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Copper(I)-Promoted Synthesis of Chloromethyl Ketones from Trichloromethyl Carbinols

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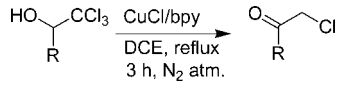

Reaction of several trichloromethyl carbinols with 2 equiv of CuCl/bpy in refluxing DCE for 3 h afforded chloromethyl ketones in excellent yield by 1,2-H shift in the copper-chlorocarbenoid intermediate.

Chloromethyl ketones are versatile synthetic intermediates for the preparation of compounds of considerable importance in medicine and agriculture.[1] Some chloromethyl ketones are known to be enzyme inhibitors and affinity labeling agents.[2] Therefore, numerous methods have been reported for the synthesis of chloromethyl ketones. A majority of these methods employ direct chlorination of ketones with elemental chlorine or various inorganic or organic chlorinating agents.[1a,3] However, these methods are not regiospecific and are not suitable for the preparation of chloromethyl ketones from methyl alkyl ketones having a hydrogen atom at the α′-carbon atom because chlorination occurs predominantly at the more substituted α′-carbon atom. Some of these methods also suffer from the problem of overchlorination,[3g–i,k,l,n] nuclear chlorination of activated aromatic ring,[3g–i] failure with deactivated aromatic ring,[3g,j,m] or incompatibility with olefinic bonds[3b] and acid-sensitive or easily oxidizable groups.[3i] Chlorination of the kinetic enolates or the corresponding silyl enol ethers provided a solution to the regiochemical problem to some extent.[4] Notwithstanding these limitations, a few of these reagents have been found to be useful in enantioselective α-chlorination of carbonyl compounds.[5]

There are only a few methods available for regiospecific synthesis of chloromethyl ketones. Some of these methods employ introduction of a chloroacetyl group through Friedel−Crafts reaction[1d,h] with activated aromatics or organometallic reactions.[1f,6] In another approach, a chloromethyl group has been linked to a carbonyl group by reaction of a suitable carbonyl compound with a carbenoid reagent. This approach includes the classical reaction of acid chlorides with CH_2N_2/HCl, which has been found to be very useful for the synthesis of bioactive chloromethyl ketones derived from sugars,[1i] amino acids, and peptides;[2a,b] a practical alternative involves the reaction of esters with $LiCH_2Cl$[7] or $CH_2{=}S(O)Me_2$/HCl[8] without the use of hazardous diazomethane, the reaction of aldehydes with $LiCCl_2S(O)Ph$[9] or $LiCHCl_2$,[10] and the reaction of aldehydes[11] or esters[9] with LiCHClS(O)Ph. Several aryl and heteroaryl chloromethyl ketones have recently been obtained by the reaction of dichloroacetaldehyde diethyl acetal with aryl- or heteroaryllithiums followed by acid hydrolysis of the products 1-aryl/heteroaryl-1-ethoxy-2-chloroethenes.[12] However, most of these reactions

(1) (a) DeKimpe, N.; Verhe, R. In *The Chemistry of α-Haloketones, α-Haloaldehydes and α-Haloimines*; Patai, S., Ed.; Wiley: Chichester, UK, 1988; pp 1−119. For some recent references, see: (b) Fan, X.; Song, Y.-L.; Long, Y.-Q. *Org. Proc. Res. Dev.* **2008**, *12*, 69–75. (c) Malkov, A. V.; Stoncius, S.; Kocovsky, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 3722–3724. (d) Gerby, B.; Boumendjel, A.; Blanc, M.; Bringuier, P. P.; Champelovier, P.; Fortune, A.; Ronot, X.; Boutonnat, J. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 208–213. (e) Yu, L.-T.; Ho, M.-T.; Chang, C.-Y.; Yang, T.-K. *Tetrahedron: Asymmetry* **2007**, *18*, 949–962. (f) Tanis, S. P.; Evans, B. R.; Nieman, J. A.; Parker, T. T.; Taylor, W. D.; Heasley, S. E.; Herrinton, P. M.; Perrault, W. R.; Hohler, R. A.; Dolak, L. A.; Hester, M. R.; Seest, E. P. *Tetrahedron: Asymmetry* **2006**, *17*, 2154–2182. (g) Kojima, S.; Suzuki, M.; Watanabe, A.; Ohkata, K. *Tetrahedron Lett.* **2006**, *47*, 9061–9065. (h) Wei, Q.-L.; Zhang, S.-S.; Gao, J.; Li, W.; Xu, L.-Z.; Yu, Z.-G. *Bioorg. Med. Chem.* **2006**, *14*, 7146–7153. (i) Adamo, M. F. A.; Adlington, R. M.; Baldwin, J. E.; Day, A. L. *Tetrahedron* **2004**, *60*, 841–849. (j) Hamada, T.; Torii, T.; Izawa, K.; Ikariya, T. *Tetrahedron* **2004**, *60*, 7411–7417. (k) Yasuda, M.; Tsuji, S.; Shigeyoshi, Y.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 7440–7447.

(2) For reviews, see: (a) Kam, C.-M.; Hudig, D.; Powers, J. C. *Biochim. Biophys. Acta* **2000**, *1477*, 307–323. (b) Willams, E. B.; Mann, K. G. *Methods Enzymol.* **1993**, *222*, 503–513. For a recent reference, see: (c) Conde, S.; Perez, D. I.; Martinez, A.; Perez, C.; Moreno, F. J. *J. Med. Chem.* **2003**, *46*, 4631–4633.

(3) For reviews, see: (a) Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; Wiley-VCH: New York, 1999; pp 709−727. (b) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin/Cummings: San Francisco, 1972; pp 459−478. For some other references, see: (c) Xu, Z.; Zhang, D.; Zou, X. *Synth. Commun.* **2006**, *36*, 255–258. (1,3-dichloro-5,5-dimethylhydantoin/PTS). (d) Lee, J. C.; Park, H. J. *Synth. Commun.* **2006**, *36*, 777–780. ($AlCl_3$/urea-hydrogen peroxide/ionic liquid). (e) Lee, J. C.; Park, J. Y.; Yoon, S. Y.; Bae, Y. H.; Lee, S. J. *Tetrahedron Lett.* **2004**, *45*, 191–193. (PhI(OTs)(OH)/$MgCl_2$/microwave). (f) Lee, J. C.; Bae, Y. H.; Chang, S.-K. *Bull. Korean Chem. Soc.* **2003**, *24*, 407–408. (NCS/PTS). (g) Yakabe, S.; Hirano, M.; Morimoto, T. *Synth. Commun.* **1998**, *28*, 131–138. [$NaOCl_2$/moist alumina/cat. $Mn(acac)_3$]. (h) Lee, J. G.; Park, I. S.; Seo, J. W. *Bull. Korean Chem. Soc.* **1995**, *16*, 349–355. (SeO_2/Me_3SiCl). (i) Kim, H. J.; Kim, H. R.; Kim, J. N.; Ryu, E. K. *Bull. Korean Chem. Soc.* **1990**, *11*, 184–186. (*m*-CPBA/HCl/DMF). (j) Kajigaeshi, S.; Kakinami, T.; Moriwaki, M.; Fujisaki, S.; Maeno, K.; Okamoto, T. *Synthesis* **1988**, 545–546. (benzyltrimethylammonium dichloroiodate). (k) Fraser, R. R.; Kong, F. *Synth. Commun.* **1988**, *18*, 1071–1077. (Me_3SiCl/DMSO/cat. Bu_4NBr). (l) Hiegel, G. A.; Peyton, K. B. *Synth. Commun.* **1985**, *15*, 385–392. (trichloroisocyanuric acid/$BF_3{\cdot}Et_2O$/AcOH). (m) Guy, A.; Lemaire, M.; Guette, J.-P. *Synthesis* **1982**, 1018–1020. (hexachloro-2,4-cyclohexadienone). (n) Keana, J. F. W.; Schumaker, R. R. *Tetrahedron* **1970**, *26*, 5191–5194. (NCS/Schiffs base with ethanol amine/acid hydrolysis)

(4) (a) Brummond, K. M.; Gesenberg, K. D. *Tetrahedron Lett.* **1999**, *40*, 2231–2234. (PTS/LDA/−78 °C). (b) Vaz, A. D. N.; Schoellmann, G. *J. Org. Chem.* **1984**, *49*, 1286–1288. (NCS/LDA/0 to−70 °C). (c) Ito, Y.; Nakatsuka, M.; Saegusa, T. *J. Org. Chem.* **1980**, *45*, 2022–2024. (silyl enol ethers/$CuCl_2$)

(5) For recent reviews, see: (a) Marigo, M.; Jorgensen, K. *A. Chem. Commun.* **2006**, 2001–2011. (b) Guillena, G.; Ramon, D. J. *Tetrahedron: Asymmetry* **2006**, *17*, 1465–1492. (c) Oestreich, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 2324–2327. (d) Lectka, T. *Eur. J. Org. Chem.* **2005**, 475–479.

(6) (a) Rosen, J.; Steinhuebel, D.; Palucki, M.; Davies, I. *Org. Lett.* **2007**, *9*, 667–669. (ArZnX/cat. $CuCl_2$/−65 °C). (b) Hirao, T.; Misu, D.; Yao, K.; Agawa, T. *Tetrahedron Lett.* **1986**, *27*, 929–932. (organovanadium/−78 °C). (c) Bunnett, J. F.; Tarbell, D. S. *J. Am. Chem. Soc.* **1945**, *67*, 944–1946. (organovanadium/0 °C)

(7) Onishi, T.; Nakano, T.; Hirose, N.; Nakazawa, M.; Izawa, K *Tetrahedron Lett.* **2001**, *41*, 5887–5890.

(8) Wang, D.; Schwinden, M. D.; Radesca, L.; Patel, B.; Kronenthal, D.; Huang, M.-H.; Nugent, W. A. *J. Org. Chem.* **2004**, *69*, 1629–1633.

(9) Satoh, S.; Mizu, T.; Kawashima, T.; Yamakawa, K. *Tetrahedron* **1995**, *51*, 703–710.

(10) Taguchi, H.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1592–1595.

(11) Reutrakul, V.; Kanghae, W. *Tetrahedron Lett.* **1977**, 1225–1226.

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are performed at subzero temperatures, and the highly basic organometallic reaction conditions used are not apparently compatible with many common functional groups. An oxidative method involving oxidation of vinyl chlorides with NaOCl, which requires acetic acid as a cosolvent, afforded chloromethyl ketones in good yields.[13]

Trichloromethyl carbinols are easily accessible useful synthons for the synthesis of a variety of organic compounds.[14] These have been used to prepare some chloromethyl ketones in four steps under rather harsh reaction conditions.[15] A few aliphatic trichloromethyl carbinols have been reported to react with 2 equiv of BuLi at −78 °C followed by acidification to give α-chloro ketones exclusively[10] or as the major product along with α-chloroaldehydes[16] in low to moderate total yields. The products have been proposed to arise by 1,2-H and alkyl shift, respectively, in the lithium chlorocarbenoid intermediate. Recently, Mioskowski and Falck et al.[17] reported the conversion of two trichloromethyl carbinols to chloromethyl ketones by reaction with $CrCl_2$ in anhydrous THF and proposed a mechanism involving 1,2-H shift in chromium chlorocarbenoid intermediate for the formation of the products. However, the scope of the reaction has not been thoroughly investigated. Since $CrCl_2$ has considerably high reducing ability,[18] easily reducible groups, such as a nitro group may not be tolerated under the conditions. Furthermore, apparently a large excess (6 equiv) of $CrCl_2$ was used in the reaction which seems to be a delicate reaction, quite sensitive to the reaction conditions.[19] Therefore, there is still a need for a simple regiospecific method of general applicability for the synthesis of chloromethyl ketones.

We have recently observed that CuCl/bpy with a lower reducing power shows considerable similarity with $CrCl_2$ toward its reaction with trichloroethyl alkyl ethers.[20] Therefore, it was considered worthwhile to examine the reaction of trichloromethyl carbinols with CuCl/bpy with a view to develop a simple method for regiospecific synthesis of chloromethyl ketones. Thus, the trichloromethyl carbinols **1** (Scheme 1) were easily prepared by the reaction of aldehydes with chloroform in the presence of DBU[21] or with trichloroacetic acid in DMSO as reported in the literature.[22] Reaction of the trichloromethyl carbinols **1** with an equimolar mixture of CuCl and bpy (2 equiv each) in refluxing DCE under a nitrogen atmosphere for 3 h

SCHEME 1. Reaction of Trichloromethyl Carbinols 1 with CuCl/bpy

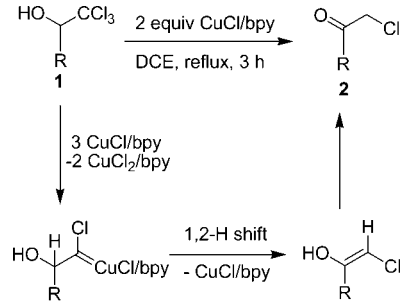


TABLE 1. Copper(I)/bpy-Promoted Synthesis of Chloromethyl Ketones 2 from Trichloromethyl Carbinols 1[a]

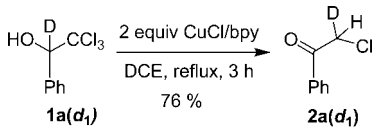
		isolated yield (%)		
entry	R	**1**[b]	**2**[c]	overall **2**[d]
1	**a**: C_6H_5	95	96	91
2	**b**: 2-ClC_6H_4	90	95	86
3	**c**: 4-ClC_6H_4	95	93	88
4	**d**: 3-BrC_6H_4	96	84	81
5	**e**: 4-BrC_6H_4	98	92	90
6	**f**: 4-$NO_2C_6H_4$	52	89	46
7	**g**: 3-MeC_6H_4	94	96	90
8	**h**: 4-MeC_6H_4	90	92	83
9	**i**: 4-$MeOC_6H_4$	95	90	86
10	**j**: 2-$MeOC_6H_4$	92	93	86
11	k: 3,4-$(MeO)_2C_6H_3$	92	96	88
12	**l**: 2-$(CH_2{=}CHCH_2O)C_6H_4$	79	82	65
13	**m**: 4-$C_2H_5OOCCH_2OC_6H_4$	88	91	80
14	**n**: *E*-PhCH=CH	60	91	55
15	**o**: $PhCH_2CH_2$	63[e]	84[f]	53
16	**p**: Ph(Me)CH	79	97	77
17	**q**: *n*-C_6H_{13}	86	92[f]	79
18	**r**: 2-furanyl	86	95	82
19	**s**: 2-pyridyl	89	94	84

[a] Unless otherwise indicated, all the reactions were performed at 0.005 mol scale in refluxing DCE under a nitrogen atmosphere for 3 h. [b] From aldehyde. [c] One step, from **1**. [d] Two step, from aldehyde. [e] From **1n**. [f] Reaction time 5 h.

followed by filtration, evaporation, and rapid chromatography on a short-path silica gel column afforded the chloromethyl ketones **2** in excellent yields (Table 1). The two-step overall yields of the products from aldehydes were also found to be generally high, and the relatively lower overall yields in some cases (entries 6, 14, and 15) are primarily due to exceptions in the preparation of trichloromethyl carbinols. All of the products have been characterized by spectroscopic analysis and comparison with the reported data. The reaction occurs at almost neutral pH and innocuous redox conditions. The present method appears to be quite general, being applicable to the synthesis of aryl (entries 1−13), alkyl (entries 15−17), heteroaryl (entries 18 and 19), and conjugated (entry 14) chloromethyl ketones. Entries 15 and 16 show the applicability of the method to the synthesis of chloromethyl alkyl ketones having even a more reactive α′-primary or secondary benzylic hydrogen. The method works well for the synthesis of α-chloroacetophenones with both electron-withdrawing (entries 2−6) and electron donating (entries 7−13) substituents on the benzene ring. Activated aromatic ring (entries 8−11) and a number of common functional groups, such as a conjugated (entry 14) or isolated olefinic bond (entry 12), nitro (entry 6), ester (entry 13), nuclear chloro or bromo (entries 2−5), and allyl ether groups (entry 12) survive the reaction conditions. A nitro group, which

(12) Yoshimatsu, M.; Sakai, M.; Moriura, E. *Eur. J. Org. Chem.* **2007**, 498–507.
(13) VanBrunt, M. P.; Ambenge, R. O.; Weinreb, S. M. *J. Org. Chem.* **2003**, *68*, 3323–3326.
(14) For a review, see: Reeve, W. *Synthesis* **1971**, 131–138.
(15) Shono, T.; Kise, N.; Yamazaki, A.; Ohmizu, H. *Tetrahedron Lett.* **1982**, *23*, 1609–1612.
(16) Villieras, J.; Bacquet, C.; Normant, J. F. *J. Organomet. Chem.* **1972**, *40*, C1−C4.
(17) Bejot, R.; Tisserand, S.; Li, D. R.; Falck, J. R.; Mioskowski, C *Tetrahedron Lett.* **2007**, *48*, 3855–3858.
(18) For reviews, see: (a) Ho, T.-L. *Synthesis* **1979**, 1–20. (b) Hanson, J. R. *Synthesis* **1974**, 1–8. For a recent reference, see: (c) Hari, A.; Miller, B. *Tetrahedron Lett.* **1999**, *40*, 245–248.
(19) It forms (*Z*)-1-chloroalkenes along with other products in the presence of water. Trichloromethylcarbinols were reported earlier also to give (*Z*)-1-chloroalkenes with $CrCl_2$ in anhydrous or aqueous THF and aq DMF, see: (a) Baati, R.; Barma, D. K.; Falck, J. R.; Mioskowski, C. *Tetrahedron Lett.* **2002**, *43*, 2183–2185. (b) Wolf, R.; Steckhan, E. *J. Chem. Soc., Perkin Trans. 1* **1986**, 733–739.
(20) Similar to $CrCl_2$: (a) Bejot, R.; Tisserand, S.; Reddy, L. M.; Barma, D. K.; Baati, R.; Falck, J. R. *Mioskowski, C. Angew. Chem. Int. Ed.* **2005**, *44*, 2008–2011. CuCl/bpy also promotes 1,2-H shift in the copper−chlorocarbenoid intermediate in 2,2,2-trichloroethyl alkyl ethers to form 1-alkoxy-2-chloroethenes: (b) Ram, R. N.; Manoj, T. P. *Org. Lett.* **2008**, *10*, 2243–2246.
(21) Aggarwal, V. K.; Mereu, A. *J. Org. Chem.* **2000**, *65*, 7211–7212.
(22) Atkins, P. J.; Gold, V.; Wassef, W. N. *Chem. Commum.* **1983**, 283–284.

SCHEME 2. Reaction of 2,2,2-Trichloro-1-deuterio-1-phenylethanol 1a(d_1) with CuCl/bpy



1a(d_1) **2a(d_1)**

deactivates the benzene ring in Friedel−Crafts acylation and is also known to have inhibitory effect in some of the reported methods,[3g,j,m] does not appear to affect the reaction adversely (entry 6). α,β-Unsaturated chloromethyl ketones, which are known to be difficult candidates to prepare,[3k,6b] can be obtained by this method in acceptable overall yield (entry 14). However, the reaction of trichloromethyl carbinol derived from 4-*N*,*N*-dimethylaminobenzaldehyde was not clean. The reaction mixture showed continuous streak on TLC and could not be purified by column chromatography. Probably the instability of the expected product, if formed, under the conditions due to the presence of mutually incompatible nucleophilic dimethylamino and electrophilic reactive chloromethyl ketone functionalities would render its isolation and purification difficult.

A mechanism involving 1,2-H shift in a copper-chlorocarbenoid intermediate has been proposed for the reaction as shown in Scheme 1. The mechanism is supported by our earlier observations on the CuCl/bpy-promoted 1,2-H shift in trichloroethyl ethers to afford 1-alkoxy-2-chloroethenes[20] as well as by the formation of α-deuterio-α-chloroacetophenone **2a(d_1)** from the reaction of 2,2,2-trichloro-1-deuterio-1-phenylethanol **1a(d_1)** under similar conditions (Scheme 2).

In conclusion, the present work describes a simple, convenient, regiospecific, efficient, and fairly general method for the preparation of chloromethyl ketones. It is free from many complications associated with several of the reported methods, is complementary to the oxidative methods and provides a useful addition to the existing methods for the preparation of chloromethyl ketones.

Experimental Section

Typical Procedure for the Synthesis of Chloromethyl Ketones: 4-Nitrophenacyl Chloride 2f. In a two-necked, flame-dried, round-bottomed flask equipped with a reflux condenser and rubber septum was created an oxygen-free nitrogen atmosphere by Schlenk technique. The flask was charged with 2,2,2-trichloro-1-(4-nitrophenyl)ethanol **1f** (1.35 g, 0.005 mol), CuCl (1.00 g, 0.01 mol), and dry 1,2-dichloroethane (DCE) (10 mL). The contents of the flask were stirred with a magnetic bar, and a solution of 2,2′-bipyridine (bpy) (1.56 g, 0.01 mol) in DCE (10 mL) was injected into the flask through the rubber septum. The reaction mixture was heated at reflux with stirring, and the progress of the reaction was monitored by TLC. After the completion of the reaction (3 h), the reaction mixture was cooled and filtered through a Celite pad, and the filtrate was evaporated under reduced pressure. The crude product was purified by flash column chromatography on a short silica gel (60−120 mesh) column using a solution of 10% ethyl acetate in hexane as the solvent for elution to give pure 4-nitrophenacyl chloride **2f** (0.89 g, 89%) as a yellow solid: mp 89 °C (lit.[23] mp 87−89.5 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.73 (s, 2H), 8.15 (d, J = 8.7 Hz, 2H), 8.36 (d, J = 8.7 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.6 (CH_2), 124.1 (CH), 129.7 (CH), 138.5 (C), 150.7 (C), 189.9 (C) ppm; IR (KBr) 3112 (m), 3049 (w), 2945 (m), 2856 (w), 1706 (s), 1600 (m), 1520 (s), 1341 (s), 1203 (s), 1106 (w), 999 (m), 849 (s), 771 (s), 747 (s), 679 (m), 557 (w), 500 (w) cm^{-1}.

2-Allyloxyphenacyl chloride 2l: colorless solid; mp 59 °C (lit.[24] mp 59 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (d, J = 5.4 Hz, 2H), 4.81 (s, 2H), 5.35−5.47 (m, 2H), 6.05−6.14 (m, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.05 (dt, J = 7.9, 0.9 Hz, 1H), 7.51 (dt, J = 9.0, 1.8 Hz, 1H), 7.88 (dd, J = 7.8, 1.5 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.1 (CH_2), 69.7 (CH_2), 112.7 (CH), 119.1 (CH_2), 121.2 (CH), 125.2 (C), 131.4 (CH), 132.1 (CH), 134.7 (CH), 157.9 (C), 192.3 (C) ppm; IR (KBr) 3104 (w), 3010 (w), 2947 (w), 1683 (s), 1595 (m), 1484 (m), 1452 (m), 1309 (m), 128 (m), 1237 (s), 1188 (s), 1161 (m), 1002 (s), 939 (m), 761 (s) cm^{-1}.

Ethyl 2-[4-(chloroethanoyl)phenoxy]acetate 2m: colorless solid; mp 58 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, J = 7.2 Hz, 3H), 4.28 (q, J = 7.2 Hz, 2H), 4.67 (s, 2H), 4.70 (s, 2H), 6.97 (d, J = 8.7 Hz, 2H), 7.94 (d, J = 8.7 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1 (CH_3), 45.7 (CH_2), 61.6 (CH_2), 65.1 (CH_2), 114.6 (CH), 127.9 (C), 130.9 (CH), 162.1 (C), 167.9 (C), 189.5 (C) ppm; IR (KBr) 2985 (m), 2935 (m), 1752 (s), 1691 (s), 1600 (s), 1510 (m), 1443 (m), 1206 (s), 1174 (s), 1075 (s), 1024 (m), 835 (m), 787 (m), 604 (m) cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{12}H_{13}O_4ClNa$ 279.0400, found 279.0401.

(*E*)-1-Chloro-4-phenylbut-3-en-2-one 2n: colorless solid; mp 55 °C (lit.[25] mp 56 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.30 (s, 2H), 6.98 (d, J = 16.2 Hz, 1H), 7.40−7.43 (m, 3H), 7.57−7.61 (m, 2H), 7.72 (d, J = 16.2 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 47.4 (CH_2), 121.6 (CH), 128.6 (CH), 129.0 (CH), 131.1 (CH), 133.9 (C), 145.2 (CH), 191.2 (C) ppm; IR (KBr) 3013 (w), 2926 (m), 1697 (s), 1613 (s), 1394 (m), 1329 (m), 1079 (s), 986 (s), 919 (m), 773 (s), 748 (s) cm^{-1}.

1-Chloro-3-phenylbutan-2-one 2p[26]: colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (d, J = 6.9 Hz, 3H), 3.99−4.12 (m, 3H), 7.21−7.38 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5 (CH_3), 47.1 (CH_2), 50.0 (CH), 127.6 (CH), 127.8 (CH), 129.2 (CH), 139.2 (C), 202.0 (C) ppm; IR (neat) 3028 (w), 2977 (m), 2934 (m), 1731 (s), 1494 (w), 1450 (m), 1388 (w), 1284 (m), 1072 (m), 1026 (m), 758 (m) cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{10}H_{11}OClNa$ 205.0396, found 205.0390.

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Supporting Information Available: Detailed experimental procedures, ^{1}H and ^{13}C NMR, and IR data and copies of ^{1}H and ^{13}C NMR spectra of **1a**, **1a(d_1)**, **1l**, **1m**, **2a-2s**, and **2a(d_1)**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(23) Miyahara, Y. *J. Hetrocycl. Chem.* **1979**, *16*, 1147–1151.
(24) Ito, Y.; Nakatsuka, M.; Saegusa, T. *J. Org. Chem.* **1980**, *45*, 2022–2024.
(25) Fraser, R.; Kong, F. *Synth. Commun.* **1988**, *18*, 1071–1077.
(26) Panizzi, L.; Pepe, G. Ann. Chim. 1953, *43*, 29−37; Chem. Abstr. 1954, *48*, 10934.