

Inductive and Field Effects in Aromatic Substitution. Part VII.¹ Hydrogen-isotope Exchange in a Bridged Anthracene Derivative carrying a Nitrogen Pole

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The ¹H n.m.r. spectra of *trans*-11-amino-9,10-dihydro-12-methyl-9,10-ethanoanthracene (III) in chloroform solutions containing varying amounts of the shift reagent Eu(dpm)₃ show an almost complete separation of the peaks corresponding to the aromatic protons. These peaks have been divided into sets corresponding to the two aromatic rings by spin-decoupling and assigned almost completely by use of the equation for pseudo-contact interactions. This identification has been used to study aromatic hydrogen-deuterium exchange in solutions of (III) in the mixed solvent CF₃CO₂D-D₂SO₄-D₂O. The extent of exchange has been calculated from the n.m.r. spectra of neutralised samples of the reaction mixture. The kinetic results indicate that reaction occurs through the conjugate acid of (III) and that the $\overset{+}{N}H_3$ pole deactivates both rings to a similar extent, despite the fact that the distances of the pole from the centres of two rings are very unequal (3.5 and 5.2 Å). Approximate partial rate factors have been calculated for exchange in the conjugate acid of (III).

PARTS IV—VI¹⁻³ have been concerned with the substituent effects of the $[CH_2]_n\overset{+}{N}R_3$ groups (R = H, Me, or alkyl) in aromatic substitution and in particular with the dependence of these substituent effects on the conformation of the carbon chain. In the course of this work, the reactivities in nitration² and hydrogen isotope¹ exchange of the compounds (I) and (II) have been compared: this provides evidence on the conformational dependence of the substituent effect of the $[CH_2]_2\overset{+}{N}R_3$ group. For the nitration of the compounds with R = H, the reactivity of the bridged substrate (II) is less than that of the open-chain substrate (I) by a factor of 100;

¹ Part VI, R. Danieli, A. Ricci, and J. H. Ridd, *J.C.S. Perkin II*, 1972, 2107.

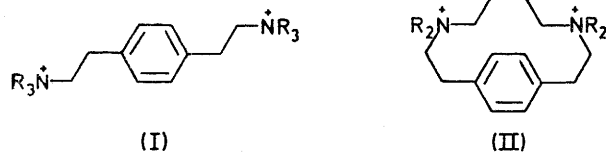
this has been attributed to the difference in the field effect of the nitrogen poles as a consequence, in part, of the shorter distance between the nitrogen poles and the ring in the bridged substrate. This interpretation assumes that, for the open chain substrate, the electrostatic interaction between each nitrogen pole and the charge on the ring in the transition state will lead to reaction in the extended conformation shown for (I).

However, it was recognised in the previous work² that the relative reactivity of substrates (I) and (II) could be influenced by other factors besides the ring-pole distance. Thus, in the open chain substrate (I), much of the space

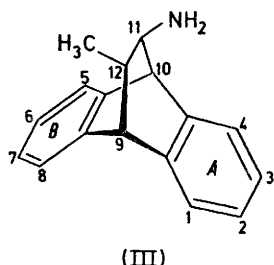
² A. Ricci, R. Danieli, and J. H. Ridd, *J.C.S. Perkin II*, 1972, 1547.

³ A. Ricci and J. H. Ridd, *J.C.S. Perkin II*, 1972, 1544.

between the pole and the ring is occupied by the solvent whereas, in the bridged substrate (II), this space is mainly included in the molecular cavity; this could markedly change the electrostatic interactions.⁴ It is



also possible that the bridging groups in (II) hinder the solvation of the Wheland intermediate relative to that in the open-chain substrate (I). For the further analysis of these substituent effects, it is helpful to consider the rate of aromatic substitution in the conjugate acid of the bridged anthracene derivative (III), for the ring-pole distances in this ion combine those of structures (I) and (II) so that both types of interaction occur within the same molecular cavity. We are indebted to Dr. A. J. Layton for pointing out the potential value of structure (III) for the purposes of this work.



Studies of the relative rate of nitration of the aromatic rings in the conjugate acid of (III) had unfortunately to be abandoned because of difficulties in determining the product composition: there are eight possible mononitro-compounds and 16 possible dinitro-compounds. However, we now report the kinetics of hydrogen-isotope exchange at the different aromatic positions. This has been made possible by the effectiveness of a europium shift reagent in separating the aromatic proton signals in the n.m.r. spectrum of the amine (III).

Analysis of the N.m.r. Spectrum of the Amine (III).—A solution of this amine in deuteriochloroform gives a complex broad peak at δ 7.0–7.4 for the aromatic protons. On the addition of a europium shift reagent [Eu(dpm)₃], this aromatic peak shows a downfield shift⁵ together with a partial separation into its components. Thus, with the ratio 0.48 mole Eu(dpm)₃ : mole amine, the 100 MHz spectrum of the aromatic protons is as shown in Figure 1. Integration shows that each of the two low field signals at δ 10.72 and 9.50 corresponds to a single proton while each of the three groups of bracketted peaks corresponds to two protons.

⁴ J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, 1938, **6**, 506, 513.

⁵ J. K. M. Sanders and D. H. Williams, *J. Amer. Chem. Soc.*, 1971, **93**, 641.

The use of spin decoupling by double resonance makes it possible to divide this spectrum into the contributions from the two aromatic rings but does not show which group of protons belongs to which ring. Thus irradiation of the low field triplet at δ 10.72 (Figure 1) changes the two-proton signal at δ 8.35 to a doublet and changes the complex four-proton peak at δ 9.50 to a regular triplet; the

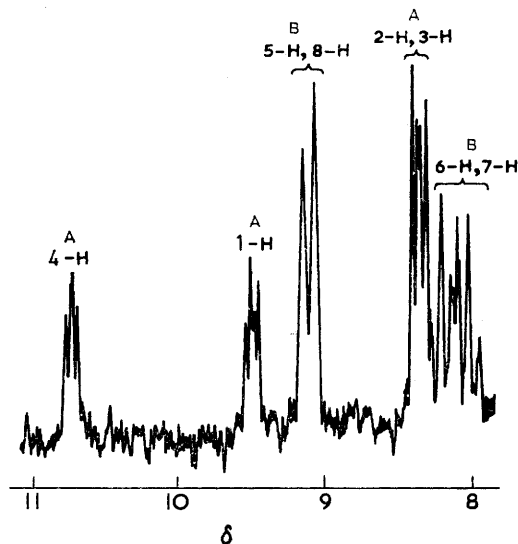


FIGURE 1 N.m.r. spectrum (CDCl₃; 100 MHz) of the aromatic protons of the amine (III) in the presence of 0.48 mole Eu(dpm)₃ : mole amine

protons giving rise to these signals belong therefore to the same ring. The results of irradiation at the other absorption frequencies accord with this interpretation.

The comparison of the order of the observed shifts ($\Delta\delta$) with that calculated for pseudo-contact interactions⁶ [equation (1)] confirms this division of the spectrum and leads to the assignment of the peaks.

$$\Delta\delta = K(3\cos^2\phi - 1)r^{-3} \quad (1)$$

In this equation, K is a constant for a particular europium complex at a given temperature, r is the proton-europium distance and ϕ is the proton-europium-nitrogen internuclear angle. The use of this equation requires a knowledge of the position of the europium atom in relation to the amine but inspection of a model of the seven co-ordinate complex [amine, Eu(dpm)₃] suggests that the direction of the N-Eu bond is largely determined by steric considerations and that steric interactions are minimised when this bond approximately eclipses the C-H bond on the adjacent carbon atom. This direction has therefore been assumed together with a C-N-Eu angle of 140° and a N-Eu bond length of 3.5 Å.⁷

For each proton signal, the variation of the shift ($\Delta\delta$) with the molar ratio Eu(dpm)₃ : amine is linear over the region 0.1–0.5 mole Eu(dpm)₃ per mole amine.

⁶ H. M. McConnell and R. E. Robertson, *J. Chem. Phys.*, 1958, **29**, 1361.

⁷ Cf. A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.*, 1973, **73**, 553.

The slopes of these plots (G) have, as usual, been taken as a measure of the $\Delta\delta$ shifts and have been plotted against the geometrical factor of equation (1) for different assignments of the protons. The assignment shown in Figure 1 gives rise to the linear plot shown in Figure 2: assignments in which the ring A peaks in Figure 1 are attributed to the aromatic ring furthest from the nitrogen pole did not give linear plots (see inset to Figure 2).

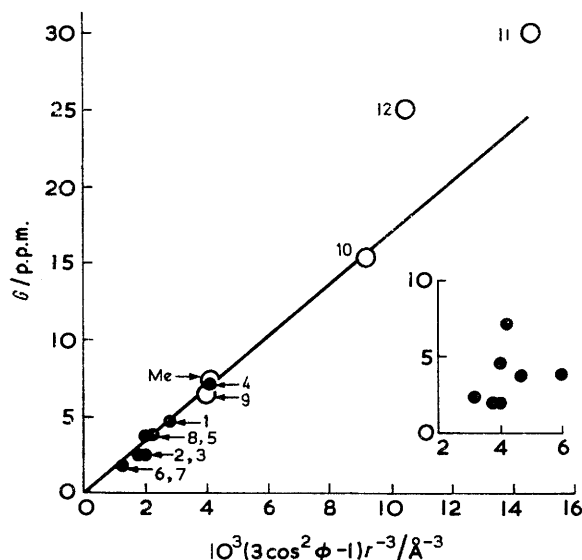


FIGURE 2 Plot of the shifts induced by $\text{Eu}(\text{dpm})_3$ against the geometrical factor of equation (1). The assignment of the aromatic protons is chosen to give the best approximation to a linear plot. Inset: the effect of exchanging the assignment of signals in rings A and B. Aromatic signals ●, aliphatic signals ○

The assignment shown in Figure 1 also accords with the multiplicity of the individual proton signals. Studies with somewhat higher $\text{Eu}(\text{dpm})_3$: amine ratios show that the β protons of ring B then give rise to triplets and the α -protons to doublets corresponding to a simple first-order spectrum. At first sight, it may seem surprising that the assignment in Figure 1 implies that the α -protons in ring A give rise to triplets but this is a known consequence⁸ of coupling in an ABX system when, as here, the chemical shifts of the A and B protons (3- and 2-H) are very similar. The same type of spectrum is observed for the aromatic protons of furfuryl alcohol.⁹ The assignment of Figure 1 has therefore been used in the interpretation of the exchange experiments.

One possible weakness in the above analysis comes from the sensitivity of the calculated shifts [equation (1)] to the assumed position of the europium atom. Independent evidence on the correctness of this position is provided by the effect of the shift reagent on the

absorption of the five types of aliphatic proton present in the amine. The positions and multiplicities of these peaks enable them to be assigned with little ambiguity: thus, the methyl and bridgehead protons give rise to sharp doublets and the others to more complex peaks. The observed and calculated effects of the shift reagent on these peaks are included in Figure 2: for the methyl and bridgehead protons, agreement is excellent but the shifts of the methine protons on the bridge are *ca.* 30% greater than the expected values. It is possible that this discrepancy could be removed by a slight change in the position of the europium atom but since these are the nearest protons to the europium atom the discrepancy could also arise by contact interaction¹⁰ transmitted through the σ -bonds. The fact that the peaks for the aromatic protons and the other aliphatic protons lie on the same line suggests that the assumed position of the europium atom is essentially correct.

Hydrogen-isotope Exchange.—These experiments were carried out by dissolving the amine (III) in the deuterating acid, maintaining the solution at 25° for an appropriate time, and then neutralising the solution and extracting the partially deuterated amine with chloroform. The integrated absorption of the aromatic peak in the n.m.r. spectrum of the product was used as a measure of the overall extent of deuteration and the integrated absorptions of the individual peaks in the presence of $\text{Eu}(\text{dpm})_3$ were used to calculate the extent of exchange at the different aromatic positions. In these calculations, the integrated absorptions of the bridgehead and methyl protons were used as standards. The shapes and relative intensities of the aliphatic peaks do not change during deuteration. The conditions used and the results obtained are shown in Table 1. Under these conditions, the n.m.r. spectra of the deuterated amine give no evidence of side-reactions accompanying deuteration, but some side-reaction (probably sulphonation)¹¹ does occur when the D_2O is omitted from the reaction mixtures.

The integrated proton absorptions in Table 1 are based on a number of integrations usually extending over several concentrations of $\text{Eu}(\text{dpm})_3$. With the exception of one measurement, all the integrated absorptions lie within ± 0.1 of the quoted values so these will be taken as the effective limits of error. The accuracy is sufficient to establish the three main features of this set of relative reaction rates.

The most surprising feature is the similar reactivity of the two aromatic rings. For the complete set of results in Table 1, the mean ratio (exchange in ring A) : (exchange in ring B) = 1.07. These reactions must involve attack on the protonated amine (see below) and so it appears that the nitrogen pole deactivates both rings to a similar extent.

The results also show that, for both rings, the total

⁸ J. W. Emsley, J. Feeney, and L. H. Sutcliffe, 'High Resolution Nuclear Magnetic Spectroscopy,' Pergamon, Oxford, 1965, vol. 1, p. 365.

⁹ R. J. Abraham and H. J. Bernstein, *Canad. J. Chem.*, 1961, **9**, 216.

¹⁰ R. K. Mackie and T. M. Shepherd, *Org. Magnetic Resonance*, 1972, **4**, 557.

¹¹ R. Taylor in 'Comprehensive Chemical Kinetics,' eds. C. H. Bamford and C. F. H. Tipper, Elsevier, Amsterdam, 1972, vol. 13, p. 255.

rate of exchange in the β -positions is much faster than that in the α -positions. Thus, when positions 6 and 7 have exchanged 1.6 protons, positions 5 and 8 have exchanged 0.47 protons (Table I, run 4). This difference was expected since the β -protons of triptycene are more reactive than the α -protons by a factor¹² of *ca.* 7 for hydrogen-isotope exchange in trifluoroacetic acid.

Finally the results indicate that the pair of α - or β -positions in a given ring exchange at markedly unequal rates. For the α -positions in ring A, this result is

based on the first four runs in Table I. Exchange at the 1-position leads to a rate coefficient of $1.7 \times 10^{-6} \text{ s}^{-1}$. Exchange at the β -positions leads to a curved plot as would be expected from the different reactivity of the two β -positions in each ring. Since exchange at the more reactive β -position is essentially complete after 94 h, the result for 142 h has been used to calculate the rate coefficient for exchange at the less reactive β -position giving $1.8 \times 10^{-6} \text{ s}^{-1}$. The use of this value in conjunction with the earlier results gives a rate coefficient of

TABLE I
Deuteration of the aromatic positions of the amine (III) at 25°

Run no.	Solvent composition /mole %			[amine]/ M	t/h^{-1}	Exchange (%)	Integrals of proton signals ^a				
	CF ₃ CO ₂ D	D ₂ SO ₄	D ₂ O				4-H	1-H	5-H, 8-H	2-H, 3-H	6-H, 7-H
1	79.6	12.5	7.9	0.15	16	14	1.0	0.93	1.93	1.5	1.5
2	79.6	12.5	7.9	0.15	40	28	0.93	0.87	1.87	1.05	1.1
3	79.6	12.5	7.9	0.15	94	41	0.9	0.6	1.86	0.7	0.6
4	79.6	12.5	7.9	0.15	142	51	0.83	0.53	1.63	0.4	0.4
5	82.8	10.5	6.6	0.15	41.5	22	1.0	0.9	2.0	1.1	1.2
6	4.9	38.8	56.3	5×10^{-3}	22	43	0.9	0.75	1.8	0.6	0.5
7 ^b	0.0	46.8	52.4	9×10^{-3}	0.08	10	1.0	1.0	2.0	1.6	1.6

^a After calibration in terms of proton numbers. ^b 0.8 mole % dimethyl sulphoxide also present.

obvious from the integrated absorptions and, for the β -positions in ring A, this result comes from the form of the n.m.r. spectrum. Thus, the spectrum of run 3 (Figure 3) shows that when the total exchange in the 2- and 3-positions is 1.3 protons, the 4-H signal is a singlet and the 1-H signal a triplet. This is consistent with almost complete exchange at the 3-position and partial exchange at the 2-position. The highest concentration of Eu(dpm)₃ used (0.98 mol per mole amine) leads to a partial separation of the β -protons in ring B and the spectrum of run 3 shows that exchange at the more reactive β -position is then effectively complete.

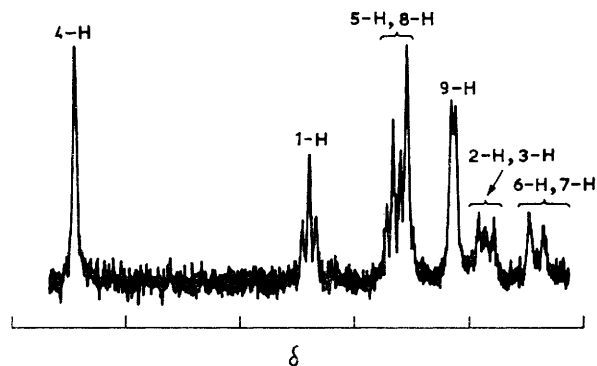


FIGURE 3 N.m.r. spectrum (60 MHz) of the reaction product of run 3 (Table I) in the presence of 0.98 mole Eu(dpm)₃: mole amine. Under these conditions, the signal of one of the bridge-head protons (9-H) is present in the aromatic region of the spectrum

The accuracy of the results in Table I is barely sufficient to justify a more detailed kinetic analysis but this has been attempted for the more reactive positions and the conventional first-order plots are shown in Figure 4

¹² R. Taylor, G. J. Wright, and A. J. Homes, *J. Chem. Soc. (B)*, 1967, 780; see also footnote in ref. 11, p. 245.

$1.0 \times 10^{-5} \text{ s}^{-1}$ for exchange at the more reactive β -position. These rate coefficients, together with that for exchange in benzene under these conditions (1.1×10^{-5}

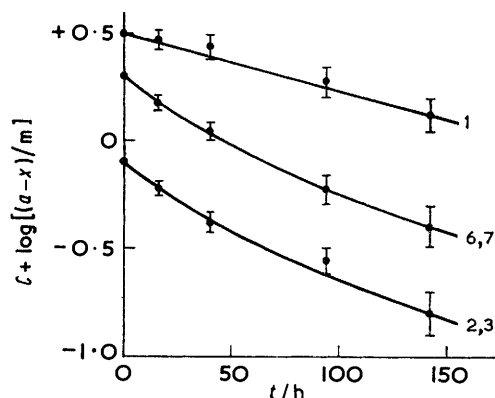
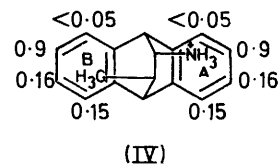


FIGURE 4 The variation of the logarithm of the integrated proton signals ($a-x$) with time for the more reactive positions in the conjugate acid of the amine (III). The constant C has the values: 1-H, 0.5; 6-H, 7-H, 0.0; 2-H, 3-H, -0.4. For conditions see text. The indicated errors correspond to ± 0.1 in ($a-x$)

s^{-1}) give the approximate partial rate factors shown in (IV). For ring A, the identity of the more reactive α - and β -positions is clear from the n.m.r. spectrum and the



figures below assume that the similarity in the overall reactivity of the α - and β -positions in the two rings comes from a similarity in the reactivity of corresponding positions.

DISCUSSION

In the absence of the deactivating effect of the nitrogen pole, the reactivity of the aromatic positions of (IV) to deuteration in trifluoroacetic acid would be expected to be similar to those of triptycene (f_α 51, f_β 363).¹³ The nitrogen pole therefore deactivates the more reactive β -position in the ion (IV) by a factor of *ca.* 360 and the more reactive α -position by a factor of *ca.* 500. These figures rule out the possibility of any significant reaction through the free amine form, from the pK_a of aliphatic amines (*ca.* 10.6) and the H_0 value of trifluoroacetic acid (*ca.* -3),¹⁴ less than one molecule in 10^{13} should be present as the free base.

Considered as a reaction of the conjugate acid, the most surprising feature of the above results is the similar reactivity of the two aromatic rings. The distances between the nitrogen pole and the centres of the two rings (3.5 and 5.2 Å) are very similar to those in structures (I) and (II) respectively. From this comparison, the reactivity of the two rings of (IV) was expected to differ by a factor of 10 in nitration² and by rather more in hydrogen-isotope exchange.¹

The absence of this reactivity difference can hardly be ascribed to an error in the assignment of the proton signals since the assignment of the proton signals to the two rings comes not merely from equation (1) but also from the double resonance experiments and is confirmed by the spin-spin splitting in the partly deuteriated reaction products. Various special mechanisms of exchange have been considered, in which the NH_3^+ group facilitates substitution in ring A by proton transfers during substitution but these appear to be ruled out by the fact that the NH protons do not exchange with the solvent during reaction in the acidic medium: these protons give rise to absorption *ca.* 1 p.p.m. upfield from the aromatic signal. The equal reactivity of the two rings is not a special consequence of reaction in trifluoroacetic acid (*e.g.* because of ion-pairing) but occurs also for reaction in aqueous sulphuric acid (Table 1, run 7).

It appears therefore that the equal deactivation of the two rings is not a consequence of the particular reaction conditions or of some special mechanism of substitution but truly reflects the substituent effect of the nitrogen pole which, in this system, behaves as if it were transmitted solely through the chemical bonds. This interpretation receives support from the pattern of reactivities within a given ring for, at least in ring A, the less reactive α - and β -positions are respectively *ortho* and *para* to the shortest carbon chain between the nitrogen pole and the ring. The reason for the apparent absence of the field effect of the nitrogen pole is not clear, but discussion of this problem is deferred until after the consideration of further experimental work in the following papers.

EXPERIMENTAL

Materials.—The amine (III) was prepared by the addition of 1-nitropropane to anthracene as described by Noland

¹³ Calculated from the rate coefficients given in ref. 11, p. 244—245.

*et al.*¹⁵ followed by reduction of the nitro-adduct to the corresponding amino-compound. This reduction was found to occur more readily with Fe-HCl than with the recommended¹⁵ Raney Ni-H₂. The product, after recrystallisation from ethanol had m.p. 109—112° (lit.,¹⁵ 111—113°), (Found: C, 86.4; H, 7.1; N, 5.9. Calc. for C₁₇H₁₇N: C, 86.8; H, 7.3; N, 6.0%). AnalaR benzene was used without further purification. Deuteriosulphuric acid (Ciba; 96—98%; >99.5 atom % D) was diluted with deuterium oxide (Norske-Hydro, 99.8 atom % D). These solutions were standardised by titrating a known weight against aqueous sodium hydroxide using phenolphthalein as indicator. Solvents for the kinetic runs were prepared by dissolving a known weight of the standardised D₂SO₄-D₂O solution in a known weight of deuteriotrifluoroacetic acid (Ciba; >99.5 atom % D). The shift reagent trisdipivaloylmethanatoeuropium(III) was obtained from Alfa Inorganics.

N.m.r. Measurements.—Spectra were recorded on either a Varian HA100 or a Varian T 60 instrument; the former was used for the double resonance experiments and the latter for the integrations required in the kinetic studies. In the assignment of the proton signals, a quantity of the amine (0.02—0.05 g) was weighed into an n.m.r. tube, dissolved in chloroform, and successive known weights of Eu(dpm)₃ added. The slopes of the induced shifts against the Eu(dpm)₃: amine ratio are listed in Table 2. The initial part of these plots was non-linear, probably because of traces of water in the solvents used.¹⁶

The calculation of the geometrical factors required in equation (1) and Figure 2 were carried out on a 1 in to 1 Å model of the geometry described above. The relevant quantities are included in Table 2.

TABLE 2

Comparison of the geometrical factor for pseudo-contact interactions [$(3\cos^2\phi - 1)r^{-3}$] with the slopes (G) of the plots of induced shift ($\delta\Delta$) against the shift reagent ratio [mol Eu(dpm)₃: mol amine]. The assignment of the aromatic protons is chosen to give the linear plot in Figure 2

Proton	$r/\text{Å}$ ^a	ϕ (°) ^b	$10^3(3\cos^2\phi - 1)r^{-3}/\text{Å}^{-3}$	$G/\text{p.p.m.}$
4	6.55	32.5	4.07	7.08
3	8.2	35.5	1.81	2.35
2	9.1	26	1.89	2.35
1	8.6	17	2.74	4.54
8	9.7	11	2.07	3.74
7	10.75	21.5	1.28	1.87
6	9.9	31.5	1.22	1.87
5	7.85	33	2.28	3.74
10	5.45	25	9.12	15.3
9	7.85	12.5	3.84	6.4
12	5.4	20.5	10.4	25.0
11	4.65	25	14.5	30.0
CH ₃	6.5	33	4.02	7.2

^a H-Eu distance. ^b H-Eu-N internuclear angle.

The spectra of the partly deuteriated amines were measured as described above. The integrated absorptions listed in Table 1 are based on a number of separate integrations carried out with different concentrations of Eu(dpm)₃.

¹⁴ R. A. Garber and W. H. Hyman, *J. Amer. Chem. Soc.*, 1959, **81**, 1847.

¹⁵ M. S. Baker, H. I. Freeman, and W. E. Noland, *J. Amer. Chem. Soc.*, 1956, **78**, 188.

¹⁶ J. K. M. Sanders, S. W. Hanson, and D. H. Williams, *J. Amer. Chem. Soc.*, 1972, **94**, 5325.

Kinetic Studies.—The amine (III) was dissolved in the deuterating solvent (*ca.* 2 cm³ at 25 ± 0.1°) to give the concentrations listed in Table 1. For runs 1—5 (Table 1), the progress of the reaction was monitored by following the change in the integrated absorption of the aromatic protons. After a suitable time, the reaction mixture was neutralised with sodium hydrogen carbonate, made up to 20 cm³ with water and extracted with AnalaR chloroform (4 × 20 cm³). The organic layer was washed with water (4 × 20 cm³) and dried (Na₂SO₄); the solvent was then removed using a rotary evaporator. Weighed samples of the amine were then dissolved in deuteriochloroform and treated with Eu(dpm)₃ as described above. The neutralisation and product analysis for runs 6 and 7 were carried out as described above but the low concentrations of the amine

made it impossible to monitor the progress of these reactions from the n.m.r. spectrum of the acidic medium. The experiments with benzene were carried out by the addition of benzene (15μl) to the deuterating medium (0.5 cm³; CF₃-CO₂D, 79.6; D₂SO₄, 12.5; D₂O, 7.9 mol %) in an n.m.r. tube containing toluene in a sealed capillary. The variation in the integrated absorption of the protons of benzene with time was calibrated with respect to that of the aromatic protons of toluene and used to calculate the first-order rate coefficient in the usual way. Linear plots were obtained up to 70% reaction.

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