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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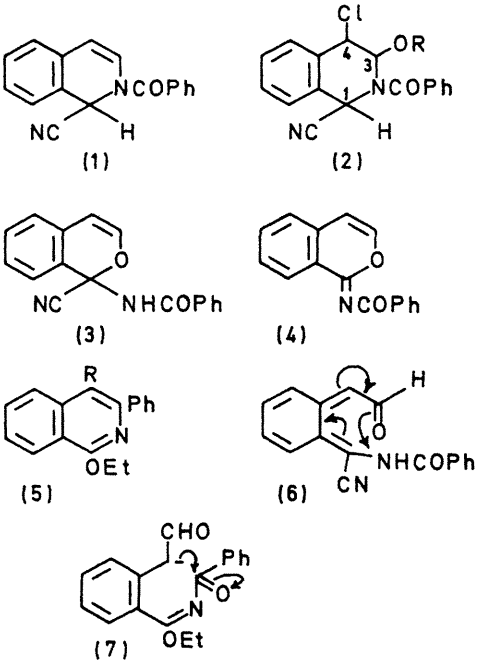
Summary The Reissert compound, 2-benzoyl-1-cyano-1,2-dihydroisoquinoline (**1**), forms a chlorohydrin (**2**; R = H) which, when treated with base, eliminates hydrogen chloride to give, depending upon conditions, the rearranged heterocycles, 1-benzoylamino-1-cyanoisochromene (**3**), 1-benzoyliminoisochromene (**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°; τ [$(CD_3)_2SO$] 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°; ν_{max} (KBr) 3263 (NH) and 1663 (C=O) cm^{-1}; τ [$(CD_3)_2SO$] — 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: ν_{max} (KBr) 1658 cm^{-1} (C=O); τ ($CDCl_3$) 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°; ν_{max} 1671 cm^{-1} (C=O); τ ($CDCl_3$) — 0·14 (s, CHO). Reduction with sodium borohydride gave a primary alcohol (**5**; R = CH_2OH) and decarbonylation[1] with palladium–carbon gave the known[2] isoquinoline (**5**; R = H) which was hydrolysed to 3-phenylisoquinolone.[2] 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.

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[1] J. O. Hawthorne and M. H. Wilt, *J. Org. Chem.*, 1960, **25**, 2215.
[2] S. Gabriel, *Ber.*, 1886, **19**, 835 and 2358.