

**347. Stereochemical Studies of Olefinic Compounds. Part III. Ring Scission of 3-Halogeno-2-alkyltetrahydrofurans as a Route to Alk-3-en-1-ols of Known Configuration and as a Method of Chain Extension by Four Methylene Groups.**

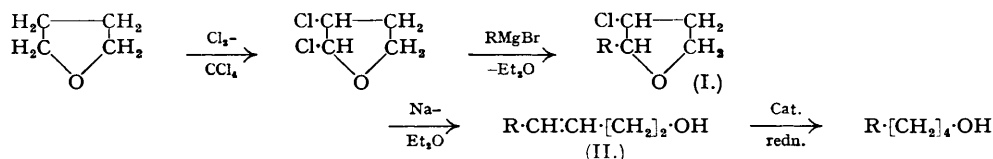
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The preparation and ring scission of 3-chloro-2-alkyltetrahydrofurans is investigated as a route to alk-3-en-1-ols and thence, by catalytic reduction, as a method of chain extension by four methylene groups.

Interaction of 2:3-dichlorotetrahydrofuran with methylmagnesium bromide gives *cis*- and *trans*-3-chloro-2-methyltetrahydrofuran, separable by distillation. Although ring scission, with sodium, of the *trans*-isomer gives *trans*-*n*-pent-3-en-1-ol containing not more than a trace of the *cis*-alcohol, the *cis*-isomer gives a mixture of *cis*- and *trans*-*n*-pent-3-en-1-ol, containing a substantial proportion of the *cis*-alcohol. The scission of *cis*- and *trans*-3-chloro-2-ethyltetrahydrofuran to *n*-hex-3-en-1-ol gives similar results. Assignments of configurations of the alcohols are based on comparison with authentic specimens of the *cis*- and *trans*-alcohols (Part I), through their infra-red absorption and mixed melting points of derivatives. In confirmation the alcohols derived from the *cis*-3-chloro-2-alkyltetrahydrofurans are converted, by carboxylation of the Grignard reagents derived from the bromides, into *n*-hex- and *n*-hept-4-enoic acids respectively. Crystallisation of the *p*-bromophenacyl esters gives in each case the known *cis*- and *trans*-derivatives.

In contrast to the ring scission of 3-chloro-2-alkyltetrahydrofurans (Part II), scission of the mixed *cis*- and *trans*-3-chloro-2-alkyltetrahydrofurans, for the cases we have examined, does not lead to alk-3-en-1-ols of a single configuration. Mechanisms for these ring scissions are discussed.

IN Part II (preceding paper) we described the preparation of 2-1'-halogenoalkyltetrahydrofurans and of *cis*- and *trans*-3-chloro-2-alkyltetrahydrofurans and the investigation of their ring scission by sodium with particular reference to the stereochemistry of the alk-4-en-1-ols formed. In this paper we describe a similar investigation of the preparation and ring scission of *cis*- and *trans*-3-chloro-2-alkyltetrahydrofurans (I) as a route to alk-3-en-1-ols (II). No 3-chloro-2-alkyltetrahydrofurans had been described when this study was started, so the following scheme was examined :



2:3-Dichlorotetrahydrofuran had been prepared by the chlorination of tetrahydrofuran in carbon tetrachloride at 0°, under anhydrous conditions (Repe and Kröper, to I. G. Farbenind. A.-G., G.P. 703,956, 1941). Normant (*Compt. rend.*, 1948, **226**, 185) has since claimed yields of up to 90%, though Stoll and Commarmont (*Helv. Chim. Acta*, 1949, **32**, 597) obtained only 34%. We find that chlorination at 30–35° gives consistent yields of 70%. Addition of 2:3-dichlorotetrahydrofuran (1 mol.) in ether to the alkylmagnesium bromide (1.5 mols.) gave the 3-chloro-2-alkyltetrahydrofuran (I; R = Me and Et) in good yield. Each of these products was separated by fractional distillation into two isomers boiling some 15° apart, which differed appreciably in physical properties (Table I) and gave different infra-red absorption spectra. On the assumption that the Auwers-Skita generalisations are applicable to tetrahydrofurans, we assign the *cis*-configuration to the higher-boiling isomers and the *trans*-configuration to the lower-boiling. At this stage Normant (*Compt. rend.*, 1948, **226**, 733) briefly reported a similar investigation, but gave only single boiling points for his 3-chloro-2-alkyltetrahydrofurans. Subsequently he stated (*L'Ind. Parfumerie*, 1948, **3**, 138) that his products had a spread of boiling point and were probably *cis-trans*-mixtures. Fractional distillation of the precursory 2:3-dichlorotetrahydro-

uran gave no indication of heterogeneity, so that either the *cis*- and *trans*-isomers have similar boiling points or the substitution gives substantially one isomer.

Ring scission with sodium of the mixed *cis*- and *trans*-3-chloro-2-methyltetrahydrofurans gave a pentenol similar to that recorded by Normant (Table II). It was shown to be *n*-pent-3-en-1-ol (II; R = Me) by catalytic reduction to *n*-amyl alcohol and by the isolation of acetaldehyde as the sole volatile aldehyde on ozonisation. However, when this ( $\alpha + \beta$ )-*n*-pent-3-en-1-ol was converted into the bromide and the derived Grignard reagent carboxylated, the *n*-hex-4-enoic acid\* so obtained gave a heterogeneous *p*-toluidide and *p*-bromophenacyl ester. Similarly ( $\alpha + \beta$ )-*n*-hex-3-en-1-ol (II; R = Et) (Table III) obtained on ring scission of the mixed *cis*- and *trans*-3-chloro-2-ethyltetrahydrofurans yielded a *n*-hept-4-enoic acid giving heterogeneous derivatives. In contrast therefore to the ring scission of *cis*- and *trans*-3-chloro-2-alkyltetrahydropyrans, in which both isomers yield the *trans*-*n*-alk-4-en-1-ol, scission of the mixed *cis*- and *trans*-3-chloro-2-methyl(and -ethyl)tetrahydrofurans gives both *cis*- and *trans*-*n*-pent(and hex)-3-en-1-ol.

TABLE I.

3-Chloro-2-alkyltetrahydrofuran.	B. p.	$d_4^{20}$ .	$n_D^{20}$ .	[ $R_L$ ] <sub>D</sub> .	
				Found.	Calc.
<i>trans</i> -2-Methyl- .....	130°	1.087	1.4420	29.36	29.60
<i>cis</i> -2-Methyl- .....	145	1.098	1.4520	29.38	29.60
<i>trans</i> -2-Ethyl- .....	150	1.058	1.4463	33.95	34.22
<i>cis</i> -2-Ethyl- .....	165	1.078	1.4553	33.90	34.22

TABLE II.

<i>n</i> -Pent-3-en-1-ol.	B. p.	$n_D^{20}$ .	1-Naphthyl-	<i>p</i> -Nitrophenyl	Ref.
			urethane, m. p.	urethane, m. p.	
( $\alpha + \beta$ )- .....	137—138°	1.4356	—	—	1
	137—138	—	—	—	2
$\alpha$ - .....	136—137	1.4343	92°	77°	1
$\beta$ - .....	137—138	1.4355	74—76	71	1
<i>cis</i> - .....	139—141	1.4386	88—89	76	3
<i>trans</i> - .....	136—137	1.4340	93	80	3
Corresponding <i>n</i> -hex-4-enoic acid.	M. p.	B. p.	$n_D^{20}$ .	<i>p</i> -Bromophenacyl ester, m. p.	Ref.
( $\alpha + \beta$ )- .....	—	117—119°/24 mm.	1.4380	—	1
$\alpha$ - .....	— 1° to + 1°	102—103°/13 mm.	1.4388	82.0—82.5°	1
$\beta$ - .....	—17° to —15	98°/11 mm.	1.4396	{ 54.0—55.5 81.0—82.5	1
<i>cis</i> - .....	—35° to —34	106°/14 mm.	1.4403	55	4
<i>trans</i> - .....	— 1° to + 1	108—109°/19 mm.	1.4387	82.5	4

<sup>1</sup> Crombie and Harper, this paper. <sup>2</sup> Normant, *Compt. rend.*, 1948, **226**, 733. <sup>3</sup> Crombie and Harper, Part I, *J.*, 1950, 873. <sup>4</sup> Crombie and Harper, *J.*, 1950, 1152.

TABLE III.

<i>n</i> -Hex-3-en-1-ol.	B. p.	$n_D^{20}$ .	1-Naphthyl-	3:5-Dinitro-	<i>p</i> -Nitrophenyl-	4-Diphenyl-	Ref.
			urethane, m. p.	benzoate, m. p.	urethane, m. p.	urethane, m. p.	
( $\alpha + \beta$ )- .....	67—71°/19 mm.	1.4377	—	—	—	—	1
( $\alpha + \beta$ )- .....	60°/12 mm.	—	—	—	—	—	2
( $\alpha + \beta$ )- .....	58—60°/12 mm.	1.4398	—	20—22°	—	—	3
$\alpha$ - .....	63—64°/16 mm.	1.4385	68—69°	46—47.5	84—85°	99.5°	1
$\beta$ - .....	63—64°/15 mm.	1.4395	60.0—60.5	27—29	76—79	73—77	1
<i>cis</i> - .....	66—67°/19 mm.	1.4384	69—70	49	72.5—73.5	91.0—91.5	4
<i>trans</i> - .....	52—53°/9 mm.	1.4374	69—70	47—48	84—85	101	4
Corresponding <i>n</i> -hept-4-enoic acids.		B. p.	$n_D^{20}$ .	<i>p</i> -Bromophenacyl ester, m. p.	Ref.		
( $\alpha + \beta$ )- .....		123—125°/20 mm.	1.4407	—	1		
$\beta$ - .....		114—115°/13 mm.	1.4416	47°, 78—79°	1		
<i>cis</i> - .....		115—116°/12 mm.	1.4403	46	5		
<i>trans</i> - .....		104—105°/7 mm.	1.4398	78—79	5		

<sup>1</sup> Crombie and Harper, this paper. <sup>2</sup> Normant, *Compt. rend.*, 1948, **226**, 733. <sup>3</sup> Stoll and Comarmon, *Helv. Chim. Acta*, 1949, **32**, 597. <sup>4</sup> Crombie and Harper, Part I, *J.*, 1950, 873. <sup>5</sup> Crombie and Harper, forthcoming publication.

The separated *trans*- and *cis*-3-chloro-2-methyltetrahydrofurans were each subjected to ring scission, to give  $\alpha$ - and  $\beta$ -*n*-pent-3-en-1-ol respectively (Table II), while *trans*- and *cis*-3-chloro-2-

\* Geneva numbering.

ethyltetrahydrofuran similarly gave  $\alpha$ - and  $\beta$ -*n*-hex-3-en-1-ol (Table III). Although the 1-naphthylurethanes of the  $\alpha$ - and  $\beta$ -alcohols had different melting points, when admixed there was no appreciable depression. The infra-red absorption spectra of  $\alpha$ - and  $\beta$ -*n*-hex-3-en-1-ol (Figs. 1 and 2) show a similar location of the main bands, each has a strong band at 9.55  $\mu$ . (primary

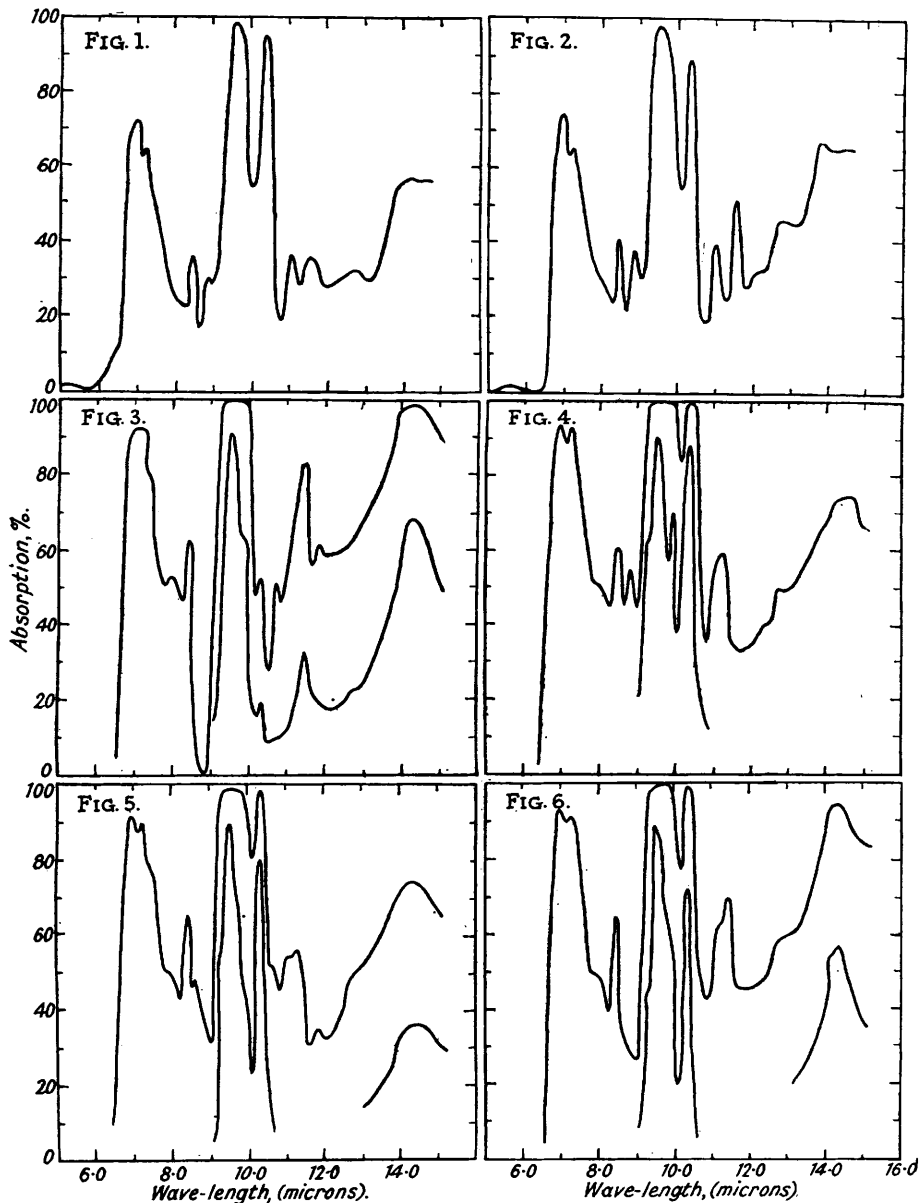


FIG. 1.— $\alpha$ -*n*-Hex-3-en-1-ol.

FIG. 3.—*cis*-*n*-Pent-3-en-1-ol.

FIG. 5.— $\alpha$ -*n*-Pent-3-en-1-ol.

FIG. 2.— $\beta$ -*n*-Hex-3-en-1-ol.

FIG. 4.—*trans*-*n*-Pent-3-en-1-ol.

FIG. 6.— $\beta$ -*n*-Pent-3-en-1-ol.

hydroxyl), but the intensity of the band at 10.3  $\mu$ . (" *trans* ") is lower in the case of the  $\beta$ -alcohol. Comparison of the spectrum of  $\alpha$ -*n*-hex-3-en-1-ol with that of authentic *trans*-*n*-hex-3-en-1-ol (Crombie and Harper, Part I, *J.*, 1950, 873; Fig. 2) suggested identity of the alcohols, which was confirmed by the absence of melting-point depression on admixture of the 1-naphthylurethanes and the 3;5-dinitrobenzoates. The spectrum of  $\beta$ -*n*-hex-3-en-1-ol is consistent with

this alcohol being a mixture of *cis*- and *trans*-*n*-hex-3-en-1-ol, since it shows both the "trans" band at 10.3  $\mu$ . and the band at 11.5  $\mu$ . which is present strongly in the spectrum of the pure *cis*-isomer (*loc. cit.*, Fig. 1). In addition, the increase in intensity at 13.9  $\mu$ . and minor details of the spectrum are consistent with the presence of a substantial proportion of the *cis*-isomer. Attempts to resolve the 1-naphthylurethane of  $\beta$ -*n*-hex-3-en-1-ol by crystallisation were unsuccessful. The alcohol was therefore converted, *via* the bromide, into a *n*-hept-4-enoic acid (Table III) and the *p*-bromophenacyl ester fractionally crystallised. Two isomeric esters were isolated, the less soluble being identical with *p*-bromophenacyl *trans*-*n*-hept-4-enoate, prepared from authentic *trans*-*n*-pent-2-en-1-ol, and the more soluble with the ester prepared from authentic *cis*-*n*-hex-3-en-1-ol.  $\beta$ -*n*-Hex-3-en-1-ol is therefore rigidly established as a mixture of commensurate proportions of *cis*- and *trans*-*n*-hex-3-en-1-ol.

The  $\alpha$ - and  $\beta$ -*n*-pent-3-en-1-ols exhibited analogous properties. That the  $\alpha$ -form is substantially *trans*-*n*-pent-3-en-1-ol was shown by the identity of its 1-naphthylurethane with authentic *trans*-*n*-pent-3-en-1-yl 1-naphthylurethane (Part I, *loc. cit.*). Conversion of the  $\beta$ -form into a *n*-hex-4-enoic acid (Table II) and fractional crystallisation of the *p*-bromophenacyl ester gave *p*-bromophenacyl *cis*- and *trans*-*n*-hex-4-enoates, identical with authentic specimens (Crombie and Harper, *J.*, 1950, 1152; therein described as hex-3-enoic acid, according to the nomenclature then used in the *Journal*). For comparison the infra-red absorption spectra of the pure *cis*- and *trans*-*n*-pent-3-en-1-ols, prepared by us (Part I, *loc. cit.*), have now been determined (Figs. 3 and 4). The spectrum of the *trans*-isomer shows the characteristic strong band at 10.3  $\mu$ ., whilst the *cis*-isomer possesses a very weak band at this wave-length, but a new band at 11.5  $\mu$ .. Furthermore the intensity at 14—15  $\mu$ . is greater in the case of the *cis*-isomer. These features parallel those already described for the *trans*- and *cis*-*n*-hex-3-en-1-ols. The spectrum of  $\alpha$ -*n*-pent-3-en-1-ol (Fig. 5) is generally similar to that of the *trans*-isomer and is, in accordance with the chemical evidence, quite dissimilar from that of the *cis*-isomer. There are, however, signs that  $\alpha$ -*n*-pent-3-en-1-ol contains a trace of the *cis*-isomer for the trough at 8.8  $\mu$ . and the pip at 11.3  $\mu$ . may be due to this cause. It is possible that this is due to the difficulty of achieving a sharp separation of the precursory *cis*- and *trans*-3-chloro-2-methyltetrahydrofurans. The  $\beta$ -alcohol is clearly a mixture of *cis*- and *trans*-*n*-pent-3-en-1-ols, for the spectrum (Fig. 6) contains the characteristic features of both isomers; this again accords with the chemical evidence. Thus the ring scission of mixed *cis*- and *trans*-3-chloro-2-alkyltetrahydrofurans, for the cases examined here, is unsuitable for the extension of carbon chains by the stereochemically homogeneous unit,  $\cdot\text{CH}_2\text{CH}(\text{CH}_2)_2\text{OH}$ , but is suitable for extension by the unit,  $\cdot[\text{CH}_2]_4\text{OH}$ , after catalytic hydrogenation.

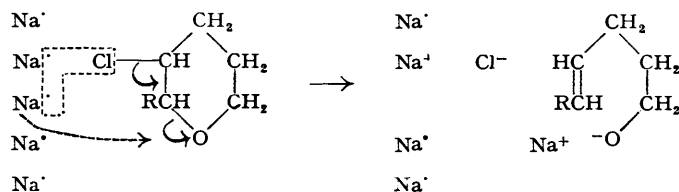
Stoll and Commarmont (*loc. cit.*) have recently repeated the ring scission described by Normant on what, from the evidence given here, was a mixture of *cis*- and *trans*-3-chloro-2-ethyltetrahydrofuran. They converted the alcoholic product into a 3:5-dinitrobenzoate (m. p. 20—22°), which after repeated crystallisation gave a small amount of pure derivative (m. p. 46.5—48°). This was not identical with *cis*-*n*-hex-3-enyl 3:5-dinitrobenzoate (m. p. 48°) and they suggested it was the product of a side-reaction, probably the ester of a *n*-hex-2-en-1-ol. In the light of this paper it is clearly the 3:5-dinitrobenzoate of *trans*-*n*-hex-3-en-1-ol, the main product of the ring scission, and we have confirmed this conclusion by a mixed melting-point determination with a specimen kindly provided by Dr. M. Stoll. In connection with Stoll and Commarmont's paper it will be apparent that our early views as to the nature of the ring scission product, recorded as a footnote to their paper, have now been revised as we had not then detected the presence of *cis*-*n*-hex-3-en-1-ol. Stoll and Commarmont's crude product, like our own (Table III), was a mixture of *cis*- and *trans*-isomers. The confusion was due to incorrect data in the literature for what had been claimed as pure *trans*-*n*-hex-3-en-1-ol; this we have since corrected (Part I, *loc. cit.*).

The data presented in this and the preceding paper, relating configurations of certain 3-chloro-2-alkyltetrahydropyrans, 3-chloro-2-alkyltetrahydrofurans, and 2-1'-bromoalkyltetrahydrofurans to those of the ethylenic alcohols formed on ring scission, permit a preliminary discussion of the mechanism of this reaction.

Three earlier suggestions have been made as to the course of similar fissions. Paul (*Bull. Soc. chim.*, 1933, [iv], 53, 421) considered the ring scission of tetrahydrofurfuryl bromide by magnesium to proceed through an intervening Grignard reagent; but Robinson and Smith (*J.*, 1936, 195) and more recently Amstutz (*J. Org. Chem.*, 1944, 9, 310) have clearly shown that a Grignard reagent is not formed. Paul subsequently (*Bull. Soc. chim.*, 1935, [v], 2, 745) suggested the intervention of the sodium "alkyl" when using sodium, but by analogy this is improbable. Although we invariably observe a blue to purple colour during these ring scissions with sodium,

similar to those observed during the Wurtz reaction, which might be attributed to the intervention of a sodium alkyl, the colour is probably due to the inclusion of sodium atoms in the sodium chloride crystal lattice (cf. Fritz Ephraim, "Inorganic Chemistry," 5th Edn., Gurney and Jackson, p. 247). Robinson and Smith (*loc. cit.*) represented the ring scission of tetrahydrofurfuryl bromide by magnesium as proceeding from the metal acting as an electron donor to the bromine, thereby inducing electron recession through the  $\beta$ - and the  $\alpha$ -carbon atom to break the  $\alpha$ -carbon-oxygen bond—essentially a heterolytic process as illustrated. In contrast Amstutz (*loc. cit.*) postulated homolytic fission of the carbon-halogen bond to yield a free radical ( $R\cdot O\cdot CH_2\cdot CH_2\cdot$ ) which then undergoes either Wurtz coupling or fission at the  $\beta$ -carbon-oxygen bond. We regard a free radical mechanism for the ring scission by sodium as improbable. Certainly the ethylenic alcohol is formed to the extent of  $\sim 90\%$ , so that any other reactions proceed to a very minor extent.

Reaction must proceed at the surface of the metallic sodium where, on the approach of a suitably orientated molecule, we suggest ring scission is initiated by nucleophilic attack on the halogen of the surface electrons, followed by electron recession to the  $\alpha$ -carbon atom and thereafter fission of the  $\alpha$ -carbon-oxygen bond with concomitant release of two sodium ions, *e.g.* :



As regards ring scission of the 3-chloro-2-alkyltetrahydropyrans, examination of models shows that, if the reaction proceeds by a "normal" bimolecular mechanism ( $S_N2$  with reference to the  $\alpha$ -carbon atom) through the duplet of electrons liberated by the breaking of the carbon-chlorine bond attacking the  $\alpha$ -carbon atom on the opposite side to that at which the  $\alpha$ -carbon-oxygen bond simultaneously breaks (*i.e.*, "inversion" of the  $\alpha$ -carbon atom), then *trans*-3-chloro-2-alkyltetrahydropyrans would give *trans*-*n*-alk-4-en-1-ols, whilst the *cis*-pyrans would give *cis*-alcohols. In contrast, if after separation of the chlorine the  $\alpha$ -carbon-oxygen bond also breaks, leaving the  $\alpha$ -carbon atom as a carbonium ion ( $S_N1$  with respect to the  $\alpha$ -carbon atom), then ethylenic-bond formation can occur without inversion at the  $\alpha$ -carbon atom. This type of substitution is generally accompanied by "racemisation" of the  $\alpha$ -carbon atom owing to the formation of a planar carbonium ion. Steric or other factors, however, may cause subsequent union in one of the two possible ways to be inhibited, with the result that somewhat more than 50% of one of the isomers is produced. Repulsion of the alkyl side-chain from the sodium surface might facilitate union with retention of configuration. By this scheme *trans*-pyrans would give both *cis*- and *trans*-*n*-alk-4-en-1-ols, with the former predominating, whilst *cis*-pyrans would give mixtures with the *trans*-isomer greatly predominating, for the repulsion of the alkyl group would be greater in the case of the *cis*-pyrans owing to its closer proximity to the chlorine and hence to the sodium surface. We have shown, certainly for methyl and most probably for ethyl, *n*-propyl, and *n*-butyl, that both *trans*- and *cis*-3-chloro-2-alkyltetrahydropyran give solely the *trans*-*n*-alk-4-en-1-ol. The ring scissions of the *trans*- and *cis*-pyrans must therefore proceed by different mechanisms, the incidence of an  $S_N1$  mechanism being caused by the steric suppression of the more "normal"  $S_N2$  reaction by the change of geometric configuration. For *trans*-pyran to give solely *trans*-alcohol the scission must proceed by the  $S_N2$  mechanism, whereas, for *cis*-pyran to give *trans*-alcohol with no more than a trace of *cis*-alcohol, scission must proceed by the  $S_N1$  mechanism with substantially complete retention of configuration. As this change of mechanism to  $S_N1$  with nearly complete retention of configuration occurs for the smallest possible alkyl group (methyl) it appears that a bimolecular scission of a *cis*-pyran cannot be realised, *i.e.*, *cis*-*n*-alk-4-en-1-ols are not accessible by the direct ring scission of 3-chloro-2-alkyltetrahydropyrans.

Next, with regard to the 3-chloro-2-alkyltetrahydrofurans, where we have shown that, for methyl and ethyl, the *trans*-furan gives *trans*-*n*-alk-3-en-1-ol, it is clear that the ring scission parallels that of the *trans*-pyrans in proceeding by a  $S_N2$  mechanism. However, as we have shown, the *cis*-furans give mixtures of *cis*- and *trans*-alcohols, in which the latter predominate. This is capable of two explanations: either the ring scission proceeds mainly by the  $S_N1$

mechanism without inversion, to give *trans*-alcohol, and partly by the  $S_N2$  mechanism to give *cis*-alcohol; or the ring scission proceeds only by the  $S_N1$  mechanism but with substantial inversion leading to both *trans*- and *cis*-alcohols. The latter appears preferable, particularly as the  $S_N2$  mechanism clearly does not participate in the presumably analogous scission of the *cis*-pyrans. This change must be connected with the differing geometry of the two systems, where in comparison with the presumably puckered and flexible six-membered tetrahydropyran ring, the five-membered tetrahydrofuran ring is both rigid and substantially planar. Further their geometry requires that in the *cis*-furans the alkyl group will be slightly farther from the chlorine than in the *cis*-pyrans. This will reduce the hindering effect of the alkyl group to the approach of the chlorine atom to the sodium surface and also the tendency of the  $\alpha$ -carbon atom to react with retention of configuration; *i.e.*, substantial "racemisation" will occur leading to the observed results. If this view is correct, increasing the steric effect of the alkyl group should lead to stronger repulsion from the sodium surface and hence to greater union without inversion; *i.e.*, by suitable variation of the alkyl group it should be possible to suppress the formation of *cis*-alcohol and to obtain solely *trans*-*n*-alk-3-en-1-ol from the ring scission of both *cis*- and *trans*-3-chloro-2-alkyltetrahydrofurans. This possibility will be investigated.

The single case of the ring scission of a 2-1'-halogenoalkyltetrahydrofuran, where alkyl is methyl, that we have examined appears at first sight to parallel the ring scission of *cis*-3-chloro-2-methyl(or -ethyl)tetrahydrofuran in giving a mixture of *trans*- and *cis*-*n*-alk-4-en-1-ol, in which the former predominates. The problem is however more complex. The bromide presumably consists of two racemic pairs of diastereoisomers, which incidentally may account for its observed spread of boiling point, and these correspond to the *trans*- and *cis*-furans. Their varying modes of ring scission, by  $S_N2$  and  $S_N1$  mechanisms, will parallel those discussed above but will lead to *trans*-*cis*-mixtures of alk-4-en-1-ols of varying composition. However a detailed analysis is too speculative in view of the limited experimental data.

#### EXPERIMENTAL.

Microanalyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected. The infra-red absorption spectra were determined by Miss I. M. Friedmann, to whom we are indebted, with a Grubb Parsons spectrometer using the pure liquids in cells of 20—50- $\mu$ . thickness.

**2 : 3-Dichlorotetrahydrofuran.**—Commercial tetrahydrofuran, containing a phenolic antioxidant, was distilled from sodium wire, and the portion, b. p. 66—67°, used immediately. Chlorine, from a cylinder, dried by passage through concentrated sulphuric acid, was passed into a solution of the distilled tetrahydrofuran (216 g.) in dry carbon tetrachloride (200 ml.) containing iodine (1 g.). Chlorination was started at 25° and within a few minutes the brown colour disappeared and the temperature rose to 30—35°, at which it was kept by cooling in running water. An efficient reflux condenser was necessary on the exit side of the all-glass apparatus to prevent loss of the volatile tetrahydrofuran. Evolution of hydrogen chloride was evident after 4 hours and chlorination was continued until reaction ceased (24—30 hours), as shown by a fall in temperature and passage of unreacted chlorine. Dry nitrogen was then bubbled through the solution to remove most of the dissolved chlorine and hydrogen chloride. The carbon tetrachloride was removed through a column under partly reduced pressure and the residue distilled through a 40-cm. Dufton column, to give 2 : 3-dichlorotetrahydrofuran (300 g., 71%), b. p. 65.5—70°/23 mm., which was sufficiently pure for preparative purposes. On redistillation the bulk (275 g.) had b. p. 63—66°/21 mm.,  $n_D^{20}$  1.4841 (Found : C, 34.9; H, 4.7; Cl, 49.2. Calc. for  $C_4H_6OCl_2$  : C, 34.1; H, 4.3; Cl, 50.3%). In our initial experiments at 0°, we found that sunlight was necessary for the reaction to start. On one occasion the chlorine merely dissolved until the flask was removed from the ice-bath, reaction then beginning suddenly with some violence. Most batches of 2 : 3-dichlorotetrahydrofuran assumed a red colour when kept which was not removed by redistillation.

**3-Chloro-2-methyltetrahydrofuran.**—2 : 3-Dichlorotetrahydrofuran (260 g., 1.0 mol.) was dropped slowly into a well stirred (Hershberg wire stirrer) ice-cold Grignard reagent prepared from methyl bromide vapour and magnesium turnings (67.5 g., 1.5 g.-atoms) in anhydrous ether (600 ml.). After storage at room temperature, usually overnight, the excess of Grignard reagent was decomposed by the careful addition of cold ammonium chloride solution, with stirring and external cooling. The ethereal layer was separated and the aqueous layer just acidified with concentrated hydrochloric acid and further extracted with ether. The extracts were bulked, washed, and dried ( $Na_2SO_4$ — $K_2CO_3$ ). Distillation gave mixed *cis*- and *trans*-3-chloro-2-methyltetrahydrofurans (177 g., 82%), b. p. 40—50°/19 mm.,  $n_D^{20}$  1.4487. This mixture was fractionated through a 50 × 1.5-cm. helices-packed column with variable take-off and electrically heated jacket, at atmospheric pressure, to give the lower-boiling *trans*- (Found : C, 49.8; H, 7.6; Cl, 29.6.  $C_6H_8OCl$  requires C, 49.8; H, 7.5; Cl, 29.4%) and *cis*-3-chloro-2-methyltetrahydrofuran (Found : C, 49.8; H, 7.6; Cl, 29.6%) (see Table I).

**3-Chloro-2-ethyltetrahydrofuran.**—By the procedure used for the lower homologue 2 : 3-dichlorotetrahydrofuran (68 g., 1.0 mol.) was treated with the Grignard reagent prepared from ethyl bromide (79 g., 1.5 mols.) and magnesium (17.6 g.) in dry ether (300 ml.), to give the mixed *cis*- and *trans*-3-chloro-2-ethyltetrahydrofuran (56.5 g., 85%), b. p. 60—72°/21 mm.,  $n_D^{20}$  1.4510. This mixture was fractionally distilled to give quite readily the higher-boiling *cis*-3-chloro-2-ethyltetrahydrofuran (b. p. 165°) (Found : C, 53.3; H, 8.5; Cl, 26.3.  $C_6H_{10}OCl$  requires C, 53.55; H, 8.2; Cl, 26.3%), but the b. p. of the *trans*-3-chloro-2-ethyltetrahydrofuran (Found : C, 53.4; H, 8.4; Cl, 25.7%) was rather wide (150—155°) and the purity of this isomer was judged by the refractive indices and densities of successive fractions. The

physical properties of these isomers are recorded in Table I. The *trans*-3-chloro-2-methyl( and -ethyl)-tetrahydrofurans had the pleasanter odours and were stable to light, whereas the *cis*-isomers became yellow in a few hours and eventually deep brown.

**Ring Scission of 3-Chloro-2-methyltetrahydrofuran.**—The same procedure was used as that for the ring scission of 3-chloro-2-methyltetrahydropyran (p. 1712). In this way the mixed *cis*- and *trans*-3-chloro-2-methyltetrahydrofuran (160 g.) gave ( $\alpha + \beta$ )-*n*-pent-3-en-1-ol (97 g., 83%), b. p. 137—138°,  $n_D^{20}$  1.4356. The yield was between 80 and 90% in three other preparations.

Ring scission of separated *trans*-3-chloro-2-methyltetrahydrofuran (31.7 g.) similarly yielded  $\alpha$ -*n*-pent-3-en-1-ol (13.1 g., 57%), b. p. 136—137°,  $n_D^{20}$  1.4343 (Found : C, 69.0; H, 11.9. Calc. for  $C_5H_{10}O$  : C, 69.7; H, 11.7%). This alcohol (130 mg.) was heated with 1-naphthyl isocyanate (243 mg.) in a sealed tube at 100° for 30 minutes. The contents of the tube were extracted with light petroleum (b. p. 60—80°), and a small quantity of dinaphthylurea was filtered off. The 1-naphthylurethane (240 mg.) separated from the filtrate in needles, m. p. 86—88°, which 3 further crystallisations raised to 92° (Found : C, 75.5; H, 6.6; N, 5.2. Calc. for  $C_{18}H_{17}O_2N$  : C, 75.3; H, 6.7; N, 5.3%). This m. p. was not depressed (92—93°) on admixture with the 1-naphthylurethane of authentic *trans*-*n*-pent-3-en-1-ol (p. 877). By a similar procedure  $\alpha$ -*n*-pent-3-en-1-ol (84 mg.) and *p*-nitrophenyl isocyanate (164 mg.) gave the *p*-nitrophenylurethane (200 mg.) as needles which after two crystallisations from light petroleum (b. p. 60—80°; 3 parts by vol.)-carbon tetrachloride (1 part) had m. p. 77° (Found : N, 10.7.  $C_{12}H_{14}O_4N_2$  requires N, 11.2%). This m. p. was not depressed on admixture with the *p*-nitrophenylurethane of *trans*-*n*-pent-3-en-1-ol (below), but was depressed to 70.5—73° on admixture with the derivative of *cis*-*n*-pent-3-en-1-ol (below). These procedures for the preparation of urethanes were also used in the earlier Parts of this series.

Ring scission of *cis*-3-chloro-2-methyltetrahydrofuran (33 g.) proceeded more vigorously than that of the *trans*-isomer, to give  $\beta$ -*n*-pent-3-en-1-ol (17.1 g., 71%), b. p. 136—137°,  $n_D^{20}$  1.4355 (Found : C, 70.2; H, 11.2%). This alcohol (130 mg.) treated as above gave the 1-naphthylurethane (250 mg.) as felted needles, m. p. 74—76°, which was unchanged after 2 further crystallisations (Found : C, 74.6; H, 6.7; N, 5.5%). A 1 : 1 mixture with the "a" 1-naphthylurethane softened at 75° and cleared at 85°. The *p*-nitrophenylurethane (180 mg. from 84 mg. of alcohol) crystallised as needles, m. p. 71°, which was not raised by recrystallisation (Found : N, 10.7%). A 1 : 1 mixture with the "a" *p*-nitrophenylurethane had m. p. 70—73°.

*trans*-*n*-Pent-3-en-1-ol (p. 877) has been further characterised by the preparation of the *p*-nitrophenylurethane, which after purification by treatment with charcoal and crystallisation from a mixture of light petroleum (b. p. 40—60°) and carbon tetrachloride was obtained as small colourless crystals, m. p. 80° (Found : C, 57.3; H, 5.75; N, 11.5.  $C_{12}H_{14}O_4N_2$  requires C, 57.6; H, 5.65; N, 11.2%). *cis*-*n*-Pent-3-en-1-ol (p. 877) has similarly been further characterised by preparation of the *p*-nitrophenylurethane, m. p. 76° (Found : C, 57.1; H, 5.55; N, 11.4%). A mixture of these two derivatives melted unsharply at 71—73°.

Both  $\alpha$ - and  $\beta$ -*n*-pent-3-en-1-ol were recovered unisomerised after being heated with a crystal of iodine in a sealed tube at 100° for 8 hours: the  $\alpha$ -alcohol so treated gave a 1-naphthylurethane, m. p. 86—87°, and the  $\beta$ -alcohol gave a 1-naphthylurethane, m. p. 74°.

**Ozonisation of  $\alpha$ - and  $\beta$ -*n*-Pent-3-en-1-ol.**—The calculated volume of ozonised oxygen was passed through ( $\alpha + \beta$ )-*n*-pent-3-en-1-ol (500 mg.) in carbon tetrachloride (15 ml.) cooled in ice. Water (20 ml.) was then added and the volatile aldehyde swept into a solution of dimedon in water by a slow stream of nitrogen during 24 hours. The dimedon derivative of acetaldehyde (420 mg.) separated, having m. p. 139°, which recrystallised from aqueous ethanol as needles or plates, m. p. 140.5°, and did not depress the m. p. of an authentic specimen (m. p. 140—141°).

Ozonisation of  $\alpha$ - and  $\beta$ -*n*-pent-3-en-1-ol separately gave similar results. Thus the dimedon derivative (100 mg.) of the volatile aldehyde from the  $\alpha$ -alcohol (170 mg.) had m. p. 140—141°, with softening at 138°, without crystallisation. One recrystallisation gave m. p. 141° and when admixed with authentic acetaldehyde dimedon derivative this derivative had m. p. 141.0—141.5°. The  $\beta$ -alcohol (300 mg.) gave on ozonolysis 240 mg. of dimedon derivative, m. p. 139—142°. One crystallisation from ethanol raised this to m. p. 141—142° (a 1 : 1 mixture with an authentic sample had m. p. 141—142°).

**Hydrogenation of  $\alpha$ - and  $\beta$ -*n*-Pent-3-en-1-ol.**—( $\alpha + \beta$ )-*n*-Pent-3-en-1-ol (163 mg.) was hydrogenated at atmospheric pressure in ethyl acetate (10 ml.), using pre-reduced palladium-barium sulphate (100 mg.; 5% Pd). Hydrogen (40.5 ml. at N.T.P.) was absorbed in 20 minutes (calc. : 43.0 ml.), whereafter absorption stopped. Filtercel was then added and the catalyst filtered off. The ethyl acetate was carefully distilled off and the residual alcohol converted into its 3 : 5-dinitrobenzoate, m. p. 43—44°, not depressed on admixture with authentic *n*-amyl 3 : 5-dinitrobenzoate, m. p. 46—47° (43—45°).

$\alpha$ -*n*-Pent-3-en-1-ol (194 mg.) absorbed hydrogen (48.0 ml. at N.T.P.) during 20 minutes (calc. : 50.5 ml.), and the 3 : 5-dinitrobenzoate of the reduction production had m. p. 43.0—43.5°. The  $\beta$ -alcohol (245 mg.) absorbed hydrogen (63.0 ml. at N.T.P.) (Calc. : 64 ml.) and the saturated product gave a 3 : 5-dinitrobenzoate, m. p. 42.5—44.0°. On admixture with authentic *n*-amyl 3 : 5-dinitrobenzoate neither of the above m. p.s were depressed.

**$\alpha$ - and  $\beta$ -*n*-Pent-3-enyl Bromides.**—Phosphorus tribromide (140 g.) was added during 3 hours to a stirred mixture of ( $\alpha + \beta$ )-*n*-pent-3-en-1-ol (112 g.) and pyridine (30 g.), cooled in ice. After a further 2 hours at room temperature the crude bromide was distilled out by direct heating of the flask until the orange residue frothed up. The crude bromide was diluted with light petroleum (b. p. 40—60°), to aid separation, and washed twice with 10% hydrochloric acid, then 10% sodium hydroxide, and water. After drying ( $Na_2SO_4$ ) and removal of the light petroleum the residue was twice distilled under partly reduced pressure, to give ( $\alpha + \beta$ )-*n*-pent-3-enyl bromide (142 g.), b. p. 89—97°/225 mm.,  $n_D^{25}$  1.4700.

$\alpha$ -*n*-Pent-3-enyl bromide prepared from the  $\alpha$ -alcohol had b. p. 90—94.5°/260 mm.,  $n_D^{20}$  1.4690, while the  $\beta$ -bromide prepared from the  $\beta$ -alcohol had b. p. 95—98°/280 mm.,  $n_D^{20}$  1.4670.

**$\alpha$ - and  $\beta$ -*n*-Hex-4-enoic Acids.**—Magnesium turnings (25.5 g.) were covered with anhydrous ether (60 ml.) and reaction started by the addition of a few ml. of ( $\alpha + \beta$ )-*n*-pent-3-enyl bromide. Further

ether (200 ml.) was then added and the remainder of the bromide (130 g. in all) dropped in during 3 hours. After a further hour the reaction mixture was cooled in alcohol-solid carbon dioxide, and carbon dioxide, dried by concentrated sulphuric acid, was passed in with stirring. When the mass became pasty and difficult to stir, a large excess of powdered solid carbon dioxide was added and the mixture stirred by hand and left for 2 hours. The product was decomposed by ice-cold 25% sulphuric acid, and the ethereal layer separated. The aqueous phase was thoroughly extracted with ether, and the bulked ethereal extracts were washed with water. The ethereal solution was then extracted with 50-ml. portions of 10% sodium hydroxide solution, until a test portion gave no turbidity on acidification. The alkaline extracts were covered at 0° with a layer of light petroleum (b. p. 40–60°), and 25% sulphuric acid was added with stirring until the aqueous phase was just acid to Congo-red. Separation of the light petroleum layer, washing, drying, and removal of the solvent gave ( $\alpha + \beta$ )-*n*-hex-4-enoic acid, which when distilled had b. p. 117–119°/24 mm. and  $n_D^{20}$  1.4380 (64.5 g., 65%). The *p*-toluicide and the *p*-bromophenacyl ester of this acid were heterogeneous and melted over a range.

In like manner  $\alpha$ -*n*-pent-3-enyl bromide (4.1 g.) was converted into  $\alpha$ -*n*-hex-4-enoic acid (2.1 g., 67%), m. p. -1° to +1°, b. p. 102.5–103.0°/13 mm.,  $n_D^{20}$  1.4388 (Found: equiv., 114.1. Calc. for  $C_8H_{10}O_2$ : equiv., 114.1). Letch and Linstead (*J.*, 1934, 1994) record m. p. +1°, b. p. 102°/12 mm.,  $n_D^{20}$  1.4367, for a specimen of *n*-hex-4-enoic acid, which from its mode of preparation must have the *trans*-configuration (cf. Crombie and Harper, p. 1152; therein named as hex-3-enoic acid). The *p*-bromophenacyl ester of the  $\alpha$ -acid formed colourless needles, m. p. 82.0–82.5°, unchanged on admixture with authentic *trans*-ester (Crombie and Harper, *loc. cit.*) (m. p. 81.5–82.5°).

Similarly  $\beta$ -*n*-pent-3-enyl bromide (2.8 g.) was converted into  $\beta$ -*n*-hex-4-enoic acid (0.95 g., 45%), m. p. -17° to -15°, b. p. 98°/11 mm.,  $n_D^{20}$  1.4396 (equiv., 115.7). The *p*-bromophenacyl ester was clearly heterogeneous and was therefore crystallised from aqueous ethanol. The less soluble fractions were collected and crystallised 3 times from ethanol, giving light colourless needles, m. p. 81.0–82.5°, which failed to depress the m. p. of authentic *trans*-ester on admixture (mixed m. p. 82.0–82.5°). The more soluble fraction, isolated by dilution of the mother-liquors with water, melted at 49–53°, after softening. Recrystallisation from ethanol-water gave a product, as colourless plates, m. p. 56°, which when admixed with authentic *p*-bromophenacyl *cis*-*n*-hex-4-enoate (colourless plates, m. p. 55°) (Crombie and Harper, *loc. cit.*) had m. p. 54–55.5°.

**Ring Scission of 3-Chloro-2-ethyltetrahydrofuran.**—By the procedure described above the mixed *cis*- and *trans*-3-chloro-2-ethyltetrahydrofuran (81 g.) were converted into ( $\alpha + \beta$ )-*n*-hex-3-en-1-ol (49 g., 81%), b. p. 67–71°/19 mm.,  $n_D^{20}$  1.4377.

Ring scission of *trans*-3-chloro-2-ethyltetrahydrofuran (15.3 g.) was slow in starting and proceeded much less vigorously than that of the *cis*-isomer, to give  $\alpha$ -*n*-hex-3-en-1-ol (7.4 g., 53%), b. p. 63–64°/16 mm.,  $n_D^{20}$  1.4385 (Found: C, 72.0; H, 12.2. Calc. for  $C_8H_{14}O$ : C, 71.9; H, 12.1%). This alcohol was characterised by the 1-naphthylurethane, which formed glistening flat needles, m. p. 68–69° (after 2 crystallisations) depressed on admixture with *cis*-*n*-hex-3-en-1-yl 1-naphthylurethane (m. p. 71°) (p. 876) to 59–60°, but not (68–70°) on admixture with *trans*-*n*-hex-3-en-1-yl 1-naphthylurethane (m. p. 69–70°) (*loc. cit.*).

$\alpha$ -*n*-Hex-3-en-1-ol (500 mg.) and 3:5-dinitrobenzoyl chloride (1.2 g.) in benzene containing pyridine gave the crude ester (1.05 g.). One crystallisation from light petroleum (b. p. 40–60°) gave a sample, m. p. 38.5–40.5°, which by repeated crystallisation was raised to 46.0–47.5°. Admixture of this with authentic *cis*-*n*-hex-3-enyl 3:5-dinitrobenzoate (m. p. 49°) (*loc. cit.*) gave a depression of the m. p. to 34°, but admixture with authentic *trans*-ester (m. p. 47°) (*loc. cit.*) gave no depression. The *p*-nitrophenylurethane, m. p. 84–85°, and the 4-diphenylurethane, m. p. 99.5°, of *trans*-*n*-hex-3-en-1-ol described previously (*loc. cit.*) were prepared from this alcohol, made by ring scission of *trans*-3-chloro-2-ethyltetrahydrofuran. When either of these derivatives was mixed with the corresponding derivative of *cis*-*n*-hex-3-en-1-ol (*loc. cit.*) depressions of the m. p. was observed. We have now prepared the *p*-nitrophenylurethane and 4-diphenylurethane of *trans*-*n*-hex-3-en-1-ol, made by reduction of *n*-hex-3-yn-1-ol (kindly provided by Dr. F. Sondheimer; cf. this vol., p. 881) with sodium in liquid ammonia. These derivatives had m. p. 84–85° and m. p. 101° respectively after recrystallisation and are cited in Table III.

Ring scission of *cis*-3-chloro-2-ethyltetrahydrofuran (21 g.) by the above method proceeded vigorously, to yield  $\beta$ -*n*-hex-3-en-1-ol (13.5 g., 86%), b. p. 63–64°/15 mm.,  $n_D^{20}$  1.4395 (Found: C, 72.5; H, 12.3%). The heterogeneity of the  $\beta$ -alcohol was demonstrated by preparation of the 1-naphthylurethane, which crystallised from light petroleum (b. p. 40–60°) as glistening needles, m. p. 59°, raised by two further crystallisations only to m. p. 60.0–60.5° (Found: C, 75.9; H, 6.6; N, 5.3. Calc. for  $C_{17}H_{19}O_2N$ : C, 75.8; H, 7.1; N, 5.2%). The 3:5-dinitrobenzoate separated as an oil, which eventually solidified and, crystallised as needles from light petroleum (b. p. 40–60°) (cooling to -80°), had m. p. 28°. The *p*-nitrophenylurethane and 4-diphenylurethane likewise melted over a range, 76–79° and 73–77° respectively.

$\alpha$ - and  $\beta$ -*n*-Hex-3-enyl Bromides.—( $\alpha + \beta$ )-*n*-Hex-3-en-1-ol (46 g.) and pyridine (10 g.) were treated with phosphorus tribromide (50 g.), following the procedure used for the lower homologue, to give ( $\alpha + \beta$ )-*n*-hex-3-enyl bromide (53 g., 71%), b. p. 47–53°/15 mm.,  $n_D^{20}$  1.4690.

$\beta$ -*n*-Hex-3-enyl bromide prepared from  $\beta$ -*n*-hex-3-en-1-ol had b. p. 81–83°/77 mm.,  $n_D^{20}$  1.4708.

$\alpha$ - and  $\beta$ -*n*-Hept-4-enoic Acids.—( $\alpha + \beta$ )-*n*-Hex-3-enyl bromide (50 g.) was converted into the Grignard reagent with magnesium (9.0 g.) in anhydrous ether (120 ml.) and carboxylated by the procedure described for the lower homologue. The resulting ( $\alpha + \beta$ )-*n*-hept-4-enoic acid (26.6 g., 68%) had b. p. 123–125°/20 mm.,  $n_D^{20}$  1.4407 (Found: equiv., 127.7. Calc. for  $C_7H_{12}O_2$ : equiv., 128.2).

In like manner  $\beta$ -*n*-hex-3-enyl bromide was converted into  $\beta$ -*n*-hept-4-enoic acid, b. p. 114–115.5°/14 mm.,  $n_D^{20}$  1.4416 (Found: equiv., 128.7). The *p*-bromophenacyl ester was clearly heterogeneous and when crystallised from aqueous ethanol was easily resolved into two esters. The more soluble ester, when recrystallised from ethanol, had m. p. 47°, and did not depress the m. p. of authentic *cis*-ester (m. p. 46.5°). As first isolated, the less soluble ester melted poorly at about 68°, but 2 crystallisations from ethanol raised this m. p. to 78–79°. On admixture with authentic *p*-bromophenacyl



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*trans-n*-hept-4-enoate (m. p. 78—79°) the mixture had m. p. 78—79°. The preparation of these two reference esters will be described in a forthcoming part of this series.

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