crystallization from 25 ml. of methanol gave fine yellow crystals with m.p. 182.5–184°; $\nu_{max}^{CHCl_3}$ 3.03 μ (N–H stretching), 5.76 μ (ester C=O).

Anal. Calcd. for $C_{23}H_{24}N_4O_{11}$: C, 51.88; H, 4.54; N, 10.52. Found: C, 51.86; H, 4.79; N, 10.21.

2,4-*O*-*p*-Dimethylaminobenzylidene-D-ribose Di-*n*-propyl Dithioacetal (X).—D-Ribose di-*n*-propyl dithioacetal (1.136 g., 4 mmoles) was added to a solution of *p*-dimethylaminobenzaldehyde (0.672 g., 4.5 mmoles) in 3 ml. of dioxane, and the solution was cooled to 5–10°. To this was added a mixture of 2 ml. of concentrated HCl (sp. gr. 1.16) and 5 ml. of water, previously cooled to 5–10°, and the resulting mixture was shaken vigorously with intermittant cooling for 20 min. A yellow solution was obtained which was poured into a separating funnel containing 100 ml. of ethyl acetate as well as 120 ml. of saturated aqueous $NaHCO_3$ solution. The ethyl acetate solution was then washed twice with 50 ml. of cold water and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure yielded 1.4 g. of a yellow oil. Crystallization was accomplished with the aid of a mixture of 2 ml. of ethyl acetate and 8 ml. of petroleum ether (b.p. 60–80°), yielding 0.73 g. (4.4%) of a crystalline material with m.p. 125–127°; $\nu_{max}^{CHCl_3}$ 2.82, 2.94 μ (OH).

Anal. Calcd. for $C_{26}H_{33}NO_4S_2$: C, 57.84; H, 7.95; N, 3.37. Found: C, 57.41; H, 7.88; N, 3.07.

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Some New Arylphosphonic and Diarylphosphinic Acids

LEON D. FREEDMAN AND G. O. DOAK

Department of Chemistry, North Carolina State University, Raleigh, North Carolina

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In earlier papers[1,2] we have reported that some arylphosphonic ($ArPO_3H_2$) and diarylphosphinic (Ar_2PO_2H) acids have appreciable *in vitro* activity against *Treponema pallidum*, the causative agent of syphilis. The preparation of eleven of the acids tested[2] has not yet been described. Nine of these were new compounds while two were known compounds which we prepared by methods different from those used previously. The present note describes the preparation and chemical properties of these eleven compounds. Their analyses, yields, and melting points are listed in Table I. Ultraviolet absorption data for some of the compounds are given in Table II.

Experimental Section

***p*-Iodophenylphosphonic Acid.**—Dry *p*-iodobenzenediazonium fluoroborate was suspended in isopropyl acetate and treated with PCl_3 and CuBr in the usual manner.[3] After the reaction mixture was hydrolyzed and steam distilled, the residual liquid in the distilling flask was filtered while hot in order to remove a brown oil. The filtrate was evaporated on the steam bath to incipient crystallization and then cooled. The crude phosphonic acid thus obtained was recrystallized from water.

***p*-Acetylphenylphosphonic Acid. A. From the Diazonium Fluoroborate and PCl_3.**—*p*-Nitroacetophenone (Eastman) in ethyl acetate was reduced with Raney nickel and hydrogen at 3.5 kg./cm.^{2} (50 lb.). After the catalyst was removed, the amine was isolated by evaporating the solvent *in vacuo* and purified by recrystallization from 95% ethanol. The yield of pure *p*-aminoacetophenone was 82%, m.p. 105–107° (lit.[4] m.p. 106–107°).

p-Acetylbenzenediazonium fluoroborate was prepared from the above amine and allowed to react with PCl_3 and CuBr in ethyl acetate. The phosphonic acid was isolated in the usual manner and was purified by procedure A as previously described.[3] Before analysis, it was dried *in vacuo* at 100°.

B. From *p*-Aminophenylphosphonic Acid and Acetaldoxime.—*p*-Aminophenylphosphonic (phosphanilic) acid[5] (43.3 g.) in 200 ml. of 3.4 *N* H_2SO_4 was diazotized at 0–5°. The resulting solution was neutralized to congo red and then allowed to react with acetaldoxime under conditions similar to those described for the conversion of *p*-chloroaniline to *p*-chloroacetophenone.[6] After the reaction mixture was acidified to congo red and made even more strongly acidic by the addition of 230 ml. of concentrated HCl, the solution was evaporated on the steam bath to 100 ml. and cooled, whereupon crude *p*-acetylphenylphosphonic acid crystallized. It was purified by extraction with absolute alcohol in a Soxhlet apparatus, evaporation of the resulting solution to dryness, and recrystallization of the residue from 6 *N* HCl. The infrared spectra of samples of *p*-acetylphenylphosphonic acid made by both methods were identical.

***m*-Phenoxyphenylphosphonic Acid.** ***m*-Bromophenylphosphonic acid**[7] (5.0 g.) was allowed to react with phenol, K_2CO_3, and copper powder under conditions similar to those described for conversion of *o*-bromophenylphosphonic acid to the corresponding phenoxy compound.[8] When the reaction mixture was steam distilled (to remove excess phenol) and then acidified, the hemipotassium salt[3] of *m*-phenoxyphenylphosphonic acid crystallized from solution. This salt was added to 100 ml. of boiling 6 *N* HCl, and sufficient 95% ethanol was added to dissolve the suspended solid. The solution was cooled and extracted with three 30-ml. portions of benzene. The benzene layers were combined and evaporated to dryness. Recrystallization of the residue from a mixture of heptane–toluene (1:2) yielded pure material.

***p*-Phenoxyphenylphosphonic Acid.**—The method used to prepare and isolate the hemipotassium salt of *p*-phenoxyphenylphosphonic acid was similar to that described for the *ortho* and *meta* isomers. The free acid was obtained by recrystallization of the salt from a mixture of 1 vol. of 95% ethanol to 3 vol. of 6 *N* HCl.

2-(*p*-Tolyloxy)phenylphosphonic Acid and 2-(*p*-Tolyloxy)-*p*-tolylphosphonic Acid.—*o*-Bromophenylphosphonic acid[5] and 2-bromo-*p*-tolylphosphonic acid[9] were allowed to react with redistilled *p*-cresol under conditions similar to those used in the preparation of the phenoxy derivatives. The hemipotassium salts obtained were converted to the free acids by recrystallization from a mixture of 1 vol. of 95% ethanol to 2 vol. of 6 *N* HCl.

Bis(*p*-phenoxyphenyl)phosphinic Acid.—An intimate mixture of 8.0 g. of bis(*p*-bromophenyl)phosphinic acid,[7] 20 ml. of redistilled phenol, 10.0 g. of anhydrous K_2CO_3, and 0.2 g. of copper powder was heated under reflux for 16 hr. After the excess phenol was removed by steam distillation, the reaction mixture was filtered and then acidified to congo red. The crude phosphinic acid thus obtained was purified by recrystallization from acetone–absolute alcohol (1:2).

2-Nitro-5-bromophenylphosphonic Acid.—A solution of *m*-bromophenylphosphonic acid[7] (10.0 g.) in 50 ml. of fuming HNO_3 (*d* 1.5) was evaporated to dryness, and the residue was recrystallized from 3 *N* HCl. The structure of this phosphonic acid was not established unequivocally, but it is probably 2-nitro-5-bromophenylphosphonic acid for the following reasons. (1) The compound does not form a water-insoluble magnesium salt either at room temperature or when heated. This behavior is characteristic of arylphosphonic acids containing bulky *ortho* substituents such as the nitro group.[10] (2) The nitration of *m*-bromobenzenearsonic acid yields 2-nitro-5-bromobenzenearsonic acid,[11] and the nitration of *m*-bromobenzoic acid yields mainly 2-nitro-5-bromobenzoic acid.[12] Since the electronic structure of the phos-

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(9) The preparation of 2-bromo-*p*-tolylphosphonic acid and bis(2-bromo-*p*-tolyl)phosphinic acid have been previously described [L. D. Freedman, H. Tauber, G. O. Doak, and H. J. Magnuson, *J. Am. Chem. Soc.*, **75**, 1379 (1953)] but were erroneously called "2-Br-5-$CH_3C_6H_3PO_3H_2$" and "(2-Br-5-$CH_3C_6H_3)_2PO_2H$," respectively.

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TABLE I
ARYLPHOSPHONIC AND DIARYLPHOSPHINIC ACIDS

Compd.	Yield, %	M.p., °C.[a]	Formula	Phosphorus, %[b] Calcd.	Found	Neut. equiv.[c] Calcd.	Found
p-Iodophenylphosphonic acid[d]	30	221–223	$C_6H_6IO_3P$	10.91	10.96	142.0	141.0
p-Acetylphenylphosphonic acid[e]	4,[f] 10[g]	163–167	$C_8H_9O_4P$	15.48	15.15	100.1	100.3
m-Phenoxyphenylphosphonic acid	45	92.5–93.5	$C_{12}H_{11}O_4P$	12.38	12.13	125.1	126.2
p-Phenoxyphenylphosphonic acid[h]	78	173.5–174.5	$C_{12}H_{11}O_4P$	12.38	12.34	125.1	124.9
2-Nitro-5-bromophenylphosphonic acid[i]	80	214–217 dec.[j]	$C_6H_5BrNO_5P$	10.98	10.99	141.0	140.2
Azoxydi-*p*-phenylenediphosphonic acid[k]	79	270–275 dec.	$C_{12}H_{12}N_2O_7P_2$	17.29	16.96	89.5	*l*
2-(*p*-Tolyloxy)phenylphosphonic acid	57	203–204	$C_{13}H_{13}O_4P$	11.72	11.55	132.1	133.6
2-(*p*-Tolyloxy)-*p*-tolylphosphonic acid	66	194–196	$C_{14}H_{15}O_4P$	11.13	11.03	139.1	141.4
Bis(*p*-iodophenyl)phosphinic acid	83	209–210	$C_{12}H_9I_2O_2P$	6.59	6.50	470.0	470.5
Bis(*p*-phenoxyphenyl)phosphinic acid	76	203–206	$C_{24}H_{19}O_4P$	7.70	7.53	402.4	398.5
4,4′-Phosphinicobis(3-bromobenzoic acid)[m]	46	278–282	$C_{14}H_9Br_2O_6P$	6.68	6.74	154.7	155.3

[a] Melting points were taken as previously described; *cf.* ref. 3. [b] Phosphorus was determined by the method of B. C. Stanley, S. H. Vannier, L. D. Freedman, and G. O. Doak, *Anal. Chem.*, **27,** 474 (1955). [c] The indicator used for the phosphonic acids was thymolphthalein; the indicator used for the phosphinic acids was phenolphthalein. [d] Previously prepared by G. M. Kosolapoff [*J. Am. Chem. Soc.*, **70,** 3465 (1948)] *via* the Sandmeyer reaction. [e] *Anal.* Calcd.: C, 48.01; H, 4.53. Found: C, 47.90; H, 4.34. [f] From *p*-acetylbenzenediazonium fluoroborate. [g] From *p*-aminophenylphosphonic acid. [h] Previously prepared as a monohydrate by W. C. Davies and C. J. O. R. Morris [*J. Chem. Soc.*, 2880 (1932)] *via* the Friedel–Crafts reaction. [i] *Anal.* Calcd.: Br, 28.34; N, 4.97. Found: Br, 28.38; N, 4.96. [j] This decomposition point was observed when a sample was placed on the melting point block preheated to 205° and the temperature of the block was slowly raised. [k] *Anal.* Calcd.: C, 40.24; H, 3.38; N, 7.82. Found: C, 39.94; H, 3.20; N, 7.60. [l] Determination of this neutral equivalent was not convenient because of the yellow color of dilute solutions of the compound. [m] *Anal.* Calcd.: Br, 34.44. Found: Br, 33.98.

TABLE II
ULTRAVIOLET ABSORPTION MAXIMA[a]

Compd.	λ_{max}, mμ	ϵ_{max}
p-Acetylphenylphosphonic acid	249	15,700
	284	1,600
m-Phenoxyphenylphosphonic acid	208	25,800
	272.5	1,960
	278.5	2,220
p-Phenoxyphenylphosphonic acid	236	15,700
	277.5	1,190
Bis(*p*-phenoxyphenyl)phosphinic acid	246.5	29,500
2-Nitro-5-bromophenylphosphonic acid	264.5	5,300
(Azoxydi-*p*-phenylene)diphosphonic acid	231.5	8,800
	268.5	9,880
	330	19,000

[a] All spectra were determined in 95% ethyl alcohol by the procedure previously described by H. H. Jaffé and L. D. Freedman, *J. Am. Chem. Soc.*, **74,** 1069 (1952).

phono group is very similar to that of the arsono group and also resembles that of the carboxy group, it seems reasonable to assume that the nitration of *m*-bromophenylphosphonic acid gives 2-nitro-5-bromophenylphosphonic acid.

Azoxydi-*p*-phenylenediphosphonic Acid.—A solution of *p*-nitrophenylphosphonic acid[3] (4.87 g.) in 25 ml. of water was added to a solution of 4.52 g. of arsenic oxide and 7.2 g. of NaOH in 25 ml. of water. The resulting mixture was refluxed for 8 hr. and then cooled. Acidification yielded a red precipitate which was recrystallized from a mixture of equal volumes of 95% ethanol and 6 *N* HCl. The ultraviolet absorption spectrum of this compound is similar to that of azoxybenzene,[13] which has maxima at 231 mμ (ε 8300), 260 (7000), and 323 (14,500).

Bis(*p*-iodophenyl)phosphinic Acid.—Bis(*p*-aminophenyl)phosphinic acid[5] (5.7 g.) in 25 ml. of water and 4.0 ml. of concentrated H_2SO_4 was diazotized at 0–5° with 3.5 g. of $NaNO_2$ in 6 ml. of water. The resulting solution was filtered from a trace of undissolved material and then added dropwise to a solution of 17.5 g. of KI and 17.5 g. of iodine in 25 ml. of water. The reaction mixture was stirred for 18 hr. at room temperature, and the precipitate of crude product was removed by filtration. It was purified by suspension in 100 ml. of 10% aqueous sodium bisulfite and subsequent recrystallization from 50% aqueous ethanol.

4,4′-Phosphinicobis(3-bromobenzoic Acid).—Bis(2-bromo-*p*-tolyl)phosphinic acid[9] (5.0 g.), dissolved in a mixture of 25 ml. of pyridine and 15 ml. of water, was oxidized with 25 g. of $KMnO_4$ by the method of Morgan and Herr.[14] After the excess pyridine was removed by steam distillation, the reaction mixture was filtered, decolorized with charcoal, and evaporated to 100 ml. on the steam bath. The resulting solution was added slowly with good stirring to 100 ml. of 10% HCl, whereupon the crude carboxy compound separated from solution. It was purified by recrystallization from aqueous acetone.

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Substituted 1,4-Diazepin-2-ones

RUDDY LITTELL AND DUFF S. ALLEN, JR.

Organic Chemical Research Section,
Lederle Laboratories Division,
American Cyanamid Company, Pearl River, New York

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In view of current interest in 1,4-benzodiazepin-2-ones as psychotherapeutic agents,[1] a program to prepare novel analogs to be screened for pharmacological activity was initiated. Since the procedures used to prepare these analogs were essentially those described in the literature,[2] no experimental details are herein presented.

Compounds I and II (Table I) were prepared by Friedel–Crafts reactions.[2] Compounds III, IV, and V (Table I) were prepared from 6-chloro-2-methyl-4H-3,1-benzoxazin-4-one[3] by Grignard syntheses[2b,4] in yields of 20 (including hydrolysis), 38, and 39%, respectively. The preparation of the Grignard reagents from the appropriately substituted bromobenzenes failed in ethyl ether but proceeded satisfactorily in refluxing tetrahydrofuran.[5] The acetamides obtained as Grignard products

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(5) W. J. Gensler and J. E. Stauffer [*J. Org. Chem.*, **23,** 908 (1958)] reported their failure to prepare 3,4-methylenedioxyphenylmagnesium bromide and cited the difficulty of others in preparing organomagnesium compounds from the related 4-bromo- and 4-iodoveratroles.