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A NEW METHOD FOR SYNTHESIS OF α-KETOGLUTARIC ACID

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ABSTRACT

The purpose of this study is the preparation of α-ketoglutaric acid.

INTRODUCTION

α-ketoglutaric acid was first synthesized by Blaise and Gault (Blaise and Gault, 1908). Then, it was synthesized by the literature cited (Ingold, 1921; Hidemoto, 1968, Takahashi, 1974). Nowadays, α-ketoglutaric acid is being synthesized biochemically. In this study, its preparation was succeeded by the hydrolysis and decarboxylation of ethylooxalylsuccinonitrile which was obtained by Claisen condensation of diethyl oxalate with succinonitrile. The aim of the study was mainly to increase the yield of α-ketoglutaric acid.

EXPERIMENTAL

Melting points (uncorrected) were determined using a Thomas-Hoover melting point apparatus. IR spectra were recorded on Perkin-Elmer 377. ^{1}H NMR spectra were recorded at 60 MHz on Varian A-60.

Succinonitrile

1.28 mole of KCN was dissolved in 40 ml of distilled water in double neck flask carrying a seperatory funnel and a reflux condenser. Then, 0.40 mole of ethylene bromide in 150 ml of ethanol was added in a half hour and refluxed on a water bath at 55 °C for 12 hours. The solvent was removed by a rotary evaporator and succinonitrile was extracted with ethyl acetate from the residue. The solution was filtrated on a Buchner funnel by suction, dried over Na_2SO_4 ethyl acetate was remo-

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ved by distillation and residue was distilled under reduced pressure to obtain succinonitrile (Vogel, 1981). Yield: 18 g (50 %), bp. 134 °C/ 10 mmHg; IR (KBr): 2930, 2200, 1430 cm^{-1}.

Diethyl oxalate

The preparation was carried out according to the method taken from the literature (Vogel, 1981). Diethyl oxalate was purified by distillation. bp. 180 °C/ 760 mmHg; IR (KBr): 2995, 1700, 1200 cm^{-1}.

Ethyloxalylsuccinonitrile

Ethyloxalylsuccinonitrile was obtained by condensation of succinonitrile with oxalic acid in strongly alkaline medium. 0.05 mol of oxalic acid diester and 0.06 mol of succinonitrile solution in ether were added into potassium ter-butoxide in dry ether. This procedure was accomplished in a salt-ice bath with vigrous stirring. The potassium salt of condensation product was filtered and washed with ether then was hydrolysed with 5 % HCl solution.

Ethyloxalylsuccinonitrile was extracted with ether, dried over Na_2SO_4 ether was removed, the crude ethyl oxalylsuccinonitrile was crystallized from 1:1 alcohol-water mixture. The product had a mp. of 154-157 °C, insoluble in water, soluble in alcohol and acetone. Yield: 3.2 g (35 %). IR (KBr): 3450–3330, 3000, 2260, 1710 1630–1560 cm^{-1}.

α-Ketoglutaric acid

Ethyloxalylsuccinonitrile was kept in 20 % HCl solution at room temperature for two days. The solution was heated on an oil bath at 140 °C and then evaporated to dryness, the residue was extracted with ether and crystalized from acetone-benzene mixture. Yield: 0.31 g (12 %), mp. 109–110 °C; IR (KBr): 3600-2750, 1720 cm^{-1}; ^{1}H-NMR (CD_3COCD_3) δ (ppm) 2.8 (2H, t), 3.4 (2H, t), 14 (1H, s).

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