The Use of a Nitro-group to ensure Intermolecular Acylation by *p*-Nitrohydrocinnamic Acid and *p*-Nitro-γ-phenylbutyric Acid

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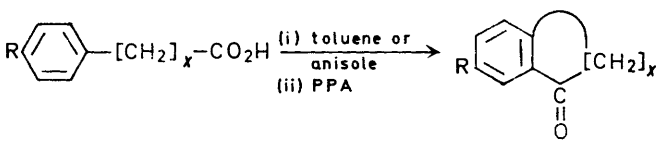
The deactivating effect of the nitro-group in *p*-nitrohydrocinnamic acid (VII) and *p*-nitro-γ-phenylbutyric acid (VIII) facilitates intermolecular acylation with toluene and anisole to provide the corresponding open-chain ketones in the presence of polyphosphoric acid. Intramolecular acylation of *p*-nitro-γ-phenylbutyric acid (VIII) in polyphosphoric acid gave 7-nitro-α-tetralone (XI) in low yield.

HYDROCINNAMIC acid (I), γ-phenylbutyric acid (II), and *p*-methoxy-γ-phenylbutyric acid (III) readily undergo intramolecular acylation to form α-hydrindone (IV),[1] α-tetralone (V),[1] and 7-methoxy-α-tetralone (VI)[2] in high yields. We have treated these carboxylic acids with toluene and anisole in the presence of polyphosphoric acid in order to determine their relative tendencies to form inter- and intra-molecularly acylated products. The tendency for intramolecular acylation was found to be so great that even when the reactions were carried out under conditions expected to favour intermolecular acylation, only the intramolecularly acylated products were obtained; yields were, however, slightly diminished (see Scheme 1). Compounds (I)—(III) were subject to



(I) R = H, x = 2 (IV) R = H, x = 2
(II) R = H, x = 3 (V) R = H, x = 3
(III) R = OMe, x = 3 (VI) R = OMe, x = 3

SCHEME 1

intramolecular acylation because of the presence of one or more activating substituents on the aromatic ring. In order to obtain products from an intermolecular acylation we used compounds containing a deactivating group in the aromatic ring, *i.e. p*-nitrohydrocinnamic acid (VII)[3] and *p*-nitro-γ-phenylbutyric acid (VIII).[4] Condensation of toluene with (VII) and (VIII) in the presence of polyphosphoric acids gave good yields of the corresponding open-chain ketones *p'*-methyl-β-(*p*-nitrophenyl)propiophenone (IX) and *p'*-methyl-γ-(*p*-nitrophenyl)-butyrophenone (X). Intermolecular acylation reaction of anisole also went smoothly with (VII) and (VIII) to yield *p'*-methoxy-β-(*p*-nitrophenyl)propiophenone (XII) and *p'*-methoxy-γ-(*p*-nitrophenyl)butyrophenone (XIII). The n.m.r. spectra indicated that the acylated products were homogeneous (see Scheme 2).

Cyclisation reactions (intramolecular acylation) with (VII) gave only tar, whereas (VIII) gave 7-nitro-α-tetralone (XI) though in much diminished yield.

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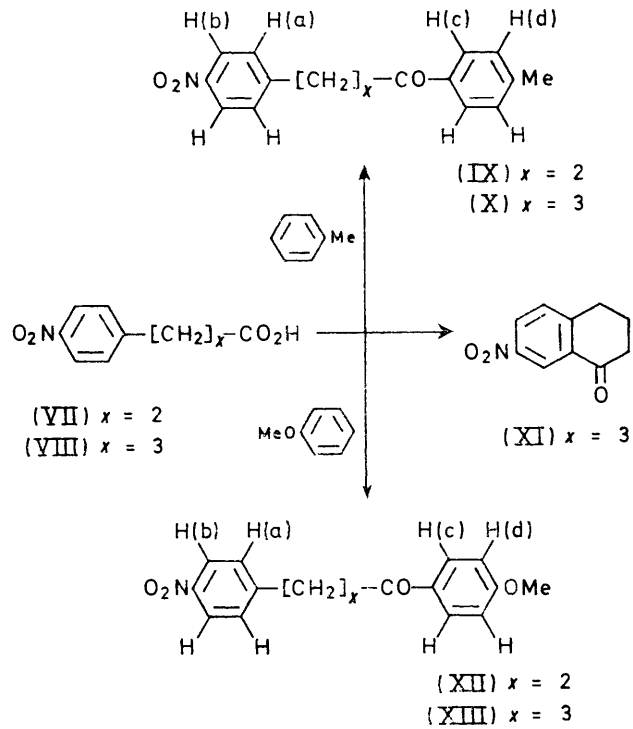
[2] G. S. K. Rao and S. Dev, *J. Indian Chem. Soc.*, 1957, **34**, 255.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 421 spectrophotometer. N.m.r. spectra were measured with a Varian A-60 (60 MHz) and HA 100 spectrometer (100 MHz)



(IX) x = 2
(X) x = 3
(VII) x = 2
(VIII) x = 3
(XI) x = 3
(XII) x = 2
(XIII) x = 3

SCHEME 2

for solutions in deuteriochloroform with tetramethylsilane as internal standard. M.p.s were taken on a Hershberg melting point apparatus using a set of Anschutz thermometers.

General Procedure for the Preparation of the Ketones.—To a stirred solution of polyphosphoric acid[5] prepared by dissolving anhydrous phosphorus pentoxide in 85% phosphoric acid generally in 2 : 1 ratio was added a mixture of the carboxylic acid and the compound to be acylated. The reaction mixture was heated at 120—125° in an oil-bath for ½ hr. Addition of ice–water yielded an oil. The mixture was extracted twice with ether, washed with 10% sodium carbonate solution, and dried ($MgSO_4$). Evaporation of the dry solvent gave the desired product which was crystallised.

[3] E. Feltenstein, *Ann. chim.* (*France*) [13], 1957, **2**, 587 (*Chem. Abs.*, 1958, **52**, 6258f).
[4] E. A. Smirnov, *J. Gen. Chem.* (*U.S.S.R.*), 1955, **25**, 769 (*Chem. Abs.*, 1956, **50**, 2481a).
[5] F. D. Popp and W. E. McEwen, *Chem. Rev.*, 1958, **58**, 321.

p'-*Methyl*-β-(p-*nitrophenyl*)*propiophenone* (IX).—A solution of *p*-nitrohydrocinnamic acid (VII) (3 g., 0·015 mole) and toluene (5·6 g., 0·06 mole) in polyphosphoric acid (30 g.) was treated and worked-up as in the foregoing procedure to give compound (IX) (3 g., 73%), m.p. 104—105°. Crystallisation from methanol gave pale yellow needles, m.p. 106° (Found: C, 71·35; H, 5·6; N, 5·3. $C_{16}H_{15}NO_3$ requires C, 71·35; H, 5·6; N, 5·2%), $\nu_{max.}$ (KBr) 1670, 1600, 1505, 1340, 1175, 845, and 805 cm.$^{-1}$, τ 1·95, 2·18, 2·63, and 2·8 (8H, 4d, J_{ab} 8·5 Hz and J_{cd} 8·0 Hz, Ar–H), 6·52—6·95 (4H, m, 2 × CH_2), and 7·65 (3H, s, Ar–CH_3).

It afforded a 2,4-dinitrophenylhydrazone, as needles, m.p. 238—239° (from chloroform) (Found: C, 58·6; H, 4·3; N, 15·4. $C_{22}H_{19}N_5O_6$ requires C, 58·8; H, 4·25; N, 15·6%).

p'-*Methyl*-γ-(p-*nitrophenyl*)*butyrophenone* (X).—Toluene (5·6 g., 0·06 mole), *p*-nitro-γ-phenylbutyric acid (VIII) (3 g., 0·014 mole), and polyphosphoric acid (30 g.) were allowed to react to give the ketone (X) (3 g., 74%) which crystallised from methanol as pale yellow needles, m.p. 88° (Found: C, 72·0; H, 6·2; N, 4·9. $C_{17}H_{17}NO_3$ requires C, 72·05; H, 6·05; N, 4·95%), $\nu_{max.}$ (KBr) 1680, 1605, 1520, 1342, 1180, 1110, 865, 810, and 755 cm.$^{-1}$; τ 1·9, 2·15, 2·67, and 2·85 (8H, 4d, J_{ab} 8·0 Hz and J_{cd} 8·5 Hz, Ar–H), 6·95—7·3 (4H, m, 2 × CH_2), 7·92 (2H, quintet, 1 × CH_2), and 7·64 (3H, s, Ar–CH_3).

A 2,4-dinitrophenylhydrazone had m.p. 218—219° (chloroform–pentane) (Found: C, 59·3; H, 4·56; N, 14·9. $C_{23}H_{21}N_5O_6$ requires C, 59·6; H, 4·57; N, 15·1%).

p'-*Methoxy*-β-(p-*nitrophenyl*)*propiophenone* (XII).—A solution of anisole (5·4 g., 0·05 mole) and *p*-nitrohydrocinnamic acid (VII) (1·95 g., 0·01 mole) in polyphosphoric acid (20 g.) was allowed to react to furnish the product (XII) (1·9 g., 67%), which recrystallised from methanol to give pale yellow needles, m.p. 129° (Found: C, 67·2; H, 5·3; N, 4·8. $C_{16}H_{15}NO_4$ requires C, 67·35; H, 5·3; N, 4·9%), $\nu_{max.}$ (KBr) 1665, 1600, 1510, 1335, 1250, 1205, 1180, 1105, and 840 cm.$^{-1}$; τ 1·9, 2·1, 2·62, and 3·1 (8H, 4d, J_{ab} 8·0 Hz and J_{cd} 8·5 Hz, Ar–H), 6·18 (3H, s, Ar–OCH_3), and 6·58—6·98 (4H, m, 2 × CH_2).

The ketone (XII) afforded a 2,4-dinitrophenylhydrazone, as prisms, m.p. 246—247° (from chloroform) (Found: C, 56·6; H, 4·2; N, 14·7. $C_{22}H_{19}N_5O_7$ requires C, 56·7; H, 4·1; N, 15·05%).

p'-*Methoxy*-γ-(p-*nitrophenyl*)*butyrophenone* (XIII).—A mixture of *p*-nitro-γ-phenylbutyric acid (VIII) (5 g., 0·023 mole) and anisole (10·8 g., 0·1 mole) was condensed in polyphosphoric acid (50 g.). Removal of the solvent gave the ketone (XIII) (6 g., 85%) which crystallised from methanol as pale yellow needles, m.p. 114° (Found: C, 68·2; H, 5·7; N, 4·75. $C_{17}H_{17}NO_4$ requires C, 68·2; H, 5·7; N, 4·7%), $\nu_{max.}$ (KBr) 1670, 1592, 1510, 1350, 1255, 1225, 1170, and 825 cm.$^{-1}$; τ 1·88, 2·1, 2·65 and 3·1 (8H, 4d, J_{ab} 8·6 Hz and J_{cd} 9·0 Hz, Ar–H), 6·15 (3H, s, Ar–OCH_3), 6·95—7·28 (4H, m, 2 × CH_2), and 7·92 (2H, quintet, 1 × CH_2).

It gave a 2,4-dinitrophenylhydrazone, m.p. 210—211° (from chloroform–pentane) (Found: C, 57·5; H, 4·5; N, 14·8. $C_{23}H_{21}N_5O_7$ requires C, 57·6; H, 4·4; N, 14·6%).

7-*Nitro*-α-*tetralone* (XI) *from* p-*Nitro*-γ-*phenylbutyric Acid* (VIII).—To a well stirred solution of polyphosphoric acid (30 g.) was added *p*-nitro-γ-phenylbutyric acid (VIII) (3 g., 0·014 mole). The temperature was raised to 120—125° during ½ hr. and held at that temperature for another ½ hr. It was cooled and work-up gave the desired compound (XI) (1 g., 37%), m.p. 101—102°. Crystallisation from ethanol gave the needles, m.p. 105—106° (lit.,[6] m.p. 105°) which was identical with an authentic sample [6] as shown by mixed m.p. and comparison of i.r. spectra (Found: C, 62·5; H, 4·73; N, 7·5. $C_{10}H_9NO_3$ requires C, 62·8; H, 4·7; N, 7·32%).

Intramolecular Acylation of the Carboxylic Acids (I), (II), *and* (III) *in the Presence of Toluene and Anisole.*—A solution of toluene (0·15 mole) or anisole (0·15 mole) and one of the acids (I)—(III) (0·025 mole) was treated with polyphosphoric acid (50 g.) to give the ketones (IV)—(VI) (*ca.* 70—80%). The i.r. and n.m.r. spectra of these materials were identical with those of the authentic samples.[1,2] Furthermore, the 2,4-dinitrophenylhydrazones of the products (IV)—(VI) were identical (mixed m.p. and i.r. spectrum) with those of the authentic samples.[1,2]

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[6] W. Reppe, *Annalen*, 1955, **596**, 120.