Nuclear Magnetic Resonance Spectra of Anilides

I. Acetanilide, N-Methylacetanilide and Related Compounds

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The NMR spectra of various anilides, in which the alkyl substituent on both the nitrogen and the carbonyl carbon has been varied, have been determined at 60 Mc/s in chloroform-*d* solutions. Special attention has been devoted to acetanilide and N-methylacetanilide, whose 2,4,6-d_3 derivatives (*ca.* 80 % deuterated) have been prepared in order to ascertain the individual chemical shifts of the various aromatic protons. It is found that the resonance for the *ortho* protons in the spectrum of acetanilide is shifted 0.29 ppm *downfield* from the corresponding resonance in the spectrum of N-methylacetanilide. The *meta* and *para* proton resonances in acetanilide are both shifted *upfield* (0.16 and 0.28 ppm, respectively). The downfield shift is attributed primarily to the fact that the anisotropic carbonyl group points towards the aromatic ring in acetanilide but in the opposite direction in N-methylacetanilide. The upfield shift (at least for the *para* proton) is concluded to be primarily the result of the difference in degree of mesomeric interaction in these two molecules due to the difference in dihedral angle between the aromatic ring and the acet-amido group. The chemical shifts for the aromatic protons in the anilides are compared with those in the corresponding anilines and discussed in terms of changes in π-electron density at the ring carbon atoms and the influence of effects transmitted through space.

It has been concluded from dipole moment,[1-4] infrared,[2,5] and nuclear magnetic resonance [6] studies that the preferred conformation of acetanilide in solution is the same as that in the solid state, *viz.* the *endo* [7] conformation with the carbonyl group pointing towards the aromatic ring (*cf.* Fig. 1a). According to the work of Brown and Corbridge,[8] who determined the structure
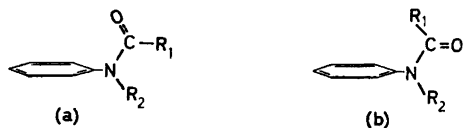

Fig. 1. The *endo* (a) and *exo* (b) forms of an open-chain anilide.

of acetanilide in the solid state by X-ray crystallography, the dihedral angle θ between the ring plane and the plane of the acetamido group (with the nitrogen atom common to both planes) is 37°54'. A recalculation of this angle,[9] based on the atomic coordinates derived by Brown and Corbridge,[8] and carried out on the Datasaab D21 computer at the Department of Medical Biochemistry of the University of Göteborg, gives a value of 17°42'. The dihedral angle θ represents the combined effect of the torsional angles about the C_7-N and C_1-N bonds. These angles were also estimated by computer calculation based on the data of Brown
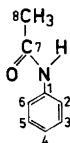
and Corbridge,[8] and were found to be 4°9' and 16°56', respectively. Thus, the most important contribution to θ is made by the C_1-N twist, which is reasonable considering the relative amounts of resonance energy involved in the two available possibilities for mesomeric interaction of the lone pair on nitrogen. The resonance energy of the acetamido group should be of the order of 20 kcal/mole;[10,11] that of the nitrogen-ring interaction can be roughly estimated to be slightly greater than 6 kcal/mole,* since this is the value given by Pauling[11] for aniline and it is to be expected that the change in hybridization on going from aniline to acetanilide (pyramidal to planar sp^2) should increase somewhat the availability of the nitrogen lone pair for conjugation with the ring. New evidence for pyramidal hybridization in aniline has recently been obtained from a microwave study,[12] and Roberts and his co-workers[13] have recently obtained new evidence for sp^2 hybridization in acetanilide from ^{15}N magnetic resonance spectroscopy.

The *exo*[7] conformation of acetanilide, in which the carbonyl group is directed away from the aromatic ring (*cf.* Fig. 1b), occurs only to the extent of about 0.1 % in pyridine solution.[6] It is remarkable that the presence of a methyl group on the anilide nitrogen atom completely reverses the conformational preference of the molecule: Pedersen and Pedersen[6] have studied N-methylacetanilide in the solid state by X-ray crystallography as well as in pyridine solution by NMR spectroscopy, and they report that the molecule exists in the *exo* conformation in the solid state, and in the same conformation to the extent of about 99.5 % in solution. The angle between the ring plane and the plane of the acetamido group is 90° in this case; resonance interaction between the nitrogen lone pair and the aromatic ring is thus at a minimum.

The work reported in this paper is an investigation of the NMR spectra of various anilides in which the alkyl substituent on the carbonyl group and the alkyl substituent on the nitrogen have been varied. Acetanilide and N-

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* *Note added in proof.* The work of Evans (*Spectrochim. Acta* **16** (1960) 428) has recently come to the author's attention. From IR measurements, Evans calculates the barrier to internal rotation in aniline to be 3.54 kcal/mole.

methylacetanilide are taken as prototypes for N-unsubstituted and N-substituted anilides, respectively, and have thus been studied in more detail than the other anilides whose NMR data are reported here. The spectra of aniline and N-methylaniline are compared with those of the anilides and the results are discussed in terms of changes in π-electron density at the ring carbon atoms and the influence of effects transmitted through space.

The fact that Pedersen and Pedersen [6] used pyridine as solvent for their NMR studies of acetanilide and N-methylacetanilide precluded observation of the aryl proton regions in the spectra of these compounds. Their conclusions are based on differences in $COCH_3$ peak positions and comparisons with the corresponding resonances in *ortho*-diiodoacetanilides of known conformation, prepared by Pedersen *et al.*[14] for use as X-ray contrasting agents. All of the spectra reported in this paper were determined in chloroform-d solutions, which allows observation of the aryl proton region, and thus complements the work of Pedersen and Pedersen [6] in this regard.

Table 1. Chemical shifts in aniline, N-methylaniline, acetanilide and N-methylacetanilide determined on the residual proton spectra of the corresponding partially deuterated $(80-82 \% \ 2,4,6-d_3)$ compounds in $CDCl_3$ solutions.

| Compound	Mole fraction	Chemical shift [a]				
				aromatic protons		
		$N-CH_3$	$COCH_3$	*ortho*	*meta*	*para*
Aniline	0.11_5	—	—	6.60	7.11	6.71
	0.10	—	—	6.61 [b]	7.12 [b]	6.71 [b]
	0.06_1	—	—	6.64	7.12	6.72
	0.04_2	—	—	6.66	7.14	6.73
	0.03_2	—	—	6.66	7.14	6.73
N-Methylaniline	0.11	2.74	—	6.55	7.16	6.68
	0.10	2.75 [b]	—	6.56 [b]	7.16 [b]	6.68 [b]
	0.06_1	2.79	—	6.58	7.17	6.68
	0.04_1	2.80	—	6.59	7.17	6.68
	0.03_1	2.81	—	6.59	7.17	6.69
Acetanilide	0.10	—	2.09	7.49	7.24	7.05
	0.05_3	—	2.11	7.47	7.26	—
	0.04_0	—	2.12	7.47	7.28	—
	0.03_2	—	2.12	7.47	7.28	—
N-Methylacetanilide	0.10	3.26	1.88	7.20	7.40	7.33
	0.05_4	3.26	1.88	7.19	7.40	—
	0.04_1	3.26	1.88	7.19	7.40	—
	0.03_3	3.26	1.88	7.19	7.40	—

[a] Ppm downfield from internal TMS.
[b] Determined by graphic interpolation.

RESULTS AND DISCUSSION

The aromatic protons in acetanilide form an AA'BB'C system, which gives rise to a fairly complex pattern centered at $\delta = 7.24$ * in a 10 mole % chloroform-d solution. The width of this pattern is 46 cps, measured at the baseline. The corresponding peaks in the spectrum of N-methylacetanilide form a similar pattern centered at $\delta = 7.32$ in a solution of the same concentration, but the width of the pattern (29 cps) is significantly less than that of acetanilide. A comparison of the residual proton spectra of acetanilide-2,4,6-d_3 and N-methylacetanilide-2,4,6-d_3 (see Table 1) shows that it is primarily the difference in shift for the *ortho* protons compared to that of the *meta* (or *para*) protons in these two molecules which gives rise to the difference in width of the AA'BB'C patterns. The resonance for the *ortho* protons of acetanilide occurs at $\delta = 7.49$ in a 10 mole % solution in chloroform-d, and the internal chemical shift $\delta_{ortho} - \delta_{meta}$ is $+ 0.25$ ppm. All of the aromatic proton shifts in acetanilide were found to be concentration-dependent (see Table 1). In N-methylacetanilide, on the other hand, the internal chemical shift $\delta_{ortho} - \delta_{meta}$ is -0.20 ppm since the *ortho* proton resonance comes furthest *upfield* at $\delta = 7.19$ in this case; all chemical shifts were found to be independent of concentration within experimental error (about ± 0.01 ppm).

The deuterated compounds contained $18-20$ mole % protium distributed in positions 2, 4, and 6, as estimated by NMR analysis. The following species ** were thus present in the deuterated samples:

I   II   III
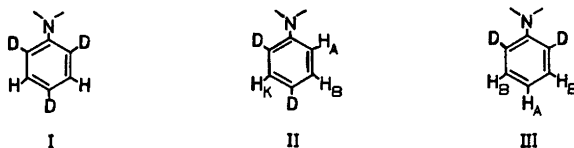
Spectral analysis. The proton spectra of these different species were easily recognizable in the total spectrum, and in most cases the peaks in each "sub-spectrum" could be unambiguously assigned. The most intense peak was of course due to the *meta* protons, and the *meta* proton shift was thus readily obtained directly from the spectrum. The residual *ortho* protons gave rise to a doublet, while the *para* proton resonance consisted of four peaks. The analysis of the *ortho* proton "sub-spectrum" was simplified by neglecting the effect of H_K (*cf.* II) on the chemical shift of H_A. If the small H—D coupling is neglected, the ring protons in II may be regarded as a three-spin system (ABK) composed of two fairly strongly coupled nuclei (H_A and H_B), both of which are relatively weakly spin coupled to a third nucleus (H_K). The fact that the chemical shift ν_B is identically equal to ν_K does not affect the argument since the *para* coupling constant J_{AK} is much smaller than J_{AB} and thus the degree of mixing

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* All chemical shifts in this paper are reported in ppm downfield from internal tetramethyl-silane (TMS), except where noted.
** The concentration of molecules containing more than three ring protons may be neglected for the purposes of this study, assuming no equilibrium isotope effects.

between A and K spin states will be correspondingly small. As discussed by Hoffman and Forsén,[15] the degree of mixing may be defined as the ratio between $|H_{pq}|$, the magnitude of the appropriate off-diagonal element of the spin Hamiltonian and $|H_{pp}-H_{qq}|$, the magnitude of the *difference* between the corresponding diagonal elements. If $|H_{pq}| < < |H_{pp}-H_{qq}|$, a low degree of mixing is indicated. The ratio $|H_{pq}|/|H_{pp}-H_{qq}|$ is of the order of 0.6 for the A and B spin states, but only *ca.* 0.03 for the A and K spin states. These ratios were estimated using the observed values of J_{AB} and the chemical shift (in cps) $\nu_A-\nu_B = \nu_A-\nu_K$ (*vide infra*), and reasonable assumed values for J_{AK} and J_{BK} (0.5 and 2.0 cps, respectively [16]), which are not obtainable from the observed spectrum. An accurate value of the *meta* proton chemical shift $\nu_B = \nu_K$ could be obtained by direct measurement, as indicated above. The chemical shift of the A proton (ν_A) was estimated by an iterative procedure, using the equations derived for an AB spin system.[17] The chemical shift parameter $|\nu_A-\nu_B|$ was varied in successive approximations until acceptable agreement with the observed spectrum was obtained. Such a procedure is justified in view of the low degree of mixing between the A and K spin states. It may easily be shown that the error introduced by using an AB analysis on the A part of the spectrum is only of the order of $\pm$ 0.5 cps.

The protons in III form an AB_2 system. The chemical shift of the *para* proton (ν_A) could thus be obtained directly from the spectrum,[18] and this was done where feasible. The coupling constant J_{AB} was calculated by determining the value of the parameter $J/|\nu_A-\nu_B|$ which best reproduced the observed spectrum.

The *ortho* coupling constants obtained from the spectra of the deuterated compounds are presented in Table 2. They are of the magnitude expected for

Table 2. Coupling constants between *meta* and *ortho* (J_{23}) and *meta* and *para* (J_{34}) protons in aniline, N-methylaniline, acetanilide, and N-methylacetanilide, as determined on the residual proton spectra of the partially deuterated (*ca.* 80 % 2,4,6-d_3) compounds in $CDCl_3$ solutions.

Compound	Coupling constants, cps	
	$|J_{23}|$	$|J_{34}|$
Aniline	8.5	7.5
N-Methylaniline	8.7	7.5
Acetanilide	8.6	7.6
N-Methylacetanilide	8.5	—

aromatic *ortho* proton-proton couplings,[16,19] and the coupling constant J_{23} is seen to be consistently larger than J_{34}, which is apparently a general phenomenon in monosubstituted benzenes.[19] The change from amine to anilide has essentially no effect on the size of the coupling constants, which is not surprising in view of the minor importance of substituents in general in the determination of the size of aromatic coupling constants.[19]

All of the lines in the aromatic proton spectra of the deuterated compounds were broadened by unresolved H—D spin-spin coupling. The line positions

could nonetheless be determined with sufficient accuracy for the purposes of this investigation.

The change in chemical shift for the *ortho* protons between aniline and acetanilide or between N-methylaniline and N-methylacetanilide is brought about through space by the diamagnetic anisotropy and electric field effects of the carbonyl group and by the anisotropy of the various carbon-nitrogen bonds, and through bonds by alterations in the mesomeric and inductive effects of the nitrogen atom. The tendency for the lone pair electrons to migrate into the ring is diminished, but the *total* migration of nonbonding electrons from nitrogen is increased, thus raising the effective electronegativity of the nitrogen atom.[20] The latter consequence of acetylation is expected to decrease the electron density at the *ortho* carbon atom, which should give rise to a downfield shift of the *ortho* proton resonance. Baba and Suzuki[20] have carried out a molecular orbital calculation on both aniline and acetanilide, from which the difference in excess π-electron density at the *ortho* carbon may be calculated to be 0.027. Application of the expression $\delta = aq$ relating chemical shift and π-electron density [21-23] in the form $\Delta\delta = a\Delta q$ with $a = 10$ ppm/electron[21] leads to an estimated downfield shift of about 0.3 ppm for the *ortho* protons in acetanilide from those in aniline due to mesomeric effects transmitted through the bonds. This is the *minimum* shift due to such effects, since Baba and Suzuki[20] made their calculations for a planar acetanilide molecule. Any twist about the aryl C—N bond will further decrease the excess π-electron density at the *ortho* and *para* positions and thus increase the size of the downfield shift. Assuming a $\cos^2$ relation between the angle of twist and the degree of resonance interaction,[24] it may be roughly estimated that the excess π-electron densities calculated by Baba and Suzuki[20] for the *ortho* and *para* positions in acetanilide should be decreased by a factor of the order of 0.1 if the torsional angle about the aryl C—N bond is 17°. In view of the approximations involved in the theoretical estimation of chemical shifts in aromatic molecules from π-electron density data, this correction leads to no significant change in the values calculated on the basis of the original π-electron densities, and will therefore be neglected in the following discussion. The change in the inductive effect of the nitrogen atom between aniline and acetanilide may be expected to increase the size of the downfield shift of the *ortho* proton resonance by an unknown (but probably small) amount, and thus the entire shift of 0.9 ppm (based on 10 mole % solutions in chloroform-*d*) may be tentatively separated into 0.3 ppm due to mesomeric effects plus 0.6 ppm due to a combination of inductive and through-space effects.

The shift of the *para* proton resonance between aniline and acetanilide may be similarly estimated. The predicted shift is about 0.2 ppm, which is in fair agreement with the observed shift of 0.34 ppm, based on 10 mole % solutions. This agreement is not unexpected since the *para* proton should be much less influenced by intramolecular through-space and inductive effects than the *ortho* (and *meta*) protons.

The chemical shift of the *para* proton in N-methylacetanilide in a 10 mole % chloroform-*d* solution was found to be 7.33 ppm, which is close to the shift of benzene under the same conditions (7.32 ppm). That this agreement is not entirely fortuitous may be made plausible by considering the reasonable

assumption that the dihedral angle θ in N-methylacetanilide has, in solution, a value near that of 90° found in the crystal.[6] Since through-space effects are at a minimum at the *para* position, it may then be plausibly predicted that the π-electron density at the *para* position is approximately the same as that in benzene, and thus it is not surprising that the chemical shifts are similar. The excess π-electron density at the *para* position in N-methylaniline may be estimated from the chemical shift data in Table 1 to be 0.064 (see Table 3).

Table 3. Aromatic chemical shifts and excess π-electron densities in aniline, N-methylaniline, acetanilide and N-methylacetanilide based on measurements in 10 mole % $CDCl_3$ solutions.

Compound	Position	δ_{obs} [a] (ppm)	q_{obs} [b]	q_{calc} [c]
Aniline	*ortho*	+ 0.71	0.071	0.081
	meta	+ 0.20	0.020	− 0.003
	para	+ 0.61	0.061	0.064
N-Methylaniline	*ortho*	+ 0.76	0.076	—
	meta	+ 0.16	0.016	—
	para	+ 0.64	0.064	—
Acetanilide	*ortho*	− 0.17	− 0.017	0.054
	meta	+ 0.08	0.008	− 0.002
	para	+ 0.27	0.027	0.042
N-Methylacetanilide	*ortho*	+ 0.12	0.012	—
	meta	− 0.08	− 0.008	—
	para	− 0.01	− 0.001	—

[a] The chemical shift of benzene in a 10 mole % $CDCl_3$ solution is used as reference (7.32 ppm from TMS). A + sign implies an upfield shift.
[b] Based on the equation $\delta = aq$ with $a = 10$ ppm per electron.[21]
[c] From the work of Baba and Suzuki.[20]

The shifts of the *ortho* and *para* proton resonances between acetanilide and N-methylacetanilide (see Table 1) may be discussed in terms of i) the effect of *endo vs. exo* conformational differences and ii) the effect of the difference in dihedral angle in these two compounds. The *ortho* proton resonance in the spectrum of acetanilide is shifted 0.29 ppm downfield from that for N-methyl-acetanilide, whereas the *para* proton resonance is shifted 0.28 ppm upfield. The latter shift will be least affected by i), and may be primarily attributed to ii). The change in dihedral angle from 18° to 90° on going from acetanilide to N-methylacetanilide will result in a decrease in the degree of mesomeric interaction between the nitrogen lone pair and the aromatic π-electrons, which will decrease the excess π-electron density at the *para* position. The observed shift is in the direction expected on the basis of this argument. This shift may be predicted to be about 0.4 ppm on the basis of the calculated π-electron density at the *para* position in acetanilide.[20] A similar calculation of the *expected*

shift of the *ortho* proton resonance leads to a value of 0.5 ppm upfield. The fact that the observed shift is 0.29 ppm in the opposite direction is an indication of the overriding importance of effect *i*) above: thus, the proximity of the anisotropic carbonyl group to the *ortho* protons in the *endo* conformation (acetanilide) is assumed to lead to the observed downfield shift.

It is of interest to note that the *para* position in acetanilide is more reactive in electrophilic bromination by a factor of 10^3 than the *para* position in N-methylacetanilide.[25] This difference in reactivity has been attributed in part to the loss of N—H hyperconjugation,[25,26] but it is recognized [26] that this cannot explain the entire factor of 10^3. Steric hindrance to planarity in the transition state has been suggested as an alternative explanation,[27] but, as pointed out by de la Mare and Ridd,[26] *ortho*-methylacetanilide chlorinates only 20 times slower than acetanilide in the *para* position even though steric inhibition of conjugation in this system must be similar to that in the N-methyl compound. Another factor to be taken into account is the importance of hydrogen bonding with the solvent for the stabilization of the transition state or the intermediate in these reactions. This is of course difficult to evaluate, but in combination with loss of N—H hyperconjugation, steric hindrance to planarity in the transition state, and *the decrease in π-electron density at the para position in the ground state due to the change in dihedral angle* between acetanilide and N-methylacetanilide, as discussed above, the thousandfold difference in reactivity may be given a plausible explanation.

The $COCH_3$ protons in N-methylacetanilide give rise to a peak at $\delta = 1.88$, which is 0.21 ppm upfield from the corresponding resonance in the spectrum of acetanilide at $\delta = 2.09$. Both of these values were determined on solutions of essentially the same concentration (10 mole %). Dilution had no effect outside experimental error on the peak position in the case of N-methylacetanilide, but led to a downfield shift of 0.07 ppm on going from a 10 mole % to a 0.5 mole % solution in the case of acetanilide itself. This shift is almost certainly due to the presence of intermolecular N—H⋯O hydrogen bonds which are broken on dilution, thus changing the environment of the $COCH_3$ group. Evidence for such hydrogen bonding in solutions of acetanilide has been obtained from both dipole moment [1,2] and infrared spectroscopic studies.[2] The absence of a significant dilution shift in the case of N-methylacetanilide is of course expected on the basis of the above argument. The "true" shift of the $COCH_3$ protons in acetanilide in chloroform-*d* solution is that obtained upon extrapolation to infinite dilution, 2.16 ppm. The difference between this shift and that of the $COCH_3$ protons in N-methylacetanilide, 0.28 ppm, is readily rationalized in terms of the difference in conformation of these two molecules: the $COCH_3$ protons in N-methylacetanilide are shifted upfield compared to those in acetanilide because of their position over the plane of the benzene ring and their proximity to the anisotropic aryl C—N bond. A calculation using the data of Johnson and Bovey [28] and approximate distances measured on Dreiding models leads to an estimated shift of 0.3 ppm for the $COCH_3$ protons in N-methylacetanilide upfield from those in acetanilide. On the basis of Pople's modified ring current,[29] the estimated shift becomes 0.2 ppm. In such an approximate calculation the effect of the anisotropic aryl C—N bond is of course neglected, but it is encouraging that the estimated

shift is in the same direction and of the same order of magnitude as the observed.

The aromatic proton spectra of propionanilide, isobutyranilide, and pival-anilide are quite similar in general appearance to that of acetanilide. As seen in Table 4, the N—H proton resonance moves upfield in this series from 8.58

Table 4. NMR data for various anilides measured on 10 mole % chloroform-*d* solutions.

$C_6H_5-N\begin{smallmatrix} COR_1 \\ \\ R_2 \end{smallmatrix}$		Chemical shifts [a]			Width of aryl multiplet (cps) [d]
R_1	R_2	R_1 [b]	R_2	Aryl H [c]	
CH_3	H	2.09 (2.16)	8.58	7.24	46
CH_3CH_2	H	1.17 (1.24); 2.34 (2.38)	8.26	7.20	54
$CH(CH_3)_2$	H	1.17 (1.25); 2.53 (2.51)	8.18	7.25	49
$C(CH_3)_3$	H	1.27 (1.32)	Under aryl peaks	7.31	44
CH_3	CH_3	1.88	3.26	7.32	29
CH_3	CH_3CH_2	1.83	1.11; 3.76	7.29	30
CH_3	$CH_2C(CH_3)_3$	1.88	0.861; 3.70	7.33	32
CH_3CH_2	CH_3	1.05; 2.10	3.26	7.29	29
$C(CH_3)_3$	CH_3	1.04;	3.21	7.29	29

[a] ppm downfield from TMS.
[b] The values in parentheses were obtained by extrapolation to infinite dilution.
[c] Center of aryl multiplet.
[d] Measured at the baseline.

ppm in acetanilide to 8.18 ppm in isobutyranilide. (The N—H peak in pival-anilide comes under the aryl proton peaks, and it was thus impossible to determine its position accurately at the concentration — 10 mole % — used for the other anilides.) This is quite probably a reflection of the different degrees of intermolecular hydrogen bonding which may be expected to occur in these different anilides for steric reasons.

The aromatic proton spectra of N-ethylacetanilide, N-neopentylacet-anilide, N-methylpropionanilide and N-methylpivalanilide are similar in width (29—32 cps) to that of N-methylacetanilide. The peak(s) for the alkyl substi-tuent on the carbonyl group in these compounds occur(s) upfield from the corresponding peak(s) in the spectra of the unsubstituted anilides (see Table 4).

On the whole, the results seem to indicate that the *exo* conformation is preferred by open-chain anilides with N-alkyl substituents, while the *endo* conformation is preferred by open-chain anilides in which the nitrogen is unsubstituted.*

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* In the cyclic anilide N-acetylindoline, the *endo* conformation is apparently preferred, judging from the large downfield shift of the proton in the 7-position.[30]

Long-range coupling. A long-range coupling of about 0.36 cps between the N-methyl group and the acetyl methyl group was observed in N-methylacetanilide in the N-methyl peak. A coupling of similar magnitude was observed in the N-methyl peak in N-methylpropionanilide. The corresponding coupling in N-neopentylacetanilide could not be resolved, but a line width comparison indicated that both the $-CH_2-$ and $COCH_3$ peaks were broadened. The half-width of the $-CH_2-$ peak is 0.9 cps, that of the $COCH_3$ peak is 0.8 cps, whereas the peak for the t-butyl group has a half-width of less than 0.6 cps. In the case of N-ethylacetanilide, the effect of the long-range coupling (if present) could not be unambiguously detected in the $-CH_2-$ peaks due to the presence of second-order fine structure.[31] In no case was multiplet structure observed in the $COCH_2R$ (R = H, CH_3) peak, but the latter was consistently broadened in all cases where the effect of a putative coupling was observed in the corresponding N-alkyl peak(s). In the case of N-methylacetanilide, it was confirmed by a double resonance experiment * that the observed multiplet structure in the N-methyl peak is not due to coupling with the nitrogen nucleus. The N-methyl peak collapsed to a singlet upon irradiation at the acetyl methyl frequency.

EXPERIMENTAL

Melting points were determined on a Kofler Hot-Stage Microscope.

Acetanilide was a commercial product which was recrystallized from water containing a small amount of ethanol. M.p. 115—116°; lit.[32] m.p. 113—114°.

Propionanilide was prepared by treating aniline with propionic anhydride. Recrystallization from ethanol-water led to a product with m.p. 105—107°. (Lit.[33] m.p. 105°).

Pure samples of *isobutyranilide* and *pivalanilide* were obtained from Dr. Bo Lamm.

N-Methylacetanilide was prepared by the reaction of N-methylaniline with acetic anhydride. Recrystallization from water led to a product with m.p. 100—101°. (Lit.[32] m.p. 102—104°.)

N-Ethylacetanilide was obtained from the reaction of freshly distilled N-ethylaniline with acetic anhydride. The product crystallized slowly with the help of seed crystals; it was then washed with water and dried in the air. M.p. 51—52°; lit.[34] m.p. 51—53° (54.5°).

N-Neopentylacetanilide was obtained from Dr. Bo Lamm as a clear oil which slowly crystallized; m.p. 38—40°. This substance had been prepared by the reaction of N-neopentylaniline with acetic anhydride,[35] and unambiguous confirmation of the proposed structure was provided by the NMR spectrum.

N-Methylpropionanilide was prepared from N-methylaniline by reaction with propionic anhydride. Distillation of the product *in vacuo* led to an oil which crystallized to a solid with m.p. 54—56°; lit.[35] m.p. 58.5°.

N-Methylpivalanilide was obtained from the reaction of N-methylaniline with pivaloyl chloride (obtained from Dr. Bo Lamm). The product had m.p. 80—82°; lit.[37] m.p. 82°.

Acetanilide-2,4,6-d₃ and *N-methylacetanilide-2,4,6-d₃*; see the following paragraph.

Aniline-2,4,6-d₃ and *N-methylaniline-2,4,6-d₃* were prepared by refluxing a solution of the corresponding undeuterated hydrochloride (0.1 mole) in excess D_2O (25 g, 1.25 mole; Norsk Hydro, 99.7 % D) for 24 h.[38] The reaction mixture was poured into excess sodium carbonate solution, and the product was extracted with ether. The residue after evaporation of the solvent was divided into two portions, one of which was treated directly with acetic anhydride to obtain the corresponding anilide. The other portion was distilled at reduced pressure (*ca.* 1 mm) to obtain a pure sample of the free base.

NMR spectra were determined on a Varian A-60 spectrometer. The spectra were calibrated by the usual side-banding technique, using sidebands from internal tetramethylsilane generated by a Hewlett-Packard model 200 CD wide range oscillator. The sideband frequency was measured by a Hewlett-Packard model 3734A frequency counter. All spectra were measured on chloroform-*d* (Fluka, 99.5 % D) solutions made up in the following way: a carefully weighed amount of the anilide was dissolved in 300 μl of solvent delivered from a volumetric micropipet. For dilution studies, 300 μl portions of chloroform-*d* were successively added to the original solution in the NMR tube, and spectra were determined after allowing time for complete mixing. Extrapolations to infinite dilution were made on plots of chemical shift *vs.* mole fraction for solutions with mole fraction ≤ 0.01.

REFERENCES

1. Gomel, M. and Lumbroso, H. *Bull. Soc. Chim. France* **1962** 1196.
2. Suzuki, I., Tsuboi, M., Shimanouchi, T. and Mizushima, S. *Spectrochim. Acta* **16** (1960) 471.
3. Smith, J. W. *J. Chem. Soc.* **1961** 4700.
4. Thompson, H. B. and Hallberg, K. M. *J. Phys. Chem.* **67** (1963) 2486.
5. Dyall, L. K. and Kemp, J. E. *Spectrochim. Acta* **22** (1966) 483, and references therein.
6. Pedersen, B. F. and Pedersen, B. *Tetrahedron Letters* **1965** 2995.
7. Holtermann, H., Haugen, L. G., Haavaldsen, J., Nordal, V., Wille, K. and Tjønneland, K. *Resuméer av sektionsföredrag 11. Nordiske Kjemikermöte,* Åbo 1962, p. 34. (See Ref. 6.).
8. Brown, C. J. and Corbridge, D. E. C. *Acta Cryst.* **7** (1954) 711.
9. Carter, R. E. and Innes, M. *Unpublished.* See Brown, C. J. *Acta Cryst.* **21** (1966) 442.
10. Syrkin, J. K. and Dyatkina, M. E. *Structure of Molecules,* Butterworths, London 1950, p. 252.
11. Pauling, L. *The Nature of the Chemical Bond,* 3rd Ed., Cornell University Press, Ithaca, N.Y. 1960, pp. 197—198.
12. Lister, D. G. and Tyler, J. K. *Chem. Commun.* **1966** 152.
13. Binsch, G., Lambert, J. B., Roberts, B. W. and Roberts, J. D. *J. Am. Chem. Soc.* **86** (1964) 5564.
14. Pedersen, B., Holtermann, H. and Haavaldsen, J. *To be published* in Acta Chem. Scand., see Ref. 6.
15. Hoffman, R. A. and Forsén, S. In Emsley, J. W., Feeney, J. and Sutcliffe, L. H. (Eds.) *Progress in NMR Spectroscopy,* Pergamon, New York 1966, Appendix I.
16. Emsley, J. W., Feeney, J. and Sutcliffe, L. H. *High Resolution Nuclear Magnetic Resonance Spectroscopy,* Pergamon, London 1965, p. 180.
17. Pople, J. A., Schneider, W. G. and Bernstein, H. J. *High-resolution Nuclear Magnetic Resonance,* McGraw, New York 1959, p. 119 *ff.*
18. *Ibid.,* p. 126.
19. Bothner-By, A. A. *Advan. Magnetic Resonance* **1** (1965) 208, and Table XXVII.
20. Baba, H. and Suzuki, S. *J. Chem. Phys.* **32** (1960) 1708.
21. Fraenkel, G., Carter, R. E., McLachlan, A. and Richards, J. H. *J. Am. Chem. Soc.* **82** (1960) 5846.
22. Smith, I. C. and Schneider, W. G. *Can. J. Chem.* **39** (1961) 1158.
23. Schaefer, T. and Schneider, W. G. *Can. J. Chem.* **41** (1963) 966.
24. Wepster, B. M. In Klyne, W. and de la Mare, P. B. D. (Eds.), *Progress in Stereochemistry,* Butterworths, London 1958, Vol. 2, p. 99, and references therein. See also Freedman, H. H. *J. Am. Chem. Soc.* **82** (1960) 2454.

25. Robertson, P. W., de la Mare, P. B. D. and Swedlund, B. E. *J. Chem. Soc.* **1935** 782.
26. De la Mare, P. B. D. and Ridd, J. H. *Aromatic Substitution*, Butterworths, London 1959, p. 145.
27. Norman, R. O. C. and Taylor, R. *Electrophilic Substitution in Benzenoid Compounds*, Elsevier, Amsterdam 1965, pp. 139 *ff*.
28. Johnson, C. E. and Bovey, F. A. *J. Chem. Phys.* **29** (1958) 1012; Ref. 11, p. 595.
29. Pople, J. A. *J. Chem. Phys.* **41** (1964) 530.
30. McLean, S. *Can. J. Chem.* **38** (1960) 2278.
31. See, for example, Ref. 17, pp. 154—155.
32. *Handbook of Chemistry and Physics*, 46th Ed., Chemical Rubber Co., Ohio 1965—1966, p. C-82.
33. *Ibid.*, p. C-493.
34. *Ibid.*, p. C-80.
35. Lamm, B. *Unpublished results*.
36. Norton, L. M. and Allen, A. W. *Ber.* **18** (1885) 1995.
37. Degnan, W. M. and Shoemaker, C. J. *J. Am. Chem. Soc.* **68** (1946) 104.
38. Best, A. P. and Wilson, C. L. *J. Chem. Soc.* **1946** 239.