

Epoxyannellation with 1,4-Dichloro-butan-2-one

By S. DANISHEFSKY* and G. A. KOPPEL

(Department of Chemistry, University of Pittsburg, Pittsburg, Pennsylvania 15213)

Summary The reaction of carbanions of β -ketoesters and β -diketones with 1,4-dichloro-butan-2-one leads to epoxyannellation and annelated chlorohydrins.

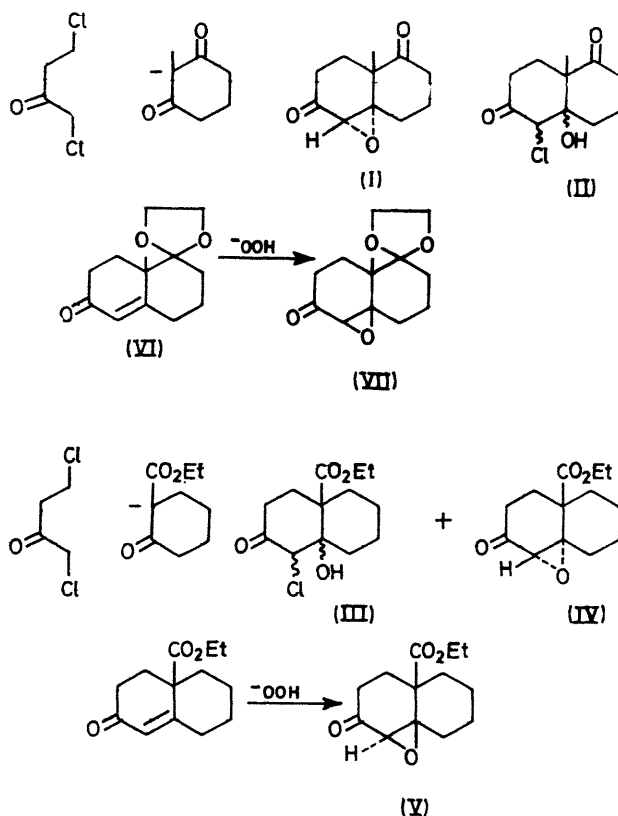
EPOXYKETONES are usually prepared by the action of alkaline hydrogen peroxide on $\alpha\beta$ -unsaturated ketones.¹ This may require a blocking-deblocking sequence to protect other vulnerable functional groups from oxidation. We report a direct route to the α -epoxyketone system.

Treatment of 1 equiv. of the sodium salt of 2-methylhydroresorcinol with 1 equiv. of 1,4-dichloro-butan-2-one in 10:1 dimethoxyethane-ethanol containing 1 equiv. of sodium ethoxide for 4 days gave a 43% yield of epoxydiketone† (I) [m.p. 81–82°; λ_{\max} (CHCl₃) 5.85 and 8.0 μ m]. A minor product (11%) [m.p. 152–153; λ_{\max} (CHCl₃) 2.80 and 5.82 μ m] is formulated as chlorohydrin (II)†.

Similar treatment of 2-ethoxycarbonylcyclohexanone gave a 22% yield of a 25:1 mixture (g.l.c.) of two epoxyketones and a 33% yield of a chlorohydrin [m.p. 111–114°; λ_{\max} (CHCl₃) 2.75, 5.79 μ m] formulated as (III).† The major component of the epoxyketones was obtained in pure form, m.p. 38–39°,† by chromatography on Florasil. The minor component was identical (g.l.c.) to the product (m.p. 47–49°) obtained by treating 4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one with alkaline hydrogen peroxide. By analogy,¹ the latter stereoisomer would be formulated as (V) and therefore the former as (IV). The n.m.r. resonance of the methine signal of the epoxide linkage of the stereoisomer of m.p. 38–39° occurs at τ 7.20 while that for the stereoisomer of m.p. 47–49° appears at τ 6.93. On the basis of the proposed structure, this corresponds to greater shielding of the conformationally rigid axial proton [in (IV)] relative to the conformationally mobile proton [in (V)]. Such a pattern is certainly well precedented for epoxy-protons² but has never been rigorously established for α -epoxyketones.

The alkaline epoxidation of the Wieland-Miescher ketone was unsuccessful but the corresponding acetal (VI), underwent epoxidation to give an epoxyketone which by analogy² was formulated as (VII) [m.p. 95.5–98°; λ_{\max} (CCl₄) 5.86, 8.0 and 9.0 μ m]. While we were unable to effect deacetalization of (VII) or acetalization of (I) the n.m.r. resonances of the methine protons of the epoxy-linkage are

again in the same order [τ (I) 7.13; τ (VII) 6.95] indicating that they belong to a different stereochemical series.



These results suggest that epoxyannellation affords the *trans*-stereochemistry at the junction which is not directly accessible *via* alkaline epoxidation of the enone. The factors which influence this stereochemistry and possibly control the production of unwanted chlorohydrins are under investigation.

(Received, January 4th, 1971; Com. 009.)

† Satisfactory elemental analyses were obtained.

¹ J. Bull, *Tetrahedron Letters*, 1968, 5959, and references therein.

² A. D. Cross, *J. Amer. Chem. Soc.*, 1962, **84**, 3206.