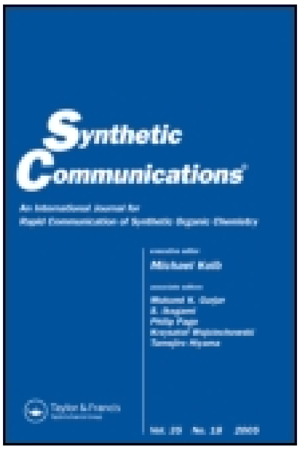

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α-Chlorination of Carboxylic Acids Using Trichloroisocyanuric Acid

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α-Chlorination of Carboxylic Acids Using Trichloroisocyanuric Acid

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ABSTRACT

Carboxylic acids are chlorinated in the α position by heating with trichloroisocyanuric acid after formation of a small amount of the acid chloride using phosphorus trichloride.

Key Words: Chlorination; α-Chlorination; α-Chloro acids; 2-Chloro acids; Carboxylic acids; Chloro acids; Substitution; Synthesis; Preparation; Trichloroisocyanuric acid.

α-Halogenation of carboxylic acids is generally known as the Hell–Volhard–Zelinsky reaction[1,2] and involves the conversion of the carboxylic

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acid partially or completely into an acid halide followed by reaction with a suitable halogenating agent. The synthesis of α-chloro carboxylic acids has been accomplished using a variety of reagents including chlorine,[3] sulfuryl chloride,[4] thionyl chloride,[5] and LDA with CCl_4.[6] We wish to report that trichloroisocyanuric acid (**1**) [1,3,5-trichloro-1,3,5-triazine-2,4,6-(1H,3H,5H)-trione; TCICA], a stable, easily handled solid, is also a suitable reagent for the chlorination reaction.

Our initial studies using thionyl chloride to generate a small amount of the acid chloride led to unpredictable results. Some of these reactions gave mainly the α-isomer and others gave a complex mixture of products, presumably through radical chlorination. A by-product from using thionyl chloride is hydrogen chloride, and hydrogen chloride reacts with **1** to form chlorine[7] which could then take part in a radical chain reaction. However, when phosphorus trichloride was used to generate the acid chloride, the reaction proceeded smoothly to give the α-chloro acid.

Two satisfactory procedures were developed. One in which **1** was the limiting reagent and the carboxylic acid was in excess, and the other in which a slight excess of **1** was used. After warming the carboxylic acid with PCl_3 to convert a portion to the acid chloride, **1** was added slowly using a solid addition funnel while warming the reaction mixture. If **1** was added too rapidly, the reaction became excessively exothermic and splashing took place. In a previously reported study on the effect of reaction temperature on the chlorination reaction of cyclohexanecarboxylic acid using chlorine, it was shown that the optimum reaction temperature was about 160°C.[8] Low temperatures resulted in radical chlorination and higher temperatures resulted in elimination of hydrogen chloride. Our results are shown in Table 1.

Table 1. Conversion of carboxylic acids to α-chloro acids.

α-Chloro acid	Procedure	Bath temperature	Yield	GC purity
2-Chloroacetic acid	Excess **1**	130°C	88%	99.4%
2-Chloropropanoic acid	Excess **1**	160°C	76%	98.4%
2-Chloropropanoic acid	Excess acid	160°C	52%	97.7%
2-Chlorobutanoic acid	Excess acid	178°C	48%	96.2%
2-Chlorobutanoic acid	Excess **1**	140°C	67%	95.8%
2-Chlorobutanoic acid	Excess **1**	140°C	73%	94.5%

EXPERIMENTAL

Gas chromatography was performed using a Hewlet-Paackard 5890 Series II instrument with a 6 ft × 1/8 in 10% Carbowax 20 M column. FT-IR spectra were recorded using a Perkin Elmer 1650. ^{1}H-NMR spectra were recorded on an Anasazi-modified Varian EFT 90 MHz instrument in $CDCl_3$ or CCl_4. All reagents were used as received except for pentane which was distilled. **1**, 99%, was obtained from Chem Lab Products. Acetic acid, 99%, was from Fisher. Propanoic acid, 99%, and hexanoic acid, 99%, were from MCB. Butanoic acid, 99%, phorphorous trichloride, 99%, and methylene chloride were from Aldrich. All products were distilled.

Preparation of 2-Chloroacetic Acid with an Excess of 1

In a 100 mL three-neck round-bottom flask were placed a magnetic stir bar, 10.196 g (0.1698 mol; 0.1698 eq) acetic acid and 0.611 g (0.0044 mol; 0.0133 eq) PCl_3. The flask was flushed with N_2 and two stoppers and a condenser fitted with a drying tube were added. The flask was heated in a 130°C oil bath for 10 min. GC analysis indicated that 2.1% acid chloride was present. Then the center stopper was replaced with a solid addition funnel with a N_2 inlet at the top and containing 16.113 g (0.06930 mol; 0.2079 eq) **1**. A gentle flow of N_2 through the funnel kept acid vapor and **1** from collecting at the tip of the funnel. After wrapping the apparatus with foil and turning off the lights, **1** was added at a slow rate over 10 min while heating was continued. The addition funnel was then replaced with a stopper.

After 19 hr, the flask was removed from the heating bath and mixture crystallized. Diethyl ether was added to dissolve the chloro acid and excess **1** was destroyed by the slow addition of solid $NaHSO_3$ until a wet iodide-starch paper test was negative. The cyanuric acid by-product was filtered and washed with ether, and the ether was removed with a rotary evaporator. The crude product was vacuum distilled through a Vigreux column to give 14.023 g (88%) 2-chloroacetic acid, b.p. 103.8–104.8°C (27.3–29.5 torr), 99.4% pure by GC. The GC retention time, FT-IR, and ^{1}HNMR were identical to those of an authentic sample.

Preparation of 2-Chloropropanoic Acid with an Excess of Propanoic Acid

In a 100 mL three-neck round-bottom flask were placed a magnetic stir bar, 16.769 g (0.2264 mol; 0.2264 eq) acetic acid and 1.486 g (0.01081 mol;

0.03243 eq) PCl_3. The flask was flushed with N_2 and two stoppers and a condenser fitted with a drying tube were added. The flask was heated in a 160°C oil bath for 10 min. GC analysis indicated that 3.4% acid chloride was present. Then the center stopper was replaced with a solid addition funnel with a N_2 inlet at the top and containing 4.997 g (0.0215 mol; 0.0645 eq) **1**. A gentle flow of N_2 through the funnel kept acid vapor and **1** from collecting at the tip of the funnel. After wrapping the apparatus with foil and turning off the lights, **1** was added at a slow rate over 40 min while heating was continued. The addition funnel was then replaced with a stopper.

After 23 hr, the flask was removed from the heating bath and excess **1** was destroyed by the slow addition of solid $NaHSO_3$ until a wet iodide-starch paper test was negative. Diethyl ether was added, the cyanuric acid by-product was filtered and washed with ether, and the ether was removed with a rotary evaporator. The crude product was vacuum distilled through a concentric tube column to give 3.659 g (52%) 2-chloropropanoic acid, b.p. 82.0–84.5°C (10.3–10.5 torr), 97.7% pure by GC. The GC retention time, FT-IR, and ^{1}HNMR were identical to those of an authentic sample.

2-Chlorobutanoic Acid

Equivalent ratio of **1** : butanoic acid 1.260, yield 67% (95.8% pure by GC), b.p. 104.0–105.8°C (16.6–17.0 torr): FT-IR (film) 3703–2352, 2695, 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 10.42 (s, 1, OH), 4.29 (ABX, $J_{ax} + J_{bx} = 13.4$ Hz, 1, + CH), 2.00 (m, 2, CH_2), 1.09 (t, $J = 7.2$ Hz, CH_3). Anal. calcd. for $C_4H_7O_2Cl$: C, 39.20; H, 5.76; found: C, 39.16; H, 6.05%.

2-Chlorohexanoic Acid

Equivalent ratio of **1** : hexanoic acid 1.301, yield 73% (94.5% pure by GC), b.p. 89.0–91.4°C (0.5–0.9 torr): FT-IR (film) 3649–2380, 2695, 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 10.19 (s, 1, OH), 4.32 (ABX, $J_{ax} + J_{bx} = 13.6$ Hz, 1, CH), 2.01 (m, 2, $C\mathbf{H}_2CH$), 1.42 (m, 4, $CH_3C\mathbf{H}_2C\mathbf{H}_2$), 0.93 (m, 3, CH_3). HRMS calcd. for $C_6H_{11}O_2Cl$ (M + H) 151.05258; found: 151.05269.

REFERENCES

1. Sonntag, N.O.V. The reactions of aliphatic acid chlorides. Chem. Rev. **1953**, *52*, 237–416.

2. Harwood, H.J. Reactions of the hydrocarbon chain of fatty acids. Chem. Rev. **1962**, *62*, 99–154.
3. Crawford, R.J. An improved α-chlorination of carboxylic acids. J. Org. Chem. **1983**, *48*, 1364–1366.
4. Galat, A. An improved synthesis of *dl*-lysine. J. Amer. Chem. Soc. **1947**, *69*, 86.
5. Rodin, R.L.; Gershon, H. Photochemical α-chlorination of fatty acid chlorides by thionyl chloride. J. Org. Chem. **1973**, *38*, 3919–3921.
6. Snider, B.B.; Kulkarni, Y.S. Preparation of unsaturated α-chloro acids and intramolecular [2 + 2] cycloadditions of chloroketenes derived from them. J. Org. Chem. **1987**, *52*, 307–310.
7. Hiegel, G.A.; Abdala, M.H.; Burke, S.V.; Beard, D.P. Methods for preparing aqueous solutions of chlorine and bromine for halogen displacement reactions. J. Chem. Educ. **1987**, *64*, 156.
8. Little, J.C.; Sexton, A.R.; Tong, Y.C.; Zurawic, T.E. Chlorination II. Free radical vs. Hell-Volhard-Zelinsky chlorination of cyclohexanecarboxylic acid. J. Amer. Chem. Soc. **1969**, *91*, 7098–7103.

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