

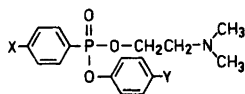
Effect of *para* Substituents on Decomposition Rates of 2-(*N,N*-Dimethylamino)ethyl Phenyl Phenylphosphonates

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Spontaneous decomposition of nineteen of the title phosphonates to their 1,1,4,4-tetramethylpiperazinium salts was followed in 50 % aqueous ethanol at different temperatures. The effect of substituents of the phenyl group on reaction rates was about twice as great as the effect substituents of the phenoxy group and an electron attracting substituent at either *para* position increase the decomposition rate. A linear dependence was found between logarithms of rate constants and σ_p^o parameters of *para* substituents of the phenyl group and a poorer linear correlation for *para* substituents of the phenoxy group. The dual substituent parameter approach using σ_1 and σ_R^o was applied.

In an earlier study the decomposition of dialkyl 2-(*N,N*-dimethylamino)ethyl phosphates was followed in water and ethanol.¹ Logarithms of rate constants were plotted against σ^{ph} parameters and a reasonable linear correlation was found. Substituent effects of phosphorus compounds are studied further here, with the same reaction but with substituents at a greater distance from the phosphorus atom so that they do not have steric effects on the other groups containing phosphorus. The compounds are 2-(*N,N*-dimethylamino)ethyl phenyl phenylphosphonates (Scheme 1).



Scheme 1. 2-(*N,N*-Dimethylamino)ethyl phenyl phenylphosphonates. X=Me₂N, MeO, Me, H, F, Br and Y=MeO, Me, H, F, Cl, Br.

In plotting reactivities against substituent properties we have concentrated on σ_p^o constants and their components instead of on phosphorus specific constants,² because in some cases these constants are linearly related to σ_p^o and σ^* constants, and in others (*e.g.*, where resonance effects are strong) the σ^{ph} parameter has to be separated into inductive and resonance components of different weight to obtain a satisfactory linear correlation. Moreover, the σ_p^o parameter and its components have been found to correlate well the NMR chemical shifts of phosphorus of the oxalates of these phosphonates.³

RESULTS AND DISCUSSION

Rate constants were determined at different temperatures and activation parameters were calculated as before¹ (Table 1).

Aqueous ethanol was chosen as solvent because the studied compounds were not soluble in water and some reactions were too slow in pure ethanol. The X and Y substituents do not interfere with the substituent properties of the other as found also in NMR study,³ and therefore the mean values of $\log(k_{XY}/k_{HY})$ and $\log(k_{XY}/k_{XH})$ were used to express the effects of X and Y, respectively (Table 2).

Thermodynamic parameters were determined only for methoxy, methyl, hydrogen and bromine substituents (not shown). The overall pattern of the enthalpies of activation suggest that the values decrease as substituents become more electron attracting (range from 91 to 101 kJ mol⁻¹), and entropies of activation are clearly negative (range from -16 to -38 J K⁻¹ mol⁻¹). The

Table 1. Rate constants and their logarithms for the decomposition of 2-(*N,N*-dimethylamino)ethyl phenyl phenylphosphonates (Scheme 1) in 50 % ethanol.

X	Y	313.2 K		323.2 K		333.2 K	
		$k/10^{-5}s^{-1}$	log k	$k/10^{-5}s^{-1}$	log k	$k/10^{-5}s^{-1}$	log k
Me ₂ N	Me	—	—	1.19(1)	-4.925	—	—
MeO	MeO	1.07(1)	-4.971	3.67(4)	-4.435	11.8(1)	-3.928
	Me	1.04(1)	-4.983	3.62(4)	-4.441	10.6(2)	-3.975
	H	1.26(2)	-4.900	4.30(8)	-4.367	13.2(8)	-3.879
	Br	2.17(2)	-4.664	7.25(8)	-4.140	22.0(3)	-3.658
Me	MeO	1.27(3)	-4.896	4.44(8)	-4.353	13.9(2)	-3.857
	Me	1.21(1)	-4.917	4.12(5)	-4.385	12.6(3)	-3.900
	H	1.55(2)	-4.810	5.14(6)	-4.289	15.9(2)	-3.799
	F	—	—	6.61(7)	-4.180	—	—
	Cl	—	—	8.31(6)	-4.081	—	—
	Br	2.63(4)	-4.580	8.86(2)	-4.053	26.8(3)	-3.572
H	MeO	1.81(2)	-4.743	6.29(8)	-4.201	18.9(2)	-3.724
	Me	1.70(6)	-4.770	5.94(8)	-4.226	18.3(3)	-3.738
	H	2.22(4)	-4.654	6.92(11)	-4.160	21.7(5)	-3.664
	Br	4.47(8)	-4.350	13.1(3)	-3.883	38.8(6)	-3.411
F	Me	—	—	8.71(8)	-4.060	—	—
Br	MeO	3.95(9)	-4.403	12.7(2)	-3.896	37.6(5)	-3.425
	Me	3.87(7)	-4.412	12.5(5)	-3.903	36.6(5)	-3.437
	H	4.47(5)	-4.350	14.1(3)	-3.851	39.4(9)	-3.405

Table 2. Mean values of log (k_{XY}/k_{HY}) (effect of X) and log (k_{XY}/k_{XH}) (effect of Y) determined at different temperatures (the respective H-substituted derivative as reference compound). Standard deviations are shown in parentheses. Substituent constants from Ref. 5.

X	log (k_{XY}/k_{HY})			Substituent constant		
	313.2 K	323.2 K	333.2 K	σ_p^o	σ_I	σ_R^o
Me ₂ N	—	-0.699 ^a	—	-0.44	+0.10	-0.54
MeO	-0.251(45)	-0.228(23)	-0.226(20)	-0.16	+0.25	-0.41
Me	-0.172(39)	-0.153(18)	-0.150(13)	-0.12	-0.05	-0.10
F	—	0.166 ^a	—	+0.17	+0.52	-0.35
Br	0.334(28)	0.312(9)	0.286(24)	+0.26	+0.45	-0.19
Y	log (k_{XY}/k_{XH})					
MeO	-0.075(17)	-0.054(13)	-0.049(21)			
Me	-0.092(25)	-0.072(18)	0.076(31)			
F	—	0.109 ^b	—			
Cl	—	0.208 ^b	—	+0.27	+0.47	-0.20
Br	0.257(41)	0.247(27)	0.234(17)			

^a Only the Y=Me series was studied. ^b Only the X=Me series was studied.

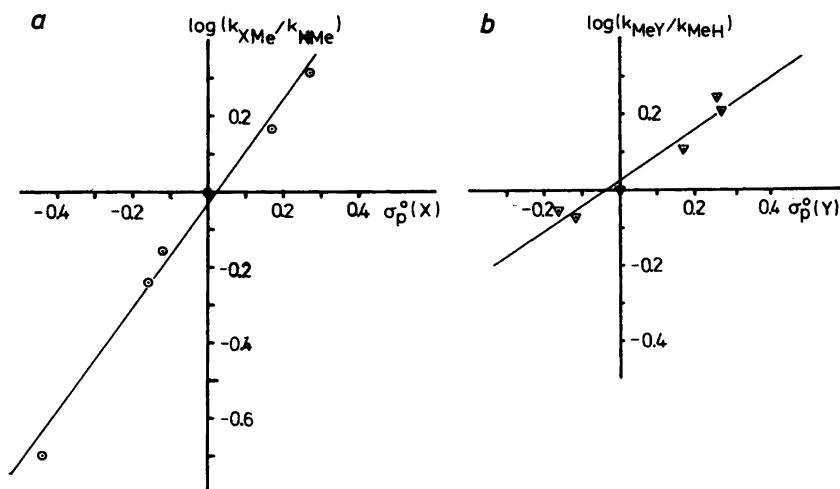


Fig. 1. Dependence of the logarithm of the decomposition rate on substituent constants σ_p^o , (a) effect of X and (b) effect of Y (from Table 2).

variation in activation parameters from one substituent to another is small and without pattern, however, making further conclusions unreasonable.

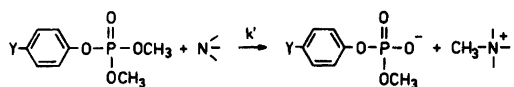
Surprisingly the effect of X on reaction rates was only about twice as great as that of Y (Table 2), whereas the effect of X on the phosphorus chemical shift of oxalates of these phosphonates was over five times as great as the effect of Y.³ The plot of $\log(k_{XY}/k_{HY})$ against the σ_p^o parameter shows a reasonably good linear dependence (Fig. 1a) ($r=0.993$, $\rho=1.40(8)$, values from Table 3, 323.2 K). The weaker effect of Y and the greater deviation of the plot from linearity [$r=0.974$, $\rho=0.70(80)$] is clearly seen in Fig. 1b. Some curving of the plot is evident in both correlations.

Despite claims that substituent constants may not be "fundamental" parameters describing "fundamental" effects,⁴ we continue for the present to use these when discussing substituent effects. The constants have a practical use and are successfully applied every day, at least qualitatively, by organic chemists when evaluating the reactivity of reagents in syntheses and reaction studies. Nevertheless the great number of substituent scales makes it difficult to select the "correct" and best scale for interpreting the observed results. When fitting with common substituent constants (e.g. σ_p^o) fails, the applica-

tion of the dual substituent parameter method (*dsp*) using the equation $\log k/k_o = \rho(\sigma_1 + \lambda\sigma_R)$ would be the next best approach to the problem. However, when multiple parameter regressions are used the statistical significance of coefficients of regression need, of course, to be carefully evaluated before they are used to explain chemical phenomena.

The measured values fit reasonably well with σ_p^o parameters and no significant improvement can be obtained by the *dsp*-method. Interestingly, however, when the latter method was applied to the data (Table 2, 323.2 K, $n=6$) using the above equation the regression gave $\lambda_X=1.18$ (F-test value 99.92 %) which is near to $\lambda_X=1.15$ obtained from NMR data,³ but $\lambda_Y=0.93$ (F-test 99.01 %) differs markedly.

An analogous reaction to the present decomposition reaction has been thoroughly investigated by Jentzsch *et al.*⁶ Alkylation of trimethylamine and 4-(4-nitrobenzylpyridine) with substituted alkyl and aryl dimethyl phosphates was followed in acetone and good linear correlations between logarithms of rate constants and σ_p^o constants were found (Scheme 2). This second order reaction (actually pseudo first order, rate constant k') correlates linearly with the first order spontaneous decomposition (rate constant k) studied here (substituents $Y=MeO, Me, H, Cl$).



Scheme 2. Methylation of tertiary amines with aryl dimethyl phosphates.⁶ Dependence of the studied decomposition rate (k) on the methylation rate (k') of trimethylamine: $\log k = -0.25 + 0.70 \log k'$, $r = 0.986$.

Jentzsch *et al.* did not find a satisfactory linear dependence between $\delta^{31}\text{P}$ and chemical reactivity of studied compounds. Here, however, the phosphorus chemical shifts (of the oxalates) have been found to correlate linearly with logarithms of decomposition rates for changes of X and the relationship can be expressed as four parallel lines for different Y substituents (Table 3).

Chemical reactivity and NMR studies of the present compounds show that the *para* substituent of the phenyl group (X) has a similar effect on logarithms of rate constants and chemical shifts of phosphorus, whereas the effects of *para* substituents of the phenoxy group (Y) are much more sensitive to variation in the chemical or physical system and not easily predicted.

EXPERIMENTAL

Preparations

The preparation of most of the ammonium oxalates of the studied phosphonates has been described earlier.³ The structure and the purity of four additional compounds synthesized for this study were confirmed by NMR.

4-Fluorophenylphosphonic dichloride. This intermediate was prepared from 4-fluorobromobenzene and triethyl phosphite. The formed

diethyl 4-fluorophenylphosphonate (b.p. 150–151 °C/931 Pa, 67 %) was transformed with phosphorus pentachloride to 4-fluorophenylphosphonic dichloride (b.p. 123–125 °C/931 Pa, 64 %).

4-Methylphenylphosphonic dichloride. Use of the Friedel-Crafts reaction resulted in the formation of both the *para* and *ortho* isomers. To avoid this the triethyl phosphite method as above was applied. Diethyl 4-methylphenylphosphonate (b.p. 150–152 °C/1064 Pa, 76 %). 4-Methylphenylphosphonic dichloride (b.p. 150–153 °C/1064 Pa, 90 %).

4-Dimethylaminophenylphosphonic dichloride. Tricoordinated 4-dimethylaminophenylphosphonic dichloride was prepared from dimethylaniline and phosphorus trichloride (b.p. 140–150 °C/3 Pa, ca. 30 %) and was oxidized with dimethylsulfoxide to the desired product (b.p. 155–165 °C/3 Pa, low yield).⁷

Oxalates of 2-(N,N)dimethylamino)ethyl phenyl phenylphosphonates. The method used earlier was slightly modified because purification of high boiling phenyl phenylphosphonic chlorides by distillation is difficult. Substituted diphenyl phenylphosphonates were first prepared from phenylphosphonic dichlorides and were then by transesterification changed to the desired 2-(N,N-dimethylamino)ethyl phenyl phenylphosphonate using an equivalent amount of sodium salt of the amino alcohol. The yields of transesterification were low (ca. 30 %). The products were recrystallized and stored as oxalates as described earlier.³ Melting points and $\delta^{31}\text{P}$ chemical shifts of the oxalates (in dimethylsulfoxide- d_6 , reference $(\text{HO})_2\text{P}^+\text{ClO}_4^-$) (see Scheme 1) are: (X=Me, Y=Cl) 142–3 °C, $\delta^{31}\text{P}$ 16.56 ppm; (Me, F) 138–9 °C, 16.63 ppm, $J(\text{P}-\text{F})$ 1.83 Hz; (Me_2N , Me) 108–9 °C, 19.00 ppm and (F, Me) 139–40 °C, 14.60 ppm, $J(\text{P}-\text{F})$ 1.53 Hz.

Decomposition reactions

The studied phosphonates were liberated from oxalates with sodium carbonate and extracted into ether, which was dried and evaporated. The remaining liquid phosphonates were used immediately in the decomposition reaction. The reaction was followed by titrating the samples with HCl solution. The end point of titration was determined by pH meter to pH 5.3.–5.2. The basicity of the reaction medium during the reaction was typically about 8.5–9.5 owing to tertiary amino group. The 50 % ethanol solution was prepared by measuring exactly 50 cm³ of ethanol and filling the flask up to the 100 cm³ mark with water at 295 K.

Table 3. Relationship between decomposition rates of studied compounds and phosphorus chemical shift of respective oxalates.³

$$\log k_{\text{XY}} = A + B \delta^{(31)\text{P}}$$

Y	A	B	r
MeO	0.22(19)	-0.24(1)	0.998
Me	0.19(25)	-0.25(1)	0.997
H	0.02(29)	-0.24(2)	0.995
Br	0.46(37)	-0.24(2)	0.997

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