a hydrogenated diester. The areas of the adduct peaks were used to calculate the ratio of adducts in the reaction, which was found to be 62:38 **16**:**15**.

4-Carbomethoxy-1,7,8,9,10,10-hexachlorotricyclo[5.2.1.$0^{2,6}$]-deca-3,8-diene (**17**).—A solution of 1.20 g (4.8 mmoles) of diester **11a** and 2.45 g (9.0 mmoles) of hexachlorocyclopentadiene in 15 ml of dioxane was heated at 100° for 18 hr. The dioxane was evaporated and the residual oil was dissolved in warm petroleum ether. On cooling and further evaporation, a solid product and an oil containing hexachlorocyclopentadiene were formed. The solid (1.00 g, 28%) was recrystallized from dichloromethane–petroleum ether to give large prisms of **17**, mp 142–144°.

Anal. Calcd for $C_{12}H_8Cl_6O_2$: C, 36.31; H, 2.03; Cl, 53.60. Found: C, 36.50; H, 2.10; Cl, 53.35.

Treatment of a mixture of 58% of **12a** and 42% of **11a** with hexachlorocyclopentadiene in dioxane in the same manner gave a 36% yield of **17**.

Kinetics.—Attempts to analyze for TCNE in diglyme solutions by the formation of the blue dye with N,N-dimethylaniline, as applied to the kinetics of dissociation of the cyclopentadiene–maleic anhydride adduct by Berson,[17] gave erratic results with known solutions. Other methods of analysis of TCNE were therefore investigated. The purple π complex of TCNE with naphthalene has been used for a spectrophotometric analysis of TCNE.[18] To avoid interference from the weaker, yellow π complex of TCNE with diglyme, small aliquots of the reaction solution were added to a large excess of a 3.0% solution of naphthalene in chloroform. This method was found to be suitable for determining the concentration of TCNE in dilgyme accurately to better than ±1%.

The apparatus consisted of a 50-ml, three-necked flask equipped with a mechanical stirrer, a rubber septum, and a condenser topped with a drying tube and was mounted on a movable stand for immersion of the flask in a constant temperature (± 0.2°) oil bath. The reactants were weighed into the flask, the solvent was added, and samples were withdrawn for determination of initial concentration. The reaction flask was heated rapidly to the desired temperature in an auxiliary bath maintained at 30 to 50° above the constant-temperature bath. When the contents of the flask had reached the desired temperature (2–6 min), the reaction flask was moved to the constant-temperature bath and 25-μl samples were withdrawn every 2–4 min. The samples were added to 3.00 of a 3% solution of naphthalene in chloroform and the concentration of TCNE in the reaction solution was determined by reading the absorption of the TCNE–naphthalene π complex at 430 or 555 mμ. Standard curves were made from solutions of weighed amounts of TCNE in diglyme.

TCNE was always used in slight excess in the kinetic runs to provide readable values on the spectrophotometer. The concentration of diester **11a** in the reaction solution was calculated from the difference between the observed concentration of TCNE and the concentration of TCNE at infinite time. A plot of the log of the concentration of **11a** against time showed a straight-line decrease from the end of the preliminary heating period through at least three half-lives (20–30 points), where the concentration of **11a** was less than the limit of error in the TCNE determination. A plot of the logarithm of the ratio of the concentrations of **11a** and TCNE against time showed a pronounced upward curvature, indicating that the reaction was not a pseudo-first-order reaction, but was first order with respect to the diester, only. The first-order rate constants were determined from the half-lives. The rate constants and temperatures are given in Table II. A plot of log k against the reciprocal of the temperature for the reactions in diglyme was used to calculate E_a and log A. These empirical values were used to calculate[14] ΔH^* and ΔS^*.

Registry No.—**3b**, 15230-99-6; **11a**, 15275-62-4; **11d**, 15231-00-2; **12a**, 15231-01-3; **12d**, 15231-02-4; **13**, 15231-03-5; **14a**, 15231-04-6; **14b**, 15231-05-7; **15**, 15231-06-8; **16**, 15231-07-9; 1-carboxy-5,6-(N-phenyldicarbimido)-2-norbornene, 15231-08-0; 1-carbomethoxy-2,3-(N-phenyldicarbimido)norbornane, 15231-09-1; **17**, 15275-63-5.

Acknowledgment.—We wish to thank Mr. Gordon J. Boudreaux for his valuable assistance in determining the nmr spectra. The authors are also grateful to the Cotton Producers Institute for partial support of this work.

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[17] J. A. Berson and W. A. Mueller, *J. Am. Chem. Soc.*, **83**, 4940 (1961).

[18] G. H. Schenk and M. Ozolius, *Talanta*, **8**, 109 (1961).

Phosphonic Acids and Esters. XIX. Syntheses of Substituted Phenyl- and Arylphosphonates by the Photoinitiated Arylation of Trialkyl Phosphites[1]

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The syntheses of a variety of nuclear substituted (methyl, ethyl, methoxy, hydroxy, amino, formyl) phenylphosphonates **3** and other aryl- (1-naphthyl-, 2-thienyl-, 2-furyl-) phosphonates have been carried out by the low-temperature ultraviolet photolyses of the corresponding aryl iodides in excess trialkyl (methyl or ethyl) phosphite **1**. The process constitutes an experimentally simple one-step procedure for the synthesis of these compounds in good yield. The nitroiodobenzenes are the only class of compounds examined which failed to yield the corresponding **3**; photolyses of these compounds in the presence of **1** resulted in deoxygenation to yield the corresponding phosphate and, presumably, an electron-deficient nitrogen intermediate. Infrared and proton magnetic resonance data are presented for certain **3**, particularly *para*-substituted compounds and those structures capable of exhibiting intra- or intermolecular hydrogen bonds.

In a preceding study,[2] it was shown that the photolysis of iodobenzene in the presence of trialkyl phosphites **1** results in the formation of dialkyl phenylphosphonates **2** (eq 1). This reaction effectively constitutes a photolytic modification of the Michaelis–Arbuzov reaction;[3] high yields of **2** can be realized by carrying out the reaction at low temperatures in the presence of a large excess of **1**. Thus, the irradiation of iodobenzene for 24 hr at 0° in a three- to fivefold excess of trimethyl phosphite results in the formation of dimethyl phenylphosphonate (**2**, R = CH_3) in quantitative yield.[2]

$$C_6H_5I + \underset{\mathbf{1}}{P(OR)_3} \longrightarrow \underset{\mathbf{2}}{C_6H_5P(O)(OR)_2} + RI \qquad (1)$$

The high yields of **2** obtained by this reaction and the experimental simplicity of the process suggested

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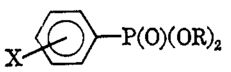
[1] Part XVIII: D. J. Martin, M. Gordon, and C. E. Griffin, *Tetrahedron*, **23**, 1831 (1967).

[2] J. B. Plumb, R. Obrycki, and C. E. Griffin, *J. Org. Chem.*, **31**, 2455 (1966).

[3] R. G. Harvey and E. R. DeSombre in "Topics in Phosphorus Chemistry," Vol. I, M. Grayson and E. J. Griffith, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, Chapter 3.

that the reaction might be applied profitably to the synthesis of nuclear substituted phenylphosphonates **3**. Each of the methods currently available for the



3

synthesis of **3**[4] suffers from one or more practical limitations affecting product purity or homogeneity. Thus, the direct phosphonation of arenes or electrophilic aromatic substitutions of **2** commonly result in the formation of positional isomers of **3**,[4a] while the reactions of aryl Grignard and diazonium reagents with phosphorus halides give, in addition to **3**, small amounts of the corresponding alkyl diarylphosphinates.[4] Wolf and Kharasch[5] have reported that the photolyses of a wide variety of nuclear substituted iodobenzenes **4** in benzene result in the formation of the appropriate biphenyls without rearrangement of the moiety derived from **4**. Consequently, the photolyses of **4** in the presence of trialkyl phosphites should result in the formation of isomerically homogeneous **3**.

Accordingly, the photolyses of a series of nuclear substituted iodobenzenes **4** in trimethyl and triethyl phosphites have been examined; the reaction conditions employed and the yields of the various products obtained are listed in Table I. Reactions were generally carried out utilizing the optimal conditions established in the studies with iodobenzene,[2] namely irradiation of **4** in a three- to fivefold excess of **1** at a maximum reaction temperature of 0° for 24 hr. Longer irradiation times were employed in reactions with triethyl phosphite and, in two cases with this phosphite, the reaction was carried out at 25°; relatively little effect is observed on yields in reactions carried out with triethyl phosphite at the higher reaction temperature. In one instance (compound **11**), the bromo- rather than the iodobenzene was employed; the longer reaction time necessary reflects the results previously obtained with bromobenzene.[2] Simple isolation procedures, generally direct distillation of the intact reaction mixtures, were employed; compounds **18**–**21** crystallized after removal of unreacted **1** and were purified by recrystallization.

In general, the yields of **3** listed in Table I are acceptable to excellent; the yields given are of material of essentially analytical purity. However, it is probable that the yields of several of the phosphonates could be increased by modifications of the reaction conditions; no attempt was made to establish optimum conditions for each reaction.[6] For example, the yield of **17** could probably be increased by the use of a fivefold excess of **1**. Compound **18** separated from solution during formation and as a consequence efficient stirring was inhibited; it is probable that the yield of **18** could have been increased by removing **18** from the reaction mixture periodically during the period of irradiation.

TABLE I

PREPARATION AND PROPERTIES OF DIALKYL ARYLPHOSPHONATES[a]

$$\underset{\mathbf{4}}{XC_6H_4I} + \underset{\mathbf{1}}{P(OR)_3} \rightarrow \underset{\mathbf{3}}{XC_6H_4P(O)(OR)_2} + RI$$

Compd	X	R	[**1**]/[**4**]	Reacn time, hr	Yield of **3** (%)	Bp, °C (mm) [mp, °C]
5	*o*-CH_3	CH_3	5	24	91	96–97 (0.25)[b]
6	*o*-CH_3	C_2H_5	4	48	73	105–107 (0.3)
7	*m*-CH_3	CH_3	5	24	87	106–107 (0.45)[b]
8	*m*-CH_3	C_2H_5	4	20	70	104–105 (0.4)
9	*p*-CH_3	CH_3	5	24	95	93–94 (0.05)[b]
10[c]	*p*-CH_3	C_2H_5	4	93	95	148–149 (4.0)
11[c,d]	*o*-C_2H_5	C_2H_5	4	92	52	130–132 (3.0)
12	*o*-CH_3O	CH_3	5	24	87	110–112 (0.1)
13	*o*-CH_3O	C_2H_5	4	18	70	120–121 (2.0)
14	*m*-CH_3O	CH_3	5	24	82	116–117 (0.1)
15	*p*-CH_3O	CH_5	5	24	92	113–114 (0.1)
16[c]	*p*-CH_3O	C_2H_5	4	69	70	177–178 (0.4)
17	*o*-NH_2	CH_3	3	24	34	117–118 (0.25)
18[e]	*p*-NH_2	CH_3	5	24	53	[107–108][f]
19[e]	*o*-OH	CH_3	5	24	53	[97–98]
20[e]	*m*-OH	CH_3	5	24	65	[91–92]
21[e]	*p*-OH	CH_3	5	24	66	[77–78]
22	*o*-CHO	CH_3	4	26	34	126–127 (0.45)

[a] For general procedural details, see Experimental Section. Unless otherwise noted, all reactions were carried out at 0 to −8°. [b] Lit.[8] bp: **5**, 107–110° (1.0 mm); **7**, 141° (4.0 mm); **9**, 106–106.5° (1.0 mm). [c] Reaction carried out at 25°. [d] Aryl bromide was photolyzed. [e] For details of experimental procedure and product isolation, see Experimental Section. [f] Lit.[9] mp 105–106.5°.

In addition to those compounds cited in Table I, five other dimethyl arylphosphonates were prepared by this procedure: dimethyl 2,6-dimethylphenyl- (**23**, 50%), 3,5-dimethoxyphenyl- (**24**, 83%), 1-naphthyl- (**25**, 81%), 2-thienyl- (**26**, 32%), and 2-furyl- (**27**, 26%) phosphonates were obtained by photolyses of the corresponding aryl iodides in trimethyl phosphite.[7] The yield of **23** is low, particularly in view of the high yield (91%) obtained under identical reaction conditions for the mono-*o*-methyl analog **5**. This result may indicate a steric limitation to the reaction; 2,6-dimethyliodobenzene was the only di-*ortho*-substituted **4** examined in this study. The heteroarylphosphonates **26** and **27** were also obtained in low yield, a result attributable to both the purity of the starting iodide (for **27**) and the photolytic instability of the products (see Experimental Section). An attempted reaction with 2-iodoquinoline failed to yield a characterizable product.

The structures of products **5**–**27** were confirmed by physical methods (infrared and proton magnetic resonance spectra) and by elemental analyses; compounds **5**,[8] **7**,[8] **9**,[8] and **18**[9] have been described previously. For each compound examined, the substitution pattern of the starting aryl iodide was retained in the product; no contamination of the products by

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(4) For reviews of the preparative chemistry of arylphosphonates, see (a) L. D. Freedman and G. O. Doak, *Chem. Rev.*, **57**, 479 (1957); (b) K. Sasse in "Methoden der Organischen Chemie," Vol. 12, part 1, E. Müller, Ed., Georg Thieme Verlag, Stuttgart, Germany, 1963, pp 338 ff.

(5) W. Wolf and N. Kharasch, *J. Org. Chem.*, **30**, 2493 (1965).

(6) The normally employed reaction time of 24 hr for reactions of aryl iodides with trimethyl phosphite may be excessive in some instances, but was chosen for convenience. A pmr study of the formation of **15** indicated the reaction to be initially rapid and essentially complete after 12 hr. The following yields of **15** at the indicated times were determined by pmr measurements: 46% (4 hr), 69% (8 hr), 87% (12 hr), 98% (24 hr).

(7) A preliminary report of the preparation of three additional examples of **3** (diethyl *o*-carboxy- and *o*- and *p*-carbethoxyphenylphosphonates) has appeared: M. Gordon, V. A. Notaro, and C. E. Griffin, *J. Am. Chem. Soc.*, **86**, 1898 (1964). The corresponding reaction with vinyl iodides has been shown to result in the formation of dialkyl vinylphosphonates: W. M. Daniewski, M. Gordon, and C. E. Griffin, *J. Org. Chem.*, **31**, 2083 (1966).

(8) C. E. Griffin, R. B. Davison, and M. Gordon, *Tetrahedron*, **22**, 561 (1966).

(9) F. Kagan, R. D. Birkenmeyer, and R. E. Strube, *J. Am. Chem. Soc.*, **81**, 3026 (1959).

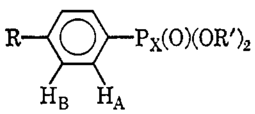
positional or other isomers was observed. The homogeneity of a number of products was confirmed by glpc analysis.

The infrared spectra of all of the arylphosphonates were in complete accord with the assigned structures. With the exceptions noted below, all group absorptions fell within the characteristic limits cited by Rao.[10] The following characteristic absorptions were observed: ν_{PO} 1242–1258; ν_{POCH_3} 1179–1188; $\nu_{POC_2H_5}$ 1145–1161; ν_{POC} 1018–1036 cm.$^{-1}$ Additionally, the expected aromatic substitution bands for 1,2- 1,3- and 1,4-disubstituted benzenes were observed in the 730–860-cm^{-1} region.[10] The only compounds exhibiting infrared absorptions outside the ranges cited above were those structures capable of inter- or intramolecular hydrogen bonding, *i.e.*, the amino- (**17**, **18**) and hydroxy-(**19**–**21**) phenylphosphonates. In each of these compounds, the phosphoryl absorption was shifted to a lower frequency (1203–1230 cm^{-1}); such shifts would be expected to result from hydrogen bonding interactions in which the phosphoryl oxygen functioned as donor atom.[10] Comparable phosphoryl frequency shifts have been observed for the intermolecular complexes of phenols and amines with phosphoryl compounds.[11] On the basis of studies carried out to date, no choice can be made between intra- and intermolecular bonding.[12] The existence of hydrogen bonding in these compounds is further supported by the absence of stretching frequencies (*ca.* 3600 cm^{-1}) due to free phenolic hydroxyl, *i.e.*, no absorptions at frequencies higher than 3165 cm^{-1} are observed for **19**.

The assigned structures of the products were also fully supported by their proton magnetic resonance (pmr) spectra. In all cases, the anticipated chemical shifts and peak multiplicities were observed and acceptable integrated intensities were obtained. For the methyl esters, the P–O–CH$_3$ doublet was observed in the range τ 6.19–6.36 ppm with J_{PH} = 10.6–11.2 Hz. For the ethyl esters, typical P–O–CH$_2$–CH$_3$ resonances were observed: τ 8.69–8.75 (triplets, CH$_3$) and 5.86–6.05 ppm (quintets, CH$_2$, *i.e.*, doublets of quartets with $J_{HH} \cong J_{PH}$ = 7–8 Hz). Chemical shifts for nuclear substituents (alkyl, methoxyl, hydroxyl, amino, formyl) fell within normally accepted ranges; these data are given in the Experimental Section. Although a first-order analysis of the aromatic portions of the spectra of these phosphonates was not possible in all cases, the appearance of these multiplets was consistent with the assigned orientation. For six of the *para*-substituted compounds (**9**, **10**, **15**, **16**, **18**, **21**), a complete first-order analysis was possible (Table II). The aromatic resonances of these compounds were of the A_2B_2X classification; all eight lines of the A and B portions were cleanly resolved without overlap. The details of the analysis employed have been reported previously.[8,13] The coupling constants observed for these phenylphosphonates (J_{AB} = 8.2–8.7, J_{AX} = 12.2–12.9, J_{BX} = 3.3–4.2 Hz) are quite similar to those observed for the analogous tris(*p*-substituted phenyl)phosphine oxides (J_{AB} = 8.0–8.9, J_{AX} = 10.5–11.5, J_{BX} = 2.1–3.4 Hz).[13] The slightly greater magnitude observed for $^{31}P-^{1}H$ couplings in the phosphonates compared to those in phosphine oxides is consistent with the behavior of such coupling constants in other phosphonates and phosphine oxides.[8] A complete first-order analysis of the aromatic resonances of dimethyl 3,5-dimethoxyphenylphosphonate (**24**) was also possible. The spectrum is of the A_2BX classification and all of the expected transitions were observed and resolved. The following parameters were observed: τ_A 3.27, τ_B 3.55 ppm (J_{AB} = 2.2, J_{AX} = 14.5, J_{BX} = 0.6 Hz). A partial analysis of the aromatic portion of the spectra of two other phenylphosphonates (**5**,[8] **13**) was also possible.[14] For **13**, the single proton (H_A) *ortho* to the phosphonate function is sufficiently deshielded (τ 2.25 ppm) so that a first-order multiplet is observed; the protons *meta* (H_B) and *para* (H_C) to the phosphonate and *ortho* (H_D) to the methoxyl group have similar chemical shifts (τ 2.63–3.02 ppm). The appearance of the H_A resonance is that of the A portion of an ABCX spectrum (X = ^{31}P) with J_{AX} = 14.9, J_{AB} = 7.8, and J_{AC} = 2.0 Hz. Similar parameters have been reported previously for **5**.[8]

TABLE II

AROMATIC PROTON MAGNETIC RESONANCE PARAMETERS FOR *para*-SUBSTITUTED PHENYLPHOSPHONATES[a]



Compd	R	R′	τ_A	τ_B	J_{AB}	J_{AX}	J_{BX}	Solvent
9	CH$_3$	CH$_3$	2.42	2.82	8.3	12.9	4.2	CCl$_4$[b]
10	CH$_3$	C$_2$H$_5$	2.39	2.81	8.2	12.7	3.9	CCl$_4$
15	CH$_3$O	CH$_3$	2.30	3.03	8.6	12.2	3.4	CCl$_4$
16	CH$_3$O	C$_2$H$_5$	2.47	3.15	8.7	12.4	3.3	CCl$_4$
18	NH$_2$	CH$_3$	2.52	3.28	8.4	12.3	3.6	CDCl$_3$
21	OH	CH$_3$	2.33	2.88	8.6	12.5	3.8	CDCl$_3$

[a] Chemical shifts are given in ppm relative to internal tetramethylsilane (τ 10.00 ppm); coupling constants (J) are given in hertz. [b] A_2B_2X spectrum unresolved in neat liquid.

The photolyses of two other classes of aryl iodides (halo and nitro substituted) in the presence of **1** have also been examined. Reactions with dihalobenzenes have been shown to result in the formation of mixtures of halo phenylphosphonates and phenylene bisphosphonates;[15] in these reactions, the unexpected photolytic displacements of both chloro and fluoro substituents were observed.

An attempted extension of this reaction to the formation of nitro-substituted phenylphosphonates was unsuccessful. The photolysis of *o*-iodonitrobenzene in trimethyl phosphite gave trimethyl phosphate (**28**, 6%) as the sole isolable product; an 80% recovery of reactants was achieved. A similar photoly-

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(10) C. N. R. Rao, "Chemical Applications of Infrared Spectroscopy," Academic Press Inc., New York, N. Y., 1963.

(11) T. Gramstad, *Spectrochim. Acta*, **19**, 497, 829, 1363 (1963); T. Gramstad and W. J. Fuglevik, *ibid.*, **21**, 503 (1965).

(12) The existence of intramolecular hydrogen bonds in the *ortho* isomers (**17**, **19**) and of intermolecular hydrogen bonds in the *meta* and *para* isomers (**18**, **20**, **21**) is supported by the results of preliminary dilution studies and by the chemical shifts observed for phenolic and amino protons in these compounds (see Experimental Section). A detailed study of hydrogen bonding in these compounds is in progress.

(13) C. E. Griffin, *Tetrahedron*, **20**, 2399 (1964).

(14) A complete analysis of the spectra of the heteroarylphosphonates **26** and **27** has also been carried out: M. Gordon, Ph.D. Thesis, University of Pittsburgh, Pittsburgh, Pa., 1965. Details of these analyses will be presented elsewhere.

(15) R. Obrycki and C. E. Griffin, *Tetrahedron Letters*, 5049 (1966); similar results have been obtained by Dr. M. Grayson, private communication, 1967.

sis of the *meta* isomer again gave **28** (60%) as the major product; a large amount of intractable tar also resulted from the reaction. Glpc analysis of the reaction mixture showed the presence of only trace amounts of unreacted iodonitrobenzene. Since only trace amounts of phosphates had been observed among the products of those reactions cited in Table I, it appeared that the formation of **28** arose from a photoinitiated deoxygenation of the nitro function by trimethyl phosphite. In order to establish this point, the photolysis of nitrobenzene in trimethyl phosphite was examined; **28** (80%) was isolated in addition to a noncharacterizable tar. This tar was subjected to column chromatography and the infrared spectra of several fractions indicated the presence of a P=N group. Only very small amounts of these fractions were available and further characterization was not attempted. Similar results were obtained for the photolysis of nitrobenzene in triethyl phosphite; the phosphate was obtained in 50% yield. A control reaction of trimethyl phosphite and nitrobenzene at −20° in the dark for 32 hr gave no reaction.

Based on the above results, it is most probable that these photolytic reactions parallel the corresponding thermal reactions, which have been the subject of investigations by Cadogan[16] and Sundberg.[17] These workers have shown that the reactions of **1** and nitroarenes, generally at elevated temperatures, result in deoxygenation to yield the phosphate and an electron-deficient nitrogen species (nitrene) which may either insert into a C–H bond or be trapped by reaction with excess **1**. Thus, it has been shown that 2-nitrobiphenyls react with triethyl phosphite to give the corresponding carbazoles[16b] and *o*-nitroethylbenzene reacts with the same phosphite to give a phosphorimidate (o-$C_2H_5C_6H_4N{=}P(OC_2H_5)_3$).[17b] One example of a similar photoinitiated reaction has been reported. Taylor and Garcia[18] showed that irradiation of a mixture of triethyl phosphite and a 5-nitro-6-styrylpyrimidine resulted in deoxygenation of the nitropyrimidine to form the phosphate; the resulting nitrene inserted into a styryl C–H bond to produce a low yield of a pyrrolopyrimidine.

Despite the failures of this reaction with nitro-substituted iodobenzenes, the results of this study indicate the photolysis of iodoarenes in trialkyl phosphites to be a generally useful one-step method for the synthesis of arylphosphonates. In view of the range of structures which have been prepared by this reaction, the ease of experimental procedure, and the avoidance of the limitations of older methods of arylphosphonate synthesis, this method can be considered the method of choice for the preparation of a major number of representatives of this class of compounds.

Experimental Section[19]

General Procedure for Photoinitiated Arylation of Trialkyl Phosphites.—The procedure is essentially that described previously for the corresponding phenylation reactions.[2] A mixture of the iodoarene (usually 0.04 mole) and the trialkyl phosphite (0.12–0.20 mole) was placed in a 45-ml double-jacketed silica reaction vessel which has been described previously.[2] The mixture was degassed by flushing with dry nitrogen for *ca.* 5 min and irradiated with a 450-w Hanovia (Model 679A-10) high pressure quartz mercury vapor lamp fitted with an aluminum reflector head; the lamp was placed 5 cm from the inner portion of the reaction vessel. The specified reaction temperature (±1°) was maintained by circulation of coolant from a thermostatically controlled refrigeration unit through the outer jacket of the reaction vessel. An atmosphere of nitrogen was maintained over the reaction mixture which was protected from moisture with a calcium chloride drying tube; continuous stirring was maintained with a magnetic stirrer. The precise reaction conditions and times are given in Table I and the text.

Isolation of Products.—On completion of the specified reaction time, the reaction mixture was stripped of trialkyl phosphite **1** and alkyl iodide at room temperature under water pump vacuum. The residue, which contained the desired product **3** and small amounts of **1**, dialkyl alkylphosphonate, aryl iodide, and alkyl iodide, was fractionated under nitrogen at reduced pressure. The boiling points of products **5–17** and **22** are listed in Table I. The following boiling points were obtained for other products: **23**, 92–93° (0.3 mm); **24**, 120–122° (0.2 mm); **25**, 129–131° (0.15 mm); **26**, 101–103° (0.3 mm); **27**, 111–114° (0.4 mm). In general, the pmr spectrum of a compound was used as the primary criterion of identity and purity and elemental analyses (Table III) were not obtained until redistillation of the product gave satisfactory integrated intensities and showed the absence of contaminants. The major contaminant normally present in these products was dimethyl methylphosphonate; this material was readily detected since the P–CH_3 doublet (τ 8.6 ppm, J_{PH} = *ca.* 18 Hz) was generally well separated from any resonances attributable to **3**.

TABLE III

ANALYTICAL DATA FOR DIALKYL ARYLPHOSPHONATES

		Calcd, %			Found, %		
Compd	Formula	C	H	P	C	H	P
6	$C_{11}H_{17}O_3P$	57.88	7.51	13.57	58.10	7.38	13.46
8	$C_{11}H_{17}O_3P$	57.88	7.51	13.57	57.59	7.66	13.70
10	$C_{11}H_{17}O_3P$	57.88	7.51	13.57	57.93	7.77	13.39
11	$C_{12}H_{19}O_3P$	59.49	7.91	12.79	59.60	8.09	13.02
12	$C_9H_{13}O_4P$	50.00	6.06	14.33	50.09	6.11	14.39
13	$C_{11}H_{17}O_4P$	54.09	7.02	12.68	53.81	6.94	12.43
14	$C_9H_{13}O_4P$	50.00	6.06	14.33	49.83	5.99	14.51
15	$C_9H_{13}O_4P$	50.00	6.06	14.33	49.78	6.31	14.11
16	$C_{11}H_{17}O_4P$	54.09	7.02	12.68	54.24	7.10	12.73
17	$C_8H_{12}NO_3P$	47.76	6.01	15.39	47.83	5.77	15.21
18	$C_8H_{12}NO_3P$	47.76	6.01	15.39	48.01	5.97	15.30
19	$C_8H_{11}O_4P$	47.53	5.48	15.32	47.71	5.35	15.11
20	$C_8H_{11}O_4P$	47.53	5.48	15.32	47.30	5.19	15.08
21	$C_8H_{11}O_4P$	47.53	5.48	15.32	47.41	5.30	15.14
22	$C_9H_{11}O_4P$	50.47	5.18	14.47	50.28	5.09	14.66
23	$C_{10}H_{15}O_3P$	56.07	7.06	14.41	55.88	6.93	14.59
24	$C_{10}H_{15}O_5P$	48.78	6.14	12.58	49.00	6.36	12.74
25	$C_{12}H_{13}O_3P$	61.02	5.55	13.11	60.84	5.80	13.05
26	$C_6H_9O_3PS$	37.50	4.72	16.20	37.41	5.01	16.08
27	$C_6H_9O_4P$	40.92	5.15	17.59	40.74	5.31	17.75

Four of the products (**18–21**) were crystalline materials. Both **18** and **20** were insoluble in their reaction mixtures and separated during the course of the reaction; these products were removed by filtration. The remaining portions of **18** and **20** and products **19** and **21** crystallized after removal of volatile materials at water pump vacuum. Compound **19** was partially distilled (bp 78° (0.05 mm)), but distillation was discontinued when the

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[16] (a) P. J. Bunyan and J. I. G. Cadogan, *J. Chem. Soc.*, 42 (1963); (b) J. I. G. Cadogan, M. Cameron-Wood, R. K. Mackie, and R. J. G. Searle, *ibid.*, 483 (1965).

[17] (a) R. J. Sundberg, *Tetrahedron Letters*, 477 (1966); (b) R. J. Sundberg, *J. Am. Chem. Soc.*, **88**, 3781 (1966); (c) R. J. Sundberg and T. Yamazaki, *J. Org. Chem.*, **32**, 290 (1967).

[18] E. C. Taylor and E. E. Garcia, *ibid.*, **30**, 655 (1965).

[19] Infrared spectra were determined as films or CCl_4 solutions on a Beckman IR-8 spectrophotometer calibrated with a polystyrene film at several wavelengths. Pmr spectra were determined on a Varian Associates A-60 spectrometer at ambient probe temperatures. Chemical shifts are reported on the τ scale in parts per million from internal tetramethylsilane (τ 10.00 ppm) and are accurate to at least ± 0.015 ppm. Coupling constants were taken from spectra recorded at 50-Hz sweep widths and are accurate to ± 0.2 Hz. Unless otherwise noted, all reactants were commercial materials and were used without prior purification.

compound solidified in the condenser. The products were purified by recrystallization: **18** ($CHCl_3$–CCl_4), **19** and **21** (CCl_4–hexane), and **20** (CCl_4). Compounds **18** and **21** were further purified by recrystallization from diethyl ether.

With the exception of **22**, all of the compounds prepared in this study are stable at room temperature; on standing, **22** becomes highly viscous and eventually sets to a semisolid. With two exceptions, the products also appear to be photolytically stable. The low yields obtained in the syntheses of the heteroarylphosphonates **26** and **27** are apparently a result of their photolytic instability. The photolysis of 50-mg samples of these compounds at 0° for 24 hr results in approximately 50% decomposition to polymeric materials. Additionally, the low yield of the furylphosphonate **27** can be attributed in part to the purity of the reactant, 2-iodofuran. The iodofuran, prepared by the method of Gilman and Wright,[20] is apparently unstable since, upon distillation, the pure compound turned black and tarry almost immediately. As a consequence, impure (*ca.* 80–90% by pmr analysis) 2-iodofuran was used in synthetic reactions.

Photoinitiated Reactions of Nitroarenes with Trialkyl Phosphites.—Similar procedures were employed in all reactions; the reaction with *o*-iodonitrobenzene will be cited as an example. A mixture of 7.47 g (0.03 mole) of the arene and 18.60 g (0.15 mole) of trimethyl phosphite was irradiated at −8° for 24 hr. Glpc analysis of the reaction mixture showed it to contain trimethyl phosphite, trimethyl phosphate, and the arene.[21] Careful distillation (pot temperature <50° until all phosphite had been removed) gave these fractions: (1) bp 26–35° (20 mm), 14.66 g; (2) bp 27–84° (0.13 mm), 0.48 g; (3) bp 84–87° (0.13 mm), 5.85 g. Fractions 1 and 2 were identified as the phosphite and phosphate, respectively, by glpc comparisons with authentic samples. Fraction 3 solidified to a yellow material which was identified as the starting arene by melting point and infrared spectral comparisons with an authentic sample.

Pmr Spectra.—In addition to the ester and aromatic proton resonances cited in the text, resonances attributable to nuclear substituents were observed for most of the arylphosphonates prepared in this study. Unless otherwise noted, all spectra were recorded on solutions of the phosphonate in CCl_4. The following resonances were observed: **5** (CH_3, τ 7.50); **6** (CH_3, 7.48); **7** (CH_3, 7.62); **8** (CH_3, 7.60); **9** (CH_3, 7.95); **10** (CH_3, 7.93); **11** (C–CH_2, 6.87, C–C–CH_3, 8.75); **12** (OCH_3, 6.17); **13** (OCH_3, 6.32); **14** (OCH_3, 6.20); **15** (OCH_3, 6.12); **16** (OCH_3, 6.23); **17** (NH_2, 4.38); **18** (NH_2, 5.50 ($CDCl_3$)); **19** (OH, 0.32 ($CDCl_3$)); **20** (OH, 0.48 ($CDCl_3$)); **21** (OH, 0.57 ($CDCl_3$)); **22** (CHO, −0.60); **23** (CH_3, 7.43, J_{PH} = 1.7 Hz); **24** (OCH_3, 6.22 ppm).

Registry No.—**5**, 6840-23-9; **6**, 15286-11-0; **7**, 15286-12-1; **8**, 15286-13-2; **9**, 6840-25-1; **10**, 1754-46-7; **11**, 15286-15-4; **12**, 15286-16-5; **13**, 15286-17-6; **14**, 15286-18-7; **15**, 15286-19-8; **16**, 3762-33-2; **17**, 15286-21-2; **18**, 15286-22-3; **19**, 15286-23-4; **20**, 15286-24-5; **21**, 15286-25-6; **22**, 15286-26-7; **23**, 15286-27-8; **24**, 15286-28-9; **25**, 15286-29-0; **26**, 13640-94-3; **27**, 13640-97-6.

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(20) H. Gilman and F. Wright, *J. Am. Chem. Soc.*, **55**, 3302 (1933).

(21) Glpc analyses were carried out on an F & M Model 300 chromatograph using a 6-ft stainless steel 20% silicone oil 710 on 60–80 mesh Chromosorb P column. The injection port was maintained at 160° and the column temperature was programmed as follows: 75° (0 min), 150° (22 min). A helium flow rate of 50 cc/min was used. Under these conditions, trimethyl phosphate and *o*-iodonitrobenzene had retention times of 13.5 and 42.0 min, respectively.

Derivatives of 2-Aminoethanethiol Related to Spermine and Spermidine[1]

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The development of methods involving hydrogen bromide cleavage of 3-substituted 2-oxazolidinones and concomitant detosylation of tosylamide functions in the substituent made possible the synthesis of N-(2-bromoethyl)amine hydrobromides from which potentially radioprotective compounds related to spermine and spermidine were derived. Thus, the method applied to N,N′-bis[3-(2-oxo-3-oxazolidinyl)propyl]-N,N′-tetramethylenebis-*p*-toluenesulfonamide (**3**) provided the spermine-related N,N′-bis[3-(2-bromoethylamino)propyl]-1,4-butanediamine tetrahydrobromide (**4**), which was converted into the corresponding bis Bunte salt **5a**, bisphosphorothioate **5b**, and dithiol **5c**. Synthesis of the spermidine-related N-[3-(2-bromoethylamino)propyl]-1,4-butanediamine trihydrobromide (**11**) involved acetyl protection of the terminal amino group. Retention of acetamido and phthalimido groups during oxazolidinone ring cleavage enabled the synthesis of the spermidine-related S-2-[3-(4-acetamidobutylamino)propylamino]ethylphosphorothioic acid (**13**) and the analogous phthalimido-substituted Bunte salt **22a** and phosphorothioate **22b**. Special problems of stoichiometry encountered in displacement reactions of polyfunctional N-(2-bromoethyl)amine hydrobromides with acid-labile thio anions are exemplified by the conversion of **11** into the corresponding Bunte salt **12a** and phosphorothioate **12b**; the thiol **12c**, as well as the thiol **5c**, were conveniently prepared by acid hydrolysis of the corresponding phosphorothioates.

In a preliminary report,[2] we briefly described syntheses of uniquely substituted N-(2-bromoethyl)amines by sequences consisting of preparations of 3-substituted 2-oxazolidinones and their facile ring cleavage with hydrogen bromide. Thus, syntheses beginning with 3-(3-chloropropyl)-2-oxazolidinone[3] (**2**) and derivatives of 1,4-butanediamine (**6**) afforded spermine- and spermidine-related N,N′-bis[3-(2-bromoethylamino)propyl]-1,4-butanediamine tetrahydrobromide (**4**) and N-[3-(2-bromoethylamino)propyl]-1,4-butanediamine trihydrobromide (**11**). These examples typify a versatile route to otherwise difficultly accessible intermediates that are convertible into analogs of 2-aminoethanethiol and related radioprotective agents containing multiple amine functions. In this report we describe development of these methods and conversions of the N-(2-bromoethyl)amines thus obtained into potential radioprotectors.

The initial step in the synthesis of **4**, which is outlined in Scheme I, was the alkylation of N,N′-tetramethyl-

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(1) This investigation was supported by the U. S. Army Medical Research and Development Command under Contract No. DA-49-193-MD-2028.

(2) J. R. Piper, R. D. Elliott, C. R. Stringfellow, Jr., and T. P. Johnston, *Chem. Ind.* (London), 2010 (1966).

(3) Asta-Werke AG, Brackwede (Westf.), Germany.