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

The Electrical Effect of the Diethoxyphosphinyl Group[1]

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RECEIVED SEPTEMBER 13, 1954

The *m*- and *p*-isomers of diethoxyphosphinylbenzoic acid, -aniline and -phenol have been prepared, and their acid (or base) dissociation constants have been determined. From these data we have calculated the following substituent constants for the diethoxyphosphinyl group [$-PO(OC_2H_5)_2$]: $\sigma_m = 0.55$; $\sigma_p = 0.60$; $\sigma_p^* = 0.78$.

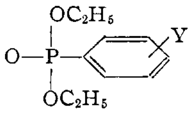
Although more than a hundred arylphosphonic acids have been described,[2] little is known about the effect of the dihydroxyphosphinyl ($—PO_3H_2$) group on the reactivity of the benzene ring and of side chains attached to it. The nitration of phenylphosphonic acid apparently requires vigorous reaction conditions and produces *m*-nitrophenylphosphonic acid in yields of about 60%.[3] These observations indicate that the PO_3H_2 group deactivates the benzene ring to electrophilic substitution. However, since the percentage of other isomers formed in the nitration is not known, we cannot make even a qualitative comparison of the electron attracting power of this group and other deactivating substituents such as NO_2, CN and $COCH_3$.

Probably the most useful measure of the electrical effect of the PO_3H_2 group in arylphosphonic acids would be the Hammett substituent constants.[4] However, it may be difficult to determine these constants for the un-ionized PO_3H_2 group since arylphosphonic acids are so strong ($pK_1 \sim 2$) that they are present partly or wholly as anions under the conditions of most reactions.[5] It has been suggested[6] that, for a given position, a single substituent constant should be applicable to the free and esterified carboxy groups. Consequently, it appears reasonable to expect that the substituent constants for the free and esterified dihydroxyphosphinyl groups do not differ appreciably. This expectation is further supported by the fact that diethyl phenylphosphonate, like the free acid, is nitrated mainly in the *meta* position.[7]

Accordingly, the *m*- and *p*-isomers of diethoxyphosphinylbenzoic acid, -aniline and -phenol have been prepared by methods described in the Experimental section, and their acid (or base) dissociation constants have been determined. From these data we were able to calculate the "normal" σ-values for the *m*- and *p*-$PO(OC_2H_5)_2$ groups as well as the σ^*-value[6] for the latter group. Table I summarizes this information together with the relevant *pK*'s.

TABLE I

pK_a's OF



Y =	pK_a	σ	ρ^a
p-COOH	3.60	0.60	1.000
p-NH_3^+	2.22	.84	2.767
p-OH	8.28	.73	2.113
m-COOH	3.65	.55	1.000
m-NH_3^+	3.09	.53	2.767
m-OH	8.66	.56	2.113

[a] Taken from ref. 6.

The σ-values determined from the three *m*-substituted compounds are virtually identical. Hence we can assign a σ-value of 0.55 to the *m*-diethoxyphosphinyl group and can conclude that this group has a smaller electron affinity than the NO_2, CN and SO_2CH_3 groups but a greater affinity than the $COCH_3$ and COOH groups.

Table I also indicates that the *p*-$PO(OC_2H_5)_2$ group belongs to the class of electron-attracting groups which require the use of larger σ-values (denoted by σ^*) for reactions of anilines and phenols than for reactions of other benzene derivatives. However, the difference ($\sigma^* - \sigma = 0.19 \pm 0.06$) in this case is appreciably smaller than for a number of other electron-attracting groups. Thus, the difference between σ and σ^* amounts to 0.91 for *p*-CHO, 0.43 for *p*-NO_2, 0.37 for CN, 0.36 for $COCH_3$, and 0.32 for SO_2CH_3.[6] Such differences have been interpreted as evidence for resonance interactions of the substituent with amino, hydroxy and similar groups.[8,9] Presumably, therefore, the electrical effect of the *p*-$PO(OC_2H_5)_2$ group involves conjugative as well as inductive factors.

Bordwell and Cooper[9] found that the σ^*-value obtained for the *p*-SO_2CH_3 group from the *pK* of *p*-methylsulfonylphenol was smaller than the value obtained from *p*-methylsulfonylaniline. Table I shows that a similar relation exists for the σ^*-values obtained from the *pK*'s of *p*-diethoxyphosphinylphenol and -aniline. Although it is doubtful that this difference is significant, it is noteworthy that this type of relation has been observed only in these two substituents, both of

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[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). In the body of this paper the compounds are named, for convenience, as diethoxyphosphinyl derivatives, while the more customary diethyl arylphosphonate names are used in the Experimental section.

[2] G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 162–167; see also L. D. Freedman, H. Tauber, G. O. Doak and H. J. Magnuson, THIS JOURNAL, **75**, 1379 (1953) and papers cited therein.

[3] D. R. Nijk, *Rec. trav. chim.*, **41**, 461 (1922).

[4] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII.

[5] Substituent constants for the PO_3H^- and the $PO_3^=$ groups have already been proposed; *cf.* H. H. Jaffé, L. D. Freedman and G. O. Doak, THIS JOURNAL, **75**, 2209 (1953).

[6] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

[7] G. M. Kosolapoff, THIS JOURNAL, **71**, 4021 (1949).

[8] G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941, pp. 257, 417.

[9] F. G. Bordwell and G. D. Cooper, THIS JOURNAL, **74**, 1058 (1952); see also F. G. Bordwell and H. M. Anderson, *ibid.*, **75**, 6019 (1953).

TABLE II

DIETHYL ARYLPHOSPHONATES

$YC_6H_4PO(OC_2H_5)_2$ Y =	Yield, %	B.p. °C.	B.p. Mm.	M.p.,[a] °C.	Phosphorus, %[b] Calcd.	Phosphorus, %[b] Found	Nitrogen, %[c] Calcd.	Nitrogen, %[c] Found
m-$COOC_2H_5$	79	137–149	0.3		10.82	10.67		
p-$COOC_2H_5$	80	143–147	.3		10.82	10.90		
m-COOH	92			85–86	12.00	11.82		
p-COOH	93			105–107	12.00	11.70		
m-NO_2	79	133–137	.2		11.95	11.92	5.40	5.29
p-NO_2	88	139–144	.3		11.95	11.91	5.40	5.32
m-NH_2	95			47–50	13.52	13.47	6.11	6.10
p-NH_2	76			115–119	13.52	13.19	6.11	6.09
m-OH	15			67–69	13.46	13.00		
p-OH	47			93–94	13.46	13.31		

[a] Melting points were taken as previously described; *cf.* ref. 11. [b] Phosphorus was determined by a modification of the method of M. D. Bachofer and E. C. Wagner, *Ind. Eng. Chem., Anal. Ed.*, **15**, 601 (1943). [c] Nitrogen was determined by a micro-Kjeldahl procedure.

which can exert a $-M$ effect only by expansion of the valence shell of the central (sulfur or phosphorus) atom.

Kosolapoff[7] has found that the principal by-product of the nitration of diethyl phenylphosphonate is diethyl *o*-nitrophenylphosphonate. This fact is consistent with the above conclusion that the $PO(OC_2H_5)_2$ group is conjugated with the ring, since purely inductive *meta*-directing substituents promote the formation of the *p*-isomer as a by-product while the *o*-isomer is favored when resonance is possible between the *meta*-directing substituent and the ring.[10]

Experimental

Preparation of Materials.—The preparation of the phosphonic acids used in the syntheses given below have been reported previously.[5,11] The esters prepared, together with their analyses, yields and m.p.'s (or b.p.'s) are listed in Table II.

Diethyl *m*-Carbethoxyphenylphosphonate.—*m*-Carboxyphenylphosphonic acid (11.4 g.) and 37 g. of phosphorus pentachloride were intimately mixed in a three-necked 250-ml. flask which was then quickly equipped for vacuum distillation. Both the air leak for the prevention of bumping and the vacuum line were protected from moisture by drying tubes. The flask was heated gently; when no solid particles remained, vacuum from a water pump was carefully applied. After the phosphorus oxychloride formed in the reaction and the excess phosphorus pentachloride had been removed, 15 ml. of dry carbon tetrachloride was added to the reaction flask. Then 37 ml. of absolute alcohol was introduced under conditions similar to the esterification procedure described by Toy.[12] The carbon tetrachloride and excess alcohol were stripped off at the water pump; high-vacuum distillation of the residue gave the pure ester.

Diethyl *p*-carbethoxyphenylphosphonate was prepared by the method used for the *m*-isomer.

Diethyl *m*-Nitrophenylphosphonate and Diethyl *p*-Nitrophenylphosphonate.—These compounds were obtained by the method described above except that 2.1 moles of phosphorus pentachloride per mole of phosphonic acid was used.

Diethyl *m*-Carboxyphenylphosphonate.—Diethyl *m*-carbethoxyphenylphosphonate (5.77 g.) was dissolved in a mixture of 40 ml. of alcohol and 40.9 ml. of 0.494 *N* sodium hydroxide solution. After about 24 hours at room temperature the *p*H of the resulting solution had fallen to 8.7. The solution was concentrated *in vacuo* to about 30 ml. and filtered. When the solution was acidified to congo red with dilute hydrochloric acid, an oil separated. The mixture was extracted with three 30-ml. portions of benzene. The combined benzene solutions were filtered through paper. Evaporation of the filtrate yielded a colorless viscous oil which readily crystallized. Analysis of the crystals showed that one ester group had been saponified. Since the hydroxamic acid test[13] was negative, the compound cannot contain a carboxylic ester group. Hence, we may conclude that the material is the desired compound.

Diethyl *p*-carboxyphenylphosphonate was prepared by the method used for the *m*-isomer.

Diethyl *m*-Aminophenylphosphonate.—A solution of 15.2 g. of diethyl *m*-nitrophenylphosphonate in 100 ml. of absolute alcohol was shaken with Raney nickel catalyst under an initial hydrogen pressure of 40 lb. After the uptake of hydrogen ceased, the catalyst was removed by filtration and the solvent distilled off under vacuum. The resulting sirup solidified when kept at −25° overnight. The solid was purified by dissolution in warm benzene, treatment of this solution with charcoal, and evaporation of the clarified solution to dryness.

Diethyl *p*-Aminophenylphosphonate.—Diethyl *p*-nitrophenylphosphonate was reduced by the method described for the *m*-isomer. The catalyst was removed by filtration, and 200 ml. of water was added to the filtrate. The resulting solution was cooled in a deep-freeze at −25°. The crystals obtained were dried *in vacuo* at 100°.

Diethyl *m*-Hydroxyphenylphosphonate.—Diethyl *m*-aminophenylphosphonate (8.17 g.), dissolved in 35 ml. of water and 10 ml. of concentrated hydrochloric acid, was diazotized at 0° with ethyl nitrite. After a starch–iodide test remained positive for five minutes, the solution was warmed until the evolution of nitrogen was completed at which time an oil separated. The mixture was extracted with three 30-ml. portions of benzene. The combined benzene solutions were extracted with three 30-ml. portions of 10% sodium carbonate solution. The combined aqueous alkaline extracts were acidified to congo red and extracted with three 30-ml. portions of benzene. The combined benzene extracts were filtered, and the organic solvent removed by evaporation. The oily residue crystallized when placed in a deep-freeze at −25°.

Diethyl *p*-hydroxyphenylphosphonate was prepared by the method used for the *m*-isomer.

***pK* Determinations.**—The *pK*'s were determined by standard methods of potentiometric titration[5] in 0.04 *M* aqueous solution at 23 ± 1°. For the amino compounds the *pK*'s reported are those of the corresponding ammonium ions. *pK* measurements were reproducible to ±0.03 unit.

Acknowledgment.—The authors wish to thank Mrs. Barbara Stanley for performing the analyses necessary for this research and Mr. Edward L. Petit and Mrs. Caroline Sasser for skilled technical assistance. The continued interest of Dr. G. O. Doak is gratefully acknowledged.

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(10) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 261.

(11) G. O. Doak and L. D. Freedman, THIS JOURNAL, **73**, 5658 (1951).

(12) A. D. F. Toy, U. S. Patent 2,400,577 (May 21, 1946).

(13) F. Feigl, "Qualitative Analysis by Spot Tests," translated by J. W. Matthews, "Elsevier," Amsterdam, Holland, 1939, p. 295. See also T. Lies, R. E. Plapinger and T. Wagner-Jauregg, THIS JOURNAL, **75**, 5755 (1953).