

THE ALUMINUM CHLORIDE PROMOTED DEMETHYLATION OF SOME DIMETHOXYINDOLES.

TWO REVISED STRUCTURES.

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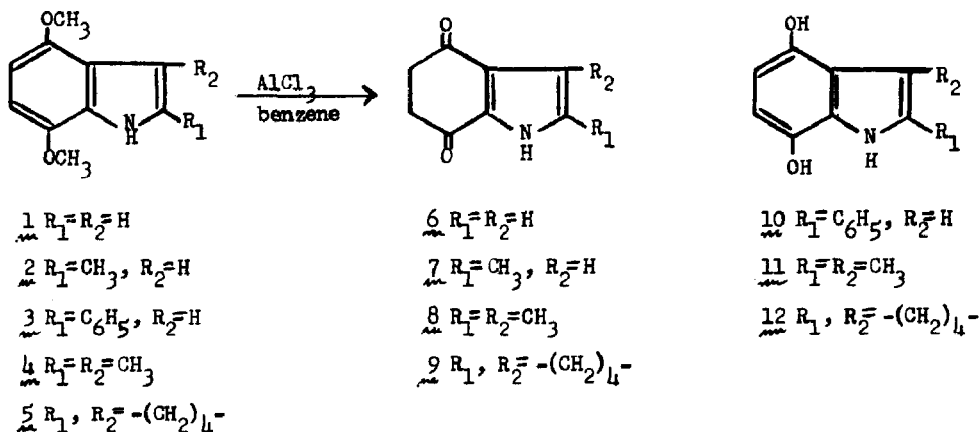
(Received in USA 6 December 1971; received in UK for publication 3 January 1972)

Malesani and co-workers have recently reported the demethylation of the 4,7-dimethoxyindoles 1⁽¹⁾ and 2⁽²⁾ by aluminum chloride in benzene to yield the corresponding 4,7-dioxo compounds 6 and 7 rather than the expected 4,7-dihydroxy tautomers. The 2-phenyl compound 3, on the other hand, was reported⁽²⁾ to give the dihydroxy compound 10, which could be easily converted to the corresponding dioxo compound.

The Italian workers were apparently unaware of earlier work by Blackhall and Thomson⁽³⁾, who reported the demethylation of 2,3-dimethyl-4,7-dimethoxyindole 4, and 1,2,3,4-tetrahydro-5,8-dimethoxycarbazole 5 by means of the same reagents. These workers assigned the dihydroxy structures 11 and 12, respectively, to the reaction products apparently solely on the basis of the ability of the materials to form diacetates. Since the Italian workers assigned structures 6 and 7 unequivocally on the basis of modern instrumental techniques, the structures 11 and 12 assigned to products obtained from closely related starting materials was somewhat in doubt.

Since compounds 8 and 9 were required for a synthetic study, the earlier work was reinvestigated. Preparation of 4 and 5 and subsequent demethylation proceeded uneventfully as previously described⁽³⁾. The product obtained from 4 had mp 210-213°d. (reported⁽³⁾ mp 205-6°d.). The infrared spectrum (nujol mull) shows a strong carbonyl band at 1645 cm⁻¹ and a band at 3200 cm⁻¹ assigned to the pyrrole N-H absorption. The NMR spectrum (60 MHz., CDCl₃) shows a singlet at δ 2.95 (5 and 6 protons, 4H), and overlapping singlets at δ 2.30 and δ 2.37 (2 and 3-methyl groups, 6H). The N-H proton appears as a very broad absorption at δ 10.5. Similarly, the material obtained from 5, mp 235-7°d. (reported⁽³⁾ mp 225°d.), shows bands in the infrared at 3180 cm⁻¹ and 1645 cm⁻¹; the

NMR spectrum exhibits a singlet at δ 2.94 (4H), multiplets at δ 2.77 (4H) and δ 1.83 (4H), and a broad absorption at $\sim\delta$ 10.5 (\sim 1H). This data clearly shows the structures to be the dioxo forms 8 and 9 and not the dihydroxy structures 11 and 12. Neither of these compounds gives the characteristic color reaction with FeCl_3 solution. Both are readily soluble in 1N NaOH giving pale yellow solutions, stable under nitrogen, but which rapidly darken on exposure to air⁽⁴⁾. It appears that 8 and 9 are readily isomerized to 11 and 12, respectively, explaining the facile acetylation of these compounds previously observed by Blackhall and Thomson. Interestingly, Malesani et. al. reported that 6 was insoluble in 5% NaOH, and that both 6 and 7 failed to react with acetic anhydride-pyridine. No apparent explanation is at hand for the difference in behavior of these structurally similar compounds.



References and Footnotes

1. G. Malesani, G. Rigatti, and G. Rodighiero, *Tetrahedron Lett.*, 4173 (1969).
2. G. Malesani, G. Chiarelto, F. Marcolin, and G. Rodighiero, *Il Farmaco (Ed. Sci.)*, 25, 972 (1970).
3. A. Blackhall and R.H. Thomson, *J. Chem. Soc.*, 1954, 3916.
4. Both 4- and 7-hydroxyindoles dissolve in 1N NaOH yielding solutions which rapidly darken on exposure to air. These compounds also give the characteristic violet color reaction with 3% FeCl_3 . J.G. Berger, unpublished observations.