Chem. Ber. **115**, 2872–2891 (1982)

Conformation in Solution of Tetraaryl-3,7-diazabicyclo[3.3.1]-nonanes and Tetra- and Pentaaryl-1,3-diazaadamantanes. A Nuclear Magnetic Resonance Study

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Received December 29, 1981

The proton NMR spectra of a series of tetraaryl-3,7-diazabicyclo[3.3.1]nonanes, **5** – **12**, have been assigned with the aid of nuclear Overhauser difference spectroscopy. The NOE's together with spin lattice relaxation times have been used to show that these molecules adopt the chair-boat conformation with all aryl groups being equatorial. This conformation and the torsional angles of the aryl groups are similar to those found in the solid state. Analogous studies have been carried out with tetra- and pentaaryl-1,3-diazaadamantanes, **3**, **4**, **13**, and **14**. A surprisingly low barrier of rotation (**4b**: $\Delta G^{\neq}_{298}$ = 42 kJ · mol^{-1}) has been found for the two 1,3-diaxially oriented aryl groups in these systems. Carbon-13 chemical shift data are reported for the above compounds. Those of the 3,7-diazabicyclononanes **5** – **12** are found to be consistent with the proposed chair-boat conformation. Nitrogen-15 chemical shift data and ^{13}C-^{15}N coupling constants are also in accord with this conformation. A stereoselective reduction of 4,8,9,10-tetrakis(3,5-dimethylphenyl)-1,3-diaza-6-adamantanone (**4b**) to the corresponding alcohol **15** and the ready acid-catalyzed rearrangement of this alcohol to **16**, the first example of the 9-oxa-1,5-diazatricyclo-[5.3.1.0^{3,8}]undecane ring system, is described.

Konformation von Tetraaryl-3,7-diazabicyclo[3.3.1]nonanen und Tetra- und Pentaaryl-1,3-diaza-adamantanen in Lösung. Eine NMR-Studie

Die ^1H-NMR-Spektren einer Reihe von Tetraaryl-3,7-diazabicyclo[3.3.1]nonanen **5** – **12** wurden mit Hilfe der Kern-Overhauser-Differenz-Spektroskopie zugeordnet. Aufgrund der NOE-Effekte und Spin-Gitter-Relaxationszeiten ließ sich zeigen, daß diese Moleküle die Sessel-Boot-Konformation einnehmen, wobei alle Arylgruppen äquatorial stehen. Diese Konformation und die Torsionswinkel der Arylgruppen ähneln denen, die im festen Zustand gefunden wurden. Analoge Untersuchungen wurden mit den Tetra- und Pentaaryl-1,3-diazaadamantanen **3**, **4**, **13** und **14** durchgeführt. Die beiden 1,3-diaxial orientierten Arylgruppen zeigen in diesen Systemen eine überraschend niedrige Rotationsbarriere (**4b**: $\Delta G^{\neq}_{298}$ = 42 kJ · mol^{-1}). Die chemischen Verschiebungen in den ^{13}C-NMR-Spektren aller Verbindungen werden mitgeteilt. Die der 3,7-Diazabicyclo[3.3.1]nonane **5** – **12** stehen im Einklang mit der vorgeschlagenen Sessel-Boot-Konformation. Das gleiche gilt für die chemischen Verschiebungen in den ^{15}N-NMR-Spektren und die ^{13}C-^{15}N-Kopplungskonstanten. Die Reduktion des 4,8,9,10-Tetrakis(3,5-dimethylphenyl)-1,3-diaza-6-adamantanons (**4b**) führt stereoselektiv zum Alkohol **15**, der sich säurekatalysiert leicht in **16** umlagert, den ersten Vertreter des 9-Oxa-1,5-diazatricyclo[5.3.1.0^{3,8}]undecan-Ringsystems.

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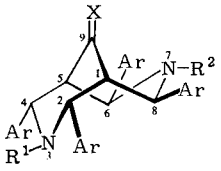
A following paper[2] describes the synthesis and the X-ray crystallographic structural studies of several tetraaryl-3,7-diazabicyclo[3.3.1]nonanes **1** and of the related 1,3-diazaadamantanes **3** and **4**. These studies unequivocally afforded both the structures and stereochemical configurations of the compounds. In addition, for the former, the X-ray crystallography established a chair-boat conformation **1** of the two piperidine rings of the bicyclo system, in the crystalline state. Previously[3], we had argued on the basis of a remarkable (but unfortunately deceptive) similarity between differential proton chemical shifts in the 1,3-diazaadamantanes **3** and **4** and the 3,7-diazabicyclononane series that the latter adopt the chair-chair conformation **2** in solution. It therefore seemed highly desirable to undertake further experiments which would be definitive in establishing the actual solution conformation of the 3,7-diazabicyclononanes. We have made extensive use of proton nuclear Overhauser enhancements (NOE), which, depending as they do on dipole-dipole interactions with their inverse sixth power dependence on internuclear separations, have proved particularly efficacious for solving these conformational problems. The enhancements are conveniently determined by FT difference spectroscopy[4].



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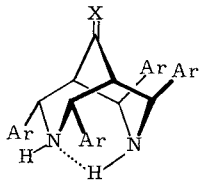

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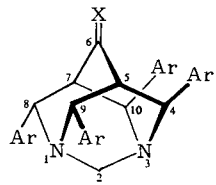


3: X = H_2
4: X = O

	Ar
a	4-Methylphenyl
b	3,5-Dimethylphenyl

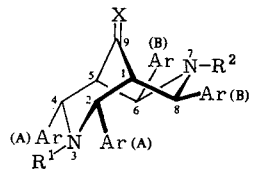
The proton spectra of *N*-substituted 3,7-diazabicyclononanes show evidence of slow rotation of the aryl substituents. This phenomenon is of interest in its own right and we will report a detailed study of the kinetics of the rotational processes at a later date. In the present context it has been sufficient to make use of the effect of saturation transfer in the NOE difference spectra to assign resonances to pairs of protons related by slow mutual exchange.

Proton NMR Spectroscopy

2,4,6,8-Tetraaryl-3,7-diazabicyclo[3.3.1]nonanes

The 200 MHz proton spectrum of 2,4,6,8-tetrakis(3,5-dimethylphenyl)-*N*,*N'*-dimethyl-3,7-diazabicyclo[3.3.1]nonane (**9b**) is shown in Figure 1 which also contains a series of NOE difference spectra.

Although the aromatic region exhibits the expected four resonances with intensity ratios of 1:1:2:2 compatible with two pairs of dissimilar 3,5-dimethylphenyl residues,



5-10 (≡ 1)

	X	R^1	R^2
5	H_2	H	H
6	O	H	H
7	H_2	H	Me
8	O	H	Me
9	H_2	Me	Me
10	O	Me	Me

	Ar
a	4-Methylphenyl
b	3,5-Dimethylphenyl

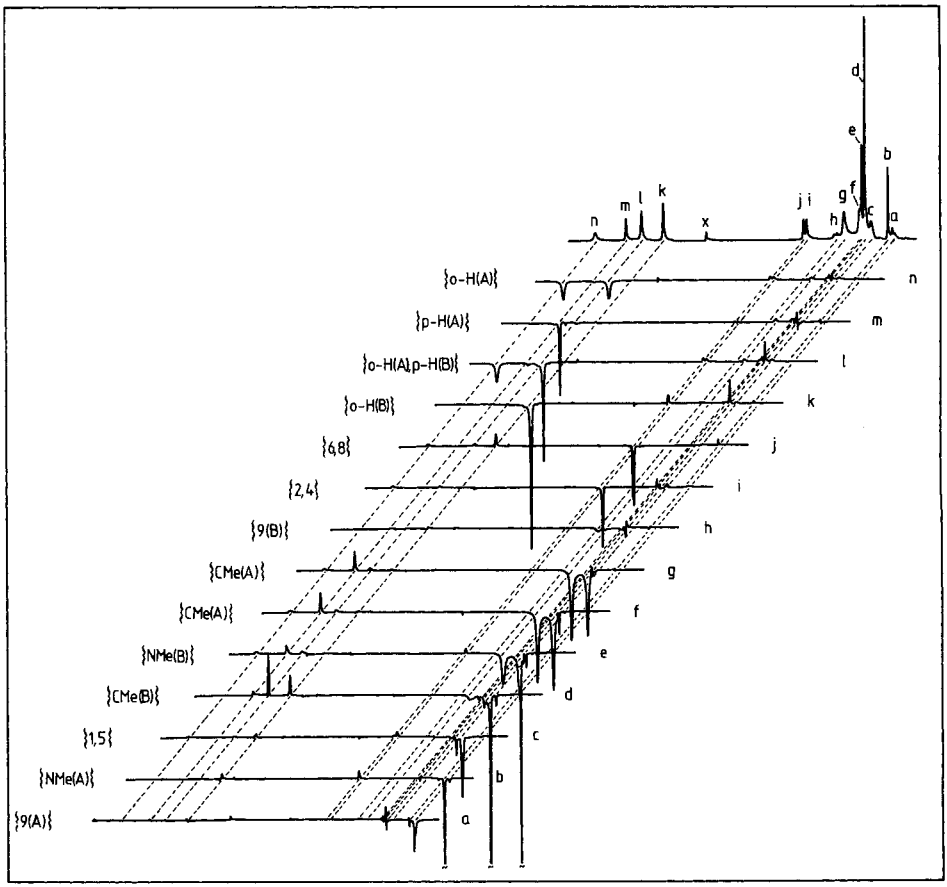


Fig. 1. 200 MHz ^{1}H NMR spectra of the *N,N'*-dimethyl-3,7-diazabicyclononane **9b** for [D_2]dichloromethane solution showing the relation between the normal spectrum and the NOE difference spectra. X: Solvent signal

the assignments are, in fact, more complex. Irradiation of the somewhat broad band at $\delta = 7.61$ (Fig. 1n) produces a *negative* signal at 6.65 which is due to saturation transfer. Thus, the peak at 7.61 and *half* that at 6.65 arise from the *ortho*-protons of an equivalent pair of 3,5-dimethylphenyl residues which are rotating at a rate which is slow on

the NMR time scale. This interpretation is confirmed by the observation of coalescence of these resonances at higher temperatures and lower field strength. Similarly, the broad resonances at 2.21 and 2.54 are assigned to the methyl groups of the same pair of rings since appropriate irradiations (Fig. 1f and 1g) also cause saturation transfer between the two sets of nuclei. For convenience, we will refer to this slowly rotating pair of rings as the pair of "slow" aryl groups and the other pair as the "fast" aryl groups and denote them by A and B, respectively.

Assignment of the signal at 6.97 to the *para*-protons of the slow ring follows from their proximity to the methyl groups as evidenced by the complimentary NOE's exhibited in Fig. 1f, 1g, and 1m. The *ortho*- and *para*-protons of the fast rings therefore absorb at 6.20 and 6.65, respectively, and the methyl groups give rise to the intense signal at 2.11. The bridgehead protons are assigned to the broad signal at 1.99 and the *N*-methyl groups to the sharp singlets at 2.17 and 1.63. The two types of benzylic protons are observed in the region 3.3 and the protons of the bridge methylene group, which have widely different chemical shifts (H_A: 1.52 and H_B: 2.71), absorb as doublets of triplets exhibiting the expected large geminal coupling (12.0 Hz).

The remaining problem is to assign these last three pairs of resonances to the one or other side of the 3,7-diazabicyclononane ring system. Since irradiation (Fig. 1b) of the *N*-methyl signal at 1.63 causes an enhancement of the benzylic proton signal at 3.36 as well as of the signal (6.20) arising from the *ortho*-protons of the fast rings, these protons must be on the same side as the fast rings. Related experiments (particularly 1i and 1j) confirm this conclusion. Finally, irradiation (Fig. 1h) of the down-field (H_B, 2.71) methylene proton, as well as causing the expected enhancements of the signals of its geminal and vicinal neighbours, produced a significant intensification of the resonance of the *ortho*-protons of the fast aromatic ring. This observation, together with the remarkable downfield shift of the methylene proton H_B requires the close approach of the fast ring to the bridging methylene group. This is only possible if the aryl groups are *cis* to the bridge. Thus all the proton resonances are unequivocally assigned and the slowly rotating aryl groups are equatorially oriented ones at positions 2 and 4 in **1**. The chemical shifts and coupling constants are included in Table 1.

A closer inspection of the NOE values and of the chemical shifts of the aromatic protons leads to a rather accurate picture of the preferred solution conformation of the whole molecule. Irradiation of the *ortho*-protons of the slow ring produces significant enhancement ($\eta = 0.08$; $\eta_{max} = 0.5$) of the benzylic protons at *both* the 2(4) and 8(6) positions as well as a smaller enhancement of the bridgehead resonance (Fig. 1l and 1n). Remembering that, because of saturation transfer, both *ortho*-protons of the slow ring will be effective in producing NOE's of the absorptions of neighbouring protons, it can be seen that the slow ring must adopt the conformation shown in Fig. 2. In contrast, irradiation of the *ortho*-protons of the fast ring only enhances the signal of the benzylic proton adjacent to that ring. That the fast aryl groups are *cis* to the bridging methylene group is evident from the fact that irradiation of the bridgehead proton (Fig. 1c) causes a much smaller enhancement (0.03 vs. 0.08) of the signal of the benzylic protons adjacent to the fast aromatic rings than for those adjacent to the slow aromatic rings, reflecting, of course, the greater internuclear distance in the former situation. The conformation of the fast rings is established as represented in Fig. 2 since, as mentioned

Table 1. Proton chemical shifts [ppm] and proton proton coupling constants [Hz] (in square brackets) of some 3,7-diazabicyclononanes and 1,3-diazaadamantanes in [D]chloroform

	Heterocyclic Ring System								Aryl Groups							
3,7-Diazabicyclononanes	$H_A-C(9)-H_B$		$H_C-C(1,5)$	J_{AB}	J_{AC}	J_{BC}	2-H 4-H Chair	6-H 8-H Boat[a]	NH[b]	*N*-Methyl Chair	*N*-Methyl Boat	Aryl A on Chair *o*-H	*m*-H	Me	Aryl B on Boat *o*-H	*m*-H	Me
5a[2]	1.68	2.69	2.09	12	2	4	4.10		1.04 1.70			7.42	7.17	2.40	6.68	6.83	2.20
7a	1.64[c]	2.79	2.20	12	2.4	3.6	4.04	3.34 [1.8]	1.78		1.67	7.43	7.18	2.42	6.57	6.87	2.25
9a	1.53	2.71	2.06	12.0	2.7	4.0[d]	3.36 [3.3	3.46 3.3]		2.15	1.63	7.1 – 7.6[e]		2.40	6.51	6.83	2.18
6a[2]			2.81				(4.29 | 4.67) [3]	1.35 2.05			7.47	7.20	2.40	6.60	6.87	2.20
8a			2.83				(4.18 | 3.94) [2.4]	2.00		1.62	7.43	7.18	2.37	6.55	6.85	2.20
10a			2.77				(3.69 [2.6 | 4.20) 2.6]		2.20	1.56	7.1 – 8.1[e]		2.38	6.52	6.82	2.18
11[2]			2.85				(4.30 | 4.72) [3]	1.50 2.70			7.47	7.20	2.43	6.6 – 7.2[f]		–
12			2.78				(3.70 [2.7 | 4.13) 2.7]		2.22	1.57	7.1 – 8.2[e]		2.38	6.6 – 7.1[f]		–
												o-H	*p*-H		*o*-H	*p*-H	
5b	[g]	2.46	1.96	15	?	3.9	4.04		1.1[g]			7.14	6.96	2.31	6.25	6.66	2.04
9b[h]	1.520	2.708	1.988	12.0	2.7	3.9	3.295 [2.1	3.363 2.1]		2.172	1.633	7.606 6.654	6.972	2.208 2.541	6.201	6.654	2.111
6b			2.75				4.24	4.64 [3]	1.40			7.19	7.00	2.36	6.26	6.70	2.09
10b			2.70				(3.60 [2.7 | 4.03) 2.7]		2.25	1.63	7.43[e]	6.97	2.35[e]	6.22	6.67	2.10

Table 1 (*continued*)

	Heterocyclic Ring System								Aryl Groups					
Tetraaryl-1,3-diazaadamantanes						Aryl eq.	Aryl ax.[a]							
	$H_A-C(6)-H_B$		$H_C-C(5,7)$	J_{AB}	J_{AC}	J_{BC}	8-H 4-H	N–CH–N	Aryl equatorial			Aryl axial		
							9-H 10-H	2-H	*o*-H	*m*-H	Me	*o*-H	*m*-H	Me
3a[2]	2.3[e]	3.36	2.83	13	?	3	4.73 4.24	4.20	7.55	7.12	2.34	7.00	6.69	2.11
4a[2]			3.90				(4.64 4.82)	4.39	7.47	7.17	2.34	6.87	6.58	2.08
13[2]			3.94				(4.72 4.83)	4.41	7.50	7.20	2.37	6.5–7.1[f]		–
									o-H	*p*-H		*o*-H	*p*-H	
3b	2.3[e]	3.56	2.82	13	?	3	(4.67 4.29)	4.24	7.25	6.90	2.31	6.75	6.47	2.07
15[i]	4.71	–	3.35	–	2	–	4.61 4.55	4.38	7.29	6.95	2.36	7.21	6.62	2.16
4b			3.85				4.60 4.70	4.42	7.22	6.95	2.33	6.60	6.38	2.07
Pentaaryl-1,3-diazaadamantanones									Ar–H				Me	
14a			3.75[k]				4.68 4.97	5.83	6.5–8.3 m				2.08	2.10
							5.07 5.17						2.28	2.32
													2.39	
									o-H	*p*-H				
14b[h]			5-H 3.70				4-H 4.85	5.79	2-Ar 7.80		7.02		2.44	
			7-H 3.67				8-H 4.58		4-Ar 6.75		6.42		2.08	
							9-H 5.08		8-Ar 7.16		6.87		2.25	
							10-H 4.92		9-Ar 7.39		6.92		2.35	
									10-Ar 6.79		6.42		2.08	

[a] Values in parenthesis are by analogy with those assigned on the basis of NOE's. – [b] No attempt was made to assign the NH signals. – [c] Signals are partially hidden under other signals. – [d] The coupling constants were taken from a 360 MHz spectrum in [D_2]dichloromethane. – [e] Broadened signal. – [f] Phenyl multiplet. – [g] Signal hidden under other signals. – [h] These values were obtained from a 200 MHz spectrum in [D_2]dichloromethane. – [i] These values were obtained from a 400 MHz spectrum. The assignment of the benzylic and *ortho*-protons may be exchanged. No signal of the hydroxy proton was found; the coupling constant for H–C–O–H is 11.9 Hz. – [k] In [D_6]benzene the two bridgehead protons give rise to separate signals at 3.58 and 3.83 ppm.

above, there must be a reasonably short internuclear separation between the bridge methylene proton and the *ortho*-protons. Furthermore, the large NOE (0.14) observed (Fig. 1k) for the benzylic proton by irradiation of the adjacent *ortho*-protons is consistent with this conformation.

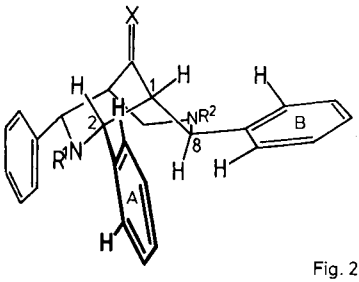


Fig. 2a

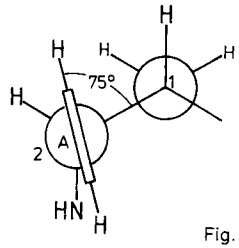


Fig. 2b

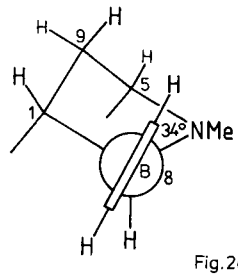


Fig. 2c

Fig. 2. Fig. 2a: Conformation of the tetraaryl-3,7-diazabicyclo[3.3.1]nonanes **5** – **12** and the approximate positions of the bridgehead, benzylic, and *ortho*-protons, cf. Table 3. The aryl ring at C-6 and the methyl groups have been omitted. Fig. 2b: View along the axis of the *p*-tolyl ring A on the chair ring of **7a**. Fig. 2c: View along the axis of the *p*-tolyl ring B on the boat ring of **7a**[2)]

Essentially the same results have been obtained for the *p*-tolyl analogue **9a**, the 360 MHz spectrum of which is shown in Fig. 3. It is noted that, in this molecule, all four ring protons of the slow ring give rise to discrete, albeit broad signals.

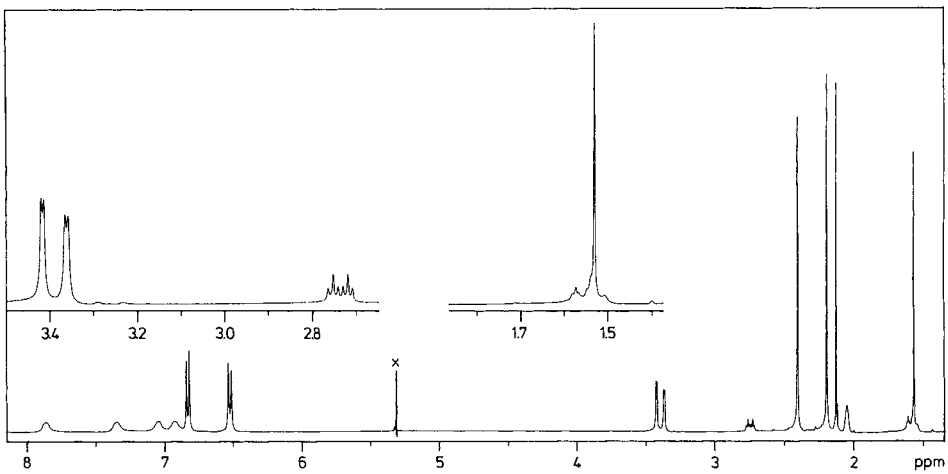


Fig. 3. 360 MHz ^{1}H NMR spectrum of *N,N'*-dimethyl-2,4,6,8-tetrakis(4-methylphenyl)-3,7-diazabicyclo[3.3.1]nonane (**9a**) in [D_2]dichloromethane solution. X: Solvent signal

The qualitative conclusions regarding the conformations in solutions of **9a** and **b** can be placed on a sounder basis by determining the contributions of the various protons to the spin lattice relaxation times ($T_1^{i(j)}$) of their neighbour and using these quantities to evaluate effective interproton distances, r_{ij}. The experimental spin lattice relaxation

times, T_1^i (obs) (Table 2), were obtained by the inversion-recovery method and the $T_1^{i\{j\}}$ were then calculated by equation (1), in which η_i^j is the measured enhancement of the signal of H(*i*) obtained by irradiating H(*j*).

$$T_1^{i\{j\}} = T_1^i\,(\text{obs}) \cdot \eta_{max}/(\eta_i^j + \eta_k^j \cdot \eta_i^k) \qquad (1)$$

$\eta_{max} = 0.5$ for proton-proton interactions and the denominator in equation (1) is the *direct* contribution of H(*j*) to the enhancement of the signal of H(*i*). This expression is adequate for the systems under investigation since, in all cases, no more than one indirect pathway ($j \rightarrow k \rightarrow i$) was observed[5]. For a rigid molecule undergoing isotropic rotational diffusion relative internuclear distances are given by equation (2).

$$r_{ij} = K\,(T_1^{i\{j\}})^{1/6} \qquad (2)$$

K is a constant which includes nuclear parameters and the isotropic rotational diffusion correlation time. The assumption of overall isotropic rotational diffusion for the molecules considered has probably introduced only minor errors whereas the assumption of molecule rigidity is much more questionable. Conformational flexibility can give rise to two types of errors. First, relatively free rotation of the aryl groups could result in a decreased correlation time for the reorientation of internuclear vectors involving the aromatic protons thus giving rise to increased values of T_1's and of the r_{ij}'s calculated therefrom. Secondly, conformational freedom corresponds to vibrations with low force constants and large amplitudes. The r_{ij}'s uncorrected for vibrational averaging may therefore differ substantially from the equilibrium values.

Table 2. Spin lattice relaxation [s] for protons of 2,4,6,8-tetrakis(3,5-dimethylphenyl)-*N*,*N*'-dimethyl-3,7-diazabicyclo[3.3.1]nonane (**9b**) in [D_2]dichloromethane at 22 °C. The observed relaxation times, T_1 (obs), are given in parentheses along the principal diagonal

Relaxed Nucleus	Source of Relaxation				
	1-H	2-H	8-H	*o*-H(2-Ar)	*o*-H(8-Ar)
1-H	(0.759)	4.7	–	6.8	10.9
2-H	3.3	(0.557)	–	4.0	–
8-H	9.6	–	(0.599)	3.9	2.0
o-H(2-Ar)	16	7.2	6.0	(1.08)	–
o-H(8-Ar)	27	–	5.8	–	(1.23)

We have computed averaged values of *K* for each compound by using $T_1^{1\{2\}}$, $T_1^{2\{1\}}$, $T_1^{1\{8\}}$, and $T_1^{8\{1\}}$ together with values of r_{12} and r_{18} obtained by averaging those found in the X-ray structures of **7a** (r_{12} = 238, r_{18} = 265 pm) and **10a** (r_{12} = 235, r_{18} = 266 pm). The internuclear distances between the *ortho*-protons and 1-H, 2-H, and 8-H were then estimated by equation (2) using only the contributions of the former groups to the T_1's of the latter and the results are presented in Table 3. It is seen that there is rather good agreement between the distances calculated from the solution data and those found for the molecules in single crystals. In particular, the close approach of the *ortho*-proton of

the A ring (pointing down in Fig. 2a) to the benzylic proton on the other side of the molecule is reproduced. We conclude that not only are these molecules in the chair-boat conformation in solution but that even the aryl groups have the same conformation in the solution and crystalline phases. Furthermore, the aryl groups are evidently rather rigidly constrained in their preferred conformations in agreement with the observation of relatively slow rotation on the proton NMR time scale.

Table 3. Interproton distances [pm] calculated from relaxation data and X-ray structure determination for the *ortho* protons of the aryl groups in tetraaryl-3,7-diazabicyclo[3.3.1]nonanes. The distances refer to the nearer of the two *ortho*-protons in each case. Cf. Fig. 2a

Nuclei	a)	Tetraaryl-3,7-diazabicyclo[3.3.1]nonane			
		6b	**7a**	**9a**	**9b**
H(2-Ar) – 1-H	265	259	264	–	255
H(2-Ar) – 2-H	248	237	264	277	234
H(2-Ar) – 8-H	260	247	248	250	233
H(8-Ar) – 1-H	330	273	307	299	276
H(8-Ar) – 8-H	246	241	229	271	209

a) The average of the distances found in the X-ray structures of **7a** and **10a**[2]. In no case the individual values deviate by more than 10 pm from this average[2].

The predominant conformation provides a proper basis for understanding the observed chemical shifts of the aromatic protons in **9a** and **b**. The *ortho*-protons of the fast ring (B) spend half their time in the strongly shielding region above the slow ring (A) and are therefore shielded. Conversely, the protons of the slow ring spend half their time close to and in the plane of the fast ring and are abnormally deshielded. The strong deshielding of the bridge methylene proton *syn* to the fast rings must be due, in part, to being in the deshielding region of these rings, although it is probable that it is also influenced by the lone pair of the nitrogen which is presumably axially oriented.

The spectrum of the *N*(7)-methyl-tetratolyl-3,7-diazabicyclononane **7a** is shown in Figure 4. The assignment of the spectrum is greatly facilitated by the observation of

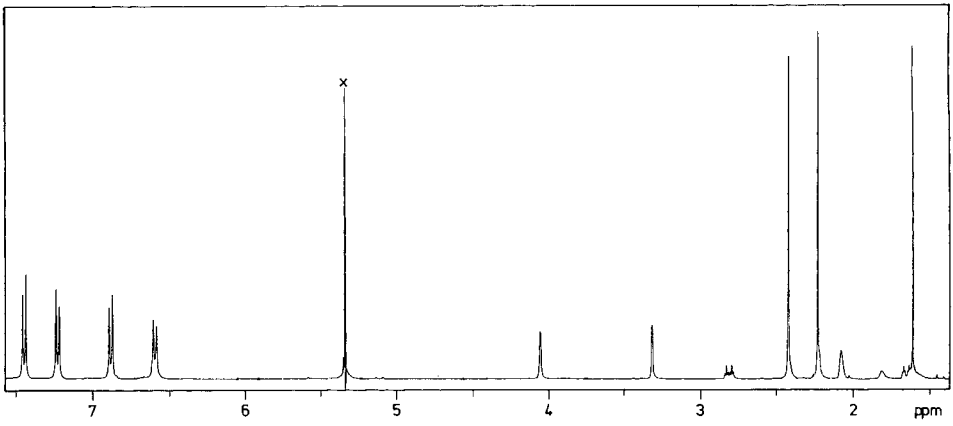


Fig. 4. 360 MHz ^{1}H NMR spectrum of the *N*-methyl-3,7-diazabicyclononane **7a** in [D_2]dichloromethane solution. X: Solvent signal

NOE's for the signals of the 2(4)-benzyl proton and the *ortho*-protons of the 2(4)-*p*-tolyl groups on irradiation of the *N*(3)-proton. It is noteworthy that rotation of both pairs of aryl groups is now fast on the NMR time scale at room temperature, indicating that the *N*(3)-methyl group plays an important role in controlling the barrier for rotation of the 2(4)-aryl groups in the *N,N'*-dimethyl series[6]. The internuclear distances (Table 3) calculated from the NOE and T_1 data, however, show that the conformation about the C(2) – Ar bond is unaffected by the removal of the *N*-methyl group. This is also true in the crystalline state[2].

Finally, the ketone **6b** which lacks both *N*-methyl groups was investigated and found (Table 3) to have the same conformation as the three systems discussed above, once again resembling the solid state conformation[2].

Polyaryl-1,3-diazaadamantanes

We have examined the spectra of three 4,8,9,10-tetraaryl-1,3-diazaadamantanes **3a**, **4b**, and **15** as well as the pentaaryl derivative **14b**.

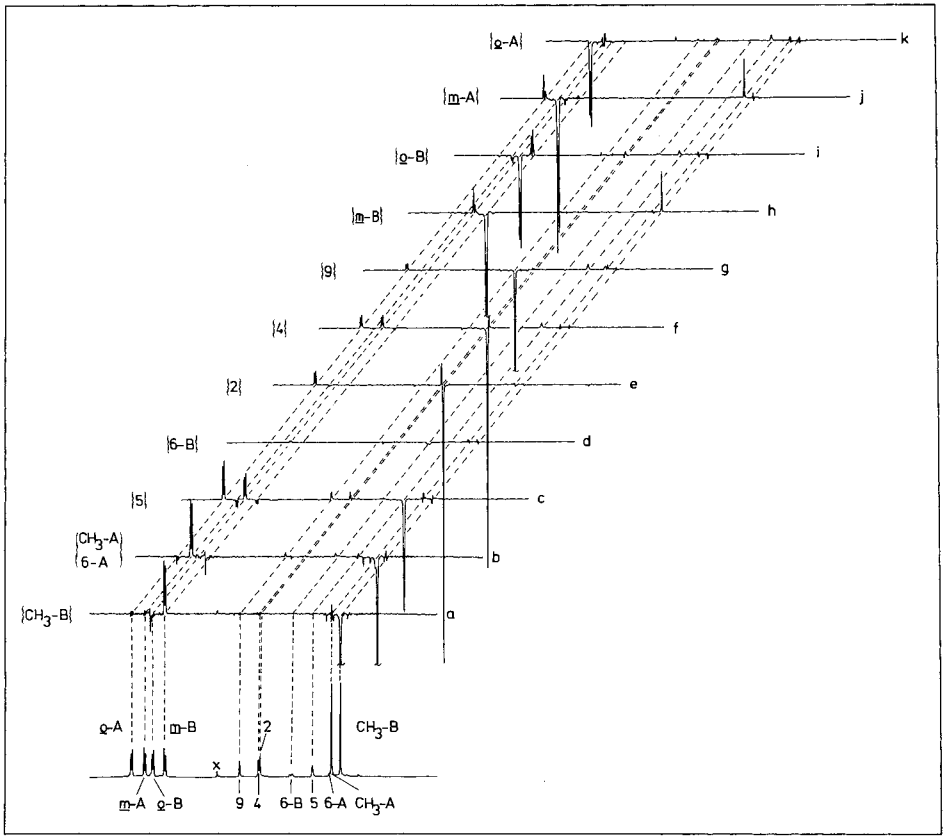


Fig. 5. 200 MHz ^{1}H NMR spectra of the tetra-*p*-tolyl-1,3-diazaadamantane **3a** for [D_2]dichloromethane solution showing the relation between the normal spectrum and the NOE difference spectra. X = Solvent signal

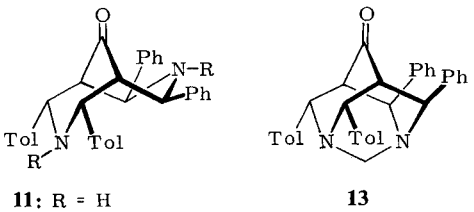
The normal and NOE difference spectra for the 1,3-diazaadamantane **3a** are shown in Figure 5. Observation of a small enhancement of the *ortho*-protons of one pair of aromatic rings on irradiation of the 2-protons and an enhancement of the signals of *ortho*-protons of the other pair of rings on irradiation of the down field proton H_B of the 6-methylene group, permits the distinction between the resonances arising from the two sides of the molecule and allows a total assignment of the proton spectrum. Irradiation of bridgehead protons leads to a large enhancement of both sets of *ortho*-protons and a very significant *negative* NOE for the *meta*-protons on *both* rings. This phenomenon is characteristic of an approximately linear arrangement of the three proton system 5-H-H(*ortho*)-H(*meta*)[5] and thus roughly defines the conformation of the 1,3-diequatorially arranged aryl groups. The other pair, which is 1,3-diaxially oriented, is virtually held in one conformation for which the arrangement of the three protons is also almost linear. Similar conclusions can be drawn concerning the conformation of **4b**.

The pentakis(3,5-dimethylphenyl)-1,3-diazaadamantane **14b** has no element of symmetry apart from the internal symmetry of the aryl groups. It should therefore exhibit twenty two discrete resonances and in fact does in [D_6]benzene. In [D_2]dichloromethane, only twenty signals are resolved, the *meta* methyl and *ortho*-protons of the 4- and 10-aryl substituents being accidentally isochronous. The complete assignment of the latter spectrum was made on the basis of NOE's, many of which are presented in Table 4. Identification of the three sets of resonances belonging to the same aromatic ring was established for each of the five rings by NOE's produced by irradiation of the *meta*-methyl protons. The absorption of 2-H was assigned on the basis of its unique chemical shift and by the observation that it is not enhanced by irradiation of either bridgehead proton. 2- and 10-H exhibit large, mutual enhancements and irradiation of 8- and 10-H significantly enhances 7-H. As expected, irradiation of 8-H did not lead to enhancement of the signals of the other benzylic protons but did produce NOE's for two of the *ortho*-proton signals. One of these *ortho*-proton signals was also enhanced by irradiation of 10-H and is therefore assignable to the 8-aryl group; the other belongs to 9-aryl ring. Irradiation of the *ortho*-protons of the 9-aryl group allows the assignment of 9-H. Finally, the distinction between the *ortho*-protons of 2- and 4-aryl groups follows from the fact that the latter signal is only enhanced by irradiating 4-H. A number of other results in Table 4 confirm these assignments.

Interproton distances between the *ortho*-protons and the protons of the adamantyl system were determined as described in the previous section and are presented in Table 5. Their relative values are in qualitative agreement with those obtained from X-ray structures of **13** and **14a**[2] with the exception of the torsional angle involving the 8(9)-aryl group(s) for which a wide range of values is found for **13** in the crystalline state (Table 5). Evidently the potential function for rotation about the aryl – C(8)-[C(9)]-bond is rather flat. Since the barrier of rotation of the analogous aryl groups in the 3,7-diazabicyclononanes is evidently quite high (see above), it is likely that the potential minima are much more sharply defined in which case it is possible for one conformation to be predominantly populated. Probably this is why the agreement between the X-ray and relaxation data is better than for the 1,3-diazaadamantanes.

Table 4. NOE's and T_1's for the pentakis(3,5-dimethylphenyl)-1,3-diazaadamantanone **14b**. The T_1's [s] are given in parentheses along the principal diagonal

Observed	Irradiated											
	Ring Protons							*ortho* Protons				
	2-H	4-H	5-H	7-H	8-H	9-H	10-H	H(2-Ar)	H(4-Ar)	H(8-Ar)	H(9-Ar)	H(10-Ar)
2-H	(0.48)						0.24	0.03		0.04		
4-H		(0.47)	0.02			0.19		0.03	0.04			
5-H		0.025	(0.45)			0.06			0.11		0.12	
7-H				(0.39)	0.06		0.025			0.125		0.15
8-H				0.06	(0.96)	0.02				0.04	0.06	
9-H		0.175	0.02			(0.47)		0.04			0.025	
10-H	0.19			0.02			(0.045)			0.01		0.10
H(2-Ar)	0.025	0.03				0.04		(0.075)	0.06	0.02	0.05	0.04
H(4-Ar)		0.05	0.05			−0.01			(0.078)		−0.02	
H(8-Ar)	0.03			0.06	0.025		0.02	0.025		(0.70)	0.01	
H(9-Ar)		−0.01	0.04		0.04	0.03		0.04	−0.01	0.025	(0.77)	
H(10-Ar)	−0.02			0.05			0.05					(0.95)



11: R = H
12: R = Me

Tol = 4-Methylphenyl

13

14

a: Ar = 4-Methylphenyl
b: Ar = 3,5-Dimethylphenyl

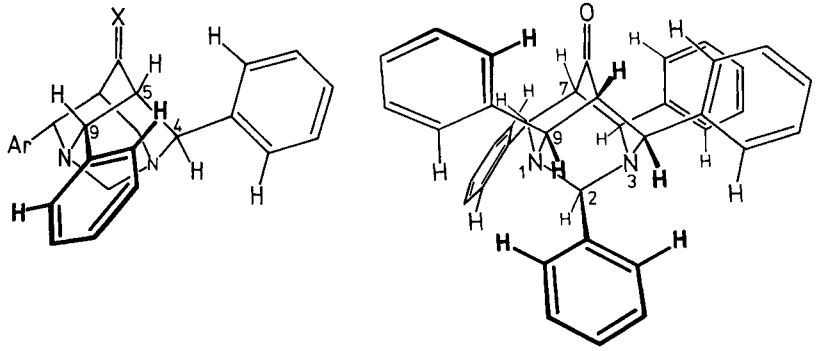


Fig. 6. Conformation of the 1,3-diazaadamantanes **3**, **4**, **13** (left side), and **14** (right side) and approximate positions of the bridgehead, benzylic, and *ortho*-protons, cf. Table 5. The aryl ring at C(10) of **3**, **4**, and **13** and the methyl groups have been omitted

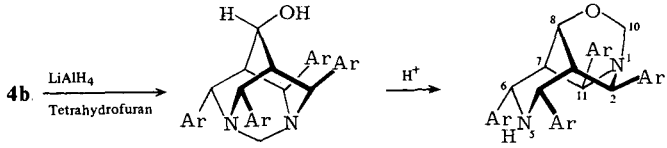
Table 5. Interproton distances (pm) for *ortho*-protons of the aryl groups in 1,3-diazaadamantanes by X-ray[2] and spin lattice relaxation (T_1) methods. The distances refer to the nearer of the two protons in each case, cf. Fig. 6

Nuclei	**13** (X-ray)[a,b]	**3a** (T_1)	**4b** (T_1)	**14a** (X-ray)[b]	**14b** (T_1)
H(2-Ar) – 2-H				292	245
H(2-Ar) – 4-H				286	240
H(2-Ar) – 9-H				265	227
H(4-Ar) – 4-H	242 – 271	298	219	235	231
H(4-Ar) – 5-H	212 – 243	265	194	261	192
H(8-Ar) – 2-H				258	231
H(8-Ar) – 7-H	213 – 225	228	181	214	184
H(8-Ar) – 8-H	272 – 306	273	242	294	254
H(8-Ar) – 10-H	246 – 303	298	234	288	282
H(9-Ar) – 5-H	213 – 225	228	181	219	190
H(9-Ar) – 8-H				279	241
H(9-Ar) – 9-H	272 – 306	273	242	302	246
H(10-Ar) – 7-H	212 – 243	265	194	210	179
H(10-Ar) – 10-H	242 – 271	298	219	281	195

[a] These values indicate the range of interproton distances found for the pair of chemically equivalent positions for each of the two crystallographically distinct molecules **13A** and **13B**. – [b] The torsional angles involving the 8(9)-aryl group(s) and the bridgehead carbon atoms are 14.9 and 24.1° for the different sides in **13A**, 31.0 and 38.2° for the different sides in **13B**, and 33.7° for **14a**.

The spectra of the 1,3-diazaadamantanes **3a**, **4b**, and **14b** at room temperature show no evidence of slow rotation of the 4- and 10-aryl substituents even though they are 1,3-diaxially oriented with respect to each other. Slow rotation of the 4- and 10-(3,5-dimethylphenyl) groups of **4b** is, however, observed at 360 MHz at low temperatures and lineshape analysis of their *meta* methyl resonances in the temperature range of -10 to $-87\,^{\circ}C$ gave $\Delta G^{\ddagger}_{298} = 42\ kJ \cdot mol^{-1}$, $\Delta H^{\ddagger} = 36\ kJ \cdot mol^{-1}$, $\Delta S^{\ddagger} = -19\ J \cdot degree^{-1}$ (coalescence temperature 191.5 K, limiting chemical shifts for the methyl groups δ = 2.01 and 1.90 ppm at 186 K). In contrast, even at 186 K and at 360 MHz there is no evidence of slow rotation of the 4- and 10-*p*-tolyl groups of **3a** although the signals of the *ortho*-protons of the 8- and 9-*p*-tolyl substituents are perceptibly broadened.

We have also prepared **15** by a diastereoselective reduction of **4b** by lithium tetrahydrido aluminate, the proof of configuration being based on its rapid acid catalyzed conversion to **16**[7], a reaction which may be facilitated by the steric repulsion between the 1,3-diaxially oriented aryl groups. Even in **15**, in which the hydroxy group appears to be sandwiched between the 4- and 10-aryl groups, there is no evidence of hindered rotation at room temperature. In summary, the 4- and 10-aryl groups in this series of compounds appear to be remarkably mobile.



Ar = 3,5-Dimethylphenyl

We considered the possibility that the rotation might occur by opening the $N-CH_2-N$ bridge, as a result of acid impurities but the spectra are unaltered in the presence of strong bases. In any case, the substantially higher barrier observed for the 3,5-dimethylphenyl compared with the *p*-tolyl substituents can only be explained in terms of their 1,3-diaxial relationship. The projection of the X-ray structure of **13** presented in Fig. 7[2] shows that the two rings are inclined rather than parallel, to one

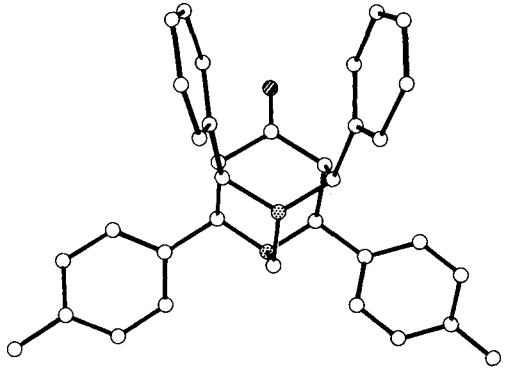


Fig. 7. X-ray structure of the 1,3-diazaadamantane **13** showing the relative positions of the 4- and 10-phenyl groups[2]

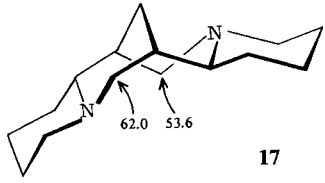
another. The angle between the axes of the axial phenyl rings of **13** is 26.2 and 30.7°, respectively, for the two crystallographically distinct molecules[2]. Nevertheless, further gross distortions must occur during rotation since Fig. 7 implies that the *meta*-methyl protons of **4b** would approach within 100 pm of the adjacent aromatic ring. This situation is reminiscent of that of the 1,8-diarylnaphthalenes. *House, Campbell,* and *Gall*[8] found a barrier of $\Delta G^{\ddagger}_{298} = 67\ \text{kJ} \cdot \text{mol}^{-1}$ for the rotation of a phenyl group and *Clough* and *Roberts*[9] report $\Delta G^{\ddagger}_{298} = 100\ \text{kJ} \cdot \text{mol}^{-1}$ for *o*-tolyl groups. The X-ray structure of 1,4,5,8-tetraphenylnaphthalene[10] reveals considerable in-plane and out-of-plane distortion of the *peri*-substituents. We must conclude that the 1,3-diazaadamantane system allows substantially greater flexibility than the naphthalene ring, possibly because of low frequency bending modes involving the pyramidal nitrogen atoms.

Carbon-13 NMR Spectroscopy

Carbon-13 chemical shift data are presented in Table 6. The assignments are based on single frequency off resonance experiments.

Eliel et al.[6] have successfully applied the analysis of carbon-13 chemical shift differences to the elucidation of the stereochemistry of 2,4-diaryl-3-azabicyclo[3.3.1]nonanes, by considering the contributions of γ-*gauche* effects to the observed shifts. We have found that the method is also useful for defining the conformations of the heterocyclic rings in the 2,4,6,8-tetraaryl-3,7-diazabicyclo[3.3.1]nonanes. That this should be possible, seemed likely since *Bohlmann* and *Zeisberg*[11] have shown very significant differences in chemical shifts in the chair and boat rings of sparteine (**17**). Inspection of the data in Table 6 reveals similar differences in the shifts for the benzylic carbon atoms for the chair and the boat rings of the tetraaryl-3,7-diazabicyclononanes. These differences are also probably the result of the γ-*gauche* effect since the 8-aryl group is γ-*gauche* to C-2 but the 2-aryl group is not γ-*gauche* to C-8.

It is also noteworthy that *N*-methylation effects by about 9 ppm to lower field[12] the shifts of the benzylic carbon atoms adjacent to that ring. Carbon-13 NMR thus provides a convenient means of establishing the structures of the monomethyl analogues in this series of compounds.



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Nitrogen-15 NMR Spectroscopy

We have determined the nitrogen-15 chemical shifts for the two nitrogen atoms in ^{15}N labelled compounds [$^{15}N_2$]-**3a**, [$^{15}N_2$]-**7a**, and [$^{15}N_2$]-**9a** (Table 7). The assignment of the mono-*N*-methyl derivative [$^{15}N_2$]-**7a** follows from the fact that the resonance of the secondary amino nitrogen is split by the attached proton. In the case of the *N,N'*-dimethyl derivative [$^{15}N_2$]-**9a** the assignment was made through the observation of the

Table 6. Carbon-13 chemical shifts [ppm] of some 3,7-diazabicyclononanes and 1,3-diazaadamantanes in [D]chloroform

	C-9	Heterocycle Bridge-head-C	NCHR[a]	NCHR[b]	Substituents *ipso*-C	*o*-C	*m*-C	*p*-C	$ArCH_3$	NCH_3
3,7-Diazabicyclononanes										
5a[2) c)]	27.4	42.6	54.4	63.6	140.7 145.9	125.8 126.9	128.5 128.8	135.2 136.3	21.0 21.1	
7a	27.5	43.7	63.3	63.4	140.3 146.4	125.7 126.8	128.6	134.8 136.1	20.8 21.0	41.8
9a	26.3	45.2	63.7	72.8	139.5 146.5	125.7	128.6	134.9 136.0	21.1	42.1 42.6
5b	27.3	42.8	54.6	63.8	143.7 148.7	124.9 126.3	137.1 137.7	127.4 128.3	21.2 21.5	
9b	26.3	45.2	64.2	73.2	142.6 149.1	123.6 126.8[d)]	137.1[e)]	127.1 128.0	21.2[e)]	42.5 42.8
3,7-Diazabicyclononan-9-ones										
6a[2) c)]	211.9	58.3	62.0	63.3	137.7 142.8	126.2 126.5	128.8 129.2	136.4 137.3	21.0 21.1	
8a	212.0	62.0	63.2	67.7	137.2[f)] 143.5	126.5 126.6	128.9 129.1	135.9 137.2[f)]	21.0 21.1	41.1
10a	211.5	62.4	68.1	73.4	136.9[f)] 143.3	126.4 128.2	128.8 129.0[d)]	135.8 136.9[f)]	21.0 21.1	41.1 41.4
11[2) c)]	211.7	58.7	61.9	63.3	137.4 145.6	126.4 126.5	128.2 129.3	126.9 137.6	21.1	
12	211.3	62.3	68.4	73.3	137.0 146.1	126.5	128.2 129.0[d)]	136.8	21.1	41.2 41.4
6b	211.7	58.4	62.1	63.5	140.7 145.5	123.9 124.6	137.4 138.1	128.3 129.1	21.1 21.4	
10b	211.6	62.5	68.6	73.8	139.9 145.9	124.2 126.2[d)]	137.4[d)] 137.8	128.7 128.9	21.1 21.5[d)]	41.6

Table 6 (*continued*)

	C-6	Heterocycle Bridge-head-C	NCHR[g]	NCHR[h]	NCH_2N	Substituents *ipso*-C	*o*-C	*m*-C	*p*-C	$ArCH_3$	NCH_3
Tetraaryl-1,3-diazaadamantanes											
3a[2]	28.7	25.9	58.3	68.4	69.0	137.8 138.0	126.3 126.5	127.7 129.2	134.4 135.9	20.7 21.0	
3b	29.4	26.4	58.7	68.9	69.4	141.0	124.3 125.7	136.0 137.9	127.0 128.2	21.2 21.7	
15[i]	77.4	33.9	59.0	68.0	71.5	140.6 141.4	124.7 126.6	136.8 138.6	127.9 128.8	21.5 21.8	
4a[2]	213.9	50.4	63.9	69.3	68.2	136.9	126.8 127.8	128.0 129.6	135.1 135.5	20.7 21.0	
4b	213.7	50.6	64.1	69.7	68.6	138.2 140.0	124.6 125.9	136.3 138.4	127.7 129.0	21.1 21.6	

			N–CH–R		NCHRN	Aryl-CH			quart. Aryl-C			Me	
Pentaaryl-1,3-diaza-6-adamantanones													
14a	212.7	49.8 50.5	63.0 65.0	64.0 66.6	79.0	126.3 128.1	126.5 129.4	127.7 129.6	135.3 136.2 136.9	135.6 136.6 137.1	135.9 136.8 137.4	20.7[j] 21.0	20.8 21.1
14b	212.8	50.2 50.6	63.3 65.4	64.4 66.8	79.2	124.1 125.5 127.7 129.1	124.4 126.2 128.8	124.5 127.4 129.0	136.3 138.4 139.9	136.4 139.2 140.4	138.1 139.5	21.2 21.6[j]	21.2 21.7

[a] Aryl groups at the boat piperidine ring. – [b] Aryl groups at the chair piperidine ring. – [c] In ref.[2] the signals of the two quaternary aryl carbon atoms have been exchanged. – [d] Broadened signal. – [e] Presumably, an additional, broadened signal is hidden under this signal. – [f] These two carbon atoms fortuitously give rise to a single signal. – [g] Axial aryl groups. – [h] Equatorial aryl groups. – [i] These values were obtained from a 100 MHz spectrum in [D_2]dichloromethane. – [j] The signal arises from two methyl groups.

expected negative NOE's caused by irradiation of the *N*-methyl groups. The assignments of the resonances in the 1,3-diazaadamantane [$^{15}N_2$]-**3a** are based on small, but significant NOE's associated with irradiation of the resonances of the two sets of *ortho*-protons.

There is a small dependence of the nitrogen-15 chemical shift on stereochemistry in [$^{15}N_2$]-**9a** and the expected[13] change on methylation on going from [$^{15}N_2$]-**7a** to [$^{15}N_2$]-**9a**. The difference in chemical shifts of the two nitrogens in the 1,3-diazaadamantane [$^{15}N_2$]-**3a** is striking and is not readily interpreted in terms of γ-effects. It is possible that the difference reflects a change in hybridization of the nitrogen atom brought about by the overcrowding in the ring bearing 1,3-diaxial *p*-tolyl groups.

We have also determined ^{15}N-^{13}C coupling constants for the 1,3-diazabicyclononane [$^{15}N_2$]-**9a**, and the values are given in Table 8. The small differences for the couplings to the benzylic and *ipso*-carbons cannot be readily interpreted. The fact that only one of the nitrogen atoms is coupled to the 9-methylene carbon atom is of stereochemical significance since this involves coupling in a three-bond interaction and should be governed by a *Karplus* type relation with the dihedral angle. This angle is 0° and 60° for the boat and chair conformations, respectively, and we conclude that the value of 4.5 Hz is characteristic of the boat conformation. This is confirmed by the observation that the corresponding C-8,9 resonance in the proton decoupled spectrum of 1,3-diazaadamantane [$^{15}N_2$]-**3a** is a singlet.

Table 7. Nitrogen-15 chemical shifts of the 1,3-diazaadamantane [$^{15}N_2$]-**3a** and the 3,7-diazabicyclononanes [$^{15}N_2$]-**7a** and [$^{15}N_2$]-**9a** in [D_2]dichloromethane

Compound	Nitrogen	[ppm][a]	{H} [ppm][b]	^{15}N-NOE [%][c]
[$^{15}N_2$]-**3a**	N-1	49.9	7.554	–
	N-3	63.4	7.000	5
[$^{15}N_2$]-**7a**	N-3	49.8[d]	–	–
	N-7	44.5	–	–
[$^{15}N_2$]-**9a**	N-3	42.7	2.119	–
	N-7	44.5	1.558	20

[a] Referenced with external 1 M ammonium chloride (5% enriched) in 10 M hydrochloric acid which absorbs at 30.3 ppm[14]. – [b] Chemical shift of the proton irradiated in the $^{15}N\{^1H\}$-NOE experiment. – [c] $NOE_{max} = 3.93$. – [d] $^1J_{N,H} = 67.1$ Hz.

Table 8. ^{15}N-^{13}C Coupling constants [Hz] in the 3,7-diazabicyclononane [$^{15}N_2$]-**9a**

			^{13}C Nuclei				
^{15}N Nuclei	N^3-CH_3	N^7-CH_3	C-2 C-4	C-6 C-8	*ipso*-C of ring A	*ipso*-C of ring B	C-9[a]
N-3	4.6		3.7		2.5		0–1
N-7		4.6		4.5		3.4	4.6

[a] See text for discussion of the coupling constant assignment.

The results presented above exemplify the usefulness of proton-proton NOE and T_1 data for determining the preferred conformations of organic molecules in solution. In this work we have used only data for protons but a logical alternative involves the relaxation times for carbon-13 nuclei with directly attached protons for the determination of the rotational diffusion parameters, provided sufficient material is available for such measurements. For the compounds studied, there is a reasonably close correspondence between the solution and solid state conformations. It is probable that this is a rather general phenomenon. Exceptions are expected when the differences in energies of possible conformations are small, as appears to be the case for the fast aryl rings in the 1,3-diazaadamantanes, or in situations in which strong intermolecular interactions, such as hydrogen bonding, may come into play.

The authors express their gratitude to Dr. *K. Peters,* Max-Planck-Institut für Festkörperforschung, Stuttgart, for providing geometric parameters from the X-ray crystallographic structures. They also express their gratitude to *N.A.T.O.* for Research Grant No. 1763 (to L.M.J. and H.Q.) and to the *Alexander von Humboldt-Stiftung* for a Senior U.S. Scientist Award (to L.M.J). Financial support for this work was provided by the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie.*

Experimental Part

NMR spectra: Bruker WH 90, WP 200, WM 360 and WM 400 spectrometers. Proton relaxation measurements were made on carefully degassed solutions using the inversion-recovery (180°-τ-90°-T) sequence and calculations of T_1's were done by a three parameter, non-linear least squares analysis. The proton NOE measurements were made at 200 MHz using the FT difference method. The data were obtained using the PAPS sequence. Four FID's were acquired with the decoupler set exactly on a given resonance; four FID's with the decoupler off-resonance were then subtracted. This procedure was repeated until an adequate signal-to-noise ratio was achieved. A 90° observation pulse and a recovery time of 10 T_1 were used.

[^{15}N]Ammonium chloride with 95% ^{15}N was obtained from VEB Berlin-Chemie, Berlin-Adlershof.

All 3,7-diazabicyclononanes and 1,3-diazaadamantanes investigated in this study, except **15** and the ^{15}N-labelled compounds, have been reported[2,3].

The ^{15}N-labelled tetrakis(4-methylphenyl)-3,7-diazabicyclo[3.3.1]nonanes [$^{15}N_2$]-**5a**, [$^{15}N_2$]-**7a**, and [$^{15}N_2$]-**9a**, and the tetrakis(4-methylphenyl)-1,3-diazaadamantane [$^{15}N_2$]-**4a** were prepared according to the procedures reported for the nonlabelled compounds. Mass spectrometry indicated complete labelling (> 95%). – [$^{15}N_2$]-**5a**: Yield 83%, m.p. 223 – 224°C, from cyclohexane/ethanol (1 : 1) (**5a**[3]): Yield 90%, m.p. 228°C). – [$^{15}N_2$]-**7a**: Yield 86%, m.p. 258 – 259°C, from ethanol (**7a**[2]): Yield 86%, m.p. 264°C). – [$^{15}N_2$]-**9a**: Yield 80%, m.p. 234 – 235°C, from ethanol (**9a**[2]): Yield 65%, m.p. 235 – 236°C). – [$^{15}N_2$]-**4a**: Yield 84%, m.p. 249 – 251°C, from ethanol (**4a**[3]): Yield 51%, m.p. 251 – 253°C).

*rel-(2R,4S,6S,8R)-2,4,6,8-Tetrakis(4-methylphenyl)-3,7-[$^{15}N_2$]diazabicyclo[3.3.1]nonan-9-one ([$^{15}N_2$]-**6a**) and -hydrazone:* 1.00 g (18.4 mmol) of [^{15}N]ammonium chloride, 1.80 g (22 mmol) of sodium acetate, 0.54 g (9.35 mmol) of acetone, and 4.60 g (38.3 mmol) of 4-methylbenzaldehyde were magnetically stirred for 7 days at 20 – 25°C. The colourless precipitate was filtered, washed with methanol and water, and dried. Yield 2.70 g (59%), m.p. 232 – 233°C (lit. 30%, m.p.

245 – 246 °C[15], 242 – 243 °C[3]). The *hydrazone* was obtained in 54% yield according to the procedure for the non-labelled compound[2] as colourless needles containing 1 mol of ethanol, m.p. 224 – 225 °C (dec.) (lit.[2] yield 52%, m.p. 223 – 224 °C).

(6s)-rel-(4R,8S,9R,10S)-4,8,9,10-Tetrakis(3,5-dimethylphenyl)-1,3-diazatricyclo[3.3.1.1^{3,7}]-decan-6-ol (**15**): 2.50 g (4.38 mmol) of **4b** and 1.00 g (26.4 mmol) of lithium tetrahydrido aluminate in 160 ml of tetrahydrofuran were heated under reflux for 3 h. After cooling, 3.5 ml of water and 1.5 ml of a 10% sodium hydroxide solution were added. Filtration of the resulting mixture, removal of the solvent from the filtrate under vacuum, and trituration of the residue with 50 ml of hot ethanol yielded 2.07 g (83%) of colourless crystals melting at 252 – 255 °C. – IR (CCl_4): 3555 cm^{-1} (OH).

$C_{40}H_{46}N_2O$ (570.8) Calc. C 84.17 H 8.12 N 4.91 **15**: Found C 83.82 H 7.96 N 4.71
16: Found C 83.74 H 8.13 N 4.78

rel-(2R,4R,6S,11S)-2,4,6,11-Tetrakis(3,5-dimethylphenyl)-9-oxa-1,5-diazatricyclo[5.3.1.0^{3,8}]-undecane (**16**): To a solution of 1.14 g (2.0 mmol) of **15** in 100 ml of chloroform was added 0.050 ml (0.67 mmol) of trifluoroacetic acid. After standing for 2 h at 20 – 25 °C the acid was removed by stirring the mixture with 5.0 g (36 mmol) of potassium carbonate for 5 min. Filtration, removal of the solvent under vacuum, and trituration of the residue with 20 ml of hot ethanol afforded 0.85 g (74%) of colourless needles melting at 279 – 280 °C. Crystallisation from ethanol/chloroform (10:1) raised the m.p. to 281 °C. – IR (CCl_4): 3320 cm^{-1} (NH), 2790 (Bohlmann band). – ^{1}H-NMR ($CDCl_3$): δ = 1.79 (NH), 2.15, 2.29 (CH_3), 2.77 (3,7-H), 4.02 (t, J = 3.8 Hz, 8-H), 4.08 (10-H), 4.33 (benzylic H), 4.43 (d, J = 5.0 Hz, benzylic H), 6.65, 7.17 (*o*-H), 6.75, 6.88 (*p*-H). – ^{13}C-NMR ($CDCl_3$): δ = 21.2, 21.3 (CH_3), 45.2 (C-3,7), 59.0, 62.1 (benzylic C), 70.2 (C-8), 72.9 (C-10), 124.5, 125.6 (*o*-C), 127.7, 128.8 (*p*-C), 136.7, 138.0 (*m*-C), 141.1, 141.9 (*ipso*-C).

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