Substituent Effects. 5.[1-4] Resonance Saturation Effects in Anilines Having a π-Donor Group in Para Position

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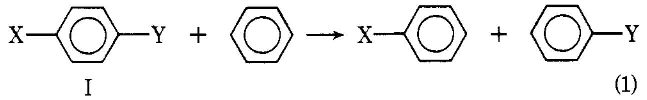
Abstract: The exaltation of σ_p for π donors in aromatic amines decreases regularly when the aniline resonance is sterically inhibited to an increasing extent; when inhibition is complete $\sigma_p \sim \sigma^n$. This is argued to be further evidence for resonance saturation, i.e., saturation of the electron release by two π donors in the 1,4 position. Derived saturation energies are in reasonable agreement with quantum-mechanical results. An expression is proposed which gives the saturation energies as a function of $\sigma_R{}^n$ values. Large saturation energies do not necessarily lead to appreciable exaltation of σ_p values, and this is exemplified for phenols. Some remarks are made on the applicability of the Hammett equation and its extensions.

Recently, Pople et al.[5,6] reported on quantum-mechanical calculations of the energy changes in the formal reaction 1 with Y = OH and with Y = NH_2.



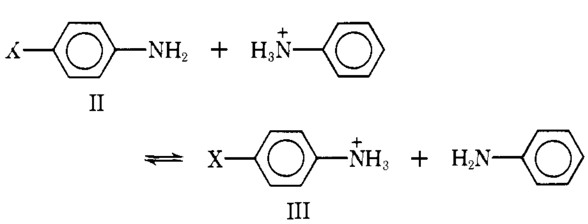
I

(1)

These energy changes, which are a measure of the interaction energy in the para-disubstituted compound, I, were found to be endothermic if X is a π acceptor (−M effect). This means stabilization in I and corresponds with the concept of through-resonance. The calculated interaction energies are surprisingly and encouragingly close to those derived from data in solution on the basis of an extension of the Hammett equation[7] or the theory of steric inhibition of (through-)resonance.[8]

The energy changes of reaction 1 were found to be exothermic if X is a π donor (+M effect). This means destabilization in I and corresponds with a "resonance saturation effect". The calculated interaction energies are virtually the same for corresponding aniline and phenol derivatives and are of the order of 1 kcal/mol. Some values are given in Table I.

In the Hammett $\rho\sigma$ treatment of the basic strength of anilines, $ArNH_2$, a destabilizing interaction in I should give rise to an exaltation of the σ values of π donors; the observed σ values should be more negative or less positive than the normal sigma values,[1] σ^n. This "negative σ shift" can be elucidated by considering the proton-transfer equilibrium 2, log K' of which equals the substituent effect log K_X − log K_H in the $ArNH_2$ series. Let us assume the following extra resonance energies: $PhNH_2$, a; $PhNH_3{}^+$, 0 (zero); XPh and III, b (see below); and II, $a + b + m$. If $m = 0$, i.e., if X and NH_2 act independently in II, the substituent effect of X is reflected by σ^n. If X is a π acceptor, m represents the stabilizing through-resonance factor; the basic strength is decreased to the equivalent of m, and there is a positive σ shift [e.g.,[4] $\sigma^n(4\text{-}NO_2) = 0.78$; observed $\sigma(4\text{-}NO_2) \equiv \sigma^-(4\text{-}NO_2) = 1.23$]. If, on the other hand, X is a π donor and resonance saturation occurs, m is destabilizing, the basic strength of II is increased to the equivalent of m, and there is a negative σ shift with respect to σ^n.



II

III

(2)

As a referee pointed out, the above analysis shows a fallacy in the generally accepted view that increasingly negative σ values imply more electron donation. Thus, in 1-amino-4-methoxybenzene the methoxy substituent donates less charge to the ring than in methoxybenzene; nevertheless the observed σ value should be (and is) more negative than σ^n. The correct sign of the σ shift can be obtained here by concentrating on the functional group, the electron donation of which is decreased in comparison with aminobenzene so that its basic strength is increased. However, examination of both sides of the equilibrium remains every man's duty, any day, and this paper contains some further illustrations.

As to the magnitude of the σ shift, this is related with the para interaction through eq 3.[1] With $\rho = -3.55$ for $ArNH_2$

$$-\Delta\Delta G_p = \rho(\sigma - \sigma^n)2.3RT \tag{3}$$

in 50% ethanol at 25 °C, a saturation energy $m = -1$ kcal/mol corresponds with $\sigma - \sigma^n = -0.20$.

Some years ago[9] we used the above line of thought[10] and the term "saturation effect" in an explanation of exaltations of σ of this magnitude observed in aniline reactivities for the substituents NH_2, NMe_2, OH, and OMe (and F[11]), and smaller exaltations of about −0.05 σ units for Cl, Br, and Me. In support it was noted[12] that the basic strength of 6-aminobenzoquinuclidine, in which compound the more basic ring-nitrogen atom does not resonate with the benzene ring,[13] yields a σ value for the para (6-)amino group which is less negative than that from the basic strength of 1,4-diaminobenzene.

We now report on the substituent effects and σ_p values of π donors as to the basic strength of: $ArNH_2$, $ArNMe_2$, ArNH-t-Bu, 2-Me-$ArNMe_2$, ArNMe-t-Bu, and benzoquinuclidines. The essential feature is that along the series the resonance of the reaction center with the benzene ring decreases gradually to zero. Hence, the saturation effect decreases, and σ should approach σ^n the closer the stronger the inhibition of the resonance.

The order of increasing steric inhibition of resonance in the above series of amines follows from ϵ/ϵ_0,[14] the ratio of the observed maximum molar extinction coefficients in the electronic spectrum of the parent compound in question (e.g., PhNMe-t-Bu) and that of a related one (PhNMeBu) in which the resonance is considered to be uninhibited (Table I). It will be oserved that the ρ values of the tertiary amines follow the same order, varying rather strongly from −4.3 to −2.9. Since the interactions in the ammonium ions may be taken to be approximately the same in each series, this variation in ρ can be largely ascribed to the decrease of the mesomeric dipole and its interaction with the substituent.[15,16]

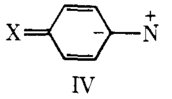
Table I. Substituent Effects, σ Values, and Resonance Saturation Energies in Anilines and Phenols Having a π Donor in Para Position[a]

Conjugate base	ϵ/ϵ_0 iso	ϵ/ϵ_0 50%	ρ_m 50%	NH_2	NMe_2	OH	OMe	F	Br	Me	NHAc
						ΔpK_a^* (50% ethanol)					
$ArNH_2$	(1)	(1)	3.552	−1.50[b]		−1.17	−0.81	0.11[c]	1.01	−0.50	−0.03
NMe_2	(1)	(1)	4.288		−1.39[b]	−1.19	−0.80	0.19	1.20	−0.51	−0.02
NH-*t*-Bu	0.84	0.67	3.942	−1.22	−1.15	−0.85	−0.52	0.32	1.01	−0.38	−0.01
2-Me-NMe_2	0.41	0.50	3.839[d]	−1.17			−0.41	0.49	1.08	−0.33	0.04
NMe-*t*-Bu	0.30	0.26	3.396	−0.99	− 0.92	−0.53	−0.25	0.56	1.00	−0.25	0.07
Benzoquinuclidine	<0.003	<0.004	2.873	−0.74	−0.67			0.55	0.91		0.15
							$\bar{\sigma}_p$				
$ArNH_2$				−0.42[b]		−0.33	−0.23	0.03[c]	0.28	−0.14	−0.01
NMe_2					−0.32[b]	−0.28	−0.19	0.04	0.28	−0.12	−0.01
NH-*t*-Bu				−0.31	−0.29	−0.22	−0.13	0.08	0.26	−0.10	0.00
2-Me-NMe_2				−0.30			−0.11	0.13	0.28	−0.09	0.01
NMe-*t*-Bu				−0.29	−0.27	−0.16	−0.07	0.17	0.29	−0.07	0.02
Benzoquinuclidine				−0.26	−0.23			0.19	0.32		0.05
							$\bar{\sigma}_p^n$ and σ_p^n				
				−0.25	−0.25	−0.17	−0.11	0.16	0.28	−0.12	0.09
				−0.24	−0.24	−0.12	−0.09	0.18	0.30	−0.10	0.14
							$\bar{\sigma}_p$ (water)				
ArOH (Water)			2.205[e]	−0.28	−0.17	−0.14[e]	−0.12	0.05	0.28[e]	−0.13[e]	
						Saturation energies in I (kcal/mol)					
ArOH Pople et al.[f]				−1.5		−1.4		−0.9		−0.4	
$ArNH_2$ Pople et al.[g]				−1.6		−1.5		−0.8		−0.5	
$ArNH_2$ eq 3				−0.8		−0.8	− 0.8	−0.8[c]	−0.2	−0.3	−0.3
$ArNMe_2$ eq 3					−0.5	−0.7	−0.7	−0.8	−0.2	−0.3	−0.4
$ArNH_2$ and $ArNMe_2$ eq 4				−0.8	−0.8	−0.9	−0.8	−0.8	−0.3	−0.1	−0.3

[a] ϵ_0, at about 250 nm, from PhNHBu, $PhNMe_2$, PhNMeBu, and $PhNMe_2$, respectively; iso, isooctane; 50%, 50 volumes of absolute ethanol in 100 volumes final solution (0.01 N in KOH in the uv measurements); ρ_m, reaction constant based on primary meta σ values (ref 4); ΔpK_a^*, thermodynamic pK_a^* parent *minus* thermodynamic pK_a^* para-substituted derivative; thermodynamic pK_a^* values in 50% ethanol as defined above, at 25 °C: $PhNH_2$ 4.04, $PhNMe_2$ 4.16, PhNH-*t*-Bu 6.37, 2-Me-*N*,*N*-dimethylaniline 4.93, PhNMe-*t*-Bu 6.63, benzoquinuclidine 6.75 (PhOH in water 10.00); $\bar{\sigma}_p = \Delta pK_a^*/\rho_m$; $\bar{\sigma}_p^n$ and σ_p^n: first row $\bar{\sigma}_p^n$, second row σ_p^n (ref 4). [b] Corrected statistically. [c] In water ΔpK_a −0.02, $\bar{\sigma}_p$ −0.01, saturation energy −0.7. [d] 2-Me-5-X-*N*,*N*-dimethylaniline. [e] Reference 1. [f] Reference 5. [g] Reference 6.

Table I lists the substituent effects in 50% ethanol in terms of the usual pK_a^* values of the conjugate acids and the derived σ values. The changes are in the expected direction if saturation effects decrease from top to bottom and are as regular as one might reasonably hope for.[17] Of course, the fact that the systems are so closely related and that the measurements pertain to one and the same solvent help to reduce complications to a minimum. In addition to the regularity it is of interest that the σ values for the benzoquinuclidines (and for ArNMe-*t*-Bu) are quite close to σ^n values as published recently[4] and given in Table I. These aspects deserve some special comment.

Above we have assumed additivity in the protonated species III when taking the extra resonance energies in III and in XPh to be the same, *b*. This is certainly not strictly true. The XAr moiety will be more strongly polarized in III than in XPh and II. In resonance terms this corresponds with an increase of the contribution of the quinonoid structure IV due to the positive charge. This "enhanced resonance" stabilizes III and thus affects *K'* in the same direction as the destabilizing resonance saturation in II. Two points can now be made with regard to our data. The first is that the enhanced resonance in III should hardly influence the vertical *variations* in Table I because in each column it is constant or very nearly so, being the interaction of an ammonio site with one and the same 4-XAr system. Hence, the vertical variations of ΔpK_a^* and σ (taking proper account of ρ) can be taken to reflect the saturation effect in II. The second point is that, notwithstanding the enhanced resonance in III, the σ values from the benzoquinuclidines are not more negative (or less positive) than σ^n. This does not mean that enhanced resonance is of no importance. It rather emphasizes that these resonance differences are absorbed in σ^n; they form a component of σ_p in σ^n type reactivities which differs from one substituent to another but which is approximately constant for each of them. Of course, the energy differences involved are much smaller in, e.g., the σ^n series $ArCH_2COOH$ than in the benzoquinuclidines, but so are the ρ values (0.7^4 vs. 2.9 in 50% ethanol), and, apparently, these factors compensate with respect to σ^n. A similar situation, similarly explained, was encountered[3] in the series $ArNHCH_2CH_2COOH$, $ArNHCH_2COOH$, and $ArNHNH_3^+$, with ρ varying from 0.2–1.6, where $\sigma(4\text{-}NO_2)$ shows approximately the same exalted value, ~1.3, although the interaction energies responsible for the exaltation must differ strongly. We note, finally, that the data for 4-NH_2 and 4-NMe_2 can also be regarded as a confirmation of our conclusion[4] that older values of σ^n (σ^0) and σ_R^n (σ_R^0) for these groups are in error.



IV

Our data also give the "saturation energies" through eq 3. Since the ρ values change regularly in the series, the pattern of these energies is similar to that of the σ values. Table I gives the energies calculated for the systems $ArNH_2$ and $ArNMe_2$, using the σ value of the benzoquinuclidines (or ArNMe-*t*-Bu) as σ^n. As to comparison with the quantum-mechanical data, it would seem fit to stress the reasonable correspondence with respect to order of magnitude and trends.

The saturation energies calculated by us can be subdivided in two groups: those for the simple first-row substituents NH_2, OH, OMe, and F are large and about the same (NMe_2 is doubtful), those for the other substituents are smaller and variable (and also less reliable). This subdivision is similar to that found for σ in Part 1[1] (see above). It also concurs with the values of $\sigma_R{}^n = \sigma^n - \sigma_I$ obtained in Part 4:[4] $\sigma_R{}^n = -0.34$ for NH_2, NMe_2, OMe, and F, and -0.37 for OH, whereas Br, Me, and NHAc gave values of -0.15, -0.05, and -0.14, respectively. On this basis, eq 4 can be proposed to represent the

$$-\Delta G_p{}^{sat} = 5\sigma_R{}^n(X)\sigma_R{}^n(Y)2.3RT \qquad (4)$$

saturation effect in individual species. It has the same form as an equation covering through-resonance, due to Hine[18] and recently discussed by us,[2,3] but it uses $\sigma_R{}^n$ as the substituent parameter (rather than $\Delta\sigma_R{}^+$ which is also numerically incompatible with our data and the quantum-mechanical ones[19]). Table I gives the saturation energies from eq 4, the proportionality constant of which, 5, was chosen so as to obtain concurrence for the first-row substituents.

In the phenol series, in water, the groups NH_2,[20] NMe_2,[20] OH, and OMe show σ_p values close to σ^n (Table I). This means that the saturation in, e.g., *para*-aminohydroxybenzene does turn up in the basic strength of the amino group, but does not in the acid strength of the hydroxyl group. This paradox can be resolved by considering, once more, that differences between factor and product are involved, so that if the saturation changes little in the dissociation of the OH group, σ will be hardly affected. In terms of eq 4 this holds if $\sigma_R{}^n(O^-) - \sigma_R{}^n(OH) = \sigma_R{}^n(O^-) + 0.37$ is much smaller than $\sigma_R{}^n(NH_2) - \sigma_R{}^n(NH_3{}^+) = -0.34 - 0 = -0.34$. Unfortunately, this cannot be checked directly since $\sigma_R{}^n(O^-)$ is not well known from reactivities,[21] but an indirect argument is fairly convincing. The $\Delta\sigma_R{}^+$ values of the groups F, OH, NH_2, and O^- vary widely: -0.28, -0.79, -1.23, and -1.8, respectively.[4] If, now, for the first three groups, the $\sigma_R{}^n$ values are "compressed" to -0.34, -0.37, and -0.34, then $\sigma_R{}^n(O^-)$ will not be very different, and, therefore, $\sigma_R{}^n(O^-) - \sigma_R{}^n(OH)$ will be small.[21] Attention may be drawn to the position of 4-F. Its σ value in the phenols, 0.05, must be regarded as exalted and corresponds with an increase of the saturation of 0.3 kcal/mol when 4-F-phenol dissociates. This is indeed less than in 4-F-aniline, 0.7 kcal/mol in water, but larger than to be expected from the data on the other groups. We have no explanation, but note that in the gas phase the substituent effect in 4-F-phenol has been found to be considerable and not far below that in 4-Cl-phenol ($\Delta\Delta G_{298}{}^0$ -2.1 and -2.9 kcal/mol, respectively[22]).

The above discussion of saturation effects calls for some remarks on the applicability of the Hammett equation. In a sense, the evaluation of the aniline data may be judged to have "reached the point of absurdity",[23] or to "border on the ridiculous",[24] in that substituent effects from the para position are considered abnormal for π acceptors (through-resonance) as well as for π donors (saturation). This leaves little space for normal behavior of para substituents and one may wonder why the $\rho\sigma$ relation, or, more specifically, the $\rho_m\sigma^n$ relation works so well in many other reactions.

With respect to π-donor saturation (+M vs. +M) the answer is twofold. First, the protonation of anilines is rather exceptional inasmuch as a large +M effect is reduced to (essentially) zero. In other systems the functional group has a small resonance effect, if any, in factor and product or transition state ($ArCH_2COOR$), or the resonance effects are large but differ little (ArOH). Secondly, with the weaker +M effects (Br) saturation effects are smaller already in the favorable situation of Table I, and, therefore, will hardly ever exceed the noise level of the $\rho_m\sigma^n$ relation.

With respect to π-acceptor saturation (−M vs. −M), as in 4-nitrobenzoic acid, we believe that saturation is of no importance. Branch and Calvin[10] discussed this case and concluded that the effect should be smaller (energetically) than in *para*-aminophenol, because (in their terminology) the latter case concerns a cross-conjugation and the former a cross-conjugation of a cross-conjugation. A more quantitative estimate follows from the substituent effects of the nitro group in 4-nitrobenzoic acid, 4-nitro-3,5-dimethylbenzoic acid, and 4-nitro-3,5-di-*tert*-butylbenzoic acid.[25] In the latter two compounds the resonance interaction between the nitro group and the rest of the system is largely eliminated.[8] Accordingly, the effect of the nitro group should decrease, and the decrease should reflect the sum of the influences of the nitrobenzene resonance, the enhanced resonance, and the saturation which enters here as a difference between acid and anion. Since these influences have the same sign, and the observed decrease amounts to only 0.10 σ unit, the saturation effect must be small. This conclusion is substantiated by the substituent effects of the nitro group in 4-nitro-2-*tert*-butyl-*N,N*-dimethylaniline and 4-nitro-2,5-di-*tert*-butyl-*N,N*-dimethylaniline.[26] These also differ by about 0.10 σ units, although the saturation effect cannot play a role here, and the aniline resonance and the through-resonance are practically absent.[27] Hence, the contribution of the saturation effect in 4-nitrobenzoic acid is at most a few hundredths of a σ unit and, therefore, can be neglected. The same holds, a fortiori, for $3-NO_2$ substitution.[25,26] Finally, we wish to mention some extra delocalization energies in benzene derivatives as obtained by Hückel MO calculations,[28] expressed in β units and positive for stabilization: $1-NH_2-4-NO_2$, 0.0606; $1-NH_2-4-NH_2$, -0.0616; $1-COO^--4-NO_2$, -0.0080; $1-NH_2-3-NO_2$, -0.0026; $1-NH_2-3-NH_2$, -0.0014; $1-COO^--3-NO_2$, -0.0008. The results are quite acceptable with respect to the para +M,−M and +M,+M combinations and the smallness of meta vs. para interactions. Accordingly, the order-of-magnitude difference between +M,+M and −M,−M combinations may be viewed with some confidence.

Thus, the present work, although emphasizing once more that the search for unique σ values is a vain one, does not unduly depreciate the usefulness of the σ^n concept. Deviations due to resonance saturation can be anticipated, and eq 3 and 4 may be employed for theoretical or predictive purposes, just as previous equations in cases of through-resonance.

A full account of our work on the amine systems of Table I will be given in future papers.

References and Notes

(1) Part 1: H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **78**, 815 (1959).

(2) Part 2: B. M. Wepster, *J. Am. Chem. Soc.*, **95**, 102 (1973).

(3) Part 3: A. J. Hoefnagel, J. C. Monshouwer, E. C. G. Snorn, and B. M. Wepster, *J. Am. Chem. Soc.*, **95**, 5350 (1973).

(4) Part 4: A. J. Hoefnagel and B. M. Wepster, *J. Am. Chem. Soc.*, **95**, 5357 (1973).

(5) L. Radom, W. J. Hehre, J. A. Pople, G. L. Carlson, and W. G. Fateley, *Chem. Commun.*, 308 (1972).

(6) W. J. Hehre, L. Radom, and J. A. Pople, *Chem. Commun.*, 669 (1972).

(7) Reference 1, 2, and 4, Pople et al.[5,6] give, e.g., the following figures (kcal/mol): 4-nitroaniline, 2.2–3.0; 4-nitrophenol, 1.3; 4-cyanophenol, 0.8; we found 1.8, 1.2, and 0.7, respectively.

(8) J. Burgers, M. A. Hoefnagel, P. E. Verkade, H. Visser, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **77**, 491, 509 (1958); see also ref 2.

(9) Reference 1, p 832–833.

(10) The earliest consideration of a saturation effect we know of is that by G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry", Prentice-Hall, New York, N.Y., 1941, p 250–252; cf. N. V. Hayes and G. E. K. Branch, *J. Am. Chem. Soc.*, **65**, 1555 (1943). Later discussions from various viewpoints are by: C. M. Judson and M. Kilpatrick, *J. Am. Chem. Soc.*, **71**, 3115, 3118 (1949); M. Kilpatrick and C. A. Arenberg, *ibid.*, **75**, 3812, 3820 (1953); L. D. McKeever and R. W. Taft, *ibid.*, **88**, 4544 (1966); A. D. Baker, D. P. May, and D. W. Turner, *J. Chem. Soc. B*, 22, 32 (1968); R. T. C. Brownlee, D. G. Cameron, R. D. Topsom, A. R. Katritzky, and A. F. Pozharsky, *J. Chem. Soc., Perkin Trans. 2*, 247, 252 (1974). As to the possible role in reactions of "electron-rich alkenes", see R. Huisgen and G. Steiner, *Tetrahedron Lett.*, 3763 (1973); the 1,2-diethoxyethylenes react more slowly than the 1-ethyl-2-ethoxyethylenes (due to the loss of resonance energy), but less so than would have to be expected if resonance saturation did not occur.

(11) See footnote 17 of ref 1; cf. ref 4.

(12) Footnote 16 of ref 1.

(13) B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **71**, 1159, 1171 (1952); *Prog. Stereochem.*, **2**, 117, 122, 150 (1958).

(14) See, e.g., ref 8, and B. M. Wepster, *Prog. Stereochem.*, **2**, 110, 117, 119, 122, 146 (1958).

(15) This interpretation of the respective ρ values suggests that mesomeric dipoles will often be of importance for the magnitude of ρ. As a rule the picture will be more complicated than in the present case due to the presence of mesomeric dipoles in both factor and product (phenols) or the uncertainties of transition state structure. As an example we mention the relatively low ρ values for the solvolysis of ArC(*t*-Bu)$_2$-*p*-nitrobenzoates as observed by H. Tanida and H. Matsumura, *J. Am. Chem. Soc.*, **95,** 1586 (1973) and by J. S. Lomas and J. E. Dubois, *Tetrahedron Lett.*, 407 (1976).

(16) The ρ values corroborate the rule that interposition of a CH$_2$ group decreases ρ by a factor 2. In 50% ethanol, ρ_m for benzoquinuclidines and ArCH$_2$NH$_2$, −2.87 and −1.27 (unpublished), already conform reasonably, and ρ_m of ArCH$_2$NMe$_2$ will be somewhat more negative than that of the primary amine. From this point of view the ρ_m values of ArNH$_2$ and ArNMe$_2$ are "abnormally" highly negative due to the aniline resonance.

(17) Our data in H$_2$O and 10% and 75% ethanol are less complete but display the same pattern. Again, the groups NH$_2$ and NHAc in meta position show variations which are much smaller.

(18) J. Hine, *J. Am. Chem. Soc.*, **81,** 1126 (1959); *ibid.*, **82,** 4877 (1960).

(19) Expressions containing $\sigma_R{}^n(X) - \sigma_R{}^n(Y)$, as used by Katritzky, Topsom et al. in their infrared work (see footnotes 10 and 21), obviously are not appropriate either. This emphasizes the differences between chemical and infrared criteria.

(20) Due to decomposition during the measurements, our potentiometric pK_a values pertaining to the hydroxy group in the aminophenols are not very accurate. However, they confirm literature values and are sufficiently reliable for the present work.

(21) In ref 4 we gave $\sigma_R{}^n(O^-) = -0.4$, but we now believe its derivation is wanting for reasons which will be apparent from later papers in this series. All required $\sigma_R{}^n(\sigma_R{}^0)$ values have been obtained from ^{19}F NMR [R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *J. Am. Chem. Soc.*, **85,** 3146 (1963)], and from infrared intensities [A. R. Katritzky and R. D. Topsom, *Angew. Chem., Int. Ed. Engl.*, **9,** 87 (1970), and later papers]. The NMR data give $\sigma_R{}^0(NH_3{}^+) - \sigma_R{}^0(NH_2) = 0.48$ as against $\sigma_R{}^0(OH) - \sigma_R{}^0(O^-) = 0.17$; the infrared data give 0.29 and 0.17, respectively. Thus, these differences are indeed smaller for phenols than for anilines. However, there is some doubt as to the applicability of these $\sigma_R{}^0$ values to the present phenomena (cf. footnote 19). In particular it is difficult to accept that donation by NH$_3{}^+$ and NMe$_3{}^+$ would be larger than by CH$_3$ and *t*-Bu, as indicated by the infrared data.

(22) R. T. McIver, Jr., and J. H. Silvers, *J. Am. Chem. Soc.*, **95,** 8462 (1973).

(23) C. G. Swain and E. C. Lupton, Jr., *J. Am. Chem. Soc.*, **90**, 4328 (1968).

(24) M. J. S. Dewar, "The Molecular Orbital Theory of Organic Chemistry", McGraw-Hill, New York, N.Y., 1969, p 423.

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(26) B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **75,** 1473 (1956). The published pK_a's are apparent values; thermodynamic values are now available and give for $\Delta pK_a{}^*$ (4-NO$_2$) in 50% ethanol,[3] at 25 °C ($\rho_m = 3.93$): 2-*tert*-butyl-*N*,*N*-dimethylaniline, 2.69; 2,5-di-*tert*-butyl-*N*,*N*-dimethylaniline, 2.37. For $\Delta pK_a{}^*$ (5-NO$_2$): 2-*tert*-butyl-*N*,*N*-dimethylaniline, 2.79; 2,4-di-*tert*-butyl-*N*,*N*-dimethylaniline, 2.86.

(27) B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **76,** 357 (1957); cf. also ref 14.

(28) We thank Mr. J. J. M. Potters (Laboratory of Physical Chemistry) for carrying out these calculations (1971). The parameters chosen were: NH$_2$, $\alpha_N = \alpha + 0.65\beta$; NO$_2$ and COO$^-$, $\alpha_N = \alpha + 0.5\beta$; $\alpha_0 = \alpha + 1.0\beta$.

Mechanism of Aminolysis of δ-Lactones. Kinetic Behavior of Tri-*O*-methyl-2-deoxyglucono-δ-lactone, Solvent Deuterium Isotope Effects, and Transition-State Characterization[1]

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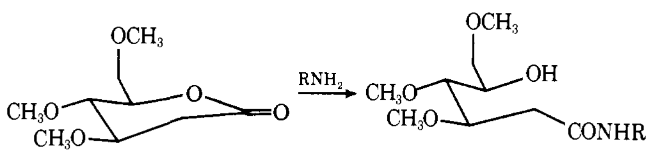
Abstract: Polarimetric and spectrophotometric methods have been used to study the aminolysis of tri-*O*-methyl-2-deoxyglucono-δ-lactone over a wide pH and buffer concentration range at 25.0 °C. Throughout the entire pH and amine nucleophile concentration range, the reaction was found to adhere to the kinetic expression in eq 1. The high reactivity towards aminolysis, the lack of change in the rate-determining step over the entire experimental pH range, and the first-order nucleophilic Bronsted slope of 0.85 place the aminolysis reactions of this δ-lactone within the family of the moderately reactive trifluoroethyl and phenyl acetates. The amines used in the present study (hydroxylamine, glycine ethyl ester, hydrazine, glycinamide, morpholine, 2-methoxyethylamine, ammonia, and glycine) exhibit one or more terms in $[N_f]$. The term for the hydroxide ion catalyzed hydroxylaminolysis is $k_3[N_f]a_{OH^-}$, with a solvent deuterium isotope effect ($k_3{}^H/k_3{}^D$) of 0.6 ± 0.1. The higher-order term $k[N_f]^2a_{OH^-}$ cannot be detected in this reaction. With morpholine the uncatalyzed first-order term in $[N_f]$, k_1, arises from a general-base-catalyzed hydrolysis as shown by product analysis and an isotope effect of 1.9 ± 0.2. The overall results indicate that the ring structure in δ-lactones mimics the effect of the better leaving alkoxy group in open chain esters. These observations are discussed in terms of previously proposed mechanisms for ester aminolysis.

In our continuing effort to characterize the effects of ring structure on the kinetic and mechanistic behavior of lactones in aqueous solution, we have examined the aminolysis of tri-*O*-methyl-2-deoxyglucono-δ-lactone. In previous studies on δ-lactone hydrolysis,[2] it was shown that the presence of the ring causes marked departures from the hydrolytic behavior of straight-chain alkyl esters. By analogy, it was felt that the aminolysis reaction of δ-lactones might also produce novel kinetic departures from those encountered with straight-chain alkyl esters.



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We report here on a detailed examination of the effect of the ring on the relative contributions to the rate expression of the various aminolysis terms shown in eq 1.[3a-f] In addition this paper also addresses itself to the question of whether or not a change in the rate-determining step is observed with decreasing pH. A break in the pH-rate profile that is caused by a change in the rate-determining step has been used to infer the existence of a tetrahedral intermediate in ester aminolysis.[4-6]

The δ-lactone which we have chosen as the substrate for the present study is the tri-*O*-methyl-2-deoxyglucono-δ-lactone. This lactone combines several important properties which are highly advantageous in the study of its aminolysis reactions.