Generation of Darzens Intermediates by Conjugate Addition

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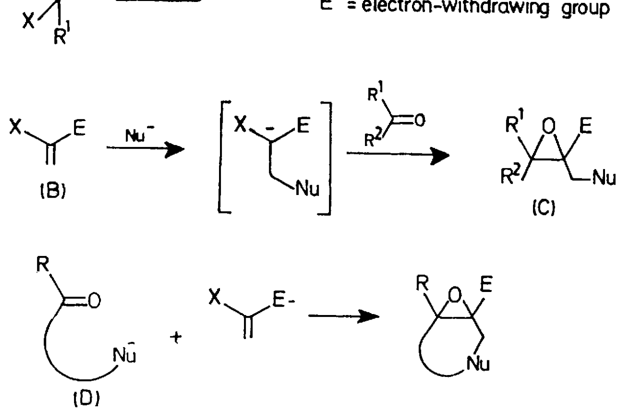
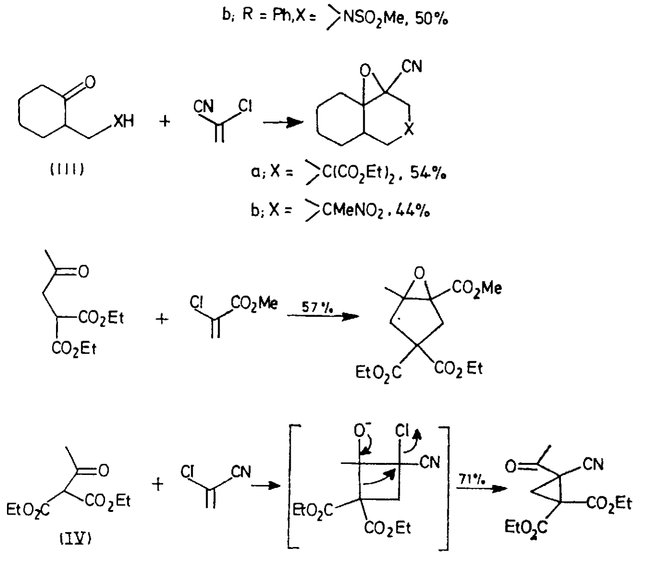
Summary Conjugate addition of nucleophiles to activated halogeno-olefins gives Darzens intermediates which react with carbonyl groups to give epoxides.

The Darzens intermediate (A), a stabilized halogeno-carbanion, is usually generated by deprotonation[1] of α-halogenoesters. It has also been formed by reduction[2,3] of polyhalogenoesters. We describe the formation and use of the Darzens intermediate by conjugate addition of a nucleophile, Nu, to an activated olefin (B) (Scheme 1). In the presence of a carbonyl compound an epoxide (C) is formed.



Scheme 1



Scheme 2

When the electron-withdrawing group, E, is cyano, sulphoxide, sulphone, or nitro, the epoxide (C) has a latent carbonyl group at the carbon bearing E. If the original carbonyl group and the nucleophilic element are connected as in (D), annulation results. Single and fused rings, both carbocyclic and heterocyclic, containing five or more atoms may be formed. If strain prevents formation of the epoxide ring [*e.g.* with compound (IV)] a cyclopropane ring is formed.

Non-optimized yields of isolated, pure products are given in Scheme 2. All compounds were characterized by i.r., n.m.r., and high resolution mass spectrometry.†

In a typical example, a solution in benzene of diethyl acetonylmalonate (Ia) (20 mmol) and $KOBu^t$ (22 mmol) was stirred under nitrogen for 20 min at room temperature. α-Chloroacrylonitrile (22 mol) was added dropwise. After 1 h, additional α-chloroacrylonitrile (4·4 mmol) and base (4·4 mmol) were added. The usual workup was followed by chromatography on silica gel to give 61% of the product (IIa).

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† G.l.c. on OV 17 shows that reactions with (IIIa and b) give two isomers in the ratios of 2·2 : 1 and 1·8 : 1, respectively.

[1] M. S. Newman and B. J. Magerlein, 'Organic Reactions,' Vol. V, ed. R. Adams, Wiley, New York, 1949.
[2] G. Darzens, *Compt. rend.*, 1936, **203**, 1374; G. Darzens and A. Levy, *ibid.*, 1937, **204**, 272.
[3] J. Villieras, G. Lavielle, and J. C. Combret, *Bull. Soc. chim. France*, 1971, 898.