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1-METHYL-2-HYDROXYINDOLO[1,2-a]AZEPINIUM BROMIDE: AN AZONIA-AZULENIUM SALT

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As part of a programme of study of aromatic systems iso-electronic with the quinolizinium ion we have investigated routes to 'azonia-azulenium' salts in which the nitrogen atom is at a bridgehead position. We report here the first example of such a system, the hydroxy derivative (8).

The reaction between the skatyl anion (from skatole and sodium hydride in dimethoxyethane) and 4-tosyloxybutyl chloride gave the N-substituted indole (1), b.p. 129 - 131°/0.25 mm. (80%). Treatment of (1) with NaCN in DMSO at 90 - 110° gave the nitrile (2), b.p. 148 - 150°/0.1 mm. (73%); attempted cyclisation of the nitrile (2) with boron trifluoride failed to give the tricyclic ketone (5). Treatment of the nitrile (2) with polyphosphoric acid at 130° gave only the amide (3), b.p. 200 - 210°/0.15 mm. Hydrolysis of the nitrile (2) with boiling 20% aqueous alcoholic NaOH gave the acid (4), m.p. 76 - 77° (almost quantitative) cyclized by polyphosphoric acid at 90 - 95° to the tricyclic ketone (5), m.p. 70 - 71° (50%), $\nu_{max.}^{CHCl_3}$ 1655 cm^{-1}. Compounds (1) to (4) showed the indole 2-proton as a singlet at 3.0 - 3.2 p.p.m. (all shifts are δ in p.p.m. from TMS); the singlet was absent in ketone (5) thus confirming cyclization in the sense shown, and not to the alternative 7 position. Bromination of the ketone (5) with phenyl trimethylammonium perbromide (2 moles) gave the yellow dibromoketone (6), m.p. 118 - 119° (80%), $\nu_{max.}^{CHCl_3}$ 1668 cm^{-1}. The n.m.r. spectrum ($CDCl_3$) of the ketone (6) showed triplets at 4.28 (NCH_2) and 3.0 p.p.m. (CBr_2CH_2) and a multiplet centred at 2.35 p.p.m. each equivalent to two protons, confirming the structure (6). Treatment of the dibromoketone (6) with lithium chloride (3 moles) in dimethylformamide at 150° gave an orange compound, m.p. 124 - 125°, analysing for $C_{14}H_{11}NO$, (83%) with $\nu_{max.}^{CHCl_3}$ 1656 cm^{-1}. The n.m.r. spectrum ($CDCl_3$) showed only the methyl singlet between 0 and 5 p.p.m.; the position of the methyl singlet, 2.83 p.p.m. showed a downfield shift due to the changed geometry around the peri carbonyl group. The other 8 protons were in the region from 4.6 to 8.0 p.p.m. These spectral properties were in accord with the formulation (7 ↔ 7a), confirmed by the n.m.r. spectrum of the protonated form (8) in TFA. A one-proton doublet at 9.1 p.p.m. (J = 9 c.p.s.) is assigned to proton 6 (by analogy with the quinolizinium system), a doublet at 7.23 p.p.m. (J = 11 c.p.s.) to proton 3, and a triplet (or pair of overlapping doublets) at 6.7 p.p.m. to proton 5; all these signals showed line broadening indicative of 'meta' coupling. The methyl singlet was at 3.2 p.p.m. in good agreement with the methyl position in other quaternary systems. Treatment of a chloroform solution of ketone (7) with dry HBr gave almost black crystals of 1-methyl-2-hydroxyindolo[1,2-a]azepinium bromide, m.p. from 115° (dec.). The electronic spectrum of the ion (8) in concentrated sulphuric acid (deep blue-green solution) showed maxima at 315, 395, 573, and 603 (sh) mμ.

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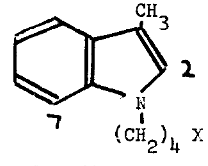
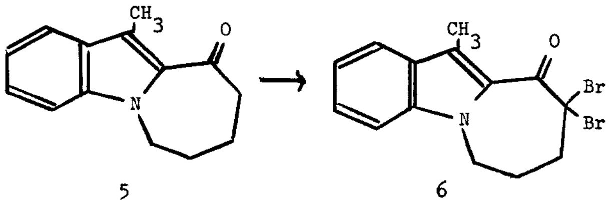
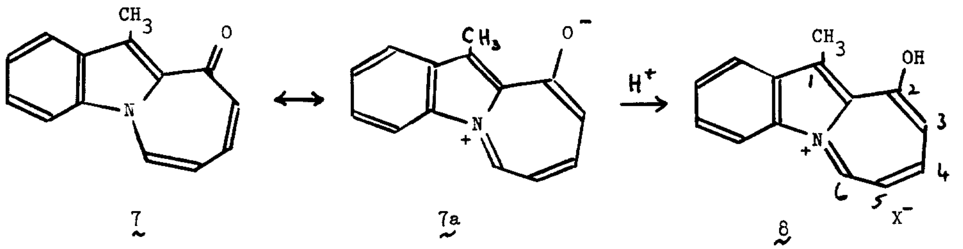


1, X = Cl
2, X = CN
3, X = $CONH_2$
4, X = CO_2H



5 6



7 7a 8