23-5; trichloroethylene, 79-01-6; 1,1,1-trichloroethane, 71-55-6; 1,2-dichloroethane, 107-06-2; methylene chloride, 75-09-2; chloroform, 67-66-3; tetrachloroethylene, 127-18-4; 1,1,2,2-tetrachloroethane, 79-34-5; *n*-butyl chloride, 109-69-3; 1,2-dibromoethane, 106-93-4; *trans*-1,2-dichloroethylene, 156-60-5; pentachloroethane, 76-01-7; methylene bromide, 74-95-3; methylene iodide, 75-11-6; perfluoro-*n*-octane, 307-34-6; perfluoro-*n*-heptane, 335-57-9; perfluorodimethyldecalin, 54471-59-9; perfluorotri-*n*-butylamine, 311-89-7; perfluoro-*n*-hexane, 355-42-0; *tert*-butyl alcohol, 75-65-0; 2-propanol, 67-63-0; *n*-butanol, 71-36-3; ethanol, 64-17-5; methanol, 67-56-1; 2-phenylethanol, 60-12-8; ethylene glycol, 107-21-1; benzyl alcohol, 100-51-6; 2-chloroethanol, 107-07-3; water, 7732-18-5; *n*-propanol, 71-23-8; trifluoroethanol, 75-89-8; hexafluoroisopropanol, 920-66-1; 2-fluoroethanol, 371-62-0; 2-methoxyethanol, 109-86-4; pyridine *N*-oxide, 694-59-7; 5-fluoroindole, 399-52-0; *n*-heptane, 142-82-5.

Reaction of Triflates with Potassium Diethyl Phosphite. Formation of Phosphate Esters

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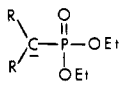
Phenyl triflate and substituted analogues react with potassium diethyl phosphite in liquid ammonia to form aryl diethyl phosphate esters. The reaction formally involves loss of trifluoromethanesulfinate ion from the triflate and concomitant oxidation of phosphorus to the phosphate stage. Preliminary data suggest that, in a series of triflates, reactivity follows the order aryl > cyclohexenyl > cyclopropyl > alkyl. Studies on aryl triflates with added labeled phenoxide rule out a mechanism involving free phenoxide ion, i.e., displacement of phenoxide by nucleophilic attack of diethyl phosphite ion on sulfur followed by phosphorylation of displaced phenoxide. Three potential mechanisms, including one involving initial attack of phosphorus at sulfur, a biphilic insertion mechanism, and one involving nucleophilic attack on oxygen, are suggested, all of which could account for these observations.

The diethylphosphonate group is a well-known carbanion-stabilizing substituent.[1] This feature permits facile generation of anions of general structure **1**. Recently we



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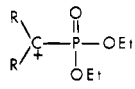
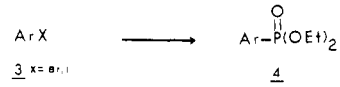


2

have generated carbocations of general structure **2** by the solvolytic route.[2] In view of the unexpected ease of generation of **2**, we wanted to evaluate the electronic properties, both conjugative and inductive, of the diethyl phosphonate group. We therefore wanted to introduce this group onto an aromatic nucleus for potential measurement of σ^+ values and also for potential measurement of effects on benzylic-type free radicals.

Various methods for substitution of $PO(OEt)_2$ for halogen on an aromatic ring have been developed.[3-6] Since the requisite aryl iodides and bromides necessary for the transformation shown below are not always readily

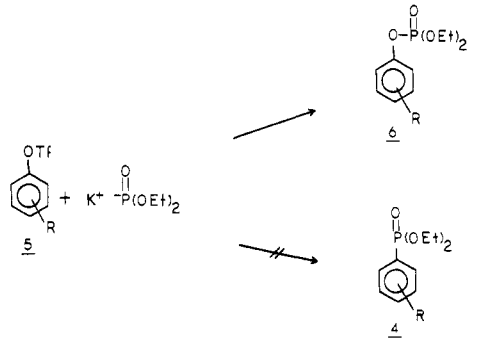


3 X = Br, I **4**

available, we sought to develop a method starting with the more accessible phenols. In principle, conversion of a phenol to the aryl triflate followed by displacement of the triflate leaving group with the anion of diethyl phosphite would lead to the aryl phosphonate **4**. It was hoped that the displacement of the excellent nucleofugic triflate group could be accomplished by either an $S_{RN}1$ mechanism,[7] an SnAr process,[8] or possibly even a direct displacement of triflate.[9] Reported here are the results of a study of the reaction of aryl triflates with potassium diethyl phosphite in liquid ammonia.

Results and Discussion

A variety of phenols were converted to the corresponding triflates **5**. These were added to potassium diethyl phosphite in liquid ammonia at −33 °C. Under these conditions, even in the dark, the triflates were all consumed. However, none of the aryl phosphonates **4** were



5 **6** **4**

formed. The major products were the phosphate esters **6**, along with small amounts of the original phenol (see Table I). The phosphate ester products represent a formal

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(6) (a) Tavs, P. *Chem. Ber.* **1970**, *103*, 2428–2436. (b) Tavs, P.; Korte, F. *Tetrahedron* **1967**, *23*, 4677–4679.

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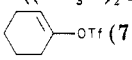
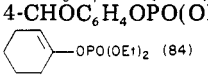
(8) (a) Bunnett, J. F. *Q. Rev., Chem. Soc.* **1958**, *12*, 1–16. (b) Pietra, F. *Ibid.* **1969**, *23*, 504–521.

(9) The possibility of such a process occurring in nucleophilic vinylic substitution has been discussed. See: Rappoport, Z. *Acc. Chem. Res.* **1981**, *14*, 7–15.

0022-3263/83/1948-2887$01.50/0

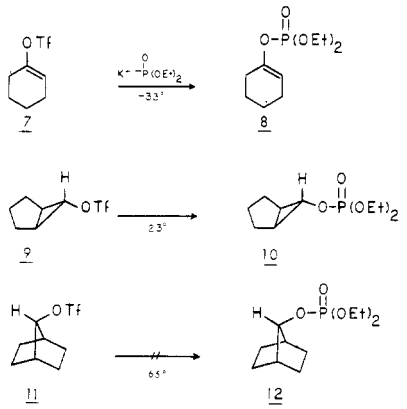
Table I. Reaction of Triflates with Potassium Diethyl Phosphite in Liquid Ammonia

triflate	reaction time, h	products (% yield)[a]
PhOTf (5a)	20	$PhOPO(OEt)_2$ (82), PhOH (13)[b]
4-$CH_3C_6H_4OTf$ (5b)	19	4-$CH_3C_6H_4OPO(OEt)_2$ (89), ArOH (5)[c]
3-$CH_3C_6H_4OTf$ (5c)	6	3-$CH_3C_6H_4OPO(OEt)_2$ (81)[e]
4-*i*-PrC_6H_4OTf (5d)	8	4-*i*-$PrC_6H_4OPO(OEt)_2$ (79)[e]
2,6-$(CH_3)_2C_6H_3OTf$ (5e)	21	2,6-$(CH_3)_2C_6H_3OPO(OEt)_2$ (82), ArOH (12)
4-$CH_3OC_6H_4OTf$ (5f)	18	4-$CH_3OC_6H_4OPO(OEt)_2$ (91), ArOH (*d*)
4-ClC_6H_4OTf (5g)	2.5	4-$ClC_6H_4OPO(OEt)_2$ (79), ArOH (17)[b]
3-ClC_6H_4OTf (5h)	2.5	3-$ClC_6H_4OPO(OEt)_2$ (67), ArOH (30)[c]
4-$((CH_3O)_2CH)C_6H_4OTf$ (5i)	4	4-$CHOC_6H_4OPO(OEt)_2$ (76)[e]
 (7)	32	 (84)

[a] Isolated yield unless otherwise indicated. [b] Yield determined by GC. [c] Estimated yield. [d] Trace amount. [e] Phenol not analyzed for.

oxidation of phosphorus. The sulfur–oxygen bond of the triflate has also been cleaved. Phenyl mesylate was unreactive, even after 1 month in sealed tubes at room temperature.

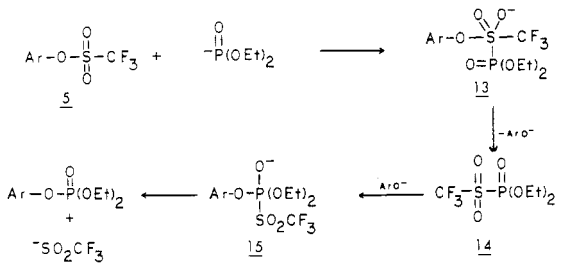
The reaction is relatively insensitive to steric effects as evidenced by the fact that 2,6-dimethylphenyl triflate (**5e**) also reacts quite readily. Qualitatively, electron-withdrawing groups have a slight rate enhancing effect, while the electron donor *p*-methyl and *p*-methoxy groups have little effect on the rate. One sees the reactivity order as *p*-Cl, *m*-Cl > *p*-H, *p*-CH_3, *p*-OCH_3. However, the rate spread is not large; the reactivity range is only about a factor of ten. Cyclohex-1-enyl triflate (**7**) gave an analogous



reaction but at a somewhat slower rate than phenyl triflate. The cyclopropyl triflate **9** reacted quite sluggishly. After 18 h at −33 °C (refluxing ammonia) only a trace of the phosphate **10** was produced. However, over a period of 1 week in sealed tubes at room temperature, **9** was smoothly converted to **10**. Triflate **11** gave no reaction after 1 day in refluxing ammonia or at room temperature. Even at 65 °C no phosphate ester **12** was formed. Reactivity therefore appears to follow the order aryl > vinyl > cyclopropyl > aliphatic triflate.

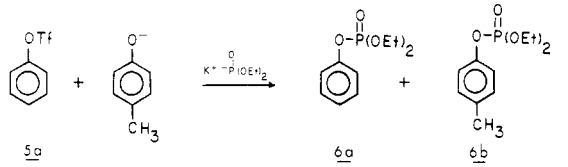
In terms of mechanism, one is tempted to suggest a process involving nucleophilic attack by diethyl phosphite anion at sulfur, loss of phenoxide, and phosphorylation of the expelled phenoxide by $CF_3SO_2PO(OEt)_2$ (**14**, Scheme I). There exists precedence for nucleophilic attack at sulfur of sulfonate esters. Aryl sulfonate esters,[10] aryl

Scheme I



triflates,[11] and vinyl triflates,[12] under more rigorous conditions, are cleaved by nucleophilic attack on sulfur to give phenols. However, in view of the mild conditions (−33 °C) under which the aryl triflates react with diethyl phosphite ion, we sought to obtain further evidence for this mechanism.

It was assumed that if free phenoxide were involved (as in Scheme I), then externally added phenoxide would also intercept the phosphorylating agent, $CF_3SO_2PO(OEt)_2$ (**14**). Accordingly, phenyl triflate was reacted with potassium diethyl phosphite in the presence of an equivalent amount of potassium *p*-methylphenoxide. Under these conditions, at completion of the reaction, both phosphate esters **6a** and **6b** were produced in a 45:55 ratio. A control



experiment showed that **6a** is not converted to **6b** in the presence of *p*-methyl phenoxide. However, more careful monitoring of the reaction showed that the ratio of phosphates **6a** and **6b** was not constant throughout the reaction but *decreased* with time. During the early stages of reaction, at any given time, the *p*-methylphenoxide/phenoxide ratio would be very large. If Scheme I were operating, one would therefore predict that **6b** would be produced in large excess over **6a**. This is exactly the op-

(10) (a) Schmid, H.; Karrer, P. *Helv. Chim. Acta* **1949**, *32*, 1371–1378. (b) Kenner, G. W.; Murray, M. A. *J. Chem. Soc.* **1950**, 406. (c) Bunton, C. A.; Frei, Y. F. *Ibid.* **1951**, 1872–1873. (d) Bunton, C. A.; Welch, V. A. *Ibid.* **1956**, 3240–3242. (e) Oal, S.; Fukumoto, T.; Kiritani, R. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 346–348. (f) Bunnett, J. F.; Bassett, J. Y., Jr. *J. Am. Chem. Soc.* **1959**, *81*, 2104–2109. (g) Bunnett, J. F.; Bassett, J. Y., Jr. *J. Org. Chem.* **1962**, *27*, 2345–2348. (h) Oae, S.; Kiritani, R. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 765–770. (i) Broxton, T. J.; Mac, Y. C.; Parker, A. J.; Ruane, M. *Aust. J. Chem.* **1966**, *19*, 521–523.

(11) (a) Subramaman, L. R.; Hanack, M.; Chang, L. W. K.; Imhoff, M. A.; Schleyer, P. v. R.; Effenberger, F.; Kurtz, W.; Stang, P. J.; Dueber, T. E. *J. Org. Chem.* **1976**, *41*, 4099–4103. (b) Landvatter, S. W.; Katzenellengoben, J. A. *J. Med. Chem.* **1982**, *25*, 1300–1307.

(12) (a) Summerville, R. H.; Senkler, C. A.; Schleyer, P. v. R.; Dueber, T. E.; Stang, P. J. *J. Am. Chem. Soc.* **1974**, *96*, 1100–1110. (b) Stang, P. J.; Magnum, M. G.; Fox, D. P. Haak, P. *Ibid.* **1974**, *96*, 4562–4569. For related examples of nucleophilic attack on sulfur of sulfonate esters see also: (c) Frydman, N.; Bixon, R.; Sprecher, M.; Mazur, Y. *Chem. Commun.* **1969**, 1044–1045. (d) Mendel, A. *J. Org. Chem.* **1966**, *31*, 3445–3446. (e) Gassman, P. G.; Hornback, J. M.; Pascone, J. M. *Tetrahedron Lett.* **1971**, 1425–1526. (f) Bordwell, F. G.; Pitt, B. M.; Knell, M. *J. Am. Chem. Soc.* **1951**, *73*, 5004.

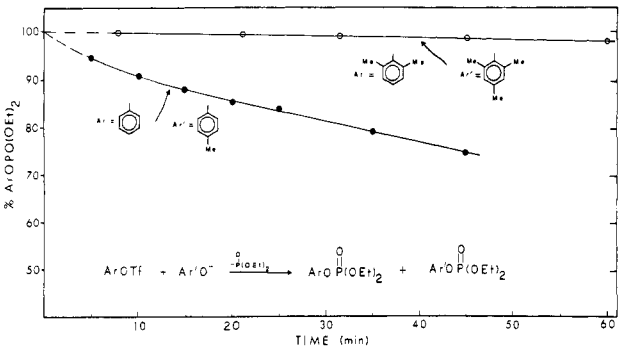
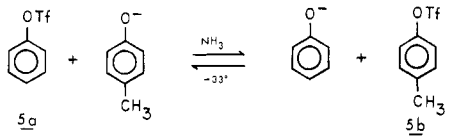


Figure 1. Reaction of ArOTf with potassium diethyl phosphite with added $Ar'O^-$. A plot of percent $ArOPO(OEt)_2$ vs. time.

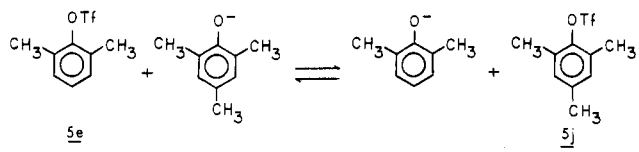
posite of what is observed. Figure 1 shows a plot of the fraction of **6a** formed as a function of time. As the reaction time approaches zero, essentially all of the product is **6a**. This suggests that **6b** arises by some mechanism other than reaction of *p*-methylphenoxide with $CF_3SO_2PO(OEt)_2$.

A control experiment reveals the probable source of **6b**. In the presence of *p*-methylphenoxide, phenyl triflate (**5a**) converts to *p*-methylphenyl triflate, (**5b**) at a rate com-



parable to the rate of reaction of phenyl triflate with diethyl phosphite anion. This surprising facile transformation in liquid ammonia probably occurs by nucleophilic attack on sulfur with expulsion of phenoxide ion.

Figure 1 suggests that free phenoxide is *not* involved in the conversion of phenyl triflate (**5a**) to phosphate **6a** with potassium diethyl phosphite. Further evidence for this suggestion comes from the reaction of 2,6-dimethylphenyl triflate (**5e**) with $K^{+-}PO(OEt)_2$ with added 2,4,6-trimethylphenoxide. After 8 min of reaction time, greater than 99.7% of the product is 2,6-dimethylphenyl diethyl phosphate (**6e**). After 30 min about 1% of the product is now 2,4,6-trimethylphenyl diethyl phosphate, and after 1 h, the amount has increased to 2%. The final ratio of 2,6-dimethylphenyl diethyl phosphate to 2,4,6-trimethylphenyl diethyl phosphate is 88:12. These results are consistent with the expected slow conversion of **5e** to **5j**

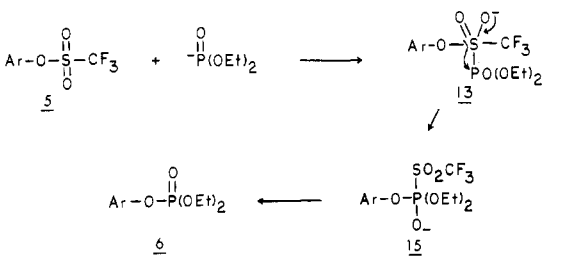


due to steric effects, an expectation born out by a control experiment. However, the conversion of **5e** to **5j** still occurs in liquid ammonia, albeit more slowly than the conversion of **5a** to **5b**. As before, free 2,6-dimethylphenoxide does not appear to be involved in the conversion of **5e** with potassium diethyl phosphite to the phosphate ester **6e**.

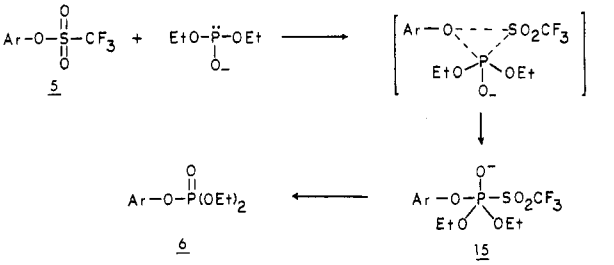
To account for these observations, a certain alternative to Scheme I comes to mind. Intramolecular migration of phenoxide (Scheme II) in the adduct **13** could produce the intermediate **15**. Loss of trifluoromethanesulfinate from **15** would account for the observed product with no incorporation of externally added phenoxide.

An attractive alternative (Scheme III) involves formation of the intermediate **15** via a direct insertion of diethyl phosphite ion into the S–O bond. This concerted insertion (where bond making to S and O may not be completely

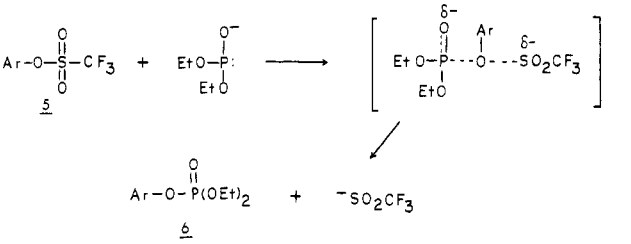
Scheme II



Scheme III



Scheme IV



synchronous) accomplishes steps 1–3 of Scheme I and steps 1 and 2 of Scheme II in a single process. An analogous mechanism has been suggested for the reaction of trialkyl phosphites and phosphines with peroxides[13] and has been termed a "biphilic insertion" mechanism. This process is suggested[13b] to involve interaction of the filled nonbonding orbital of phosphorus with the σ^* antibonding oxygen–oxygen orbital. Concurrently an available d orbital on phosphorus can accept a σ bonding electron pair associated with the oxygen–oxygen bond. Phosphorus will therefore have both nucleophilic and electrophilic properties in such a transformation and hence is termed a biphilic reagent. The mechanism is analogous to the addition of singlet carbenes in a concerted process to a carbon–carbon π bond.[14]

In Scheme III, the S–O bond strength of the triflate should be important in controlling the rate of this biphilic insertion process. The reduced reactivity of **9** and **11** may reflect the expected greater S–O bond strength in the aliphatic triflates **9** and **11** relative to the aryl triflates **5** and cyclohex-1-enyl triflate (**7**).

One additional scheme (Scheme IV) that should be considered is direct displacement of trifluoromethanesulfinate by nucleophilic attack of diethyl phosphite ion on oxygen.[15] This would represent one extreme of the biphilic insertion mechanism. Nucleophilic attack at sulfur

(13) (a) Denney, D. B.; Jones, D. H. *J. Am. Chem. Soc.* **1969**, *91*, 5821–5825. (b) Denney, D. B.; Denney, D. Z.; Hall, C. D.; Marsi, K. L. *Ibid.* **1972**, *94*, 245–249. (c) Baumstark, A. L.; McCloskey, C. J.; Williams, T. E.; Chrisope, D. R. *J. Org. Chem.* **1980**, *45*, 3593–3597. (d) Clennan, E. L.; Heah, P. C. *Ibid.* **1981**, *46*, 4105–4107.

(14) Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971.

(15) Analogous processes involving nucleophilic attack of trivalent phosphorus on halogen have much precident. See: Miller, B. In "Topics in Phosphorus Chemistry"; Wiley: New York, 1965; Vol. 2, p 133–199.

represents the other extreme. In view of the "oxophilic" nature[16] of phosphorus in the phosphite oxidation state and the leaving group ability of trifluoromethanesulfinate ion,[17] such a mechanism must be considered.

Such a displacement on oxygen is also consistent with all of the available data. In this process, electron-withdrawing groups on the aromatic ring are expected to slightly enhance rates. The low reactivity of aliphatic triflates **9** and **11** could be a result of decreased rate of nucleophilic attack at the nonbenzylic oxygen atom in these systems. The same features which lend to increased rates of nucleophilic displacement at benzylic carbon[18] could be operating in such displacements at benzylic oxygen. The lack of a significant steric effect in the reaction of triflate **5e** could be a reflection of a transition state in which phosphorus becomes bonded to a relatively unencumbered divalent oxygen.[19] Clearly, further studies are necessary to determine which of these mechanisms is operative in the conversion of triflates to phosphate esters.

Experimental Section

Preparation of Aryl Triflates. General Procedure. The preparation of aryl triflates **5** was similar to the previously described procedure.[11a] A solution of the appropriate phenol (1 part) in pyridine (7 parts) was cooled to 0 °C, and 1.2 equiv of triflic anhydride was added dropwise. After warming to room temperature and being stirred for 1 h, the mixture was taken up into ether, washed with two portions of water, dilute hydrochloric acid, and saturated sodium chloride solution, and dried over $MgSO_4$. After filtration, the solvent was removed by rotary evaporator, and the residue was distilled at reduced pressure to give the pure triflates **5**. Yields ranged from 91% to 95%.

Preparation of Triflate 5i. *p*-Toluenesulfonic acid dihydrate (50 mg) was added to a solution of 2.18 g of *p*-formylphenyl triflate (prepared as described above from *p*-hydroxybenzaldehyde) in 20 mL of methanol containing 1.24 g of trimethyl orthoformate. A slightly exothermic reaction ensued. The mixture was stirred for 17 h at room temperature. About 20 mg of sodium methoxide was then added, and the solvent was removed by rotary evaporator. Distillation of the residue gave 2.54 g (98%) of triflate **5i**: bp 70–73 °C (0.04 mm); NMR ($CDCl_3$) δ 7.7–7.1 (4 H, AA'BB' q), 5.41 (1 H, s), 3.33 (6 H, s). Anal. Calcd for $C_{10}H_{11}F_3O_5S$: C, 40.00; H, 3.69. Found: C, 39.76; H, 3.65.

Reaction of Triflates with Potassium Diethyl Phosphite in Liquid Ammonia at −33 °C. General Procedure. Potassium metal (0.55 g) was added to 170 mL of freshly distilled anhydrous ammonia under nitrogen. Diethyl phosphite (1.95 g) was added dropwise. Upon completion of the addition the blue color was discharged. The appropriate triflate **5** (0.5 equiv relative to potassium diethyl phosphite) was then added to the stirred solution at reflux temperature. Samples were periodically removed by using a U-shaped dip tube, quenched in ether–water, and analyzed by gas chromatography. After an appropriate reaction time (as determined by GC), the ammonia was allowed to evaporate, and a standard aqueous workup followed. The ether extract was dried over $MgSO_4$, and the solvent was removed by rotary evaporator. The phosphate esters **6** were isolated by distillation at reduced pressure. The following procedure is representative.

p-Methylphenyl triflate (**5b** 1.66 g) was added to the potassium diethyl phosphite solution prepared as described from 0.55 g of potassium and 1.95 g of diethyl phosphite in 170 mL of NH_3. After 19 h, NH_4Cl was added, and the ammonia was allowed to evaporate. An aqueous workup with ether extraction followed. Gas chromatographic analysis showed the presence of about 5% *p*-cresol along with phosphate **6b**. The solution was washed with a dilute KOH solution and saturated sodium chloride solution and dried over $MgSO_4$. After solvent removal by rotary evaporator, the residue was distilled to give 1.50 g (89%) of **6b**: bp 99–101 °C (0.03 mm); NMR ($CDCl_3$) δ 7.16 (4 H, s), 4.20 (4 H, quintet, J = 7.5 Hz), 2.30 (3 H, s), 1.32 (6 H, t, J = 7.5 Hz). The NMR and infrared spectra of **6b** were identical with those of an authentic sample[20] prepared by reaction of phenol with diethyl chlorophosphate in pyridine or NaOH solution. Gas chromatographic analysis showed no phosphonate **4** (R = *p*-CH_3; which could be prepared by the $S_{RN}1$ reaction of *p*-iodotoluene with potassium diethyl phosphite).[3]

Reaction of Cyclohex-1-enyl Triflate (7) with Potassium Diethyl Phosphite. Triflate **7**[21] (636 mg) was added to a solution prepared from 0.22 g of potassium and 0.76 g of diethyl phosphite in 70 mL of ammonia. After 1 h only a small amount of phosphate **8** was present. After 8 h, about 25% of unreacted **7** remained. After 32 h, the ammonia was allowed to evaporate, and a standard workup followed. Distillation gave 541 mg (84%) of **8**:[22] bp 82–83 °C (0.08 mm); NMR ($CDCl_3$) δ 5.48 (1 H, m), 4.16 (4 H, quintet, J = 7.3 Hz), 2.4–1.9 (4 H, m), 1.9–1.4 (4 H, m), 1.35 (6 H, t, J = 7.3 Hz).

Preparation of *exo*-Bicyclo[3.1.0]hex-6-yl Triflate (9). A mixture of *exo*- and *endo*-bicyclo[3.1.0]hexan-6-ol[24a] (exo/endo ratio of 1.8:1) was prepared by using the procedure described for the preparation of *exo*- and *endo*-bicyclo[4.1.0]heptan-7-ol.[23] This alcohol mixture (1.66 g) was added to a solution of 5.70 g of triflic anhydride in 20 mL of pyridine at 0 °C. The mixture was stirred at room temperature for 10 h, and a standard aqueous workup followed. Pyridine was removed from the ether extract by washing with dilute hydrochloric acid. After the organic phase was dried, the solvent was removed by rotary evaporator. Distillation gave 1.89 g (76% based on *exo*-alcohol) of pure triflate **9**,[24] bp 56–59 °C (3.5 mm). No *endo*-triflate was present.

Reaction of *exo*-Bicyclo[3.1.0]hex-6-yl Triflate (9) with Potassium Diethyl Phosphite. Triflate **9** (1.50 g) was added to a solution prepared from 0.51 g of potassium and 1.80 g of diethyl phosphite in 160 mL of ammonia. After 100 min a sample was withdrawn and analyzed by gas chromatography. No reaction was apparent. After 18 h at −33 °C, a trace of phosphate **10** could be seen by GC. Samples of the reaction mixture were then sealed in tubes and allowed to stand at room temperature. After 22 h, a tube was opened (after cooling in dry ice), and the contents were analyzed by gas chromatography after an aqueous workup. About 60% reaction had occurred. After 2 days about 85% reaction had occurred. After 1 week at room temperature, greater than 99% of **9** had reacted. A sample of phosphate **10** was isolated by preparative gas chromatography: NMR ($CDCl_3$) δ 4.12 (4 H, quintet, J = 7 Hz), 3.61 (1 H, s), 1.95–1.45 (7 H, m), 1.35 (6 H, t, J = 7 Hz) 1.10–0.85 (1 H, m). Anal. Calcd for $C_{10}H_{19}O_4P$: C, 51.28; H, 8.18. Found: C, 51.05; H, 8.35.

Preparation of 7-Norbornyl Triflate (11). Bicyclo[2.2.1]-heptan-7-ol[25] (1.00 g; prepared by catalytic hydrogenation of

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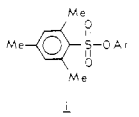
(18) For a discussion of this effect and a compilation of pertinent data, see: Streitwieser, A., Jr. *Chem. Rev.* **1956**, *56*, 571–752.

(19) A relevant study is that of Bunnett and Bassett,[10f,g] who have reported a minimal steric effect in the reactions of i with nucleophiles. Nucleophilic attack at sulfur is not encumbered by the *o*-methyl substituents.



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commercially available 7-acetoxynorbornadiene followed by treatment with methyllithium) was added to a mixture of 3.0 g of triflic anhydride in 15 mL of pyridine at 0 °C. After 90 min at 0 °C a standard aqueous workup was used to isolate 11. Ether was used for extractions. After solvent removal by rotary evaporator, the residue was distilled to give 1.40 g (64%) of triflate 11:[24b] bp 63–65 °C (3 mm); NMR (300 MHz) ($CDCl_3$) δ 4.97 (1 H, brs), 2.38 (2 H, m), 1.92 (2 H, m) 1.65 (2 H, m), 1.44 (2 H, AB q), 1.33 (2 H, AB q).

Reaction of 7-Norbornyl Triflate (11) with Potassium Diethyl Phosphite. 7-Norbornyl triflate (0.60 g) was added to a solution of potassium diethyl phosphite prepared from 0.19 g of potassium and 0.68 g of diethyl phosphite in 100 mL of ammonia. After vigorous stirring of the mixture for 20 min, the triflate dissolved. Gas chromatographic analysis showed no reaction after 10 h at −33 °C. Samples of the solution were sealed in tubes. After 1 day at room temperature, no reaction was apparent. A sample (sealed tube) was then placed in a steel bomb, and liquid ammonia was introduced into the cooled bomb. After sealing, the bomb was placed in a bath and maintained at 65 °C for 35 h. After cooling, the bomb was opened and the tube was removed. After being cooled in dry ice, the tube was opened, and an aqueous workup followed. No phosphate ester **12** was present by gas chromatographic analysis. Much of the triflate **11** had been consumed. Two products of shorter gas chromatographic retention time than **11** were observed along with unreacted **11**. Samples of each product were isolated by preparative gas chromatography. The major product, which could be extracted with dilute hydrochloric acid, was identified as 7-norbornyl amine. The minor product was identified as bicyclo[2.2.1]heptan-7-ol by comparison with an authentic sample.[25]

Reaction of Phenyl Triflate (5a) with Potassium Diethyl Phosphite in the Presence of *p*-Methylphenoxide. A solution of potassium diethyl phosphite in 170 mL of liquid ammonia was prepared as previously described from 0.55 g of potassium and 1.95 g of diethyl phosphite. Potassium (0.26 g) was then added followed by 0.72 g of *p*-cresol. The color was discharged. Phenyl triflate (**5a**, 1.50 g) was then added, and samples were periodically withdrawn, diluted with ether, and extracted with water. The ether extracts were analyzed by gas chromatography. Both phosphates **6a** and **6b** were present. Figure 1 gives the area percent of phosphate **6a** as a function of time. After 17 h, the ratio of **6a** to **6b** was 45:55.

Reaction of 2,6-Dimethylphenyl Triflate (5e) with Potassium Diethyl Phosphite in the Presence of 2,4,6-Trimethylphenoxide. A solution of potassium diethyl phosphite in 170 mL of ammonia was prepared as previously described from 0.55 g of potassium and 1.95 g of diethyl phosphite. Potassium (0.27 g) was added followed by 0.93 g of 2,4,6-trimethylphenol. 2,6-Dimethylphenyl triflate (**5e**, 1.74 g) was added, and the mixture was stirred vigorously for 5 min to dissolve the triflate **5e**. Samples were periodically withdrawn and diluted with ether, and water was added. The ether extracts were analyzed by gas chromatography. After 8 min greater than 99.7% of the product was phosphate **6e**. After 30 min, about 99% of the product was **6e** and 1% of 2,4,6-trimethylphenyl diethyl phosphate had appeared. After 1 h, 2% of this product was present and 8% after 5 h. On completion of the reaction (25 h) the ratio of phosphate **6e** to 2,4,6-trimethylphenyl phosphate was 88:12.

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Registry No. **5a**, 17763-67-6; **5b**, 29540-83-8; **5c**, 32578-31-7; **5d**, 86364-01-4; **5e**, 86364-02-5; **5f**, 66107-29-7; **5g**, 29540-84-9; **5h**, 86364-03-6; **5i**, 86364-04-7; **5** (R = *p*-formyl), 17763-69-8; **6a**, 2510-86-3; **6b**, 4877-08-1; **6c**, 14143-01-2; **6d**, 16462-76-3; **6e**, 39604-15-4; **6f**, 5076-68-6; **6g**, 5076-63-1; **6h**, 32019-36-6; **6i**, 22955-88-0; **7**, 28075-50-5; **8**, 4452-32-8; **9**, 25327-17-7; **10**, 86364-05-8; **11**, 25354-43-2; **12**, 86364-06-9; *p*-toluenesulfonic acid, 104-15-4; *exo*-bicyclo[3.1.0]hexan-6-ol, 13830-42-7; *endo*-bicyclo[3.1.0]hexan-6-ol, 13830-09-6; triflic anhydride, 358-23-6; bicyclo[2.2.1]heptan-7-ol, 2566-48-5; 7-acetoxynorbornadiene, 13426-49-8; potassium *p*-methylphenoxide, 1192-96-7; potassium 2,4,6-trimethylphenoxide, 79719-34-9; 2,4,6-trimethylphenyl diethyl phosphate, 67951-88-6; potassium diethyl phosphite, 54058-00-3.

Conformational and Configurational Studies on *N*-(Substituted phenyl)pyranosylamine Derivatives by High-Resolution Nuclear Magnetic Resonance Spectroscopy[1]

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A series of *N*-(substituted phenyl)-tri-*O*-acetyl-D-xylopyranosylamines (Ia–h) and *N*-(para-substituted phenyl)per-*O*-acetylglycopyranosylamines, including four hexose derivatives (D-glucose, II; D-galactose, III; D-mannose, IV; and L-rhamnose, V) and two pentose derivatives (D-arabinose, VI; D-ribose, VII), has been synthesized and characterized by 270- and 500-MHz NMR spectroscopy. The configuration and conformation of these carbohydrate derivatives were determined by analyzing the chemical shifts and coupling constants by NMR spectroscopy. Most of the synthesized compounds were found to exist in the *C*1 (D) conformation, with the exception of the rhamnosyl and arabinosyl derivatives V and VI which favored the 1*C* (L) and 1*C* (D) conformations, respectively. Compounds Ia–h, II, and III existed in the β configuration, and the rest of the compounds (IV–VII) favored the α configuration.

A series of *N*-glycopyranosylamines has been synthesized,[3a-c] with the objective being the development of agents capable of modifying the biosynthesis of glycosaminoglycans by serving as artificial acceptors for biosynthetic

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(3) (a) Presented in part at the 182nd National Meeting of the American Chemical Society. See: Wang, L.; Maniglia, C. A.; Mella, S. L.; Sartorelli, A. C. In "Abstracts of Papers", 182nd National Meeting of the American Chemical Society, New York, New York, Aug 23–28, 1981; American Chemical Society: Washington, DC; Abstract CARB 23. (b) Wang, L.; Maniglia, C. A.; Mella, S. L.; Sartorelli, A. C. *J. Med. Chem.* **1983**, *26*, 629. (c) Wang, L.; Maniglia, C. A.; Mella, S. L.; Sartorelli, A. C. *J. Med. Chem.*, in press.

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