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

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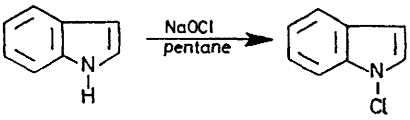
Summary *N*-Chloroindole (**2**) is an intermediate in the chlorination of indole (**1**) with aqueous sodium hypochlorite and rearranges to give 3-chloroindole (**4**).

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



(1) (2)

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 titrametrically observed intermediate is (**2**) and not 3-chloroindolenine (**3**).[4] The i.r. spectrum of (**2**) in pentane showed the complete absence of both the indole NH stretching frequencies (3500 and 3400 cm^{-1}) and the characteristic stretching frequency (1630—1590 cm^{-1}) assigned to the imino group in indolenines.[5] The u.v. spectrum of (**2**) in hexane showed a maximum at 265 $m\mu$, which is also present in indole (**1**). The u.v. maxima of 3-chloro-2,3-dimethylindolenine and 2,3-dimethylindole appear at 266 $m\mu$ (sh 292 $m\mu$) and 280

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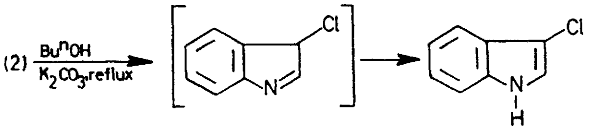
† Solutions of (**2**) are light yellow and can be analysed by visual iodometric methods.

$m\mu$ respectively.[1] The n.m.r. spectrum of (**2**) in pentane showed δ 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[6] 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.



(3) (4)

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 recrystalized from petroleum ether to give a 75% yield of (**4**) whose melting point and spectral properties are in agreement with those previously reported.[6] Halogenation of (**1**) gives products substituted at C(3).[7] 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.[1]

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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[1] P. G. Gassman, G. A. Campbell, and G. Mehta, *Tetrahedron*, 1972, **28**, 2749.

[2] P. Haberfield and D. Paul, *J. Amer. Chem. Soc.*, 1965, **87**, 5502; P. G. Gassman and G. A. Campbell, *ibid.*, 1971, **93**, 2567; 1972, **94**, 3891.

[3] Presented in part at the XXIVth Annual Convention of the Venezuelan Association for the Advancement of Science, Maracaibo, Venezuela, October 1974.

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

[5] B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, 1951, **73**, 2188 and references therein.

[6] J. C. Powers, *J. Org. Chem.*, 1966, **31**, 2627.

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