

An Unusually Reactive Pyrrole (1)

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Facile electrophilic substitution is a characteristic feature of π -excessive heterocycles (2). 1-Methyl-2-phenyl-4-methoxypyrrole, **1**, is unusually reactive in this regard (3), and we wish to report here some reactions involving this π -excessive system.

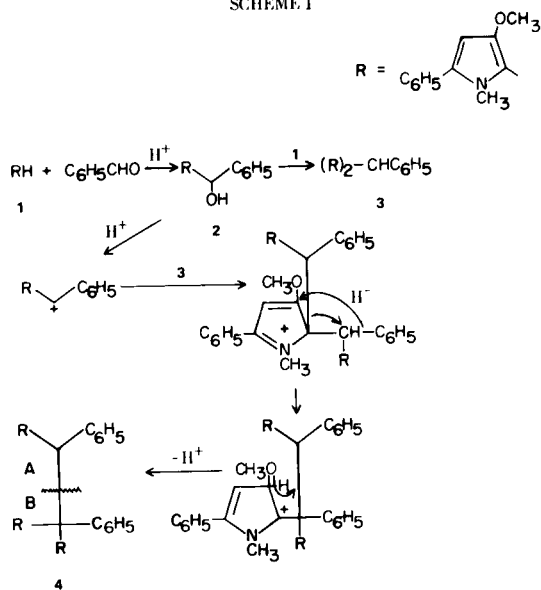
First, the readily available 1-methyl-2-phenyl-4-methoxypyrrole (**1**) (**3**) was treated with benzaldehyde in the presence of an acid catalyst in the hope of synthesizing triarylmethane **3** (4a,b) (Scheme I). When this experiment was performed, however, the somewhat surprising result was the formation of the penta-arylethane, 1,1,2-tris[1'-methyl-3'-methoxy-5'-phenyl-2'-pyrryl]-1,2-diphenylethane, **4**. It seems that the desired triarylmethane must have formed but then, in another manifestation of the reactivity of these 1-methyl-3-methoxypyrroles, proceeds to react with the stable, diaryl carbonium ion formed from the diarylcarbinol **2** under the acidic conditions of the reaction. The indicated (Scheme I) hydride shift, alkyl migration, and loss of a proton would then give the observed **4**.

The structure of **4** was confirmed by nmr and mass spectrum. Integration of the nmr spectrum of **4** clearly estab-

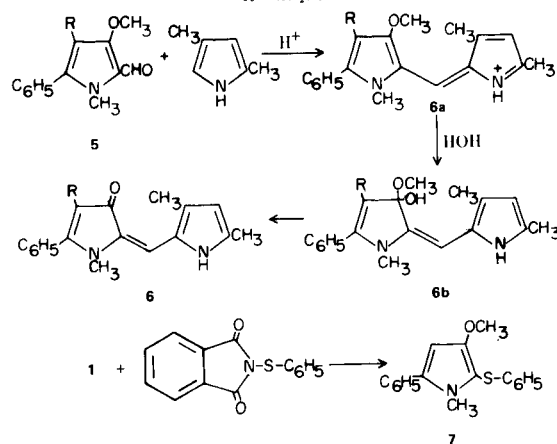
lished that there were a total of five phenyl groups in the molecule and that there were three pyrrole nuclei containing NCH₃, OCH₃ and H-4 protons. Nmr also clearly showed the single proton on C-2 of the ethane structure. The mass spectrum showed a molecular ion at *m/e* 737 which, by exact mass measurements, confirmed the molecular formula, C₅₀H₄₇N₃O₃. Also, the mass spectrum shows, as the two most prominent fragments, *m/e* 276, corresponding to fragment A (cf. **4**, Scheme I) and *m/e* 462, corresponding to fragment B, increased one mass unit by the transfer of a hydrogen atom.

In another interesting reaction of one of these 1-methyl-2-phenyl-4-methoxypyrrole systems we obtained an unusual condensation product from the reaction of 1-methyl-3-methoxy-4-ethoxycarbonyl-5-phenylpyrrole-2-carboxaldehyde, **5**, and 2,4-dimethylpyrrole (Scheme II). Corwin (5a,b) has shown that when aldehydes of *N*-methylpyrroles are condensed with *N*-unsubstituted pyrroles always result. However, when the aldehyde **5** and 2,4-dimethylpyrrole were condensed in chloroform using dry hydrogen chloride as the catalyst, 1-methyl-3-oxo-4-ethoxycarbonyl-5-phenyl-3-(3',5'-dimethyl-2'-pyrrylmethylidene)-4-pyrroline, **6**, was obtained. It seems that the indicated dipyrromethene (**6a**) must form initially

SCHEME I



SCHEME II

R = CO₂Et

but upon protonation it is hydrated rapidly by traces of water in the reaction mixture or in the workup to give **6b**, the hemiketal of **6** (Scheme II).

Finally, we were able to sulfenylate pyrrole **1** with *N*-phenylthiophthalimide in tetrahydrofuran, giving 1-methyl-2-phenylthio-3-methoxy-5-phenylpyrrole (**7**, Scheme II) in moderate yield. Although Gronowitz *et al.* (**6**) were successful in sulfenylating pyrrole in low yield with methanesulfonyl chloride to give a mixture of products, *N*-phenylthiophthalimide is a mild sulfenylating agent not previously used in pyrrole chemistry.

EXPERIMENTAL

Melting points were obtained on a Mel-Temp capillary melting point apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer model 137 infrared spectrometer. Nmr spectra were taken on a Varian Associates' HA-100 instrument operating in the frequency sweep mode and using tetramethylsilane as the standard. Mass spectra were determined on a Varian MAT CH-7 spectrometer or an Associated Electrical Industries' MS-9 spectrometer at 70eV.

Thin layer chromatography was done on glass slides, coated with silica gel GF-254 (Brinkmann). The slides were eluted with 10% tetrahydrofuran in benzene and visualization was by ultraviolet light. Analyses were obtained by courtesy of Galbraith Laboratories, Knoxville, Tennessee.

Diethyl 2,4-dimethylpyrrole-3,5-dicarboxylate was purchased from ICN-K&K (Cleveland) and had m.p. 134-135° (Lit. (7) m.p. 136°). This diester was treated according to Corwin and Krieble (8) to give 2,4-dimethylpyrrole (2,4-DMP), nmr (carbon tetrachloride) 1.96 (s, 3H, 4-CH₃), 2.10 (s, 3H, 2-CH₃), 5.50 (s, broad, 1H, H-3), 6.08 (s, broad, 1H, H-5).

1,1,2-Tris(1'-methyl-3'-methoxy-5'-phenyl-2'-pyrrol)-1,2-diphenylethane (**4**).

1-Methyl-3-methoxy-5-phenylpyrrole-2,4-dicarboxylic acid (1.0 g., 3.14 mmoles) was decarboxylated as previously described (3), the resulting liquid **1** was carefully dissolved in 1 ml. of THF under nitrogen and sealed with a rubber septum. To this solution was added *via* syringe 0.20 g. (1.59 mmoles) of benzaldehyde in 1 ml. of THF containing 1 drop of concentrated hydrochloric acid. A deep purple color developed immediately and after 15 minutes the reaction mixture was poured into 10 ml. methylene chloride, washed with two 10 ml. portions of saturated sodium bisulfite solution, and dried. Concentration of the solvent under reduced pressure gave purple crystals which were tan after one recrystallization from methanol (0.68 g., 77%), m.p. 90-95° (dec.). These tan crystals started turning purple again after 48 hours. Thin layer chromatography gave one spot (rf. ca. 0.9) with a little purple color at the origin. This spot was initially colorless but turned intensely purple after 30 minutes. The nmr was obtained by dissolving 50 mg. of this material in 2 ml. benzene-d₆ and passing it over a small pad of neutral alumina before taking the spectrum; δ 3.34 (s, 9H, NCH₃ or OCH₃), 3.38 (s, 9H, OCH₃ or NCH₃), 5.86 (s, 3H, H-4 or pyrrole), 6.18 (s, 1H, H-2 of ethane), 7.10 (s, broad, 25H, phenyl H's). M.W. Calcd. for C₅₀H₄₇N₃O₃: 737.3620. Found: M⁺ 737.3657.

1-Methyl-3-methoxy-4-ethoxycarbonyl-5-phenylpyrrole-2-carboxaldehyde (**5**).

Ethyl 1-methyl-2-phenyl-4-methoxypyrrole-3-carboxylate (3) (6.1 g., 0.024 mole) was dissolved in 15 ml. of dry DMF under nitrogen. A solution of 30 ml. dry DMF and 3.7 g. (0.024 mole) of phosphorus oxychloride was prepared in an ice bath and the solution of the pyrrole in DMF was added slowly with a syringe. The reaction mixture was allowed to warm to room temperature over 60 minutes and then poured over ice. This solution was then made basic with saturated aqueous sodium acetate, warmed gently for a few minutes on a steam bath, and the white crystals of **5** that formed filtered directly from the warm aqueous solution. One recrystallization from petroleum ether gave 5.3 g. (79%) of **5**, m.p. 67-68°; ir. (potassium bromide) 5.85 (C=O, ester), 6.00μ (C=O, vinylogous formamide); nmr (carbon tetrachloride): δ 0.90 (t, 3H, J = 7 Hz, 3-CO₂CH₂CH₃), 3.54 (s, 3H, NCH₃), 3.90 (q, 2H, J = 7 Hz, 3-CO₂CH₂CH₃), 3.92 (s, 3H, OCH₃), 7.10-7.32 (m, 5H, aryl H's), 9.58 (s, 1H, CHO).

Anal. Calcd. for C₁₆H₁₇NO₄: C, 66.88; N, 5.96; O, 4.88. Found: C, 66.99; H, 5.92; N, 4.83.

1-Methyl-3-oxo-4-ethoxycarbonyl-5-phenyl-2-(3',5'-dimethyl-2'-pyrrylmethylidene)-4-pyrroline (**6**).

A solution of 2,5-dimethylpyrrole (0.118 g., 1.25 mmoles) and the aldehyde **5** (0.352 g., 1.23 mmoles) in 4 ml. of chloroform was treated with 0.5 ml. of anhydrous ethyl ether which was saturated with dry hydrogen chloride. After 5 minutes the reaction was treated with 1 ml. of concentrated aqueous ammonia. The residue that remained after drying and evaporating the organic phase was chromatographed on 30 g. of neutral alumina (10% THF/benzene) to separate the major component of the mixture from a few highly colored contaminants. Concentration of the golden yellow fractions gave crystals of **6** that could be recrystallized from cyclohexane, m.p. 199-200° (dec); ir. (potassium bromide) 5.95 (C=O, unsaturated ester), 6.15μ (C=O, unsaturated ketone); nmr (deuteriochloroform): δ 1.04 (t, 3H, J = 7 Hz, 4-CO₂CH₂CH₃), 2.22 (s, 3H, 3'-CH₃), 2.32 (s, 3H, 5'-CH₃), 3.20 (s, 3H, NCH₃), 4.08 (q, 2H, J = 7 Hz, 4-CO₂CH₂CH₃), 5.96 (d, 1H, J = 2 Hz, H-4'), 6.63 (s, 1H, *meso*-CH), 7.18-7.44 (m, 5H, aryl H's).

Anal. Calcd. for C₂₁H₂₂N₂O₃: C, 71.98; H, 6.33; N, 8.00; M.W. 350. Found: C, 71.86; H, 6.50; N, 7.89; M.W., M⁺ 350.

1-Methyl-2-phenylthio-3-methoxy-5-phenylpyrrole (**7**).

1-Methyl-3-methoxy-5-phenylpyrrole-2,4-dicarboxylic acid (1.0 g., 3.14 mmoles) was decarboxylated (3) and the resulting liquid **1** was dissolved in 3 ml. of THF under nitrogen. This solution was added *via* syringe to 0.93 g. of *N*-phenylthiophthalimide (**9**) (3.65 mmoles) in 10 ml. of THF stirring under nitrogen. After stirring for 16 hours at room temperature TLC showed starting materials remaining, so an additional 1.5 mmoles of *N*-phenylthiophthalimide was added and the reaction refluxed for 2 hours. At the end of this time starting materials still remained, so the solvent was evaporated under reduced pressure and the mixture separated on 110 g. of silica gel (MCB, grade 62), eluting with 1:1 benzene/cyclohexane. Consolidation and evaporation of the fractions containing the new material gave 0.54 g. of **7** (50%) as a viscous oil that was homogeneous to TLC; nmr (carbon tetrachloride): δ 3.60 (s, 3H, NCH₃), 3.85 (s, 3H, OCH₃), 6.05 (s, 1H, H-4), 7.10 (s, 5H, aromatics), 7.45 (s, 5H, aromatics); M.W. Calcd. for C₁₈H₁₇NOS: 295.10308. Found: M⁺, 295.10289.

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