(8) A. L. Green, G. L. Sainsbury, B. Saville, and M. Stanfield, *J. Chem. Soc.*, 1583 (1958).
(9) J. Epstein, P. L. Cannon, Jr., H. O. Michel, B. E. Hackley, Jr., and W. A. Mosher, *J. Am. Chem. Soc.*, **89**, 2937 (1967).
(10) (a) R. I. Ellin and J. H. Wills, *J. Pharm. Sci.*, **53**, 995 (1964); (b) R. I. Ellin and J. Henry Wills, *ibid.*, **53**, 1143 (1964); (c) N. Bodor, E. Shek, and T. Higuchi, *Science*, **190**, 155 (1975); (d) N. Bodor, E. Shek, and T. Higuchi, *J. Med. Chem.*, **19**, 102 (1976); (e) E. Shek, T. Higuchi, and N. Bodor, *ibid.*, **19**, 108 (1976); (f) *ibid.*, **19**, 113 (1976).
(11) (a) C. A. Bunton and L. G. Ionescu, *J. Am. Chem. Soc.*, **95**, 2912 (1973); (b) K. Martinek, A. V. Levashov, and I. V. Berezin, *Tetrahedron Lett.*, 1275 (1975); (c) Tabushi, Y. Kuroda, and S. Kita, *ibid.*, 643 (1974); (d) T. Kunitake, U. Okahata, and T. Sakamoto, *Chem. Lett.*, 459 (1975).
(12) R. A. Moss, R. C. Nahas, S. Ramaswami, and W. J. Sanders, *Tetrahedron Lett.*, 3379 (1975).
(13) U. Tonellato, *J. Chem. Soc., Perkin Trans. 2*, 771 (1976).
(14) (a) A. Ray and P. Mukerjee, *J. Phys. Chem.*, **70**, 2138 (1966); (b) J. E. Adderson and H. Taylor, *J. Pharm. Pharmacol.*, **16**, 147T (1964); (c) G. C. Kresheck, E. Hamori, G. Davenport, and H. A. Scheraga, *J. Am. Chem. Soc.*, **88**, 246 (1966); (d) B. C. Bennion and E. M. Eyring, *J. Colloid Interface Sci.*, **32**, 286 (1970).
(15) J. H. Fendler, E. J. Fendler, G. A. Infante, P. S. Shih, and L. K. Patterson, *J. Am. Chem. Soc.*, **97**, 89 (1975).
(16) J. Epstein, J. J. Callahan, and V. E. Bauer, *Phosphorus*, **4**, 157 (1974).
(17) J. J. Kaminski, K. W. Knutson, and N. Bodor, *Tetrahedron*, in press.
(18) We are indebted to Dr. G. T. Davis and M. M. Demek for supplying these data.
(19) C. Tanford, "The Hydrophobic Effect", Wiley, New York, N.Y., 1973, p 81.
(20) The partition coefficients of isopropyl methylphosphonofluoridate between nonpolar solvents such as hexane and carbon tetrachloride and water are less than one (R. W. Rosenthal, R. Proper, and J. Epstein, *J. Phys. Chem.*, **60**, 1596 (1956)).
(21) G. E. Delory and E. J. King, *Biochem. J.*, **39**, 245 (1945).
(22) G. L. Ellman, K. D. Courtney, V. Anders, Jr., and R. M. Featherstone, *Biochem. Pharmacol.*, **7**, 88 (1961).

The Intermediate from the Triphenylphosphine–Tetrachloromethane–Alcohol Reaction: Relative Rates of Intermediate Formation, Kinetics, and Mechanism of Intermediate Decomposition

L. A. Jones, C. E. Sumner, Jr., B. Franzus,* T. T.-S. Huang, and E. I. Snyder

Department of Chemistry, East Tennessee State University, Johnson City, Tennessee 37601

Received October 13, 1977

The rate of formation of the phosphorylated intermediate formed by reacting triphenylphosphine, carbon tetrachloride, and an alcohol is only slightly influenced by steric effects. The relative rates of intermediate formation are primary > secondary > neopentyl. The relative rates of intermediate decomposition follow the order primary > secondary > neopentyl. Thus neopentyl alcohol reacted with the phosphorylating agent at room temperature to form an intermediate without concomitant decomposition to neopentyl chloride. The structure of the intermediate was elucidated by ^1H NMR and ^{31}P decoupling. Rates of decomposition to the respective alkyl chlorides of the phosphorylated intermediates formed from neopentyl alcohol and from 1,1-dideuterio-2,2-dimethylpropanol were run at various temperatures. Clean first-order kinetics were obtained as well as the energetics for the decomposition reaction. A small positive α hydrogen kinetic isotope effect was obtained and the various mechanisms of intermediate decomposition to chloride product are discussed in terms of rate constants, the energetics, and the isotope effects.

The reaction of triphenylphosphine, carbon tetrachloride, and alcohols gives rise to an elegant method for the synthesis of primary and secondary alkyl chlorides.

$$(C_6H_5)_3P + CCl_4 + ROH \rightarrow RCl + (C_6H_5)_3PO + CHCl_3 \quad (1)$$

In 1966, the preparation of acyl chlorides[1] by the reaction of a carboxylic acid with triphenylphosphine and carbon tetrachloride was extended to the preparation of alkyl chlorides from alcohols, triphenylphosphine, and carbon tetrachloride.[2]

Similarly, tri-*n*-octylphosphine and carbon tetrachloride were used to convert primary and secondary alcohols to the corresponding chlorides with inversion of configuration; the production of tertiary chlorides gave very poor yields, possibly due to elimination being the primary reaction.[3] The use of carbon tetrabromide, trialkyl- or triarylphosphines, and primary or secondary alcohols led to alkyl bromides. Again, inversion of configuration seemed to predominate in this synthetic procedure.[3] The ease with which chlorides were formed with inversion of configuration was explored by R. G. Weiss and E. I. Snyder in several papers.[4a-c]

The various pathways for intermediate formation have been investigated by Appel and have been summarized in an excellent review article by the same author.[5] The overall mechanism of the reaction is presumed to proceed via eq 2.[5]

$$(C_6H_5)_3P + CCl_4 \rightarrow [(C_6H_5)_3PCl]^+CCl_3^-$$

$$[(C_6H_5)_3PCl]^+CCl_3^- + ROH \rightarrow [(C_6H_5)_3POR]^+Cl^- + HCCl_3$$

$$[(C_6H_5)_3POR]^+Cl^- \rightarrow RCl + (C_6H_5)_3PO \quad (2)$$

In more detail, the formation of the intermediate can be formulated in part as follows:[5]

$$(C_6H_5)_3\overset{\delta+}{P}\cdots Cl\cdots\overset{\delta-}{C}Cl_3 \rightarrow [(C_6H_5)_3POR]^+Cl^- + HCCl_3 \quad (3)$$

(R–O–H)

Appel[5] has also described other minor routes to the phosphorylated intermediate involving $(C_6H_5)_3PCl_2$ and $(C_6H_5)_3PCCl_2$, but they will not be discussed in this manuscript.

There are a number of gaps in this mechanistic picture that need to be filled and clarified: First, it must be noted that nowhere is there any mention of the relative rates of formation and decomposition of the intermediate. Second, it will be noted that the intermediate has been described as an ion pair with a phosphorus–oxygen–carbon bond. At present there is no hard evidence for this assumption. Third, it must be emphasized that although the intermediate has been described as undergoing a first-order decomposition to product, there is no concrete evidence to date that this implied kinetic order is a reality.

0022-3263/78/1943-2821$01.00/0

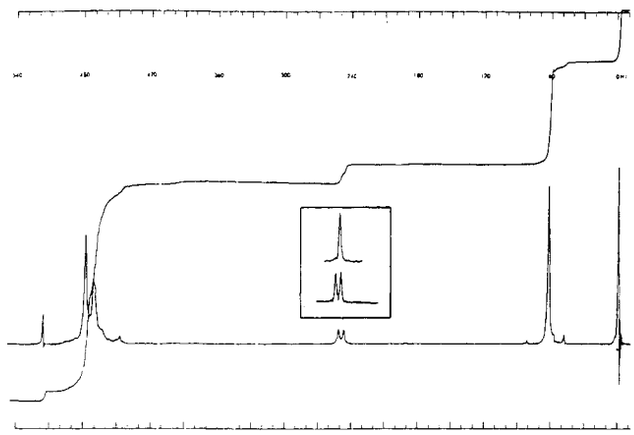
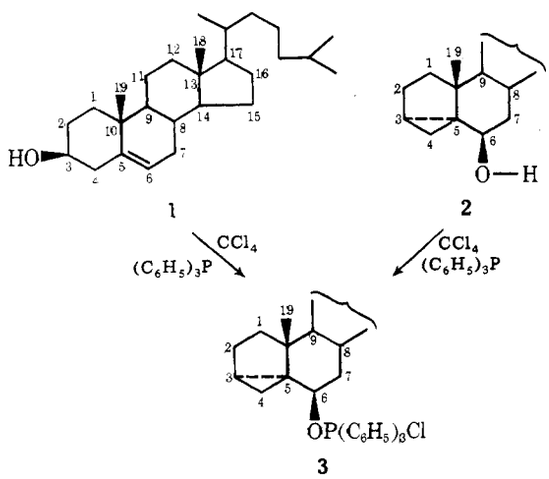


Figure 1. The ^1H NMR spectrum of compound **6** in $CDCl_3$–CCl_4. The inset shows the CH_2–O–^{31}P doublet and its collapse to a singlet peak upon ^{31}P irradiation.

First, we propose to show that for sterically unhindered primary alcohols the rate of intermediate decomposition to alkyl chloride is faster than the rate of intermediate formation; for secondary alcohols the rate of intermediate decomposition is slowed much more dramatically than the rate of intermediate formation, and for the neopentyl alcohol system, the rate of intermediate formation is many times faster than the rate of intermediate decomposition. Second, we will show that the intermediate contains a phosphorus–oxygen–carbon bond. Third, we have run decomposition kinetics on the phosphorylated neopentyl intermediate to neopentyl chloride and have verified that indeed the decomposition is first order. Finally, we have run decomposition kinetics on 1,1-dideuterio-2,2-dimethylpropanol and obtained an α hydrogen kinetic isotope effect showing that the decomposition proceeds via an intramolecular S_N2 substitution.[6]

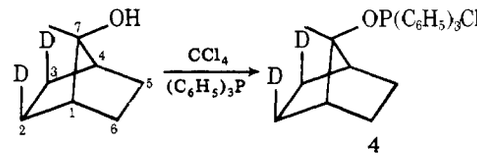
Results

The isolation of a crude intermediate has been noted by Aneja, Davies, and Knaggs[7] where some intermediate phosphorylated derivative (**3**) was obtained both from the reaction of cholesterol (**1**) and from isocholesterol (**2**). The "proof" of

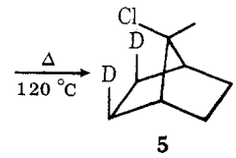


3

structure of **3** resided in the fact that the chemical shift for the 19-CH_3 was at δ 0.4 suggesting spacial proximity to the substituent at C-6. The only other known case was that of Weiss and Snyder[4b] who had shown that a crude preparation of *anti*-**4** could be isolated and decomposed thermally (with approximate first-order kinetics) to *syn*-**5**. It is well known that reactions in the 7-substituted norbornyl system proceed slowly with inversion.[8] So, in order to duplicate this type of



4



5

system in the acyclic series, neopentyl alcohol was chosen as a model compound since displacement with inversion on neopentyl-substituted compounds also proceeded slowly. When neopentyl alcohol was treated with triphenylphosphine and carbon tetrachloride, it was observed that the hydroxyl proton area decreased and at the same time underwent a shift to lower field. For example, at the beginning of the reaction, the hydroxyl proton appeared at δ 2.97, and after 513 min the last vestiges of the **OH** appeared at δ 6.77. At the same time the **OH** was shifting and decreasing in area, the CH_2O (δ 3.32) area of the original alcohol was decreasing and a new peak appeared as a doublet ($J \simeq 4.3$ Hz) at δ 4.17. The increase in area of the new peak was equal to the decrease in area of the CH_2O peak of the alcohol. The ^1H NMR data were consistent with compound **6.** Since it was known for trineopentyl phosphate (**7**) that the J_{CH_2OP} coupling constant was 5.24 Hz,[9] it was presumed that the doublet arose from a ^{31}P coupling. That this was indeed a ^{31}P coupling was further substantiated by ^{31}P irradiation of the intermediate which resulted in collapse of the doublet to a singlet. (See Figure 1.) Thermal treatment of intermediate **6** led to formation of neopentyl chloride.

$$(CH_3)_3CCH_2OH \xrightarrow[CCl_4]{(C_6H_5)_3P} (CH_3)_3CCH_2OP(C_6H_5)_3Cl$$

6

$$J_{CH_2OP} = 4.3 \text{ Hz}$$

$$[(CH_3)_3CCH_2O-]_3P{=}O$$

7

$$J_{CH_2OP} = 5.24 \text{ Hz}$$

We were able to follow this, not only by product isolation but by ^1H NMR spectroscopy. Thus, the CH_2O doublet of the intermediate (δ 4.17) collapsed to a singlet (CH_2Cl, δ 3.27) of the product. We also noted that as the intermediate *tert*-butyl group decreased in area there was a concomitant increase in the area of the product *tert*-butyl group. Since the reaction involving intermediate formation is a result of front-side attack (see eq 3), we assumed that the rate of intermediate formation should be essentially free of any steric requirements. To test this hypothesis, the relative rates of disappearance of benzyl alcohol vs. neopentyl alcohol were determined by ^1H NMR spectroscopy. In the case of benzyl alcohol no intermediate was detected by ^1H NMR, so it was assumed that the rate of intermediate decomposition was much faster than its rate of formation. Thus by ^1H NMR we were able to observe benzyl alcohol, benzyl chloride, neopentyl alcohol, and the neopentyl intermediate (**6**). Furthermore, by assuming that the alcohols were consumed unimolecularly, it was determined that the relative rate of benzyl alcohol disappearance to neopentyl alcohol disappearance was about 7.4/1. The data did range in relative rates from a high of 8.5 to a low of 6.5. However, it does support the front-side attack hypothesis (eq 3) since it is known that for back-side displacement reactions the relative rate of $PhCH_2X$/neopentyl-X is about 30 000 000/1.0.[10] The above compounds were chosen at opposite extremes of nucleophilic displacement reactions to emphasize that to

Table I. Material Balance for Competition Kinetics of 3-Methyl-1-butanol vs. 1-Pentanol[a]

Time, min	1-Pentanol A[c]	Isoamyl OH B[c]	1-Chloropentane[c]	Isoamyl Cl[c]	Int. A[b]	Int. B[b]
15	1.60	1.75	0.09	0.03	0.51	0.42
75	1.45	1.67	0.45	0.15	0.30	0.38
138	0.82	1.09	0.82	0.35	0.56	0.76
210	0.31	0.57	1.57	0.63	0.32	1.00
300	0.10	0.25	1.80	0.75	0.30	1.20
390	0.02	0.02	1.99	1.17	0.19	1.01
T_∞	0.02	0.02	2.00	2.01	0.18	0.17
58	1.62	1.80	0.34	0.17	0.24	0.23
127	0.81	1.11	0.77	0.38	0.62	0.71
195	0.45	0.70	1.56	0.57	0.19	0.93
268	0.33	0.60	1.61	0.80	0.26	0.80
376	0.05	0.07	1.88	1.13	0.27	1.00
T_∞	0.01	0.02	1.99	2.00	0.20	0.18

[a] Run in excess chlorinating agent. Initial alcohols: 2.20 mmol of each alcohol. [b] Intermediates are assumed for material balance of original alcohol minus alcohol and chloride at time t as the amount of phosphate intermediate which has not decomposed. [c] Units are millimoles.

Table II. Material Balance for Competitive Kinetics of 1-Pentanol vs. 2-Pentanol[a]

Time, min	1-Pentanol A[c]	2-Pentanol B[c]	1-Chloropentane[c]	2-Chloropentane[c]	Int. A[b]	Int. B[b]
10	1.80	2.00			0.40	0.20
72	1.48	1.84	0.43	0.10	0.29	0.26
135	1.12	1.60	0.81	0.20	0.27	0.40
210	0.73	1.32	1.36	0.32	0.11	0.56
278	0.15	0.81	1.94	0.42	0.11	0.97
343	0.02	0.48	2.00	0.52	0.18	1.20
T_∞	0.02	0.02	2.01	1.98	0.17	0.20
15	1.60	1.90			0.60	0.30
150	0.85	1.45	0.90	0.22	0.45	0.53
230	0.36	1.00	1.38	0.32	0.46	0.88
290	0.17	0.69	1.74	0.43	0.29	1.08
T_∞	0.02	0.02	1.99	1.98	0.19	0.20

[a] Run with excess chlorinating agent. Initial alcohols: 2.20 mmol of each alcohol. [b] Intermediates are assumed for material balance of original alcohol minus alcohol and chloride at time t as the amount of phosphate intermediate which has not decomposed. [c] Units are mmoles.

a large extent intermediate formation is *not* sterically controlled. To determine the possibility of intermediate formation in simple, acyclic systems, 1-pentanol vs. 2-pentanol and 1-pentanol vs. 3-methyl-1-butanol (isoamyl alcohol) were reacted competitively with triphenylphosphine and carbon tetrachloride. If an intermediate were being formed, this would be reflected by the relative rates of 1-pentanol vs. the other two alcohols showing only a small difference in rates, presumably due to small secondary effects of steric hindrance.

Competitive kinetics for the disappearance of alcohol or appearance of alkyl chloride by GLC can be misleading in this type of system. The reason for this caveat lies in the fact that the decomposition of intermediate has a high energy of activation (this will be discussed later) so that volatilization of the sample in the injection port of the chromatograph caused an increase of intermediate decomposition to alkyl chloride. In order to minimize the results due to intermediate decomposition, thermostated samples consisting of alcohol, triphenylphosphine, chloroform-*d*, and tetrachloromethane were removed from time to time and connected to a high vacuum system to trap all the alkyl chloride, $CDCl_3$, CCl_4, and much of the unreacted alcohol. As described in the Experimental Section, the alcohol and alkyl chlorides were determined (quantitatively) by GLC using an internal standard. Essentially *all* the volatile alkyl chloride (plus a large amount of alcohol) was removed under vacuum leaving a small amount of the less volatile unreacted alcohol and the intermediate. This residue was analyzed separately by GLC using an internal standard. Thus the amount of alcohol that had reacted was a reliable value since all the CCl_4 which could form intermediate was removed under vacuum; there is of course an inherent source of error overestimating the amount of alkyl chloride formed and underestimating the amount of intermediate present in the reaction mixture at any time. This of course arises from the amount of intermediate which decomposes to alkyl chloride. Nevertheless, the material balance was relatively reliable and consistent in almost all our experiments and at no time was the material balance over 20% and was generally well within the 10% mark. Consistently, it was noted that 1-pentanol reacted only 1.4 times as fast as isoamyl alcohol and only 2.2 times as rapidly as 2-pentanol with both excess chlorinating agent and excess alcohol. These relative rates were fully consistent with the formation of a discrete intermediate. However, as shown in Tables I and II, which summarize the material balance of 1-pentanol vs. isoamyl alcohol (Table I) and 1-pentanol vs. 2-pentanol (Table II), the intermediate from 1-pentanol increased only very slightly during the course of the reaction, but the intermediate from both isoamyl alcohol and 2-pentanol increased markedly in the first part of the reaction and then decreased. If the case of isoamyl alcohol were taken and it was assumed that as much as 0.2 mmol of product and/or intermediate could not be found (Table I, top portion), it would be noted that at 300 min there was 1.2 mmol of isoamyl intermediate. Even with an error of 0.2 mmol, there was still at least 1.0 mmol of intermediate

Table III. Rates and Kinetic Isotope Effects for Decomposition of Intermediates from Neopentyl Alcohol and 1,1-Dideuterio-2,2-dimethylpropanol (10)

Temp, °C	$k_H \times 10^5$, s^{-1} [a]	$k_D \times 10^5$, s^{-1}	k_H/k_D
40	1.40	1.30	1.077
49.8	5.57	5.02	1.109
59.9	20	17	1.176
70.3	66	63	1.047
		k_H/k_D (av)	1.102 ± 0.055

[a] Average of two kinetic runs at each temperature.

formed. This value was too large to ignore and graphically illustrated the intermediate formation.

It was quite apparent from our competitive studies that the slow step in alkyl chloride formation was due to rate of intermediate decomposition rather than rate of intermediate formation for secondary alcohols and neopentyl alcohol. Sterically unhindered primary alcohols not only formed intermediate rapidly but the intermediate, in turn, quickly decomposed to primary alkyl chloride. From Tables I and II it will be noted that even with a large excess of 1-pentanol in the early part of the reaction (10 to 150 min) there is always much more 1-chloropentane formed than intermediate present, strongly suggesting that the rate of intermediate decomposition of unhindered primary alcohol is more rapid than the rate of intermediate formation. This is certainly true for benzyl alcohol.

Once we had established the relative rates of intermediate formation and decomposition of various substrates, it became of interest for us to look at the rate of intermediate decomposition more critically in order to absolutely ascertain the order of the decomposition reaction, the energetics of the decomposition, and the kinetic isotope effect for the rate of decomposition. These results are of utmost importance when evaluating any proposed decomposition mechanism. Any mechanism that is proposed must be consistent with the stereochemistry of the reaction, the kinetics, the energetics, and the isotope effect. We needed an alcohol which would form intermediate much more rapidly than the corresponding intermediate would decompose to alkyl chloride; in addition we needed to know the stereochemical course of intermediate decomposition of this specific alcohol. The alcohol of choice was neopentyl alcohol (2,2-dimethylpropanol). We had found from competitive kinetics that we could readily form the neopentyl intermediate at ambient temperatures with insignificant intermediate decomposition; in addition it is known that the reaction of (*R*)-1-deuterio-2,2-dimethylpropanol (8) with tetrachloromethane and triphenylphosphine proceeds with greater than 85% inversion to form (*S*)-1-deuterio-2,2-dimethylpropyl chloride (**9**).[4c]

$$(R)\text{-}(CH_3)_3CCHDOH + CCl_4 + (C_6H_5)_3P \rightarrow (S)\text{-}(CH_3)_3CCDHCl$$

8 **9**

Not only did we need a system that would give reliable kinetics, but in addition we needed a system whereby we could study the kinetic isotope of an α,α-dideuterated system in order to get some conception of the amount of bond making and bond breaking of the intermediate to form the deuterated neopentyl chloride. To this end we synthesized 1,1-dideuterio-2,2-dimethylpropanol (**10**) via the $LiAlD_4$ reduction of methyl trimethylacetate (methyl pivalate). The alcohol obtained (**10**) had 1.95 D per molecule.

Table IV. Energetics for Decomposition of Intermediates from Neopentyl Alcohol and 1,1-Dideuterio-2,2-dimethylpropanol (10)

Compd	E_a, kcal/mol	$\Delta S^{\ddagger}$, eu
$(CH_3)_3CCH_2OP(C_6H_5)_3Cl$	27.14 ± 0.34	4.05 ± 0.02
$(CH_3)_3CCD_2OP(C_6H_5)_3Cl$	27.18 ± 0.34	3.98 ± 0.02

$$(CH_3)_3CCO_2CH_3 + LiAlD_4 \rightarrow \rightarrow (CH_3)_3CCD_2OH$$

10

We were able to monitor disappearance of neopentyl alcohol, appearance of intermediate, and appearance of neopentyl chloride by ^1H NMR spectroscopy. However, we did not have the CH_2O peak for the dideuterated derivative so we used the difference in the chemical shift of the *tert*-butyl group in the neopentyl series to monitor the reaction.

$$(\mathbf{CH_3})_3CCH_2OH \quad (\mathbf{CH_3})_3CCH_2OP(C_6H_5)_3Cl$$
$$\delta\ 0.875 \qquad \delta\ 1.033$$
$$(\mathbf{CH_3})_3CCH_2Cl$$
$$\delta\ 0.967$$

In addition we were able to obtain kinetics by ^1H NMR spectroscopy by measuring relative peak heights of intermediate and product.

Clean first-order kinetics were obtained up to and even over three half-lives of reaction for both neopentyl alcohol and the deuterated alcohol, compound **10**. We ran the kinetics simultaneously on the deuterated and nondeuterated neopentyl alcohols so that even if it should have turned out that our kinetic method may not have been absolute our relative kinetic isotope effect would have been valid. Our fears were ungrounded, however, and we obtained good first-order kinetics with correlation coefficients ranging from 0.997 to 0.999. In addition we were able to get correlation coefficients of 0.9998 on our Arrhenius plots. The kinetic data are summarized in Table III. It is possible that the values of the individual rate constants may not be accurate to the precision listed in the table. However, the relative values of the kinetic isotope effect should be reliable to the significant digits shown in the fourth column of Table III. It will be noted that the average experimental kinetic isotope effect (k_H/k_D) is 1.102 with small but abnormal temperature dependence. If one looks at the effect of just one deuterium, the kinetic isotope effect is 1.050. Indeed, this is a *very small* kinetic isotope effect. It can be seen in Table IV that the energies of activation for both neopentyl alcohol and compound **10** are essentially equal, the only small difference really residing in a slightly larger $\Delta S^{\ddagger}$ for the hydrogen isomer.

Discussion

We can now briefly summarize both our results and those of other authors in the preparation of alkyl chlorides by reaction of an alcohol with triphenylphosphine and carbon tetrachloride:

(i) Reactions generally proceed in two steps as in (a) and (b)

$$ROH + (C_6H_5)_3P + CCl_4 \rightarrow [(C_6H_5)_3\underset{\displaystyle Cl}{\overset{|}{P}}OR] + CHCl_3 \quad (a)$$

$$(C_6H_5)_3\underset{\displaystyle Cl}{\overset{|}{P}}OR \rightarrow RCl + (C_6H_5)_3PO \quad (b)$$

(ii) In the case of primary alcohols (sterically unhindered) step (a) is probably slower than (b) but for secondary alcohols and neopentyl alcohol step (a) is faster than step (b).

(iii) There is hard evidence for an intermediate, in particular, $(CH_3)_3CCH_2OP(C_6H_5)_3Cl$.

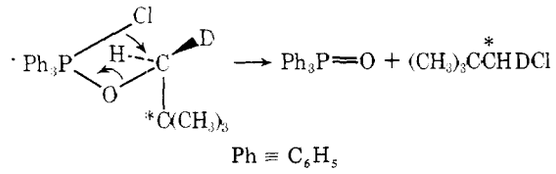
(iv) The rate of decomposition of the above intermediate follows clean first-order kinetics with an energy of activation of about 27 kcal/mol and an entropy of activation of about +4 eu.

(v) A greater than 85% inversion of configuration has been noted for the neopentyl system;[4c] thus greater than 92% back-side attack must be assumed for the thermal decomposition of $(CH_3)_3CCH_2OP(C_6H_5)_3Cl$ to $(CH_3)_3CCH_2Cl$.

(vi) The very small isotope effect per deuterium ($k_H/k_D \sim 1.050$) indicates a nearly balanced bond-making, bond-breaking process.

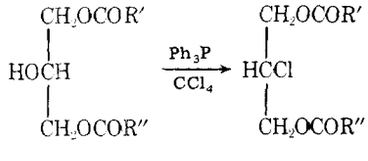
From a purely operational point of view the thermal decomposition of $(CH_3)_3CCH_2OP(C_6H_5)_3Cl$ to $(CH_3)_3CCH_2Cl$ must be an intramolecular S_N2 process with very little ion-pair character.[6] We can state this with complete confidence because of the large amount of inversion and the very small kinetic isotope effect. The kinetic isotope effect argument that this process has a nearly balanced bond making and bond breaking in what is usually known as an S_N2 process proceeds as follows.[11] From a theoretical point of view, the hydrogen kinetic isotope effects (KIE) depend on the symmetry properties of the transition state. The very small KIE that we experienced could be contributed totally from the temperature independent factor (TIF), namely the isotopic rate ratio resulting from the reaction coordinate, $\nu_H^{\ddagger}/\nu_D^{\ddagger}$, the variation of KIE over the limited temperature range could be explained as the result of the EXC (excitation) term. This argument fits our data rather well, since only a small isotope effect in entropy of activation can be accounted for from our experimental results. The zero-point energy difference (ZPE) is negligible; the small contribution must be from EXC assuming that for an intramolecular S_N2 the contribution from the moment of inertia change is small.

There have been a couple of interesting approaches toward the mechanism of intermediate decomposition. Under the assumption that the intermediate is a trigonal bipyramid, there is the so-called four-center mechanism whereby P–Cl bond breaking precedes somewhat C–O bond cleavage in a very tight ion pair.[4b]

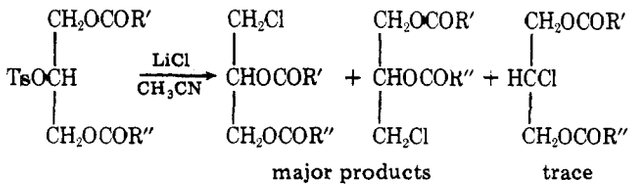


Ph ≡ C_6H_5

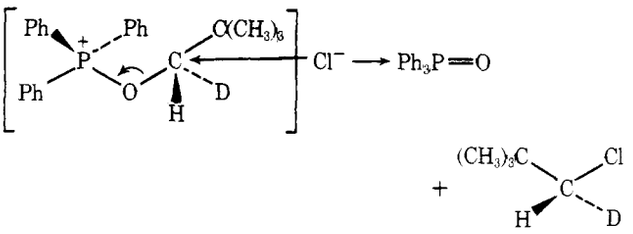
With sufficient C–O bond cleavage the above mechanism would require a measurable retention of configuration as has been noted by both Snyder[4b] and Mosher.[12] The nonconcerted P–Cl, C–O bond cleavage postulated by Snyder[4b] in the four-centered mechanism has been disputed by Aneja, Davies, and Knaggs.[13] These authors reacted acylglycerols with triphenylphosphine and tetrachloromethane and obtained only configurational inversion and no rearrangement due to acyloxy neighboring group participation.



If the corresponding *p*-toluene sulfonate (tosylate ≡ Ts) was reacted with lithium chloride in acetonitrile then both 1- and 3-substituted chlorodeoxydiacylglycerols were the major products resulting from acyloxy neighboring group participation.



Since *no* neighboring group was observed with $Ph_3P + CCl_4$, these authors disputed the prior P–Cl bond cleavage postulated by Weiss and Snyder.[4b] This argument is not valid since it is the extent of C–O cleavage which is involved in neighboring group participation of the acyloxy group *not* the amount of P–Cl cleavage. If the intermediate is written as an



ion pair with the phosphorus tetrahedrally coordinated[5] then the inversion of configuration and the energetics of the thermal decomposition are readily rationalized by the above mechanism.

The energetics observed for this type of process is not unreasonable. Thus, it is known that the nucleophilic substitution of neopentyl bromide with ethoxide ion in ethanol has an energy of activation of 26.2 kcal/mol.[14] This is quite close to our observed value of 27.1 kcal/mol and presumably 5–6 kcal/mol of this activation energy is steric in origin due to the bulk of the neopentyl group. The observed entropy of activation of +4 eu is fairly close to zero and is consistent with the above picture of an intramolecular S_N2 reaction. Indeed we would anticipate that the entropy of activation would increase markedly as the amount of C–O bond rupture increased; the above mechanism is therefore in accordance with the small isotope effect and the observed stereochemistry.

There are some flaws in the above picture; we have artificially placed the nucleophilic chloride adjacent to the electrophilic carbon and separated the positive phosphorus from the negative chloride in order to satisfy our steric requirements for a reaction of greater than 92% back-side attack. Such a charge separation is energetically unreasonable. If, however, we postulate that the ion pair is *not* a lone entity but is instead structured as a cluster of ion pairs in two and/or three dimensions wherein a positive phosphorus in one ion pair is in part electrically neutralized by a negative chloride from (an) other ion pair(s), then the ion-pair electrostatic picture becomes more reasonable. Rationalization for this model is remotely justified by noting that even interaction of *R–S* enantiomers is sufficiently strong so that the ^1H NMR of a racemic mixture can differ measurably from that of the pure enantiomer in an achiral solvent.[15]

Another flaw in the above model resides in the fact that an external nucleophile such as cyanide ion was unable to compete with chloride ion in the reaction of 2-phenylethanol, with triphenylphosphine–carbon tetrachloride in dimethyl sulfoxide.[4c] Yet 2-phenylethyl tosylate in dimethyl sulfoxide gave better than 19/1 2-phenylethyl cyanide to 2-phenylethyl chloride starting with equimolar amounts of cyanide and chloride ion.[4c] This could, of course, be a result of a very tight ion pair, but operationally it becomes difficult to distinguish between the tight ion pair with that of a covalent compound. We do not mean to imply that the phosphonium oxide group (Ph_3PO) is not a good leaving group; indeed this is considered to be a strong possibility in the reaction of tertiary alcohols

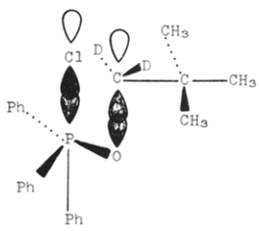


Figure 2. The decomposition of the intermediate $(CH_3)_3CCD_2$–$OPCl(C_6H_5)_3$ in a ${}_\sigma2_s + {}_\sigma2_a$ pericyclic reaction.

with tetrachloromethane–triphenylphosphine which leads to alkenes presumably due to prior formation of a tertiary carbenium ion.[3]

The ion-pair, four-centered mechanism is not unique in accounting for the stereochemistry, isotope effect, and the observed energetics. Indeed, Aneja, Davies, and Knaggs[7] proposed a $\sigma_{2_s} + \sigma_{2_a}$ thermal pericyclic reaction to account for the stereochemistry although there was no direct proof of this concerted process. However, this mechanism does account for the inversion of configuration and in a concerted process there could be almost equal C–Cl bond making and C–O bond breaking to account in full for the small isotope effect that we observed. First-order kinetics are also completely consistent with this mechanism. The intermediate that we have pictured in Figure 2 is that of a trigonal bipyramid (dsp^3) but there is no reason why we could not picture the intermediate as a square pyramid. What we do require is that one of the reacting groups be in the apical position (like the chloride in Figure 2) and the other group be in an equatorial position. Thus by breaking the P–Cl and the C–O bonds suprafacially (dark lobes) and also in a concerted process making a C–Cl bond via the front (dark) lobe of the Cl and the back (light) lobe of the C–O we have a symmetry-allowed ${}_\sigma2_s + {}_\sigma2_a$ pericyclic reaction in which the bonds are presumed to be heterolytically cleaved.

The one major flaw in the ${}_\sigma2_s + {}_\sigma2_a$ mechanism resides in the fact that the neopentyl system is only slightly hindered by front-side steric hindrance. Yet the neopentyl intermediate decomposes many times slower than benzyl, amyl, isoamyl, or 2-amyl alcohol intermediates. This is more in line with back-side steric hindrance than a concerted process involving front-side attack.

Examination of molecular models of the trigonal bipyramid structure (see Figure 2) would indicate that back-side displacement by chloride with this model would be a *very* difficult process. The ${}_\sigma2_s + {}_\sigma2_a$ mechanism is not really consistent with the slow decomposition of the neopentyl intermediate, although our other data do not rule out such a mechanism. At present, the intramolecular S_Ni displacement from the ion pair seems to be most consistent with both our data and that of other authors. Clearly, the energetics of decomposition of some simpler phosphonium intermediates are needed to more critically examine the microscopic decomposition pathways.

Experimental Section

^1H NMR spectra were determined with a JEOL C-60H spectrometer. Purity evaluations of all alcohols, cyclohexane, other internal standards, alkyl halides, carbon tetrachloride, and chloroform were performed on a Perkin-Elmer 990 gas chromatograph using a $\frac{1}{8}$ in. × 12 ft column, packed with 20% FFAP on Chromosorb W. All melting points (uncorrected) were taken on a Thomas-Hoover capillary melting point apparatus.

Triphenylphosphine, obtained from Strem Chemical Co., was recrystallized from cyclohexane prior to use and found to have a melting point of 78 to 80 °C. Reagent grade carbon tetrachloride (greater than 99% purity) from Fisher Scientific Co. was distilled from triphenylphosphine, placed in a brown bottle under nitrogen, and stored in the dark prior to use. Deuterated chloroform of 99.8% purity was obtained from Thomas-Packard, Inc.

Typical ^1H NMR Procedure for Following Intermediate and Halide Formation. Neopentyl alcohol (mp 55–56.2 °C) was greater than 99% pure as determined by GLC. To a ^1H NMR tube were added 0.0969 g (1.1 mmol) of neopentyl alcohol, 0.300 g (1.14 mmol) of triphenylphosphine, 0.2 mL (0.319 g, 2.07 mmol) of carbon tetrachloride, 0.4 mL of chloroform-*d* and a trace amount of tetramethylsilane (Me_4Si) as an internal ^1H NMR standard. In some cases, a known amount of cyclohexane (99% pure) was added as an internal standard for integration purposes. The reaction was scanned for a period of 24 h. The disappearance of alcohol was followed by noting the area change in the $\mathbf{OCH_2}$ peak and the *tert*-butyl peak of the neopentyl alcohol.

Heteronuclear Decoupling Experiment. A solution of 0.100 g of neopentyl alcohol, 0.300 g of triphenylphosphine, 0.2 mL of carbon tetrachloride, 0.4 mL of chloroform-*d*, and tetramethylsilane (trace) was added to a ^1H NMR tube and allowed to react at room temperature for 4 h. The reaction was scanned by ^1H NMR and the appearance of a doublet indicative of ^{31}P coupling was noted. Irradiation of the sample at the ^{31}P resonance frequency collapsed the doublet to a singlet.

Competitive Kinetics as Determined by ^1H NMR. To a high-precision ^1H NMR tube, 0.044 g (0.500 mmol) of neopentyl alcohol, 0.051 mL (0.053 g; 0.490 mmol) of benzyl alcohol, 0.300 g (1.143 mmol) of triphenylphosphine, 0.054 mL (0.77 g; 0.914 mmol) of cyclohexane, deuterated chloroform, and tetramethylsilane were added. After an initial scan, with no carbon tetrachloride, 0.200 mL (0.292 g; 1.898 mmol) of carbon tetrachloride was added and the reaction was observed for a period of 24 h. The areas of the $\mathbf{CH_2}$ peaks were observed both for the disappearance of the alcohol and the formation of halide and/or intermediate. Three duplicate runs were examined.

Typical Gas-Liquid Phase Chromatographic Procedure for Following the Disappearance of Alcohol and Formation of Halide. All GLC data were determined with a Perkin-Elmer 990 gas chromatograph. Two columns were used for both the molar response data and the competitive kinetics: a $\frac{1}{8}$ in. × 12 ft column packed with 20% FFAP on Chromosorb W and a $\frac{1}{8}$ in. × 20 ft silicone column. The reaction was first examined using an excess of chlorinating agent and a minimum of alcohol then the reaction was followed using an excess of alcohol and a minimum of chlorinating agent. The triphenylphosphine used was recrystallized from cyclohexane. Just prior to use, the chloroform was shaken with alumina to remove traces of ethanol stabilizer. All of the reactants used, except isoamyl alcohol (3-methyl-1-butanol), were found to be greater than 99% pure as determined by GLC. Isoamyl alcohol was purified by preparatory GLC, using a 0.5 in. × 20 ft FFAP column in a preparative Varian 1800 Aerograph gas chromatograph. The internal standards, *o*-chlorotoluene, ethylbenzene, and *p*-dichlorobenzene, were also found to be greater than 99% pure. The carbon tetrachloride was distilled from triphenylphosphine. A vacuum apparatus was used for trapping the volatile reactants (and thus quenching the reaction). The apparatus was made by Lab Glass, Inc. and consisted of three U-tube traps connected to each other in series with a ball and socket connection and protected at each end with glass stopcock valves. This evacuation apparatus was connected at one end to a rotary evaporator and at the other end to a vacuum pump. Three Dewars of liquid nitrogen were used to cool the traps. Prior to following the competitive kinetics of the alcohols, the following molar responses were obtained: (i) 1-pentanol, 2-pentanol, 3-methyl-1-butanol vs. *o*-chlorotoluene in chloroform–carbon tetrachloride, (ii) 1-chloropentane, 2-chloropentane, 3-methyl-1-chlorobutane, and *o*-chlorotoluene in chloroform–carbon tetrachloride vs. *p*-dichlorobenzene and/or vs. ethylbenzene.

In examining the relative competitive kinetics of this reaction two pairs of alcohols were used: (1) 1-pentanol vs. 2-pentanol; and (2) 1-pentanol vs. 3-methyl-1-butanol. Each of the two pairs of alcohols were reacted under conditions of excess chlorinating agent and under conditions of excess alcohol. Each reaction was run in duplicate.

The following description of a reaction using the first pair of alcohols illustrates a typical kinetic run. Just prior to use, all glassware was cleaned first with a detergent–water solution, rinsed with distilled water then acetone, dried in a 110 °C oven for an hour, and cooled by a stream of dry nitrogen. Into a 10.00-mL volumetric flask was placed 0.24 mL (0.194 g; 2.2 mmole) of 1-pentanol, 0.23 mL (0.194 g; 2.2 mmol) of 2-pentanol, 0.18 mL (0.193 g; 1.5 mmol) of *o*-chlorotoluene, and 2.31 g (8.8 mmol) of triphenylphosphine. The reaction was timed after dilution to 10.00 mL with a 60:40 (v/v) chloroform–carbon tetrachloride mixture. A 1-mL aliquot was withdrawn from the reaction solution immediately after the addition of the chloroform–carbon tetrachloride mixture. The volumetric flask with the remaining reaction mixture was placed in a 25 °C water bath where it remained

for the duration of the examination. The 1.00-mL aliquot was transferred to a 50-mL round-bottomed flask which in turn was connected to a rotary evaporator. A 30–32 °C water bath was raised into place underneath the round-bottomed flask and the spin rate of the rotary evaporator was turned to its highest speed. The vacuum apparatus had previously been evacuated and the Dewars of liquid nitrogen were raised into place to cool the traps. The valve connecting the evaporator to the vacuum apparatus was opened slowly, care being taken to trap as much of the vapors as possible in the first trap. After this was accomplished, the needle valve on the manifold was closed slowly and the system, which was now under a vacuum of 0.1 mm, was evacuated for 0.5 h. At that time, the valves to the vacuum pump and the rotary evaporator were closed. Then the set of valves to each U-tube were closed and the Dewars were lowered to allow the U-tubes' contents to thaw. To two 1.00-mL calibrated volumetric flasks approximately 1 mmol of *p*-dichlorobenzene was added. Using chloroform as a wash, the liquid from the three U-tube traps was placed in one of the flasks while the syruplike material which remained in the 50-mL round-bottomed flask was dissolved in chloroform and placed in the remaining volumetric flask. These flasks were filled to the mark with chloroform. Then the material from each flask was transferred to a labeled 5-mL Erlenmeyer flask, corked, covered with Nalge plastic, and placed in the refrigerator until ready for GLC analysis. At that time they were placed on ice until the GLC analysis was completed.

The areas of the peaks obtained by GLC were determined first by the standard peak height times peak width at half-height and in the last stages of this research by direct area reading via a voltage to frequency converter (Model 2210 by Dymec) and an electronic counter (Model 2725 by Simpson).

Competitive Kinetics. ^{1}H NMR competitive kinetics between neopentyl alcohol and benzyl alcohol were run at 25 °C using cyclohexane as an internal standard. The area of the cyclohexane standard was divided by 12 to obtain a standard area for hydrogen. The $\mathbf{CH_2OH}$ and $\mathbf{CH_2Cl}$ areas of the benzyl alcohols, benzyl chloride, neopentyl alcohol, and neopentyl intermediate were normalized to the standard, and the relative reactivity of the alcohols was determined from the disappearance of the alcohol (assuming the alcohol molecularity was first order) using the expression

$$k_A/k_B = \log [[A_i]/[A_f]] \log [[B_i]/[B_f]]$$

where k_A/k_B is the relative rate constant for reaction with alcohol A and alcohol B while $[A_i]/[A_f]$ and $[B_i]/[B_f]$ are the ratios of the initial to final alcohol concentrations for alcohols A and B, respectively.[16] For GLC kinetics, the amounts of alcohol and alkyl halides were determined from molar response data with given standards. The same kinetic expression was used to determine relative rates of disappearance of alcohols.[16]

Preparation of 1,1-Dideuterio-2,2-dimethylpropanol (10). To a three-necked 500-mL flask equipped with dropping funnel, condenser, and thermometer was added 5.403 g (0.128 mole) of lithium aluminum deuteride (99% Stohler Isotope) in 250 mL of anhydrous ether. To this solution was added 14.0 g (0.12 mol) of methyl trimethylacetate (methyl pivalate 99% by GLC; Aldrich Chemical) in 125 mL of ether in a dropwise manner for 45 min at 0 °C and 30 min at room temperature. When the supernatant liquid showed no carboxyl stretch (1710 cm^{-1}) in the infrared, the reaction was quenched with wet sodium sulfate followed by 6 M sulfuric acid. The ether layers were combined, washed with saturated sodium chloride, and dried over anhydrous potassium carbonate. The ether was carefully distilled in a Todd column and the product was distilled from a microdistillation flask. A forerun (3 g) containing some ethyl ether was not used but the main fraction (6.0 g; 0.68 mol, 57%) had bp 106 °C (725 Torr) and mp 49–50 °C. Theory would predict 16.66 atom % excess D; 16.25 atom % excess D was found (Josef Nemeth Labs, Urbana, Il.). This corresponds to 1.95 D/molecule.

Preparation of Kinetic Samples. A 3.300-g sample of triphenylphosphine (12.6 mmol) and 0.660 g of neopentyl alcohol (7.5 mmol) were placed in a 50-mL flask. To this flask was added 2.20 mL of tetrachloromethane (22.8 mmol) and 5.00 mL of chloroform-*d* as solvent. This solution was allowed to stand about 5 h and was monitored for intermediate formation by ^{1}H NMR spectroscopy. After the intermediate had formed, the solution was transferred into ^{1}H NMR tubes and sealed. This same procedure was followed for the 1,1-dideuterio-2,2-dimethylpropanol except that 0.665 g (7.5 mmol) of the latter alcohol was used. The sealed NMR tubes were placed in a thermostated bath and removed from time to time and quenched by immersing the tubes in an isopropyl alcohol ice bath at −12 °C. The quenched samples were placed in a freezer and the ^{1}H NMR's were all run at the same time.

Kinetics. The fraction reacted (Φ) was determined as the height of the *tert*-butyl portion of the neopentyl chloride isomer (δ 0.967) divided by the height of the *tert*-butyl portion of the intermediate (δ 1.033) plus the height of the *tert*-butyl portion of the neopentyl chloride. Using the standard first-order equation $kt = \ln (1/(1 - \Phi))$ we obtained good plots of $\ln (1/(1 - \Phi))$ vs. t. All rates were obtained using least squares and correlation coefficients of 0.997 to 0.999 were obtained for all rates.

Acknowledgment is made to Mrs. Susan Campbell for her aid in the drawings and preparation of the manuscript. One of us (B.F.) acknowledges the assistance of Dr. Frank C. Spencer of New York University School of Medicine without whose aid this manuscript could never have been written.

Registry No.—6, 66085-08-3; **10,** 7210-87-9; neopentyl alcohol, 75-84-3; triphenylphosphine, 603-35-0; carbon tetrachloride, 56-23-5; methyl trimethylacetate, 598-98-1; 1-pentanol, 71-41-0; isoamyl alcohol, 123-51-3; 1-chloropentane, 543-59-9; isoamyl chloride, 107-84-6; 2-pentanol, 6032-29-7; 2-chloropentane, 625-29-6; $(CH_3)_3CCD_2OPCl(C_6H_5)_3$, 66085-09-4.

Supplementary Material Available: Listing of a least-squares plot for E_{act} and two tables on relative rates with excess and minimum of chlorinating agent (3 pages). Ordering information is given on any current masthead page.

References and Notes

(1) J. B. Lee, *J. Am. Chem. Soc.*, **88,** 3440 (1966).
(2) I. M. Downie, J. B. Holmes and J. B. Lee, *Chem. Ind. (London)*, 900 (1966).
(3) J. Hooz and S. S. H. Gilani, *Can. J. Chem.*, **46,** 86 (1968).
(4) (a) R. G. Weiss and E. I. Snyder, *Chem. Commun.*, 1358 (1968); (b) *J. Org. Chem.*, **35,** 1627 (1970); (c) *ibid.*, **36,** 403 (1971)
(5) R. Appel, *Angew. Chem., Int. Ed. Engl.*, **14,** 801 (1975).
(6) We realize that this first-order reaction cannot be a true S_N2 reaction. However, this term is used so that the S_N2 type transition state structure of this reaction can be emphatically understood.
(7) R. Aneja, A. P. Davies, and J. A. Knaggs, *Tetrahedron Lett.*, 67 (1974).
(8) J. T. Lamb and G. H. Whitman, *Chem. Commun.*, 400 (1966).
(9) J. W. Emsley, J. Feeney, and L. G. Sutcliff, "High Resolution Nuclear Magnetic Resonance Spectroscopy", Vol. 2, Pergamon Press, New York, N.Y., 1965, p 1063.
(10) A Streitwieser, Jr., *Chem. Rev.*, **56,** 571 (1956).
(11) (a) M. Wolfsberg and M. J. Stern, *Pure Appl. Chem.*, **8,** 325 (1964); (b) T. T.-S. Huang, W. J. Kass, W. E. Budderbaum, and P. E. Yankwich, *J. Phys. Chem.*, **72,** 4431 (1968); (c) R. P. Bell, *Chem. Soc. Rev.*, **3,** 513 (1974).
(12) B. Stephenson, G. Solladié, and Harry S. Mosher, *J. Am. Chem. Soc.*, **94,** 4184 (1972).
(13) R. Aneja, A. P. Davies, and J. A. Knaggs, *Chem. Commun.*, 110 (1973).
(14) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, N.Y., 1953, pp 408 and 409.
(15) T. Williams, R. G. Pitcher, P. Bonner, J. Gutzwiller, and M. Uskoković, *J. Am. Chem. Soc.*, **91,** 1871 (1969); H. Wynberg and B. Feringa, *Tetrahedron*, **32,** 2831 (1976).
(16) W. A. Thaler and B. Franzus, *J. Org. Chem.*, **29,** 2226 (1964).