Mechanism of the Triphenylphosphine-Tetrachloromethane-Alcohol Reaction: Pericyclic or Clustered Ion Pairs?

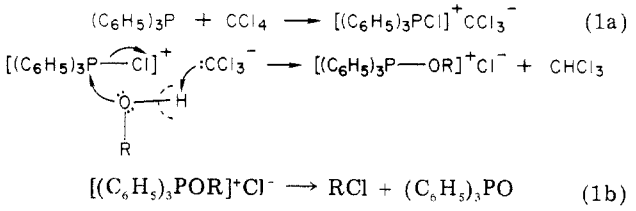
J. D. Slagle, T. T.-S. Huang, and B. Franzus*

Department of Chemistry, East Tennessee State University, Johnson City, Tennessee 37614

Received February 4, 1981

The intermediate formed from tetrachloromethane–triphenylphosphine and neopentyl alcohol decomposes bimolecularly in acetonitrile and not unimolecularly as in $CDCl_3$. This kinetic order is not consistent with a pericyclic pathway but is consistent with an ion-pair mechanism. Consistent with the ion-pair mechanism in acetonitrile is the incorporation of external nucleophiles in the neopentyl skeleton by addition of added nucleophiles to the system. Consistent with the enhanced polarity of acetonitrile is the increased amount of carbon–oxygen cleavage resulting in extensive racemization of the reaction product from (*R*)-(+)-2-octanol. The preparation of neopentyl thiocyanate and neopentyl isothiocyanate from the corresponding alcohol illustrates the synthetic utility of this reaction in more polar solvents.

The formation of primary and secondary alkyl bromides and chlorides from the corresponding alcohols, a trialkyl- or triarylphosphine, and a tetrahalomethane (or hexachloroacetone) proceeds with both high conversions and yields.[1] The halogenation reaction sequence has been elegantly summarized by Appel in a review article;[2] the reaction proceeds in two steps, intermediate formation (eq 1a) and intermediate decomposition (eq 1b) as shown with



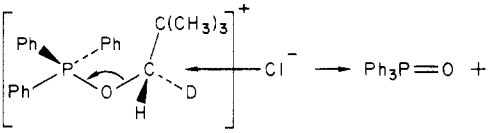
$$(C_6H_5)_3P + CCl_4 \longrightarrow [(C_6H_5)_3PCl]^+CCl_3^- \quad (1a)$$

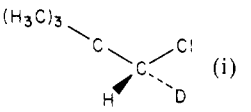
$$[(C_6H_5)_3P{-}Cl]^+ \; :CCl_3^- \longrightarrow [(C_6H_5)_3P{-}OR]^+Cl^- + CHCl_3$$

$$[(C_6H_5)_3POR]^+Cl^- \longrightarrow RCl + (C_6H_5)_3PO \quad (1b)$$

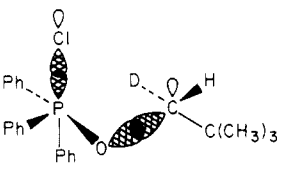
triphenylphosphine and tetrachloromethane as the chlorinating agent. Intermediate decomposition occurs with extensive inversion of configuration,[3a] rendering this synthetic technique as one of the better methods for obtention of alkyl chlorides with known stereochemical integrity.[3] It has been shown that the decomposition proceeds unimolecularly, exhibits a kinetic isotope effect (k_H/k_D) of 1.05 per hydrogen[4] for the decomposition reaction (eq 1b), and, as previously noted, occurs with predominant inversion of configuration.[3] Indeed, the possible mechanisms of intermediate decomposition (eq 1b) were narrowed to two alternative mechanisms: (i) first-order decomposition of a cluster of intimate ion pairs in two and/or three dimensions stabilized by virtue of a positively charged phosphorus in one ion pair adjacent to a negative chloride from another ion pair and (ii) to $\sigma 2_s + \sigma 2_a$ thermal pericyclic reaction[4,5] wherein the P–Cl is broken suprafacially (dark lobes suprafacial) and the C–Cl bond made antarafacially (dark lobe of Cl and rear light lobe of carbon).

From examination of molecular models which show that the neopentyl system is only slightly hindered by front-side attack but is, however, highly hindered by back-side attack, it is difficult to rationalize the high energy of activation (27.1 kcal/mol)[4] for the displacement in the neopentyl





(i)



(ii)

system for a pericyclic reaction mechanism which is relatively insensitive to steric effects. On the other hand, all of the kinetic, energetic, stereochemical, and isotopic data are completely consistent with the clustered ion-pair mechanism except for one fact; in dimethyl sulfoxide, 2-phenylethanol with triphenylphosphine, carbon tetrachloride, and added sodium cyanide gave only 2-phenylethyl chloride without concomitant formation of 2-phenylethyl cyanide. This indicates no competition from an external nucleophile and casts doubt on the ion-pair concept.[3c]

Results and Discussion

Initially, we attempted to obtain sufficient intermediate from some hindered alcohols to enable us to follow the decomposition of these intermediates. We were, however, surprised to find that under our experimental conditions we were unable to detect (by NMR spectroscopy) any intermediate with 2-propanol. All we observed were 2-propanol and 2-chloropropane. We were able to observe an intermediate from isobutyl alcohol; however, the intermediate decomposition was sufficiently rapid that determination of the kinetics by NMR spectroscopy was not feasible. We therefore decided to reexamine the neopentyl system where it was known that intermediate decomposition was slower than intermediate formation. We reexamined this system with a more polar solvent, acetonitrile, since it has been reported that halogenation occurs very rapidly in this particular solvent.[6] The rationale for examination of the solvent effect resides in the fact that, in general, pericyclic reactions are relatively insensitive to large variations in solvent polarity;[7] alternatively, both

(1) (a) Downie, I. M.; Holmes, J. B.; Lee, J. B. *Chem. Ind. (London)* **1966** 900. (b) Hooz, J.; Gilani, S. S. H. *Can. J. Chem.* **1968**, *46*, 86. (c) Magid, R. M.; Fruchey, O. S.; Johnson, W. L.; Allen, T. G. *J. Org. Chem.* **1979**, *44*, 359.

(2) Appel, R. *Angew. Chem., Int. Ed. Engl.* **1976**, *14*, 801.

(3) (a) Weiss, R. G.; Snyder, E. I. *J. Org. Chem.* **1971**, *36*, 403. (b) Weiss, R. G.; Snyder, E. I. *Chem. Commun.* **1968**, 1358. (c) Weiss, R. G.; Snyder, E. I. *J. Org. Chem.* **1970**, *35*, 1627.

(4) Jones, L. A.; Sumner, C. E., Jr.; Franzus, B.; Huang, T. T.-S.; Snyder, E. I. *J. Org. Chem.* **1978**, *43*, 2821.

(5) Aneja, R.; Davies, A. P.; Knaggs, J. A. *Tetrahedron Lett.* **1974**, 67.

(6) Cristol, S. J.; Strom, R. M.; Stull, D. P. *J. Org. Chem.* **1978**, *43*, 1150.

0022-3263/81/1946-3526$01.25/0

bimolecular and unimolecular substitutions do show significant solvent effects with increased solvent polarity.[8] As in our previous study,[4] we first had to ascertain the lifetime of intermediate 1 in acetonitrile. Much to our

$$\mathrm{ROH} + (\mathrm{C_6H_5})_3\mathrm{P} + \mathrm{CCl_4} \xrightarrow[k_1]{\mathrm{CH_3CN}} \underset{\mathbf{1}}{[(\mathrm{CH_3})_3\mathrm{CCH_2OP}(\mathrm{C_6H_5})_3]^+\mathrm{Cl}^-} + \mathrm{CHCl_3} \quad (2)$$

$$\mathrm{R} \equiv (\mathrm{CH_3})_3\mathrm{CCH_2}$$

$$\underset{\mathbf{1}}{[(\mathrm{CH_3})_3\mathrm{CCH_2OP}(\mathrm{C_6H_5})_3]^+\mathrm{Cl}^-} \xrightarrow[k_2]{\mathrm{CH_3CN}} \underset{\mathbf{2}}{(\mathrm{CH_3})_3\mathrm{CCH_2Cl}} + (\mathrm{C_6H_5})_3\mathrm{PO} \quad (3)$$

suprise we found that it was the first step in the halogenation sequence rather than the second that proceeded so rapidly. Compound 1 formed in about 250 s in sharp contrast to formation of 1 in CCl_4 which occurred in 4.5 h (16 200 s). This large relative rate of intermediate formation of 60/1 *may* account in part for some reported enhanced rates in acetonitrile.[6] Again, as in our previous study, we were fortunate that $k_1 \gg k_2$ and we could therefore study the rate of intermediate decomposition to product. We were able to monitor the reaction in CD_3CN by NMR spectroscopy by following the relative heights of the singlet *tert*-butyl group in intermediate 1 and the singlet *tert*-butyl group of neopentyl chloride (2). Al-

$[(CH_3)_3CCH_2OP(C_6H_5)_3]^+Cl^-$	$(CH_3)_3CCH_2Cl$
δ 1.02 (s) δ 4.00 (d)	δ 1.00 (s) δ 3.33 (s)
1	**2**

though the singlet *tert*-butyl chemical shift differences between 1 and 2 were not large, we chose to follow the reaction by *tert*-butyl peak height analysis of 1 and 2 rather than by NMR integration of the CH_2 groups of the product (singlet) and the CH_2 of the intermediate (doublet due to ^{31}P coupling) because of the inherent inaccuracy of NMR integration. The chemical shift differences (between the reactant and product *tert*-butyl groups) of 0.02 ppm (1.2 Hz) was sufficient to allow us to monitor the reaction to about 65% conversion since resolution on the C-60H NMR spectrometer was better than 0.4 Hz.

In our initial runs we assumed (incorrectly) that the decomposition of intermediate 1 would follow first-order kinetics as had previously been observed.[4] We could not have been further from the truth; there was absolutely no possibility that the intermediate decomposed to product unimolecularly as it did in both CCl_4 and $CDCl_3$.[4] Since the product, neopentyl chloride (2), could only arise from intermediate 1, we could assume that the rate of formation of 2 was dependent only on the concentration of 1 to the nth power. That is

$$\text{rate} = \text{rate of formation of } \mathbf{2} = k[\mathbf{1}]^n$$

$$\log \text{rate} = \log k + n \log [\mathbf{1}]$$

Thus when log rates vs. log [1] was plotted, the order of the reaction,[9] n, was 2.32 ± 0.23 (correlation coefficient 0.96). This value of n was sufficiently close to 2 to encourage us to plot the results as a second-order reaction. Although we could not follow the reaction to more than 65% conversion due to the inherent difficulty of separating the *tert*-butyl peaks of the intermediate and neopentyl chloride, there was no doubt that our k_2 (obsd) = (1.57 ± 0.10) × 10^{-4} L mol^{-1} s^{-1} (correlation coefficient 0.99) was indeed that for a second-order reaction.

It was clear to us that we could now rule out a pericyclic pathway for intermediate decomposition and opt in favor of an ion-pair mechanism. In tetrachloromethane the mechanistic pathway would be via three-dimensional clustered ion pairs. In the cluster there would be *one* chloride anion associated with *one* alkoxytriphenylphosphonium cation which would collapse unimolecularly with back-side attack to form the alkyl chloride.[10] In acetonitrile it would appear as if the route to product involved collision between two ion pairs. As a consequence of the latter mechanistic pathway it can be predicted that in acetonitrile, addition of other nucleophiles should be in competition with chloride ion for the neopentyl group. We added ammonium thiocyanate to neopentyl alcohol, carbon tetrachloride, and triphenylphosphine all in CD_3CN. After the intermediate formed, we heated the reaction mixture to 50 °C for 9 h. We were again able to monitor intermediate and product formation by NMR spectroscopy. The compounds predicted from our proposed mechanism with added nucleophiles are shown in eq 5.

$$\mathrm{ROH} + (\mathrm{C_6H_5})_3\mathrm{P} + \mathrm{CCl_4} \xrightarrow{\mathrm{CD_3CN}} \underset{\mathbf{1}}{[(\mathrm{CH_3})_3\mathrm{CCH_2OP}(\mathrm{C_6H_5})_3]^+\ \mathrm{Cl}^-} + \mathrm{CHCl_3} \quad (4)$$

$$\mathrm{R} \equiv (\mathrm{CH_3})_3\mathrm{CCH_2}$$

$$\mathbf{1} + \mathrm{NH_4SCN} \xrightarrow{\mathrm{CD_3CN}} \underset{\mathbf{2}}{(\mathrm{CH_3})_3\mathrm{CCH_2Cl}} + \underset{\mathbf{3}}{(\mathrm{CH_3})_3\mathrm{CCH_2SC{\equiv}N}} + \underset{\mathbf{4}}{(\mathrm{CH_3})_3\mathrm{CCH_2N{=}C{=}S}} \quad (5)$$

As will be noted in this paper, a 90/10 mixture of neopentyl thiocyanate and neopentyl isothiocyanate was synthesized. From infrared assignments of known alkyl thiocyanates and isothiocyanates[11] we were able to ascertain which of the NMR absorptions could be attributed to the thiocyanate and which could be assigned to the isothiocyanate. The SC≡N group has a strong and sharp absorption at 2137–2566 cm^{-1} (2150 cm^{-1} observed) whereas the N=C=S group has a strong but somewhat broader absorption at 2080–2100 cm^{-1} (2080 cm^{-1} observed). Since the 2150 cm^{-1} absorption was so much stronger than the 2080 cm^{-1} absorption, we were then able to designate the neopentyl thiocyanate as the dominant isomer. Thus, by measuring the relative heights of the new NMR peaks, we were able to assign both $(CH_3)_3C$ and CH_2 chemical shifts to both neopentyl thiocyanate and neopentyl isothiocyanate. As will be noted in Figure 1, compounds 1–4 can all clearly be identified by the chemical shifts of the $(CH_3)_3C$ and CH_2 groups. That this formation of 3 and

$(CH_3)_3CCH_2Cl$	$(CH_3)_3CCH_2SC{\equiv}N$	$(CH_3)_3CCH_2N{=}C{=}S$
δ 1.00 δ 3.33	δ 1.07 δ 2.93	δ 1.03 δ 3.17
2	**3**	**4**

(7) Marchand, A. P.; Lehr, R. E. In "Pericyclic Reactions"; Marchand, A. P., Lehr, R. E., Eds.; Academic Press: New York, 1977; Vol. I, pp 34–37.
(8) Ingold, C. K. "Structure and Mechanism in Organic Chemistry"; Cornell University Press: Ithaca, NY, 1953.
(9) Laidler, K. J. "Chemical Kinetics", 2nd ed.; McGraw-Hill: New York, 1965; p 15.
(10) Note added in proof: In a recent prepublication manuscript by Ramos and Rosen, it was noted that monoalkoxytriphenylphosphonium triflates substituted slowly or not at all with negative nucleophiles; however, several bis(alkoxytriphenylphosphonium triflates) when sterically constrained as close neighbors reacted rapidly with negative nucleophiles at room temperature. All of their observations were not only consistent but also were rationalized in terms of the ion-pair cluster mechanism. We thank Professor Rosen for presenting us with a copy of his manuscript prior to publication.
(11) Bellamy, L. J. "Advances in Infrared Group Frequencies"; Methuen and Co. Ltd: New York, 1968, p 58.

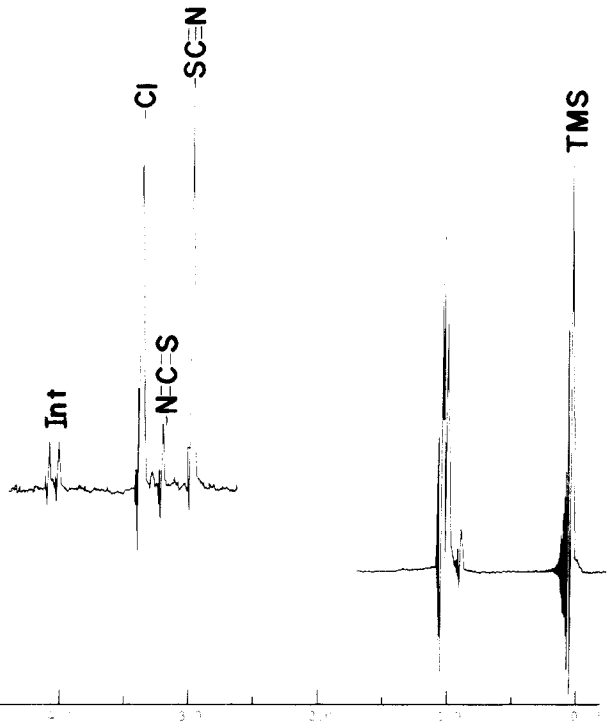


Figure 1. NMR spectra of products from the reaction: $(CH_3)_3CCH_2OH + CCl_4 + (C_6H_5)_3P + NH_4SCN$ (as an external nucleophile). The $(CH_3)_3C$ groups all appear upfield at $\delta \sim 1.0$. The CH_2 protons range from $\delta \sim 3$ to ~ 4. The spectrometer gain was increased for the downfield protons so that they would be observable in this figure.

4 was due to anion interchange of the ion pairs and not due to reaction of neopentyl chloride with ammonium thiocyanate follows from our observation that neopentyl chloride gave absolutely *no* product with ammonium thiocyanate even after heating at 80 °C for 9 h.

The previous objection to the clustered ion-pair concept arose from the observation that 2-phenylethanol, tetrachloromethane, and triphenylphosphine in dimethyl sulfoxide with cyanide as the added nucleophile did not incorporate cyanide in the final product.[3c] This result is in sharp contrast to the observed reaction of sugars in dimethyl sulfoxide with added sodium cyanide, wherein there is apparent intervention with added cyanide to form nitriles.[12] Although we are unable to reconcile the differences between the previous investigations, there can be no doubt from our own data in acetonitrile that incorporation of the external thiocyanate in the final product does and has occurred, fully supporting the ion-pair mechanistic concept.

Increased polarity of acetonitrile over both tetrachloromethane and chloroform was effective in disturbing the three-dimensional lattice such that the kinetic order changed from unimolecular to bimolecular; this also allowed for sufficient separation of ion pairs to, in effect, promote anion interchange. The observed solvent effect caused us to reflect on the possibility that increased solvent polarity might affect intermediate decomposition such that carbon–oxygen cleavage might be considerably enhanced over carbon–chloride bond formation. We tested this possibility by allowing (*R*)-(+)-2-octanol to react with triphenylphosphine and tetrachloromethane in acetonitrile and found that the 2-chlorooctane obtained was 78% *racemic*. Indeed, in the more polar solvent acetonitrile, carbon–oxygen cleavage was sufficiently extensive that a caveat against using acetonitrile (rather than CCl_4 or $CHCl_3$) for reactions requiring high stereospecificity must be noted. On the other hand, if stereospecificity is not of prime importance, the technique of using an alcohol, triphenylphosphine, and tetrachloromethane in acetonitrile with an added nucleophile is an excellent procedure for going from the alcohol to the final product without stopping at the intermediate halide (eq 6), where M^+ is

$$ROH + (C_6H_5)_3P + CCl_4 + M^+Nu^- \xrightarrow{CH_3CN} (C_6H_5)_3PO + CHCl_3 + M^+Cl^- + RCl + RNu \quad (6)$$

some metal and Nu^- is the added nucleophile. In our hands we were able to prepare a 90/10 mixture of neopentyl thiocyanate/neopentyl isothiocyanate in 22% yield using ammonium thiocyanate as the added nucleophile. This 90/10 ratio is higher than that obtained with alkoxyisothiocyanatophosphoranes[13] (60/40) but lower than had been obtained with $(C_6H_5)_3P(SCN)_2$[14] (100%). Although there is essentially 100% conversion of neopentyl alcohol (as determined by NMR spectroscopy) to the corresponding chloride, thiocyanate, and isothiocyanate, the conversion to the thiocyanate–isothiocyanate mixture was about 50%. Thus recovery of the "desired product" was only half of that theoretically possible, presumably due to losses in our workup procedure.

Intuitively, chemists realize that before a substance crystallizes from a saturated solution the substance in question, whether organic or inorganic, must be agglomerated in some large three-dimensional "liquid" lattice such that on subsequent precipitation, the gain in lattice energy is greater than the energy originally gained from the heat of solution. We now have a procedure in a particular reaction system for operationally determining whether we have separate ion pairs or a three-dimensional lattice; interestingly, this procedure is based purely on a kinetic reaction order.

Experimental Section

^1H NMR spectra were determined with a JEOL C60H NMR spectrometer. Infrared spectra were run on a Perkin-Elmer Model 521 spectrometer; purity determinations of volatile compounds such as solvents, starting alcohols, and carbon tetrachloride in addition to neopentyl chloride and neopentyl thiocyanate were done on a Perkin-Elmer 990 gas chromatograph with an attached Hewlett-Packard Model 3380A integrator using a $^1/_8$ in. × 12 ft column packed with 20% FFAP on Chromosorb W. Mass spectral analyses were obtained with the use of a JEOL JMS D100 mass spectrometer. All elemental analyses were performed by Galbraith Laboratories.

Typical Sample Preparation for a Kinetic Run. To a 10.00-mL volumetric flask was added 3.3824 g (12.9 mmol) of triphenylphosphine and 2.20 ± 0.05 mL (3.5 g, 22.7 mmol) of carbon tetrachloride (>99% by GLC). Then 1.5–2.0 mL of CD_3CN (Norell Chemical Co., Inc.) was added to the volumetric flask. The mixture was cooled to about 0–4 °C and to this cold mixture was added 0.701 g (7.97 mmol) of neopentyl alcohol (mp 55–56 °C; >99% pure by GLC) in a small amount of CD_3CN. To this cold mixture was added a small amount of tetramethylsilane and enough CD_3CN to make almost 10.00 mL of solution. The mixture was allowed to warm until an exothermic reaction occurred to give the intermediate. Before this exothermic reaction the triphenylphosphine was not in solution; however, after the reaction a true solution was formed, cooled, and brought to the 10.00 mL mark with CD_3CN. Portions of this cold mixture (~0.5–0.7 mL) were pipetted into an NMR tube; the NMR tube was purged with dry nitrogen and then sealed. Two NMR tubes were kept at −10°

(12) Brett, D.; Downie, I. M.; Lee, J. B. *J. Org. Chem.* **1967**, *32*, 855.

(13) Burski, J.; Kieszkowski, J.; Pakulski, T.; Skowronska, A. *Chem. Commun.* **1978**, 940.

(14) Tamura, Y.; Kawasaki, T.; Adachi, M.; Kita, Y. *Tetrahedron Lett.* **1977**, 4417.

C as initial controls (t_0), and the remaining tubes were placed in a thermostated bath controlled at 55.00 ± 0.02° C by using a Fisher proportional temperature controller to maintain these isothermal conditions. NMR tubes were removed from the bath from time to time, cooled, and analyzed for reactant and product by NMR spectroscopy.

Kinetic Analysis. The fraction reacted (Φ) was determined from the height of the *tert*-butyl portion of the neopentyl chloride (δ 1.00) divided by the height of the *tert*-butyl portion of the intermediate (δ 1.02) plus the height of the *tert*-butyl portion of the neopentyl chloride. Because of the close proximity of the chemical shifts of the *tert*-butyl portions of the intermediate and the chloride, an expansion of 0.5× was used. In those cases where one could compare, the 0.5× expansion and the original observation gave identical results. Since Φ is known at any time t, a plot of the concentration of intermediate vs. time was made, and tangents to this curve at various times t were drawn. Each tangent line drawn at time t is the rate of the reaction at that time. Since the rate and the concentration of intermediate are known at time t, the slope of the line for a plot of log rate vs. log (concentration) would yield the order of the reaction (see eq 7 and 8). A value

$$\text{rate} = k[\text{int}]^n \quad (7)$$

$$\log \text{rate} = \log k + n \log [\text{int}] \quad (8)$$

of $n = 2.30 \pm 0.23$ (correlation coefficient 0.96) was obtained. The order was sufficiently close to 2 to plot the results as purely bimolecular. A standard second-order expression, $\Phi/a(1 - \Phi) = k_2t$, can be obtained, where a is the initial concentration of intermediate. A plot of $\Phi/(1 - \Phi)$ vs. t gave a good straight line (correlation coefficient 0.99). The rate constant obtained was 1.57 ● 0.10×10^{-4} L mol^{-1} s^{-1} at 55 °C.

Relative Rates of Intermediate Formation. To an NMR tube were added 0.266 g (1.05 mmol) of triphenylphosphine, 0.058 g (0.66 mmol) of neopentyl alcohol, and 0.4 mL of CD_3CN. To this mixture was added 0.2 mL (0.318 g, 2.07 mmol) of carbon tetrachloride. An electronic timer was then started. The NMR tube was shaken to effect solution, placed in the NMR spectrometer at ambient temperature, and scanned at δ 1.0–1.5 and at δ 3.0–4.5. The first observation was at 180 s, and a small amount of unreacted alcohol was still present. The second scan was at 250 s, and only intermediate with no trace of alcohol was present in solution. The rate of intermediate formation in $CDCl_3$ which is assumed to proceed at least as rapidly as in CCl_4 was ascertained in the following manner. To 3.300 g (12.5 mmol) of triphenylphosphine and 0.660 g (7.5 mmol) of neopentyl alcohol in 5.5 mL of $CDCl_3$ was added 2.20 mL (3.5 g, 22.7 mmol) of carbon tetrachloride. All substances were in solution, and no heat evolution was noted. The solution was allowed to stand at ambient temperature and was analyzed periodically by NMR spectroscopy to determine the extent of alcohol to intermediate formation. After 4.5 h (16 200 s) all the alcohol had reacted. Thus the relative rate of intermediate formation in $CDCl_3$ (16 200 s) to that in CD_3CN (250 s) was at least 60/1.

Typical Run for Capture of Thiocyanate Ion. To a flask were added 0.7649 g (10.05 mmol) of ammonium thiocyanate, 0.6154 g (6.99 mmol) of neopentyl alcohol, and 4.5 mL of CD_3CN to effect solution. To this solution was added 3.2620 g (12.4 mmol) of triphenylphosphine which did not dissolve. Addition of 2.20 mL (3.5 g, 22.7 mmol) of carbon tetrachloride resulted in solution accompanied by heat evolution. After being heated for 9 h at 50 °C, the solution was examined by NMR spectroscopy, and as denoted by the $CH_2O^{31}P$ doublet, about 90% of the intermediate had decomposed to product. As is customary in bimolecular reactions, some unreacted starting material was anticipated. The major products appeared to be neopentyl thiocyanate and neopentyl chloride in about a 55/45 ratio. This ratio was adduced from the relative heights of the $CH_2SC{\equiv}N$ and CH_2Cl singlet peak heights.

Control Run: Neopentyl Chloride plus Ammonium Thiocyanate. To a 10-mL round-bottomed flasked were added 0.5559 g (7.31 mmol) of ammonium thiocyanate, 0.9569 g (3.44 mmol) of triphenylphosphine oxide, 2.7 mL of CD_3CN, 0.75 mL (1.19 g, 7.8 mmol) of carbon tetrachloride, and 0.43 mL (0.373 g, 3.49 mmol) of neopentyl chloride (>99.9% pure by GLC). This mixture "approximated" the composition of the thiocyanate capture run. About 0.5–0.6 mL of this mixture was added to an NMR tube along with a small amount of tetramethylsilane. The tube was sealed and placed in a thermostated bath at 80 ± 0.3 °C. The extent of the reaction could be determined by NMR spectroscopy by following the formation of neopentyl thiocyanate from neopentyl chloride. The extent of the reaction was ascertained at 3.5, 5.0, 6.5, and 9.0 h. No reaction was in evidence even after 9 h, indicating that neopentyl thiocyanate did not arise from neopentyl chloride as its precursor.

Reaction of (*R*)-(+)-2-Octanol with Tetrachloromethane–Triphenylphosphine in Acetonitrile. To a 250-mL round-bottomed flask were added 32.32 g (0.123 mol) of triphenylphosphine and 11.412 g (0.088 mol) of (*R*)-(+)-2-octanol ($[\alpha]^{20}_D$ +8.42°; 85% optically pure based on the $[\alpha]^{20}_D$ for pure (*R*)-(+)-2-octanol of +9.92°[15]). The 50 mL of acetonitrile (dried and distilled from P_2O_5) and 22 mL (35 g, 0.23 mol) of carbon tetrachloride were added to the flask. After the exothermic formation of intermediate was complete, the reaction mixture was refluxed for 3 h. After the mixture cooled, 150 mL of water and 80 mL of dichloromethane were added to the reaction mixture. The dichloromethane layer was separated and the aqueous layer extracted two more times with 70- and 60-mL portions of dichloromethane. The combined dichloromethane layers were washed three times with 100-mL portions of water. The organic layer was dried over anhydrous calcium chloride and concentrated by distillation of the dichloromethane at atmospheric pressure. When the pot temperature reached 136 °C and the head temperature reached 80 °C, all the volatiles were distilled under vacuum (20 torr) at 45–60 °C and collected in a single receiver cooled to liquid nitrogen temperatures. This distillate was redistilled, and a fraction with a boiling point of 52–54° C (8–12 torr) was collected. The product, 6.35 g (0.043 mol) of (*S*)-(–)-2-chlorooctane, was obtained in a 48.7% yield and had an $[\alpha]^{20}_D$ of –7.2°; on the assumption that pure (*S*)-(-)-2-chlorooctane has an $[\alpha]^{20}_D$ of –37.43°,[16] the absolute optical purity was 7.2°(100)/37.43°(0.85) = 22.6%. If, however, one assumes that pure (*S*)-(-)-2-chlorooctane has an $[\alpha]^{20}_D$ of –38.29°,[3b] then the absolute optical purity is 22.1% (7.2°(100)/38.29°(0.85)). In order to ascertain if chiral 2-chlorooctane would racemize under the reaction conditions,[17] we refluxed (*S*)-(-)-2-chlorooctane ($[\alpha]^{20}_D$ –31°; 83% optically pure based on an $[\alpha]^{20}_D$ for pure (*S*)-(-)-2-chlorooctane of –37.43°)[16] in dry acetonitrile in the presence of triphenylphosphine, triphenylphosphine oxide, and chloroform, thus approximating the experimental conditions for the preparation of (*S*)-2-chlorooctane in acetonitrile shown above. (*S*)-(-)-2-Chlorooctane was prepared from (*R*)-(+)-2-octanol ($[\alpha]^{20}_D$ 8.42°; 85% optically pure based on an $[\alpha]^{20}_D$ for pure (*R*)-(+)-2-octanol of 9.92°)[15] by using triphenylphosphine–tetrachloromethane as the chlorinating agent.[3] To a 10.00-mL volumetric flask was added 1.3 g (0.0088 mol) of (*S*)-(-)-2-chlorooctane, 0.9 g (0.0034 mol) of triphenylphosphine, 2.4 g (0.0086 mol) of triphenylphosphine oxide, and 2.2 mL of $CDCl_3$. This mixture was diluted exactly to 10.00 mL with CH_3CN (dried and distilled over P_2O_5). The observed optical rotation of the reaction mixture was 3.75 ± 0.1°. After the mixture was refluxed for 3 h under anhydrous conditions, the observed optical rotation of the mixture was 3.95 ± 0.2°. Thus no detectable racemization of the product occurred under the experimental conditions.

Preparation of Neopentyl Thiocyanate. To a 250-mL round-bottomed flask were added 32.81 g (0.125 mol) of triphenylphosphine, 7.31 g (0.083 mol) of neopentyl alcohol, and 8.37 g (0.110 mol) of ammonium thiocyanate. To this solid mixture were added 60 mL of acetonitrile (dried and distilled from P_2O_5) and 23 mL (36.6 g, 0.24 mol) of carbon tetrachloride. The reaction mixture was prepared for reflux with a drying tube (filled with indicating anhydrous calcium sulfate) atop the reflux condenser to maintain anhydrous conditions. The mixture was stirred (magnetic stirrer) for 5–8 min after which the reaction mixture

(15) Brauns, H. *Recl. Trav. Chim. Pays-Bas* **1946**, *65*, 803.
(16) Hoffman, H. *J. Chem. Soc.* **1964**, 1249.
(17) This manuscript was presented at the 181st National Meeting of the American Chemical Society, Atlanta, GA, Mar 29–Apr 3, 1981, at which time it was noted that there was a possibility that chiral 2-chlorooctane could racemize under the experimental conditions. We thank Dr. Magnuson for bringing this to our attention.

increased in temperature (formation of intermediate), started to reflux, turned a bright yellow, and finally became homogeneous. The mixture was gently refluxed for 10 h. An NMR spectrum of the solution indicated mainly neopentyl thiocyanate (plus some neopentyl isothiocyanate) and neopentyl chloride as the reaction products. A solid had formed during the reaction; the solid was filtered and washed with pentane, and the pentane was added to the filtrate. The solvent was removed at 25–38 °C under water aspirator vacuum by using a rotary evaporator. When the mixture was concentrated, much of the triphenylphosphine oxide formerly in solution was precipitated by the addition of pentane. The solid which was formed was filtered and then triturated with pentane; the pentane extracts were combined, dried, and further distilled to concentrate the organic layer. This whole procedure was repeated and the final concentrated liquid distilled under vacuum. The final product (2.3 g, 0.018 mol, 21.7% yield) had a boiling point of 62 °C at 12 torr. Its purity was >99% by GLC (105–190 °C, temperature programmed at 24 °C/min). Anal. Calcd for $C_6H_{11}NS$: C, 55.77; H, 8.58; N, 10.84; S, 24.81. Found: C, 55.52; H, 8.58; N, 10.79; S, 24.58. NMR analysis by relative peak heights indicated a 90/10 mixture of neopentyl thiocyanate ($(CH_3)_3C$, δ 1.07; $CH_2SC{\equiv}N$, δ 2.93) and neopentyl isothiocyanate ($(CH_3)_3C$, δ 1.03; $CH_2N{=}C{=}S$, δ 3.17). Infrared (neat) clearly indicated absorptions at 2960 (CH alkane), 2150 (sharp, $SC{\equiv}N$), and 2080 cm^{-1} (br, $N{=}C{=}S$, small peak). These results are still consistent with the 90/10 thiocyanate/isothiocyanate mixture. Mass spectral analysis showed a parent peak (M) of m/e 129, an M - 15 peak at m/e 114, and m/e 72 (CH_2SCN), 71 (C_5H_{11}), 58 (SCN), 57 (C_4H_9), 55 (C_4H_7), 43 (C_3H_7), 41 (C_3H_5), 29 (C_2H_5), and 27 (HCN). The mass spectral analysis is consistent with both neopentyl thiocyanate and neopentyl isothiocyanate.

Acknowledgment is made to the East Tennessee State Research Advisory Council for financial assistance, to Mrs. Susan Campbell for her aid in the drawings and preparation of the manuscript, and to Dr. J. L. Miller for his valuable discussions. 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. 1, 66085-08-3; 3, 69626-79-5; 4, 25343-65-1; neopentyl alcohol, 75-84-3; (*R*)-(+)-2-octanol, 5978-70-1; (*S*)-(−)-2-chlorooctane, 16844-08-9.

Models for the Ion-Pair Cluster Mechanism in Nucleophilic Substitution Reactions

Socorro Ramos and William Rosen*

Department of Chemistry, University of Rhode Island, Kingston, Rhode Island 02881

Received April 1, 1981

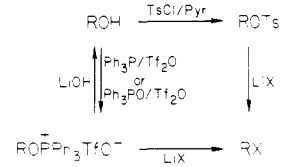
Several bis(alkoxytriphenylphosphonium) salts have been prepared. When sterically constrained, as close neighbors, the leaving groups of these cations react rapidly at room temperature with negative nucleophiles to produce the expected substitution product. When sterically unconstrained, these types of functional groups behave as if they were mono(alkoxytriphenylphosphonium) salts, substituting very slowly or not at all at room temperature. The ion-pair cluster mechanism is discussed in light of these results.

The reactions leading to the formation of tetracovalent phosphorus moieties are numerous.[1] In several of these reactions, alkoxyphosphonium salts have been implicated as important intermediates rather than stable entities. This is particularly true in those reactions where an alcohol functionality is transformed to another function by the use of a phosphine(ite) in conjunction with different reagents. Examples are the Michaelis–Arbusov reaction,[2] the Lee reaction,[3] and the DEAD reaction.[4] Recently, Hendrickson and Schwartzman have shown that some of the suspected alkoxytriphenylphosphonium intermediates from these reactions can be easily prepared as relatively stable compounds when the anion is the trifluoromethanesulfonyl (triflate) group.[5] As a result, we have been able to prepare several bis(alkoxytriphenylphosphonium) systems[6] which shed considerable light on the mechanism of nucleophilic substitution in these important reactions.

The nucleophilic substitution mechanism is one of the most important concepts in chemistry. Recently, several variations of this important concept have been proposed to explain the results obtained in the Lee reaction.[7] One of these variations proposes an unusual clustering process involving ion pairs, and it is to this mechanism that we address ourselves in this report.

The clustering of molecular entities is a phenomenon of increasing import.[8] It is becoming recognized by chemists as an area of study which should help to bridge the gap that exists between the chemistry of monomolecular units and polymolecular moieties. This may be nowhere more true than in reactions leading to nucleophilic

Scheme I.[a,b] Cycle of Reactions Used To Verify the Integrity for the Carbon Skeletons of the Alkoxytriphenylphosphonium Salts Studied



[a] See Table I for the alkyl groups. [b] X = Cl, Br, or I; R = alkyl; Ph = phenyl; Ts = *p*-toluenesulfonyl; Pyr = pyridine.

(1) Kirby, A. J.; Warren, S. G. "The Organic Chemistry of Phosphorus"; Elsevier: New York, 1967.
(2) Harvey, R. G.; LeSombre, E. G. *Top. Phosphorus Chem.* **1964**, *1*, 58.
(3) Appel, R. *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 801.
(4) Mitsunobu, O. *Synthesis* **1981**, 1.
(5) Hendrickson, J. B.; Schwartzman, S. M. *Tetrahedron Lett.* **1975**, 277. See also: Aaberg, A.; Gramstad, T.; Husebye, S. *Ibid.* **1979**, 2263.
(6) Ramos, S.; Rosen, W. *Tetrahedron Lett.* **1981**, 35.
(7) Jones, L. A.; Sumner, C. E., Jr.; Franzus, B.; Huang, T. T.-S.; Snyder, E. I. *J. Org. Chem.* **1978**, *43*, 2821.
(8) See for examples: Kenney-Wallace, G. A. *Acc. Chem. Res.* **1978**, *11*, 434. Geoffroy, G. L. *Ibid.* **1980**, *13*, 469.

0022-3263/81/1946-3530$01.25/0