^{17}O and ^{18}O Labeling Studies by NMR. Mechanism of Rearrangement of an α-Thiophosphoryl Trifluoroacetate to an α-Phosphoryl Thiotrifluoroacetate

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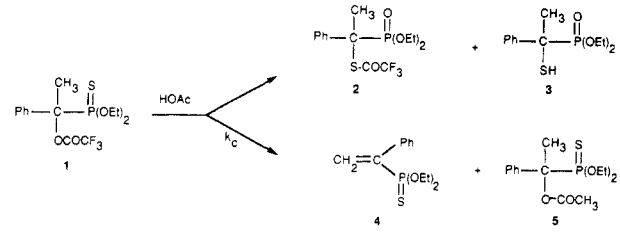
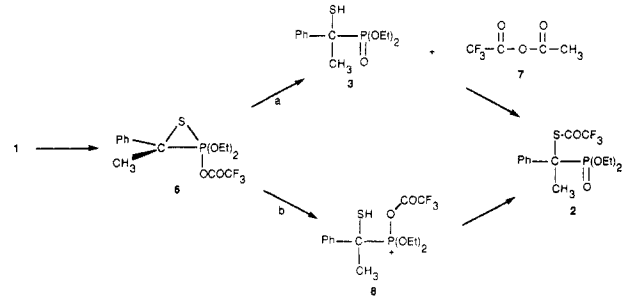
Abstract: Acetophenone-^{17}O and acetophenone-^{18}O have been condensed with hydrogen diethylthiophosphonate, and the resultant oxygen-labeled α-hydroxythiophosphonates, $PhC(CH_3)(*OH)PS(OEt)_2$, **13**, were converted to the labeled trifluoroacetates $PhC(CH_3)(*OCOCF_3)PS(OEt)_2$, **1**-$^{17}O$ and **1**-^{18}O. Under acetolysis conditions, the major product from rearrangement of unlabeled **1** is the rearranged product $PhC(CH_3)(SCOCF_3)PO(OEt)_2$, **2**. The mechanism of this rearrangement has been investigated using the labeled substrates **1**-^{17}O and **1**-^{18}O. These substrates rearrange under acetolysis conditions to give a labeled product, **2***, which has 80% of the label incorporated in the phosphoryl group and 20% of the label incorporated in the carbonyl group. In the case of **1**-^{17}O, the label position was determined directly by ^{17}O NMR spectroscopy. The acetolysis of **1**-^{18}O was also directly monitored by ^{31}P NMR where the chemical shift of phosphorus bonded to ^{16}O differs from that of phosphorus bonded to ^{18}O. These complimentary labeling studies rule out a concerted mechanism for the formation of **6**, the key intermediate in this rearrangement. A k_Δ mechanism, involving neighboring thiophosphoryl participation leading to an ion pair, where internal return of trifluoroacetate occurs at phosphorus, is the most probable mechanism leading to formation of the intermediate **6**. Internal return of trifluoroacetate at phosphorus does not result in complete oxygen scrambling. Capture of the oxygen that was originally bonded to the incipient ionization center is 4 times more probable than capture of the more remote of the functionally nonequivalent trifluoroacetate oxygen atoms in the ion pair. Acetolysis of **1**-^{18}O in the presence of unlabeled thiol $PhC(CH_3)(SH)PO(OEt)_2$, **3**, gave no incorporation of this unlabeled material in the product **2**-^{18}O. This study shows that the subsequent rearrangement of **6** to **2** is an intramolecular process not involving free thiol **3**. Intramolecular trifluoroacetyl group transfer, after opening of **6**, offers a reasonable rationale for the formation of **2**. These studies illustrate the utility of ^{17}O NMR and ^{31}P NMR for direct determination of the position of a labeled oxygen in mechanistic studies.

We recently reported[1] that the α-thiophosphoryl trifluoroacetate **1** reacts in acetic acid to give the products **2**–**5**. The major product (63%) was the isomeric thiotrifluoroacetate **2**. In this transformation, the thiophosphoryl group of **1** had been converted to an O-phosphoryl group in **2**. Also produced was a smaller amount (27%) of the deacetylated rearranged thiol **3**. We have concluded



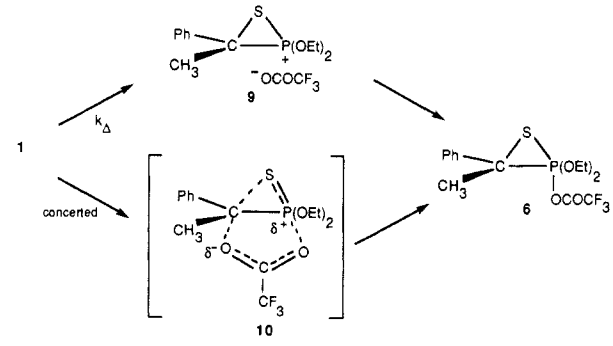
that the two other minor products, **4** and **5**, are derived from a k_c process in which a thiophosphoryl-substituted carbocation undergoes proton loss or solvent capture. We were interested in the mechanism of formation of the major product **2** in which sulfur and oxygen have formally interchanged positions. We therefore wanted to determine which oxygen (if any) of the trifluoroacetate group in **1** became the phosphoryl oxygen of **2**.

We have suggested[1] that **6** (which could not be detected) is the key intermediate in conversion of **1** to **2**. There are two plausible pathways by which the intermediate **6** could be converted to the observed products. We initially suggested that opening of **6** by



attack of acetic acid (or acetate ion) at the carbonyl group of **6** would lead to the thiol **3** as well as the mixed acetic trifluoroacetic anhydride **7**. Subsequent trifluoroacetylation of **3** would give the observed product **2**. Alternatively, opening of **6** via the ionic intermediate **8** followed by intramolecular transfer of the trifluoroacetyl group would also give **2**.

The key cyclic intermediate **6** was suggested to be derived from a k_Δ process, involving neighboring thiophosphoryl participation, leading to the ion pair **9**, based on kinetic data. However a



concerted process (where sulfur participation and carbonyl group bonding to phosphorus are simultaneous) with a charge-separated transition state as in **10** could not be ruled out. We therefore wanted to further investigate the mechanism of formation of the proposed intermediate **6** and the mechanism of the subsequent conversion of **6** to the observed product **2**.

In principle, an oxygen-labeled substrate **1** could be of value in elucidating the mechanism of the transformation of **1** to **2**. Oxygen labeling studies have been used in the past to elucidate subtle details in solvolytic studies.[2-5] We have now investigated

(1) Creary, X.; Mehrsheikh-Mohammadi, M. E. *J. Org. Chem.* **1986**, *51*, 7–15.

(2) Diaz, A. F.; Lazdins, I.; Winstein, S. *J. Am. Chem. Soc.* **1968**, *90*, 1904–1905.

(3) For representative examples, see: (a) Goering, H. L.; Anderson, R. P. *J. Am. Chem. Soc.* **1978**, *100*, 6469–6474. (b) Goering, H. L.; Humski, K. *J. Org. Chem.* **1975**, *40*, 920–922. (c) Goering, H. L.; Thies, R. W. *J. Am. Chem. Soc.* **1968**, *90*, 2967–2968. (d) Georing, H. L.; Thies, R. W. *Ibid.* **1968**, *90*, 2968–2970. (e) Goering, H. L.; Briody, R. G.; Levy, J. F. *Ibid.* **1963**, *85*, 3059–3061.

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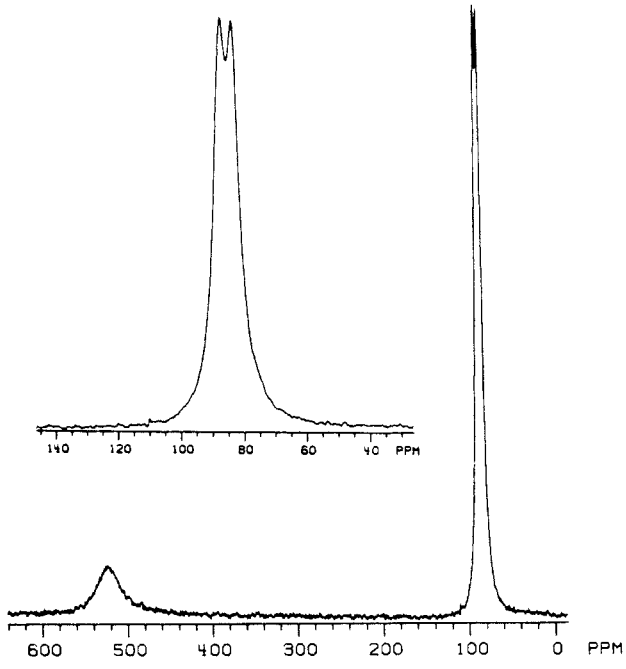


Figure 1. ^{17}O NMR spectrum (40.7 mHz) in $CDCl_3$ of the products **2**-^{17}O formed on acetolysis of **1**-^{17}O. Insert shows the expanded P=^{17}O region.

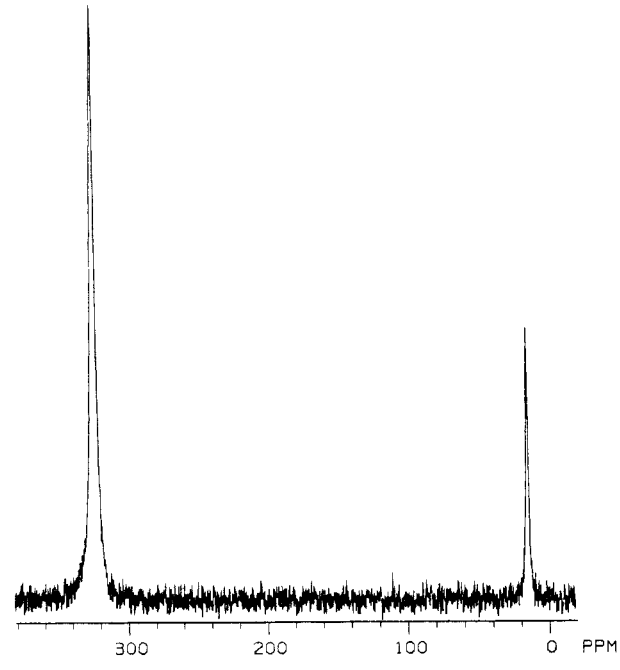
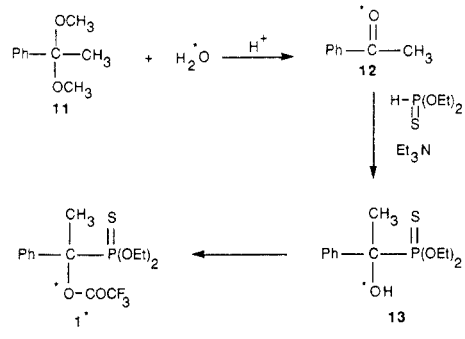


Figure 2. ^{17}O NMR spectrum (40.7 mHz) in Et_2O of **14**-^{17}O (50 mg) which is formed on acetolysis of **1**-^{17}O followed by cleavage of **2**-^{17}O with NH_3. The peak at δ 14.3 is due to the ether solvent.

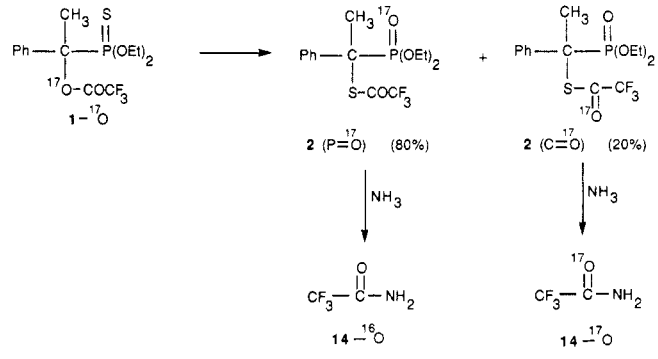
the conversion of **1** to **2** in more detail using ^{17}O- and ^{18}O-labeled substrates. These studies have been useed in an attempt to distinguish between the suggested ion-pair mechanism and the concerted process for formation of the key intermediate **6**. We have also monitored the reaction by ^{31}P NMR to determine the subtle details of the mechanism of conversion of **6** to the observed products. Reported here are the results of these studies.

Results

Synthesis of Labeled Substrates. The acid-catalyzed hydrolysis of acetophenone dimethyl acetal with $H_2{}^{17}O$ (23% enriched) or $H_2{}^{18}O$ (97% enriched) gave the appropriately labeled acetophenone.[6] This was converted as previously described[1] to the labeled trifluoroacetate **1**. Mass spectroscopic analysis of the $H_2{}^{18}O$ hydrolysis reaction product showed the acetophenone to be 96% enriched in ^{18}O. The trifluoroacetate **1**-^{18}O was also 96% enriched in ^{18}O by mass spectral analysis.



Solvolysis of 1-^{17}O. Mechanistic studies employing ^{17}O NMR for determing the label position have only become feasible with the advent of modern NMR techniques.[7] In the solvolytic area, the only ^{17}O NMR studies that we are aware of are two recent le Noble studies[5] which used this method for monitoring solvolyses of ^{17}O-labeled norbornyl sulfonate esters. We have now monitored the solvolysis of **1**-^{17}O by using ^{17}O NMR spectroscopy. The labeled substrate **1**-^{17}O, which shows a broad ^{17}O signal at δ 171 (H_2O reference), was solvolyzed in acetic acid at 100 °C as previously described.[1] Spectral results are shown in Figure 1.



The doublet at δ 85 due to ^{17}O incorporation into the phosphoryl group of the product **2** can be clearly seen (J_{P-O} = 145 Hz).[8] An unusually far downfield and broad ^{17}O signal at δ 524 due to the carbonyl oxygen of **2** can also be seen. That this broad signal is actually due to ^{17}O incorporation into the carbonyl group can be verified by cleavage of the product **2** with ammonia. The much sharper ^{17}O signal (Figure 2) of the labeled amide product **14**-^{17}O appears at δ 324. The ratio of phosphoryl-^{17}O to carbonyl-^{17}O is 4 to 1 as determined by integration of the ^{17}O NMR signals. These results suggest that the label is *unequally scrambled to both the carbonyl and phosphoryl positions* of the product.

Solvolysis of 1-^{18}O. Relaxation times are rapid for ^{17}O, and there is no Overhauser effect. However, because of the inherent difficulties in recording NMR spectra of this nucleus,[9] we sought further verification of the reliability of ^{17}O NMR integration as a quantitative measure of the oxygen distribution. Therefore, the study has been repeated using the labeled **1**-^{18}O (96% ^{18}O in-

(4) Paradisi, C.; Bunnett, J. F. *J. Am. Chem. Soc.* **1981**, *103*, 946–948.
(5) (a) Chang, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1983**, *105*, 3708–3709. (b) Chang, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1984**, *106*, 810–811.
(6) For an analogous hydrolysis in ^{18}O-enriched water which leads to complete incorporation of the label into the carbonyl group, see: Stasuik, F.; Sheppard, W. A. *Can. J. Chem.* **1956**, *34*, 123–127.
(7) For a discussion of ^{17}O NMR spectroscopy and the problems associated with recording spectra of this nucleus, see: Krintzinger, J.-P. In *Oxygen-17 and Silicon-29*; Diehl, P., Fluck, E.; Kosfeld, R., Ed.; Springer-Verlag: New York, 1981.
(8) Gray, G. A.; Albright, T. A. *J. Am. Chem. Soc.* **1977**, *99*, 3243–3250.
(9) A major problem is a distorted base line in the Fourier transformed spectrum due to rf pulse breakthrough as a result of short delay times between the rf pulse and data aquisition. This problem was minimized in the present case as described in the Experimental Section.

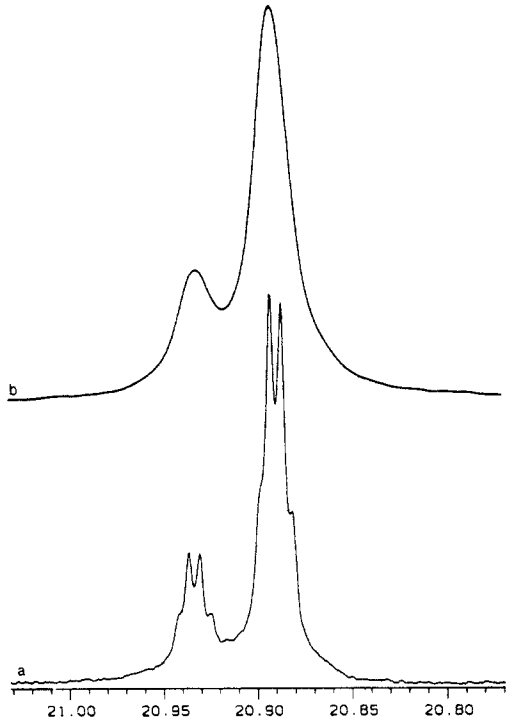


Figure 3. ^{31}P NMR spectrum (121.5 mHz) in $CDCl_3$ of **2**-^{18}O formed on acetolysis of **1**-^{18}O. (a) Line broadening = 0.1 Hz. (b) Line Broadening = 1.0 Hz.

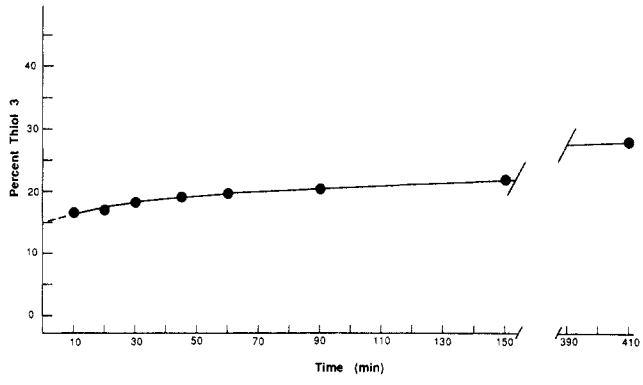


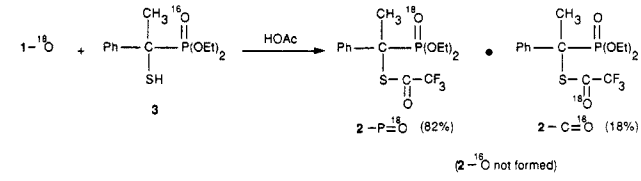
Figure 4. Plot of percent thiol **3** formed in solvolysis of **1** at 100 °C vs. time.

corporation). This system offers a unique opportunity for direct analysis of the label position by ^{31}P NMR spectroscopy.

The ^{31}P NMR spectrum of the thiotrifluoroacetate product obtained in acetolysis of **1**-^{18}O is shown in Figure 3. Long-range coupling to fluorine (0.7 Hz) can be seen when the line broadening is 0.1 Hz. This coupling is not apparent when the line broadening is 1 Hz. Unlabeled **2** shows a single ^{31}P signal at δ 20.94, while the product of solvolysis of **1**-^{18}O clearly shows two signals at δ 20.89 and 20.94 in a 79:21 (±2%) ratio.[10] The peak at δ 20.89 is presumably due to an ^{18}O isotopic shift. Such isotope effects on the chemical shift of ^{31}P have previously been observed.[11] This allows one to directly determine the extent of ^{18}O label in the phosphoryl group. One must take into acocunt the fact that the starting material has 4% unlabeled **1**. The 79:21 peak ratio in Figure 3 therefore corresponds to 82 ± 2% incorporation of the original ^{18}O label (from 100% **1**-^{18}O) into the phosphoryl group. This is, within experimental error, the same result as determined from the original ^{17}O-labeling experiment.

When **1**-^{18}O was reacted for 1 half-life and the unreacted **1**-^{18}O was recovered, cleavage with ammonia gave trifluoroacetamide **14** which showed 5% incorporation of the ^{18}O label into the carbonyl group. This control experiment shows that **1**-^{18}O undergoes scrambling of the label to the carbonyl group at a slower rate than it rearranges to **2**-^{18}O. Oxygen scrambling in **1**-^{18}O therefore does not account for the much larger fraction (20%) of label which ends up in the carbonyl group of **2**-^{18}O.

Solvolysis of 1-^{18}O in HOAc in the Presence of Thiol 3. The question of whether **6** is converted to **2** by an intramolecular trifluoroacetyl group transfer or an intermolecular transfer involving the mixed anhydride **7** has been addressed by using a labeling experiment. The solvolysis of **1**-^{18}O was monitored in

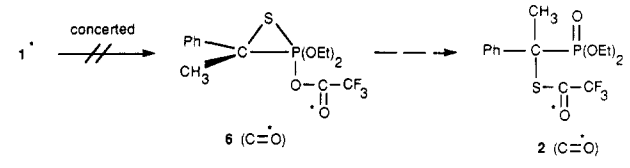


the presence of unlabeled thiol **3**. The ratio of P ^{16}O to P ^{18}O in the product **2** was the same as in the absence of added thiol **3** even at low conversion. The product **2** formed under these reaction conditions therefore is not derived from unlabeled **3**. Therefore, the trifluoroacetyl group never becomes free during the reaction; i.e., the thiol **3** is not a precursor to the product **2**.[12]

We have also examined the acetolysis of **1** by ^{31}P NMR as a function of time. Figure 4 shows that the ratio of thiol **3** (^{31}P NMR (in HOAc) δ 26.34) to thiotrifluoroacetate **2** (^{31}P NMR (in HOAc) δ 21.44) does not remain constant. The amount of **3** increases with time as a result of slow conversion of **2** to **3** under the reaction conditions.[12] Interestingly, extrapolation to time zero shows that a small amount (approximately 15%) of **3** is formed. Thiol **3** is therefore a primary product, but **3** is not involved in the production of **2**.

Discussion

Both the ^{17}O- and the ^{18}O-labeling experiments indicate substantial incorporation of the label into the P=O group of the product **2**. This result rules out the concerted process. This



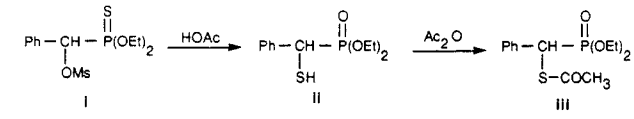
process, which would have given the intermediate **6**(C=O*), predicts *no* label incorporation into the phosphoryl group and complete incorporation into the carbonyl group. This leaves the ion-pair mechanism as the most plausible. We can now use the labeling data to say something about the nature of the proposed ion pair. The label is not equally scrambled into the phosphoryl and carbonyl groups. Therefore, the trifluoroacetate oxygens are functionally nonequivalent in the ion-pair intermediate. We picture an ion pair, as in **15**, where internal return at phosphorus by way of the labeled oxygen is 4 times more probable than capture at the more remote unlabeled oxygen.

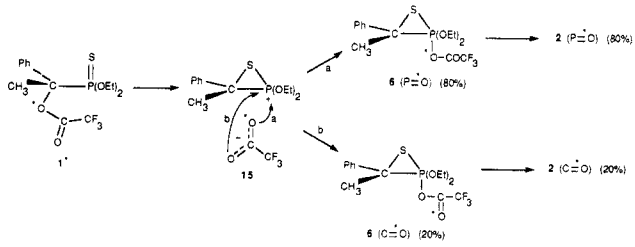
Where do these results fit into the scheme of ion-pair mechanisms? The present findings strongly contrast with an earlier

(10) This ratio was determined by computer simulated deconvolution of the partially overlapped spectrum in Figure 3b.

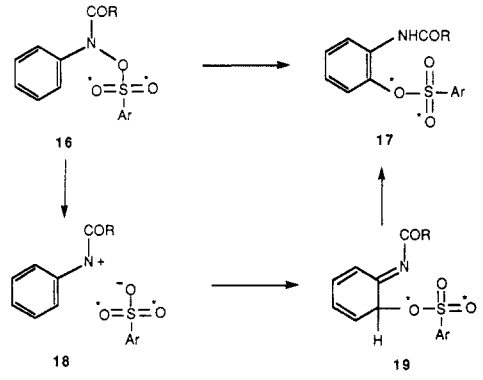
(11) (a) Cohn, M.; Hu, A. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 200–203. (b) Webb, D. R.; McDonald, G. G.; Trentham, D. R. *J. Biol. Chem.* **1978**, *253*, 2908–2911. (c) Bock, J.; Cohn, M. *J. Biol. Chem.* **1978**, *253*, 4082–4085. (d) Van Etten, R. L.; Risley, J. M. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 4784–4787. (e) Taira, K.; Fanni, T.; Gorenstein, D. G. *J. Am. Chem. Soc.* **1984**, *106*, 1521–1523.

(12) This result contrasts with our earlier observation[1] where the thioacetate iii is formed on acetolysis of i by acetylation of the intermediate thiol ii.

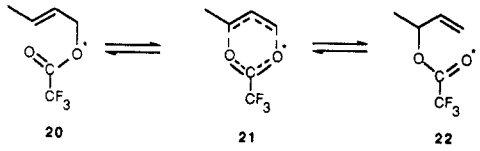




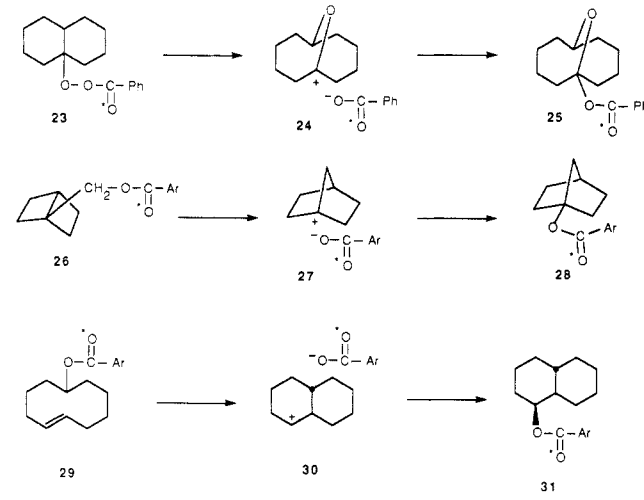
^{18}O-labeling study on the rearrangement of **16** to **17**.[13] In this process, the sulfonyl oxygen is the one which becomes attached to the aromatic ring during the rearrangement. This rearrangement was initially discussed in terms of a concerted process. However, recent studies by Gassman[14] on mesylate analogues of **16** support the involvement of nitrenium ion–sulfonate ion pairs. Hence, the ion-pair mechanism, where the original sulfonyl oxygen of the functionally nonequivalent sulfonate oxygen atoms is preferentially captured by the electron-deficient ring carbon, offers the best rationale for the available data. By way of contrast, in the rearrangement of **1**, the oxygen covalently bonded to the incipient ionization center is the one that is preferentially reattached in the ion pair.



The gas-phase thermal allylic rearrangement of trifluoroacetate **20**[15] also contrasts with the present solvolysis results. In this rearrangement, a concerted Cope-like process, as shown in **21**, accounts for the major incorporation of the labeled oxygen into the carbonyl group of the product.



The behavior of the ion pair **15** is reminiscent of the behavior of carboxylate ion in the Criegee rearrangement of the perester **23**.[16] In this rearrangement, which occurs via ion pair **24**, internal return occurs preferentially at the same oxygen which was directly bonded to the substrate and not at the original carbonyl oxygen. The same phenomenon has been observed in the ion-pair rearrangements of **26**.[17] Another pertinent reaction is the solvolysis of **29**, which gives a substantial amount of the rearrangement ester **31**, without complete scrambling of the labeled oxygen, despite the relatively large distance that the carboxylate ion must migrate in this rearrangement.[18] These rearrangements all involve rather short-lived ion pairs which apparently do not rach the "solvent separated" stage. A similarly short-lived ion pair is presumably involved in the acetolysis of **1**.



Conversion of **6** to the product **2** involves an intramolecular transer of the trifluoroacetyl group. This is shown by the lack of incorporation of unlabeled thiol **3** into the product when **1**-^{18}O is solvolyzed in the presence of unlabeled **3**. This rules out the process involving cleavage of **6** to **3** with acetic acid followed by trifluoroacetylation using the mixed anhydride **7** that would be formed in such a process. The alternative process involving opening of **6** to **8**, followed by intramolecular transfer of the trifluoroacetyl group, appears most plausible.

Conclusions. The rearrangement of **1**-^{17}O or **1**-^{18}O to **2** under acetolysis conditions proceeds with 80% incorporation of the label into the phosphoryl group and 20% label incorporation into the carbonyl group. In the case of **1**-^{17}O, the label position was determined directly by ^{17}O NMR spectroscopy, while the label position in acetolysis of **1**-^{18}O was directly monitored by ^{31}P NMR. These complimentary studies rule out a concerted mechanism for the formation of **6**, the key intermediate in this rearrangement. An ion-pair mechanism, where internal return of trifluoroacetate occurs at phosphorus, is the most probable mechanism. Capture of the oxygen that was originally bonded to the incipient ionization center is 4 times more probable than capture of the more remote of the functionally nonequivalent trifluoroacetate oxygen atoms in the ion pair. As deduced by further labeling studies, the subsequent rearrangement of **6** to **2** is an intramolecular process not involving free thiol **3**. Intramolecular trifluoroacetyl group transfer in the ionic intermediate **8** offers a reasonable rationale for the formation of **2**.

Experimental Section

NMR spectra were recorded on a Nicolet NB 300 spectrometer. Chemical shifts for ^{17}O spectra are relative to H_2O. Chemical shifts for ^{31}P spectra are relative to 85% H_3PO_4. ^{17}O spectra were recorded at 40.7 MHz using a pulse width of 35 μs and a delay of 500 μs before data aquisition. Before Fourier transformation of the data the command LS was applied 1, 2, or 3 times to the FID. Each LS command shifts the data one point to the left and thereby removes extraneous data points due to rf pulse breakthrough. This procedure proved useful in eliminating the base-line roll (which makes accurate integration of spectra difficult) in the Fourier transformed spectrum.

Preparation of Acetophenone-^{18}O. To a carefully dried flask was added 498 mg of $H_2{}^{18}O$ (Merck Sharp & Dome Isotopes, 97% ^{18}O). Fifteen milliliters of tetrahydrofuran was distilled directly into the flask (from Na/benzophenone) under nitrogen. Acetophenone dimethyl ketal (3.582 g) was then added followed by 20 mg of concentrated H_2SO_4. After 30 min, 3 drops of Et_3N was added, and the solvent was removed by using a rotary evaporator. The residue was distilled to give 2.528 g (98%) of acetophenone-^{18}O, bp 61–63 °C (2 mm). Mass spectral analysis by examination of the peaks at *m/e* 108 $(Ph^{13}C^{18}O)^+$ and 105 $(Ph^{12}C^{16}O)^+$ indicated 96% incorporation of ^{18}O in the product.

Reaction of Acetophenone-^{18}O with Hydrogen Diethylthiophosphite. The procedure was analogous to that described for the reaction of unlabeled acetophenone.[1] A mixture of 2.41 g of acetophenone-^{18}O, 3.20 g of $HPS(OEt)_2$, and 1.05 g of freshly distilled Et_3N (from $LiAlH_4$) was heated at 65–69 °C for 4 h and 20 min in a tightly stoppered flask. After being allowed to stand at room temperature for 12 h, the lower boiling unreacted starting materials and Et_3N were removed by evacuation of

(13) Tisue, G. T.; Grassmann, M.; Lwowski, W. *Tetrahedron* **1968**, *24*, 999–1006.
(14) (a) Gassman, P. G.; Granrud, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 1498–1499. (b) Gassman, P. G.; Granrud, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 2448–2449.
(15) Lewis, E. S.; Hill, J. T. *J. Am. Chem. Soc.* **1969**, *91*, 7458–7462.
(16) Denney, D. D.; Denney, D. G. *J. Am. Chem. Soc.* **1957**, *79*, 4806–4808.
(17) Dauben, W. G.; Chitwood, J. L. *J. Org. Chem.* **1969**, *34*, 726–729.
(18) Goering, H. L.; Myers, R. F. *J. Am. Chem. Soc.* **1969**, *91*, 3386–3387.

the flask at 15 mmHg pressure and then by lowering the pressure to 0.05 mmHg and heating the flask in an oil bath at 60–70 °C. The crude product weighed 4.02 g (74%) and showed only a trace of acetophenone when examined by 300-mHz NMR. The NMR spectrum was identical with the previously reported spectrum of unlabeled **13**-^{18}O. This crude product was converted without purification to the trifluoroacetate.

Preparation of Trifluoroaceate 1-^{18}O. The procedure was analogous to that described for the preparation of unlabeled **1**.[1] A solution of 4.018 g of **13**-^{18}O in 35 mL of freshly distilled pyridine (from P_2O_5) was cooled at 0 °C as 4.80 g of trifluoroacetic anhydride was added dropwise. The mixture was stirred at room temperature for 4 h and then taken up into 50 mL of ether and 50 mL of Skelly F. The mixture was washed with three portions of cold water, cold 10% HCl, and saturated NaCl solution and dried over $MgSO_4$. The solvents were removed by using a rotary evaporator, and the residue was distilled to give 4.978 g (92%) of **1**-^{18}O, bp 94–97 °C (0.05 mm). Mass spectral analysis by examination of the peaks at *m/e* 373 (M + 1 peak for **1**-^{18}O) and *m/e* 370 (parent peak for **1**-^{16}O) indicated 96% ^{18}O incorporation in the product trifluoroacetate.

Preparation of Trifluoroacetate 1-^{17}O. Acetophenone-^{17}O was prepared by hydrolysis of acetophenone dimethyl acetal with $H_2{}^{17}O$ (Merck Shape & Dome Isotopes, 23% ^{17}O) using a procedure analogous to that described above. The ^{17}O NMR of acetophenone-^{17}O showed a signal at δ 539. Conversions to **13**-^{17}O (^{17}O NMR δ 40.3) and **1**-^{17}O (^{17}O NMR δ 170.7) were also analogous to the procedures described above.

Acetolysis of Trifluoroacetate 1-^{17}O. The procedure was analogous to that described for the acetolysis of unlabeled **1**.[1] A solution of 1.956 g of **1**-^{17}O (23% ^{17}O) in 60 mL of 0.1 M NaOAc in acetic acid containing 1% acetic anhydride was heated for 11 h at 100 °C. A standard aqueous workup followed as previously described. The thiol **3** was removed by extraction with K_2CO_3 solution. After solvent removal by using a rotary evaporator, the ^{17}O NMR spectrum of the crude residue (which contained **2**-^{17}O and small amounts of **4** and **5**) was recorded (Figure 1). The spectrum shown corresponds to 44 000 scans with an aquisition time of 0.295 s/scan. The spectrum shows signals at δ 85 (doublet, J = 145 Hz, P=^{17}O) and 524 (C=^{17}O) in a 399:100 ratio (±3%) respectively. The spectrum is identical with that of a sample of pure **2**-^{17}O isolated by preparative gas chromatography.

Reaction of 2-^{17}O with Ammonia. The crude solvolysis product obtained above (660 mg) was placed in a 25-mL flask, and 10 mL of liquid ammonia (distilled from sodium) was condensed into the flask under nitrogen by using a cold finger condenser. After 90 min at −33 °C, the ammonia was allowed to evaporate and a short-path distillation head was attached. The flask was evacuated at 20-mmHg pressure, and the receiver flask was then cooled to −78 °C. The pressure was then lowered to 0.05 mmHg, and the flask was heated to about 70 °C. The solid amide **14** was sublimed and condensed in the short-path condenser. The solid **14** (75 mg; 37%) was collected and washed with a small amount of Skelly F. The product is relatively insoluble in $CDCl_3$. Recrystallization from $CDCl_3$ gave a sample which had a infrared spectrum identical with that of an authentic sample of unlabeled **14**. Figure 2 shows the ^{17}O NMR spectrum of 50 mg of this mixture of **14**-^{17}O and **14**-^{16}O in 3.5 mL of diethyl ether. The spectrum shown corresponds to 15 000 scans with an aquisition time of 0.2147 s/scan. **14**-^{17}O shows a signal at δ 324, while the ether solvent appears at δ 14.3.

Acetolysis of Trifluoroacetate 1-^{18}O. The procedure was analogous to that described for the acetolysis of unlabeled **1**. Reaction of 270 mg of **1**-^{18}O (96% ^{18}O) in 14 mL of HOAc at 100 °C for 9 h gave, after a standard aqueous workup, 194 mg of a mixture of **2**-^{18}O, **4**, and **5**. (The thiol **3** was removed by an aqueous K_2CO_3 extraction.) This mixture was analyzed by ^{31}P NMR. The phosphoryl region of this spectrum is shown in Figure 3. The relative areas of the P=^{16}O signal at δ 20.95 and the P=^{18}O signal at δ 20.89 were determined by computer simulation of the partially overlapped spectrum obtained when the spectrum is recorded with a line broadening of 1 Hz (Figure 3b).

Acetolysis of Trifluoroacetate 1-^{18}O with Added Unlabeled Thiol 3. A mixture of 80 mg of **1**-^{18}O and 29 mg of **3** (prepared from solvolysis of unlabeled **1** in formic acid)[1] was heated in 3 mL of 0.075 M sodium acetate in acetic acid containing 1% acetic anhydride at 100 °C for 25 min (25% reaction). The mixture was analyzed directly in the acetic acid solvent by ^{31}P NMR which showed a P=^{16}O signal at δ 21.44 and a P=^{18}O signal at δ 21.40 in a 20:80 ratio. After 60 min (50% reaction) the P=^{16}O to P=^{18}O ratio was identical.

Acetolysis of Trifluoroacetate 1. Product Study as a Function of Time. A solution of 120 mg of unlabeled **1** in 3 mL of 0.075 M sodium acetate in acetic acid containing 1% acetic anhydride was heated at 100 °C in a NMR tube. At certain time intervals, the tube was analyzed by ^{31}P NMR for **2** (which appears at δ 26.34) and **3** (which appears at δ 21.44) by integration of the appropriate signals. Results are presented graphically in Figure 4.

Acetolysis of Trifluoroacetate 1-^{18}O for 1 Half-Life. Analysis of Recovered Unreacted 1-^{18}O. A solution of 600 mg of **1**-^{18}O in 22 mL of HOAc was heated at 100 °C for 60 min (1 half-life), and a standard aqueous workup followed. The residue, after solvent removal, was chromatographed on 17 g of silica gel and eluted with 10% ether in Skelly F. The unreacted **1**-^{18}O and olefin **4** (11.6:1 ratio) eluted immediately with no trace of **2** or **3**. This mixture (296 mg) was placed in a 10 mL flask, and 4 mL of anhydrous ammonia was condensed under nitrogen. After 90 min at −33 °C, the ammonia was allowed to evaporate and the trifluoroacetamide **14** was isolated as previously described above. The crude **14** (65 mg; 53%) was washed with Skelly F and recrystallized from $CDCl_3$. Mass spectral analysis showed 95% of **14**-^{16}O and 5% of **14**-^{18}O.

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Registry No. **1**-^{18}O, 103712-06-7; **1**-^{17}O, 103712-09-0; **2**(C=^{17}O), 103712-10-3; **2**(P=^{17}O), 103712-11-4; **3**, 99668-46-9; **4**, 99668-44-7; **5**, 99668-45-8; **11**, 4316-35-2; **12**-^{17}O, 103712-07-8; **12**-^{18}O, 73007-56-4; **13**-^{17}O, 103712-08-9; **13**-^{18}O, 103712-05-6; **14**-^{16}O, 354-38-1; **14**-^{17}O, 103712-12-5; **14**-^{18}O, 103712-13-6; ^{17}O, 13968-48-4; ^{18}O, 14797-71-8; $HP(S)(OEt)_2$, 991-01-9.

Novel Benzyllithium Structures

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Abstract: Novel benzyllithium systems, e.g., **2**, **4**, and **5**, have been prepared and characterized via chemical and NMR spectroscopic evidence. The important experimental aspects of this work are the method of carbanion preparation via reductive cleavage of σ-bonds and the multinuclear NMR (^1H, ^{13}C, ^7Li, ^6Li) approach. It appears that carbanion and dianion structures are deeply affected by the intramolecular interaction between a carbanion moiety and a remote π-system as well as by the interaction of two carbanion subunits.

The structures of lithiated hydrocarbons are the subjects of extensive experimental and theoretical studies.[2] An important question is concerned with the hybridization of the carbanion center and, thus, the degree of covalent or ionic bonding.[2-7] The

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