346. *Stereochemical Studies of Olefinic Compounds. Part II.* Ring Scission of 2-1′-Halogenoalkyltetrahydrofurans and 3-Halogeno-2-alkyltetrahydropyrans as a Route to Alk-4-en-1-ols of Known Configuration and as a Method of Chain Extension by Five Methylene Groups.*

By Leslie Crombie and Stanley H. Harper.

The preparation and ring scission of 2-1′-bromoalkyltetrahydrofurans and 3-chloro-2-alkyltetrahydropyrans are investigated as routes to alk-4-en-1-ols and thence, by catalytic reduction, as a means of chain extension by five methylene groups. Although 2-1′-hydroxyethyltetrahydrofuran is readily prepared, conversion into a halide in acceptable yield is difficult. Ring scission of the bromide with sodium gives a moderate yield of *n*-hex-4-en-1-ol, shown to be predominately *trans*, though the infra-red absorption indicates the presence of some of the *cis*-isomer.

The same objective is reached more effectively from 3-chloro-2-alkyltetrahydropyrans. 2 : 3-Dichlorotetrahydropyran and methylmagnesium bromide give *cis*- and *trans*-3-chloro-2-methyltetrahydropyran, separable by distillation but both converted by ring scission into exclusively *trans*-*n*-hex-4-en-1-ol in high yield. Configurations are assigned by comparison with authentic *cis*- and *trans*-*n*-hex-4-en-1-ol, made by catalytic semi-hydrogenation and by reduction by sodium in liquid ammonia, respectively, of *n*-hex-4-yn-1-ol, through mixed melting points of derivatives, and through the infra-red absorption of the alcohols. *n*-Hept-, *n*-oct-, and *n*-non-4-en-1-ols are also prepared by this method and assigned the *trans*-configuration from their infra-red absorption.

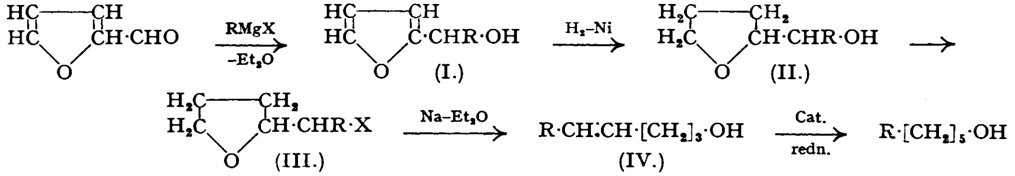
The ring scission of 3-chloro-2-alkyltetrahydropyrans is believed to provide a general route to *trans*-alk-4-en-1-ols.

When a β-halogeno-ether is treated with one of the more electro-positive metals, halogen elimination and scission of the β-carbon–oxygen bond occurs with formation of an olefin and a metal alkoxide : $\mathrm{R{\cdot}O{\cdot}CH_2{\cdot}CH_2X + 2M \longrightarrow R{\cdot}OM + CH_2{:}CH_2 + MX}$

Thus reaction of 2-phenoxyethyl bromide with magnesium or sodium gives ethylene and the phenoxide (Grignard, *Compt. rend.*, 1904, **138**, 1048; Wohl and Berthold, *Ber.*, 1910, **43**, 2175); Boord and his co-workers (*J. Amer. Chem. Soc.*, 1930, **52**, 651, 3396; 1931, **53**, 1505, 2427; 1932, **54**, 751; 1933, **55**, 3293, 4930) generalised the reaction with zinc as a method of preparing olefinic hydrocarbons of the types $\mathrm{RCH{:}CH_2}$, $\mathrm{RCH{:}CHR'}$, $\mathrm{RR'C{:}CH_2}$, and $\mathrm{RR'C{:}CHR''}$; and 2-bromoethyl alkyl ethers with magnesium give ethylene and the bromomagnesium alkoxide (Tallman, *ibid.*, 1934, **56**, 126). When the ether is cyclic the hydroxyl and the ethylenic link are produced within the same molecule by ring scission. Thus tetrahydrofurfuryl chloride or bromide with magnesium or sodium in ether gives *n*-pent-4-en-1-ol in high yield (Paul, *Bull. Soc. chim.*, 1933, [iv], **53**, 424; 1935, [v], **2**, 745; Paul and Normant, *ibid.*, 1943, [v], **10**, 484; *Org. Synth.*, 1945, **25**, 84; Robinson and Smith, *J.*, 1936, 195), and 3-bromotetrahydrofuran is attacked by lithium in ether to give *n*-but-3-en-1-ol (Amstutz, *J. Org. Chem.*, 1944, **9**, 310).

It appeared that ring scission of cyclic β-halogeno-ethers should be capable of extension to provide routes to various ethylenic alcohols of known configuration and, by subsequent catalytic hydrogenation, afford methods for the extension of carbon chains by several methylene groups at a time. The unit added would be terminated by a functional group suitable for a repetition of the process or for other standard reactions. In this and the following paper a study of three such ring scissions, with particular reference to the stereochemistry of the products, is presented. Examples of the use of these reactions have already been given by us (Crombie and Harper, *Nature*, 1949, **164**, 534, 1053; *J.*, 1950, 1152).

When this work was started (1947), no satisfactory procedure for the preparation of tetrahydrofurfuraldehyde was available (cf. Owen, *Ann. Reports*, 1945, **42**, 152)—though it has since been made readily available by the work of Bremner, Coats, Robertson, and Allan (*J.*, 1949, S 25)—and the following route to alk-4-en-1-ols (IV) through the ring scission of 2-1′-halogenoalkyltetrahydrofurans (III) was examined :



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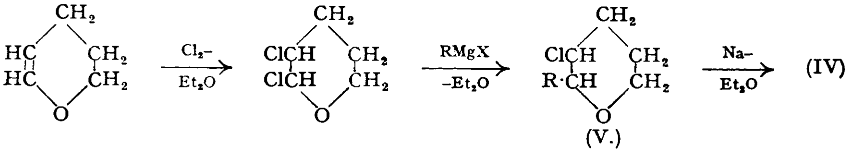
* " 'Leaf Alcohol' and the Stereochemistry of the *cis*- and *trans*-*n*-Hex-3-en-1-ols and *n*-Pent-3-en-1-ols " (Crombie and Harper, *J.*, 1950, 873) is regarded as Part I of this series.

Furfuraldehyde was converted into 2-1′-hydroxyethylfuran (I; $R = Me$) by the Grignard reaction (Peters and Fischer, *J. Amer. Chem. Soc.*, 1930, **52**, 2079; Paul, *Bull. Soc. chim.*, 1937, [v], **4**, 846) and thence by hydrogenation over Raney nickel into 2-1′-hydroxyethyltetrahydrofuran (II; $R = Me$) in high yield. Prolongation of the reduction time led to a lower yield through the formation of higher-boiling material, probably diols formed by hydrogenolysis of the furan ring. Conversion of this carbinol into a halide was unexpectedly difficult, for thionyl chloride, anhydrous hydrogen chloride, and phosphorus and iodine gave very poor yields of impure halides, while phosphorus tribromide gave only 34% of the bromide (III; $R = Me$, $X = Br$), which was difficult to purify. This bromide reacted vigorously with sodium to give a non-homogeneous *n*-hex-4-en-1-ol (IV; $R = Me$) (evidence is given below that this is the *trans*-alcohol, probably in admixture with the *cis*-isomer). In view of the mediocre yields and the apparent impurity of the product this route was unsatisfactory. At this time Paul and Riobé (*Compt. rend.*, 1947, **224**, 474) recorded a similar failure to convert 2-1′-hydroxy-*n*-amyltetrahydrofuran (II; $R = Bu^n$) satisfactorily into a halide, but reached the same objective, *n*-non-4-en-1-ol (IV; $R = Bu^n$), by the ring scission of 3-chloro-2-*n*-butyltetrahydropyran (V; $R = Bu^n$), which Paul (*ibid.*, 1944, **218**, 122) had earlier reported, though without details, as obtained from 2 : 3-dichlorotetrahydropyran and *n*-butylmagnesium chloride.

We therefore turned our attention to the following as a route to alk-4-en-1-ols:



Following details suggested by Dr. R. Paul (private communication in December, 1947) dihydropyran (1 mol.) in ether was chlorinated at 0° and without isolation the 2 : 3-dichlorotetrahydropyran was added to the appropriate Grignard reagent (1·5 mols.) ($R = Me$, Et, Pr^n, and Bu^n); this provides a general route to 3-chloro-2-alkyltetrahydropyrans (V). In further experiments with Mr. J. H. Brookman we have found it possible to reduce the excess of Grignard reagent without causing resinification or seriously diminishing the yield, if vigorous stirring is maintained towards the end of the addition when solid tends to separate. If local concentrations of 2 : 3-dichlorotetrahydropyran are set up resinification occurs. We have not found it profitable to reduce the proportion of alkyl halide below 1·1—1·2 mols., since the formation of the Grignard reagent is not quantitative and contamination of the product with unchanged 2 : 3-dichlorotetrahydropyran is undesirable. When methylmagnesium iodide (1 mol.) was added to 2 : 3-dichlorotetrahydropyran (1 mol.) in ether resinification occurred and scarcely any of the desired product (V; $R = Me$) was obtained.

Riobé (*ibid.*, 1947, **225**, 334) showed that the 3-chloro-2-alkyltetrahydropyrans (V; $R = Me$, Et, and Pr^n) so obtained are separable into lower- and higher-boiling isomeric forms. From the relative values of the physical constants of the pairs of isomers he concluded that the former is *trans* and the latter *cis*. These configurations are consistent with the relative speeds of reaction with ethanolic sodium ethoxide and with the products formed on treatment with potassium hydroxide in diethylene glycol (*ibid.*, 1948, **226**, 1625; *Ann. Chim.*, 1949, **4**, 593).* Riobé stated that on ring scission the *cis*- and the *trans*-isomer gave the same alcohol (IV), the evidence being that neither the ethylenic alcohols nor their acetates could be fractionated by distillation into isomers. Since the boiling points of such *cis*- and *trans*-olefinic alcohols (cf. Crombie and Harper, Part I, *J.*, 1950, 873) are generally very close, fractionation would need to be very

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* In his earliest paper Riobé designated the lower-boiling (*trans*-)isomer the α- and the higher-boiling (*cis*-)isomer the β-form. In his later papers he reversed this nomenclature without comment. To avoid further confusion it is desirable to discontinue the use of Greek prefixes, as applied to the 3-chloro-2-alkyltetrahydropyrans, since actual configurations can now be assigned with reasonable certainty. However, for the purposes of this and the following paper, it is necessary to designate the alcohols derived from the *trans*-, by ring scission with sodium, as α and those derived from the *cis*-3-chloro-2-alkyltetrahydro-pyrans (or -furans) as β. The stereochemistry of these alcohols is elucidated later in these papers and this notation too then becomes redundant. Paul and Tchelitcheff (*Bull. Soc. chim.*, 1948, [v], **15**, 1199) have separated the isomeric 3-chloro-2-*n*-hexyltetrahydropyrans and assigned the *cis*-configuration to the lower-boiling isomer; on the basis of the Auwers–Skita generalisations we believe this to be incorrect.

[*Added in proof, May 15th,* 1950.] Dr. R. Paul (private communication) concurs with us that the assignments of configuration made by Paul and Tchelitcheff should be reversed.

refined to be a convincing test. We have therefore investigated the homogeneity and the stereochemistry of the alcohols formed in this reaction.

Fractional distillation of crude 3-chloro-2-methyltetrahydropyran yielded the higher- and the lower-boiling isomer, whose physical properties differ somewhat from those reported by Riobé (Table I). On the assumption that the Auwers–Skita generalisations are applicable to tetrahydropyrans, we agree with Riobé's assignment of configurations. During distillation of the precursory 2 : 3-dichlorotetrahydropyran we observed no appreciable spread of boiling point; we believe that this consists of one geometrical form only, since addition of halogens to a double bond, here *cis*, is known to occur *trans* and would give *trans*-2 : 3-dichlorotetrahydropyran (cf. Hammett, " Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, 1940, p. 147; Raphael, *J.*, 1949, S 44, and references cited therein). When therefore this 2 : 3-dichlorotetrahydropyran reacts with the Grignard reagent, $C_{(2)}$ becomes planar owing to the formation of a carbonium ion (S_N1 mechanism), and both *cis*- and *trans*-3-chloro-2-alkyltetrahydropyran are produced.

TABLE I.

3-Chloro-2-methyl-tetrahydropyran.	B. p.	d_4^{21}.	n_D^{21}.	$[R_L]_D$.		Ref.
				Found.	Calc.	
trans-	154°; 51°/18 mm.	1·071	1·4551	34·09	34·22	1
	56°/23 mm.	1·058	1·4543	34·43	34·22	2
cis-	172°; 66°/18 mm.	1·091	1·4626	33·97	34·22	1
	72°/23 mm.	1·090	1·4646	34·09	34·22	2

[1] Crombie and Harper, this paper. [2] Riobé, *Ann. Chim.*, 1949, **4**, 593.

Subjecting *cis*- and *trans*-3-chloro-2-methyltetrahydropyran separately to ring scission we observed that the *cis*- reacted more vigorously with sodium than did the *trans*-isomer. The α- and β-*n*-hex-4-en-1-ol had nearly identical physical properties (Table II) and gave identical 1-naphthyl- and 4-diphenylyl-urethanes. Furthermore, conversion of (α + β)-*n*-hex-4-en-1-ol, made by ring scission of the mixed *cis*- and *trans*-3-chloro-2-methyltetrahydropyrans, into *n*-hept-5-enoic acid,* through the *n*-hex-4-enyl bromide and carboxylation of the derived Grignard reagent, gave an acid which from the purity of its derivatives was homogeneous (to be reported later). We conclude, in agreement with Riobé, that this ring scission gives a single stereoisomer of *n*-hex-4-en-1-ol. We have also prepared (α + β)-*n*-hept-, (α + β)-*n*-oct-, and (α + β)-*n*-non-4-en-1-ol, by ring scission of the appropriate 3-chloro-2-alkyltetrahydropyran (V; R = Et, Pr^n, and Bu^n) and have observed no indications of the presence of more than one stereoisomer.

TABLE II.

n-Hex-4-en-1-ol.	B. p.	n_D^{20}.	1-Naphthylurethane, m. p.	4-Diphenylylurethane, m. p.
α-	158°	1·4403	73°	93—94°
β-	159	1·4402	73	92—93
cis-	158—159	1·4420	74—75	77·5
trans-	158	1·4402	72	93

To elucidate the configuration of the isomer formed in the ring scission we have prepared *cis*- and *trans*-*n*-hex-4-en-1-ol by unambiguous routes. (α + β)-*n*-Hex-4-en-1-ol was brominated in ether below 0° and the 4 : 5-dibromohexanol dehydrobrominated by sodamide in liquid ammonia, to yield *n*-hex-4-yn-1-ol, characterised as its 1-naphthylurethane. From this hexynol, authentic *cis*-*n*-hex-4-en-1-ol was prepared by semi-hydrogenation over palladium–calcium carbonate at room temperature. This procedure is known to give a *cis*-double bond (Campbell and Campbell, *Chem. Reviews*, 1942, **31**, 90; Part I, *loc. cit.*). Reduction of the hexynol with sodium in liquid ammonia, which is known to proceed by *trans*-addition (Campbell and Campbell, *loc. cit.*; Sondheimer, *J.*, 1950, 877; Part I, *loc. cit.*), yielded *trans*-*n*-hex-4-en-1-ol. These alcohols were characterised as their 1-naphthyl- and 4-diphenylyl-urethanes (Table II), and mixed melting points established the identity of the α- and the β-*n*-hex-4-en-1-ol with the *trans*-isomer.

The assignment of the *trans*-configuration to the alcohol formed by ring scission is supported by infra-red absorption measurements. The spectra of α-, β-, and *trans*-*n*-hex-4-en-1-ol (Figs. 1—3 respectively) are closely similar and differ markedly from that of the *cis*-isomer

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* In this and succeeding papers we use Geneva numbering for carboxylic acids.

(Fig. 4). Strong absorption at 10·3 μ. is characteristic of the *trans*-forms (cf. Part I, *loc. cit.*), absorption here being very much weaker for the *cis*-form. In the spectrum of *cis*-*n*-hex-3-en-1-ol (*loc. cit.*, Fig. 1) there is marked absorption at 11·5 μ., but careful examination has failed to reveal a corresponding peak in that of *cis*-*n*-hex-4-en-1-ol; the latter has however characteristic absorption at 9·65 μ. The spectra of the α- and β-alcohols give no indication of the presence of *cis*-isomer. In particular the relative intensities of the 9·4-μ. (primary hydroxyl) and the 10·3-μ. ("*trans*") band correspond closely with those for the pure *trans*-isomer; any *cis*-isomer should be easily detected by decrease in absorption at 10·3 μ. Thus on chemical and spectroscopic evidence the product of the ring scission of both *cis*- and *trans*-3-chloro-2-methyltetrahydropyran is *trans*-*n*-hex-4-en-1-ol, free from any detectable quantity of the *cis*-isomer. The infra-red absorption spectra of (α + β)-*n*-hept-, (α + β)-*n*-oct-, and (α + β)-*n*-non-4-en-1-ol (Figs. 6—8 respectively) all exhibit the strong "*trans*" peak at 10·3 μ. Reference samples of the corresponding authentic *cis*- and *trans*-alcohols have not been prepared, but from the spectroscopic evidence coupled with the apparent chemical homogeneity, we conclude that these too are pure *trans*-isomers.

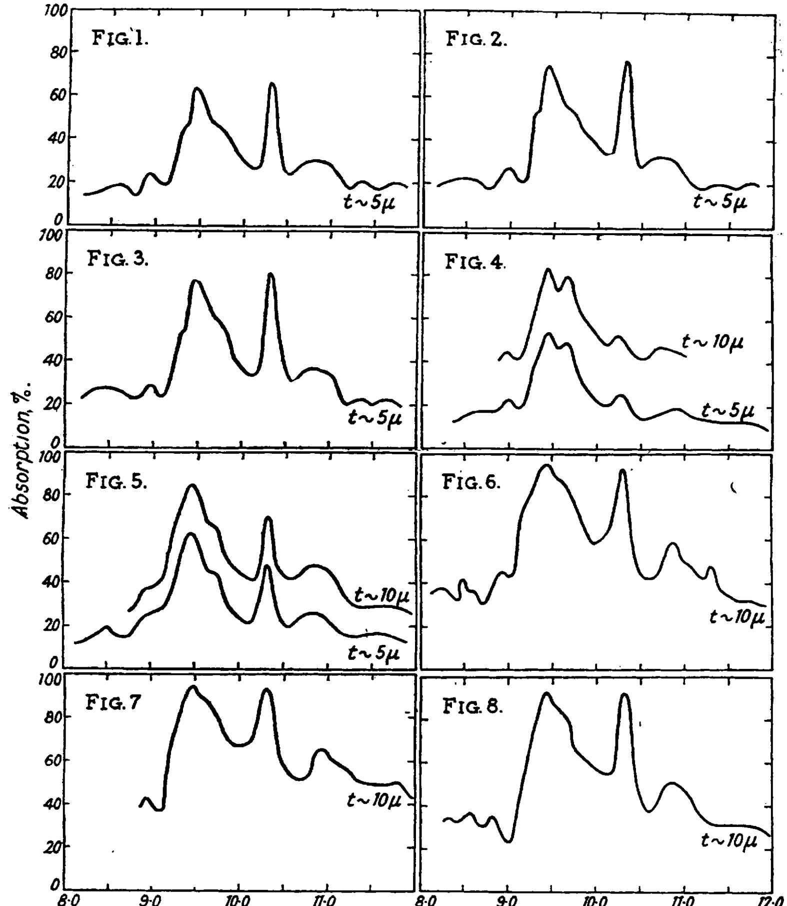

Fig. 1.—*α-n-Hex-4-en-1-ol.*
Fig. 2.—*β-n-Hex-4-en-1-ol.*
Fig. 3.—trans-n-*Hex-4-en-1-ol.*
Fig. 4.—cis-n-*Hex-4-en-1-ol.*
Fig. 5.—n-*Hex-4-en-1-ol from ring scission of 2-1′-bromoethyltetrahydrofuran.*
Fig. 6.—(α + β)-n-*Hept-4-en-1-ol.*
Fig. 7.—(α + β)-n-*Oct-4-en-1-ol.*
Fig. 8.—(α + β)-n-*Non-4-en-1-ol.*

In view of the exclusive formation of the *trans*-alcohol in this ring scission we have re-examined the specimen of *n*-hex-4-en-1-ol obtained by ring scission of 2-1′-bromoethyltetrahydrofuran. The melting point of its 4-diphenylylurethane was not sharp but was raised on admixture with that of the authentic *trans*-derivative. The alcohol thus appears to be largely but not entirely *trans*-*n*-hex-4-en-1-ol. This view is supported by the infra-red spectrum (Fig. 5) which bears a general similarity to that of the *trans*-alcohol (Fig. 3) but differs in two important features. First, there are signs of a new absorption maximum appearing at ~9·7 μ., this being more distinct than the inflexion which occurs in this region for the *trans*-isomer. Secondly, the intensity of absorption of the 10·3-μ. ("*trans*") band relative to that of the 9·4-μ. (primary hydroxyl) peak is markedly reduced. Both these observations suggest that the contaminant is *cis*-*n*-hex-4-en-1-ol and that the ring scission of 2-1′-bromoethyltetrahydrofuran gives a mixture of *cis*- and *trans*-*n*-hex-4-en-1-ols.

We reserve discussion of the mechanism of these ring scissions until the following paper.

EXPERIMENTAL.

Microanalyses, apart from the halogen determinations, are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected. Infra-red absorption spectra were determined by one of us (L. C.) with a Grubb Parsons spectrometer coupled to a Brown recorder, using the pure liquids in a cell of 5—10-μ. thickness (not constant). The spectra were measured over the range 6—15 μ. but only the most important portion (8—12 μ.) is reproduced. We are indebted to Dr. W. C. Price for this facility.

2-1′-Hydroxyethylfuran.—Freshly distilled furfuraldehyde (240 g., 1·0 mol.) was added dropwise during 4 hours to the vigorously stirred ice-cold Grignard reagent prepared from methyl iodide (444 g., 1·25 mols.) and magnesium (80 g.) in dry ether (900 ml.). Next day the product was treated with iced water and the aqueous slurry thrice further extracted with ether. The ethereal extract was washed with aqueous sodium hydrogen sulphite and then water, and dried (K_2CO_3). A few drops of aniline were added, the ether was removed, and the residue distilled to give 2-1′-hydroxyethylfuran (182 g., 65%), b. p. 80·5°/21 mm., n_D^{20} 1·4794. Peters and Fischer (*J. Amer. Chem. Soc.*, 1930, **52**, 2079) record b. p. 76—77°/23 mm., n_D^{25} 1·4785. This carbinol was particularly sensitive to acids and was therefore stored in the presence of a little base.

2-1′-Hydroxyethyltetrahydrofuran.—2-1′-Hydroxyethylfuran (70·5 g.) in ethanol (200 ml.) was hydrogenated at 100°/125 atm. in a metal autoclave fitted with a magnetically operated agitator in the presence of Raney nickel (7 g.). After 3 hours the reduction was stopped, the suspension filtered, and the ethanol evaporated under a column. Distillation of the residue gave 2-1′-hydroxyethyltetrahydrofuran (65 g., 89%), b. p. 75—77°/20 mm., n_D^{20} 1·4480 (Found : C, 62·3; H, 10·15. Calc. for $C_6H_{12}O_2$: C, 62·1; H, 10·3%), which possessed a mushroom-like odour. Paul (*Bull. Soc. chim.*, 1937, [v], **4**, 846) records b. p. 71°/16 mm., n_D^{17} 1·4500. In another reduction, when the hydrogenation was continued for 18 hours at 100°, the yield dropped to 80% and there was a larger proportion of high-boiling residue.

Attempts to Prepare 2-1′-Halogenoethyltetrahydrofurans.—Thionyl chloride and pyridine (cf. *Org. Synth.*, 1945, **25**, 84), even at −20°, caused resinification and gave only a trace of the required chloride, as did anhydrous hydrogen chloride.

Red phosphorus (0·55 g.) was mixed with 2-1′-hydroxyethyltetrahydrofuran (5·8 g.), and then iodine (6·35 g.) added in portions. The mixture became hot and the reaction was completed at 100° during 1 hour. The product was diluted with ether and filtered through glass wool, and the filtrate washed with aqueous potassium hydroxide. After drying and evaporation the residue was distilled at 3 mm. to give fractions : b. p. 45—78°, n_D^{22} 1·4845 (1·7 g.) (Found : I, 45·7) ; b. p. 78—100°, n_D^{22} 1·5304 (0·9 g.) (Found : I, 58·1) ; and b. p. 100—103°, n_D^{22} 1·5540 (1·2 g.) (Found : I, 62·1. Calc. for $C_6H_{11}OI$: I, 56·2%). Much decomposition occurred on attempting to distill the crude iodide at 45 mm.

2-1′-Hydroxyethyltetrahydrofuran (27 g.), mixed with pyridine (3 ml.), was added dropwise slowly to a mixture of phosphorus tribromide (22·4 g.) and pyridine (1 ml.) kept at 0° (cf. Robinson and Smith, *J.*, 1936, 195). After 48 hours at room temperature the product was distilled off under vacuum and had b. p. 74°/21 mm. to 140°/45 mm. This crude bromide was twice fractionated by distillation at 14 mm. to give fractions : b. p. below 68°, n_D^{23} 1·4712 (0·7 g.) ; b. p. 68—70°, n_D^{23} 1·4744 (4·4 g.) (Found : Br, 45·5%) ; b. p. 70—80°, n_D^{23} 1·4742 (2·0 g.) ; b. p. 80—90°, n_D^{23} 1·4740 (3·8 g.) ; b. p. 90—100°, n_D^{23} 1·4740 (4·0 g.) (Found : Br, 46·4. Calc. for $C_6H_{11}OBr$: Br, 44·7%). Repetition of this distillation gave no better results. In another experiment the carbinol (13·5 g.) was added during 30 minutes to phosphorus tribromide (11·2 g.) kept at −5°, in the absence of pyridine. The product was worked up following the procedure of Gerrard (*J.*, 1945, 848) and distilled at 18 mm. to give fractions : b. p. 46—70°, n_D^{25} 1·4842 (1·4 g.) ; b. p. 70—80°, n_D^{25} 1·4791 (1·4 g.) ; and b. p. 80—95°, n_D^{25} 1·4810 (2·1 g.).

Ring Scission of 2-1′-Bromoethyltetrahydrofuran.—The bromide (10·0 g. ; b. p. 68—100°/14 mm.) in anhydrous ether (25 ml.) was added dropwise to a stirred suspension of powdered sodium (3·5 g., well rinsed with ether to remove xylene) in anhydrous ether (25 ml.). An exothermic reaction ensued, sufficient to cause gentle refluxing of the ether, whilst the sodium became purple. When reaction had finished water was added, and the ethereal layer separated, washed, and dried ($MgSO_4$). Careful removal of the ether and distillation of the residue gave a fraction, b. p. 130—180°, n_D^{20} 1·4426 (3·0 g., 54%). This crude *n*-hex-4-en-1-ol was redistilled at 11 mm. to give three fractions : (i) b. p. 52—54°, n_D^{20} 1·4408 (0·6 g.) ; (ii) b. p. 54—59°, n_D^{20} 1·4401 (0·5 g.) ; and (iii) b. p. 59—66°, n_D^{20} 1·4442 (0·8 g.). Similar results were obtained in other experiments [Found (for a sample redistilled at atmospheric pressure) : C, 72·3 ; H, 11·5. Calc. for $C_6H_{12}O$: C, 71·9 ; H, 12·1%].

After 2 years, fraction (iii) was redistilled ; it then had b. p. 159°, n_D^{20} 1·4413. Its 4-diphenylylurethane had m. p. 81—84° after two crystallisations from light petroleum (b. p. 80—100°) ; when admixed with authentic *trans*-*n*-hex-4-en-1-yl 4-diphenylylurethane (see below ; m. p. 93°) it had m. p. 82—86° and admixed with authentic *cis*-derivative (m. p. 78°) had m. p. 75—80°.

3-Chloro-2-methyltetrahydropyran.—Dihydropyran (168 g.) in dry ether (400 ml.) was kept between

0° and 5°, and dried chlorine passed into the solution until it acquired a green tinge due to excess of chlorine (*ca.* 2·5 hours). Excess of chlorine was then removed by the dropwise addition of dihydropyran until the solution of 2 : 3-dichlorotetrahydropyran (310 g., 1·0 mol.) was again colourless. Meanwhile methylmagnesium bromide (1·5 mols.) was prepared in dry ether (500 ml.) from magnesium (72 g.) and gaseous methyl bromide. This reagent was cooled in an ice-bath and well stirred by means of a Hershberg wire stirrer while the 2 : 3-dichlorotetrahydropyran solution prepared above was added dropwise. After storage at room temperature, usually overnight, the excess of methylmagnesium bromide was decomposed by the cautious addition of cold ammonium chloride solution, with stirring and external cooling. Concentrated hydrochloric acid (98 ml.) was then added and the ethereal layer separated and dried (K_2CO_3). The ether was removed, and the residue distilled to give, after elimination of lower-boiling material, the mixed *cis-* and *trans*-3-chloro-2-methyltetrahydropyrans (164 g., 61%), b. p. 150—175° (mainly), $n_{\rm D}^{20}$ 1·4594. This mixture was fractionally distilled, first at 13 mm. and then at atmospheric pressure, through a 50 × 1·5-cm. helices-packed column with variable take-off and electrically heated jacket, to give the lower-boiling *trans-* and the higher-boiling *cis*-isomer (see Table I). The *cis*-form darkened when kept, whereas the *trans*-form remained colourless.

Ring Scission of 3-*Chloro*-2-*methyltetrahydropyran.*—Sodium (144 g., 2·2 g.-atoms) was powdered under xylene, then thoroughly rinsed with dry ether, and covered with this solvent (1 l.). A little 3-chloro-2-methyltetrahydropyran (*cis-* + *trans-*) was added and the suspension stirred with a Hershberg wire stirrer until reaction commenced as shown by the surface of the sodium assuming an indigo-blue colour and by refluxing of the ether. The remaining 3-chloro-2-methyltetrahydropyran (380 g. in all, 1 mol.) was now added dropwise, so that steady refluxing was maintained. The thick blue suspension was stirred for a further 2 hours and then kept at room temperature overnight. Next day ice and water were cautiously added. The ethereal layer was separated and the aqueous layer further extracted with ether. After being washed and dried (Na_2SO_4), the ether was removed under a column from the combined ethereal extracts, and the residue distilled to give (*trans-*)*n*-hex-4-en-1-ol (230 g., 82%), b. p. 68·5°/15 mm., $n_{\rm D}^{20}$ 1·4403.

In like manner *trans*-3-chloro-2-methyltetrahydropyran (18 g.) gave α-*n*-hex-4-en-1-ol (11·6 g., 87%), b. p. 158°, $n_{\rm D}^{20}$ 1·4403, characterised as the 1-naphthylurethane, needles [from light petroleum (b. p. 40—60°)], m. p. 73°, and as the 4-diphenylylurethane, clumps of short needles [from light petroleum (b. p. 80—100°)], m. p. 93—94°.

Similarly *cis*-3-chloro-2-methyltetrahydropyran (17 g.) with sodium (6·5 g.) gave β-*n*-hex-4-en-1-ol (9·9 g., 78%), b. p. 159°, $n_{\rm D}^{20}$ 1·4402, characterised as the 1-naphthylurethane (needles), m. p. 73°, and as the 4-diphenylylurethane (clumps of needles), m. p. 92—93°. Neither the 1-naphthyl- nor the 4-diphenylyl-urethane of the α- and β-alcohols showed depressions of the m. p. when mixed, or when mixed with the corresponding derivatives of authentic *trans-n*-hex-4-en-1-ol (see below). These derivatives were obtained pure more readily (1 or 2 crystallisations) than those of *trans-n*-hex-4-en-1-ol obtained by reduction of *n*-hex-4-yn-1-ol with sodium in liquid ammonia.

n-*Hex*-4-*yn*-1-*ol.*—Bromine (99 g.) was added slowly to the (*trans-*)*n*-hex-4-en-1-ol (61·5 g.), obtained by ring scission of *cis-* + *trans*-3-chloro-2-methyltetrahydropyran, diluted with an equal volume of anhydrous ether, at $<$10° (external cooling). When addition was complete (2—3 hours), the ether was sucked off by a water-pump at room temperature from the crude *erythro*-4 : 5-dibromohexanol. To a solution of sodamide [from sodium (70 g.) and liquid ammonia (2 l.) in the presence of ferric nitrate (cf. Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120)], the 4 : 5-dibromohexanol was added rapidly, with cooling in alcohol–solid carbon dioxide. After 3 hours' stirring the flask was removed from the cooling bath, ether (100 ml.) added, and the ammonia allowed to evaporate overnight. Next day water was added and the alcohol removed by 5 extractions with ether. The extracts were washed with dilute acid and then water and dried, and the ether removed under a column. Distillation of the brown residue gave the crude alcohol (25 g., 41%), b. p. 160—178°, which was refractionated to give n-*hex*-4-*yn*-1-*ol* (18·6 g., 31%), b. p. 165—168°, $n_{\rm D}^{20}$ 1·4586 (Found: C, 73·35, 73·4; H, 10·5, 10·55. $C_6H_{10}O$ requires C, 73·4; H, 10·25%). The 1-*naphthylurethane*, which crystallised from light petroleum (b. p. 40—60°), had m. p. 82° (Found: C, 76·25; H, 6·45; N, 5·55. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·25%).

trans-n-*Hex*-4-*en*-1-*ol.*—*n*-Hex-4-yn-1-ol (5·0 g.) was added dropwise to a stirred solution of sodium (5 g.) in liquid ammonia (250 ml.), cooled in alcohol–solid carbon dioxide. The alcohol was washed in with a little ether, and the mixture stirred for a further 90 minutes, whereafter solid ammonium chloride was added cautiously until the blue colour was discharged. The solution was covered with ether (15 ml.), and the ammonia allowed to evaporate overnight. Next day water (50 ml.) and more ether (10 ml.) were added, and the ethereal layer was separated. The aqueous layer was extracted 3 times with ether and the combined ethereal extracts were washed with 10% sulphuric acid, then water, and dried. Removal of the ether through a column and distillation of the residue gave trans-n-*hex*-4-*en*-1-*ol* (3·95 g., 72%), b. p. 158°, $n_{\rm D}^{20}$ 1·4402 (Found: C, 71·35; H, 11·95. $C_6H_{12}O$ requires C, 71·9; H, 12·1%). The 1-*naphthylurethane*, forming needles from light petroleum (b. p. 40—60°) after 4 crystallisations, had m. p. 72° (Found: C, 75·5; H, 6·9; N, 5·55. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1; N, 5·2%), whilst the 4-*diphenylylurethane* formed clumps of short needles [from light petroleum (b. p. 80—100°)], having m. p. 93° (Found: C, 77·0; H, 7·25. $C_{19}H_{21}O_2N$ requires C, 77·25; H, 7·25%).

cis-n-*Hex*-4-*en*-1-*ol.*—*n*-Hex-4-yn-1-ol (5·24 g.) was hydrogenated at atmospheric pressure over pre-reduced palladium–calcium carbonate (5%), no solvent being used, until 1200 ml. of hydrogen had been absorbed at 16° and 758 mm. (Calc. for semi-hydrogenation: 1275 ml.). Ether and Filtercel were added, and the catalyst was filtered off. Distillation gave cis-n-*hex*-4-*en*-1-*ol* (4·6 g., 75%), b. p. 156—160°, of which the bulk had b. p. 158—159° on redistillation, $n_{\rm D}^{20}$ 1·4420 (Found: C, 72·5; H, 11·7. $C_6H_{12}O$ requires C, 71·9; H, 12·1%). The 1-*naphthylurethane* crystallised as long needles [from light petroleum (b. p. 40—60°)], m. p. 74—75° (Found: C, 75·95; H, 6·8; N, 5·55%), which on admixture with the *trans-* 1-naphthylurethane softened at 63° and melted unsharply at 65—68°. The 4-*diphenylylurethane* crystallised as needles [from light petroleum (b. p. 80—100°)], m. p. 77·5° (Found: C, 77·55; H, 6·85%), which on admixture with the *trans*-4-diphenylylurethane had m. p. 75—77°.

3-*Chloro-2-ethyltetrahydropyran* [with J. H. Brookman].—A series of experiments was carried out under comparable conditions to discover the effect of varying the ratio of Grignard reagent to 2 : 3-dichlorotetrahydropyran. Following the procedure for the lower homologue, 2 : 3-dichlorotetrahydropyran [prepared by chlorination of dihydropyran (84 g., 1·0 mol.) in ether (200 ml.)] was added to ethylmagnesium bromide (1·5—0·9 mol.) in the appropriate volume of ether. Discoloration and resin formation were mitigated by dropping the ethereal 2 : 3-dichlorotetrahydropyran into the middle of the well-stirred (Hershberg wire stirrer) Grignard solution. By working up as previously described, the products were distilled to give the following fractions of the *cis*- and *trans*-3-chloro-2-ethyltetrahydropyrans (foreruns and residues are omitted) :

Ethylmagnesium bromide.	B. p.	n_D^{20}.	Wt., g.	Yield, %.
1·5 mols.	52—63°/11 mm.	1·4499	34	23
	63—72°/11 mm.	1·4608	37	25
	72—81°/12 mm.	1·4638	19	13
	Total		90	61
1·3 mols.	*ca.* 50—67°/14 mm.	1·4514	26	16
	67—74°/14 mm.	1·4588	36	24
	74—82°/14 mm.	1·4653	19	13
	Total		81	53
1·1 mols.	*ca.* 50—65°/13 mm.	1·4474	23	15
	65—73°/13 mm.	1·4607	36	24
	73—81°/13 mm.	1·4651	19	13
	Total		78	52
0·9 mol.	49—65°/14 mm.	1·4563	27	19
	65—74°/14 mm.	1·4674	35	23
	74—82°/14 mm.	1·4801	(17)	—
	Total		62	42

The top fraction of the last run evidently contained unchanged 2 : 3-dichlorotetrahydropyran (Paul, *Compt. rend.*, 1944, **218**, 122, records b. p. 89—90°/20 mm., n_D^{17} 1·4957), and was dark brown (the top fractions of the other runs were only yellow to pale brown and did not contain resin). On storage of this fraction colourless needles separated, being presumably di-3-chloropyran-2-yl ether (cf. Paul, *loc. cit.*) formed by hydrolysis of the 2 : 3-dichlorotetrahydropyran. Riobé (*Ann. Chim.*, 1949, **4**, 593) obtained a 70% yield of the mixed *cis*- and *trans*-3-chloro-2-ethyltetrahydropyrans using 1·5 mols. ethylmagnesium bromide, and recorded for the *trans*-isomer, b. p. 69°/22 mm., n_D^{20} 1·4559, and for the *cis*-isomer, b. p. 84°/22 mm., n_D^{20} 1·4651. The presence of *cis*- and *trans*-isomers in our preparations is evident.

trans-n-*Hept*-4-*en*-1-*ol*.—Ring scission of the mixed *cis*- and *trans*-3-chloro-2-ethyltetrahydropyrans, by the procedure used for the lower homologue, gave *trans*-*n*-hept-4-en-1-ol, b. p. 74—76°/11 mm., n_D^{20} 1·4439. Riobé (*loc. cit.*) recorded b. p. 81·5°/17 mm., n_D^{20} 1·4442.

3-*Chloro*-2-n-*propyltetrahydropyran*.—By the procedure used for the lower homologues, 2 : 3-dichlorotetrahydropyran [prepared by chlorination of dihydropyran (210 g., 1·0 mol.) in ether (500 ml.)] was added to the Grignard reagent prepared from *n*-propyl bromide (370 g., 1·2 mols.) and magnesium (73 g.) in dry ether (750 ml.). Towards the end of the addition the ice-bath was allowed to melt and the ether refluxed gently. When 80 ml. of the ethereal 2 : 3-dichlorotetrahydropyran had still to be added, solid began to separate and stirring became difficult, but the addition was completed. After being worked up as previously described, the product was distilled through a Dufton column. After elimination of a forerun, b. p. 60—82°/18 mm., the mixed *cis*- and *trans*-3-chloro-2-*n*-propyltetrahydropyrans (249 g., 62%) were collected, b. p. 82—89°/18 mm., mainly at 85—87°, n_D^{20} 1·4588. Riobé (*loc. cit.*) obtained a 60% yield using 1·5 mols. of *n*-propyl bromide and recorded for the *trans*-isomer, b. p. 88°/23 mm., n_D^{18} 1·4577, and for the *cis*-isomer, b. p. 101°/23 mm., n_D^{18} 1·4659. Our product appears to consist largely of the *trans*-form.

trans-n-*Oct*-4-*en*-1-*ol*.—Ring scission of the largely *trans*-3-chloro-2-*n*-propyltetrahydropyran (245 g.), using powdered sodium (77 g.), and following the procedure for the lower homologues, gave *trans*-*n*-oct-4-en-1-ol (170 g., 88%), b. p. 86—88°/11 mm., n_D^{20} 1·4456. Another preparation [with J. H. Brookman] had b. p. 104—106·5°/30 mm., n_D^{20} 1·4451. Riobé (*loc. cit.*) recorded b. p. 95°/17 mm., n_D^{20} 1·4462.

3-*Chloro*-2-n-*butyltetrahydropyran* [with J. H. Brookman].—By the procedure used for the lower homologues, 2 : 3-dichlorotetrahydropyran [prepared by chlorination of dihydropyran (252 g., 1·0 mol.) in ether (600 ml.)] was added to the Grignard reagent prepared from *n*-butyl bromide (452 g., 1·1 mols.) and magnesium (81 g.) in dry ether (550 ml.). Before all the ethereal 2 : 3-dichlorotetrahydropyran could be added the reaction mixture set solid and the addition was discontinued. The unused solution corresponded to 21 g. of dihydropyran, showing that 1·2 mols. of *n*-butylmagnesium bromide had been used. After working up as previously described, the product was distilled, and after elimination of a forerun the mixed *cis*- and *trans*-3-chloro-2-*n*-butyltetrahydropyrans (303 g., 63%) were collected in three fractions : b. p. 83—90°/11 mm., n_D^{20} 1·4532 (33 g.) ; b. p. 90—103°/11 mm., n_D^{20} 1·4618 (264 g.) ; and b. p. 103—108°/11 mm., n_D^{20} 1·4670 (6 g.). Riobé (*loc. cit.*) obtained a 73% yield of mixed *cis*- and *trans*-isomers using 1·5 mols. of *n*-butylmagnesium bromide and recorded for the *trans*-isomer, b. p. 101°/21 mm., n_D^{23} 1·4571, and for the *cis*-isomer, b. p. 114°/21 mm., n_D^{23} 1·4659. Our lower and upper fractions, therefore, are substantially pure *trans*- and *cis*-forms respectively.

trans-n-*Non-4-en-1-ol* [with J. H. BROOKMAN].—Ring scission of the mixed *cis-* and *trans*-3-chloro-2-n-butyltetrahydropyrans (270 g.), as above, with powdered sodium (78 g.), gave *trans-n*-non-4-en-1-ol (183 g., 84%), b. p. 101—105°/13 mm., n_D^{20} 1·4476. Riobé (*loc. cit.*) recorded a 90% yield of this alcohol having b. p. 108·5°/17 mm. and n_D^{18} 1·4494.

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