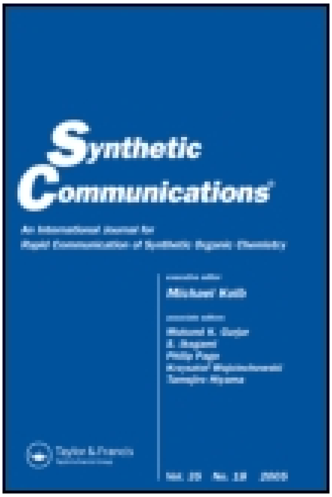

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A General and Simple Synthesis of Phenylglyoxylic Esters via the Oxidation of Mandelic Esters with Ammonium Chlorochromate Adsorbed on Alumina

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To cite this article: Gui-Sheng Zhang & Hui Gong (1999) A General and Simple Synthesis of Phenylglyoxylic Esters via the Oxidation of Mandelic Esters with Ammonium Chlorochromate Adsorbed on Alumina, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 29:18, 3149-3153, DOI: 10.1080/00397919908085939

To link to this article: http://dx.doi.org/10.1080/00397919908085939

SYNTHETIC COMMUNICATIONS, 29(18), 3149-3153 (1999)

A GENERAL AND SIMPLE SYNTHESIS OF PHENYLGLYOXYLIC ESTERS VIA THE OXIDATION OF MANDELIC ESTERS WITH AMMONIUM CHLOROCHROMATE ADSORBED ON ALUMINA

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ABSTRACT: A general method for preparation of phenylglyoxylic esters by oxidation of mandelic esters with readily available ammonium chlorochromate adsorbed on alumina is described.

α-Keto acids play an important role in biological studies and asymmetric synthesis. For example, they are usually used as precursors for biosynthesis of α-amino acids and human body's other necessary elements such as fats, carbohydrates, proteins and so on.[1] Phenylglyoxylic esters, being a special sort of α-keto esters, have attracted our attentions to search their new and easily preparative approaches.

Esterification is usually under consideration to obtain those esters. However, owing to specific reactive characteristics of α-keto acids, such reaction conditions

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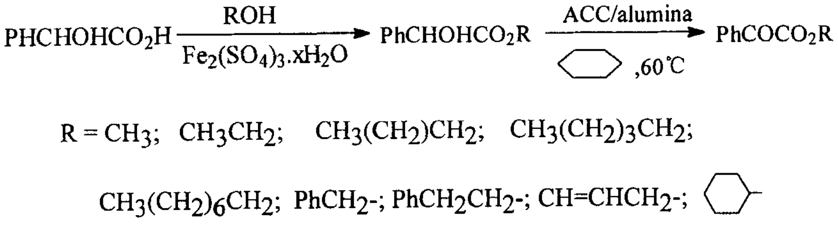
is less satisfactory in preparation of phenylglyoxylic esters.[2] J.Villieras[3] and co-workers reported that Grignard Reagent could be used for this purpose. They treated phenylmagnesium bromide with diethyl oxalate and finally produced ethyl phenylglyoxylic esters. Oxidation of phenylacetylene derivatives can also be utilized for synthesis of α-keto esters. L. Caglioti[4] and co-workers afforded methyl phenylglyoxylate via ozonolysis of 1-bromo phenylacetylene followed by reduction reaction with potassium iodide. P. Bulman[1] improved oxidation by treatment of trimethylsilyl phenylacetylenes with oxidative system of osmium tetroxide and t-butyl hydroperoxide in methanol solution to get identical product that L. Caglioti has gained. Though methods mentioned above could all be used in laboratory preparation of desired esters, their difficult manipulation or needing expensive reagents or relatively low yields prevented them from generalization.

We have previously reported that ammonium chlorochromate adsorbed on alumina (ACC/alumina) could be used as an efficient reagent for the oxidation of alcohols[5] and deoximes[6] to corresponding carbonyl compounds under non-aqueous conditions. Herein, we report a mild , convenient and economical method for the synthesis of phenylglyoxylic esters via the oxidation of mandelic esters in high yields by using ACC/alumina. Mandelic esters can be easily prepared by the esterification of mandelic acid with alcohols using $Fe_2(SO_4)_3 \cdot xH_2O$ as catalyst.

Our experiments show that mandelic esters are converted to their corresponding phenylglyoxylic esters in cyclohexane with advantages of mild reaction conditions, ease of work-up and high yields. Further oxidation by cleavage of the bond (CHOH-COOR) to benzoic acids was not observed. The results obtained from the preparation of 9 phenylglyoxylic esters are listed in Table. In conclusion, with the easily available oxidant, high yields, mild conditions and easy operation, Scheme



we think that the present work described herein may provide a convenient and efficient synthetic method of phenylglyoxylic esters.

Experimental Section

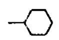
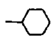
General Procedure for the Preparation of Mandelic esters

Place a mixture of mandelic acid (10mmol), alcohol (20mL) and catalyst (0.1g) in a 50mL two-necked flask, equipped with a condenser and mechanical stirrer. Heat the mixture, with stirring, in a oil bath for 4-12h, The progress of the reaction is followed by TLC. Remove the excess of alcohol by distillation under reduced pressure. Dilute the residue with ether (40mL) and filter off the catalyst. Treat the filtrate with 5% sodium bicarbonate solution and saturated brine solution. Drying over anhydrous magnesium sulfate, filtration and evaporation to give the crude product. The pure products are obtained by recrystallization or on a silica-gel column. The yields are 50-85%.

General Procedure for the Preparation of Phenylglyoxylic Esters

1mmol substrate was dissolved in 20 ml cyclohexane in three-necked flask which was equipped with mechanical stirrer and a thermometer. The oxidant powder (2mmol) was added in parts during period of 1 hour at 60℃ with stirring. The

Table Oxidation of Mandelates to α-Keto Phenylacetates [a]

Substrate	Product	Time (h)	Yield [b] (%)
$\mathrm{PhCHOHCO_2CH_3}$	$\mathrm{PhCOCO_2CH_3}$	2	73
$\mathrm{PhCHOHCO_2CH_2CH_3}$	$\mathrm{PhCOCO_2CH_2CH_3}$	2	78
$\mathrm{PhCHOHCO_2CH_2\ (CH_2)CH_3}$	$\mathrm{PhCOCO_2CH_2(CH_2)CH_3}$	2	75
$\mathrm{PhCHOHCO_2CH_2(CH_2)_3CH_3}$	$\mathrm{PhCOCO_2CH_2(CH_2)_3CH_3}$	13.5	80
$\mathrm{PhCHOHCO_2CH_2(CH_2)_6CH_3}$	$\mathrm{PhCOCO_2CH_2(CH_2)_6CH_3}$	2	78
$\mathrm{PhCHOHCO_2\text{-}CH_2Ph}$	$\mathrm{PhCOCO_2\text{-}CH_2Ph}$	2	80
$\mathrm{PhCHOHCO_2\text{-}CH_2CH_2Ph}$	$\mathrm{PhCOCO_2\text{-}CH_2CH_2Ph}$	2	85
$\mathrm{PhCHOHCO_2\text{-}CH_2CH{=}CH_2}$	$\mathrm{PhCOCO_2\text{-}CH_2CH{=}CH_2}$	2	70
$\mathrm{PhCHOHCO_2}$ 	$\mathrm{PhCOCO_2}$ 	1.5	69

a. Reactions carried out at 60℃ in cyclohexane solvent. Oxidant added in batches. The ratio of substrate to oxidant: 1mmol to 1.5g ACC/alumina (2mmol equivalent of CrO_3). *b*.Yields based on isolated products which were purified by column chromatography with mixed eluent and determined on their IR spectra .

mixture was stirred for additional hours. The procedure was traced by TLC. After the reaction finished, the reaction mixture was filtered and the precipitate was washed with cyclohexane (2×10mL). The products were obtained by removing solvent from the combined filtrates under reduced pressure and purifying the residue on silica-gel column chromatography with the mixture eluent (cy-C_6H_{12}:ether = 4:1).

Acknowledgment

Project 29577273 Supported by National Science Foundation of China.

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Received in the UK 13 November 1998