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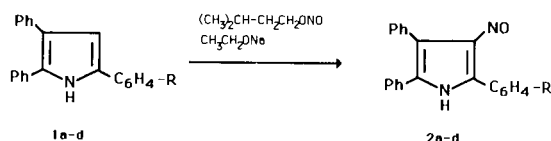
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A comparison of the behaviour on the nitrosation of the isomers 5-(2-methoxyphenyl)- (**1a**) 5-(3-methoxyphenyl)- (**1b**) and 5-(4-methoxyphenyl)-2,3-diphenylpyrroles (**1c**) carried out in the usual way with *iso*-amyl nitrite in a solution of sodium ethoxide in ethanol evidences that **1a** is dramatically less reactive with respect to **1b** and **1c**. The different reactivity was ascribed to the occurrence of a strong hydrogen bond involving pyrrole N-H and the *ortho*-methoxy group.

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It is known that 1-*H*-pyrroles may be nitrosated under basic conditions with alkyl nitrites in the presence of sodium ethoxide [1], and this reaction is the more used one for the synthesis of 2,5-diaryl- and 2,4,5-triaryl-3-nitrosopyrroles [1-4], which constitute key synthons for the preparation of the corresponding amino- [1] and diazopyrroles [1-3]. As we had interest, for a mass spectrometric study [5], in the synthesis of  $\beta$ -diazopyrroles bearing different substituents at the 5-position, the 5-anisylpyrrole isomers **1a**, **1b** and **1c** were treated with the usual nitrosating agents, stoichiometric amounts of freshly distilled *iso*-amyl nitrite and sodium ethoxide [1-4] at room temperature. While the behaviour of **1b** and **1c** parallels those of the 2,3,5-triphenylpyrrole **1d** [1-4], giving the corresponding 3-nitrosopyrroles **2b,c** (yields 75-85%), the pyrrole **1a** was almost unreacted under the same conditions, its nitrosation requiring more drastic conditions. In fact the 2,3-diphenyl-5-(2-methoxyphenyl)-4-nitrosopyrrole **2a** was obtained only on refluxing for 15 hours with an excess of *iso*-amyl nitrite (yield 35%).

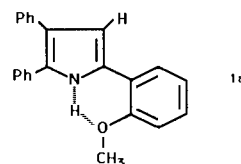
## Scheme



a. R = *ortho*-OCH<sub>3</sub>    c. R = *para*-OCH<sub>3</sub>  
b. R = *meta*-OCH<sub>3</sub>    d. R = H

The <sup>1</sup>H nmr spectrum of **1a** in deuteriochloroform shows the N-*H* absorption 1.5 ppm downfield with respect to those of **1b** and **1c** and **1d**. When the spectra are recorded using DMSO-*d*<sub>6</sub>, a suitable solvent for the formation of strong intermolecular hydrogen bonds, the N-*H* signals lie in a narrow range (Table 1). It is also remarkable that, while the N-*H* protons of **1b**, **1c** and **1d** are completely exchanged by the addition of deuterium oxide (<sup>1</sup>H nmr, deuteriochloroform) within 2 hours, in the case of **1a**, a small peak (about 10%) due to the N-*H* proton is also still present for 24 hours after the deuterium oxide addition.

In addition, the ir spectra (nujol mull) show the N-*H* stretching absorption band of **1a** at 3355 cm<sup>-1</sup> while those of **1b**, **1c** and **1d** lie in the narrow range between 3425 cm<sup>-1</sup> and 3435 cm<sup>-1</sup>. All these findings are evidence for an intramolecular hydrogen bond between the N-*H* hydrogen and the methoxyl oxygen of **1a** which involves the formation of a stable six membered ring.



Even if the only evidence in this regard is the fact that 1-methylpyrroles are not nitrosated under basic conditions [6], it is reported that nitrosation under these conditions should involve nucleophilic attack by the pyrrol anion on the alkyl nitrite [1]; hence, the different reactivity of the three isomeric pyrroles can be attributable to the strong hydrogen bond which makes the proton abstraction by sodium ethoxide from **1a** energetically more expensive than with **1b** and **1c**.

## EXPERIMENTAL

The <sup>1</sup>H nmr spectra were recorded on a Varian EM-360 A spectrometer using tetramethylsilane as internal standard. The ir spectra (nujol mull) were recorded on a Jasco IR-810 spectrometer. The melting points were determined in an open glass capillary tube and are uncorrected. The mass spectra were run on a Jeol JMS-01-SG-2 mass spectrometer, with an electron beam energy of 75 eV, an accelerating voltage of 10 kV and an electron current of 100  $\mu$ A. The samples were introduced into the ionization chamber with a probe.

Synthesis of 2,3,5-Triarylpyrroles **1a**, **1b**, **1c** and **1d**.

The pyrroles **1**, **1a**, **1b**, **1c** and **1d** were prepared according to the usual procedure [2].

The appropriate methoxyacetophenone, **1a**, **1b**, **1c**, or acetophen-

Table  
<sup>1</sup>H-NMR Chemical Shifts of Compounds **1a-d** [a,b]

Compound	N-H	Pyrrole-C-H	Aromatic	OCH <sub>3</sub>	Solvent
<b>1a</b>	10.10 [c] (s, broad)	6.93 (d, J = 3.0 Hz) [d]	7.00-8.00 (m)	4.01 (s)	CDCl <sub>3</sub>
	11.20 (s, broad)	6.94 (d, J = 3.0 Hz)	7.00-8.20 (m)	3.97 (s)	DMSO-d <sub>6</sub>
<b>1b</b>	8.50 [e] (s, broad)	6.78 (d, J = 3.0 Hz) [d]	6.96-7.65 (m)	3.84 (s)	CDCl <sub>3</sub>
	11.50 (s, broad)	6.90 (d, J = 3.0 Hz)	7.10-7.70 (m)	3.89 (s)	DMSO-d <sub>6</sub>
<b>1c</b>	8.45 [e] (s, broad)	6.71 (d, J = 3.0 Hz) [d]	6.99-7.75 (m) [f]	3.86 (s)	CDCl <sub>3</sub>
	11.50 (s, broad)	6.82 (d, J = 3.0 Hz)	7.10-8.10 (m) [g]	3.92 (s)	DMSO-d <sub>6</sub>
<b>1d</b>	8.40 [e] (s, broad)	6.72 (d, J = 3.0 Hz) [d]	7.20-7.70 (m)	----	CDCl <sub>3</sub>
	11.50 (s, broad)	6.80 (d, J = 3.0 Hz)	7.20-8.00 (m)	----	DMSO-d <sub>6</sub>

[a] The spectra were recorded on a Varian EM-360 A spectrometer; the chemical shifts are given in ppm downfield from TMS. [b] The multiplicity of the signals is indicated in parentheses by the following abbreviations: s = singlet, d = doublet, m = multiplet. [c] The proton exchanges very slowly, about the 90% was exchanged in 24 hours. [d] This signal appears as a singlet after a complete exchange. [e] Exchanges slowly, but complete exchange was observed between 1-2 hours. [f] The signals appear as doublet centered at  $\delta$  7.07 (J = 9.0 Hz) integrated for 2 protons and a multiplet at  $\delta$  7.25-7.75 integrated for 12 protons. [g] The signals appear as doublet centered at  $\delta$  7.15 (J = 9.0 Hz) integrated for 2 protons, a doublet centered at  $\delta$  7.99 (J = 9.0 Hz) integrated for 2 protons and a multiplet at  $\delta$  7.3-7.8 integrated for 10 protons.

one **1d** (0.05 mole), benzoin (0.05 mole), and potassium cyanide (1.2 g) in ethanol (30 ml) and water (4 ml) was refluxed for 2 hours. On standing (12 hours), a yellow precipitate was obtained. The precipitate, solubilized in hot ethanol, was added an equal weight of ammonium acetate and was refluxed for 4 hours. The solvent was removed under reduced pressure, the residue was solubilized in ether and shaken with aqueous saturated solution of sodium bicarbonate. The organic phase was dried over anhydrous sodium sulfate, and the solvent removed at reduced pressure; the resinous product was purified by crystallization from methanol and then from acetic acid.

#### 2,3-Diphenyl-5-(2-methoxyphenyl)pyrrole **1a**.

This compound (yield 85%) was obtained as white crystals (from acetic acid), mp 185-186°; ms: m/z (I%) 325 (100, M<sup>+</sup>), 324 (4), 310 (43), 282 (5).

*Anal.* Calcd. for C<sub>23</sub>H<sub>19</sub>NO: C, 84.89; H, 5.89; N, 4.30. Found: C, 85.01; H, 5.99; N, 4.20.

#### 2,3-Diphenyl-5-(3-methoxyphenyl)pyrrole **1b**.

This compound (yield 80%) was obtained as white crystals (from acetic acid), mp 116-118°; ms: m/z (I%) 325 (100, M<sup>+</sup>), 324 (5), 310 (2), 282 (18).

*Anal.* Calcd. for C<sub>23</sub>H<sub>19</sub>NO: C, 84.89; H, 5.89; N, 4.30. Found: C, 84.75; H, 5.79; N, 4.48.

#### 2,3-Diphenyl-5-(4-methoxyphenyl)pyrrole **1c**.

This compound (yield 75%) was obtained as white crystals (from acetic acid), mp 182-184°; ms: m/z (I%): 325 (100, M<sup>+</sup>), 324 (2), 310 (25), 282 (10).

*Anal.* Calcd. for C<sub>23</sub>H<sub>19</sub>NO: C, 84.89; H, 5.89; N, 4.30. Found: C, 85.13. H, 5.71; N, 4.42.

#### 2,3,5-Triphenylpyrrole **1d**.

Analytical and physical data are identical to those reported in the literature [2].

#### Nitrosation of 2,3-Diphenyl-5-(2-methoxyphenyl)pyrrole **1a**.

Pyrrole **1a** (10<sup>-3</sup> mole) was dissolved in an ice-cold solution of sodium ethoxide (10<sup>-3</sup> mole of sodium in 30 ml of absolute ethanol) and *iso*-amyl nitrite (0.2 ml) was added dropwise. After refluxing for 8 hours *iso*-amyl nitrite (0.2 ml) was added again and refluxed for another 7 hours. The dark brown mixture was poured into water (50 ml) and an orange-brown powder precipitated. After neutralization with ammonium chloride, extraction with ether (4 x 50 ml), the organic phase was dried over sodium sulfate and the solvent was removed under reduced pressure. The

2,3-diphenyl-5-(2-methoxyphenyl)-4-nitrosopyrrole was separated from the starting pyrrole and from other by-products by flash column chromatography using Hoechst silica gel (0.032-0.063 mm) and cyclohexane/ethyl acetate 9/1 as the eluent mixture.

#### 2,3-Diphenyl-5-(2-methoxyphenyl)-4-nitrosopyrrole **2a**.

This compound (yield 35%) was obtained as yellow crystals (from ethanol) mp 195-197°; ir:  $\nu$  3150 broad (N-H), 1580 (N=O)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  from TMS 8.80 (1 H, broad, N-H, deuterium oxide-exchangeable), 7.60-7.00 (14 H, m, aromatic protons), 4.20 (3 H, s,  $\text{OCH}_3$ ); ms:  $m/z$  (I%) 354 (100,  $\text{M}^+$ ), 353 (5), 340 (15), 339 (11), 338 (7), 337 (17), 326 (12), 325 (15), 324 (54), 323 (57), 322 (17), 310 (22), 244 (15), 205 (14), 204 (41), 203 (22), 190 (17), 189 (27), 178 (20), 177 (22), 176 (18), 165 (16), 104 (12), 77 (27).

*Anal.* Calcd. for  $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_2$ : C, 77.95; H, 5.12; N, 7.91. Found: C, 78.00; H, 4.98; N, 8.02.

Nitrosation of 2,3-Diphenyl-5-(3-methoxyphenyl)pyrrole **1b**, 2,3-Diphenyl-5-(4-methoxyphenyl)pyrrole **1c** and 2,3,5-Triphenylpyrrole **1d**.

The appropriate pyrrole ( $10^{-3}$  mole) was dissolved in an ice-cold solution of sodium ethoxide ( $10^{-3}$  mole of sodium in 30 ml of absolute ethanol) and *iso*-amyl nitrite (0.3 ml) was added dropwise with stirring. After two days at room temperature the dark brown mixture was poured into water (50 ml) and a brown powder precipitated. After neutralization with ammonium chloride, extraction with ether (4 x 50 ml), the organic phase was dried over sodium sulfate, and the solvent was removed under reduced pressure. The  $\beta$ -nitrosopyrrole was separated from the starting pyrrole and from other by-products by flash column chromatography using Hoechst silica gel (0.032-0.063 mm) and cyclohexane/ethyl acetate 9/1 as the eluent mixture.

#### 2,3-Diphenyl-5-(3-methoxyphenyl)-4-nitrosopyrrole **2b**.

This compound (yield 75%) was obtained as a brown powder (from ethanol), mp 96-98°; ir (nujol):  $\nu$  3260 (N-H), 1590 (N=O)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  from TMS 7.95 (1 H, broad, N-H, deuterium oxide-exchangeable), 7.70-6.80 (14 H, m, aromatic protons) 3.80 (3 H, s,  $\text{OCH}_3$ ); ms:  $m/z$  (I%) 354 (100,  $\text{M}^+$ ), 353 (7), 340 (17), 339 (5), 338 (15), 337 (25), 326 (7), 325 (10), 324 (10), 323 (24), 280 (20), 204 (22), 203 (9), 190 (12), 189 (14), 128

(22), 127 (14), 126 (12), 165 (12), 77 (26).

*Anal.* Calcd. for  $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_2$ : C, 77.95; H, 5.12; N, 7.91. Found: C, 77.82; H, 4.98; N, 8.02.

#### 2,3-Diphenyl-5-(4-methoxyphenyl)-4-nitrosopyrrole **2c**.

This compound (yield 80%) was obtained as a brown powder (from ethanol), mp 196-198°; ir:  $\nu$  3300 (N-H or O-H, *iso*-nitroso form), 1610 (N=O)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  from TMS 9.70 (1 H, broad, N-H, deuterium oxide-exchangeable), 8.25 (2 H, d,  $J = 8.4$  Hz), 7.40-7.30 (10 H, m, aromatic protons), 7.25 (2 H, d,  $J = 8.4$  Hz), 4.00 (3 H, s,  $\text{OCH}_3$ ); ms,  $m/z$  (I%) 354 (100,  $\text{M}^+$ ), 353 (6), 340 (55), 339 (19), 338 (36), 337 (32), 326 (11), 325 (34), 324 (18), 323 (18), 309 (12), 308 (25), 280 (16), 235 (13), 205 (18), 204 (30), 203 (15), 128 (50), 127 (22), 126 (24), 165 (17), 77 (36).

*Anal.* Calcd. for  $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_2$ : C, 77.95; H, 5.12; N, 7.91. Found: C, 77.77; H, 4.93; N, 8.01.

#### 2,3,5-Triphenyl-4-nitrosopyrrole **2d**.

This compound was obtained with a yield of 85%;  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  from TMS 9.48 (1 H, broad, N-H, deuterium oxide-exchangeable), 7.08-7.94 (15 H, m, aromatic protons); the other analytical and physical data are identical to those reported in the literature [2-4].

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- \* Author to whom the correspondence should be addressed.
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