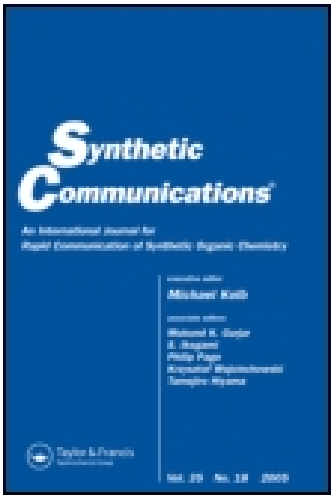

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M. Narender [a], M. Somi Reddy [a], V. Pavan Kumar [a] & K. Rama Rao [a]
[a] Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad, India
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Organic Reactions in Water: Synthesis of Phenacyl Esters from Phenacyl Bromide and Potassium Salts of Aromatic Acids in the Presence of β-Cyclodextrin

M. Narender, M. Somi Reddy, V. Pavan Kumar, and K. Rama Rao
Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad, India

Abstract: A convenient and facile synthesis of phenacyl esters is reported by the reaction of phenacyl bromide with potassium salts of aromatic acids in the presence of β-cyclodextrin in water under neutral conditions.

Keywords: β-Cyclodextrin, phenacylbromide, phenacyl esters, potassium salts of carboxylic acids, water

INTRODUCTION

The synthesis of phenacyl esters has many advantages in organic chemistry because they are usually solids and provide a useful means of characterizing acids and phenols. The classical synthesis of phenacyl esters consists of treating the sodium or potassium salts of acids with α-bromoacetophenones,[1] but are associated with problems such as low yields, slow reaction times, hydrolysis of the alkylating agents,[2] and contamination of the product with the starting alkylating reagent. To overcome these disadvantages, a number of methods have been developed such as potassium fluoride in glacial acetic acid,[3] polymer-supported reagents,[4] crown ether in conjunction with

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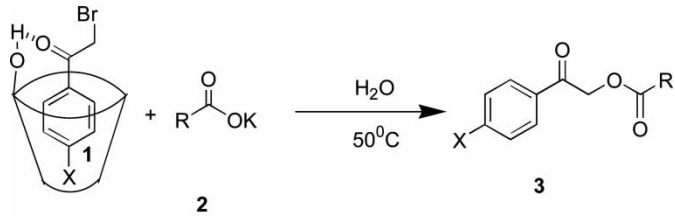
Address correspondence to K. Rama Rao, Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad 500 007, India. Tel.: +91-40-27193164; Fax: +91-40-27160757; E-mail: drkrrao@yahoo.com

phase transfer catalyst (PTC),[5] crown ether under reflux conditions,[6] and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene,[7] which is carcinogenic. Even recently, Liu et al.[8] reported the synthesis of phenacyl esters from α-tosyloxy ketones in ionic liquids. We saw the need to develop a mild and widely applicable approach for the synthesis of phenacyl esters in water under neutral conditions.

RESULTS AND DISCUSSION

Cyclodextrins, which are cyclic oligosaccharides, have excited much interest as enzyme models because of their ability to bind substrates selectively and catalyze chemical reactions by supramolecular catalysis involving the reversible formation of host–guest complexes with the substrates by noncovalent bonding as seen in enzyme complexation processes.[9] Complexation depends on the size, shape, and hydrophobicity of the guest molecule. The synthesis of phenacyl esters in the presence of β-cyclodextrin has been examined (Scheme 1). In general, these reactions were carried out by dissolving β-cyclodextrin in water, followed by the addition of phenacyl bromide **1** and potassium salt of carboxylic acid **2** to obtain the corresponding phenacyl ester. All the products were characterized by ^{1}H NMR, IR, and mass spectroscopy. Although these reactions were carried out in situ, the cyclodextrin complexes were isolated and characterized by ^{1}H NMR in D_2O. There is an upfield shift of C_3 and C_5 protons of cyclodextrin indicating the formation of inclusion complex.[10] These reactions did not proceed in the absence of β-cyclodextrin. We believe that β-cyclodextrin activates the phenacyl bromide by forming the hydrogen bond and also acts as a solubilizing agent. These cyclodextrins can also be recovered and reused.

This method has many advantages over the existing methodologies, offering an environmentally benign protocol with the practical convenience of not having to handle flammable and anhydrous organic solvents, and is a practical method involving carboxylic acid salts.



X=H, Cl, Br, Me, NO_2

R=Ph, $PhCH_2$, PhCH=CH

Scheme 1.

EXPERIMENTAL

Materials

All reactions were carried out without any special precautions in an atmosphere of air. Chemicals and solvents were purchased from Fluka and S. D. Fine Chemicals and used as received. The ^{1}H NMR spectra were recorded on a 300 or 400 MHz spectrometer. IR spectra were recorded on a NICOLET FT-IR spectrometer. Mass spectra were observed on V. G. Auto spectrometer.

General Procedure

To a solution of β-cyclodextrin (1 mmol) in water (25 mL) at 50°C phenacyl bromide (1 mmol) in acetone (1 mL) was added. After 10 min, the potassium salt of carboxylic acid (1.2 mmol) was added. After completion of the reaction, the organic material was extracted with ethyl acetate, washed with sodium bicarbonate and brine, and dried over sodium sulphate. On solvent removal, the crude product was purified on silica gel by using ethylacetate–hexane (2:98) as an eluent.

1-(2-Phenylcarbonyloxyacetyl) benzene (1). White solid, yield 90%, mp 116–118°C; IR (KBr) 1720 cm^{-1}, 1685 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 5.55 (s, 2H), 7.40–7.70 (m, 6H), 7.95 (d, 2H, $J = 7.9$ Hz), 8.15 (d, 2H, $J = 7.5$ Hz); Anal. calcd. for $C_{15}H_{12}O_3$ requires C, 74.99; H, 5.03; found: C, 74.85; H, 5.12.

2-Oxo-2-phenylethyl 2-phenylacetate (2). Brown oil, yield 95%, IR (KBr) 1715 cm^{-1}, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.82 (s, 2H), 5.32 (s, 2H), 7.25–7.40 (m, 5H), 7.47 (t, 2H, $J = 9.4$ Hz), 7.63 (t, 1H, $J = 9.4$ Hz), 7.93 (d, 2H, $J = 9.4$ Hz). Anal. calcd. for $C_{16}H_{14}O_3$ requires C, 75.58; H, 5.55; found: C, 75.45; H, 5.65.

2-Oxo-2-phenylethyl 3-phenyl-(E)-2-propenoate (3). White solid, yield 88%, mp 110°C; IR (KBr) 1702 cm^{-1}, 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 5.45 (s, 2H), 6.60 (d, 1H, $J = 16.4$ Hz), 7.37–7.42 (m, 3H), 7.45–7.70 (m, 5H), 7.80 (d, 1H, $J = 16.4$ Hz), 7.95 (d, 2H, $J = 9.6$ Hz). Anal. calcd. for $C_{17}H_{14}O_3$ requires C, 76.68; H, 5.30; found: C, 76.52; H, 5.40.

4-Chloro-1-(2-phenylcarbonyloxyacetyl) benzene (4). White solid, yield 92%, mp 117–119°C; IR (KBr) 1732 cm^{-1}, 1702 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.48 (s, 2H), 7.40–7.50 (m, 4H), 7.59 (t, 1H, $J = 9.3$ Hz), 7.93 (d, 2H, $J = 9.0$ Hz), 8.12 (d, 2H, $J = 9.0$ Hz); Anal. calcd. for

$C_{15}H_{11}O_3Cl$ requires C, 65.59; H, 4.04; Cl, 12.91; found: C, 65.45; H, 4.13; Cl, 12.79.

2-(4-Chlorophenyl)-2-oxoethyl 2-phenylacetate (5). White solid, yield 90%, mp 73–75°C; IR (KBr) 1750 cm^{-1}, 1695 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 3.80 (s, 2H), 5.25 (s, 2H), 7.25–7.40 (m, 5H), 7.47 (d, 2H, $J = 9.2$ Hz), 7.85 (d, 2H, $J = 9.2$ Hz). Anal. calcd. for $C_{16}H_{13}O_3Cl$ requires C, 66.56; H, 4.54; Cl, 12.28; found: C, 66.43; H, 4.65; Cl, 12.44.

2-(4-Chlorophenyl)-2-oxoethyl 3-phenyl-(E)-2-propenoate (6). white solid, yield 90%, mp 135°C; IR (KBr) 1709 cm^{-1}, 1632 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 5.40 (s, 2H), 6.60 (d, 1H, $J = 14.6$ Hz), 7.35–7.45 (m, 3H), 7.45–7.55 (m, 4H), 7.80 (d, 1H, $J = 14.6$ Hz), 7.95 (d, 2H, $J = 9.3$ Hz). Anal. calcd. for $C_{17}H_{13}O_3Cl$ requires C, 67.89; H, 4.36; Cl, 11.79; found: C, 67.75; H, 4.53; Cl, 11.53.

4-Bromo-1-(2-phenylcarbonyloxyacetyl) benzene (7). White solid, yield 93%, mp 119–120°C; IR (KBr) 1734 cm^{-1}, 1701 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 5.52 (s, 2H), 7.46 (t, 2H, $J = 9.4$ Hz), 7.57 (t, 1H, $J = 9.4$ Hz), 7.67 (d, 2H, $J = 9.4$ Hz), 7.85 (d, 2H, $J = 10.0$ Hz), 8.13 (d, 2H, $J = 10.0$ Hz); Anal. calcd. for $C_{15}H_{11}O_3Br$ requires C, 56.45; H, 3.47; Br, 25.04; found: C, 56.30; H, 3.67; Br, 25.18.

2-(4-Bromophenyl)-2-oxoethyl 2-phenylacetate (8). White solid, yield 88%, mp 77°C; IR (KBr) 1749 cm^{-1}, 1697 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ: 3.80 (s, 2H), 5.30 (s, 2H), 7.30–7.40 (m, 5H), 7.60 (d, 2H, $J = 9.0$ Hz), 7.75 (d, 2H, $J = 9.0$ Hz). Anal. calcd. for $C_{16}H_{13}O_3Br$ requires C, 57.68; H, 3.93; Br, 23.98; found: C, 57.53; H, 4.18; Br, 23.86.

2-(4-Bromophenyl)-2-oxoethyl 3-phenyl-(E)-2-propenoate (9). White solid, yield 86%, mp 137°C; IR (KBr) 1720 cm^{-1}, 1701 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ: 5.40 (s, 2H), 6.55 (d, 1H, $J = 16.7$ Hz), 7.35–7.85 (m, 10H). Anal. calcd. for $C_{17}H_{13}O_3Br$ requires C, 59.15; H, 3.80; Br, 23.15; found: C, 59.28; H, 3.71; Br, 23.02.

4-Methyl-1-(2-phenylcarbonyloxyacetyl) benzene (10). White solid, yield 88%, mp 105°C; IR (KBr) 1732 cm^{-1}, 1697 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.45 (s, 3H), 5.51 (s, 2H), 7.30 (d, 2H, $J = 8.2$ Hz), 7.45 (t, 2H, $J = 8.9$ Hz), 7.56 (t, 1H, $J = 8.9$ Hz), 7.87 (d, 2H, $J = 8.2$ Hz), 8.13 (d, 2H, $J = 8.9$ Hz); Anal. calcd. for $C_{16}H_{14}O_3$ requires C, 75.58; H, 5.55; found: C, 75.41; H, 5.41.

2-(4-Methylphenyl)-2-oxoethyl 2-phenylacetate (11). White solid, yield 90%, mp 77°C; IR (KBr) 1745 cm^{-1}, 1699 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.45 (s, 3H), 3.80 (s, 2H), 5.30 (s, 2H), 7.20–7.40

(m, 7H), 7.80 (d, 2H, $J = 9.5$ Hz). Anal. calcd. for $C_{17}H_{16}O_3$ requires C, 76.10; H, 6.01; found: C, 76.30; H, 5.87.

2-(4-Methylphenyl)-2-oxoethyl 3-phenyl-(E)-2-propenoate (12). White solid, yield 87%, mp 130°C; IR (KBr) 1725 cm^{-1}, 1695 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.45 (s, 3H), 5.40 (s, 2H), 6.55 (d, 1H, $J = 15.0$ Hz), 7.27 (d, 2H, $J = 8.8$ Hz), 7.35–7.40 (m, 3H), 7.50–7.60 (m, 2H), 7.80 (d, 1H, $J = 15.0$ Hz), 7.87 (d, 2H, $J = 8.8$ Hz). Anal. calcd. for $C_{18}H_{16}O_3$ requires C, 77.13; H, 5.75; found: C, 77.28; H, 5.88.

4-Nitro-1-(2-phenylcarbonyloxyacetyl) benzene (13). Pale yellow solid, yield 90%, mp 140–142°C; IR (KBr) 1726 cm^{-1}, 1705 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ: 5.53 (s, 2H), 7.46 (t, 2H, $J = 7.8$ Hz), 7.60 (t, 1H, $J = 7.8$ Hz), 8.10–8.18 (m, 4H), 8.39 (d, 2H, $J = 8.4$ Hz); Anal. calcd. for $C_{15}H_{11}O_5N$ requires C, 63.16; H, 3.89; N, 4.91; found: C, 63.31; H, 3.74; N, 4.76.

2-(4-Nitrophenyl)-2-oxoethyl 2-phenylacetate (14). Pale yellow solid, yield 89%, mp 87°C; IR (KBr) 1728 cm^{-1}, 1705 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ: 3.80 (s, 2H), 5.40 (s, 2H), 7.40–7.50 (m, 3H), 7.55–7.65 (m, 2H), 8.15 (d, 2H, $J = 8.8$ Hz), 8.40 (d, 2H, $J = 8.8$ Hz). Anal. calcd. for $C_{16}H_{13}O_5N$ requires C, 64.28; H, 4.38; N, 4.68; found: C, 64.43; H, 4.51; N, 4.82.

2-(4-Nitrophenyl)-2-oxoethyl 3-phenyl-(E)-2-propenoate (15). Pale yellow solid, yield 93%, mp 152°C; IR (KBr) 1728 cm^{-1}, 1705 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ: 5.40 (s, 2H), 6.55 (d, 1H, $J = 16.6$ Hz), 7.35–7.45 (m, 3H), 7.50–7.60 (m, 2H), 7.80 (d, 1H, $J = 16.6$ Hz), 8.15 (d, 2H, $J = 9.2$ Hz), 8.40 (d, 2H, $J = 9.2$ Hz). Anal. calcd. for $C_{17}H_{13}O_5N$ requires C, 65.59; H, 4.21; N, 4.50; found: C, 65.76; H, 4.05; N, 4.35.

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