

## Base-catalysed Elimination of Hydrogen Chloride from the Chlorohydrin of a Reissert Compound: Novel Interconversion of Isoquinoline and Isochromene Ring Systems

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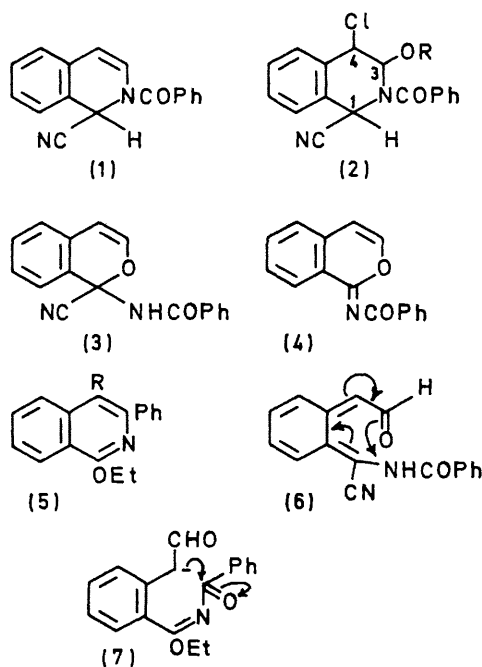
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**Summary** The Reissert compound, 2-benzoyl-1-cyano-1,2-dihydroisoquinoline (**1**), forms a chlorohydrin (**2**; R = H) which, when treated with base, eliminates hydrogen chloride to give, depending upon conditions, the rearranged heterocycles, 1-benzoylamino-1-cyanoisochromene (**3**), 1-benzoyliminoisochromene (**4**), 1-ethoxy-3-phenylisoquinoline (**5**; R = H), and 1-ethoxy-4-formyl-3-phenylisoquinoline (**5**; R = CHO).

The Reissert compound (**1**) reacted with hypochlorous acid in aqueous dioxan to give in 58% yield the chlorohydrin (**2**; R = H), m.p. 176–178°;  $\tau$  [(CD<sub>3</sub>)<sub>2</sub>SO] 3.24 (d,  $J$  4.3 Hz, OH), 3.77 (s, 1-H), 4.35 (dd,  $J$  3.1 and 4.3 Hz, 3-H), and 4.67 (d,  $J$  3.1 Hz, 4-H). The product appeared, from its physical properties, to be a single stereoisomer. The *O*-ethyl derivative (**2**; R = Et) was prepared similarly using *N*-chlorosuccinimide in ethanolic dioxan. The orientation of addition of hypochlorous acid was determined as follows. 4-Deuterioisoquinoline, prepared from 4-bromoisoquinoline by successive treatment with *n*-butyl-lithium and deuterium oxide, was converted into the correspondingly deuteriated chlorohydrin. The n.m.r. spectrum of this material still showed OH-CH vicinal coupling; the hydroxy-group was therefore attached to C-3.

The chlorohydrin (**2**; R = H) reacted with triethylamine (1 mole.) in dioxan to give a major (43%) product (**3**), m.p. 131–133°;  $\nu_{\max}$  (KBr) 3263 (NH) and 1663 (C=O) cm<sup>-1</sup>;  $\tau$  [(CD<sub>3</sub>)<sub>2</sub>SO] - 0.14 (s, NH), and 3.20 and 3.75 (doublets,  $J_{3,4}$  5.9 Hz). A minor (8%) product (**4**), m.p. 113–114°, of this reaction was obtained in better yield (43%) when aqueous sodium hydroxide (1 mole) was used as base in dioxan. The structure of compound (**4**) followed from its

near-quantitative conversion, by hydrochloric acid in aqueous dioxan, into isocoumarin and benzamide and from



the spectroscopic data:  $\nu_{\max}$  (KBr) 1658 cm<sup>-1</sup> (C=O);  $\tau$  (CDCl<sub>3</sub>) 3.02, 3.70 (doublets,  $J_{3,4}$  5.8 Hz). Treatment of the isochromene (**4**) with an excess of ethanolic sodium

hydroxide gave (52%) the formylisoquinoline (**5**; R = CHO), m.p. 110—111°;  $\nu_{\max}$  1671  $\text{cm}^{-1}$  (C=O);  $\tau(\text{CDCl}_3)$  — 0.14 (s, CHO). Reduction with sodium borohydride gave a primary alcohol (**5**; R =  $\text{CH}_2\text{OH}$ ) and decarbonylation<sup>1</sup> with palladium-carbon gave the known<sup>2</sup> isoquinoline (**5**; R = H) which was hydrolysed to 3-phenylisoquinolone.<sup>2</sup> Treatment of the chlorohydrin (**2**; R = H) with an excess of ethanolic sodium hydroxide gave directly the aldehyde (**5**; R = CHO) (31%), the isoquinoline (**5**; R = H) (27%), and benzamide (17%).

These reactions, which all took place at room temperature,

provide an unusual and simple route to 1-substituted isochromenes and to isoquinolines fully substituted in the hetero-ring. Mechanistically, 1,4-elimination of hydrogen chloride and opening of the carbinolamide ring (not necessarily in this order) might produce the diene (**6**) from the chlorohydrin (**2**; R = H). Cyclisation, as shown, could then lead to the isochromene (**3**) and thence (**4**). Attack of ethoxide on the imide system of (**4**) followed by ring opening could give the anion (**7**) from which the isoquinoline (**5**; R = CHO) could be formed by cyclisation and dehydration.

(Received, July 16th, 1970; Com. 1155.)

<sup>1</sup> J. O. Hawthorne and M. H. Wilt, *J. Org. Chem.*, 1960, **25**, 2215.

<sup>2</sup> S. Gabriel, *Ber.*, 1886, **19**, 835 and 2358.