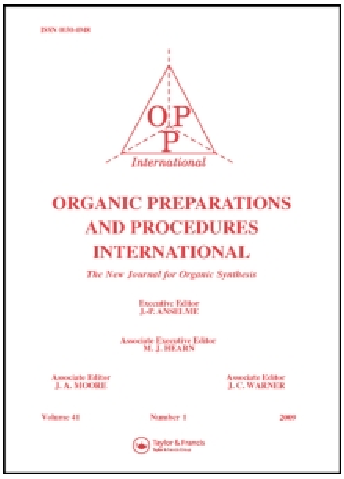

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3-(p-METHOXYBENZOYL)PROPIONIC ACID. AN IMPROVED SUCCINOYLATION PROCEDURE

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3-(p-METHOXYBENZOYL)PROPIONIC ACID. AN IMPROVED SUCCINOYLATION PROCEDURE.

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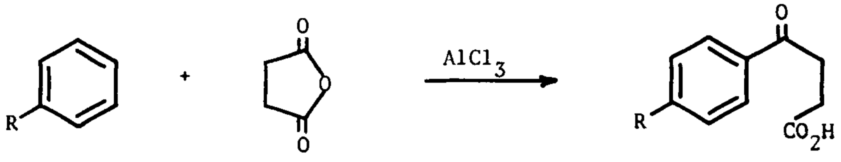
The preparation of 3-(p-methoxybenzoyl)propionic acid (2, R = OCH_3) by the Friedel-Crafts reaction between succinic anhydride and anisole in the presence of aluminum chloride is well documented in the literature.[2] This reaction has been conducted in nitrobenzene,[3] nitropropane,[4] tetrachloroethane[5] and a tetrachloroethane-nitrobenzene mixture[6] to give 75-95% yields of product. Anisole,[7] carbon disulfide[8] and benzene[9] have also been used as solvents, but result in lower yields. In most of the reports, a lengthy reaction period (24-72 hr) was followed by hydrolysis and removal of solvent by steam distillation. This procedure is inconvenient, time consuming and solvent removal by steam distillation results in some degradation of the product.



1 2

We have found that long reaction times at low temperature are unnecessary and that the product can be isolated rapidly without the necessity of a steam distillation or extractive work-up. The time expended in completing the entire preparation is less than 3 hr. The results of a systematic study of the succinoylation of anisole in various solvent systems using this procedure are indicated in Table I.

This succinoylation procedure was also found to be very satisfactory for several other monosubstituted benzenes (Table II). The success of this method is a reflection of the relative insolubility of the resulting γ-keto acids.

TABLE I

Effect of Solvent in the Preparation of 3-(p-Methoxybenzoyl)-propionic Acid.

Solvent	Isolated Yield, %
Nitromethane	80
Nitroethane	72
Nitropropane	68
Tetrachloroethane-Nitromethane[a]	80
Tetrachloroethane-Nitroethane[a]	72
Tetrachloroethane-Nitropropane[a]	93
Tetrachloroethane-Nitrobenzene[a]	82

(a) 4:1 mixture by volume.

TABLE II

Succinoylation of Monosubstituted Benzenes in a 4:1[a] Tetrachloroethane-Nitrobenzene Solvent System

Reactant	Product	mp, °C[b]	lit. mp, °C	Isolated Yield, %
Anisole	3-(p-Methoxybenzoyl)propionic Acid	146	146.5-147[c]	82
Toluene	3-(p-Methylbenzoyl)propionic Acid	124	127.5[d]	84
Chlorobenzene	3-(p-Chlorobenzoyl)propionic Acid	131	131[e]	37
Diphenyl ether[f]	3,3'-[Oxybis(p-phenylenecarbonyl)]-dipropionic Acid	221	217[g]	94

(a) By volume. (b) Melting points are uncorrected. (c) Reference 6b. (d) Reference 10. (e) Reference 11. (f) Two moles of succinic anhydride and five moles of anhydrous $AlCl_3$ were used per mole of diphenyl ether. (g) Reference 12.

EXPERIMENTAL

Succinoylation of Anisole in Tetrachloroethane-Nitrobenzene. The following experimental is representative of the general procedure. A mixture of 10.8 g (0.10 mol) of anisole and 10.0 g (0.10 mol) of succinic anhydride was taken up in 80 ml of tetrachloroethane and 20 ml of nitrobenzene. To this was added, in small portions with stirring, 40.0 g (0.30 mol) of anhydrous aluminum chloride while the temperature was kept below 50° by occasional cooling. When addition was completed, the reaction mixture was allowed to stand at room temperature for 45 min. The mixture was then added to a crushed ice-hydrochloric acid mixture, and the resulting precipitate of keto acid 2 (R = OCH_3) collected by filtration. The crude product was dissolved in potassium carbonate solution, filtered and washed once with ether. The precipitate obtained upon acidification with concentrated hydrochloric acid was filtered, washed with water and dried to give 17.1 g (82%) of pure 2 (R = OCH_3) as a white solid, mp 146°.

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