A Simple, Rapid Procedure for the Synthesis of Chloromethyl Methyl Ether (MOMCl) and Other Halo Alkyl Ethers

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Supporting Information

Chromatography Conditions S1
Reagents and Methods S1
Synthesis of α-halo ethers (table 4) S2–S4
- MOMCl (neat procedure) S2
- MOMBr, 5, S2
- 6, 7, 8, 9 S3

Synthesis of alkylated products (table 5) S5–S9
- 11, 12 S5
- 13, 14 S6
- 15, 16, 17 S7
- 18 S8

Quench Experiments S9–S10

LC Conditions: Agilent Zorbax® SB-C8 column (4.6 × 150 mm) using CH₃CN and aqueous 0.1% HClO₄ as the mobile phases, with a 10 min program starting with 2 min isocratic at 90:10 CH₃CN/aqueous followed by a gradient to 10:90 over 6 min and 2 min isocratic at 10:90. Flow rate 2 mL/min, and detection was by UV at 210 nm and 254 nm.

Reagents and Methods: All reagents were obtained from commercial suppliers at 95% purity or greater and were utilized as received. Zinc(II) salts were anhydrous, but no special precautions were taken to exclude moisture during handling. Reactions were typically conducted under a nitrogen atmosphere to minimize hydrolysis during the course of the reaction, but otherwise no measures were taken during reaction setup to exclude moisture or air from the apparatus or reagents. NMR spectra were obtained in deuteriochloroform and referenced to residual CHCl₃ at δ 7.24 ppm (¹H) and δ 77.0 ppm (¹³C). Reactions were monitored by TLC, HPLC and/or ¹H NMR analysis of aliquots removed from the reaction vessel.
Synthesis of α-halo ethers:

**Chloromethyl methyl ether** (1): A 3-neck 250 mL flask was fitted with a condenser, an addition funnel and an internal thermocouple thermometer. Anhydrous zinc bromide (5.6 mg, $2.5 \times 10^{-5}$ equiv, 0.0025 mol%) and dimethoxymethane (76.1 g, 88.5 mL, 1 mol) were charged to the flask giving a clear, colorless solution. Acetyl chloride (78.5 g, 71.1 mL, 1 mol) was charged to the addition funnel. The flask was placed in an ambient temperature external water bath and approx. 5 mL of acetyl chloride was added to the reaction mixture in a single portion, resulting in controlled self-heating of the reaction mixture to reflux over 5-10 min. At this time AcCl was added dropwise to the reaction mixture at such a rate to maintain an internal temperature of 40–45 °C. Once the addition was complete the reaction was allowed to cool to ambient temperature. Analysis of an aliquot by $^1$H NMR indicated that the exchange reaction was complete. $^1$H NMR (CDCl$_3$) δ 5.44 (s, 2H, MOMCl), 3.64 (s, 3H, MeOAc), 3.49 (s, 3H, MOMCl), 2.03 (s, 3H, MeOAc). This solution of MOMCl in MeOAc has a density of 1.00 g/mL and a concentration of 6.5 M (51.4% w/w).

**Bromomethyl methyl ether:** Dimethoxymethane (5.0 mL, 56.5 mmol) and ZnBr$_2$ (64 µL of a 20 mg/mL solution in DMM, 1.3 mg, $1 \times 10^{-4}$ equiv) were dissolved in toluene (15 mL) in a flask immersed in an ambient temperature water bath and fitted with a thermocouple thermometer. Acetyl bromide (4.17 mL, 56.5 mmol) was introduced portionwise over 15 minutes, which resulted in a mildly exothermic reaction and final reaction temperature of 32 °C. After cooling for an additional 30 minutes, an aliquot was removed and $^1$H NMR analysis of the clear, colorless solution indicated complete and clean formation of an equimolar mixture of MOMBr and MeOAc. $^1$H NMR (CDCl$_3$) δ 5.66 (s, 2H, MOMBr), 3.66 (s, 3H, MeOAc), 3.48 (s, 3H, MOMBr), 2.05 (s, 3H, MeOAc).

**Chloromethyl ethyl ether** (5): Diethoxymethane (5 mL, 40 mmol, 1 equiv) and Zn(OTf)$_2$ (1.5 mg, 0.01 mol%) were mixed in a flask immersed in an ambient water bath and AcCl (2.84 mL, 1 equiv) was added portionwise over 10 minutes, during which time the reaction warmed from 24–32 °C. The reaction slowly cooled back to ambient temperature over 1h and was allowed to stir 16h, at which time an aliquot of the clear,
colorless reaction mixture indicated reaction completion. $^1\text{H NMR (CDCl}_3\delta 5.49$ (s, 2H), 3.73 (q, $J = 7.1$ Hz, 2H), 1.24 (t, $J = 7.1$ Hz, 3H).

1-Chloro-1-Methoxypropane (6):$^1$ 1,1-Dimethoxypropane (4 mL, 32.7 mmol, 1 equiv) and Zn(OTf)$_2$ (1.1 mg, 0.01%) were mixed and oxalyl chloride (1.43 mL, 0.5 equiv) was added in roughly 15 equal portions over 20 min. After each addition the internal temperature of the reaction quickly reached 35 °C and then cooled back to ~25 °C in less than one minute. As the reaction cooled to ambient temperature it became dark red; an NMR spectrum of an aliquot after 1h indicated reaction completion and clean formation of the title product (ratio 98:2 product to starting acetal). $^1\text{H NMR (CDCl}_3\delta 5.43$ (t, $J = 5.2$ Hz, 1H), 3.50 (s, 3H), 2.01 (A of ABXY$^3$, $J_{AB} = 14.4$ Hz, $J_{AX} = 6.0$ Hz, $J_{AY} = 7.8$ Hz, 1H), 1.99 (B of ABXY$^3$, $J_{AB} = 14.4$ Hz, $J_{BX} = 4.6$ Hz, $J_{BY} = 7.3$ Hz, 1H), 1.01 (t, $J = 7.4$ Hz, 3H).

1-Chloro-1-ethoxyethane (7):$^2$ Acetal (5.69 mL, 40 mmol, 1 equiv) and ZnBr$_2$ (0.01 mol%) were mixed and AcCl (2.84 mL, 1 equiv) was added in one portion. The reaction temperature slowly increased from 23-27 °C and then gradually cooled back to ambient temperature. After 1h NMR analysis of an aliquot of the reaction mixture indicated a 92:8 ratio of product to starting acetal, which is very sensitive to hydrolysis. $^1\text{H NMR (CDCl}_3\delta 5.71$ (q, $J = 5.4$ Hz, 1H), 3.93 (dq, $J = 7.1$, 9.4 Hz, 1H), 3.53 (dq, $J = 7.1$, 9.7 Hz, 1H), 1.77 (d, $J = 5.4$ Hz, 3H), 1.23 (t, $J = 7.2$ Hz, 3H).

2-Chloro-2-methoxyethylbenzene (8):$^3$ Phenylacetaldehyde dimethyl acetal (1.0 mL, 6.02 mmol, 1 equiv) and Zn(OTf)$_2$ (1.0 mg, 0.05%) were combined in a flask immersed in an ambient temperature water bath. AcCl (428 µL, 1.0 equiv) was added slowly over 2 minutes to the reaction, resulting in a temperature increase to 30 °C before cooling back to ambient temperature. After stirring an additional 30 minutes, $^1\text{H NMR analysis of an aliquot indicated complete consumption of the AcCl and a 93:7 ratio of }\alpha\text{-chloro ether 9 to starting acetal. }^1\text{H NMR (CDCl}_3\delta 7.35\text{–}7.20$ (m, 5H), 5.61 (dd, $J = 5.0$, 6.4 Hz, 1H), 3.49 (s, 3H), 3.33 (A of ABX, $J_{AB} = 14.2$ Hz, $J_{AX} = 6.8$ Hz, 1H), 3.25 (B of ABX, $J_{AB} = 14.2$ Hz, $J_{BX} = 5.0$ Hz, 1H).

1-Chloro-1-Methoxytoluene (9):$^3$ Benzaldehyde dimethyl acetal (1.57 mL, 10.5 mmol, 1 equiv) and Zn(OTf)$_2$ (1 mg, 0.025%) were added to CH$_2$Cl$_2$ (4.5 mL, 3 vol) in a flask immersed in an ambient temperature water bath. Acetyl chloride (0.69 mL, 1.05 equiv)
was introduced over 2 minutes and the reaction was then stirred as the internal temperature slowly increased from 19–24 °C and the reaction color changed from colorless to a clear orange. After 1 hr, an aliquot was removed and \textsuperscript{1}H NMR analysis indicated complete consumption of the AcCl and PhCH(OMe)\textsubscript{2} and the presence of α-chloro ether 10:benzaldehyde in a 4:1 ratio (due to hydrolysis of the very labile product in the NMR solvent). \textsuperscript{1}H NMR (CDCl\textsubscript{3}) δ 7.47 (m, 2H), 7.38 (m, 3H), 6.43 (br, 1H), 3.68 (br s, 3H).
Alkoxyalkylation Reactions:

4-Methoxymethoxyacetophenone (11): A solution of 56 mmol MOMCl was prepared in toluene (15 mL) using 5 mL dimethoxymethane, 4 mL acetyl chloride and 0.01 mol% ZnBr₂. p-Hydroxyacetophenone (3.87g, 28 mmol) and diisopropylethylamine (5.38 mL, 1.1 equiv) were added sequentially to the MOMCl solution and the resulting slurry stirred 24h, at which time HPLC analysis indicated ~95% reaction completion (tᵣ SM 2.47 min, tᵣ product 5.42 min). The reaction mixture was diluted with ethyl acetate and washed twice with water and once with saturated aqueous NaHCO₃ solution. The organic layer was dried with Na₂SO₄ and concentrated under reduced pressure to a clear oil. Chromatography on silica gel (eluting with 4:1 hexanes:EtOAc) provided the title compound (4.42g, 24.4 mmol) as a clear, colorless oil in 87% yield. Rᵣ 0.4 (4:1 hexanes/EtOAc). ¹H NMR (CDCl₃) δ 7.89 (app d, J = 8.9 Hz, 2H), 7.04 (app d, J = 8.9 Hz, 2H), 5.20 (s, 2H), 3.45 (s, 3H), 2.53 (s, 3H). ¹³C NMR (CDCl₃) δ 196.8, 161.0, 131.1, 130.4, 115.6, 93.9, 56.2, 26.3. IR (cm⁻¹) 2935, 1674, 1598, 1269, 1236, 1150, 1078, 981, 955, 921, 836, 590, 564. Anal. Calc’d for C₁₀H₁₂O₃: C, 66.65; H, 6.71. Found: C, 66.26; H, 6.86.

Diethyl 2-allyl-2-methoxymethylmalonate (12): Sodium hydride (634 mg, 1.25 equiv, 60% in oil) was suspended in THF (15 mL) and the slurry was cooled to 0 °C in an ice bath. Diethyl allylmalonate (2.5 mL, 12.7 mmol, 1 equiv) was added dropwise over 5 minutes, and the resulting light yellow slurry was stirred 1 hr at 0 °C. At this time a solution of 1 in toluene (2.1M, 12 mL, 2 equiv) was added in one portion and the resulting colorless slurry was allowed to warm to ambient temperature with stirring overnight. The reaction was quenched with a saturated aqueous NH₄Cl solution and the layers were separated. The organic layer was washed once with brine, dried with MgSO₄ and concentrated under reduced pressure to a clear, colorless oil. Purification by distillation (OT 136 °C, 0.7 mmHg) provided the 2.49 g of the title compound as a clear, colorless oil (10.2 mmol, 80% yield). ¹H NMR (CDCl₃) δ 5.64 (ddt, J = 15.1, 10.1, 7.5 Hz, 1H), 5.14–5.06 (m, 2H), 4.17 (q, J = 7.1 Hz, 4H), 3.73 (s, 2H), 3.31 (s, 3H), 2.73 (dt, J = 7.5, 1.1 Hz, 2H), 1.22 (t, J = 7.1 Hz, 6H). ¹³C NMR (CDCl₃) δ 169.5, 132.3, 119.2, 71.9, 61.3, 59.3, 58.2, 35.1, 14.0. IR (cm⁻¹) 2983, 1730, 1446, 1296, 1199, 1109, 1014, 922, 858, 659. Anal. Calc’d for C₁₂H₂₀O₅: C, 59.00; H, 8.25. Found: C, 59.42; H, 8.43.
1-Methoxymethoxy-3-phenylbutane (13): A solution of 56 mmol of MOMCl was prepared from dimethoxymethane, AcCl and 0.01% Zn(OAc)$_2$ following the general procedure. Toluene (15 mL) and 3-phenyl-1-butanol (4.32 mL, 28 mmol, 1 equiv) were added, followed by i-Pr$_2$NEt (5.62 mL, 1.15 equiv). The reaction mixture warmed gradually and after several minutes ammonium salts precipitated. The reaction was maintained at ambient temperature for 12h, at which time analysis by TLC and HPLC indicated it was complete. The reaction mixture was partitioned between ethyl acetate and saturated aqueous NH$_4$Cl; the aqueous layer was removed and the organic layer washed once with water, once with brine, dried with MgSO$_4$ and concentrated under reduced pressure to a clear, colorless oil. No additional purification was required. A total of 5.03g of the title compound was isolated (25.9 mmol, 93% yield). $R_f$ 0.5 (5:1 hexanes/EtOAc). $^1$H NMR (CDCl$_3$) $\delta$ 7.33–7.27 (m, 2H), 7.20–7.16 (m, 3H), 4.58 (d, A of AB, $J = 6.5$ Hz, 1H), 4.56 (d, B of AB, $J = 6.5$ Hz, 1H), 3.45 (dt, A of ABX$^2$, $J_{AB} = 9.8$ Hz, $J_{AC} = 6.4$ Hz, 1H), 3.39 (dt, B of ABX$^2$, $J_{BA} = 9.8$ Hz, $J_{BC} = 7.0$ Hz, 1H), 3.33 (s, 3H), 2.88 (sextet, $J = 7.2$ Hz, 1H), 1.88 (app q, $J = 6.8$ Hz, 2H), 1.27 (t, $J = 7.0$ Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 146.8, 128.4, 126.9, 125.9, 96.4, 65.9, 55.1, 37.9, 36.5, 22.3. IR (cm$^{-1}$) 2930, 1493, 1452, 1213, 1150, 1109, 1040, 917, 761, 699, 548. Anal. Calc’d for C$_{12}$H$_{18}$O$_2$: C, 74.19; H, 9.34. Found: C, 74.07; H, 9.59.

(3-Methoxymethoxy-3-methylbutyl)benzene (14): $\alpha,\alpha$-Dimethylbenzenepropanol (4.76 mL, 28 mmol, 1 equiv), toluene (15 mL) and diisopropylethylamine (5.62 mL, 1.15 equiv) were added to a solution of 56 mmol MOMCl (2 equiv, prepared following the general procedure). The reaction warmed slightly over the next 0.5h as the color changed to light orange and ammonium salts precipitated from the solution. HPLC analysis after 1h indicated the reaction was 95% complete, and after stirring at ambient temperature for 12h, the starting material had been consumed. The reaction mixture was quenched into a mixture of EtOAc and a saturated aqueous NH$_4$Cl solution, and the organic layer was separated, washed once with water, once with brine, dried with MgSO$_4$ and concentrated to a clear, colorless oil. A total of 5.37g (92% yield) was isolated and did not require additional purification. $R_f$ 0.6 (5:1 hexanes:EtOAc). $^1$H NMR (CDCl$_3$) $\delta$ 7.30–7.15 (m, 5H), 4.74 (s, 2H), 3.39 (s, 3H), 2.67 (m, 2H), 1.80 (m, 2H), 1.28 (s, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 142.7, 128.3, 128.3, 91.0, 75.9, 55.2, 43.8, 30.4, 26.4. IR (cm$^{-1}$): 2973, 1454,
Methoxymethyl benzoate (15): Benzoic acid (1.0 g, 8.2 mmol, 1 equiv) was suspended in 5 mL toluene and then MOMCl (2.1M in toluene, 4.6 mL, 1.2 equiv) and diisopropylethylamine (1.71 mL, 1.2 equiv) were introduced via syringe. The reaction mixture briefly became homogenous before ammonium salts came out of solution, and the resulting slurry was then stirred an additional 0.5 hr at ambient temperature. Analysis of the reaction by HPLC at this point indicated reaction completion, so the solution was partitioned between EtOAc and an aqueous NH₄Cl solution. The organic layer was then washed sequentially with water and brine, dried with MgSO₄ and concentrated to 1.25 g (92% yield) of a clear, colorless oil that required no additional purification. ¹H NMR (CDCl₃) δ 8.07 (app d, 2H), 7.57 (app t, 1H), 7.44 (app t, 2H), 5.48 (s, 2H), 3.53 (s, 3H). ¹³C NMR (CDCl₃) δ 166.0, 133.2, 129.77, 129.71, 128.4, 90.9, 57.7. IR (cm⁻¹) 1718, 1452, 1268, 1161, 1053, 1023, 914, 708, 576. Anal. Calc’d for C₉H₁₀O₃, C, 65.05; H, 6.07; Found: C, 64.78; H, 6.09.

trans-Methoxymethyl cinnamate (16): trans-Cinnamic acid (1.0 g, 6.75 mmol, 1 equiv) was suspended in 5 mL toluene and a solution of MOMCl (2.1M in toluene, 3.86 mL, 1.2 equiv) and diisopropylethylamine (1.41 mL, 1.2 equiv) were introduced via syringe. After 0.5h at ambient temperature, analysis of the reaction by HPLC at this point indicated reaction completion, so the solution was partitioned between EtOAc and NH₄Cl solution. The organic layer was then washed once with water, once with brine, dried with MgSO₄ and concentrated to 1.25 g (96% yield) of a clear, colorless oil that was analytically pure. ¹H NMR (CDCl₃) δ 7.73 (d, J = 16.1 Hz, 1H), 7.53 (m, 2H), 7.38 (m, 3H), 6.44 (d, J = 16.1 Hz, 1H), 5.36 (s, 2H), 3.51 (s, 3H). ¹³C NMR (CDCl₃) δ 166.3, 145.7, 134.1, 130.5, 128.9, 128.1, 117.5, 90.5, 57.6. IR (cm⁻¹) 1711, 1634, 1450, 1310, 1136, 1089, 963, 917, 766, 710, 683, 554. Anal. Calc’d for C₁₁H₁₂O₃, C, 68.74; H, 6.29. Found, C, 68.55; H, 6.36.

4′-(1-Methoxy-2-phenylethoxy)acetophenone (17): Toluene (5 mL) was added to a solution of 6 mmol of 2-chloro-2-methoxyethylbenzene (8) in MeOAc (see above for preparation). 4′-Hydroxyacetophenone (619 mg, 0.75 equiv) and diisopropylethylamine (1.05 mL, 1 equiv) were added sequentially and the light yellow solution stirred for 0.5 hr at ambient temperature. Analysis of the reaction by HPLC at this point indicated reaction completion, so the solution was partitioned between EtOAc and an aqueous NH₄Cl solution. The organic layer was then washed sequentially with water and brine, dried with MgSO₄ and concentrated to 1.25 g (92% yield) of a clear, colorless oil that required no additional purification. ¹H NMR (CDCl₃) δ 8.07 (app d, 2H), 7.57 (app t, 1H), 7.44 (app t, 2H), 5.48 (s, 2H), 3.53 (s, 3H). ¹³C NMR (CDCl₃) δ 166.0, 133.2, 129.77, 129.71, 128.4, 90.9, 57.7. IR (cm⁻¹) 1718, 1452, 1268, 1161, 1053, 1023, 914, 708, 576. Anal. Calc’d for C₁₃H₂₀O₂, C, 74.96; H, 9.68. Found: C, 74.94; H, 9.68.
overnight. HPLC analysis of the reaction mixture at this time indicated complete consumption of the acetophenone, so the reaction mixture was partitioned between ethyl acetate and saturated aqueous NH₄Cl solution. The organic layer was then washed once with water, once with brine, dried with MgSO₄ and concentrated under reduced pressure to a yellow oil. Purification by chromatography on silica gel eluting with 5:1 hexanes:EtOAc provided the title compound (1.13g, 4.18 mmol, 93% yield based on acetophenone charge) as a clear, colorless oil. 

\[ ^{1}H \text{NMR (CDCl}_3\] δ 7.88 (app d, 2H), 7.35-7.20 (m, 5H), 6.97 (app d, 2H), 5.39 (t, \( J = 5.6 \text{ Hz}, 1\text{H} \)), 3.39 (s, 3H), 3.148 (dd, A of ABX, \( J_{AB} = 13.5 \), \( J_{AX} = 5.7 \text{ Hz}, 1\text{H} \)), 3.113 (dd, B of ABX, \( J_{AB} = 13.5 \), \( J_{BX} = 5.2 \text{ Hz}, 1\text{H} \)), 2.53 (s, 3H). 

\[ ^{13}C \text{NMR (CDCl}_3\] δ 196.7, 161.1, 135.8, 131.1, 130.5, 129.5, 128.5, 126.8, 116.4, 103.4, 53.2, 39.8, 26.4. 

IR (cm⁻¹): 2933, 1675, 1597, 1504, 1239, 1169, 1108, 954, 836, 749, 699, 589. MS (ES+) 271.3 (m+1). Anal. Calc’d for C₁₇H₁₈O₃, C, 75.53; H, 6.71; Found, C, 75.38; H, 6.78.

**Methyl (R)-2-(ethoxymethoxy)mandelate (18):** Zinc triflate (2 mg, 0.04 mol%), diethoxymethane (2.82 mL, 22.6 mmol, 1.5 equiv) and toluene (10 mL) were combined in a flask and acetyl chloride (1.61 mL, 22.6 mmol, 1.5 equiv) was added in one portion. After 6 hrs analysis of an aliquot of the solution by \(^1\text{H} \text{NMR} \) indicated the exchange reaction was complete, so (R)-methyl mandelate (2.5g, 15.0 mmol) and diisopropylethylamine (3.15 mL, 1.2 equiv) were introduced. Over the next two hours ammonium salts precipitated out of solution, and at this time HPLC analysis of the reaction mixture indicated complete consumption of the starting material. The reaction mixture was then partitioned between saturated aqueous NH₄Cl solution and ethyl acetate, and the organic phase was washed sequentially with water and brine, dried with MgSO₄ and concentrated under reduced pressure to a clear, colorless oil. Purification by chromatography on silica gel eluting with 10:1 hexanes/EtOAc provided 2.87 g of 18 (12.8 mmol, 85% yield) as a clear, colorless oil. 

\[ R_f \] 0.5 (2:1 hexanes:EtOAc). \([\alpha]_D \] −75° (c 22 mg/mL, EtOAc). 

\[ ^{1}H \text{NMR (CDCl}_3\] δ 7.42 (m, 2H), 7.34 (m, 3H), 5.18 (s, 1H), 4.79 (d, A of AB, \( J = 7.1 \text{ Hz}, 1\text{H} \)), 4.71 (d, B of AB, \( J = 7.1 \text{ Hz}, 1\text{H} \)), 3.70 (s, 3H), 3.67 (dq, A of ABX³, \( J_{AB} = 9.6 \text{ Hz}, J_{AX} = 7.1 \text{ Hz}, 1\text{H} \)), 3.54 (dq, B of ABX³, \( J_{BA} = 9.6 \text{ Hz}, J_{BX} = 7.1 \text{ Hz}, 1\text{H} \)), 1.15 (t, \( J = 7.1 \text{ Hz}, 3\text{H} \)). 

\[ ^{13}C \text{NMR (CDCl}_3\] δ 171.2, 136.1, 128.68, 128.61, 128.58, 126.8, 116.4, 103.4, 53.2, 39.8, 26.4.
127.4, 93.5, 76.6, 63.9, 52.3, 14.9. IR (cm⁻¹) 2976, 1751, 1436, 1209, 1171, 1041, 1101, 730, 697. Anal. Calc’d for C₁₂H₁₆O₄, C, 64.27; H, 7.19. Found, C, 64.33; H, 7.21.

**Quench Experiments**

An aqueous solution (20 mL of water, sat’d NH₄Cl solution, and sat’d Na₂CO₃ solution) was added quickly to a flask containing 20 mL of a 2.1 M solution of chloromethyl methyl ether in toluene/MeOAc (42 mmol) prepared by the general procedure. The quenches were conducted with internal temperature monitoring, magnetic stirring set at the highest speed, but no external temperature control. The biphasic mixture was stirred rapidly to ensure good mixing and aliquots were periodically sampled from the organic layer to assay for residual chloro-alkyl ethers. For all three aqueous solutions, the quench was mildly exothermic (temperatures increase from 21 °C to ~31–35 °C over 5 minutes) and greater than 98% of the initial charge of MOMCl was destroyed within 5 minutes of mixing.

The methoxymethylation reaction to form 13 was conducted on 56 mmol scale and the quench carefully monitored by withdrawing aliquots every five minutes after saturated NH₄Cl solution was added to assay for residual MOMCl. No residual MOMCl was observed after five minutes stirring. This quench was also mildly exothermic with a temperature maximum of 30 °C occurring four minutes after quench.
Quenches of MOMCl solutions by three aqueous mixtures (42 mmol scale)

Saturated NH₄Cl Solution

<table>
<thead>
<tr>
<th>Time</th>
<th>Molar Ratio (MOMCl/Toluene, ¹H NMR)</th>
<th>Temp (°C)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1:5</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1:400</td>
<td>31</td>
<td>White ammonium salts precipitated. Temp max at 3 min after addition.</td>
</tr>
<tr>
<td>15</td>
<td>&lt;1:1000</td>
<td>25</td>
<td>No α-halo ethers present.</td>
</tr>
</tbody>
</table>

Water

<table>
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<tr>
<th>Time</th>
<th>Molar Ratio (MOMCl/Toluene, ¹H NMR)</th>
<th>Temp (°C)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1:5</td>
<td>21</td>
<td>Clear, colorless layers. Maximum temperature at 5 minutes post quench.</td>
</tr>
<tr>
<td>5</td>
<td>&lt;1:800</td>
<td>32</td>
<td>No α-halo ethers present.</td>
</tr>
<tr>
<td>15</td>
<td>&lt;1:1000</td>
<td>27</td>
<td>No α-halo ethers present.</td>
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</tbody>
</table>

Saturated Na₂CO₃ Solution

<table>
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<tr>
<th>Time</th>
<th>Molar Ratio (MOMCl/Toluene, ¹H NMR)</th>
<th>Temp (°C)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1:5</td>
<td>21</td>
<td>Some CO₂ evolution during first part of quench followed by precipitation of NaHCO₃. Additional stirring gradually neutralizes acidic organic layer. More water accelerates this process (solubilizes carbonate base).</td>
</tr>
<tr>
<td>5</td>
<td>1:400</td>
<td>36</td>
<td>No α-halo ethers present.</td>
</tr>
<tr>
<td>15</td>
<td>&lt;1:1000</td>
<td>27</td>
<td>No α-halo ethers present.</td>
</tr>
</tbody>
</table>

1 Henze, H.R.; Benz, G.W.; Sutherland, G.L. J. Am. Chem. Soc. **1949**, *71*, 2122.
