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1,3-DIMETHYLINDOLE: NMR SPECTROSCOPY AND REACTIVITY TOWARDS ETHYL CARBONATE IN THE PRESENCE OF BUTHYL LITHIUM

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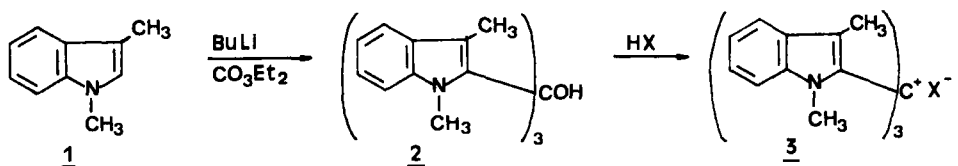
ABSTRACT

We report the reactivity of the 2-lithium derivative of 1,3-dimethylindole 1 with ethyl carbonate to prepare tris-(1,3-dimethyl-2-indolyl)methanol 2. A strong concentration dependence in $CDCl_3$ for H-2 and N-methyl protons resonances of 1 is described.

Müller et al (1) have prepared tris-(1,3-dimethyl-2-indolyl)methane with a 4% yield by reaction of 1,3-dimethylindole and ethyl orthoformate under acid catalysis and the oxidation of such triheteroarylmethane yielded the unstable salt 3 which was characterized by its visible spectroscopic data. However an analogous oxidation of tris-(3-methyl-2-indolyl)methane yielded tris-(3-methyl-2-indolyl)carbonium perchlorate as an isolable salt. These results show that the presence of the N-methyl group diminishes the stability of these salts and are in accordance to our previous work (2) reporting that tris-(1-methyl-2-indolyl) carbonium tetrafluoroborate could only be characterized by its visible spectroscopic data (3).

Following the previously reported methodology (2), we attempted the synthesis of the tetrafluoroborate salt 3 ($X^- = F_4B^-$) by acid treatment of tris-(1,3-dimethyl-2-indolyl)methanol 2 through metallated 1,3-dimethylindole 1 and diethyl carbonate.



1 2 3

Compound 1 was prepared from 3-methylindole and methyl iodide in dry dimethylsulphoxide following a described method (4) of N-alkylation of indoles and pyrroles. The carbinol 2 obtained in the experimental conditions that give the maximun lithiation yield, showed a fast decomposition in several solvents. However a solution of 2 in glacial acetic acid showed a visible spectrum corresponding to 3 ($X^- = AcO^-$) being analogous to that previously described, but attempts to obtain 3 ($X^- = F_4B^-$) through acid treatment of 2 with tetrafluoroboric acid gave decomposition products as it was expected.

Thus, both the carbinol 2 and the carbonium salt 3 are too unstable to be isolated, but while the carbonium salt 3 could only be identified by its visible spectrum, the carbinol 2 was stable enough to record its ^1H n.m.r. spectrum.

In this context we observed a strong concentration dependence for the chemical shifts of the N-CH_3 and H-2 protons in deuterochloroform solutions of 1 (TABLE 1).

TABLE 1

^1H n.m.r. chemical shifts ($CDCl_3$) of 1,3-dimethylindole N-CH_3 and C_2-H protons at different concentrations (recorded at 60 MHz, chemical shifts at $\pm$ 0.05 ppm)

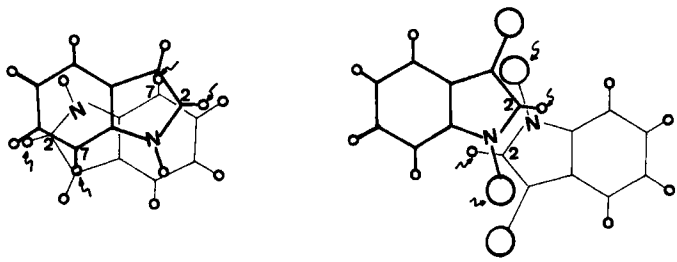
Concentration (%)	N-CH_3	C_2-H
100	2.75	5.95
83	2.85	6.10
60.5	3.05	6.30
54.5	3.15	6.35
46.5	3.25	6.40
37	3.30	6.50
30.5	3.45	6.55
12	3.55	6.70
7.5	3.60	6.75
1	3.70	6.80

N-CH_3 = 3.7 - 0.01 (%), n = 10, r^2 = 0.99

C_2-H = 6.8 - 0.0085 (%), n = 10, r^2 = 0.999

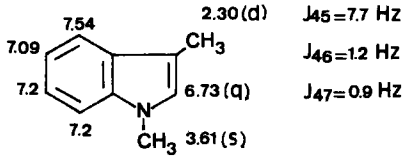
Paramagnetic shifts with polar solvents and concentration dependence of indole H-2 and H-7 protons thus far reported have been explained by the self-association depicted in FIG 1a (5,6). In our case, the observed H-2 and N-CH_3 resonance effects (not observed for H-7) suggest a different head-to-tail complex as is proposed in FIG 1b.

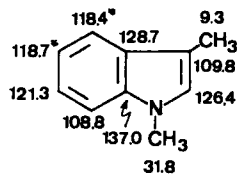
FIG 1



a b

Although the ^{1}H n.m.r. spectrum (60MHz) of 1,3-dimethylindole in Cl_4C has been described (7) without any indication of the concentration employed, it is clear that due to the dilution dependence of δ values (up to ~ 1 ppm), the chemical shifts should be given with an indication of the precise concentration value. Using a 7.5% $CDCl_3$ solution we have recorded the n.m.r. spectra of 1 at 200 MHz (^{1}H) and at 20 MHz (^{13}C).





A long range coupling between the C-methyl and H-2 protons of 1.0 Hz has been observed in the ^{1}H n.m.r. spectrum. The assignements are based on a recent study (8) of 1-methylindole (^{1}H and ^{13}C n.m.r. in Cl_3CD).

EXPERIMENTAL

All melting points were recorded on a Buchi capillary melting point apparatus. The ^{1}H n.m.r. spectra (60 MHz) were recorded on a Perkin-Elmer R24-B spectrometer; the ^{1}H n.m.r. spectrum at 200 MHz was recorded on a Bruker AM-200 spectrometer; ^{13}C n.m.r. spectrum (20 MHz) was recorded on a Bruker WP 80 SY spectrometer. The electronic spectrum was recorded on a spectrophotometer Bausch and Lomb Spectronic 2000 between 800 and 200 nm.

1,3-Dimethylindole (1). This compound was obtained in a 93% yield using the procedure described in reference 4. Starting from 3-methylindole (1.3 g, 0.01 mol) and methyl iodide (2.8 g, 0.02 moles), a residual oil was obtained after removal the solvent. The product was purified by column chromatography on silica gel (eluent: dichloromethane-hexane 1:1) (Found:C, 82.46; H, 7.83;

N, 9.47. Calc. for $C_{10}H_{11}N$: C, 82.72; H, 7.63; N, 9.64%).

Tris-(1,3-dimethyl-2-indolyl)methanol (2). 1,3-Dimethylindole (4g, 0.027 moles) was dissolved in dry tetrahydrofuran (75 ml). With stirring and under nitrogen stream, butyl-lithium (17.2 ml of a 1.6 M ethereal solution) was added and the mixture refluxed for 14h. When the solution reached room temperature, diethyl carbonate (1.07 g, 0.009 moles) in dry tetrahydrofuran (25 ml) was added. After 7h at room temperature, the mixture was refluxed for 17h and the cold reaction was poured into water (100 ml). The aqueous solution was extracted with ether, the combined extracts were dried over sodium sulfate and evaporated under vacuum to yield an oil. This oil, after treatment with petroleum ether, gave (2) as a solid in 23% yield, m.p. 144-149°C (dec.) (Found: C,80.45; H, 6.85; N, 9.22. Calc. for $C_{31}H_{31}N_3O$: C, 80.65; H, 6.76; N, 9.10%). δ_H ($CDCl_3$, 60 MHz) 1.45 (9H, s, 3-CH_3); 3.7 (9H, s, 1-CH_3); 3.8 (1H, s, OH); 6.9-7.6 (12H, m, aromatic protons).

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