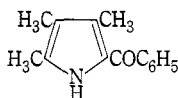


## PYRROLE STUDIES\*

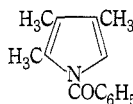
### III.† THE BENZOYLATION OF ALKYL PYRROLES

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In the course of our work on the stepwise synthesis of *meso*-substituted porphyrins<sup>1</sup> we prepared 3,4,5,3',4',5'-hexamethyl-*ms*-phenyldipyrromethene by the reaction of 2,3,4-trimethylpyrrole with benzoyl chloride in acetic acid. As a by-product of this reaction, we also isolated a compound, m.p. 136–137°, with analytical figures corresponding to C<sub>14</sub>H<sub>15</sub>NO. One might reasonably expect that 2-benzoyl-3,4,5-trimethylpyrrole (I) would be an intermediate in the reaction and the presence of bands at 3450 and 1593 cm<sup>-1</sup> ( $\nu_{\text{NH}}$  and  $\nu_{\text{CO}}$ ) in the infrared spectrum of the unknown compound suggested that this was the product which we had isolated.



(I)



(II)

However, the melting point of (I) corresponded to that of a compound, prepared by Treibs and Derra-Scherer<sup>2</sup> from 2,3,4-trimethylpyrrole and benzoyl chloride in excess sodium hydroxide, which they described as the 1-benzoyl compound (II). This discrepancy prompted us to make an investigation of the benzylation of pyrroles.

Treibs<sup>2,3</sup> reported that benzylation of pyrroles with benzoyl chloride in sodium hydroxide gave the 1-benzoyl compounds, and several text books,<sup>4,5</sup> and reviews<sup>6</sup> have quoted this work. However, Pleininger, Bauer, and Katritzky<sup>7</sup> recently showed that 2-ethoxy-3,4-dimethylpyrrole benzylation in the 5-position under similar conditions to those reported by Treibs.

In our hands pyrrole, 2,4-dimethylpyrrole, and 2,3,4-trimethylpyrrole gave only the *C*-benzoyl derivatives on benzylation with benzoyl chloride in excess sodium hydroxide. The melting point of 2-benzoyl-3,5-dimethylpyrrole (118.5–119°) was close to that recorded for 1-benzoyl-2,4-dimethylpyrrole (119°) by Treibs and different from that of his 2-benzoyl-3,5-dimethylpyrrole (136°).<sup>3</sup> The identification of

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† Part II, *Aust. J. Chem.*, 1964, **17**, 894.

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<sup>1</sup> Badger, G. M., Jones, R. A., and Laslett, R. L., *Aust. J. Chem.*, in press.

<sup>2</sup> Treibs, A., and Derra-Scherer, H., *Liebigs Ann.*, 1954, **589**, 188.

<sup>3</sup> Treibs, A., and Michl, K. H., *Liebigs Ann.*, 1952, **577**, 115.

<sup>4</sup> Stevens, T. S., in "Chemistry of Carbon Compounds." (Ed. E. H. Rodd.) Vol. IVA (Elsevier: Amsterdam 1957.)

<sup>5</sup> Katritzky, A. R., and Lagowski, J. M., "Heterocyclic Chemistry." p. 175. (Methuen: London 1960.)

<sup>6</sup> Baltazzi, E., and Krimen, L. I., *Chem. Rev.*, 1963, **63**, 511.

<sup>7</sup> Pleininger, H., Bauer, H., and Katritzky, A. R., *Liebigs Ann.*, 1962, **654**, 165.

our products was obtained by comparison with the 1-benzoyl derivatives, which were prepared by the general method of Rainey and Adkins,<sup>8</sup> and authentic samples of the 2-benzoyl derivatives prepared by Houben-Hoesch acylation. Also, the infrared spectra of all the 2-benzoyl compounds showed absorption bands near 3450 and 1600  $\text{cm}^{-1}$  ( $\nu_{\text{NH}}$  and  $\nu_{\text{CO}}$ ), whereas the 1-benzoyl compounds absorbed near 1690  $\text{cm}^{-1}$  ( $\nu_{\text{CO}}$ ).

### Experimental

#### 3,4,5,3',4',5'-Hexamethyl-ms-phenyldipyrromethene

Potassium 3,4,5-trimethylpyrrole-2-carboxylate<sup>9</sup> (5 g) and benzoyl chloride (5 ml) in glacial acetic acid (10 ml) were refluxed for 90 min and then poured into water. The aqueous mixture was extracted with benzene (3  $\times$  50 ml) and the benzene extracts were washed with ammonium hydroxide and water. The benzene extracts were dried and concentrated. Chromatography on alumina using benzene for elution gave two products. The first, an orange solid (2.05 g, 37%), on recrystallization from hexane gave 2-benzoyl-3,4,5-trimethylpyrrole as pale yellow needles, m.p. 136–137° (Found: C, 79.2; H, 7.0; N, 6.5%.  $\text{C}_{14}\text{H}_{15}\text{NO}$  requires C, 78.8; H, 7.1; N, 6.5%). The second fraction gave 3,4,5,3',4',5'-hexamethyl-ms-phenyldipyrromethene (1.75 g, 44%), dark green plates from hexane, m.p. 193–195° (Found: C, 82.7; H, 8.1; N, 9.6%.  $\text{C}_{21}\text{H}_{24}\text{N}$  requires C, 82.9; H, 8.0; N, 9.2%).

#### 1-Benzoylpyrroles

Potassium pyrrole,<sup>8</sup> prepared from pyrrole (10 g), was refluxed in toluene (200 ml) with benzoyl chloride (26 ml) for 3 hr. The toluene was removed and the product distilled to give 1-benzoylpyrrole (18.0 g, 70%), b.p. 94–96°/0.2 mm (lit.<sup>10</sup> 276°/715 mm).

1-Benzoyl-2-methylpyrrole (14%), b.p. 160–162°/23 mm (Found: C, 77.1; H, 6.0; N, 7.1%.  $\text{C}_{13}\text{H}_{11}\text{NO}$  requires C, 77.8; H, 6.0; N, 7.6%); 1-benzoyl-2,4-dimethylpyrrole (39%), b.p. 126–128°/0.5 mm (lit.<sup>3</sup> m.p. 119°) (Found: C, 77.9; H, 6.6; N, 6.8%.  $\text{C}_{15}\text{H}_{13}\text{NO}$  requires C, 78.4; H, 6.6; N, 7.0%); 1-benzoyl-2,5-dimethylpyrrole (40%), b.p. 106°/0.3 mm, m.p. 38° (pale yellow prisms from hexane) (Found: C, 78.3; H, 6.9; N, 7.0%); and 1-benzoyl-2,3,4-trimethylpyrrole (45%), b.p. 110–114°/0.02 mm (Found: C, 78.6; H, 6.9; N, 6.7%.  $\text{C}_{14}\text{H}_{15}\text{NO}$  requires C, 78.8; H, 7.1; N, 6.5%) were prepared by methods analogous to that used for 1-benzoylpyrrole.

#### 2-Benzoylpyrrole

Benzoyl chloride (20 ml) was added dropwise to pyrrole (8.25 g) in aqueous sodium hydroxide (10%, 25 ml) at 0° over a period of 10 min. The solution was stirred at room temperature for 3 hr and then extracted with chloroform (3  $\times$  50 ml). The extracts were washed with sodium hydroxide and water, and then dried. Removal of the solvent gave a solid, m.p. 100–120°, which on further washing with sodium hydroxide and extraction with ether gave an oil. Chromatography of the oil on alumina using hexane as the eluant gave 2-benzoylpyrrole (2.0 g, 10%), m.p. 78–79° (lit.<sup>11</sup> 79°).

#### 2-Benzoyl-5-methylpyrrole

Benzoyl chloride (1.2 ml) in ether (10 ml) was added to the Grignard derivative of 2-methylpyrrole,<sup>12</sup> prepared from magnesium (0.22 g), ethyl bromide (1.06 g), and 2-methylpyrrole (0.7 g), over a period of 10 min. The mixture was refluxed for 18 hr and then cooled to 0°. Saturated ammonium chloride was added and the ethereal layer separated and dried. Removal of the solvent gave 2-benzoyl-5-methylpyrrole (0.56 g, 35%), yellow prisms from hexane, m.p. 142° (Found: C, 77.7; H, 6.1; N, 7.4%.  $\text{C}_{12}\text{H}_{11}\text{NO}$  requires C, 77.8; H, 6.0; N, 7.6%).

<sup>8</sup> Rainey, J. L., and Adkins, H., *J. Amer. Chem. Soc.*, 1939, **61**, 1104.

<sup>9</sup> Badger, G. M., Harris, R. L. N., Jones, R. A., and Sasse, J. M., *J. Chem. Soc.*, 1962, 4329.

<sup>10</sup> Pietet, A., and Rudstein, S., *Ber. dt. chem. Ges.*, 1904, **37**, 2796.

<sup>11</sup> Fischer, H., and Orth, H., "Die Chemie des Pyrrols." Vol. I. (Akademische Verlagsgesellschaft: Leipzig 1934.)

<sup>12</sup> Cornforth, J. W., and Firth, M. E., *J. Chem. Soc.*, 1958, 1091.

*2-Benzoyl-3,4-dimethylpyrrole*

This compound (23%), m.p. 76–77°, needles from hexane (Found: C, 78.7; H, 6.6; N, 6.9%.  $C_{13}H_{13}NO$  requires C, 78.4; H, 6.6; N, 7.0%) was prepared from 3,4-dimethylpyrrole<sup>13</sup> by a method analogous to that used for 2-benzoyl-5-methylpyrrole.

Benzoylation using benzoyl chloride and sodium hydroxide gave a mixture of inseparable products.

*2-Benzoyl-3,5-dimethylpyrrole*

(i) 2,4-Dimethylpyrrole<sup>14</sup> was shaken with excess benzoyl chloride in aqueous sodium hydroxide. The product (52%) obtained was recrystallized from hexane to give 2-benzoyl-3,5-dimethylpyrrole, m.p. 118.5–119° (Found: C, 78.2; H, 6.7; N, 7.3%). Treibs<sup>2</sup> gave m.p. 119° for 1-benzoyl-2,4-dimethylpyrrole.

(ii) The Houben–Hoesch procedure employed by Treibs<sup>2</sup> for the preparation of 2-benzoyl-3,5-dimethylpyrrole gave a product (28%), m.p. 117–118°, identical with the above. (Treibs<sup>2</sup> gave m.p. 136° for 2-benzoyl-3,5-dimethylpyrrole.)

*2-Benzoyl-3,4,5-trimethylpyrrole*

(i) 2,3,4-Trimethylpyrrole<sup>15</sup> was shaken with excess benzoyl chloride in aqueous sodium hydroxide. Sublimation of the crude product at 100°/0.5 mm and crystallization from hexane gave 2-benzoyl-3,4,5-trimethylpyrrole (36%) as pale yellow needles, m.p. 136–137°.

(ii) Benzonitrile (3.6 g) was added to 2,3,4-trimethylpyrrole (2.16 g) in ether (30 ml) and the solution was saturated at 0° with hydrogen chloride. After keeping the solution at 0° for 12 hr, the ether was removed under reduced pressure. Water (30 ml) was added to the residual oil and the mixture was refluxed for 6 hr. On allowing the mixture to stand for 2 days at room temperature 2-benzoyl-3,4,5-trimethylpyrrole (1.2 g, 31%), m.p. 135–137°, crystallized.

(iii) Ethyl 2,4-dimethylpyrrole-3-carboxylate<sup>11</sup> gave 2-benzoyl-3,4,5-trimethylpyrrole, m.p. 135–137°, by the method described by Treibs<sup>2</sup> for the synthesis of 1-benzoyl-2,3,4-trimethylpyrrole. (Treibs<sup>2</sup> gave m.p. 136° for 1-benzoyl-2,3,4-trimethylpyrrole.)

The products obtained from all three methods were identical with the by-product of the synthesis of 3,4,5,3',4',5'-hexamethyl-*ms*-phenyldipyrromethene. There was no depression of melting point with mixed samples and the infrared spectra of all specimens were identical.

*Acknowledgments*

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<sup>13</sup> Booth, H., Johnson, A. W., Johnson, F., and Langdale-Smith, R. A., *J. Chem. Soc.*, 1963, 655.

<sup>14</sup> Corwin, A. H., and Kreible, R. H., *J. Amer. Chem. Soc.*, 1941, **63**, 1829.

<sup>15</sup> Treibs, A., and Zinsmeister, R., *Chem. Ber.*, 1957, **90**, 87.