Mild Halogenation of Stabilized Ester Enolates by Cupric Halides

Xiao-Xin Shi and Li-Xin Dai*

Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Ling-Ling Road, Shanghai 200032, China

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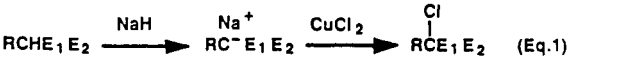
The reactions of various stabilized ester enolates of 2-keto, 2-(alkoxycarbonyl), 2-phosphoryl, and 2-(benzenesulfonyl) esters with cupric chloride or cupric bromide have been examined. The reactions lead to 2-halo esters in good to excellent yields under mild condition. Enolates which contain an unsaturated functionality such as a double bond, a triple bond, or an allylic or a benzylic moiety react with high chemoselectivity.

Halogenation in organic chemistry is a fundamental process for a wide scope of chemical transformations.[1] It remains, however, of considerable interest for the development of new methods. Carbonyl compounds can be halogenated at the α position by numerous reagents.[2] Direct α-halogenation of carbonyl compounds normally requires acidic and relatively vigorous reaction conditions.[3] The same result can be achieved in a mild and selective way through preformation of enolates, enol ethers, enol silanes, or enol esters. For halogenation of these enol derivatives of ketones several methods have been reported,[2b] but methods for the halogenation of ester enol derivatives are rare.[4] Metal halides which are effective for the halogenation of ketone enol compounds[5] have not been used as halogenating agents for ester enol compounds. Several papers have described halogenation of ketones, aldehydes, and ketone enol silanes with cupric halides,[6] but the corresponding halogenation of esters by cupric halides is relatively unknown.[7]

Now, we would like to report our results on the chlorination and bromination of stabilized sodium enolates of 2-carbonyl, 2-sulfonyl, or 2-phosphoryl esters with cupric chloride or cupric bromide.[8]

Table I. Reaction of Sodium Enolates with Cupric Chloride



1 2 3

entry	enolates (2) E_1	E_2	R	condns	time (h)	product 3 (yield, %)[a]
1	COOEt	COOEt	Me	DMSO, 40 °C	12	**3a** (88)
2	COOEt	COOEt	Me	DMF, 40 °C	12	**3a** (86)
3	COOEt	COOEt	H	DMSO, 40 °C	16	**3b** (90)
4	COOMe	COOMe	Bu	DMSO, 40 °C	12	**3c** (85)
5	COOMe	COOMe	Bn	DMSO, rt	10	**3d** (98)
6	COOMe	COOMe	Cn[b]	DMSO, rt	8	**3e** (97)
7	COOEt	COOEt	Pg[c]	DMSO, 40 °C	9	**3f** (84)
8	COOPn[d]	COOPn	Me	DMSO, 40 °C	10	**3g** (79)
9	COMe	COOEt	Me	DMSO, rt	10	**3h** (81)
10	COMe	COOEt	H	DMSO, rt	7	**3i** (77)[e]
11	COMe	COOEt	Bu	DMSO, rt	9	**3j** (85)
12	COMe	COOEt	Bn	DMSO, rt	5	**3k** (98)
13	COMe	COOEt	Pn	DMSO, rt	11	**3l** (86)
14	COMe	COOEt	Cn	DMSO, rt	4	**3m** (91)
15	COMe	COOEt	Pg	DMSO, rt	8	**3n** (85)
16[f]	$CO(CH_2)_n$	COOEt	$(CH_2)_{5-n}$	DMSO, rt	6	**3o** (79)
17	$PO(OEt)_2$	COOEt	Me	DMSO, 40 °C	16	**3p** (92)
18	SO_2Ph	COOEt	Me	DMSO, rt	15	**3q** (85)
19	COMe	COMe	Me	DMSO, rt	8	**3r** (70)
20	SO_2Ph	COPh	H	DMSO, rt	11	**3s** (92)

[a] Isolated yields by preparative TLC. [b] Cn = cinnamyl. [c] Pg = propargyl. [d] Pn = 3-propenyl. [e] Unstable on prolonged standing. [f] The substrate of entry 16 is 2-(ethoxycarbonyl)cyclohexanone.

Reaction of Sodium Ester Enolates with Anhydrous Cupric Chloride. Stabilized sodium ester enolates **2** were treated with 2 or 3 molar equiv of cupric halide at room temperature or 40 °C for 4–16 h; 2-chloro esters **3** were produced in good to excellent yields. The results are listed in Table I.

The choice of solvent was crucial. The use of DMSO or DMF was important. In THF, CH_2Cl_2, or other common nonprotic solvents the reaction was sluggish even at higher temperature, and yields were low.

Preformation of sodium enolates was also necessary. When diethyl 2-methylmalonate (**1a**) (but not the enolate) was directly treated with cupric chloride in DMSO or DMF, no reaction occurred and the starting malonate was recovered completely after heating for 6–8 h. The preformation of the sodium enolate of 1,3-diketones also accelerated the chlorination rate (Table I, entry 19) as compared with the direct chlorination of the same 1,3-diketone by Kosower's methods[6e,9] which required 2 days at room temperature.

The chlorination reaction was applicable to several types

(1) Trost, B. M.; Fleming, I. *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, 1991; Vol. 7, pp 120–123 and 527–540.

(2) (a) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; Chapter 8, pp 459–478. (b) Larock, R. C. *Comprehensive Organic Transformations*; VCH Publishers Inc.: New York, 1989; pp 369–380.

(3) (a) Clarke, H. T.; Taylor, E. R. *Organic Syntheses*; Wiley: New York, 1941; Collect. Vol. I, p 115. (b) Marvel, C. S.; Duvigneaud, V. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 93.

(4) (a) Rathke, M. W.; Lindert, A. *Tetrahedron Lett.* **1971**, 3995. (b) Stotter, P.; Hill, K. *Tetrahedron Lett.* **1972**, 4067. (c) Arnold, R. T.; Kulenovic, S. T. *J. Org. Chem.* **1978**, *43*, 3687. (d) Sasson, Y.; Webster, O. W. *J. Chem. Soc., Chem. Commun.* **1992**, *17*, 1200. (e) Evans, D. A.; Britton, T. C.; Ellman, J. A.; Dorow, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 4011.

(5) (a) Stefani, H. A.; Chieffi, A.; Comasseto, J. V. Organometallics **1991**, *10*, 1178. (b) Motohashi, S.; Satomi, M. *Synthesis* **1982**, 1021. (c) Ito, Y.; Nakatsuka, M.; Saegusa, T. *J. Org. Chem.* **1980**, *45*, 2022. (d) Rubottom, G. M.; Mott, R. C. *J. Org. Chem.* **1979**, *44*, 1731.

(6) (a) Doifode, K. B.; Marathy, M. G. *J. Org. Chem.* **1964**, *29*, 2025 and references cited therin. (b) King, L. C.; Ostrum, G. K. *J. Org. Chem.* **1964**, *29*, 3459. (c) Kosower, E. M.; Cole, W. J.; Wu, G-S.; Cardy, D. E.; Meisters, G. *J. Org. Chem.* **1963**, *28*, 630. (d) Lorenzini, A.; Walling, C. *J. Org. Chem.* **1967**, 32, 4008. (e) Kosower, E. M.; Wu, G-S. *J. Org. Chem.* **1963**, *28*, 633. (f) Louw, R. *J. Chem. Soc., Chem. Commun.* **1966**, 544. (g) Brown, H. C.; Rogic, M. M.; Rathke, M. W. *J. Am. Chem. Soc.* **1968**, *90*, 6218.

(7) The production of 2-bromo esters as side products from the Cu(II)-promoted dimerization of lithium ester enolates has been mentioned by Rathke et al.; see: Rathke, M. W.; Lindert, A. *J. Am. Chem. Soc.* **1971**, *93*, 4065.

(8) The reaction of 2-keto esters with NCS or NBS in the presence of a base gives 2-halodeacylation products. See: Mignani, G.; Morel, D.; Grass, F. *Tetrahedron Lett.* **1987**, *28*, 5505.

0022-3263/93/1958-4596$04.00/0

of stabilized ester enolates: malonate or 2-substituted malonates (Table I, entries 1–8), acyclic and cyclic keto esters (entries 9–16), a 2-phosphoryl carboxylate (entry 17), and a 2-(benzenesulfonyl) carboxylate (entry 18). The reaction of these ester enolates gave the corresponding 2-chloro products in good to excellent yields. The reaction was also applicable to a 1,3-diketone (entry 19) and a 2-benzenesulfonyl ketone (entry 20).[10] It must be pointed out that the chlorination reaction was not applicable to a 2-cyano ester or a malononitrile. None of the 2-halo product could be isolated from these reactions.

The reaction was also applicable to substrates containing an unsaturated functionality such as a double bond (entries 6, 13, 14), a triple bond (entries 7 and 15), or a benzene moiety (entries 5 and 12). Furthermore, the allyl group of an allyl ester (entry 8) was unchanged during the reaction with no chlorination occurring at the allylic position. The selective chlorination products **3e**, **3l**, and **3m** could be easily transformed into the dienoates by elimination of HCl,[11] and the products **3f** and **3n** could be used to prepare enynoates by elimination of HCl.[12]

Dimerization of lithium enolates of ketones or esters by 1 molar equiv cupric halide has been documented in the literature. 1,4-Diketones were obtained in high yields from lithium enolates of ketones with 1 molar equiv $CuCl_2$,[13] and substituted succinates were obtained from the lithium enolates of mono esters with 1 molar equiv $CuBr_2$.[7] In the present reaction, no dimerized product could be detected. The different reaction paths (halogenation vs dimerization) could not be attributed to different metal ions because the addition of lithium chloride in the present reaction system gave no dimerization product. Moreover, the sodium enolate of methyl phenyl ketone dimerized in 42% yield.[14] Probably the bulkiness of 2-substituents in our substrates blocked the dimerization path, in accord with the results of Rathke[7] who found only 25% of dimerization product could be obtained from the lithium enolate of ethyl isobutyrate. In this case he observed an increased amount of 2-bromo ester as compared with the result from ethyl propionate. In addition, an electron-withdrawing substituent adjacent to the ester group may retard dimerization.

In the present reaction more than 2 equiv of $CuCl_2$ must be used. When the amount of $CuCl_2$ was less than 2 equiv, the yield of 2-chloro ester was lowered. If only 1 equiv of $CuCl_2$ was used, almost no reaction occured. The necessity of 2 equiv of $CuCl_2$ supports the mechanism proposed by Kosower et al.[6e] involving two-electron reduction through the simultaneous single-electron transfer of two Cu(II) species (Scheme I). A free-radical mechanism seems less probable because neither radical scavenging by the intramolecular olefinic moiety nor intermolecular radical trapping with 2-methyl-2-nitrosopropane was effective.

Scheme I

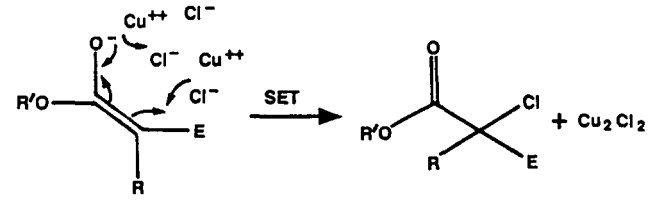
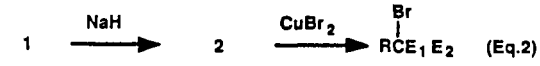


Table II. Reactions of Sodium Enolates with Cupric Bromide



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entry	enolates (2) E_1	E_2	R	condns	time (h)	product 4 (yield, %)[a]
1	COOEt	COOEt	H	DMSO, 40 °C	7	**4a** (90)
2	COOMe	COOMe	Bn	DMSO, rt	7	**4b** (97)
3	COOEt	COOEt	Pg[b]	DMSO, 40 °C	9	**4c** (76)
4	COMe	COOEt	H	DMSO, rt	5	**4d** (66)[c]
5	COMe	COOEt	Me	DMSO, rt	7	**4e** (67)
6	COMe	COOEt	Bn	DMSO, rt	5	**4f** (91)
7	COMe	COOEt	Pn[d]	DMSO, rt	6	**4g** (81)
8	COMe	COMe	Me	DMSO, rt	2	**4h** (69)
9	$PO(OEt)_2$	COOEt	Me	DMSO, 40 °C	16	**4i** (91)
10	SO_2Ph	COOEt	Me	DMSO, rt	15	**4j** (80)

[a] Isolated yields by preparative TLC. [b] Pg = propargyl. [c] Unstable on prolonged standing. [d] Pn = 3-propenyl.

For the chlorination of unsubstituted esters such as diethyl malonate or acetoacetate (Table I, entries 3 and 10), 2 equiv, not 3 equiv, of $CuCl_2$ must be used in order to avoid formation of the 2,2-dichloro ester.

Reaction of Sodium Ester Enolates with Anhydrous Cupric Bromide. Sodium ester enolates **2** were also treated with a 2 or 3 molar excess of cupric bromide in DMSO to give 2-bromo esters **4** in moderate to good yields. The results are listed in Table II.

Cupric bromide is more reactive than cupric chloride. The bromination rate was faster than that of the chlorination under the same conditions. For unsaturated substrates, 2-bromo esters were obtained in high yields without affecting the double or triple bond. Although the disproportionation of cupric bromide to cuprous bromide and bromine has been noted,[15] there was no bromination of the double bond or triple bond (Table II, entries 3 and 7).

In conclusion, because of its simplicity, high selectivity, and high yields, we believe that the method presented here will prove valuable for the synthesis of 2-chloro esters and 2-bromo esters with an electron-withdrawing group substituted at the C2 position. Moreover, the method is especialy useful for the synthesis of 2-halo esters containing an unsaturated functionality such as a double bond, a triple bond, or an allylic or benzylic moiety, which is sensitive to normal halogenation methods.

Experimental Section

Chemical shifts in ^1H NMR spectra were relative to tetramethylsilane. All solvents were distilled over calcium hydride. Anhydrous cupric chloride and bromide were prepared by heating at 100–120 °C on a vacuum line bearing a drying apparatus. Sodium hydride from Aldrich was washed with pentane and

(9) (a) Johnson, W. S.; Wiedhaup, K.; Brady, S. F.; Olson, G. L. *J. Am. Chem. Soc.* **1968**, *90*, 5277. (b) Johnson, W. S.; Li, T-T.; Faulkner, D. J.; Campbell, S. F. *J. Am. Chem. Soc.* **1968**, *90*, 6225.

(10) (a) Okada, R.; Yamakawa, K. *Tetrahedron Lett.* **1992**, 1455. (b) Satoh, T.; Onda, K.-I.; Yamakawa, K. *J. Org. Chem.* **1991**, *56*, 4129.

(11) (a) Backvall, J. E.; Ericsson, A. M.; Plobeck, N. A.; Juniunen, S. K. *Tetrahedron Lett.* **1992**, 131. (b) Trost, B. M.; Schmidt, T. J. *J. Am. Chem. Soc.* **1988**, *110*, 2303. (c) Ma, D.; Lin, Y.; Lu, X.; Yu, Y. *J. Org. Chem.* **1989**, *54*, 1105.

(12) (a) Beaudet, I.; Parrian, J. L.; Quintard, J.-P. *Tetrahedron Lett.* **1992**, 3647 and references cited therein. (b) Dabdoub, M. J.; Dabdoub, V. B.; Comasseto, J. V. *Tetrahedron Lett.* **1992**, 2261.

(13) Ito, Y.; Konoike, T.; Saegusa, T. *J. Am. Chem. Soc.* **1975**, *97*, 2912.

(14) Kauffmann, T.; Beissner, G.; Berg, H.; Koppelmann, E.; Legler, J.; Schonfelder, M. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 540.

(15) Castro, C. E.; Gaughan, E. J.; Owsley, D. C. *J. Org. Chem.* **1965**, *30*, 587.

dichloromethane in turn. All experiments were performed under a nitrogen atmosphere. The 2-alkyl-2-substituted esters 1 were prepared according to the literature procedure.[4b]

General Procedure. An ester (3 mmol) was dropped into a suspension of sodium hydride (90 mg, 80%, 3 mmol) in 15 mL of DMSO. After the mixture had stirred at 20 °C for 2 h, anhydrous cupric chloride (0.81–1.21 g, 6–9 mmol) or cupric bromide (1.34–2.01 g, 6–9 mmol) was added. The mixture was stirred at rt or 40 °C and analyzed by TLC. After the reaction was complete, 50 mL of dilute HCl (5%) was added, and then the aqueous solution was extracted three times with 60 mL of ether. The combined extracts were washed with 10 mL of water and dried over anhydrous magnesium sulfate. After removal of ether, the crude product was purified by preparative TLC. Some representative purified compounds are characterized as follows:

Dimethyl 2-benzyl-2-chloromalonate (3d): colorless oil; IR (neat) 2890, 1740, 1735, 1640 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 3.52 (s, 2H), 3.76 (s, 6H), 7.24 (m, 5H); MS *m/z* 259 (M^+ + 3, 12), 257 (M^+ + 1, 38), 189 (100). Anal. Calcd for $C_{12}H_{13}ClO_4$: C, 56.15; H, 5.10; Cl, 13.81. Found: C, 56.07; H, 5.12; Cl, 13.41.

Dimethyl 2-chloro-2-cinnamylmalonate (3e): colorless oil; mixture of trans and cis isomers (trans:cis = 64:36); IR (neat) 2900, 2800, 1735 (br), 1480, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.89 and 3.20 (2d, 2H, *J* = 6.7 and 6.7 Hz, two isomers), 3.78 and 3.86 (2s, 6H, two isomers), 6.04–6.30 (m, 1H), 6.46–6.63 (m, 1H), 7.36 (m, 5H); MS *m/z* 285 (M^+ + 3, 0.2), 284 (M^+ + 2, 0.3), 283 (M^+ + 1, 0.7), 282 (M^+, 0.6), 117 (100). Anal. Calcd for $C_{14}H_{15}ClO_4$: C, 59.48; H, 5.35; Cl, 12.54. Found: C, 59.26; H, 5.55; Cl, 12.20.

Diethyl 2-chloro-2-propargylmalonate (3f): colorless oil; IR (neat) 3250, 2900, 1765, 1740, 1440 cm^{-1}; ^1H NMR (C_6D_6) δ 0.94 (t, 6H, *J* = 7.0 Hz), 1.92 (t, 1H, *J* = 2.5 Hz), 3.31 (d, 2H, *J* = 2.5 Hz), 4.01 (q, 4H, *J* = 7.0 Hz); MS *m/z* 235 (M^+ + 3, 2), 233 (M^+ + 1, 7), 133 (100). Anal. Calcd for $C_{10}H_{13}ClO_4$: C, 51.62; H, 5.63; Cl, 15.24. Found: C, 51.51; H, 5.79; Cl, 15.01.

Di-3-propenyl 2-chloro-2-methylmalonate (3g): colorless oil; IR (neat) 2900, 2800, 1740, 1640, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.95 (s, 3H), 4.75 (d, 4H, *J* = 6.0 Hz), 5.39 (m, 4H), 5.71 (m, 2H); MS *m/z* 235 (M^+ + 3, 9), 233 (M^+ + 1, 22), 43 (100). Anal. Calcd for $C_{10}H_{13}ClO_4$: C, 51.62; H, 5.63; Cl, 15.24. Found: C, 51.30; H, 5.64; Cl, 14.90.

Ethyl 2-benzyl-2-chloroacetoacetate (3k): colorless oil; IR (neat) 2900, 1730, 1705, 1600, 1480, 1440 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 1.21 (t, 3H, *J* = 7.0 Hz), 2.25 (s, 3H), 3.20 (s, 2H), 4.22 (q, 2H, *J* = 7.0 Hz), 7.24 (m, 5H); MS *m/z* 257 (M^+ + 3, 13), 255 (M^+ + 1, 45), 43 (100). Anal. Calcd for $C_{13}H_{15}ClO_3$: C, 61.30; H, 5.94; Cl, 13.92. Found: C, 61.67; H, 5.89; Cl, 13.70.

Ethyl 2-chloro-2-(3-propenyl)acetoacetate (3l): colorless oil; IR (neat) 2900, 1740, 1710, 1630, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (t, 3H, *J* = 7.0 Hz), 2.35 (s, 3H), 2.93 (dd, 2H, *J* = 6.0, 4.5 Hz), 4.30 (q, 2H, *J* = 7.0 Hz), 5.21 (m, 2H), 5.80 (m, 1H); MS *m/z* 207 (M^+ + 3, 3), 205 (M^+ + 1, 9), 44 (100). Anal. Calcd for $C_9H_{13}ClO_3$: C, 52.82; H, 6.40; Cl, 17.32. Found: C, 51.49; H, 6.60; Cl, 17.03.

Ethyl 2-chloro-2-cinnamylacetoacetate (3m): pale yellow oil; mixture of trans and cis isomers (trans:cis = 81:19). IR (neat) 2950, 2900, 1740, 1720, 1590, 1480, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 and 1.31 (2t, 3H, *J* = 7.0 and 7.0 Hz, two isomers), 2.41 (s, 3H), 3.13 (m, 2H), 4.19 and 4.32 (2q, 2H, *J* = 7.0 and 7.0 Hz, two isomers), 6.22 (m, 1H), 6.54 (m, 1H), 7.36 (m, 5H); MS *m/z* 282 (M^+ + 2, 0.1), 280 (M^+, 0.5), 43 (100). Anal. Calcd for $C_{15}H_{17}ClO_3$: C, 64.17; H, 6.10; Cl, 12.63. Found: C, 64.01; H, 6.15; Cl, 12.29.

Ethyl 2-chloro-2-propargylacetoacetate (3n): colorless oil; IR (neat) 3200, 2900, 1745, 1730, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (t, 3H, *J* = 7.2 Hz), 2.12 (t, 1H, *J* = 2.6 Hz), 2.40 (s, 3H), 3.09 (m, 2H), 4.30 (q, 2H, *J* = 7.2 Hz); MS *m/z* 205 (M^+ + 3, 5), 203 (M^+ + 1, 16), 44 (100). Anal. Calcd for $C_9H_{11}ClO_3$: C, 53.35; H, 5.47; Cl, 17.50. Found: C, 53.25; H, 5.49; Cl, 17.21.

Dimethyl 2-benzyl-2-bromomalonate (4b): colorless oil; IR (neat) 2950, 2900, 1745, 1730, 1590, 1480, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.64 (s, 2H), 3.77 (s, 6H), 7.26 (m, 5H); MS *m/z* 303 (M^+ + 2, 4), 301 (M^+, 5), 91 (100). Anal. Calcd for $C_{12}H_{13}BrO_4$: C, 47.86; H, 4.35; Br, 26.53. Found: C, 47.48; H, 4.39; Br, 26.30.

Diethyl 2-bromo-2-propargylmalonate (4c): colorless oil; IR (neat) 3250, 2950, 1760, 1740, 1460, 1440, 1410 cm^{-1}; ^1H NMR (C_6D_6) δ 0.93 (t, 6H, *J* = 7.0 Hz), 1.93 (t, 1H, *J* = 2.5 Hz), 3.41 (d, 2H, *J* = 2.5 Hz), 4.01 (q, 4H, *J* = 7.0 Hz); MS *m/z* 279 (M^+ + 2, 25), 277 (M^+, 25), 151 (100). Anal. Calcd for $C_{10}H_{13}BrO_4$: C, 43.34; H, 4.73; Br, 28.83. Found: C, 43.03; H, 4.79; Br, 28.49.

Ethyl 2-benzyl-2-bromoacetoacetate (4f): colorless oil; IR (neat) 2920, 1735, 1715, 1590, 1490, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (t, 3H, *J* = 7.0 Hz), 2.35 (s, 3H), 3.52 (d, 1H, *J* = 14.0 Hz), 3.65 (d, 1H, *J* = 14.0 Hz), 4.21 (t, 2H, *J* = 7.0 Hz), 7.28 (m, 5H); MS *m/z* 301 (M^+ + 2, 3), 299 (M^+, 3), 43 (100). Anal. Calcd for $C_{13}H_{15}BrO_3$: C, 52.19; H, 5.05; Br, 26.71. Found: C, 52.37; H, 5.36; Br, 26.36.

Ethyl 2-bromo-2-(3-propenyl)acetoacetate (4g): colorless oil; IR (neat) 2900, 1740, 1715, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (t, 3H, *J* = 7.0 Hz), 2.40 (s, 3H), 3.00 (m, 2H), 4.29 (q, 2H, *J* = 7.0 Hz), 5.13–5.26 (m, 2H), 5.70–5.92 (m, 1H); MS *m/z* 251 (M^+ + 2, 21), 249 (M^+, 19), 43 (100). Anal. Calcd for $C_9H_{13}BrO_3$: C, 43.40; H, 5.26; Br, 32.08. Found: C, 43.39; H, 5.28; Br, 32.30.

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Supplementary Material Available: ^1H NMR, IR, and MS spectral data for compounds **3a–c,h–j,o–s** and **4a,d,e,h–j** and elemental analysis data for compounds **3c,j,o–q,s** and **4i,j** (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.