

Isolation of the Intermediate in a Heterocyclic Ring Expansion Reaction

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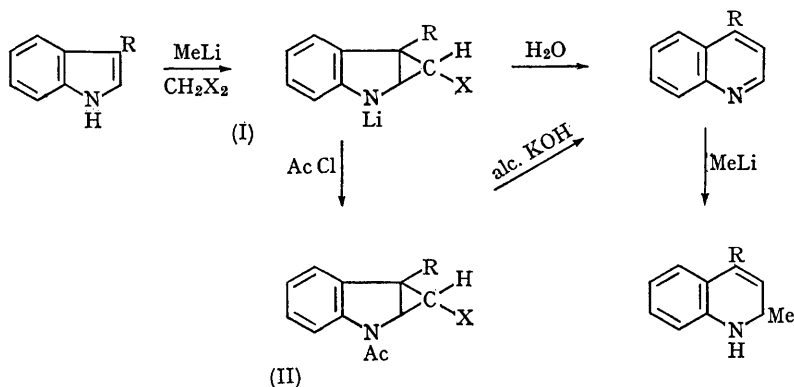
(U.K. Atomic Energy Research Establishment, Wantage, Berks)

WHEN methyl-lithium is added to indole in methylene chloride solution the indole undergoes ring expansion to quinoline.¹ Quinoline reacts rapidly with methyl-lithium in ether solution to give 1,2-dihydro-2-methylquinoline. Yet, when indole (1 mole) is allowed to react with excess of methyl-lithium in ether solution in the presence of a limited quantity of methylene chloride (1 mole), for a prolonged period, a mixture of quinoline and 1,2-dihydro-2-methylquinoline is formed. The presence of quinoline in the final product indicates the existence of an intermediate, that does not react readily with methyl-lithium, and is converted into quinoline in the final stage of the reaction when the excess of methyl-lithium is decomposed.

were found to be 1:1.8 respectively, by using a radiotracer technique. This confirms that the reactive species is an electrophile.

3-Methylindole was treated with methyl-lithium and carbon-14-labelled methylene chloride. Acetyl chloride was added, and the excess finally decomposed with water. From the reaction mixture a radioactive oil, that was insoluble in acid, was isolated. On hydrolysis with alcoholic potassium hydroxide the oil was shown by dilution analysis to yield 4-methylquinoline. Purification of the neutral compound by column chromatography yielded an amber oil which showed well-defined absorption peaks at 860 and 1020 cm^{-1} , providing strong evidence for a cyclopropane structure (II).

Labelled methylene chloride and methylene



It has been postulated^{1,2} that the ring expansion proceeds *via* attack of chlorocarbene on the 2,3-double bond of indole with the formation of a cyclopropane intermediate (I). The relative, competitive reaction rates of indole and 3-methylindole with methyl-lithium and methylene

bromide both gave radioactive neutral compounds when treated with indole, methyl-lithium, and acetyl chloride. On hydrolysis both compounds were converted into radioactive quinoline.

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¹ G. L. Closs and G. M. Schwartz, *J. Amer. Chem. Soc.*, 1961, **26**, 2609.

² C. W. Rees and C. E. Smithen, *J.*, 1964, 928.

³ L. J. Bellamy, "Infra Red Spectra of Complex Molecules", 2nd Edn., Methuen, p. 29.