Intramolecular Cyclization of 3,4-Epoxy-alcohols; Oxetan Formation

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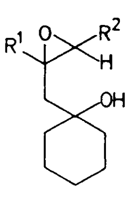
Summary 1-($\beta\gamma$-Epoxypropyl)cyclohexan-1-ol (**1**) and its methyl analogues (**2**) and (**3**), when treated with base in 75% aqueous Me_2SO, gave the corresponding oxetans (**4**)–(**6**) as the main products, while treatment of (**1**) under anhydrous conditions afforded the oxolan dimer (**11**) as the sole identified product.

INTRAMOLECULAR cyclization of epoxy-alcohols by ring cleavage usually leads to the formation of oxirans, oxolans, and/or oxans.[1] We describe herein the reactions of 3,4-epoxy alcohols with bases, which involve regiospecific attack of the alkoxy anion at C-3 under controlled conditions.[2]

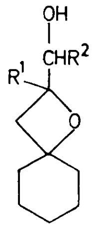
TABLE. Reactions of 3,4-epoxy-alcohols with bases in aqueous solvent.[a]

Compound	Base	Time/min	Products (%)
(**1**)	KOH	90	(**4**) (49), (**7**) (32)
(**1**)	NaOH	45	(**4**) (49), (**7**) (32)
(**1**)	LiOH	15	(**4**) (49), (**7**) (32)
(**2**)	KOH	60	(**5**) (67), (**8**) (14)
(**3**)	KOH	60	(**6**) (73), (**9**) (9)

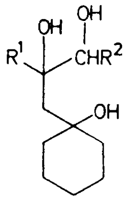
[a] Reactions were carried out by heating (bath temp. 140—150 °C) with 10 mol. equiv. of base in 75% aqueous Me_2SO, and ceased when the starting epoxide was consumed.



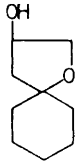
(1) $R^1 = R^2 = H$
(2) $R^1 = Me, R^2 = H$
(3) $R^1 = H, R^2 = Me$



(4) $R^1 = R^2 = H$
(5) $R^1 = Me, R^2 = H$
(6) $R^1 = H, R^2 = Me$



(7) $R^1 = R^2 = H$
(8) $R^1 = Me, R^2 = H$
(9) $R^1 = H, R^2 = Me$



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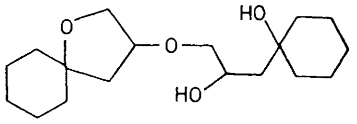

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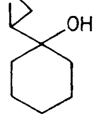

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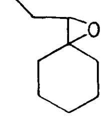

(13)

Treatment of 1-($\beta\gamma$-epoxypropyl)cyclohexan-1-ol (**1**) and its methyl analogues (**2**) and (**3**) with a base in 75% aqueous Me_2SO produced a mixture of the corresponding oxetans (**4**)–(**6**) and the triols (**7**)–(**9**), no oxolan (**10**) being detected (Table). Evidently, the oxetans resulted from attack of the alkoxy anion at C-3 because (**7**) was not converted into (**4**) (recovered unchanged) under these conditions. It is emphasized that (i) the oxetans were formed preferentially under the hydrolysis conditions,[3] regardless of the relative degree of substitution of the epoxy ring, (ii) the yields of oxetans increased with the number of substituents on the epoxy-alcohols,[4] and (iii) the reaction of (**1**) with different bases gave the products (**4**)–(**7**) in the same ratio (**49**:32), with the reaction rate varying slightly but definitely depending on the nature of the base used. On the other hand, reactions of (**1**) with bases under anhydrous conditions [*e.g.*, with NaH, BuLi, or $LiNPr^i_2$ in tetrahydrofuran (THF), Me_2SO, $(MeOCH_2)_2$, THF–hexamethylphosphoric triamide, or THF–dimethylformamide] affected formation of a five-membered ether and produced the oxolan dimer (**11**) and oligomers (not completely identified); the monomer (**10**) or oxetan (**4**) were not detected. These results are not readily explained on the basis of the current 'S_N mechanisms'. Treatment of (**12**) in aqueous Me_2SO under the same conditions afforded the corresponding oxiran (**13**), as a single product in 78% yield. In view of the recent reports on cyclobutane formation by intramolecular cyclization of epoxycarbanions,[5] the present result is significant and constitutes a new non-photochemical synthesis of oxetans.[2]

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