CHEMICAL AND PHOTOCHEMICAL BEHAVIOURS OF 5-BENZOYLAMIDO-4-DIAZO-1-METHYL-3-PHENYLPYRAZOLE

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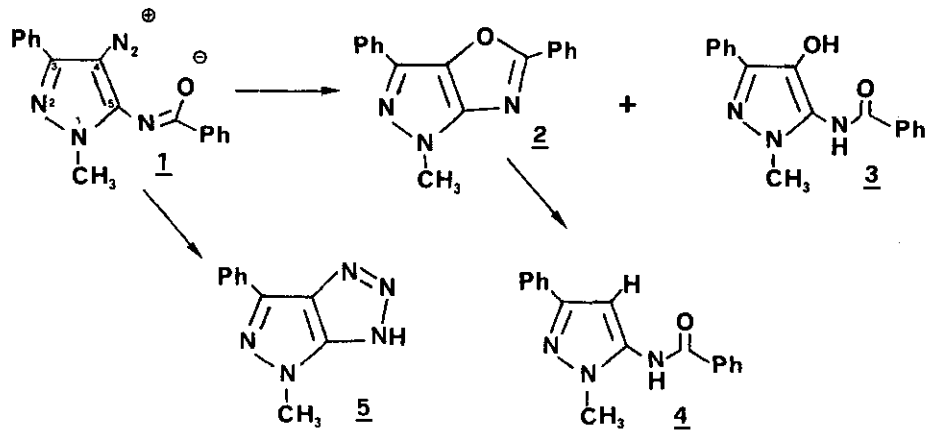
Abstract - Diazo compound (1) photochemically reacts to give rise mainly to compound (2). Alkaline hydrolysis of (1) yields compound (5).

As a part of our program aimed at the synthesis of potential antitumor agents containing the pyrazole ring[1-3] we have recently described the synthesis and the reactivity of 5-benzoylamido-4-diazo-1-methyl-3-phenylpyrazole which exsists in the zwitterionic structure (1)[4] . This compound can be regarded as a potential antitumor agent, since it has been shown that the cytostatic activity of dacarbazine is to be attributed to the *in vivo* formation of a diazo compound[5].

Compound (1) is a very stable product if sheltered from light, thus in this paper we report its chemical and photochemical behaviours. When it is irradiated[6] in the solid state, adsorbed on silica gel or in (75%) acetone-water solution, the photoproduct (2) is mainly obtained, with respective yields ranging from 90% to 42%.



Compound (2) has mp 141-142°C (from acetone/water); ms: m/z 275 M^+; ^{1}H-nmr δ (DMSO-d_6): 8.3-7.3 (m, 10H, benzene protons), 4.00 (s, 3H, CH_3); ir: 1220, 1052, 1020, 903, 770, 726, 692, and 638 cm^{-1} [7].

A very small amount (< 10%) of 5-benzoylamido-4-hydroxy-1-methyl-3-phenylpyrazole (3) is also isolated by column chromatography from the photoreaction mixture (eluating system: $CHCl_3/CH_3CN$, 10:1). Compound (3), mp 79-80°C (from ethanol) is characterized from the following evidences: ms: m/z 293 M^+; ^{1}H-nmr δ (DMSO-d_6): 10.05 (br s, 1H, exchangeable NH/OH), 8.53 (s, 1H, exchangeable OH/NH), 8.2-7.8 (m, 4H, benzene protons), 7.7-7.2 (m, 6H, benzene protons), 3.67 (s, 3H, CH_3); ir: 3250 (v br), 1660, 1605, 1530, 1332, 1296, 1270, 765, and 682 cm^{-1}. When compound (3) is heated at its melting point, compound (2) is obtained.

When a methanolic solution of (2) (500 mg) is catalytically hydrogenated (Pd/C,100 mg) at room temperature and atmospheric pressure it gives rise, for hydrogenolysis of the C_4-O bond, to 5-benzoylamido-1-methyl-3-phenylpyrazole (4)[8], mp 165-167°C (from ethyl acetate); ^{1}H-nmr δ (DMSO-d_6): 10.43 (br s, 1H, exchangeable NH), 8.2-7.2 (m, 10H, benzene protons), 6.73 (s, 1H, C_4 proton), 3.80 (s, 3H, CH_3); ir: 3250 (br), 1660, 1575, 1310, 1300, 1200, 1028, 960, 765, and 695 cm^{-1}.

Compound (1) is recovered unaltered when irradiated in anhydrous benzene and also whem heated under vacuum at its melting point. Thus we suggest that the mechanism of the photoreaction of (2) proceeds through the nucleophicic attack of the $C\text{-}O^{(-)}$ to the C_4 cation formed by N_2 loss.

When sodium (40 mg) in methanol (2.5 ml) is added to a benzene (50 ml) solution of (1) (500 mg) and irradiated for 12 h a mixture of (2) and 1-methyl-3-phenylpyrazolo [4,5-d] [1,2,3] triazole (5) (80% and 10% respectively) is formed. To investigate the mechanism of the formation of (5) we treated (1) with 5N sodium hydroxide at room temperature and sheltered from light and the starting material was recovered unchanged.

On the other hand when (1) is refluxed, still sheltered from light, with 5N sodium hydroxide it gives rise, after acidification, to the sole compound (5); mp 277-280°C (from ethyl acetate/cyclohexane); ms: m/z 199 M^+; ^{1}H-nmr δ (DMSO-d_6): 8.2-7.9 (m, 2H, benzene protons), 7.6-7.1 (m, 3H, benzene protons), 3.82 (s, 3H, CH_3); ir: 3400 (v br), 1575, 1492, 1303, 1274, 1127, 1080, 1070, 1030, 920, and 770 cm^{-1}.

This result suggests that the formation of (5) proceeds by cyclization of the 5-amino-4-diazo intermediate initially formed by alkaline hydrolysis of (1).

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6) All samples were irradiated with the light of a G.E.C. 250 W mercury lamp.

7) All melting points were determined on a Büchi 510 capillary melting point apparatus and are uncorrected. Mass spectra were determined with a Perkin-Elmer 270 mass spectrometer and samples were introduced by direct inlet probe. Operating conditions: ion accelerating voltage 2.5 kV, electron energy 70 eV, and ion source temperature 160°C. ^{1}H-nmr spectra were recorded with a Varian EM 360 instrument: chemical shifts are reported in δ (ppm) downfield from internal TMS. Ir spectra were measured for potassium bromide discs with a Perkin-Elmer 283 spectrophotometer. Silica gel plates (Merck F_{254}) and silica gel 60 (Merck; 70-230 mesh) were used for analytical and column chromatography respectively.

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