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Note

Preparation of 4,4-dimethoxybutyl chloride from γ-butyrolactone†

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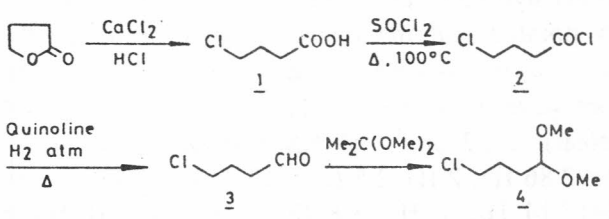
4,4-Dimethoxybutyl chloride **4**, an important alternate for the synthesis of 1,5- and 1,6-dicarbonyl functionalities, has been synthesized from γ-butyrolactone.

4,4-Dimethoxybutyl chloride **4** is extensively used in organic synthesis as a building block for the synthesis of 1,5- or 1,6-dicarbonyl functionalities which are common entries for the synthesis of five and six membered ring systems[1]. γ-Butyrolactone has been utilized for the preparation of 4-chlorobutyric esters by passing hydrogen chloride gas in the presence of the corresponding alcohols[2]. 4-Chlorobutanoyl chloride has been prepared by the reaction of γ-butyrolactone and $SOCl_2$ in the presence of a catalytic amount of $ZnCl_2$[3]. Other derivatives such as 2,3-halopropyl-1,3-dioxolane[4], and acetals of 3-halo-propanal[5-6] have been reported recently. A method for the synthesis of **4** from γ-butyrolactone is described in this communication, 4,4-Dimethoxybutyl chloride is an important intermediate for the synthesis of the antimigrane drug "sumatryptan".

4-Chlorobutanoic acid **1** was prepared by the reaction of γ-butyrolactone with calcium chloride and concentrated hydrochloric acid. Under reflux at 100 °C for 72 hr. The chloroacid was extracted with dichloromethane and the solvent evaporated to obtain a liquid which was distilled at 210 °C/20 mm.

4-Chlorobutanoyl chloride **2** was prepared by the addition of thionyl chloride to 4-chlorobutanoic acid **1**. The reaction mixture was stirred overnight and distilled at 110 °C/20 mm.

Reduction of 4-chlorobutanoyl chloride **2** with 10% Pd-$BaSO_4$ under hydrogen atmosphere gave 4-chlorobutyraldehyde **3**.



The target compound **4** was obtained by the interaction of 4-chlorobutyaldehyde **3** and 2,2-dimethoxypropane in the presence of a catalytic amount of *p*-toluenesulfonic acid and stirring the reaction mixture overnight. The compound **4** was extracted with chloroform and distilled at 120 °C/40 mm.

Experimental Section

General. ^{1}H NMR spectra were measured on a Varian Gemini (200 MHz) spectrometer using tetramethylsilane as internal standard for solution in deuterated chloroform. IR spectra were taken on a Perkin-Elmer 1310 spectrometer. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 40 °C.

4-Chlorobutanoic acid 1. To a stirred solution of γ-butyrolactone (110 g, 1.28 moles) and calcium chloride (400 g, 3.60 moles) cooled to 0 °C, conc. Hydrochloric acid (300 mL) was added dropwise over a period of 1 hr. After the addition of acid was over, the reaction mixture was heated at 100 °C for 72 hr. The acid was extracted in dichloromethane and distilled to give **1** (124 g, 80%) as colourless liquid, b.p. 210 °C/20 mm, (lit.[7], bp 84-85 °C/3 mm); IR neat: 1760 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.1 (m, 2 H), 2.5 (q, *J*=12.5 Hz, 2 H), 3.6 (t, *J*=20 Hz, 2 H).

4-Chlorobutanoyl chloride 2. A mixture of **1** (127 g, 1.036 moles) and $SOCl_2$ (100 mL) was stirred at reflux overnight. The excess of $SOCl_2$ was distilled off and the product was distilled under reduced pressure to give **2** (143 g, 97%) as colourless liquid, bp 110 °C/20 mm (lit.[2], b.p. 69-74 °C/14 mm); IR (Neat): 1780 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.2 (q, *J*=24 Hz, 2 H), 3.1 (t, *J*=12 Hz, 2 H), 3.6 (t, *J*=16 Hz, 2 H).

4-Chlorobutyraldehyde 3. Compound **2** (10 g,

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0.066 mole) and (10%) Pd-$BaSO_4$ (1.1 g) were taken in a mixture of xylene (70 mL) and toluene (30 mL). The mixture was heated at 120 °C for 6 hr in the presence of a catalytic amount of quinoline under hydrogen atmosphere at 20 psi. Solvent was evaporated and the residue without filtering the catalyst, on distillation under vacuum at 65 °C/30 mm gave **3** (5.74 g, 76%) as a brown liquid, IR (Neat): 1727 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.1 (q, *J*=22.86 Hz, 2 H), 2.5 (t, *J*=17.14 Hz, 2 H), 3.6 (t, *J*=17.14 Hz, 2 H), 8.8 (b, 1 H) [lit.[8] ^1H NMR (CCl_4): δ 2.07 (q, *J*=7 Hz, 2 H), 2.63 (t, *J*=7 Hz, 2 H), 3.58 (t, *J*=7 Hz, 2 H), 9.45 (s, 1 H)].

4,4-Dimethoxybutyl chloride 4. A mixture of **3** (5 g) and 2,2-dimethoxypropane (50 mL) was stirred overnight in presence of a catalytic amount of *p*-toluenesulfonic acid. The compound was extracted in $CHCl_3$ (100 mL) and washed several times with $NaHCO_3$ followed by final washing with brine.The organic layer was concentrated and distilled to give **4** (3.58 g, 50%) as a light yellow liquid, b.p. 120 °C/40 mm (lit.[9], b.p. 76-78 °C/20 mm); ^1H NMR ($CDCl_3$): δ 2.15 (m, 4 H), 3.6 (t, *J*=15.38 Hz, 2 H), 3.7 (s, 6 H), 4.2 (t, 1 H) [lit[10]. ^1H NMR ($CDCl_3$): δ 1.67-1.90 (m, 4 H), 3.30 (s, 6 H), 3.6 (t, 2 H), 4.38 (t, 1 H).

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