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tert-Butyl Peroxybenzoate-Promoted α-Methylation of 1,3-Dicarbonyl Compounds

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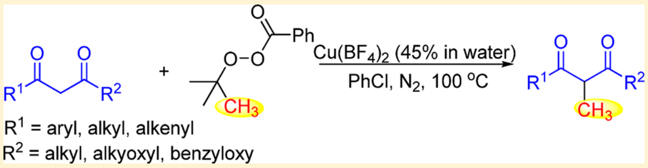
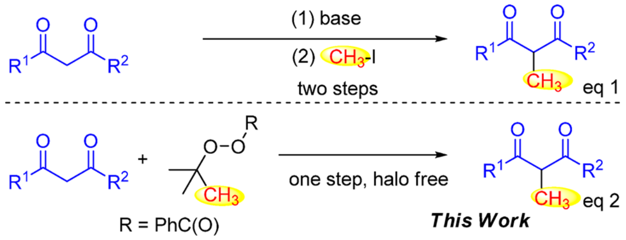
Supporting Information

ABSTRACT: A *tert*-butyl peroxybenzoate (TBPB)-promoted direct α-methylation of 1,3-dicarbonyl compounds has been developed, providing α-methyl derivatives in moderate to good yields. In this procedure, TBPB plays a dual role, serving as both the methyl source and radical initiator. This work represents a key complement to the traditional α-methylation of 1,3-dicarbonyl compounds using methyl iodide.



The methylation of C−H bonds is one important transformation in organic chemistry and the pharmaceutical industry because the introduction of a methyl group can improve a molecule's biological activity and physical properties, which is known as the magical methyl effect.[1−8] Thus, it is common that medicinal chemists examine methylated variants of a drug lead after replacing C−H with C−Me. In many instances, however, methylation of an advanced drug intermediate can be achieved only through de novo synthesis. Compared with sp^2 C−H methylation,[9−11] the methylation of sp^3 C−H bonds has been less investigated because of their low polarity.[12−14] Recently, a lot of progress in the α-methylation of carbonyl compounds has been made. For example, Donohoe reported Rh-catalyzed α-methylation of ketones using methanol as the methylating reagent under mild conditions.[15] Xiao and co-workers also developed the Ru-catalyzed methylation of ketone compounds with DMF as the carbon source.[16] However, in the case of 1,3-dicarbonyl compounds, α-methylation is generally limited to a two-step procedure: deprotonation of the activated methenyl by a strong base followed by quenching of the intermediate anion with an electrophile such as methyl iodide (Scheme 1, eq 1).[17−21] Such a methylation reagent is poisonous and generates halogen-containing wastes. Nevertheless, this method is valid as long as the substrate tolerates strongly basic reaction conditions. Very recently, the in situ-formed methyl radicals derived from various peroxides have been widely applied in the methylation of arenes, carboxylic acids, amides, and activated alkenes.[22−27] Meanwhile, the radical coupling of 1,3-dicarbonyl compounds in C−C bond formation has been well-documented.[28−41] As a result, the development of a one-step direct methylation of such a compound by the in situ-formed methyl radical is reasonable (Scheme 1, eq 2). Herein we report our study on such a method. This procedure features (1) selective monomethylation under nearly neutral reaction conditions and (2) the use of *tert*-butyl peroxybenzoate (TBPB) rather than methyl iodide as the methyl source, thus avoiding the generation of halogen-containing waste.

Scheme 1. α-Methylation of 1,3-Dicarbonyl Compounds



We selected the combination of ethyl 3-oxo-3-phenylpropanoate (**1a**), di-*tert*-butyl peroxide (DTBP) (2 equiv), and Bu_4NI (5 mol %) in chlorobenzene (3 mL) at 100 °C as the model reaction. Fortunately, the monomethylated product **3a** was selectively obtained, although in a low yield of 10% (Table 1, entry 1). Under similar reaction conditions, a 22% yield of **3a** was isolated by catalysis using $FeCl_2$ (entry 2), but other catalysts, such as $Fe_2(SO_4)_3$, I_2, $Cu(OTf)_2$, and CuF_2, failed to promote this transformation (entries 3−6). Further optimization showed that when $Cu(BF_4)_2$ was utilized, the yield of **3a** increased dramatically to 43% (entry 7). To obtain better results, other potential methyl sources, such as TBHP, DCP, and TBPB were analyzed (entries 8−10). TBPB was found to be the best, allowing **3a** to be isolated in 78% yield (entry 10). Other copper salts, including $Cu(OTf)_2$ and $Cu(acac)_2$, were less effective under exactly the same conditions (entries 11 and 12). Solvent screening showed that common solvents such as MeCN, DMF, and THF were not effective at all (entries 13−15). In addition, reducing the amount of solvent or elevating the reaction temperature decreased the total yield because of the formation of an increased amount of acetophenone as a byproduct, as detected by GC−MS (entries 16 and 17). A

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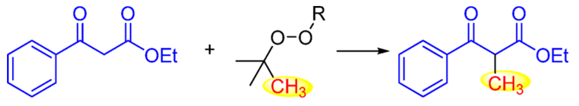
Table 1. Selected Results for Screening the Optimized Reaction Conditions[a]



1a **2** **3a**

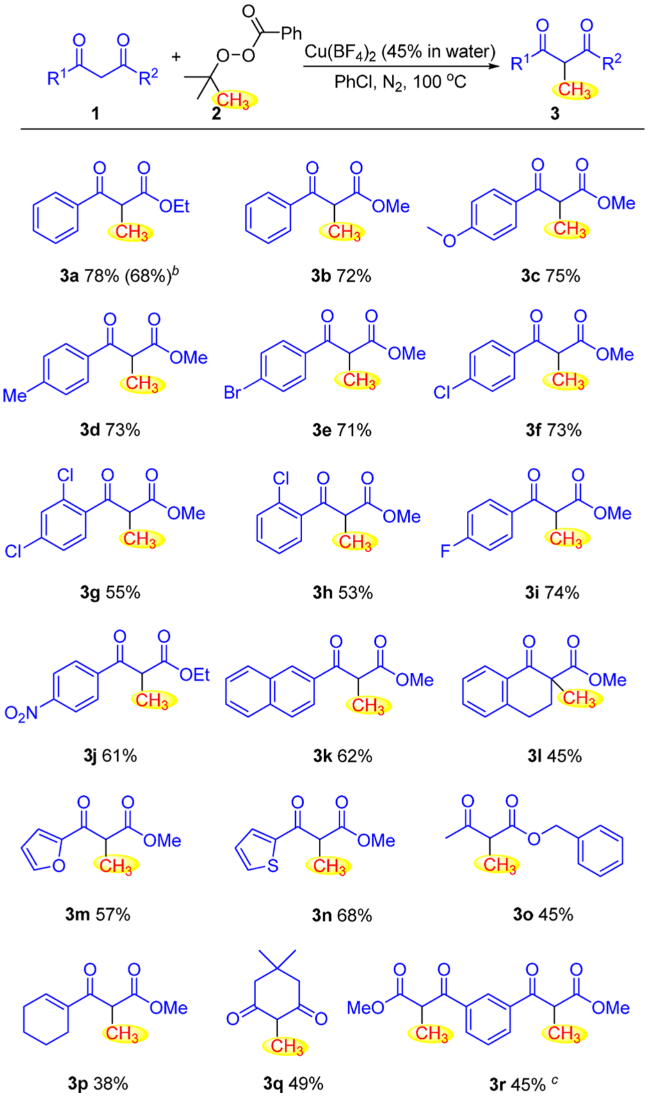
entry	catalyst	2	solvent	yield (%)
1	Bu_4NI	DTBP	PhCl	10
2	$FeCl_2$	DTBP	PhCl	22
3	$Fe_2(SO_4)_3$	DTBP	PhCl	<1
4	I_2	DTBP	PhCl	<1
5	$Cu(OTf)_2$	DTBP	PhCl	<1
6	CuF_2	DTBP	PhCl	<5
7	$Cu(BF_4)_2$	DTBP	PhCl	43
8	$Cu(BF_4)_2$	TBHP	PhCl	<1
9	$Cu(BF_4)_2$	DCP	PhCl	32
10	$Cu(BF_4)_2$	TBPB	PhCl	78
11	$Cu(OTf)_2$	TBPB	PhCl	70
12	$Cu(acac)_2$	TBPB	PhCl	32
13	$Cu(BF_4)_2$	TBPB	MeCN	<1
14	$Cu(BF_4)_2$	TBPB	DMF	<1
15	$Cu(BF_4)_2$	TBPB	THF	<5
16[b]	$Cu(BF_4)_2$	TBPB	PhCl	65
17[c]	$Cu(BF_4)_2$	TBPB	PhCl	60
18	–	TBPB	PhCl	<1

[a] Reaction conditions: **1a** (0.5 mmol), catalyst (5 mol %), and **2** (1.0 mmol, 2 equiv) (TBHP = *tert*-butyl hydroperoxide, DTBP = di-*tert*-butyl peroxide, TBPB = *tert*-butyl peroxybenzoate, DCP = dicumyl peroxide) in PhCl (3 mL) at 100 °C under N_2 for 2 h in a sealed tube. TBHP (70% in water), $Cu(BF_4)_2$ (45% in water). [b] PhCl (1 mL). [c] At 120 °C.

control experiment revealed that no product was detected in the absence of any catalyst (entry 18). Ultimately, the optimal reaction conditions were found to be the following: 1,3-dicarbonyl compound **1a** reacting with TBPB in chlorobenzene (3 mL) catalyzed by $Cu(BF_4)_2$ at 100 °C for 2 h.

Under the optimized reaction conditions, the substrate scope of 1,3-dicarbonyl compounds was studied, as shown in Scheme 2. As expected, almost all of the substrates reacted smoothly under the standard procedure. Methyl, ethyl, and benzyl esters were all well-tolerated. Generally, the reaction was not sensitive to the electronic property of the substituent on the phenyl ring, as both electron-donating and electron-withdrawing groups could provide the corresponding products in good yields (**3a**–**k**). Notably, the tolerance of halogens offers an opportunity for subsequent functionalizations to synthesize various α-methylated 1,3-dicarbonyl derivatives (**3e**–**i**). A substrate with an *ortho* substituent resulted in a lower yield, maybe because of steric hindrance (**3h**). Particularly, an α-substituted 1,3-dicarbonyl substrate also reacted smoothly to produce the quaternary carbon center (**3l**). To our delight, heteroaryl keto esters were also suitable substrates in this methylation process, and **3m** and **3n** were isolated in 57% and 68% yield, respectively. Generally, alkyl and alkenyl keto esters gave lower yields than their aryl keto ester analogues (**3o** and **3p**). Unfortunately, acyclic 1,3-diketone compounds failed to produce the desired product. On the contrary, a cyclic 1,3-diketone gave the α-methylated product in moderate yield (**3q**). A compound with two 1,3-dicarbonyl substituents also worked well, and the dual-methylated product was obtained in moderate yield (**3r**). To further evaluate the practicability of this procedure, the reaction was conducted on a 5 mmol scale, and the desired product **3a** was obtained in a comparable 68% yield.

Scheme 2. Scope of Dicarbonyl Compounds[a]

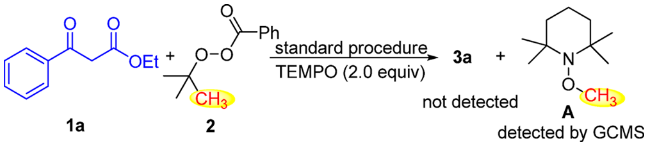


[a] Reaction conditions: **1** (0.5 mmol), $Cu(BF_4)_2$ (0.025 mmol, 5 mol %), and TBPB (1.0 mmol, 2 equiv) in PhCl (3 mL) at 100 °C under N_2 for 2 h in a sealed tube. Isolated yields are shown. [b] **1a** (5 mmol), $Cu(BF_4)_2$ (0.25 mmol, 5 mol %), and TBPB (10.0 mmol, 2 equiv) in PhCl (30 mL) at 100 °C under N_2 for 3 h in a sealed tube. [c] 4 equiv of TBPB was used.

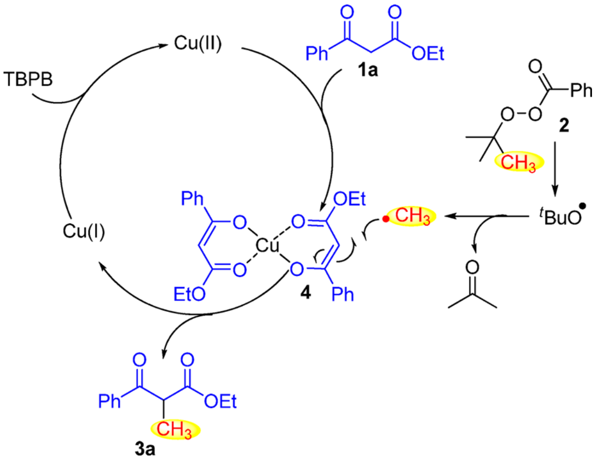
To gain some insight into the reaction mechanism, we investigated the reaction in the presence of the radical scavenger 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO). After the addition of 2.0 equiv of TEMPO into the standard reaction procedure, the methylation process was completely shut off and no **3a** was detected. In addition, the TEMPO–CH_3 adduct **A** was detected by GC–MS (Scheme 3; also see the Supporting Information), which could indicate that this methylation involves free radical intermediates.

A tentative mechanism for this novel α-methylation process by the reaction of 1,3-dicarbonyl compounds with TBPB is proposed in Scheme 4. First, thermally promoted homolytic cleavage of the radical initiator TBPB produces the *tert*-butoxy radical $^{t}BuO\cdot$, which converts to the methyl radical by releasing

Scheme 3. Radical Capture Experiment



Scheme 4. Proposed Mechanism



1 equiv of acetone.[26] Then the copper(II) reacts with the 1,3-dicarbonyl compound to generate copper enolate intermediate **4**. Finally, the methyl radical reacts with enolate **4** to produce the *α*-methylated 1,3-dicarbonyl compound **3** and regenerate Cu(I), which is oxidized to Cu(II) for further reactions. Alternatively, the reaction could be considered as a simple free-radical addition onto a double bond of a copper benzoylacetate.[42] At the current stage, neither of these two possible pathways could be thoroughly ruled out.

In conclusion, we have developed a direct and selective TBPB-promoted monomethylation of 1,3-dicarbonyl compounds in moderate to good yields. This procedure tolerates a series of functional groups and avoids the use of poisonous methyl iodide. Thus, it represents a facile and straightforward pathway leading to *α*-methyl 1,3-dicarbonyl compounds.

■ EXPERIMENTAL SECTION

General Information. All chemicals were used as received without further purification unless stated otherwise. ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a 300 or 400 MHz NMR spectrometer (75 or 100 MHz for ^{13}C). NMR chemical shifts (δ) are reported in parts per million (ppm) and were referenced to $CDCl_3$ (7.26 or 77.0 ppm) as the internal standard. Coupling constants (J) are given in hertz. Column chromatography was performed using EM Silica gel (300–400 mesh). IR spectra were recorded on a spectrometer using KBr discs.

Experimental Procedure for the Methylation of 1,3-Dicarbonyl Compounds. Under N_2, a Schlenk tube equipped with a stir bar was charged with 1,3-dicarbonyl compound **1** (0.5 mmol), $Cu(BF_4)_2$ (45% in water, 7 μL, 0.025 mmol, 5 mol %), TBPB (190 μL, 1.0 mmol, 2 equiv), and PhCl (3 mL) and sealed. The reaction mixture was stirred at 100 °C for 2 h. After completion of the reaction (as monitored by TLC), the solvent was concentrated in vacuum, and the residue was purified by flash column chromatography on silica gel with petroleum ether/EtOAc as the eluent to give the desired product.

Ethyl 2-Methyl-3-oxo-3-phenylpropanoate (3a).[17] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) gave **3a** (80.6 mg, 78% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.98–7.95 (m, 2H), 7.60–7.54 (m, 1H), 7.49–7.44 (m, 2H), 4.37 (q, J = 7.1 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 1.48 (d, J = 7.1 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 195.8, 170.8, 135.8, 133.4, 128.6, 128.5, 61.3, 48.3, 13.9, 13.7.

Methyl 2-Methyl-3-oxo-3-phenylpropanoate (3b).[43] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) gave **3b** (69.3 mg, 72% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98–7.95 (m, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.4 Hz, 2H), 4.41 (q, J = 7.1 Hz, 1H), 3.67 (s, 3H), 1.49 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 195.8, 171.3, 135.6, 133.5, 128.7, 128.5, 52.4, 48.0, 13.8.

Methyl 3-(4-Methoxyphenyl)-2-methyl-3-oxopropanoate (3c).[44] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:10) gave **3c** (83.0 mg, 75% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (d, J = 8.9 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 4.36 (q, J = 7.1 Hz, 1H), 3.86 (s, 3H), 3.67 (s, 3H), 1.47 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 194.3, 171.5, 163.8, 130.9, 128.6, 113.9, 55.5, 52.4, 47.7, 13.9.

Methyl 2-Methyl-3-oxo-3-(*p*-tolyl)propanoate (3d).[45] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:30) gave **3d** (75.4 mg, 73% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 4.40 (q, J = 7.1 Hz, 1H), 3.68 (s, 3H), 2.41 (s, 3H), 1.49 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 195.4, 171.4, 144.4, 133.1, 129.4, 128.7, 52.3, 47.8, 21.6, 13.8.

Methyl 3-(4-Bromophenyl)-2-methyl-3-oxopropanoate (3e).[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) gave **3e** (96.0 mg, 71% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82 (d, J = 8.6 Hz, 2H), 7.60 (d, J = 8.6 Hz, 2H), 4.33 (q, J = 7.1 Hz, 1H), 3.66 (s, 3H), 1.47 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 194.7, 170.9, 134.4, 132.0, 130.0, 128.7, 52.5, 48.0, 13.6.

Methyl 3-(4-Chlorophenyl)-2-methyl-3-oxopropanoate (3f).[47] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:30) gave **3f** (83.0 mg, 73% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.89 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 4.34 (q, J = 7.1 Hz, 1H), 3.65 (s, 3H), 1.46 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 194.5, 170.9, 139.9, 134.0, 129.9, 129.0, 52.5, 47.9, 13.6.

Methyl 3-(2,4-Dichlorophenyl)-2-methyl-3-oxopropanoate (3g). Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) gave **3g** (72.0 mg, 55% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.55 (s, 0.74H), 7.46–7.44 (m, 2.50H), 7.33–7.29 (m, 1.73H), 7.27–7.25 (m, 1.07H), 4.33 (q, J = 7.1 Hz, 0.93H), 3.84 (s, 2.34H), 3.68 (s, 3.00H), 1.58 (s, 2.34H), 1.47 (d, J = 7.1 Hz, 3.00H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 197.7, 173.6, 170.4, 166.2, 137.7, 136.6, 135.8, 133.4, 132.8, 132.0, 130.7, 130.4, 130.4, 129.7, 127.4, 127.2, 99.0, 52.5, 52.0, 51.6, 13.1, 12.1. MS (EI): 260 (M^+). HRMS (ESI-TOF): calcd for $C_{11}H_{11}Cl_2O_3$ $(M + H)^+$ 261.0080, found 261.0107. IR (KBr) ν 3090, 2953, 2853, 1747, 1709, 1657, 1626, 1583, 1555, 1439, 1348, 1273, 1238, 1159, 1103, 1061, 825, 812 cm^{-1}.

Methyl 3-(2-Chlorophenyl)-2-methyl-3-oxopropanoate (3h).[48] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:30) gave **3h** (60.1 mg, 53% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.59 (s, 0.38H), 7.47–7.30 (m, 5.71H), 4.35 (q, J = 7.1 Hz, 0.94H), 3.83 (s, 1.31H), 3.67 (s, 3.00H), 1.58 (s, 1.34H), 1.47 (d, J = 7.2 Hz, 3.00H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 199.0, 173.8, 170.6, 167.4, 138.4, 134.2, 132.4, 132.0, 130.9, 130.5, 130.4, 129.8, 129.8, 129.3, 127.0, 126.8, 98.6, 52.4, 51.9, 51.8, 13.2, 12.1.

Methyl 3-(4-Fluorophenyl)-2-methyl-3-oxopropanoate (3i). Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:30) gave **3i** (77.4 mg, 74% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02–7.97 (m, 2H), 7.16–7.10 (m, 2H), 4.35 (q, J = 7.1 Hz, 1H), 3.67 (s, 3H), 1.47 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 194.1, 171.1, 165.9 (d, J_{C-F} = 254.2 Hz), 132.1 (d, J_{C-F} = 3.0 Hz), 131.2 (d, J_{C-F} = 9.4 Hz), 115.9 (d, J_{C-F} = 21.8 Hz), 52.5, 48.0, 13.7. MS (EI): 210 (M^+). HRMS (ESI-TOF):

calcd for $C_{11}H_{12}FO_3$ $(M + H)^+$ 211.0765, found 211.0766. IR (KBr) ν 2993, 2955, 1747, 1688, 1682, 1599, 1506, 1456, 1435, 1329, 1302, 1286, 1231, 1159, 1101, 1084, 978, 951, 849, 606, 569 cm^{-1}.

Ethyl 2-Methyl-3-(4-nitrophenyl)-3-oxopropanoate (3j).[49] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:30) gave **3j** (76.9 mg, 61% yield) as a pale-yellow oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.29 (d, J = 8.8 Hz, 2H), 8.11 (d, J = 8.8 Hz, 2H), 4.36 (q, J = 7.0 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 1.49 (d, J = 7.0 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 194.3, 170.0, 150.3, 140.4, 129.5, 123.8, 61.7, 48.8, 13.8, 13.3.

Methyl 2-Methyl-3-(naphthalen-2-yl)-3-oxopropanoate (3k). Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:30) gave **3k** (74.9 mg, 62% yield) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.50 (s, 1H), 8.04−8.02 (m, 1H), 7.98−7.96 (m, 1H), 7.91−7.86 (m, 2H), 7.63−7.53 (m, 2H), 4.58 (q, J = 7.1 Hz, 1H), 3.69 (s, 3H), 1.56 (d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 195.7, 171.3, 135.7, 133.0, 132.4, 130.4, 129.6, 128.7, 128.6, 127.7, 126.9, 124.0, 52.5, 48.0, 13.9. MS (EI): 242 (M^+). HRMS (ESI-TOF): calcd for $C_{15}H_{15}O_3$ $(M + H)^+$ 243.1016, found 243.1018. IR (KBr) ν 3059, 2951, 2878, 2845, 1747, 1682, 1626, 1595, 1466, 1454, 1435, 1281, 1202, 933, 866, 825, 758, 476 cm^{-1}.

Methyl 2-Methyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (3l).[50] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:30) gave **3l** (48.9 mg, 45% yield) as a pale-yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.06−8.03 (m, 1H), 7.49−7.44 (m, 1H), 7.33−7.28 (m, 1H), 7.23−7.20 (m, 1H), 3.66 (s, 3H), 3.08−2.87 (m, 2H), 2.64−2.56 (m, 1H), 2.09−2.00 (m, 1H), 1.50 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 196.0, 173.4, 143.1, 133.5, 131.5, 128.7, 128.0, 126.7, 53.8, 52.4, 33.9, 25.9, 20.7.

Methyl 3-(Furan-2-yl)-2-methyl-3-oxopropanoate (3m).[48] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:20) gave **3m** (52.2 mg, 57% yield) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.63 (s, 1H), 7.30 (d, J = 3.6 Hz, 1H), 6.59−6.57 (m, 1H), 4.20 (q, J = 7.2 Hz, 1H), 3.71 (s, 3H), 1.48 (d, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 184.5, 170.8, 151.6, 146.9, 118.3, 112.5, 52.4, 48.2, 13.1.

Methyl 2-Methyl-3-oxo-3-(thiophen-2-yl)propanoate (3n).[51] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:20) gave **3n** (67.4 mg, 68% yield) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.77−7.76 (m, 1H), 7.68−7.67 (m, 1H), 7.14−7.12 (m, 1H), 4.24 (q, J = 7.1 Hz, 1H), 3.68 (s, 3H), 1.49 (d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 188.4, 170.7, 142.9, 134.7, 132.8, 128.3, 52.5, 49.2, 13.8.

Benzyl 2-Methyl-3-oxobutanoate (3o).[52] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:50) gave **3o** (46.6 mg, 45% yield) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.26 (m, 5H), 5.17 (s, 2H), 3.55 (q, J = 7.2 Hz, 1H), 2.19 (s, 3H), 1.36 (d, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 203.4, 170.3, 135.3, 128.5, 128.4, 128.2, 67.0, 53.5, 28.4, 12.6.

Methyl 3-(Cyclohex-1-en-1-yl)-2-methyl-3-oxopropanoate (3p). Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:50) gave **3p** (37.4 mg, 38% yield) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 6.93 (s, 1H), 4.11 (d, J = 7.0 Hz, 1H), 3.66 (s, 3H), 2.25−2.22 (m, 4H), 1.61−1.59 (m, 4H), 1.33 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 196.6, 171.7, 141.5, 138.3, 52.2, 46.3, 26.2, 23.2, 21.7, 21.3, 14.1. MS (EI): 196 (M^+). HRMS (ESI-TOF): calcd for $C_{11}H_{17}O_3$ $(M + H)^+$ 197.1172, found 197.1172. IR (KBr) ν 3312, 2937, 2862, 1744, 1666, 1636, 1450, 1435, 1383, 1215, 1088, 1072, 986, 901, 856 cm^{-1}

2,5,5-Trimethylcyclohexane-1,3-dione (3q). Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:10) gave **3q** (38.1 mg, 49% yield) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.35 (s, 1H), 3.68 (s, 3H), 2.25 (s, 2H), 2.19 (s, 2H), 1.05 (s, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 199.5, 177.0, 101.1, 55.6, 50.7, 42.6, 32.5, 28.2, 28.2. MS (EI): 154 (M^+). HRMS (ESI-TOF): calcd for $C_9H_{15}O_2$ $(M + H)^+$ 155.1067, found 155.1068. IR (KBr) ν 2958, 2941, 2872, 1661, 1609, 1373, 1225, 1153 cm^{-1}.

Dimethyl 3,3′-(1,3-Phenylene)bis(2-methyl-3-oxopropanoate) (3r). Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:5) gave **3r** (68.6 mg, 45% yield) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.54 (s, 1H), 8.17 (d, J = 7.8 Hz, 2H), 7.60 (t, J = 7.8 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 3.68 (s, 6H), 1.49 (d, J = 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 194.9, 170.8, 136.3, 136.2, 133.1, 133.1, 129.4, 129.4, 128.6, 128.5, 52.6, 48.1, 48.0, 13.6. MS (EI): 306 (M^+). HRMS (ESI-TOF): calcd for $C_{16}H_{19}O_6$ $(M + H)^+$ 307.1176, found 307.1180. IR (KBr) ν 3069, 2993, 2953, 2880, 2845, 1747, 1693, 1597, 1456, 1435, 1207, 1086, 945, 862, 679, 588 cm^{-1}.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Radical capture experiments and ^1H and ^{13}C NMR spectra of compounds **3a−r.** This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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