Synthesis of Pyridyl *meso* Substituted Dipyrrylmethanes

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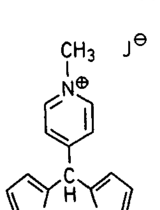
Despite current interest in the chemistry of porphyrins there are few reports on the synthesis of dipyrrylmethanes. Dipyrrylmethanes and their derivatives are by far the most suitable starting materials for the total synthesis of porphyrin complexes. Few of the reported works on dipyrrylmethanes[2] deal with *meso* carbon substituted systems. In connection with our work on dipyrrylmethanes, we wish to report a successful synthetic route for previously unreported *meso* substituted dipyrrylmethanes (**1**, **2**).



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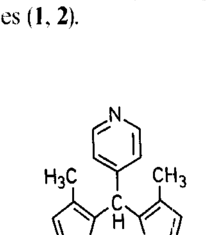

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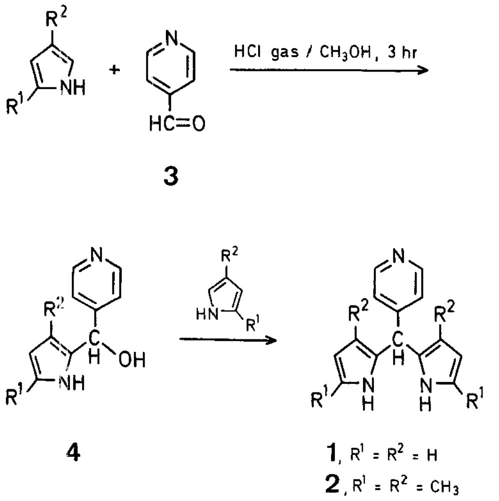
In general the synthesis of 4-(dipyrrylmethyl)-*N*-methylpyridinium iodide (**1**) and bis[2,4-dimethylpyrryl]-4-pyridylmethane (**2**) depends upon the ease with which the α-position of pyrrole is attacked by the electrophillic reagent 4-pyridinecarboxaldehyde (**3**). The mechanism[3] involves an addition step involving a pyrrole and 4-pyridinecarboxaldehyde to produce a carbinol (**4**), which need not be isolated in the course of the synthesis. A second molecule of pyrrole condenses with the carbinol to yield the dipyrryl system.



Compounds (**1**, **2**) are isolated as their hydrochloride salts, which following neutralization yield the free bases. The pyridine nitrogen of the free base forms a quaternary salt with iodomethane (**1**).

The scope of the outlined synthesis is not limited to pyridyl *meso* substituted dipyrrylmethanes. It is applicable to other aromatic systems substituted at the *meso* position of dipyrrylmethanes. However, the method is limited to symmetric dipyrrylmethanes. With different pyrroles, a mixture of products is obtained and due to the marked similarity in properties of the different dipyrrylmethanes the desired product is difficult to isolate.

2,4-Dimethylpyrrole:

The method in the literature[4] for this preparation gives unreliable results. The following procedure gives yields up to 98%.

2,4-Dimethyl-3,5-dicarbethoxypyrrole[5] (48 g, 0.5 mol) is ground with 85% potassium hydroxide (78 g, 1.2 mol) and made into a paste with chloroform (25 ml). The paste is placed into a steel bomb, sealed and heated in an oil bath at 170° for 5 to 6 hours. A pressure of 310 psi develops within the steel bomb, indicating the completion of the reaction. On cooling to room temperature, a dark brown liquid is obtained in addition to crystalline potassium carbonate. The liquid is extracted with ether and the ether extract is steam distilled. The distillate is saturated with sodium chloride and is extracted several times with ether. The ether extract is dried over anhydrous sodium sulfate, evaporated, and 2,4-dimethylpyrrole distilled under vacuum; b.p. 56°/10 torr. The 2,4-dimethylpyrrole is stored in a colored bottle flushed with nitrogen; yield: 18.3 g (98%).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 6.4$ (s, $1H_{arom}$), 5.75 (s, $1H_{arom}$), 2.15 ppm (d, 6H).

Preparation of pyridyl *meso* substituted dipyrrylmethanes:

4-Pyridinecarboxaldehyde (**3**, 10 g, 0.094 mol) was added dropwise with stirring at room temperature into a methanolic solution of the desired pyrrole (0.2 mol) while hydrogen chloride gas was bubbled through the reaction mixture. Dark red crystalls separated from the mixture three hours after the addition of the aldehyde. The hydrochloride salt was recrystallized from methanol/dichloromethane; yield: about 70%. The aqueous hydrochloride solution was converted to the free base by neutralization with ammonia. The free base was washed with water and recrystallized from acetone. The overall yield of the synthesis is about 60%. The hydrochloride salts of the dipyrrylmethanes are extremely hygroscopic, however they can be stored as stable solids following recrystallization in a dry box.

The pyridine nitrogen forms a quaternary salt with iodomethane in dry ether at room temperature. The quaternary salts can be stored as stable solids following recrystallization from methanol/ether in a dry box.

4-(Dipyrrylmethyl)-*N*-methylpyridinium iodide (1):

This compound was prepared according to the procedure mentioned above, using pyrrole (13.4 g, 0.2 mol) and 4-pyridinecarboxaldehyde (10.7 g, 0.1 mol). The free base (2.4 g, 0.01 mol) was stirred in ether with iodomethane (2.0 g, 0.014 mol) to yield the quaternary salt (**1**). Recrystallized from methanol/ether; yield: 55%; m.p. 183 (dec).

$C_{15}H_{16}N_3J$	calc.	C 49.36	H 4.38	N 11.49
(365.2)	found	49.60	4.20	11.32

^{1}H-N.M.R. (DMSO-d_6): $\delta = 8.4$ (m, $2H_{arom}$), 7.6 (m, $3H_{arom}$), 6.9 ppm.

Bis[2,4-dimethylpyrryl]-4-pyridylmethane (2):

This compound was prepared according to the typical procedure mentioned above, using 2,4-dimethylpyrrole (19 g, 0.2 mol) and 4-pyridinecarboxaldehyde (10.7 g, 0.1 mol). The free base is recovered following recrystallization from acetone. Yield: 60%; m.p. 142 (dec).

$C_{18}H_{21}N_3$	calc.	C 77.38	H 7.57	N 15.04
(279.34)	found	74.79	7.70	14.37

The probable explanation for the disparity in calculated and analyzed values is due to the presence of water, one water molecule for two molecules of bis[2,4-dimethylpyrryl]-4-pyridylmethane.

^{1}H-N.M.R. (CDCl$_3$): $\delta = 8.3$ (d, $2H_{arom}$), 7.6 (b, $2H_{arom}$), 7.1 (d, $2H_{arom}$), 5.8 (s, $2H_{arom}$), 5.4 (s, 1H), 2.0 (s, 6H), 1.8 ppm (s, 6H).

Bis[2,4-dimethylpyrryl]-4-phenylmethane:

To prove the applicability of the above mentioned procedure, benzaldehyde was condensed with 2,4-dimethylpyrrole. The desired product was obtained. The structure of which was confirmed by the nuclear magnetic resonance spectrum.

^{1}H-N.M.R. (CDCl$_3$): $\delta = 7.24$ (s, $5H_{arom}$), 5.4 (m, 3H), 1.92 (s, 6H), 1.77 ppm (s, 6H).

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