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UNUSUAL REACTIVITY PATTERNS IN *BIS*-TRIPHENYLALKOXYPHOSPHONIUM SALTS

Socorro Ramos and William Rosen*
Department of Chemistry
University of Rhode Island
Kingston, Rhode Island 02881

Abstract: Alkoxyphosphonium triflates have been prepared and reacted with a number of nucleophiles. Only negatively charged nucleophiles initiate substitution reactions. Nucleophile association with the phosphorus entity, prior to nucleophilic displacement, is implied.

The preparation of oxyphosphonium salts has been known for some time.[1] Unlike tetracarbophosphonium salts, monoxy-tricarbo-phosphonium salts are much less stable. Recently, Hendrickson and Schwartzman have shown that triphenylalkoxyphosphonium triflate salts can be prepared from the corresponding alcohol by reaction with a mixture of triphenyl phosphine oxide (Ph_3PO) and triflic anhydride (Tf_2O).[2] Once formed, these salts tended to eliminate in the presence of base at elevated temperatures.

Triphenylalkoxyphosphonium salts have recently been shown to be important intermediates in several synthetically useful reactions. For example, when triphenyl phosphine (Ph_3P) and an alcohol are reacted in carbon tetrachloride, alkyl chlorides are obtained.[3] Similarly, diethylazodicarboxylate, Ph_3P and alcohols lead to a variety of products depending upon the conditions.[4] In both cases, the mechanism appears to involve formation of the alkoxy-phosphonium salt with retention of configuration at carbon, followed by S_N2 displacement of Ph_3PO by an active nucleophile to produce the inverted product.[3,4]

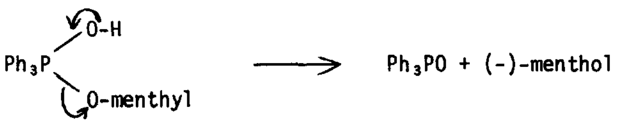
In the course of another investigation, we had need to prepare some *bis*-phosphonium salts such as 1g. Attempts to prepare these from standard precursors of 1 were not successful because of the facile conrotatory opening of the cyclobutene ring when temperatures were raised above 60-70°C. As a consequence, we searched for a low temperature preparative method for these phosphonium ions. Since it is known that the triflate ion is an extremely good leaving group,[5] we decided to prepare the *bis*-triflate of 1a, i.e. 1f, and then convert it to the desired ditriflate salt, 1g. It was during this phase of our study that we gained access, unexpectedly, to the *bis*-triphenylalkoxyphosphonium salt 1b. Subsequent inquiry into the reactivity of 1b led to some unusual observations about these types of systems and thus we present our preliminary results here.

Reaction of 1a with Tf_2O and a nine mole excess of Ph_3P in CH_2Cl_2 at -20°C produced the *bis*-triphenylalkoxyphosphonium ditriflate 1b in 70% yield.[6,7] The only other isolable products were the excess Ph_3P and some Ph_3PO. When the above reaction was carried out in the solvent pyridine, the only cyclobutenyl product isolated in good yield was 1h.[8] Originally, suspecting that the *bis*-triflate 1f was intervening in these reactions, we prepared it from 1a, Tf_2O and 2,6-di-*tert*-butylpyridine in CH_2Cl_2 at -20°C. Isolation of 1f was possible,[8] but, because of its instability, cleaner subsequent reactions were obtained when its isolation was avoided. Reaction of 1f with an excess of Ph_3P yielded Ph_3PO as the only readily identifiable product. Reaction of 1f directly with Ph_3PO yielded 1b *albeit* in very poor yield. In contrast, reaction of 1a with a mixture of Ph_3PO and Tf_2O produced **1b** as the only cyclobutenyl product in moderate yield.[9] Finally, reaction of Ph_3P with Tf_2O in CH_2Cl_2 at -20°C produced Ph_3PO in nearly quantitative yield. These data indicate, but do not conclusively prove, that **1b** is derived from a reaction sequence that does not involve **1f**. Our best guess is that these reaction sequences can be modeled after those alluded to previously[3,4] and thus we propose the scheme shown in Figure I.

Reaction of **1b** with nucleophiles provided an unusual and interesting reaction pattern. Negative nucleophiles, such as hydroxide, chloride, bromide and iodide, reacted rapidly at 25°C with **1b** to produce **1a**, **c**, **d**, and **e**,[10] respectively. This reaction was a very fast one, occurring instantaneously upon mixing, whether the reactants were present in the same phase or not.[11] Neutral nucleophiles, on the other hand, were kinetically unreactive towards **1b** at 25°C. Pyridine, Ph_3P, $(CH_3)_2S$ and CH_3OH all returned **1b** in unchanged form, even with prolonged, intimate contact at 25°C in CH_2Cl_2. This dichotomy of reactivity is unusual and implies that association of a negatively charged entity with the positive phosphonium ion prior to nucleophilic displacement is necessary.[3]

In order to verify that the cyclobutenyl ring system was not contributing to the above noted reactivity patterns, we prepared and examined two other bis-triphenylalkoxyphosphonium salts, **2**[12] and **3**.[13] The dihydro derivative of **1b**, **2**, reacted in complete analogy to the above. Reactions of **3**, however, were much more sluggish with negative nucleophiles such as bromide ion. Upon ion exchange with bromide ion in acetone only the normal, primary position was substituted by the nucleophile. At elevated temperatures in acetone, however, both the normal and neo-pentyl primary carbons reacted with bromide ion to produce (1R,3S)-1,2,2-trimethyl-1,3-bis(bromomethyl)-cyclo-pentane, which is of some interest as a precursor of natural products.[14]

The reaction of negative nucleophiles with the prepared alkoxyphosphonium salts proceeds rapidly in most cases, and with apparent inversion of configuration at carbon. Utilizing (-)-menthol, we could easily prepare the optically active triphenyl-(-)-menthoxyphosphonium triflate.[2] The previously noted susceptibility to decomposition of this secondary system prevented complete purification but partially purified samples could be conveniently subjected to nucleophilic substitution conditions. In all cases, negative nucleophiles yielded the (+)-neomenthyl derivative[15] while neutral nucleophiles produced many different products. The most interesting example from this set of experiments, was that where hydroxide ion was the nucleophile. One could argue that coordination of the hydroxide ion should have yielded a five coordinate phosphorus complex that could then lead to retention of configuration by the mechanism shown below.



Instead, we observed only (+)-neomenthol which implied that a mechanism involving ion-pairs was operative or the five coordinate complex reacted via a ${}_{\sigma}2_{s} + {}_{\sigma}2_{a}$ pericyclic reaction. Since this latter alternative has been discounted, it would appear that an ion-pair mechanism must be given serious consideration.[3]

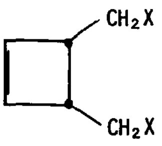
Acknowledgement: We wish to thank the Research Corporation for financial support of this project.

Figure I

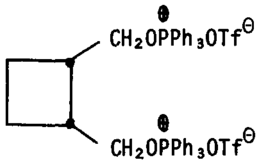
$$Ph_3P + Tf_2O \longrightarrow Ph_3\overset{\oplus}{P}\text{-}OTf + Tf^{\ominus}$$

$$Ph_3PO + Tf_2O \longrightarrow Ph_3\overset{\oplus}{P}\text{-}OTf + OTf^{\ominus}$$

$$ROH + Ph_3\overset{\oplus}{P}\text{-}OTf \longrightarrow Ph_3\overset{\oplus}{P}\text{-}OR + OTf^{\ominus} + H^{\oplus}$$



1



2

1a X = -OH

1b X = $-O\overset{\oplus}{P}Ph_3OTf^{\ominus}$

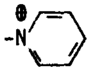
1c X = -Cl

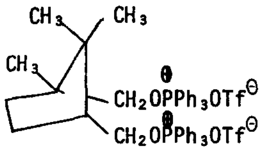
1d X = -Br

1e X = -I

1f X = -OTf

1g X = $-\overset{\oplus}{P}Ph_3OTf^{\ominus}$

1h X =  $OTf^{\ominus}$



3

Ph = Phenyl

Tf = CF_3SO_2

References and Footnotes

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6. The compound 1b can best be prepared by adding a precooled mixture of Tf_2O in CH_2Cl_2 to a mixture of Ph_3P and 1a in CH_2Cl_2 at -20°C. The product can be isolated pure by

chromatography on silica gel, elution with acetone.

7. **1**b; 'HNMR (CDCl$_3$): δ 3.20-3.6 (m,2H), 4.3-4.8 (m,4H), 6.0 (s,2H), 7.3-8.1 (m,30H).*
8. **1**f; 'HNMR (CDCl$_3$): δ 3.1-3.6 (m,2H), 4.5-4.7 (dd,4H), 6.2 (s,2H).
   1h; 'HNMR (accetone-d$_6$): δ 3.7-4.2 (m,2H), 5.1-5.4 (2 overlapping doublets,4H), 6.35 (s, 2H), 8.1-9.4 (m,10H).
9. The material made by Hendrickson's procedure is the pure ditriflate while our materials always contained some of the triflinate anion.
10. **1**a; 'HNMR (CDCl$_3$): δ 3.0-3.6 (m,2H), 3.65-4.0 (dd,4H), 4.25 (bs,2H), 6.1 (s,2H).
    1c; 'HNMR (CDCl$_3$): δ 3.05-3.8 (overlapping multiplets,6H), 6.25 (s,2H).
    1d; 'HNMR (CDCl$_3$): δ 3.2-3.7 (overlapping multiplet,6H), 6.2 (s,2H).
    1e; 'HNMR (CDCl$_3$): δ 2.85-3.5 (m,6H), 6.2 (s,2H).
11. Reaction could be conducted in the same liquid phase, i.e. acetone, in a two phase liquid system such as CH$_2$Cl$_2$ and H$_2$O, or on passing an acetone solution of the salt over an appropriate ion exchange resin.† Negative nucleophiles such as azide and benzoate ions, in aqueous solution, only reacted through the equilibrium amount of hydroxide ions producing **1**a. Under anhydrous conditions, the insolubility of these anions prevented any pronounced reactivity.
12. **2**; 'HNMR (CDCl$_3$): δ 1.65-2.1 (m,4H), 2.7-3.2 (m,2H), 4.0-5.0 (m,4H), 7.3-8.2 (m,30H).*
13. **3**; 'HNMR (CDCl$_3$): δ 0.65 (s,3H), 0.95 (s,3H), 1.1 (s,3H), 1.2-1.6 (m,5H), 4.1-4.6 (m,4H), 7.6-8.2 (m,30H).*
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*The coupling constant between phosphorous and the methylene hydrogens in **1**b, **2** and **3** is approximately 6 cps. This is consistent with a POCH$_2$ coupling system rather than a PCH$_2$ coupling system. [Compare Denney, D. B., and Relles, H. M., *Tetrahedron Lett.*, 573 (1964) to Hendrickson, J. B., Maddox, M. L., Sims, J. J., and Kaesz, H. D., *Tetrahedron*, **20**, 449 (1964)]. In addition, it was shown by ^{31}P NMR and conductivity measurements that **1**b, **2** and **3** are all 2:1 oxyphosphonium electrolytes in chloroform and methanol, respectively.

†The other product in all these nucleophilic reactions was shown to be triphenylphosphine oxide by isolation.

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