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Studies on the Proton Magnetic Resonance Spectra in Aromatic Systems. XVIII.[1] Tris(dipivalomethanato)europium Induced Shift of *para*- and *meta*-Substituted Deuteroanilines[2]

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The S values, those are the paramagnetic shift parameters of deuterated and undeuterated and undeuterated *para*- and *meta*-substituted aniline derivatives induced by tris (dipivalomethanato)europium, were measured. The observed S values of compounds in the *para*-substituted series were linearly related with the substituent constants σ_π, whereas those of the *meta*-substituted series were linearly related with σ_i.

The following results were obtained for the magnitudes, S_h and S_d, and the slopes, ρ_h and ρ_d, of the undeuterated and deuterated compounds in the two series: $S_d > S_h$ and $\rho_d/\rho_h = 1.35$.

Introduction

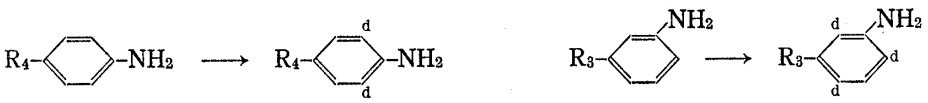
There are numerous papers on the practical utilities of tris(dipivalomethanato)europium $Eu(DPM)_3$ in nuclear magnetic resonance (NMR) spectroscopic studies on aliphatic and aromatic amines because the nitrogen lone pair electrons have a remarkable effect on the induced chemical shift. Recently, Beauté, *et al.*[4] suggested that the basicity scale of amine shown by protonation was not satisfactory because of the marked steric hindrance of the shift reagent. However, Ernst and Mannschreck[5] showed a linear relation between the magnitudes of the induced shift and the pK_a values of compounds in the *para*-substituted aniline series. This result suggests that there is also a linear relation between the $Eu(DPM)_3$/substrate equilibrium constant and ΔE_π.[6] In this work, we examined the correlation of the $Eu(DPM)_3$ induced paramagnetic effects on the ring proton chemical shifts of *meta*- and *para*-substituted deuteroanilines with the substituent constants σ_i and σ_π.[7]

Experimental

All *meta*- and *para*-substituted aniline derivatives were of the J.I.S. grade, and were purified by redistillation or recrystallization. The mps, bps and other physical constants of the purified compounds agreed well with reported values. The aromatic ring proton/deuterium exchange reaction was carried out by the electrophilic substitution reaction catalyzed by D^+ in 99.5% D_2O with a small amount of PtO_2 catalyst[8] in sealed glass tube for 90 hr at 150—155°. The free base was extracted by a standard procedure, and the solid reaction products were purified by column chromatography on basic or neutral Al_2O_3/ether, whereas the liquids were distilled under the reduced pressure.[9]

1) Part XVII: Y. Sasaki and M. Suzuki, *Chem. Pharm. Bll.* (Tokyo), **18**, 1799 (1970).
2) This work was presented at the 11th Japanese Symposium on NMR, in Osaka, on October 16, 1972.
3) *a) Toneyama 6-1-1, Toyonaka, Osaka; b) Kowakae 321, Higashi-Osaka, Osaka.*
4) C. Beauté, Z.W. Wolkowski, and N. Thoai, *Tetrahedron Letters*, **1971**, 817.
5) L. Ernst and A. Mannschreck, *Tetrahedron Letters*, **1971**, 3023.
6) P-O. Lowdin and B. Pullman, Molecular Orbitals in Chemistry, Physics and Biology, Academic Press, New York, 1964, p. 475.
7) Y. Yukawa and Y. Tsuno, *Nippon Kagaku Zasshi*, **86**, 873 (1965).
8) L.L. Garnett, L.J. Henderson, and W.A. Sollich, *Tetrahedron Letters.*, **1961**, 516.
9) Details of the aromatic H/D exchange reaction will be published elsewhere in the near future.

The proton magnetic resonance spectra of deuterated free bases were examined, and deuteration was found to occur as shown in the following scheme:



For example, *m*-nitroaniline and *p*-aminoacetophenone afford the following spectra (Fig. 1 and Fig. 2).

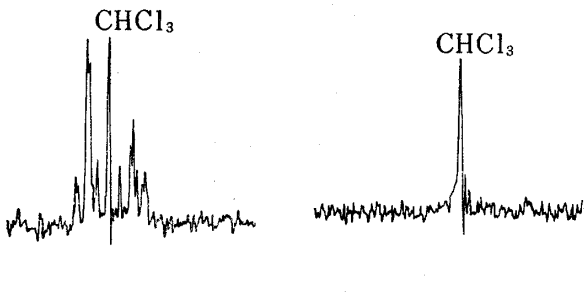


Fig. 1. NMR Spectra of *meta*-Nitroaniline

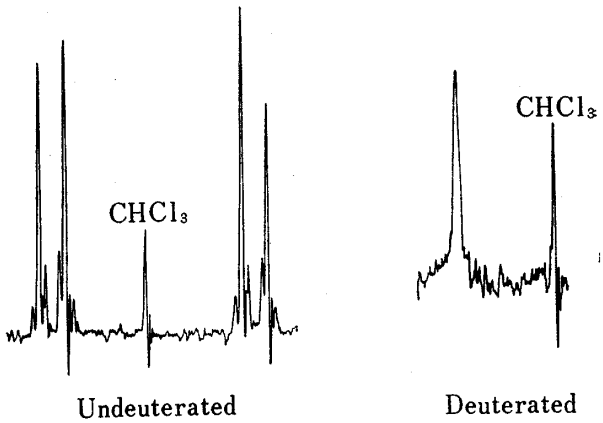


Fig. 2. NMR Spectra of *para*-Aminoacetophenone

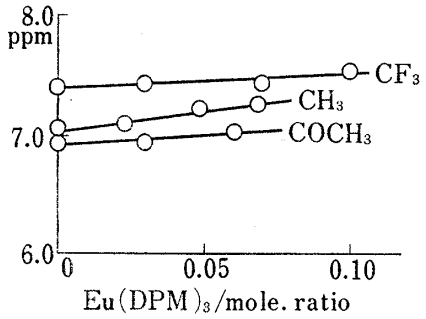


Fig. 3a. Correlations between H-5 Proton Chemical Shifts of *meta*-Substituted Aniline Derivatives and Eu(DPM)$_3$/ligand Mole. Ratios

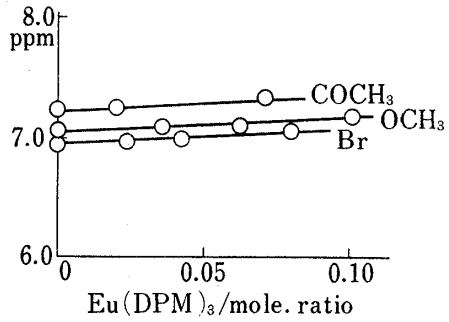


Fig. 3b. Correlations between H-5 Proton Chemical Shifts of *meta*-Substituted-2,4,6-trideuterioaniline Derivatives and Eu(DPM)$_3$/ligand Mole. Ratios

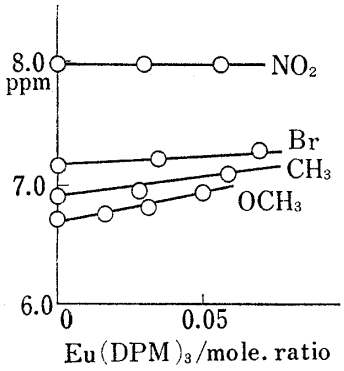


Fig. 4a. Correlations between H-3 Proton Chemical Shifts of *para*-Substituted Aniline Derivatives and Eu(DPM)$_3$/ligand Mole. Ratios

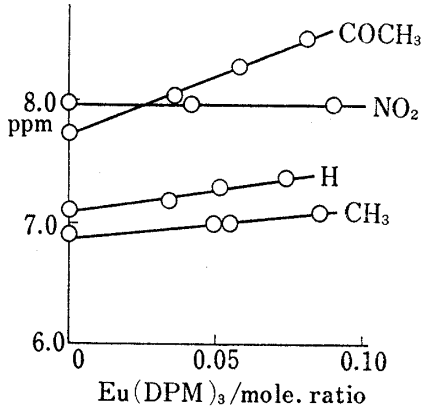


Fig. 4b. Correlations between H-3 Proton Chemical Shifts of *para*-Substituted-2,6-dideuterioaniline Derivatives and Eu(DPM)$_3$/ligand Mole. Ratios

All spectra were measured with an Hitachi R-20A type spectrometer (solvent, $CDCl_3$; internal reference, TMS).

The induced shift at 34° due to an equilibrium reaction——base + $Eu(DPM)_3$ $\rightleftarrows$ complex——was correlated with the molar ratio of $Eu(DPM)_3$/ligand$\lesssim$0.10, where the ligand concentration was 0.5 mole in $CDCl_3$.

The gradients of these correlations were taken as the S values.[10] Some examples are illustrated in the following Figures (Fig. 3 and Fig. 4).

Result and Discussion

Ring Proton Chemical Shifts of *para*- and *meta*-Substituted Deuteroanilines

In the absence of the shift reagent, the H-3 and H-5 of *p*-substituted-2,6-dideuteroanilines are situated at the *ortho* positions of the substituent groups, whereas those of the H-5 of *m*-substituted-2,4,6-trideuteroanilines are at the *meta* positions. These results are supported by the spectral patterns and the simple sum rule of the substituent effects on the ring proton chemical shifts.[11a-c] The observed ring proton chemical shifts are summarized in Table I, and as shown in Fig. 5 and Fig. 6, the former shifts are linearly related with σ_π, and the

Table I. Observed and Calculated Ring Proton Chemical Shifts of *para*- and *meta*-Substituted Deuteroanilines (Concentration: 0.5 mole. $CDCl_3$, Me_4Si as internal reference)

R	*p*-R-C_6H_4-NH_2 H-3 ppm		*m*-R-C_6H_4-NH_2 H-5 ppm	
	Obs.	Calcd.	Obs.	Calcd.
OMe	6.71	6.55	7.06	6.90
Me	6.98	6.86	7.02	6.90
F	6.80	6.78	7.08	7.04
Cl	6.95	6.90	7.00	6.77
Br	7.20	7.05	6.98	6.71
H	7.10	7.03	7.10	7.03
CF_3			7.18	7.19
CO_2Me	7.83	7.81		
COMe	7.75	7.65	7.22	7.11
NO_2	8.06	7.87	7.20	7.24

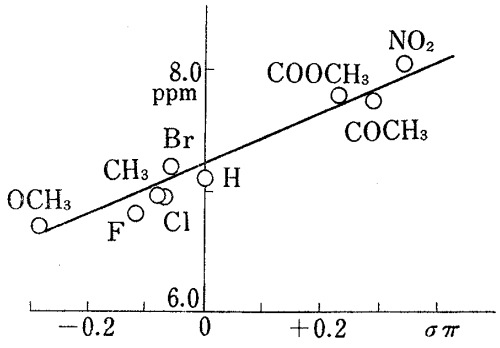


Fig. 5. Correlations between H-3 Proton Chemical Shifts of *para*-Substituted-2,6-dideuterioaniline Derivatives and Substituent Constants, σ_π

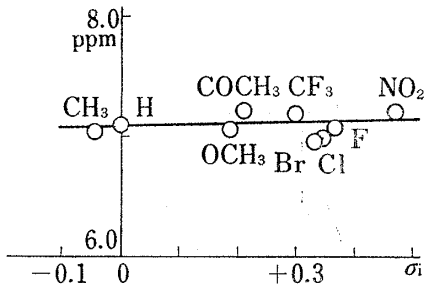


Fig. 6. Correlations between H-5 Proton Chemical Shifts of *meta*-Substituted-2,4,6-trideuterioaniline Derivatives and Substituent Constants, σ_i

10) A.F. Cockerill and D.M. Rackham, *Tetrahedron Letters*, **1970**, 5149 5153.

11) *a*) K. Hayamizu and O. Yamamoto, *J. Mol. Spectry.*, **25**, 422 (1968); *b*) P. Diehl, *Hel. Chim. Acta.*, **44**, 829 (1961); *c*) G.W. Smith, *J. Mol. Spectry.*, **12**, 146 (1964).

latter with σ_i. The linear relation observed in Fig. 5 is an interesting correlation, because, contrary to expectation, it seems as if the contribution of the steric effect of the substituent groups is not effective at the *ortho* positions. This is probably due to the removal of the steric factor because of the induced mesomeric interaction between the NH_2 group and substituent groups.

S Values

The observed *S* values of H-3 and H-5 chemical shifts of *p*-substituted-2,6-dideuteroanilines and those H-5 of *m*-substituted-2,4,6-trideuteroanilines are summarized in Table III. These *S* values are linearly related with the substituent constants σ_i and σ_π, as shown in Fig. 7a—b, respectively. These results indicate that the *S* values of these series are determined by the substituent effect on the amino group. In other words, the equilibrium between the shift reagent and substrate is under the control of the polar effect ——resonance or inductive—— of the substituent group. From this, we can predict that the shift parameters are of an electric character. These two linear relations also suggest that the steric interference of the chelation between the shift reagent and the ligand molecule does not operate, at least not on the *meta* position from the amino group.

TABLE II. Eu(DPM)$_3$ Induced Shift Parameters, *S* Values, of *para*- and *meta*-Substituted Aniline Derivatives

R	S_{H-3} of *para*-R.$C_6H_4NH_2$		S_{H-5} of *meta*-R.$C_6H_4NH_2$	
	Deuterated	Undeuterated	Deuterated	Undeuterated
OMe	5.5	4.0	2.5	1.7
Me	4.0	3.0	4.5	3.0
F	4.5	3.0	3.5	2.5
Cl	4.0	2.0	2.5	2.0
Br	3.0	1.5	2.0	0.5
H	3.5		3.5	
CF_3			1.5	1.5
CO_2Me	11.0	1.5		
COMe	10.0	2.0	2.0	2.0
CN	6.0	1.5		
NO_2	0	0	0	0

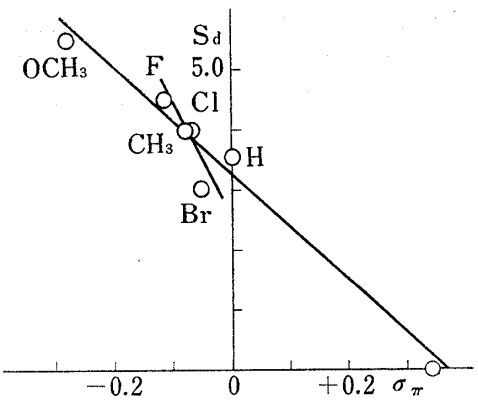


Fig. 7a. Correlations between Induced Shift Parameters, S_d, of H-3 Protons of *para*-Substituted-2,6-dideuterioanilines and Substituent Constants, σ_π

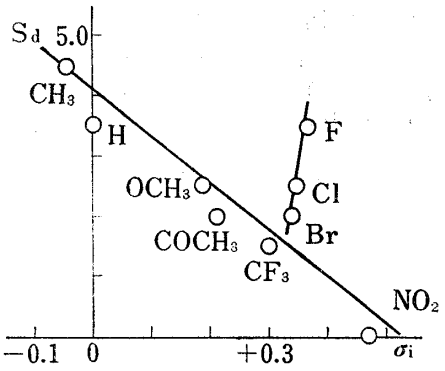


Fig. 7b. Correlations between Induced Shift Parameters, S_d, of H-5 Protons of *meta*-Substituted-2,4,6-trideuterioanilines and Substituent Constants, σ_i

Isotope Effect of Deuterium on the *S* Value

Next, the *S* values of undeuterated starting materials were measured and results are summarized in Table II. Except for substituent groups with a magnetic anisotropy effect

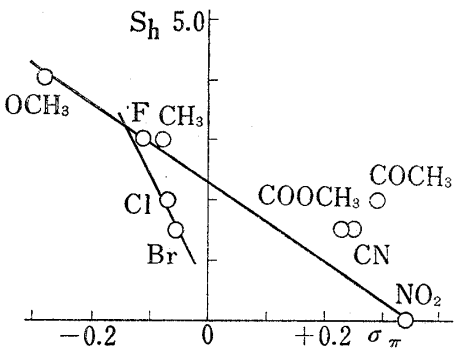


Fig. 8a. Correlations between Induced Shift Parameters, S_h, of H-3 Protons of *para*-Substituted Anilines and Substituent Constants, σ_π

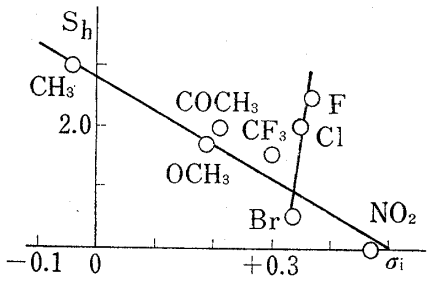


Fig. 8b. Correlations between Induced Shift Parameters, S_h, of H-5 Protons of *meta*-Substituted Anilines and Substituent Constants, σ_I

TABLE III. Slopes of S Values for Undeuterated (ρ_h) and Deuterated (ρ) *para*- and *meta*- Substituted Aniline Derivatives

para-Substituted anilines		*meta*-Substituted anilines	
H-3	$\rho_h=-6.57$	H-5	$\rho_h=-5.70$
	$\rho_d=-8.78$		$\rho_d=-7.74$
	$\rho_d/\rho_h=1.36$		$\rho_d/\rho_h=1.34$

(*i.e.* CO_2Me, COMe and CN), these S values are linearly related with the substituent constants σ_π and σ_I, as shown in Fig. 8a—b. The observed trend of $S_d>S_h$ seen in Table II indicates that the removal of the steric effect due to $Eu(DPM)_3$ in an equilibrium reaction with the ligand is facilitated by the H–D exchange at both sides of the NH_2-group. Consequently, it seems that the steric factor adjacent to the coordination site strongly influences the S value.[12] The observed slopes ρ_d and ρ_h of the deuterated (*cf.* Fig. 7a—b) and undeuterated series indicate that the isotope effect due to the deuterium exchange affects the slope of the S values of the *meta*-protons from the NH_2-group (*cf.* Table III). The observed ratios of the slopes of undeuterated and deuterated aniline derivatives are similar. This is because the deuteriums are situated at the *ortho*- and *para*-positions of the observed protons in these series. This trend also applies to *para*-halogeno-aniline derivatives, but for the *meta*-substituted series, the sign of the slope is positive. These anomalous behaviors and orders ——F>Cl>Br—— are thought to be compatible with the predominance of the mesomeric contributions rather than the inductive ones through space.

12) G.V. Smith, W.A. Boyd, and C.C. Hinckley, *J. Am. Chem. Soc.*, **93**, 6319 (1971).