Reactions of Hydrazonoyl Halides with Imidazoles and Benzimidazoles

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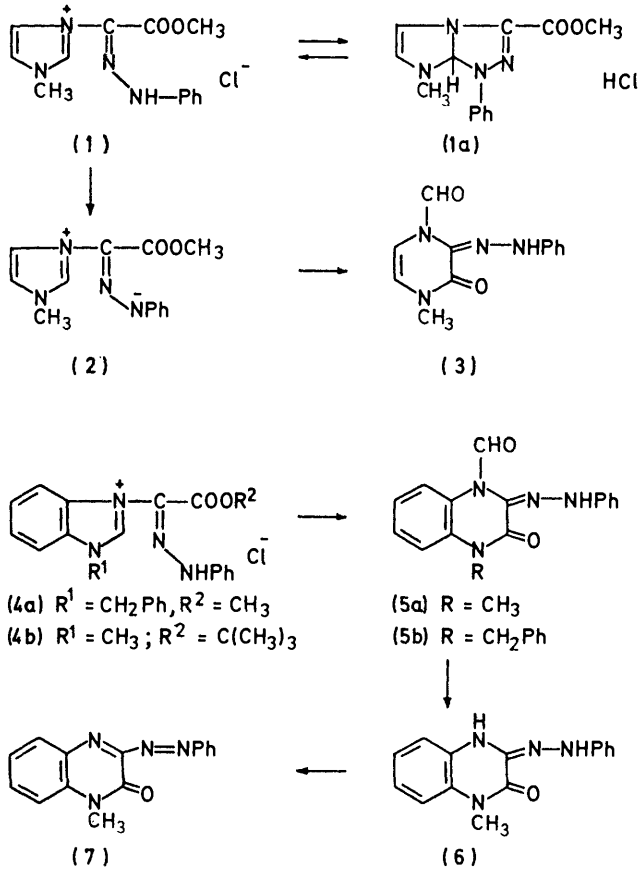
Hydrazonoyl halides upon reaction with *N*-methylimidazole and *N*-substituted benzimidazoles yield ring opened 1 : 1 adducts. The action of aqueous sodium hydroxide on these adducts leads to the formation of pyrazin-2-one or quinoxalin-2-one derivatives *via* ring expansion.

As part of our interest in the cycloadditions of 1,3-dipoles to give heterocyclic systems [1,2] we have investigated the reaction of several five-membered ring heterocyclic imines with hydrazonoyl halides. Methyl α-chloroglyoxylate phenylhydrazone reacted, in the presence of triethylamine, with *N*-methylimidazole in chloroform, at room temperature, to give a 1 : 1 adduct isolated as chloride (1) by addition of hydrogen chloride



to the mixture. In the absence of triethylamine the reaction does not occur.

The ring opened structure was assigned to (1) on the basis of analytical and spectroscopic data. The n.m.r. spectrum shows signals at δ 8.9, 7.9, and 7.8 typical of an imidazolium cation. Protonation of the imidazole system causes a downfield shift of the nuclear proton signals from δ 7.2, 6.9, and 6.7 (free base) to δ 9.1, 7.9, and 7.7 (protonated base) respectively for the hydrogen atoms in the 2-, 5-, and 4-positions.

The alternative bicyclic structure (1a) was ruled out due to the lack of any proton signal for the ring junction in the expected region of δ 4.5—6.0 usual for this type of ring system.[3]

Structure (1) was also confirmed by the following chemical transformations. Pyrolysis gave *N*-methylimidazole and 3,6-bismethoxycarbonyl-1,4-diphenyl-1,4-dihydro-*s*-tetrazine from dimerisation of the intermediate nitrile imide. Treatment with an equimolar amount of sodium hydroxide in a two phase system (water–chloroform) at low temperature afforded the ylide (2). This compound, unstable in moistened protic solvents, was converted into aqueous ethanol into 4-formyl-1-methyl-3-phenylhydrazono-3,4-dihydropyrazin-2-one (3).

The n.m.r. spectrum of (3) by comparison with that of (1) strongly suggests the assigned structure since it contains three singlets at δ 3.95, 9.5, and 13.2, attributed respectively to the protons of the NCH_3, CHO, and NH groups. In the i.r. spectrum there are two strong absorptions at 1 680 and 1 640 cm^{-1} assigned to formyl and lactam carbonyl groups.

In the case of *N*-alkylbenzimidazoles also reaction with hydrazonoyl halides afforded ring opened adducts (4) which on treatment with sodium hydroxide in aqueous ethanol yielded 1-alkyl-4-formyl-3-phenylhydrazono-3,4-dihydroquinoxalin-2-ones (5).

The most interesting aspect of the chemical behaviour of adducts (1) and (4) was the observed ring enlargement from five- to six-membered heterocyclic systems. This was due to nucleophilic attack of a hydroxide ion on the 2-position of the imidazolium or benzimidazolium system with the formation of a pseudo-base (A) in tautomeric equilibrium with the opened form (B) which can cyclise, by reaction with the ester group, to give pyrazinone or quinoxalinone.

The structure of the ring expanded products was confirmed on the basis of analytical and spectroscopic data and by hydrolytic removal of the formyl group. Reaction of (5a) with 50% aqueous acetic acid gave 1-methyl-3-phenylhydrazono-3,4-dihydroquinoxalin-2-one (6) * which was also prepared in a different way by reacting *N*-benzyl-*N*-methyl-*o*-phenylenediamine with methyl

* This compound is easily oxidised by air to the corresponding 1-methyl-3-phenylazoquinoxalin-2-one (7).

α-chloroglyoxylate phenylhydrazone followed by catalytic debenzylation of the intermediate condensation product. Finally treatment with sodium methoxide in refluxing methanol gave (6). The characteristics (n.m.r., i.r., and mixed m.p.) of the product were identical with those of the compound obtained by hydrolysis of (5a).

EXPERIMENTAL

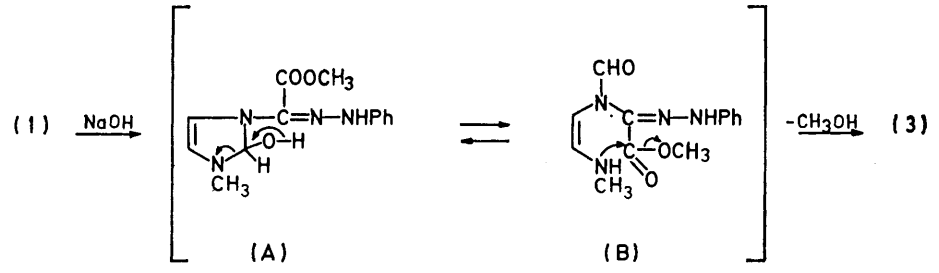
N.m.r. spectra were measured with a Varian A-60 spectrometer (Me_4Si internal standard). I.r. spectra were recorded with a Perkin-Elmer 377 spectrophotometer. M.p.s were determined on a Buchi apparatus (capillary method) and were uncorrected.

General Method for the Preparation of Adducts.—Triethylamine (0.01 mol) was added to a stirred solution of heterocyclic base (0.01 mol) and of hydrazonoyl halide [1,4] (0.01 mol) in chloroform (50 ml) and the mixture was kept overnight. Hydrogen chloride was bubbled into the solution, the solvent was evaporated, and the residue purified by crystallisation: 1-[*methoxycarbonyl*(*phenylhydrazono*)*methyl*]-3-*methylimidazolium chloride* (1) (75%), m.p. 165—167 °C (ethanol) (Found: C, 52.1; H, 5.05; N, 18.6. $C_{13}H_{11}ClN_4O$ requires C, 53.0; H, 5.1; N, 19.0%); δ(C_2D_6SO) 3.8 (3 H, N-CH_3), 4.0 (3 H, $COOCH_3$), 7.5—7.0 (5 H, C_6H_5), 7.8, 7.9, and 8.9 (3 H, imidazolium 4, 5-, and 2-H), and 12 (1 H, NH); $\nu_{max.}$(Nujol) 1 700 cm^{-1} (C=O); 3-*benzyl*-1-[*methoxycarbonyl*(*phenylhydrazono*)*methyl*]-*benzimidazolium chloride* (4a) (55%), m.p. 166—168 °C (decomp.) (ethyl acetate) (Found: C, 65.85; H, 5.25; N, 13.45. $C_{23}H_{21}ClN_4O_2$ requires C, 65.65; H, 5.0; N, 13.3%); δ($CDCl_3$) 3.85 (3 H, $COOCH_3$), 4.9 (2 H, CH_2Ph), and 6.7—8.9 (9 H, m, ArH); $\nu_{max.}$($CHCl_3$) 1 660 cm^{-1} (C=O); 3-*methyl*-1-[*t-butoxycarbonyl*(*phenylhydrazono*)*methyl*]*imidazolium chloride* (4b) (70%), m.p. 148—150 °C (ethyl acetate) (Found: C, 62.0; H, 5.4; N, 14.3. $C_{20}H_{22}ClN_4O_2$ requires C, 62.3; H, 5.7; N, 14.5%).

Pyrolysis of (1).—Compound (1) (0.5 g) was heated in an oil-bath at 180 °C for 10 min and the residue was taken up in water–benzene (1 : 5; 30 ml). From the organic layer was recovered 3,6-*bismethoxycarbonyl*-1,4-*diphenyl*-1,4-*dihydro*-s-*tetrazine* (0.2 g, 66%), m.p. 170—172 °C (methanol) (Found: C, 61.4; H, 4.65; N, 15.6. $C_{18}H_{16}N_4O_4$ requires C, 61.35; H, 4.6; N, 15.9%). The aqueous phase was strongly basified and extracted with ether. The extract was dried and evaporated *in vacuo*. The residue was identified as *N*-methylimidazole (0.12 g, 85%) by g.l.c. comparison with an authentic sample.

Reaction of (1) *with Sodium Hydroxide in a Two Phase System.*—Chloroform (20 ml) and sodium hydroxide (0.27 g, 6.8 mmol) were added to an ice-cooled solution of (1) (2 g, 6.8 mmol) in water (10 ml). The mixture was vigorously stirred for 5 min and then the organic layer was separated and dried (Na_2SO_4). The solvent was evaporated and the residue crystallised from benzene to give *methoxycarbonyl*(3-*methylimidazolio*)*methyleneaminoanilide* (2) (1 g, 58%); m.p. 142—144 °C (Found: C, 60.05; H, 5.35; N, 21.8. $C_{13}H_{14}N_4O_2$ requires C, 60.45; H, 5.45; N, 21.7%); δ(C_2D_6SO) 3.65 (3 H, NCH_3), 3.90 (3 H, $COOCH_3$), 6.7—7.4 (5 H, m, C_6H_5), and 7.7, 7.8, and 8.9 (3 H, imidazolium 4-, 5-, and 2-H); $\nu_{max.}$($CHCl_3$) 1 650 cm^{-1} (C=O).

Ring Expansion Reaction. General Procedure.—A solution of adduct (0.01 mol) in 50% aqueous ethanol (50 ml) was treated with sodium hydroxide (0.01 mol) and stirred at room temperature overnight. The precipitate was



filtered off and purified by crystallisation: 4-*formyl*-1-*methyl*-3-*phenylhydrazono*-1,4-*dihydropyrazin*-2-*one* (3) (55%), m.p. 163—165 °C (n-butanol) (Found: C, 58.65; H, 5.1; N, 22.65. $C_{12}H_{12}N_4O_2$ requires C, 59.0; H, 4.95; N, 22.95%); δ(C_2D_6SO) 3.95 (3 H, NCH_3), 6.8—7.2 (5 H, m, C_6H_5), 7.7 and 8.1 (2 H, dd, 4- and 5-H), 9.5 (1 H, CHO), and 13.2 (1 H, NH); $\nu_{max.}$(Nujol) 3 380, 1 680, and 1 640 cm^{-1} (NH, C=O); 4-*formyl*-1-*methyl*-3-*phenylhydrazono*-1,4-*dihydroquinoxalin*-2-*one* (5a) (71%), m.p. 189—191 °C (ethanol) (Found: C, 64.95; H, 4.5; N, 18.8. $C_{16}H_{14}N_4O_2$ requires C, 65.3; H, 4.8; N, 19.05%); δ($CDCl_3$) 3.55 (3 H, NCH_3), 6.8—7.7 (9 H, m, ArH), 8.65 (1 H, CHO), and 9.45 (1 H, NH); $\nu_{max.}$(Nujol) 3 300, 1 700, and 1 650 cm^{-1} (NH, C=O); 1-*benzyl*-4-*formyl*-3-*phenylhydrazono*-1,4-*dihydroquinoxalin*-2-*one* (5b) (50%), m.p. 133—135 °C (ethanol) (Found: C, 70.95; H, 5.05; N, 15.25. $C_{22}H_{18}N_4O_2$ requires C, 71.35; H, 4.9; N, 15.15%); $\nu_{max.}$(Nujol) 3 280 (NH), 1 700, and 1 660 cm^{-1} (C=O).

1-*Methyl*-3-*phenylhydrazono*-1,4-*dihydroquinoxalin*-2-*one* (6).—The formyl derivative (5a) (0.5 g) in 50% aqueous acetic acid (50 ml) was heated under reflux for 6 h. The solution was evaporated, the residue treated with 1N-sodium hydroxide, and the crude product filtered off. Purification by column chromatography [silica gel; benzene–ethyl acetate (75 : 25)] gave (6) (0.3 g, 65%) as *crystals*, m.p. 185—187 °C (ethanol) (Found: C, 67.8; H, 5.3; N, 20.7. $C_{15}H_{14}N_4O$ requires C, 67.65; H 5.3; N, 21.05%); $\nu_{max.}$ (Nujol) 3 280 (NH) and 1 660 cm^{-1} (C=O).

1-*Methyl*-3-*phenylazoquinoxalin*-2-*one* (7).—Air was bubbled for 6 h into a solution of (6) (0.5 g) in methanol (25 ml). The solvent was evaporated off and the residue, crystallised from di-isopropyl ether, gave the product as red *prisms*, m.p. 124—126 °C (Found: C, 67.95; H, 4.4; N, 20.85. $C_{15}H_{12}N_4O$ requires C, 68.15; H, 4.6; N, 21.2%); $\nu_{max.}$($CHCl_3$) 1 660 cm^{-1} (C=O).

Preparation of an Authentic Sample of (6).—A mixture of *N*-benzyl-*N*-methyl-*o*-phenylenediamine [5] (2.5 g, 11.8 mmol) and of methyl α-chloroglyoxylate phenylhydrazone (2.66 g, 11.8 mmol) in acetonitrile (50 ml) was boiled under reflux for 4 h in the presence of triethylamine (1.2 g, 11.8 mmol). The solvent was evaporated and the residue was shaken

with ether and water. The organic solvent was evaporated and the residue, dissolved in methanol (25 ml), was debenzylated with hydrogen and 5% palladium–charcoal (0.2 g). After removal of the catalyst the solution was heated at 60 °C for 4 h, under nitrogen, in the presence of a catalytic amount of sodium methoxide. Evaporation of the methanol and crystallisation of the residue gave (6) (0.8 g, 25%), m.p. 185—187 °C (ethanol).

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