

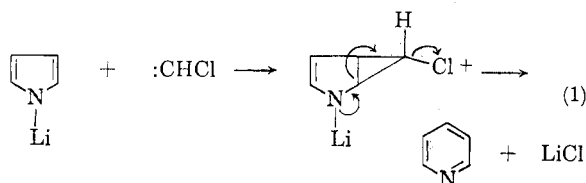
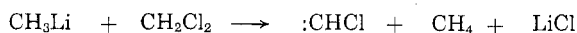
Ring-Expansion of Pyrrole and Indole

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The formation of halogen-substituted ring-expansion products in the Reimer-Tiemann reaction of pyrrole and indole with haloforms is well known.¹ There can be little doubt that these reactions involve the intermediate formation of dihalocarbenes² which are known to be generated from haloforms in basic reaction media.³

Electrophilic addition of the carbene to the double bond of the heterocycle may lead to a hypothetical bicyclic intermediate which can rearrange with loss of halide ion to form the halogenated six-membered aromatic system. Methylene halides are known to be unreactive under Reimer-Tiemann conditions, the only exception being methylene iodide which produces traces of pyridine on reaction with pyrrole and sodium ethoxide.⁴ This observation is readily understood in terms of a carbene mechanism, since much a stronger base than aqueous alkali hydroxide is required to effect α -elimination from methylene halides. Recent work in this laboratory has shown that chlorocarbene can be generated *via* α -elimination from methylene chloride when such strong bases as alkyllithium compounds are employed.⁵ It was of interest to investigate the reaction of this carbene with pyrrole and indole, ring expansion of which would lead to pyridine (sequence 1) and quinoline, respectively.



When a solution of methyllithium in diethyl ether was slowly added to a solution of pyrrole in

(1) H. Wynberg, *Chem. Revs.* **60**, 169 (1960).

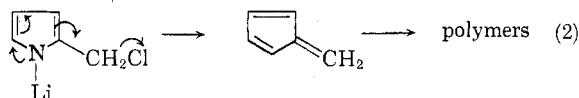
(2) J. Hine and J. M. Van Der Veen, *J. Am. Chem. Soc.*, **81**, 6446 (1959).

(3) J. Hine, *J. Am. Chem. Soc.*, **72**, 2438 (1950).

(4) M. Dennstedt and J. Zimmerman, *Ber.*, **18**, 3316 (1885); G. L. Ciamician, *Ber.*, **37**, 4201 (1904); E. R. Alexander, A. B. Herrick, and J. M. Roder, *J. Am. Chem. Soc.*, **72**, 2760 (1950).

(5) G. L. Closs and L. E. Closs, *J. Am. Chem. Soc.*, **82**, 5723 (1960).

methylene chloride, 32% of pyridine was isolated from the reaction mixture. Similarly, when indole was used as the substrate, quinoline was found in 13% yield. Both reactions were accompanied by the formation of large amounts of polymers, and no other products could be identified. The absence of substitution products, which predominate in the Reimer-Tiemann reaction, is readily understood considering that chloromethylpyrrole and 3-chloromethylindole will not survive the reaction conditions. Instead, elimination of lithium chloride can be expected to convert these compounds into polymeric materials (sequence 2).



EXPERIMENTAL

Reaction of pyrrole with methylene chloride and methyllithium. A solution of methyllithium (0.4 mole) in diethyl ether (235 ml.) was added with vigorous stirring to a solution of pyrrole (7.0 g.; 0.104 mole) in methylene chloride. The addition was carried out under a protective atmosphere of nitrogen, and the temperature was maintained at 25°. After the addition was complete (2 hr.) the reaction mixture was hydrolyzed with ice water and the polymeric material removed by filtration over cellulose powder. The solution was acidified and nonbasic material was extracted with ether. The aqueous layer was then made basic, saturated with potassium carbonate and exhaustively extracted with ether. The combined ether extracts were dried with potassium carbonate and the solvent was distilled off over a Vigreux column. The residue was distilled over a micro Vigreux column. Pyridine (2.60 g.; 0.033 mole; 32%) was collected between 114 and 114.5° and was identified through its infrared spectrum and mixed melting point of its picrate with an authentic sample (m.p. 162–163°).

A similar run in which the ratio of pyrrole to methyllithium was 1:3 gave 24% of pyridine.

Reaction of indole with methylene chloride and methyllithium. A solution of methyllithium (0.4 mole) in diethyl ether (230 ml.) was added with vigorous stirring to a solution of indole (12 g.; 0.1 mole) in methylene chloride. The addition was carried out under nitrogen and the temperature was held at 25 to 30°. After the addition was complete (2 hr.) the reaction mixture was worked up in the same manner as described for the reaction of pyrrole with methyllithium and methylene chloride. Quinoline (1.7 g.; 0.013 mole; 13%) was identified by its infrared spectrum and mixed melting point of its picrate with an authentic sample (207–209°).

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