closed and swept with nitrogen. The formaldehyde was then added and the dropper rinsed with 0.4 ml. of water. The reaction mixture was slowly warmed to 100°. A rapid evolution of carbon dioxide started at 85° and continued for about twenty minutes. After this, the mixture was refluxed for four hours at 100–105°. The reaction mixture was cooled, 0.9 ml. of 6 *N* hydrochloric acid was added and the flask connected through the Dry Ice cooled trap to a vacuum line. Then the mixture was warmed under reflux for ten minutes.

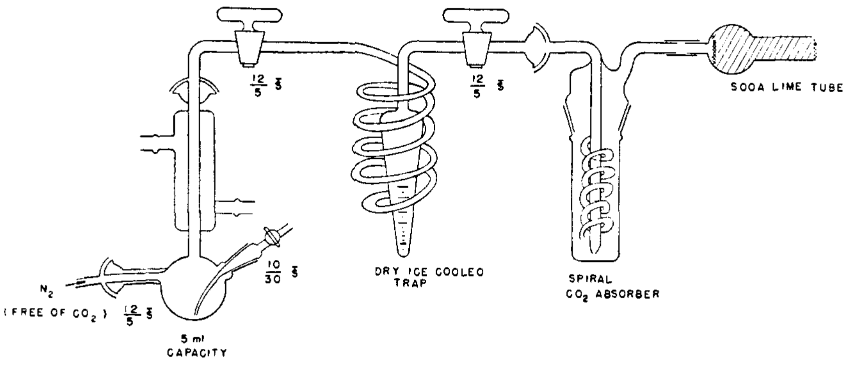

Fig. 1.

The Dry Ice cooled trap was then removed and 3 mg. of the dimethone derivative of formaldehyde recovered and the specific activity determined.

To the sodium hydroxide solution 7 ml. of 4.4 *N* ammonium chloride and 43 ml. of 1.4 *M* barium chloride were added. The precipitate of barium carbonate was dried (1.02 g., 5.2 mmoles) and the specific activity determined.

The remaining volatile material in the flask, hydrochloric and formic acids, was then removed *in vacuo*. The crude product, a soft yellow solid was dissolved in chloroform, filtered, and the chloroform removed *in vacuo*. A first crop of 463 mg. of demerol was obtained by crystallization from acetone, m. p. 187–188°. The specific activity of this material was 215 μc/mmole, or 0.79 μc/mg. Second and third crops, totaling 455 mg., were crystallized from a chloroform–ether mixture. The combined yield was 78% based on the formaldehyde used to begin the synthesis. The analysis of an inactive sample prepared by the above method and corresponding to the first fraction with the same melting point is as follows: *Anal.* Calcd. for $C_{15}H_{22}O_2HCl$: C, 63.48, H, 7.81; N, 4.94; Cl, 12.49. Found: C, 63.69; H, 7.91; N, 5.14; Cl, 12.68.

The material was analyzed by two-dimensional paper chromatography using butanol–propionic acid in one direction and phenol–water in the other.[12] Only one radioactive spot was found when the paper was exposed to X-ray film.

**Preparation Using Labeled Formic Acid.**—The reaction was carried in the same manner as the previous run using, however, 4.4 mmoles of 4-phenyl-4-carbethoxypiperidine, 4.4 mmoles of formaldehyde and 9.4 mmoles of formic acid-$C^{14}$. Most of the excess formic acid (4.6 mmoles) was recovered from the cold trap as sodium formate as well as 3.4 mg. of the dimethone derivative of formaldehyde. The specific activity of the several fractions was measured.

**Acknowledgment.**—The authors wish to thank Professors M. Calvin, R. T. Arnold and H. H. Anderson for their help and encouragement in this work.

## Summary

1. Demerol-N-methyl-$C^{14}$ has been synthesized using the formate–formaldehyde reductive methylation method.

2. By the use of labeled formaldehyde in one reaction and labeled formic acid in another it has been shown that in this reaction the formaldehyde is the source of the N-methyl group, that the only major source of the reductive action is formic acid going to carbon dioxide, and that there is no exchange between the formic acid and formaldehyde.

BERKELEY, CALIFORNIA RECEIVED MAY 16, 1950

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[12] Calvin, *et al.*, THIS JOURNAL, **72**, 1710 (1950).

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY, AND FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

# Reactions of Organometallic Compounds with Alkyl Halides. II. On Sodium Ethyl and (+)2-Chloroöctane

BY STEPHEN E. ULRICH,[1] FRANKLIN H. GENTES, JOHN F. LANE AND EVERETT S. WALLIS

The first paper of this series[2] presented the results of an investigation on the action of sodium ethyl on (−)2-bromoöctane. The products of the reaction were shown to be octylene and octane, together with smaller amounts of the products of substitution, 3-methylnonane and 7,8-dimethyltetradecane. The first of these substitution products was almost completely (97%) racemized; the latter was optically inactive.

These results were considered in conjunction with the earlier finding of Wallis and Adams[3] that the action of sodium on (+)2-bromobutane gave optically inactive 3,4-dimethylhexane. It was pointed out that in both instances the optical inactivity of the di-*s*-alkyl hydrocarbon could have resulted from one of the three following causes:

(1) The hydrocarbon was produced by a concerted ($S_N2$) displacement reaction between sodium *s*-alkyl and *s*-alkyl halide in such a fashion as to give exclusively the *meso*-form.

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[1] American Chemical Society Fellow in Rutgers University, 1946–1949.

[2] Brink, Lane and Wallis, THIS JOURNAL, **65**, 943 (1943).

[3] Wallis and Adams, *ibid.*, **55**, 3838 (1933).

(2) It was produced by dimerization of optically inactive *s*-alkyl radicals.

(3) It was produced by a two stage ionic substitution process ($S_N1$) involving racemization of the *s*-alkyl carbonium ion initially formed

$$s\text{-AlkBr} \xrightarrow{\text{slow}} Br^{\ominus} + dl\text{-}s\text{-Alk}^{\oplus} + dl\text{-}s\text{-Alk}^{\ominus}\,Na^{\oplus} \xrightarrow{\text{fast}} dl + meso\text{-}(s\text{-Alk})_2 + NaBr$$

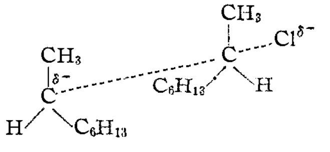
Of these possibilities (3) was not at that time considered very likely, since in general such processes have been found to occur chiefly in media of relatively high dielectric constant and with weakly basic substituting agents.[4]

The present investigation, however, offers results which render impossible the acceptance of hypotheses (1) and (2), results, indeed, which joined with the additional evidence brought forth in the succeeding paper,[5] strongly support hypothesis (3) as the true explanation of the observed racemizations.

When (+)2-chlorooöctane, $[\alpha]^{20}D$ + 26.61° (homogeneous), was subjected, as described in the Experimental Part, to the action of sodium ethyl, there was produced octylene (37%), octane (8.5%), (+)3-methylnonane (6.4%), $[\alpha]^{25}D$ + 5.16° (homogeneous), and (+)7,8-dimethyltetradecane (3.7%), $\alpha^{23}D$ + 0.96° (homogeneous, 1 dm. tube.)

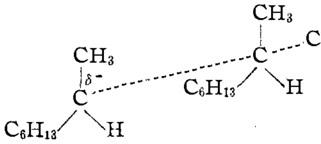
These results lead to the following conclusions. First, from the maximal rotations of the halide[6] ($[\alpha]^{20}D \pm 38.3°$) and of 3-methylnonane[7] ($[\alpha]^{25}D \pm 9.30°$) it is evident that, had no racemization occurred, the 3-methylnonane produced here should have exhibited a rotation $[\alpha]^{25}D$ + 6.46°. Comparison of this value with the value $[\alpha]^{25}D$ + 5.16° observed experimentally indicates that racemization occurred to the extent of only 20%. Furthermore, as previously noted,[2] retention of rotational sign is here associated with a Walden inversion in the replacement of halogen by ethyl. Hence, the displacement reaction displays the stereochemical characteristics of concerted nucleophilic substitution ($S_N2$)[4]: namely, inversion without appreciable racemization.

Second, since the 7,8-dimethyltetradecane formed possessed appreciable optical activity, a substantial portion of it must have resulted from a displacement of halogen by *s*-octyl which preserved optical activity, and which, presumably, involved concerted substitution analogous to that occurring in the formation of 3-methylnonane. The transition-state for this process may be pictured:



I

Accompanying this to some extent was, in all probability, the corresponding substitution involving the enantiomorphic *s*-octyl group, *e. g.*,



II

which produced the *meso* form. In any event, the results clearly indicate that the energy of the transition state II cannot be appreciably less than that of I. Since these relative energies cannot be much altered by replacing chlorine with bromine, this kind of displacement, operating with the corresponding bromide, should have given an optically active product, not exclusively the *meso* form. That such was not the case[2] requires a different mechanism for the bromide and rules out hypothesis (1) above.

Third, if free *s*-alkyl radicals had been present in the reaction of sodium ethyl with the bromide, they should equally well have been present here, since in either case their source would be the sodium *s*-octyl, produced by metal–halogen interchange

$$Na^{\oplus}C_2H_5^{\ominus} + s\text{-}C_8H_{17}X = NaX + Na^{\oplus}C_8H_{17}^{\ominus} \quad (X = Cl, Br).$$

Had the 7,8-dimethyltetradecane arisen from them, it should have been optically inactive in both reactions. Accordingly, hypothesis (2) can be rejected.

The only reasonable explanation which remains is that the (−)2-bromooöctane reacts with sodium alkyls by a two stage process involving the initial production of a carbonium ion which racemizes before combining with the alkyl carbanion. This concept will be developed in greater detail in the fourth paper of this series.

## Experimental

**Materials.**—(+)2-Chlorooöctane, $[\alpha]^{25}D$ + 26.41°, $[\alpha]^{20}D$ + 26.61° (homogeneous), b. p. 66–67° at 17 mm., $d^{25}_4$ 0.8607, was prepared from (−)2-octanol, $[\alpha]^{25}D$ −7.66 (homogeneous), b. p. 85–87° at 20 mm., $d^{25}_4$ 0.8165, in 77% yield by a method essentially like that of Clark and Streight,[8] but in which chloroform was used as the solvent. The (−)2-octanol was obtained from the resolution of *dl*-2-octanol (Eastman Kodak Co., White Label) according to Kenyon.[9] Mercury diethyl, b. p. 55–57° at 15 mm., was prepared in 67% yield according to the procedure of Marvel and Gould[10] as improved by Gilman and Brown.[11] Analysis of this compound according to Koten and Adams[12] showed it to be 99% pure. The *n*-pentane used in these experiments was a product of the Phillips Petroleum Company and was distilled from sodium, b. p. 36–37°. No unsaturates were detected, and a sample in a 2 dm. tube showed no optical activity.

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(4) *Cf.* Hughes, *Trans. Far. Soc.*, **37**, 603 (1941).

(5) Ulrich and Lane, THIS JOURNAL, **72**, 5130 (1950).

(6) Hughes, Ingold and Masterman, *J. Chem. Soc.*, 1196 (1937).

(7) Letsinger and Traynham, THIS JOURNAL, **72**, 849 (1950).

(8) Clark and Streight, *Trans. Roy. Soc. Can.*, [3] **23**, Sect. 3, 77 (1929).

(9) Kenyon, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 410.

(10) Marvel and Gould, THIS JOURNAL, **44**, 153 (1922).

(11) Gilman and Brown, *ibid.*, **52**, 3314 (1930).

(12) Koten and Adams, *ibid.*, **46**, 2769 (1924).

**Action of Sodium Ethyl on (+)2-Chloroöctane.**—Reaction between these substances was carried out under nitrogen in the fashion previously described[2] for the reaction between sodium ethyl and (−)2-bromoöctane, except that somewhat longer reaction times were employed. Table I summarizes for the different runs the amounts of material and the times of reaction at 10° and room temperature.

TABLE I

MATERIALS AND CONDITIONS EMPLOYED IN THE REACTION BETWEEN SODIUM ETHYL AND (+)2-CHLOROÖCTANE

| | Materials | | | | Temperature and reaction time, hr. | |
|---|---|---|---|---|---|---|
| Expt. | Pentane, ml. | Sodium, g. atom | Mercury diethyl, mole | 2-Chloro-octane, mole | −10° | Room temp. |
| 1 | 300 | 0.0683 | 0.331 | 0.265 | 9 | 12 |
| 2 | 400 | .0731 | .351 | .568 | 12 | 36 |
| (2)[a] | | .272 | .123 | | 16 | 32 |
| 3 | 180 | .87 | .369 | .491 | 18 | 36 |

[a] Retreatment of reaction mixture 2.

To each of the reaction mixtures was finally added 300 ml. of water and the layers were separated from each other and from the partially decomposed amalgam. The aqueous layer was then analyzed for chloride ion by the Volhard method. From this was calculated the extent of reaction of the halide. The amalgam was then freed from unreacted sodium by treatment with dilute sulfuric acid and the remaining mercury dried and weighed. From this was calculated the yield of sodium ethyl. These data are summarized in Table II.

TABLE II

YIELD OF SODIUM ETHYL AND EXTENT OF ITS REACTION WITH (−)2-CHLOROÖCTANE

| Expt. | Chloride ion, mole | Extent of reaction, % | Mercury, mole | Yield of sodium ethyl, % |
|---|---|---|---|---|
| 1 | 0.256 | 97 | 0.280 | 85 |
| 2 | .430 | 96 | .284 | 80 |
| (2) | .117 | | | |
| 3 | .485 | 99 | .344 | 93 |

The united pentane layers were dried over magnesium sulfate and most of the pentane was removed through an 8-bulb Snyder column at 36°. Ether was added and the solution saturated with dry hydrogen chloride. After removal by filtration of the precipitated ethyl mercuric chloride the solution was freed from ether by distillation through the Snyder column and then chilled to precipitate the remaining ethyl mercuric chloride. After filtration the solution was fractionated through a 55 mm. column packed with glass helices, and 68.2 g. of material boiling between 121.5° and 125.5° was obtained. Analysis for unsaturation by the method of Uhrig and Levin,[13] showed that this fraction contained 55.5 g. (0.49 mole, 37%) of octylene and 12.7 g. (0.11 mole, 8.5%) of octane. Between 125.5° and 142° only 0.9 g. of material was collected.

At this point the fractionation was discontinued and the residual liquid in the boiler was taken up in 98% ethanol. To the gently refluxing solution was added 15 g. of sodium in small pieces over a period of three hours, after which 70 ml. of 95% ethanol was added and the mixture refluxed for an additional three hours. The mixture was cooled, diluted with water and extracted with five 50-ml. portions of pentane. The united pentane extracts were washed twenty times with concentrated sulfuric acid and five times with saturated magnesium sulfate solution, and the solution was finally dried over magnesium sulfate and potassium carbonate. The bulk of the pentane was removed through the Snyder column and a 2-ml. portion of the residual liquid (50 ml.) was analyzed for chloride by the method of Rauscher.[14] No chloride could be detected.

The solution was now fractionated through the 55-cm. column filled with glass helices. Data on the fractions obtained between the temperatures of 123 and 210° are given in Table III.

TABLE III

PHYSICAL CHARACTERISTICS OF FRACTIONS BOILING BETWEEN 123 AND 210° (769 MM.)

| Fraction | B. p., °C. | Weight, g. | $n^{20}$D | $\alpha^{25}$D(°)[a] |
|---|---|---|---|---|
| 1 | 123–156 | 4.0 | 1.4011 | 0.74 |
| 2 | 160–165.3 | 1.8 | 1.4109 | 3.16 |
| 3 | 166.2–167.1 | 2.4 | 1.4126 | 3.70 |
| 4 | 167.1–167.2 | 4.1 | 1.4129 | 3.76 |
| 5 | 167.3–168.1 | 1.6 | 1.4133 | 3.74 |
| 6 | 178–210 | 1.1 | 1.4179 | 3.07 |

[a] Homogeneous, 1-dm. tube.

Fractions 3, 4 and 5 are substantially pure 3-methylnonane. Fraction 4 had $d^{25}_4$ 0.7286, $[\alpha]^{25}$D + 5.16°.

*Anal.*[15] Calcd. for $C_{10}H_{22}$: C, 84.41; H, 15.59. Found: C, 84.46; H, 15.74.

Since the contaminants of fractions 1 and 2 (octane, octylene) are optically inactive, the amounts of (+)3-methylnonane in them are calculated from the rotations to be, respectively, 0.8 g. and 1.5 g. Fraction 6 is contaminated with 7,8-dimethyltetradecane ($n^{20}$D 1.4423, see below.) From refractive indices the amount of (+)3-methylnonane in this fraction is estimated at 0.8 g. The total weight of (+)3-methylnonane obtained is thus 11.3 g. The yield (based on the 96% of material fractionated) is 6.4%.

The high boiling residue from the fractionation was distilled at 9 mm. from a small Claisen flask and yielded three fractions, the characteristics of which are given in Table IV.

TABLE IV

CHARACTERISTICS OF HYDROCARBON PRODUCTS BOILING BETWEEN 129–226° AT 9 MM.

| Fraction | B. p., °C., uncor. | Wt., g. | $n^{20}$D | $\alpha^{22}$D[a] (°) |
|---|---|---|---|---|
| 1 | 129–135 | 0.8 | 1.4421 | 1.04 |
| 2 | 135–151 | 4.8 | 1.4423 | 0.90 |
| 3 | 151–226 | 1.7 | 1.4524 | 0.16 |
| 4 | Residue | 0.7 | | |

[a] Homogeneous, 1-dm. tube.

Fraction 2 was redistilled at 9 mm. from a 10-ml. distilling flask and five fractions, each of about 1 ml., were collected. Their physical characteristics are given in Table V.

TABLE V

CHARACTERISTICS OF FRACTIONS OBTAINED ON REDISTILLATION OF FRACTION 2 FROM TABLE IV

| Fraction | B. p.,[a] °C. | $n^{20}$D | $\alpha^{23}$D (°)[b] | Micro b. p., °C. (cor.)/ 769 mm. |
|---|---|---|---|---|
| 2a | 169–214 | 1.4422 | 1.02 | |
| 2b | 219–260 | 1.4422 | 1.02 | 275 |
| 2c | 261–262 | 1.4423 | 0.96 | 278 |
| 2d | 263–264 | 1.4422 | 0.86 | |
| 2e | 265–269 | 1.4438 | 0.64 | |

[a] °/760–763 mm. (uncor.). [b] Homogeneous, 1-dm. tube.

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(13) Uhrig and Levin, *Ind. Eng. Chem., Anal. Ed.*, **13**, 90 (1941).

(14) Rauscher, *ibid.*, **9**, 296 (1937).

(15) Analysis by Mr. Joseph Alicino, Squibb Institute for Medical Research, New Brunswick, New Jersey.

*Anal.* (2c)[15] Calcd. for $C_{16}H_{34}$: C, 84.86; H, 15.14; mol. wt., 226. Found: C, 85.21; H, 14.74; mol. wt. (cryoscopic, benzene), 222.

## Summary

The action of sodium on (+)2-chlorooctane has been found to give octylene (37%), octane (8.5%), (+)3-methylnonane (6.4%), $[\alpha]^{25}D$ + 5.16° and (+)7,8-dimethyltetradecane (3.7%), $\alpha^{23}D$ + 0.96° (homogeneous, 1-dm. tube.) It is suggested that the optically active hydrocarbons are formed by a concerted displacement reaction with accompanying Walden inversion. The known extensive racemization of the same hydrocarbons produced by the action of sodium ethyl on (−)2-bromooctane is interpreted as indicating that this halide reacts with sodium alkyls by a two-stage process involving initial production of a racemizable *s*-octyl carbonium ion.

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RECEIVED APRIL 20, 1950

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY]

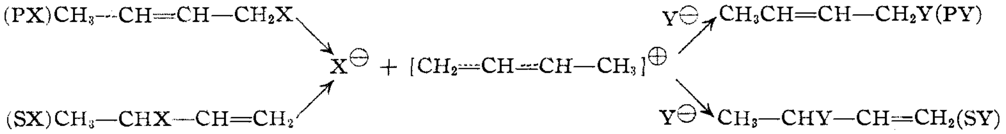
# Reactions of Organometallic Compounds with Alkyl Halides. III. On Sodium Ethyl and Butenyl Chlorides

BY STEPHEN E. ULRICH[1] AND JOHN F. LANE

In the first two papers of this series[2,3] it has been shown that interaction of sodium alkyls with an optically active alkyl chloride led to the production of optically active hydrocarbons. On the other hand, with the corresponding alkyl bromide extensively or completely racemized products were obtained. These results have been interpreted[3] as indicating that the displacement of chlorine by alkyl carbanions is a concerted, one step process attended by Walden inversion but little racemization, while displacement of bromine by the same carbanions is a two stage process involving preliminary ionization of the halide to give a racemizable carbonium ion.

The occurrence of this kind of displacement in a medium of low dielectric constant and with an entering anion of high basicity is somewhat surprising. It was, therefore, considered desirable to explore the possibility of its occurring with certain additional halides which are prone to undergo displacement reactions by way of intermediate carbonium ions.

It is well known that allylic halides are of this type. Furthermore, much evidence has been presented[4,5] to substantiate the conclusion that with a pair of allylic isomers, the two stage ionic replacement of one group by another ($S_N1$) leads from each isomer to the same mixture of products, *e. g.*



$$\begin{array}{l}(PX)CH_3{-}CH{=}CH{-}CH_2X \searrow \\ \qquad\qquad X^{\ominus} + [CH_2{\cdots}CH{\cdots}CH{-}CH_3]^{\oplus} \\ (SX)CH_3{-}CHX{-}CH{=}CH_2 \nearrow \end{array} \begin{array}{l} \nearrow Y^{\ominus}\ CH_3CH{=}CH{-}CH_2Y(PY) \\ \\ \searrow Y^{\ominus}\ CH_3{-}CHY{-}CH{=}CH_2(SY)\end{array}$$

while, on the other hand, concerted one stage displacement usually leads to "normal" products ($Y + PX \rightarrow PY + X^{\ominus}$, $S_N2$) and sometimes to "inverse" products ($Y + PX \rightarrow SY + X^{\ominus}$, $S_N2'$), it never leads to mixtures.

In the present study the isomeric butenyl chlorides, 1-chloro-2-butene (PCl) and 3-chloro-1-butene (SCl), were separately allowed to react in pentane with sodium ethyl. In each case the only clearly isolable product was (chiefly *trans*) 2-hexene ($PC_2H_5$), although the lower boiling fractions may have contained traces of the isomeric 3-methyl-1-pentene ($SC_2H_5$). This behavior indicates formation in each case of a mixture of products in which the thermodynamically more stable hexene-2 is predominant.[6] That ionic replacement of chlorine by ethyl should, in this system, lead to a mixture of products resembling the thermodynamically stable one is quite reasonable. This has, indeed, been shown to be true[4a] in the conversion of the corresponding alcohols (POH, SOH) to the bromides by an ionic mechanism.

These results strongly suggest that with these reactive halides the replacement of chlorine by ethyl has not proceeded by the concerted one stage mechanism, but rather by way of a resonating butenyl carbonium ion.

## Experimental

**Materials.**—The isomeric butenyl chlorides were obtained by fractionation, through a 90-cm. Todd column, of the commercial mixture of the Shell Development Company. 3-Chloro-1-butene boiled at 64.9–65.0° (771 mm.)

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[1] American Chemical Society Fellow in Rutgers University, 1946–1949.

[2] Brink, Lane and Wallis, THIS JOURNAL, **65**, 943 (1943).

[3] Ulrich, Gentes, Lane and Wallis, *ibid.*, **72**, 5127 (1950).

[4] (a) Young and Lane, *ibid.*, **60**, 847 (1938); (b) Roberts, Young and Winstein, *ibid.*, **64**, 2197 (1942).

[5] Hughes, *Trans. Far. Soc.*, **37**, 603 (1941).

[6] Am. Pet. Inst., "Selected Values of Properties of Hydrocarbons," Vol. III, Table 8p, gives the following free energies of formation ($\Delta F_{298}$, kcal.): $PC_2H_5$, *trans*, 18.46, *cis* 19.18, $SC_2H_5$, 20.28. From these the composition of the thermal equilibrium mixture is estimated to be: $PC_2H_5$, *trans*, 70.4%, *cis* 26.3%, $SC_2H_5$, 3.3%.