Acknowledgment. We thank the Belgian National Science Foundation for financial support and for fellowships to P.V. and M.VDA.

Appendix

Starting from the kinetic Scheme I and considering equations for the rates of CIP and SSIP formations, the following classical differential equations are found

$$\ddot{Y} + (k_{DX} + k_{DY})\dot{Y} + (k_{DX}k_{DY} - k^*_1k^*_{-1})[Y^*] = 0 \quad (10)$$

$$\ddot{X} + (k_{DX} + k_{DY})\dot{X} + (k_{DX}k_{DY} - k^*_1k^*_{-1})[X^*] = 0 \quad (11)$$

where

$$\ddot{Y} = d^2[Y^*]/dt^2,\ \ddot{X} = d^2[X^*]/dt^2,$$
$$\dot{Y} = d[Y^*]/dt,\ \dot{X} = d[X^*]/dt$$

The solution of this system of equations is given by eq 4-6 from which the following R and S values may be extracted

$$R = \Lambda\{(k^*_1k_{FY} - k_{FX}(k_{DX} + \lambda_2))\alpha + (k^*_{-1}k_{FY} - k_{FY}(k_{DY} + \lambda_2))(1 - \alpha)\}$$

$$S = \Lambda\{(k^*_{-1}k_{FY} + k_{FX}(k_{DX} + \lambda_1))\alpha + (-k^*_{-1}k_{FX} + k_{FY}(k_{DY} + \lambda_2))(1 - \alpha)\}$$

where $\Lambda = 1/(\lambda_1 - \lambda_2)$, and α and $(1 - \alpha)$ represent the molar fractions of the excited CIP and SSIP, respectively.

Acetylenic Esters. Preparation and Characterization of Alkynyl Dialkyl Phosphates, RC≡COPO(OR′)$_2$†

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Abstract: The first synthesis of acetylenic phosphates is reported. Reaction of PhIO with $BF_3{\cdot}OEt_2$ followed by treatment with aqueous $NaO_2P(OR')_2$, or anion exchange of alkynyl(phenyl)iodonium tosylates with $NaO_2P(OR')_2$, gives good yields of alkynyl dialkyl phosphates. These new phosphate esters are characterized by spectral means and show highly characteristic IR and ^{13}C NMR absorptions. The scope and limitations of this methodology are discussed along with mechanistic considerations.

Acetylenic esters represent a distinct, new class of compounds that combine two of the most valuable and important functionalities in organic chemistry into a single, unusual derivative. Recently we reported the synthesis and characterization of alkynyl sulfonates[2] and alkynyl carboxylates,[3] the first known members of the family of alkynyl esters. Besides sulfonate and carboxylate esters the third major and significant class of esters are phosphates. Phosphate esters play a key role in mechanistic and bioorganic chemistry.[4] Despite the importance and variety of phosphate esters as well as the availability of numerous functionalized acetylenes[5] alkynyl phosphates are to date unknown. Hence, we wish to report a general, simple procedure for the preparation as well as the spectral characterization of a variety of alkynyl dialkyl phosphates.[6]

Results and Discussion

Phosphate esters, like carboxylate esters, are normally prepared by reaction of an appropriate phosphorus halide with the respective alcohol, or an enolate if a vinyl phosphate ester is desired. As ynols, RC≡COH, are unknown,[7] this simple, standard procedure cannot be employed for the formation of alkynyl phosphates. Likewise, the standard methods for acetylene formation[5] are, at least in our hands, inapplicable to the synthesis of alkynyl phosphates. Hence, the lack of simple, standard methods for the preparation of alkynyl phosphates might at least partially account for the hitherto unknown nature of this unusual, albeit simple, class of functionalized organic derivatives.

Our recent success in the preparation of alkynyl sulfonate esters[2] and alkynyl carboxylates[3] via tricoordinate iodonium species prompted us to examine this novel route as a possible means to the desired alkynyl phosphate esters. Specifically, we explored the formation, and subsequent decomposition, of alkynyl(phenyl)iodonium phosphates **5** as outlined in Scheme I.

Three different methods were examined for the formation of alkynyl(phenyl)iodonium phosphate **5**, the key intermediate in our tricoordinate iodine methodology for alkynyl esters preparation. Method A involves the interaction of readily available 1-alkynylsilanes **1** with iodosobenzene, **2**, in analogy with our recently reported,[11] much improved, synthesis of the analogous tricoordinate

† Dedicated to Professor William G. Dauben on the occasion of his 70th birthday.

(1) (a) HOECHST AG Postdoctoral Fellow. (b) DFG Postdoctoral Fellow.

(2) Stang, P. J.; Surber, B. W.; Chen, Z. C.; Roberts, K. A.; Anderson, A. G. *J. Am. Chem. Soc.* **1987**, *109*, 228.

(3) Stang, P. J.; Boehshar, M.; Wingert, H.; Kitamura, T. *J. Am. Chem. Soc.* **1988**, *110*, 3272.

(4) Inter alia: Walsh, C. *Enzymatic Reaction Mechanisms*; W. H. Freeman & Co.: San Francisco, 1979. *Transition States of Biochemical Processes*; Grandour, R. D., Schowen, R. L., Eds.; Plenum Press: New York, 1978. Metzler, D. *Biochemistry: The Chemical Reactions of Living Cells*; Academic Press: New York, 1977. Lehninger, A. *Biochemistry*, 2nd ed.; Worth: New York, 1975.

(5) Reviews: Viehe, H. G. *Chemistry of Acetylenes*: Marcel Dekker: New York, 1969. Jäger, V.; Viehe, H. G. In *Methoden der Organischen Chemie* (Houben-Weyl); Georg Thieme Verlag: Stuttgart, Federal Republic of Germany, 1977; 5/2a, Chapter 1, pp 1-961. *The Chemistry of the Carbon-Carbon Triple Bond*; Patai, S., Ed.; Wiley-Interscience: London, 1978; Parts 1 and 2.

(6) For a preliminary report, see: Stang, P. J.; Boehshar, M.; Lin, J. *J. Am. Chem. Soc.* **1986**, *108*, 7832.

(7) Alkynols, analogous to enols, are in tautomeric equilibrium with ketenes: RC≡COH ⇄ RCH=C=O. Ab initio calculations[8] indicate that ketene is 36 kcal/mol more stable than the parent hydroxyacetylene. This is considerably greater than the calculated enol-keto energy difference of 11 kcal/mol for the vinyl-alcohol-acetaldehyde system. Yet the barrier to interconversion of HC≡COH → H_2C=C=O is very high at 73 kcal/mol as determined by calculations.[8] Stable enols are well known.[9] Recently the parent hydroxyacetylene HC≡COH was observed by tandem mass spectrometry in the gas phase.[10]

(8) Bouma, W. J.; Nobes, R. H.; Radom, L.; Woodward, C. E. *J. Org. Chem.* **1982**, *47*, 1869 and references therein.

(9) For a review on stable enols, see: Hart, H. *Chem. Rev.* **1979**, *79*, 515. For simple enols and more recent references, see: Chiang, Y.; Kresge, A. J.; Walsh, P. A. *J. Am. Chem. Soc.* **1986**, *108*, 6314.

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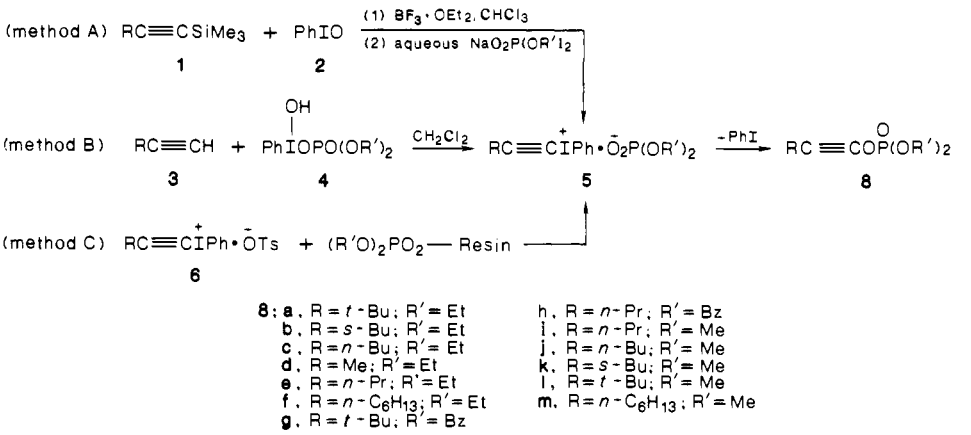
Scheme I



alkynyl(phenyl)iodonium arylsulfonates **6**. Method B parallels our initially reported[2] formation of analogous **6**, via the interaction of terminal alkynes with phenylhydroxyiodonium phosphate **4**, based upon procedures originally developed by Koser and coworkers[12] involving the related phenylhydroxyiodonium tosylate, **9** PhIOH·OTs.[13] Finally, method C takes advantage of the ionic character[2] of tricoordinate iodonium salts. In analogy with our alkynyl benzoate formation[3,6] exchange of the tosylate in **6**, by means of an amberlyst ion-exchange resin, leads to the formation of **5** and thence to **8**.

Our observations suggest that alkynyl(phenyl)iodonium phosphates **5** are intermediate in stability between the related stable, isolable[2] alkynyl(phenyl)iodonium arylsulfonates **6** and the not isolable, unstable[3] alkynyl(phenyl)iodonium carboxylates, $RC{\equiv}CI^{+}Ph{\cdot}{}^{-}O_2CR'$. Specifically, **5a–c**, where **a**, R = *t*-Bu; R' = Et; **b**, R = *t*-Bu; R' = C_6H_5; and **c**, R = *s*-Bu, R' = Ph, were isolated and characterized as stable crystals, whereas all other alkynyl(phenyl)iodonium phosphates **5** could not be isolated as they decomposed, under the reaction conditions, via loss of iodobenzene, to give the desired alkynyl phosphates **8**. In fact, upon standing at room temperature for a few hours, or slight warming, in CH_2Cl_2 or $CHCl_3$, *all* alkynyl(phenyl)iodonium phosphates **5** smoothly decomposed, via loss of iodobenzene, to the product alkynyl phosphate esters **8** as summarized in Table I.

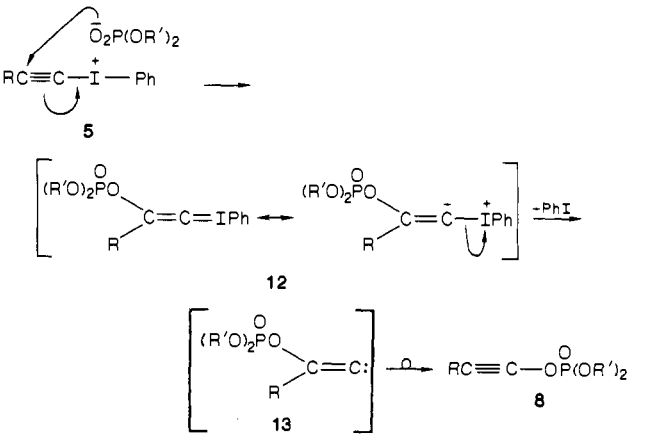
As the data in Table I indicate method A consistently resulted in higher yields of alkynyl phosphate esters **8** than either method B or C and hence is clearly the method of choice for the ready preparation of these novel, new phosphate esters. As seen in Table I this method readily affords a wide variety of alkynyl dialkyl phosphates in reasonable isolated yields (31–58%). These new alkynyl dialkyl phosphate esters **8** are stable, yellow, clear, liquid compounds.

Characterization of Alkynyl Phosphates 8. All new alkynyl phosphates were characterized by spectral and analytical means as summarized in Table I and the Experimental Section.

In particular, all alkynyl phosphates give characteristic mass spectra via chemical ionization (CI) using methane (CH_4) as the ionizing gas. Appropriate high resolution mass spectra are reported for all new compounds. The infrared shows very characteristic, strong absorptions between 2260 and 2295 cm^{-1} due to the unsymmetrical carbon–carbon triple bond along with typical, intense P=O absorption between 1275 and 1305 cm^{-1}.

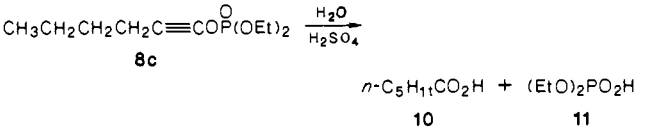
All proton NMR absorptions for **8** are consistent with the proposed structures. Particularly characteristic are the long range couplings of about 8 Hz between the phosphorus and the hydrogen(s) on the α-carbon of the dialkyl moiety. Uniquely characteristic and particularly valuable are the ^{13}C NMR signals,

Scheme II



especially the resonances due to the two acetylenic carbons. The α-carbons resonate between 78 and 80 ppm and have a long range phosphorus–carbon coupling of $^2J_{P,C} = 10 \pm 1$ Hz, whereas the β-carbons absorb between 35 and 48 ppm and have a long range phosphorus–carbon coupling of $^3J_{P,C} = 6$ Hz. Likewise the α-carbons on the dialkyl moeity have a long range carbon–phosphorus coupling of $^2J_{P,C} = 6$ Hz. The upfield shifts of the β-acetylenic carbons, as expected, are typical for these electron-rich unsymmetrical alkynes.[2,3]

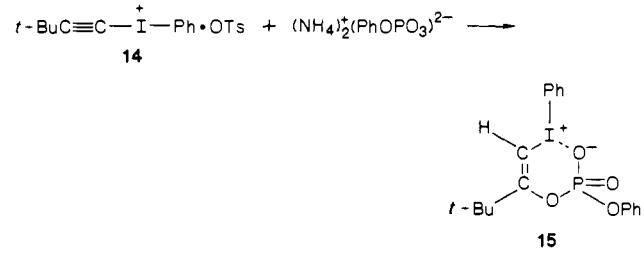
Chemical characterization is afforded by the acid-catalyzed hydrolysis of these alkynyl phosphates. For example, reaction of diethyl 1-hexynyl phosphate (**8c**) in aqueous sulfuric acid gives[14] the expected *n*-hexanoic acid, **10**, derived from the alkynyl moiety along with the diester **11** from the acyl portion of the molecule



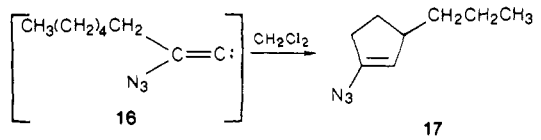
Mechanistic Considerations. Unlike the coupling of alkynyl(phenyl)iodonium sulfonates to give alkynyl sulfonates[2] and analogous to the rapid spontaneous decomposition of alkynyliodonium carboxylates to alkynyl carboxylates,[3] the loss of iodobenzene from alkynyl phosphates **5** to give esters **8** does not require metal catalysis. Hence, this process is likely to involve alkylidenecarbenes and/or their iodonium ylides as outlined in Scheme II. Addition of the nucleophilic phosphate ion to the β-carbon of **5** gives carbene ylide **12**. Evidence for such a β-addition and ylide formation derives from the isolation[15] of zwit-

(10) Schwarz, H.; Weiske, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 282.
(11) Kitamura, T.; Stang, P. J. *J. Org. Chem.* **1988**, *53*, 4105.
(12) Rebrovic, L.; Koser, G. F. *J. Org. Chem.* **1984**, *49*, 4700. Koser, G. F.; Rebrovic, L.; Wettach, R. H. *J. Org. Chem.* **1981**, *46*, 4324.
(13) Koser, G. F.; Wettach, R. H. *J. Org. Chem.* **1977**, *42*, 1476. See, also: Neiland, O.; Karele, B. *J. Org. Chem. USSR (Engl. Transl.)* **1970**, *6*, 889.
(14) Allen, A. D.; Tidwell, T. T.; Roberts, K. A.; Kitamura, T.; Stang, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 622.
(15) Stang, P. J.; Wingert, H.; Arif, A. M. *J. Am. Chem. Soc.* **1987**, *109*, 7235.

terionic species **15** from **14**. Loss of iodobenzene from **12** results



in alkylidenecarbene **13** that rapidly rearranges to the product phosphate ester **8**. Evidence for the possible involvement of **13** comes from the intramolecular trapping via C–H insertion of the analogous ylide derived β-azidocarbene **16** to give **17** in 58%



yield.[16] A similar intramolecular trapping of an iodonium ylide derived alkylidenecarbene has been reported by Ochiai[17] who also recently reported the generation and trapping of alkylidenecarbenes generated via the iodonium ylide derived from vinyl(phenyl)-iodonium tetrafluoroborates.[18] The subsequent rapid rearrangement of alkylidenecarbenes, such as **13**, to alkynes is well established.[19]

Conclusions

Hitherto unknown alkynyl phosphates, the third major member of the novel family of acetylenic esters that combine two of the common and simple organic functionalities into a single, unusual derivative, have been prepared. A variety of alkynyl dialkyl phosphates **8** were isolated in reasonable yields via alkynyl(phenyl)iodonium dialkyl phosphates **5** obtained in a single step from simple precursors. Alkynyl phosphates **8** are stable pale yellow oils with very characteristic infrared and ^{13}C NMR properties. Further work on the chemistry and biochemistry[20] of these novel phosphate esters is underway and will be the subject of future reports.

Experimental Section

General Methods. Melting points (uncorrected) were obtained with a Mel-Temp capillary melting point apparatus. NMR spectra were recorded on either a Varian EM 390 or a Varian XL 300 spectrometer. Chemical shifts (^1H, ^{13}C) are reported relative to internal tetramethylsilane. EI, CI, and high resolution mass spectra were obtained on a VG Micromass 7070-E double focusing high resolution mass spectrometer, operating at 5 kV with a VG Analytical DS 2050 data system.

Materials. Iodosobenzene was prepared from commercial (Aldrich) iodobenzene diacetate and sodium hydroxide via a standard procedure.[21] Acetylenes were purchased from Farchan Laboratories. The preparation of alkynyl(phenyl)iodonium tosylates **6** has been described in detail.[2,11] Dibenzyl and diphenyl phosphates were purchased from Aldrich, and their sodium salts were prepared by mixing with anhydrous sodium carbonate. The sodium salts of diethyl and dimethyl phosphates were prepared by literature procedure.[22] BF_3 etherate was purchased from MCB and distilled from granular CaH_2 prior to use. Phenylhydroxyiodonium tosylate, **9**, was prepared by Koser's method.[13] 1-Trimethylsilylacetylenes were prepared from 1-alkynes by established methods. Silica gel (Davisil) was not activated prior to use.

Phenylhydroxyiodonium Diethyl Phosphate (4). A solution of phenylhydroxyiodonium tosylate,[13] **9** (3.9 g, 10 mmol), and sodium diethyl phosphate (1.76 g, 10 mmol) in methanol (35 mL) was stirred for 12 h at room temperature under argon. After evaporation of the methanol CH_2Cl_2 was added, and the precipitated sodium tosylate filtered off. The CH_2Cl_2 was evaporated, and the residual oil was dried in vacuo resulting in 3.7 g (99%) of **4** as a pale yellow viscous oil. Attempts to crystallize **4** failed; the viscous oil may be used as is: IR (neat) cm^{-1} 3400–2100 (br, shallow, OH), 3060 (m), 2980 (vs), 2950 (s), 2900 (s), 1570 (m), 1470 (s), 1440 (s), 1390 (s), 1230–1150 (vs), 1070–950 (vs); ^1H NMR ($CDCl_3$) δ 1.16 (t, $^3J_{H,H}$ = 7 Hz, CH_3), 3.83 (dq, $^3J_{H,H}$ = 7 Hz, $^3J_{P,H}$ = 12 Hz, CH_2), 7.20–7.46 (m, ArH), 7.83–7.95 (m, ArH), 11.30 (br s, OH); ^{13}C NMR ($CDCl_3$) δ 16.01 (d, $^3J_{P,C}$ = 7 Hz, CH_3), 61.96 (d, $^2J_{P,C}$ = 6 Hz, CH_2), 125.02, 130.42, 131.03, 132.64 (Ar C).

General Procedure for the Preparation of Alkynyl Phosphates. *n*-Butylethynyl Diethyl Phosphate (8c). Method A. To a suspension of iodosobenzene (1.1 g, 5 mmol) and 1-trimethylsilyl-1-hexyne (0.77 g, 5 mmol) in $CHCl_3$ (10 mL) at 0 °C was slowly added 0.6 mL (5 mmol) of $BF_3{\cdot}OEt_2$, and after addition the mixture was stirred at room temperature for 3 h (until the PhIO depolymerized, and the suspension became a clear, homogeneous yellow solution). The organic solution was recooled to 0 °C, a solution of sodium diethyl phosphate (3.5 g, 20 mmol) in water (30 mL) was added, and the mixture was vigorously stirred for about 3–5 min. The organic layer was separated, and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was washed with water and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a yellow oil whose infrared adsorption (2170, 2140–2100, 1080 cm^{-1}) indicated the presence of crude *n*-butylethynyl(phenyl)iodonium diethyl phosphate **5** i.e., **5b**. Stirring this yellow oil in CH_2Cl_2 (40 mL) for 16 h at room temperature resulted in crude **8c**, iodobenzene, and impurities. After evaporation of the solvent the crude mixture was purified by column chromatography on silica gel (100 g) by using first a mixture of CH_2Cl_2/hexane as eluent followed by pure CH_2Cl_2 resulting in 0.37 g (31%) of **8c** as a yellow oil. HRMS (CI; CH_4 as ionizing gas) for $C_{10}H_{19}PO_4(M^+)$ calcd 234.1021, found 234.1023.

***n*-Butylethynyl Diethyl Phosphate (8c). Method B.** A solution of phenylhydroxyiodonium diethyl phosphate (3.75 g, 10 mmol), 1-hexyne (3.4 mL, 30 mmol), and t.h.e. desicant (10 g) in CH_2Cl_2 (60 mL) was refluxed for 3 h. After removal of the desiccant the solvent was evaporated, and the residue was chromatographed on silica gel (120 g). Successive elution with 50% CH_2Cl_2–hexane, pure CH_2Cl_2, 5% acetone–, 10% acetone–, and 20% acetone–CH_2Cl_2 gave, after evaporation of the solvent, 0.44 g (19%) of **8c**.

***n*-Butylethynyl Diethyl Phosphate (8c). Method C (Ion-Exchange Reaction). (a) Preparation of Ion-Exchange Resin.** A chromatography column was loaded with Amberlyst A-26 ion-exchange resin (100 mL) and was successively rinsed with H_2O (300 mL), 1 M NaOH (300 mL), H_2O (300 mL), 1 M aqueous $NaO_2P(OEt)_2$ (300 mL), H_2O (300 mL), CH_3CN (300 mL), and finally with CH_2Cl_2 (300 mL). The resulting diethyl phosphate-loaded amberlyst resin was air dried and then dried in vacuo.

(b) Ion-Exchange Reaction. A chromatography column packed with the above diethyl phosphate-loaded resin (100 mL) was rinsed with CH_2Cl_2. A solution of *n*-butylethynyl(phenyl)iodonium tosylate[2] (2.03 g, 4.44 mmol) in CH_2Cl_2 (5 mL) was placed on the resin and then eluted with CH_2Cl_2 (150 mL) at a rate of about 1 drop/s. After evaporation of the CH_2Cl_2 the crude residue was subjected to column chromatography on silica gel (100 g) and eluted with CH_2Cl_2/hexane and CH_2Cl_2 followed by 5% acetone/hexane, resulting in 0.177 g (17%) of **8c**.

***sec*-Butylethynyl Diethyl Phosphate (8b). Method B.** A solution of phenylhydroxyiodonium diethyl phosphate (3.74 g, 10 mmol), 3-methyl-1-pentyne (1.8 g, 22 mmol), and t.h.e. desiccant (4 g) in CH_2Cl_2 (60 mL) was refluxed for 9 h. Workup gave 1.09 g (46%) of **8b** as a yellow oil: HRMS (CI; CH_4) for $C_{10}H_{20}PO_4$ (M^+ + H) calcd 235.1099, found 235.1103.

***sec*-Butylethynyl Diethyl Phosphate (8b). Method C.** A solution of *sec*-butylethynyl(phenyl)iodonium tosylate[2] (2.3 g, 5 mmol) in CH_2Cl_2 (5 mL) was chromatographed with 200 mL of CH_2Cl_2 on a column loaded with diethylphosphate resin. After evaporation of the solvent, the residue was stirred in $CHCl_3$ (2 mL) for 20 h at room temperature. Workup gave 300 mg (25%) of **8b**.

***tert*-Butylethynyl Diethyl Phosphate (8a). Method A.** A mixture of 3,3-dimethyl-1-(trimethylsilyl)-1-butyne (1.54 g, 10 mmol), iodosobenzene (2.2 g, 10 mmol), and $BF_3{\cdot}OEt_2$ (1.2 mL, 10 mmol) in $CHCl_3$ (20 mL) was stirred at room temperature for 3 days followed by reaction with a solution of $NaO_2P(OEt)_2$ (7.0 g, 40 mmol) in water (40 mL). Extraction with $CHCl_3$ and removal of the solvent gave a yellow oil (probably the iodonium diphosphate) that was stirred in CH_2Cl_2 at room temperature for 24 h. Workup gave 1.3 g (55%) of **8a** as a yellow oil:

(16) Kitamura, T.; Stang, P. J. *Tetrahedron Lett.* **1988**, *29*, 1887.
(17) Ochiai, M.; Kunishima, M.; Nagao, Y.; Fuji, K.; Shiro, M.; Fujita, E. *J. Am. Chem. Soc.* **1986**, *108*, 8281.
(18) Ochiai, M.; Takaoka, Y.; Nagao, Y. *J. Am. Chem. Soc.* **1988**, *110*, 6565.
(19) Stang, P. J. *Acc. Chem. Res.* **1982**, *15*, 348. Stang, P. J. *Chem. Rev.* **1978**, *78*, 383.
(20) The analogous alkynyl carboxylates are potent inhibitors of serine-based proteases: Segal, D.; Shalitin, Y., private communication.
(21) Saltsman, H.; Sharefkin, J. G. *Organic Synthesis*; Wiley: New York, Collect. Vol. 4, p 659.
(22) McIvor, R. A.; McCarthy, G. D.; Grant, G. A. *Can. J. Chem.* **1956**, *34*, 1819.

Table I. Summary of Yield and Spectral Properties of Alkynyl Phosphates **8**

alkynyl phosphates	yield (%)	IR [cm^{-1}]	^1H NMR ($CDCl_3$, δ)	^{13}C NMR ($CDCl_3$, δ)	MS (CI, CH_4) [m/z, %]
8a	55[a] 33[b] 50[c]	2965–2910 (vs), 2865 (s), 2290 sh [C≡C], 2270 (s), [C≡C], 1475 (s), 1305–1280 (vs) [PO], 1060–1010 (vs) [POEt]	4.23 (dg, $^3J_{H,H}$ = 7.5, $^3J_{P,H}$ = 8.5 Hz, $POCH_2$), 1.36 (dt, $^3J_{H,H}$ = 7.5, $^4J_{P,H}$ = 1.3 Hz, $POCCH_3$), 1.17 (s, *t*-Bu)	79.07 (d, $^2J_{P,C}$ = 11.4 Hz, C-α), 65.84 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$), 47.75 (d, $^3J_{P,C}$ = 6 Hz, C-β), 31.24 [$(CH_3)_3$], 26.18 (CMe_3), 15.98 (d, $^3J_{P,C}$ = 6 Hz, $POCCH_3$)	469 [54] $2M^+ + 1$, 371 [71] $2M^+$ – BuC≡CO, 235 [100] $M^+ + 1$, 179 [92] $M^+ + 1 - C_4H_8$, 138 [24] $PO(OEt)_2$, 97 [69] BuC≡CO
8b	46[b] 25[c]	2965 (vs), 2930 (vs), 2875 (s), 2280 (vs) [C≡C], 1455 (s), 1305–1280 (vs) [PO], 1230 (vs), 1060–1010 (vs) [POEt]	4.28 (dq, $^3J_{H,H}$ = 7.5, $^3J_{P,H}$ = 8.5 Hz, $POCH_2$), 2.34 (m, CH_3), 1.40 (m, CH_2 and dt, $^3J_{H,H}$ = 7.5, $^4J_{P,H}$ = 1.3 Hz, $POCCH_3$), 1.13 (d, $^3J_{H,H}$ = 7.0 Hz, CH_3), 0.97 (t, $^3J_{H,H}$ = 7.5 Hz, CH_3)	80.16 (d, $^2J_{P,C}$ = 9 Hz, C-α), 65.88 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$), 43.86 (d, $^3J_{P,C}$ = 6 Hz, C-β), 30.09, 26.01, 20.98, 11.71 (*s*-Bu), 16.02 (d, $^3J_{P,C}$ = 8 Hz, $POCCH_3$)	389 [3] $M^+ + H_2O_2P(OEt)_2$, 291 [4], M^+ + Bu, 235 [23] $M^+ + 1$, 179 [16] $M^+ + 1 - C_4H_8$, 155 [100] $H_2O_2P(OEt)_2$, 137 [51] $PO(OEt)_2$, 127 [66] $H_2O_2PO(OEt)$, 109 [96], HOPO(OEt), 97 [92] BuC≡CO
8c	31[a] 19[b] 17[c]	2980 sh (s), 2955 (s), 2930 (s), 2860 (s), 2280 (s) [C≡C], 1465–1430 (m), 1295 (vs) [PO], 1230 (vs), 1060–1005 (vs) [POEt]	4.23 (dq, $^3J_{H,H}$ = 7.5, $^3J_{P,H}$ = 8.5 Hz, $POCH_2$), 2.12 (m, CH_2), 1.40 (m, CH_2CH_2 and dt, $3J_{H,H}$ = 7.5, $^4J_{P,H}$ = 1.3 Hz, $POCCH_3$), 0.90 (m, CH_3)	79.37 (d, $^2J_{P,C}$ = 10 Hz, C-α), 65.73 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$), 39.53 (d, $^3J_{P,C}$ = 6 Hz, C-β), 30.78, 21.61, 16.26, 13.33 (*n*-Bu), 15.77 (d, $^3J_{P,C}$ = 8 Hz, $POCCH_3$)	469 [76] $2M^+ + 1$, 389 [10] $M^+ + H_2O_2P(OEt)_2$, 371 [5] $2M^+$ – BuC≡CO, 291 [11] M^+ + Bu, 235 [100] $M^+ + 1$, 155 [36] $H_2O_2P(OEt)_2$, 127 [14] $H_2O_2PO(OEt)$, 109 [16] HOPO(OEt)
8d	40[a]	2980 (s), 2920 (s), 2860 (m), 2290 (s) [C≡C], 1440 (s), 1290–1280 (vs) [PO], 1245 (vs), 1050–1010 (vs) [POEt]	4.27 (dq, $^3J_{H,H}$ = 7, $^3J_{P,H}$ = 8.5 Hz, $POCH_2$), 1.73 (d, $^5J_{P,H}$ = 4 Hz, MeC≡C), 140 (dt, $^3J_{H,H}$ = 7, $^4J_{P,H}$ = 1 Hz, $POCCH_3$)	78.01 (d, $^2J_{P,C}$ = 10 Hz, C-α), 65.62 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$), 35.00 (d, $^3J_{P,C}$ = 6 Hz, C-β), 15.62 (d, $^3J_{P,C}$ = 6 Hz, $POCCH_3$) 0.96 (Me)	193 [87] $M^+ - 1$, 192 [11] M^+, 165 [12] $M^+ + 1 - C_2H_4$, 137 [100] $OP(OEt)_2$, 109 [78] HOPO(OEt)
8e	44[a]	2990 sh (s), 2970 (vs), 2915 sh (s), 2875 (s), 2290 (vs) [C≡C], 1460–1440 (m), 1300–1290 (vs) [PO], 1230 (vs), 1060–1010 (vs) [POEt]	4.20 (dq, $^3J_{H,H}$ = 7, $^3J_{P,H}$ = 8.5 Hz, $POCH_2$), 2.07 (dt, $^3J_{H,H}$ = 7, $^5J_{P,H}$ = 3.5 Hz, CH_2), 1.53 (m, CH_2), 137 (dt, $^3J_{H,H}$ = 7, $^4J_{P,H}$ = 1 Hz, $POCCH_3$), 0.93 (t, $^3J_{H,H}$ = 7 Hz, CH_3)	79.21 (d, $^2J_{P,C}$ = 10 Hz, C-α), 65.38 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$), 38.93 (d, $^3J_{P,C}$ = 6 Hz, C-β), 21.77, 18.18, 12.74 (*n*-Pr), 15.38 (d, $^3J_{P,C}$ = 5 Hz, $POCCH_3$)	221 [79] $M^+ + 1$, 193 [44], $M^+ + 1 - C_2H_4$, 192 [42] $M^+ + 1 - C_2H_5$, 137 [97] $OP(OEt)_2$, 109 [100] HOPO(OEt)
8f	42[a]	2990 sh (s), 2960 (vs), 2935 (vs), 2860 (vs), 2290 (vs) [C≡C], 1470–1435 (m), 1300–1290 (vs) [PO], 1230 (vs), 1055–1015 (vs) [POEt]	4.27 (dq, $^3J_{H,H}$ = 7, $^3J_{P,H}$ = 8.5 Hz, $POCH_2$), 2.12 (m, CH_3), 1.38 (dt, $^3J_{H,H}$ = 7, $^4J_{P,H}$ = 1 Hz, $POCCH_3$), 1.33 ($CH_2CH_2CH_2CH_2$), 0.90 (m, CH_3)	79.18 (d, $^3J_{P,C}$ = 10 Hz, C-α), 65.47 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$), 39.27 (d, $^3J_{P,C}$ = 6 Hz, C-β), 30.91, 28.46, 28.02, 22.14, 16.33, 13.55 (*n*-Hex), 15.52 (d, $^3J_{P,C}$ = 6 Hz, $POCCH_3$)	263 [56] $M^+ + 1$, 163 [17] $M^+ + 1 - C_5H_{10}$, 155 [100] $H_2O_2P(OEt)_2$, 137 [14] $OP(OEt)_2$, 127 [60] $H_2O_2P(OEt)$, 109 [49] HOPO(OEt)
8g	57[a]	3065 (m), 3035 (m), 2970 (vs), 2930 (m), 2900 (m), 2865 (m), 2300 (s) [C≡C], 2275 (s) [C≡C], 1495 (m), 1475 (m), 1455 (s), 1300 (vs) [PO], 1140 (vs), 1040–995 (vs) [POBz]	7.23 (s, Ph), 5.10 (d, $^3J_{P,H}$ = 8 Hz, $POCH_2$), 1.13 (s, *t*-Bu)	134.47 (d, $^3J_{P,C}$ = 7 Hz, Ar C), 128.66, 128.39, 127.83 (Ar C), 78.80 (d, $^2J_{P,C}$ = 10 Hz, C-α), 70.85 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$-), 48.06 (d, $^3J_{P,C}$ = 6 Hz, C-β), 31.14 (CMe_3), 26.11 (d, $^4J_{P,C}$ = 2 Hz, CMe_3)	358 [4] M^+, 343 [4] $M^+ - CH_3$, 267 [12] $M^+ - CH_2Ph$, 245 [6] $P(OCH_2Ph)_2$, 173 [63] $H_2O_2P(OCH_2Ph)$, 91 [100] CH_2Ph
8h	45[a]	3065 (m), 3035 (m), 2965 (s), 2935 (m), 2870 (m), 2295 (s) [C≡C], 1495 (m), 1455 (s), 1295 (vs) [PO], 120 (vs), 1050–990 (vs), [POBz]	7.23 (s, Ph), 5.10 (d, $^3J_{P,H}$ = 8 Hz, $POCH_2$), 2.03 (dt, $^3J_{H,H}$ = 7, $^5J_{P,H}$ = 4 Hz, CH_2), 1.43 (m, CH_2), 0.90 (t, $^3J_{H,H}$ = 7 Hz, CH_3)	134.33 (d, $^3J_{P,C}$ = 7 Hz, Ar C, 128.57, 128.28, 127.80 (Ar C), 79.30 (d, $^2J_{P,C}$ = 10 Hz, C-α), 70.77 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$-), 39.90 (d, $^3J_{P,C}$ = 6 Hz, C-β), 22.06, 18.60, 13.25 (*n*-Pr)	344 [2] M^+, 253 [6] $M^+ - CH_2Ph$, 91 [100] CH_2Ph
8i	41[a]	2965 (vs), 2935 (s), 2875 (s), 2290 (vs) [C≡C], 1460–1450 (s), 1300 (vs) [PO], 1230 (vs), 1060–1030 (vs), [POMe]	3.90 (d, $^3J_{P,H}$ = 12 Hz, POMe), 2.10 (dt, $^3J_{H,H}$ = 7, $^5J_{P,H}$ = 3 Hz, CH_2), 1.43 (m, CH_2), 1.30 (m, CH_3)	79.37 (d, $^2J_{P,C}$ = 10 Hz, C-α), 55.84 (d, $^2J_{P,C}$ = 6 Hz, PO*Me*), 39.66 (d, $^3J_{P,C}$ = 6 Hz, C-β), 22.17, 18.65, 13.27 (*n*-Pr)	207 [5] $M^+ + CH_3$, 193 [6] $M^+ + 1$, 179 [6] 207-Et, 164 [5] M^+ + 1-Et, 127 [51] $H_2O_2P(OMe)_2$, 109 [48] $OP(OMe)_2$, 84 [100] PrC≡COH
8j	36[a]	2960 (vs), 2935 (vs), 2870 (s), 2290 (vs), [C≡C], 1460–1450 (s), 1300–1290 (vs) [PO], 1230 (vs), 1070–1030 (vs) [POMe]	3.88 (d, $^3J_{P,H}$ = 11 Hz, POMe), 2.12 (m, CH_3), 1.40 (m, CH_2CH_2), 0.90 (m, CH_3)	79.21 (d, $^2J_{P,C}$ = 10 Hz, C-α), 55.83 (d, $^2J_{P,C}$ = 6 Hz, POMe), 39.78 (d, $^3J_{P,C}$ = 6 Hz, C-β), 30.82, 21.73, 16.32, 13.45 (*n*-Bu)	221 [8] $M^+ + CH_3$, 207 [7] $M^+ + 1$, 165 [31], $M^+ + 1 - C_3H_6$, 151 [6] $M^+ + 1 - C_4H_8$, 127 [100] $H_2O_2P(OMe)_2$, 113 [35] 109 [38] $OP(OMe)_2$, BuC≡COH + CH_3, 81 [31] C_6H_9

Table I (Continued)

alkynyl phosphates	yield (%)	IR [cm^{-1}]	^{1}H NMR ($CDCl_3$, δ)	^{13}C NMR ($CDCl_3$, δ)	MS (CI, CH_4) [m/z, %]
8k	23[b]	2970 (vs), 2930 (vs), 2875 (s), 2280 (vs) [C≡C], 1450 (s), 1300 (vs) [PO], 1230 (vs), 1185 (vs), 1060–1030 (vs) [POMe]	3.87 (d, $^3J_{P,H}$ = 11 Hz, POMe), 2.36 (m, CH_3), 1.43 (m, CH_2), 1.12 (d, $^3J_{H,H}$ = 7 Hz, CH_3), 0.95 (m, CH_3)	79.83 (d, $^2J_{P,C}$ = 10 Hz, C-α), 55.74 (d, $^2J_{P,C}$ = 6 Hz, PO*Me*), 43.42 (d, $^3J_{P,C}$ = 6 Hz, C-β), 29.83, 25.73, 20.65, 11.43 (*s*-Bu)	235 [6] M^+ + Et, 221 [7] M^+ + CH_3, 207 [14] M^+ + 1, 191 [9] M^+ + 1 − CH_4, 177 [8] M^+ + 1 − C_2H_6, 151 [6] M^+ + 1 − C_4H_8, 127 [100] $H_2O_2P(OMe)_2$, 109 [36] $OP(OMe)_2$, 97 [33] BuC≡CO, 81 [42] C_6H_9
8l	58[a]	2970–2910 (vs), 2860 (s), 2290 sh (s) [C≡C], 2270 (vs) [C≡C], 1450 (s), 1290 (vs) [PO], 1135 (vs), 1050–1020 (vs) [POMe]	3.90 (d, $^3J_{P,H}$ = 11 Hz, POMe), 1.22 (s, *t*-Bu)	78.49 (d, $^2J_{P,C}$ = 9 Hz, C-α), 55.50 (d, $^2J_{P,C}$ = 6 Hz, POMe), 47.26 (d, $^3J_{P,C}$ = 6 Hz, C-β), 30.75 (CMe_3), 25.73 (CMe_3)	315 [14] 2M^+ − BuC≡CO, 221 [16] M^+ + CH_3, 207 [20] M^+ + 1, 191 [50] M^+ + 1 − CH_4, 165 [13] M^+ + 1 − C_3H_6, 151 [100] M^+ + 1 − C_4H_8, 127 [61] $H_2O_3P(OMe)_2$, 109 [72] $OP(OMe)_2$, 97 [20] BuC≡CO
8m	38[a]	2970–2920 (vs), 2835 (s), 2290 (vs) [C≡C], 1450 (m), 1295 (vs) [PO], 1230 (vs), 1050–1020 (vs) [POMe]	3.90 (d, $^3J_{P,H}$ = 12 Hz, POMe), 2.10 (m, CH_3), 1.32 (m, $CH_2CH_2CH_2CH_2$), 0.88 (m, CH_3)	79.17 (d, $^2J_{P,C}$ = 10 Hz, C-α), 55.75 (d, $^2J_{P,C}$ = 6 Hz, POMe), 39.75 (d, $^3J_{P,C}$ = 6 Hz, C-β), 31.14, 28.66, 28.28, 22.39, 16.58, 13.84 (*n*-Hex)	249 [6] M^+ + CH_3, 235 [5] M^+ + 1, 165 [34] M^+ + 1 − C_5H_{10}, 127 [100] $H_2O_2P(OMe)_2$, 109 [41] $OP(OMe)_2$, 86 [45] C_6H_{14}, 84 [69] C_6H_{12}

[a] Method A. [b] Method B. [c] Method C. [d] See text and Experimental Section.

HRMS (CI; CH_4) for $C_{10}H_{20}PO_4$ (M^+ + H) calcd 235.1099, found 235.1103.

***tert*-Butylethynyl Diethyl Phosphate (8a). Method B.** A solution of phenylhydroxyiodonium diethyl phosphate (5 mmol), 3,3-dimethyl-1-butyne (20 mmol), and t.h.e. desiccant (5 g) in CH_2Cl_2 (25 mL) was refluxed for 24 h. Workup gave 0.38 g (33%) of **8a**.

***tert*-Butylethynyl Diethyl Phosphate (8a). Method C.** A solution of *tert*-butylethynyl(phenyl)iodonium tosylate[2] (2.3 g, 5 mmol) in 25 mL of CH_2Cl_2 was subjected to chromatography on the diethyl phosphate loaded resin. Elution with 200 mL of CH_2Cl_2 and evaporation of the solvent gave a yellow oil that was crystallized from ether/pentane resulting in 800 mg (36%) of **5a** as a pale yellow solid: mp 65–67 °C (dec); IR (KBr, cm^{-1}) 2970 (s), 2925 (m), 2895 (m), 2165 (m), 2135 (w, C≡C), 1438 (m), 1245–1220 (vs, P=O), 1060–1040 (vs, POEt); ^{1}H NMR ($CDCl_3$, δ) 1.23 (t, $^3J_{H,H}$ = 7.5 Hz, CH_3), 1.25 (s, *t*-Bu), 3.85 (quint. $^3J_{P,H} \cong {}^3J_{H,H}$ = 7.5 Hz, CH_2), 7.20–7.50 (m, ArH), 8.07–8.25 (m, ArH); ^{13}C NMR ($CDCl_3$) δ 16.31 (d, $^3J_{P,C}$ = 9 Hz, CH_3), 29.10 (CMe_3), 30.11 [$C(CH_3)_3$], 35.28 (C_α), 61.00 (d, $^2J_{P,C}$ = 5 Hz, $POCH_2$), 113.62 (C_β), 120.41, 130.63, 130.98, 132.65 (Ar C). Anal. Calcd for $C_{16}H_{24}IPO_4$: C, 43.85; H, 5.52; P, 7.06; I, 28.95. Found: C, 43.33; H, 5.98; P, 7.44; I, 29.30. Stirring of **5a** in $CHCl_3$ at room temperature for 20 h gave after workup 600 mg (51%) of **8a**.

1-Propynyl Diethyl Phosphate (8d). Method A. A mixture of 1-(trimethylsilyl)-1-propyne (1.12 g, 10 mmol), iodosobenzene (2.2 g, 10 mmol), and $BF_3{\cdot}OEt_2$ (1.2 mL, 10 mmol) in $CHCl_3$ (20 mL) was stirred at room temperature for 4 h and then reacted with a solution of $NaO_2P(OEt)_2$ (7.0 g, 40 mmol) in water (40 mL). After extraction with $CHCl_3$ and removal of the solvent the resulting yellow oil was stirred in CH_2Cl_2 (30 mL) at room temperature for 12 h. Workup gave 0.77 g (40%) of **8d** as a yellow oil: HRMS (CI; CH_4) for $C_7H_{14}PO_4$ (M^+ + H) calcd 193.06296, found 193.06147.

1-Pentynyl Diethyl Phosphate (8e). Method A. A mixture of 1-(trimethylsilyl)-1-pentyne (1.4 g, 10 mmol), iodosobenzene (2.2 g, 10 mmol), and $BF_3{\cdot}OEt_2$ (1.2 mL, 10 mmol) in $CHCl_3$ (20 mL) was stirred at room temperature for 6 h and then reacted with a solution of $NaO_2P(OEt)_2$ (7.0 g, 40 mmol) in water (40 mL). After extraction with $CHCl_3$ and removal of the solvent the resulting yellow oil was stirred in CH_2Cl_2 (30 mL) at room temperature for 19 h. Workup gave 0.97 g (44%) of **8e** as a yellow oil: HRMS (CI; CH_4) for $C_9H_{18}PO_4$ (M^+ + H) calcd 221.0943, found 221.0933.

1-Octynyl Diethyl Phosphate (8f). Method A. A mixture of 1-(trimethylsilyl)-1-octyne (1.7 g, 10 mmol), iodosobenzene (2.2 g, 10 mmol), and $BF_3{\cdot}OEt_2$ (1.2 mL, 10 mmol) in $CHCl_3$ (20 mL) was stirred at room temperature for 17 h and then reacted with a solution of $NaO_2P(OEt)_2$ (7.0 g, 40 mmol) in water (40 mL). After extraction with $CHCl_3$ and removal of the solvent the resulting yellow oil was stirred in CH_2Cl_2 (50 mL) at room temperature for 24 h. Workup gave 1.09 g (42%) of **8f** as a yellow oil: HRMS (CI; CH_4) for $C_{12}H_{24}PO_4$ (M^+ + H) calcd 263.1413, found 263.1403.

***tert*-Butylethynyl Dibenzyl Phosphate (8g). Method A.** A mixture of 3,3-dimethyl-1-(trimethylsilyl)-1-butyne (0.31 g, 2 mmol), iodosobenzene (0.44 g, 2 mmol), and $BF_3{\cdot}OEt_2$ (0.24 mL, 2 mmol) in $CHCl_3$ (5 mL) was stirred at room temperature for 19 h and then reacted with a solution of $NaO_2P(OEt)_2$ (1.4 g, 8 mmol) in water (20 mL). After extraction with $CHCl_3$ and removal of the solvent the resulting yellow oil was stirred in CH_2Cl_2 (20 mL) at room temperature for 26 h. Workup gave 0.41 g (57%) of **8g** as a yellow oil: HRMS (CI; CH_4) for $C_{20}H_{23}PO_4(M^+)$ calcd 358.1334, found 358.1345.

1-Pentynyl Dibenzyl Phosphate (8h). Method A. A mixture of 1-(trimethylsilyl)-1-pentyne (0.42 g, 3 mmol), iodosobenzene (0.66 g, 3 mmol), and BF_3OEt_2 (0.36 mL) in $CHCl_3$ (10 mL) was stirred at room temperature for 6 h and then reacted with a solution of $NaO_2P(OEt)_2$ (1.8 g, 10 mmol) in water (20 mL). After extraction with $CHCl_3$ and removal of the solvent the resulting yellow oil was stirred in CH_2Cl_2 (20 mL) at room temperature for 15 hrs. Workup gave 0.47 g (45%) of **8h** as a yellow oil: HRMS (CI; CH_4) for $C_{19}H_{21}PO_4(M^+)$ calcd 344.1177, found 344.1175.

1-Pentynyl Dimethyl Phosphate (8i). Method A. A mixture of 1-(trimethylsilyl)-1-pentyne (1.4 g, 10 mmol), iodosobenzene (2.2 g, 10 mmol), and $BF_3{\cdot}OEt_2$ (1.2 mL, 10 mmol) in $CHCl_3$ (20 mL) was stirred at room temperature for 4 h then reacted with a solution of $NaO_2P(OMe)_2$ (5.92 g, 40 mmol) in water (40 mL). After extraction with $CHCl_3$ and removal of the solvent the resulting yellow oil was stirred in CH_2Cl_2 (30 mL) at room temperature for 21 h. Workup gave 0.79 g (41%) of **8i** as a yellow oil. HRMS (CI; CH_4) for $C_7H_{14}PO_4$ (M^+ + H) calcd 193.06296, found 193.06147.

1-Hexynyl Dimethyl Phosphate (8j). Method A. A mixture of 1-(trimethylsilyl)-1-hexyne (1.54 g, 10 mmol), iodosobenzene (2.2 g, 10 mmol), and $BF_3{\cdot}OEt_2$ (1.2 mL, 10 mmol) in $CHCl_3$ (20 mL) was stirred at room temperature for 4 h and then reacted with a solution of $NaO_2P(OMe)_2$ (5.92 g, 40 mmol) in water (40 mL). After extraction with $CHCl_3$ and removal of the solvent the resulting yellow oil was stirred in CH_2Cl_2 (30 mL) at room temperature for 21 h. Workup gave 0.73 g (36%) of **8j** as a yellow oil. HRMS (CI, CH_4) for $C_8H_{16}PO_4$ (M^+ + H) calcd 207.0786, found 207.0771.

***sec*-Butylethynyl Dimethyl Phosphate (8k). Method B.** A solution of phenylhydroxyiodonium dimethyl phosphate (10 mmol, prepared from phenylhydroxyiodonium tosylate,[13] **9**, and $NaO_2P(OMe)_2$), 3-methyl-1-pentyne (2.46 g, 30 mmol), and t.h.e. desiccant (**5g**) in CH_2Cl_2 (50 mL) was refluxed for 21 h. After removal of the desiccant and solvent, chromatographic workup on silica gel (CH_2Cl_2 eluent) gave 0.47 g (23%) of **8k** as a yellow oil. HRMS (CI; CH_4) for $C_8H_{16}PO_4$ (M^+ + H) calcd 207.0786, found 207.0771.

***tert*-Butylethynyl Dimethyl Phosphate (8l). Method A.** A mixture of 3,3-dimethyl-1-(trimethylsilyl)-1-butyne (1.54 g, 10 mmol), iodosobenzene (2.2 g, 10 mmol), and $BF_3{\cdot}OEt_2$ (1.2 mL, 10 mmol) in $CHCl_3$ (20 mL) was stirred at room temperature for 26 h and then reacted with a solution of $NaO_2P(OMe)_2$ (5.92 g, 40 mmol) in water (40 mL). After

extraction with $CHCl_3$ and removal of the solvent the residual yellow oil was stirred in CH_2Cl_2 (50 mL) at room temperature for 48 h. Workup gave 1.2 g (58%) of **8l** as a yellow oil: HRMS (CI; CH_4) for $C_8H_{16}PO_4$ ($M^+ + H$) calcd 207.0786, found 207.0771.

***tert*-Butylethynyl Dimethyl Phosphate (8l). Method B.** A solution of $PhIOH{\cdot}OTs$[13] (3.9 g, 10 mmol) and $NaO_2P(OMe)_2$ (1.48 g, 10 mmol) in methanol (135 mL) was stirred at room temperature under argon for 12 h. Removal of the precipitated NaOTs and evaporation of the solvent gave 3.5 g of $PhIOH{\cdot}O_2P(OMe)_2$: IR (neat, cm^{-1}) 3400-2050 (br, shallow, OH), 3060 (m), 2990 (m), 2950 (s), 2850 (s), 1570 (m), 1465 (s), 1440 (s), 1230-1170 (vs), 1060-980 (vs); ^1H NMR ($CDCl_3$, δ) 3.57 (d, $^3J_{P,H}$ = 11 Hz, CH_3), 7.17-7.50 (m, ArH), 7.83-7.93 (m, ArH), 12.57 (br s, OH); ^{13}C NMR ($CDCl_3$; δ) 53.26 (d, $^2J_{P,C}$ = 6 Hz, CH_3), 124.94, 130.57, 131.33, 132.93 (Ar C). A solution of $PhIOH{\cdot}O_2P(OMe)_2$ (10 mmol), 3,3-dimethyl-1-butyne (2.5 g, 30 mmol), and t.h.e. desiccant (**5g**) in CH_2Cl_2 (50 mL) was refluxed for 21 h. After removal of the desiccant and evaporation of the solvent chromatographic workup of the residue on silica gel (CH_2Cl_2 as eluent) gave 0.76 g (37%) of **8l**.

1-Octynyl Dimethyl Phosphate (8m). Method A. A mixture of 1-(trimethylsilyl)-1-octyne (1.72 g, 10 mmol), iodosobenzene (2.2 g, 10 mmol), and $BF_3{\cdot}OEt_2$ (1.2 mL, 10 mmol) in $CHCl_3$ (20 mL) was stirred at room temperature for 18 h and then reacted with a solution of $NaO_2P(OMe)_2$ (5.92 g, 40 mmol) in water (40 mL). After extraction with $CHCl_3$ with removal of the solvent the resulting yellow oil was stirred in CH_2Cl_2 (50 mL) at room temperature for 24 h. Workup gave 0.90 g (38%) of **8m** as a yellow oil: HRMS (CI; CH_4) for $C_{10}H_{20}PO_4$ ($M^+ + H$) calcd 235.1099, found 235.1108.

***tert*-Butylethynyl(phenyl)iodonium Diphenyl Phosphate (5: R = *t*-Bu, R′ = C_5H_5). Method C.** A diphenyl phosphate-loaded resin (50 mL) was prepared in a manner described above for the diethyl phosphate system. A solution of *tert*-butylethynyl(phenyl)iodonium tosylate (2.28 g, 5 mmol) in $CHCl_2$ (25 mL) was placed on the column and eluted with 200 mL of CH_2Cl_2. Evaporation of the CH_2Cl_2 gave a yellow oil that crystallized upon standing giving 2.40 g (88%) of *tert*-butylethynyl(phenyl)iodonium diphenyl phosphate as an off white powder: mp 108-110 °C (dec); IR (KBr, cm^{-1}) 2970, 2170, 2140, 1585, 1480, 1250-1200, 1070; ^1H NMR ($CDCl_3$, δ) 1.15 (s, *t*-Bu), 6.80-7.50 (m, ArH), 7.85-8.00 (m, Ar H); ^{13}C NMR ($CDCl_3$, δ) 29.30 ($C(CH_3)$), 30.90 (CH_3), 31.71 (C-1), 114.10 (C-2), 119.53, 120.17, 122.86, 128.84, 130.69, 130.99, 132.74, 152.47 (d, $^2J_{P,C}$ = 7 Hz).

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Mechanism of Autoxidation of 5,7-Dihydroxytryptamine: ^{18}O Is Incorporated on C-4 during Oxidation with $^{18}O_2$

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Abstract: Oxidation of 3-[2-((ethoxycarbonyl)amino)ethyl]-5,7-dihydroxyindole (**12**) with $^{18}O_2/H_2O$ (pH ~8) at 25 °C gave the corresponding unlabeled 5-hydroxyindole-4,7-dione **13** and ^{18}O-labeled isotopomer **14** in a ratio of 32:68 as indicated by mass spectral data. An ^{18}O-isotope effect (of 0.05 ppm) on the ^{13}C chemical shift for C-4 of **14** (vs unlabeled **13**) confirmed that the ^{18}O label of **14** was attached to C-4. Oxidation of **12** with $O_2/H_2{}^{18}O$ as above gave **13** and ^{18}O-labeled **13** in a ratio of 75:25. Treatment of **13** with $H_2{}^{18}O$ under identical conditions gave **13** and ^{18}O-labeled **13** in a ratio of 76:24. These results were interpreted to suggest that during the autoxidation of 5,7-dihydroxytryptamine (**1**) to 5-hydroxytryptamine-4,7-dione (**6**), virtually all of the incorporated oxygen on C-4 is derived from O_2 and not from H_2O.

The neurodegenerative effects of 5,7-dihydroxytryptamine (5,7-DHT, **1**, Scheme I), a selective serotonergic neurotoxin,[7] are believed to be the result of the cytotoxic effects of its products of autoxidation.[1-3] Consequently, much effort has been directed toward characterizing the mechanism and the products of autoxidation of 5,7-DHT. 5,7-DHT, which exhibits pronounced phenol-keto tautomerism[4] with **2** being the predominant keto tautomer[5] at pH 7.4, undergoes rapid autoxidation at the same pH. On the basis of kinetic and various circumstantial evidence, we proposed[5] that 5,7-DHT reacts with O_2 to produce initially hydroperoxide **4** via the carbon radical-superoxide complex **3**. The secondary hydroperoxide **4** then breaks down to quinone **5**, which rearranges to produce more stable para quinone **6**. It was postulated that these quinones in turn may decompose to other products. Among the postulated products of autoxidation, so far only quinone **6** has been isolated[6] and its structure has been confirmed by an unambiguous synthesis.[7]

An alternate mechanism, in which *p*-quinoneimine **7** (Scheme II) is the initial product of autoxidation of 5,7-DHT, has not yet been ruled out. *p*-Quinoneimine **7**, long regarded[8] as the product of autoxidation of 5,7-DHT, appears to be the initial, transient product of electrochemical oxidation of 5,7-DHT under acidic pH. When generated electrochemically, **7** undergoes addition of H_2O followed by electrochemical oxidation to produce quinone **6**

(1) For selected reviews see: (a) Jacoby, J. H.; Lytle, L. D., Eds. Serotonin Neurotoxins. *Ann. N.Y. Acad. Sci.* **1978**, *305*, 1-702. (b) Baumgarten, H. G.; Klemm, H. P.; Sievers, J.; Schlossbarger, H. G. In *Biology of Serotonergic Transmission*; Osborne, N. N., Ed.; Wiley: New York, 1982; Chapter 10. (c) Jonsson, G. In *Handbook of Chemical Neuroanatomy*; Bjorklund, A., Hokfelt, T., Eds.; Elsevier: Amsterdam, 1983; Vol. 1, Methods in Chemical Neuroanatomy, Chapter XII. (d) Shallert, T.; Wilcox, R. E. In *Neuromethods*; Boulton, A. A., Baker, G. B., Eds.; Humana Press: Clifton, 1985; Vol. 1, General Neurochemical Techniques, pp 343-387.

(2) Baumgarten, H. G.; Bjorklund, A.; Nobin, A.; Rosengren, E.; Schlossberger, H. G. *Acta Physiol. Scand. Suppl.* **1975**, *429*, 1.

(3) Sinhababu, A. K.; Borchardt, R. T. *Neurochem. Internat.* **1988**, *12*, 273.

(4) Schlossberger, H. G. *Ann. N.Y. Acad.* Sci. **1978**, *305*, 25.

(5) Sinhababu, A. K.; Borchardt, R. T. *J. Am. Chem. Soc.* **1985**, *107*, 7618.

(6) Wrona, M. Z.; Lemordant, D.; Lin, L.; Blank, C. L.; Dryhurst, G. *J. Med. Chem.* **1986**, *29*, 499.

(7) Sinhababu, A. K.; Borchardt, R. T. *J. Heterocycl. Chem.* **1988**, *25*, 1155.

(8) (a) Baumgarten, H. G.; Klemm, H. P.; Lachenmayer, L.; Bjorklund, A.; Lovenberg, W.; Schlossberger, H. G. *Ann. N.Y. Acad. Sci.* **1978**, *305*, 3. (b) Creveling, C. R.; Rotman, A. *Ibid.* **1978**, *305*, 57.

0002-7863/89/1511-2230$01.50/0