved by the reaction of **5a** in the presence of 0.2 equiv of NaOAc in dry THF under O_2 condition with addition of 0.1 mL of isotope labeled H_2O^{18}, which generated **4a** with HRMS at 407.1477 ($M + Na^+$) (Table 4, entry 4).

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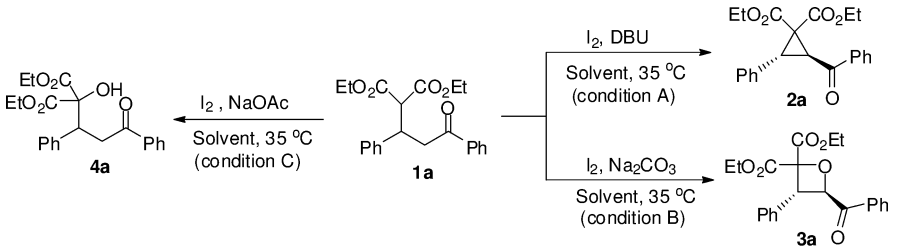
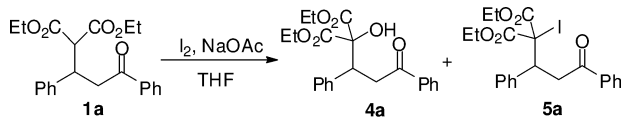
Table 2. Screening of the Reaction Conditions[a]



		condition A				condition B				condition C			
				yield (%)[b]				yield (%)[b]				yield (%)[b]	
entry	solvent	molar ratio [1a:I_2:DBU]	time (h)	2a	4a	molar ratio [1a:I_2:Na_2CO_3]	time (h)	3a	4a	molar ratio [1a:I_2:NaOAc]	time (h)	3a	4a
1	EtOH	1:1:1	3	61	tr	1:1:1	70	71	0	1:1:1	48	7	79
2	EtOH	1:1:2	3	91	tr	1:1:2	48	85	0	1:1:2	48	43	39
3	EtOH	1:1:3	2	92	tr	1:2:2	48	81	0	1:1:3	48	45	34
4	EtOH	1:1:4	2	91	tr	1:2:4	48	67	0	1:1:4	48	57	25
5	dioxane	1:1:2	3	79	8	1:1:2	72	21	55	1:1:1	80	tr	69
6	DME	1:1:2	3	72	9	1:1:2	72	79	10	1:1:1	48	0	82
7	DMF	1:1:2	3	83	4	1:1:2	30	91	0	1:1:1	18	30	45
8	CH_3CN	1:1:2	3	82	tr	1:1:2	72	18	49	1:1:1	48	tr	53
9	toluene	1:1:2	3	79	0	1:1:2	48	0	tr	1:1:1	48	0	tr
10	CH_2Cl_2	1:1:2	3	81	0	1:1:2	48	0	tr	1:1:1	48	0	tr
11	DMSO	1:1:2	3	87	tr	1:1:2	24	80	0	1:1:1	18	43	36
12	THF	1:1:2	3	75	10	1:1:2	72	59	26	1:1:1	48	0	88

[a]All the reactions were performed with 0.5 mmol of **1a**, 0.5 mmol of I_2, and corresponding amount of base in 5 mL of solvent at 35 °C for designated time; [b]Isolated yield based on substrate **1a**; tr = trace.

Table 3. Reaction of 1a with I_2/NaOAc under Air or N_2 Conditions[a]

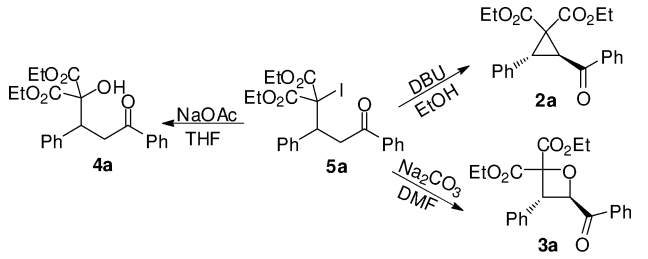


		yield (%)	
entry	conditions	4a	5a
1	**1a**:I_2:NaOAc = 1:1:1, THF, N_2, 60 h	tr	59
2	**1a**:I_2:NaOAc = 1:1:1, THF, air, 7 h	38	43
3	**1a**:I_2:NaOAc = 1:1:1, THF, air, 48 h	96	0
4	**1a**:I_2:NaOAc = 1:0.2:0.2, THF, air, 48 h	96	0
5	**1a**:I_2:NaOAc = 1:0.2:0.2, with additive of 3 equiv of TEMPO, THF, air, 50 h	13	7
6	**1a**:I_2:NaOAc = 1:0.2:0.2, dry THF, O_2, 5 Å molecular sieve, 48 h	96	0

[a]All reactions were performed with 0.5 mmol of **1a** in 5 mL of solvent at 35 °C.

The α-hydroxymalonate **4a** could be cyclized to **3a** in high yield under either I_2/Na_2CO_3/DMF or I_2/DBU/EtOH condition (Table 5, entries 1 and 4). This transformation required at least 1 equiv of I_2, and the O_2 had no influence on the reaction (Table 5, entries 2 and 3). However, under I_2/NaOAc/THF condition, the conversion of **4a** to **3a** was difficult perhaps owing to the weak basicity of NaOAc (Table 5, entry 5). It is interesting that under I_2/DBU/EtOH condition **1a** converted only to **2a** because the transformation of intermediate **5a** to **4a** was forbidden. Consequently, the base-controlled selective conversion of Michael adducts of malonates with enones was realized.

Table 4. Investigation on the Conversion of 5a to 2a, 3a, and 4a[a]



entry	conditions	product	yield (%)
1	NaOAc (0.2 equiv), THF, air, 24 h	**4a**	97
2	NaOAc (0.2 equiv), THF, N_2, 22 h	**4a**	tr
3	NaOAc (0.2 equiv), dry THF, O_2, 5 Å molecular sieve, 22 h	**4a**	95
4	NaOAc (0.2 equiv), dry THF, O_2, H_2O^{18}, 24 h	**4a**	95
5	NaOAc (0.2 equiv), TEMPO (3 equiv), THF, air, 24 h	**4a**	22
6	Na_2CO_3 (0.2 equiv), DMF, air, 48 h	**3a**	35
7	Na_2CO_3 (1 equiv), DMF, air, 18 h	**3a**	95
8	Na_2CO_3 (1 equiv), DMF, N_2, 24 h	**3a**	tr
9	DBU (1 equiv), EtOH, 3 h	**2a**	96

[a]All reactions were performed with 0.5 mmol of **5a** in 5 mL of solvent at 35 °C.

On the basis of these results and those reported radical reactions of iodo-compounds,[16] a possible reaction mechanism is proposed in Scheme 1. The Michael adduct of diethyl malonate with chalcone (**1a**) reacts with I_2 to give the crucial intermediate **5a**. Under DBU condition, **5a** converts to **2a** directly through intramolecular S_N2 reaction. The first step

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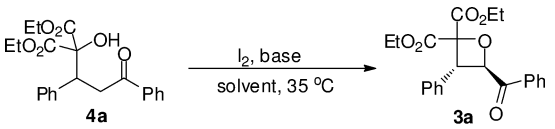
Table 5. Cyclization of 4a to 3a[a]



entry	conditions	yield (%)
1	I_2 (1 equiv), Na_2CO_3 (2 equiv), DMF, air, 24 h	95
2	I_2 (1 equiv), Na_2CO_3 (2 equiv), DMF, N_2, 24 h	95
3	I_2 (0.2 equiv), Na_2CO_3 (2 equiv), DMF, air, 24 h	19
4	I_2 (1 equiv), DBU (2 equiv), EtOH, air, 24 h	93
5	I_2 (1 equiv), NaOAc (2 equiv), THF, air, 24 h	0

[a]All reactions were performed with 0.5 mmol of **5a** in 5 mL of solvent at 35 °C.

iodination reaction needs 1 equiv of I_2 and 1 equiv of DBU, and the second step substitution reaction needs 1 equiv of DBU. However, under NaOAc and Na_2CO_3 condition, the homolytic cleavage of the C−I bond of **5a** generates the carbon radical **6**, which reacts with molecular oxygen to generate the peroxyl radical **7**, subsequently coupling with iodine radical to form iodoperoxide **8**. Homolytic cleavage of the O−O bond of **8** generates oxygen radical **9**, which is then trapped by iodine radical to form hypoiodite **10** that is a good electrophilic reagent as I^+. Hypoiodite **10** reacts with the Michal adduct **1a** to form α-hydroxymalonate **4a** and the intermediate **5a**, which undergos the next cycle. Therefore, the conversion of **1a** to **4a** needs only a catalytic amount of I_2 and NaOAc. Under I_2/Na_2CO_3 condition, **4a** continues to react with 1 equiv of I_2 and 1 equiv of Na_2CO_3 to generate **11**, with subsequent intramolecular S_N2 reaction with 1 equiv of Na_2CO_3 to afford **3a**. Therefore, the conversion of **1a** to **3a** can be accomplished by 1 equiv of I_2 and 2 equiv of Na_2CO_3. When **5a** is treated with Na_2CO_3, the path A is blocked. Intramolecular electrophilic reaction of hypoiodite **10** will generate **11** (path B), with further intramolecular S_N2 reaction to yield **3a**. For this reason, 1 equiv of Na_2CO_3 is required for the conversion of **5a** to **3a**. To prove this radical reaction mechanism, we introduced TEMPO to the system to trap the radical intermediate. Although we failed to capture the carbon radical with TEMPO, the reaction became sluggish in the presence of TEMPO (Table 3, entry 5 and Table 4, entry 5).

It is interesting that the transformation of **10** to **11** is difficult when NaOAc is used as the base in THF. Therefore, under I_2/NaOAc/THF and I_2/Na_2CO_3/DMF condition, α-hydroxymalonate **4a** and oxetane **3a** are the main products, respectively.

With the optimized conditions in hand, the scope of this reaction was extended to various substrates. The results presented in Table 6 demonstrate that the reactions proceeded well when R^1 and R^2 were both aryl groups and gave gratifying yields of cyclopropanes **2**, oxetanes **3**, and α-hydroxylmalonates **4**, respectively (Table 6, entries 1−10). The electronic effect of the substituent group on the phenyl ring had no significant impact on the reaction. The conversion of **1n** with a bulky ester group was relatively slower (Table 6, entry 14). When R^1 was a phenyl group and R^2 was a pyridyl group, cyclopropane **2k** and oxetane **3k** were also obtained in good yield. However, under NaOAc condition, a mixture of α-hydroxyl malonate **4k** and hemiketal **5k** (in a ratio of 2.23:1, analysis of ^{1}H NMR spectrum), which was formed from **4k** by intramolecular attack of the hydroxyl on carbonyl, was yielded (Scheme 2). A similar hemiketal also could be observed for **4i**, **4j**, and **4l**. A trend toward increasing ratio of hemiketal as electron-withdrawing ability of R^2 increased was also found. When R^1 was phenyl group and R^2 was methyl group, only a trace of cyclopropane **2l** was detected. As for the Michael adduct of cyclic enone with diethylmalonate (**1o**), only the α-hydroxyl malonate **4o** was obtained using either Na_2CO_3 or NaOAc as the base. It should be noted that **1e**, **1j**, **1l**, and **1n**, which could not afford oxetane poducts using the recently reported procedure,[7] also gave moderate to good yields of **3** under I_2/Na_2CO_3/DMF condition.

CONCLUSION

In summary, we report here an efficient base-controlled selective conversion of Michael adducts of malonates with enones in the presence of I_2. Highly functionalized cyclopropane and oxetane derivatives are divergently synthesized in moderate to good yields with high diastereoselectivity. The high stereoselectivity in cyclopropane is due to thermodynamic stability of the *trans*-product.[3c] Oxetane **3** with *trans*-orientation of both phenyl and benzoyl groups are stable because the two groups are both in the equatorial position. A novel strategy of direct α-hydroxylation of malonate derevatives using a catalytic

Scheme 1. Possible Reaction Mechanism for the Selective Conversion

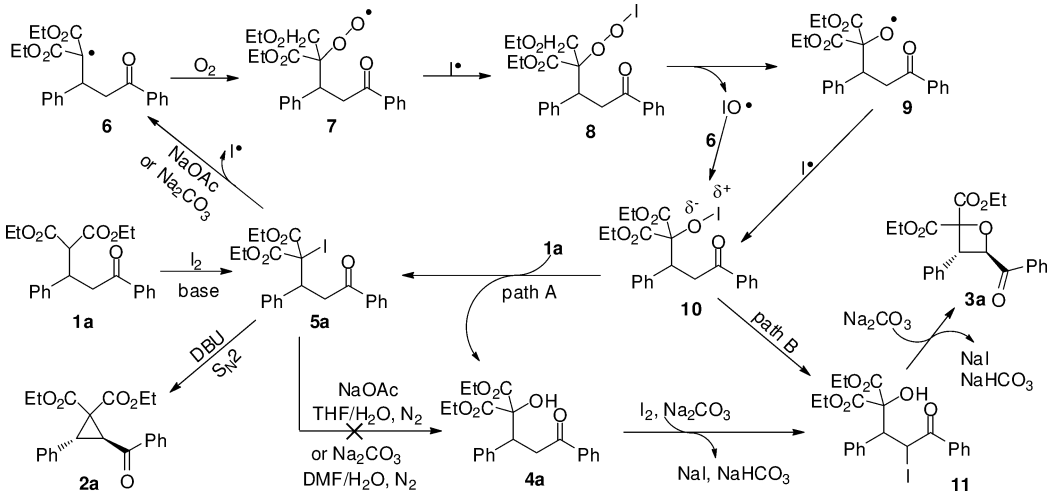


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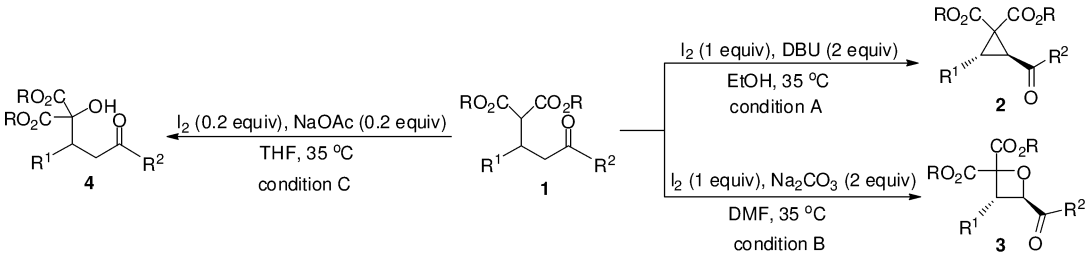
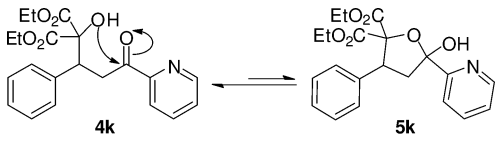
Table 6. Base-Controlled Selective Conversion of Michael Adducts of Malonates with Enones[a]



	substrate				condition A			condition B			condition C		
entry		R^1	R^2	R	time (h)		yield of **2** (%)[b]	time (h)		yield of **3** (%)[b]	time (h)		yield of **4** (%)[b]
1	**1a**	Ph	Ph	Et	3	**2a**	90	36	**3a**	91	48	**4a**	93
2	**1b**	4-MeO-C_6H_5	Ph	Et	3	**2b**	87	48	**3b**	82	48	**4b**	87
3	**1c**	4-Me-C_6H_5	Ph	Et	3	**2c**	89	36	**3c**	90	48	**4c**	89
4	**1d**	4-Cl-C_6H_5	Ph	Et	3	**2d**	92	36	**3d**	91	48	**4d**	91
5	**1e**	4-NO_2−C_6H_5	Ph	Et	3	**2e**	95	36	**3e**	88	48	**4e**	86
6	**1f**	3-NO_2-C_6H_5	Ph	Et	3	**2f**	93	36	**3f**	92	48	**4f**	84
7	**1g**	Ph	4-MeO-C_6H_5	Et	3	**2g**	89	36	**3g**	89	48	**4g**	92
8	**1h**	Ph	4-Me-C_6H_5	Et	3	**2h**	88	36	**3h**	90	48	**4h**	90
9	**1i**	Ph	4-Cl-C_6H_5	Et	3	**2i**	88	36	**3i**	91	48	**4i**	87 (95:5)[e]
10	**1j**	Ph	4-NO_2-C_6H_5	Et	3	**2j**	86	36	**3j**	91	48	**4j**	85 (85:15)[e]
11	**1k**	Ph	2-pyridyl	Et	3	**2k**[c]	92[c]	36	**3k**	79	48	**4k**	71 (69:31)[e]
12	**1l**	Ph	CH_3	Et	24	**2l**	tr	60	**3l**	42	24	**4l**	95 (86:14)[e]
13	**1m**	H	Ph	Et	3	**2m**	97	48	**3m**	90	48	**4m**	84
14	**1n**	Ph	Ph	t-Bu	12	**2n**	80	72	**3n**	87	72	**4n**	73
15	**1o**	R^1, R^2 = -$(CH_2)_3$-		Et	48	**2o**	0	48	**4o**[d]	41	24	**4o**	88

[a]All reactions were performed with 1.0 mmol of **1** in 10 mL of solvent at 35 °C for the designated time. [b]Isolated yield based on **1**. [c]Contains little *cis*-isomer. [d]No oxetane product was observed in the reaction. [e]Anlysis of the NMR showed that it is a mixture of the α-hydroxylated malonate and hemiketal.

Scheme 2. Formation of Hemiketal 5k from 4k



amount of I_2/NaOAc was also explored. O_2 was found to be crucial to the formation of oxetane and α-hydroxylated malonate derevatives. The influence of the solvent and molar ratio of reactants on the selective reaction was investigated in detail. Our further investigations on the construction of azetidines and thietanes under similar conditions are currently underway.

EXPERIMENTAL SECTION

General Method. All reactions were performed under atmosphere. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ at 500 and 125 MHz, respectively. FT-IR spectra were taken in KBr pellets and were reported in cm^{-1}. High-resolution mass spectra (HRMS) were obtained with a positive EI or positive ESI mode. All of the known products were confirmed by comparison of their ^{1}H NMR spectral data with those reported in literature. The identification of new compounds was fully confirmed by their HRMS, ^{1}H NMR, ^{13}C NMR, and FTIR spectra.

General Procedure for the Synthesis of Cyclopropane Derivatives 2. A mixture of the Michael adducts of malonates with enones (**1**, 1 mmol), I_2 (254 mg, 1 mmol), and DBU (305 mg, 2 mmol) was stirred in 10 mL of ethanol at 35 °C for designated time. Most of the solvent was removed *in vacuo*, and 20 mL of cold water was added. To the mixture was added saturated $Na_2S_2O_3$ until the disappearance of umber, and the mixture was then extracted with dichloromethane (15 mL × 3). The organic layer was dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether) to provide the corresponding cyclopropanes **2**.

Diethyl 2-phenyl-3-picolinoylcyclopropane-1,1-dicarboxylate ***2k***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (d, *J* = 4.6 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.7, 1.6 Hz, 1H), 7.52 (ddd, *J* = 7.6, 4.8, 1.0 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.25 (t, *J* = 7.3 Hz, 1H), 5.09 (d, *J* = 7.6 Hz, 1H), 4.23−4.33 (m, 2H), 3.92−4.02 (m, 2H), 3.78 (d, *J* = 7.6 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.6, 166.4, 165.6, 152.9, 149.4, 136.9, 133.9, 128.9, 128.2, 127.53, 127.50, 122.01, 61.73, 61.67, 46.6, 37.9, 33.0, 14.0, 13.7; IR (KBr) ν/cm^{-1} 2983, 2937, 1736, 1692, 1584, 1442, 1300, 1284, 1250, 1215, 1184, 1108, 1025, 745, 698; TOF-MS (EI) calcd for $C_{21}H_{21}NO_5$ [M^+] 367.1420, found 367.1429.

General Procedure for the Preparation Derivatives 3. A mixture of the Michael adducts of malonates with enones (**1**, 1 mmol), I_2 (254 mg, 1 mmol), and Na_2CO_3 (212 mg, 2 mmol) were stirred in 10 mL of DMF upon exposure to air at 35 °C for designated time. To the mixture was added 40 mL of cold water and saturated $Na_2S_2O_3$ until the disappearance of umber, and then the mixture was extracted with dichloromethane (20 mL × 3). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether) to provide the corresponding oxetanes **3**.

Diethyl 4-Benzoyl-3-(4-nitrophenyl)oxetane-2,2-dicarboxylate ***3e***. Mp 99−100 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.7 Hz, 2H), 7.99 (d, *J* = 7.8 Hz, 2H), 7.58−7.65 (m, 3H), 7.48 (t, *J* = 7.8 Hz, 2H), 6.13 (d, *J* = 7.6 Hz, 1H), 5.17 (d, *J* = 7.6 Hz, 1H), 4.36 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.28 (dq, *J* = 10.7, 7.1 Hz, 1H), 4.00 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.89 (dq, *J* = 10.7, 7.1 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.9, 167.0, 166.4, 147.9, 141.6, 134.5, 133.3, 129.3, 129.2, 129.0,

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123.9, 86.7, 81.9, 63.0, 62.4, 48.1, 14.0, 13.8; IR (KBr) ν/cm^{-1} 1743, 1678, 1599, 1524, 1348, 1300, 1263, 1169, 1071, 1016, 975, 853, 693; TOF-MS (EI) calcd for $C_{22}H_{21}NO_8$ [M$^+$] 427.1267, found 427.1271.

Diethyl 4-(4-Nitrobenzoyl)-3-phenyloxetane-2,2-dicarboxylate ***3j***. Mp 84−86 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 8.8 Hz, 2H), 8.12 (d, J = 8.8 Hz, 2H), 7.45 (d, J = 7.2 Hz, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.36 (t, J = 7.0 Hz, 1H), 6.09 (d, J = 7.4 Hz, 1H), 5.00 (d, J = 7.4 Hz, 1H), 4.33 (dq, J = 10.7, 7.1 Hz, 1H), 4.26 (dq, J = 10.7, 7.1 Hz, 1H), 3.92 (dq, J = 10.7, 7.1 Hz, 1H), 3.85 (dq, J = 10.7, 7.1 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H), 0.83 (t, J = 7.1 Hz, 3H); NMR (125 MHz, $CDCl_3$) δ 194.3, 167.1, 166.4, 150.9, 137.9, 133.7, 130.3, 129.1, 128.9, 128.2, 124.1, 87.4, 82.8, 62.85, 62.2, 49.0, 14.0, 13.6; IR (KBr) ν/cm^{-1} 2994, 2960, 2917, 1759, 1740, 1698, 1602, 1525, 1353, 1298, 1254, 1125, 1065, 1016, 983, 854, 839, 791, 751, 709, 566; TOF-MS (EI) calcd for $C_{22}H_{21}NO_8$ [M$^+$] 427.1267, found 427.1264.

Diethyl 3-Phenyl-4-picolinoyloxetane-2,2-dicarboxylate ***3k***. Mp 94−95 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 4.6 Hz, 1H), 8.08 (d, J = 7.8 Hz, 1H), 7.83 (td, J = 7.7, 1.5 Hz, 1H), 7.52 (d, J = 7.4 Hz, 2H), 7.39−7.42 (m, 1H), 7.37 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.5 Hz, 1H), 6.66 (d, J = 7.5 Hz, 1H), 4.85 (d, J = 7.5 Hz, 1H), 4.39 (dq, J = 10.7, 7.1 Hz, 1H), 4.32 (dq, J = 10.7, 7.1 Hz, 1H), 3.87 (dq, J = 10.7, 7.1 Hz, 1H), 3.82 (dq, J = 10.7, 7.1 Hz, 1H), 1.34 (t, J = 7.1 Hz, 3H), 0.82 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 167.8, 166.7, 150.9, 149.2, 137.1, 134.5, 128.6, 128.4, 128.1, 127.9, 122.6, 87.3, 82.1, 62.7, 61.8, 49.9, 14.1, 13.7; IR (KBr) ν/cm^{-1} 2979, 2935, 1760, 1736, 1708, 1584, 1442, 1290, 1272, 1258, 1117, 1062, 1045, 962, 855, 801, 753, 701; TOF-MS (EI) calcd for $C_{21}H_{21}NO_6$ [M$^+$] 383.1369, found 383.1388.

Diethyl 4-Acetyl-3-phenyloxetane-2,2-dicarboxylate ***3l***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.38 (m, 5H), 5.38 (d, J = 7.9 Hz, 1H), 4.74 (d, J = 7.8 Hz, 1H), 4.29−4.41 (m, 2H), 3.89 (dq, J = 10.7, 7.1 Hz, 1H), 3.82 (dq, J = 10.7, 7.2 Hz, 1H), 2.31 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H), 0.81 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 167.5, 166.5, 133.8, 128.8, 128.5, 128.1, 87.1, 83.7, 62.7, 62.0, 49.2, 25.4, 14.0, 13.6; IR (KBr) ν/cm^{-1} 2984, 2939, 1743, 1456, 1369, 1278, 1175, 1122, 1053, 1011, 856, 747, 700; TOF-MS (EI) calcd for $C_{17}H_{20}O_6$ [M$^+$] 320.1260, found 320.1252.

Diethyl 4-Benzoyloxetane-2,2-dicarboxylate ***3m***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.9 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 2H), 5.78 (dd, J = 8.5, 6.7 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 4.23 (q, 7.1 Hz, 2H), 3.43 (dd, J = 12.2, 6.7 Hz, 1H), 3.36 (dd, J = 12.2, 8.6 Hz, 1H), 1.34 (t, J = 7.2 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.6, 168.2, 167.5, 133.8, 133.3, 128.8, 128.7, 81.9, 77.8, 62.4, 62.2, 31.0, 13.9, 13.7; IR (KBr) ν/cm^{-1} 2984, 2940, 1746, 1693, 1598, 1450, 1370, 1301, 1277, 1231, 1140, 1061, 857, 695; TOF-MS (EI) calcd for $C_{16}H_{18}O_6$ [M$^+$] 306.1103, found 306.1095.

Di-tert-Butyl 4-Benzoyl-3-phenyloxetane-2,2-dicarboxylate ***3n***. Mp 118−120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 7.8 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.47 (d, J = 7.3 Hz, 2H), 7.41 (t, J = 7.7 Hz, 2H), 7.37 (d, J = 7.6 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 6.06 (d, J = 7.3 Hz, 1H), 4.91 (d, J = 7.4 Hz, 1H), 1.50 (s, 9H), 1.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.5, 166.4, 165.5, 134.4, 133.9, 133.6, 129.0, 128.8, 128.7, 128.6, 128.3, 87.3, 83.2, 82.9, 81.9, 48.5, 27.8, 27.4; IR (KBr) ν/cm^{-1} 2980, 2934, 1756, 1740, 1685, 1598, 1451, 1370, 1300, 1272, 1256, 1169, 1141, 1125, 976, 840, 705; TOF-MS (EI) calcd for $C_{26}H_{30}O_6$ [M$^+$] 438.2042, found 438.2031.

General Procedure for the Conversion of Michael Adducts of Malonates with Enones to α-Hydroxylmalonates 4. A mixture of the Michael adducts of malonates with enones (**1**, 1 mmol), I_2 (51 mg, 0.2 mmol), and NaOAc (17 mg, 0.2 mmol) were stirred in 10 mL of THF upon exposure to air at 35 °C for designated time. Most of the solvent was removed *in vacuo*, and 20 mL of water was added. To the mixture was added saturated $Na_2S_2O_3$ until the disappearance of umber, and then the mixture was extracted with dichloromethane (15 mL × 3). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether) to provide the corresponding α-hydroxylmalonates **4**.

Diethyl 2-Hydroxy-2-(1-(4-methoxyphenyl)-3-oxo-3-phenylpropyl)malonate ***4b***. Mp 111−113 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.8 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H), 6.75 (d, J = 8.7 Hz, 2H), 4.40 (dd, J = 10.4, 2.9 Hz, 1H), 4.24−4.32 (m, 2H), 4.07 (dq, J = 10.7, 7.1 Hz, 1H), 4.00 (dq, J = 10.7, 7.1 Hz, 1H), 3.99 (s, 1H), 3.73 (s, 3H), 3.68 (dd, J = 17.3, 10.4 Hz, 1H), 3.33 (dd, J = 17.3, 3.1 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 170.0, 169.6, 158.9, 137.1, 133.1, 130.60, 130.56, 128.6, 128.2, 113.6, 82.2, 63.0, 62.8, 55.2, 44.1, 40.3, 14.1, 14.0; IR (KBr) ν/cm^{-1} 3560, 2976, 2926, 1739, 1686, 1613, 1518, 1447, 1252, 1221, 1178, 1127, 1051, 818, 762, 690; TOF-MS (EI) calcd for $C_{23}H_{26}O_7$ [M$^+$] 414.1679, found 414.1667.

Diethyl 2-Hydroxy-2-(1-(4-methylphenyl)-3-oxo-3-phenylpropyl)-malonate ***4c***. Mp 107−108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.8 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H), 7.01 (d, J = 7.9 Hz, 2H), 4.40 (dd, J = 10.2, 2.9 Hz, 1H), 4.24−4.32 (m, 2H), 4.07 (dq, J = 10.7, 7.1 Hz, 1H), 3.99 (s, 1H), 3.98 (dq, J = 10.7, 7.1 Hz, 1H), 3.70 (dd, J = 17.3, 10.3 Hz, 1H), 3.44 (dd, J = 17.3, 3.1 Hz, 1H), 2.24 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 170.1, 169.6, 137.1, 137.0, 135.4, 133.1, 129.4, 128.9, 128.6, 128.2, 82.1, 63.0, 62.8, 44.5, 40.2, 21.2, 14.1, 14.0; IR (KBr) ν/cm^{-1} 3562, 2976, 2927, 1740, 1688, 1595, 1446, 1251, 1220, 1126, 1048, 761, 689; TOF-MS (EI) calcd for $C_{23}H_{26}O_6$ [M$^+$] 398.1729, found 398.1727.

Diethyl 2-Hydroxy-2-(1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)-malonate ***4d***. Mp 103−105 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.8 Hz, 2H), 7.53 (d, J = 7.4 Hz, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 4.43 (dd, J = 10.4, 2.9 Hz, 1H), 4.25−4.32 (m, 2H), 4.08 (dq, J = 10.7, 7.1 Hz, 1H), 4.01 (s, 1H), 4.00 (dq, J = 10.7, 7.1 Hz, 1H), 3.75 (dd, J = 17.9, 10.6 Hz, 1H), 3.44 (dd, J = 17.9, 2.9 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 169.8, 169.4, 137.3, 136.9, 133.4, 133.3, 131.0, 128.7, 128.4, 128.2, 81.9, 63.2, 63.0, 44.1, 40.2, 14.1, 14.0; IR (KBr) ν/cm^{-1} 3560, 2978, 2929, 1740, 1688, 1596, 1446, 1252, 1220, 1126, 753, 691; TOF-MS (EI) calcd for $C_{22}H_{23}ClO_6$ [M$^+$] 418.1183, found 418.1171.

Diethyl 2-Hydroxy-2-(1-(4-nitrophenyl)-3-oxo-3-phenylpropyl)-malonate ***4e***. Mp 76−78 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.8 Hz, 2H), 7.89 (d, J = 7.9 Hz, 2H), 7.67 (d, J = 8.8 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 4.58 (dd, J = 10.5, 2.8 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 4.19 (s, 1H), 4.09 (dq, J = 10.7, 7.1 Hz, 1H), 4.02 (dq, J = 10.7, 7.1 Hz, 1H), 3.75 (dd, J = 17.9, 10.6 Hz, 1H), 3.44 (dd, J = 17.9, 2.9 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7. 169.1, 168.9, 147.0, 146.6, 136.3, 133.2, 130.5, 128.5, 127.9, 122.9, 81.4, 63.0, 62.9, 44.2, 39.9, 13.8, 13.7; IR (KBr) ν/cm^{-1} 3550, 2983, 2933, 1746, 1686, 1598, 1520, 1449, 1344, 1243, 1217, 1133, 858, 748, 707, 692; TOF-MS (EI) calcd for $C_{22}H_{23}NO_8$ [M$^+$] 429.1424, found 429.1421.

Diethyl 2-Hydroxy-2-(1-(3-nitrophenyl)-3-oxo-3-phenylpropyl)-malonate ***4f***. Mp 81−82 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (t, J = 1.8 Hz, 1H), 8.06 (dd, J = 8.3, 2.1 Hz, 1H), 7.90 (d, J = 7.9 Hz, 2H), 7.81 (d, J = 7.8 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.41 (t, J = 7.8 Hz, 1H), 4.57 (dd, J = 10.4, 2.8 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 4.09 (dq, J = 10.7, 7.1 Hz, 1H), 4.06 (s, 1H), 4.03 (dq, J = 10.7, 7.1 Hz, 1H), 3.77 (dd, J = 17.9, 10.6 Hz, 1H), 3.44 (dd, J = 17.9, 2.9 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 169.5, 169.1, 148.1, 141.0, 136.6, 136.1, 133.5, 129.0, 128.8, 128.2, 124.8, 122.6, 81.6, 63.4, 63.2, 44.2, 40.1, 14.1, 14.0; IR (KBr) ν/cm^{-1} 3435, 2991, 2906, 1748, 1679, 1529, 1449, 1350, 1292, 1259, 1222, 1136, 1033, 978, 752, 706, 685; TOF-MS (EI) calcd for $C_{22}H_{23}NO_8$ [M$^+$] 429.1424, found 429.1415.

Diethyl 2-Hydroxy-2-(3-(4-methoxyphenyl)-3-oxo-1-phenylpropyl)malonate ***4g***. Mp 64−65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.9 Hz, 2H), 7.41 (d, J = 7.2 Hz, 2H), 7.20 (t, J = 7.3 Hz, 2H), 7.15 (t, J = 7.3 Hz, 1H), 6.87 (d, J = 8.9 Hz, 2H), 4.44 (dd, J = 10.2, 3.1 Hz, 1H), 4.24−4.31 (m, 2H), 4.06 (s, 1H), 4.05 (dq, J = 10.7, 7.1 Hz, 1H), 3.97 (dq, J = 10.7, 7.1 Hz, 1H), 3.82 (s, 3H), 3.67 (dd, J = 17.1, 10.3 Hz, 1H), 3.31 (dd, J = 17.1, 3.2 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 196.1, 169.9, 169.6, 163.5, 138.7, 130.5, 130.2, 129.5, 128.1, 127.4, 113.7, 82.1, 63.0, 62.8, 55.5, 45.0, 39.8, 14.1, 13.9; IR (KBr) ν/cm^{-1} 3479, 2982, 2937, 1739, 1678, 1601, 1455, 1303, 1257, 1223, 1171, 1134, 1208, 703; TOF-MS (EI) calcd for $C_{23}H_{26}O_7$ [M$^+$] 414.1679, found 414.1672.

Diethyl 2-Hydroxy-2-(3-(4-methylphenyl)-3-oxo-1-phenylpropyl)-malonate ***4h***. Mp 83−84 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 2H), 7.41 (d, J = 7.2 Hz, 2H), 7.18−7.23 (m, 4H), 7.20 (t, J = 7.2 Hz, 1H), 4.44 (dd, J = 10.2, 3.0 Hz, 1H), 4.25−4.31 (m, 2H), 4.05 (dq, J = 10.7, 7.1 Hz, 1H), 4.00 (s, 1H), 3.98 (dq, J = 10.7, 7.1 Hz, 1H), 3.70 (dd, J = 17.3, 10.2 Hz, 1H), 3.33 (dd, J = 17.3, 3.1 Hz, 1H), 2.37 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 169.7, 169.3, 143.5, 138.6, 134.3, 129.4, 129.0, 128.0, 127.8, 127.2, 81.9, 62.6, 62.5, 44.7, 39.9, 21.4, 13.8, 13.6; IR (KBr) ν/cm^{-1} 3540, 2984, 2941, 1748, 1718, 1674, 1608, 1458, 1301, 1261, 1227, 1132, 1095, 1028, 702; TOF-MS (EI) calcd for $C_{23}H_{26}O_6$ [M$^+$] 398.1729, found 398.1731.

Diethyl 2-(3-(4-Chlorophenyl)-3-oxo-1-phenylpropyl)-2-hydroxy-malonate ***4i***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.6 Hz, 2H), 7.39 (d, J = 7.4 Hz, 2H), 7.37 (d, J = 8.6 Hz, 2H), 7.21 (t, J = 7.2 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 4.41 (dd, J = 10.2, 3.0 Hz, 1H), 4.23−4.33 (m, 2H), 4.05 (dq, J = 10.7, 7.1 Hz, 1H), 4.03 (s, 1H), 3.98 (dq, J = 10.7, 7.1 Hz, 1H), 3.66 (dd, J = 17.3, 10.3 Hz, 1H), 3.36 (dd, J = 17.3, 3.1 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.4, 169.8, 169.4, 139.4, 138.4, 135.2, 129.5, 129.4, 128.8, 128.1, 127.5, 81.8, 62.9, 62.7, 44.8, 40.2, 14.0, 13.8; IR (KBr) ν/cm^{-1} 3479, 2983, 2938, 1739, 1688, 1590, 1300, 1260, 1221, 1134, 1093, 1032, 1051, 702; TOF-MS (EI) calcd for $C_{22}H_{23}ClO_6$ [M$^+$] 418.1183, found 418.1171.

Diethyl 2-Hydroxy-2-(3-(4-nitrophenyl)-3-oxo-1-phenylpropyl)-malonate ***4j***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J = 8.8 Hz, 2H), 8.04 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 7.0 Hz, 2H), 7.22 (t, J = 7.2 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H), 4.39 (dd, J = 10.2, 3.0 Hz, 1H), 4.24−4.35 (m, 2H), 4.07 (s, 1H), 4.06 (dq, J = 10.7, 7.1 Hz, 1H), 3.98 (dq, J = 10.7, 7.1 Hz, 1H), 3.71 (dd, J = 17.3, 10.3 Hz, 1H), 3.48 (dd, J = 17.3, 3.1 Hz, 1H), 1.30 (t, J = 7.1 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.4, 169.8, 169.4, 150.4, 141.4, 138.1, 129.4, 129.3, 128.3, 127.8, 123.9, 81.7, 63.2, 62.9, 44.8, 41.0, 14.1, 13.9; IR (KBr) ν/cm^{-1} 3476, 2983, 2938, 1739, 1697, 1604, 1526, 1455, 1348, 1260, 1221, 1134, 856, 745, 711; TOF-MS (EI) calcd for $C_{22}H_{23}NO_8$ [M$^+$] 429.1424, found 429.1419.

Diethyl 2-Hydroxy-2-(3-oxo-1-phenyl-3-(pyridin-2-yl)propyl)-malonate ***4k***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, J = 4.7 Hz, 1H), 7.89 (d, J = 7.9 Hz, 1H), 7.74 (td, J = 7.7, 1.7 Hz, 1H), 7.45 (d, J = 7.2 Hz, 2H), 7.41 (ddd, J = 7.5, 4.8, 1.1 Hz, 1H), 7.31 (t, J = 7.4 Hz, 1H), 7.21 (t, J = 7.3 Hz, 2H), 4.46 (dd, J = 10.2, 3.2 Hz, 1H), 4.23−4.30 (m, 2H), 4.14 (dd, J = 18.4, 10.3 Hz, 1H), 4.06 (dq, J = 10.7, 7.2 Hz, 1H), 4.05 (s, 1H), 3.99 (dq, J = 10.7, 7.2 Hz, 1H), 3.52 (dd, J = 18.3, 3.3 Hz, 1H), 1.28 (t, J = 7.2 Hz, 3H), 1.13 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.2, 169.9, 169.6, 153.3, 148.9, 138.9, 136.8, 129.7, 127.9, 127.2, 127.1, 121.7, 82.1, 62.7, 62.6, 44.6, 39.5, 14.0, 13.8.

Diethyl 2-Hydroxy-2-(3-oxo-1-phenylbutyl)malonate ***4l***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 7.0 Hz, 2H), 7.17−7.26 (m, 3H), 4.25−4.33 (m, 2H), 4.21 (dd, J = 10.1, 3.2 Hz, 1H), 4.04 (dq, J = 10.7, 7.1 Hz, 1H), 3.96 (dq, J = 10.7, 7.1 Hz, 1H), 3.93 (s, 1H), 3.11 (dd, J = 17.1, 10.2 Hz, 1H), 2.85 (dd, J = 17.1, 3.2 Hz, 1H), 2.01 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 169.8, 169.4, 138.4, 129.4, 128.2, 127.5, 81.7, 62.9, 62.7, 45.0, 44.6, 30.5, 14.0, 13.8; IR (KBr) ν/cm^{-1} 3484, 2984, 2939, 1739, 1455, 1367, 1255, 1220, 1135, 1096, 1023, 860, 702; TOF-MS (EI) calcd for $C_{17}H_{22}O_6$ [M$^+$] 322.1416, found 322.1429.

Diethyl 2-Hydroxy-2-(3-oxo-3-phenylpropyl)malonate ***4m***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.8 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 4.25−4.31 (m, 4H), 3.94 (s, 1H), 3.11 (t, J = 7.7 Hz, 2H), 2.50 (t, J = 7.7 Hz, 2H), 1.30 (t, J = 7.1 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.1, 170.4, 136.7, 133.2, 128.7, 128.2, 78.2, 62.7, 32.8, 29.2, 14.1; IR (KBr) ν/cm^{-1} 3479, 2983, 2939, 1739, 1686, 1598, 1449, 1368, 1267, 1227, 1191, 1129, 1026, 859, 745, 691; TOF-MS (EI) calcd for $C_{16}H_{20}O_6$ [M$^+$] 308.1260, found 308.1271.

Di-tert-butyl 2-Hydroxy-2-(3-oxo-1,3-diphenylpropyl)malonate ***4n***. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.9 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.45 (d, J = 7.2 Hz, 2H), 7.39 (t, J = 7.8 Hz, 2H), 7.20 (t, J = 7.4 Hz, 2H), 7.14 (t, J = 7.3 Hz, 1H), 4.37 (dd, J = 10.4, 2.6 Hz, 1H), 4.03 (s, 1H), 3.70 (dd, J = 17.4, 10.5 Hz, 1H), 3.34 (dd, J = 17.4, 2.7 Hz, 1H), 1.49 (s, 9H), 1.24 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 169.1, 168.8, 139.5, 137.2, 133.0, 129.8, 128.5, 128.2, 128.0, 127.2, 83.8, 83.2, 82.3, 44.3, 40.9, 27.9, 27.6; IR (KBr) ν/cm^{-1} 3492, 2978, 2934, 1739, 1688, 1596, 1452, 1370, 1316, 1260, 1242, 1144, 841, 753, 706, 691; TOF-MS (EI) calcd for $C_{26}H_{32}O_6$ [M$^+$] 440.2199, found 440.2187.

Diethyl 2-Hydroxy-2-(3-oxocyclohexyl)malonate ***4o***. Mp 93−96 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.25−4.31 (m, 4H), 3.81 (s, 1H), 2.77−2.85 (m, 1H), 2.35−2.44 (m, 2H), 2.18−2.30 (m, 2H), 2.05−2.14 (m, 1H), 1.62−1.77 (m, 3H), 1.30 (t, J = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.6, 169.7, 169.6, 81.2, 63.2, 62.9, 42.6, 41.8, 41.0, 25.0, 24.5, 14.2, 14.1; IR (KBr) ν/cm^{-1} 2983, 2960, 2909, 1750, 1732, 1698, 1262, 1220, 1192, 1151, 1024, 862, 668, 519; TOF-MS (EI) calcd for $C_{13}H_{20}O_6$ [M$^+$] 272.1260, found 272.1251.

Synthesis of Diethyl 2-Iodo-2-(3-oxo-1,3-diphenylpropyl)-malonate 5a. *Method A*. A mixture of the Michael adduct of diethyl malonate with chalcone (**1a**, 368 mg, 1 mmol), I_2 (254 mg, 1 mmol), and NaOAc (82 mg, 1 mmol) was stirred in 10 mL of THF upon exposure to air at 35 °C for 7 h (detected by TLC). The similar operation process as above provides **5a** (212 mg, 43%), unreacted **1a**, and **4a** (146 mg, 38%).

Method B. A mixture of the Michael adduct of diethyl malonate with chalcone (**1a**, 368 mg, 1 mmol), I_2 (254 mg, 1 mmol), and NaOAc (82 mg, 1 mmol) was stirred in 10 mL of THF under N_2 atmosphere at 35 °C for 60 h. The similar operation process as above provides **5a** (291 mg, 59%) and unreacted **1a**. **5a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 8.1 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.39−7.44 (m, 4H), 7.20−7.25 (m, 3H), 4.18−4.28 (m, 2H), 4.01−4.15 (m, 3H), 3.84−3.86 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 168.1, 166.8, 138.3, 136.6, 132.9, 129.3, 128.4, 127.90, 127.88, 127.76, 63.1, 62.8, 52.7, 47.1, 45.5, 13.54, 13.51; HRMS (+ESI) calcd for $C_{22}H_{23}INaO_5$ [M + Na$^+$] 517.0488, found 517.0475.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General method and NMR spectra of all the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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