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REACTIONS OF OXIRANES WITH ALKALI METALS: INTERMEDIACY OF RADICAL-ANIONS

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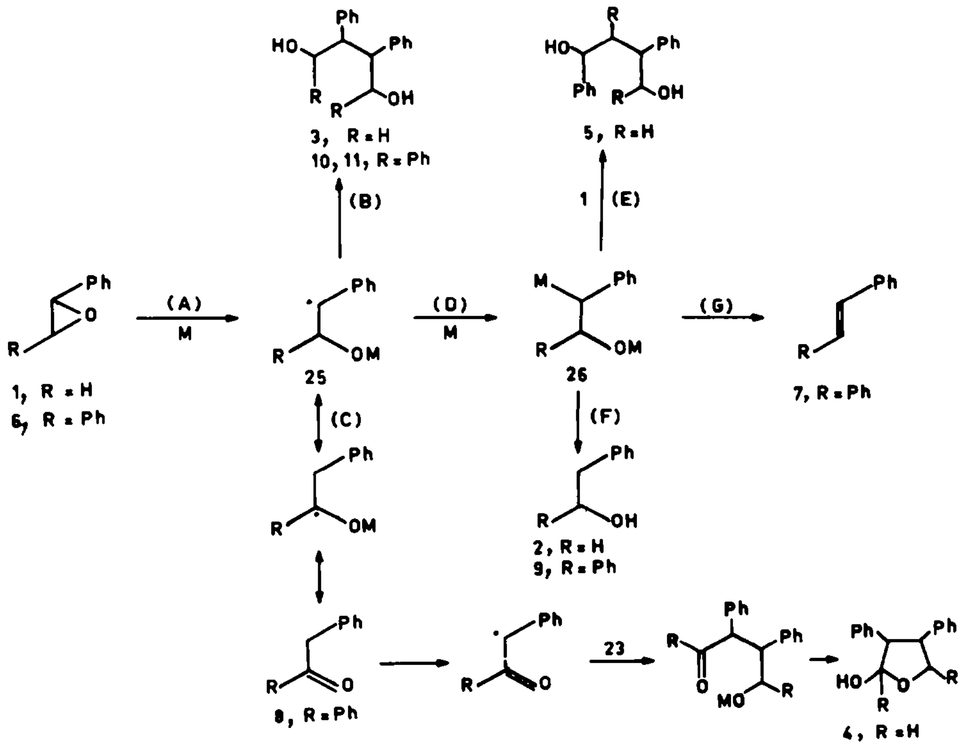
Abstract—Reaction of oxiranes with alkali metals in aprotic solvents yields a variety of products depending on the nature of the metal and the structure of the oxirane. Deoxygenation to olefins is the major reaction in case of lithium. Rearrangement to carbonyl compounds, reduction to alcohols and formation of dimeric products occur when oxiranes are treated with sodium. All the reactions could be rationalised by a mechanism involving an initial single electron transfer leading to the formation of a radical-anion intermediate.

Reduction of oxiranes with alkali metals in ammonia[1] and amines[2] is well known. However, apart from some stray and inconsistent reports, there is surprisingly little information on the reaction of these heterocycles with alkali metals in aprotic solvents. Stryene oxide **1** on reaction with sodium in tetrahydrofuran (THF) was reported[3] to give 2,3-diphenylbutane-1,4-diol **3** in 73% yield, but in another report[4] from the same laboratory, it was demonstrated to yield 2-sodio-2-phenylethoxide which could either be hydrolysed to 2-phenylethanol or be reacted with benzyl chloride to give 2,3-diphenylpropan-1-ol. The epoxides of monoterpenes, α-pinene,[5], limonene,[6] and 3-carene[7] reportedly gave different proportions of hydrocarbons, alcohols and ketones when treated with sodium in benzene.

We have recently reported[8] that oxiranes are deoxygenated to olefins by the action of lithium in THF. The reaction is of general synthetic utility in the sense that mono-, di-, tri- and tetra-substituted oxiranes (both cyclic and acyclic) readily yielded olefins in very good yields. Thus, there appears to be a dramatic difference in the reaction of oxiranes with lithium and sodium. A detailed and definitive study of the reaction of oxiranes with alkali metals in aprotic solvents, would significantly contribute to the understanding of the mechanism of the reaction as well as to develop convenient synthetic methods. We now report the results of our investigations in this direction using representative examples and discuss a possible reaction pathway to rationalise the products formed.

On the basis of our earlier experience with the



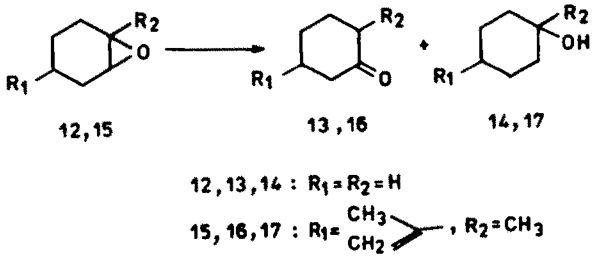
Scheme 1.

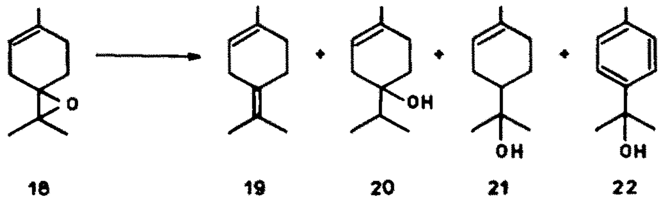
reaction of oxiranes with lithium and in order to draw meaningful comparisons with those results, the present experiments with sodium were carried out under the same conditions using 2.2 equivalents of sodium in THF. The results are summarised in Table 1. Contrary to the earlier reports,[3,4] reaction of styrene oxide with sodium gave 2,3-diphenylbutane-1,4-diol **3** only as a minor product; the major product was 1,3-diphenylbutan-1,4-diol **5**. The ^1H NMR spectrum of **5** showed, apart from signals due to two phenyl groups and two hydroxyl groups (Table 1), a methylene α to OH as a double doublet; another benzylic proton appeared at δ 3.15 as a ABX multiplet (5 lines). The most interesting and revealing was a ABMX (14 lines) pattern at δ 2.10 for the methylene flanked by the two benzylic carbons. The non-equivalence at the two geminal protons is explainable as due to the adjacent asymmetric carbon atoms. Another hitherto unreported product formed in the reaction is the tetrahydrofuranol derivative, **4**. The methylene flanked by the ether bridge and the benzylic carbon appeared at δ 4.20 (ABX, 5 lines) and the methine α to OH at δ 5.50. The two benzylic methines and the ten aromatic protons appeared at δ 3.35 and 7.20 respectively. The identity of **4** was confirmed by its oxidation to 2,3-diphenyl-γ-butyrolactone (ν_{max} 1775 cm^{-1}).

Stilbene oxide (**6**) under similar conditions as above also gave a number of products, the major product being the dimer, 1,2,3,4-tetraphenylbutan-1,4-diol in the racemic (**10**) and meso (**11**) forms. **10** was easily identified by the two sets of doublets (J = 6 Hz) for the benzylic protons (2 each) at δ 3.50 and 5.20 (α to OH) and the two OH protons (δ 1.80) which exchanged with D_2O. For reasons of solubility, the ^1H NMR spectrum of **11** was recorded in D_6-DMSO-TFA wherein the two sets of benzylic protons appeared at δ 3.35 and 4.30. The identity of **10** and **11** were confirmed by their oxidation to the single compound, 1,2,3,4-tetraphenylbutan-1,4-dione and comparison with the product obtained by coupling of desyl chloride (α-chlorobenzyl phenyl ketone) by Zn–Cu couple. Of the two isomers, the major product (**11**) is considered to the meso isomer and the other (**10**) the racemate for steric reasons.[9]

Cyclohexene oxide (**12**) gave, with sodium, cyclohexanone (**13**) and cyclohexanol (**14**) in almost equal proportions, while limonene oxide (**15**) gave mainly the alcohol, β terpineol (**17**) (mixture of *cis* and *trans* isomers, 2:5). The tetrasubstituted spirooxirane, terpinolene oxide (**18**) yielded 4-terpinenol (**20**)[10] as the major product accompanied by α-terpineol (**21**), α,α-dimethylbenzyl alcohol (**22**), and a small quantity of terpinolene (**19**). Effects of solvent (benzene, ether, THF) and temperature (25°, reflux) on the reaction were studied using **18** the product composition remaining essentially unchanged, while the time required for completion ranged from 32 h in benzene at 25° to 12 h in refluxing THF. Addition of 1 mole% of biphenyl to refluxing THF speeded up the reaction by 50% (to 8 h). Reaction of sodium with phenyl trimethyloxirane (**23**) furnished 2-methyl-3-phenyl-2-butanol (**24**) almost exclusively.

As already recorded,[8] the above compounds on treatment with lithium in THF readily furnished the corresponding olefins by reductive elimination (except that styrene from styrene oxide underwent polymerisation). Terpinolene oxide with lithium gave 75% of terpinolene and the remainder was found to be a mixture of the three alcohols **20**, **21** and **22** in the ratio 4:2:1; this indicated that while the products formed with sodium and lithium are qualitatively





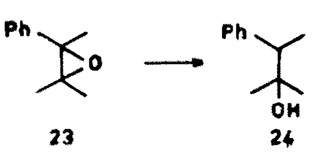


Table 1. Reaction of oxiranes with sodium in THF

Oxirane	Reaction Temp. (°C)	Time(h)	Product	Yield (%)	B.p. Torr or m.p.(°C)	^{1}H N.M.R.
1	25	12	**2**	12	74/1.5	1.95(1H,s,OH),2.83(2H,t,J=8Hz), 3.75(2H,t,J=8Hz),7.27(5H,br).
			3	16	139	1.25(2H,br,OH),3.10(2H,br),3.55(4H,br), 7.40(10H,s).
			4	10	95	3.35(2H,m),4.20(2H,5 lines), 5.50(1H,br), 7.20(10H,br).
			5	45	85–86	2.10(2H,14 lines), 2.70(2H,br,OH), 3.15(1H,5 lines), 3.80(2H,d,J=6Hz), 4.60(1H,dd,J=3Hz, 10.5Hz), 7.40(10H,s).
6	25	5	**7**	7	118	7.12(2H,s), 7.35(10H,m).
			8	8	59	4.20(2H,s), 7.20(5H,s),7.45(2H,m),8.00(3H,m)
			9	30	66	1.80(1H,br,OH),2.95(2H,d,J=7Hz), 4.80(1H,t,J=7Hz),7.15(5H,m), 7.30(5H,s).
			10	8	169–170	1.80(2H,br,OH),3.50(2H,br,d,J=6Hz), 5.20(2H,br,d,J=6Hz), 7.20(20H,m)
			11	40	263–264	3.35(2H,s), 4.30(2H,s), 7.00(20H,m), (D_6 – DMSO + TFA).
12	25	16	**13**	42	152–3/690	1.85(6H,br), 2.25(4H,br).
			14	36	155.5/690	1.35(6H,br), 1.90(4H,br), 2.85(1H,br), 3.60(1H,m).
15	65	14	**16**	20	176/690	1.05(3H,d,J=8Hz),1.80(3H,s),4.80(2H,s).
			17	70	198/690	1.20(3H,s), 1.73(3H,s), 4.70(2H,s).
18	65	12	**19**	4	66/5	1.67(s,9H), 1.95(2H,t,J=6Hz),2.30(2H,t,J=6Hz) 2.67(2H,d,J=1Hz), 5.35(1H,m).
			20	48	82–83/4	0.93(6H,d,J=6.5Hz),1.70(3H,s),2.05(4H,m) 5.30(1H,br).
			21	26	70–72/0.5	1.10(6H,s),1.64(3H,s),1.95(5H,br),3.20(1H,s) 5.40(1H,br).
			22	16	155/690	1.30(6H,s),2.20(3H,s),7.05(4H,A_2B_2)
23	65	5	**24**	85	102/2	1.13(6H,s),1.30(3H,d,J=7.5Hz) 2.73(1H,q,J=7.5Hz), 7.30(5H,s)

similar, the difference is in their relative proportion. It is also found that while both *cis* and *trans* stilbene oxide gave *trans* stilbene, isomerically pure *cis* or *trans* 9-octadecenyl methyl ether epoxides gave a 45:55 mixture of the *cis* and *trans* olefins.[11]

The above results of the reduction of different oxiranes with lithium and sodium clearly indicate that the first step involves a single electron transfer from the metal to the oxirane (reaction A) giving rise to a radical-anion (**25**).[12] Subsequent dimerization (reaction B), rearrangement to carbonyl compounds (reaction C) or abstraction of another metal atom (reaction D) may occur leading to different types of products as shown in Scheme 1. Dimerisation of the radical-anion (**25**) is favoured in case of aryl substituted compounds presumably due to the longer life of the radical. (Dimerization of the radical-anion from **23** did not occur apparently due to steric reasons.) Rearrangement to a carbonyl compound (reaction C) or abstraction of a metal atom to form a dialkali metal salt **26** (reaction D) predominates in case of aliphatic compounds. The dialkali metal salt (**26**) can also take part in Grignard type reactions (reaction E) or yield alcohols on hydrolysis (reaction F).

Reaction D also predominates when the metal is lithium, understandably due to the lower electropositivity of the metal relative to sodium. The more covalent nature of C–Li and O–Li bonds in **26** (M = Li) is also probably responsible for facile elimination of Li_2O leading, in all cases studied, to olefins (route G). The ease with which reductive elimination of cyclic oxiranes occurs indicates that the elimination is *trans*. The planar radical intermediate **25** explains the formation of mixtures of *cis* and *trans* olefins in case of dialkyl substituted oxiranes; formation of *trans* stilbene in case of *cis* as well as *trans* stilbene oxide may be due to the ready isomerization of *cis* stilbene to *trans* in presence of alkali metals.

EXPERIMENTAL

M.ps and [illegible] are uncorrected. GLC is carried out on Hewlett-Packard 5734 gas chromatograph using 3 mm × 1.8 m column of 10% carbowax on chromosorb W, temp 120–8–200°. ^1H NMR spectra were recorded on Varian EM-390 instrument using TMS as internal standard. The oxiranes used in the reactions were obtained by standard methods by treating the appropriate olefins with 40% peracetic acid in CH_2Cl_2 buffered with NaOAc.

Reaction of oxiranes with sodium

The oxirane (20 moles) in anhydrous THF (100 ml) was stirred with atomised sodium (0.05 g atom). At the end of the reaction, the mixture was carefully diluted with water and extracted with ether. The ether extract after drying (Na_2SO_4) and removal of solvent was charged on a silica gel column prepared in hexane and eluted with increasing proportion of EtOAc (1–10%) in hexane. The reaction conditions, the products obtained and the yields of the isolated products are listed in Table 1. The identity of compounds 2, 7, 8, 9, 13, 14, 16, 17, 19, 20, 21 and 22 were established by direct comparison with authentic samples on GLC; other compounds were identified by their spectral data.

Oxidation of **4**

Compound **4** (20 mg) in acetone (5 ml) was stirred at room temperature with 7% chromic acid (0.2 ml). After 15 min the organic layer was decanted from the inorganic salts diluted with ether and washed successively with dil HCl and aq $NaHCO_3$. The organic layer was then dried, evaporated and the residue chromatographed on silica gel (3 g, hexane:acetone, 95:5) yielding 2,3-diphenylbutyrolactone[13] as colourless crystals from hexane (10 mg), m.p. 96°; δ (CCl_4): 3.85 (2H, d, J = 4.5 Hz), 4.25 (1H, m), 4.65 (1H, m). 7.30 (10H, br).

Oxidation of **10**

Compound **10** (20 mg) was oxidised using Jones reagent as described above yielding 1,2,3,4-tetraphenylbutan-1,4-dione,[14] m.p. 248–249°; δ ($CDCl_3$): 5.80 (2H, s), 7.30 (20H, m), ν_{max} 1640–1660 cm^{-1}.

Oxidation of **11**

CrO_3 (60 mg) in CH_2Cl_2 (1 ml) was stirred for 15 min with pyridine (0.2 ml). **11** (20 mg) was then added and the stirring continued for 12 h. The organic layer was decanted from the salts, washed with dil HCl followed by aq $NaHCO_3$ and evaporated. The compound was purified as above and crystallised from $CHCl_3$, m.p. 248°.

1,2,3,4-*Tetraphenylbutan*-1,4-*dione*

A mixture of Zn–Cu couple[15] (5.02 g), KI(1.164 g), $NaHCO_3$ (1.165 g) and desyl chloride[16] (3.5 g) was placed in a 3-necked flask, flushed with N_2 and treated with dry DMSO (50 ml), added dropwise with stirring.[17] The mixture was stirred at 60°C for 1 h and, after addition of satd NH_4Cl (25 ml), extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (50 g, hexane: EtOAc, 95:5) yielding pure 1,2,3,4-tetraphenylbutan-1,4-dione, m.p. 252°. ^1H NMR and IR Spectra were identical with those obtained above.

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