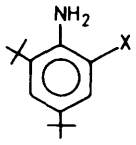
Derivatives of *m*-Di-t-butylbenzene. Part 8.[1] Dissociation Constants of 2-Halogeno-4,6-di-t-butylanilines, and ^{1}H Nuclear Magnetic Resonance Spectra of the Corresponding Acetanilides

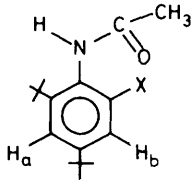
Adrianus Jan de Koning †
Department of Chemistry, National University of Lesotho, Roma, Lesotho

The dissociation constants of 2-halogeno-4,6-di-t-butylanilines have been compared with those of 2-halogenoanilines. The base-weakening effect of the t-butyl group *ortho* to the amino group is greatly reduced by the presence of the *ortho* halogen atom. The ^{1}H n.m.r. spectra of 2'-halogeno-4',6'-di-t-butylacetanilides show the presence of geometrical isomers as a result of restricted rotation around the bond between the nitrogen atom and the acetyl group.

The preparation of several 2-halogeno-4,6-di-t-butylanilines (1) and the corresponding acetanilides (2)—(4) has been described in Part 6.[1] The present paper deals with the abnormal dissociation constants of the substituted anilines, and the restricted rotation in the substituted acetanilides observed by ^{1}H n.m.r. spectroscopy.



(1)



(2) X = Cl
(3) X = Br
(4) X = I
(5) X = H

Results and Discussion

In Table 1 are listed the dissociation constants (in 50% ethanol at 25 °C) of four 2-halogeno-4,6-di-t-butylanilines (1) and the related 2-halogenoanilines. From these dissociation constants (expressed as pK_a values) it may be deduced that the base-weakening effect of a halogen *ortho* to the amino group is smaller in the first series than in the second: the difference is 0.43 pK_a units for Cl, 0.34 units for Br, and 0.35 units for I. It is well known that an *ortho*-t-butyl group decreases the relative basic strength of aniline, by 1.3 pK_a units.[2] This decrease can be ascribed to steric hindrance to solvation: the non-polar t-butyl group destabilises the anilinium ion by disturbing its solvation shell. It now appears that an *ortho*-halogen atom also reduces the steric hindrance to solvation of the t-butyl group, by about 0.40 pK_a units, *i.e.* much less than an *ortho*-t-butyl group. This seems understandable: a t-butyl group can replace mobile solvent molecules from the solvation shell in 2-t-butylaniline but not a polar halogen linked to the benzene ring in 2-halogeno-4,6-di-t-butylanilines.

^{1}H N.m.r. spectra (at 60 and 200 MHz) of 2'-halogeno-4',6'-di-t-butylacetanilides (2)—(4) showed the presence of *Z*- and *E*-isomers in the proportions 68 : 32 for (2), 72 : 28 for (3), and 74 : 26 for (4). In the 200 MHz spectrum of the iodo-derivative (4) (Figure) the signals of the isomers are completely separated. A similar picture was obtained for the bromo-derivative (3). In the spectrum of the chloroacetanilide (2) no separation of the aromatic proton signals was discerned for the *Z*-isomer, but the aromatic proton signals of the *E*-isomer were clearly separated.

Chemical shifts, coupling constants, and isomer distributions are shown in Table 2, along with relevant data for 2',4'-di-t-butylacetanilide (5). In this substance *Z*- and *E*-isomers were found in the ratio 76 : 24, respectively (Kessler and Rieker [3] quote 75 : 25 for 2'-t-butylacetanilide). No splitting of the t-butyl signal was observed (even at 200 MHz) but unambiguous assignment of signals of the aromatic protons of both isomers was possible. Molecular models show that in 2'-halogeno-4',6'-di-t-butylacetanilides the acetamido group is out of the plane of the benzene ring, and it must be the restricted rotation around the N–Ac bond which gives rise to the two isomers (see Figure). This type of restricted rotation was first observed by Phillips [4] in the ^{1}H n.m.r. spectrum of *N*,*N*-dimethylformamide, and it has since been found in other amides (*cf.* ref. 5), including 2'-t-butylacetanilide and 2',4',6'-tri-t-butylacetanilide.[3] It seems certain that the high field methyl signal can be attributed to the *E*-isomer, since then the methyl group will be situated over the benzene ring and experience extra shielding. Comparison of the chemical shifts of the two t-butyl groups with shifts of t-butyl groups in related substances allows identification of the signals.‡ The high field signal (δ 1.29—1.32) can be assigned to the t-butyl group in position 4 and the low field signal (δ 1.36—1.40) to the group in position 6. It is surprising that the splitting of the 4-t-butyl signal is more pronounced than that for the group in position 6 (*i.e.* close to the acetamido group). The results in Table 2 show that the percentage of *Z*-isomer increases from 68 to 74 in going from the chloro to the iodo derivative. This increase may be related to the increase in size of the halogen atom, but in 2'-alkylacetanilides and 2',6'-dialkylacetanilides an increase in the size of the alkyl group results in a decrease in the proportion of the *Z*-isomer.[3] Similarly, the isomer composition of 2',4'-di-t-butylacetanilide (5) does not fit into the pattern of the three 2'-halogeno-4',6'-di-t-butylacetanilides, but does fit the behaviour of the alkyl-substituted acetanilides.[3] This is another example where a polar halogen and a non-polar alkyl group or hydrogen

† *Present address:* Fishing Industry Research Institute, University of Cape Town, Rondebosch 7700, Cape Town, Republic of South Africa.

‡ For example in 3',5'-di-t-butylacetanilide the t-butyl groups absorb at δ 1.33; in 2',6'-dibromo-3',5'-di-t-butylacetanilide at δ 1.51, and in 3-bromo-4,6-di-t-butylacetanilide at δ 1.50 (position 4) and 1.38 (position 6). In addition the t-butyl groups in 1,3-diacetamido-4,6-di-t-butylbenzene absorb at δ 1.38 (unpublished observations).

Table 1. pK_a Values of some substituted anilines in 50% (by vol.) ethanol at 25 °C

	pK_a	ΔpK_a		pK_a	ΔpK_a
2,4-Di-t-butylaniline	3.83	0.00	Aniline	4.30	0.00
2-Chloro-4,6-di-t-butylaniline	2.33	1.50	2-Chloroaniline	2.37	1.93
2-Bromo-4,6-di-t-butylaniline	2.18	1.65	2-Bromoaniline	2.31	1.99
2-Iodo-4,6-di-t-butylaniline	2.13	1.70	2-Iodoaniline	2.25	2.05

Table 2. N.m.r. spectra (δ values; *J* in Hz) of 2′-X-4′,6′-di-t-butylacetanilides in $CDCl_3$ at 200 MHz and 22 °C

	Methyl (%)		t-Butyl 4		t-Butyl 6		NH [a]	
X	*Z*	*E*	*Z*	*E*	*Z*	*E*	*Z*	*E*
H_c	2.177 (76%)	1.877 (24%)	1.304		1.398		7.158	7.038
Cl	2.216 (68%)	1.812 (32%)	1.296	1.321	1.377	1.394	6.800	6.769
Br	2.218 (72%)	1.810 (28%)	1.295	1.320	1.373	1.388	6.816	6.770
I	2.218 (74%)	1.788 (26%)	1.288	1.313	1.359	1.371	6.912	6.832

	Aromatic protons H_a		H_b		H_c	
X	*Z*	*E*	*Z*	*E*	*Z*	*E*
H_c	7.422 (d, *J* 2.1)	7.471 (d, *J* 2.1)	7.233 (dd, *J* 2.1 and 8.2) [d]		7.351 (d, *J* 8.2)	7.000 (d, *J* 8.2)
Cl	7.350 (s) [b]	7.340 (d, *J* 2.1) [c]	7.350 (s) [b]	7.374 (d, *J* 2.1) [c]		
Br	7.405 (d, *J* 2.2)	7.450 (d, *J* 2.2)	7.532 (d, *J* 2.2)	7.555 (d, *J* 2.2)		
I	7.437 (d, *J* 2.3)	7.480 (d, *J* 2.3)	7.779 (d, *J* 2.3)	7.810 (d, *J* 2.3)		

[a] All NH signals are broad bands with two peaks. [b] H_a and H_b have identical shifts in the *Z*-isomer. [c] It seems likely that H_b has the larger chemical shift. [d] H_b of the *Z*- and the *E*-isomer have identical chemical shifts.

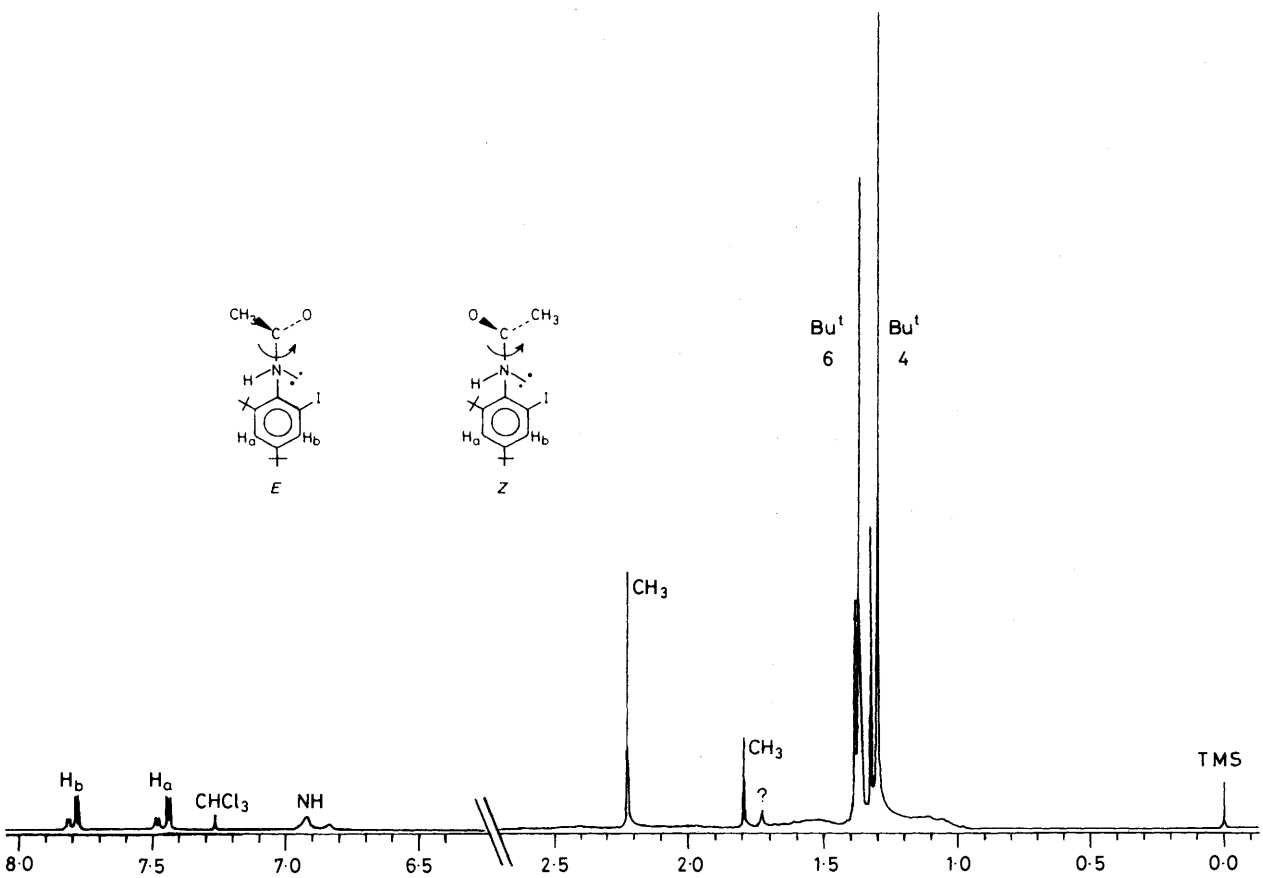


Figure. ^1H N.m.r. spectrum (200 MHz) of the iodoanilide (4)

atom show opposite behaviour (*cf.* the rate of deacetylation of *ortho*-substituted acetanilides in methanolic sodium methoxide.[1]

Experimental

The dissociation constants of the anilines were determined by titration of *ca.* 0.5 mmol of substance in 20 ml of 50% aqueous ethanol (by vol.) at 25 °C with 0.05M-HCl in 50% ethanol, using an Electronic Instruments Ltd. 7020 pH meter with combined glass electrode. pH Values at half neutralisation were converted to pK_a values using the expression (i).* The

$$pK_a = pH + \log\left(\frac{[salt] - [H^+]}{[base] + [H^+]}\right) \qquad (i)\ *$$

instrument was standardised with aqueous buffers of pH 4.00 and 6.84. The pK_a value of aniline under these conditions was 4.30 (lit.,[6] 4.26) and that of 2,4-di-t-butylaniline 3.83 (lit.,[6] 3.80). ^1H N.m.r. spectra (60 MHz) were taken for $CDCl_3$ solutions (*ca.* 50 mg ml^{-1}) at 28 °C with a Varian EM 360 spectrometer. 200 MHz Spectra were taken for $CDCl_3$ solutions (*ca.* 50 mg ml^{-1}) at 22 °C with a Nicolet NT 200 spectrometer equipped with an Oxford Instruments wide-bore superconducting magnet. The isomer compositions determined at 60 and at 200 MHz were identical. The syntheses of 2-chloro-4,6-di-t-butylaniline, 2-bromo-4,6-di-t-butylaniline (this substance has now been obtained crystalline with m.p. 30—31 °C), 2-iodo-4,6-di-t-butylaniline, and their acetylated derivatives have been described.[1] 2,4-Di-t-butylaniline and 2′,4′-di-t-butylacetanilide were prepared according to ref. 7. Aniline, 2-chloroaniline, 2-bromoaniline, and 2-iodoaniline were purified by distillation or recrystallisation.

* An error exists in the pK_a values reported in Part 5[1] owing to the use of pK_a = pH at half neutralisation and neglect of the logarithmic term. Since we are dealing with two closely related series of compounds having similar pK_a values, this error does not affect the conclusions reached in Part 5,[1] but the absolute values are incorrect. The correct values have been published as an erratum in *Recl. Trav. Chim. Pays-Bas*, 1983, **105**, 399.

Acknowledgements

I thank Mr. A. Sinnema and Dr. J. A. Peters, Laboratory of Organic Chemistry, Delft University of Technology, for recording and interpreting the 200 MHz spectra. The work was supported by a research grant from the National University of Lesotho.

References

1 Part 7, A. J. de Koning, *Recl. Trav. Chim. Pays-Bas*, 1982, **101**, 385; Part 6, A. J. de Koning, *ibid.*, 1981, **100**, 421; Part 5, A. J. de Koning, *ibid.*, 1978, **97**, 147.
2 B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, 1957, **76**, 357.
3 H. Kessler and A. Rieker, *Z. Naturforsch.*, 1967, **22**, 456; H. Kessler and A. Rieker, *Liebigs Ann. Chem.*, 1967, **708**, 57.
4 W. D. Phillips, *J. Chem. Phys.*, 1955, **23**, 1363.
5 W. E. Stewart and T. H. Sidall, *Chem. Rev.*, 1970, **70**, 517.
6 J. Burgers, M. A. Hoefnagel, P. E. Verkade, H. Visser, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, 1958, **77**, 491.
7 J. Burgers, W. van Hartingsveldt, J. van Keulen, P. E. Verkade, H. Visser, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, 1956, **75**, 1327.

Received 7th February 1983; *Paper* 3/171