The Stereochemistry of Additions to Olefins. III. The Prins Reaction with *cis*- and *trans*-4-Octene

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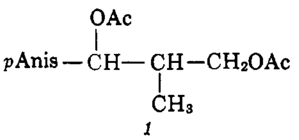
Received October 5, 1962

Prins reactions were carried out with pure *cis*- and *trans*-4-octene and the product *m*-dioxanes were isolated and purified. Hydrolysis afforded mixtures of the diastereomeric 3-propyl-1,3-hexanediols. Analysis indicated that the *erythro/threo* ratios of these diols (and of the *m*-dioxanes from which they were generated) were 1.3 and 4.2 from the *cis* and *trans* olefins, respectively. These results are interpreted in terms of a general mechanistic scheme for the Prins reaction. Several other products were isolated from the Prins reactions.

Recent studies concerning the stereochemical nature of the Prins reaction[2] of cyclohexenes have clearly demonstrated that the condensations proceeded exclusively with *trans*[3,4] diaxial[5] addition. However, with anethole, an equilibrium mixture of the diacetates *1* was obtained from reaction with formaldehyde in acetic acid.[6] The *m*-dioxane *2* was also produced and was suspected to be a mixture of *cis* and *trans* isomers. These observations were interpreted in terms of thermodynamic control, involving a highly stabilized *p*-anisyl cation intermediate. It was not stated whether the kinetic and equilibrium compositions of mixture *1* were identical. We have examined the reaction of formaldehyde in the presence of an acid catalyst with the *cis* and *trans* isomers of 4-octene. In the present case of an aliphatic olefin, it was expected that the product diols and *m*-dioxanes would be stable under the reaction conditions, and that analysis would indicate the kinetic composition of the reaction mixture.

cis- and *trans*-4-octenes were obtained by the reduction of 4-octyne with diborane and sodium in ammonia, respectively, and were purified by gas chromatography. Each of the olefins was added to a slurry of paraformaldehyde in a sulfuric acid–dioxane mixture at room temperature. The products were isolated by fractional distillation and were purified by gas chromatography. The major products were found to be 4,5-di-*n*-propyl-*m*-dioxane (*3*) and 3-ethyl-5-*n*-propyltetrahydropyran-4-ol (*4*). The minor products consisted of 2-ethyl-4-*n*-propyltetrahydrofuran (*5*), 3-*n*-propyl-4-(*trans*-1′-propenyl)tetrahydrofuran (*6*), and 3-*n*-propyl-4-(1′-hydroxy-1′-propyl)tetrahydrofuran (*7*). Several additional minor components were not identified.



$$p\text{Anis}-\overset{\overset{\displaystyle OAc}{|}}{C}H-\underset{\underset{\displaystyle CH_3}{|}}{C}H-CH_2OAc$$

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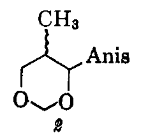

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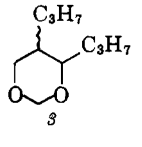

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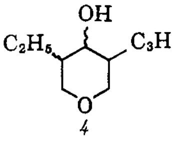

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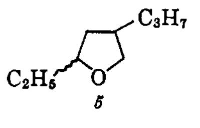

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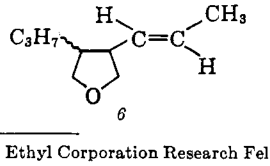

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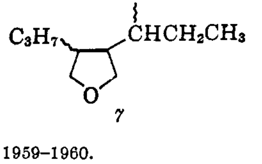

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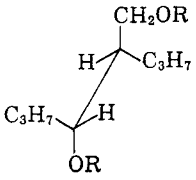
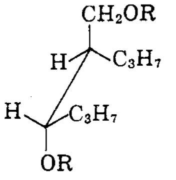
One of the major products of the Prins reactions from both isomeric olefins was a mixture of the diastereomeric *m*-dioxanes *3a* and *3b*. The assignment of structure was supported by infrared spectral data. Ring cleavage was effected by heating with methanolic sulfuric acid and the dimethyl formal was converted to the 2,4-dinitrophenylhydrazone of formaldehyde. It was assumed that hydrolysis of the *m*-dioxane took place without affecting the asymmetric center at position 4,[7] and that the composition of the mixture of the diastereometric diols *8a* and *8b* obtained by distillation, was identical with the composition of the original dioxane mixture *3* (a and b).



8a. R = H

9a. R = $\underset{\underset{\displaystyle O}{\|}}{C}NHC_6H_5$



8b. R = H

9b. R = $\underset{\underset{\displaystyle O}{\|}}{C}NHC_6H_5$

In order to establish the correct structure of the diol *8*, an authentic sample of 2-propyl-1,3-hexanediol was synthesized *via* a Reformatsky reaction between *n*-butyraldehyde and ethyl α-bromovalerate. The resulting ethyl 3-hydroxy-2-propylcaproate was reduced with lithium aluminum hydride. The synthetic diol was assumed to be a mixture of the diastereomers *8* and showed the same retention time on gas chromatography. The infrared spectra were identical.

The bisphenylurethan was prepared and fractional crystallization afforded the *threo* isomer *9b* as the higher melting derivative. The *erythro* product *9a* was isolated from the mother liquors. This synthetic diol was subjected to the conditions of hydrolysis of the *m*-dioxanes. The recovered diol was converted to the bisphenylurethans, which were separated; the isolated total weight of derivative was slightly lower; however, the relative proportion was unchanged. The *m*-dioxanes, obtained from *trans*- and *cis*-4-octene, were individually cleaved to the diol mixture *8*. Both products were converted to the bisphenylurethans, and the diastereomers were separated by fractional crystallization. From this analysis, the relative amounts of *cis*- and *trans*-4,5-di-*n*-propyl-1,3-dioxane

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(1) Ethyl Corporation Research Fellow, 1959–1960.

(2) H. J. Prins, *Chem. Weekblad*, **16**, 1510 (1919); *Cf.* also E. E. Arundale and L. A. Mikeska, *Chem. Rev.*, **51**, 505 (1952).

(3) E. E. Smissman and R. A. Mode, *J. Am. Chem. Soc.*, **79**, 3447 (1957).

(4) A. T. Blomquist and J. Wolinsky, *ibid.*, **79**, 6025 (1957).

(5) E. E. Smissman and D. T. Witiak, *J. Org. Chem.*, **25**, 471 (1960).

(6) P. S. Portoghese and E. E. Smissman, *ibid.*, **27**, 719 (1962).

(7) F. W. Brugman and J. F. Arens. *Rec. Trav. Chim.*, **74**, 209 (1955).

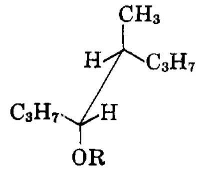
Table I

Analysis of the Bisphenylurethans of 2-Propyl-1,3-hexandiol (*8*)

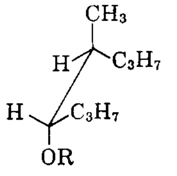
Source	*erythro* (*9a*), %	*threo* (*9b*), %	Recovery, %
Synthetic	67	33	80
3 from Prins reaction of *trans*-4-octene	81	19	73
3 from Prins reaction of *cis*-4-octene	54	46	70

produced in the Prins reactions could be determined. These results are summarized in Table I.

The assignments of configuration to the diols *8a* and *8b* were carried out as follows. Each of the derivatives *9a* and *9b* was hydrolyzed to the pure diastereomeric diols, *8a* and *8b*, respectively. Monotosylation of the primary hydroxyl group followed by lithium aluminum hydride reduction afforded pure samples of *erythro*-5-methyl-4-octanol (*10a*) and *threo*-5-methyl-4-octanol (*10b*). These alcohols were characterized by conversion to the phenylurethans (*11a* and *11b*, respectively). Assignments of configuration were based upon the following applications of the rule of asymmetric induction.[8] The reduction of 5-methyl-4-octanone with sodium borohydride afforded a crude alcohol from which a crystalline phenylurethan, identical with *11a*, was obtained in 58% yield. On the other hand, the crude alcohol from the reaction of 2-methylvaleraldehyde with *n*-propylmagnesium bromide, gave a 63% yield of the phenylurethan *11b*. A more direct and less ambiguous route involved the reaction between *cis*-4-octene oxide and dimethylmagnesium. The product alcohol was isolated and was converted to the phenylurethan (*11b*) of *threo*-5-methyl-4-octanol (*10b*). Thus, it appears certain that the compounds *3a*, *8a*, *9a*, *10a*, and *11a* belong to the *erythro* series.



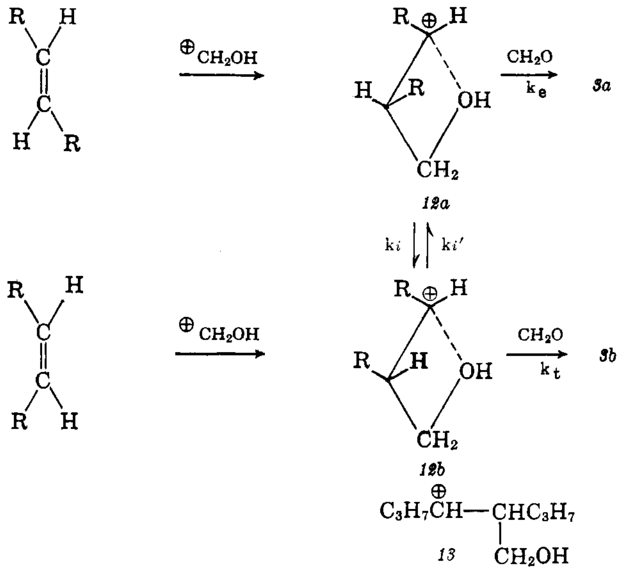
10a. R = H
11a. R = $\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{NHC_6H_5}$



10b. R = H
11b. R = $\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{NHC_6H_5}$

It is generally agreed that the first step in the Prins reaction involves the addition of a protonated formaldehyde molecule to the olefin to give an intermediate which has been described as a free carbonium ion[9,10] or a solvated trimethylene oxide.[11] The observed stereospecific *trans* additions to cyclohexene and *trans*-Δ^2-octalin can be accounted for by *trans* opening of this solvated trimethylene oxide with neutral formaldehyde or solvent. However, in the case of 4-octene, the reaction is nonstereospecific; but different ratios of *cis*- and *trans*-*m*-dioxanes (*3a* and *3b*) are obtained from the *trans* and *cis* olefins. Thus, the experimental results cannot be accommodated simply by involving an "open" carbonium ion or a solvated trimethylene oxide, but rather by a combination of the two.

A possible rationale is given by the mechanistic sequence outlined in Scheme I. At this time, it should be noted that either *trans*- or *cis*-4-octene could be recovered from the Prins reaction mixtures and were found to be unchanged. Further, when *cis*-4-octene was subjected to the reaction conditions except that the formaldehyde was not added, it was recovered in nearly quantitative yield. Thus no isomerization of the starting olefin took place during the course of the reaction. Addition of a protonated formaldehyde to the *trans* and *cis* olefins can be presumed to give rise to the solvated trimethylene oxide species *12a* and *12b*, respectively. These species are interconvertible by rotation about the single bond, presumably through the "open" carbonium ion *13*. We prefer to treat the intermediates *12a* and *12b* as stable conformations of the carbonium ion *13*, interconvertible by the equilibrium expressed in the rate constants k_i and k_i'. Some question may arise as to the validity of assignment of *12a* and *12b* as conformational isomers, since their interconversion might be said to involve the breaking of a carbon–oxygen bond. We visualize this carbon-oxygen "bond", as given in the structural formulae, as an electronic *interaction* which does not lead to trimethylene oxide formation. Thus *12a* and *12b* are at lower potential energy minima than *13*, and may be referred to as interacted conformations. The intermediate *12a* is expected to be more stable than *12b* because of eclipsing effects; therefore $k_i' > k_i$. Furthermore, we assume that *12a* undergoes *trans* attack by formaldehyde to give the *cis* (*erythro*) product *3a* (after rotation and ring closure); and that *12b* will lead to *3b*. The product ratio is then determined by the relative magnitudes of the rate constants k_e, k_i, k_t, and k_i' and by the concentration of neutral formaldehyde. The experimental results suggest that complete equilibration between *12a* and *12b* is not attained, and that the rates of the product forming steps are not much different from the rates of equilibration. If, in the case of the production of *12a* from pure *trans* olefin, equilibrium with *12b* is reached; the reaction with formaldehyde apparently affords an 80:20 ratio of *3a* to *3b*. On this basis it is apparent that *12b*, pro-



Scheme I

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[8] D. J. Cram and F. A. Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952).

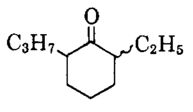
[9] C. C. Price, *Ind. Eng. Chem.*, **40**, 257 (1948).

[10] J. W. Baker, *Nature*, **161**, 171 (1948).

[11] H. E. Zimmerman and J. English, *J. Am. Chem. Soc.*, **75**, 2367 (1953).

duced from pure *cis* olefin, must react to give product (*3b*) before complete equilibration is reached. Viewed in this light, the Prins reaction follows a stereoselective *trans* addition course. Since the product forming steps are presumed to be first order in intermediate and first order in neutral formaldehyde, the stereoselectivity should be increased with increasing formaldehyde concentration. This treatment is consistent with the observed stereospecificity in cyclohexene systems, since an interconversion of the type *12a* ⇄ *12b* cannot be established.

It is entirely possible that, in the present case employing solvent dioxane, a dual mechanism is being observed, whereas in studies with cyclohexene and formaldehyde in acetic acid the solvent of lower cation-solvating ability allows for the observed stereospecificity. An interpretation could follow that intermediates *12a* (from *trans* olefin) and *12b* (from *cis* olefin) are to some extent—*but different in each case*—subject to direct *trans* attack by formaldehyde before rotation can take place, and, in addition, are converted to dioxane solvated cations which react to give a mixture of products. Until further work regarding the effect of solvents upon the stereospecificity of the Prins reaction is completed, we can make no definite choice between these possibilities.



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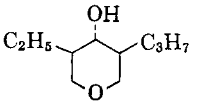
The second major product produced in the reaction of *cis*- and *trans*-4-octene with formaldehyde was a solid alcohol to which the structure 3-ethyl-5-*n*-propyltetrahydropyran-4-ol (*4*) was assigned. This structure was supported by the infrared spectrum and by preparation of derivatives. Oxidation afforded a ketone *14* which showed a carbonyl band at 1725 cm.$^{-1}$. Although compound *4* was a single isomer, the ketone *14* gave a mixture of *cis*- and *trans*-isomeric 2,4-dinitrophenylhydrazones. The ratio of these derivatives was determined to be about 3:2. We have assigned to *4* the *trans*, *trans* stereochemistry *15* on the basis of the nmr spectra[12] of the acetate and *p*-nitrobenzoate derivatives, which show simple triplet patterns at δ = 4.50 p.p.m. (J = 9.6 c.p.s.) and δ = 4.84 p.p.m. (J = 10.4 c.p.s.), respectively; attributed to the axial C-4 proton split by two equivalent vicinal axial protons. The mechanism of formation of this product (*vide infra*) supports this assignment in that the ethyl and hydroxyl groups would be expected to be *trans* oriented. The *n*-propyl group would then adopt the more stable orientation in the final product.



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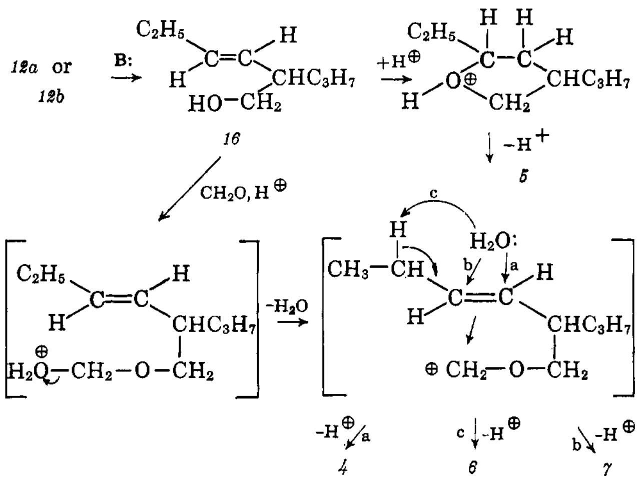
An additional secondary alcohol *7* was isolated as a minor component of the Prins reactions. Infrared spectra suggested a tetrahydrofuran structure. Oxidation afforded a ketone which was not a cyclopentanone, and which gave a negative iodoform test. From mechanistic considerations, the structure *7* is reasonable, however no information concerning stereochemistry has been obtained.

A *trans* olefin of similar structure was also detected as a by-product. This olefin *6* was hydroborated to give a low yield of an alcohol identical with *7* and was assigned the structure 3-*n*-propyl-4-(*trans*-2′-propenyl)-tetrahydrofuran.

The final by-product that was isolated in pure form was assigned the structure 3-ethyl-4-*n*-propyltetrahydrofuran (*5*). Support for this assignment—in addition to the infrared spectrum—was the fact that minor quantities of *5* were detected from the sulfuric acid-catalyzed hydrolysis of *3a* and *3b*.

The mechanism of the formation of these by-products can be considered analogous to that route proposed[3,13] for the production of 3-oxabicyclo[3.3.1]-nonan-9-ol from cyclohexene. The common intermediate is assumed to be the *trans*-homoallylic alcohol 16.[14]



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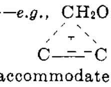
(12) The n.m.r. spectra were obtained with a Varian DP-60 high resolution spectrometer. Solutions of approximately 20% w./v. in carbon tetrachloride were used and tetramethylsilane was the internal standard. We are indebted to Dr. Merle Emerson for these determinations.

(13) In a recent manuscript [L. J. Dolby, *J. Org. Chem.*, **27**, 2971 (1962)], a modified mechanism has been proposed for the Prins reaction which involves a three-membered cyclic ion—*e.g.*,  All of the products observed in the present work can be accommodated by this mechanism; in fact, the formation of product *7* is quite analogous to that of the new alcohol reported. If this mechanism obtains in the formation of *m*-dioxane from *cis*- and *trans*-4-octene under our conditions, it appears that this cyclic ion intermediate is not as effective as, for example, the suggested "bromonium ion" in providing stereospecific *trans* addition. This is not entirely surprising, since the extent of importance of cyclic ion intermediates in addition reactions has been related to the ability of the moiety to act as a neighboring group. Saturated carbon appears to act as a neighboring group only in special cases. The chief arguments presented in favor of the three-membered cyclic ion mechanism concern the absence of significant anchimeric assistance by oxygen *via* a four-membered cyclic oxonium ion intermediate. However, it can be pointed out that the failure to observe participation in the rate-determining step does not rule out the fact that an oxonium ion intermediate might subsequently participate in maintaining the configuration of a carbonium ion center. In view of these considerations, it would seem that the cyclic three-membered ion—although aesthetically pleasing and certainly plausible—would have no distinct advantage over the four-membered cyclic ion as far as accounting for *m*-dioxane or diol formation in the Prins reaction. As for the formation of alcohols *4* and *7*, the three-membered cyclic ion analogous to that proposed for the formation of *trans*-6-hydroxy-*cis*-3-bicyclo[4.3.0]nonane and *trans*-9-hydroxy-3-oxabicyclo[3.3.1]nonane is very attractive. However, with the limited data available in support of such intermediates we have chosen to treat the products *4* and *7* as arising by way of addition of $^{\oplus}CH_2$—O—R to the olefinic linkage followed by a rapid *trans* attack of the external nucleophile, water.

(14) *Cf.* N. C. Yang and D. D. Yang, *J. Am. Chem. Soc.*, **81**, 133 (1959).

Experimental[15]

4-Octyne and *cis*- and *trans*-4-Octene.—4-Octyne, b.p. 128–129°, n^{25}D 1.4203 was obtained from Columbia Organic Chemicals, Inc., and also *via* the alkylation of acetylene with *n*-propyl bromide. Reduction with sodium in liquid ammonia afforded a 60% yield of *trans*-4-octene, b.p. 122–122.1°, n^{25}D 1.4108 (lit.,[16] b.p. 122.37°, n^{20}D 1.4122).

Hydroboration according to the procedure of Brown and Zweifel[17] gave a 72% yield of *cis*-4-octene, b.p. 122.3–122.5°, n^{25}D 1.4180 (lit.,[16] b.p. 122.8°, n^{20}D 1.4147).

Prins Reaction of *trans*-4-Octene.—In a 300-ml., three-necked flask equipped with a stirrer, a condenser, and a dropping funnel was added 110 g. of dioxane, 16 g. of 96% sulfuric acid, and 12.6 g. (0.4 mole) of 91% paraformaldehyde. The mixture was stirred briefly at room temperature and was then cooled to 0°. *trans*-4-Octene (22.4 g.; 0.2 mole) was added slowly and the mixture was stirred at room temperature for 130 hr. After pouring onto crushed ice, the products were extracted with ether and the ether solution was washed with sodium carbonate solution and water, dried, and fractionally distilled through a 2-ft. spinning-band column. After the removal of a forerun which contained the unchanged olefin and some dissolved formaldehyde, two major fractions were obtained: fraction A, 13.3 g. (39% based on formaldehyde), b.p. 80–100° (5 mm.); fraction B, 17.7 g. (52%), b.p. 90° (1 mm.). The first fraction was shown to give three peaks on gas chromatography. The retention times were 6, 9.75, and 13.25 min. respectively, at 170° and 8 p.s.i.g. The second fraction gave one broad peak with a retention time of 22.5 min.

Prins Reaction of *cis*-4-Octene.—Employing the same procedure as with the *trans*-olefin, two major fractions were obtained: fraction C, 18.7 g. (55% based on formaldehyde), b.p. 80–100° (5 mm.); fraction D, 11.6 g. (43%), b.p. 90° (1 mm.). These fractions on gas chromatography were found to contain all of the components observed in fractions A and B; however, the relative amounts were different.

Olefin Stability during the Prins Reactions.—Prins reactions were carried out with *cis*-4-octene and *trans*-4-octene in the manner previously described for a period of 90 hr. The reaction mixtures were poured onto crushed ice and extracted with pentane. The pentane layers were washed, dried, and concentrated. Distillation of the more volatile components (b.p. to 100° at 80 mm.) afforded recovery of the unchanged olefins. Analytical gas chromatography employing a column containing a saturated solution of silver nitrate in tetraethylene glycol suspended on firebrick showed the olefins to be identical with their respective pure samples. No isomerization was observed.

Stability of *cis*-4-Octene under Acidic Conditions.—A mixture of 25 g. of dioxane and 3.6 g. of concd. sulfuric acid was cooled to 0° and 5 g. of *cis*-4-octene was slowly added with stirring. The mixture was allowed to warm to room temperature and was stirred for 130 hr. The mixture was poured onto crushed ice and extracted with pentane. The pentane layer was washed, dried, and concentrated. Analytical gas chromatography of the crude residue (silver nitrate column) showed the material to be nearly identical with the pure *cis*-4-octene Less than 1% isomerization had occurred.

4,5-Di-*n*-propyl-*m*-dioxane (*3a* and *3b*).—The Prins reaction on *trans*-4-octene yielded 19.4% of 4,5-di-*n*-propyl-*m*-dioxane (mixture of diastereomers), b.p. 80–90° (5 mm.), n^{25}D 1.4380. Pure *m*-dioxane was obtained by preparative gas chromatography of fraction A. Analytical gas chromatography showed this material to be homogeneous with a retention time of 13.25 min. at 170° and 8 p.s.i.g. The Prins reaction on *cis*-4-octene yielded from fraction C in the same manner 40.2% of 4,5-di-*n*-propyl-*m*-dioxane (mixture of diastereomers), b.p. 80–85° (5 mm.), n^{25}D 1.4382. A synthetic mixture of the two *m*-dioxanes was analyzed and one peak was observed.

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.74; H, 11.62.

3-Ethyl-5-*n*-propyltetrahydropyran-4-ol (*4*).—The Prins reaction with *trans*-4-octene yielded 49.1% of 3-ethyl-5-*n*-propyltetrahydropyran-4-ol, m.p. 82–82.5°. An analytical sample of *4* was obtained by two recrystallizations from pentane. The Prins reactions with *cis*-4-octene yielded 32.4% of *4*. A mixture melting point was not depressed.

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.81; H, 11.66.

The ***p*-nitrobenzoate** was prepared in pyridine and was recrystallized from 95% ethanol, m.p. 85.5–86.5°.

Anal. Calcd. for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36. Found: C, 63.45; H, 7.27; N, 4.46.

The **acetate** was prepared by heating with excess acetic anhydride. Distillation afforded a liquid, n^{25}D 1.4464.

Anal. Calcd. for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35. Found: C, 66.98; H, 10.18.

3-Ethyl-5-*n*-propyltetrahydrofuran (*5*).—The Prins reaction on *trans*-4-octene yielded 7.3% of 3-ethyl-5-*n*-propyltetrahydrofuran b.p. 90–95° (5 mm.), n^{25}D 1.4255. Pure *5* was obtained by preparative gas chromatography of fraction A. Analysis indicated this material to be homogeneous with a retention time of 6 min. at 170° and 8 p.s.i.g. The Prins reaction on *cis*-4-octene yielded 5.4% of *5* from fraction C. A synthetic mixture of the two tetrahydrofurans was analyzed and one peak was observed.

Anal. Calcd. for $C_9H_{18}O$: C, 76.00; H, 12.75. Found: C, 75.63; H, 12.66.

3-*n*-Propyl-4-(*trans*-1′-propenyl)tetrahydrofuran (*6*).—The Prins reaction with *trans*-4-octene yielded 11.6% of 3-*n*-propyl-4-(*trans*-1′-propenyl)tetrahydrofuran, b.p. 95–100° (5 mm.), n^{25}D 1.4484. Pure *6* was obtained by preparative gas chromatography of fraction A. The material was homogeneous with a retention time of 9.75 min. at 170° and 8 p.s.i.g. The Prins reaction of *cis*-4-octene yielded 9.3% of *6* from fraction C. A synthetic mixture of the tetrahydrofurans was analyzed and one peak was observed.

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.75; H, 11.93.

3-*n*-Propyl-4-(1′-hydroxy-1′-propyl)tetrahydrofuran (*7*).—The Prins reaction of *trans*-4-octene yielded 2.6% of 3-*n*-propyl-4(1′-hydroxy-1′-propyl)tetrahydrofuran, b.p. 90–95° (1 mm.), n^{25}D 1.4630. Since *7* codistilled with *4* (fraction B), the mixture (17 g.) was chromatographed on 680 g. of Merck acid-washed alumina. The column was eluted successively with 200 ml. of pentane, 500 ml. of 3% ether–pentane, 500 ml. of 5% ether–pentane, 500 ml. of 10% ether–pentane, 500 ml. of 50% ether–pentane, and 100% ether. Fractions 25–45 afforded 800 mg. of *7*. Fractions 46–55 afforded 8.8 g. of 4 which solidified upon standing. The Prins reaction with *cis*-4-octene yielded 1.7 % of *7* from chromatography of fraction D. A synthetic mixture of the tetrahydrofurans was analyzed with a retention time of 22.5 min. at 170° and 8 p.s.i.g.

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.96; H, 11.82.

The ***p*-nitrobenzoate** was prepared in 60% yield, after recrystallization from 95% ethanol, m.p. 91–92°.

Anal. Calcd. for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36. Found: C, 63.27; H, 7.00; N, 4.44.

Ethyl 3-Hydroxy-2-propylcaproate.—A Reformatsky reaction was carried out in the usual manner with ethyl α-bromovalerate and *n*-butyraldehyde. Fractionation afforded 27 g. (34%) of the β-hydroxy ester, b.p. 91° (2.5 mm.), n^{25}D 1.4345, infrared, 3591 and 1739 cm.$^{-1}$.

Anal. Calcd. for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.36; H, 10.83.

The **hydrazide** was prepared from 85% hydrazine hydrate in ethanol solution. Recrystallization from water afforded 1.1 g. (36%) of pure hydrazide, m.p. 140–141°.

Anal. Calcd. for $C_9H_{20}O_2N_2$: C, 57.41; H, 10.71; N, 14.88. Found: C, 57.10; H, 10.90; N, 14.81.

There was also obtained in the Reformatsky reaction 13 g. (17%) of 2-ethyl-3-hydroxyhexanal, b.p. 113° (2.5 mm.), n^{25}D 1.4422.

Anal. Calcd. for $C_8H_{16}O_2$: C, 66.72; H, 11.18. Found: C, 67.04; H, 11.05.

2-Propyl-1,3-hexanediol (*8*).—To a solution of 2.84 g. (0.07 mole) of lithium aluminum hydride in 90 ml. of anhydrous ether was added 15.2 g. (0.07 mole) of ethyl 3-hydroxy-2-propylcaproate. After an additional hour's stirring, 25 ml. of water was

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[15] All melting and boiling points are uncorrected. The infrared spectra were determined with a Beckman IR-4 recording spectrophotometer using a cell thickness of 0.1 mm. We are indebted to Mrs. Mary L. Bergishagen for these measurements. Gas chromatography analyses were carried out employing an 8-mm. o.d. × 7-in. glass column packed with 20% by weight of silicone GE-SF 96 or 30% silicone 550 fluid on 80–100-mesh firebrick.

[16] A. L. Henne and K. W. Greenlee, *J. Am. Chem. Soc.*, **65**, 2020 (1943).

[17] H. C. Brown and G. Zweifel *ibid.*, **81**, 1512 (1959).

added dropwise with cooling, followed by dilute sulfuric acid solution. The product was extracted with ether and the ether solution was washed with sodium carbonate solution and water. The extract was dried and concentrated. Distillation of the residue, employing a 2-ft. Podbielniak column, furnished 11.2 g. (86%) of 2-propyl-1,3-hexanediol (a mixture of diastereomers), d.p. 104–105° (1.25 mm.), n^{25}D 1.4500.

Anal. Calcd. for $C_9H_{20}O_2$: C, 67.45; H, 12.58. Found: C, 67.68; H, 12.50.

The **bisphenylurethan** (a mixture of diastereomers) was prepared in the usual manner and was fractionally crystallized from chloroform to yield 655 mg. (26%) of pure *threo* isomer, *9b*, m.p. 132–134°.

Anal. Calcd. for $C_{23}H_{30}O_4N$: C, 69.32; H, 7.59; N, 7.03. Found: C, 69.30; H, 7.40; N, 7.22.

The *erythro* isomer, *9a*, melting at 82–84°, was recovered from the mother liquors by trituration with pentane, followed by recrystallization from a chloroform–pentane mixture. The yield was 1287 mg. (54%).

Anal. Calcd. for $C_{23}H_{30}O_4N$: C, 69.32; H, 7.50; N, 7.03. Found: C, 69.39; H, 7.64; N, 7.02.

erythro-**2-Propyl-1,3-hexanediol** (*8a*).—In a 100-ml. flask equipped with a condenser was added a 2.5 g. of the bisphenylurethan melting at 82–84° and 30 ml. of 20% alcoholic potassium hydroxide. The mixture was heated overnight and then 10 ml. of water was added and the mixture was heated for an additional 2 hr. After the usual work-up the residue was distilled to yield 800 mg. (80%) of *erythro*-2-propyl-1,3-hexanediol, b.p. 105–106° (1.25 mm.), n^{25}D 1.4485.

Anal. Calcd. for $C_9H_{20}O_2$: C, 67.45; H, 12.58. Found: C, 67.53; H, 22.64.

threo-**2-Propyl-1,3-hexanediol** (*8b*).—The bisphenylurethan (2.5 g.) melting at 132–134° was hydrolyzed and the residue was distilled to yield 750 mg. (75%) of *threo*-2-propyl-1,3-hexanediol, b.p. 105–106° (1.25 mm.), n^{25}D 1.4463.

Anal. Calcd. for $C_9H_{20}O_2$: C, 67.45; H, 12.58. Found: C, 67.25; H, 12.36.

Hydrolysis of 4,5-Di-*n*-propyl-*m*-dioxane. A. From *cis*-4-Octene.—In a 50-ml. flask equipped with a condenser was added 400 mg. of 4,5-di-*n*-propyl-*m*-dioxane, 10 ml. of methyl alcohol, and 12 drops of 96% sulfuric acid. The solution was heated to reflux for 10 hr. The solvent and volatile acetal were distilled directly into 2,4-dinitrophenylhydrazine reagent to isolate the formaldehyde that was formed in the reaction. Water was added to the solution and the product was extracted with ether. The extract was washed with dilute sodium carbonate solution and water. The solution was dried and concentrated and the residue was distilled to yield 372 mg. (80%) of 2-propyl-1,3-hexanediol, b.p. 105–106° (1.25 mm.), n^{25}D 1.4482.

The **bisphenylurethan** (a mixture of diastereomers) was prepared in the usual manner and was fractionally crystallized from chloroform to yield 201 mg. (33%) of pure *threo* isomer, m.p. 132–134°. The *erythro* isomer, melting at 82–84; was recovered from the mother liquors. The yield was 240 mg. (38%).

B. From *trans*-4-Octene.—Employing the same procedure outlined above 356 mg. (76%) of 2-propyl-1,3-hexanediol, b.p. 105–106° (1.25 mm.), n^{25}D 1.4481 was obtained from 500 mg. of the dioxane.

The **bisphenylurethan** (a mixture of diastereomers) was prepared in the usual manner and was fractionally crystallized from chloroform to yield 83 mg. (14%) of pure *threo* isomer, m.p. 132–134°. The *erythro* isomer, melting at 82–84°, was recovered from the mother liquors. The yield was 362 mg. (56%).

erythro-**5-Methyl-4-octanol** (*10a*). **Procedure A.**—A solution of 500 mg. (0.003 mole) of *erythro*-2-propyl-1,3-hexanediol and a 10% excess (650 mg.) of *p*-toluenesulfonyl chloride in pyridine was stirred for 12 hr. The mixture was then extracted with methylene chloride. The extract was washed, dried and concentrated and the crude product was used directly for the reduction. The crude tosylate was added to 300 mg. (0.008 mole) of lithium aluminum hydride in ether. The mixture was refluxed for 1 hr. and was worked up in the usual manner. The product was distilled to yield 257 mg. (58%) of *erythro*-5-methyl-4-octanol, b.p. 65° (0.6 mm.), n^{25}D 1.4270.

Anal. Calcd. for $C_9H_{20}O$: C, 74.93; H, 13.98. Found: C, 74.83; H, 13.94.

The **phenylurethan** (*11a*) was prepared in the usual manner and was recrystallized from methyl alcohol (58%), m.p. 75–77°.

Anal. Calcd. for $C_{16}H_{25}O_2N$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.82; H, 9.48; N, 5.42.

Procedure B.—A solution of 1.2 g. (0.04 mole) of sodium borohydride in 25 ml. of methanol was cooled, and 6 g. (0.04 mole) of 5-methyl-4-octanone was slowly added keeping the mixture at 5–10°. The solution was stirred for 3 hr. To the mixture was then added dilute hydrochloric acid solution. The product was extracted with ether and the ether solution was washed, dried and concentrated. Distillation of the residue afforded 5.6 g. (80%) of *erythro*-5-methyl-4-octanol, b.p. 51–52° (1.5 mm.), n^{26}D 1.4285.

Reaction with phenyl isocyanate and recrystallization of the product from methanol afforded a 58% yield of the phenylurethan of *erythro*-5-methyl-4-octanol, m.p. 75–77°.

threo-**5-Methyl-4-octanol** (*10b*). **Procedure A.**—Employing the same procedure used for the *erythro* isomer, 500 mg. (0.003 mole) of *threo*-2-propyl-1,3-hexanediol was converted to the tosylate. Reduction of the crude ester with lithium aluminum hydride afforded 173 mg. (40%) of *threo*-5-methyl-4-octanol, b.p. 65° (0.6 mm.), n^{25}D 1.4291.

Anal. Calcd. for $C_9H_{20}O$: C, 74.93; H, 13.98. Found: C, 74.63; H, 13.87.

The **phenylurethan** (*11b*), was prepared in the usual manner and was recrystallized from methyl alcohol (61%), m.p. 71–72°.

Anal. Calcd. for $C_{16}H_{25}O_2N$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.84; H, 9.55; N, 5.30.

Procedure B.—The Grignard reagent, prepared from 2.4 g. (0.1 g.-atom) of magnesium and 12.3 g. (0.1 mole) of *n*-propyl bromide in 100 ml. of anhydrous ether, was heated to reflux and 9 g. (0.09 mole) of 2-methylvalerylaldehyde was added slowly over a period of 30 min. After the usual work-up, the residue was distilled to yield 9.7 g. (75%) of *threo*-5-methyl-4-octanol, b.p. 75–76° (1 mm.), n^{26}D 1.4298.

Reaction with phenyl isocyanate and recrystallization of the product from methanol afforded a 63% yield of the phenylurethan of *threo*-5-methyl-4-octanol, m.p. 71–72°.

Procedure C.—A 0.15 *N* solution of dimethylmagnesium[18] in ether (400 ml.) was concentrated until 35 ml. remained. Dry dioxane (24 ml.) was then added at the same rate that the ether distilled. While the stirred solution was refluxed gently, 1.72 g. of *cis*-4-octene oxide in 5 ml. of dioxane was added dropwise. The reaction mixture was stirred and refluxed for 28 hr. The reaction was worked up by cooling the mixture in ice, slowly adding 75 ml. of saturated ammonium chloride solution followed by water and ether until the precipitate had dissolved. The organic layer was washed twice with water, dried, and distilled. The residue was distilled to yield 1.14 g. (59%) of *threo*-5-methyl-4-octanol, b.p. 65° (0.6 mm.) n^{25}D 1.4269.

The phenylurethan melted at 71–72°, m.m.p. 71–72°.

cis-**4-Octene Oxide.**—*cis*-4-Octene (12.0 g., 0.11 mole) was added dropwise during a period of 30 min. with stirring to 32.5 ml. of 40% peracetic acid to which 6.5 g. of sodium acetate trihydrate had been added. The temperature was maintained at 0–10° during the addition. After 3 hr. at room temperature, the mixture was added to crushed ice and neutralized to litmus by adding 30% sodium hydroxide solution. The epoxide was taken up in ether and the ether layer was washed with water and dried. The solvent was distilled and the product was fractionated using a 1-ft. Vigreux column to yield 8.9 g. 65% of *cis*-4-octene oxide, b.p. 155–156°, n^{25}D 1.4136. The infrared spectrum of the *cis* isomer was characterized by bands at 909 cm.$^{-1}$ and 888 cm.$^{-1}$. *cis*-4-Octene oxide was shown to give only one peak on gas chromatography through a silicone 550 fluid column. The retention time was 24 min. at 98° and 7 p.s.i.g.

Anal. Calcd. for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 75.18; H, 12.40.

3-Ethyl-5-*n*-propyltetrahydropyran-4-one (*14*).—3-Ethyl-5-*n*-propyltetrahydropyran-4-ol (945 mg. 5.5 mmoles) was dissolved in 10 ml. of acetone freshly distilled from potassium permanganate. The mixture was cooled to 0° and 1.4 ml. of chromium trioxide reagent (prepared from 2.67 g. chromium trioxide 2.3 ml. of concd. sulfuric acid, diluted to 10 ml. with water) was added slowly with stirring. The reaction was allowed to warm to room temperature for 1 hr. and was then stored overnight at 0°. Sufficient isopropyl alcohol was added to destroy the yellow color. The mixture was filtered through a very small alumina (Woelm) column. The acetone was distilled and the residue was taken up in pentane. The pentane layer was washed, dried, and concentrated. Vacuum distillation of the residue afforded 813 mg. (86%)

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[18] B. G. Christiansen, *et al.*, *J. Am. Chem. Soc.*, **82**, 3995 (1960).

of 3-ethyl-5-*n*-propyltetrahydropyran-4-one, bath temperature 80° (1.5 mm.), n^{25}D 1.4481.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.28; H, 10.59.

The 2,4-dinitrophenylhydrazone (mixture of geometric isomers) was prepared in the usual manner and was fractionally crystallized from 95% ethanol to yield 346 mg. (38%) of an isomer m.p. 147–148°, λ_{max}^{EtOH} 362 mμ, log ε 4.7.

Anal. Calcd. for $C_{16}H_{22}N_4O_5$: C, 54.84; H, 6.33: N, 15.99. Found: C, 54.92; H, 6.40; N, 15.73.

A second isomer, melting at 122–123.5°, was recovered from the mother liquors, λ_{max}^{EtOH} 362 mμ, log ε 5. The yield was 265 mg. (29%).

Anal. Calcd. for $C_{16}H_{22}N_4O_5$: C, 54.84; H, 6.33; N, 15.99. Found: C, 54.89; H, 6.55; N, 15.55.

When the oxidation was carried out with chromic acid-pyridine complex, the ketone *14* was obtained in 80% yield. Preparation and crystallization of the 2,4-dinitrophenylhydrazones gave 50% of the isomer melting at 147–148° and 20% of the isomer melting at 122–123.5°.

Equilibration of 3-Ethyl-5-*n*-propyltetrahydropyran-4-one.—To a 50-ml. flask equipped with a condenser was added 500 mg. (0.003 mole) of 3-ethyl-5-*n*-propyltetrahydropyran-4-one followed by 20 ml. of benzene and 20 mg. of *p*-toluenesulfonic acid and the mixture was heated to reflux for 3 hr. After the usual work-up, distillation of the product afforded 450 mg. (90%) of *cis*-3-ethyl-5-*n*-propyltetrahydropyran-4-one. This product showed one peak on gas chromatography.

The **2,4-dinitrophenylhydrazone** (a mixture of geometric isomers) was prepared in the usual manner and was fractionally crystallized from 95% ethanol to yield 80 mg. (20%) of an isomer, m.p. 147–148°.

The second isomer, melting at 111–115°, was recovered from the mother liquors. The yield was 200 mg. (50%).

3-*n*-Propyl-4-propionyltetrahydrofuran.—A sample of 3-*n*-propyl-4-(1′-hydroxy-1′-propyl)tetrahydrofuran (500 mg., 0.003 mole) was oxidized with chromium trioxide–pyridine in the usual manner. Distillation afforded 310 mg. (75%) of 3-*n*-propyl-4-propionyltetrahydrofuran, bath temperature 110–120° (2 mm.), n^{25}D 1.4494.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.32; H, 10.58.

The **2,4-dinitrophenylhydrazone** (a mixture of geometric isomers) was prepared and was fractionally crystallized from 95% ethanol to yield 175 mg. (54%) of pure isomer, m.p. 95.5–97°.

Anal. Calcd. for $C_{16}H_{22}O_5N_4$: C, 54.84; H, 6.33; N, 15.99. Found: C, 54.64; H, 6.42; N, 15.55.

A second isomer, melting at 84–86°, was recovered from the mother liquors. The yield was 86 mg. (26%).

Anal. Calcd. for $C_{16}H_{22}O_5N_4$: C, 54.84; H, 6.33; N, 15.99. Found: C, 55.00; H, 6.28; N, 15.85.

Hydroboration of 3-*n*-Propyl-4-(*trans*-1′-propenyl)tetrahydrofuran.—3-*n*-Propyl-4-(*trans*-1′-propenyl)tetrahydrofuran (90 mg. 0.006 mole) was hydroborated in diglyme with sodium borohydride and boron trifluoride etherate.[17] After oxidation with 30% hydrogen peroxide, the mixture was poured into water. The product was extracted with ether, and the residual diglyme was removed by several washings with ice–water. Distillation followed by further purification by means of gas chromatography yielded 43 mg., 90% yield (based on recovered starting material) of 3-*n*-propyl-4-(1′-hydroxy-1′-propyl)tetrahydrofuran. Gas chromatography showed this material to be homogeneous with a retention time of 9.75 min. at 170° and 8 p.s.i.g.

The *p*-nitrobenzoate was prepared in the usual manner in 15% yield after recrystallization from 95% ethanol, m.p. 88–93°, m.m.p. 88–93°.

Acknowledgment.—This investigation was supported by generous grants from the Alfred P. Sloan Foundation and the Research Corporation.

Azo Compounds. XLI.[1] Decomposition of 2,2′-Azobis-2-cyclopropylpropionitrile. A Possible Rearrangement of a Cyclopropylcarbinyl Free Radical.

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Received October 9, 1962

Solution decomposition of 2,2′-azobis-2-cyclopropylpropionitrile has been shown to yield predominantly polymer along with *sym*-dimethyldicyclopropyl succinonitrile and 1-methylcyclopenten-5-one azine, whereas solid state decomposition gives predominantly dinitrile, some polymer and no azine. Proof of structure of the azine was obtained through spectral evidence along with unequivocal synthesis. Formation of azine is postulated as arising from rearrangement of a cyclopropylcarbinyl free radical in the form of its ketenimine resonance hybrid. Differences in product composition arising from solution *vs.* bulk decompositions are explained as being due to restricted motion of free radicals in the solid state.

The rate of thermal decomposition of azonitriles has been shown to be relatively insensitive to structural variations.[3–5] Throughout the course of their decomposition, solutions have been observed to remain clear and colorless, yielding upon work-up predominantly the correspondingly substituted succinonitriles.[3–7] However, 2,2′-azobis-2-cyclopropylprionitrile I has been found to decompose at an anomalously rapid rate,[4,5] forming colored solutions in the process. In an attempt to elucidate the reasons for this behavior, the nature of the decomposition products under various conditions was investigated.

Results

Decomposition of 2,2′-azobis-2-cyclopropylpropionitrile I[3–5] in hexane at 69° gave predominantly an unidentified brown polymeric material of low molecular weight. This material gradually decomposed upon heating to 300° without exhibiting a definite melting point. It was insoluble in all common organic solvents except acetic acid and did not reprecipitate from solution upon dilution with water unless basified. The solid gradually evolved ammonia upon standing. Infrared and n.m.r. spectra showed the presence of the cyclopropyl group and the absence of unsaturation. The infrared spectrum also showed the presence of the

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[1] This is the 41st in a series of papers concerned with the preparation and decomposition of azo compounds. For the previous paper in this series, see C. G. Overberger and G. Kesslin, *J. Org. Chem.*, **27**, 3898 (1962).

[2] Taken from the dissertation submitted by Martin Tobkes to the Faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1963, and from the thesis of Arnold Zweig for the degree of Bachelor of Science in Chemistry. 1955.

[3] C. G. Overberger, M. T. O'Shaughnessy, and H. Shalit, *J. Am. Chem. Soc.*, **71**, 2661 (1949).

[4] C. G. Overberger and M. B. Berenbaum, *ibid.*, **73**, 2618 (1951).

[5] C. G. Overberger and A. Lebovits, *ibid.*, **76**, 2722 (1954).

[6] J. Thiele and K. Heuser, *Ann.*, **290**, 1 (1896).

[7] A. F. Bickel and W. A. Waters, *Rec. trav. chim.*, **69**, 1490 (1950).