Tetrahedron. Vol. 32, pp. 2339 to 2342. Pergamon Press 1976. Printed in Great Britain

DIAZEPINES—XXII

^{13}C NMR SPECTRA OF 2,3-DIHYDRO-1,4-DIAZEPINIUM SALTS[1]

D. LLOYD,* R. K. MACKIE, H. MCNAB and K. S. TUCKER
Department of Chemistry, Purdie Building, University of St. Andrews, St. Andrews, Fife, Scotland

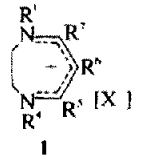
and

D. R. MARSHALL
School of Physical and Molecular Sciences, University College of North Wales, Bangor, Gwynedd, Wales

(*Received in the UK 22 March 1976; Accepted for publication 16 April 1976*)

Abstract—The ^{13}C NMR spectra of a number of 2,3-dihydro-1,4-diazepinium salts, like ^{1}H NMR spectra, confirm shape, and charge distribution for these compounds. The ring has a half-chair shape which is inverting rapidly at room temperature. The atoms in the conjugated portion of the ring show alternating polarity, and phenyl groups attached to these positions act, respectively, as electron-donors or electron-acceptors. A methyl substituent in the saturated portion of the ring shows equal preference for quasi-equatorial and quasi-axial conformations. Some comparisons are drawn between present results and similar results obtained with related benzene derivatives.

^{13}C NMR studies of molecules which have complete cyclic conjugated systems clearly show that the chemical shifts are little affected by ring-current but are strongly dependent on the charge densities at the carbon atoms.[2] The 2,3-dihydro-1,4-diazepinium salts **1** are thus ideally suited for ^{13}C NMR studies. Since their conjugation is not completely cyclic the question of ring-current is irrelevant, while their interesting properties[3] are closely connected with the charge distribution within the molecules.



1

^{1}H NMR spectra had previously indicated the alternating polarity of the conjugated portion of the ring (atoms 4-7, **1**) in that signals for H(5,7) appear at much lower field than signals for H(6).[4] There is similarly a spectacular difference in chemical shift between C(6) (δ *ca.* 90 ppm) and C(5,7) (δ *ca.* 160 ppm) (see Tables 1 and 3). These results are in accord with studies on cyanines,[5] which have a related electronic system, and with MO–LCAO calculations on α,ω-diazapolymethines.[6]

The signal for the 6-carbon atom is at much higher field than is usually found in nitrogen heterocycles,[7] but approaches that of the meso-position in porphyrins[8] and

Table 1. ^{13}C-NMR shifts for dihydrodiazepinium cations **1** (δ, ppm downfield from Me_4Si)

Substituent groups[ref.]					δ	δ	δ	δ
R^1	R^7	R^6	R^5	R^4	C(6)	C(5,7)	C(2,3)	other C
H	H	H	H	H[15]	88.01	157.31	48.81	
Me	H	H	H	H[a]	87.43	158.53 156.06	47.64 47.07	1-Me, 56.47
Me	H	H	H	Me[16]	87.04	157.21	46.71	1,4-Me, 55.20
H	Me	H	Me	H[17]	91.39	166.96	47.87	5,7-Me, 23.67
H	Me	H	Ph	H[18]	90.42	167.66 164.54	48.49 47.66	5-Me, 23.79; 7-Ph, 135.67, 131.69, 128.76, 127.97
H	Ph	H	Ph	H[14]	90.64	166.33	49.34	5,7-Ph, 136.54, 132.43, 129.46, 128.63
Me	Ph	H	Ph	H[14]	93.52	168.00 163.92	48.72 45.37	1-Me, 57.06; 5,7-Ph, 136.74, 136.21, 131.59, 130.75 128.85, 128.36, 127.94
Ph	H	H	H	Ph[19]	92.64	155.40	55.84	1,4-Ph, 144.97, 129.73, 128.29, 122.62
Ph	Me	H	Me	Ph[20]	96.34	165.45	58.67	5,7-Me, 25.14; 1,4-Ph, 144.73, 130.06, 129.07, 125.70
H	Me	Br	Me	H[21]	84.53	166.65	48.20	5,7-Me, 28.40
H	Me	NO_2	Me	H[22]	126.65	162.52	47.55	5,7-Me, 21.29
H	Me	OMe	Me	H*[21]	124.75	164.31	47.75	5,7-Me, 19.48; 6-MeO, 61.31; picrate, 125.22
H	H	Ph	H	H[23]	102.68	157.30	48.70	6-Ph, 138.71, 128.66, 127.19, 126.17

*Picrate anion. [a]Not previously reported; see Experimental.

Table 2. ^{13}C-NMR shifts for phenyl substituents in dihydrodiazepinium cations (δ, ppm downfield from Me_4Si)

Substituent groups					δ	δ	δ	δ	
R^1	R^7	R^6	R^5	R^4	(para)	(meta)	(ortho)	(l)	δ(m)–δ(p)
H	Me	H	Ph	H	131.69	128.76	127.97	135.67	−2.93
H	Ph	H	Ph	H	132.43	129.46	128.63	136.54	−2.97
Me	Ph	H	Ph	H	131.59	128.85	128.36	136.74	−2.74
					130.75		127.94	136.21	−1.90
Ph	H	H	H	Ph	128.29	129.73	122.62	144.97	+1.44
Ph	Me	H	Me	Ph	129.01	130.01	125.70	144.73	+1.00
H	H	Ph	H	H	126.17	128.66	127.19	138.71	+2.49

Table 3. ^{13}C-NMR shifts for 2-substituted dihydrodiazepinium cations **5**, **6** and **9** (δ, ppm downfield from Me_4Si)

Diazepinium salt[ref.]	Temp.	δ C(6)	δ C(5,7)	δ C(2,3)	δ 5-Me	δ 7-Me	δ 2-Me
(5) X = Cl[4]	+40°	96.92	164.58	55.80	25.48	27.24	25.28
			168.76	60.44			
	−20°	96.76	164.33	55.50	25.59	27.27	—
			168.58	60.28			
	−40°	96.70	164.22	55.37	25.63	27.26	23.44
			168.51	60.23			26.57
(5) X = H[24]	+40°	92.02	164.97	55.71	23.17	24.84	24.84
			168.41	58.89			
	+20°	92.02	164.93	55.61	23.17	24.80	—
			168.35	58.84			
	−40°	91.88	164.69	55.42	23.13	24.71	23.13
			168.16	58.74			26.51
(6)[24]	+30°	91.97	166.26	52.17	23.45	24.33	17.05
			168.38	54.54			
	−40°	91.82	165.90	52.17			
			166.16	53.31	23.58	23.92	16.15
			167.90	53.76	23.72	24.60	17.87
			168.39	55.59			
(9)[24]	+40°	91.92	167.06	60.45	23.69		24.26[a]
							31.45[b]
	−40°	91.69	166.66	60.01	23.54		24.08[a]
							31.24[b]

[a]4',5'-C of cyclohexane ring; [b]3',6'-C of cyclohexane ring.

that of the methine carbon in the enol form of β-diketones.[9] It is also very close to that for the 3-position of the isoelectronic pentadienide anion,[10] thus nicely demonstrating the ironical fact that this is an electron-rich cation. Application of an empirical relation[11] provides an estimated π-electron density of *ca.* 1.3 electrons at C(6) and 0.8 electrons at C(5, 7), suggesting that the π-electrons must be predominantly associated with the nitrogen atoms (*ca.* 1.6 electrons each).

Methyl groups at C(5, 7) cause downfield shifts of the carbon atom to which they are attached of *ca.* 10 ppm, an effect quantitatively similar to that observed for benzene derivatives.[12] They also cause smaller downfield shifts of the signal for C(6). N-Methyl substituents on the other hand cause an upfield shift of the C(6) signal; N,N'-dimethyl substitution produces no overall effect on the C(5, 7) resonances but mono-N-methyl substitution splits the C(5, 7) signal symmetrically into two signals. As would be expected from the electron densities of the ring sites to which they are attached, the N-methyl groups provide signals much further downfield than do the 5,7-methyl groups.

The qualitative effects of substituents at the 6-position also resemble those observed for aryl derivatives.[12] 6-Nitro- and 6-methoxy-groups cause pronounced downfield shifts for the C(6) signal, and a 6-chloro-substituent causes a smaller downfield shift, whereas a 6-bromo-substituent causes an upfield shift. In addition 6-nitro- and 6-methoxy-groups cause upfield shifts of the signals due to vicinal methyl groups, while a 6-bromo-atom causes a downfield shift; a 6-chloro-atom also causes a small downfield shift. This again finds a parallel in spectra of aryl derivatives for the methyl groups of mesitylene appear at δ 21.10, whereas the 1,3-methyl groups of 2-nitro-, 2-methoxy- and 2-bromo-mesitylene appear, respectively, at δ 17.28, 15.84 and 23.54. The signals for the 5-methyl groups in these mesitylene derivatives are relatively slightly affected by these 2-substituents, and are uniformly shifted upfield, appearing respectively at δ 20.85, 20.54 and 20.53. The upfield shifts caused by the vicinal methoxy- and nitro-groups may be due to steric compression shifts;[13] this factor will be less important when there is a vicinal bromine atom which, owing to its greater bonding radius, causes less crowding than do the other groups. A difference between the effects caused by vicinal methoxy- and nitro-groups on the one hand, and

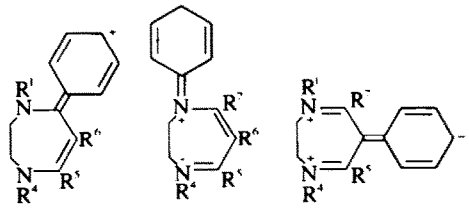
halogen atoms on the other hand, has been observed also in variable temperature ^{1}H NMR investigations of dihydrodiazepinium salts.[4]

Some special interest centres on the cases of substituent phenyl groups at different positions, because it has been pointed out[4] that conjugative interaction of such groups with the dihydrodiazepinium ring is necessarily electron-withdrawing at the 1,4,6-positions and electron-donating at the 5,7-positions. Also, UV[14] and ^{1}H NMR[4] spectra suggest that the coplanarity of phenyl groups with the seven-membered ring may be prevented by adjacent methyl substituents.

As in the case of benzene derivatives, the effect of a substituent phenyl group is generally deshielding, but the different types of conjugation between the two rings, depending upon the site of the substituent phenyl group, is clear from the signals due to the phenyl carbon atoms (see Table 2).

In assigning the phenyl signals it has been assumed that the most downfield peak is due to the 1-carbon atom, and that the p-carbon atom gives rise to the other peak of low intensity. The signal at 129.5 ± 1 ppm is assigned to the m-carbon atom, since it shows the least deviation from the signal for the carbon atoms in benzene (*cf.* Ref. 12). The assignment of the o- and m-signals is unambiguous except in the case of the 5,7-diphenyl compound, but even if the signals are misassigned for this compound it does not affect the qualitative argument.

The difference between the signals for the m- and p-positions shows the difference between 5,7-phenyl groups and 1,4,6-phenyl groups, the p-position of the former being relatively electron-deficient and of the latter being electron-rich. This is in accord with contributions from the canonical forms **2**, **3** and **4** respectively. From the values for δ(m)–δ(p) it appears that the contribution of form **3** is relatively less important than the contributions from forms **2** and **4** to the respective dihydrodiazepinium cations.

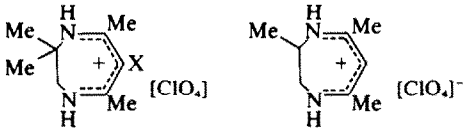


2 **3** **4**

The lessened conjugation of phenyl groups with the dihydrodiazepinium ring when they are flanked by methyl groups, presumably because they are forced out of coplanarity with the seven-membered ring, is again evident from these spectra. The difference between the two phenyl groups in the 1-methyl-5,7-diphenyl derivative is particularly illustrative.

A high resolution study of the unsubstituted dihydrodiazepinium cation shows coupling between hydrogen atoms and the carbon atoms to which they are attached as follows: $J_{6C\text{-}6H}$ = 165.9 Hz, $J_{5(7)C\text{-}5(7)H}$ = 172.7 Hz, $J_{2(3)C\text{-}2(3)H}$ = 144.7 Hz. These values are all in accord with the assigned structure of the molecule (cf. 163.0 and 170.0 Hz for the 3- and 2-positions, respectively, in pyridine). Longer range couplings are also evident as follows: $J_{6C\text{-}5(7)H}$ = 4.1 Hz, $J_{6C\text{-}1(4)H}$ = 4.1 Hz, $J_{2(3)C\text{-}3(2)H}$ = 3.7 Hz, $J_{2(3)C\text{-}7(5)H}$ = 9.3 Hz.

Variable temperature ^{1}H NMR studies had shown that the dihydrodiazepinium ring has a half-chair shape, which is rapidly inverting at ambient temperature.[4] Similar ^{13}C NMR studies have now been carried out and, as in the case of the ^{1}H NMR investigations, it has proved convenient to use the 2,2-dimethyldihydrodiazepinium salts **5**, and also the 2-methyl derivative **6**, for this purpose. Results are shown in Table 3.

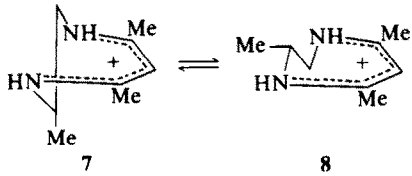


5 **6**

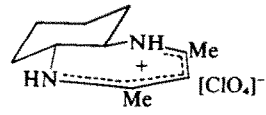
At +40°, the methyl signals for (**5**, X = Cl) appear at 25.28, 25.48 and 27.24. When the solution is cooled to −40° there are four signals, at 23.44, 25.63, 26.57 and 27.26. The peaks at ~25.5 and ~27.25 persist throughout the temperature range but the peak at 25.28 (+40°) disappears below 0° to be replaced by two signals at still lower temperatures. The persistent signals may be ascribed to the 5,7-methyl groups, while the other signals arise from the 2-methyl groups, which appear as distinct quasi-axial and quasi-equatorial groups at low temperatures, but are averaged out by inversion at higher temperatures.

In the case of (**5**, X = H), there are only two signals (at 23.17, 24.84) at +40°, and only three (at 23.13, 24.71, 26.51) at −40°. At +40° the signal at ~23.15 is much greater than that at ~24.8, but at −40° the ratio is reversed, while at ~ +20°, the two signals are of approximately equal height and are apparently superimposed upon a flat signal. It seems therefore that these two signals arise from the 5,7-methyl groups, and that at +40° an averaged signal for the two 2-methyl groups is superimposed upon the lower field signal; this latter signal disappears when the solution is cooled to near +20° and then reappears at lower temperatures at two signals due to separate quasi-axial and quasi-equatorial methyl groups, and one of these separate signals is now superimposed on the higher field signal due to the 5,7-methyl groups.

The situation with regard to **6** is more complex in that inversion is not between two equivalent conformers, as in the case of **5**, but between two distinct species **7** and **8**.



7 **8**



9

Therefore when inversion is rapid, there should be one signal due to the 2-methyl group, and two due to each of the 5,7-methyl groups, 5,7-ring atoms, and 2,3-ring atoms, while at lower temperatures there should be two signals due to the 2-methyl group, and four signals for each of the 2,3-ring atoms, 5,7-ring atoms, and 5,7-methyl groups. The experimental result confirms this (see Table 3).

All these results thus confirm the shape previously deduced for this heterocyclic system.[4] The low temperature spectra for **6** indicate an approximately equal contribution for the quasi-axial **7** and quasi-equatorial **8** conformers. This is also in agreement with the earlier findings from ^{1}H NMR. At −50° the signals due to the protons of the 2-methyl group appear as doublets of equal intensity. Hence, in contrast to the behaviour of cyclohexane derivatives, there is no preference for a substituent methyl group in the saturated part of a dihydrodiazepinium ring to adopt an equatorial position. The difference obviously arises from the absence of other axial substituents in the other part of the ring, which in turn leads to an absence of 1,3-diaxial interactions.

The cyclohexanodihydrodiazepinium salt **9** must be rigid, and cannot invert. In accord with this, its ^{13}C NMR spectrum does not change over the temperature range +40° to −40° (see Table 3).

If it may be assumed that for the 2-substituted dihydrodiazepinium salts the chemical shift due to the 5-methyl group is more likely than the signal due to the 7-methyl group to resemble the shift for 5,7-methyl groups in the 2-unsubstituted analogue (**1**, $R^1 = R^4 = R^6 = H$; $R^5 = R^7 = Me$), since the 5-methyl group is further away from the 2-substituent(s), then the 5-methyl signal appears uniformly at lower field than the 7-methyl signal in the 2-methyl derivatives.

EXPERIMENTAL

The spectra in Tables 1 and 2 were recorded at 20 MHz for 10% solutions, normally in [^{2}H$_6$]DMSO, but also with the addition of trifluoroacetic acid, or in deuteriotrifluoroacetic acid, in the case of high-resolution studies. The variable-temperature spectra recorded in Table 3 were for solutions in [^{2}H$_6$]acetone. The counter-ion was usually perchlorate, except where otherwise indicated; the effect of the counter-ion appears from other experiments with related compounds to be very small.

All the salts had been reported before with the exception of the following case.

2,3-Dihydro-1-methyl-1,4-diazepinium perchlorate

N-Methylethylenediamine (0.22 g, 3 mmoles) in methanol (100 ml) and 1,5-diaza-1,5-diphenylpentadienium perchlorate[15] (0.97 g, 3 mmoles) in methanol (100 ml) were added over a period of *ca.* 3 h to boiling methanol (500 ml). Evaporation of the solvent *in vacuo*, followed by addition of ether, promoted the crystallisation of the dihydrodiazepinium perchlorate (0.3 g, 48%), m.p. 102–103° (from ethanol), λ_{max} (MeOH) = 336 nm (ϵ = 15,000), ν_{max} (Nujol mull) = 3340, 1640, 1570, 1330, 1100, 800 cm^{-1}, τ ([^{2}H$_6$]acetone) 2.25 (2H, complex), 4.87 (1H, t), 6.10 (4H, s), 6.45 (3H, s) (NH signal not apparent). (Found: C, 34.25; H, 5.4; N, 13.25. $C_6H_{11}ClN_2O_4$ requires: C, 34.2; H, 5.25; H, 13.3%).

Acknowledgements—We thank Mrs. Melanja Smith for recording the spectra. We are also grateful to the SRC and the University of St Andrews for the awards of research studentships to H.M. and K.S.T., respectively.

REFERENCES

[1]Part XXI. D. Lloyd, H. McNab and D. R. Marshall, *Austral. J. Chem.* in press.
[2]Inter alia: H. Günther, H. Schmickler, H. Königshafen, K. Recker and E. Vogel, *Angew. Chem.* **85**, 261 (1973); *Angew. Chem. Internat. Edn.* **12**, 243 (1973); H. Günther, H. Schmickler, U. H. Brinker, E. Nachtkamp, J. Wassen and E. Vogel, *Angew. Chem.* **85**, 762 (1973); *Angew. Chem. Internat. Edn.* **12**, 760 (1973); H. Günther and H. Schmickler, *Pure and Applied Chem.* in press.
[3]D. Lloyd, H. P. Cleghorn and D. R. Marshall, *Adv. Heterocyclic Chem.* **17**, 1 (1974).
[4]D. Lloyd, R. K. Mackie, H. McNab and D. R. Marshall, *J. Chem. Soc. Perkin II* 1729 (1973).
[5]R. Radeglia, C. Engelhardt, E. Lippmaa, T. Pehk, K-D. Nolte and S. Dähne, *Org. Magn. Resonance* **4**, 571 (1972); H-U. Wagner, *Chem. Ber.* **107**, 634 (1974).
[6]J. Fabian and H. Hartmann, *J. Mol. Structure* **27**, 67 (1975); *Theoret. Chim. Acta* **36**, 351 (1975).
[7]G. C. Levy and G. L. Nelson, *Carbon-13 Nuclear Magnetic Resonance for Organic Chemists*, p. 96. Interscience, New York (1972).
[8]R. J. Abraham, G. E. Hawkes and K. M. Smith, *J. Chem. Soc. Perkin II* 627 (1974).
[9]L. F. Johnson and W. C. Jankowski, *Carbon-13 NMR Spectra*, pp. 115, 463. Academic Press, New York (1972).
[10]W. T. Ford and N. Newcomb, *J. Am. Chem. Soc.* **96**, 309 (1974).
[11]J. B. Stothers, *Carbon-13 NMR Spectroscopy*, p. 91. Academic Press, New York (1972).
[12]Ref. 7, p. 81.
[13]D. M. Grant and B. V. Cheney, *J. Am. Chem. Soc.* **89**, 5315 (1967).
[14]A. M. Gorringe, D. Lloyd and D. R. Marshall, *J. Chem. Soc.* (C), 1081 (1969).
[15]D. Lloyd, H. McNab and D. R. Marshall, *Synthesis* 791 (1973).
[16]D. Lloyd, H. McNab and D. R. Marshall, *J. Chem. Soc. Perkin I* 1260 (1975).
[17]G. Schwarzenbach and K. Lütz, *Helv. Chim. Acta* **23**, 1144 (1940).
[18]A. M. Gorringe, D. Lloyd and D. R. Marshall, *J. Chem. Soc.* (C), 2340 (1967).
[19]B. Eistert and F. Haupter, *Chem. Ber.* **93**, 264 (1960).
[20]C. Barnett, H. P. Cleghorn, G. E. Cross, D. Lloyd and D. R. Marshall, *J. Chem. Soc.* (C), 93 (1966).
[21]D. Lloyd and D. R. Marshall, *J. Chem. Soc.* 118 (1958).
[22]C. Barnett, *J. Chem. Soc.* (C), 2436 (1967); A. M. Gorringe, D. Lloyd and D. R. Marshall, *Ibid.* 617 (1970).
[23]K. Feldmann, E. Daltrozzo and G. Scheibe, *Z. Naturforsch.* **22b**, 722 (1967).
[24]D. Lloyd, R. H. McDougall and D. R. Marshall, *J. Chem. Soc.* (C), 780 (1966).