416. *The Influence of Steric Factors on the Properties of 4-Nitropyridines.*

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The basic strengths at three temperatures, the ultraviolet absorption spectra of the free bases and cations, and the frequencies of the N–O stretching bands are reported for a series of 3-substituted 4-nitropyridines. The nitro-group is shown to influence the basic strength of the ring-nitrogen atom by exercise only of its inductive effect. The twisting of the nitro-group by the 3-substituent diminishes the intensity of the main $\pi \longrightarrow \pi^*$ band of the 4-nitropyridine spectrum, but increases the intensity of $n_O \longrightarrow \pi^*$ absorption, the latter effect being especially marked with the cations.

Recently we reported a study of the influence of steric factors on the properties of 4-aminopyridine derivatives.[1] The interaction between a 4-dimethylamino-, 4-methylamino-, or 4-amino-substituent and the pyridine nucleus was examined by the device of introducing a hindering substituent at position 3.

Since the nitro-group is planar, the situation with it is simpler than with the amino-group. With the latter, the degree to which the group deviates from planarity must change to accompany the change in hybridisation of the nitrogen orbitals caused by the amino-group's being forced out of conjugation with the nucleus. Steric inhibition of resonance in aromatic nitro-compounds has, in fact, been extensively studied,[2,3] by measurement of dipole moments,[4] and of ultraviolet [5] and infrared absorption spectra,[6] and by *X*-ray structural analyses.[7] Wepster [5] also examined the way in which steric hindrance around the nitro-group influenced the latter's effect upon the basic strength of a *p*-amino-group. We now report a study of a number of 3-alkyl-4-nitropyridines by some of the physical methods just mentioned, which parallels our earlier work on the 4-aminopyridines.

In Table 1 are collected ionisation data for the 4-nitropyridines. From the values of ΔpK_a, the difference between pK_a for a particular nitropyridine and pK_a for the analogous compound unsubstituted at position 4, it can be seen that 4-nitropyridine is a weaker base than pyridine by 3·66 units of pK_a. The nitro-group is, in fact, base-weakening in every case, but ΔpK_a changes only very slightly and irregularly with 3-substitution. The studies mentioned above, and results discussed later in this paper, leave no doubt that the 3-substituents force the nitro-group and the pyridine ring out of coplanarity, and

Table 1.

Ionisation results * for 4-nitropyridines in water at 20°.

Subst.	pK_a	ΔpK_a †	ΔG	ΔH	$-T\Delta S$
—	1·61	−3·66	2·16 ± 0·03	1·06 ± 0·02	1·10 ± 0·02
3-Me	2·22	−3·57	2·97 ± 0·39	1·98 ± 0·27	0·99 ± 0·27
3-Et	2·20	−3·60	2·95 ± 0·27	1·99 ± 0·19	0·96 ± 0·19
3-Pr^i	2·21	−3·67	2·97 ± 0·29	2·12 ± 0·20	0·85 ± 0·20
3,5-Me_2	2·52	−3·71	3·38 ± 0·17	2·79 ± 0·17	0·59 ± 0·17
2,3,5,6-Me_4	4·08	−3·80	5·47 ± 0·07	5·04 ± 0·05	0·43 ± 0·05

* Values of ΔG, ΔH, and $T\Delta S$ are in kcal./mole, and are recorded with their standard errors.
† Obtained by using pK_a values reported earlier for the alkylpyridines.[1]

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[1] Essery and Schofield, *J.*, 1961, 3939.

[2] Wheland, "Resonance in Organic Chemistry," Wiley and Sons Inc., New York, 1955.

[3] Wepster in "Progress in Stereochemistry," ed. Klyne and de la Mare, Vol. II, Butterworths Scientific Publns., London, 1958.

[4] Birtles and Hampson, *J.*, 1937, 10; Kofod, Sutton, de Jong, Verkade, and Wepster, *Rec. Trav. chim.*, 1952, **71**, 521; Kofod, Sutton, Verkade, and Wepster, *ibid.*, 1959, **78**, 790.

[5] Wepster, *Rec. Trav. chim.*, 1957, **76**, 335.

[6] van Veen, Verkade, and Wepster, *Rec. Trav. chim.*, 1957, **76**, 801.

[7] Trotter, *Canad. J. Chem.*, 1959, **37**, 351, 825, 1487.

consequently it is concluded that the 4-nitro-group causes base-weakening solely by exercising its inductive influence upon the ring nitrogen atom.

Table 1 shows that for the 4-nitropyridines the increases in ΔG for the 3-substituted compounds, above the value for 4-nitropyridine, are paralleled by increases in the enthalpy terms and also in the entropy terms. If the effects of the alkyl groups are allowed for, by making use of the earlier data,[1] it is seen (Table 2) that the contribution of ΔH to the ΔG term for introduction of the nitro-group does not change significantly, and the values show no trend in the series. This is in accord with the view that the nitro-group causes base-weakening only by its inductive effect. The contribution of the entropy term to the change in ΔG is in each case important, but no trend in the values is discernible. We cannot explain satisfactorily the gradual increase in $T\Delta S$ shown in Table 1.

TABLE 2.

Comparative values of ΔG, ΔH, and $T\Delta S$ for 4-nitropyridines.*

Subst.	$\Delta(\Delta G)$	$\Delta(\Delta H)$	$\Delta(-T\Delta S)$	Subst.	$\Delta(\Delta G)$	$\Delta(\Delta H)$	$\Delta(-T\Delta S)$
—	-4.91	-3.31	-1.60	3-Pr^i	-4.92	-3.45	-1.47
3-Me	-4.79	-2.66	-2.13	3,5-Me_2	-4.97	-2.50	-2.47
3-Et	-4.82	-3.31	-1.51	2,3,5,6-Me_4	-5.10	-3.04	-2.06

* Obtained by combining data from Table 1 above with data from Table 2 of ref. 1.

From the Hammett plot given earlier[1] for pyridine derivatives, and ΔpK_a for 4-nitropyridine recorded above, the value $\sigma = +0.617$ can be deduced for the 4-nitro-group. This is in satisfactory agreement with the value $\sigma_I = +0.63$ obtained by Taft[8] from nuclear magnetic shielding parameters. Taft[9] used his result to deduce a value of log (K/K_0) due to the effect of a completely resonance-inhibited *p*-nitro-group on the ionisation of the anilinium ion. The value deduced was in precise agreement with that estimated by Wepster[10] from the linear relationship existing between $\varepsilon_{max.}$ (ultraviolet) and ΔpK_a for *p*-nitroanilines. The σ-value for the *p*-nitro-group quoted by Jaffé[11] is $+0.778$, being made up of the inductive, σ_I, and resonance, σ_R, contributions. The value of σ from the present work, and its agreement with Taft's σ_I value, confirm the conclusion that the nitro-group in 4-nitropyridine exerts only an inductive effect upon the ring-nitrogen atom. The conclusion is also in agreement with dipole-moment studies, which show the unimportance of resonance interaction between the pyridine ring and a 4-nitro-, 4-ethoxycarbonyl, or 4-cyano-group.[12]

Table 3 records the frequencies of the infrared absorption bands due to N–O stretching vibrations in the substituted 4-nitropyridines. For 4-nitropyridine the frequencies of absorption due to the antisymmetric stretching vibration (ν_a) and the symmetric stretching vibration (ν_s) are close to those (1536 and 1349 cm.$^{-1}$) for nitrobenzene in cyclohexane solution.[6] The variations observed in the values of ν_a and ν_s are similar to those found in a series of *o*-alkyl-substituted nitrobenzenes.[6] Thus, the variation in ν_a is small and not systematic, whilst the value of ν_s increases with the steric requirement of the alkyl group. It is concluded that in 4-nitropyridine there is *p*-orbital overlap between the nitro-group

TABLE 3.

Infrared N–O stretching vibrations for 4-nitropyridines in cyclohexane.

Subst.	ν_a (cm.$^{-1}$)	ν_s (cm.$^{-1}$)	Subst.	ν_a (cm.$^{-1}$)	ν_s (cm.$^{-1}$)
—	1536	1350	3,5-Me_2	1538	1369
3-Me	1533	1351	2,3,5,6-Me_4	1538	1370
3-Et	1537	1357	(Nitromethane	1569	1378)
3-Pr^i	1543	1362			

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[8] Taft, *J. Amer. Chem. Soc.*, 1957, **79**, 1045.

[9] Taft, *J. Chem. Phys.*, 1957, **27**, 1427.

[10] Wepster, *Rec. Trav. chim.*, 1958, **77**, 491.

[11] Jaffé, *Chem. Rev.*, 1953, **53**, 191.

[12] Leis and Curran, *J. Amer. Chem. Soc.*, 1945, **67**, 79; Katritzky, Randall, and Sutton, *J.*, 1957, 1769.

and the pyridine nucleus (though the overlap causes no charge deficiency in the ground state at the ring-nitrogen atom, as is shown by the ionisation data), and that steric hindrance interferes with this overlap. Consequently, as the steric hindrance to co-planarity of the nitro-group and the aromatic ring increases, the value of ν_s gradually approaches that for an aliphatic nitro-group.

The ultraviolet extinction curve of 4-nitropyridine shows a strong maximum at 229·5 mμ (Table 4). This peak is affected by the introduction of 3-alkyl groups in a manner characteristic of $\pi \longrightarrow \pi^*$ bonds, suffering diminution in intensity and almost elimination. Numerous examples of such behaviour are known.[1,3] More interesting is the appearance in the spectra of the free bases, for the last three members of the series, of a weak band at about 272 mμ. This is most intense (though still weak) in 2,3,5,6-tetramethyl-4-nitropyridine among the free bases, but becomes much more marked for the cations (*e.g.*, $\lambda_{max.}$ 278 mμ, ε 5150, for 2,3,5,6-tetramethyl-4-nitropyridinium ion). The behaviour of this peak strongly suggests that it arises from mixing of $n_O \longrightarrow \pi^*$ with $\pi \longrightarrow \pi^*$ absorption, the mixing being made possible by the twisting of the nitro-group by the 3-alkyl substituents, which brings the non-bonding oxygen orbitals into the correct relationship with the nuclear π-orbitals. The resulting absorption is intensified in the cations by the influence of the powerfully electron-attracting $:NH^{\cdot+}$ group. A similar situation is found in *cis*-azobenzene.[13] Thus, the ultraviolet spectral data confirm the assumption that in this series of 4-nitropyridines adjacent alkyl groups force the nitro-group out of the plane of the pyridine ring. There is, in consequence, inhibition of the excited state resonance responsible for the major $\pi \longrightarrow \pi^*$ absorption band, but at the same time enhancement of the interaction responsible for a particular $n \longrightarrow \pi^*$ transition.

TABLE 4.

Ultraviolet spectral data for 4-nitropyridines in aqueous solution.

	Base		Cation	
Subst.	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
—	229·5, 284	7860, 1810	222, 280	7010, 3300
3-Me	222, 294	5520, 1990	— 287	— 2875
3-Et	— 292	— 1750	— 282	— 2865
3-Pr^i	— 271	— 2110	— 273·5	— 4100
$3,5\text{-Me}_2$	— 272	— 2025	— 276	— 4530
$2,3,5,6\text{-Me}_4$	— 273	— 2350	— 278	— 5150

TABLE 5.

Thermodynamic pK_a values of 4-nitropyridines in aqueous solution.

Temp.	Subst.	pK_a	Subst.	pK_a
5·4°	—	1·65 ± 0·02	3-Pr^i	2·29 ± 0·02
20	—	1·61 ± 0·01	,,	2·22 ± 0·02
35	—	1·57 ± 0·01	,,	2·13 ± 0·02
5·4	3-Me	2·29 ± 0·01	$3,5\text{-Me}_2$	2·63 ± 0·02
20	,,	2·23 ± 0·02	,,	2·51 ± 0·02
35	,,	2·14 ± 0·01	,,	2·42 ± 0·02
5·4	3-Et	2·28 ± 0·01	$2,3,5,6\text{-Me}_4$	4·28 ± 0·02
20	,,	2·19 ± 0·02	,,	4·08 ± 0·02
35	,,	2·13 ± 0·02	,,	3·90 ± 0·02

Experimental.—The preparation of the nitropyridines has been described,[14] as have the methods of obtaining the physical data.[1] Table 5 contains the " thermodynamic " pK_a values, from which the data of Table 1 were obtained as has been described.[1]

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[13] Mason, *Quart. Rev.*, 1961, **15**, 317.
[14] Essery and Schofield, *J.*, 1960, 4953.