Amine Oxidation. Part X.[1] The Oxidation of Some 4-Substituted *NN*-Dimethylbenzylamines and a Selection of Other Amines with 1-Chlorobenzotriazole

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1-Chlorobenzotriazole in benzene converts substituted *NN*-dimethylbenzylamines into *NN*-disubstituted aminoalkylbenzotriazoles and a product containing positive chlorine. Hydrolytic work-up gives substituted benzaldehydes and benzylmethylamines. Kinetic studies show that the consumption of 1-chlorobenzotriazole, corrected for the positive chlorine in the product, obeys the rate law $-d[\text{chlorobenzotriazole}]/dt = k_2'[\text{amine}][\text{chlorobenzotriazole}]$. Correlation of the logarithm of the second-order rate constants for oxidation of the *NN*-dimethylbenzylamines using the Hammett and Brönsted relationships gives ρ −0.71 and α 0.63 respectively. Comparative kinetic measurements with *NN*-dimethylbenzylamine and *NN*-dimethyl[α-$^2H_2$]benzylamine give $k_2'H/k_2'D$ = 1·3. Product studies reveal information about the factors that control the direction of the oxidative dealkylation. The identity of the active chlorine product although not conclusively established is assigned as the *NN*-dimethylbenzylchloroammonium ion.

In the suggested mechanism the predominant role of 1-chlorobenzotriazole involves an initial one-electron abstraction from the amine followed by a product-determining deprotonation of the resulting aminium radical. Chlorine transfer is a minor route.

Information obtained from the reaction of a selection of other amines supports the dual nature of these oxidations.

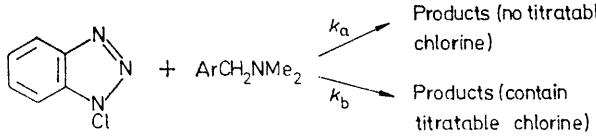
1-CHLOROBENZOTRIAZOLE is a versatile organic reagent capable of oxidising alcohols, ethers, and hydrazo and sulphur compounds,[2] chlorinating aromatic and saturated aliphatic compounds and sulphoxides,[3] and adding to olefins.[4] This reactivity towards a wide range of compounds, which it shares with a variety of other *N*-halogeno-compounds,[5] is in part due to its ability to serve as a source of positive chlorine [4] (ionic reactions) or chlorine atoms (radical reactions).[2a] This paper describes an investigation of the reactions of this reagent with a selection of amines and in particular kinetic and product studies with 4-substituted *NN*-dimethylbenzylamines.

RESULTS

Kinetic Studies.—The reactions were followed iodimetrically by measuring the change in concentration of positive chlorine species with time. The validity of the iodimetric estimation was tested with standard solutions of 1-chlorobenzotriazole, *N*-chlorosuccinimide, 2-chloroamino-2-methylpropane, and dibutylchloroamine.

In reactions with an excess of *NN*-dimethylbenzylamine over 1-chlorobenzotriazole the titratable positive chlorine decays rapidly to a value *ca.* 10—20% that of the initial oxidant concentration. Further loss of chlorine is very slow. The value of the levelling off point is unaffected by varying the excess of the amine.

These observations fit the Scheme. Assuming k_a/k_b is



SCHEME

constant throughout the reaction it is possible to correct the value of the positive chlorine concentration obtained from each titre for that in the product. Making this correction the decay of the concentration of 1-chlorobenzotriazole is found to follow the simple kinetic relationship, $-d[\text{chlorobenzotriazole}]/dt = k_1'[\text{chlorobenzotriazole}]$.

In all the studies with excess of amine the pseudo-first-order plots were linear for more than three half-lives. A computer was used to obtain the kinetic data by means of a least-mean-square program.

Table 1 summarises the kinetic data for the oxidation of some substituted *NN*-dimethylbenzylamines in benzene.

[1] Part IX, J. R. Lindsay Smith and D. Masheder, *J.C.S. Perkin II*, 1976, 47.

[2] (*a*) C. W. Rees and R. C. Storr, *J. Chem. Soc.* (*C*), 1969, 1474; (*b*) W. D. Kingsbury and C. R. Johnson, *ibid.*, p. 365.

[3] (*a*) H. Oelschlager and E. Ehlers, *Pharm. Acta Helv.*, 1972, **13**, 23; (*b*) P. M. Bowyer, D. H. Iles, and A. Ledwith, *J. Chem. Soc.* (*C*), 1971, 2775; (*c*) M. Cinquini and S. Collonna, *Synthesis*, 1972, **5**, 259.

[4] C. W. Rees and R. C. Storr, *J. Chem. Soc.* (*C*), 1969, 1478.

[5] R. Filler, *Chem. Rev.*, 1963, **63**, 21.

There is a good linear relationship between the pseudo-first-order rate constant, k_1', and the amine concentration for *NN*-dimethylbenzylamine. The slope of the straight line corresponds to the second-order rate constant, k_2', in the full rate equation, $-$d[Chlorobenzotriazole]/dt = k_2'[Amine][Chlorobenzotriazole]. Correlation of the logarithm of these values with the Hammett σ substituent

TABLE 1

Kinetic data for the oxidation of 4-substituted *NN*-dimethylbenzylamines by 1-chlorobenzotriazole (2.52×10^{-3}M) in benzene

Substituent	10^2[substrate]/M	Rate constants $10^3k_1'$/s^{-1}	Rate constants $10^5k_2'$/m^3 mol^{-1} s^{-1}
(A) 282.4 K			
H	2.67	1.8 ± 0.08	6.78 ± 0.29
H	3.88	2.55 ± 0.05	6.58 ± 0.12
H	4.03	2.77 ± 0.06	6.88 ± 0.15
H	5.11	3.60 ± 0.07	7.05 ± 0.13
(B) Temp. 280.4 K			
OMe	2.63		7.29 ± 0.18
H	2.63		4.98 ± 0.22
Cl	2.63		3.08 ± 0.03
NO_2	2.63		1.34 ± 0.06

constants or the pK_a * values of the amines gives a ρ value of -0.71 ± 0.03 (r 0.998) and a Brönsted α of 0.63 ± 0.05 (r 0.993) respectively.

Changing the solvent from benzene to benzene–methanol (90 : 10 v/v) increases the second-order rate constant for the oxidation of *NN*-dimethylbenzylamine by a factor of 3.1. With 20% methanol the reaction became too fast to measure iodimetrically. A blank experiment showed that by comparison the rate of oxidation of methanol by 1-chlorobenzotriazole is neligible.

The second-order rate constant for the oxidation of *NN*-dimethyl[α-$^2H_2$]benzylamine in benzene is slower than the protio-analogue by a factor of 1.3.

Product Studies.—(a) *Before hydrolytic work-up.* *NN*-Dimethylbenzylamine hydrochloride equivalent to 87 ($\pm$5)% of the added oxidant is precipitated from the reaction of *NN*-dimethylbenzylamine and 1-chlorobenzotriazole in benzene. Analyses by g.l.c. of the benzene solution proved unsatisfactory since the products were involatile or unstable. Only unchanged amine and some minor components were detected; g.l.c.–mass spectrometry revealed that none of these contained chlorine. Tests with authentic materials showed that it would have been possible to detect dimethylchloroamine but not *N*-benzylmethylchloroamine by this method. Passing a stream of nitrogen through the reaction in benzene and collecting the effluent gas in acidified potassium iodide released a minimal amount of iodine; control experiments showed that this procedure would have detected dimethylchloroamine or chlorine.

Attempts to crystallise the reaction products from the benzene solution were only successful in the presence of aqueous methanol when 1-hydroxymethylbenzotriazole and 1-(*N*-benzyl-*N*-methylaminomethyl)benzotriazole were obtained.†

The reaction of *NN*-dimethylbenzylamine with 1-chlorobenzotriazole, in a 2 : 1 molar ratio, in [$^2H_6$]benzene, after removal of precipitated amine hydrochloride, was analysed by n.m.r. spectroscopy. From a comparison of this spectrum with that obtained from *NN*-dimethyl[α-$^2H_2$]-benzylamine and those of authentic materials, the following products were assigned: benzotriazole, 1- and 2-(*N*-benzyl-*N*-methylaminomethyl)benzotriazole, 1- and 2-*NN*-dimethylaminobenzylbenzotriazole, *NN*-dimethylbenzylamine, and benzaldehyde. Flushing the reaction mixture with nitrogen caused no significant change in the spectrum. There were four significant singlet absorptions (δ 4.87, 2.60, 2.53, and 2.00) which could not be assigned.

(b) *After hydrolytic work-up.* Table 2 summarises the products from the oxidation of some 4-substituted *NN*-dimethylbenzylamines and *NN*-dimethyl- and 4-nitro-*NN*-dimethyl[α-$^2H_2$]benzylamine. All the reactions were carried out with a three-fold molar excess of amine at room temperature. The product distributions were unaffected by the presence or absence of air or light. In all the reactions there was a good recovery of unchanged amine and oxidation products. The following compounds were shown to be absent from the reaction of *NN*-dimethylbenzylamine in benzene: bibenzyl, benzyl chloride, benzyl alcohol, benzylamine, and 4-chloro-*NN*-dimethylbenzylamine. The presence of formaldehyde was confirmed by the chromotropic acid test.[7]

The time taken for *NN*-dimethylbenzylamine hydrochloride to be precipitated from a reaction of the free amine and 1-chlorobenzotriazole in diethyl ether was unaffected by the presence of 5 mole % of 1,4-benzoquinone or tetrachloro-1,4-benzoquinone, or by degassing the solutions with a stream of nitrogen.

(c) *The reaction of 1-chlorobenzotriazole with a selection of other amines.* No oxidation product was detected from 1-azabicyclo[2.2.2]octane. The presence of 4- and 5-chlorobenzotriazoles and two dichlorobenzotriazoles in the reaction mixture accounted for part of the active chlorine consumed.

1,4-Diazabicyclo[2.2.2]octane in benzene gave 1,4-bis-(benzotriazolylmethyl)piperazine. An e.s.r. study of the reaction in methanol showed the presence of the aminium radical.[8] *NNN'N'*-Tetramethyl-1,4-diaminobenzene in benzene or methanol was also oxidised to its aminium radical.

The primary amines 2-amino-2-methylpropane and benzylamine gave the corresponding monochloroamines and a precipitate of the ammonium benzotriazolate.

N-Benzyl-*N*-methylaminomethylbenzotriazole was inert to oxidation by 1-chlorobenzotriazole.

DISCUSSION

Prior to hydrolysis the major products from the reaction of 1-chlorobenzotriazole and dimethylbenzylamines in benzene are 1- and 2-*NN*-dimethylaminobenzylbenzotriazoles (V) and 1- and 2-(*N*-benzyl-*N*-methyl aminomethyl)benzotriazoles (VI), hydrogen chloride, and an active chlorine compound. Hydrolysis gives the aldehydes and secondary amines typical of oxidative dealkylation in aqueous solution. The kinetic results are best interpreted assuming that the 1-chlorobenzo-

* pK_a in aqueous solution.

† In solution this material exists as an equilibrium mixture of the 1- and 2-isomers.[6]

[6] J. R. Lindsay Smith and J. S. Sadd, *J.C.S. Perkin I*, 1975, 1181.

[7] C. E. Bricker and H. R. Johnson, *Ind. and Eng. Chem. (Analyt. Edn.)*, 1945, **17**, 400.

[8] T. M. McKinney and D. H. Geske, *J. Amer. Chem. Soc.*, 1965, **87**, 3013.

triazole reacts by a dual mechanism to give the aminoalkylbenzotriazoles on the one hand, and the active chlorine compound on the other.

The identity of the active chlorine product has not been conclusively established. However, it is unlikely to be a secondary chloroamine, formed by chlorination of secondary amine arising from hydrolysis of intermediates by traces of water in the reaction medium. Nor is it likely that it arises from further reaction of an aminoalkylbenzotriazole derivative with the oxidant, for as found in the kinetic studies the proportion of the observations. A free radical chain reaction analogous to that proposed for the oxidation of alcohols using 1-chlorobenzotriazole [2] or sunlight with *N*-bromodiphenylketimine [10] can be eliminated for the oxidation of the tertiary amines has no induction period and is unaffected by light, oxygen, or inhibitors. Alternative mechanisms are discussed below.

The rate law derived from equations (1)—(5) gives $-d[\text{chlorobenzotriazole}]/dt = k_1[\text{amine}][\text{chlorobenzotriazole}]$. This is in agreement with the observed kinetics, when corrected for active chlorine products, of an

TABLE 2

Yields (% based on substrate) of products from the oxidation of some substituted *NN*-dimethylbenzylamines with 1-chlorobenzotriazole at room temperature

Substrate $4\text{-XC}_6\text{H}_4\text{CY}_2\text{NMe}_2$			Products			Ratio $4\text{-XC}_6\text{H}_4\text{CHO}$: $4\text{-XC}_6\text{H}_4\text{CY}_2\text{NHMe}$
X	Y	Solvent	$4\text{-XC}_6\text{H}_4\text{CHO}$	$4\text{-XC}_6\text{H}_4\text{CY}_2\text{NHMe}$	Unreacted substrate	
OMe	H	C_6H_6	14.1	13.4	66.4	1.05
		MeOH	5.6	19.5	70.7	0.29
H	H	C_6H_6	15.3	13.4	65.7	1.14
		C_6H_6 *	13.9	13.5	66.5	1.03
		Et_2O	14.0	13.5	64.5	1.03
		MeOH	4.6	22.5	70.0	0.20
H	D	C_6H_6	10.6	17.3	64.6	0.61
		MeOH	2.9	24.4	69.9	0.12
Cl	H	C_6H_6	15.8	13.8	71.1	1.14
		Et_2O	13.7	13.1	70.6	1.05
		Et_2O–MeOH (95 : 5)	11.3	12.8	75.0	0.89
		Et_2O–MeOH (50 : 50)	9.3	16.5	76.0	0.56
		MeOH	5.7	21.4	75.3	0.27
		MeOH–H_2O (95 : 5)	4.9	19.2	77.4	0.26
NO_2	H	C_6H_6	16.6	4.5	76.4	3.66
		MeOH	3.7	23.8	68.6	0.16
NO_2	D	C_6H_6	12.5	6.6	72.3	1.9
		MeOH	1.6	26.6	66.9	0.06

* In the dark.

active chlorine product was independent of the excess of the substrate, and there was no evidence of a reaction when *N*-benzyl-*N*-methylaminomethylbenzotriazole was mixed with 1-chlorobenzotriazole. In the absence of positive evidence to implicate other species we suggest that the active chlorine species is the *NN*-dimethylbenzylchloroammonium ion. Although trialkylhalogenoammonium salts have been reported [9] attempts to prepare and isolate a pure sample of *NN*-dimethylbenzylchloroammonium chloride from the tertiary amine and chlorine were unsuccessful. Direct observation of the chloroammonium ion in the reaction mixture by n.m.r. spectroscopy was not possible. Rapid exchange of chlorine between the chloroammonium ion and the unchanged amine would have given a time averaged spectrum. Attempts to detect the related species, the 1-chloro-1-azoniabicyclo[2.2.2]octane ion, in the reaction of 1-azabicyclo[2.2.2]octane and 1-chlorobenzotriazole were also unsuccessful. N.m.r. studies at several temperatures (−100 to 36°) using authentic 1-azabicyclo[2.2.2]octane and its chloroammonium chloride confirmed the rapid Cl^+ exchange.

Mechanism A for the formation of the aminoalkylbenzotriazoles is in agreement with the experimental overall second-order process, first order in each reactant. Two other reaction mechanisms, one involving hydride abstraction (Mechanism B), and the other an initial chlorine transfer and loss of hydrogen chloride (Mechanism C) each followed by reaction of the iminium ions (VII) and (VIII) with benzotriazolate to give (V) and (VI), also obey the observed rate law. In a third possibility, analogous to that proposed by Lee and Srinivasan [11] for the oxidation of *NN*-dimethylbenzylamine by bromine in aqueous acetic acid, the rate-determining step is the concerted transfer from the substrate of two electrons to the oxidant and an α-proton to a second molecule of substrate to give (VII) and (VIII). However, this scheme would not show overall second-order kinetics and can be eliminated.

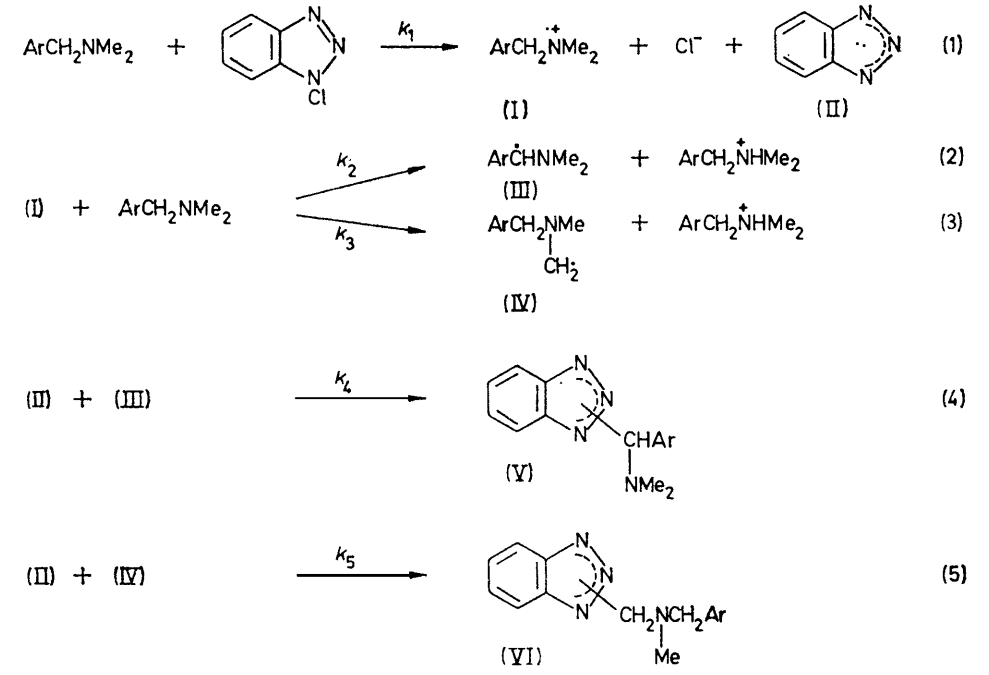
The rate enhancement when the oxidations are carried out in solvents more polar than benzene is explicable in terms of equation (1) (assuming that there is no change in mechanism) for the transition state in the initial electron transfer will be more polar than the reactants. A similar effect would be expected for Mechanisms B and C.

The kinetic isotope effect obtained from *NN*-dimethyl-[α-$^2H_2$]benzylamine, k'_1H/k'_1D 1.3, is typical of secondary isotope effects reported for electron abstraction from

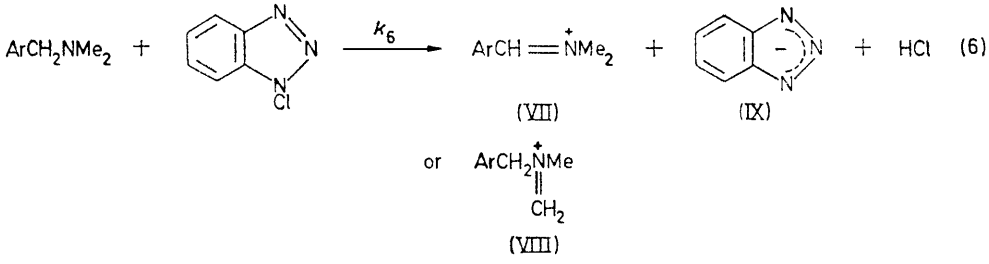
[9] H. Bohme and W. Krause, *Chem. Ber.*, 1951, **84**, 170.
[10] C. G. McCarty and C. G. Leeper, *J. Org. Chem.*, 1970, **35**, 4245.
[11] D. G. Lee and R. Srinivasan, *Canad. J. Chem.*, 1973, **51**, 2546.

tertiary amines.[12,13] Mechanism B would have a primary kinetic isotope effect for debenzylation of 1.82.* This value is low for a primary isotope effect and would require an unsymmetrical or non-linear transition state loss of hydrogen chloride is rate determining, a value approaching a typical primary effect.

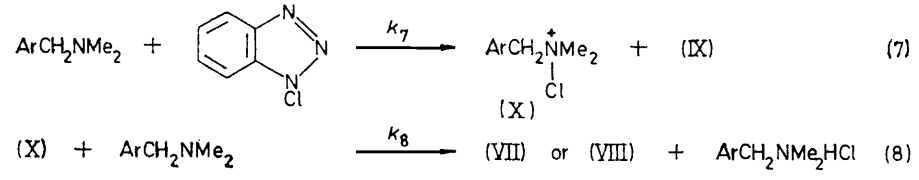
The Hammett ρ value of −0.71 ± 0.03 and Brönsted α of 0.63 ± 0.05 agree well with the values reported for



MECHANISM A



MECHANISM B



MECHANISM C

for α-C–H cleavage.[14] In Mechanism C α-deuteriation should favour the transfer of chlorine to the amine in the manner that it favours the quaternisation of amines.[13a,15] This would lead to a negative isotope effect or, if the the one-electron oxidation of these amines in aqueous solution [ρ −0.984 and α 0.99, and ρ −0.924 and α 0.812 for oxidation with potassium hexacyanoferrate-(III)[16] and chlorine dioxide[17] respectively]. For Mechanism B the Hammett plot of σ values against the second-order rate constants for debenzylation † shows a

* This value is calculated assuming the reaction leading to demethylation is unaffected by the benzylic deuterons.

† The measured rate constants are corrected for the proportion of reaction that gives demethylation.

[12] J. R. Lindsay Smith and L. A. V. Mead, *J.C.S. Perkin II*, 1973, 206.

[13] (*a*) L. A. Hull, G. T. Davis, D. H. Rosenblatt, H. K. R. Williams, and R. C. Weglein, *J. Amer. Chem. Soc.*, 1967, **89**, 1163; (*b*) D. H. Rosenblatt, G. T. Davis, L. A. Hull, and G. D. Forberg, *J. Org. Chem.*, 1968, **33**, 1649.

[14] F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265.

[15] (*a*) E. A. Halevi, *Progr. Phys. Org. Chem.*, 1963, **1**, 109; (*b*) E. S. Lewis, *Tetrahedron*, 1959, **5**, 143.

[16] C. A. Audeh and J. R. Lindsay Smith, *J. Chem. Soc.* (*B*), 1971, 1741.

[17] D. H. Rosenblatt, L. A. Hull, D. C. de Luca, G. T. Davis, R. C. Weglein, and H. K. R. Williams, *J. Amer. Chem. Soc.*, 1967, **89**, 1158.

distinct curvature. The best straight line gives ρ −0.54 ± 0.04. This small negative ρ is inconsistent with a hydride abstraction process. A ρ value of −2.0 has been reported for the hydride-transfer oxidation of amines by the triphenylmethyl cation.[18] A ρ value more negative than −1.0 might be expected for *N*-chlorination in Mechanism C; for comparison ρ −1.14 is obtained from a correlation of the pK_a values of the substituted dimethylbenzylamines[17] with the σ substituent constants. From the kinetic isotope effect coupled with the Hammett ρ value Mechanism C seems unlikely.

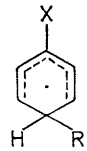
The yield of substituted benzaldehyde relative to the corresponding substituted *N*-methylbenzylamine after hydrolytic work-up of the oxidation of a substituted *NN*-dimethylbenzylamine is equivalent to k_2/k_3. If we assume that k_3, the rate constant for loss of a proton from the methyl group, is not significantly affected by substitution in the aromatic nucleus or by deuteriation of the benzylic hydrogens, then the product distribution gives a measure of how the rate constant for debenzylation (k_2) is affected by these factors.

Comparison of the product distributions of *NN*-dimethylbenzylamine and 4-nitro-*NN*-dimethylbenzylamine with those of their [α-$^2H_2$]-isomers gives a primary kinetic isotope effect, k_2H/k_2D, for loss of a benzyl proton of 1.9 in benzene for each pair of substrates and 1.7 and 2.5 respectively in methanol. The small sizes of these values suggest that the transition states for proton abstraction either resemble the aminium radical (I) (slight α-C–H stretching) or the α-amino-radical (III) or (IV) (almost complete α-C–H bond breakage).

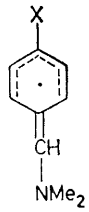
For a transition state that resembles the aminium radical the product distribution should be controlled by the relative acidities of the α-hydrogens and the proportion of debenzylation should increase with the electron-withdrawing character of the substituent. Further, calculations by Cedheim reported by Ross and his co-workers[19] for the *NN*-dimethylbenzylaminium radical suggest that a methyl hydrogen should be twice as reactive as a benzyl one to loss as a proton.

A measure of the expected influence of substituents on the stability of the α-amino-radical (III) can be obtained from the partial rate factors for radical attack at the 4-position of monosubstituted benzene derivatives, *i.e.*, the intermediate (XI) serves as a model for the α-amino-radical (III). The values for phenylation[20] (R = Ph), $PhNO_2$ (9.05), PhCl (1.48), and PhOMe (1.29), show that each substituent would stabilise (III) more than hydrogen but 4-nitro most dramatically so.

The product distributions from the reactions in benzene indicate that the transition states for deprotonation of the aminium radical have characteristics of both the aminium radical and the α-amino-radical but more closely resemble the latter. In no instance is demethylation preferred over debenzylation.



(XI)



(III)

There are no kinetic data for the reactions in the more polar protic solvent methanol; however, it is noteworthy that there is a steady trend from a situation favouring benzyl cleavage to one giving a near statistical distribution of products with a slight preference for demethylation with increasing polarity of the solvent. Similar non-selective dealkylations have been reported from oxidations in aqueous solution (chlorine dioxide, pH 8)[17] and aqueous alkaline methanol (controlled potential electrolysis, 10^{-3}M-sodium hydroxide).[1]

The data from the reaction of 1-chlorobenzotriazole with the miscellaneous amines support the dual nature of the oxidations. The aminium radicals derived from 1,4-diazabicyclo[2.2.2]octane and *NNN'N'*-tetramethyl-1,4-diaminobenzene most probably arise by an electron-transfer analogous to equation (1) although the alternative route *via* *N*-chlorination, followed by homolysis[21] or disproportionation respectively, cannot be eliminated. *N*-Chlorination is certainly the major process in the reactions of primary amines where the alternative electron abstraction is no longer favoured; electrochemical studies have shown that the oxidation potentials of primary amines are significantly higher than those of the corresponding tertiary compounds.[22] It is noteworthy that this reaction might be used for the synthesis of monochloroamines especially where benzotriazole is precipitated as its ammonium salt.

The oxidative fragmentation of 1,4-diazabicyclo-[2.2.2]octane could proceed by either chlorine- or electron-transfer; Rosenblatt and his co-workers[23] have proposed both alternatives for the oxidation of this diamine by hypochlorous acid and chlorine dioxide. No oxidation products from 1-azabicyclo[2.2.2]octane were detected although some of the substrate was consumed; a minor part of the active chlorine was recovered in the *C*-chlorobenzotriazoles. It seems likely that these materials arise from chlorination of benzotriazolate by the 1-chloro-1-azoniabicyclo[2.2.2]octane ion, in agreement with this conclusion this reaction was shown to give a mixture of *C*-chlorobenzotriazoles. Presumably this reaction assumes importance owing to the unfavourable alternative of electron transfer from the bridgehead nitrogen.[12]

[18] N. C. Deno and R. E. Fruit, *J. Amer. Chem. Soc.*, 1968, **90**, 3502.
[19] J. E. Barry, M. Finkelstein, E. A. Mayeda, and S. D. Ross, *J. Org. Chem.*, 1974, **39**, 2695.
[20] R. Ito, T. Migita, N. Morikawa, and O. Simamura, *Tetrahedron*, 1965, **21**, 955.
[21] D. H. Rosenblatt, M. M. Demek, and G. T. Davis, *J. Org. Chem.*, 1972, **37**, 4148.
[22] C. K. Mann, *Analyt. Chem.*, 1964, **36**, 2424.
[23] W. H. Dennis, L. A. Hull, and D. H. Rosenblatt, *J. Org. Chem.*, 1967, **32**, 3783.

EXPERIMENTAL

E.s.r. spectra were recorded on a Varian E3 instrument using a flow system.[24] All other spectroscopic and chromatographic methods have been reported previously.[1,12,16]

Materials.—AnalaR benzene and diethyl ether were sodium-dried before use. All organic materials, except those described below, were available commercially and were purified before use. 1-Chlorobenzotriazole was prepared following Rees and Storr [2] and had m.p. 104—105° (from methylene dichloride) (lit.,[2] 104—106°). The preparations of the 4-substituted *NN*-dimethylbenzylamines [1] and 4-nitro-*NN*-dimethyl[α-$^2H_2$]benzylamine [25] have been reported. *NN*-Dimethyl[α-$^2H_2$]benzylamine was prepared by lithium aluminium deuteride reduction of *NN*-dimethylbenzamide and had b.p. 70—72° at 18 mmHg (lit. protio-analogue,[26] 66—67° at 15 mmHg). Mass spectral analysis showed that the deuterium content was >99%. 4-Methoxy-*N*-methylbenzylamine was prepared following Wojahn and Erdelmeier [27] and had b.p. 119—121° at 14 mmHg (lit.,[28] 114—120° at 15 mmHg). 4-Nitro- and 4-chloro-*N*-methylbenzylamines were prepared by the method of Eliel *et al.*[29] and had b.p. 156—158° at 15 mmHg (lit.,[30] 68—72° at 0.25 mmHg) and 98—100° at 13 mmHg (lit.,[31] 118—121° at 23 mmHg), respectively.

The preparation of 1-hydroxymethylbenzotriazole and the aminoalkylbenzotriazoles, except for *NN*-dimethylaminobenzylbenzotriazole and 1,4-bis(benzotriazolylmethyl)piperazine, have been reported.[6] *NN*-Dimethylaminobenzylbenzotriazole was prepared by the addition of benzaldehyde (11.7 g) in methanol (50 cm^3) dropwise over 1 h to a cooled (−18°) solution of benzotriazole (11.9 g) and dimethylamine (9.0 g) in methanol (50 cm^3) under nitrogen. The mixture was allowed to warm to room temperature and anhydrous calcium sulphate was added. After two days stirring the drying agent was removed by filtration and the filtrate was concentrated under reduced pressure in a nitrogen atmosphere. The residual gum was very readily hydrolysed and satisfactory analytical data were not obtained, δ ($CDCl_3$; −30°) 8.1—7.6 (2 H, m), 7.4—7.1 (8 H, m), 6.7 (1 H, s), and 2.4 and 2.3 (6 H, 2s).

1,4-*Bis(benzotriazolylmethyl)piperazine* [6] had m.p. 237—239° (decomp.) (Found: C, 61.85; H, 6.0; N, 32.3. $C_{18}H_{20}N_8$ requires C, 62.1; H, 5.8; N, 32.2%). 2-*Ammonio-2-methylpropane benzotriazolate* was prepared in quantitative yield by mixing equimolar amounts of 2-amino-2-methylpropane and benzotriazole in diethyl ether (Found: C, 62.8; H, 8.5; N, 29.35. $C_{10}H_{16}N_4$ requires C, 62.5; H, 8.4; N, 29.1%). 5-Chlorobenzotriazole prepared following Fagel and Ewing [32] had m.p. 157—158.5° (lit.,[32] 156—157°). An ethereal solution of dimethylchloroamine was prepared following Bock and Kompa.[33] Benzylmethylchloroamine was obtained by the method of Neale and Walsh [34] but was not distilled, δ 7.4—7.0 (5 H, m), 3.85 (2 H, s), and 2.7 (3 H, s). 2-Chloroamino- and 2-dichloroamino-2-methylpropane were prepared from the hydrochloride salt of the primary amine and sodium hypochlorite in the presence of diethyl ether and methylene dichloride respectively. Their spectra were consistent with published data.[35] 1-*Chloro*-1-*azoniabicyclo*[2.2.2]*octane* was prepared by passing chlorine through a stirred solution of 1-azabicyclo[2.2.2]octane (0.13 g) in dry tetrachloromethane (50 cm^3) at −20° for 10 min. The white precipitate which was dried in a vacuum desiccator did not melt at <300° and had δ[$(CD_3)_2SO$] 3.2 (6 H, m) and 1.8 (7 H, m) (Found: C, 46.3; H, 7.1; N, 7.8. $C_7H_{13}NCl_2$ requires C, 46.2; H, 7.2; N, 7.7%).

Nitrogen was British Oxygen white-spot grade and was purified by passage through, successively, chromium(II) chloride solution, concentrated sulphuric acid, and potassium hydroxide pellets.

Kinetic Studies.—A standard solution of 1-chlorobenzotriazole and one containing a known amount of the substrate each in benzene were allowed to equilibrate for 1 h in a thermostatted bath. The required amount of oxidant solution was pipetted into the substrate solution and the mixture was shaken. A stop-watch was started when half the oxidant had been added. Portions were removed at intervals by pipette and quenched with acidified potassium iodide solution. The time was noted when half a portion had been quenched. The iodine liberated was titrated immediately against 0.01M-sodium thiosulphate solution using B.D.H. ' Iodine indicator.'

Product Studies: Reaction of Tertiary Amines with 1-Chlorobenzotriazole.—(a) *N.m.r. spectra of products before hydrolytic work-up.* A solution of *NN*-dimethylbenzylamine (72.7 mg) in [$^2H_6$]benzene (0.2 cm^3) was mixed with 1-chlorobenzotriazole (41.6 mg) in the same solvent (0.6 cm^3). After 1 h the solution was filtered, tetramethylsilane was added, and the n.m.r. spectrum recorded. A stream of nitrogen was passed through the solution for 5 min and the spectrum was re-recorded.

The experiment was repeated with *NN*-dimethyl[α-$^2H_2$]-benzylamine.

(b) *Products after hydrolytic work-up.* A solution of 1-chlorobenzotriazole (*ca.* 3mM) in the required solvent was added in one portion to the tertiary amine (*ca.* 9mM) in the same solvent. After 0.5—1.0 h, 2M-hydrochloric acid (150 cm^3) with some ether, to aid separation of the phases, was added and the organic layer was separated and washed with 2M-hydrochloric acid. The aqueous solution and washings were extracted with ether (2 × 150 cm^3) and the combined organic solutions were dried ($MgSO_4$), concentrated, and analysed.

1,2-Diaminoethane (15mM) was added to the aqueous acid solution and after 15 min this was made strongly alkaline (NaOH) and extracted with ether (3 × 150 cm^3). The ether solution was worked-up as above. This work-up procedure was checked using authentic samples of aminoalkylbenzotriazoles.

When the yield of amine hydrochloride in the product

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was needed, the salt was removed by filtration, prior to the addition of the hydrochloric acid, washed with dry benzene, and estimated gravimetrically.

Isolation of 1-*Hydroxymethylbenzotriazole and* N-*Benzyl*-N-*methylaminomethylbenzotriazole from a Reaction Mixture.*—*NN*-Dimethylbenzylamine (5.19 g) in benzene (50 cm^3) was mixed with 1-chlorobenzotriazole (2.92 g) in benzene (50 cm^3). After 15 min, filtration removed the amine hydrochloride and the filtrate was concentrated to 5 cm^3 before methanol (25 cm^3) and water (75 cm^3) were added. The lower layer was separated and on standing for two days in contact with water gave 1-hydroxymethylbenzotriazole (i.r. and n.m.r. spectra identical to those of authentic material).

The upper layer was recrystallised to give *N*-benzyl-*N*-methylaminomethylbenzotriazole (0.22 g), m.p. 61.5—62.5° (lit.,[6] 62—62.5°) (i.r. and n.m.r. spectra identical to those of authentic material).

Estimation of Any Volatile Active Chlorine Compounds produced in the Reactions of 1-*Chlorobenzotriazole.*—A stream of nitrogen was passed through the reaction mixture into a solution of acidified potassium iodide containing soluble starch. Any colour liberated was titrated against 0.01M-sodium thiosulphate. A control experiment using a solution of dimethylchloroamine in benzene showed that this procedure would have detected volatile active chlorine products.

Reaction of 1-*Chloro*-1-*azoniabicyclo*[2.2.2]*octane Chloride with Sodium Benzotriazolate.*—1-Chloro-1-azoniabicyclo-[2.2.2]octane chloride (0.053 g) and sodium benzotriazolate (0.064 g) were heated as a suspension in refluxing benzene. After 1 h no positive chlorine remained and the solution was concentrated and analysed by g.l.c.

E.s.r. Studies.—A 0.1M solution of 1,4-diazabicyclo-[2.2.2]octane in methanol was mixed with 0.01M-1-chlorobenzotriazole in methanol, using a two-way flow system, prior to passage through the resonance cavity of the e.s.r. spectrometer. The spectrum of 1,4-diazabicyclo[2.2.2]-octane aminium radical was obtained, a_N 1.685, a_H 0.733 mT (lit.,[8] a_N 1.676 ± 0.008, a_H 0.734 ± 0.008 mT).

Reaction of NNN'N'-*Tetramethyl*-1,4-*diaminobenzene with* 1-*Chlorobenzotriazole.*— *NNN'N'*-Tetramethyl-1,4-diaminobenzene was converted by 1-chlorobenzotriazole (2 : 1 molar ratio) in methanol to its aminium radical. The spectrum was identical to that reported by Michaelis *et al.*[36]

Reaction of Primary Amines with 1-*Chlorobenzotriazole.*—A solution of the primary amine (20mM) in benzene or methylene dichloride was mixed with a solution of 1-chlorobenzotriazole (10mM) in the same solvent. Filtration of the solution gave the alkylammonium benzotriazolate, identical with the authentic material, and iodimetric titration showed that the filtrate contained all the active chlorine. The yield of the alkylammonium benzotriazolate was quantitative from 2-amino-2-methylpropane.

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