THE RELATION BETWEEN STRUCTURE AND REACTIVITY IN FIVE-MEMBERED HETEROAROMATIC COMPOUNDS—I

EFFECT OF ASSUMED MOLECULAR GEOMETRY ON CNDO/2 ELECTRON DISTRIBUTION FOR SOME TETRAZOLE DERIVATIVES

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Abstract—Two parallel sets of CNDO/2 calculations have been carried out for 1H-5-aminotetrazole (**1**), 2-methyl-5-aminotetrazole (**2**), 1,3-dimethyl-5-aminotetrazolium cation (**3**) and the tetrazolate anion (**4**). In one set, the molecular geometry was represented by a regular pentagon 1·33 Å on a side, and in the other the experimentally determined molecular geometries were used. The calculated electronic structures from the two sets of calculations are compared; both sets predict similar trends in variation of atomic charges and bond indices with structure. Where comparison is possible, these trends seem to be generally in agreement with expectations based on classical concepts such as resonance. It is noted that the relative magnitudes of σ-electron bond indices seem to parallel those of the π-electron bond indices in many cases, although the σ-bond indices show much smaller variation in absolute magnitude as compared with the π-bond indices. A brief discussion of the relative merits of various geometrical models is presented; it is suggested that, in order to combine the advantages of both approaches, standard and experimentally-determined geometries should be used side-by-side whenever possible. A procedure for speeding convergence by use of a damping factor is described.

We have recently begun a study of the relation between structure and reactivity in azole derivatives.[2-5] Preliminary presentations have been given for CNDO/2 calculations on substituent effects exerted by azapyrrole rings[3] and on C–H acidities of azolium cations,[5] as well as experimental and theoretical work on the substituent effects exerted by tetrazole rings.[2,4] In this work, variations in the reactivities of side chains attached to azole rings are examined. Results in this paper include calculations on the following:

ity of cases, experimentally determined molecular geometries for the particular molecules under study are not available. Furthermore, extensive minimization of molecular geometry against calculated energy does not seem economically feasible or scientifically desirable for molecules of the size presently under consideration. Consequently, a number of authors[7] have chosen to represent heteroaromatic rings by regular pentagons or hexagons of appropriate dimensions.

Another argument in favor of idealized assumed

1	**2**	**3**	**4**
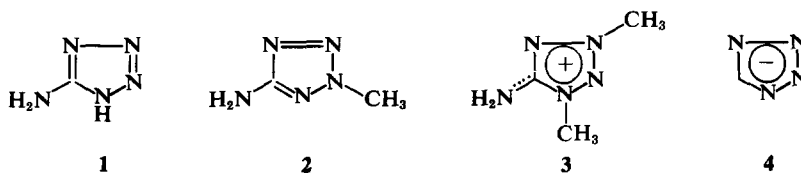
In the course of this work, we will be attempting to judge the importance of resonance, field and other classical organic effects on the relative reactivities of these compounds; one means of accomplishing this will be through the use of electronic structures calculated by CNDO/2[6a] and other molecular orbital methods.[6]

The input required for calculations of this type includes a set of bond lengths and angles for the molecule being calculated. However, in the major-

geometries is that, as pointed out by Pople and Gordon[8a] in a paper on acyclic aliphatic systems, the use of one standard geometrical convention throughout a series of calculations may allow more insight into trends in electronic structure. This is because individual geometrical features are themselves caused by the electronic structure. However, the present work deals with cyclic molecules; when a series of heterocyclic molecules or ions is represented by a constant, regular polygonal ring geom-

etry throughout, no account is taken of the fact that, for example, pure single C–C, C–N and N–N bonds are expected to have different lengths because of the differing atomic radii of carbon and nitrogen.

The discussion in the preceding paragraphs suggests that, in studying trends in calculated electronic structures for heterocyclic compounds, idealized and experimental (or optimized) geometrical models each have their respective strong and weak points. Consequently, it seemed desirable to obtain some information as to the effect of reasonable changes in assumed molecular geometry on calculated electronic structures for some compounds representative of those to be studied in the future. Accordingly, in the present paper, the CNDO/2 calculated electronic structures of some tetrazole derivatives are compared between regular-pentagonal and crystallographic assumed molecular geometries.

Calculations

The CNDO/2 calculations[8a] were performed in double precision on the Naval Postgraduate School IBM 360/67, in single precision on the Naval Weapons Center Univac 1108, or in single precision (72-bit word) on the Ballistic Research Laboratories "BRLESC" computers, using a program written by one of us (W.M.T.). The input consisted of atomic numbers, bond angles, and bond lengths. The coordinates were generated by the appropriate rotation and translation of the coordinate system. Iteration was continued until the elements of the bond-order charge-density matrix from successive iterations were consistent to within 0·0001.

The matrix elements converged very slowly for some of these and related molecules. Inspection of intermediate results revealed that the orbital charge densities were oscillating with each successive iteration, as shown in Table 1 for 1H-5-aminotetrazole (1). In order to improve the convergence for this method, a damping factor was calculated every second iteration and applied

according to the method described in the following paragraph.

The criterion for oscillation, O, was first determined by comparison of the results of three consecutive iterations. O is given by the equation

$$O = \frac{\sum_a \left\{ \frac{(P''_{aa} - P'_{aa}) \, | \, (P''_{aa} - P'_{aa}) \, |}{(P'_{aa} - P_{aa})} \right\}}{\sum_a \, | \, (P''_{aa} - P'_{aa}) \, |}$$

where a is an atomic orbital and P_{aa} is a diagonal element of the population matrix (charge-density bond-order matrix). P_{aa} represents a given iteration, P'_{aa} represents the next iteration, and P''_{aa} represents the next iteration after that. In practice it was convenient to set limits on the value of O chosen such that

$$-2·00 < O < 0·33.$$

The damping factor, D, is initially set equal to unity and then modified every second iteration according to the equation

$$D^{new} = (1 - R)D + R[D/(1 - O],$$

where R determines the rate at which D approaches the "ideal" value. Convenient values for R have been found to be between 0·3 and 0·5.

The equations for the population matrix are modified to include this damping factor. Letting the primes retain their previous significance, an improved set of matrix elements P^{new}_{ab} and P^{new}_{AA} is obtained according to the equations

$$P^{new}_{ab} = P'_{ab}(1 - D) + P''_{ab}D$$

and

$$P^{new}_{AA} = P'_{AA}(1 - D) + P''_{AA}D$$

where a and b are atomic orbitals, and P_{AA} throughout is the net charge on atom A. Use of this method markedly reduced the number of iterations nec-

Table 1 CNDO/2 total atomic charges[a] for first six iterations on 1H-5-aminotetrazole (1) 1·33 Å pentagon

	Atomic charges					
Iteration	1	2	3	4	5	6
N(1)	+284	−268	+97	−155	+23	−111
H(1)	+137	+135	+96	+124	+102	+119
N(2)	−220	−109	−25	−168	−20	−159
N(3)	−215	+121	−165	+87	−114	+52
N(4)	−463	−51	−339	−126	−289	−165
C(5)	+375	+187	+342	+243	+306	+229
N(NH$_2$)	−201	−323	−248	−265	−255	−259
H$_1$(NH$_2$)	+152	+173	+124	+143	+129	+138
H$_2$(NH$_2$)	+153	+136	+117	+117	+118	+116

[a]In units of 0·001 electronic charge.

essary for convergence. Several instances were found in calculating these and related heterocyclic ring compounds in which convergence was not reached after over 40 iterations. Application of the above method reduced the number of iterations in some cases to 20. The damping factor which seems most ideally suited for these calculations seems to be less than unity when convergence is nearly reached. In all cases examined an improvement in computer time was noted with the above technique.

The above extrapolation technique is a modification of that reported by Roothan and Bagus.[8b] For a choice of $\mathbf{R}$ equal to unity, and if the value of O is calculated for each element P_{ab}, the result is mathematically identical with that suggested by Hartree.[8b] Utilizing this method, however, the effects of oscillation are averaged throughout the eigenvectors rather than calculated for each eigenvector element. This method offers the additional advantage that only the diagonal elements of a matrix need be stored for three successive iterations rather than the entire matrix, as suggested by Hartree. The authors wish to thank one of the referees for referral to these more conventional extrapolation techniques.

The tetrazole rings were represented by regular pentagons 1·33 Å on a side, or by crystallographic geometries, as specified in the Tables. For the regular-pentagon calculations, the C–NH$_2$ bond length was taken as 1·37 Å for 1 and 2 and 1·29 Å for 3; other bond lengths and angles were, unless specified to the contrary, assumed to have the values suggested by Pople and Gordon.[8a]

In the experimental-geometry calculation on 1, the ring CNH angle was estimated from a series of calculations on 1H-tetrazole in which the tetrazole ring was assumed to have the geometry found experimentally for 1H-5-aminotetrazole (1) and CNH angle was varied until an energy minimum was found to within 0·1°; this occurred at 132·3°. References to crystallographic measurements are given in the footnotes to the Tables.

The bond index between atomic orbitals a and b is defined by the equation

$$W_{ab} = P_{ab}^2,$$
$$P_{ab} = 2 \sum_i c_{ia} c_{ib},$$

where W_{ab} is the bond index, P_{ab} is the bond order between orbitals a and b (a ≠ b), and c_{ia} and c_{ib} are the coefficients of orbitals a and b in the i'th occupied molecular orbital. The bond index between two atoms is the sum of the bond indices between the orbitals on those atoms; these quantities seem to be related to bond character.[9]
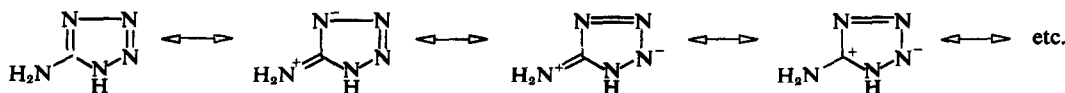
RESULTS

Our CNDO/2 atomic charges and bond indices for 1–4 are presented in Tables 2 and 3 respectively.

The calculated dipole moments for 1 were 6·53 D from the regular-pentagon calculation and 6·28 D from the experimental-geometry calculation. The experimental value for 5-aminotetrazole is 5·7 D.[10] The corresponding quantities for 2 are 2·07, 1·88 and ca 2·6 D.[11] Better dipole moments and lower total energies were obtained when the amino groups were taken to the tetrahedral (rather than coplanar as in the Pople-Gordon[8a] geometrical convention); these results are summarized in Table 4. However, the experimental values given were measured in solution, and hence are subject to complexities due to factors such as intermolecular association and tautomerism; these are especially pertinent in the present case due to the N–H bonds in the molecules under consideration.

DISCUSSION

Examination of Tables 2 and 3 shows that, although absolute magnitudes do vary somewhat, the regular (1·33 Å)-pentagon and experimental-geometry calculations show very much the same trends in calculated atomic charges and bond indices. Both sets of calculations show π-electron bond indices alternating as expected from classical organic chemical structural formulas. The σ-electron bond indices tend to alternate in the same way as the π-electron bond indices. The regular-pentagon calculation on 1 (Table 3) shows σ-electron bond indices of 0·995 and 0·993 in the 2–3 and 4–5 bonds respectively, and 0·948, 0·977 and 0·951 in the 1–2, 3–4 and 1–5 bonds respectively. Possibly this alternation in σ-electron bond indices is related to the charge alternation noted by Pople and Gordon[8a] and by Hehre and Pople[13] in nonheteroaromatic systems.

Our calculations (Table 2) show considerable σ-electron polarization in these molecules and ions; this is in agreement with previous results[7a] for a number of unsubstituted azoles.

The π-electron charges behave about as expected classically. For example, both sets of calculations show quite high negative charges at positions 2 and 4 of 1 (Table 2); this is expected on the basis of resonance among forms such as those shown below

The calculations predict more π-electron withdrawal by resonance from the amino group in 1H-5-aminotetrazole (1) than from that in 2-methyl-5-aminotetrazole (2). This follows from the fact that both sets of calculations show a significant positive π-charge on the amino nitrogen and larger C–NH$_2$

Table 2. Effect of assumed molecular geometry on CNDO/2 atomic charges for some tetrazole derivatives

Molecule or Ion	Position	Atomic charges^a							
		1·33 Å Pentagon^b				Experimental Geometry			
		σ	π	Total	H	σ	π	Total	H
1H-5-Aminotetra-zole (1)^c	1	−460	+404	−56	+112	−446	+336	−110	+115
	2	+157	−257	−100	—	+146	−211	−65	—
	3	+28	−44	−16	—	+5	−8	−3	—
	4	+80	−302	−222	—	+112	−366	−254	—
	5	+201	+86	+287	—	+190	+133	+323	—
	NH₂	−369	+112	−257	+118,^d +134^e	−375	+115	−260	+119,^d +135^e
2-Methyl-5-amino-tetrazole (2)^f	1	+110	−336	−226	—	+130	−368	−238	—
	2	−416	+511	+95	—	−405	+509	+104	—
	3	+65	−102	−37	—	+41	−56	−15	—
	4	+44	−234	−190	—	+67	−279	−212	—
	5	+194	+73	+267	—	+188	+96	+284	—
	CH₃	+55	+0	+55	+17,^g +20^h	+46	+1	+47	+17,^g +17^h
	NH₂	−356	+102	−254	+117,^d +119^e	−366	+112	−254	+115,^d +118^e
1,3-Dimethyl-5-aminotetrazolium cation (3)^i	1	−472	+493	+21	—	−438	+432	−6	—
	2	+173	−161	+12	—	+168	−159	+8	—
	3	−505	+701	+196	—	−515	+744	+229	—
	4	+177	−360	−183	—	+201	−389	−188	—
	5	+215	+132	+347	—	+195	+156	+351	—
	CH₃(1)	+89	−30	+59	+48,^g +62^h	+84	−23	+61	+41,^g +57^h
	CH₃(3)	+88	−45	+43	+68,^j +72^k	+79	−47	+32	+69,^f +72^k
	NH₂	−416	+193	−223	+168,^d +189^e	−424	+217	−207	+176,^d +194^e
Tetrazolate anion (4)^l	1(4)	−37	−233	−270	—	−23	−271	−294	—
	2(3)	+20	−216	−196	—	+15	−198	−183	—
	5	+145	−101	+44	−115	+144	−61	+83	−129

^a In units of 0·001 electronic charge; σ, π and total charges given for CH₃ and NH₂ are those for C or N alone.

^b Ring geometry represented by a regular pentagon 1·33 Å on a side; exocyclic C–N bond lengths given in section entitled "Calculations"; other bond lengths and angles as suggested by J. A. Pople and M. Gordon, *J. Am. Chem. Soc.* **89**, 4253 (1967).

^c Experimental bond lengths and angles involving C and N only taken from K. Britts and I. L. Karle, *Acta Crystallogr.* **22**, 308 (1967); bond angles involving N–H bond in position 1 were estimated as described under "Calculations"; other bond lengths and angles involving hydrogen estimated as in footnote b.

^d Proton *syn* to position 1.

^e Proton *anti* to position 1.

^f Experimental bond lengths and angles involving C and N only taken from J. H. Bryden, *Acta Crystallogr.* **9**, 874, (1956); those involving hydrogen estimated as in footnote b.

^g Two equivalent protons oriented *syn* to position 1.

^h Proton in plane of ring and oriented *anti* to position 1.

^i Experimental bond lengths and angles involving C and N only taken from J. H. Bryden, *Acta Crystallogr.* **8**, 211 (1955); those involving hydrogen estimated as in footnote b.

^j Two equivalent protons oriented *anti* to position 4.

^k Proton in plane of ring *syn* to position 4.

^l Experimental C–N and N–N bond lengths and angles taken from G. J. Palenik, *Acta Crystallogr.* **16**, 596 (1963); C–H bond lengths estimated as in footnote b.

π-bond indices and π-charges on nitrogen in **1** than in **2**.

We conclude that the results of the calculations seem to be in accord with classical organic theory and that, subject of course to the reliability of the method used in carrying out the calculations, it should be possible in many cases to make meaningful predictions as to trends and relative magnitudes of resonance, field, inductive and other classical organic effects from either experimental-geometry or regular-pentagon calculations. Adam, Grimison and Rodriguez^7b reached an analogous conclusion from Extended Huckel calculations on pyridine and the diazines.

The material covered in the introduction to the present paper suggests that, as bases for conclusions concerning *trends* in electronic structure, ideal and experimental assumed geometries each have their individual strong and weak points. The experimentally observed geometries give the most reliable picture of the electron distribution in the actual molecule or ion under consideration, but are usually unavailable for one or more members of the particular series of molecules being studied.

Table 3. Effect of assumed molecular geometry on CNDO/2 bond indices[a] for some tetrazole derivatives

Molecule or Ion	Bond	Bond indices					
		1·33 Å Pentagon[b]			Experimental Geometry[b]		
		σ	π	Total	σ	π	Total
1H-5-Aminotetrazole (1)	1–2	0·948	0·175	1·123	0·932	0·124	1·056
	2–3	0·995	0·614	1·609	1·023	0·722	1·745
	3–4	0·977	0·294	1·271	0·956	0·207	1·163
	4–5	0·993	0·475	1·468	0·998	0·511	1·509
	5–1	0·951	0·316	1·267	0·957	0·289	1·246
	5-NH$_2$	0·983	0·122	1·105	0·979	0·130	1·109
2-Methyl-5-aminotetra-zole (2)	1–2	0·952	0·199	1·151	0·939	0·168	1·107
	2–3	0·951	0·371	1·322	0·962	0·403	1·365
	3–4	0·996	0·453	1·449	0·988	0·442	1·430
	4–5	0·976	0·349	1·325	0·972	0·329	1·301
	5–1	1·045	0·423	1·468	0·988	0·496	1·484
	2-CH$_3$	0·977	0·033	1·010	0·976	0·023	1·008
	5-NH$_2$	0·981	0·109	1·090	0·977	0·122	1·099
1,3-Dimethyl-5-aminotetra-zolium cation (3)	1–2	0·973	0·255	1·228	0·970	0·210	1·180
	2–3	0·970	0·519	1·489	0·976	0·561	1·537
	3–4	0·944	0·233	1·177	0·944	0·234	1·178
	4–5	1·001	0·427	1·428	0·986	0·401	1·387
	5–1	0·933	0·287	1·220	0·931	0·274	1·205
	1-CH$_3$	0·944	0·026	0·970	0·956	0·029	0·985
	3-CH$_3$	0·934	0·033	0·967	0·937	0·032	0·969
	5-NH$_2$	1·011	0·218	1·229	1·015	0·251	1·266
Tetrazolate anion (4)	1(4)-2(3)	0·982	0·364	1·346	0·973	0·323	1·296
	2(3)-3(2)	0·987	0·464	1·451	1·005	0·518	1·523
	5-1(4)	0·998	0·449	1·447	1·001	0·460	1·461

[a]K. B. Wiberg, *Tetrahedron* 24, 1083 (1968).
[b]Assumed geometries are summarized in the footnotes to Table 2.

Table 4. CNDO/2 dipole moments and total energies for some 5-aminotetrazole derivatives

Molecule	Geom.[a]	Dipole moment (D)	Total energy (a.u.)
1H-5-Aminotetrazole (1) (Coplanar NH$_2$)	1·33 Å	6·53	−67·765
	Exp	6·28	−67·733
1H-5-Aminotetrazole (1) (Tetrahedral NH$_2$)	1·33 Å	6·00	−67·775
2-Methyl-5-Aminotetrazole (2) (Coplanar NH$_2$)	1·33 Å	2·07	−76·450
	Exp.	1·88	−76·464
2-Methyl-5-Aminotetrazole (2) (Tetrahedral NH$_2$)	1·33 Å	2·93	−76·462
	Exp.	2·81	−76·472

[a]Assumed molecular geometries are summarized in footnotes to Table 2.

The use of a constant, regular geometrical convention throughout a series, however, allows the calculations to be extended to all members of the series. Such a convention can also remove perturbations due to steric and other effects, or to experimental uncertainty in atomic positions; this allows better insight into trends and substituent effects. However, regular-pentagonal or hexagonal models for heteroaromatic molecules have the disadvantage that they do not allow for differences in pure single or pure double bond lengths between atoms of different atomic number.

Consequently, we feel that it would be best to handle the problem of molecular geometry by carrying out regular-pentagon calculations for all molecules under consideration and, where feasible, backing these up with a parallel set of calculations assuming experimental or optimized geometries. In addition to giving some notion of the degree of dependence of calculated electronic structures on

assumed molecular geometry, this approach combines the advantages of the regular-pentagon and experimental geometries given in the preceding paragraph. This procedure will improve our ability to distinguish between the effect on calculated electron distributions of the following: (a) the electronegativities of ring atoms and substituents; and (b) changes in bond lengths and angles among the members of the series under consideration.

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