REACTIONS OF 1,2-EPOXYOCTANE

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ABSTRACT

The synthesis of 1,2-epoxyoctane (6) and the stereospecifically labelled mono and dideuterated derivatives (7) and (8) are described. The BF_3 : etherate catalysed rearrangement of 1,2-epoxyoctanes (6), (7) and (8) in ether gave products identified as 1-ethoxy-octan-2-ol (9a), (1S, 2S)1R, 2R-1-d-1-ethoxy-octan-2-ol (10a) and (1R, 2S)1S, 2R-1,2-dideutero-1-ethoxy-octan-2-ol (11a) respectively. The BF_3 : etherate catalysed rearrangement of 1,2-epoxyoctane (6) gave aldehyde (14) by selective migration (ca. 1.41 : 1) of the hydrogen atom (Hb) <u>trans</u> to the long chain aliphatic group.

INTRODUCTION

Acid Catalysed Rearrangement of Epoxides

The chemistry of epoxides[1-4] has been widely studied. Epoxides undergo rearrangement when heated and in the presence of acid or base catalysts. Acid catalysed rearrangements of epoxides have been the most studied.

When a Lewis acid or a strong proton acid coordinates with an epoxy-oxygen lone pair, one of the C-O bonds of the epoxide ring is polarised and cleaved. This may be accompanied by a variety of processes, the most important being;

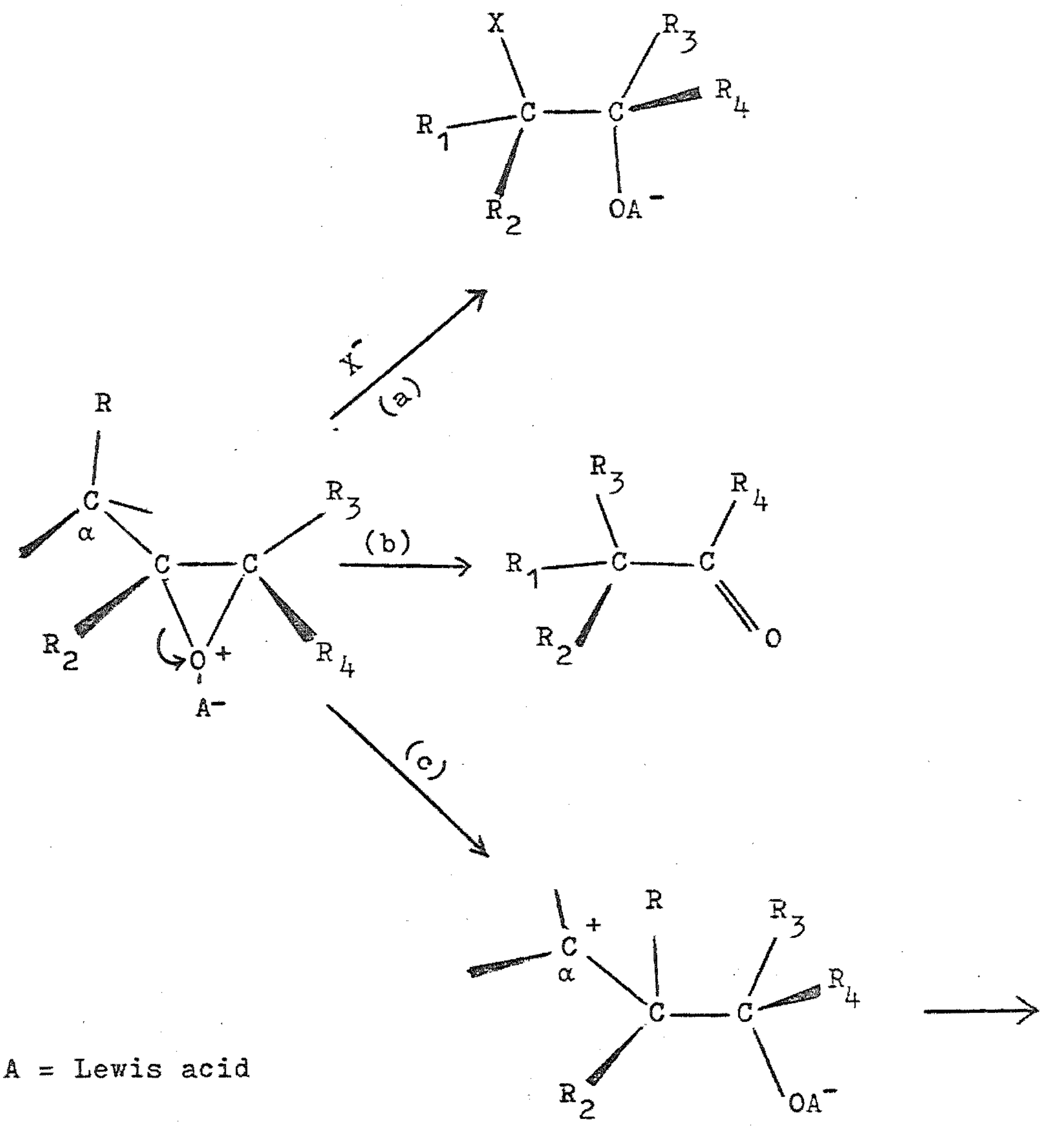
a) attack by an external nucleophile, X^-

b) migration of a substituent from one carbon of the epoxide ring to the other, leading to the formation of a carbonyl compound.

c) the 1,2-shift of a group from the α-carbon atom of one of the substituents to the carbon involved in C-O cleavage.

Process (a) involves attack by an external or conveniently placed internal nucleophile[5]. In the absence of a suitable nucleophile the orientation of ring opening is determined principally by the combined electron donating power of the substituents on the epoxy-carbons[2,3]; epoxide ring opening being favoured at tertiary > secondary > primary centre. However, in the presence of suitable nucleophiles acid catalysed ring opening may occur at the least substituted centre. The less substituted epoxide carbon atom is also sterically less hindered and thus more accessible to nucleophilic attack.

Rearrangement to a carbonyl containing product (process (b) Fig. (1)) is favoured in an inert solvent in the absence of good



A = Lewis acid

Fig. 1

nucleophiles. This rearrangement involves the migration of a substituent on one carbon of the epoxide ring to the other carbon and the choice of migrating substituent (R_3 or R_4) depends both on the relative migratory aptitudes and on the steric environments. Migratory aptitudes of groups involving 1,2 shifts to electron deficient centres follow the general trend aryl > acyl > hydrogen > alkyl[2].

Process (c), fig. 1, can lead to the formation of many interesting products among which are products of subsequent fragmentation[6,7,8] processes.

The initial step in the acid catalysed rearrangement of an epoxide involves coordination of the acid with the oxygen lone pair and this process is followed by cleavage of one of the C-O bonds. The strong electronic substituent effect controlling the orientation of ring opening suggests that there is a marked separation of charge in the transition state. Parker and Isaacs[2] postulated that there are two possible mechanisms for the rearrangement leading to carbonyl compounds (Fig. 2):-

a) a two-step mechanism in which the rate determing step leads to a discrete carbonium ion intermediate, followed by a rapid migration of a substituent to that centre.

b) a one-step 'concerted' mechanism in which carbon-oxygen bond breaking is more important than bond making.

There is, however, no evidence that the carbonyl-compound forming rearrangements proceed <u>via</u> this latter pathway (b, Fig. 2) for epoxides containing at least one tertiary carbon. With the Lewis acid catalyst, BF_3, fluorohydrin may be

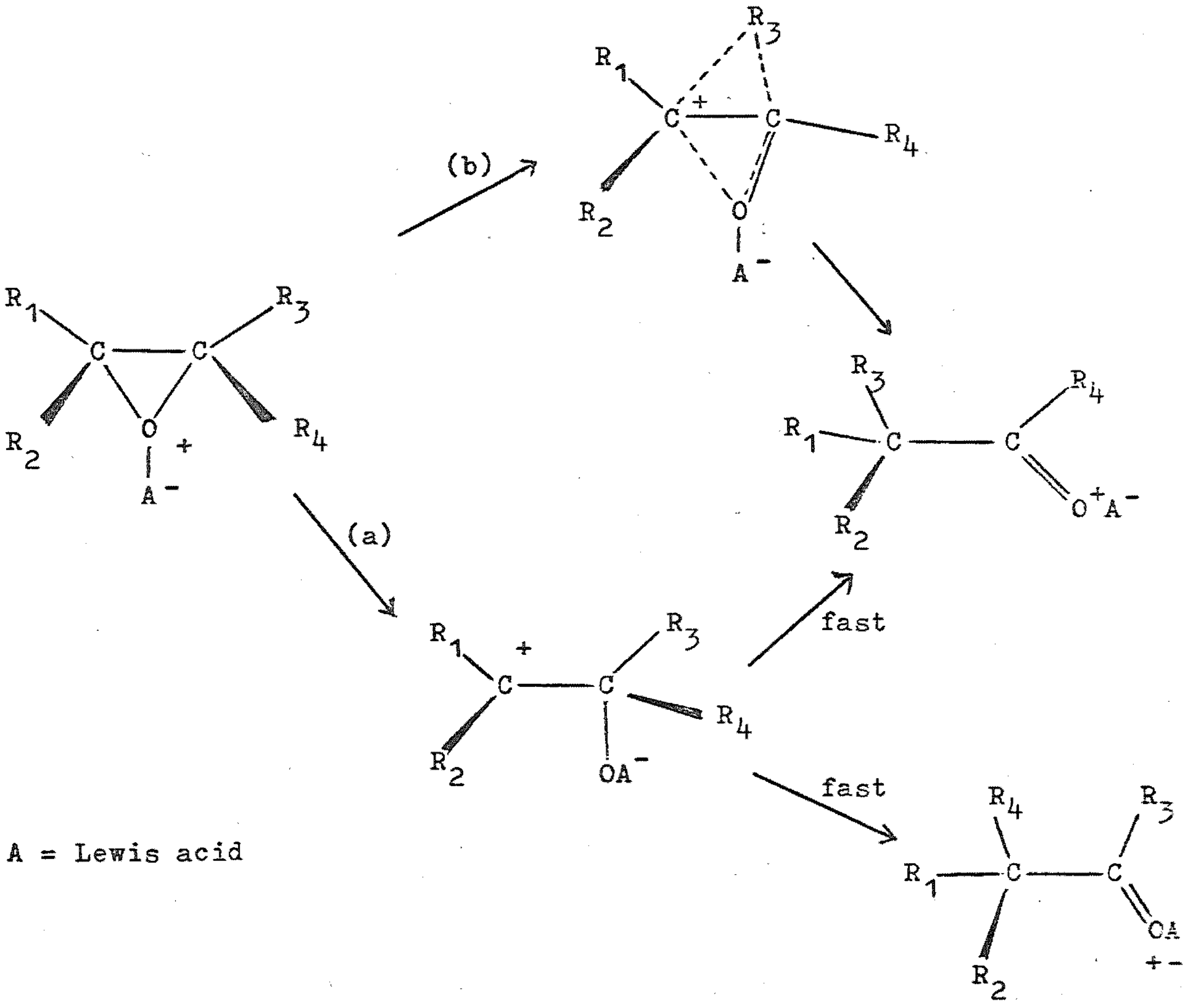


Fig. 2

a reaction intermediate in some cases (Fig. 3). Further reaction of the fluorohydrin with Lewis acid may give products by a concerted pathway or by a two step mechanism.

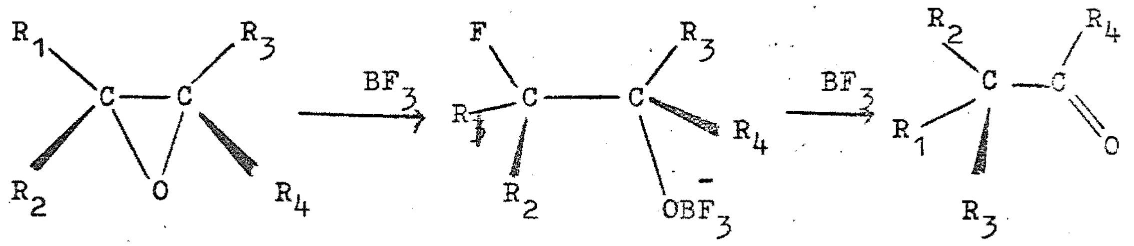


Fig. 3

Rearrangements of epoxides containing a tertiary carbon[7,8,9,10] are thought to proceed via discrete carbonium ion intermediates. The aldehyde product ratios obtained from rearrangement of exocyclic methylene epoxides[8] (e.g. Fig. 4) necessitates the intermediary of a carbonium ion in the rearrangement process.

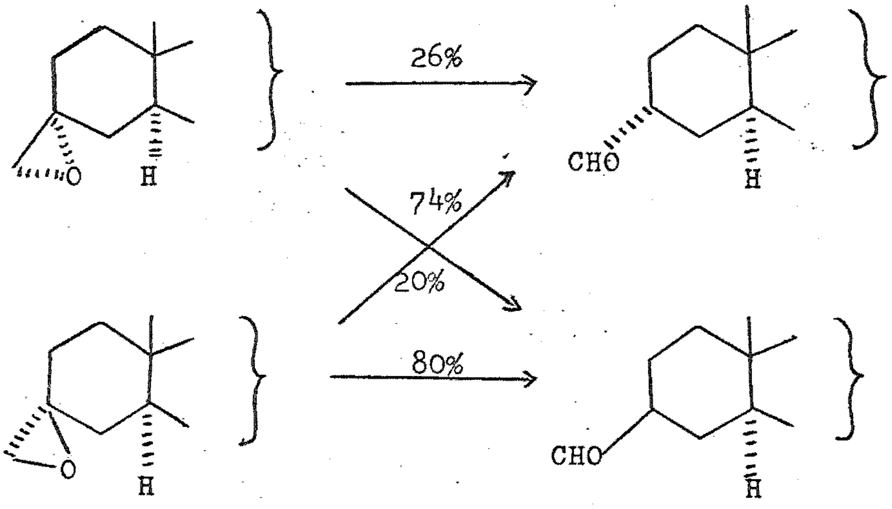


Fig. 4

If hydride migration were concerted with C-O cleavage there would be only one aldehyde formed from each epoxide. The formation of both epimeric aldehydes results from hydrogen migration to the intermediate tertiary carbonium ion.

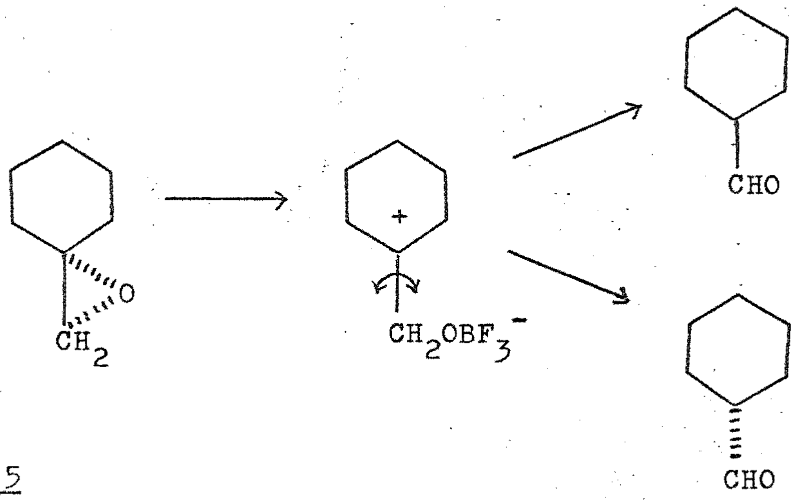


Fig. 5

Alexander and Dittmer[11], and House[12] have secured evidence of stereochemical specificity in the isomerisation of *cis*- and *trans*-2,3-epoxybutane with Lewis acid as catalyst. The *trans*-isomer yielded a substantial proportion of isobutylaldehyde (ca. 10%) by methyl migration and the *cis*-isomer yielded mostly the 2-butanone (54%) (Fig. 6).

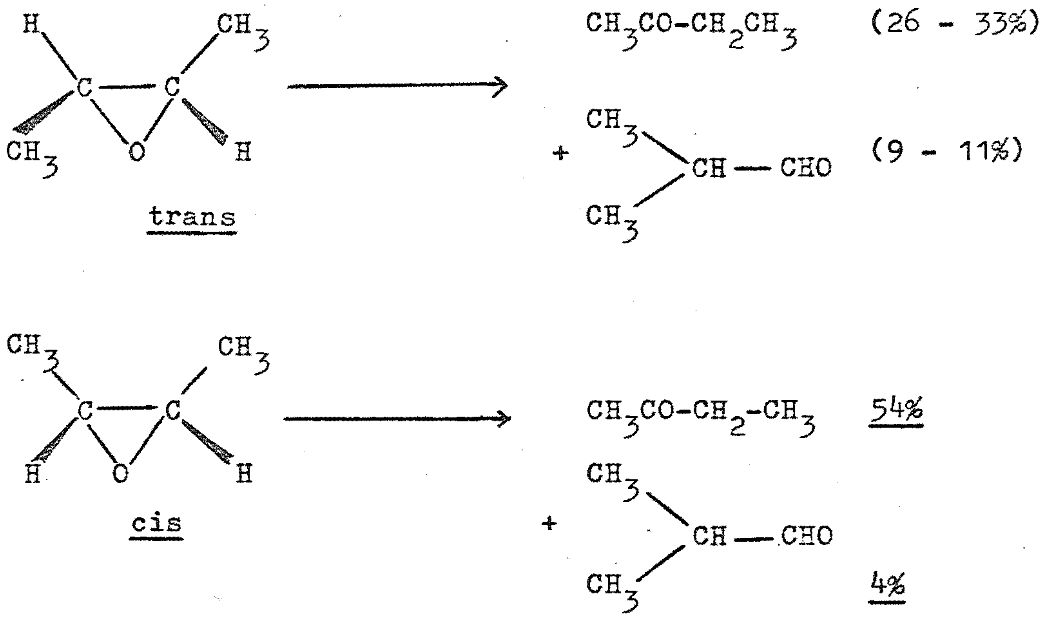


Fig. 6

Rosowsky[1] suggests that the rearrangement of the epoxide proceeds *via* abridged-intermediate (concerted pathway) rather than an open carbonium ion but Blackett has disputed his conclusions[14,15]. Swallow rationalises the BF_3: etherate catalysed isomerisations of *cis* and *trans*-epoxybutane in terms of secondary carbonium ion intermediates[16] where rotation about the C-C bond of the epoxide is possible. The product ratio of aldehyde is thought to reflect the torsional strain between the substituent groups and the migratory aptitudes of the hydride and methyl groups.

In an extensive study of the BF_3 catalysed rearrangement of 2,3,3-trimethylepoxybutane Blackett[17] established the comparability of the rate constant for a hydride shift (k_H 1.71) to that of the conformational change (k^1, k^{-1} 1.84) of a carbonium ion intermediate (Fig. 7). He also established that the boron trifluoride catalysed rearrangement of the epoxide to give the corresponding aldehyde proceeds by selective (1.9:1) migration of the hydrogen atom (H b) *cis* to methyl group.

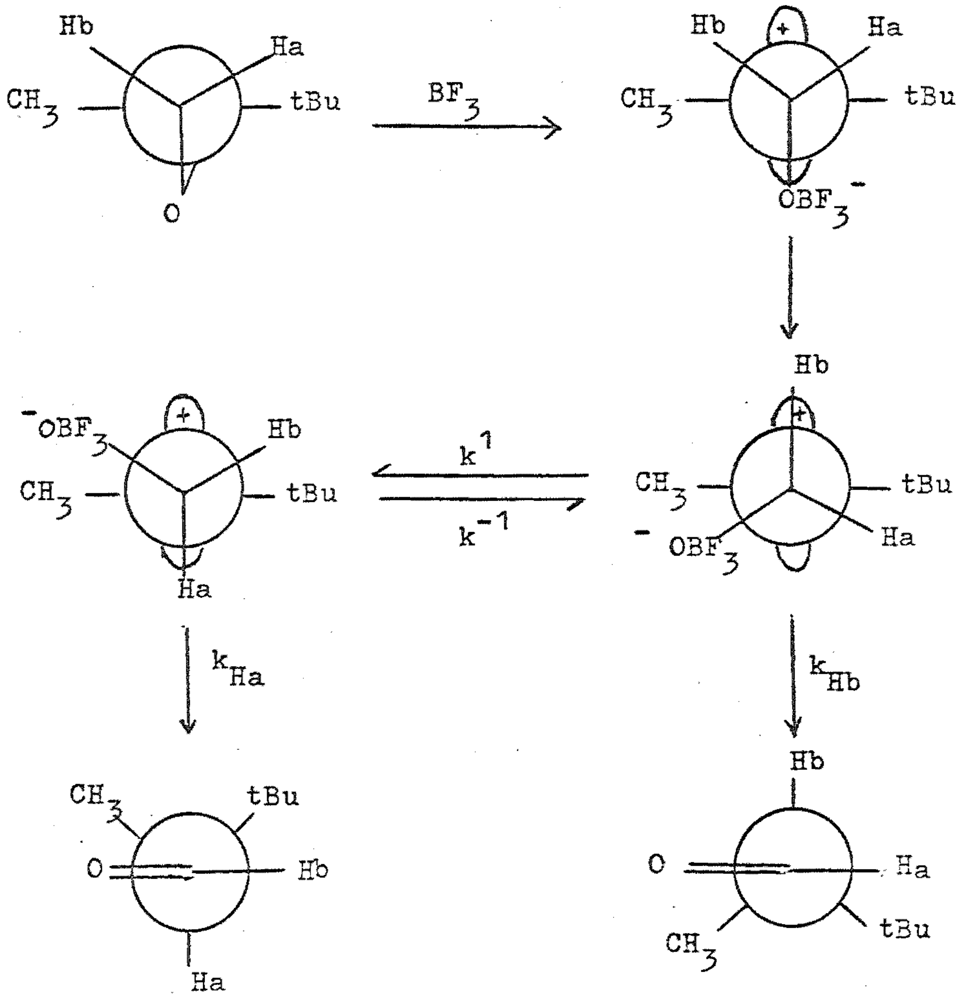


Fig. 7

The mechanism of rearrangement of epoxides at secondary and primary centres is not certain. A carbonium ion intermediate may be involved although other mechanisms are possible. A primary carbonium ion is of higher energy than a secondary carbonium ion which in turn is of higher energy than a tertiary carbonium ion[18].

The purpose of the current study has been to examine in some detail the rearrangement of 1,2-epoxyoctane containing a primary and a secondary epoxy carbon atom in order to probe the mechanism of the acid catalysed reaction involving cleavage of a secondary carbon-oxygen bond.

DISSCUSSION

The boron trifluoride catalysed rearrangement of the unsymmetrical epoxide[17] (2,3,3-trimethylepoxybutane) to give the aldehyde (2,3,3-trimethylbutylaldehyde) exhibited a preference for the migration of the hydrogen cis to the methyl group to the extent of ca. 1.9. The stereoselectivity of hydride migration results from the comparability of energy of activation for rotation and hydride migration (i.e. $k_{rotation} \simeq k_{Hmigration}$) (Fig. 7).

As an extension of this study the rearrangement of 1,2-epoxyoctane (6) with Lewis acid has been examined. 1,2-Epoxyoctane has both a primary and secondary epoxy-carbon atom and an acid catalysed rearrangement would be expected to give products resulting from cleavage of the secondary C-O bond. The difference in size of the two substituents (hydrogen atom and long chain aliphatic group) at C(2) in 1,2-epoxyoctane is comparable to the difference in the corresponding substituents (methyl and tertiary butyl) of 2,3,3-trimethyepoxybutane, and hence if the mechanism for the reactions are similar some stereoselectivity would be expected.

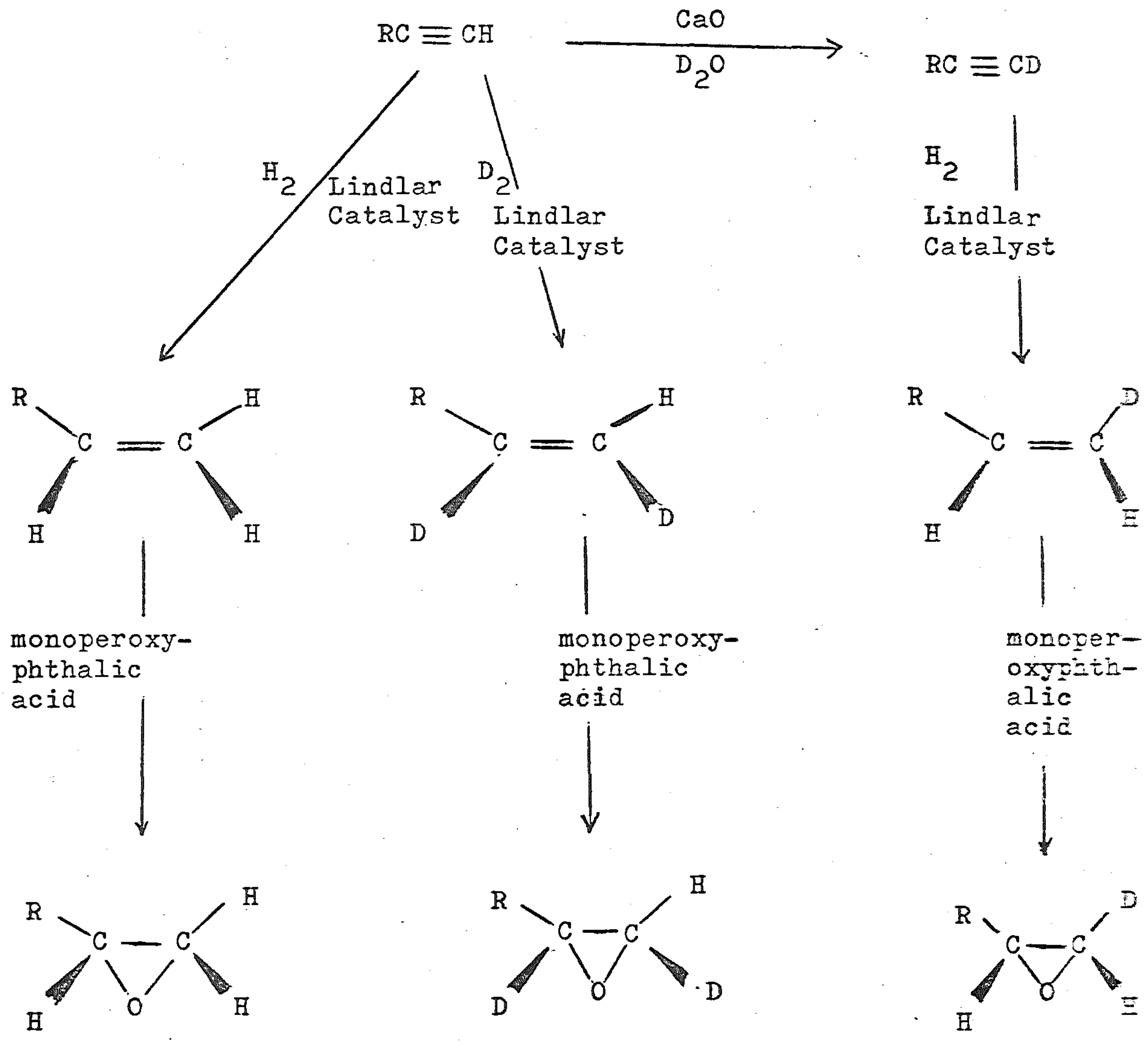
In the present study of stereoselectivity in substituent migration for the 1,2-epoxyoctane (6), synthesis and rearrangement of both its stereospecifically labelled C-1 monodeuterated (7) and C-1 and C-2 dideuterated derivative (8) were carried out (Fig. 8).

To prepare the (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) from 1-octyne (1), it was necessary to exchange the terminal hydrogen of the 1-octyne (1) with deuterium[19]. 1-d-1-Octyne (2) was prepared by the agitation of the 1-octyne (1) for several hours at 70°C with successive portions of D_2O and CaO. The increase in deuteration was determined from the infra-red spectra which showed a decrease of peak intensity at 3350 cm^{-1} (C≡C-H stretching) and an increase of peak intensity at 2610 cm^{-1} (C≡C-D stretching). Repeated washing with fresh D_2O and CaO finally gave alkyne which was $>$ 95% 1-d-1-octyne (2). Semihydrogenation of the 1-d-1-octyne (2) gave (Z)-1-d-1-octene (4a). Oxidation of the alkene with monoperoxyphthalic acid gave (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) (Fig. 8).

The (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) was prepared from 1-octyne. Semideuteration of 1-octyne (1) gave (E)-1,2-dideutero-1-octene (5a) and subsequent oxidation yielded the required (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) (Fig. 8).

Reduction of 1-octyne (1) with Lindlar catalyst and quinoline[20] in the presence of an atmosphere of hydrogen gave a high yield of 1-octene (3). The nmr spectra of the 1-octene (3) showed a multiplet centred at δ 5.83 ((C2)Hc), a doublet at δ 4.83 and 5.13, J = 18 Hz; ((C1)Ha) another doublet at δ 4.83 and 5.01, J = 11 Hz; ((C1)Hb), a multiplet centred at δ 2.06 ((C3)H_2), another multiplet centred at δ 1.33, ($Wh/_2$ = 11 Hz); ((C4)H_2), and a triplet centred at δ 0.90 ((C1)H_3). The nmr spectra was identical to that of an authentic sample.

Reaction Pathways



R = $CH_3(CH_2)_5$

Fig. 8

Table 1

Products of semihydrogenation of alkynes

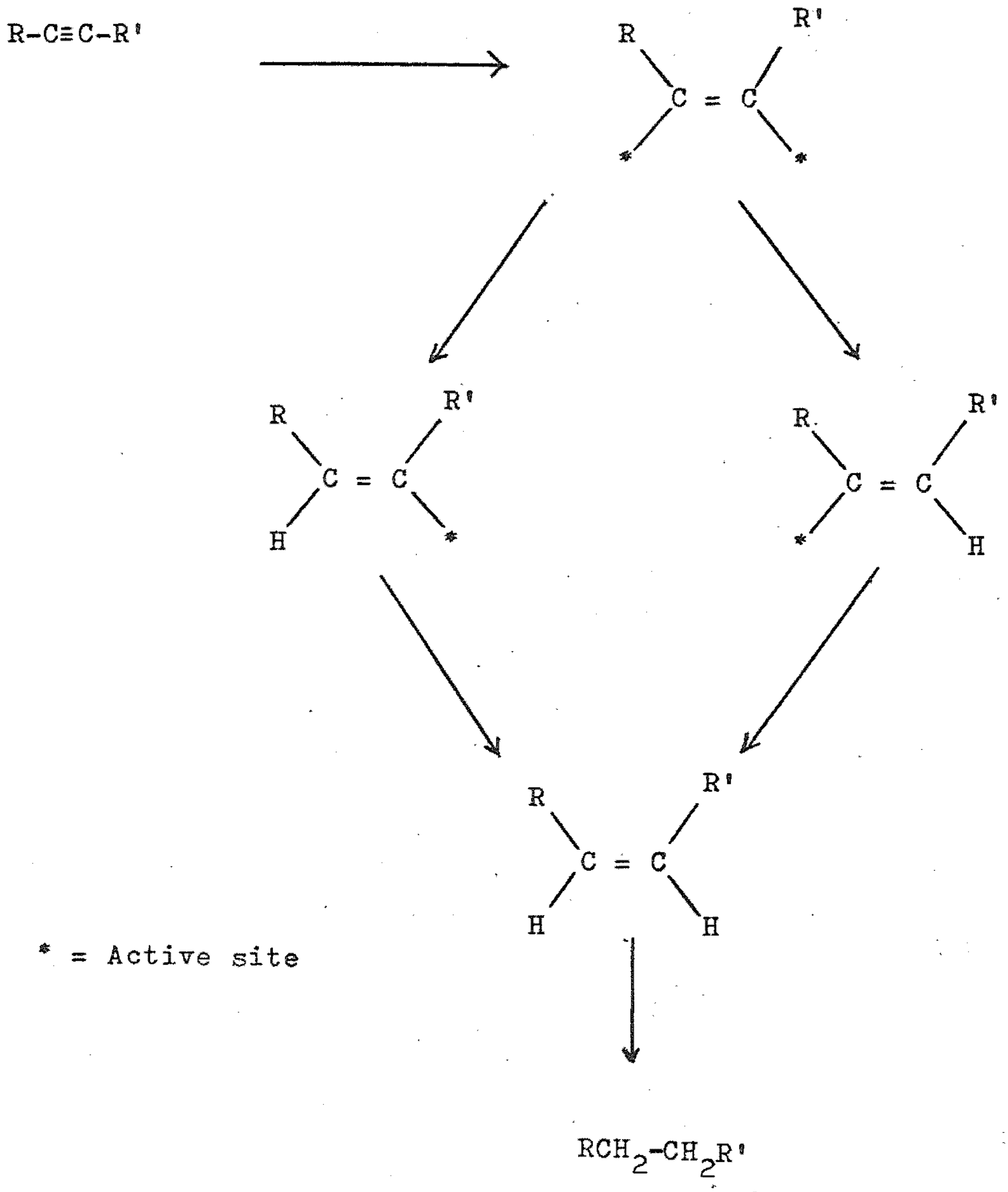
			Ref.
$C_6H_9C{\equiv}CH$	$C_6H_9C{=}CH_2$	89%	
	$C_6H_9CH_2{-}CH_3$	8%	21
	$C_6H_9C{\equiv}CH$	6%	
$C_6H_9C{\equiv}C{-}CH_3$	$C_6H_9C{=}CHCH_3$		
	cis	76%	
	trans	2%	21
	$C_6H_9CH_2CH_2CH_3$	8%	
	$C_6H_9C{\equiv}C{-}CH_3$	5%	
Hex-3-yne	3-hexene	91.2%	
	trans 3-hexene	4.3%	
	cis 2-hexene	1.4%	22
	trans 2-hexene	1.4%	
	hexane	1.6%	
Hept-2-yne	*trans* isomer	1%	
Dec-5-yne	*trans* isomer	5%	25

Products of semideuteration of alkynes

1-Butyne	1-butene	99.1%	23
	2-butene		
	cis	0.2%	
	trans	0.2%	
2-Butyne	2-butene		
	cis	97.5%	21
	trans	1.0%	
	butane	1.0%	
	1-butene	0.5%	

Hydrogenation (deuteration) of an alkyne is believed to be stereospecific and *cis*[21,22,23]. The selectivity of deuterium addition to a terminal alkyne approaches 100%. Monosubstituted acetylenes have higher selectivity than the disubstituted acetylenes. The order of bond selectivity is HC≡CR > R-C≡C-R > CH_2=CHR > RCH=CHR (Table 1). The high selectivity is thought to be due to two factors[24]: high activity of the catalyst and strong absorption by the catalyst. Lindlar catalyst has higher activity[26,27,28] for absorption by an acetylenic bond than an ethylenic bond. No hydrogenation of the double bond takes place while acetylene is present. The mechanism involves adsorption of the catalyst onto the acetylene with the opening of one π-bond followed by reaction with two active H or D atoms as shown in Fig. 9.

Mechanism of semihydrogenation of triple bond to double bond



* = Active site

Fig. 9

Reduction of 1-d-1-octyne (2) gave 90% (Z)-1-d-1-octene (4a), 5% 1-d-octyne (2) and 5% octane. The nmr spectra of (Z)-1-d-1-octene (4a) showed a doublet at δ 4.83 and 5.01 J = 10 Hz; ((C1)Hb), a weak peak (compared with nmr spectra of 1-octene) at δ 5.13 which corresponded to (C1)Ha ($J_{Ha,\ Hc}$ = 18 Hz) and a multiplet at δ 5.83 ((C2)Hc). From the nmr spectra it was estimated that 4% of undeuterated 1-octene (3) was present.

Deuterium gas manufactured by Matheson (99.8% pure) was used to prepare the (E)-1,2-dideutero-1-octene (5a). Analysis by g.l.c. showed the reaction product to contain ca. 90% (E)-1,2-dideutero-1-octene (5a) and 5% each of 1-octyne (1) and octane. 1-Octyne separated by preparative g.l.c. was found to contain no deuterium. Octane was not separated. The nmr spectra of (E)-1,2-dideutero-1-octene (5a) showed a broad singlet at δ 5.00, $Wh/_2$ = 8 Hz; (CC1)Ha) and weak peaks beside the broad singlet which may be due to the presence of traces of 1-octene (3). With the 0.2% impurity of hydrogen in the deuterium gas, the formation of some undeuterated 1-octene (3) was inevitable and this was estimated from nmr as $<$ 3%. A second attempt to prepare (E)-1,2-dideutero-1-octene (5a) was carried out using deuterium gas prepared from reaction of D_2O on aluminium turnings and mercurous chloride. The octene was found to be less than 90% dideuterated.

Epoxides (6), (7) and (8) were prepared by oxidation of alkenes (3), (4a) and (5a) respectively in dry ether with monoperoxyphthalic acid at room temperature for 7 days. The reaction was followed by g.l.c. and high yields of epoxides were obtained. In each case the epoxides were purified by preparative g.l.c. The nmr spectra of epoxide (6) showed a triplet at δ 0.90 $(C8)H_3$), a multiplet at δ 1.33, $((C3)H_2$-$(C7)H_2$) and the three protons Ha, Hb, Hc between δ 2.30 and 3.10. From the nmr spectra of (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) and (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) the coupling constants of Ha, Hb and Hc can be estimated. The (C1)Ha proton of 1,2-epoxyoctane (6) appeared as a doublet of doublets centred at δ 2.43, $J_{Ha, Hc} = 3$ Hz; $J_{Ha, Hb} = 5$ Hz and the (C1)Hb centred at δ 2.72 appeared as a doublet of doublets; $J_{Ha, Hb} = 5$ Hz; $J_{Hb, Hc} = 5$ Hz. (1R, 2S)1S, 2R-1-d-1,2-Epoxyoctane (7) in the nmr had a doublet centred at δ 2.72, J = 3 Hz; ((C1)Hb) and a multiplet centred at δ 2.88 ((C2)Hc). (1S, 2S)1R, 2R-1,2-Dideutero-1,2-epoxyoctane (8) showed a singlet at δ 2.43 ((C1)Ha.

Efforts to determine the percentage of epoxide (6) in epoxide (7) by integration of the proton signals in the nmr spectra was of limited success because the protons Ha, Hb and Hc of the epoxide (6) appeared as an ABC multiplet. However, a pure sample of epoxide (8) would only have a singlet due to (C1)Ha at δ 2.43. Therefore, the percentage of undeuterated epoxide (6) in epoxide (8) could be estimated..

Further attempts were made to determine the percentage of deuterium at C1(Ha) for the (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) and at C1 and C2 for the (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctene (8).

The first involved the reduction of epoxides (6), (7) and (8) with lithium aluminium hydride in dry ether to give the secondary alcohols (19), (20) and (21). It was hoped that nmr studies with $Eu(fod)_3$ on the three alcohols might enable the integrals of the C1, C2 and C3 protons to be measured and from their integrals the percentage of deuterium at C1 and C2 for the epoxide (7) and (8) to be deduced.

Octan-2-ol (19) was identified from the infra-red absorption at 3350 cm^{-1} and the nmr spectra which showed a triplet centred at δ 0.88 ($(C8)H_3$), another triplet centred at 1.23 ($(C1)H_3$), a multiplet centred at 1.35 ($Wh/_2$ = 11 Hz; CH_2 groups, $(C3)H_2$-$(C7)H_2$), a singlet at δ 1.82 ((C2)OH) and a multiplet centred at 3.78 ($Wh/_2$ = 16 Hz; (C2)H). The nmr spectra of 1-d-octan-2-ol (20) gave a singlet at 1.93 ((C2)OH) and a multiplet centred at 3.73 ($Wh/_2$ = 18 Hz, (C2)H), while the spectra of 1,2-dideutero-octan-2-ol (21) showed a singlet centred at δ 2.30 ((C2)OH) and a very weak multiplet centred at 3.76 ((C2)H) resulting from the presence of undeuterated epoxide in the starting material.

Nmr studies using $Eu(fod)_3$ shift reagent on 1-d-octan-2-ol (20) gave poor spectra. The $(C3)H_2$ shifted faster on addition of $Eu(fod)_3$ than the $(C1)H_2D$ and the (C2)H was hidden with the (C3) protons.

The second method involved the preparation of (1S, 2S)1R, 2R-1-d-1-ethoxy-2-acetoxyoctane (10b) and (1R, 2S)1S, 2R-1,2-dideutero-1-ethoxy-2-acetoxyoctane (11b) from epoxides (7) and (8) respectively by reaction of the respective epoxide with sodium ethoxide. Acetylation with acetic anhydride-pyridine resulted in formation of the acetates (10b) and (11b). From integration of the appropriate signals in the nmr spectra of acetates (10b) and (11b) it was hoped to determine the deuterium enrichment of the samples. An unlabelled sample of acetate (9b) exhibited absorptions at δ 5.00 (C2)Hc, a multiplet centred at δ 3.48 due to $OC\underline{H_2}Me$, (C1)Ha and (C1)Hb and a singlet at δ 2.05 (OAc). Integration (average of five integrals) of these three signals was in the ratio 1:4:3 for the acetate (9b). Similar measurements on (1S, 2S)1R, 2R-1-d-1-ethoxy-2-acetoxyoctane (10b) and (1R, 2S)1S, 2R-1,2-dideutero-1-ethoxy-2-acetoxyoctane (11b) are shown in Tables 2 and 3 below.

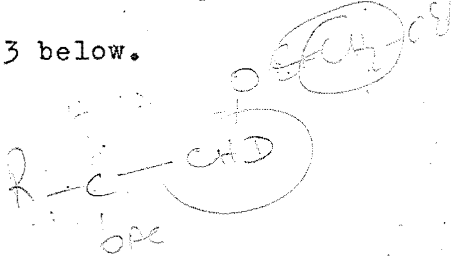


Table 2

Determination of Deuterium content of (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) using (1S, 2S)1R, 2R-1-d-1-ethoxy-2-acetoxyoctane (10b)

Sample	(C2)Hc δ 5.00		(C1)Ha, Hb and $OC\underline{H}_2Me$ δ 3.50		(C2)OAc δ 2.05		Percentage D at C1
		s.d.		s.d.		s.d.	
1	11.60	0.4	35.1	0.2	41.55	0.7	97.5
2	10.15	0.2	31.75	0.2	38.50	0.5	87.2

Average percentage at C-1 is 92.3% s.d. 5.0

Because of the inherent error in integration as evidenced (sample no. 1 and 2) in Table 2, this method was shown to be of insufficient accuracy in the determination of percentage deuteration of epoxide (7).

Table 3

Determination of Deuterium content of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) using (1R, 2S)1S, 2R-1,2-dideutero-1-ethoxy-2-acetoxyoctene (11b)

(C2)Hc δ 5.00		(C1)Ha, Hb and $OC\underline{H}_2Me$ δ 3.50		(C2)OAc δ 2.05		Percentage D at C1 and C2	
	s.d.		s.d.		s.d.		s.d.
1.45	0.6	32.35	0.9	39.0	1.0	86%	1.5

For the dideuterated compound it is assumed that hydrogen at C-2 will equate with an equal amount of hydrogen at C-1. The acetate (11b) in Table 3 was prepared from epoxide (8) which in turn was prepared from (E)-1,2-dideutero-1-octene (5a) obtained by deuteration of 1-octyne (1) using deuterium gas prepared from D_2O on aluminium turnings and mercurous chloride.

Deuterium content of epoxide (8) prepared from deuterium gas from the cylinder was not determined by the above method. An alternative procedure was carried out involving the comparison of the nmr spectrum of both the alkenes and epoxides prepared from deuterium gas from two different sources. It was estimated that the epoxide (8) prepared from deuterium gas manufactured by Matheson gave 97% deuteration.

The percentage deuterium at C-1 of epoxide (7) could be determined from the infra-red spectra of the starting 1-octyne (1) and 1-d-1-octyne (2) and comparing the ratios of the intensity of the $C\equiv C-H$ (1-d-1-octyne) with respect to the C-H stretches at 2950 and 2875 cm^{-1} after deuterium exchange and the intensity of the corresponding peaks in an undeuterated sample as shown in Table 4A and 4B below.

Table 4 (A)

IR peak intensities in arbitrary units.

First sample

IR peaks	Intensities			Intensity Ratios		
	$RC\equiv CD$ after washing with D_2O and CaO	$RC\equiv CH$		$RC\equiv CD$ after washing with D_2O and CaO	$RC\equiv CH$	$\frac{RC\equiv CD}{RC\equiv CH} \times 100$
a) C-H stretch at 2950 cm^{-1}	44.7	60.7	$\frac{C\equiv C-H}{C-H(a)}$	0.0224	0.678	3.29%
b) C-H stretch at 2875 cm^{-1}	29.2	46.2				
$C\equiv C-H$ stretch at 3325 cm^{-1}	1.0	41.2	$\frac{C\equiv C-H}{C-H(b)}$	0.0342	0.892	3.84%

Average of undeuterated 1-octyne is 3.56%   s.d. = 0.3

The percentage of deuterium at C-1 of epoxide (7) was therefore (96.4 ± 1)%

Table 4 (B)

IR peak intensities in arbitrary units.

Second sample

IR peaks	Intensities			Intensity Ratios		
	RC≡CD after washing with D_2O and CaO	RC≡CH		RC≡CD after washing with D_2O and CaO	RC≡CH	$\frac{RC\equiv CD}{RC\equiv CH} \times 100$
a) C-H stretch at 2950 cm^{-1}	38.9	60.7	$\frac{C\equiv C\text{-}H}{C\text{-}H(a)}$	0.0359	0.678	5.3%
b) C-H stretch at 2875 cm^{-1}	25.8	46.2				
C≡C-H stretch at 3325 cm^{-1}	1.4	41.2	$\frac{C\equiv C\text{-}H}{C\text{-}H(b)}$	0.0543	0.892	6.1%

Average of undeuterated 1-octyne is 5.7%   s.d. = 0.4

The percentage of deuterium at C-1 of epoxide (7) was found to be (94.3 ± 1)%.

Therefore the percentages of deuterium at C-1 for the two samples of epoxide (7) were (96.0 ± 1)% and (94.0 ± 1%).

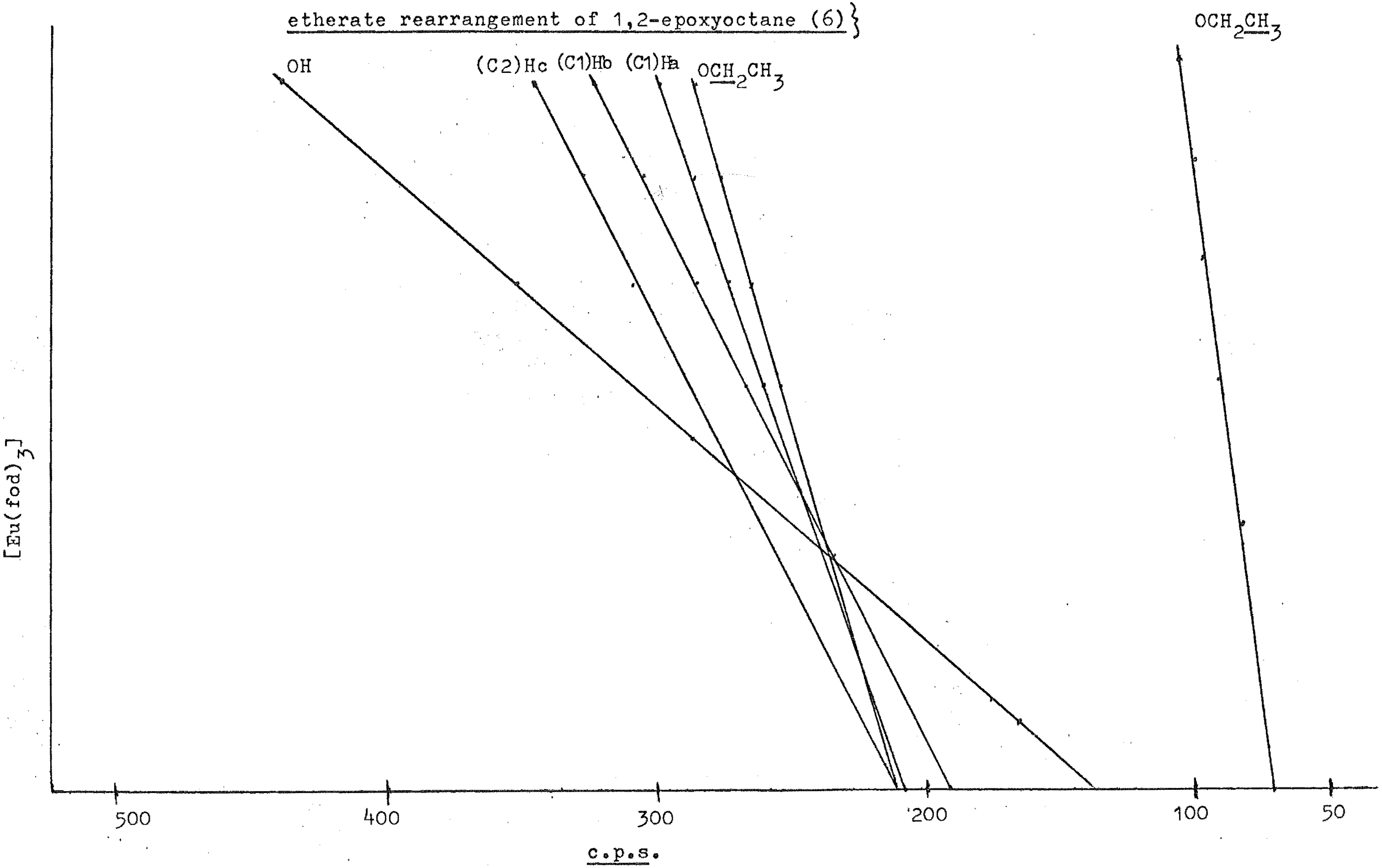
Acid Catalysed rearrangement of 1,2-epoxyoctane

Rearrangements of 1,2-epoxyoctane in THF, benzene, CCl_4 and ether were performed by bubbling through the solution BF_3 gas. The reactions were not reproducable probably due to the difficulty in controlling the BF_3 gas flow.

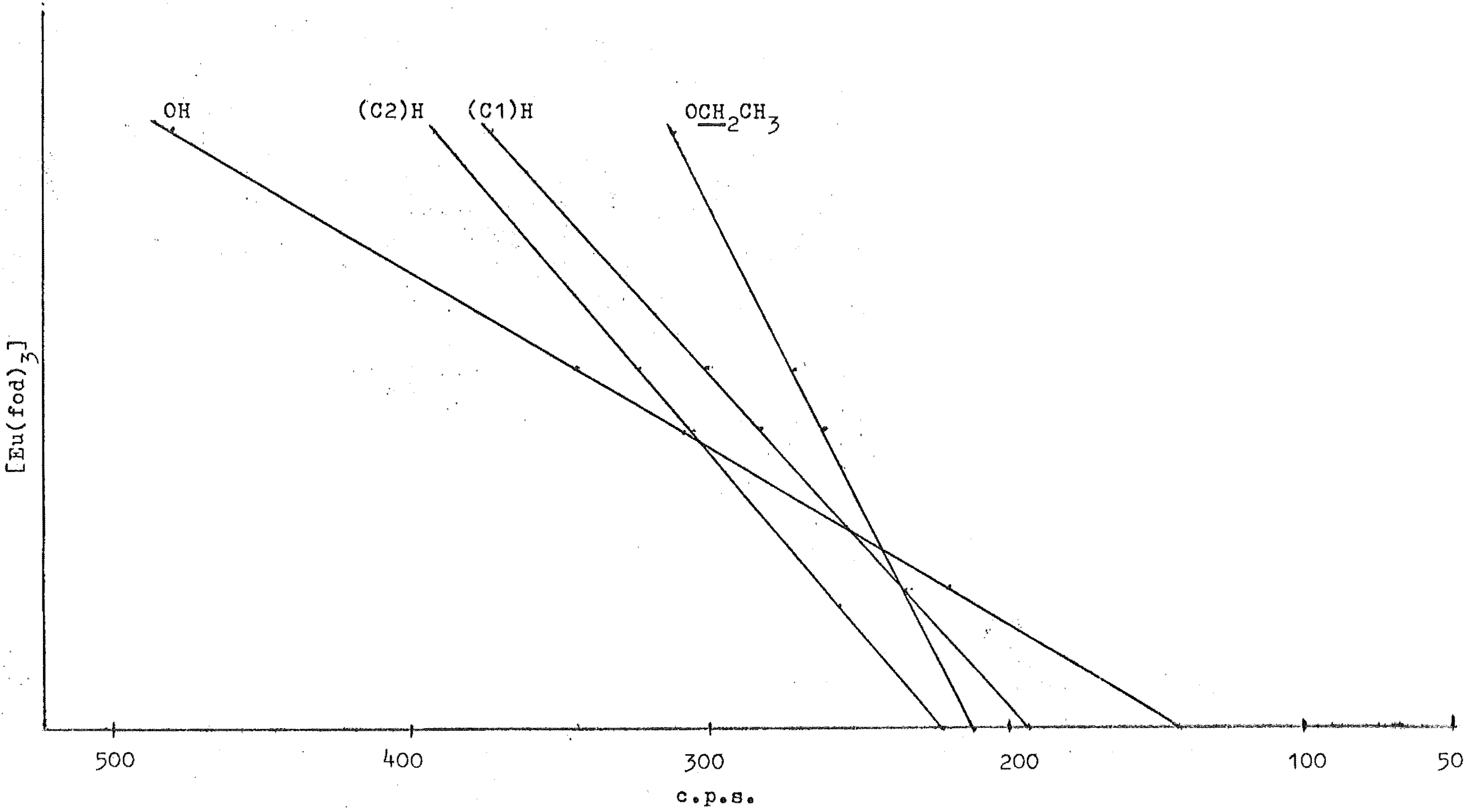
Reaction of the epoxide (6) with BF_3 etherate in dry ether at room temperature for 5 hours and then quenching the reaction mixture with anhydrous K_2CO_3 gave a crude product consisting of aldehyde (14, 12%) and ethoxyalcohol (9a, 60%) and an unidentified compound (28%). The products were separated by preparative g.l.c. The nmr spectra of aldehyde (14) was identical to an authentic sample. The ethoxyalcohol (9a) was identified by microanalysis, IR, nmr, $Eu(fod)_3$ shifts and decoupling experiments. Further reaction of the ethoxyalcohol to the acetate (9b) further confirmed the structure of the starting compound.

The infra-red spectra of 1-ethoxy-2-octanol (9a) indicated the presence of an OH group at 3450 cm^{-1}. The nmr spectrum exhibited a multiplet centred at δ 3.60 (5 protons) and a hydroxyl singlet peak at δ 2.30. On adding $Eu(fod)_3$ shift reagent, it was found that the OH shifted far downfield and the five proton cluster gradually spread out resulting in a multiplet centred at δ 6.20, a triplet centred at 5.80 ($J = 8$ Hz), a doublet of doublets centred at δ 5.25 ($J = 8$ Hz, $J = 3$ Hz) and a quartet centred at δ 4.97. Decoupling was performed at this stage. Irradiation on the doublet of doublets centred at 5.25 effected collapse of the triplet at 5.80 due to (C1)Hb. Irradiation on the multiplet centred at 6.20, ((C2)Hc) effected collapse of the doublet of doublets centred at 5.25 ((C1)Ha) to a doublet. Further assignment of the proton spectra was possible by $Eu(fod)_3$ shift studies on the monodeuterated and dideuterated ethoxyoctan-2-ols (10a and 11a). For the monodeuterated alcohol (10a), after addition of an appropriate quantity of $Eu(fod)_3$ shift reagent, the doublet

Graph 1 [Eu(fod)$_3$] v's Chemical Shift of 1-ethoxyoctan-2-ol (9a) {Reaction product of BF$_3$: etherate rearrangement of 1,2-epoxyoctane (6)}

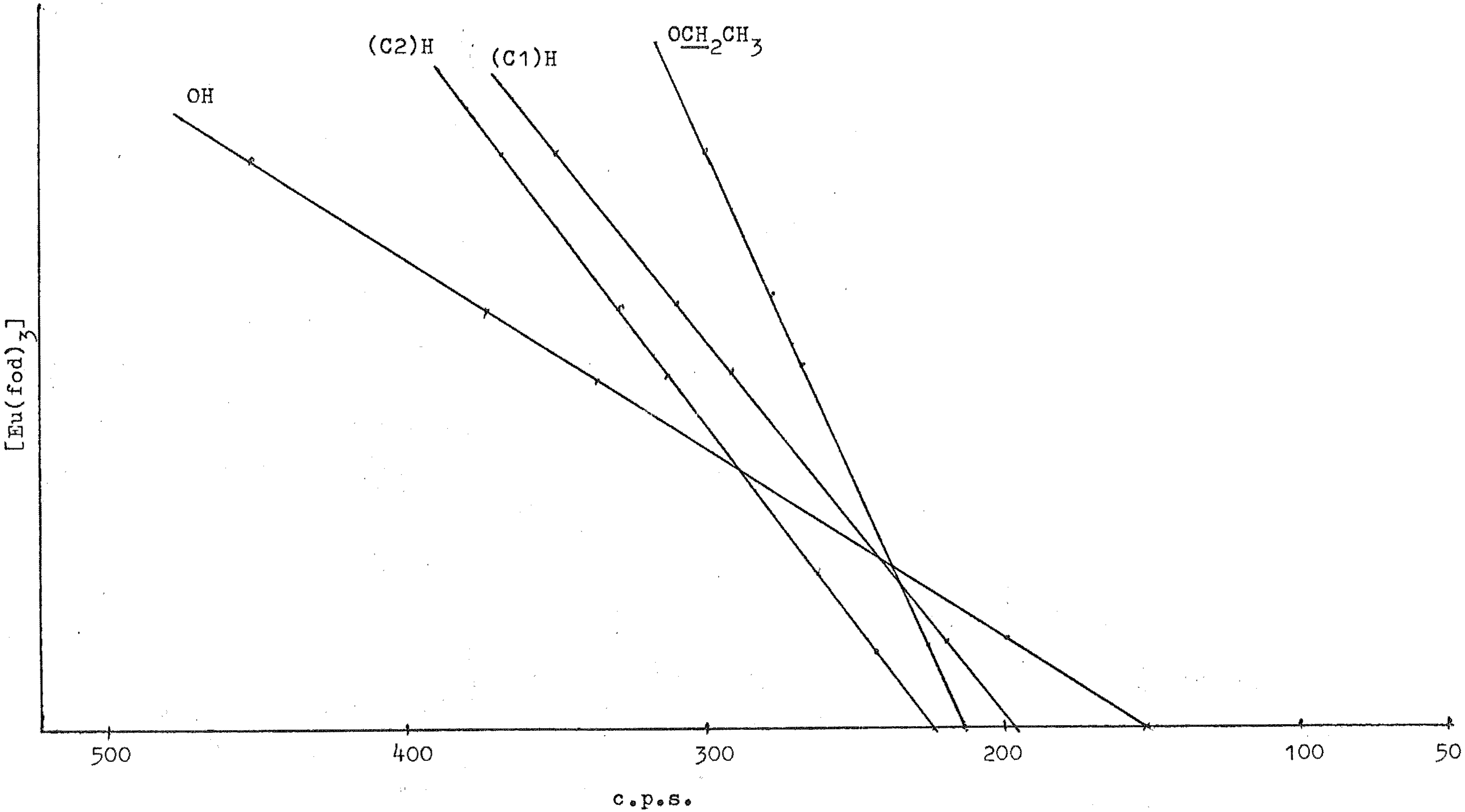


Graph 2 $[Eu(fod)_3]$ v's Chemical Shift of (1S, 2S)1R, 2R-1-d-1-ethoxyoctan-2-ol (10a) {Reaction product of BF_3 : etherate rearrangement of (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7)}

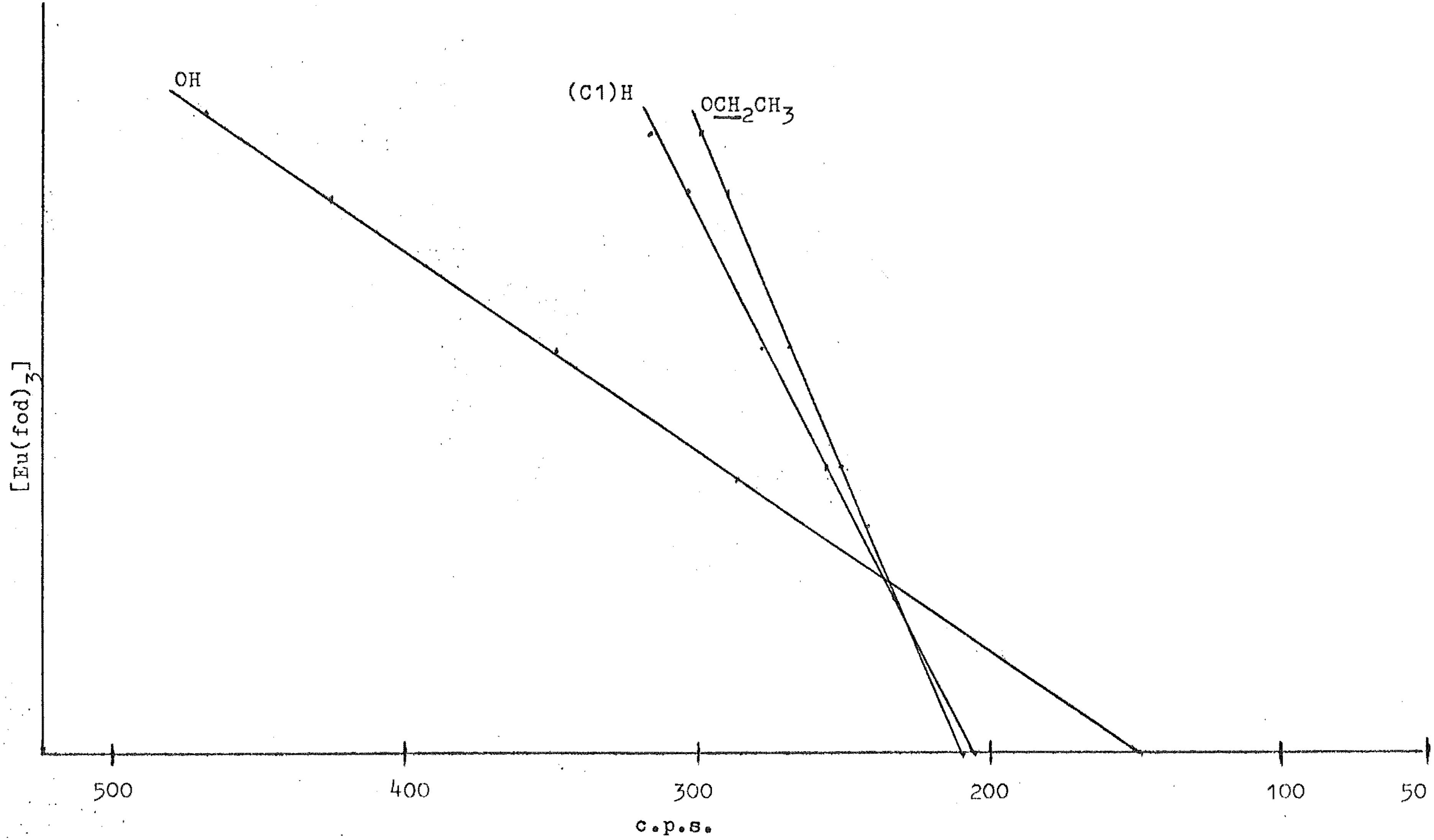


Graph 3 [Eu(fod)$_3$] v's Chemical Shift of (1S, 2S)1R, 2R-1-d-1-ethoxyoctan-2-ol (10a)

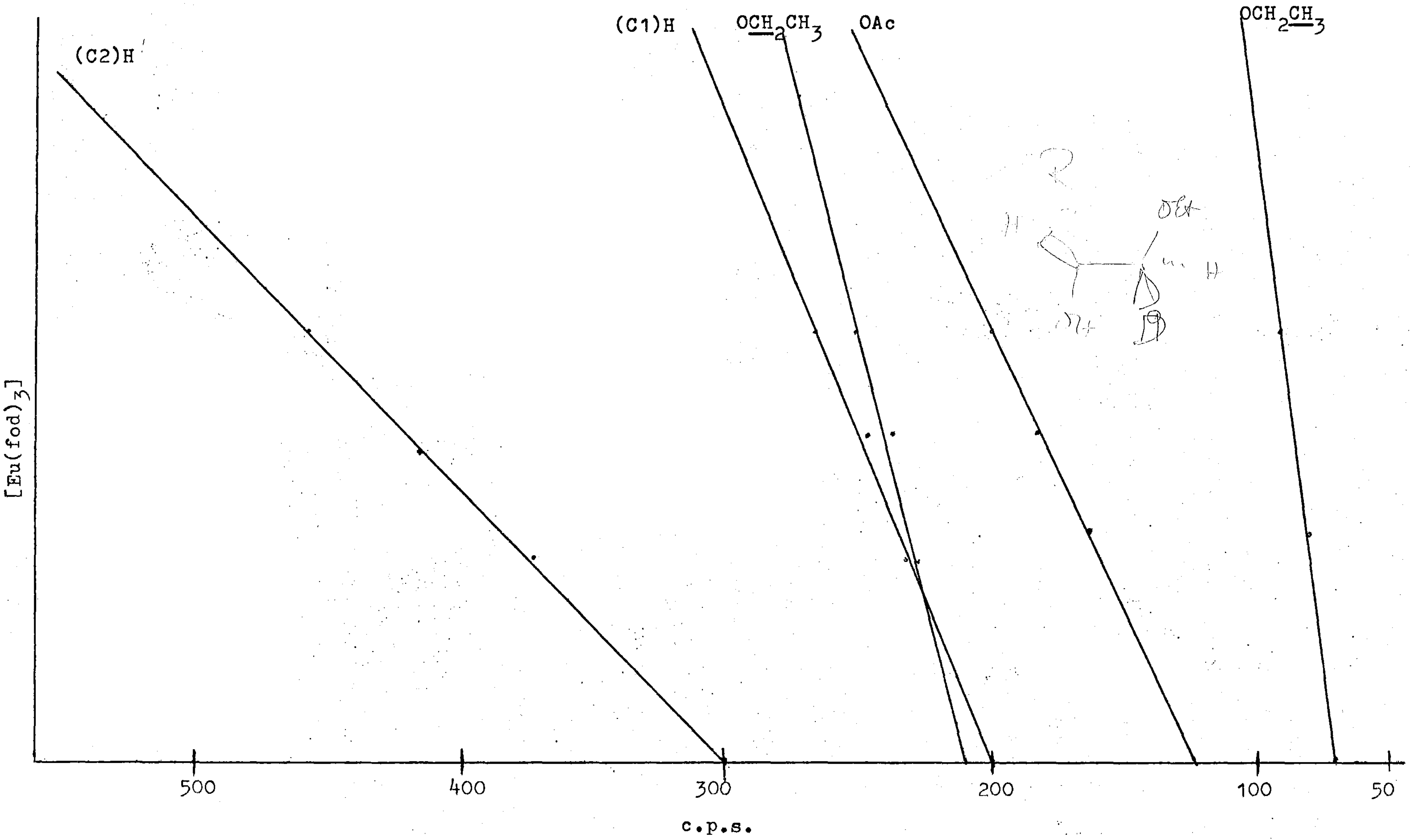
{Reaction product of NaOEt and (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7)}



Graph 4 [Eu(fod)$_3$] v's Chemical Shift of (1R, 2S)1S, 2R-1,2-dideutero-1-ethoxyoctan-2-ol (11a) {Reaction product of BF$_3$: etherate rearrangement of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8)}



Graph 5 [Eu(fod)$_3$] v's Chemical Shift of (1S, 2S)1R, 2R-1-d-1-ethoxy-2-acetoxyoctane (10b)



of doublets centred at 5.25 totally disappeared, indicating the absorption to result from the (C1)Ha proton. The doublet of doublets (J = 8 Hz; J = 8 Hz) centred at δ 5.80 became a doublet (J = 8 Hz). For the dideuterated sample the triplet centred at δ 5.80 and multiplet centred at δ 6.20 both disappeared. The doublet of doublets centred at δ 5.25 in the undeuterated analogue became a singlet confirming the initial assignment of the (C1)Ha proton. Nmr studies using $Eu(fod)_3$ shift reagent on the alcohols (10a and 11a) collected from the BF_3 : etherate catalysed rearrangement were identical in all respects with analogous compounds prepared from reactions of sodium ethoxide with the appropriate epoxide.

Reaction of epoxide (6) with sodium ethoxide in dry ethanol under reflux for 5 hours gave exclusively the 1-ethoxyoctan-2-ol (9a). The ethoxy ion attacks the terminal epoxide carbon atom[29] with inversion occurring at that centre. The 1-ethoxyoctan-2-ols (10a, 11a) and their acetates (10b and 11b) were prepared by the standard procedures.

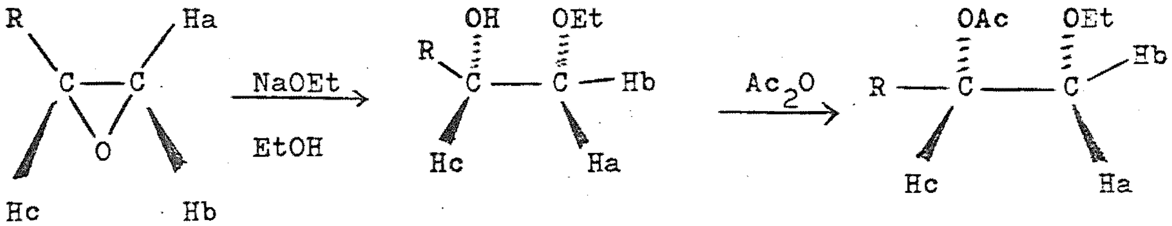


Fig. 10

Kolaczinski et.al.[18] have reported the formation of 1-ethoxy-2-octanol 4 and 2-ethoxy-1-octanol 3 (fig. 11) from

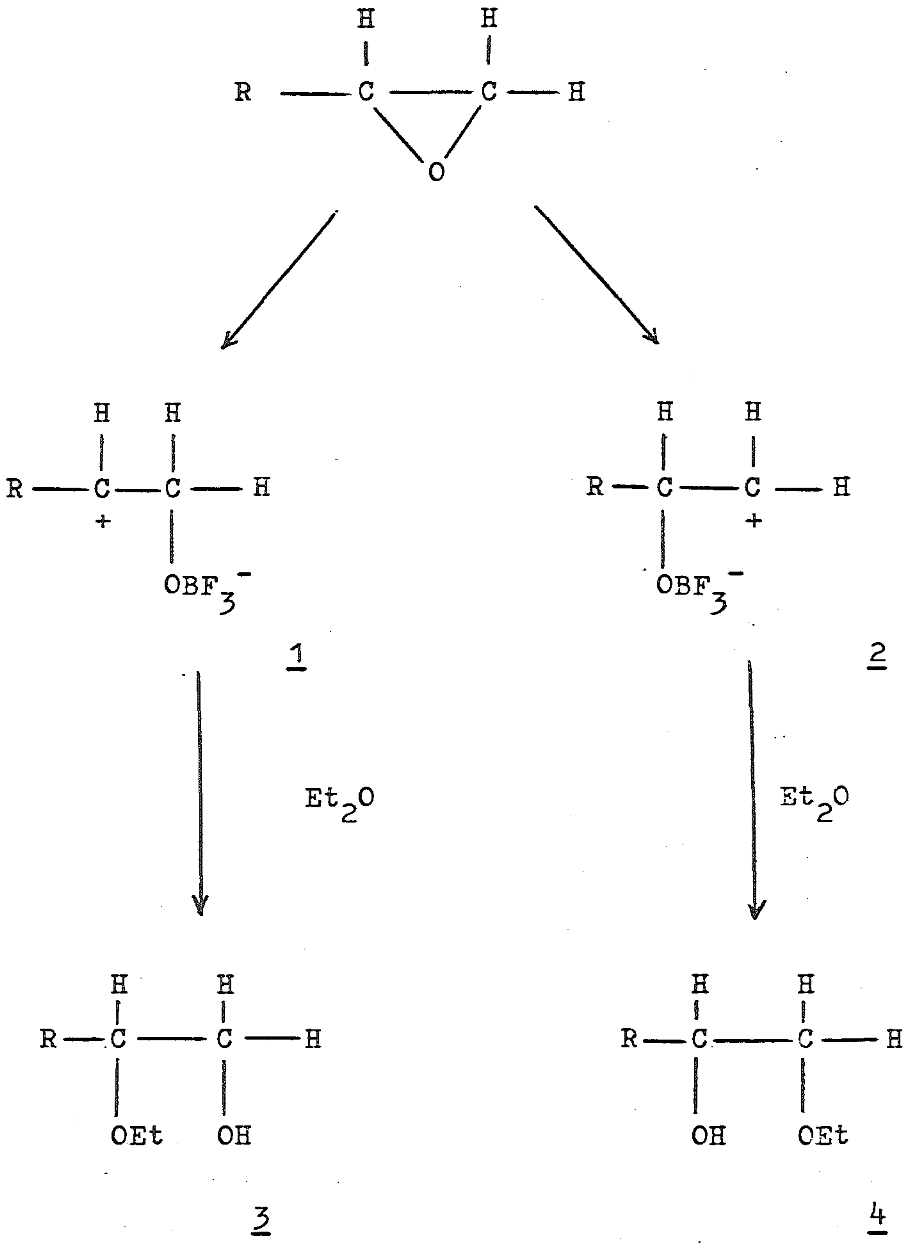


Fig. 11

the reaction of 1,2-epoxyoctane with BF_3 : etherate in ether and suggested the reaction proceeded via carbonium ion intermediates. The ethoxy group was thought to come from the solvent ether, since no other nucleophile was present.

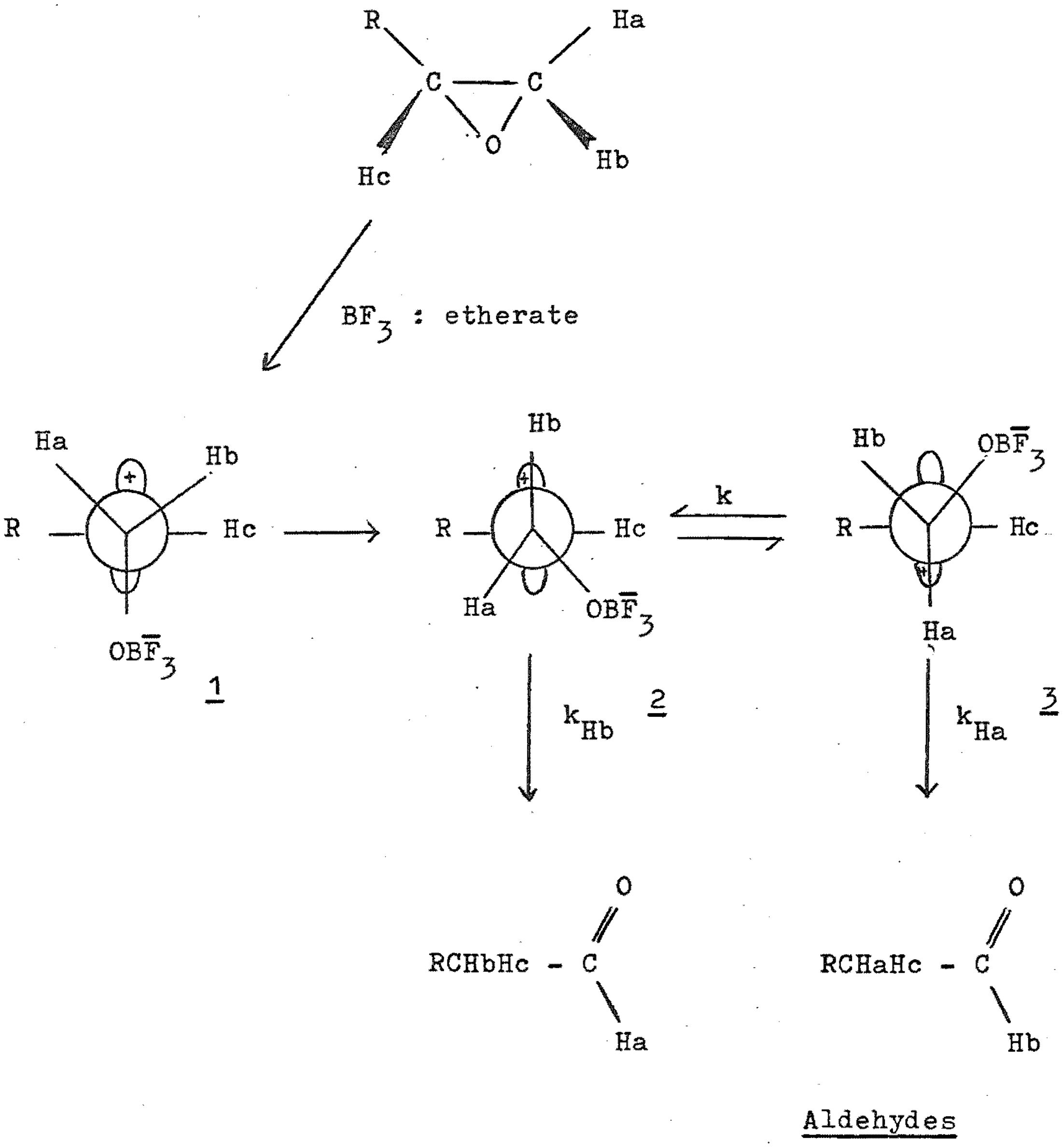
In our hands the major products were 1-ethoxy-2-octanol (9a, 60%) and aldehyde (14, 12%). A trace of 2-ethoxy-1-octanol could possibly be formed, as published in the literature, but could not be detected.

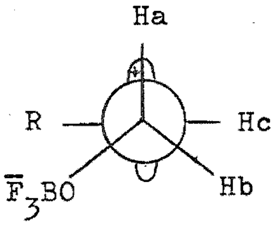
The stereochemistry of hydroxy-ether formation from reaction of epoxide with BF_3 : etherate in ether was examined by undertaking a study on both the mono and di-deuterated epoxides. In each case the product was found to have been formed with inversion at C(1).

The rearrangement of epoxide (6) with BF_3 : etherate in dioxane was fast, reaction being complete (g.l.c.) after 15 minutes. Gas chromatography analysis of the crude reaction product showed aldehyde (14, 60%) and three high boiling compounds. Attempts to separate the high boiling compounds on glass and steel preparative g.l.c. columns (to 180°C) was unsuccessful. No starting material was found. The aldehyde (14) was found to be identical to an authentic sample.

Reaction of each deuterated epoxide (7 and 8) with BF_3 : etherate in dioxane gave products from which mixtures of the deuterated aldehydes (15, 16) and (17, 18) respectively were separated. The ratio of aldehydes (15, 16) due to H or D migration from the reaction of epoxide (7) was determined from the relative integrals of the nmr resonances due to the methylene hydrogen ($\delta 2.41$) and the aldehyde proton ($\delta 9.78$).

Mechanistic Model of the BF_3 : Catalysed Rearrangement of 1,2-Epoxyoctane





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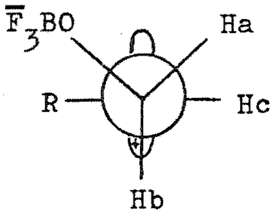

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Fig. 12

The presence of undeuterated epoxide (6) in the deuterated and dideuterated epoxides (7 and 8) was compensated for (see Appendices I and II). The ratio of aldehydes (15, H-migration: 16, D-migration) formed from epoxide (7) was found to be 4.78 : 1 (Table V). The ratio of aldehydes (17 and 18) formed from epoxide (8) was found in a similar manner to be 3.09 : 1 (Table VI). These results show a preference for the migration of hydrogen to deuterium.

The above results can be analysed in terms of the mechanistic model shown in Fig. 12 involving cleavage of the C-O bond in epoxide (6) to give a carbonium ion. The subsequent rotation about the C-C bond is directed by the interaction between the long chain aliphatic group (R) and the solvated OBF_3^- group. Conformer $\underline{2}$ is formed which allows Hb to migrate. Competing with Hb migration, the reversible equilibrium to conformer $\underline{3}$ is established in which Ha is favourably orientated to migrate. Conformers $\underline{4}$ and $\underline{5}$, due to *gauche* interaction between the large OBF_3^- and the R groups, are considered unlikely, and are not included in the calculation.

The relative values of the rate constants compared with $k_D = 1$ are calculated as $k_H = 4.36$ and $k = 10.6$ as evaluated by substituting the experimental ratios 1 : 4.78 for epoxide (7), [Ha = D and Hb = H] and 3.09 : 1 for epoxide (8), [Ha = H and Hb = D] into the following expression (Appendix III).

$$\frac{\text{Hb migration}}{\text{Ha migration}} = \frac{k_{Hb}}{k_{Ha}} \left[1 + \frac{k_{Ha}}{k}\right]$$

These results allow a measure for epoxide (6) of the preferred migration of Hb of ca. 1.41 : 1. This stereoselectivity confirms that the Hb migration (trans to R group) is more favourable than the Ha migration (cis to R group). For rearrangement of epoxide (6) the comparability in rate of hydride migration (k_H) and rate of the conformational change (k) is responsible for the stereoselectivity observed in the reaction rearrangement.

EXPERIMENTAL

Melting points are uncorrected. Infra-red spectra were recorded on a Shimadzu IR27G or a Perkin-Elmer 337 infra-red spectrophotometer, and are for liquid films only. Nuclear magnetic resonance spectra were obtained on a Varian T 60 spectrometer using $CDCl_3$ solutions with T.M.S. and $CHCl_3$ as internal standards. Analysis of apparent coupling is by first order. Micro-analyses were determined at the University of Otago. Mass spectra were determined on an AEI model M.S. 9 spectrometer. Analytical gas chromatography was performed on a Varian Aerograph 1200 using 2½% E.G.A. and SE 30 with stainless steel columns. Preparative g.l.c. was performed on an Aerograph Autoprep 705 using stainless steel columns packed with 8% E.G.A. and SE 30.

Fractional distillations were carried out using Nester Faust annular teflon two-foot spinning band columns.

The BF_3-etherate used was distilled until clear and distilled again immediately before use, collecting at 125 - 126°. Dioxane used was dried over molecular sieves for two weeks before use. Ethanol used was purified using magnesium turnings and iodine.

1-d-1-Octyne (2)

1-Octyne (1, 20 ml) in a 50 ml round bottomed flask fitted with a condenser and drying tube was agitated and heated to 70°C with deuterium oxide (5 ml) and calcium oxide (ca. 10 g) for 12 hours. The exchange of hydrogen with deuterium using fresh calcium oxide and deuterium oxide was repeated four times until no further exchange was apparent from the infra-red spectra. The increase in deuteration was followed from the intensity decrease of the ≡C-H stretch; (1-octyne) ν_{max} 3350 (≡C-H stretch), 2950, 2130 (C≡C stretch), 1460 cm^{-1}, nmr δ 0.88 (triplet, $(C8)H_3$), 1.38 (multiplet, $Wh/_2$ = 11 Hz; $(C4)H_2$-$(C7)H_2$), 1.90 (triplet, C≡C-H, J = 2 Hz), 2.18 (multiplet, $(C3)H_2$). (1-d-1-octyne) ν_{max} 2950, 2610 C≡C-D stretch), 1730 ~~1640~~ (C≡C stretch, very weak), 1460 cm^{-1} nmr δ 0.88 (triplet, $(C8)H_3$), 1.36 (multiplet, $Wh/_2$ = 11 Hz; $(C4)H_2$-$(C7)H_2$), 2.16 (distorted triplet, $(C3)H_2$).

The percentage of 1-d-1-octyne was calculated by comparison of infra-red peak intensities at 2950 cm^{-1} and 2875 cm^{-1} (C-H stretches) with the 3350 cm^{-1} (C≡C-H stretch) and showed that the mixture contained 96 ±1% of 1-d-1-octyne and 4% undeuterated 1-octyne. This result was consistant with mass spectra[30] intensity measurements on the M-1 and M-2 peaks (M-1 and M-2 peaks intensities were taken to be proportional to the M and M-1 peaks respectively). Another sample of the 1-d-1-octyne prepared and analysed by the same methods as above was found to contain 6% undeuterated 1-octyne.

1-Octene (3)

A 25 ml reaction flask of a low pressure hydrogenation apparatus was charged with 1-octyne (1, 2 ml), Lindlar catalyst (0.1 g), quinoline (0.5 ml) and pentane (7 ml). The apparatus was evacuated and hydrogen admitted to a pressure slightly above 1 atmosphere. Rapid absorption of hydrogen took place as stirring was started. After the absorption of 1 mole equivalent of hydrogen, the reaction mixture was filtered and solvent removed by distillation. A sample of 1-octene (3) was purified using preparative gas liquid chromotography (SE 30). ν_{max} 3100, 2950, 1648, 1460, 990, 913 cm^{-1}, nmr δ0.90 (triplet,(C8)H_3), 1.33 (multiplet, Wh/$_2$ = 7 Hz;(C4)H_2-(C7)H_2), 2.06 (multiplet, Wh/$_2$ = 11 Hz;(C3)H_2), 4.90 (doublet of doublets, $J_{Ha, Hc}$ = 18 Hz; $J_{Ha, Hb}$ = 2 Hz;(C1)Ha), 5.00 (doublet of doublets, $J_{Hb, Hc}$ = 10 Hz; $J_{Hb, Ha}$ = 2 Hz;(C1)Hb), 5.85 (multiplet,(C2)Hc).

(Z)-1-d-1-octene (4a)

(Z)-1-d-1-Octene (4a) was prepared from 1-d-1-octyne (2, 2 ml) using the same procedure as above. After the usual work-up, the olefin was isolated by fractional distillation. A small sample of (2)-1-d-1-octene (4a) was separated using preparative g.l.c. nmr δ 0.88 (triplet,(C8)H_3), 1.33 (multiplet, Wh/$_2$ = 8 Hz;(C4)H_2-(C7)H_2), 2.03 (multiplet, Wh/$_2$ = 12 Hz;(C3)H_2), 4.90 (doublet, $J_{Hb, Hc}$ = 10 Hz;(C1)Hb), 5.80 (multiplet, Wh/$_2$ = 19 Hz;(C2)Hc).

(E)-1,2-Dideutero-1-octene (5a)

(E)-1,2-Dideutero-1-octene (5a) was prepared by reduction of 1-octyne (1, 2 ml) with deuterium gas from a cylinder manufactured by Matheson in the presence of Lindlar catalyst. After the usual work-up, the solvent was removed by distillation and a small sample of (E)-1,2-dideutero-1-octene (5a) was separated for nmr using preparative g.l.c. nmr δ 0.88 (triplet,$(C8)H_3$), 1.33 (multiplet, $Wh/_2 = 7$ Hz;$(C4)H_2$-$(C7)H_2$), 2.03 (multiplet,$(C3)H_2$), 5.00 (singlet, $Wh/_2 = 8$ Hz;-(C1)Ha).

Preparation of deuterium gas [31]

Aluminium turnings (8 g) and mercurous chloride as catalyst were placed in a dried, three necked, 500 ml pear-shaped flask. The flask was connected to a nitrogen inlet, a separating funnel with D_2O (10 ml) and to the hydrogenation apparatus. The system was evacuated and flushed two times with nitrogen gas before D_2O was added to the aluminium turnings. The reaction mixture was slightly heated until D_2 gas started evolving. The deuterium gas was collected in a 2 litre glass cylinder in the hydrogenation apparatus ready for use. When sufficient deuterium gas was collected the reaction mixture was cooled using acetone dry ice.

(E)-1,2-Dideutero-1-octene (5a)

The second sample of (E)-1,2-dideutero-1-octene (5a) was prepared by semideuteration of 1-octyne (1, 2 ml) with deuterium gas prepared above in the presence of Lindlar catalyst. After the usual work-up, the solvent was removed by careful distillation and a small sample of (E)-1,2-dideutero-1-octene (5a) separated for nmr using preparative g.l.c.

The nmr spectra of the dideuterated octene indicated the sample was less pure than that prepared from deuterium gas manufactured by Matheson.

Preparation of monoperoxyphthalic acid

An ether solution of monoperoxyphthalic acid was prepared by stirring finely ground phthalic anhydride (70 g) and hydrogen peroxide (130 ml; 30%) in ether (600 mls) until all the solid had dissolved (ca. 4 hours). The solution was washed 5 times with saturated aqueous $(NH_4)_2SO_4$ and dried over anhydrous $MgSO_4$. The concentration of monoperoxyphthalic acid was determined by titration with thiosulphate.

1,2-Epoxyoctane (6)

Oct-1-ene (3, 20 ml) was treated with an excess of freshly prepared monoperoxyphthalic acid in ether (0.8 M) at room temperature for 7 days. The solution was washed several times with aqueous Na_2CO_3 and dried over anhydrous $MgSO_4$ (50 g). The product was purified by spinning band distillation to give 1,2-epoxyoctane (15 ml); (b.p.$_{17\ mm}$ 62.5 - 63.0^o), ν_{max} 3050, 2930, 2850, 1458, 1245, 918, 833, nmr δ 0.90 (triplet, (C8)H_3), 1.33 (multiplet, Wh/$_2$ = 15 Hz; (C3)H_2-(C7)H_2), 2.43 (doublet of doublets; $J_{Ha,\ Hc}$ = 3 Hz; $J_{Ha,\ Jb}$ = 5 Hz; (C1)Ha), 2.72 (doublet of doublets; $J_{Ha,\ Hb}$ = 5 Hz; $J_{Hb,\ Hc}$ = 5 Hz; (C1)Hb), 2.88 (multiplet, (C2)Hc).

(1R, 2S) 1S, 2R-1-d-1,2-Epoxyoctane (7)

The solution of the (Z)-1-d-1-octene (4a, 5 ml; crude solution of olefin prepared as above) was treated with a solution of monoperoxyphthalic acid in ether (20 g in 250 ml) and kept at room temperature for 7 days. After the usual work-up, the solvent was removed by careful distillation and epoxide isolated by preparative g.l.c. ν_{max} 2950, 2875, 1465, 1240, 920, 840 cm^{-1}, nmr δ0.90 (triplet(C8)H_3), 1.33 (multiplet, Wh/$_2$ = 16 Hz;(C3)H_2-(C7)H_2), 2.72 (doublet, $J_{Hb, Hc}$ = 3 Hz; (C1)Hb), 2.88 (multiplet,(C2)Hc).

(1S, 2S)1R, 2R-1,2-Dideutero-1,2-epoxyoctane (8)

The solution of the (E)-1,2-dideutero-oct-1-ene (5a, 5 ml; 97% D_2, crude solution of olefin) was treated with a solution of monoperoxyphthalic acid in ether (20 g in 250 ml) and kept at room temperature for 7 days. After the usual work-up, fractionation of solvents and preparative g.l.c. gave the (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8). ν_{max} 2950, 2850, 1458, 900, nmr δ 0.90 (triplet,(C8)H_3), 1.33 (multiplet, Wh/$_2$ = 16 Hz; (C3)H_2-(C7)H_2), 2.43 (singlet,(C1)Ha). Another sample of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) was prepared by the same method as above using the (E)-1,2-dideutero-oct-1-ene (5a, 5 ml; 86% D_2, crude solution of olefin prepared from deuterium gas obtained from aluminium turnings and D_2O). After the usual work-up, fractionation of solvents and preparative g.l.c. gave the (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8). The nmr spectra of the epoxide was found to be less pure than that above prepared from deuterium gas from the cylinder.

Rearrangement of 1,2-epoxyoctane (6) with BF_3: etherate in ether

To a solution of epoxide (6, 1 ml) in sodium dried ether (100 ml) was added BF_3: etherate (4 ml). The reaction was stirred and kept at room temperature for 5 hours and then quenched with saturated potassium carbonate (5 ml). After a further 15 minutes stirring, anhydrous potassium carbonate was added and the reaction mixture left to stir for another 20 mins. The solid was removed by filtration and the solvent by careful distillation. The crude reaction product was shown by g.l.c. to contain aldehyde (14, 12%) and 1-ethoxy-octan-2-ol (9a, 60%). Octyldehyde (14); ν_{max} 2950, 1730, 1460 cm^{-1}, nmr 0.88 (triplet(C8)H_3), 1.33 (multiplet, $Wh/_2 = 7$ Hz; (C3)H_2-(C7)H_2), 2.41 (distorted triplet, J = 7 Hz; (C2)H_2), 9.78 (triplet, $J_{CHO,\ CH_2} = 1$ Hz; CHO). The nmr spectrum was identical in all aspects with an authentic sample. 1-Ethoxy-octan-2-ol (9a), ν_{max} 3450, 2950, 1470 cm^{-1}, nmr δ 0.88 (triplet,(C8)H_3), 1.20 (triplet, $-O-CH_2-\underline{CH_3}$), 1.33 (multiplet, $Wh/_2 = 5$ Hz; (C3)H_2-(C7)H_2), 2.30 (singlet, $Wh/_2 = 6$ Hz; OH), 3.53 (quartet, J = 7 Hz; $O-\underline{CH_2}-CH_3$), 3.20 (doublet of doublets, $J_{Ha,\ Hb} = 8$ Hz; $J_{Hb,\ Hc} = 8$ Hz; (C1)Hb), 3.47 (doublet of doublets; $J_{Ha,\ Hb} = 8$ Hz; $J_{Ha,\ Hc} = 3$ Hz; (C1)Ha), 3.50 (multiplet, $Wh/_2 = 15$ Hz; Hc). Found : C, 69.36; H, 13.12; $C_{10}H_{22}O_2$ requires C, 68.92; H_2 12.72 (Lit. cit.[18] C, 68.73; H, 12.78). The nmr spectrum was found to be identical to an authentic sample prepared by reaction of epoxide (6) with sodium ethoxide.

Rearrangement of (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) with BF_3 : etherate in ether

The rearrangement of monodeuterated epoxide (7, 1 ml) in ether was carried out in the manner described for the undeuterated epoxide (6). The major product, (1S, 2S)1R, 2R-1-d-1-ethoxy-octan-2-ol (10a), was isolated using preparative g.l.c. nmr δ 0.88 (triplet, $(C8)H_3$, 1.20 (triplet, $O\text{-}CH_2\text{-}\underline{CH_3}$), 1.33 (multiplet, $Wh/_2$ = 8 Hz; $(C2)H_2\text{-}(C7)H_2$), 2.33 (singlet, $Wh/_2$ = 8 Hz; OH), 3.52 (quartet, J = 7 Hz; $\text{-}O\text{-}\underline{CH_2}\text{-}CH_3$), 3.21 (doublet, $J_{Hb,\ Hc}$ = 8 Hz; (C1)Hb), 3.50 (multiplet, Hc). The nmr spectrum was found to be identical to an authentic sample prepared by reaction of epoxide (7) with sodium ethoxide.

Rearrangement of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) with BF_3 : etherate in ether

The rearrangement of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8, 1 ml) in ether was carried out in the same fashion as described for the undeuterated epoxide (6). The major product, (1R, 2S)1S, 2R-1,2-dideutero-1-ethoxy-octan-2-ol (11a), was isolated using preparative g.l.c. nmr δ 0.88 (triplet, $(C8)H_3$), 1.20 (triplet, $O\text{-}CH_2\text{-}\underline{CH_3}$), 1.33 (multiplet, $Wh/_2$ = 8 Hz; $(C3)H_2\text{-}(C7)H_2$), 2.49 ($Wh/_2$ = 2.5 Hz), 3.51 (quartet, J = 7 Hz; $O\text{-}\underline{CH_2}\text{-}CH_3$), 3.41 (singlet, (C1)Ha). The nmr spectrum was identical to an authentic sample prepared by reaction of epoxide (8) with sodium ethoxide.

(1-Ethoxy-octan-2-ol (9a)). Reaction of 1,2-epoxyoctane (6) with sodium ethoxide in ethanol

Sodium ethoxide was prepared by gradually adding sodium pieces (0.2 g) to dried ethanol (50 ml) in a 50 ml round bottomed flask fitted with condenser and drying tube. The 1,2-epoxyoctane (6, 100 mg) was added to the ethoxide and the reaction mixture was heated under reflux for 5 hours. The reaction mixture was then poured into a 50 : 50 mixture of ether and water. The ether layer was separated and dried over $MgSO_4$. The solvent was removed under slight vacuum to give the 1-ethoxy-octan-2-ol (9a). nmr δ 0.88 (triplet, $(C8)H_3$), 1.20 (triplet, $-O-CH_2-\underline{CH_3}$), 1.33 (multiplet, $W_{h/2}$ = 5 Hz; $(C3)H_2-(C7)H_2$), 2.30 (singlet, $W_{h/2}$ = 6 Hz; OH), 3.53 (quartet, J = 7 Hz; $O-\underline{CH_2}-CH_3$), 3.20 (doublet of doublets, $J_{Ha, Hb}$ = 8 Hz; $J_{Hb, Hc}$ = 8 Hz; (C1)Hb), 3.47 (doublet of doublets; $J_{Ha, Hb}$ = 8 Hz; $J_{Ha, Hc}$ = 3 Hz; (C1)Ha), 3.50 (multiplet, $W_{h/2}$ = 15 Hz; Hc).

[(1S, 2S)1R, 2R-1-d-Ethoxy-octan-2-ol (10a)]. Reaction of (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) with sodium ethoxide in ethanol

The reaction of sodium ethoxide and (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) was carried out as for the undeuterated epoxide (6). After work-up the solvent was removed under slight vacuum and the resulting alcohol (10a) was obtained. nmr δ 0.88 (triplet, $(C8)H_3$), 1.20 (triplet, $O-CH_2-\underline{CH_3}$), 1.33 (multiplet, $W_{h/2}$ = 8 Hz; $(C3)H_2-(C7)H_2$), 2.33 (singlet, $W_{h/2}$ = 8 Hz, OH), 3.52 (quartet, J = 7 Hz; $-O-\underline{CH_2}-CH_3$), 3.21 (doublet, $J_{Hb, Hc}$ = 8 Hz; (C1)Hb), 3.50 (multiplet, Hc).

[(1R, 2S)1S, 2R-1,2-Dideutero-1-ethoxy-octan-2-ol (11a)] Reaction of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) with sodium ethoxide in ethanol

The reaction of sodium ethoxide and (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) was carried out as for the undeuterated epoxide (6). After work-up the solvent was removed under a slight vacuum and the resulting alcohol (11a) was obtained. nmr δ 0.88 (triplet, $(C8)H_3$), 1.20 (triplet, $O\text{-}CH_2\text{-}\underline{CH_3}$), 1.33 (multiplet, $Wh/_2$ = 8 Hz; $(C3)H_2\text{-}(C7)H_2$), 2.49 ($Wh/_2$ = 2.5 Hz), 3.51 (quartet, J = 7 Hz; $O\underline{CH_2}CH_3$), 3.41 (singlet, (C1)Ha).

Acetylation of 1-ethoxyoctan-2-ol (9a)

Acetic anhydride (0.5 ml) was added to a solution of 1-ethoxyoctan-2-ol (9a, 100 mg) in dry pyridine (2 ml) and the reaction left overnight at room temperature. The reaction mixture was poured into water-ether mixture (50 ml) and then washed several times with very dilute H_2SO_4 (3% concentration) and with $NaHCO_3$ aq. The ether layer was then washed with water and dried over $MgSO_4$. Isolation of the product in the usual manner gave a quantitative yield of acetate (9b). ν_{max} 3000, 2950, 1755, 1470, 1370, 1245, 1130 cm^{-1}. nmr δ 0.90 (triplet, $(C8)H_3$), 1.18 (triplet, $O\text{-}CH_2\text{-}\underline{CH_3}$), 1.33 (multiplet, $Wh/_2$ = 5 Hz; $(C3)H_2\text{-}(C7)H_2$), 2.05 (singlet, OAc), 3.46 (doublet, $J_{Ha,\ Hb}$ = 5 Hz; (C1)Ha and (C1)Hb), 5.00 (quintet, J = 5 Hz; (C2)Hc), 3.50 (quartet, J = 7 Hz, $O\text{-}\underline{CH_2}\text{-}CH_3$).
Found: C, 66.17; H, 10.67; $C_{12}H_{24}O_3$ requires C, 66.63; H, 11.18.
Mass spectrum (70 ev) $m/_e$ = 173 ($M\text{-}CH_3CO^+$), 156 ($M\ \text{-}CH_3COOH^+$), 97 ($156\text{-}C_2H_5OCH_2^+$), 85 ($C_6H_{13}^+$), 59 ($C_2H_5OCH_2^+$), 43 (CH_3CO^+).

Acetylation of (1S, 2S)1R, 2R-1-d-1-ethoxy-octan-2-ol (10a)

Acetylation of the secondary alcohol (10a) was effected as above. After work-up the solvent was removed under slight vacuum. The product (1S, 2S)1R, 2R-1-d-1-ethoxy-2-acetoxy-octane (10b) was obtained. ν_{max} 2950, 1740, 1230 cm^{-1}, nmr δ 0.88 (triplet, $(C8)H_3$), 1.17 (triplet, $O\text{-}CH_2\text{-}\underline{CH_3}$), 1.33 (multiplet, $Wh/_2 = 5$ Hz; $(C3)H_2\text{-}(C7)H_2$, 2.05 (singlet, -OAc), 3.50 (quartet, $O\underline{CH_2}\text{-}CH_3$), 5.00 (multiplet, (C2)Hc), 3.43 (doublet, J = 6 Hz, (C1)Hb). Mass spectrum (70 ev) $m/_e$ = 174 ($M\text{-}CH_3CO^+$), 157 ($M\ \text{-}CH_3COOH^+$), 97 ($157\text{-}C_2H_5OCHD^+$), 85 ($C_6H_{13}^+$), 60 ($C_2H_5OCHD^+$), 43 (CH_3CO^+).

Acetylation of (1R, 2S)1S, 2R-1,2-dideutero-1-ethoxy-octan-2-ol (11a)

Acetylation of the secondary alcohol (11a) was carried out in the same manner as for the undeuterated alcohol (9a). After work-up the solvent was removed under vacuum to give (1R, 2S)1S, 2R-1,2-dideutero-1-ethoxy-2-acetoxyoctane (11b). ν_{max} 2950, 1740, 1235 cm^{-1}. nmr δ 0.88 (triplet, $(C8)H_3$), 1.18 (triplet, $\text{-}OCH_2\text{-}\underline{CH_3}$), 1.33 (multiplet, $Wh/_2 = 5$ Hz; $(C3)H_2\text{-}(C7)H_2$), 2.07 (singlet, -OAc), 3.43 (singlet, (C1)Ha), 3.50 (quartet, $O\text{-}CH_2\text{-}CH_3$). Mass spectrum (70 ev) $m/_e$ = 175 ($M\text{-}CH_3CO$), 158 ($M\ \text{-}CH_3COOH^+$), 98 ($158\text{-}C_2H_5OCHD^+$), 60 ($C_2H_5OCHD^+$), 43 (CH_3CO^+).

Reaction of 1,2-epoxyoctane (6) with lithium aluminium hydride

The epoxide (6, 80 mg) in ether (5 ml) was reacted with 3 equivalents of LAH and the mixture refluxed for 2 hours. Excess LAH was removed by careful addition of hydrated crystals of sodium sulphate, followed by a few drops of water till the mixture formed a white precipitate. The solution was filtered, dried with anhydrous $MgSO_4$ and after removal of solvent gave octan-2-ol (19). ν_{max} 3350 cm^{-1}, nmr δ 0.88 (triplet, $(C8)H_3$), 1.23 (triplet $(C1)H_3$), 1.35 (multiplet, $Wh/_2$ = 11 Hz; $(C3)H_2$-$(C7)H_2$, 1.82 (singlet, (C2)OH), 3.78 (multiplet, $Wh/_2$ = 16 Hz; -C$\underline{H}$-OH Me).

Reaction of (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) with lithium aluminium hydride

The reduction reaction with LAH was carried out on epoxide (7), similar to that of the undeuterated epoxide (6) above. After work-up the solvent was removed giving 1-d-octan-2-ol. (20). ν_{max} 3350 cm^{-1}, nmr δ 0.88 (triplet, $(C8)H_3$), 1.17 (doublet, J = 7 Hz; $(C1)CDH_2$), 1.35 (multiplet, $Wh/_2$ = 11 Hz; $(C3)H_2$), 1.93 (singlet, (C2)OH), 3.73 (multiplet, $Wh/_2$ = 18 Hz; -C$\underline{H}$-OH-CH_2D).

Reaction of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) with lithium aluminium hydride

Similar reduction reaction was carried out using epoxide (8) and LAH as above. After work-up the solvent was removed giving 1,2-dideutero-octan-2-ol (21). ν_{max} 3350 cm^{-1}, nmr δ 0.88 (triplet, $(C8)H_3$), 1.18 (singlet, $(C1)CH_2D$), 1.35 (multiplet, $Wh/_2$ = 11 Hz; $(C3)H_2$-$(C7)H_2$), 2.13 (singlet, (C2)OH).

Rearrangement of 1.2-epoxyoctane (6) with BF_3 etherate in dioxane

To a solution of epoxide (6, 500 mg) in dry dioxane (3 ml) was added BF_3 : etherate (500 mg). The reaction was stirred at room temperature for 15 minutes. Anhydrous potassium carbonate was added and the reaction mixture was further stirred for another half an hour. The solid was removed by filtration and solvent by careful distillation. The crude reaction product shown by g.l.c. contained aldehyde (14, 60%) and inseparable high boiling compounds. Octyldehyde (14), ν_{max} 1730 cm^{-1}.

nmr δ 0.88 (triplet, $(C8)H_3$), 1.33 (multiplet, $Wh/_2$ = 7 Hz; $(C3)H_2$-$(C7)H_2$), 2.41 (distorted triplet, $(C2)H_2$), 9.78 (triplet, J_{CHO, CH_2} = 2 Hz; C$\underline{H}$O). Mass spectra showed parent peak at $m/_e$ at 128.

Rearrangement of (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7) with BF_3 : etherate in dioxane

The rearrangement of monodeuterated epoxide (7, 500 mg) in dioxane (3 ml) was carried out in the same fashion as described for the undeuterated epoxide (6). After the usual work-up, the solvent was removed by careful distillation and the monodeuterated aldehydes (15 and 16) obtained by preparative g.l.c. ν_{max} 1730 cm^{-1}, nmr δ 0.88 (triplet, $(C8)H_3$), 1.33 (multiplet, $Wh/_2$ = 7 Hz; $(C3)H_2$-$(C7)H_2$), 2.40 (distorted triplet, $(C2)H_2(HD)$, 9.75 ($Wh/_2$ = 1 Hz, CHO(CDO)). Mass spectra showed parent peak at $m/_e$ 129.

Also in the mixture of aldehydes (15 and 16) was the undeuterated aldehyde (14) due to the presence of epoxide (6), 4% (6%) (determined from infra-red spectra of the starting octyne) in the starting epoxide. (Samples 1, 2 and 3 in Table 5 were from epoxide (7) containing 4% undeuterated epoxide (6) and sample 4 was from epoxide (7) containing 6% undeuterated epoxide (6)). The total integral A* (average of 5 integrals) of the C-2 proton(s) at δ 2.41 and B(average of 5 integrals) of the C-1 proton at δ 9.75 were recorded for these mixtures. The ratio of hydrogen migration to deuterium migration for epoxide (7) was determined (Appendix I) and tabulated. (Table 5).

Table 5

Rearrangement of (1R, 2S)1S, 2R-1-d-1,2-epoxyoctane (7)

C-1 and C-2 integrals are in arbitrary units.

Rearrangement of

A^* integral of C2-H ; B relative integral of C1-H

Corrections to allow for 4% undeut. epoxide

Exp	A*	s.d.	B	s.d.	A*+B	M"	M	B' D migr	M-B' H migr	$\frac{M-B'}{B'}$ hydrogen / deuterium
1.	34.0	0.6	3.88	0.07	37.88	18.57	17.83	3.14	14.69	4.68
2.	38.3	0.4	4.24	0.07	42.54	20.85	20.02	3.40	16.61	4.88
3.	33.8	0.5	3.79	0.10	37.59	18.43	17.69	3.05	14.64	4.79
4.	31.8	0.5	3.86	0.05	35.66	17.31	16.27	2.82	13.45	4.76

The average ratio of hydrogen migration to deuterium migration is $\frac{M-B'}{B'} = \frac{M_H^D}{M_D^H} = \underline{4.78}$ s.d. 0.06.

Rearrangement of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxyoctane (8) with BF_3 : etherate in dioxane

The rearrangement of dideuterated epoxide (8, 500 mg) in dioxane was carried out in the same manner as that for the undeuterated epoxide (6). After the usual work-up, the solvent was removed by careful distillation and the dideuterated aldehydes (17 and 18) obtained by preparative g.l.c. ν_{max} 1725 cm^{-1}, nmr δ 0.88 (triplet, $(C8)H_3$), 1.33 (multiplet, $Wh/_2$ = 7 Hz; $(C3)H_2$-$(C7)H_2$), 2.40 (distorted triplet, $(C2)H_2$), 9.78 (singlet, $Wh/_2$ = 1 Hz; $CD_2C\underline{H}O$(CDHCDO). Mass spectra showed parent peak at $m/_e$ 130.

Also in the mixture of aldehydes (17 and 18) was the undeuterated aldehyde (14) due to the presence of epoxide (6), 3% (14%) (estimated from nmr spectrum of dideuterated alkene and epoxide) in the starting epoxide. (Samples 1, 2 and 3 in table 6 were from epoxide (8) containing 3% undeuterated epoxide (6) and sample 4 was from epoxide (8) containing 14% undeuterated epoxide (6)). The total integral A (average of 5 integrals) of the C-2 proton at δ 2.41 and B of the C-1 proton at δ 9.78 were recorded for these mixtures. The ratio of hydrogen migration to deuterium migration for the epoxide (8) was then determined (Appendix II) and tabulated below (Table 6).

Table 6

Rearrangement of (1S, 2S)1R, 2R-1,2-dideutero-1,2-epoxy-octane (8)

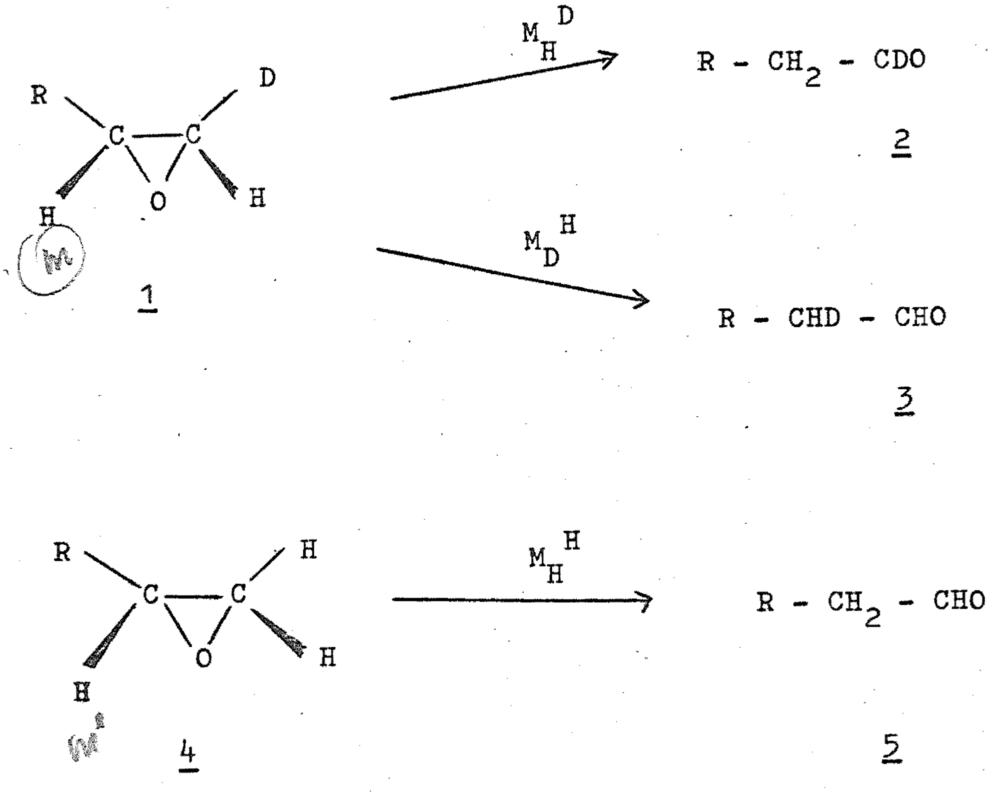
C-1 and C-2 integrals are in arbitrary units.

	A		B		A+B	M"	M	B'	M-B'	$\frac{M-B'}{B'}$
		s.d.		s.d.						
1	30.3	0.9	10.1	0.1	40.4	38.11	36.97	8.96	28.01	3.13
2	42.1	1.0	13.9	0.1	56.0	52.83	51.25	12.31	38.93	3.16
3	30.2	0.9	9.9	0.1	40.1	37.83	36.69	8.77	27.92	3.18
4	25.3	0.9	9.9	0.1	35.2	27.50	23.65	6.05	17.60	2.91

Similar values were obtained in expts using 80% dideuterated epoxide

The average $\frac{M-B'}{B'} = \frac{\text{H migration}}{\text{D migration}}$ = $\underline{3.09}$ s.d. $\underline{0.09}$

APPENDIX I



M + M' = M''

M_H^D = migration of hydrogen from a CHD carbon.

M_D^H = migration of deuterium from a CHD carbon.

M_H^H = migration of hydrogen from a CH_2 carbon.

Fig. 13

Epoxide 1 rearranges to aldehydes 2 and 3 and epoxide 4 rearranges to aldehyde 5.

A* and B were total integrals of C-2 and C-1 protons (aldehydes 2, 3 and 5) respectively.

Let M = the integral of (C2)H in epoxide 1 and M' = the integral of (C2)H in epoxide 4. M + M' = M" = total integral measurement of (C2)H in epoxides 1 and 4.

Then for monodeuterated epoxide with 96% D at C-1;

$$M = {}^{96}/_{100}\, M''$$

and $$M' = {}^{4}/_{100}\, M''$$

From Fig. 13 above;

$$A^* = CH_2(\underline{2}) + CHD(\underline{3}) + CH_2(\underline{5}) \qquad (1)$$

$$B = CHO(\underline{3}) + CHO(\underline{5}) \qquad (2)$$

$$\underline{B'} = CHO(\underline{3}) \text{ (a measure of deuterium migration)}$$

$$\therefore B' = B - CHO(\underline{5})$$

$$B' = B - M' \qquad (3)$$

$\underline{M - B'}$ = an integral measurement of hydrogen migration from C-1 to C-2 in epoxide 1 and

M' = an integral measurement of hydrogen migration from C-1 to C-2 in epoxide 4.

From equation (1);

$$A^* = CH_2(\underline{2}) + CHD(\underline{3}) + CH_2(\underline{5})$$

$$= M + M' + M - B' + M'$$

2

Equating in terms of M";

$$A^* = M'' + \frac{96}{100} M'' - (B - M') + {}^{4}/_{100}\, M''$$

$$A^* = 2.04\, M'' - B$$

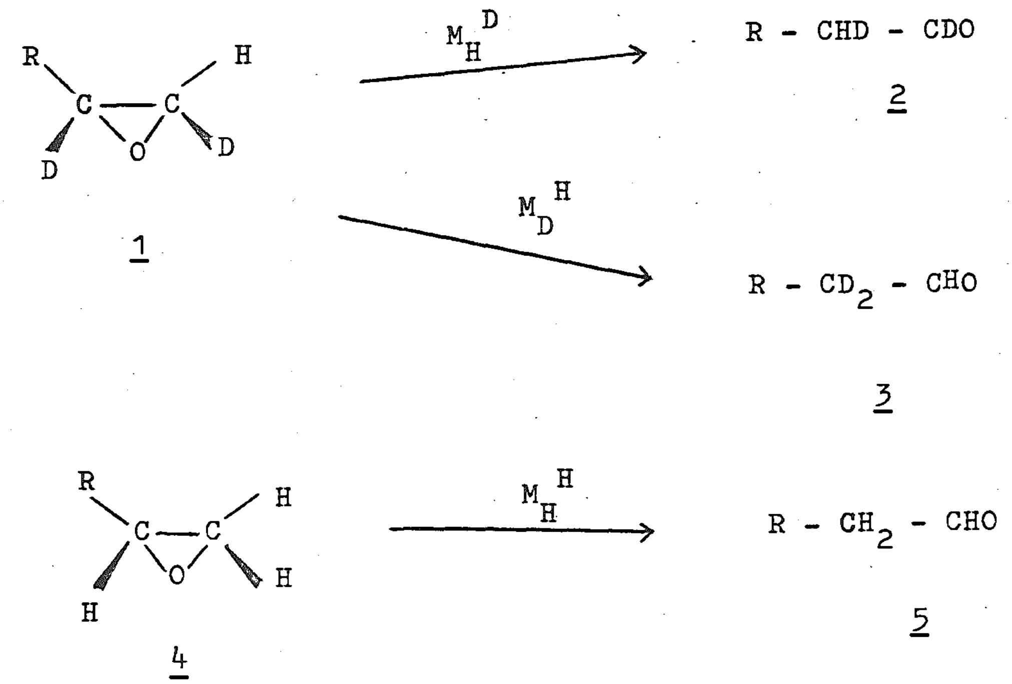
$$M'' = \frac{A^* + B}{2.04} \qquad (4)$$

$\frac{A^* - B}{2} = M''$

Similarly, we can work out the equation for M" for the monodeuterated epoxide containing 94% D at C-1.

$$M'' = \frac{A^* + B}{2.06} \qquad (5)$$

APPENDIX II



M_H^D, M_D^H and M_H^H are as defined in Appendix I.

Fig. 14

Dideuterated epoxide 1 and epoxide 4 rearranged to aldehydes 2, 3 and 5 respectively.

A and B were total integrals of C-2 and C-1 protons for the aldehyde mixtures containing 2, 3 and 5.

Let M = the integral measurement of 1 proton in epoxide 1

and M' = the integral measurement of 1 proton in epoxide 4

then M + M' = M'' = total integral measurement of the (C1)H in epoxide 1 and the (C2)H in epoxide 4.

For dideuterated epoxide with 97% D at C-1 and C-2

$$M = {}^{97}/_{100}\ M''$$

$$M' = {}^{3}/_{100}\ M''$$

From Fig. 14 above;

$$A = CHD(\underline{2}) + CH_2(\underline{5}) \qquad (1)$$

$$B = CHO(\underline{3}) + CHO(\underline{5}) \qquad (2)$$

$\underline{B'} = CHO(\underline{3})$ (a measure of deuterium migration)

$$\therefore B' = B - CHO(\underline{5})$$

$$B' = B - M' \qquad (3)$$

$\underline{M - B'}$ = an integral measurement of hydrogen migration from C-1 to C-2 in epoxide $\underline{1}$ and,

M' = an integral measurement of hydrogen migration from C-1 to C-2 in epoxide $\underline{4}$.

From equation (1);

$$A = CHD(\underline{2}) + CH_2(\underline{5})$$

$$= M - B' + M' + M'$$

Equating A in terms of M";

$$A = {}^{97}/_{100}\, M'' - (B - {}^{3}/_{100}\, M'') + 2({}^{3}/_{100}\, M'')$$

$$A = 1.06\, M'' - B$$

$$M'' = \frac{A + B}{1.06} \qquad (4)$$

Similarly, we can work out the equation for M" for dideuterated epoxide containing 86% D at C-1 and C-2.

$$M'' = \frac{A + B}{1.28} \qquad (5)$$

APPENDIX III

Calculation of the ratio of Hb to Ha migration for the reaction scheme Fig. 12.

Using the area integration method, the ratio of products, P and Q resulting from the simplified reaction scheme below, substrate S and intermediates A and B and T can be evaluated.

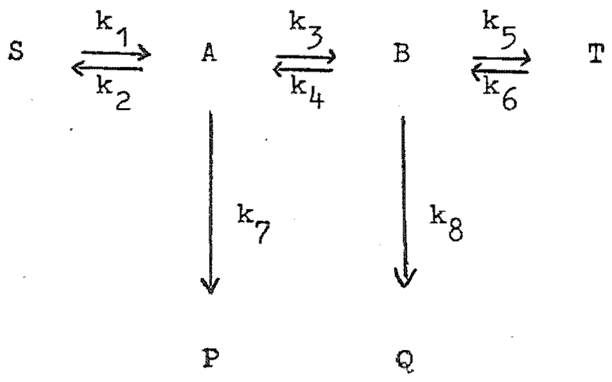


Fig. 15

Let x_i be concentration of I at time t. (I = S, A, B or T).

For intermediate T,

$$\frac{d(x_t)}{dt} = k_5x_b - k_6x_t$$

Integrating from t = 0 to t = ∞

$$[x_t]_o^{\infty} = k_5S_b - k_6S_t = 0 \qquad (1)$$

For intermediate B,

$$\frac{d(x_b)}{dt} = k_3x_a + k_6x_t - (k_4 + k_5 + k_8)x_b.$$

Integrating from $t = 0$ to $t = \infty$

$$[x_b]_0^{\infty} = k_3S_a + k_6S_t - (k_4 + k_5 + k_8)Sb = 0 \qquad (2)$$

Subtracting (1) from (2)

$$k_3Sa - (k_4 + k_8)Sb = 0 \qquad (3)$$

The ratio of P and Q for complete reaction is

$$\frac{Sa}{Sb} = \frac{k_4 + k_8}{k_3}$$

$$\frac{m_p}{m_q} = \frac{k_7Sa}{k_8Sb} = \frac{k_7}{k_8}\,\frac{(k_4 + k_8)}{k_3} \qquad (4)$$

k_1, k_2, k_5 and k_6 were eliminated in the subtracting and hence not enter the equation.

Taking S to represent epoxide (6), T its epimers, and A and B the carbonium ion (Fig. 12) in conformation <u>2</u> and <u>3</u> respectively, then $k_3 = k_4 = k$, $k_7 = k_{Ha}$ and $k_8 = k_{Hb}$. Equation (4) gives

$$\frac{\text{Ha migration}}{\text{Hb migration}} = \frac{k_{Ha}}{k_{Hb}}\left[1 + \frac{k_{Hb}}{k}\right] \qquad (5)$$

Similarly, taking $k_7 = k_{Hb}$ and $k_8 = k_{Ha}$, equation (4) gives

$$\frac{\text{Hb migration}}{\text{Ha migration}} = \frac{k_{Hb}}{k_{Ha}}\left[1 + \frac{k_{Ha}}{k}\right]$$

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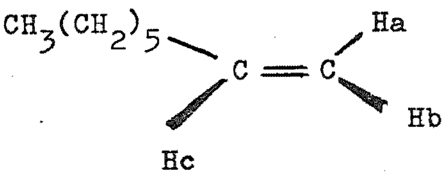
$CH_3(CCH_2)_5C\equiv CH$

1

$CH_3(CH_2)_5C\equiv CD$

2



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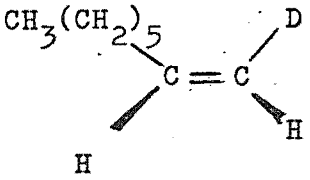

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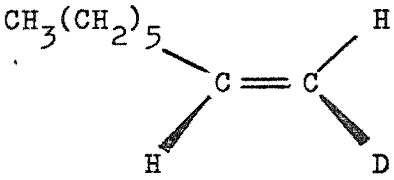
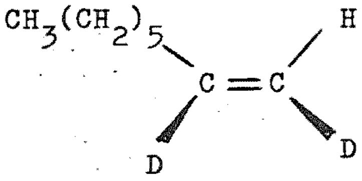
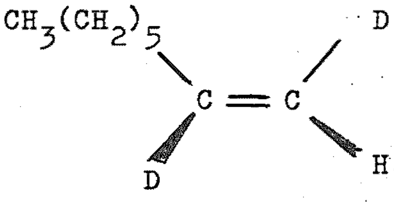


4b



5a



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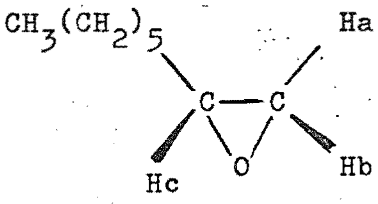

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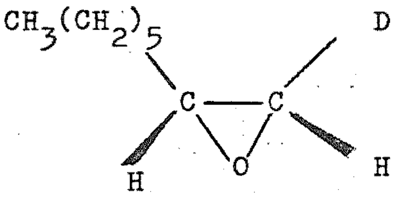

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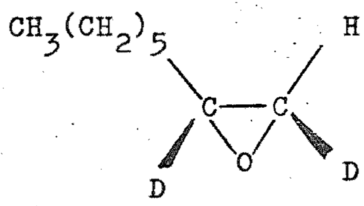

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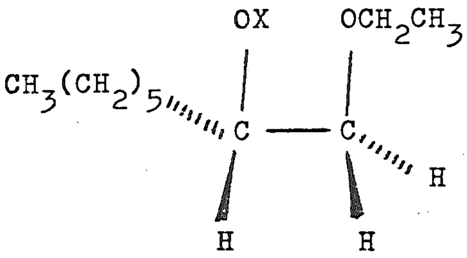
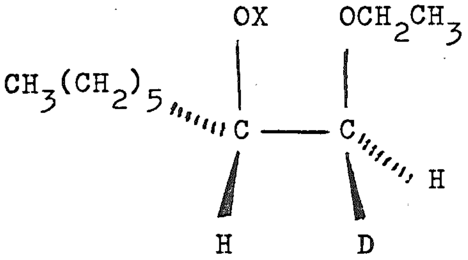


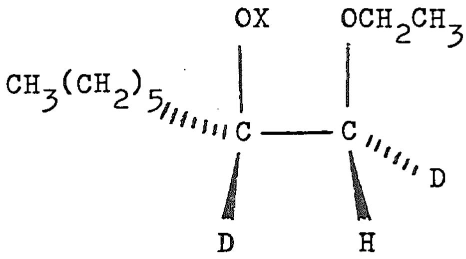
9 a) X = H

b) X = Ac



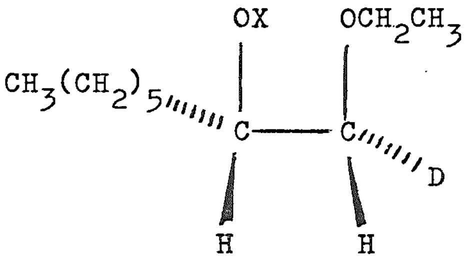
10 a) X = H

b) X = Ac



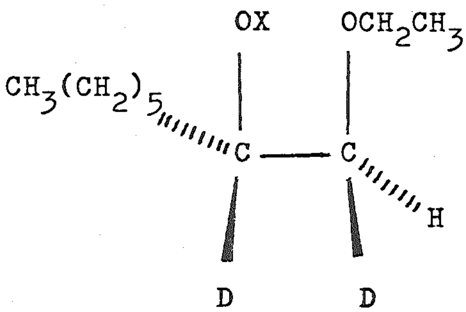
11 a) X = H

b) X = Ac



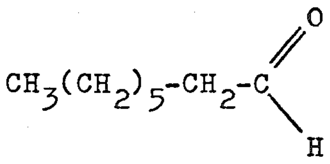
12 a) X = H

b) X = Ac



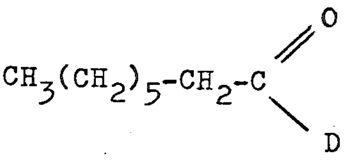
13 a) X = H

b) X = Ac



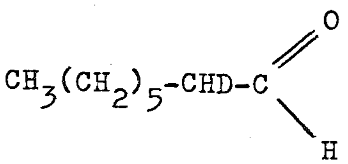
$CH_3(CH_2)_5\text{-}CH_2\text{-}C(=O)H$

14



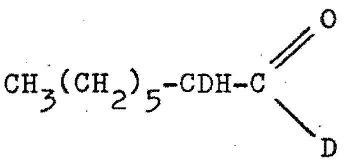
$CH_3(CH_2)_5\text{-}CH_2\text{-}C(=O)D$

15

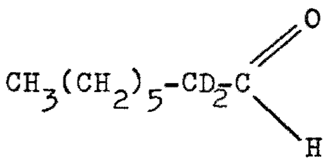


$CH_3(CH_2)_5\text{-}CHD\text{-}C(=O)H$

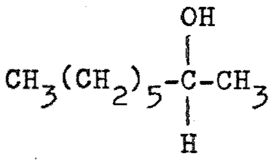
16



17

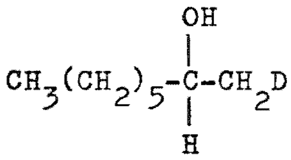


18



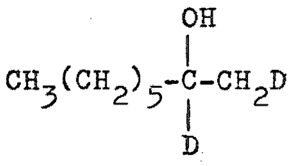
$CH_3(CH_2)_5\text{-}\overset{OH}{\underset{H}{C}}\text{-}CH_3$

19



$CH_3(CH_2)_5\text{-}\overset{OH}{\underset{H}{C}}\text{-}CH_2D$

20



$CH_3(CH_2)_5\text{-}\overset{OH}{\underset{D}{C}}\text{-}CH_2D$

21