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SUBSTITUENT EFFECTS OF PHOSPHORUS AND ARSENIC CONTAINING GROUPS IN AROMATIC SUBSTITUTION–II

NITRATION OF BENZYLPHOSPHONIC ACID AND RELATED COMPOUNDS

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Abstract—The reactivities of benzylphosphonic acid (protonated and unprotonated) and β-phenylethylphosphonic acid have been determined for nitration. The highly selective *para/ortho* orientation has been confirmed. The relative reactivities of systems PhX and $PhCH_2X$ for some substituents are discussed.

The effect of an interposed methylene group on the reactivity of the systems PhX and $PhCH_2X$ in electrophilic substitution provides an useful model for the elucidation of the relative importance of the detailed mechanisms of the substituent effects. Ridd *et al*[1] discussed recently the substituent effects of the groups X and CH_2X in *meta* nitration in terms of the variation of the transmission factors for field effect with the nature of the group X. For the —I, —M groups, the change of the reactivity of the ring, resulting from the introduction of the methylene bridge should depend strongly on the relative contribution of the mesomeric interactions to the total electron-withdrawing properties of the group X. The inductive effects should be reduced according to the change of the ring-substituent distance and of the number of the intervening σ bonds, whereas the conjugative interactions of the group X disappear in the benzyl derivative. In consequence, the greater the importance of the —M effect of a given group, the greater the relative change of the free energy of activation for the substitution should be observed when the substituent is separated from the ring by a saturated C atom.

In the preceeding paper the substituent effects of some phosphorus and arsenic containing groups in nitration have been discussed.[2] It was shown that for the PhX system, the deactivation decreases strongly in the order of phosphonium (PMe_3^+), "quasiphosphonium" ($PO_3H_3^+$), and phosphonic (PO_3H_2) groups. This order can result from the changes in the magnitudes of both inductive and conjugative effects of substituents. In the present paper we report the results obtained for the nitration of the systems where the phosphorus-containing groups have been separated from the ring by a saturated carbon chain.

The nitration of benzylphosphonic (**1**) and β-phenylethylphosphonic (**2**) acids in aqueous sulphuric acid follow second-order kinetics; values of the stoichiometric second-order rate coefficients at different acidities are set out in Table 1. These results, together with those for benzene[3] are plotted logarithmically in Fig 1.

Table 1. Rate coefficients for nitration in aqueous sulphuric acid at 25·0°

Substrate % H_2SO_4	$10^2 k_2$ (l. mole^{-1} sec^{-1}) $PhCH_2PO_3H_2$ **1**	 $PhCH_2CH_2PO_3H_2$ **2**
61·5		0·0803
64·9	0·0614	
65·1		1·94
65·6	0·123	
66·8		4·18
67·7	0·601	
68·5		22·7
71·0	7·60	
72·3	20·8	

Following the arguments presented before,[2] it can be seen from Fig 1 that for a given acidity range compounds **1** and **2** react as protonated species; the corresponding values of the slopes are 0·36 and 0·33, respectively. The relative reactivities, given therefore by a single set of log k_2 data, reflect in fact the substituent effects of the "quasiphosphonium" pole, —P(OH)$_3^+$, separated from the ring by one or two methylene groups.

Substituent effect of the unprotonated phos-

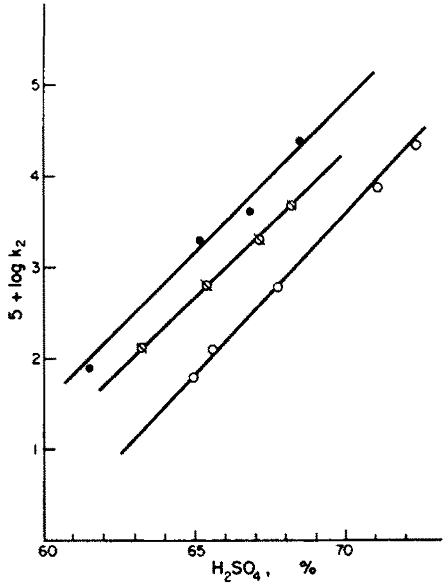


Fig 1. Variation of rate coefficients (l. mole^{-1} sec^{-1}) with acidity for nitration in sulphuric acid; ○, $PhCH_2PO_3H_2$; ∅, Benzene (Ref 3); ●, $PhCH_2CH_2PO_3H_2$.

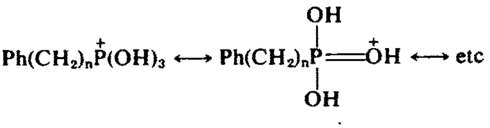
Table 2. Relative reactivities in nitration (25·0°)

Substrate	Medium	Relative reactivity (Benzene = 1)
1. Ph—$P(OH)_3^+$	aq. H_2SO_4	$1{\cdot}1 \times 10^{-5}$[a]
2. Ph—$CH_2P(OH)_3^+$	aq. H_2SO_4	0·18
2a. Ph—$CH_2CH_2P(OH)_3^+$	aq. H_2SO_4	3·2
3. Ph—PO_3H_2	Ac_2O	$2{\cdot}9 \times 10^{-3}$[a]
4. Ph—$CH_2P(O)(OEt)_2$	Ac_2O	2·6
5. Ph—PMe_3^+	aq. H_2SO_4	$1{\cdot}6 \times 10^{-7}$[b]
6. Ph—$CH_2PMe_3^+$	$MeNO_2$	0·0066[c]
7. Ph—PPh_3^+	aq. H_2SO_4	$1{\cdot}0 \times 10^{-7}$[d]
8. Ph—$CH_2PPh_3^+$	aq. H_2SO_4	0·0397[e]
9. Ph—$AsMe_3^+$	aq. H_2SO_4	13×10^{-7}[b]
10. Ph—$CH_2AsMe_3^+$	$MeNO_2$	0·0127[c]

[a] Taken from Ref 2
[b] Taken from Ref 4
[c] Taken from Ref 5
[d] Taken from Ref 6
[e] Taken from Ref 7.

phonic group can be estimated for nitration in acetic anhydride where the protonation equilibrium is not possible. Because of the very low solubility of **1** in Ac_2O, we have determined, using the method of competitive nitration, the relative reactivity of the diethyl ester of **1** for the nitration by AcO—NO_2 in Ac_2O. The difference in the effect of the —$P(O)(OEt)_2$ and —$P(O)(OH)_2$ should not be significant, and the obtained value of k_{rel} has been used for further discussion. The values of k_{rel}, together with some other taken from the literature, made it possible to compare the reactivities of systems PhX and $PhCH_2X$ for a number of phosphorus- or arsenic-containing derivatives; the pertinent data are collected in Table 2.

The relative reactivities for the series $Ph(CH_2)_nPO_3H_3^+$ (n = 0, 1, 2; compounds 1, 2, 2a of the Table) confirm the existence of the $p_\pi - d_\pi$ bonding between the O and P atoms in protonated phosphonic group. If a considerable fraction of the charge is localized on the O atoms, as represented by the structure **3a**



$$Ph(CH_2)_n\overset{+}{P}(OH)_3 \longleftrightarrow Ph(CH_2)_n\underset{OH}{\overset{OH}{P}}{=}\overset{+}{O}H \longleftrightarrow \text{etc}$$

3 **3a**

the ring-pole distance will be effectively increased, giving for the structures (**3a**) the actual number of atoms separating the C_1 carbon atom of the ring from the positively charged center as equal to (n + 1) for the system (**3**). Assuming that the differences in the polarizability of P and C atoms are of minor importance in transmittance of the —I effect of the pole, the reactivities of compounds (**3**) should be, for a given value of n similar to those of the corresponding (n + 1) compound of the series $Ph(CH_2)_nNMe_3^+$. The values of k_{rel} for both series are given below.

Relative reactivities (benzene = 1)

	n =	0	1	2
$Ph(CH_2)_nPO_3H_3^+$		$1{\cdot}1 \times 10^{-5}$	0·18	3·2
	n =	1	2	3
$Ph(CH_2)_nNMe_3^+$[a]		$7{\cdot}95 \times 10^{-5}$	0·224	3·16

[a] Taken from Ref 8

The ratio $(\delta\Delta G\ddagger_X - \delta\Delta G\ddagger_{CH_2X})/\delta\Delta G\ddagger_X$ can be considered as a measure of the relative change of the free energy of activation of the nitration of the system PhX, produced by introduction of the methylene group between the ring and the substituent X. This ratio, which can be replaced by the ratio $Y = \log (k_{rel}^{CH_2X}/k_{rel}^{X})/-\log k_{rel}^{X}$, should depend on the nature of the substituent effects of X in the sense of the relative contribution of the inductive and mesomeric interactions to the polar effect of the substituent. If we take the relationship between the function Y and the value of $-\log k_{rel}^{X}$ (the measure of the total deactivating effect of X) for the purely "inductive" (−I) substituents as a reference, we should expect the substituents of the —I, —M class to deviate from this relationship; the deviation should be, for a given value of $-\log k_{rel}^{X}$, higher (to the higher values of Y), the more conjugative interactions contribute to the electron-attracting effect of the group X. The ammonium,[1] trimethylammonium[8] and ethylsulphonyl[9] groups have been chosen as those for which the conjugative interactions with the ring in PhX can be ignored. Fig 2 illustrates the relationship between the function Y and values of $-\log k^{X}_{rel}$ for these substituents, and for the pairs of compounds collected in Table 2; a few points for some other derivatives are also included.

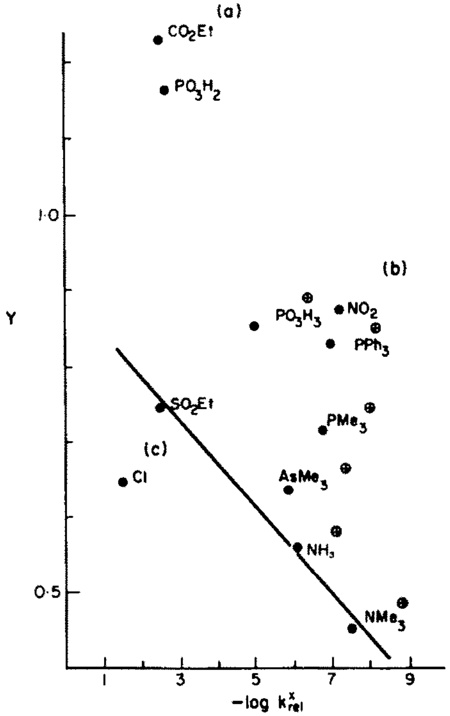


Fig 2. Variation in the values of function Y with the values of $-\log k^{X}_{rel}$; a, c, taken from Ref 9; b, taken from Ref 9, 10.

Fig 2 indicates that the —M effect operates strongly in all (charged and uncharged) phosphorus-containing substituents, being of the higher relative importance than in the case of the arsonium pole.* For substituents of similar deactivating effect (similar values of $-\log k^{X}_{rel}$) the relative contribution of the conjugative interactions to the total electron-withdrawing effect of X increase in the order: $NMe_3^+ = 0 < PMe_3^+ < PPh_3^+ < NO_2$: $NH_3^+ = 0 < AsMe_3^+ < P(OH)_3^+$; $SO_2Et = 0 < PO_3H_2 < CO_2Et$. Evidently, for substituents of the —I, +M class, the corresponding point has to be placed below the "reference" line; this is illustrated in Fig 2 by the data for the chlorobenzene/benzyl chloride system.

The preparative nitration of benzylphosphonic acid and its dialkyl esters has been carried out by several authors;[11] in all cases an almost exclusive *para*-orientation was reported. This abnormal positional selectivity remains in disagreement not only with the substituent effect of the CH_2X group in general, but also is not consistent with results obtained by Eaborn *et al*[13] who found in protodesilylation the deactivating effect of the $CH_2PO_3H_2$ group to be only 2·4 times, and of the $CH_2P(O)(OEt)_2$ only 3·3 times higher at the *meta* than at the *para* position.

We have carried out the mononitration of **1** in sulphuric or trifluoroacetic acid and examined by NMR the product, relating its spectra to that of the synthetic *p*-nitroderivative (**4**). In all cases, **4** appeared in fact to be the main product of substitution; it was however accompanied always by a significant amount of the second compound (**5**). The evidence for the formation, and the determination of the relative amounts of the two products was simplified by the fact that the PMR signal of the CH_2 group in **4** occured in conc H_2SO_4 at 0·55 ppm, and in CF_3CO_2H at 0·47 ppm to high field of the corresponding doublet of the second product (Fig 3).

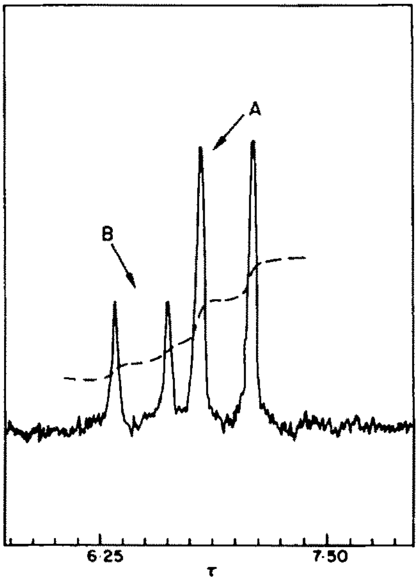


Fig 3. NMR spectrum (80 MHz) of the benzylic protons in the product from the nitration of benzylphosphonic acid; A, *p*-nitrobenzylphosphonic acid; B, *o*-nitrobenzylphosphonic acid.

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*Unfortunately, we were unable to include here the data for the system of $X = AsO_3H_2$. We attempted the nitration of benzylarsonic acid under a variety of conditions; in all cases substrate appeared to be unstable in the reaction medium. In CF_3CO_2H, C—As bond was ruptured and benzyl trifluoroacetate was formed; in H_2SO_4 aq we confirmed the previously reported[12] formation of bibenzyl; the reaction with conc HNO_3 yielded the mixture of at least ten compounds, containing the isomeric nitrobenzaldehydes and nitrobenzoic acids as main products.

The average ratio of the peaks areas (taken from six independent experiments) gave the isomer distribution equal to 74 ± 4% of the *para*-derivative and 26 ± 4% of the compound **5**. The latter has been identified as *o*-nitrobenzylphosphonic acid according to the following evidence: (i) The nitration of **1** with an excess of HNO_3 yielded a single dinitro derivative, the NMR spectrum of which was identical with that of the pure 2,4-dinitrobenzylphosphonic acid. The same compound has been obtained when the crude product of mononitration was treated with the additional amount of the nitrating agent. (ii) The nitration mixture was analysed by oxidation, separation of the bulk of *p*-nitrobenzoic acid and NMR examination of the remaining nitrobenzoic acids. Only the *o*-nitrobenzoic acid and the rest of the *p*-derivative were identified; in no case could any trace of the *m*-nitration product be detected.

For the nitration of **2**, the NMR spectrum of the reaction mixture was not a convenient guide of the product composition; the subsequent oxidation produced again merely the mixture of *o*- and *p*-nitrobenzoic acids; the relative amounts, as determined from NMR spectra, being approximately $p/o = 2:1$. In conclusion, although we have not confirmed the reported exclusive *para*-orientation of the $CH_2PO_3H_2$ group in nitration,* the substituents in **1** and **2** have to be considered as *para/ortho* directing in this reaction, with a negligible contribution of *meta*-substitution. This unexpected inhibition of *meta*-nitration is difficult to explain without taking into account some specific substituent-electrophile interactions increasing the intramolecular selectivity of the nitration.

EXPERIMENTAL

Solvents were purified by conventional methods. M.ps and b.ps are uncorrected. The commercial benzylarsonic acid (BDH, Anala Grade) was purified by crystallization from water. M.p. 179–183°, (lit.[14] m.p. 167–168°); (Found: C, 38·90; H, 3·96. $C_7H_9O_3As$ required: C, 38·91; H, 4·19%). The remaining compounds were prepared according to reported procedures: benzylphosphonic acid **1**, m.p. 169–170°, (from AcOH; lit.[15] m.p. 166°); *β*-phenylethylphosphonic acid (**2**), m.p. 137·5–139°, (lit.[11c] m.p. 138·5–140°); diethylbenzylphosphonate, b.p. 185–189°/20 mm Hg; n_D^{20} 1·4959, (lit.[11b] b.p. 160–164°/15 mm Hg; n_D^{20} 1·4938); *p*-nitrobenzylphosphonic acid (**4**), m.p. 217–219°, (lit.[11b] m.p. 226°). (Found: N, 6·38. $C_7H_8O_5NP$ requires N, 6·45%). NMR spectrum in full agreement with the assumed structure.

2,4-Dinitrobenzylphosphonic acid was obtained by nitration of **1** with an excess of conc HNO_3 at room temp, yield 100%; m.p. 216–217° (from $MeNO_2$). (Found: N, 10·12. $C_7H_7O_7N_2P$ requires N, 10·68%); λ_{max} (H_2O) 256 nm; $\epsilon_{max} = 11{\cdot}700$. IR and NMR spectra in full agreement with the assumed structure.

Acetic anhydride, nitric acid and solutions of sulphuric acid were prepared as before.[2]

Kinetic measurements of nitrations in H_2SO_4 aq were carried out as described in Part I. The required values of ϵ_s and ϵ_p were as follows: **1**, (277 nm), $\epsilon_p = 8{\cdot}400$, $\epsilon_s = 0$; (**2**), (280 nm), $\epsilon_p = 7{\cdot}000$, $\epsilon_s = 0$. For both substrates the typical second-order kinetics was observed.

The competitive nitrations of diethyl ester of **1** and benzene were carried out in Ac_2O as described previously, and the ratio of the rate coefficients was calculated in the usual way.

Product determination. **1** was dissolved in conc H_2SO_4 or anhyd CF_3CO_2H and nitrated with the stoichiometric amount of HNO_3 at room temp. After the nitration, the solns were examined by NMR.

The solns after nitrations in CF_3CO_2H were evaporated to dryness, the residue was dissolved in dil NaOH aq, and the saturated aqueous soln of the required amount of $KMnO_4$ was added dropwise at 80° with stirring. After filtration, the filtrate was concentrated under reduced pressure, acidified and the precipitate of *p*-nitrobenzoic acid was filtered off. The filtrate was then evaporated to dryness, extracted with hot acetone, and the acetone solns were examined by NMR.

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*It cannot be excluded that the nitration of dialkylbenzylphosphonates[11] yielded also the mixture of the para- and ortho-nitroderivatives; the vacuum distillation of the high-boiling oils may not afford the effective separation of two isomeric esters. The hydrolysis to the phosphonic acids can, after the purification, yield the pure *p*-nitrobenzylphosphonic acid because of the usually higher solubility of ortho isomers.