Conformational Studies by Dynamic Nuclear Magnetic Resonance Spectroscopy. Part 19.[1,2] Substituent Effects upon the Rotational Barrier of Alkylanilines

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The low-temperature n.m.r. spectra at the ^{13}C frequency (25.16 MHz) showed the non-equivalence of the *ortho*- and *meta*-carbons in a number of substituted *N*-alkylanilines. Line-shape analysis, or measurement at the coalescence temperature, yielded the free energy of activation for the rotational process about the C–N bond. The $\Delta G^{\ddagger}$ values were found to be linearly related to the Hammett constants for a variety of *para*-substituted derivatives. The barriers were found also to decrease with an increase in the size of the alkyl substituents bonded to the nitrogen atom.

CONJUGATION of the nitrogen atom with the aromatic rings in aromatic amines gives sufficient double bond character to the C–N linkage to generate restricted motion detectable by n.m.r. spectroscopy. A number of aromatic amines have been investigated by ^{1}H n.m.r.[3-8] The advent of ^{13}C n.m.r. allowed the investigation of molecules which gave ^{1}H spectra too complicted to be analysed.[9] In particular the method allowed the determination of the rotational rate constants, and therefore of the thermodynamic parameters, for the rotational process of *N*-methylaniline.[10] The present work is concerned with the effect on the rotation of substituents both at the phenyl ring and at the nitrogen atom in aromatic anilines.

RESULTS AND DISCUSSION

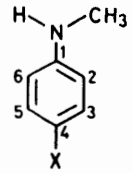
The determination of the rotational barriers ($\Delta G^{\ddagger}$) was carried out for the 4-substituted *N*-methylanilines (1)—(6).

The aromatic region of the ^{13}C spectrum of some of these molecules [(1), (3), (4), (6)] is very simple, since there are only four lines in the fast-exchange region (usually above −50 °C), which becomes six in the slow-exchange region (usually below −100 °C), due to the non-equivalence of *ortho*- and *meta*-carbons (Table 1).

By monitoring the coalescence temperatures of these lines it is possible to obtain the rate constants and the free energies of activation at these temperatures. Since the accurate line-shape analysis carried out on (3) gave [10] a negligible $\Delta S^{\ddagger}$ value, the $\Delta G^{\ddagger}$ value can be safely considered temperature independent, within experimental error, and will be thus employed as a measure of the rotational barrier.

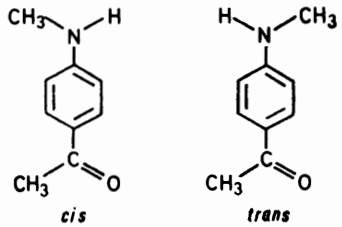
In the case of 4-fluoro-*N*-methylaniline (2) the C–F couplings (6.9, 22.0, and 229.9 Hz) make the spectrum more complex, since all the aromatic lines (except C-1) are split into doublets. For this compound complete line-shape simulation [11] was required to obtain the values of the rate constants.

When the substituent is the acetyl group, as in 4-acetyl-*N*-methylaniline (5), the dynamic phenomenon is expected also to reflect the restricted motion of the Ar–CO bond. The barrier for Ar–COR rotation was found [12] to have $\Delta G^{\ddagger}$ 8.3 kcal mol^{-1} for 4-acetyl-*NN*-dimethylaniline. The Figure shows the effect of temperature on the spectrum for three selected situations. At room temperature the customary four lines of a *para*-substituted benzene are observed. At −85 °C they become six, as in the other cases, due to the restriction of C–N rotation. At −120 °C, ten lines, with different intensity distribution, are visible. When the first



(1) X = OCH_3
(2) X = F
(3) X = H
(4) X = Cl
(5) X = $COCH_3$
(6) X = NO_2

motion (C–N rotation) is slow we simply have non-equivalent carbons, whereas when the second motion (Ar–$COCH_3$ rotation) is also slow, two isomers, *cis* and *trans*, with different stabilities are generated.



cis *trans*

In principle, different signals ought to be observed [13] also for C-1 and C-4, but their separation is expected to be much smaller, and was not detected in our experimental conditions.

Electron-attracting substituents are expected to increase the rotational barrier and the electron-releasing substituents to reduce it, because of the contribution of mesomeric structures such as (A).

since these values also depend [15] on the π electron densities at nitrogen.

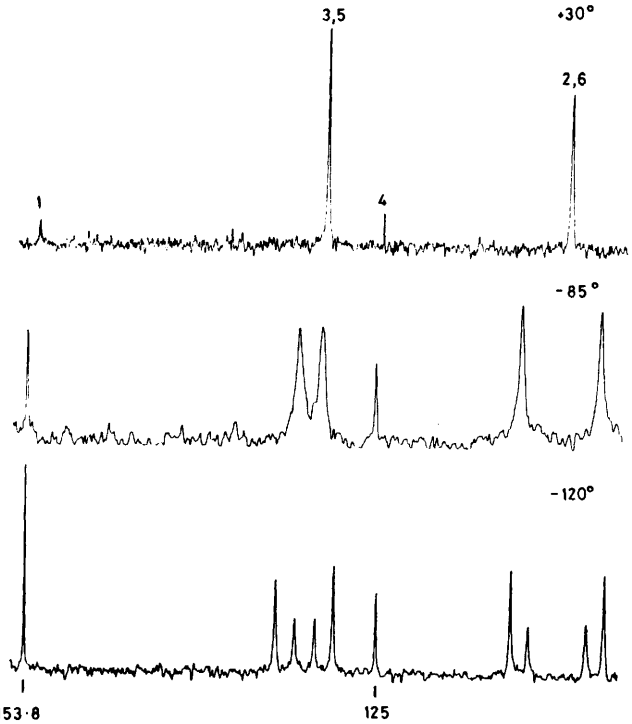
The free energy of activation has also been measured for 4-(*N*-methylamino)pyridine (7): its value (10.2 ± 0.1 kcal mol^{-1}) is relatively high and close to that of *N*-methyl-4-nitroaniline (6). The pyridine ring is known to behave similarly to nitrophenyl, at least in regard to conjugative properties.

TABLE 1

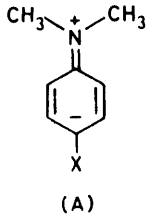
^{13}C Chemical shifts (p.p.m. from Me_4Si) for derivatives (1)—(7). The data are reported for the temperatures corresponding to slow and fast rotation. The relative assignments of C-2,-6 and C-3,-5 has been made by analogy with refs. 1 and 10. Accordingly the assignments of C-3 and -5 can be reversed. Values not reported are covered by solvent lines

Compound	*t*/°C	C-1	C-2	C-3	C-4	C-5	C-6	NCH_3	Other	Solvent
(1)	−50	152.5	114.1	115.1	144.5	115.1	114.1	31.6	55.5	CCl_2F_2–$CHCl_2F$
	−155	152.5		114.9	144.9	112.5		30.9	55.1	CHF_2Cl
(2)	−60		112.2	115.2	154.9	115.2	112.2	29.9		$(CH_3)_2O$
	−145	146.9	109.0	115.7	154.9	114.7	115.1	29.9		
(3)	−75	150.2	111.5_5	128.9	115.8	128.9	111.5_5	29.5		$(CH_3)_2O$
	−133	150.1	108.4_5	129.5	115.8	128.7_5	114.4	29.9		
(4)	−80	148.9	112.7	128.7	119.6	128.7	112.7	29.3		$(CH_3)_2O$
	−130	148.8	109.6	129.6	119.3	129.1	115.6	29.2		
(5)	−30	154.4	111.1	131.2	126.0	131.2	111.1	29.6	25.8	$(CH_3)_2O$
	−85	153.8	107.0	131.6	125.3	129.7	113.5	28.8	25.3	
	−120	153.8	(106.4; 107.8)	(133.1; 131.6)	125.0	(129.9; 128.4)	(114.0; 112.5)	28.8	25.5	
(6)	−30	156.0	112.2	126.9	136.3	126.9	112.2			$(CD_3)_2CO$
	−55	156.0	107.9	127.7	136.3	126.4	114.4			
(7)	−20		149.6	107.1		107.1	149.6	29.2		CD_2Cl_2
	−80		147.8	149.3	154.7	147.8	149.3	28.7		

The trend in $\Delta G^{\ddagger}$ was found (Table 2) to follow that of the Hammett substituent constants,[14] according to the relationship $\Delta G^{\ddagger}$ kcal mol^{-1} = 6.91 + 5.11σ. These values are also related to the J_{NH} coupling constants and to the ^{15}N chemical shifts of the corresponding anilines,

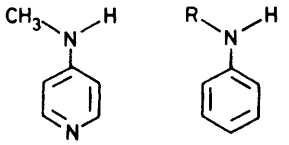


Temperature dependence of the aromatic region of the ^{13}C n.m.r. spectrum of a 4-acetyl-*N*-methylaniline (5) in dimethyl ether. At −85 °C the C–N rotation is slow but the Ar–CO rotation is still fast. At −120 °C both rotations are slow, thus showing the spectra corresponding to two conformers, *cis* and *trans*, of different stability



(A)

When alkyl substituents of increasing size are bonded to the nitrogen atom, the rotational barrier becomes smaller as shown by the results obtained for *N*-ethyl- (8), *N*-isopropyl-(9) and *N*-t-butyl-aniline (10) (Tables 2 and 3). This trend is expected whenever the ground state



(7)

(8) R = C_2H_5

(9) R = iso-C_3H_7

(10) R = t-C_4H_9

of the molecule is planar, or nearly so, and the transition state perpendicular.[16,17] If nitrogen inversion is faster [10] than Ph–N rotation (*i.e.* $\Delta G^{\ddagger}_{inv} \ll \Delta G^{\ddagger}_{rot}$) the dynamic plane of the HNR group is almost coplanar with the phenyl ring.

When alkyl substituents of size larger than methyl are introduced, the HNR plane will be twisted, and the

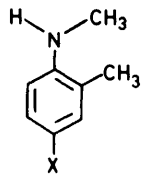
ground state destabilized owing to the reduced nitrogen–phenyl conjugation. On the other hand the transition state, where the HNR and phenyl groups are perpendicular, is not likely to be very much affected by the size of R. In consequence the difference between ground and transition states becomes smaller as R increases from methyl, to ethyl, to isopropyl, to t-butyl. Accordingly the experimental values of the free energy of activation decrease along this series.

TABLE 2

Barriers for CN rotation of (4-substituted) *N*-methylanilines (1)—(6) and *N*-alkylanilines (8)—(10). The errors were estimated by averaging the results of different temperature measurements

Compound	$\Delta G^{\ddagger}$/kcal mol^{-1}	Solvent
(1)	5.7 ± 0.2	CHF_2Cl
(2)	6.9 ± 0.0_5	$(CH_3)_2O$
(3)	7.2_4 ± 0.0_2	$(CH_3)_2O$
(4)	7.70 ± 0.0_5	$(CH_3)_2O$
(5)	9.4_5 ± 0.1_5	$(CH_3)_2O$
(6)	11.1 ± 0.1	$[^2H_6](CH_3)_2CO$
(8)	7.2 ± 0.1	$(CH_3)_2O$
(9)	6.8 ± 0.1	$(CH_3)_2O$
(10)	6.3 ± 0.1	CCl_2F_2–$CHFCl_2$

Attempts have been also made to detect rotational isomers having NCH_3 *syn* or *anti* with respect to a substituent, such as a second methyl in the *ortho*-position [compound (11)], as reported for alkylbenzaldehydes.[16]

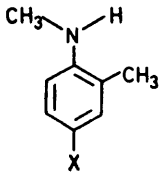


(11) X = H

(12) X = NO_2

In (11) we did not detect rotational isomers even at −150 °C; this could be attributed either to the presence of the less hindered rotamer in exceedingly large amount, or to the lowering, due to steric hindrance, of $\Delta G^{\ddagger}$, which would make impossible a distinction of two species.

The experiment was thus repeated on (12) where the presence of NO_2 in the *para*-position considerably enhances the rotational barrier. Even with a dramatic lowering of $\Delta G^{\ddagger}$ from the 11.1 kcal mol^{-1} for compound (6), it seems unlikely that, even at −150 °C, the two rotamers are undetectable. We thus conclude that, as opposed to the *o*-alkylbenzaldehydes,[16] only the *trans*-conformer is present in these derivatives.



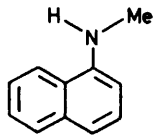
trans

A similar investigation was carried out on 1- and 2-(*N*-methylamino)naphthalene (13) and (14). Again we failed to detect rotational isomers, even at the lowest attainable temperature. In the case of (13) the double bond character of C–N should be similar to that of *N*-methylaniline (3); the failure to detect two conformers should thus be attributed to the much greater stability of the less hindered species. On the other hand, in (14) the two conformers have not too different steric requirements and the negative result should thus be attributed to a very low rotational barrier. This indicates that $\Delta G^{\ddagger}$ is probably smaller than 5.5 kcal mol^{-1}, *i.e.* at least 1.7 kcal mol^{-1} lower than in *N*-methylaniline (3). This agrees with the well known fact that conjugation at the β position of naphthalene is smaller than in the phenyl group.

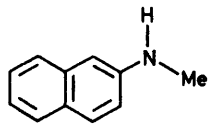
TABLE 3

^{13}C Chemical shifts (p.p.m. from Me_4Si) for derivatives (3) and (8)—(10). The values are reported for the temperatures corresponding to slow and fast rotation. The relative assignments of C-2,-6 and C-3,-5 have been made by analogy with refs. 1 and 10. Accordingly the assignments of C-3 and -5 can be reversed

Compound	*t*/°C	C-1	C-2	C-3	C-4	C-6	C-6	CH_3	Other	Solvent
(3)	−75	150.2	111.5_5	128.9	115.8	128.9	111.5_5	29.5		$(CH_3)_2O$
	−133	150.1	108.4_5	129.5	115.8	128.7_5	114.4	29.9		
(8)	−40	149.4	112.0	129.0	115.8	129.0	112.0	13.7	37.7	$(CH_3)_2O$
	−140	149.4	109.0	129.5	115.8	128.8	114.3	13.7	37.7	
(9)	−40	148.8	112.7	129.4	115.8	129.4	112.7	21.6	43.1	$(CH_3)_2O$
	−145	148.8	109.0	129.5	115.8	129.1	115.0	21.6	43.2	
(10)	−50	148.1	117.9	130.2	118.7	130.2	117.9	29.3	51.9	$CHFCl_2$–CF_2Cl_2
	−148	148.1	115.5	130.4	118.1	130.4	119.1	29.7	29.3	



(13)



(14)

EXPERIMENTAL

Derivatives (1), (3), (8), and (9) were commercially available and were distilled before use. The *N*-methyl derivatives (2), (4), (5), and (11)—(14) were obtained by methylation of the corresponding amines. An example is the preparation of 4-acetyl-*N*-methylaniline[18] (5). To a solution of 4-aminoacetophenone (6 g, 0.044 mol) in ethanol (50 ml) was added dimethyl sulphate (2 ml, 0.021 mol). The

solution was refluxed overnight and treated with aqueous NaOH; the ethanol was evaporated under reduced pressure and the residue extracted with ether. The ethereal solution was washed with water until neutrality and dried over Na_2SO_4. After elimination of ether the solid residue was chromatographed [SiO_2; benzene–ethyl acetate (3 : 7)], yield 1.5 g, m.p. 108—109° (lit.,[18] 90°).

The data for the other derivatives are as follow: compound (2) has b.p. 69° at 13 mmHg (lit.,[19] 79° at 11 mmHg); (4) has b.p. 57° at 6 mmHg (lit.,[20] 239—240°); (11) has b.p. 90° at 20 mmHg (lit.,[21] 207—208°); (12) has m.p. 140° (lit.,[22] 137); (13) has b.p. 86° at 0.04 mmHg (lit.,[22] 157—176° at 16 mmHg); and (14) has b.p. 96° at 0.04 mmHg (lit.,[23] 317°). *N*-Methyl-4-nitroaniline (6), 4-(*N*-methylamino)pyridine (7) and *N*-t-butylaniline (10) were prepared according to the literature,[24-26] and have m.p. 152°, m.p. 124°, and b.p. 83° at 17 mmHg, respectively.

Spectral Determinations.—The samples for n.m.r. measurements were prepared by condensing with liquid nitrogen the gaseous solvents (Me_2O, CCl_2F_2, CHF_2Cl, or $CHCl_2F$) into a 10-mm n.m.r. tube connected to a vacuum line; the tube contained the alkylaniline and some [$^2H_6$]acetone for locking the instrument at the deuteron resonance. The tube was sealed *in vacuo* and kept at room temperature before introduction into the spectrometer. The temperature was measured with a thermocouple inserted in a dummy tube placed in the probe before or after each spectral determination. The spectra were obtained at 25.16 MHz (Varian XL-100) in the Fourier-transform mode: the pulse angle was kept in the interval 45—60°, usually a 5 000 Hz interval was examined, and a few hundred transients were normally collected.*

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* *Note added in proof:* Recently (F.A.L. Anet and M. Ghiaci, *J. Amer. Chem. Soc.*, 1979, **101**, 6857) the barrier in derivative (6) was found equal to our value in the same solvent (acetone), but decreased by 0.8 kcal mol^{-1} in CD_2Cl_2. The barrier of (3) in Freon was also different from the present value in Me_2O by >1 kcal mol^{-1}, thus indicating a remarkable solvent effect.

REFERENCES

[1] Part 18, L. Lunazzi, D. Macciantelli, and G. Placucci, *Tetrahedron Letters*, 1980, 975.
[2] Taken in part from C. Magagnoli, Doctoral Thesis, University of Bologna.
[3] J. Heidberg, J. A. Weil, G. A. Janusonis, and J. K. Anderson, *J. Chem. Phys.*, 1964, **41**, 1033; J. Jouanne and J. Heidberg, *J. Amer. Chem. Soc.*, 1973, **95**, 487.
[4] D. D. MacNicol, *Chem. Comm.*, 1969, 933, 1516; A. R. Katritzky and G. J. Tiddy, *Org. Magnetic Resonance*, 1969, **1**, 57.
[5] I. C. Calder, P. J. Garrett, and F. Sondmeier, *Chem. Comm.*, 1967, 41.
[6] S. Brownstein, E. C. Horswill, and K. U. Ingold, *Canad. J. Chem.*, 1969, **47**, 3243; *J. Amer. Chem. Soc.*, 1970, **92**, 7217.
[7] T. Lillefors, *Org. Magnetic Resonance*, 1974, **6**, 144.
[8] L. Forlani, L. Lunazzi, and A. Medici, *Tetrahedron Letters*, 1977, 4525.
[9] L. Lunazzi, D. Macciantelli, and A. C. Boicelli, *Tetrahedron Letters*, 1975, 205.
[10] L. Lunazzi, C. Maganoli, M. Guerra, and D. Macciantelli, *Tetrahedron Letters*, 1979, 3031.
[11] D. A. Kleier and G. Binsch, Program 140 (DNMR), Quantum Chemistry Program Exchange, Indiana University, Bloomington.
[12] T. B. Grindley, A. R. Katritzky, and R. D. Topsom, *J.C.S. Perkin II*, 1975, 2443; T. Drakenberg, J. M. Sommer, and R. Jost, *Org. Magnetic Resonance*, 1976, **8**, 570.
[13] L. Lunazzi, D. Macciantelli, and G. Cerioni, *J.C.S. Perkin II*, 1976, 1791.
[14] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.
[15] T. Axenrod, P. S. Pregosin, M. J. Wieder, E. D. Becker, and G. W. A. Milne, *J. Amer. Chem. Soc.*, 1971, **93**, 6536.
[16] L. Lunazzi, A. Ticca, D. Macciantelli, and G. Spunta, *J.C.S. Perkin II*, 1976, 1121.
[17] A. Cipiciani, P. Linda, L. Lunazzi, and D. Macciantelli, *J.C.S. Perkin II*, 1979, 1045.
[18] L. Weil, *Monatsh.*, 1908, **29**, 906.
[19] F. L. Allen, R. E. Jewell, and H. Suschitzky, *J. Chem. Soc.*, 1960, 5259.
[20] R. Stoermer, *Ber.*, 1898, **31**, 2523.
[21] P. Monnet, F. Reverdin, and E. Noelting, *Ber.*, 1878, **11**, 2278.
[22] E. Bambergh, *Ber.*, 1897, **30**, 1248.
[23] R. Pschorz and W. Karo, *Ber.*, 1906, **39**, 3140.
[24] G. T. Morgan and W. R. Grist, *J. Chem. Soc.*, 1918, **113**, 690.
[25] C. W. N. Cumper and A. Singleton, *J. Chem. Soc.* (*B*), 1967, 1096.
[26] W. J. Hickinbottom, *J. Chem. Soc.*, 1933, 946.