Electrochemical Reactions. Part 19.[1] Intermolecular Radical Substitution during the Reduction of 2-Halogeno-*N*-methylbenzanilides

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The reduction of 2-halogeno-*N*-methylbenzanilides gives *N*-methyl-*N*-phenylcarbamoylphenyl radicals, which (i) react by substitution to yield phenanthridones and biphenyl-2-carboxamides or (ii) are reduced further to the *N*-methylbenzanilide. Occurrence of the substitution process confirms the presence of phenyl radical intermediates. The maximum yield of intramolecular substitution products is limited by the proportion of *syn*-amide rotamer present at equilibrium. When the halogen is chlorine, intramolecular trapping of the resulting phenyl radical is an efficient process and only the *anti*-amide rotamer forms the *N*-methylbenzanilide. When the halogen is bromine or iodine a significant proportion of the phenyl radical derived from the *syn*-amide rotamer is also converted by further reduction and protonation into the *N*-methylbenzanilide. Intramolecular radical substitution leads to both phenanthridones and biphenyl-2-carboxamides when the aniline component of the *N*-methylbenzanilide does not carry an *ortho*-substituent. Only the biphenyl-2-carboxamide is formed when an *ortho*-substituent is present on the aniline component. These results are compared with the results from related radical reactions.

THE overall reaction observed during electrochemical reduction of aryl halides is replacement of the halogeno-substituent by a hydrogen atom. For some halogenated derivatives of nitrobenzene,[2,3] benzophenone,[4] fluorenone,[4,5] and benzonitrile [6] it has been possible to demonstrate the stages in this reduction in aprotic solvents: (i) formation of a π-radical-anion which is in redox equilibrium with the substrate, (ii) decomposition of this radical-anion in a reaction with measurable first-order kinetics to generate a σ-radical and a halide ion, and (iii) either abstraction of a hydrogen atom from the solvent [3] by the σ-radical, or reduction of this σ-radical to a carbanion [1] which is protonated by traces of water remaining in the solvent. It is not, however, possible to demonstrate the individual steps in the reduction of the vast majority of aryl halides by purely electrochemical methods. It occurred to us that if the σ-radical is intermediate in the reduction of most aryl halides, as is presumed, then by choosing a substrate with a suitably placed phenyl substituent the σ-radical intermediate will be made to undergo an intramolecular cyclisation reaction in competition with other processes which may occur. A preliminary communication [7] of our first experiments on the reductive cyclisation of 2-halogeno-*N*-methylbenzanilides has appeared. We have also published parallel studies [8] on the use of the electrochemical cyclisation for the synthesis of condensed nitrogen aromatic heterocycles.

In our first experiments to demonstrate this reductive cyclisation, 2-bromo- and 2-iodo-4′-methoxy-*N*-methylbenzanilides (1a; X = Br or I) were reduced in dimethylformamide. The products were separated by chromatography and crystallisation and consisted of the benzanilide (7a) and a mixture of the phenanthridone (5a) and the biphenylcarboxamide (6a). The last two compounds can be considered as the final products of a radical cyclisation which proceeds *via* the intermediate radicals (3a) and (4a). Reduction of 2-iodo-*N*-methylbenzanilide gave *N*-methylbenzanilide, *N*-methylphenanthridone and *N*-methylbiphenyl-2-carboxamide.

The formation of (7a) along with (5a) and (6a) indicates that there is competition between the direct replacement of halogen by hydrogen and the cyclisation of intermediates. We have examined the reduction of related halogen-substituted *N*-methylbenzanilides in order to shed more light on this competition.

Hey [9] and his co-workers have carried out many studies on the cyclisation of σ-radicals of the general formula (2) derived either from *o*-aminobenzoyl-*N*-methylanilines by a diazonium reaction or from *o*-iodobenzoyl-*N*-methylanilines by a photochemical re-

[1] Part 18, J. Grimshaw and J. Trocha-Grimshaw, *J.C.S. Perkin II*, 1975, 215.

[2] J. G. Lawless and M. D. Hawley, *J. Electroanalyt. Chem.*, 1969, **21**, 365; R. P. Van Duyne and C. N. Reilley, *Analyt. Chem.*, 1972, **44**, 158; W. C. Danen, T. T. Kensler, J. G. Lawless, M. F. Marcus, and M. D. Hawley, *J. Phys. Chem.*, 1969, **73**, 4389.

[3] R. F. Nelson, A. K. Carpenter, and E. T. Seo, *J. Electrochem. Soc.*, 1973, **120**, 206.

[4] L. Nadjo and J. M. Saveant, *J. Electroanalyt. Chem.*, 1971, **30**, 41.

[5] J. Grimshaw and J. Trocha-Grimshaw, *J. Electroanalyt. Chem.*, 1974, **56**, 443.

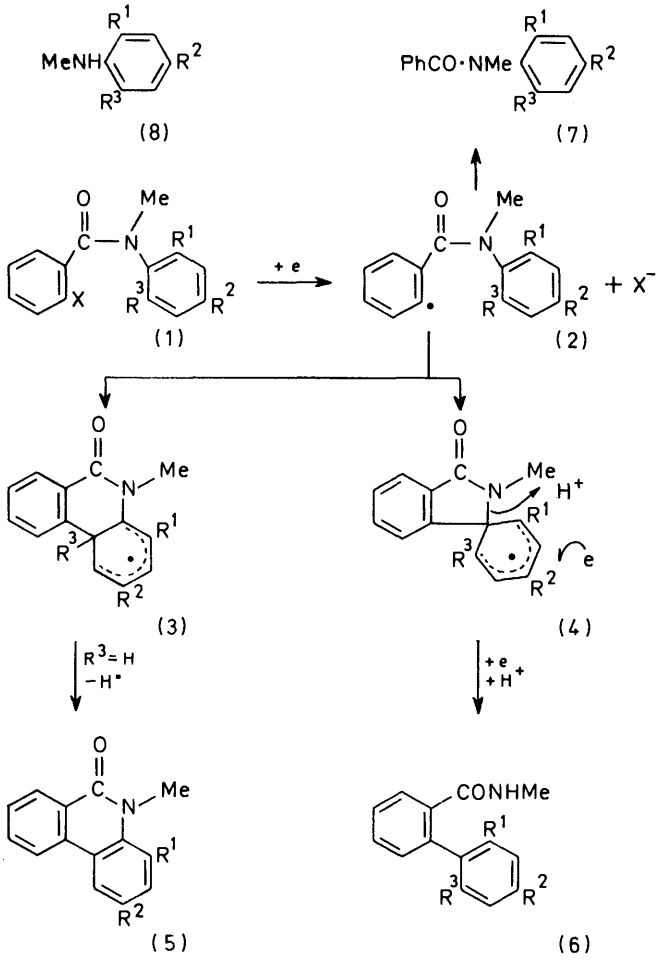
[6] D. E. Bartak, K. J. Houser, B. C. Rudy, and M. D. Hawley, *J. Amer. Chem. Soc.*, 1972, **94**, 7526; K. J. Houser, D. E. Bartak, and M. D. Hawley, *ibid.*, 1973, **95**, 6033.

[7] J. Grimshaw and J. Trocha-Grimshaw, *Tetrahedron Letters*, 1974, 993.

[8] W. J. Begley, J. Grimshaw, and J. Trocha-Grimshaw, *J.C.S. Perkin I*, 1974, 2633; J. Grimshaw and J. Trocha-Grimshaw, *Tetrahedron Letters*, 1975, 2601.

[9] Reviewed by D. H. Hey, *Quart. Rev.*, 1971, **25**, 483; see also references 18—20, 23, 26, 27, and 29.

action and interpret these results in terms of an initial cyclisation of the radical to give (3) and (4). The ultimate fate of these radicals when generated under such



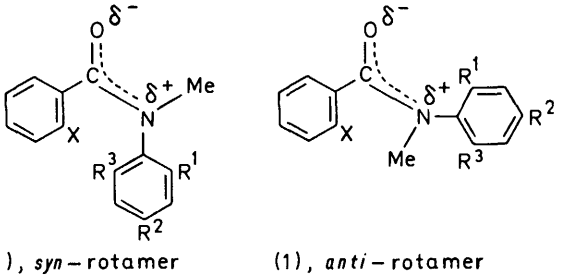
where X=Cl, Br or I and a; $R^1=R^3=H$, $R^2=OMe$
b; $R^1=R^3=H$, $R^2=Me$
c; $R^2=R^3=H$, $R^1=Me$
d; $R^2=H$, $R^1=R^3=Me$

conditions is to yield a mixture containing a large proportion of dimeric products. Hey's results and ours will be compared at the end of this paper but clearly some of the intermediate stages must be common to the reactions of both the chemically (as in Hey's case) and the electrochemically generated σ-radicals.

In a quantitative investigation of the electrochemical reaction, the yields of products formed in the reduction of 2-halogeno-*N*-methylbenzanilides were determined by n.m.r. spectroscopy. We used amides derived from the toluidines so as to have both *C*-Me and *N*-Me n.m.r. signals available as monitors of concentration. These electrochemical reductions were carried out in anhydrous dimethylformamide and the products were separated for identification purposes by column chromatography and crystallisation. After characterisation of the products, the compositions of mixtures from small-scale runs were determined after isolation of the total reaction mixture and thorough washing to remove solvent and supporting electrolyte.

The half-wave potential for reduction of the halogeno-substituent in compounds (1a—d) would be expected to be independent of the substituent on the aniline ring within ±0.03 V and this expectation was verified for a few examples in Table 6. In the following experiments the halogeno-compounds were reduced at cathode potentials near to the $E_{\frac{1}{2}}$ values reported in this Table. The reduction wave at more negative potentials around −2.5 V is due to reduction of the amide groups.

Slow Rotation about the Amide Bond.—It is well known that slow rotation about the amide bond occurs, and the equilibrium between *syn*- and *anti*-forms can be investigated by n.m.r. spectroscopy.[10] In order to interpret the product ratios which result from electrochemical reduction of the halogeno-*N*-methylbenzanilides, it is necessary first to determine the equilibrium ratio of *syn*- and *anti*-forms and to decide if the rate of interconversion of these forms is significant with respect to the rates of the steps in the process initiated by electron transfer. A few pertinent rates of interconversion are included in Table 1. There has been no systematic study made of the *N*-methylbenzanilides.



(1), *syn*-rotamer (1), *anti*-rotamer

The barrier to rotation about the amide bond occurs because of the dipolar resonance contribution to this bond. When either the carbonyl group or the nitrogen lone pair is conjugated with a phenyl substituent the barrier to rotation about the amide bond relative to dimethylformamide is lowered. This barrier is raised by the presence of an *ortho*-substituent on the benzene ring because the interaction between this *ortho*-substituent and other groups tends to force the benzene ring out of the plane of the amide group and so reduce the conjugation between the benzene ring and the amide group. Some results from the literature, together with our own results illustrating these effects, are given in Table 1.

N-Methylbenzamides show two bands in the n.m.r. spectrum due to *N*-CH_3 groups in the *syn*- and *anti*-rotamers. The assignment of such lines to a particular amide rotamer has recently been appraised critically.[11] In the case of *NN*-dimethylbenzamides, the upfield

[10] W. E. Steward and T. H. Siddall, *Chem. Rev.*, 1970, **70**, 517.
[11] A. H. Lewin and M. Frucht, *Org. Magnetic Resonance*, 1975, **7**, 206.

line is assigned to the methyl group *anti* to the carbonyl group and this line undergoes the greater upfield shift when the chloroform solvent is changed to benzene. Using these criteria on two of our *N*-methylbenzanilides, we conclude that the upfield N-CH_3 resonance is due to the *anti*-rotamer.

The *syn* : *anti* ratios for our *N*-methylbenzanilides are at equilibrium. This is the situation which would be expected as a result of steric interactions between substituents on adjacent benzene rings. Thus *ortho*-substitution in one benzene ring causes an increase in steric strain for both rotamers so that overall the equilibrium ratio is changed little. However *ortho*-substitution in both benzene rings causes more steric interaction

TABLE 1

Hindered rotation in amides

Compound	$K = \left[\frac{anti}{syn}\right]$	ΔG_c^*/kJ mol^{-1} *syn* ⟶ *anti*	T_c/°C	Solvent	Ref.
2-Methylacetanilide	0.06		15	$CDCl_3$	*a*
2,6-Dimethylacetanilide	0.35	73.2	57	$CHBr_3$	*a*
NN-Dimethylbenzamide	1.00	65.8	30	$CDCl_3$	*b*
NN,2,4,6-Pentamethylbenzamide	1.00	94.1	168	α-$C_{10}H_7Cl$–$PhCCl_3$	*c*
(1c; X = Cl)	0.37	88.1	118	$CDCl_3$	*d*
(1d; X = Cl)	1.94	See *d*	160	$CDCl_3$	*d*

[a] Ref. 13. [b] K. Spaargaren, P. K. Korver, P. J. van der Haak, and Th. J. de Boer, *Org. Magnetic Resonance*, 1971, **3**, 615. [c] A. Mannschreck, A. Mattheus, and G. Rissmann, *J. Mol. Spectroscopy*, 1967, **23**, 15. [d] This paper. For (1c; X = Cl): b_e = 1.80 Hz, $\Delta\nu$ = 20.8 Hz. For (1d; X = Cl): k(*syn* ⟶ *anti*) = 8.7 × 10^{-4} s^{-1} at 35 °C, determined by following the conversion of crystalline *syn*-rotamer into the equilibrium mixture.

TABLE 2

Data for the *N*-methylbenzanilides (1)

Compound (1)	M.p. (b.p.) (°C)	Found (%)	N.m.r. data ($CDCl_3$) τ($CDCl_3$) [a] *N*-Me	*C*-Me	Coalescence temp. (°C) for *N*-Me peaks	Ratio [b] *syn* : *anti* rotamer
R^1 = R^3 = H, R^2 = Me						
X = Cl	55—57	C, 69.1; H, 5.3; Cl, 13.7; N, 5.3 [c]	6.52	7.76	Not determined	
X = Br	66—69	C, 59.5; H, 4.7; Br, 26.2; N, 4.6 [d]	6.54	7.79	50	95 : 5 (at 10 °C)
X = I	76—78	C, 51.2; H, 4.0; I, 36.0; N, 4.0 [e]	6.58	7.82	Not determined	
X = H	46—48	(Lit.,[f] m.p. 46—48°)	6.55	7.78	Not determined	
R^1 = R^2 = H, R^3 = Me						
X = Cl	(146 at 0.2 mmHg)	C, 69.1; H, 5.4; N, 5.3 [c]	*syn*-6.60	7.68	110	73 : 27
			anti-6.88	7.61		
X = Br	73—74	C, 59.3; H, 4.5; Br, 26.3; N, 4.3 [d]	*syn*-6.61 [k]	7.65	115	72 : 28
			anti-6.92	7.61		
X = I	104—105	C, 51.2; H, 4.2; N, 4.0 [e]	*syn*-6.60	7.63	120	71 : 29
			anti-6.91	7.60		
X = H	64—65	(Lit.,[f] m.p. 65—66°)	6.76	7.81	Not determined	
R^1 = R^3 = Me, R^2 = H						
X = Cl	110—115	C, 70.5; H, 5.8; Cl, 13.1; N, 4.9 [g]	*syn*-6.64 [l]	7.70	160	34 : 66
			anti-6.97	7.63		
X = Br	122—126	C, 59.2; H, 5.2; Br, 26.2; N, 4.5 [h]	*syn*-6.55	7.59	Not determined	31 : 69
			anti-6.88	7.53		
X = I	105—130	C, 52.7; H, 4.6; N, 3.9%	*syn*-6.65	7.68	160	25 : 75
			anti-6.97	7.56		
X = H	120—121	(Lit.,[j] m.p. 127°)	*syn*-6.63	7.72	Not determined	90 : 10
			anti-6.81	7.60		

[a] At ambient temperature. Where no isomer is specified, only one coalesced peak was observed. [b] At ambient temperature unless otherwise stated. [c] $C_{15}H_{14}ClNO$ requires C, 69.4; H, 5.4; Cl, 13.7; N, 5.4%. [d] $C_{15}H_{14}BrNO$ requires C, 59.3; H, 4.6; Br, 26.3; N, 4.6%. [e] $C_{15}H_{14}INO$ requires C, 51.3; H, 4.0; I, 36.1; N, 4.0%. [f] Ref. 28. [g] $C_{16}H_{16}ClNO$ requires C, 70.2; H, 5.9; Cl, 12.9; N, 4.9%. [h] $C_{16}H_{16}BrNO$ requires C, 58.9; N, 5.3; Br, 26.1; N, 4.6%. [i] $C_{16}H_{16}INO$ requires C, 52.6; H, 4.4; N, 3.8%. [j] Ref. 30. [k] Upfield shifts in C_6D_6: *syn* 0.22, *anti* 0.46. [l] Upfield shifts in C_6D_6: *syn* 0.25, *anti* 0.52.

given in Table 2. When *ortho*-substitution is present on one benzene ring only, the *syn*-rotamer predominates at equilibrium to the extent of 90% or greater. Substitution of each benzene ring by a single *ortho*-substituent decreases the proportion of *syn*-rotamer at equilibrium. When a total of three *ortho*-substituents is present the *anti*-rotamer becomes the major component for the *syn*- than for the *anti*-rotamer and so greatly influences the isomer ratio at equilibrium.

For a given series of compounds where the halogen is changed from chlorine to iodine, there is a decrease in the amount of *syn*-rotamer at equilibrium due to the increasing size of the halogen group. This effect is particularly noticeable in the series of compounds

derived from 2,6-dimethylaniline where the halogen interacts with two *ortho*-substituents on the adjacent ring.

Electrochemical Reduction.—Reduction of the amides (1b) derived from *p*-toluidine gave results which are relatively easy to interpret because these amides exist predominantly in solution as the *syn*-rotamer (see Table 2). Product yields are collected in Table 3. The

TABLE 3

Yields of products from reduction of halogeno-*N*-methylbenzanilides in anhydrous dimethylformamide (0.1M in Pr_4NClO_4)

Compound (1)	Yields (%) of reduction products [a] (7)	(5)	(6)	(8)
	$R^1 = R^3 = H$ and $R^2 = Me$			
X = Cl	13	38	45	4
X = Br	26	33	38	3
X = I	45	26	24	5
	$R^1 = R^2 = H$ and $R^3 = Me$			
X = Cl	21	0	76	3
X = Br	50	0	49	1
X = I	72	0	23	5
	$R^1 = R^3 = Me$ and $R^2 = H$			
X = Cl	61	0	39	0
X = Br	63	0	34	3
X = I	93	0	7	0

[a] Relative yields determined by an n.m.r. method on the total reaction sample by integrating the peaks due to *N*-Me or *C*-Me. Estimated error ±3%.

accuracy of our analytical procedure is estimated at *ca.* ±3%. Thus since the amount of *anti*-rotamer present is only 5%, the accuracy of measurement does not warrant a discussion of the influence of *anti*- to *syn*-interconversion.

For the three amides (1b) the chloro-compound gives the lowest yield of product (7b) from replacement of the halogen by hydrogen, and the iodo-compound gives the highest yield of this product. This dependence of product yield on the halogen is shown also in the other series of amides which we have examined. The products (5b) and (6b) result from intramolecular radical substitution reactions. In the case of the chloro-compound the total yield of (5b) and (6b) is close to the proportion of *syn*-rotamer present at equilibrium, so the intramolecular substitution process is efficient.

For the amides (1c) derived from *o*-toluidine, the proportion of *anti*-rotamer at equilibrium is significant. Before proceeding to an interpretation of the yields of products formed from electrochemical reduction we must examine the rate of the *anti*-to-*syn* interconversion, which may be high or low relative to the rate expected for the reactions of radical (2c). These amides show two lines in the n.m.r. spectrum at ambient temperatures due to the *N*-Me groups of the *syn*- and *anti*-rotamers. The lines coalesce at *ca.* 115 °C. The rate constant for the *syn*-to-*anti* conversion was calculated at the coalescence temperature for 2-chloro-*N*,2′-dimethylbenzanilide by the method of Jaesche.[12] Spectra were taken at a range of temperatures from ambient to coalescence. Values of the natural line width b_e, the equilibrium constant K { = [*anti*-rotamer]/[*syn*-rotamer]}, and the chemical shift difference, $\Delta\nu$, between the two *N*-Me signals were then extrapolated to the coalescence temperature, T_c, from the region where they are linearly dependent on temperature. The rate constant k (13.7 s^{-1}) for the process *syn* ⟶ *anti* at T_c was then obtained by substituting the values into Jaesche's diagram. These results are given in Table 1. With sufficient accuracy for our purpose, we can neglect the dependence of ΔG^* on temperature so that application of the Eyring equation (i), where k_B is Boltzmann's constant and h is Planck's constant, gives $k = 2 \times 10^{-3}$ s^{-1}

$$k = k_B T/h \exp(-\Delta G^*/RT) \qquad \text{(i)}$$

at 25 °C. Thus the rate of interconversion of *syn*- and *anti*-rotamers, for compounds (1c) is so low as to be negligible as compared with the rate of the radical reactions which follow the addition of an electron to the molecule.

We required the *syn* : *anti* ratio in dimethylformamide which is the solvent used in the electrochemical reduction. It was not possible to determine this value directly as deuteriated solvent was not available. Instead we examined the variation of this ratio with polarity of the solvent for the bromo-compound (1c; X = Br). The results (Table 4) show that the proportion of *anti*-isomer increases with increasing polarity of the solvent but the effect is small. A similar small effect was observed for the amide (1d; X = Br) derived from 2,6-dimethylaniline. The dipolar resonance form of these amides should make a greater contribution in polar solvents and this will stabilise the ground state relative to the activated state for the *syn* ⟶ *anti* conversion.

TABLE 4

Influence of solvent on the rotational equilibrium about the amide bond in some *N*-methylbenzanilides

Compound (1)	Deuteriated solvent	Equilibrium ratio (*syn* : *anti*)
$R^1 = R^2 = H$, $R^3 = Me$, X = Br	Chloroform	72 : 28
	Benzene	73 : 27
	Acetone	69 : 31
	Acetonitrile	65 : 35
	Pyridine	61 : 39
$R^1 = R^3 = Me$, $R^2 = H$, X = Br	Chloroform	31 : 69
	Pyridine	22 : 78

There is presumably no dipolar contribution to the activated state. Thus increasing solvent polarity should also raise the rotational barrier. This solvent effect on the rotational barrier for dimethylformamide is very small and close to the limits of experimental error.[10]

The results (see Table 3) for reduction of the chloro-compound (1c; X = Cl) show that the ratio of the product (6c) [formed by cyclisation of the radical (2c)] to the product (7c) is close to the *syn* : *anti* ratio for the substrate. This suggests that cyclisation of the radical (2c) is efficient in this case. The processes which give (7c) become more competitive when the intermediates

[12] A. Jaesche, H. Muensch, H. G. Schmidt, H. Friebolin, and A. Mannschreck, *J. Mol. Spectroscopy*, 1969, **31**, 14.

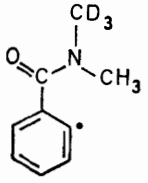
are derived from bromo- and iodo-compounds. A possible reason for this will be discussed later.

For the amides (1d) derived from 2,6-dimethylaniline the *anti*-rotamer is the more abundant at equilibrium. These amides crystallise as mixtures of individual crystals of the *syn*- and *anti*-rotamers and, when quickly precipitated, the mixture has a wide m.p. range. Relatively pure crystals of the *syn*-rotamer (1d; X = I) were obtained by slow crystallisation and their interconversion in solution was followed for the chloro-compound by the slow change in the height of peaks in the n.m.r. spectrum. For these amides the rate of interconversion of rotamers is negligible as compared with the rate of the reactions which follow the addition of an electron to the substrate. Isolation of pure rotamers of other *ortho*-substituted amides, 2,4,6-tri-t-butylacetanilide [13] and *N*-benzyl-*N*,2,4,6-tetramethylbenzamide,[14] has been achieved. The product yields from reduction of our amides (1d) are collected in Table 3. Reduction of the chloro-compound (1d; X = Cl) gives a ratio of the product (6d), formed by cyclisation of the radical (2d), to the product (7d) which is close to the *syn*:*anti* rotamer ratio at equilibrium. Again cyclisation of the radical (2) is efficient when the radical is derived from a chloro-compound but the processes which give (7d) become more competitive when the intermediates are derived from bromo- and iodo-compounds.

Discussion.—Reduction of the chloro-compounds (1b—d; X = Cl) gives close to the maximum yield of products which can be achieved from cyclisation of the intermediate radical (2) if we assume that the *syn*- and *anti*-rotamers do not undergo interconversion during the actual process of reduction. We have shown that for the examples (1c and d) where this interconversion could influence the product yields, its rate is so low that the interconversion can be neglected. We should estimate the rate of interconversion of amide rotamers of the radicals (2) since the removal of the *ortho*-substituent enables the aryl group to conjugate better with the carbonyl group and this lowers the energy of the amide rotational barrier. Ideally we need the value of the rotational barrier for the amides (1c and d with X = H) but this cannot be obtained easily because there is only 5—10% of the *anti*-rotamer present at equilibrium. These amides will however have the *ortho*-substituted aniline ring out of the plane of the amide group and the barrier to amide rotation will be close to that for *NN*-dimethylbenzamide. Cohen [15] has demonstrated that intramolecular hydrogen transfer in the aryl radical (9) is appreciably faster than rotation about the amide bond. Thus we conclude that in our radical reactions also the rate of rotation about the amide bond is sufficiently low to be neglected.

[13] H. Kessler and A. Rieker, *Annalen*, 1967, **708**, 57.
[14] A. Mannschreck, *Tetrahedron Letters*, 1965, 1341.
[15] T. Cohen, G. H. McMullen, and K. Smith, *J. Amer. Chem. Soc.*, 1968, **90**, 6866; T. Cohen, K. W. Smith, and M. D. Swerdloff, *ibid.*, 1971, **93**, 4303.
[16] W. Walter, Th. Fleck, J. Voss, and M. Gerwin, *Annalen*, 1975, 275.

The reaction of a σ-radical such as (2) with a hydrogen source is known to occcur by two mechanisms [1,3] discussed in a previous paragraph. We know that a substantial incorporation of deuterium occurs during the conversion of (1a; X = I) to (7a) in dimethylformamide



(9)

containing a little deuterium oxide.[1] Thus the reaction of radicals (2) to give (7) will proceed largely by the pathway which involves further reduction of the radical at the electrode to give a carbanion which is protonated by traces of water in the solvent. There will be a greater probability for reduction of the radical if it is generated closer to the electrode surface. Reaction of (1) with the electrode forms a radical anion which decomposes to give (2) and the rate of conversion of radical anion to (2) will increase in the order X = Cl, Br, I which is the order of decreasing C–X bond strength. Thus when X = I the radical (2) is formed closer to the electrode surface and will be further reduced at a greater rate than when X = Cl, so giving a higher yield of the product (7).

Compounds of general formula (1) can be expected to show restricted rotation about the aryl-to-carbonyl and aryl-to-nitrogen bonds because of steric interactions between bulky substituents. These interactions are equivalent to those which give rise to rotational isomerism in the biphenyl series. Rotational barriers have been measured for the aryl-to-carbonyl bond in 2-halogeno-*NN*-dimethylbenzamides [16] and the aryl-to-nitrogen bond in *ortho*-substituted *N*-alkylacetanilides.[17] The amides we have examined possess no suitable prochiral group to display these rotational phenomena in the n.m.r. spectrum. Unlike the rotamers about the amide partial π-bond, each of the low energy rotamers which results from this type of restricted rotation about a σ-bond will have an equal probability to undergo cyclisation of the derived radical for the processes here investigated.

Hey [9,18-20] and his co-workers have made a study of the intramolecular cyclisation of radicals of the general type (2). These radicals were generated either by the reduction of diazonium salts (1; with X = N_2^+ BF_4^-) in the presence of copper, or by the photolysis of iodo-compounds (1; X = I) under nitrogen. The yields of products generated by reactions of two such pairs of

[17] T. H. Siddall and W. E. Stewart, *J. Phys. Chem.*, 1969, **73**, 40.
[18] D. H. Hey, G. H. Jones, and M. J. Perkins, *J. Chem. Soc.* (*C*), 1971, 116.
[19] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972 1150.
[20] D. H. Hey, G. H. Jones, and M. J. Perkins, *J.C.S. Perkin I*, 1972, 1155.

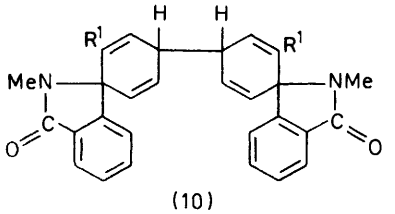
substrates are listed in Table 5. These examples are chosen because the product yields were determined by g.l.c. where practical. One pair is derived from aniline and the second from 2-methoxyaniline. The most noticeable difference between these and our electrochemical reactions is the formation of spiro-compounds such as the dimers (10), the monomer (11), and the dienone (12) which result under Hey's conditions from

TABLE 5

Comparison of yields of compounds from the photolysis of 2-iodo-*N*-methylbenzanilides in benzene under nitrogen and the Cu-catalysed decomposition of *N*-methyl-*N*-phenylcarbamoylbenzene-2-diazonium tetrafluoroborates in acetone

	Yield (%) [a] of product from (1)			
	$R^1 = R^2 = R^3 = H$		$R^1 = OMe$, $R^2 = R^3 = H$	
	X =		X =	
Product	X = I	$N_2^+BF_4^-$	X = I	N_2BF_4
N-Methylphenanthridone (5)	34—36 [b]	35—37 [b]	4 [c]	1.5 [c]
Spiro-dimers (10)	30—36	38—40	45	
Spiro-diene (11)	4—5			
Biphenylcarboxamide (6)	0.5—1			
Spiro-dienone (12)				68
Benzanilide	4—5	4—5		

[a] Determined by g.l.c., except for the dimers, which were determined by isolation. [b] Ref. 18. [c] Refs. 19 and 20.



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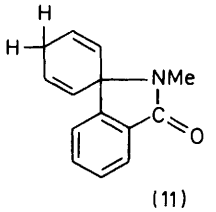

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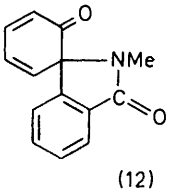

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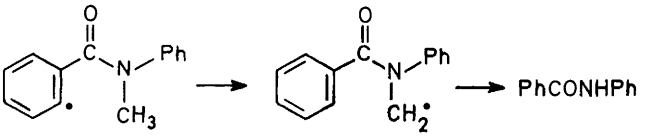
further reactions of the spiro-radical (4). In our reactions this spiro-radical is generated close to the cathode where it undergoes reduction to a carbanion with simultaneous cleavage of the carbon-to-nitrogen bond and protonation at the nitrogen atom. Thus under our conditions the spiro-radical (4) gives rise to the biphenylcarboxamide (6).

It has been shown in a previous paragraph that further reduction of the radical (2) at the electrode is unimportant when the radical is derived from a chloro-compound, unlike the situation for bromo- and iodo-compounds. Thus a comparison should be made between the yields of products from Hey's experiments and the yields from the reduction of the chloro-compounds in our experiments.

First we compare Hey's experiments [18] with iodo- and diazonium salt derivatives of *N*-methylbenzanilide and our experiments on the reduction of the chloro-compound (1b; X = Cl) derived from *p*-toluidine. The substrates here belong to the class of *N*-methylbenzanilides derived from an aniline with no *ortho*-substituent. We can take the total yield of spiro-compounds from Hey's experiments to be the equivalent of the yield of biphenylcarboxamide (6) in our experiments since these compounds are all derived from the spiro-radical (4). Within the framework thus laid down there is substantial agreement between Hey's results and our own obtained by using an n.m.r. analytical technique. In both sets of experiments there is the same degree of partitioning, within the limits of experimental error, of the radical (2) between pathways which proceed from (3) and (4). The benzanilide which was isolated in Hey's experiments was considered to arise from the *anti*-rotamer radical (13) by intramolecular hydrogen abstraction and further reactions of the $N-CH_2^{\bullet}$ radical.[19]

There is also substantial agreement between Hey's



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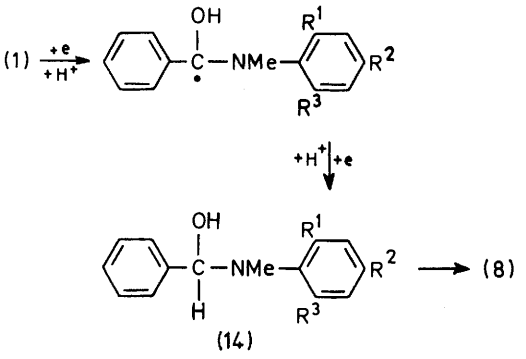
results [19,20] with substrates related to 2′-methoxy-*N*-methylbenzanilide and ours for the reduction of 2-chloro-*N*,2′-dimethylbenzanilide. The substrates here belong to a class of amides derived from an aniline with one *ortho*-substituent. In both Hey's set of experiments and ours, the derived radical (2) reacts to give almost exclusively the spiro-radical (4) and products derived from this. It is suggested that steric effects cause radicals such as (2) which bear substituents *ortho* to the amide nitrogen to adopt a conformation with the aniline ring perpendicular to the plane of the amide group. Positions 2 and 1′ are then brought within bonding distance whereas positions 2 and 2′ or 6′ are further apart. The radical (2) thus now gives products mostly derived from the spiro-radical (4) and only traces of the phenanthridone derived from radical (3). This same argument explains why reduction of the *N*-methylbenzanilides (1d) derived from 2,6-dimethylaniline also give no products of reaction *via* (3d).

In view of the good agreement with Hey's observations we have rejected the alternative hypothesis, introduced in a previous paper,[1] that the electrochemical cyclisation involves a reaction between the radical-anion from one benzene ring and the adjacent benzene ring. The small amounts of amine (8) which we isolated from electrochemical reductions probably arise by protonation of the initially formed radical-anion and then further reduction to an aldehyde-ammonia type of compound (14), which undergoes hydrolysis during work-up.

The photochemical reaction of some substituted 2-iodo-*N*-methyl benzanilides has yielded a more complex mixture of phenthridone isomers than can be explained



on the basis of the reaction sequence (1) ⟶ (2) ⟶ (3) ⟶ (5).[19] Formation of the unexpected phenanthridone isomers can be explained on the assumption that the radical (4) may rearrange by either carbon or nitrogen 1,2-migration and then give rise to a phenanthridone. The unexpected isomers were not formed after either pyridine or iodine had been added to the reaction mixture, but the reason for this is not clear. We have found no evidence in our electrochemical experiments for the formation of phenanthridones other than those expected from the route (1) ⟶ (2) ⟶ (3) ⟶ (5). The products which we obtained had physical constants which agreed with the values given in the literature where they had been obtained by the decomposition of diazonium sulphates (1; X = N_2^+ HSO_4^-) in an intramolecular electrophilic aromatic substitution reaction involving carbocations.

In conclusion, we can make predictions of the usefulness in synthesis of this reduction of 2-halogeno-*N*-methylbenzanilides. The maximum yield of intramolecular substitution products is limited by the proportion of *syn*-amide rotamer present at equilibrium and this proportion can usually be estimated by n.m.r. spectroscopy. The highest yields of products of intramolecular radical substitution result when the halogen substituent is chlorine. Both phenanthridone and biphenylcarboxamide derivatives result when the aniline component of the benzanilide bears no *ortho*-substituent. Only biphenylcarboxamides are formed when the aniline component does bear an *ortho*-substituent.

EXPERIMENTAL

N.m.r. spectra were obtained with a Varian A60 instrument ($CDCl_3$ as solvent, unless otherwise stated). Sealed sample tubes were used for measurements at elevated temperatures. Light petroleum had b.p. 40—60 °C.

Substrates.—Substituted *N*-methylbenzanilides were prepared from the appropriate acid chloride and *N*-methylaniline in pyridine solution. Where only the corresponding aniline was available, this was treated with the appropriate acid chloride and the resulting benzanilide methylated with sodium hydroxide and dimethyl sulphate (method A.)[18] This methylation process is only satisfactory for *o*-halogenobenzanilides. If the benzanilide contains no *ortho*-halogeno-substituent it is more satisfactorily methylated by first treating with sodium metal to give the sodium salt, which is treated with iodomethane (method B).[21] Physical and analytical data for the *N*-methylbenzanilides are collected in Table 2.

N,2,6-*Trimethylaniline*. Diborane was generated in a separate flask by addition of sodium borohydride (2.5 g) in anhydrous bis-(2-methoxyethyl) ether (60 ml) to boron trifluoride–ether (15 ml) dissolved in anhydrous bis-(2-methoxyethyl) ether (30 ml) and passed in a stream of nitrogen into a flask containing a solution of *N*-formyl-2,6-dimethylaniline (10 g) in tetrahydrofuran (150 ml). After 1 h the diborane generator was heated to 80 °C and the reaction was continued for a further 1 h. The mixture was then evaporated under reduced pressure and the residue dissolved in ether. N,2,6-*Trimethylaniline* was extracted into 2N-hydrochloric acid, liberated by base, collected in ether, dried ($MgSO_4$), and distilled; b.p. 83—85° at 9 mmHg (8.6 g, 93%) (Found: C, 79.1; H, 9.6; N, 10.2. $C_9H_{13}N$ requires C, 79.3; H, 9.6; N, 10.3%), τ 7.02 (s, NH), 7.26 (3 H, s, NMe), and 7.72 (6 H, s, ArMe), M^+ 135.

2-*Iodo*-2′,6′-*dimethylbenzanilide*. Prepared from 2-iodobenzoyl chloride and 2,6-dimethylaniline in pyridine at 0 °C, 2-*iodo*-2′,6′-*dimethylbenzanilide* crystallised from ethanol as needles, m.p. 183—184° (Found: C, 51.5; H, 4.0; I, 36.1; N, 4.0. $C_{15}H_{14}INO$ requires C, 51.3; H, 4.0; I, 36.1; N, 4.0%) τ (*syn*-rotamer) 6.68 and (*anti*-rotamer) 6.75 (total 6 H, ArMe). The *anti*-rotamer predominates.

2-*Iodo*-N,2′,6′-*trimethylbenzanilide*. *Method A*. Dimethyl sulphate (12 ml) was added dropwise to a refluxing solution of 2-iodo-2′,6′-dimethylbenzanilide (8 g), in acetone (100 ml) and aqueous sodium hydroxide (100 ml; 10%). After a further 30 min the mixture was poured into iced water and the product collected in ether. The solution was washed with water, dried ($MgSO_4$), and evaporated.

Method B. 2-Iodo-2′,6′-dimethylbenzanilide (3.0 g) was dissolved in xylene (30 ml) and stirred for 24 h with finely cut sodium pieces (0.4 g). Iodomethane (3.0 g) was added to the resulting suspension and the mixture stirred for 1 h. The solvent was then removed under reduced pressure and the residue dissolved in ether; the solution was washed with water, dried ($MgSO_4$), and evaporated.

Prepared by either method or from *N*,2,6-trimethylaniline, 2-*iodo*,N,2′,6′-*trimethylbenzanilide* crystallised from ethanol as a mixture of the *syn*- and *anti*-rotamers, m.p. 105—130° (see Table 2 for analytical data). A saturated ethanolic solution was allowed to evaporate at room temperature and deposited crystals of the *syn*-rotamer, m.p. 125—130°.

Procedure for Electrolytic Reduction.—The polarographic half-wave potentials for the reduction of some 2-halogeno-*N*-methylbenzanilides are given in Table 6. Preparative-scale reductions were carried out at the following controlled cathode potentials: chloro-compounds −2.10 V, bromo-compounds −2.00 V, iodo-compounds −1.66 V *vs.* s.c.e. The *N*-methylbenzanilide (5×10^{-3} mol) was dissolved in anhydrous dimethylformamide (15 ml) containing 0.1M-tetrapropylammonium perchlorate as supporting electrolyte. This was placed in the cathode compartment of an H-type electrolysis vessel fitted with a mercury cathode, a salt bridge connection to an s.c.e. reference, and a nitrogen

[21] R. F. Hunter and J. W. T. Jones, *J. Chem. Soc.*, 1930, 941.

inlet. The anode compartment contained 0.1M-electrolyte in dimethylformamide and a platinum anode. Reduction was continued until the current fell to a low value and the quantity of electricity passed (1.8—1.9 Faraday mol^{-1}) was measured with a hydrazine coulometer.[22] The catholyte was then evaporated to a small volume under vacuum, water (100 ml) was added, and the product was extracted with ether. The extract was washed with water, dried

TABLE 6

Polarographic half-wave potentials for the reduction of some benzanilides in dimethylformamide (0.1M in Pr_4NClO_4)

Compound (1)	$-E_{\frac{1}{2}}$/V *vs.* s.c.e.
$R^1 = R^3 = Me$, $R^2 = H$	
X = H	2.46
X = Cl	2.28, 2.52
X = Br	2.20, 2.52
X = I	1.67, 2.46
$R^1 = R^3 = H$, $R^2 = Me$	
X = Br	2.16
X = I	1.66

($MgSO_4$), and evaporated. N.m.r. analysis of the residue was performed on a 10% solution in $CDCl_3$; the results are collected in Table 3. Products were separated by chromatography on an alumina column and by fractional crystallisation.

Reduction of 2-*iodo*-N-*methylbenzanilide*. The reaction mixture deposited crystals of *N*-methylbiphenyl-2-carboxamide on addition of ether. The residue was chromatographed on alumina in ether–light petroleum to yield *N*-methylbenzanilide (35%), identified by mass spectrometry. Elution with ether afforded *N*-methylphenanthridone (17%) as needles (from aqueous ethanol), m.p. 108—108.5° (lit.,[23] 107—108°), M^+ 209. Elution with ethyl acetate afforded *N*-methylbiphenyl-2-carboxamide; the total amount (11%) of this compound crystallised from ether–light petroleum as needles, m.p. 167—168° (lit.,[24] 165—167°).

Reduction of 2-*iodo*-4′-*methoxy*-N-*methylbenzanilide* (1a; X = I). The reaction mixture deposited crystals of 3-methoxy-5-methylphenanthridone on addition of ether and the filtrate was chromatographed on alumina. Elution with ether–light petroleum (1 : 1) afforded 4′-methoxy-*N*-methylbenzanilide (7a) (38%), which crystallised from light petroleum as needles, m.p. 77—78° (lit.,[25] 74—77°). Elution with ether afforded 4′-methoxy-*N*-methylbiphenyl-2-carboxamide (6a), which crystallised from benzene as needles, m.p. 133—134° (lit.,[26] 131—133°). Elution with chloroform gave a mixture, easily separable by crystallisation from benzene, into the biphenyl-2-carboxamide (total yield 10%) and 3-methoxy-5-methylphenanthridone (5a) (11%), needles from benzene, m.p. 159—160° (lit.,[27] 161°).

Reduction of 2-*bromo*-4′-*methoxy*-N-*methylbenzanilide* (1a; X = Br). Separation of the products as for the previous example afforded 4′-methoxy-*N*-methylbenzanilide (35%), 4′-methoxy-*N*-methylbiphenyl-2-carboxamide (46%), and 3-methoxy-5-methylphenanthridone (9%).

Reduction of 2-*bromo*-N,2′-*dimethylbenzanilide* (1c; X = Br). The products were separated by chromatography on alumina. Elution with ether–light petroleum (1 : 1) afforded *N*,2′-dimethylbenzanilide, needles from light petroleum, m.p. 64—65° (lit.,[28] 65—66°). Elution with ether gave N,2′-*dimethylbiphenyl*-2-*carboxamide* (6c), needles from ether, m.p. 94—95° (Found: C, 80.0; H, 6.6; N, 6.2. $C_{15}H_{15}NO$ requires C, 80.0; H, 6.7; N, 6.2%), τ 7.63 (3 H, d, *J* 5.0 Hz, *N*-Me) and 8.16 (3 H, s, ArMe).

Reduction of 2-*chloro*-N,4′-*dimethylbenzanilide* (1b; X = Cl). Column chromatography did not separate the products. Preparative t.l.c. on silica gel was used with chloroform–methanol (95 : 5) as developing solvent. Compounds were isolated from appropriate bands by extraction with hot chloroform. 2,5-Dimethylphenanthridone (5b), R_F 0.8, crystallised from benzene–light petroleum as needles, m.p. 137—138° (lit.,[29] 136—137°); τ 6.26 (3 H, s, *N*-Me) and 7.52 (3 H, s, *C*-Me). N,4′-*Dimethylbiphenyl*-2-*carboxamide* (6b), R_F 0.5, crystallised from benzene–light petroleum as needles, m.p. 112—113° (Found: C, 80.0; H, 6.8; N, 6.1. $C_{15}H_{15}NO$ requires C, 80.0; H, 6.7; N, 6.2%), τ 7.33 (3 H, d, *J* 5 Hz, $NHCH_3$) and 7.62 (3 H, s, *C*-Me).

Reduction of 2-*iodo*-N,2′,6′-*trimethylbenzanilide* (1d; X = I). The products were chromatographed on alumina. Elution with ether gave *N*,2′,6′-trimethylbenzanilide (7d), needles from ethanol, m.p. 120—121° (Found: C, 80.3; H, 7.2; N, 5.9. Calc. for $C_{16}H_{17}NO$: C, 80.3; H, 7.3; N, 5.9%) (lit.,[30] m.p. 127°). Further elution with ether–methanol (200 : 1) yielded N,2,6-*trimethylbiphenyl*-2′-*carboxamide* (6d), needles from ethanol, m.p. 98—100° (Found: C, 79.8; H, 7.2; N, 5.6. $C_{16}H_{17}NO$ requires C, 80.2; H, 7.2; N, 5.9%), τ 7.41 (3 H, d, *J* 5.0 Hz, NMe) and 8.00 (6 H, s, ArMe), M^+ 238.

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