825. *A Theoretical Investigation of the Chemical Reactivity of Benziminazole.*

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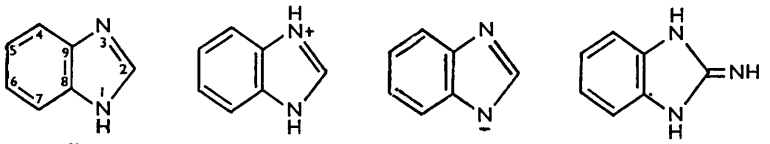
A theoretical investigation of the benziminazole molecule by the molecular-orbital method indicates that electrophilic substitution in acidic media (*e.g.*, nitration) occurs in the free base and not in the benziminazolium cation; but in alkaline solution the substitution must occur in the benziminazole anion whenever it occurs preferentially in the 2-position. Other properties of benziminazoles are also interpreted in terms of the theoretical results. It is predicted that free radicals will attack the 4-position preferentially.

Recently [1-5] we compared the results of calculations by the simple molecular-orbital approximation with the known chemical properties of some heterocyclic nitrogen compounds. In the present paper benziminazole is treated along the lines used for five-membered nitrogen heterocycles.[1,2] The approximations used for glyoxaline [1] have been adopted and in addition the overlap integral has been taken to be zero to simplify the calculations for the larger molecule. Theoretical results obtained for glyoxaline by neglecting overlap [2] do not differ qualitatively from those obtained with overlap included,[1] and the same is doubtless true for benziminazole.

π-Electron densities and atom-localization energies for electrophilic, nucleophilic, and homolytic substitutions have been calculated for various values of the electronegativity parameter, h, for the nitrogen atoms. Our earlier results suggest that from the viewpoint of the π-electrons the difference between the neutral benziminazole molecule (I), its cation



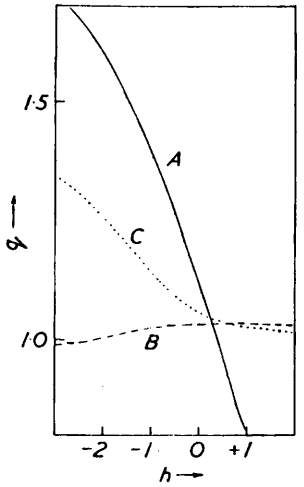
(I) (II) (III) (IV)

(II), and anion (III) can primarily be ascribed to a change in electronegativity of the nitrogen atoms. In particular they become *less* electronegative than carbon atoms in the anion (III).

The theoretical results are present in the Figures and Tables.

[1] Bassett and R. D. Brown, *J.*, 1954, 2701.
[2] Brown, *Austral. J. Chem.*, 1955, **8**, 100.
[3] Brown and Heffernan, *ibid.*, 1956, **9**, 83.
[4] Brown, *J.*, 1956, 272.
[5] Bassett, Brown, and Penfold, *Chem. and Ind.*, in the press.

FIG. 1. *π-Electron densities in benziminazole as a function of electronegativity of nitrogen.*



A, Position 2. *B*, Position 4. *C*, Position 5.

FIG. 2. *Electrophilic atom-localization energies.*

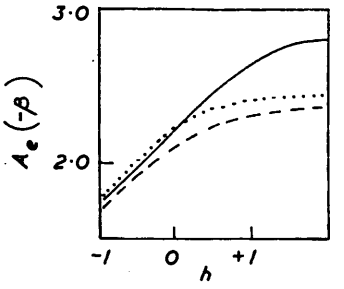


FIG. 3. *Nucleophilic atom-localization energies.*

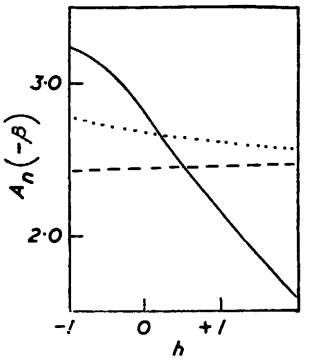


FIG. 4. *Radical atom-localization energies.*

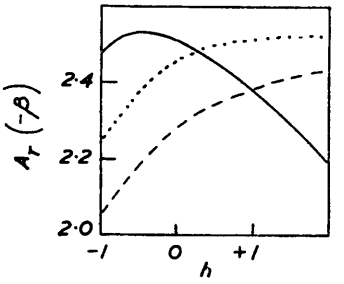


TABLE 1. *π-Electron densities.*

Position	*h*:	−∞	−3	−2	−1	−0·5	0	+0·5	+1	+2	+∞
1		0·00	0·27	0·48	0·86	1·07	1·25	1·40	1·52	—	2·00
2		2·00	1·73	1·60	1·39	1·26	1·11	0·96	0·81	—	0·00
4		1·33	0·99	1·00	1·02	1·03	1·03	1·03	1·03	1·03	1·00
5		1·33	1·35	1·26	1·14	1·09	1·06	1·04	1·03	1·02	1·00
8		1·33	1·53	1·46	1·28	1·18	1·10	1·04	1·01	—	1·00

TABLE 2. *Electrophilic atom-localization energies (units of* −β).

Position	*h*:	−1	−0·5	0	+0·5	+1	+2
2		1·73	1·96	2·22	2·46	2·65	2·80
4		1·66	—	2·12	2·23	2·30	2·37
5		1·67	—	2·23	2·35	2·41	2·46

TABLE 3. *Nucleophilic atom-localization energies (units of* −β).

Position	*h*:	−1	−0·5	0	+0·5	+1	+2
2		3·22	3·10	2·81	2·46	2·12	1·59
4		2·42	—	2·44	2·46	2·47	2·49
5		2·78	—	2·68	2·65	2·62	2·58

TABLE 4. *Homolytic atom-localization energies (units of* −β).

Position	*h*:	−1	−0·5	0	+0·5	+1	+2
2		2·48	2·53	2·51	2·46	2·39	2·19
4		2·04	—	2·28	2·34	2·38	2·43
5		2·23	—	2·46	2·50	2·51	2·52

Electron Densities.—The π-electron densities at the three different carbon atoms are plotted against the electronegativity parameter in Fig. 1. They suggest an interpretation of the substitution of benziminazole as follows:

For the neutral molecule the appropriate value [4] of h is in the vicinity of 0·5. In this region the most highly charged carbon atom is at position 5. The value of h applying to the protonated benziminazole (II) is probably 1—2 and in this range the 4-position has the greatest π-electron density. Now in acid media benziminazole is nitrated predominantly [6] in the 5-position, only a trace of 4-isomer being obtained.[7] This suggests that nitration proceeds through the very small equilibrium amount of free base (I) which remains unprotonated in the acid medium. For the free base the charge density at position 4 is not much smaller than that at position 5, so that the isolation of slight amounts of the 4-nitro-compound is understandable.

The observation [8] that benziminazole is quantitatively iodinated in aqueous sodium hydroxide at position 2 may also be interpreted in terms of the electron densities. Iodination is an electrophilic substitution [9] and the position of attack would be expected to be that of greatest π-electron density. For negative values of h the charge at position 2 is far greater than that on any other carbon atom, which suggests that benziminazole is attacked in a form in which the nitrogen atoms are less electronegative than carbon atoms. It has been suggested [1,2,5] that this situation exists in anions such as (III), and quantum-mechanical calculations of electronegativities for negatively charged, conjugated nitrogen atoms confirm this reversal.[10] Further, if the iodination of benziminazole proceeds through the anion it will be analogous to that of glyoxaline.[11]

The π-electron densities of the 2-positions in glyoxaline and benziminazole for $h = -1$, which might be appropriate for the anions, are respectively 1·458 and 1·391. These values suggest that the benziminazole anion will be iodinated more slowly than the glyoxaline anion under comparable conditions, but there is no experimental evidence about this.

The π-electron density at the 2-position in the free base (*i.e.*, for small positive values of h) is much smaller than that at any other position. From a comparison with the charges at the 2- and 4-position of pyridine [3] (for $h = 0{\cdot}5$: 2-pyridine 0·923, 4-pyridine 0·950, 2-benziminazole 0·959*) we might expect a 2-methyl substituent in benziminazole to be reactive. Indeed, 2-methylbenziminazole, like α-picoline, reacts with aldehydes [12] and other carbonyl compounds.[13] In contrast, 2-methylglyoxaline does not.[14] This is understandable from the relative electron densities at position 2 in glyoxaline and benziminazole (respectively 0·907 and 0·810 for $h = 1$).

The stability of benziminazolecarboxylic acids may also be explained in terms of the calculated electron distribution. Carboxyl groups in the benzene portion of the molecule are very stable to heat, whereas benziminazole-2-carboxylic acids are very readily decarboxylated.[15] Decarboxylation by the unimolecular mechanism [16] is facilitated by a low electron density at the carbon atom carrying the carboxyl group. However, when the electron density on that atom is neither high nor low, decarboxylation by either the S_E1 or the S_E2 mechanism proceeds with difficulty.

The properties of the aminobenziminazoles also reflect the general features of the

* The value of h appropriate for the benziminazole molecule is probably larger than that for pyridine,[5] so that the comparable charge for position 2 of benziminazole is probably appreciably smaller than this value. The observed orientation of nitration and the reactivity of the 2-methylbenziminazole relative to α-picoline suggest that the appropriate value of h is about 0·6.

[6] Fischer and Hess, *Ber.*, 1903, **36**, 3967.
[7] Fries, *Annalen*, 1927, **454**, 121.
[8] Pauly and Gundermann, *Ber.*, 1908, **41**, 3999.
[9] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, 1953, p. 291.
[10] Brown and Penfold, *J. Chem. Phys.*, 1956, **24**, 1259.
[11] Ridd, *J.*, 1955, 1238.
[12] Bamberger and Berle, *Annalen*, 1893, **273**, 303.
[13] van Alphen, *Rec. Trav. chim.*, 1940, **59**, 289.
[14] Hofmann, "Imidazole and Its Derivatives. Part I." Interscience Publ. Inc., New York, 1953, p. 278.
[15] *Op. cit.*, p. 314.
[16] B. R. Brown, *Quart. Rev.*, 1951, **5**, 131.

π-electron distribution. *Bz*-Aminobenziminazoles are typical aromatic amines,[17] in agreement with the fact that the charge densities in the benzene ring lie very close to unity in the uncharged benziminazole molecule. In contrast a 2-amino-group is not basic, which indicates a low π-electron density at the 2-position: its tendency to exist in the imide form (cf. IV) and general similarity to the amino-group in 2- and 4-aminopyridine is to be associated with a low π-electron density at the position carrying it.

The calculated electron distribution in uncharged benziminazole also explains why the 2-halogen substituents are readily displaced under conditions which leave *Bz*-substituents unchanged,[18] in agreement with the very much lower charge density at the 2-position.

Atom-localization Energies.—The electrophilic localization energies are shown as functions of h in Fig. 2. For positive values of h such as would be appropriate for the free base and the cation (II), the localization energy is smallest for position 4, and it is not possible to obtain the smallest localization energy at position 5 for any choice of h. The substitutions in the free base are thus orientated in accordance with the electron densities rather than the localization energies, *i.e.*, the chemical " non-crossing rule " does not apply.[19]

For values of h less than -1 the localization energy is still smaller at other positions than at position 2. Thus the " non-crossing rule " breaks down also for the anion (III), since it is hardly likely that the appropriate value of h for this entity will be much less than -1.

It is interesting that a somewhat similar breakdown of the non-crossing rule was found for glyoxaline,[1,2] and here also the orientation was in agreement with the charge densities rather than with the localization energies.

The nucleophilic localization energies, shown in Fig. 3, do, however, agree with the π-electron distribution. For h greater than 0·5, position 2 has the smallest localization energy; for more negative h, the localization energy is smallest for position 4.

The radical localization energies are plotted in Fig. 4. The results enable us to predict that in the free base radical attack will occur preferentially at position 4. The use of free valencies as alternative criteria of reactivities towards radical substitution cannot be justified for benziminazole;[20] however, it is of interest that for $h = 0{\cdot}5$ the free valencies of positions 2, 4, and 5 are respectively 0·416, 0·447, and 0·405, in agreement with the radical-localization energies. There appear to be no experimental data, *e.g.*, on phenylation or vapour-phase bromination, which might indicate the position of attack of benziminazole by radicals.

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[17] Lindemann and Krause, *J. prakt. Chem.*, 1927, **115**, 256.
[18] *Op. cit.*, p. 302.
[19] R. D. Brown, *Quart. Rev.*, 1952, **6**, 63.
[20] R. D. Brown, *J. Chim. phys.*, 1953, **50**, 109.