Reaction Between *N*-Methylpyrrole and n-Butyl-lithium in Hexane: 2,4- *vs.* 2,5-Dianion Formation

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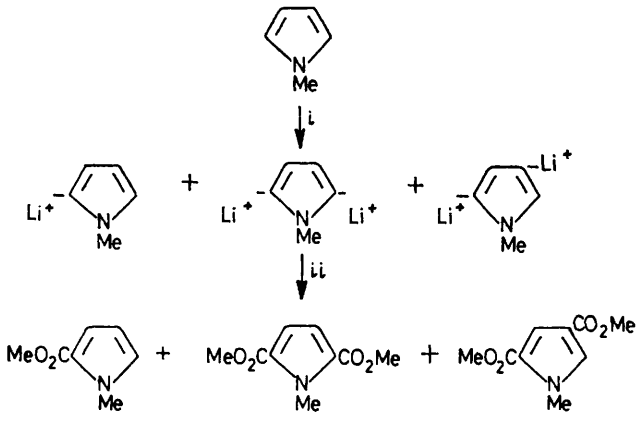
Summary *N*-Methylpyrrole reacts with n-butyl-lithium in hexane to give mainly 2,4- and 2,5-dianions whose relative proportions depend upon quantities of reagents and reaction times.

It is generally accepted[1] that *N*-alkyl-pyrroles, -furans, and -thiophens undergo hydrogen–metal exchange with Bu^nLi exclusively at α-positions unless special structural features favouring β-metallation are present.[2] For example, it is reported[3] that *N*-methylpyrrole on boiling under reflux for 12 h with a 3—3·5 molar excess of ethereal Bu^nLi yields solely the 2,5-dianion. During an attempt to use this reaction to prepare 2,5-dideuterio-*N*-methylpyrrole (by addition of D_2O to the dianion) it transpired that in addition to α-deuteriation, some deuterium (*ca.* 16%) was incorporated into β-positions. When the ether solvent was replaced by hexane, deuteriation (*ca.* 30%) occurred equally at α- and β-positions. The reaction was therefore investigated further (Scheme).

When 1:1 molar ratios of Bu^nLi (1·6M in hexane) and *N*-methylpyrrole were used, the approximate proportions of products (by g.l.c.) (I):(II):(III) were 0·3:0·65:1 (3 h reflux) and 0·6:0·95:1 (16 h reflux). When a 4·5:1 molar ratio was used, the proportions were 0·01:0·10:1 (16 h reflux). The surprising conclusions are thus that under conditions where only the mono-anion would be expected, dianions are preferred, and that by suitable adjustment of



(I) (II) (III)

SCHEME

The degree of ionic character is not implied by these representations, neither do the terms 'anions', 'dianions', *etc.* in the text imply 100% ionic characters.

Reagents i, Bu^nLi in hexane; reflux; ii, solid CO_2 in Et_2O, then 5N-HCl, then CH_2N_2 in Et_2O.

quantities of reactants, products derived from the 2,4-dianion are preferred to the extent of 90% over those from the 2,5-dianion.

The synthetic utility of these reactions is demonstrated by the isolation (in *ca.* 50% yield) of dimethyl *N*-methylpyrrole-2,4-dicarboxylate,† m.p. 97—99°, τ (CCl_4) 2·76br (d, *J* 1·9 Hz, 5-H), 2·84 (d, *J* 1·9 Hz, 3-H), 6·09 (s, Me), 6·26 (s, Me), and 6·29 (s, Me), *m/e* 197 (M^+, 66%) and 166 (100%), and (by replacing solid CO_2 with dimethylformamide in the dianion work-up) of *N*-methylpyrrole-2,4-dicarbaldehyde, m.p. 94—95°,† τ ($CDCl_3$) 0·23br (s, CHO), 0·37 (d, *J* 10 Hz, CHO), 2·53br (s, 5-H), 2·66 (d, *J* 1·7 Hz, 3-H), and 6·00 (s, Me).

That the $\alpha\beta$-dianion is the 2,4- rather than the 2,3-ion follows from the magnitude of the ring-proton coupling constants in the diester and dialdehyde, and from the comparison of the latter's physical properties with those for *N*-methylpyrrole-2,3-dicarbaldehyde.[4]

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† Satisfactory elemental analytical data were obtained.

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[4] J. Duflos, D. Letouze, G. Queguiner, and P. Pastour, *J. Heterocyclic Chem.*, 1973, **10**, 1083.