Conformation of the Dimethylamino-group in Benzene, Pyridine, Pyrimidine, and Cytosine Derivatives. ^{13}C Chemical Shift Studies of *ortho*-Methyl Substitution Effects

By **Zbigniew Proba** and **Kazimierz L. Wierzchowski,*** Institute of Biochemistry and Biophysics, Polish Academy of Sciences, 02–532 Warszawa, Rakowiecka 36, Poland

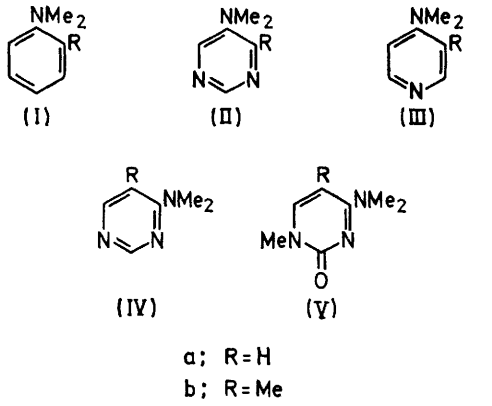
The ^{13}C n.m.r. spectra of several dimethylamino-derivatives of pyridine, pyrimidine, and 2-oxopyrimidine with and without *C*-*o*-methyl groups have been obtained. Analysis of the chemical shifts of *C*-methyl and amino *N*-methyl carbon atoms as well as C(Me) and C(NMe_2) ring carbon atoms indicates a progressive twist of the dimethylamino-group in hindered derivatives from a planar conformation in the 2-oxopyrimidine compound to the most twisted one in the benzene derivative.

OUR previous studies of *ortho*-substitution effects on protolytic equilibria and electronic absorption spectra in aminopyrimidines,[1] as well as recent i.r. and dipole moment investigations,[2] indicated that the conformation of 4-dimethylaminopyrimidine is only slightly affected by the presence of a 5-methyl group, while in the dimethylamino-4-methyl isomer pronounced steric inhibition of resonance was noted. Similar studies with 4-dimethylaminopyridines[3] also revealed steric inhibition of resonance, though weaker than that in *o*-methylated dimethylaminobenzene.[3,4] On the other hand, steric effects were hardly observed in u.v. spectra, protolytic equilibria,[1,5,6] and molecular dipole moments[7] of 4-dimethylamino-1,5-dimethyl-2-oxopyrimidine (*NN*,1,5-tetramethylcytosine).

This molecule was shown recently by *X*-ray crystallography to be in a planar conformation,[8] like unhindered cytosines,[9] which contradicts previous theoretical predictions.[7] Unique conformational properties of dimethylamino groups *para*-substituted with respect to the ring nitrogen in pyridine and pyrimidine manifest themselves also in dual fluorescence,[10,11] the long wavelength component of which apparently corresponds to the emission from a rotationally relaxed singlet excited state. All these observations prompted us to investigate further *ortho*-methyl effects on the conformation of dimethylamino substituents in benzenes, pyridines, pyrimidines, and 2-oxopyrimidines by ^{13}C n.m.r. spectroscopy. Because of the pronounced dependence of ^{13}C shieldings on electronic density and their deviation from additivity in *ortho*-substituted systems, ^{13}C n.m.r. spectroscopy offers a means of assessing steric inhibition of resonance.

[1] Z. Proba and K. L. Wierzchowski, *Acta Biochim. Polon.*, 1975, **22**, 131.
[2] E. Litońska, Z. Proba, I. Kulakowska, and K. L. Wierzchowski, submitted to *Acta Biochim. Polon.*
[3] J. M. Essery and K. Schofield, *J. Chem. Soc.*, 1961, 3939.
[4] B. M. Wepster, *Rec. Trav. chim.*, 1957, 1275.
[5] T. D. Kulikowski and D. Shugar, *Acta Biochim. Polon.*, 1971, **18**, 209.
[6] T. D. Kulikowski, B. Zmudzka, and D. Shugar, *Acta Biochim. Polon.*, 1969, **16**, 201.
[7] I. Kułakowska, M. Geller, B. Lesyng, K. Bolewska, and K. L. Wierzchowski, *Biochim. Biophys. Acta*, 1975, 407.
[8] J. K. Dattagupta, W. Saenger, K. Bolewska, and I. Kułakowska, *Acta Cryst.*, 1977, **B33**, 85.
[9] D. L. Barker and R. E. Marsh, *Acta Cryst.*, 1964, **17**, 151.
[10] J. Smagowicz and K. L. Wierzchowski, in ' Organic Molecular Photophysics,' ed. J. B. Birks, Wiley–Interscience, London, 1975, p. 24.
[11] J. Smagowicz and K. L. Wierzchowski, submitted to *J. Luminescence*.

It is known from early studies by Lauterbur [12] that shielding of the benzene carbon directly bonded to methyl or dimethylamino groups and methyl carbon shieldings of both substituents are essentially independent of the presence of other substituents in the *meta*- and *para*-positions of the ring, but may be strongly affected by an *ortho*-substituent. Thus, evaluation of *ortho*-methyl effects on chemical shifts of the four carbon atoms involved would place on a common scale differences in the whole series of compounds studied.



^{13}C N.m.r. spectra of compounds (I)—(V) were recorded. The chemical shifts δ_c and the differences $\Delta\delta_c$ are collected in Tables 1—3. Reliable assignments of ^{13}C resonance lines in the spectra of singly substituted derivatives (IIa)—(IVa), (X), and (XII) as well as of (Va) and (XVI) to particular rings and methyl carbon atoms were achieved by comparison with those known for unsubstituted parent compounds, taking into account well established signs and magnitudes of amino, alkylamino, and methyl substituent effects upon chemical shifts of ring carbons in aromatic and heteroaromatic systems (see Tables). A similar interpretation of resonances in the spectrum of (Ia) proved in full agreement with that given by Lauterbur [12] for proton-coupled spectrum. The resonances observed at high fields were also unequivocally attributed to *C*- and *N*-amino-methyl carbon atom in the spectra of *ortho*-substituted derivatives (Ib)—(Vb); they were separated by *ca.* 20 p.p.m., as expected from the spectra of the respective singly substituted derivatives, because of the relatively small magnitude of the *ortho*-effect thereon. Quaternary carbon atoms bearing dimethylamino and methyl groups were easily distinguished by the considerably reduced relative intensities of the corresponding resonance lines. Of the two low intensity signals observed in the spectra of the *ortho*-substituted derivatives (Ib), (IIIb), and (IVb) (Table 1) the one appearing at lower field was attributed to the carbon atom bearing a dimethylamino-group, in view of its large deshielding

TABLE 1

^{13}C Chemical shifts of ring carbon atoms

	δ_c [p.p.m. relative to Me_4Si]				$\Delta\delta_c$ [p.p.m. relative to (VI)—(XVI)]		$\Delta\delta_c$ [p.p.m. relative to (I)—(V)]	
Compound	C–NMe_2	*ortho*	*meta*	*para*	C–NMe_2	*ortho*	C–NMe_2	*ortho*
(Ia)	150.7	112.5	129.3	116.4	+22.3	−15.9		
(IIa)	143.6	140.2		147.5	+21.0	−17.4		
(IIIa)	155.0	106.3	149.0		+18.6	−18.2		
(IVa)	161.7	102.6	157.2 (C-2)		+4.1	−20.0		
			153.5 (C-6)					
(Va)	164.1	91.1	156.9 (C-2)		−1.8	−13.1		
			145.5 (C-6)					
(Ib)	152.9	132.2 (C-2)	131.2 (C-3)	118.5	+23.6	−5.5	+2.2	+19.7
		122.7 (C-6)	126.5 (C-5)				(+1.3)	(+10.4)
(IIb)	148.8	159.8 (C-4)		152.0	+27.8	−7.3	+5.2	+19.6
		145.7 (C-6)					(+6.8)	(+10.1)
(IIIb)	158.6	124.1 (C-3)	151.9 (C-2)		+21.3	−9.7	+3.6	+17.8
		111.7 (C-5)	148.1 (C-6)				(+2.7)	(+8.5)
(IVb)	164.4	115.6	157.3 (C-2)		+7.4	−15.3	+2.7	+13.0
			155.8 (C-6)				(+3.3)	(+4.7)
(Vb)	166.5	102.3	156.6 (C-2)				+2.4	+11.2
			146.0 (C-6)					

Values in parentheses are corrected for the α- (column 9) and β-effects of methyl substitution (column 8).

Benzene (VI) [a]	128.4
Pyrimidine (VII) [b]	157.6 (C-4), 122.6 (C-5)
Pyridine (VIII) [b]	136.4 (C-4), 124.5 (C-3)
Toluene (IX) [c]	129.3 (C-2), 137.7 (3-1)
4-Methylpyrimidine (X)	167.1 (C-4), 121.0 (C-5)
3-Methylpyridine (XI) [b]	137.3 (C-4), 133.8 (C-3)
5-Methylpyrimidine (XII)	157.0 (C-4), 130.9 (C-5)
1-Methyl-2-oxopyrimidine (XVI)	165.9 (C-4), 104.2 (C-5)

[a] 'Selected ^{13}C Nuclear Magnetic Resonance Spectral Data,' American Petroleum Institute, 1976. [b] P. C. Lauterbur, *J. Chem. Phys.*, 1965, **43**, 360. Neat liquid: J. B. Stothers, 'Carbon-13 N.M.R. Spectroscopy,' Academic Press, New York, 1972, pp. 239—253. [c] D. Lauer, E. L. Motell, D. D. Traficante, and G. E. Maciel, *J. Amer. Chem. Soc.*, 1972, **94**, 5335. Neat liquid.

between respective shifts of the parent benzene, pyridine, or pyrimidine compounds and their dimethylamino derivatives, both with and without an *o*-methyl group, similar to that noted in the corresponding parent compound (*cf.* Table 1). The other was consequently

[12] P. C. Lauterbur, *J. Chem. Phys.*, 1963, **38**, 1432.

assigned to the ring carbon atom bearing a methyl group. This assignment was also supported by the

TABLE 2

^{13}C Chemical shifts ($CDCl_3$ as solvent except where noted) of ring carbon atoms

Compound without CH_3	δ_C (p.p.m.)	Compound with CH_3	δ_C (p.p.m.)	$\Delta\delta_C$ (p.p.m)
Benzene	128.4 [a]	Toluene	137.7 [a]	+9.3
Pyrimidine (C-4)	157.6 [b]	4-Methylpyrimidine	167.1	+9.5
Pyrimidine (C-5)	122.6 [b]	5-Methylpyrimidine	130.9	+8.3
Pyridine (C-3)	124.5 [b]	3-Methylpyridine	133.8 [b]	+9.3

[a] 'Selected ^{13}C Nuclear Magnetic Resonance Spectral Data,' American Petroleum Institute, 1976. [b] P. C. Lauterbur, *J. Chem. Phys.*, 1965, **43**, 360. Neat liquid.

value of the chemical shift which is close to that on the basis of partial cancellation of deshielding by the methyl and shielding by the dimethylamino-group, somewhat reduced by steric inhibition of resonance (*cf.* Table 1), of the carbon atom in question. The reversed position of the two resonances considered in the spectrum of (IIa) led to assignment of the higher field low intensity signal, δ 148.8 p.p.m., in the spectrum of (IIb) to the C-5 and the δ 159.8 p.p.m. low intensity signal to the C-4 ring carbon. Assignment of the remaining resonance lines in the spectra of (Ib)—(IVb), corresponding to the ring carbon atoms not discussed in this paper, was based on consideration of the superposition of substituent chemical shift effects exerted thereon. The signals due to carbon atoms *ortho* to the dimethylamino-bearing atom in the spectra of (Ib)—(IIIb) were identified by their upfield shifts similar to those exhibited by symmetrically positioned C(Me) *ortho*-carbon atoms (Table 1). This permitted us to assign the fourth resonance line at δ 152.0 p.p.m. in the spectrum of (IIb) and that at δ 118.5 p.p.m. in the spectrum of (Ib), exhibiting the largest deviation, δ 2.2 p.p.m., from the predicted value, to *para*-ring carbon atoms. It should be noted that our assignment of resonance lines in the spectrum of (Ib) to C-4 and -6 ring carbons is reversed compared with that proposed by Lauterbur [12] on the basis of the proton-coupled spectrum. The resonances due to ring carbon atoms *meta* to $C(NMe_2)$ were distinguished by having the smallest deviation from the predicted chemical shift values assuming additivity of the substituent effects observed in the singly substituted parent compounds. Owing to minor changes in the spectrum of (Va) on going to (Vb), with the exception of the downfield shift with concomitant decrease in intensity of the C-5 signal due to substitution by a methyl group, all resonance lines in the spectrum of (Vb) could also be assigned reliably.

The data contained in Tables 1—3 provide an insight into the relative magnitude of ring–dimethylamino resonance interactions and the steric hindrance thereof. Deshielding of the ring carbon bearing the dimethylamino-group (positive $\Delta\delta_{CNMe_2}$, Table 1) and shielding of

TABLE 3

^{13}C Chemical shifts ($CDCl_3$ as solvent except where noted) of *C*-methyl and amino *N*-methyl carbon atoms

Compound	δ_{CMe} (p.p.m.) (relative to Me_4Si)	δ_{NMe} (p.p.m.) (relative to Me_4Si)	$\Delta\delta_{CMe}$ (p.p.m.) [relative to (XIII)—(XV)]	$\Delta\delta_{CMe}$ (p.p.m.) [relative to (IX)—(XII)]	$\Delta\delta_{NMe}$ (p.p.m.) [relative to (I)—(V)]
(Ia)		40.2			
(IIa)		39.4			
(IIIa)		38.9			
(IVa)		37.1			
(Va)		37.6			
(Ib)	18.3	44.2	+1.2	−3.1	+4.0
(IIb)	21.5	43.2		−2.6	+3.8
(IIIb)	17.0	42.4	+3.1	−1.9	+3.5
(IVb)	18.3	40.1		+2.6	+3.0
(Vb)	18.3	40.3	+5.5		+2.7
(IX)	21.4 [a]				
(X)	24.1				
(XI)	18.9 [b]				
(XII)	15.7				
o-Toluidine (XIII)	17.1				
4-Amino-3-methylpyridine (XIV)	13.9				
4-Amino-5-methyl-2-oxopyrimidine (XV)	12.8 [c]				

[a] 'Selected ^{13}C Nuclear Magnetic Resonance Spectral Data,' American Petroleum Institute, 1976. [b] P. C. Lauterbur, *J. Chem. Phys.*, 1965, **43**, 360. Neat liquid. [c] R. A. Komorski and A. Allerhand, *Biochemistry*, 1974, **13**, 369. D_2O solvent.

the ring *ortho*-carbon (negative $\Delta\delta_{ortho}$, Table 1), a general pattern characteristic of benzene substitution with donating substituents,[12] is also observed in the two heterocycles (VII) and (VIII) studied. The magnitude of $\Delta\delta_{CNMe_2}$ decreases while that of $\Delta\delta_{ortho}$ increases from (Ia) to (IVa), consistent with increasing resonance interactions. In the planar 2-oxopyrimidine derivative (Va) C-4 bearing the dimethylamino group even becomes effectively shielded by 1.8 p.p.m. compared with that of (XVI). The less negative value of $\Delta\delta_{ortho}$ (−13.1 p.p.m.) found for (Va) is apparently due to strong shielding by 18.4 p.p.m. of C-5 by the 2-oxo-group [*cf.* C-5 resonances in (VII) and (XVI)].

Upon *ortho*-methyl substitution, shielding of ring carbon atoms *ortho* with respect to that bearing the original dimethylamino-substituent is reduced (Table 1), but these atoms still remain shielded compared with the C(Me) ring carbon atoms in the monomethylated parent compounds without the dimethylamino-group (Table 1). The largest reduction in shielding, by 10.4 p.p.m. (value corrected for α-effect of methyl substitution), is shown by

the ring *ortho*-carbons in (I), whereas in (IV) the magnitude of this effect is relatively small, $\Delta\delta_{ortho}$ 4.7 p.p.m., indicating the smallest steric hindrance of resonance. Although ^{13}C n.m.r. data for 1,5-dimethyl-2-oxopyrimidine were not available to us, it is possible to include (Va and b) on account of the essential invariability of methyl substitution effects (Table 2). Differences in the chemical shifts $\Delta\delta_{ortho}$ between the pairs (Ia, b) and (Va, b) (Table 1), uncorrected for the α-effect of *ortho*-methyl substitution, should also reflect changes in the degree of steric hindrance to resonance. As seen from the data in Table 1, $\Delta\delta_{ortho}$ decreases from (Ia, b) to (Va, b).

In view of the established planarity of compound (Vb),[8] the value of $\Delta\delta_{ortho}$ in this case can be taken as a measure of the in-plane opening up by 5—8° of the exocyclic angles adjacent to dimethylamino and *ortho*-methyl groups necessary to relieve excessive steric strain which would otherwise occur.

Contrary to simple predictions based on mesomeric considerations, the *ortho*-methyl substitution effect on the carbon atoms bonded to the dimethylamino group consists in a downfield shift (Table 1). The magnitude of the shift, however, decreases in the expected order (II)—(V) with the exception of (I) where it has the smallest value. Correction for the β-effect of *ortho*-methyl substitution is not negligible and does change the order of $\Delta\delta_{CNMe_2}$ because its sign varies from compound to compound.

Analogous treatment of chemical shift data for the exocyclic *C*- and *N*-methyl carbon atoms (Table 3) affords information concerning steric non-bonded interactions between the two substituents *ortho* to each other in (Ib)—(Vb). As the two carbons are separated by four valence bonds their chemical shifts can be discussed in terms of the stereochemical dependence of δ-effects,[13,14] proven to be useful in conformational analysis of very different classes of organic compounds.[15-17]

Let us first consider the changes $\Delta\delta_{CMe}$ in *ortho*-methyl carbon shielding caused by exchanging both amino hydrogens in *o*-toluidine, 4-amino-3-methylpyridine, and 4-amino-5-methyl-2-oxopyrimidine (5-methylcytosine) for methyl groups to give (Ib), (IIIb), and 4-dimethylamino-5-methyl-2-oxopyrimidine, respectively. This generally results in deshielding of the *ortho*-methyl carbon: in (Ib) by 1.2, in (IIIb) by 3.1, and by at least as much as 5.5 p.p.m. in the pyrimidine derivative. The latter value is comparable with the 6.6 p.p.m. downfield shift of the *peri*-methyl group of the sterically crowded 1,8-dimethylnaphthalene [15] and consistent with severe in-plane non-bonded N–Me · · · Me–C interactions in 4-dimethylamino-5-methyl-2-oxopyrimidine, a very close analogue of (Vb). On the other hand, insertion of an *ortho*-dimethylamino-group into (IX)—(XI) to give (Ib)—(IIIb) causes an upfield shift of the methyl carbon signal (Table 3). The magnitude of the difference $\Delta\delta_{CMe}$ decreases gradually from (Ib) to (IIIb) and turns to a 2.6 p.p.m. downfield shift in (IVb). Upfield δ-effects of the order of 1 p.p.m. have been observed in cyclohexane [18] and norbornane [13] where the methyl groups involved are at maximum separation. A far larger upfield component to the observed δ_{CMe} shielding can certainly be contributed by the γ-effect of the dimethylamino-group due to its interaction with the *ortho*-methyl carbon through its electrical field; in primary amines it amounts on average to −4.6 p.p.m.[19] Thus the observed differences in (Ib)—(Vb) would consist in a superposition of an essentially deshielding δ-effect associated with non-bonded N–Me · · · Me–C interactions and an electrical field shielding γ-effect of the dimethylamino group. Effective shielding [$\Delta\delta_{CMe}$ −3.1 p.p.m. in (Ib)] thus indicates predominance of the γ-effect and a relatively weak δ-effect. The steric strain in (Ib) must be indeed insignificant because of the low barrier to rotation in (I), *E ca.* 5.1 kcal mol^{-1}.[20] It can easily be relieved by rotation of the dimethylamino-group about the C–N bond from its equilibrium position ϕ *ca.* 0 [21] out of the molecular plane, as commonly accepted.[22-24] In (IIIb), the *ortho*-methyl carbon is only 1.9 p.p.m. shielded relative to (XI), which implies a larger δ-effect, fully consistent with $\Delta\delta_{CMe}$ +3.1 p.p.m. (Table 3) and ring carbon deshielding (Table 1).

This can be taken as evidence that the strong mesomeric interaction between the pyridine ring and the lone-electron pair of the dimethylamino-group in (III) is not too seriously hindered by *ortho*-methyl. Shieldings of −2.6 and +2.6 p.p.m. found for (IIb) and (IVb) point to a stepwise relaxation of the molecular conformation in the series (Ib)—(Vb), as the mesomeric interaction decreases, from a strained planar conformation adopted by (Vb) and probably also by (IVb) to a twisted one in (Ib).

Non-bonded interactions between the *ortho*-methyl and amino methyl groups result in deshielding of the MeN carbon atom (Table 3), the magnitude of which decreases in the series (Ib)—(Vb), opposite to the progression of deshielding of the *ortho*-methyl carbons in this series and quite in contrast to predictions based on considerations of the δ-effect solely in terms of alkyl non-bonded van der Waals interactions. This apparent

[13] H. Spiesecke and W. G. Schneider, *J. Chem. Phys.*, 1961, **35**, 731.
[14] N. K. Wilson and J. B. Stothers, *Topics Stereochem.*, 1974, **7**, 1.
[15] S. H. Grover, J. P. Stothers, and C. T. Tan, *J. Magnetic Resonance*, 1973, **10**, 227.
[16] J. G. Batchelor, *J. Magnetic Resonance*, 1975, **18**, 212.
[17] H. Pearson, *J.C.S. Chem. Comm.*, 1975, 913.
[18] T. Pehk and E. Lippmaa, *Org. Magnetic Resonance*, 1971, **3**, 679.
[19] T. D. Brown, Ph.D. Thesis, University of Utah, 1965; 'Carbon-13 N.M.R. Spectroscopy,' J. B. Stothers, Academic Press, New York, 1972, p. 152.
[20] R. K. MacKenzie and D. D. MacNicol, *Chem. Comm.*, 1970, 1299.
[21] L. V. Vilkov and T. P. Timasheva, *Doklady Akad. Nauk S.S.S.R.*, 1965, **161**, 351.
[22] T. B. Grindley, A. R. Katritzky, and R. D. Tompson, *J.C.S. Perkin II*, 1974, 289.
[23] G. Hallas, J. D. Hepworth, P. Jones, D. A. Ibbitson, and A. M. Jones, *J.C.S. Perkin II*, 1977, **5**, 559.
[24] B. M. Wepster, *Progr. Stereochem.*, 1958, **2**, 99.

discrepancy can be rationalized when gradual rehybridization of the amino-nitrogen from an intermediate configuration between sp^3 and sp^2 in (Ib) [21] to sp^2 in (Vb) is properly taken into account. In trimethylamine the methyl carbon bonded to the sp^3 nitrogen is distinctly deshielded, δ_{NMe} 47.5 p.p.m.,[19] relative to (Ia), δ_{NMe} 40.2 p.p.m., and even more so relative to (Va), δ_{NMe} 37.6 p.p.m., where the dimethylamino-nitrogen is certainly of sp^2 configuration.[8] Hence, the observed reversed order of $\Delta\delta_{NMe}$ (Table 3) can simply be attributed to superposition of a 'pure' Me · · · Me δ-deshielding effect, expected to increase in the order (Ib)—(Vb), and of an $sp^2 \rightarrow sp^3$ rehybridization deshielding effect decreasing in that order.

We can now proceed to evaluate, at least semi-quantitatively, the differences in conformation between members of the (Ib)—(Vb) series by assuming a linear correlation between the various $\Delta\delta$ values and the angle ϕ of rotation of the dimethylamino-group about the C–N bond. Such an assumption can be valid only as a first-order approximation in view of the complex dependence of ^{13}C chemical shifts on several factors and the chemical nature of the system considered.[25]

In spite of progressive changes in hybridization of the amino nitrogen of (Ia)—(Va), the equilibrium conformation of the dimethylamino-group in all these compounds seems to correspond closely to ϕ *ca.* 0, for zero rotational angle was demonstrated in (Vb) [8] and is very probable in (Ia),[21] *i.e.* for both extremes of the series. The differences in hybridization must thus manifest themselves solely in different dimethylamino $\widehat{CNC}$ angles, as has been shown for (Ia).[21] There exist no direct experimental data concerning the conformations of *ortho*-methylated derivatives of (Ia)—(Va), except for (Vb) in which ϕ *ca.* 0 was demonstrated by *X*-ray crystallography.[8] The rotational angle in (Ib) derived from analysis of *ortho*-effects in u.v. absorption spectra is ϕ *ca.* 50° [26] and from dipole moment measurements *ca.* 30°; [23] in view of the obvious shortcomings of these approaches, these values can only be regarded as very approximate. If one thus assigns recorded $\Delta\delta$ values for (Vb) to ϕ 0 and those for (Ib) to the maximal angle ϕ 1 in the series, evaluation of intermediate angles in (IIb)—(IVb) is possible by fitting the various corresponding $\Delta\delta$ values to linear plots defined by the two known points on both ends of the ϕ scale. The relative ϕ obtained in this way are: $\phi_{(IIa)}$ 0.91 ± 0.08, $\phi_{(IIIa)}$ 0.71 ± 0.1, and $\phi_{(IVa)}$ 0.30 ± 0.1. By the same token it is also possible to assess the unknown energy barriers to rotation for (IIa) and (IIIa) assuming $E_{(Ia)}$ 5.1,[20] $E_{(IVa)}$ 10.7,[27] and $E_{(Va)}$ 16 kcal mol^{-1}.[28] By interpolation $E_{(IIa)} = 6.2$ and $E_{(IIIa)} = 7.3$ kcal mol^{-1}. Since $E_{(Ia)}$ was itself obtained by crude interpolation the estimated $E_{(IIa)}$ and $E_{(IIIa)}$ values should be viewed with circumspection. Verification of these predictions by more direct methods of determination of the geometries and energies seems worthwhile.

EXPERIMENTAL

^{13}C *N.m.r. Spectra.*—Natural abundance 22.63 MHz ^{13}C n.m.r. broad-band decoupled spectra were recorded on a Brücker HSX 72 spectrometer operating in the pulsed Fourier transform mode.

Materials.—Most compounds were prepared by the methods described in refs. 1 (aminopyrimidines) and 29 (aminopyridines). 1-Methyl-2-oxopyridine was synthesized according to ref. 30. Aniline derivatives were commercial samples purified by standard procedures.

This investigation was supported by the Polish Academy of Sciences.

[7/1729 *Received*, 30*th September*, 1977]

[25] C. H. Yoder, F. K. Sheffy, and R. Howell, *J. Org. Chem.*, 1976, **41**, 1511.
[26] J. Burgers, M. A. Hoefnagel, P. E. Verkade, H. Visser, and B. M. Wepster, *Rec. Trav. chim.*, 1958, **77**, 491.
[27] A. R. Katritzky and G. J. T. Tiddy, *Org. Magnetic Resonance*, 1969, **1**, 57.
[28] R. R. Shoup, H. T. Miles, and E. D. Becker, *J. Phys. Chem.*, 1972, **76**, 64.
[29] J. M. Essery and K. Schofield, *J. Chem. Soc.*, 1960, 4953.
[30] D. J. Brown and R. V. Foster, *J. Chem. Soc.*, 1965, 4911.