THE PHOTOCHEMISTRY OF 2-DIAZO- AND 3-DIAZOPYRROLES

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Abstract- The photochemistry of 2-diazo- and 3-diazopyrroles has been investigated. The irradiation of 2-diazo-3-cyano-4-methyl-5-phenylpyrrole in various reaction solvents brings to a photolytic singlet carbene intermediate, which evolves into 2-substituted pyrroles. A substituent effects has been recognized in the irradiations of some 3-diazopyrroles in methanol.

INTRODUCTION

The photochemistry of diazoazoles has received attention from not only theoretical and mechanistic but synthetic points of view.[1] A generalized photoreaction pattern involves extrusion of nitrogen and formation of a carbene-type intermediate from which reaction products take place through its singlet or triplet chemistry.[2] However, several parameters play an important role in developing this key species, and among these one should at the first consider the nature of the azole ring (and substituents on it) which affects reactivity and even the reaction pathway.[3] On the other hand, the photoreaction medium and the presence of reagents also play a significant role in determining final products.[1-3]

In the pyrrole series, only the photochemistry of some 3-diazo compounds [namely, the 2,5-diphenyl-[4] and the 2,4,5-triphenyl-3-diazopyrroles[5] (**9c**) and (**9d**)] has been thoroughly investigated, and the formation of photoproducts has been explained on the basis of the above considerations. *Inter alia*, irradiation of these substrates in methanol is reported to furnish essentially the reduced 2,5-diphenyl- or 2,4,5-triphenylpyrrole, (**14c**) and (**14d**) respectively, which are explained by assuming the formation of a triplet

carbene species.[6] On the other side, only a small amount (12%) of the corresponding 3-methoxy-2,5-diphenylpyrrole (**12c**) (through a competing electrophilic carbene interacting with nucleophilic reagents) have been isolated.[6] By contrast, when irradiation of the 3-diazopyrrole (**9c**) was carried out in methanol in the presence of trifluoroacetic acid, the yield of the corresponding 3-methoxy-2,5-diphenylpyrrole (**12c**) greatly increased (up to 44%), and this result was ascribed to the involvement of a 3-pyrrolediazonium intermediate as the actual photochemical species.[6] So, one could presume that particular substituents, too, would have affected the photochemical pattern of 3-diazopyrroles by affecting the acid-base equilibria in the substrates. Furthermore, as for 2-diazopyrroles, these substrates represent a new class of diazoazoles, the preparation of which has been recently pointed out by diazotization of the corresponding 2-aminopyrroles.[7] In our opinion, their photochemistry could have furnished promising results both from mechanistic and synthetic projects.

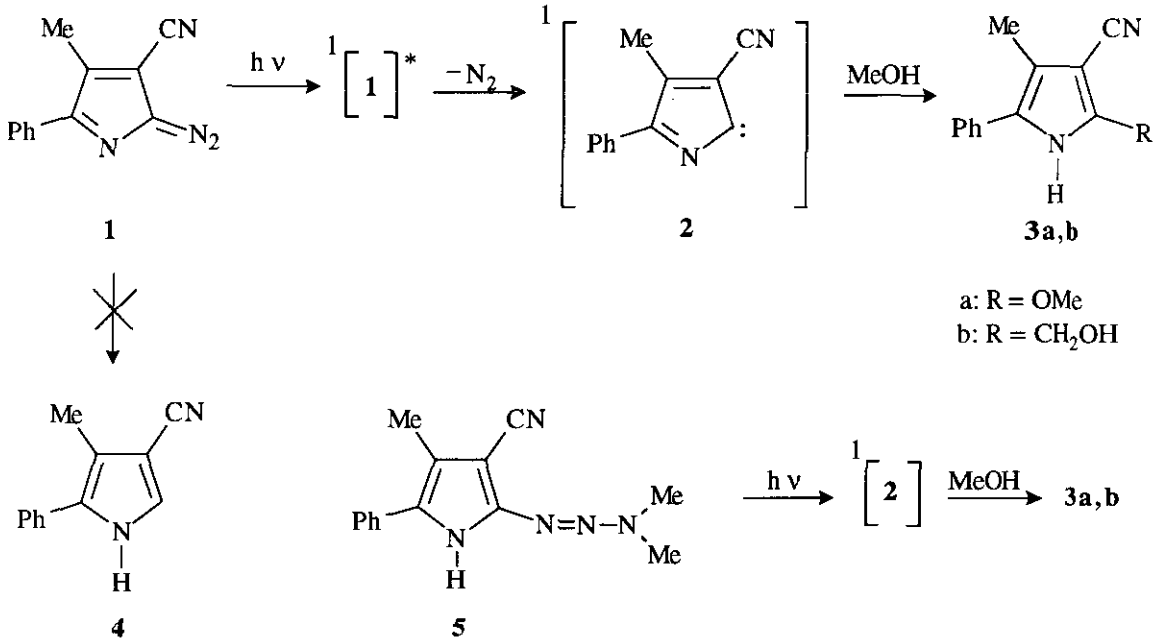
In connection with our interest in the photochemical behavior of azoles[8] and in the framework of a general study on photodynamics of pharmaceuticals, we investigated the photochemistry of variously substituted 2-diazo- and 3-diazopyrroles. Taking into account the relevance of these substrates in medicinal chemistry, an attractiveness of this study could be also recognized in having more insight in the question of photostability and photodegradation of these potential pharmaceuticals. In this paper we report the results concerning the photochemical behavior of the 2-diazopyrrole (**1**) irradiated in various reaction solvents. Moreover, to gain informations on the role of substituents in the photochemical pattern of the 3-diazopyrrole system, we investigated irradiations in methanol of some suitably substituted 3-diazopyrroles (**9a**) and (**9b**), characterized by the presence of electron withdrawing groups at the C(4) of the pyrrole ring.

RESULTS AND DISCUSSION

Diazopyrroles showed intense absorptions in the region of λ = 350 nm. Therefore, irradiations at this wavelength would be suitable. To this aim, we used a Rayonet RPR-100 photoreactor equipped with 16 irradiating Hg-lamps RPR-3500Å.

Irradiation of the diazopyrrole (**1**) in methanol essentially gave the 2-methoxy substituted pyrrole (**3a**) (70%). No reduced pyrrole (**4**) was detected, whereas some amounts (10%) of the hydroxymethyl derivative (**3b**) were isolated. This result, which differs to great extent from that observed in the before-

mentioned irradiation[4-6] of 3-diazo-2,5-diphenyl- or 3-diazo-2,4,5-triphenylpyrroles, indicates the involvement of an electrophilic carbene species which will react with the nucleophilic solvent (to produce **3a**) or undergo a C-H insertion (to give **3b**). These different behaviors could have been expected taking into account that diazoazoles containing an adjacent nitrogen atom react preferentially by an electrophilic singlet carbene.[2]

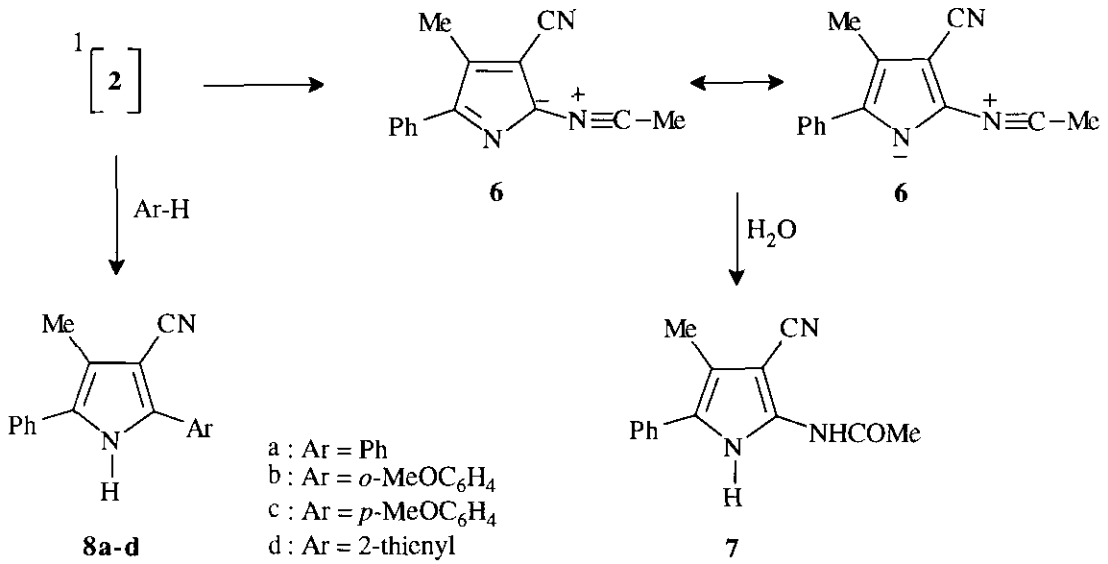


Scheme 1

On the other hand, electron withdrawing group at C(3) could also play a role in determining the photoreaction pathway. Interestingly, the same photoproducts (**3a**) (52%) and (**3b**) (10%) have been also obtained in the irradiation of the 2-triazenopyrrole (**5**) in methanol. As expected,[9] the photochemistry of **5** brings to the extrusion of the dimethylamino moiety and molecular nitrogen in one hand, and to electrophilic singlet carbene (**2**) in the other.

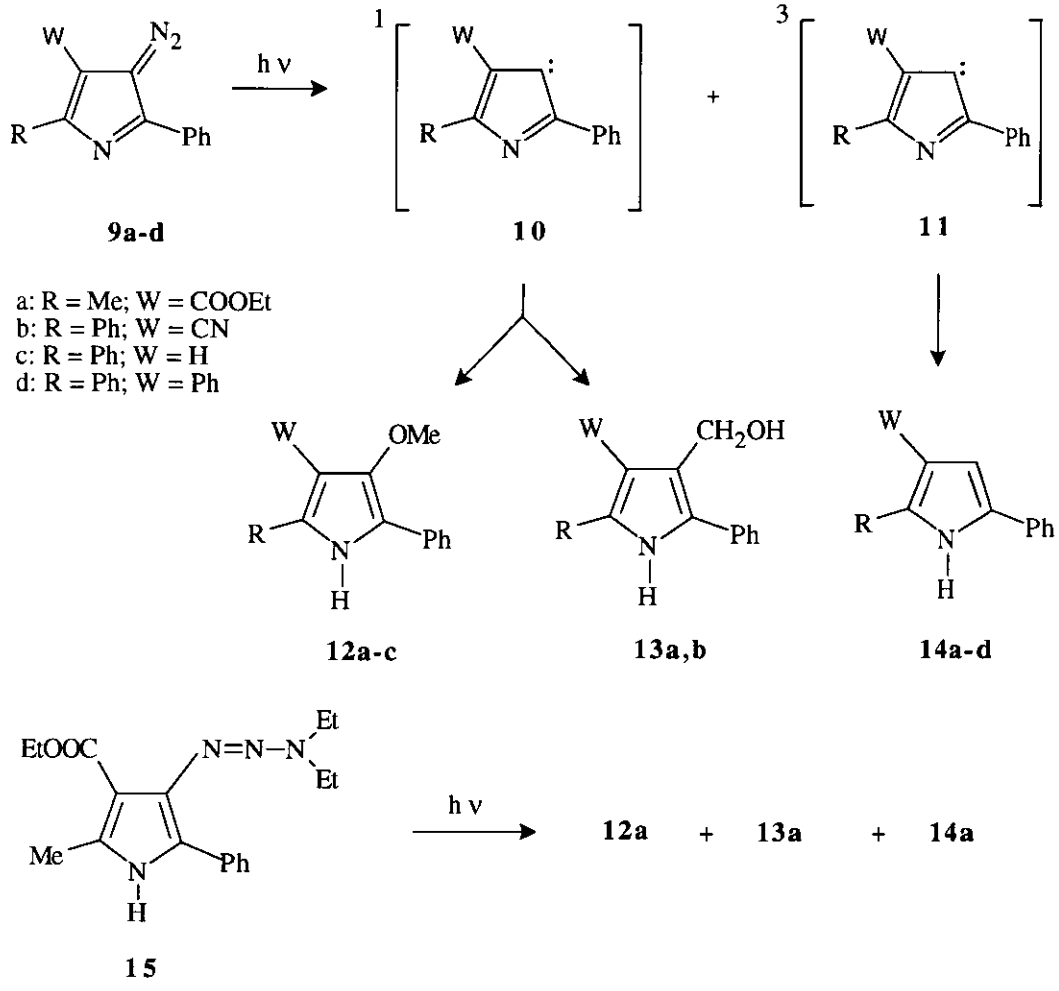
These results prompted us to exploit the photoreactivity of the 2-diazo compound (**1**) in synthetic projects. To this aim, we have investigated irradiations of **1** in the presence of various reagents, such as acetonitrile in one hand, and suitable aromatics (benzene, anisole and thiophene), in the other. As expected, irradiation of **1** in acetonitrile gave the acetylamino compound (**7**) (70%), reasonably through the ylide (**6**).

Furthermore, irradiation of **1** in benzene, anisole or thiophene gave an interesting arylation reaction leading to the 2-aryl substituted pyrroles (**8a**) (70%), (**8b**) (50%), (**8c**) (25%), and (**8d**) (55%), respectively. Clearly, formation of *ortho* and *para* isomers (**8b**) and (**8c**), as well as the formation of the α-thienyl derivative (**8d**) agrees with an electrophilic carbene-singlet pathway.



Scheme 2

To come back to the 3-diazopyrrole system, we investigated irradiations of compounds (**9a**) and (**9b**) in methanol, supposing that electron withdrawing groups at C(4) could have affected the photochemical pathway. Really, at variance with the results mentioned above regarding the photoreactivity of the 3-diazo-2,5-diphenylpyrrole (**9c**), irradiation of these substrates in methanol chiefly gave the corresponding 3-methoxy substituted pyrroles (**12a**) and (**12b**), respectively as the major products, (in about 60% yield), together with small amounts (10-15%) of 3-hydroxymethylpyrroles (**13a**) and (**13b**); only few amounts of the reduced pyrroles (**14a**) and (**14b**) (arising from a triplet carbene chemistry) were isolated. The same products have been also obtained in the irradiation of the 3-triazenopyrrole (**15**) in methanol. The formation of **12a,b** which can be reasonably explained by assuming the involvement of an electrophilic carbene chemistry, demonstrated that the nature of substituent largely affects the photoreaction pathway by a reinforcement of electron deficiency of the pyrrole ring in one hand, and by determining the singlet or triplet chemistry of the primarily-formed carbene-type intermediate.



Scheme 3

EXPERIMENTAL

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. IR spectra (Nujol) were determined with a Perkin-Elmer 257 instrument, ^{1}H NMR spectra were recorded on a Bruker 250 E spectrometer (tetramethylsilane as internal standard). MS spectra (70 eV) were recorded with a RMU-60 instrument. Flash chromatography was performed on Merck silica gel by using mixture of light petroleum (fraction boiling in the range of 40-60°C) and ethyl acetate in varying ratios. Compounds (**1**),[7] (**5**),[10] (**9a**),[11] (**9b**)[12] and (**15**)[13] which were used for irradiation were prepared as reported. Photochemical reactions were carried out in Pyrex tubes at the room temperature by using a Rayonet RPR-100 photoreactor, fitted with 16 irradiating Hg-lamps RPR-3500Å and a merry-go-round apparatus.

General Procedure for Photochemical Reactions

A sample of compounds (**1**, **5**, **9a**, **9b**, and **15**) in anhydrous methanol or in the appropriate anhydrous solvent/reagent, (acetonitrile, benzene, anisole or thiophene) was irradiated untill disappearance of the starting material. After removing the solvent under reduced pressure, the residue was chromatographed.

Irradiation of compounds (1) and (5) in methanol

Irradiation of compound (**1**) (0.3 g, 1.44 mmol) in methanol (300 mL) for 10 min gave **3a** (0.21 g, 70%) and **3b** (0.03 g, 10%). Compound (**3a**) had mp 174-175°C (from ethanol). IR 3340 (NH), 2220 (CN) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.21 (s, 3H, Me), 4.12 (s, 3H, OMe), 7.29-7.54 (m, 5H, aromatic), 11.60 (s, 1H, NH); MS *m/z*: 212 (M^+). Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.60; H, 5.68; N, 13.25. Compound (**3b**) had mp 201-202°C (from ethanol). IR 3340, 3200 (NH, OH), 2220 (CN) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.28 (s, 3H, Me), 4.56 (d, J = 5.4 Hz, 2H, CH_2), 5.43 (t, J = 5.4 Hz, 1H, OH), 7.16-7.58 (m, 5H, aromatic), 11.90 (s, 1H, NH); MS *m/z*: 212 (M^+). Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.55; H, 5.66; N, 13.14.

Irradiation of compound (**5**) (0.3 g, 1,19 mmol) in methanol (300 mL) for 40 min gave **3a** (0.15 g, 50%) and **3b** (0.03 g, 10%).

Irradiation of compound (1) in acetonitrile

Irradiation of compound (**1**) (0.3 g, 1.44 mmol) in acetonitrile (300 mL) for 10 min gave **7** (0.24 g, 70%), mp 208-209°C (from ethanol). IR 3340, 3240 (NH), 2220 (CN), 1610 (CO) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.13 (s, 3H, Me), 2.26 (s, 3H, Me), 7.32-7.50 (m, 5H, aromatic), 10.50, 11.70 (2s, 2H, 2NH); MS *m/z*: 239 (M^+). Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.22; H, 5.38; N, 17.49. An authentic sample of **7** was obtained by acetylation of the 2-amino-3-cyano-4-methyl-5-phenylpyrrole[9] with acetic anhydride.

Irradiation of compound (1) in benzene

Irradiation of compound (**1**) (0.3 g, 1.44 mmol) in benzene (300 mL) for 10 min gave **8a** (0.26 g, 70%), mp 210-211°C (from ethanol). IR 3230 (NH), 2220 (CN) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.33 (s, 3H, Me), 7.41-7.92 (m, 10H, aromatic), 12.06 (s, 1H, NH); MS *m/z*: 258 (M^+). Anal. Calcd for $C_{18}H_{14}N_2$: C, 83.69; H, 5.46; N, 10.84. Found: C, 83.56; H, 5.38; N, 10.65.

Irradiation of compound (1) in anisole

Irradiation of compound (**1**) (0.3 g, 1.44 mmol) in anisole (300 mL) for 15 min gave **8b** (0.2 g, 50%) and **8c** (0.1 g, 25%). Compound (**8b**) had mp 120-121°C (from ethanol). IR 3340 (NH), 2210 (CN) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.34 (s, 3H, Me), 3.90 (s, 3H, OMe), 7.10-7.63 (m, 9H, aromatic), 11.82 (s,

1H, NH); MS *m/z*: 288 (M^+). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.71. Found: C, 79.18; H, 5.48; N, 9.65. Compound (**8c**) had mp 206-207°C (from ethanol). IR 3240 (NH), 2220 (CN) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.31 (s, 3H, Me), 3.89 (s, 3H, OMe), 7.15 (d, J = 7 Hz, 2H, aromatic) 7.40-7.59 (m, 5H, aromatic), 7.84 (d, J = 7 Hz, 2H, aromatic) 11.91 (s, 1H, NH); MS *m/z*: 288 (M^+). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.71. Found: C, 79.05; H, 5.45; N, 9.75.

Irradiation of compound (1) in thiophene

Irradiation of compound (**1**) (0.3 g, 1.44 mmol) in thiophene (300 mL) for 15 min gave **8d** (0.18 g, 55%), mp 168-170°C (from ethanol). IR 3220 (NH), 2220 (CN) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.30 (s, 3H, Me), 7.23-7.64 (m, 8H, aromatic), 12.14 (s, 1H, NH); MS *m/z*: 264 (M^+). Anal. Calcd for $C_{16}H_{12}N_2S$: C, 72.70; H, 4.58; N, 10.60. Found: C, 72.58; H, 4.48; N, 10.65.

Irradiation of compound (9a) in methanol

Irradiation of compound (**9a**) (0.5 g, 1.96 mmol) in methanol (100 mL) for 30 min gave **14a**[14] (0.04 g, 10%), **12a** (0.3 g, 60%) and **13a** (0.05 g, 10%). Compound (**12a**) had mp 129-131°C (from ethanol). IR 3280 (NH), 1660 (CO) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 1.33 (t, J = 7 Hz, 3H, Me), 2.48 (s, 3H, Me), 3.75 (s, 3H, Me), 4.27 (q, J = 7 Hz, 2H, CH_2), 7.19-7.78 (m, 5H, aromatic), 11.32 (s, 1H, NH); MS *m/z*: 239 (M^+). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 75.28; H, 7.16; N, 17.56. Found: C, 75.40; H, 7.22; N, 17.35. Compound (**13a**) had mp 142-144°C (from ethanol). IR 3340, 3220 (NH, OH), 1650 (CO) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 1.39 (t, J = 7 Hz, 3H, Me), 2.47 (s, 3H, Me), 4.29-4.37 (m, 3H, CH_2, OH), 4.65 (q, J = 7 Hz, 2H, CH_2), 7.25-7.78 (m, 5H, aromatic), 8.84 (s,H, NH); MS *m/z*: 239 (M^+). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 75.28; H, 7.16; N, 17.56. Found: C, 75.15; H, 7.16; N, 17.33.

Irradiation of compound (9b) in methanol

Irradiation of compound (**9b**) (0.5 g, 1.85 mmol) in methanol (300 mL) for 15 min gave **14b**[15] (0.02 g, 5%), **12b** (0.3 g, 60%) and **13b** (0.08 g, 15%). Compound (**12b**) had mp 174-175°C (from ethanol). IR 3240 (NH), 2220 (CN) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 3.39 (s, 3H, Me), 7.07-7.86 (m, 10H, aromatic), 11.89 (s, 1H, NH); MS *m/z*: 274 (M^+). Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21 Found: C, 78.63; H, 4.98; N, 10.05. Compound (**13b**) had mp 165-168°C (from ethanol). IR 3380, 3240 (NH, OH), 2220 (CN), cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 4.50 (d, J = 5.3 Hz, 2H, CH_2), 5.28 (t, J = 5.3 Hz, 1H, OH), 7.29-7.98 (m, 10H, aromatic), 12.18 (s, 1H, NH); MS *m/z*: 274 (M^+). Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H,5.14; N, 10.21 Found: C, 78.72; H, 5.05; N, 10.12.

Irradiation of compound (15) in methanol

Irradiation of compound (**15**) (0.4 g, 1.22 mmol) in methanol (100 mL) for 10 h gave **14a**[14] (0.1 g, 35%), **12a** (0.15 g, 50%) and **13a** (0.03 g, 10%).

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