

A Novel Oxidative Reaction of 2,4,5-Triphenylpyrrole

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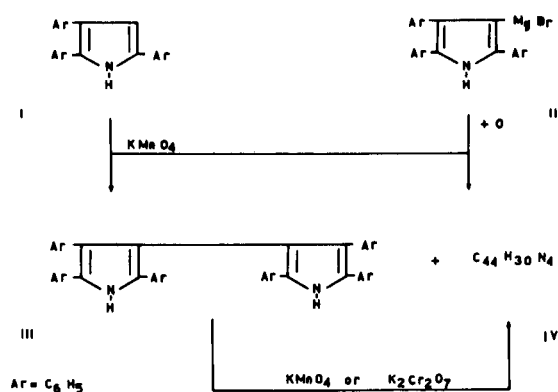
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The effect of phenyl groups on the oxidation of 2,4,5-triphenylpyrrole (I) has been investigated. By oxidation of 2,4,5-triphenylpyrrole magnesium bromide (II) with oxygen and of 2,4,5-triphenylpyrrole (I) with potassium permanganate besides 2,4,5,2',4',5'-hexaphenyl-3,3'-bipyrrole (III) another product, which has been assigned the 1,6-dihydro-2,3,4,5,6a-pentaphenylbenzo[g]pyrrole[3,2-e]indole (IV) structure, was obtained. The behaviour of IV toward further oxidation and the spectroscopic data (ir, nmr, ms) were in good agreement with the assigned structures.

Recently in the pyrrole series a few cases of formation of dimers *via* oxidation were reported (1,2,3). In connection with the work concerning polyphenylpyrrole oxidation (4) we wish to present the first proof of structural elucidation of pyrrole dimers obtained by oxidation of 2,4,5-triphenylpyrrole magnesium bromide with oxygen by direct oxidation of 2,4,5-triphenylpyrrole with potassium permanganate.

Chromatographically pure 2,4,5-triphenylpyrrole (I) was converted into the magnesium bromide derivative (II) and the boiling ethereal solution was stirred for several hours under a slow stream of oxygen. The ethereal extracts from the reaction mixture, purified by column chromatography, gave two products III m.p. 249-250°, which was the major component, and IV m.p. 269-270°. Oxidation of I with potassium permanganate (2 gram atoms of oxygen per mole) in benzene solution gave products identical with III and IV, respectively.

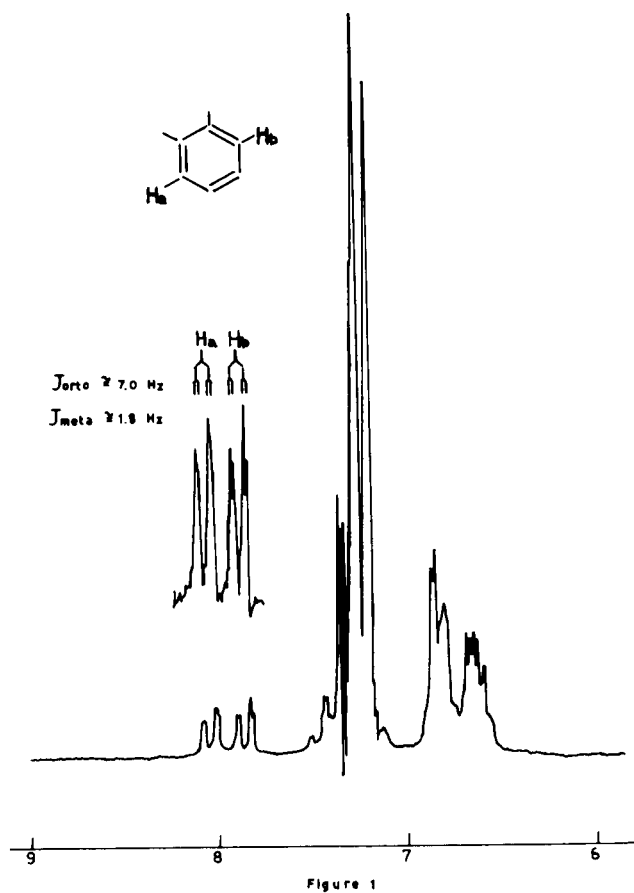
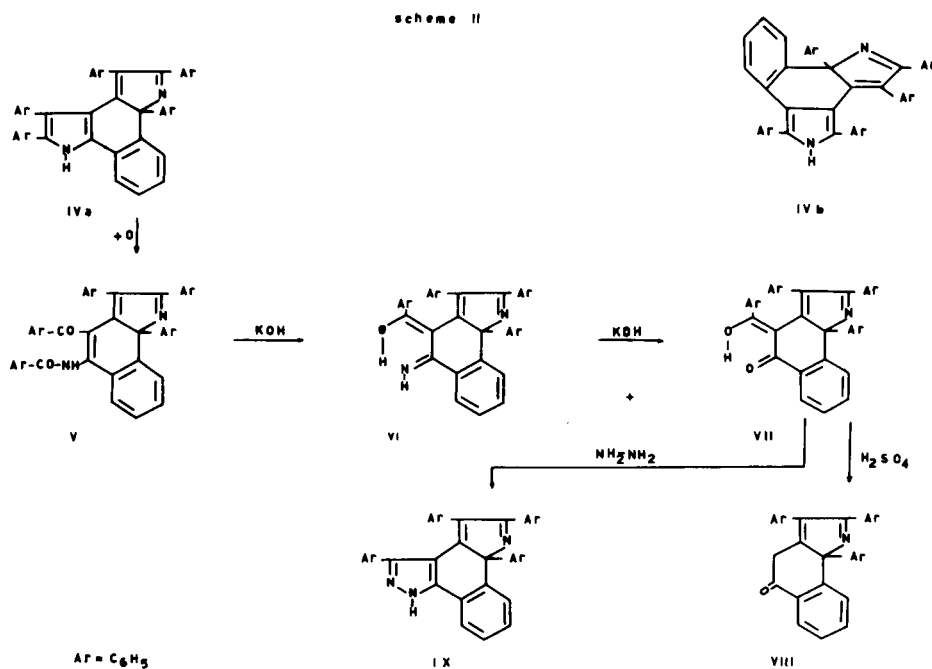
Scheme 1



The results of elemental analysis, molecular weight (C₄₄H₃₂N₂, Mass: M⁺ 588) and spectroscopic data of III supported the structure of 2,4,5,2',4',5'-hexaphenyl-3,3'-bipyrrole. The uv spectra of III were similar to that of 2,4,5-triphenylpyrrole, the ir spectrum showed a strong pyrrole NH absorption at 3380 cm⁻¹; the nmr spectrum, besides signals for aromatic protons, exhibited a singlet (two pyrrole NH) at 11.17 δ.

Compound IV (C₄₄H₃₀N₂, Mass: M⁺ 586), which was also obtained by oxidation of III with potassium dichromate or potassium permanganate (1 gram atom of oxygen per mole) showed, in comparison to III, two atoms less of hydrogen. The ir spectrum of IV showed a band at 3420 cm⁻¹ in the NH pyrrole stretching region and at 1640 cm⁻¹ (C=N); nmr spectrum at 100 MHz exhibited a singlet (1H) at 11.92 δ (NH), at 7.88 δ (1H, dd, J = 7.0 Hz, J = 1.8 Hz) 8.07 δ (1H, dd, J = 7.0 Hz, J = 1.8 Hz) (Figure 1) and 6.40-7.60 δ (27H, m, aromatic protons). Oxidation of dimer III into IV apparently involved a phenyl group forming a new ring. By considering that, on oxidation, the α position (5) of the pyrrole nucleus is involved first, the possible structures are limited. We believe that the most probable structures are IVa or IVb obtained by involving the α position of a pyrrole nucleus with the α' or β' phenyl group of the other pyrrole ring.

The behaviour of IV on further oxidation led to 1,6-dihydro-2,3,4,5,6a-pentaphenylbenzo[g]pyrrolo[3,2-e]-indole (IVa) as the preferred structure. In fact IV, very stable to hydrolytic processes in basic of acidic media, by oxidation with an excess of potassium dichromate yielded quantitatively the amide V. The structural assignment of compound V rested on the analytical data, on compatible ir and nmr spectra and the chemical behaviour. The ir



spectrum showed an absorption at 3300 cm^{-1} due to an amide NH and at 1700 and 1660 cm^{-1} due to the ketone and amide carbonyl, respectively. The nmr spectrum besides signals for aromatic protons, exhibited a singlet (1H) at $11.20\ \delta$ due to the amide NH. The mass spectrum of VI showed the significant peaks M^+ 618, 513 ($M\text{-C}_6\text{H}_5\text{CO}^+$) 105 ($\text{C}_6\text{H}_5\text{CO}^+$), 77 (C_6H_5^+ , base peak).

Alkaline degradation of V afforded two products, VI and VII, which were separated by column chromatography (for details see experimental). The latter compound VII (6) could be also obtained from VI by further alkaline hydrolysis.

Compound VII reacted with hydrazine to give the pyrazole derivative IX and also was converted into VIII by acid hydrolysis.

The formulation of VI and VII appears reasonable on the basis of nmr, ir and uv spectra; both the compounds gave a positive test with ferric chloride.

The ir spectrum of VI showed two strong absorptions at 3440 and 1680 cm^{-1} due to the $\text{C}=\text{NH}$ group, the nmr spectrum showed a signal at $8.30\ \delta$ which indicated an imine NH group. The ir spectrum of VII showed a band at 1640 cm^{-1} due to a carbonyl group strongly intramolecularly hydrogen bonded. The uv spectra of both the compounds were quite similar to each other. The mass spectra of VI and VII showed the significant peaks M^+ 514, 409 ($M\text{-C}_6\text{H}_5\text{CO}^+$ base peak), 105 ($\text{C}_6\text{H}_5\text{CO}^+$) and M^+ 515 (base peak), 438 ($M\text{-C}_6\text{H}_5$), 410 ($M\text{-C}_6\text{H}_5\text{CO}^+$) 105 ($\text{C}_6\text{H}_5\text{CO}^+$), 77 (C_6H_5^+) respectively.

Compound VIII contained two isolated uv chromophores, one of which is an α -tetralone. The uv spectrum of tetralone exhibits a major maximum at about 248 nm (8). The uv spectrum of VIII (λ max nm sh 336, sh 268 and 243) was in agreement with this standpoint. The MS spectrum of VIII showed the significant peaks M^+ 411 (base peak), 382 (M -CHO) $^+$, 77 (C_6H_5) $^+$.

Additional means for the elucidation of the structure of compound IV are being investigated.

EXPERIMENTAL

All melting points were taken on a Büchi-Tottoli capillary melting point apparatus and are uncorrected. Uv absorption spectra (ethanol) were measured on a Beckmann DB recording spectrophotometer and ir absorption spectra with Perkin-Elmer infracord 137 using nujol mulls. Nmr spectra were measured, using, tetramethylsilane as the internal standard, with a Jeol C-60H and Varian XL-100-15 spectrometer. Mass spectrometric analyses were determined with Spectrometer Hitachi Perkin-Elmer 270. Silica gel for chromatography was Merck (0.05-0.2 mm) in the inactive form.

Oxidation of 2,4,5-Triphenylpyrrole-magnesium Bromide (II) with Oxygen and Oxidation of 2,4,5-Triphenylpyrrole (I) with Permanganate.

A stream of oxygen was bubbled through a suspension of II (obtained from 3 g. of 2,4,5-triphenylpyrrole, 0.3 g. of magnesium, 100 ml. of absolute ether and 1 ml. of ethyl iodide) and the mixture was refluxed for 8 hours. After decomposition with ice and aqueous saturated ammonium chloride the layers were separated and the ether phase was dried over anhydrous sodium sulfate. The concentrated ethereal solution was purified by column (60 x 3 cm) chromatography over silica gel (100 g.). Elution with cyclohexane-benzene (1:1) (F_{1-6} each 100 ml.) gave 0.3 g. of 2,4,5-triphenylpyrrole, m.p. 140-141°. Further elution with cyclohexane-benzene (3:7) (F_{10-20} each 100 ml.) gave III, 1.8 g. Elution with benzene (F_{24-28} each 100 ml.) gave IVa, 0.3 g. Products identical with III and IVa, respectively, were obtained in the same yield by oxidation of I with potassium permanganate.

A solution of I (2.95 g., 0.01 mole) in 50 ml. of benzene was treated with 1.05 g. of potassium permanganate (0.01 gram atoms of oxygen) in 40 ml. of water and the mixture was shaken at room temperature until the reagent was completely reduced.

The suspension was filtered off and the solid residue (manganese dioxide) was washed with hot benzene. The combined organic solutions were dried and evaporated. The residue was chromatographed on a column of silica gel as above.

2,4,5,2',4',5'-Hexaphenyl-3,3'-bipyrrole (III).

Pale yellow crystals from ethanol, m.p. 249-250°, were obtained, ir 3380 cm^{-1} (pyrrole NH); uv λ max nm log ϵ 328 (4.53) sh 302 (4.46) sh 268 (3.35) sh 234 (3.43); nmr 60 M Hz (DMSO- d_6): 6.40-8.00 δ (30H, m, aromatic H), 11.17 δ (2H, s, pyrrole NH), MS: m/e 588 (M^+), 294 (M^{++}).

Anal. Calcd. for $C_{44}H_{32}N_2$: C, 89.76; H, 5.48; N, 4.76. Found: C, 89.74; H, 5.70; N, 4.93.

1,6-Dihydro-2,3,4,5,6a-pentaphenylbenzo[*g*]pyrrolo[3,2-*e*]indole (IVa).

Yellow crystals from benzene-light petroleum (b.p. 40-60°), m.p. 269-270°, were obtained. ir: 3420 cm^{-1} (pyrrole NH); uv λ max nm log ϵ 304 (4.23) 274 (4.15); nmr at 100 M Hz (DMSO- d_6): 6.40-7.60 (27H, m, aromatic H) 7.88 δ (1H, dd, $J \cong 7.0$ Hz,

$J = 1.8$ Hz aromatic H), 8.07 δ (1H, dd, $J \cong 7.0$ Hz, $J \cong 1.8$ Hz, aromatic H); 11.92 δ (1H, s, pyrrole NH), MS: m/e 586 (M^+).

Anal. Calcd. for $C_{44}H_{30}N_2$: C, 90.10; H, 5.11; N, 4.77. Found: C, 90.34; H, 5.05; N, 4.87.

Oxidation of III by Dichromate and Permanganate. 1,6a-Dihydro-2,3,4,5,6a-pentaphenylbenzo[*g*]pyrrolo[3,2-*e*]indole (IVa).

A solution of potassium dichromate (0.1 g., 0.001 gram atoms of oxygen) in 5 ml. of water was added dropwise with stirring to a solution of III (0.6 g., 0.001 mole) in acetic acid (20 ml.). The temperature was not allowed to exceed 15°. After a short period of time the mixture was added to water (100 ml.) and was neutralized with aqueous sodium bicarbonate. Extraction with ether gave, after drying (sodium sulfate) and evaporation of the ether, a yellow solid which was recrystallized from benzene-light petroleum (b.p. 40-60°), m.p. 269-270° (yield 70%).

A solution of III (0.6 g., 0.01 mole) in 20 ml. of benzene, was treated with 0.10 g. of potassium permanganate (0.01 gram atoms of oxygen) in 5.0 ml. of water and the mixture was shaken at room temperature until the reagent was completely reduced. The suspension was filtered off and the solid residue (manganese dioxide) was washed with hot benzene. The combined organic solutions were dried and evaporated. The residue was crystallized from benzene-light petroleum (b.p. 40-60°), m.p. 269-270° (yield 75%).

The products obtained by these two methods were identical with IVa (m.p. and mixed m.p., ir, nmr, uv).

Oxidation of IVa. *N*-(4-Benzoyl-2,3,9b-triphenyl-9bH-benz[*g*]indole-5-yl)benzamide (V).

To the solution of IVa (5 g.) in 100 ml. of acetic acid was added a solution of potassium dichromate (2 g.) in 10 ml. of water.

The mixture was refluxed until reduction of the reagent was complete. The precipitate obtained after cooling of the solution was crystallized from acetic acid or ethanol, yellow needles (4.5 g.) m.p. 249-250°; ir 3300 (amide CO) 1700 and 1660 cm^{-1} (amide CO and ketone CO); uv λ log ϵ sh 272 (4.25) 244 (4.05); nmr at 100 M Hz (DMSO- d_6): 6.40-8.00 δ (29H, m, aromatic H) 10.36 δ (1H, s, amide NH); MS: m/e 618 (M^+), 513 (M - C_6H_5 -CO) $^+$ 105 (C_6H_5 -CO) $^+$ 77 (C_6H_5) $^+$.

Anal. Calcd. for $C_{44}H_{30}N_2O_2$: C, 85.41; H, 4.89; N, 4.53. Found: C, 85.49; H, 4.79; N, 4.65.

Hydrolysis of V. 4- α -Hydroxybenziliden-5-imino-2,3,9b-triphenyl-9bH-benz[*g*]indole (VI) and 4- α -Hydroxybenziliden-5-keto-2,3,9b-triphenyl-9bH-benz[*g*]indole (VII).

The mixture of V (3 g.) and 4% ethanolic potassium hydroxide (100 ml.) was boiled under reflux for 6 hours. The reaction solution was concentrated under reduced pressure. Water (40 ml.) was added the mixture was extracted with ether (7). The combined organic extracts were washed with water, dried over anhydrous sodium sulfate, filtered and the filtrate was concentrated under reduced pressure.

The residue was purified by column (60 x 3 cm) chromatography over silica gel (100 g.). Elution with benzene:cyclohexane (9:1) (F_{5-20} each 100 ml.) gave 1.50 g. of 4- α -hydroxybenziliden-5-keto-2,3,9b-triphenyl-9bH-benz[*g*]indole (VII), yellow crystals, from light petroleum (b.p. 40-60°) m.p. 213-214°. The product in ethanolic solution gave a violet colouration with ferric chloride; ir: 1640 cm^{-1} (CO); uv λ max nm log ϵ 260 (4.35); nmr at 60 M Hz (deuteriochloroform): 6.40-8.50 δ (m, aromatic, H); MS:

m/e 515 (M^+), 438 ($M-C_6H_5$)⁺, 410 ($M-C_6H_5-CO$)⁺, 105 (C_6H_5-CO)⁺, 77 (C_6H_5)⁺.

Anal. Calcd. for $C_{37}H_{25}NO_2$: C, 86.19; H, 4.89; N, 2.72. Found: C, 86.14; H, 4.84; N, 2.61.

Elution with benzene-ethyl acetate (9:1) ($F_{24.30}$ each 100 ml.) gave 1.0 g. of 4- α -hydroxybenziliden-5-imino-2,3,9b-triphenyl-9bH-benz[*g*]indole (VI), yellow crystals from ethanol, m.p. 159-160° dec. The product in ethanolic solution gave a brown-red colouration with ferric chloride; ir: 3440 and 1680 cm^{-1} (C=NH); uv λ max nm log ϵ 262 (4.35); nmr at 60 M Hz (deuteriochloroform): 6.20-8.20 δ (23H, m, aromatic H) 8.30 δ (1H, broad, NH); MS: m/e 514 (M^+), 409 ($M-C_6H_5-CO$)⁺, 105 (C_6H_5-CC)⁺.

Anal. Calcd. for $C_{37}H_{26}N_2O$: C, 86.35; H, 5.09; N, 5.44. Found: C, 86.34; H, 5.21; N, 5.27.

Hydrolysis of VI. 4- α -Hydroxybenziliden-5-keto-2,3,9b-triphenyl-9bH-benz[*g*]indole (VII).

Compound VI (1.0 g.) was refluxed for 6 hours in a solution of 5.0 g. of sodium hydroxide in 50 ml. of ethanol. The solvent was distilled and 50 ml. of water added. The mixture was extracted with four 50 ml. portions of ether. The combined extracts were dried (sodium sulfate) and the solvent was distilled in a rotary evaporator to leave a solid, yellow crystals from light petroleum (b.p. 40-60°) m.p. 213-214°. The product was identical with VII obtained by the above method. (m.p. and mixed m.p., ir, uv, nmr).

Action of Hydrazine on VII. 1,6a-Dihydro-3,4,5,6a-tetraphenylbenzo[*g*]pyrrolo[3,2-*e*]indazole (IX).

Hydrazine hydrate (1.0 ml.) was added to a solution of VII (0.5 g.) in 20 ml. of ethanol and 1.0 ml. of acetic acid. The mixture was refluxed for 2 hours. The solution was evaporated to dryness on rotary evaporator and extracted with five 30 ml. portions of ether. The ether extracts were washed with water, dried (sodium sulfate) and concentrated on the flash evaporator, light yellow crystals (ethanol) m.p. 253°; ir 3350 cm^{-1} (NH); uv λ max nm log ϵ 282 sh (4.39) 252 (4.56); nmr at 100 M Hz (DMSO- d_6): 6.60-8.20 δ (1H, s, pyrazolic NH); MS. m/e 511 (M^+).

Anal. Calcd. for $C_{37}H_{25}N_3$: C, 86.88; H, 4.89; N, 8.21. Found: C, 86.57; H, 4.92; N, 8.23.

Monoacetyl derivative: white scales from ethanol m.p. 223°.

Anal. Calcd. for $C_{39}H_{27}N_3O$: N, 7.59. Found: N, 7.85.

Hydrolysis of VII. 4,9b-Dihydro-2,3,9b-triphenyl-5H-benz[*g*]indol-5-one (IX).

Compound VII (1.0 g.) was refluxed for 10 hours in a mixture of 50 ml. of dioxane and 10 ml. of 50% aqueous sulfuric acid. The dioxane was distilled under vacuum and 50 ml. of water was added. The mixture was extracted with ether (4 x 50 ml.).

The combined extracts were washed with aqueous saturated sodium bicarbonate (7), dried and the solvent was finally distilled in a rotary evaporator, white crystals from ethanol m.p. 106°; ir 1700 cm^{-1} (CO); uv λ max nm log ϵ sh 336 (3.53) sh 268 (4.02) 243 (4.23); nmr 100 M Hz (deuteriochloroform): 2.75 δ (1H, d, J = 16.0 Hz), 4.23 δ (1H, d, J \cong 16.0 Hz) 6.90-8.20 δ (19H, m, aromatic H); MS: m/e 411 (M^+), 382 ($M-CHO$)⁺, 77 (C_6H_5)⁺.

Anal. Calcd. for $C_{30}H_{21}NO$: C, 87.56; H, 5.14; N, 3.40. Found: C, 87.67; H, 5.34; N, 3.39.

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REFERENCES

- (1) K. Tomita and N. Yoshida, *Tetrahedron Letters* 1169 (1971).
- (2) K. Tomita and N. Yoshida, *Bull. Chem. Soc. Japan* 45, 3160 (1972).
- (3) G. Rio and D. Masure, *Bull. Soc. Chim. France*, 4610 (1972).
- (4) V. Sprio, *Gazz. Chim. Ital.*, 85, 569 (1955).
- (5) The presence in IV of a pyrrole NH in the ir and nmr spectra and of a C=N absorption in the ir spectrum led to the exclusion of the pyrrole NH as a participant in the cyclization.
- (6) The hydrolysis resistance of VII showed that the imine NH group was bonded to a nucleus.
- (7) Acidification of the alkaline liquors and successive extraction with ether produced benzoic acid.
- (8) M. Ramart-Lucas and M. J. Hoch, *Bull. Soc. Chim. France*, 19, 220 (1952).