

## Linear Solvation Energy Relationships. 39. A Multiple Substituent Parameter Equation for $\beta$ Values (Hydrogen-Bond Acceptor Basicities) of XYZP=O Compounds

Robert W. Taft, Wendel J. Shuely,\* Ruth M. Doherty, and Mortimer J. Kamlet

*Department of Chemistry, University of California, Irvine, California 92717, U.S. Army Chemical Research, Development, and Engineering Center, Aberdeen Proving Ground, Maryland 21010, Naval Surface Weapons Center, White Oak Laboratory, Silver Spring, Maryland 20910, and Advanced Technology and Research, Inc., 3933 Sandy Spring Road, Burtonsville, Maryland 20866*

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Phenol infrared spectral shifts,  $\Delta\nu(\text{O-H, free minus hydrogen bonded})$ , formation constants of hydrogen-bonded complexes with phenol, enthalpies of formation of hydrogen-bonded complexes with 4-fluorophenol, and a multiple substituent parameter correlation are used to obtain  $\beta$  values, which scale the hydrogen-bond acceptor abilities of 54 substituted phosphine oxides, XYZP=O. The multiple substituent parameter equation that correlates these  $\beta$  values with generally satisfactory precision shows that additive substituent field/inductive effects cause the dominant structural effects. In addition, secondary effects due to  $\pi$  electron-donating and to polarizable substituents also may contribute significantly to increase the hydrogen-bond acceptor ability. Some systematic deviations from this equation are attributed to saturation and steric twisting effects on multiple substitution of  $\pi$  electron donor substituents such as  $\text{N}(\text{CH}_3)_2$ . Evidence is presented showing that alkyl phosphates in aqueous solutions have multiple hydrogen-bond acceptor sites so that their effective  $\sum\beta$  values are significantly larger than the corresponding  $\beta_m$  values.

In earlier papers of this series<sup>1-3</sup> we have reported the formulation of three scales of solute or solvent properties. A  $\pi^*$  scale of molecular dipolarity/polarizabilities, sometimes used in combination with a "polarizability correction" parameter,  $\delta$ , measures the ability of a compound to stabilize a neighboring dipole or charge by virtue of dipole/dipole, charge/dipole, and dipole or charge/induced dipole interactions. An  $\alpha$  scale of molecular HBD (hydrogen-bond donor) acidities measures a compound's ability to donate a share of a proton (accept an electron pair) in a solute-solvent or solute-solute hydrogen bond; a  $\beta$  scale of HBA (hydrogen-bond acceptor) basicities measures a compound's ability to accept a proton share (donate an electron pair). For certain types of "family dependent" properties, a coordinate covalency parameter,  $\xi$ , is used in combination with  $\beta$ .<sup>4</sup>

We have used these parameters to correlate, rationalize, and predict large numbers of diverse physicochemical and biochemical properties of solutes and solvents through linear solvation energy relationships of the following types. For properties of a single solute or set of reactants in a series of solvents

$$\text{XYZ} = \text{XYZ}_0 + h(\delta_{\text{H}}^2)_1/100 + s(\pi^* + d\delta)_1 + a\alpha_1 + b\beta_1 \quad (1)$$

and for properties of a series of solutes in a single solvent, or distribution between a pair of solvents

$$\text{XYZ} = \text{XYZ}_0 + mV_2/100 + s(\pi^* + d\delta)_2 + a(\alpha_m)_2 + b(\beta_m)_2 \quad (2)$$

Subscript 1 indicates that the parameter applies to solvent

properties, subscript 2 to solute properties. The  $\delta_{\text{H}}$  and  $V$  parameters in eq 1 and 2 measure the solvent and solute's contributions to the cavity term,  $\delta_{\text{H}}$  being the Hildebrand solubility parameter, and  $V$  a measure of solute molar volume. The subscript  $m$  indicates that, for compounds which are capable of self-association, the parameter applies to non-self-associated "monomer" solutes. We use  $V_2/100$  and  $(\delta_{\text{H}}^2)_1/100$  so that the parameters measuring the cavity term should cover roughly the same range as the other parameters, which makes easier the evaluation of the relative contributions of the various terms to the solute-solvent interaction studied.

### Methodology and Results

**Correlation Equations for Estimation of  $\beta$  Values of XYZP=O Bases.** In this paper we report additional  $\beta$  values for phosphine oxide derivatives XYZP=O (as solutes and solvents) and examine structure-property relationships in this series. Values of  $\beta$  have been reported earlier<sup>5-7</sup> for 17 P=O compounds (1-17 of Table I). The latter were determined from formation constants,  $K_{\beta}$ , and infrared spectral shifts,  $\Delta\nu(\text{O-H, free minus hydrogen bonded})$  of phenol complexes with the HBA bases. The experimental results were those of Gramstad and co-workers;<sup>8</sup> the correlation equations used to back-calculate the  $\beta_i$  values are given by eq 3 and 4. Our practice, where possible, has been to obtain  $\beta$  values from averages of two or more  $\beta_i$  values derived from different types of measurements.

$$\Delta\nu(\text{O-H, phenol:O=PXYZ}) = -199.6 + 671\beta\text{cm}^{-1} \quad (\text{ref 7, eq 5d}) \quad (3)$$

$$\log K_{\beta}(\text{phenol:HBA}) = -1.05 + 4.31\beta \quad (\text{ref 7, eq 4}) \quad (4)$$

(1) The most recent review is given in Kamlet, M. J.; Doherty, R. M.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *CHEMTECH* 1986, 16, 566.

(2) Additional review papers: (a) Taft, R. W.; Abboud, J.-L. M.; Kamlet, M. J.; Abraham, M. H. *J. Solution Chem.* 1985, 14, 153. (b) Abraham, M. H.; Doherty, R. M.; Kamlet, M. J.; Taft, R. W. *Chem. Brit.* 1986, 22, 551. (c) Kamlet, M. J.; Taft, R. W. *Acta Chem. Scand., Ser. B* 1985, B39, 611.

(3) Comprehensive lists of solvatochromic parameters in: (a) Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* 1983, 48, 2877. (b) Kamlet, M. J.; Abboud, J.-L. M.; Taft, R. W. *Prog. Phys. Org. Chem.* 1981, 13, 485.

(4) Kamlet, M. J.; Gal, J. F.; Maria, P. C.; Taft, R. W. *J. Chem. Soc., Perkin Trans. 2* 1985, 1583.

(5) Kamlet, M. J.; Taft, R. W. *J. Am. Chem. Soc.* 1976, 98, 377.

(6) Kamlet, M. J.; Solomonovici, A.; Taft, R. W. *J. Am. Chem. Soc.* 1979, 101, 3734.

(7) Taft, R. W.; Gramstad, T.; Kamlet, M. J. *J. Org. Chem.* 1982, 47, 4557.

(8) (a) Gramstad, T.; Sandstrom, J. *Spectrochem. Acta, Part A* 1969, 25A, 31. (b) Gramstad, T. *Ibid.* 1963, 19, 497. (c) Gramstad, T. *Ibid.* 1963, 19, 829. (d) Blindheim, U.; Gramstad, T. *Ibid.* 1965, 21, 1073. (e) Gramstad, T.; Fuglevik, W. J. *Ibid.* 1965, 21, 423. (f) Gramstad, T.; Mundheim, O. *Ibid.* 1972, 28A, 1405. (g) Gramstad, T. *Acta Chem. Scand.* 1961, 15, 1337.

Table I. Estimation of Additional  $\beta$  Values

no.	XYZP=O			$\beta$ ref 3a	phenol <sup>a</sup>		phenol <sup>b</sup>		4-F-phenol <sup>c</sup>			$\beta_{ave}$
	X	Y	Z		$\log K_f$	$\beta_1$	$\Delta\nu(O-H)$	$\beta_2$	$\Delta H_f$	$\beta_3$	$\beta_4$	
1	PhO	PhO	PhO	0.62 <sup>e</sup>			225 <sup>e</sup>					
2	MeO	MeO	MeO	0.77 <sup>f</sup>			305 <sup>e</sup>		6.44 <sup>f</sup>			
3	EtO	EtO	EtO	0.77 <sup>e,f</sup>			325		6.59 <sup>f</sup>			
4	Ph	Ph	Ph	0.94 <sup>e</sup>			410 <sup>e</sup>					
5	Me	Me	Me	1.02 <sup>e</sup>			445 <sup>e</sup>					
6	Et	Et	Et	1.05 <sup>e</sup>			462 <sup>e</sup>					
7	<i>n</i> -Pr	<i>n</i> -Pr	<i>n</i> -Pr	1.04								
8	Me <sub>2</sub> N	Me <sub>2</sub> N	Me <sub>2</sub> N	1.05 <sup>e,f</sup>			470 <sup>e</sup>		8.72 <sup>f</sup>			
9	MeO	MeO	H	0.74 <sup>e</sup>			285 <sup>e</sup>					
10	MeO	MeO	Et	0.81 <sup>e</sup>			355 <sup>e</sup>					
11	EtO	EtO	CCl <sub>3</sub>	0.68 <sup>e</sup>			245 <sup>e</sup>					
12	EtO	EtO	CHCl <sub>2</sub>	0.74 <sup>e</sup>			263 <sup>e</sup>					
13	EtO	EtO	CH <sub>2</sub> Cl	0.79 <sup>e</sup>			310 <sup>e</sup>					
14	EtO	EtO	H	0.76 <sup>e</sup>			300 <sup>e</sup>					
15	EtO	EtO	Me	0.84 <sup>e</sup>			360 <sup>e</sup>					
16	EtO	EtO	Me <sub>2</sub> N	0.88								
17	<i>i</i> -PrO	<i>i</i> -PrO	<i>i</i> -PrO	0.80 <sup>e</sup>			320 <sup>e</sup>					
18	<i>n</i> -PrO	<i>n</i> -PrO	H		2.300	0.78	(320) <sup>a</sup>	0.77			0.80	0.78 ± 0.017
19	Et	Et	F		2.111	0.73	(270) <sup>a</sup>	0.70			0.76	0.73 ± 0.020
20	Et	MeO	F		1.916	0.69 <sup>e</sup>	270 <sup>e</sup>	0.70			0.68	0.69 ± 0.020
21	EtO	EtO	<i>n</i> -Pr		2.688	0.87	(350) <sup>a</sup>	0.82			0.85	0.85 ± 0.017
22	EtO	EtO	<i>i</i> -Pr		2.660	0.86 <sup>e</sup>	365 <sup>e</sup>	0.87			0.85	0.86 ± 0.007
23	PhO	PhO	CCl <sub>3</sub>		1.179	0.52 <sup>e</sup>	(195) <sup>a,f</sup>	0.59			0.50	0.54 ± 0.037
24	<i>n</i> -Pr	<i>n</i> -Pr	PhO		2.489	0.82 <sup>e</sup>	(355) <sup>a,e</sup>	0.83			0.85	0.83 ± 0.10
25	EtS	EtS	EtS		1.872	0.68	280	0.72				0.70 ± 0.020
26	PhS	PhS	PhS		1.837	0.67	240	0.66				0.67 ± 0.005
27	EtS	EtS	<i>i</i> -Pr		2.219	0.76	334	0.81				0.78 ± 0.025
28	PhS	PhS	<i>i</i> -Pr		2.182	0.75 <sup>e</sup>	(305) <sup>a,e</sup>	0.75				0.75 ± 0.00
29	EtO	EtO	Et				365	0.87 <sup>f</sup>	7.46 <sup>f</sup>	0.89	0.84	0.87 ± 0.017
30	Cl	Cl	Cl				110	0.41 <sup>f</sup>	3.71 <sup>f</sup>	0.41	0.40	0.41 ± 0.003
31	Cl	Cl	PhO				150	0.48 <sup>f</sup>	4.29 <sup>f</sup>	0.49	0.45	0.47 ± 0.017
32	Cl	Cl	Ph				182	0.54 <sup>f</sup>	4.59 <sup>f</sup>	0.52	0.60	0.55 ± 0.030
33	EtO	EtO	Cl				240	0.64 <sup>f</sup>	5.55 <sup>f</sup>	0.64	0.65	0.64 ± 0.003
34	F	F	Ph				157	0.50			0.55	0.53 ± 0.025
35	F	F	Me				156	0.49			0.54	0.52 ± 0.025
36	<i>i</i> -PrO	<i>i</i> -PrO	<i>i</i> -PrO				345	0.83			0.81	0.82 ± 0.010
37	<i>n</i> -PrO	<i>n</i> -PrO	<i>n</i> -PrO				325	0.80			0.78	0.79 ± 0.010
38	<i>n</i> -BuO	<i>n</i> -BuO	<i>n</i> -BuO				325	0.80			0.78	0.79 ± 0.010
39	Me	MeO	H				333	0.81			0.85	0.83 ± 0.020
40	Me	EtO	H				350	0.84			0.86	0.85 ± 0.010
41	Me	<i>i</i> -PrO	H				347	0.84			0.87	0.86 ± 0.015
42	PhO	PhO	H				235	0.63			0.65	0.64 ± 0.010
43	Cl	Cl	OMe				155	0.49			0.51	0.50 ± 0.010
44	Cl	Cl	OEt				162	0.50			0.52	0.51 ± 0.010
45	Cl	Cl	CCl <sub>3</sub>				123	0.43			0.40	0.42 ± 0.015
46	Cl	Cl	CHCl <sub>2</sub>				133	0.45			0.44	0.45 ± 0.005
47	Cl	Cl	Me				175	0.53			0.59	0.56 ± 0.030
48	<i>n</i> -Bu	<i>n</i> -Bu	<i>n</i> -Bu				470	1.06			1.00	1.03 ± 0.030
49	EtO	EtO	Ph				350	0.84			0.84	0.84 ± 0.00
50	EtO	EtO	<i>t</i> -Bu				367	0.87			0.86	0.87 ± 0.005
51	F	F	<i>t</i> -Bu				180	0.54			0.57	0.56 ± 0.015
52	CH=CH <sub>2</sub>	CH=CH <sub>2</sub>	Ph				415	0.96			0.96	0.96 ± 0.00
53	CH=CH <sub>2</sub>	CH=CH <sub>2</sub>	OEt				372	0.88			0.88	0.88 ± 0.00
54	CH=CH <sub>2</sub>	CH=CH <sub>2</sub>	Me <sub>2</sub> N				440	1.00			1.00	1.00 ± 0.00

<sup>a</sup>Reference 8. <sup>b</sup>References 9–11 except as noted. <sup>c</sup>Reference 12. <sup>d</sup>Calculated by eq 7. <sup>e</sup>These are the data employed to construct eq 5. <sup>f</sup>These are the data employed to construct eq 6.

To expand the data base for HBA basicity of P=O compounds, we have used eq 3 and 4 with additional  $\log K_f$  and  $\Delta\nu(OH)$  values reported by Gramstad and co-workers<sup>8</sup> to arrive at  $\beta_i$  values for compounds 18–28 of Table I. We have also used another set of infrared spectral shifts obtained for the phenol complexes by Raevskii and co-workers,<sup>9–11</sup> as well as enthalpies of formation of 4-fluorophenol complexes reported by Arnett and co-workers,<sup>12</sup> and a multiple substituent parameter correlation

(linear free energy relationship) to arrive at further  $\beta_i$  values for compounds 18–54 of Table I.

Discussing seriatim the individual calculations: (a) Formation constants of the phenol complexes in CCl<sub>4</sub> were used with eq 4 to arrive at  $\beta_1$  values for compounds 18–28. (b) Phenol infrared shifts reported by Gramstad were used with eq 3 to arrive at  $\beta_2$  values for compounds 18, 19, 21, 23, 24, and 27. (c) Earlier  $\beta$  values for compounds 1–6, 8–15, and 17 and  $\beta_1$  values for compounds 20, 22, 25, 26, and 28 were correlated with  $\Delta\nu(O-H)$  data of Raevskii and his co-workers<sup>9–11</sup> (which are indicated by footnote e in Table I) to arrive at eq 5 which, although quite precise,

(9) Raevskii, O. A.; Gilyazov, M. M.; Levin, Y. A. *Zh. Obshch. Khim.* 1983, 53, 1720.

(10) Raevskii, O. A.; Gilyazov, M. M.; Levin, Y. A. *Zh. Obshch. Khim.* 1983, 53, 1724.

(11) Raevskii, O. A.; Gilyazov, M. M.; Levin, Y. A. *Zh. Obshch. Khim.* 1983, 53, 563.

(12) Arnett, E. M.; Mitchell, E. J.; Murty, T. S. S. R. *J. Am. Chem. Soc.* 1974, 96, 3875.

$$\Delta\nu(\text{O}-\text{H}, \text{phenol}:\text{O}=\text{PXYZ}) = (-136.5 \pm 17.3) + (575.9 \pm 21.2)\beta \text{ cm}^{-1} \quad (5)$$

$$n = 19, r = 0.989, \text{sd} = 11.5 \text{ cm}^{-1}$$

is seen to differ significantly from eq 3, the equation based on the Gramstad group's data for the same property. Equation 5 was then used to back-calculate  $\beta_2$  values for compounds 20, 22, 25–27, and 29–54. [It is not evident to us why Gramstad's and the Raevskii group's data should lead to such different equations;  $\Delta\Delta\nu_{\text{calcd}}$  values (eq 3 minus eq 5) of  $-6 \text{ cm}^{-1}$  at  $\beta = 0.6$ ,  $+13 \text{ cm}^{-1}$  at  $\beta = 0.8$ , and  $+32 \text{ cm}^{-1}$  at  $\beta = 1.0$  reflect a systematic trend in the data which may derive from instrumental, concentration, or temperature differences. Since  $\Delta\nu(\text{O}-\text{H})$  depends on the strength of the hydrogen bond, and since formation constants for complexation between phenol and the HBA bases are quite temperature sensitive,<sup>8a</sup> we suspect temperature effects. It is clear, however, that serious errors may arise if one uses the data from one source with the correlation equation from the other to derive new  $\beta_i$  values.] (d) Enthalpies of formation of 4-fluorophenol: $\text{O}=\text{PXYZ}$  complexes reported by Arnett, Mitchell, and Murty<sup>12</sup> were next used to derive  $\beta_3$  values; the  $\Delta H_f$  data used were those obtained in the pure base as the solvent. Correlation of  $\Delta H_f$  with the earlier  $\beta$  values of compounds 2, 3, and 8, and the  $\beta_2$  values of compounds 29–33 (which are indicated by footnote f in Table I) led to eq 6, which was then used to back-calculate  $\Delta H_f(4\text{-FC}_6\text{H}_4\text{OH}:\text{O}=\text{PXYZ}) =$

$$(0.43 \pm 0.12) + (7.94 \pm 0.16)\beta \text{ kcal/mol} \quad (6)$$

$$n = 8, r = 0.9988, \text{sd} = 0.09 \text{ kcal/mol}$$

$\beta_3$  values for compounds 29–33. (e) The final set (4) of  $\beta_i$  values was next obtained from a multiple substituent parameter equation containing terms in  $\sum\sigma_{\alpha}$ ,  $\sum\sigma_{\text{F}}$ , and  $\sum\sigma_{\text{R}}$ , where  $\sigma_{\alpha}$  measures substituent polarizability,  $\sigma_{\text{F}}$  substituent field effect, and  $\sigma_{\text{R}}$  substituent resonance effect.<sup>13</sup> The derivation of the equation and the reasons for the choice of the data set used in the correlation are discussed in detail below. (f) Finally the  $\beta_i$  values for compounds 18–54 were averaged to obtain the  $\beta_{\text{ave}}$  values listed in the last column of Table I. None of our back-calculations indicated that any of the earlier  $\beta$  values for compounds 1–17 required revision and, accordingly, these remained unchanged.

**Multiple Substituent Parameter Equation for Estimation of  $\beta$  Values of  $\text{XYZP}=\text{O}$  Bases.** The  $\sigma_{\alpha}$ ,  $\sigma_{\text{F}}$ , and  $\sigma_{\text{R}}$  values used in the correlations are assembled in Table II. The 54 compounds of Table I have either known substituent parameters<sup>13</sup> or parameter values that could be estimated. It was assumed as an initial simplification that the sum of the substituent parameters for X, Y, and Z could be used for each of the three kinds of substituent effects. This gave correlation equation 7. The  $\sum\sigma_{\alpha}$ ,  $\sum\sigma_{\text{F}}$ ,

$$\beta = (0.84 \pm 0.02) - (0.08 \pm 0.01)\sum\sigma_{\alpha} - (0.46 \pm 0.01)\sum\sigma_{\text{F}} - (0.17 \pm 0.01)\sum\sigma_{\text{R}} \quad (7)$$

$$n = 54, r = 0.979, \text{sd} = 0.037$$

and  $\sum\sigma_{\text{R}}$  values for this data set show very low colinearity;  $r(\sigma_{\alpha} \text{ vs } \sigma_{\text{F}}) = -0.049$ ;  $r(\sigma_{\alpha} \text{ vs } \sigma_{\text{R}}) = 0.416$ ;  $r(\sigma_{\text{F}} \text{ vs } \sigma_{\text{R}}) = -0.097$ . Since phosphine oxide,  $\text{H}_3\text{P}=\text{O}$ , is an unknown compound, there is no direct confirmation of the value of the intercept ( $\beta = 0.84 \pm 0.02$  for  $\text{H}_3\text{P}=\text{O}$ ). Consequently, noncolinearity of the independent variables is particularly crucial for obtaining a valid correlation equation.

Table II. Substituent Parameters Used in Correlations<sup>a</sup>

substituent	$\sigma_{\alpha}$	$\sigma_{\text{F}}$	$\sigma_{\text{R}}$
H	0.00	0.00	0.00
CH <sub>3</sub>	-0.35	0.00	-0.08
C <sub>2</sub> H <sub>5</sub>	-0.49	0.00	-0.07
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	-0.54	0.00	-0.07
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-0.62	0.00	-0.07
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	-0.57	0.00	-0.07
<i>t</i> -C <sub>4</sub> H <sub>9</sub>	-0.75	0.00	-0.07
CH <sub>3</sub> O	-0.17	0.25	-0.42
C <sub>2</sub> H <sub>5</sub> O	-0.23	0.25	-0.45
<i>n</i> -C <sub>3</sub> H <sub>7</sub> O	(-0.26)	(0.25)	(-0.46)
<i>i</i> -C <sub>3</sub> H <sub>7</sub> O	(-0.29)	(0.24)	(-0.47)
<i>n</i> -C <sub>4</sub> H <sub>9</sub> O	(-0.27)	(0.25)	(-0.46)
C <sub>6</sub> H <sub>5</sub> O	(-0.38)	0.38	-0.32
CH <sub>2</sub> Cl	-0.54	0.23	-0.06
CHCl <sub>2</sub>	(-0.62)	(0.35)	(-0.03)
CCl <sub>3</sub>	-0.70	0.44	0.00
F	0.13	0.44	-0.25
Cl	-0.43	0.45	-0.17
C <sub>6</sub> H <sub>5</sub>	-0.81	0.10	-0.22
(CH <sub>3</sub> ) <sub>2</sub> N	-0.44	0.10	-0.64
C <sub>2</sub> H <sub>5</sub> S	(-0.74)	(0.24)	(-0.27)
C <sub>6</sub> H <sub>5</sub> S	(-0.90)	(0.26)	(0.00)
CH=CH <sub>2</sub>	-0.50	0.06	(-0.15)

<sup>a</sup> From ref 13. Values in parentheses have been estimated from these and other known values, cf. Hehre, W. J.; Pau, C.-F.; Headley, A. D.; Taft, R. W.; Topsom, R. D. *J. Am. Chem. Soc.* 1986, 108, 1711. All of these substituent parameters apply for nonsolvated substituents and for  $\pi$ -electron-donor substituents with maximal orbital overlap with the conjugated acceptor center.

Equation 7 shows that the field/inductive effects of substituents are the major ones that determine the hydrogen-bond acceptor ability of the phosphine oxides. These effects are shown to be nearly additive by the satisfactory precision of eq 7. The substituent polarizability and resonance effect terms in eq 7 are both found to be statistically significant at the 95+ % confidence level (by the Student *t*-test). Thus, if the polarizability effect term (with the smallest coefficient of  $\sigma$ ) is excluded, *sd* increases to 0.053 and the correlation coefficient worsens to 0.955. The presence of this term in eq 7 is expected on the grounds that the  $\text{P}=\text{O}$  dipole will induce a dipole in a polarizable substituent, thus increasing the value of  $\beta$ . Similarly, the presence of the resonance effect term in eq 7 is expected since the  $\text{P}=\text{O}$  group is a weak  $\pi$ -electron acceptor (weak in comparison to a  $\text{C}=\text{O}$  group, for example), and thus  $\pi$ -electron-donor substituents increase the  $\beta$  value.

## Discussion and Conclusions

### Evaluation and Partitioning of Substituent Effects.

In order to obtain further evidence regarding the effects of nonadditivity of  $\sigma_{\text{R}}$  values, three additional correlation equations were determined: (a) From the entire data set of 54, 12 trisubstituted phosphine oxides,  $\text{XYZP}=\text{O}$ , for which  $\sum\sigma_{\text{R}}$  is less negative than  $-0.25$  were excluded. This resulted in eq 7a. (b) A correlation was obtained for only

$$\beta = (0.91 \pm 0.02) - (0.10 \pm 0.01)\sum\sigma_{\alpha} - (0.48 \pm 0.01)\sum\sigma_{\text{F}} - (0.19 \pm 0.00)\sum\sigma_{\text{R}} \quad (7a)$$

$$n = 42, r = 0.984, \text{sd} = 0.033$$

the 15  $\text{X}_3\text{P}=\text{O}$  compounds of Table I. This resulted in eq 7b. (c) The 14 compounds in Table I of the family

$$\beta = (1.01 \pm 0.02) - (0.01 \pm 0.01)\sum\sigma_{\alpha} - (0.47 \pm 0.01)\sum\sigma_{\text{F}} - (0.09 \pm 0.01)\sum\sigma_{\text{R}} \quad (7b)$$

$$n = 15, r = 0.995, \text{sd} = 0.022$$

( $\text{C}_2\text{H}_5\text{O}$ )<sub>2</sub> $\text{XP}=\text{O}$  (which includes X = H) were correlated, giving eq 7c.

(13) Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* 1987, 16, 1 (Table I).

$$\beta = (0.79 \pm 0.02) - (0.12 \pm 0.03)\sigma_{\alpha} - (0.41 \pm 0.04)\sigma_{\text{F}} - (0.14 \pm 0.04)\sigma_{\text{R}} \quad (7c)$$

$$n = 14, r = 0.957, \text{sd} = 0.025$$

The independent variables in eq 7a retained a very similar level of mutual noncolinearity as for eq 7; only  $r$  for  $\sigma_{\alpha}$  vs  $\sigma_{\text{R}}$  increased slightly to 0.530. It is seen that eq 7a is quite similar to eq 7 for the entire data set, although there is a small improvement in precision of fit, with  $\rho_{\text{R}}$  and  $\rho_{\alpha}$  having increased in magnitude slightly and  $\rho_{\text{F}}$  remaining constant at  $-0.47 \pm 0.01$ .

Equation 7b for the  $\text{X}_3\text{P}=\text{O}$  family reveals quite significant movements in the values of  $\rho_{\alpha}$ ,  $\rho_{\text{R}}$ , and the intercept (calculated value for  $\text{H}_3\text{P}=\text{O}$ ), but  $\rho_{\text{F}}$  remains the same as for eq 7 and 7a. Compared to eq 7, the intercept has increased by 0.17,  $\rho_{\alpha}$  has become statistically not significant, and  $\rho_{\text{R}}$  has decreased in magnitude by a factor of 2.

The coefficients of  $\sigma_{\alpha}$ ,  $\sigma_{\text{F}}$ , and  $\sigma_{\text{R}}$  in eq 7c for the  $(\text{C}_2\text{H}_5\text{O})_2\text{XP}=\text{O}$  family are not different within the combined uncertainties of the estimates from those in eq 7 for the whole data set. The estimate of the  $\beta$  value for  $(\text{C}_2\text{H}_5\text{O})_2\text{HP}=\text{O}$  differs by 1 sd from the experimental value and can be used to estimate the value of  $\beta = 0.93 \pm 0.05$  for  $\text{H}_3\text{P}=\text{O}$ .

Taken all together, eq 7, 7a, 7b, and 7c lead us to the following conclusions: (i) The substituent effects on  $\beta$  values for  $\text{XYZP}=\text{O}$  compounds are determined largely by field/inductive effects, and these are well correlated by  $\sum\sigma_{\text{F}}$  (additivity is excellent). (ii) Although of secondary importance, substituent resonance and polarizability effects also contribute to the hydrogen-bond basicities of  $\text{XYZP}=\text{O}$  compounds. Highly polarizable substituents or strong  $\pi$  donor substituents may increase  $\beta$  values by 0.1–0.3 unit. (iii) The  $\beta$  value for the unknown parent  $\text{H}_3\text{P}=\text{O}$  can be estimated only crudely as ca.  $0.90 \pm 0.05$  due to errors introduced by nonadditivity of the secondary substituent resonance and polarizability effects. (iv) Saturation and steric twisting from coplanarity reduce  $\pi$ -electron-donating substituent effects so that  $\sigma_{\text{R}}$  values are not strictly additive with successive substitution (see below, Steric Effects). The errors introduced by the use of  $\sum\sigma_{\text{R}}$  for strong  $\pi$ -electron-donor substituents like  $(\text{C}_2\text{H}_5)_2\text{N}$  appear in the secondary terms, i.e., in values of the intercept and the coefficient of substituent polarizability,  $\sigma_{\alpha}$ . The reduced  $\sigma_{\text{R}}$  coefficient in eq 7b compared to that in eq 7 is a real manifestation of this effect. (v) Donor  $\pi$ -electron delocalization to  $\text{P}=\text{O}$  probably reduces the polarizing interaction with substituents at phosphorus. This is suggested by the lack of a statistically significant  $\sigma_{\alpha}$  value in eq 7b. (vi) Equation 7 appears to be the preferred equation for generally useful predictions. Correlation equations such as 7a, 7b, and 7c can only be useful if applied to a family having a wide range of  $\beta$  values.

In conclusion, we point out that we have not used all the data on  $\Delta\nu(\text{O}-\text{H})$  reported by Raevskii and co-workers,<sup>9–11</sup> but rather have treated a representative sampling of their 243 experimental determinations. Readers interested in estimating  $\beta$  values for additional  $\text{XYZP}=\text{O}$  compounds are advised to use eq 5 and 7 together with the additional Raevskii data. As a check of eq 7, we have, however, used some of their additional data for the families  $\text{Cl}_2\text{XP}=\text{O}$ ,  $(\text{CH}_3)_2\text{XP}=\text{O}$ ,  $\text{HXP}=\text{O}$ , and  $\text{CH}_3\text{X}_2\text{P}=\text{O}$  to arrive independently at eq 8 which is seen to agree quite well with

$$\beta = 0.86 - 0.07\sigma_{\alpha} - 0.47\sigma_{\text{F}} - 0.17\sigma_{\text{R}} \quad (8)$$

$$n = 47, r = 0.980$$

eq 7. It is important to note that the range of  $\beta$  values

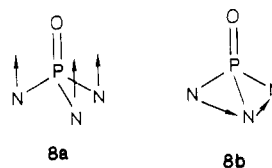
within each of the four separate families proved to be too small to permit reliable correlations within the families but, as expressed by eq 8, the combined data for all four of these families do give a satisfactory result.

**Steric Effects.** The largest deviation from eq 7 is for hexamethylphosphoramide ( $\beta_{\text{obsd}} = 1.05$ ,  $\beta_{\text{calcd}} = 1.12$ ). Also the  $\beta$  values for trialkylphosphine oxides are undercalculated by 0.04 to 0.07. These systematic deviations are in accord with the expectation that there is nonadditivity of  $\sigma_{\text{R}}$  values for strong  $\pi$ -electron donors like  $\text{N}(\text{CH}_3)_2$ . Errors introduced by the additivity assumption apparently are relatively small because the coefficient of  $\sum\sigma_{\text{R}}$  is only about one-third as large as that for  $\sum\sigma_{\text{F}}$ .

Both saturation and steric twisting effects can act to reduce  $\pi$ -donor substituent effects with each successive substitution. The  $\beta$  value for  $(\text{C}_2\text{H}_5\text{O})_2[(\text{CH}_3)_2\text{N}]_n\text{P}=\text{O}$  is 0.13 unit larger than that for  $(\text{C}_2\text{H}_5)_2\text{HP}=\text{O}$ , whereas the  $\beta$  value for  $[(\text{CH}_3)_2\text{N}]_3\text{P}=\text{O}$  is only 0.21 unit (rather than 0.39 unit) larger than the estimated value for  $\text{H}_3\text{P}=\text{O}$  (eq 7).

The gas-phase proton-transfer basicities of the phosphine oxides in the series  $(\text{CH}_3)_{3-n}[(\text{CH}_3)_2\text{N}]_n\text{P}=\text{O}$  show similar nonadditive trends for substitution of  $(\text{CH}_3)_2\text{N}$  for  $\text{CH}_3$ . The basicity difference for compounds with  $n = 1$  and  $n = 0$  is 4.2 kcal/mol; for  $n = 2$  compared to  $n = 1$ , the difference is 3.1 kcal/mol; and for  $n = 3$  compared to  $n = 2$ , the difference is 2.6 kcal/mol.<sup>14a</sup> The reduced  $\pi$ -donor resonance effects of the  $(\text{CH}_3)_2\text{N}$  substituents on successive substitution that are implied are in part imposed by steric considerations.

For hexamethylphosphoramide, maximal overlap of orbitals would require a conformation like 8a, in which the three nitrogen lone pairs (represented by the arrows) are parallel to and in the same direction as the  $\text{P}=\text{O}$  axis and wherein all six methyl groups lie in the same plane. Such a conformation, although electronically favored, is strongly disfavored sterically.



Indeed, Bollinger and co-workers<sup>14b</sup> have calculated dipole moments as functions of conformation for the various HMPA conformers, using "rigid dipole" summations (i.e., lone pairs at angles of 0°, 90°, and 180° from the direction of the  $\text{P}-\text{O}$  axis). They found that structure 8a would require a dipole of 5.82 D, compared with the experimental dipole of 4.19 D (in cyclohexane). The "rigid dipole" conformation which corresponded most closely to the experimental moment was that shown in 8b, in which one lone pair is parallel to the  $\text{P}=\text{O}$  bond, but in the opposite direction, and the two others are in a plane perpendicular to  $\text{P}-\text{O}$ . In the nonrigid system, this is equivalent to a "high pitch" propeller arrangement of the dimethylamine groups, which is also intuitively preferred.

Further, such a propeller arrangement was also found by Steudel and co-workers<sup>15</sup> in an X-ray diffraction study of the structure of  $\text{HMPA}\cdot 2\text{S}_7\text{NH}$ . Angles of 113.8°, 84.5°, and 107.3° were found between the  $\text{O}-\text{P}-\text{N}$  planes and the

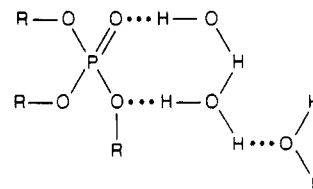
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bisectors of the P-N-C planes (which correspond to the lone pair-N-P planes). These may be regarded as the angles of twist from maximal orbital overlap.

**Multifunctional Acceptor Effects, a Caveat.** The  $\beta$  values derived here are intended to be used as measures of the HBA basicities of the XYZP=O compounds acting as either solutes or solvents. There has been a complication, however, insofar as predictions of octanol/water partition coefficients or aqueous solubilities of (RO)<sub>3</sub>P=O and possibly (RO)<sub>2</sub>XP=O and (RO)XYP=O compounds are concerned.

Using  $\beta$  values from Table I together with equations which we have reported for octanol/water partition coefficients<sup>16</sup> and aqueous solubilities<sup>17</sup> of organic nonelectrolytes has led to serious overpredictions of log  $K_{ow}$  and serious underpredictions of log  $S_w$ . We believe that this is because these compounds act as multifunctional hydrogen-bond acceptors in water, hydrogen bonding at both the P=O and R-O-P oxygens to either different or the same water clusters. In HBD solvents other than water,



such interactions at multiple HBA sites are very much less apt to occur. In water, however, *effective*  $\sum\beta$  values rather than the  $\beta$  values reported here are required to predict solubility and partition properties of the trialkyl phosphates.

We have calculated from octanol/water partition constants<sup>18</sup> that  $\sum\beta$  has values from 1.00 to 1.10 for methyl through *n*-butyl phosphates (compared to  $\beta = 0.77$ -0.82 in Table I). These values were confirmed by the finding that the  $\sum\beta$  values for the trialkyl phosphates allowed the calculation of cyclohexane/water partition coefficients through the correlation equation for that bilayer system. This is strong confirmation, since the equation for cyclohexane/water partition has significantly larger  $m$ ;  $-s$ ,  $-a$ , and  $-b$  coefficients in eq 2 than does that for octanol/water partition.

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(18) Unpublished results.

## Mild and Regiospecific Reduction of Masked 1,3-Dicarbonyl Derivatives to Monocarbonyl Compounds and Primary and Secondary Amines

José Barluenga,\* Enrique Aguilar, Bernardo Olano, and Santos Fustero

Departamento de Química Organometálica, Facultad de Química, Universidad de Oviedo, 33071 Oviedo, Spain

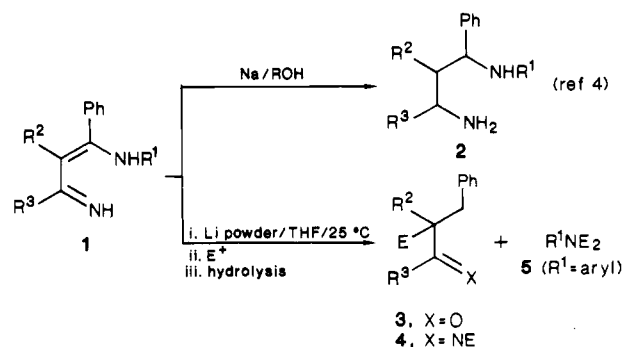
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The regiospecific reduction of masked 1,3-dicarbonyl compounds to the corresponding saturated monocarbonyl 3 or iminic 4 compounds via 3-amino-2-alkenimines 1 is described. The formation of 3 or 4 can be explained in terms of a double reduction process from 1. A simple method for the synthesis of primary and secondary amines 6 is also described.

We have been interested for some years in the readily available 3-amino-2-alkenimine systems 1,<sup>1,2</sup> both as synthons in the preparation of a wide range of heterocycles<sup>3</sup> and in the preparation of  $\beta$ - and  $\gamma$ -difunctionalized compounds by reduction processes.<sup>4-6</sup> In particular, the reduction of 1 with sodium in *i*-PrOH as protic cosolvent led to a diastereoisomeric mixture of  $\gamma$ -diamines 2<sup>4</sup> (Scheme I).

In connection with these studies, we now describe the behavior of systems 1, direct precursors of the 1,3-dicarbonyl derivatives,<sup>2</sup> when treated with lithium metal in the absence of a proton source; this process allows the regiospecific reduction of 1 to saturated carbonyl or iminic

Scheme I



compounds 3 and 4.<sup>7</sup> In addition, a new method for the synthesis of amines of type 6 is also described.

(7) Although the selective reduction of one of the carbonyl groups in 1,3-dioxo compounds has been widely studied in the preparation of  $\beta$ -hydroxy carbonyl compounds, especially from  $\beta$ -keto esters, only a few examples have been reported for the direct reduction of one of the  $>C=O$  groups to  $=CH_2$  in 1,3-dicarbonyl compounds. See, for example: (a) Oishi, T.; Nakata, T. *Acc. Chem. Res.* 1984, 17, 338. (b) Coates, R. M.; Shaw, J. E. *J. Org. Chem.* 1970, 35, 2597 and 2601.

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