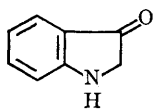


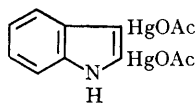
## Preparation of [2-<sup>2</sup>H]- and [2-<sup>3</sup>H]-Indole from Indoxyl, and the Structure of Diacetoxymercuri-indole

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FOR studies on the biosynthesis of indole alkaloids an unambiguous preparation of [2-<sup>3</sup>H]-indole was required. Indoxyl, obtained by hydrolysis of the diacetate<sup>1</sup> and purified by sublimation (100°, 10<sup>-4</sup>mm.), had infrared bands at 3450, 1690, and 1623 cm.<sup>-1</sup> (CHCl<sub>3</sub>) and at 3380, 1690, and 1620 cm.<sup>-1</sup> (Nujol mull), consistent<sup>2</sup> with the keto-form (I). In the n.m.r. spectrum (in CDCl<sub>3</sub>) the methylene protons appeared as a singlet at  $\tau$ 6.16 which was unchanged when the solution was shaken with D<sub>2</sub>O. Addition of a trace of trifluoroacetic acid to the D<sub>2</sub>O however caused rapid disappearance of the methylene band.



(I)



(II)

Indoxyl was shaken in chloroform with 1N-DCl for 10 min. at room temperature to give the [1,2,2-<sup>2</sup>H<sub>3</sub>] derivative. Reduction<sup>3</sup> with excess of lithium aluminium hydride in ether at room temperature then gave [2-<sup>2</sup>H]-indole. This material, m.p. 49—52°, had the expected n.m.r. spectrum. The triplet corresponding to the 2-proton in indole was absent while the 3-proton appeared as a doublet at  $\tau$ 3.63 (in CCl<sub>4</sub>),  $J_{1,3} = 1.8$  c./sec. Treatment with alkaline D<sub>2</sub>O caused

this signal to collapse to a singlet in the predicted<sup>4</sup> manner. Mass spectrometry confirmed the molecular weight of 118 and showed fragments at  $M-27$  and  $M-28$ . [2-<sup>3</sup>H]-Indole was prepared in a similar manner using acidified, tritiated water in the exchange reaction with indoxyl.

Treatment of indole with aqueous mercuric acetate (2 moles) gives a diacetoxymercuri-indole in high yield.<sup>5</sup> The structure (II) originally proposed<sup>5</sup> for this derivative has recently been re-affirmed.<sup>6</sup> [2-<sup>3</sup>H]-Indole (relative molar activity 1.0) was converted in this way into the corresponding mercurated derivative (r.m.a. 0.99) which was reduced<sup>6</sup> with lithium aluminium hydride in ether to regenerate indole (r.m.a. 0.97). Similarly, mercuration in ethanol<sup>6</sup> gave diacetoxymercuri-indole (r.m.a. 0.92) which again was converted into indole (r.m.a. 0.88). These and earlier observations<sup>7</sup> exclude structure (II) for diacetoxymercuri-indole.

Reduction of the mercurated indole (prepared in ethanol) with LiAlD<sub>4</sub> and decomposition of the product with water gave a mixture<sup>8</sup> (ca. 1:1) of indole and [3-<sup>2</sup>H]-indole (n.m.r. and mass-spectrometric analysis). The mass spectrum showed no significant amounts of dideuterated species. These results are most simply explained if diacetoxymercuri-indole is the 1,3-dimercurated derivative; an alternative 3,3-diacetoxymercuri-indolenine structure cannot rigorously be excluded at present.

(Received, June 15th, 1965; Com. 370.)

<sup>1</sup> S. J. Holt and P. W. Sadler, *Proc. Roy. Soc.*, 1958, B, 148, 481.

<sup>2</sup> B. Witkop, *J. Amer. Chem. Soc.*, 1950, 72, 614.

<sup>3</sup> E. Giovannini and T. Lorenz, *Helv. Chim. Acta*, 1957, 40, 2287.

<sup>4</sup> cf. J. A. Elvidge and R. G. Foster, *J. Chem. Soc.*, 1964, 981.

<sup>5</sup> Q. Mingoia, *Gazzetta*, 1930, 60, 509.

<sup>6</sup> L. K. Ramachandran and B. Witkop, *Biochemistry*, 1964, 3, 1603.

<sup>7</sup> E. J. Herbert and G. W. Kirby, unpublished work; E. J. Herbert, Ph.D. Thesis, London, 1964.

<sup>8</sup> Exchange of the 3-proton in indole in alkaline media is well known; see, B. C. Challis and F. A. Long, *J. Amer. Chem. Soc.*, 1963, 85, 2524.