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^{13}C CHEMICAL SHIFTS OF SOME AZAINDOLIZINES VERSUS ELECTRON CHARGE DISTRIBUTION

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ABSTRACT

Azaindolizines, which contain all possible combinations of nitrogen atoms within the five-membered ring moiety, are used as models for the investigation of a relationship between electron charge distribution and ^{13}C shifts. A linear correlation is observed between the shifts and total rather than π-charge densities as calculated by the INDO—MO method. The average excitation energy (AEE) approximation in the theory of nuclear screening is shown to hold separately for the CH moieties and the carbon atoms at the ring junction in indolizines. An empirical correlation with charge densities is obtained from the AEE method, as a result of the compensation of effects within the local paramagnetic term and the prevailing contribution to the latter of the effective nuclear charge. ^{13}C shifts afford a reasonable measure of the total net charges at the carbon atoms of indolizines. The INDO calculations indicate that the π-charges follow the pattern suggested by simple resonance structures but the overall charge density depends heavily on σ-core polarization effects.

INTRODUCTION

The chemistry of indolizine (1) and of its derivatives has attracted considerable attention [1]. Compounds from this group of heteroaromatic structures seem to provide interesting molecular models for observing relations betweeen electron charge distribution and ^{13}C chemical shifts owing to the asymmetry of their ring systems and to a variety of effects which may be exerted on the electron distribution by nitrogen atoms (compounds 1—9). The nitrogen atoms can theoretically induce both positive and negative net charges in the carbon atom framework, as may be inferred from simple considerations of possible resonance structures. Only one resonance structure without charge splitting can be written for indolizine (I). Those with charge splitting due to a delocalization of the electron pair at N-4 (II—XI) suggest that the π-charge density should be increased in the entire carbon atom pattern; the highest accumulation of charge should occur at positions 1 and

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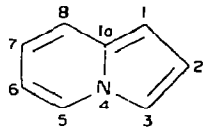

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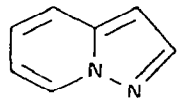

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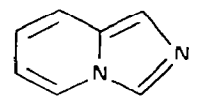

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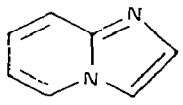

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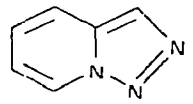

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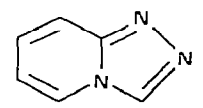

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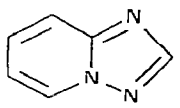

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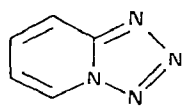

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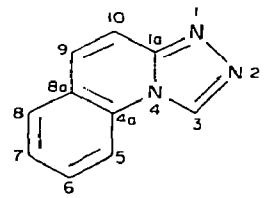

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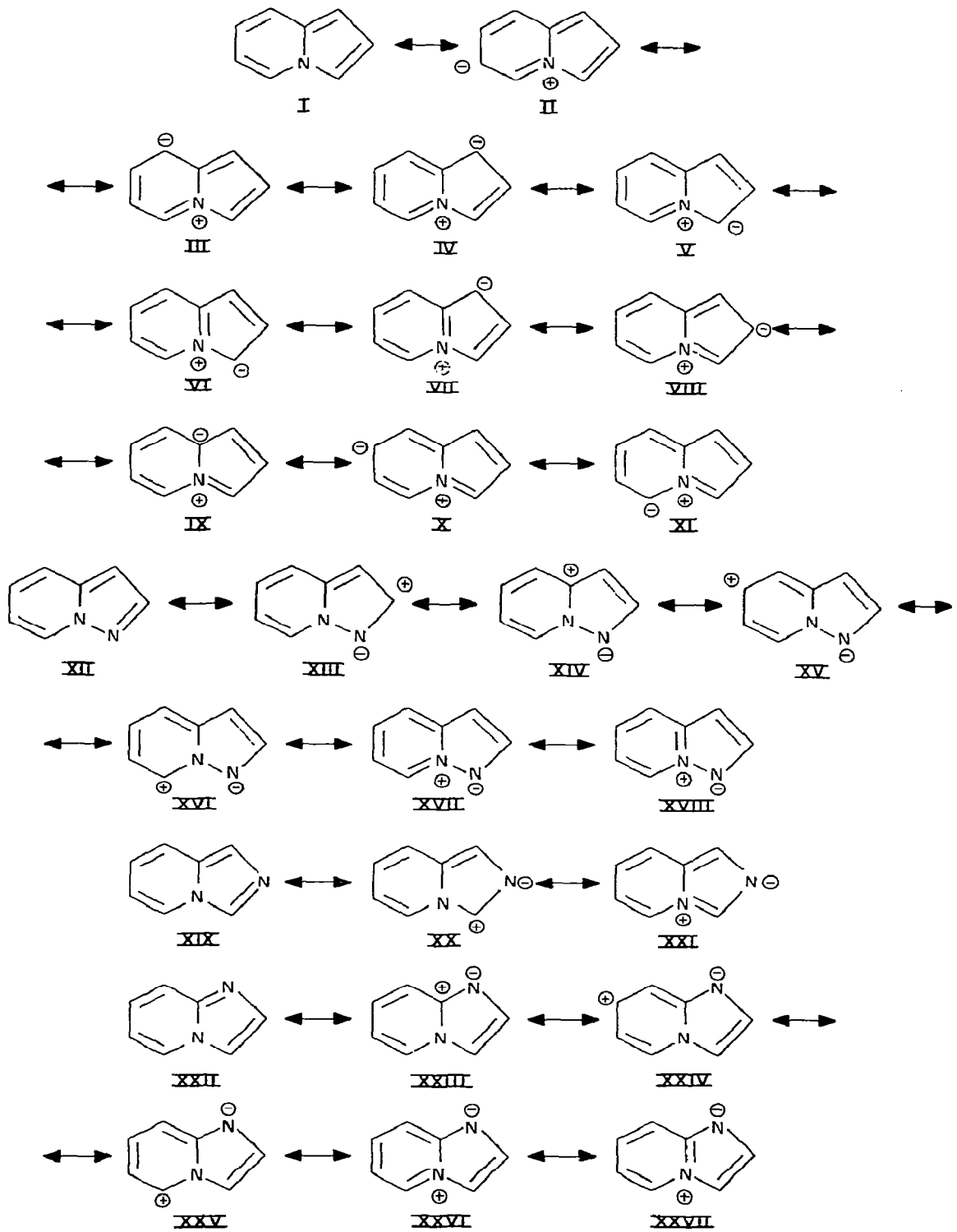
3 since a negative charge appears twice there in the resonance structures (IV—VII). The opposite effect is expected from additional nitrogen atoms in compounds 2—9, but this should be more selective. Thus the N-1 and N-3 atoms should generate positive net charges at C-1a, C-5 and C-7, and they should augment the electron pair delocalization from N-4 (structures XII—XXVII). Much less effect is expected from N-2 (structures XIX—XXI). The effect of N-4 should therefore partly compete and partly cooperate with those of N-1, N-2 and N-3 to yield net charges of either sign within the system of carbon atoms.

Pugmire et al. [2] have already measured the ^{13}C shifts for compounds 1—4 and tried to correlate them with charge distributions using a variation of the average excitation energy (AEE) approximation. They did not obtain a clear relationship and resorted to rather unrealistic assumptions about the value of the excitation energy. We feel that this was due to a rather limited set of experimental data and to some misunderstanding about the nature of the AEE approximation.

We propose to extend the measurements and theoretical considerations over all possible azaindolizines with nitrogen atoms in the five-membered ring section, with some specific questions in mind. The latter include the applicability of the AEE approximation, without any further unnecessary assumptions, to explaining the ^{13}C shifts in indolizines; the possibility of using ^{13}C-NMR as a direct measure of charge density, with a consideration of the π-electron system, the σ-bond system, and total charge density; the degree of additivity of effects on charge distribution and ^{13}C shifts which are brought about by nitrogen atoms. We are encouraged in these efforts



by the successful application of the AEE approximation to an explanation of the nitrogen chemical shifts of azaindolizines [3, 4].

EXPERIMENTAL

The compounds examined were prepared according to procedures quoted elsewhere [4]. The ^{13}C-PFT-NMR spectra were measured at 22.63 MHz and 30° with a Bruker spectrometer, using a sweep width of 6000 Hz, pulse width 8—10 s, pre-delay 143 s, post-delay 2 s, and broad-band proton decoupling.

The calculations were carried out on the CDC-7600 system of the University of London and the ODRA-1204 system of the Polish Academy of Sciences. The INDO method was used, as previously [4], incorporating standard geometries [13].

^{13}C SHIFT ASSIGNMENTS AND EMPIRICAL CORRELATIONS

We have measured the ^{13}C-NMR spectra of solutions of compounds 1—9 in acetone. For compounds 1—4, the assignments are taken from the work of Pugmire et al. [2] who used selective proton decoupling and the proton shift assignments by Black et al. [5]. We have used these data as a starting point for further assignments of the ^{13}C shifts for compounds 5—9. We have considered separately each of the eight possible positions of carbon atoms within the indolizine ring system. It is assumed that the effects on the corresponding groups of shifts induced by N-1, N-2 and N-3 are approximately additive, and therefore we have carried out a regression analysis in order to obtain the best fit for the eight groups taken together. The results are shown in Table 1, with the calculated values of increments characteristic of individual nitrogen atoms. There seems to be little doubt about the assignments since the shifts fall quite neatly into the additivity scheme, and the standard deviations do not exceed 10% of the corresponding ranges of variations of the shifts within each group.

There are some features which should be interesting from the point of view of the resonance structures discussed above. The N-1 and N-3 atoms exert a significant and deshielding effect on the C-1a, C-5 and C-7 nuclei which is compatible with the resonance structures, provided that a simple increase in shielding with increasing electron density prevails for the carbon nuclei. For other positions within the six-membered ring the effects are much smaller and variable in sign. The same is observed for the N-2 effects on all positions of the ring. For the five-membered ring moiety there is a strong deshielding of the carbon nuclei in position C-2 by N-1 and N-3, in C-3 by N-2, and in C-1 by N-2, while C-1 and C-3 are much less affected by N-3 and N-1, respectively. These trends are also in agreement with the resonance structures. However, one should be aware of the fact that the simple resonance structures are actually concerned with the charge distribution throughout the π-electron system only.

TABLE 1

^{13}C Chemical shift assignments and AEE calculations for azaindolizines

Carbon atom	Cpd.	^{13}C Shifts (p.p.m. from TMS)			σ^{loc}_{dia} (p.p.m.)	$(\sigma^{loc}_{para} \times \Delta E_{av})$ (p.p.m. × eV)	ΣQ_{AB}	$(Z_{2p})^3$
		Obs.	Calc.	Diff.				
C—1a	1	133.3	133.7	+0.4	235.59	—1813.82	2.6521	22.6547
	2	141.0	137.8	—3.2	235.51	—1845.77	2.6776	22.8342
	3	131.0	132.0	+1.0	235.65	—1801.24	2.6562	22.4630
	4	145.9	147.9	+2.0	235.26	—1894.35	2.6818	23.3983
	5	134.5	136.1	+1.6	235.58	—1828.34	2.6772	22.6220
	6	149.7	146.2	—3.5	235.32	—1891.21	2.6965	23.2326
	7	151.4	152.0	+0.6	235.23	—1910.78	2.6984	23.4560
	8	149.2	150.3	+1.1	235.27	—1905.65	2.7058	23.3294
		(Calc. shift = 133.7 + increments: +4.1(N—3); —1.7(N—2); +14.2(N—1))						
C—1	1	99.5	99.3	—0.2	236.06	—1581.75	2.4850	21.0846
	2	97.3	97.5	+0.2	236.12	—1586.49	2.5173	20.8767
	3	120.2	120.4	+0.2	235.82	—1660.30	2.5259	21.7734
	5	118.7	118.5	—0.2	235.85	—1662.83	2.5422	21.6665
		(Calc. shift = 99.3 + increments: —1.85(N—3); +21.05(N—2))						
C—2	1	114.0	115.9	+1.9	235.80	—1653.02	2.4989	21.9122
	2	142.3	140.4	—1.9	235.46	—1756.80	2.5531	22.7932
	4	134.0	132.1	—1.9	235.54	—1725.47	2.5337	22.5588
	7	154.6	156.5	+1.9	235.15	—1840.25	2.5958	23.4840
		(Calc. shift = 115.9 + increments: +24.45(N—3); +16.15(N—1))						
C—3	1	113.5	111.2	—2.3	235.90	—1621.18	2.4915	21.5540
	3	128.8	131.1	+2.3	235.60	—1711.21	2.5382	22.3325
	4	113.3	115.6	+2.3	235.93	—1614.25	2.4956	21.4268
	6	137.1	135.5	—1.6	235.64	—1709.55	2.5529	22.1824
	9	136.3	135.5	—0.8				
		(Calc. shift = 111.2 + increments: +19.9(N—2); +4.4(N—1))						
C—5	1	126.3	126.5	+0.2	235.63	—1682.91	2.4977	22.3195
	2	129.5	128.8	—0.7	235.60	—1692.44	2.5016	22.4110
	3	123.5	123.9	+0.4	235.63	—1681.32	2.4927	22.3432
	4	127.3	127.6	+0.3	235.58	—1699.84	2.5046	22.4814
	5	126.1	126.2	+0.1	235.60	—1691.39	2.5002	22.4093
	6	125.8	125.0	—0.8	235.59	—1692.81	2.4992	22.4371
	7	129.7	129.9	+0.2	235.56	—1704.03	2.5056	22.5283
	8	126.9	127.3	+0.4	235.57	—1698.90	2.5030	22.4833
		(Calc. shift = 126.5 + increments: +2.3(N—3); —2.6(N—2); +1.1(N—1))						
C—6	1	110.7	110.3	—0.4	235.86	—1645.68	2.5069	21.7451
	2	112.4	113.0	+0.6	235.87	—1642.69	2.5054	21.7189
	3	112.8	113.1	+0.3	235.85	—1646.91	2.5055	21.7735
	4	112.4	112.2	—0.2	235.89	—1639.67	2.5092	21.6463
	5	116.1	115.7	—0.4	235.85	—1645.73	2.5041	21.7705
	6	114.5	114.9	+0.4	235.87	—1645.10	2.5084	21.7246
	7	114.7	114.8	+0.1	235.89	—1638.32	2.5074	21.6442
	8	117.8	117.6	—0.2	235.86	—1644.56	2.5064	21.7347
		(Calc. shift = 110.3 + increments: +2.65(N—3); +2.75(N—2); +1.85(N—1))						

(continued overleaf)

TABLE 1 (continued)

Carbon atom	Cpd.	^{13}C Shifts (p.p.m. from TMS) Obs.	Calc.	Diff.	σ^{loc}_{dia} (p.p.m.)	$(\sigma^{loc}_{para} \times \Delta E_{av})\Sigma Q_{AB}$ (p.p.m. × eV)		$(Z_{2p})^3$
C—7	1	117.3	117.3	0.0	235.78	—1665.26	2.5061	22.0109
	2	123.9	123.3	—0.6	235.72	—1679.02	2.5099	22.1597
	3	119.5	120.1	+0.5	235.79	—1661.74	2.5055	21.9698
	4	124.6	124.8	+0.2	235.72	—1675.90	2.5045	22.1664
	5	126.1	126.1	0.0	235.74	—1675.66	2.5102	22.1122
	6	128.9	127.6	—1.3	235.72	—1676.98	2.5033	22.1909
	7	130.4	130.8	+0.4	235.69	—1685.58	2.5082	22.2611
	8	133.3	133.6	+0.3	235.68	—1687.04	2.5079	22.2830
	9(C—9)	127.1	127.6	+0.5				
	(Calc. shift = 117.3 + increments: +6.0(N—3); +2.8(N—2); +7.5(N—1))							
C—8	1	119.7	119.6	—0.1	235.85	—1636.78	2.4960	21.7221
	2	118.9	118.7	—0.2	235.88	—1632.73	2.4995	21.6378
	3	118.6	117.9	—0.7	235.83	—1640.59	2.4929	21.7999
	4	118.0	118.1	+0.1	235.91	—1618.64	2.4893	21.5393
	5	116.1	117.0	+0.9	235.85	—1637.68	2.4967	21.7277
	6	115.9	116.4	+0.5	235.89	—1623.77	2.4876	21.6226
	7	117.2	117.2	0.0	235.93	—1616.03	2.4916	21.4847
	8	116.2	115.5	—0.7	235.90	—1623.44	2.4896	21.6003
	9(C—10)	117.0	116.4	—0.6				
	(Calc. shift = 119.65 + increments: —0.92(N—3); —1.72(N—2); —1.52(N—1)							
	(Compound 9, additional peaks at 115.3, 130.1, 130.7)							

MOLECULAR ORBITAL CALCULATIONS

In order to obtain an estimate of relative contributions of σ- and π-charge densities to total charge densities in azaindolizines, we have carried out INDO molecular orbital calculations. From our experience with nitrogen chemical shifts [3, 4, 6] the INDO method seems to give more reasonable results than the CNDO/2 method used in ref. 2. The corresponding σ-, π- and total net charges obtained are given in Table 2. The results for indolizine (1) are quite instructive. The calculation suggests an overall increase in the π-electron charge at N-4, with the most remarkable changes occurring at C-1 and C-3. This is in perfect agreement with the conclusions based on the resonance structures. However, this effect is largely offset by an opposite trend in the σ-bond core from which N-4 seems to withdraw electrons by something which may be termed an inductive effect, since the most affected positions are those adjacent to N-4. The overall picture is thus fairly complicated since the net charge densities are actually differences between changes of comparable magnitude. An interesting question arises as to whether ^{13}C shifts bear any simple relationship to the total charge densities or any portions thereof.

If we try to plot the ^{13}C shifts against the calculated π- or σ-charges no reasonable correlation is obtained, but a plot against the net charges (or

total electron densities) reveals a good linear relationship (Fig. 1) with a standard deviation of 3.5 p.p.m. which amounts to 7% of the range of shifts. One should note that the correlation includes the C-1a atoms (those at ring junctions) for which some specific effects are claimed in the literature [2]. The mean spread of the points around a straight line is within the range of long-range effects on the shifts, those due to ring currents, electric field effects, etc. Recent calculations [6] of ring currents in aromatic heterocycles including indolizine suggest effects within a few p.p.m. However, at least 85% of the range of shifts is explained in terms of the total net charge which is obviously concerned with electrons localized at the nucleus involved. The ^{13}C shifts seem to be a reasonable measure of the corresponding net charges. A zero charge corresponds to 118.06 p.p.m. on the plot in Fig. 1, but the range of 114—120 p.p.m. represents small net charges of either sign, —0.04 to +0.02. Shifts lower than that (i.e. increased shielding of ^{13}C) clearly indicate a negative charge, and those in excess of 120 p.p.m. show a positive charge. The value of about 162 p.p.m. per unit electron charge obtained for the azaindolizines is in excellent agreement with the earlier value of 160 p.p.m. per π-electron, obtained by Spiesecke and Schneider [7] for the tropylium cation, benzene, and the cyclopentadienyl anion. A value of about 200 p.p.m. per electron was suggested for indolizines [2], but this resulted from an assumption of the value of mean excitation energy. This point will be discussed later; one should note, however, that it is rather dangerous to try and interpret ^{13}C shifts in terms of π-electrons only, as is shown in the

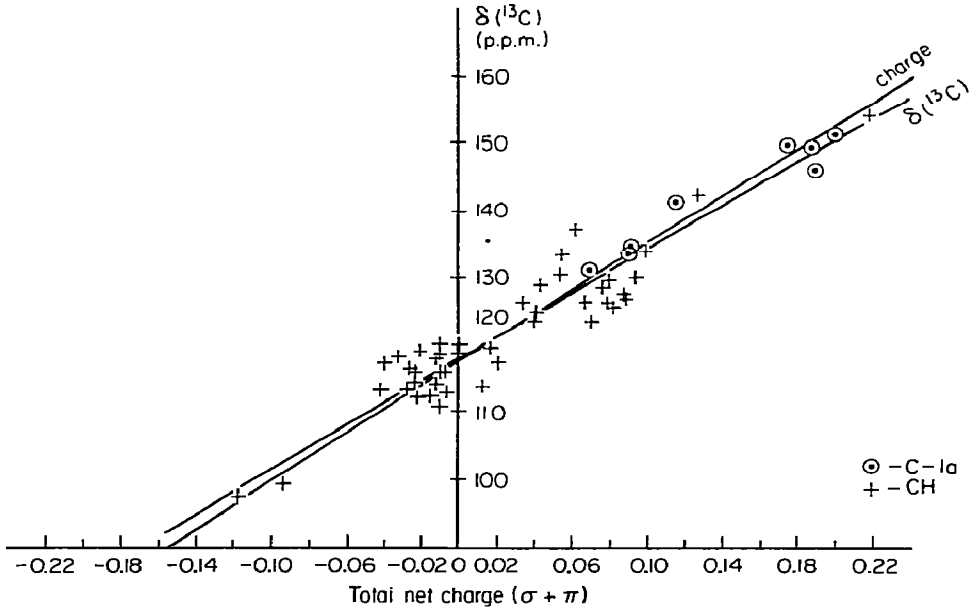


Fig. 1. Least-squares fits between $\delta(^{13}C)$ and net charge. $\delta(^{13}C) = 118.06 + 162.25$ (net charge), std. deviation ± 3.56 p.p.m.; net charge = $0.00566357\delta(^{13}C) - 0.66539$, std. deviation ± 0.02101 unit charge; linear correlation coefficient, 0.960.

TABLE 2

Net charges and ^{13}C shifts[a] in some azaindolizines

Compound	Net charge	Atom						
		1a	1	2	3	4	5	6
1	σ	+0.1543	+0.0681	+0.0323	+0.1797	−0.5288	+0.1143	+0.0287
	π	−0.0637	−0.1610	−0.0203	−0.2079	+0.5736	−0.0465	−0.0393
	Total	+0.0906	−0.0929	+0.0120	−0.0282	+0.0448	+0.0678	−0.0105
	^{13}C shift	133.3	99.5	114.0	113.5		126.3	110.7
2	σ	+0.1225	+0.0542	+0.0818	+0.1385	−0.5170	+0.1055	+0.0287
	π	−0.0072	−0.1709	+0.0455	−0.3925	+0.6141	−0.0261	−0.0442
	Total	+0.1154	−0.1167	+0.1274	−0.2540	+0.0971	+0.0795	−0.0155
	^{13}C shift	141.0	97.3	142.3			129.5	112.4
3	σ	+0.1408	+0.1360	−0.0906	+0.2288	−0.5395	+0.1187	+0.0250
	π	−0.0711	−0.1359	−0.1172	−0.1525	+0.5874	−0.0487	−0.0317
	Total	+0.0697	+0.0001	−0.2078	+0.0763	+0.0479	+0.0700	−0.0067
	^{13}C shift	131.0	120.2		128.8		123.5	112.8
4	σ	+0.1985	−0.0174	+0.0868	+0.1672	−0.5477	+0.1108	+0.0259
	π	−0.0081	−0.3089	+0.0120	−0.2091	+0.6148	−0.0233	−0.0483
	Total	+0.1904	−0.3263	+0.0988	−0.0419	+0.0671	+0.0875	−0.0224
	^{13}C shift	145.9		134.0	113.3		127.3	112.4
5	σ	+0.1120	+0.1217	−0.0477	+0.2117	−0.5369	+0.1091	+0.0248
	π	−0.0202	−0.1321	−0.0467	−0.3680	+0.6423	−0.0304	−0.0320
	Total	+0.0918	−0.0104	−0.0944	−0.1553	+0.1054	+0.0787	−0.0072
	^{13}C shift	134.5	118.7				126.1	116.1
6	σ	+0.1800	+0.0701	−0.0348	+0.2082	−0.5734	+0.1110	+0.0255
	π	−0.0056	−0.2919	−0.0809	−0.1462	+0.6083	−0.0288	−0.0383
	Total	+0.1744	−0.2218	−0.1157	+0.0620	+0.0348	+0.0822	−0.0128
	^{13}C shift	149.7			137.1		125.8	114.5
7	σ	+0.1700	−0.0266	+0.1312	+0.1241	−0.5358	+0.1034	+0.0278
	π	+0.0302	−0.3045	+0.0872	−0.3782	+0.6429	−0.0097	−0.0508
	Total	+0.2002	−0.3311	+0.2184	−0.2541	+0.1071	+0.0937	−0.0230
	^{13}C shift	151.4		154.6			129.7	114.7
8	σ	+0.1609	+0.0570	+0.0059	+0.1798	−0.5607	+0.1046	+0.0256
	π	+0.0267	−0.2740	−0.0005	−0.3432	+0.6486	−0.0164	−0.0373
	Total	+0.1876	−0.2170	+0.0054	−0.1634	+0.0879	+0.0882	−0.0117
	^{13}C shift	149.2					126.9	117.8

[a] All shifts are in p.p.m.

present work. The situation is less critical for symmetric species like those in ref. 7 which have a clear and uniform charge distribution among their CH moieties. It is also interesting that the range of net charges, from that for the tropylium cation (+1/7) to that for the cyclopentadienyl anion (−1/5), is almost the same as the calculated range for the azaindolizines examined. Having found a rather good and useful correlation between the ^{13}C shifts and total net charges at the corresponding carbon atoms, one may wonder whether this relationship can be accounted for on more theoretical grounds. We therefore proceed to calculations of the nuclear screening of ^{13}C in azaindolizines using the average excitation energy approximation [14].

7	8	H—1	H—2	H—3	H—5	H—6	H—7	H—8
+0.0366	+0.0090							
—0.0157	—0.0192							
+0.0209	—0.0102	—0.0130	—0.0193	—0.0101	—0.0107	—0.0093	—0.0239	—0.007
117.3	119.7							
+0.0270	+0.0109							
+0.0129	—0.0316							
+0.0399	—0.0207	—0.0069	—0.0132		—0.0022	—0.0045	—0.0212	—0.005
123.9	118.9							
+0.0363	+0.0091							
—0.0203	—0.0100							
+0.0160	—0.0009	—0.0108		—0.0009	—0.0118	—0.0092	—0.0231	—0.009
119.5	118.6							
+0.0300	+0.0063							
+0.0101	—0.0391							
+0.0401	—0.0328		—0.0186	—0.0080	—0.0099	—0.0062	—0.0198	+0.002
124.6	118.0							
+0.0267	+0.0105							
+0.0075	—0.0204							
+0.0342	—0.0099	—0.0030			—0.0010	—0.0034	—0.0191	—0.005
126.1	116.1							
+0.0294	+0.0073							
+0.0137	—0.0302							
+0.0431	—0.0229			+0.0022	—0.0077	—0.0038	—0.0180	+0.003
128.9	115.9							
+0.0232	+0.0075							
+0.0300	—0.0471							
+0.0532	—0.0396		—0.0080		—0.0016	—0.0018	—0.0173	+0.003
130.4	117.2							
+0.0233	+0.0094							
+0.0315	—0.0353							
+0.0548	—0.0259				+0.0020	+0.0009	—0.0147	+0.006
133.3	116.2							

AVERAGE EXCITATION ENERGY APPROXIMATION (AEE) OF ^{13}C SHIFTS

Since we consider carbon atoms which are involved in a planar σ-bond and a π-electron system, it is reasonable to employ a method based on the original LCAO formulation by Pople [8] using the closure approximation. We employ a particular realisation of this scheme which we have already used for the explanation of nitrogen chemical shifts in general [3, 4, 9], including those for azaindolizines [4]. Only the local diamagnetic term, σ_{dia}^{loc}, and the local paramagnetic term, σ_{para}^{loc}, in the expression for the screening constant are considered [14] according to equations derived elsewhere [9].

$$\sigma_{dia}^{loc} = 17.7501 \sum_i P_{ii} Z_i n_i^{-2} \quad \text{(p.p.m.)} \tag{1}$$

$$\sigma_{para}^{loc} \times \Delta E_{av} = -30.1885 (Z_{2p})^3 \sum_B Q_{AB} \quad \text{(p.p.m. eV)} \tag{2}$$

where i denotes an atomic orbital, P_{ii} is its population, Z_i is the corresponding effective nuclear charge and n_i is the principal quantum number associated with the i^{th} orbital. The last term in eqn. (2) is given by

$$Q_{AB} = (4/3)\delta_{AB}(P_{x_A x_B} + P_{y_A y_B} + P_{z_A z_B}) - (2/3)(P_{x_A x_B} P_{y_A y_B} + P_{x_A x_B} P_{z_A z_B} + P_{y_A y_B} P_{z_A z_B}) + (2/3)(P_{x_A y_B} P_{x_B y_A} + P_{x_A z_B} P_{x_B z_A} + P_{y_A z_B} P_{y_B z_A}) \tag{3}$$

where δ_{AB} is the Kronecker delta and the P's are the bond-order and charge-density matrix elements for the $2p_x$, $2p_y$ and $2p_z$ orbitals which are calculated by the INDO method. The summation over B includes all atoms in the molecule; atom A is also considered. The effective ^{13}C nuclear charges for electrons in the $1s$, $2s$ and $2p$ orbitals are estimated using the rules of Burns [10] for exponential-type orbitals. The following equations can be derived [14] for carbon atoms

$$Z_{1s} = 5.2 - 0.1(P_{2s} + P_{2p}) \tag{4}$$

$$Z_{2s} = 4.6 - 0.4\, P_{2s} - 0.35\, P_{2p} \tag{5}$$

$$Z_{2p} = 4.35 - 0.5\, P_{2s} - 0.35\, P_{2p} \tag{6}$$

where P_{2s} and P_{2p} are total orbital populations for the atom considered.

The average excitation energy, ΔE_{av}, does not bear any simple relationship to actual excited states of molecules, and it is rather pointless to speculate about its value using transitions observed in UV and visible absorption spectra [14]. One does not have to, and actually should not, assume any specific value of ΔE_{av} at the outset. The values of the product $(\sigma_{para}^{loc} \times \Delta E_{av})$ calculated according to eqn. (2), eventually corrected for some small changes in σ_{dia}^{loc} (which are usually negligible as has been shown elsewhere [11]), can be plotted against the corresponding experimental chemical shifts. If the plot is reasonably linear then it is obvious that ΔE_{av} is reasonably constant throughout the set of atoms involved and its value may be obtained from the slope of the least-squares fitted straight line. One should note that by considering only the local diamagnetic and paramagnetic terms we exclude all long-range effects on the shifts, which should not however contribute more than a few parts per million to the observed range of shifts [14].

The values of $(\sigma_{para}^{loc} \times \Delta E_{av})$ for individual carbon atoms in azaindolizines are given in Table 1 together with those for σ_{dia}^{loc}. The latter are almost constant [14], and plots of the former against the ^{13}C shifts show good linear correlations (correlation coefficient ca. 0.96) for two separate groups of carbon nuclei, those in the CH moieties and the C-1a atoms at ring junctions (Fig. 1). The standard deviations are within the range expected for

long-range effects and about 85% of the total variation of the ^{13}C magnetic screening observed is accounted for by changes in the local paramagnetic term. It is interesting that ΔE_{av} is reasonably constant for all of the CH moieties involved, independent of the number and position of nitrogen atoms present within the ring system. However, by replacing a hydrogen atom with a heavier atom (C or N), as is the case for C-1a, a lower value of $1/\Delta E_{av}$ is obtained. This should act as a warning to those who attempt to correlate carbon shifts with the results of AEE-type calculations, since aromatic CH moieties are likely to follow their own sequence which is different from that for carbon atoms with no hydrogen atoms attached to them.

One can go a little further with the AEE method and ask about the position of the absolute zero on the scale of ^{13}C chemical shifts, i.e. that of the resonance of a bare ^{13}C nucleus. In principle, the following equation should hold, if we neglect changes other than those in the local diamagnetic and paramagnetic terms

$$\delta(^{13}C)_{TMS} = \sigma^{abs}_{TMS} - \sigma^{loc}_{dia} - (1/\Delta E_{av})\,(\sigma^{loc}_{para} \times \Delta E_{av}) \qquad (7)$$

where δ is a shift from TMS on the "deshielding" scale (deshielding taken as positive). For the azaindolizines examined, we have two such linear relations with three unkowns, the absolute screening constant for ^{13}C in TMS (σ^{abs}_{TMS}), and two reciprocal average excitation energies (for the CH and C-1a carbon atoms), which may be obtained from a least-squares fitting procedure: $(1/\Delta E_{av}) = 0.205 \pm 0.005$ eV^{-1} for CH; $(1/\Delta E_{av}) = 0.194 \pm 0.009$ eV^{-1} for C-1a, and $\sigma^{abs}_{TMS} = +15.8 \pm 18.3$ p.p.m. The last is rather far from the values of about +200 p.p.m. obtained from more sophisticated calculations [12], and this discrepancy seems to stem from the nature of the AEE approximation [14]. The average excitation energy can be fairly constant over a limited range of shifts, as revealed by plots of $(\sigma^{loc}_{para} \times \Delta E_{av})$ against the shifts, but even a slight non-linearity of the correlation (corresponding to minor but regular changes in ΔE_{av}) can render a linear extrapolation highly unreliable [14, 15].

One may wonder how it is possible that good linear relationships are observed between the experimental ^{13}C shifts and the AEE values in two groups of carbon atoms while there is a single linear correlation of the shifts with total charge densities. A careful examination of the factors in the expression for the local paramagnetic term (eqn. (2) and Table 1) indicates that relative changes in $(Z_{2p})^3$ are much larger than in the ΣQ term within each group. However, there is a systematic difference in the ΣQ term between the groups which is compensated for by a corresponding change in ΔE_{av}. Thus, there is a general relationship between $(Z_{2p})^3$ and the shifts in the two groups taken together. The $(Z_{2p})^3$ term, according to eqn. (6), should give a cubic rather than linear dependence on the charge density. However, if one inserts actual values of extreme charge densities for the set of molecules considered, it is easy to show that about 90% of the change

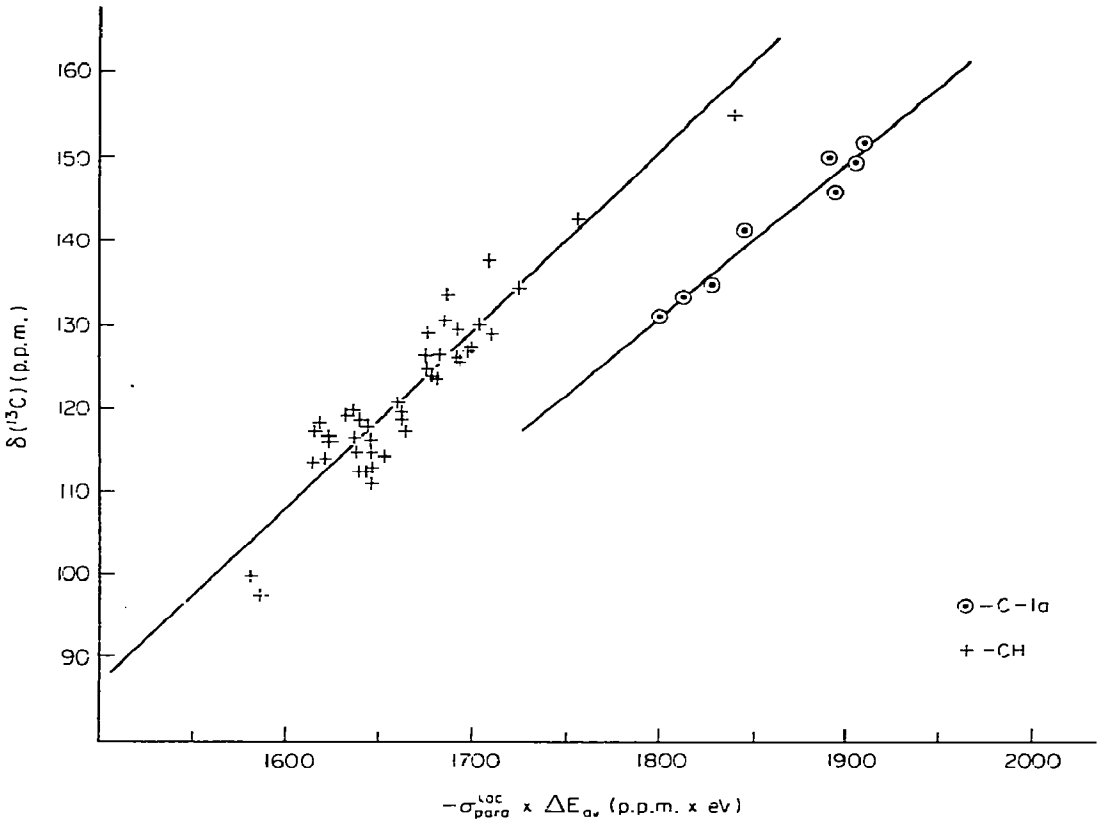


Fig. 2. Least-squares fits between $\delta(^{13}C)$ and $(\sigma^{loc}_{para} \times \Delta E)$. For CH carbon atoms, $\delta(^{13}C) = 0.210964(\sigma^{loc}_{para} \times \Delta E_{av}) - 229.75$, std. deviation ± 3.6 p.p.m., $\Delta E_{av} = 4.74$ eV; for C-1a, $\delta(^{13}C) = 0.182479(\sigma^{loc}_{para} \times \Delta E_{av}) - 197.67$, std. deviation ± 1.6 p.p.m., $\Delta E_{av} = 5.48$ eV.

in $(Z_{2p})^3$ is linear with the difference in electron charge density. Thus, there is no contradiction between the empirical and theoretical correlations obtained. Some consequences of this are interesting from the point of view of an explanation of the ^{13}C shifts in conjugated rings. The $(Z_{2p})^3$ term is a factor in the local paramagnetic term, but its contribution may be considered as an "increase in screening", since it reduces the absolute value of σ^{loc}_{para} with increasing total electron density. This factor seems to be mainly responsible for changes in the ^{13}C shifts of heteroaromatic ring structures. The contribution of ΣQ is truly a "decrease in screening", since for a given total $2p$ electron density it increases the absolute value of σ^{loc}_{para} with increasing departure from a spherical distribution of the charge. Hence, changes in this term are either less significant than those in $(Z_{2p})^3$ or they are offset by a corresponding change in ΔE_{av}. The overall result is that the ^{13}C shifts of conjugated rings can serve as a measure of net charge on the carbon atoms. Nevertheless, one should bear in mind that this is a result of the compensation of certain effects within the local paramagnetic term which may be specific

to some molecular structures. In addition, it is noteworthy that the apparent "increase in screening" changes are actually those in the local paramagnetic term rather than those in the local diamagnetic term [11].

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