0.23 g. (35%) of 1,2-diphenyl-3-benzylhydrindene, m.p. 180–182°, identical with the high melting material derived from reduction of tetraphenylthiophene.

The filtrate from above was steam distilled. A gummy residue remained which after recrystallization from methanol yielded 0.25 g. (36%) of white needles, m.p. 88–90°, identical with the tetraphenylbutane isolated above.

The same two products were isolated when 3.0 g. (0.0084 mole) of tetraphenylbutadiene in 30 ml. of ether, 10 ml. of ethylene glycol dimethyl ether and 20 ml. of benzene were stirred for 3 hours with 0.5 g. of lithium. The dark-brown solution was poured rapidly into ethanol. A total of 0.93 g. (34%) of 1,2-diphenyl-3-benzylhydrindene, m.p. 180–182°, was isolated and identified by mixed melting point with the above samples. From the filtrate was isolated 0.90 g. (30%) of tetraphenylbutane, m.p. 89–91°, identical with the other samples isolated above.

C. By Hydrogenation of Tetraphenylbutadiene.—A solution of 0.35 g. (0.00098 mole) of tetraphenylbutadiene in 35 ml. of pure dioxane was treated over 22 hr. in the presence of Raney nickel with hydrogen at 1300 p.s.i. Removal of the dioxane led to the recovery of 0.17 g. (48%) of the starting material, m.p. 183–184°, identified by mixed melting point, and 0.21 g. of white needles, m.p. 85–88°, which after recrystallization from methanol yielded 0.17 g. (48%) of tetraphenylbutane, m.p. 89–90°, identical with the material isolated above.

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[CONTRIBUTION FROM THE VENEREAL DISEASE EXPERIMENTAL LABORATORY, U. S. PUBLIC HEALTH SERVICE, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF NORTH CAROLINA]

Magnesium Salts of Arylphosphonic Acids. The Preparation of *o*-Nitrophenylphosphonic Acid[1]

BY LEON D. FREEDMAN AND G. O. DOAK

RECEIVED JUNE 23, 1955

A number of arylphosphonic acids, previously prepared in this Laboratory, were tested to determine whether they form insoluble magnesium salts. It was found that most of these acids yield no precipitates with magnesia mixture in the cold, but, when heated with magnesia mixture, form voluminous precipitates. Arylphosphonic acids containing bulky *o*-substituents do not form insoluble magnesium salts. This fact permitted the isolation of *o*-nitrophenylphosphonic acid from the mixture of isomers obtained by nitrating phenylphosphonic acid.

It has long been known that most arsonic acids when heated with magnesia mixture yield insoluble magnesium salts.[2] This reaction has often proved useful in the isolation and purification of arsonic acids. In 1941, Bauer[3] noted an analogous reaction with *p*-chloro- and *p*-aminophenylphosphonic acids. Since we had available a considerable number of arylphosphonic acids, the preparation of which has been described in recent communications[4] from this Laboratory, it seemed of interest to determine which of these compounds react with magnesia mixture.

A sample of the phosphonic acid,[5] dissolved in dilute aqueous ammonia, was treated with magnesia mixture. The resulting solution was allowed to stand at room temperature for five minutes and then boiled for one minute. The following results were obtained: (1) Only two compounds, *p*-biphenylylphosphonic and 2-hydroxy-4-nitrophenylphosphonic acids, yielded insoluble magnesium salts at room temperature. (2) Compounds containing *o*-methyl, *o*-amino, *o*-hydroxy or *o*-fluoro substituents gave sparse precipitates on heating; compounds containing other *ortho* substituents did not form insoluble magnesium salts either at room temperature or when heated. (3) With one exception, every compound that did not contain an *ortho* substituent gave a copious precipitate on heating. The exception was *m*-carboxyphenylphosphonic acid which failed to give a precipitate with magnesia mixture.

The Preparation and Properties of *o*-Nitrophenylphosphonic Acid.—The above results indicate that bulky *ortho* substituents (such as C_2H_5, CH_3O, COOH, Cl, Br and I) inhibit the formation of insoluble magnesium salts of arylphosphonic acids. It occurred to us that this effect might be used to bring about the separation of *o*-substituted phosphonic acids from mixtures with *m*- and *p*-isomers. In general, the separation of pure phosphonic acids from a mixture of these acids has proved to be extremely difficult.[6] Kosolapoff[6a] has reported that the nitration of diethyl phenylphosphonate produced a mixture of the corresponding *o*- and *m*-nitrophenylphosphonates, which he was unable to separate by fractional distillation. Furthermore, after these esters had been hydrolysed, he was unable to separate the free acids from the mixture. It was felt that it would be of interest to isolate the pure *o*-isomer, especially since the preparation of *o*-nitrophenylphosphonic acid by other methods never has been accomplished.[4a,d]

Using Kosolapoff's procedure,[6a] we prepared a mixture of isomers of nitrophenylphosphonic acid. This material was dissolved in dilute aqueous am-

(1) The organophosphorus nomenclature used in this paper is that proposed by the Organic Division's Advisory Committee on the Nomenclature of Organic Phosphorus Compounds; *cf. Chem. Eng. News*, **30**, 4515 (1952).

(2) See, for example, W. M. Dehn, *Am. Chem. J.*, **33**, 101 (1905); P. Ehrlich and A. Bertheim, *Ber.*, **40**, 3292 (1907).

(3) H. Bauer, THIS JOURNAL, **63**, 2137 (1941).

(4) (a) G. O. Doak and L. D. Freedman, *ibid.*, **73**, 5658 (1951); (b) **74**, 753 (1952); (c) **75**, 683 (1953); (d) L. D. Freedman, H. Tauber, G. O. Doak and H. J. Magnuson, *ibid.*, **75**, 1379 (1953); (e) H. H. Jaffé, L. D. Freedman and G. O. Doak, *ibid.*, **75**, 2209 (1953); (f) G. O. Doak and L. D. Freedman, *ibid.*, **75**, 6307 (1953); (g) H. H. Jaffé, L. D. Freedman and G. O. Doak, *ibid.*, **76**, 1548 (1954); (h) L. D. Freedman and G. O. Doak, *ibid.*, **77**, 173 (1955).

(5) Every phosphonic acid described in ref. 4 was used. We also tested o-tolylphosphonic acid, which was kindly made available to us by Dr. G. M. Kosolapoff of the Ross Chemical Laboratory, Alabama Polytechnic Institute.

(6) (a) G. M. Kosolapoff, *ibid.*, **71**, 4021 (1949); (b) V. L. Bell, Jr., and G. M. Kosolapoff, *ibid.*, **75**, 4901 (1953).

monia and treated with magnesia mixture. When the resulting solution was boiled, a yellow precipitate was obtained which was removed by filtration. From the filtrate we obtained a 7% yield of a nitrophenylphosphonic acid, m.p. 200–203°. Mixed m.p.'s with *m*- and *p*-nitrophenylphosphonic acids gave large depressions. These results, together with the *pK* data, ultraviolet absorption spectra and biological results described below, clearly demonstrate that we have prepared *o*-nitrophenylphosphonic acid.

We also investigated the preparation of the *ortho* isomer by the nitration of the phenylphosphonic acid. The nitration of this acid has been studied by several investigators.[7] Nijk[7b] showed that *m*-nitrophenylphosphonic acid is formed; he was unable to detect the presence of either *o*- or *p*-isomers although he made a determined effort to do so. However, it is possible (as Kosolapoff[6a] has suggested) that these isomers were missed. This possibility is strengthened by the fact that the sample of *m*-nitrophenylphosphonic acid prepared by Nijk gave a m.p. of 140° while the pure compound is known[4a] to melt at 155–156°. We have now found that phenylphosphonic acid can be nitrated with fuming nitric acid to give a virtually quantitative yield of mononitrated phenylphosphonic acid. From this material we obtained through the magnesium salt procedure a 13% yield of *o*-nitrophenylphosphonic acid and a 57% yield of *m*-nitrophenylphosphonic acid.

Table I lists some of the properties of the isomeric nitrophenylphosphonic acids. It is seen that the *pK*'s of the *o*-nitro isomer are higher than the corresponding *pK*'s of the other isomers. The "*ortho* effect" is undoubtedly due to intramolecular hydrogen bonding and can be elucidated by mechanisms previously described.[4a] The second *pK* is affected to a larger extent, since the proton to be removed in this dissociation is involved in a hydrogen bond between one of the oxygens in the phosphono group and one in the nitro group. It is noteworthy that the *pK*'s of the *o*-nitrobenzenearsonic acid are higher than the corresponding *pK*'s of the *m*- and *p*-nitrobenzenearsonic acids.[8]

TABLE I

THE ISOMERIC NITROPHENYLPHOSPHONIC ACIDS

$RC_6H_4PO_3H_2$ R =	M.p., °C.	pK_1	pK_2	$\lambda_{max.}$, mμ	$\epsilon_{max.}$
o-O_2N	200–203	1.45	6.74	251	3,740
m-O_2N	155–156[a]	1.30[b]	6.27[b]	263[c]	6,400[c]
p-O_2N	197–198[a]	1.24[b]	6.23[b]	270[c]	10,400[c]

[a] Taken from ref. 4a. [b] Taken from ref. 4e. [c] Taken from ref. 9.

The ultraviolet absorption spectra of *m*- and *p*-nitrophenylphosphonic acids are very similar to the spectrum of nitrobenzene.[9] The absorption of *o*-nitrophenylphosphonic acid is much less intense, and shows a slight hypsochromic shift. Remington[10] has shown that the absorption of an *o*-substituted nitro compound, in general, should be less intense than that of the corresponding *p*-isomer. This effect is attributed to steric interference with the resonance between the nitro group and the benzene ring.

Unpublished results of Dr. J. D. Thayer of this Laboratory show that *o*-nitrophenylphosphonic acid has no activity against a wide variety of bacterial species. Thus, this compound differs from the *m*-isomer which is active against *S. hemolyticus*, (C203), and from the *p*-isomer which inhibits the growth of a number of microörganisms.[11]

Experimental

Reaction of Magnesia Mixture with Arylphosphonic Acids.—A solution of 0.05 millimole of phosphonic acid in 1.0 ml. of 10% aqueous ammonia was mixed with 1.0 ml. of magnesia mixture.[12] The resulting solution was allowed to stand at room temperature for five minutes and then boiled vigorously for an additional minute. Except in those cases noted in the text, the magnesium salt separated immediately as a voluminous precipitate.

Magnesium *p*-Nitrophenylphosphonate.—The composition of a typical magnesium salt was determined in the following manner. A solution of 2.03 g. of *p*-nitrophenylphosphonic acid[4a] in 50 ml. of 10% aqueous ammonia was mixed with 50 ml. of magnesia mixture. The precipitate obtained by boiling was removed by filtration and dissolved in 25 ml. of 0.6 *N* hydrochloric acid. The resulting solution was filtered from a small amount of undissolved material and then made alkaline with 5 ml. of 10% aqueous ammonia. When this solution was boiled, a precipitate formed which was removed by filtration and dried *in vacuo* at 100°. The yield was 1.91 g., m.p. >300°.

Anal. Calcd. for $C_6H_4MgNO_5P \cdot 1^1/_2H_2O$: N, 5.55: P, 12.27; H_2O, 10.7. Found: N, 5.62; P, 12.14; wt. loss at 240°, 10.0.

The material dried at 240° gave satisfactory analyses for the anhydrous salt. Presumably, therefore, only water was lost when the hydrated salt was heated to this temperature.

Anal. Calcd. for $C_6H_4MgNO_5P$: N, 6.21; P, 13.74. Found: N, 6.13; P, 13.56.

The Preparation of *o*-Nitrophenylphosphonic Acid.—*o*-Nitrophenylphosphonic acid can be isolated from the mixture of isomers obtained by the hydrolysis of the diethyl nitrophenylphosphonates prepared according to ref. 6a. However, a more convenient source is the mixture of nitro acids obtained by nitrating phenylphosphonic acid. Phenylphosphonic acid (50 g.) was nitrated at 30–35° with 290 ml. of fuming nitric acid (d. 1.5) under conditions similar to those described in ref. 7c. The yield of nitrated material was 64 g., m.p. 138–140°.

Anal. Calcd. for $C_6H_6NO_5P$: N, 6.90. Found: N, 6.87.

A solution of 43 g. of this material in 270 ml. of 10% aqueous ammonia was mixed with 1 l. of magnesia mixture.[13] The resulting solution was boiled for at least 30 minutes in order to precipitate the magnesium salt of *m*-nitrophenylphosphonic acid. The precipitate was removed by filtration, washed with hot water and dried *in vacuo* over sulfuric acid. The yield was 43 g.

Anal. Calcd. for $C_6H_4MgNO_5P \cdot 1.2H_2O$: N, 5.67; P, 12.54; H_2O, 8.75. Found: N, 5.69; P, 12.24; wt. loss at 240°, 8.79.

The filtrate from the magnesium salt was adjusted to *p*H > 10 with 100 ml. of 20% sodium hydroxide solution, filtered and then aerated to remove the ammonia. The re-

(7) (a) A. Michaelis, *Ber.*, **8**, 493 (1875); A. Michaelis and E. Benzinger, *Ann.*, **188**, 275 (1877); (b) D. R. Nijk, *Rec. trav. chim.*, **41**, 461 (1922); (c) G. M. Kosolapoff, THIS JOURNAL, **70**, 3465 (1948).

(8) D. Pressman and D. H. Brown, *ibid.*, **65**, 540 (1943).

(9) H. H. Jaffé and L. D. Freedman, *ibid.*, **74**, 1069 (1952).

(10) W. R. Remington, *ibid.*, **67**, 1838 (1945).

(11) J. D. Thayer, H. J. Magnuson and M. S. Gravatt, *Antibiotics & Chemotherapy*, **3**, 256 (1953).

(12) Magnesia mixture was prepared according to the directions in "Official Methods of Analysis of the Association of Official Agricultural Chemists," Seventh Edition, Association of Official Agricultural Chemists, Washington, D. C., 1950, p. 605. This mixture was prepared by dissolving 55 g. of $MgCl_2 \cdot 6H_2O$ and 140 g. of NH_4Cl in water; 130.5 ml. of concentrated aqueous ammonia was added, and the resulting solution was diluted to one liter.

(13) An aqueous solution of $MgCl_2 \cdot 6H_2O$ (55 g./l.) is as effective as magnesia mixture.

sulting solution was stirred for 30 minutes with 350 g. of Dowex-50 (hydrogen ion form) which changed the *p*H of the solution to 1.0 or less; the resin was removed and the solution was evaporated to dryness. The residue was extracted with ether in a soxhlet apparatus until the material in the thimble gave no acid reaction. *o*-Nitrophenylphosphonic acid crystallized readily from the ether solution, and a second crop could be obtained by evaporating the ether to a small volume. The yield of pale yellow crystals was 5.6 g., m.p. 200–203°. Mixed m.p. with *p*-nitrophenylphosphonic acid was 159.5–165°; mixed m.p. with *m*-nitrophenylphosphonic acid was 133–137°.

Anal. Calcd. for $C_6H_6NO_5P$: N, 6.90; P, 15.25; neut. equiv., 101.5. Found: N, 6.84; P, 15.18; neut. equiv., 101.5.

The magnesium salt of *m*-nitrophenylphosphonic acid was converted to the free acid in the following manner. A suspension of 41 g. of the salt in 250 ml. of 6% sodium hydroxide solution was heated to boiling and then allowed to cool. The precipitated magnesium hydroxide was removed by filtration, and the filtrate was stirred with 350 g. of Dowex-50 (hydrogen ion form) which changed the *p*H of the solution to 1.0 or less. The resin was removed, and about 25 ml. of concentrated hydrochloric acid was added to the resulting solution, which was then evaporated to dryness. The residue was extracted with ether in a soxhlet apparatus. When the ethereal solution was concentrated to incipient crystallization and cooled, there was obtained 23.3 g. of *m*-nitrophenylphosphonic acid. This was identified by analysis, by mixed m.p. with an authentic sample and by ultraviolet absorption.

Physical Measurements.—The acid dissociation constants were determined by potentiometric titration in water as described in an earlier paper.[4e]

The ultraviolet absorption spectra were determined in 95% ethyl alcohol by the procedure previously used.[9] All measurements were made at room temperature with 1.0-cm. silica cells. The molar extinction coefficient, ϵ, was calculated from the equation: $\epsilon = D/lc$, where D = optical density, l = absorption cell thickness in cm., and c = the concentration of the sample in moles per liter.

Acknowledgments.—The authors wish to thank Miss Betty Jean Pegram for performing the analyses necessary for this investigation and Mr. Edward L. Petit for skilled technical assistance.

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[CONTRIBUTION FROM THE VENEREAL DISEASE EXPERIMENTAL LABORATORY, U. S. PUBLIC HEALTH SERVICE, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF NORTH CAROLINA]

The Ultraviolet Absorption Spectra of Some Biphenyl Derivatives of Phosphorus and Arsenic

BY LEON D. FREEDMAN

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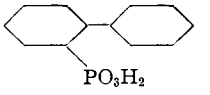
The ultraviolet absorption spectra of a number of biphenyl derivatives of phosphorus and arsenic have been determined. These spectra indicate that the *o*-PO_3H_2 and the *o*-AsO_3H_2 groups are very effective in restricting rotation around the carbon–carbon bond joining the two rings in the biphenyl molecule. The spectrum of arsafluorinic acid exhibits the intensity and the prominent fine structure characteristic of fluorene derivatives.

Biphenyl and its *meta* and *para* substituted derivatives have intense absorption ($\epsilon_{max.} > 10{,}000$) near 250 m$\mu$, due mainly to extensive resonance between the two phenyl rings.[1] *Ortho* substituents may hinder the attainment of a planar arrangement of the two rings and thus cause a considerable change in the ultraviolet absorption. For example, the presence of two bulky *ortho* substituents in 2,2′-dimethylbiphenyl reduces the molecular extinction coefficient enormously.[1b] A single *ortho* substituent ordinarily has comparatively little effect.[1d]

In a recent communication[2] from this Laboratory, evidence was presented which indicated that the two phenyl rings in *o*-biphenylylphosphonic acid(I)



I

(and in *o*-biphenylarsonic acid) are almost perpendicular to each other. This configuration, it was concluded, is reinforced by a hydrogen bond between the PO_3H_2 (or AsO_3H_2) group and one of the benzene rings. If these deductions are correct, the ultraviolet absorption spectra of these compounds should differ markedly from the spectrum of biphenyl. Table I lists the wave lengths of the absorption maxima and the corresponding molar extinction coefficients for these compounds and several related biphenyl derivatives.

TABLE I

ULTRAVIOLET ABSORPTION CHARACTERISTICS OF SOME BIPHENYL DERIVATIVES

Compound	$\lambda_{max.}$, mμ	$\epsilon_{max.}$
Biphenyl	248	16,600
p-Biphenylylphosphonic acid	255	21,900
3,3′-Biphenyldiphosphonic acid	250.5	15,600
4,4′-Biphenyldiphosphonic acid	262.5	23,300
o-Biphenylylphosphonic acid	237	8,220
	274.5	2,030
o-Biphenylarsonic acid	239	8,510
	276	2,890
Arsafluorinic acid	226	25,700
	232.5	29,600
	240	28,000
	276.5	8,210
	287.5	6,870

The ultraviolet absorption spectra of *p*-biphenylylphosphonic, 3,3′-biphenyldiphosphonic and 4,4′-biphenyldiphosphonic acids are very similar to the

(1) See, for example (a) L. W. Pickett, G. F. Walter and H. France, THIS JOURNAL, **58**, 2296 (1936); (b) M. T. O'Shaughnessy and W. H. Rodebush, *ibid.*, **62**, 2906 (1940); (c) B. Williamson and W. H. Rodebush, *ibid.*, **63**, 3018 (1941); (d) R. A. Friedel, M. Orchin and L. Reggel, *ibid.*, **70**, 199 (1948); (e) G. H. Cookson and F. G. Mann, *J. Chem. Soc.*, 2888 (1949); (f) A. J. Bilbo and G. M. Wyman, THIS JOURNAL, **75**, 5312 (1953). This last paper discusses spectral and chemical effects associated with the degree of planarity of certain biphenyl derivatives.

(2) H. H. Jaffé, L. D. Freedman and G. O. Doak, *ibid.*, **76**, 1548 (1954).