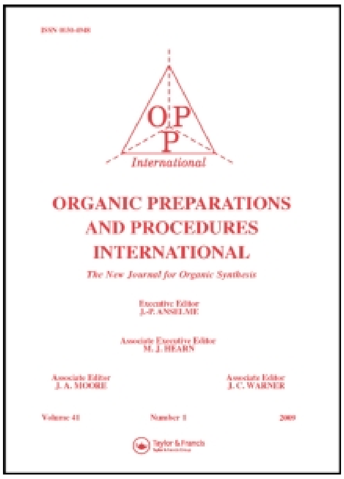

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IMPROVED TWO-STEP SYNTHESIS OF ETHYL CYCLOPROPANECARBOXYLATE AND CYCLOPROPANECARBOXYLIC ACID

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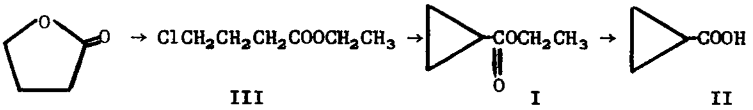
In connection with studies in cyclopropane chemistry, ethyl cyclopropanecarboxylate (I) and cyclopropanecarboxylic acid (II) were required in quantity. A two-step preparation from γ-butyrolactone via ethyl 4-chlorobutyrate (III) was developed by modification of published procedures for the preparation of III[1] and for its cyclization.[2,3] The preparations of II from 1-bromo-3-chloropropane[4] and from cyclopropyl methyl ketone[5] are more costly. On a 10-mole scale, the reaction of γ-butyrolactone with thionyl chloride and ethanol gave 85% II. Reaction of III with 5M sodium ethoxide gave 66% I; the overall yield from γ-butyrolactone was 56%. Alternatively, hydrolysis with 6N NaOH of the mixture from the reaction of III with sodium ethoxide gave 84% II; the overall yield from γ-butyrolactone was 71%.



EXPERIMENTAL

Ethyl 4-chlorobutyrate III.- A mixture of 861 g (10.0 moles) of γ-butyrolactone (practical) and 1250 g (10.5 moles) of thionyl chloride (practical) was refluxed for 1 hr. in a 3-ℓ flask fitted with an addition funnel and an efficient condenser and drying tube. Addition of 510 g

(11 moles) of absolute ethanol was accomplished in 2 hr., with stirring; the drying tube was replaced by a trap for evolved HCl. After the addition, the mixture was heated to reflux for 1 hr. The excess ethanol was removed by rotary evaporation at 15-30 mm. Foaming due to dissolved SO_2 and HCl was a problem and care was required in the disposal of condensate trapped by a Dry Ice condenser. Distillation gave 1180 g (8.53 moles, 85%) of III, bp. 77-78°/16 mm, lit.[1] bp. 94-95°/37 mm.

Ethyl cyclopropanecarboxylate. - A solution of sodium ethoxide was prepared by addition of 126.5 g (5.5 moles) of sodium metal (cut in small pieces) to 1200 ml of absolute ethanol. This reaction was best accomplished when both alcohol and sodium were added in three portions with mechanical stirring to a 3-ℓ round bottom flask fitted with an addition funnel, with an ice bath available for cooling if necessary. Heating to reflux near the end of the reaction was advisable. Addition of 753 g (5.0 moles) of III to the rapidly-stirred sodium ethoxide solution during 2 hr. was followed by heating and stirring for 1 hr. at reflux. The reaction mixture was carefully neturalized to pH 6 by the dropwise addition of 10 M H_2SO_4 to the stirred and cooled solution. The ethanol solution was decanted from the salt residue and concentrated by distillation of the ethanol through a column packed with Berle saddles, to leave a residue of crude ethyl cyclopropanecarboxylate containing some ethanol. This was combined with the salt and sufficient water was added to dissolve the salt. The ester layer was separated and the aqueous layer was extracted with 2 x 250 ml of benzene. The combined benzene and ester layers were washed with saturated $NaHCO_3$ solution until no further color was extracted, then with 2 x 100 ml of saturated NaCl solution, filtered through a cone of anhydrous sodium sulfate and dried with Drierite. Preliminary distillation through a column packed with glass helices to remove benzene and alcohol obviated the need for the final drying step, since the benzene-alcohol-water ternary azeotrope removed water. Final distillation through a short column packed with Berle saddles or stainless steel mesh gave 375 g (66%) of I, bp. 129-130°, lit.[3] bp. 133-135°/750 mm.

Cyclopropanecarboxylic acid (III). - The reaction mixture containing crude ethyl cyclopropanecarboxylate (above) was separated by decantation and the salt was filtered by suction and washed with alcohol to recover additional product. The filtrate and washings were combined with the crude ester solution in a 3-ℓ flask fitted with a distilling head and dropping funnel and 865 ml of 6N NaOH solution was added dropwise, with vigorous stirring. Heating was applied to distill alcohol until the bumping became difficult to control; rotary evaporation was then used to concentrate the sodium salt to a thick slurry. While stirring and cooling in an ice bath, 10 M H_2SO_4 was added until the mixture was strongly acid (pH 1-2). The crude acid was separated and the aqueous layer was extracted with 5 x 100 ml of benzene (cyclopropanecarboxylic acid is soluble to the extent of about 3% in saturated salt solution.) The solution was dried by reflux under a Dean-Stark trap and after final drying with Drierite benzene was removed by distillation through a short column. The residue was distilled at reduced pressure to give 363 g (84%) of II, bp. 89-90°/16 mm, lit.[4] 94-95°/20 mm.

REFERENCES

1. W. Reppe [Ann., 596, 80 (1955)] first prepared 4-chlorobutyric acid esters by saturating an alcohol solution of γ-butyrolactone with hydrogen chloride with a zinc chloride catalyst. An improved yield (85%) using no catalyst was reported by D. S. Noyce and J. H. Canfield [J. Am. Chem. Soc., 76, 3630 (1954)]

2. The cyclization of methyl and ethyl 4-chlorobutyrate has been reported in several patents: U. S. Patent 2,992,269 (1959) [Chem. Abstr., 56, 12770 g (1952)] (Using NaH); French Patent 2,093,472 (1972) [Chem. Abstr., 77, 126126 p (1972)] (Using $NaOCH_3$).

3. G. M. Lampman, D. A. Horne, and G. D. Hager [J. Chem. Eng. Data, 14, 396 (1969)] report the preparation in 88% yield from ethyl 4-bromobutyrate and NaH.

4. C. M. McCloskey and G. H. Coleman in "Organic Synthesis", Coll. Vol. III, E. C. Horning, Ed., p. 221, John Wiley and Sons, New York, 1955.

5. G. H. Jeffery and A. L. Vogel, J. Chem. Soc., 1948, 1804.

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