

## The Chlorination of Indoles with Aqueous Sodium Hypochlorite. Proof of the Existence of an *N*-Chloro Intermediate

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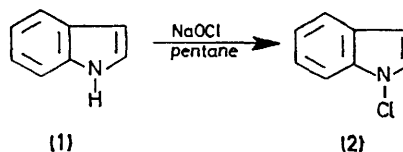
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**Summary** *N*-Chloroindole (2) is an intermediate in the chlorination of indole (1) with aqueous sodium hypochlorite and rearranges to give 3-chloroindole (4).

RECENTLY the intermediacy of an *N*-chloroindole was suggested as a possibility in the chlorination of 2,3-dimethylindole with aqueous sodium hypochlorite.<sup>1</sup> This suggestion is analogous to the known intermediacy of *N*-chloroanilines in the chlorination of aniline derivatives.<sup>2</sup> We now report the first direct evidence for the existence of an *N*-chloroindole intermediate in solution.<sup>3</sup>

Indole (1) was chosen for our initial study. *N*-Chloroindole (2) can be prepared in 90–92% yield by stirring a solution of (1) in pentane, hexane, chloroform, or carbon tetrachloride with an aqueous solution of sodium hypochlorite at 0°C for 3 h.† The spectroscopic data demonstrate conclusively that the titrimetrically observed

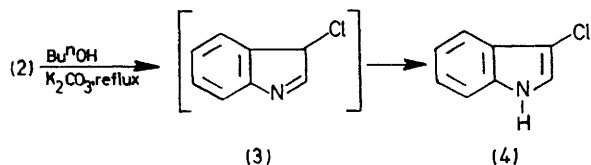
intermediate is (2) and not 3-chloroindolenine (3).<sup>4</sup> The i.r. spectrum of (2) in pentane showed the complete absence of both the indole NH stretching frequencies (3500 and 3400 cm<sup>-1</sup>) and the characteristic stretching frequency



(1630–1590 cm<sup>-1</sup>) assigned to the imino group in indolenines.<sup>5</sup> The u.v. spectrum of (2) in hexane showed a maximum at 265 mμ, which is also present in indole (1). The u.v. maxima of 3-chloro-2,3-dimethylindolenine and 2,3-dimethylindole appear at 266 mμ (sh 292 mμ) and 280

† Solutions of (2) are light yellow and can be analysed by visual iodometric methods.

$m\mu$  respectively.<sup>1</sup> The n.m.r. spectrum of (2) in pentane showed  $\delta$  6.49 (1H, d, C(3)-H, 3 Hz) and 6.81—7.68 (5H, m, C(2)-H and arom-H). The position of C(3)-H has been shifted 0.07 p.p.m. downfield relative to C(3)-H in (1). The



downfield shift of C(2)-H cannot be determined since the expected doublet overlaps with the aromatic multiplet. The reported results<sup>6</sup> for the equivalent protons in 2- and 3-chloroindole show that in 2-chloroindole C(3)-H is shifted 0.06 p.p.m. downfield relative to C(3)-H in (1), and in 3-chloroindole C(2)-H is shifted 0.49 p.p.m. downfield relative to C(2)-H.

N-Chloroindole (2) rearranges to 3-chloroindole (4) when a solution of (2) in pentane is added to n-butyl alcohol containing anhydrous potassium carbonate, heated to

distil off the pentane and refluxed for an additional 60 min. 3-Chloroindole (4) is isolated by column chromatography on silica gel using chloroform as the eluent and recrystallized from petroleum ether to give a 75% yield of (4) whose melting point and spectral properties are in agreement with those previously reported.<sup>6</sup> Halogenation of (1) gives products substituted at C(3).<sup>7</sup> Formation of (4) from (2) demonstrates that under the conditions studied, (2) is an intermediate in the chlorination of (1) with aqueous sodium hypochlorite.

We have not detected (3) in the reaction studied. It is probable that if any (3) forms, it quickly rearranges to (4), in view of the reported rearrangement of 3-chloro-2,3-dimethylindolenine at a substantially lower temperature than that used in this study.<sup>1</sup>

At present, it is not known whether the rearrangement of (2) to (4) proceeds through an inter- or intra-molecular process. This aspect is currently under investigation.

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<sup>1</sup> P. G. Gassman, G. A. Campbell, and G. Mehta, *Tetrahedron*, 1972, **28**, 2749.

<sup>2</sup> P. Haberfeld and D. Paul, *J. Amer. Chem. Soc.*, 1965, **87**, 5502; P. G. Gassman and G. A. Campbell, *ibid.*, 1971, **93**, 2567; 1972, **94**, 3891.

<sup>3</sup> Presented in part at the XXIVth Annual Convention of the Venezuelan Association for the Advancement of Science, Maracaibo, Venezuela, October 1974.

<sup>4</sup> P. G. Gassman and his co-workers have reported that 3-chloro-2,3-dimethylindolenine oxidizes iodide ion (see ref. 1).

<sup>5</sup> B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, 1951, **73**, 2188 and references therein.

<sup>6</sup> J. C. Powers, *J. Org. Chem.*, 1966, **31**, 2627.

<sup>7</sup> For a recent survey see R. J. Sundberg, 'The Chemistry of Indoles,' Academic Press, New York, 1970, pp. 14—17.