Carboxylation of Dilithium *ortho*-Toluates

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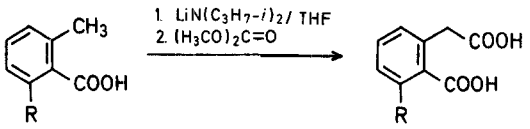
In conjunction with other work, we needed to transform an *ortho*-toluic acid to a homophthalic acid. A direct method to effect this transformation, the carboxylation of the dianion derived from the *ortho*-toluic acid with carbon dioxide, has been reported[1]. Unfortunately in the absence of hexamethylphosphoric triamide as cosolvent, the yield is only 25% and therefore the reaction is of little preparative value.

We have found an alternative, but equally direct, sequence which effects this transformation in consistently high yield. This is accomplished by generation of the dilithium anion of an *ortho*-toluic acid in the presence of excess lithium diisopropylamide and acylating with dimethyl carbonate, a masked carbon dioxide equivalent. Thus, reproducibly high conversions (85–90%) of *ortho*-toluic acid (**1a**) and 6-methoxy-*ortho*-toluic acid (**1b**) to the corresponding homophthalic acids **2a** and **2b** are obtained directly on reaction mixture work-up.



1a R = H
b R = OCH_3

2a, b

General Procedure for Carboxylation:

To a magnetically stirred solution of diisopropylamine (12.5 g, 124 mmol) in tetrahydrofuran (40 ml) under nitrogen at 0° was added *n*-butyllithium (124 mmol). The solution was stirred for 10 minutes, then cooled to −78°. A solution of the *ortho*-toluic acid **1a** or **1b** (31 mmol) and dimethyl carbonate (6.65 ml, 62 mmol) in tetrahydrofuran (40 ml) was added dropwise over 10 minutes. When the addition was completed, the cooling bath was removed and the reaction was allowed to warm to room temperature, during which time a precipitate formed in the yellow solution. The reaction mixture was stirred for 4 h, then water (50 ml) was added and stirring was continued overnight. The basic solution was evaporated at reduced pressure until water began to distill.

For homophthalic acid (**2a**), the solution was acidified (pH = 1) and extracted with ethyl acetate (4 × 75 ml). After drying ($MgSO_4$), ethyl acetate was removed at reduced pressure and the resulting solid was triturated with boiling chloroform, cooled, and filtered to give pure homophthalic acid; yield: 4.75 g (85%); m.p. 140–141 (Lit.[2], m.p. 140–141°).

For 6-methoxyhomophthalic acid (**2b**), the solution was acidified, then further evaporated until an oil precipitated. This mixture was extracted with hot ethyl acetate (4 × 75 ml). After drying ($MgSO_4$) and evaporation of the solvent, the residue was triturated with boiling ether (50 ml), cooled, and filtered to give pure 6-methoxyhomophthalic acid (**2b**); yield: 2.73 g. The filtrate was evaporated, the oily residue was diluted with water (50 ml) and a small amount of methanol, and heated in the steam bath for 15 min. After re-extraction with ethyl acetate, drying, evaporation of the solvent and ether treatment, an additional crop of pure product **2b** was obtained; yield: 2.54 g. The filtrate was again evaporated, the residue was dissolved in hot acetone which was then diluted with benzene. The resulting crystals (580 mg) were collected to bring the overall yield of pure **2b** to 5.85 g (90% yield), m.p. 164–165° (Lit.[3], m.p. 165°). An identical yield of **2b** was obtained when the reaction scale was tripled.

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