Studies of the Synthesis, Protonation and Decomposition of 2,4,6,8,10,12-Hexabenzyl-2,4,6,8,10,12-hexaazatetracyclo[5.5.0.0^{5,9}.0^{3,11}]dodecane (HBIW)

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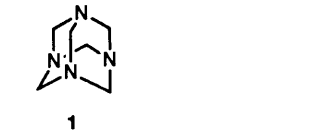
Reaction of glyoxal with benzylamine or with substituted benzylamines leads to the cage structure **3**. The X-ray crystal structure of **3c** formed from 4-chlorobenzylamine is reported. ^{1}H and ^{13}C NMR spectra of **3a–j** have been measured. Changes in spectra in the presence of acid indicate successive reaction to give mono- and di-protonated species, **4** and **5** respectively, in which the added protons bridge two nitrogen atoms. The kinetics of the decomposition of **3a** in aqueous acetonitrile are compatible with two competing pathways involving reaction of the protonated form with either water or more acid.

The reaction of aldehydes with amines may produce imines which subsequently polymerise to yield cyclic or cage structures,[1-4] such as hexamethylene tetramine (**1**). The corresponding reactions of the dialdehyde glyoxal with most aliphatic and aromatic amines yield diimines[5-9] which do not react further. However it was found recently[10] that reaction of glyoxal with benzylamine or substituted benzylamines gave the interesting cage structure **3** and the diimines **2** were implicated as reaction intermediates, as shown in Scheme 1.



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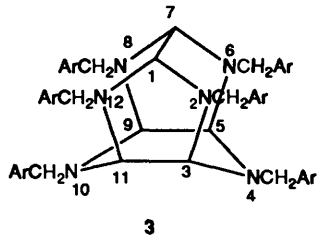


3

Scheme 1

Compound **3a**, 2,4,6,8,10,12-hexabenzyl-2,4,6,8,10,12-hexaazatetracyclo[5.5.0.0.^{5,9}0^{3,11}]dodecane is also known as hexabenzylhexaazaisowurtzitane. It is described as an isowurtzitane owing to its close relationship to the hydrocarbon wurtzitane.[11,12] The wurtzitane structure contains five six-membered rings while the isomeric isowurtzitane structure has two five-membered rings, two seven-membered rings and one six-membered ring.

We report here some studies of the synthesis of **3a** and of its ring-substituted derivatives, but our work is mainly concerned with the behaviour of **3** in acidic solutions. There is current interest[13,14] in the protonation of nitrogen-containing cage structures. Our results provide evidence for the formation of mono- and di-protonated derivatives of **3** in which protons bridge nitrogen atoms. We have also made kinetic studies of the acid-catalysed decomposition of **3a** in aqueous acetonitrile.

Results and Discussion

Synthesis and Characterisation.—**3a** was prepared by reaction in acetonitrile of glyoxal with benzylamine in a molar ratio 1:2 in the presence of acid catalyst. **3a** precipitates from solution and can be separated and recrystallised. The effects of varying both the nature and concentration of the acid catalyst were examined in detail using nitric, sulfuric, perchloric, hydrochloric, formic and ethanoic acids. Higher yields were obtained using the mineral acids with nitric acid being the most effective. An optimum yield of 67% of recrystallised product was obtained when the acid concentration (0.025 mol dm^{-3}) was twenty times smaller than the benzylamine concentration (0.50 mol dm^{-3}). Controlling the temperature had little effect on the efficiency of the reaction so that at < 16 °C the yield was 60%, at 25 °C 67% and at 35 °C 65%. Increasing the proportion of either benzylamine or glyoxal did not increase the yield.

In agreement with the proposed mechanism[10] it was found that the diimine **2a** when dissolved in acetonitrile formed **3a** in high yield (80%).

Data for **3a** and ring-substituted derivatives are in Table 1. In some cases relatively low yields were obtained, notably when the benzyl ring contained electron-withdrawing substituents, and it was thought to be of interest to try to identify other reaction products. After precipitation of **3c** from the reaction of 4-chlorobenzylamine the mother liquor was concentrated and a chromatographic separation attempted. Amongst the species present it was possible to identify unreacted 4-chlorobenzylamine, the diimine **2c** and also **3c**.

Of the ten compounds listed in Table 1, four have previously been reported.[10] The melting points for **3a** and **3e** are very close to literature values while the values for **3b** and **3c** are much lower than those previously reported, 208–211 °C and 212–214 °C respectively. It has been noted[10] that these compounds may exist in different crystalline forms and we attribute these differences to this factor. The structure and conformation of **3c** in the solid state as determined by our crystal structure analysis is shown in Fig. 1. The molecule has two-fold crystallographic symmetry, the two-fold axis passing through the mid-point of the C(1)–C(1′) bond. The six-membered C_4N_2 ring [C(3), N(4), C(5), C(3′), N(4′), C(5′)] at the base of the structure as shown in Fig. 1, is in a well-defined boat conformation with the

Table 1 Characterisation of compounds **3a–j**

Derivative	Phenyl substituent	M.p./°C	Yield (%)	Calculated				Found			
				C	H	N	Halogen	C	H	N	Halogen
a	H	153	67	81.3	6.8	11.9	—	81.4	6.8	11.8	—
b	2-Cl	182	15	62.9	4.6	9.2	23.3	62.9	4.5	9.1	22.6
c	4-Cl	191	20	62.9	4.6	9.2	23.3	62.9	4.5	9.1	23.0
d	2-Me	203	45	81.7	7.6	10.6	—	81.6	7.5	10.4	—
e	4-Me	174	62	81.7	7.6	10.6	—	81.6	7.5	10.5	—
f	2-Br	210	22	48.7	3.6	7.1	40.6	48.7	3.5	7.1	39.2
g	2-F	126	33	70.5	5.1	10.3	13.9	70.4	5.1	10.2	13.4
h	2-MeO	136	28	72.9	6.7	9.4	—	72.8	6.7	9.4	—
i	4-Cl (d_{12})[a]	192	10	62.1	—	9.1	—	62.0	—	9.0	—
j	H (d_{12})[a]	147	43	79.9	—	11.7	—	79.8	—	11.6	—

[a] Prepared from benzylamines with deuteriated methylene groups.

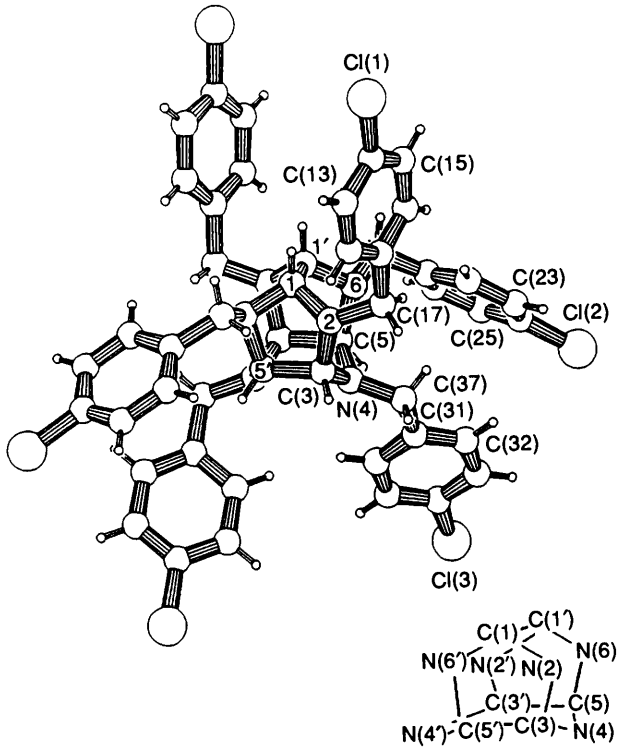


Fig. 1 A view prepared with PLUTON of **3c** giving an indication of the crystallographic numbering scheme; the two-fold symmetry axis passes through the centre of the C(1)–C(1') bond

N(4)–C(37) bond pseudo-equatorial. The five-membered C_3N_2 rings have envelope conformations; the atoms N(2), C(3), C(5'), C(6') are almost planar, with C(1) 0.650(2) Å from this plane. The seven-membered ring C(1), N(2), C(3), N(4), C(5), N(6), C(1') has a chair conformation. None of the N atoms has planar stereochemistry; the angle sums are 347.9° [N(2)], 348.5° [N(4)] and 326.6° [N(6)]. Interestingly, the N(2)–C(17) and N(4)–C(37) bonds are *endo* and the N(6)–C(27) bond is *exo*. The actual orientation of the benzyl groups in the structure is presumably that which minimises intermolecular interactions in the solid state. The C(1)–C(1') [1.579(3) Å] and C(3)–C(5') [1.561(3) Å] bonds are longer than usually found for unstrained C_{sp^3}–C_{sp^3} distances, reflecting the strain in the cage. It is possible that an anomeric effect involving nitrogen lone pairs is also operating here. The remaining dimensions (deposition material) are unexceptional and serve to establish the structure unequivocally [*e.g.* C_{sp^3}–N_{sp^3} distances in the range 1.438(3) to 1.493(3) Å, mean 1.462 Å, C–Cl 1.739(3) to 1.748(3) Å, mean 1.743 Å].

Nevertheless the NMR spectra of **3a–j** (Table 2) indicate that in solution in deuteriochloroform there are only two types of benzyl groups. Those at N(2), N(6), N(2') and N(6') become equivalent, although this may result from rapid equilibration of non-equivalent structures, but are distinct from those at N(4) and N(4'). The ^{1}H NMR spectrum is shown in Fig. 3, and the notation of hydrogen atoms is given in Fig 2. The methine hydrogens Ha and Hb give singlets at δ 3.57 and 4.16 respectively. An AB quartet (8 H) centred at δ 4.09 is observed for the methylene hydrogens Hc and Hd resulting from geminal coupling, J = 13 Hz, while a singlet (4 H) at δ 4.04 is observed from He and Hf. The assignment, which differs from that given previously,[10] was aided by the availability of compounds **3i** and **3j** prepared from benzylamine in which the methylene hydrogens had been deuteriated. These compounds showed bands for the methine hydrogens, derived from glyoxal, and aromatic hydrogens only.

^{13}C NMR shifts are in Table 3. The methine carbons, two types, absorbed in the expected region[15] at *ca.* δ 80 and the methylene carbons, two types, at *ca.* δ 50. The assignments were confirmed by comparison of proton-coupled and proton-decoupled spectra. The spectra of the deuteriated derivatives **3i** and **3j** showed bands of very low intensity due to the methylene carbon atoms attributed to saturation caused by the adjacent deuterium atoms.

Protonation.—Interesting changes in the NMR spectra occur in the presence of acid. Spectra obtained with one equivalent and with two equivalents of acid indicate reaction successively to give monoprotonated **4** and diprotonated **5** derivatives as shown in Fig. 2. ^{1}H spectra of **4a**, **4c**, **4d** and **4j** were obtained in deuteriochloroform and shifts are in Table 2. ^{13}C Data for **4a** and **4d** are in Table 3. Because kinetic measurements, reported later, were made in acetonitrile it was of interest to obtain NMR spectra in this solvent. The parent molecules **3** were insufficiently soluble in acetonitrile for spectra to be obtained. However, in the presence of acid solution occurred, allowing spectra of protonated derivatives to be obtained.

The spectra of monoprotonated derivatives **4** are consistent with a structure in which the added proton bridges the nitrogen atoms N(2) and N(6) and indicate a plane of symmetry through the added proton and bisecting the bond between C(1) and C(1'). The spectrum of **4a** in trideuterioacetonitrile is shown in Fig. 4. The methine hydrogens Ha show a pronounced paramagnetic shift on protonation to δ 4.72 (the corresponding value in $CDCl_3$ is 5.20) consistent with the proximity of the positive charge. The methine hydrogens Hb, Hb' show a much smaller shift of *ca.* 0.3 ppm on protonation. In CD_3CN they give an AB quartet, J = 7 Hz, while in $CDCl_3$ the shifts coincide. In the protonated derivatives **4** the methylene hydrogens Hc and Hc' become non-equivalent, as do Hd and

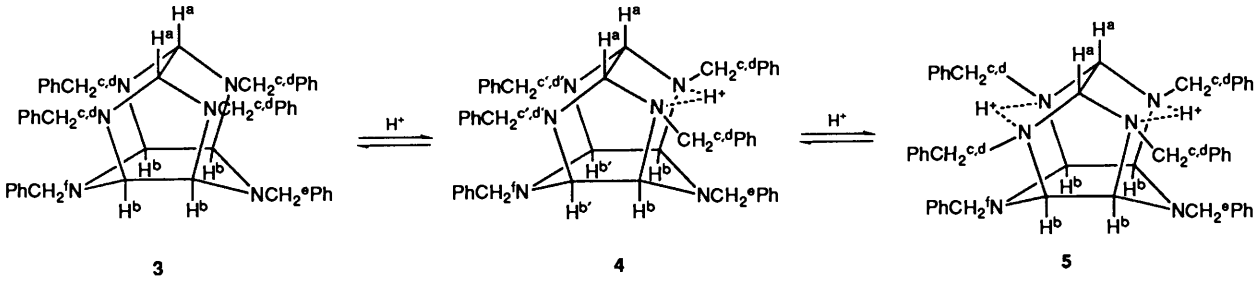


Fig. 2 Protonation of **3** to give **4** and **5**, showing notation of hydrogen atoms

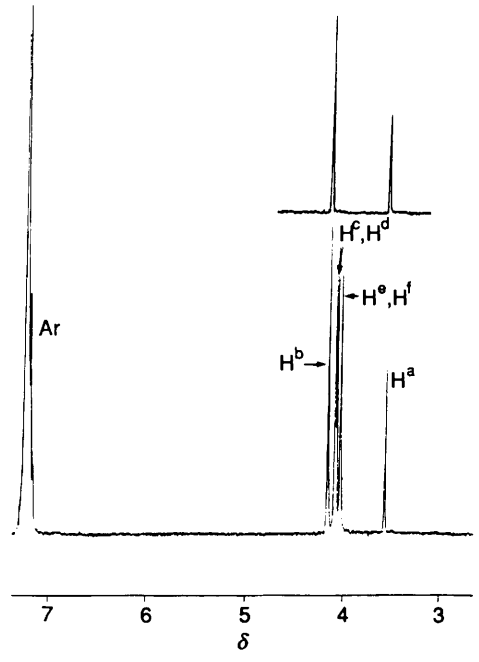


Fig. 3 ^{1}H NMR spectrum (250 MHz) of **3a** in deuteriochloroform. Inset: spectrum of methine hydrogens of **3j**.

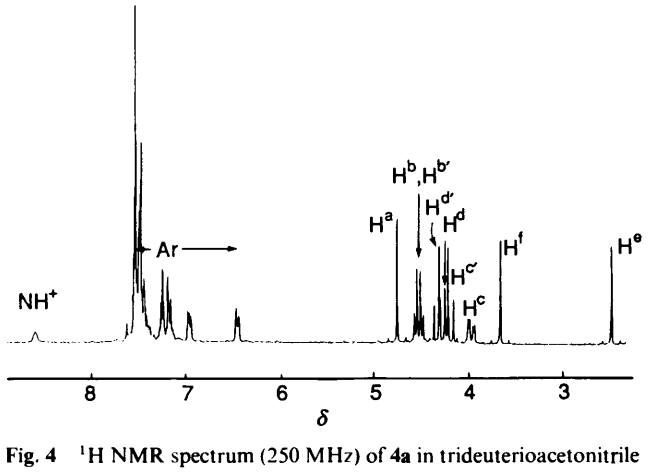


Fig. 4 ^{1}H NMR spectrum (250 MHz) of **4a** in trideuterioacetonitrile

Hd', so that now two distinct AB quartets are observed. It is interesting that spin-coupling, J = 4.8 Hz, is observed between the added ammonium proton and the two equivalent methylene hydrogens Hc (double doublet at δ 3.98 in Fig. 4). However the coupling constant between the added proton and hydrogens Hd is small so that only slight broadening of the Hd doublet is observed. This difference in values of the vicinal coupling constants indicates that the conformation of **4** is fairly firmly fixed and is consistent with dihedral angles [16] between the C–Hc and $\overset{+}{N}$–H bonds of *ca.* 210° and between C–Hd and $\overset{+}{N}$–H

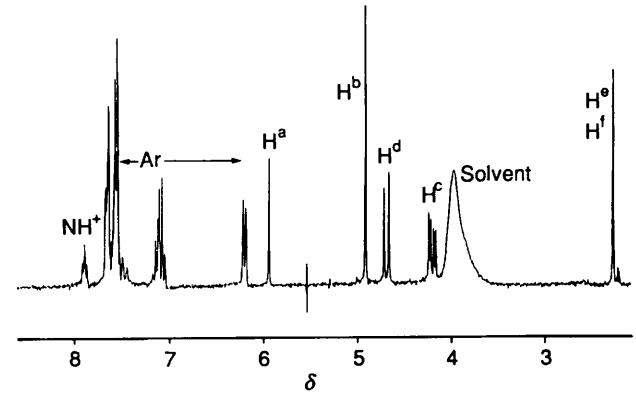
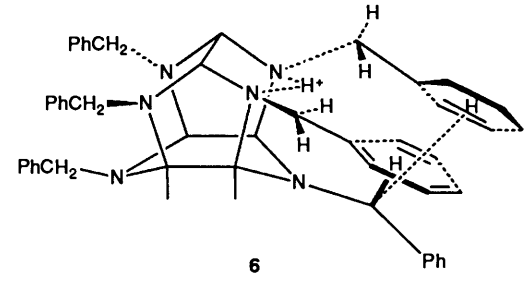


Fig. 5 ^{1}H NMR spectrum (250 MHz) of **5a** in trideuterioacetonitrile

bonds of *ca.* 90°. Another major change in the spectrum on protonation is the large upfield shift to δ 2.4 of the methylene hydrogens He. It is known [17] that the ring current in aromatic derivatives may cause diamagnetic shielding of hydrogens above or below the ring plane. The observed effect may indicate that the hydrogens He are located below the aromatic rings of benzyl groups at N(2) and at N(6) as depicted diagrammatically in **6**.



^{1}H and ^{13}C data for diprotonated derivatives **5** are in Tables 2 and 3, and the spectrum of **5a** in trideuterioacetonitrile is shown in Fig. 5. The spectra indicate that the original symmetry present in solution in the parent compounds is restored on diprotonation. This is consistent with the two protons bridging N(2) and N(6), and N(2') and N(6') respectively. In the ^{1}H spectrum the methine hydrogens Ha show a pronounced paramagnetic shift to *ca.* δ 6 while Hb absorb at δ 5. The Hc and Hd hydrogens now give a single AB quartet, and further coupling, J = 5.6 Hz, is observed between Hc and the added ammonium proton. The methylene hydrogens He and Hf give a singlet at *ca.* δ 2.2 indicating that the diamagnetic shielding depicted in **6** is now felt by all four of these hydrogens.

The spectra indicate that the added acidic protons are strongly held by the nitrogen atoms and that proton exchange either with the medium or with other molecules of **3** is slow. In media containing 0.5 equivalents of acid separate NMR bands are observed for the unprotonated and monoprotonated

Table 2 ^{1}H NMR shifts for **3** and its mono-protonated, **4**, and diprotonated, **5**, derivatives

	Ring substituent	Solvent	Methine		Methylene[a]			Aromatic	Methyl	$\overset{+}{N}H$
			Ha	Hb, Hb'	Hc, Hc'	Hd, Hd'	He, Hf			
3a	H	$CDCl_3$	3.57	4.16	4.07	4.10	4.04	7.17–7.25	—	—
3b	2-Cl	$CDCl_3$	3.57	4.29	4.15	4.17	4.24	6.71–7.48	—	—
3c	4-Cl	$CDCl_3$	3.55	4.06	3.98	4.00	3.89	6.97–7.27	—	—
3d	2-Me	$CDCl_3$	3.49	4.25	3.94	4.03	4.10	6.38–7.23	2.27, 2.35	—
3e	4-Me	$CDCl_3$	3.52	4.10	3.99	4.04	3.98	7.04–7.12	2.32, 2.33	—
3f	2-Br	$CDCl_3$	3.56	4.33	4.14	4.24	4.27	6.68–7.54	—	—
3g	2-F	$CDCl_3$	3.66	4.20	4.05	4.11	4.09	6.92–7.32	—	—
3h	2-OMe	$CDCl_3$	3.59	4.21	4.01	4.05	4.12	6.70–7.47	3.73, 3.76	—
3i	4-Cl (d_{12})	$CDCl_3$	3.55	4.06	—	—	—	7.01–7.27	—	—
3j	H (d_{12})	$CDCl_3$	3.57	4.16	—	—	—	7.19–7.25	—	—
4a	H	$CDCl_3$	5.20	4.41	3.81, 4.12	4.75, 4.41	2.35, 3.61	6.21–7.59	—	8.7
4a	H	CD_3CN	4.72	4.50,[c] 4.57[c]	3.98,[b] 4.20	4.25, 4.34	2.55, 3.70	6.40–7.64	—	8.5[b]
4c	4-Cl	$CDCl_3$	5.16	4.37	3.81, 4.07	4.65, 4.33	2.43, 3.55	6.21–7.52	—	8.6
4d	2-Me	$CDCl_3$	5.22	4.53	4.10, 4.17	4.60, 4.42	2.49, 3.60	6.06–7.46	2.29, 2.32 1.65, 1.90	8.6
4j	H (d_{12})	$CDCl_3$	5.19	4.40	—	—	—	6.22–7.54	—	8.7
4j	H (d_{12})	CD_3CN	4.71	4.50,[c] 4.56[c]	—	—	—	6.42–7.60	—	8.5
5a	H	$CDCl_3$	6.17	5.06	4.23	4.73	2.28	6.20–7.72	—	8.0 (2 H)
5a	H	CD_3CN	5.94	4.92	4.20[d]	4.70	2.27	6.20–7.67	—	7.9[d] (2 H)
5c	4-Cl	$(CD_3)_2CO$	6.25	5.34	4.64	4.97	2.41	6.25–7.85	—	8.5 (2 H)
5j	H (d_{12})	$CDCl_3$	6.19	5.08	—	—	—	6.20–7.74	—	8.0 (2 H)

[a] Geminal coupling, J = 13 Hz, is always observed between Hc and Hd, and between Hc' and Hd'. [b] Coupling, J = 4.8 Hz, is observed between the two Hc protons and NH^+. [c] Vicinal coupling, J = 7 Hz, is observed between Hb and Hb'. [d] Coupling, J = 5.6 Hz is observed between ammonium protons and Hc, and Hc'.

Table 3 ^{13}C NMR shifts[a] for **3** and mono-protonated derivatives **4**

	Ring substituent	Methine	Methylene	Aromatic	Methyl
3a	H	76.99 (4 C) 80.15 (2 C)	55.84 (4 C) 56.51 (2 C)	126–140	—
3b	2-Cl	76.77 (4 C) 79.69 (2 C)	53.15 (4 C) 54.34 (2 C)	126–138	—
3c	4-Cl	76.47 (4 C) 80.95 (2 C)	55.54 (4 C) 56.18 (2 C)	128–139	—
3d	2-Me	75.95 (4 C) 77.01 (2 C)	52.46 (4 C) 54.35 (2 C)	124–138	18.68 (2 C) 18.76 (4 C)
3e	4-Me	76.77 (4 C) 80.38 (2 C)	55.81 (4 C) 56.56 (2 C)	128–138	21.00 (2 C) 21.11 (4 C)
3f	2-Br	77.53 (4 C) 78.77 (2 C)	55.41 (4 C) 56.29 (2 C)	124–140	—
3g	2-F	76.84 (4 C) 80.83 (2 C)	49.21 (4 C) 49.57 (2 C)	114–131	—
3h	2-OMe	77.12 (4 C) 80.36 (2 C)	50.36 (4 C) 54.94 (2 C)	110–158	26.74 (2 C) 26.85 (4 C)
3i	H (d_{12})	76.36 (4 C) 80.76 (2 C)	—	128–138	—
3j	4-Cl (d_{12})	77.07 (4 C) 80.84 (2 C)	—	127–141	—
4a	H	75.09 (2 C) 80.89 (2 C) 84.31 (2 C)	54.5 (1 C), 56.1 (1 C) 55.9 (2 C), 58.1 (2 C)	127–138	—
4a	H[b]	75.38 (2 C) 81.53 (2 C) 82.84 (2 C)	54.19 (1 C), 55.19 (1 C) 54.75 (2 C), 57.21 (2 C)	127–139	—
4d	2-Me	75.06 (2 C) 81.32 (2 C) 82.91 (2 C)	52.71 (1 C), 53.43 (1 C) 52.49 (2 C), 54.78 (2 C)	116–137	18.72 19.28

[a] In deuteriochloroform unless stated. [b] In trideuterioacetonitrile.

species, similarly with 1.5 equivalents of acid bands due to mono- and di-protonated species are observed. The spectra are then, consistent with structures **4** and **5** in which the proton(s) is strongly associated with two nitrogen atoms. However it is not possible to distinguish between situations where the proton is situated symmetrically between the nitrogen atoms or alternatively equilibrates rapidly between equivalent structures involving bonding to one nitrogen atom with hydrogen-bonding to the second.

The monoprotonated derivatives **4** were found to be stable in solution for many hours, whereas the NMR spectra of diprotonated species, **5**, indicated decomposition within 1 h. This precluded determination of ^{13}C spectra of **5**. Addition of base soon after acidification regenerated the spectra of parent molecules **3**. There was no evidence for triprotonation in the presence of excess acid and it was found qualitatively that the rate of decomposition increased with increasing excess of acid.

Table 4 Rate constants for decomposition of **3a** in acetonitrile as a function of acid concentration and water content[a]

	$k_{obs}/10^{-4}$ s^{-1}				
$[HClO_4]$/ 10^{-3} mol dm^{-3}	0% H_2O[b]	0.25% H_2O[b]	0.50% H_2O[b]	0.75% H_2O[b]	1.0% H_2O[b]
1.0	0.25	—	1.21	2.19	3.28
2.0	0.39	—	1.88	2.71	3.40
4.0	0.68	—	2.10	2.85	4.36
6.0	0.84	—	2.50	4.30	5.40
9.0	1.21	—	3.10	4.51	6.10
20.0	2.5	2.8	3.6		
40.0	5.3	—	—		
60.0	8.1	4.6	3.9		
80.0	11.5	7.4	4.6		
90.0	12.8	8.7	4.5		
200	47	34	24		
500	134	88	62		

[a] Concentration of **3a** is 9.7×10^{-5} mol dm^{-3}. Temperature is 25 °C. [b] Added water, % (v/v).

Table 5 Rate constants for decomposition of **3a** in acetonitrile with low water content.[a] Fit to eqn. (2)

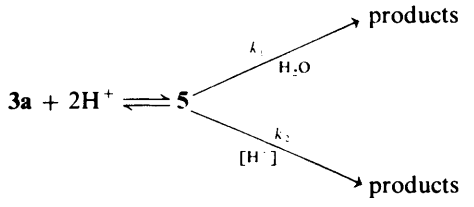
$[HClO_4]$/ 10^{-3} mol dm^{-3}	% H_2O[b]	k_{obs}/ 10^{-5} s^{-1}	$k_2[H^+]$[c]/ 10^{-5} s^{-1}	k_2[d]$/10^{-2}$ dm^3 mol^{-1} s^{-1}
1.0	0.054	2.5	1.15	1.15
2.0	0.058	3.9	2.4	1.2
3.0	0.062	5.2	3.6	1.2
4.0	0.066	6.8	5.1	1.3
5.0	0.070	7.5	5.7	1.2
6.0	0.074	8.4	6.5	1.1
7.0	0.078	10	8.3	1.2
10	0.090	12	9.8	1.0
20	0.13	30	27	1.3
40	0.21	53	48	1.2
50	0.25	73	67	1.3
70	0.33	91	83	1.2
80	0.37	107	98	1.2
90	0.41	128	118	1.3

[a] Concentration of **3a** is 9.7×10^{-6} mol dm^{-3}. [b] % (v/v). Total water content. [c] Calculated after subtraction of $k_1[H_2O]$ from k_{obs}, using a value of 2.5×10^{-4} s^{-1} for k_1 at 1% H_2O. [d] Calculated by dividing previous column by $[HClO_4]$.

Formation and Decomposition of **3a** *in Acetonitrile.*— Attempts were made to follow the formation of **3a** using UV spectrophotometry. In acetonitrile **3a** shows an inflection at 207 nm (ε 6×10^4 dm^3 mol^{-1} cm^{-1}) with a shoulder extending to 280 nm. The reactant benzylamine shows strong absorption below 230 nm with a broad band at 250 nm, while the likely intermediate **2a** has λ_{max} 220 nm with a shoulder to 280 nm. The similarity of these spectra made analysis difficult. It was, however, noted that spectra of a reaction mixture containing benzylamine, glyoxal and acid initially showed absorption due to benzylamine and with time a general increase in absorbance in the region to 300 nm occurred. Nevertheless the final spectrum did not correspond closely to that of **3a**, but corresponded more closely to the decomposition products of **3a** in acid solution. A problem with spectrophotometric measurements is the requirement, because of their high extinction coefficients, to use low (*ca.* 10^{-4} mol dm^{-3}) concentrations of reagents. In the preparation of **3a** the concentration of acid catalyst is twenty times smaller than that of benzylamine and it was difficult in the spectrophotometric measurements to maintain the acid concentration at the required level.

Studies of the acid-catalysed decomposition of **3a** were more successful. **3a** is insufficiently soluble in water even for spectrophotometric measurements so that acetonitrile was used as solvent. Here **3a** is indefinitely stable. The effects of changing the acid and water concentrations were examined, with perchloric acid being used since it is known to be completely dissociated in acetonitrile.[18,19]

The presence of acid caused an initial instantaneous decrease in absorbance of **3a** in the region 230–300 nm. This change which is quantitatively reversed by base is attributed to protonation and in view of the NMR measurements is likely to represent diprotonation. The initial rapid change in spectrum was followed by a very much slower change giving rise to increases in absorbance at 210 nm and in the range 230–300 nm. The kinetics of this process were measured at 240 nm both as a function of acid concentration and of water content in the solvent. In all cases the acid concentration was in large excess of the concentration of **3a** and first-order kinetics were observed. The data in Table 4 show that values of the rate constant increase with acid concentration. However the dependence on water content depends on the acidity. Thus in solutions where $[HClO_4] < 0.04$ mol dm^{-3} values of rate constants increase with increasing water content, whereas at higher acidities the rate constants decrease with increasing water content. These results are compatible with the presence of two competing pathways shown in eqn. (1), which leads to eqn. (2). Decomposition may involve attack by water on the diprotonated species **5a** or further reaction of **5a** with acid. The water present



(1)

$$k_{obs} = k_1[H_2O] + k_2[H^+] \quad (2)$$

may arise from that present in the solvent (0.05%), from water added with the perchloric acid or from further added water. Data in solutions of low total water content are in Table 5 and are compatible with eqn. (2) with a value for k_2 of 0.012 dm^3 mol^{-1} s^{-1} and a value for k_1 of 2.5×10^{-4} s^{-1} at 1% (v/v) water content. The latter value may be converted to a second order rate constant of 4.5×10^{-4} dm^3 mol^{-1} s^{-1} for reaction of **5a** with water. In view of the relatively small difference in values of k_1 and k_2 it seems likely that the acid-catalysed pathway involves equilibrium protonation, equilibrium constant K_2, to give a low concentration of a triprotonated species which spontaneously decomposes.

The increase in value of k_{obs} with increasing water content at low acid concentration is explained by the dominance of the first term in eqn. (2). In solutions of high acid concentration the second term in eqn. (2) will become dominant. However it is known from related work[20] that values of protonation constants, such as K_2, for nitrogen heterocycles decrease as the water content in acetonitrile increases. Hence the overall decrease in the value of k_2 with increasing water content at high acid concentrations may be attributed to this source.

The results suggest that, since a single rate process is observable, an initial C–N bond breaking step is rate determining in the decomposition pathway. It was possible, in more concentrated solutions, to isolate ammonium perchlorate as a reaction product indicating complete decomposition. It seems likely[20] that the water-catalysed route may involve attack on an imminium ion intermediate present at low concentration in equilibrium with protonated forms.

Table 6 Summary of data collection, structure solution and refinement details

Crystal data	
empirical formula	$C_{48}H_{42}Cl_6N_6$
fw	915.6
colour, habit	colourless, prism
crystal size, mm	0.43 × 0.38 × 0.62
crystal system	Monoclinic
a/Å	18.916(4)
b/Å	11.449(2)
c/Å	20.403(4)
α/°	90
β/°	90.72(2)
γ/°	90
V/Å^3	4418(1)
space group	$C2/c$
Z	4
molecular symmetry	2-fold
F(000)	1896
d_{calc}/g cm^{-3}	1.376
μ/mm^{-1}	0.43
Data acquisition[a]	
temp./°C	23
unit-cell refl. (2θ-range°)	25 (14–36)
max. 2θ (°) for refl.	53.8
hkl range of refl.	−24 24, 0 14, 0 26
variation in 3 standard refl.	< 1%
refl. measured	5290
unique refl.	4800
R_{int}	0.011
refl. with $I > 3\sigma(I)$,	2827
absorption correction type	9 ψ scans
min. max. abs. corr.	0.8090, 0.8837
Structure solution and refinement	
solution method	Direct methods
H-atom treatment	riding, C–H 0.95 Å
no. of variables in LS	272
k in $w = 1/(\sigma^2F_o + kF_o^2)$	0.0006
R,R_w, gof	0.041, 0.058, 2.19
density range in final Δ-map/e Å^{-3}	−0.20, 0.23
final shift/error ratio	0.004
sec. extnct. correction	1.5×10^{-7}

[a] Data collection on an Enraf–Nonius CAD4 diffractometer with graphite-monochromatised Mo-Kα radiation (λ 0.7093 Å).

Experimental

^{1}H and ^{13}C NMR spectra were recorded using Bruker AC250 or AMX 500 instruments with 0.01 mol dm^{-3} concentration of substrates. HPLC measurements were made with a Varian 9010 star system using a Highchrom R.P.B. column. UV spectra were recorded with a Perkin-Elmer Lambda 2 spectrophotometer. Kinetic measurements were made at 25 °C using the latter instrument with freshly prepared solutions of reagents. First-order rate coefficients were determined by standard methods.

Glyoxal (40% aqueous solution), benzylamine and substituted benzylamines were the purest available commercial specimens. The acetonitrile used as solvent for the spectrophotometric measurements was BDH, HPLC, Far-UV grade containing 0.05% water.

Synthesis of **3a**.—The following general procedure was used. Benzylamine (14 g, 0.13 mol) was added slowly to a solution of 40% glyoxal (9.48 g, 0.065 mol) in acetonitrile (250 cm^3) containing nitric acid (0.4 cm^3, 70%) over 40 min at 25 °C. The mixture was stirred overnight, the solvent was then decanted off and methanol (150 cm^3) was added to the crude product. The mixture was stirred vigorously for *ca.* 1 h and then allowed to settle after which time the methanol was decanted off and the washing was repeated with a second portion of methanol. After decanting off the methanol, acetonitrile (30 cm^3) was added and the fine white material was filtered off, washed with acetonitrile (30 cm^3) and dried. The material was recrystallised from boiling acetonitrile. The effects of varying the nature and concentration of acid catalyst, and also of varying the temperature were examined.

In the case of **3g**, after the addition of 2-fluorobenzylamine the mixture was left for 3 days, after which time the acetonitrile was removed under reduced pressure. Addition of methanol resulted in precipitation of **3g**, which was recrystallised from methanol. In the case of **3h**, after reaction in acetonitrile for 1 day the solvent was removed, the residue was left for 4 days and then a mixture of cyclohexane/chloroform [80/20 (v/v), 2 cm^3] was added to facilitate precipitation. This was followed by the addition of cold methanol (150 cm^3) after which the product was filtered off, washed with methanol and recrystallised from cyclohexane.

Synthesis of **3i, j**.—The method described for the synthesis of **3** was repeated using benzylamine-[α,α-$^2H_2$]-[N,N-$^2H_2$] to give **3j** and 4-chlorobenzylamine [α,α-$^2H_2$]-[N,N-$^2H_2$] to give **3i**. **3j** was recrystallised from acetonitrile and **3i** from methylene dichloride.

Preparation of **2a** *and* **2c**.—40% Aqueous glyoxal (4 g, 0.027 mol) was added dropwise with stirring to a solution of benzylamine (5.9 g, 0.055 mol) in aqueous ethanol (40 cm^3, 50% v/v) containing nitric acid catalyst (0.005 cm^3, 70%) over a period of 10 min while the temperature was kept below 0 °C. The precipitated white solid was washed with cold aqueous ethanol (10 cm^3) and dried under vacuum (0.1 mmHg) for 2 h. **2a** was obtained (5.8 g, 91%) as an unstable crystalline solid. $\delta_H(CDCl_3)$ 4.77 (s, 4 H, methylene), 7.10–7.37 (m, 10 H, aromatic) and 8.07 (s, 2 H, vinyl).

2c was prepared similarly starting from 4-chlorobenzylamine. $\delta_H(CDCl_3)$ 4.73 (s, 4 H, methylene), 7.15–7.34 (m, 8 H, aromatic) and 8.05 (s, 2 H, vinyl).

Crystal Structure Analysis of **3c**.—Details of the crystal data, data acquisition and refinement are concisely summarised in Table 6. The systematic absences (hkl absent if $h + k = 2n + 1$, $h0l$ absent if $l = 2n + 1$) allow the space group to be Cc or $C2/c$; the latter was chosen and confirmed by the successful refinement. All hydrogen atoms were clearly visible in difference maps and were allowed for, but not refined, in the calculations. Scattering factors and anomalous dispersion correction terms were from *International Tables for X-ray Crystallography*.[21] The final fractional atomic coordinates together with other data tables (bond lengths and angles, anisotropic thermal parameters, calculated hydrogen coordinates and torsion angles have been desposited.* Calculations were done with SDP-Plus.[22] The diagram (Fig. 1) was prepared with the aid of PLUTON;[23] analysis of the coordinates with the program PLATON[24] showed that there were no solvent-accessible voids in the crystal lattice.

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* For details of the CCDC deposition scheme, see 'Instructions to Authors,' *J. Chem. Soc., Perkin Trans. 2*, 1993, issue 1.

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