Conversion of α -Halo-Aldehydes into Acylating Agents by an Internal Redox Reaction Catalyzed by Nucleophilic Carbenes.

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Supporting Information

General Methods. All reactions were carried out under an atmosphere of argon in flame-dried glassware with magnetic stirring. Toluene was degassed with argon and passed through one column of neutral alumina and one column of Q5 reactant. Column chromatography was performed on EM Science silica gel 60 (230-400 mesh). Thin layer chromatography was performed on EM Science 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light, KMnO_4 , or aqueous ceric ammonium molybdate dips followed by heating.

Cyclohexanol was used as purchased from Mallinckrodt. All other alcohols and aniline were purchased from Aldrich Chemical Co. and used without further purification. α -Haloaldehydes were prepared by an adaptation of a literature procedure.¹ Previously synthesized compounds matched reported spectra and new esters are characterized below.

Infrared spectra were obtained on a Nicolet Avatar 320 FT-IR spectrometer. ^1H NMR and spectra were recorded on a Varian 300, 400, or 500 MHz spectrometer at ambient temperature. Data are reported as follows: chemical shift in parts per million (δ , ppm) from an internal standard [tetramethylsilane (TMS) or deuterated chloroform (CDCl_3)], multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), integration, and coupling constant (Hz). ^{13}C NMR were recorded on a Varian spectrometer at 75, 100, or 125 MHz at ambient temperature. Chemical shifts are reported in ppm from CDCl_3 taken as 77.0 ppm. Mass spectra were obtained on Fisons VG Autospec.

General procedure for the internal redox reaction of α -halo-aldehydes: A flame-dried round-bottomed flask was charged with azolium salt (0.2 eq). Toluene (sufficient to attain a final concentration of 0.15M in substrate), triethylamine (1.0 eq), and alcohol (1.0 eq) were added via syringe and the solution was stirred at ambient temperature for 10 minutes. α -Halo-aldehyde was then added via syringe and the reaction was stirred at room temperature for the time indicated. The reaction mixture was then subjected directly to column chromatography eluting with 99:1 hexane/ Et_2O affording the pure product.

3-Phenyl-propionic acid 4-phenyl-butyl ester: R_f = 0.40 (9:1 Hex/ EtOAc); ^1H NMR (300 MHz, CDCl_3) δ 7.20-7.36 (m, 10H),

¹ Halland, N.; Braunton, A.; Bachmann, S.; Marigo, M.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 4790-4791.

4.12-4.16 (m, 2H), 3.00 (t, 2H, $J = 7.7, 8.1$ Hz), 2.67 (t, 4H, $J = 8.1, 7.3$ Hz), 1.67-1.72 (m, 4H); ^{13}C NMR (300 MHz, CDCl_3) δ 172.7, 141.9, 140.4, 128.4, 128.3, 128.2, 128.1, 126.1, 125.7, 65.8, 64.3, 36.0, 35.5, 31.0, 28.3, 27.7; IR (NaCl, neat), 1733, 1496, 1454, 1162 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{19}\text{H}_{22}\text{O}_2$, 283.1698, Found 283.1699.

3-Phenyl-propionic acid 1-ethyl-prop-2-ynyl ester: $R_f = 0.45$ (9:1 Hex/EtOAc); ^1H NMR (400 MHz, CDCl_3) δ 7.24–7.33 (m, 5H), 5.36 (td, 1H, $J = 6.4, 6.5, 2.2, 2.2, 2.0$ Hz), 3.01 (t, 2H, $J = 7.7, 7.9$ Hz), 2.68-2.74 (m, 2H), 2.48 (d, 1H, $J = 2.2$ Hz), 1.76-1.86 (m, 2H), 1.02 (t, 3H, $J = 7.3, 7.5$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 171.8, 140.3, 128.5, 128.3, 126.3, 81.0, 73.5, 64.9, 35.8, 30.8, 27.8, 9.2; IR (NaCl, neat), 1739, 1455, 1159 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{14}\text{H}_{16}\text{O}_2$, 217.1229. Found 217.1230.

Cyclohexanecarboxylic acid 2-hydroxy 1,2-diphenyl-ethyl ester. R_f (4:1 hexane to ethyl acetate) = 0.5; $[\alpha]_D^{23} = +5.8^\circ$ (CDCl_3); HPLC analysis – Chiracel AD column 90:10 hexanes to isopropanol 0.5 mL/min. Major: 23.3 minutes, Minor: 29.0 minutes; ^1H NMR (400 MHz, CDCl_3) δ 7.26 (10H, m), 5.87 (1H, d, $J = 6.4$ Hz), 4.93 (1H, d, $J = 6.4$ Hz), 2.24-2.10 (2H, m), 1.78-1.56 (5H, m), 1.30-1.11 (5H, m); ^{13}C NMR (400 MHz, CDCl_3) δ 174.9, 139.8, 137.1, 128.5, 128.5, 128.3, 127.8, 127.3, 78.5, 76.8, 43.4, 28.9, 28.9, 25.9, 25.5; IR (NaCl, CH_2Cl_2) 3480, 2929, 2854, 1727, 1445; HRMS (FAB+) calcd for $\text{C}_{21}\text{H}_{24}\text{O}_3$ 324.1725. Found 324.1759.

Spectra:

nr-4june-4aPROD

13C OBSERVE

nr-4june-4b-PRODHL

¹³C OBSERVE