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CONFORMATIONAL ANALYSIS AND ELECTRONIC STRUCTURE OF PHENYLTHIAZOLES AND THEIR PROTONATED FORMS

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Abstract—The most probable conformation of 2-, 4-, and 5-phenylthiazole and their protonated forms has been investigated using the Extended Hückel molecular orbital approach and it has been found to be non-planar, the angle of twist about the interring linkage increasing in the order: 4- < 2- < 5-. For the energetically most favourable geometry the charge distribution calculated using the CNDO/2 method is found to be consistent with the observed dipole moment.

OUR RECENT INTEREST in MO calculations on the preferred conformation of compounds consisting of two aromatic rings linked together through an essential single bond[1] prompts us to report here our efforts in predicting the equilibrium conformation and related electronic properties of the monophenyl-thiazoles and their protonated forms.

For molecules formed by two conjugated rings joined by an essentially single bond there are two factors mainly responsible for their conformation. These are: (a) the π-interaction between the aromatic rings which tends to keep them coplanar (the conjugative factor), and (b) the non-bonded interactions which are minimized when the terminal units are perpendicular (the steric factor). The equilibrium conformation of the molecule is determined by a delicate balance of these two. It is therefore necessary to include both effects in calculations in order to provide a reliable estimate for the potential energy function of rotation about the interring bond.

SCF MO methods dealing only with the π-electrons give the energetic contribution resulting solely from π-electron delocalization and therefore, in order to obtain the correct conformation of the investigated molecule, the non-bonded interactions must be considered in some way. This was done, for example, by Dewar and Harget,[2] who predicted a quite reasonable conformation of biphenyl using their variant of the SCF π-MO method and the Bartell[3] potential functions for calculating the non-bonded interactions between C and H atoms. Unfortunately, no satisfactory function is as yet available to account for the non-bonded interactions of H atoms with lone pairs on S or N atoms as, for example, those appearing in systems like phenylthiazoles. Thus, an approach considering only π-electrons and neglecting the non-bonded interactions between H atoms and lone pairs on the heteroatoms (by assuming these to be rather small in comparison with the other non-bonded interactions) may give unreliable information about the preferred geometry of the phenylthiazoles. In fact, this was attempted previously[4] with the result that 2-phenylthiazole should exist in a planar conformation, while its N-protonated form should stabilize in non-planar conformation, the angle of twist being 10°.

In connection with recent extensive studies[5–9] on the chemistry and physical properties of the monophenyl-thiazoles, a thorough investigation of the problem of their conformations has become rather important. We decided to perform this study with the aid of the Extended Hückel (EH) method,[10] because well-established experience of this methodology[11] suggests that, although estimates of the twist angles were sometimes found to be somewhat exaggerated,[11] the prediction of a planar or distorted conformation for a number of molecules has agreed with the experimental information. On the other hand, we would like to mention that we did not attempt to use the CNDO/2 approach because of its known shortcomings[12–14] in predicting conformations. However, since the EH MO theory is unreliable for predicting the charge distributions especially in heteroatomic systems,[11] we determined with the aid of the CNDO/2 method the charge distribution of each molecule in the energetically most favourable geometry.

COMPUTATIONAL DETAILS AND RESULTS

The standard EH MO method[10] was used. All valence electrons were explicitly treated and all overlap integrals were included. Slater-type orbitals used as the basis set were 1s of H, 2s and 2p of C and N, and 3s and 3p of S: a total of 51 orbitals for the neutral species and 52 orbitals for the protonated species. In the present calculations we did not include the 3d orbitals of sulphur because some of our earlier results[1b,c] indicated that the inclusion of sulphur 3d orbitals causes no change in the geometry and has only a small effect on the height of the rotational barrier in systems like phenyl-thiophenes and diphenyl-sulphide. The values of the valence state ionization potentials were taken from Hoffmann and Imamura[15] for H, C, and N, and from Hinze and Jaffé[16] for S. Slater exponents were assumed for all orbitals except 1s of H, where 1·3[14] was preferred to the usual value of 1·0.

Since structural data are lacking, the molecular geometries were derived by taking the unsubstituted 1,3,4-thiadiazole structure[17] and replacing a C–H by a C–Ph group, with standard parameters for Ph (C–C of 1·396 Å, all angles 120°). The N–H distance was set equal to 1·00 Å. Only the length of the interannular bond was varied (1·426 Å and 1·465 Å)[4] in order to investigate if the interannular bond length has any influence on the deviation from planarity.*

Calculations were carried out from 0° to 90° with a scanning of 10°. The plots of the calculated total energy *vs.* the angle of twist are given in Fig.s 1–3. For the energetically most favoured geometry of each molecule, the ground-state charge distribution was calculated by means of the CNDO/2 formalism and the parametrization given by Clark.[18] The net atomic charges are presented in Table 1.

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* The variation of the interannular distance did not affect either the barrier of rotation or the value of dihedral angle. For both interannular distances used the same result was reached. Hereafter reference will be made to the results obtained with the distance of 1·426 Å.

DISCUSSION

Inspection of Figs. 1-3 shows that deviation from planarity leads to a greater conformational stability for the phenylthiazoles. In particular, the minimum energy is achieved at a twist angle of ~30° for 4-phenylthiazole, ~40° for 2-phenylthiazole, and ~45° for 5-phenylthiazole. Slightly larger angles of twist are found for the corresponding N-protonated derivatives. Overestimation of steric factors with respect

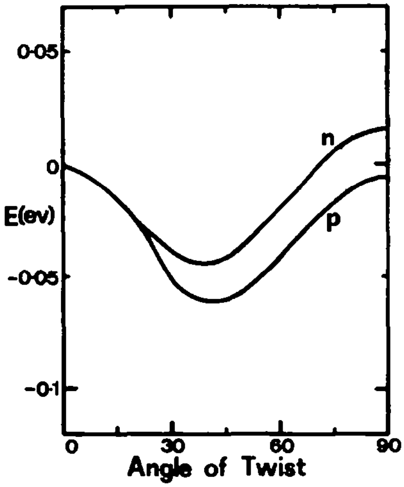


Fig. 1. Extended Hückel energy *vs.* angle of twist for neutral (n) and protonated (p) 2-phenylthiazole. The energy zero has been arbitrarily assigned to the planar conformation.

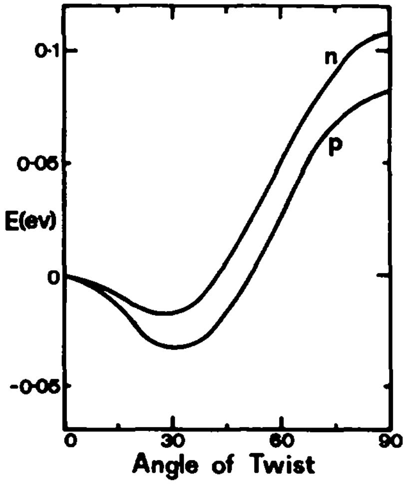


Fig 2. Extended Hückel energy *vs.* angle of twist for neutral (n) and protonated (p) 4-phenylthiazole. The energy zero has been arbitrarily assigned to the planar conformation.

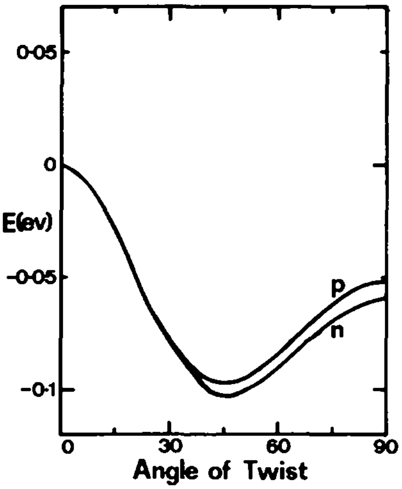


FIG 3. Extended Hückel energy *vs.* angle of twist for neutral (n) and protonated (p) 5-phenylthiazole. The energy zero has been arbitrarily assigned to the planar conformation.

to the conjugative factor is a distinctive feature of EH MO calculations and even in the present cases leads presumably to theoretical twist angles being larger than those one might obtain from experiment. Leaving aside the precise determination of deviation from planarity, we can however conclude that the ground-state conformation of the phenylthiazoles should be non-planar in the gaseous state. This is in accord with our experience with like systems[1b] and X-ray information about a similar compound, N-phenylpyrazole.[19]

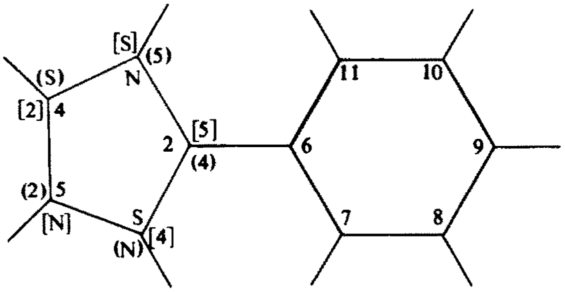
Whereas a non-planar conformation for 4- and 5-phenylthiazole and the three protonated species can be readily anticipated in view of the mere presence of reasonably small H-H contacts, the twisted geometry predicted by the EH theory for 2-phenylthiazole, which has apparently no steric problems, is rather unexpected and deserves particular comment. This results is, indeed, clearly diagnostic of the fact that the relatively diffuse lone-pairs of nitrogen and, particularly, sulphur are able to interact so strongly with the rather distant *ortho* H atoms of the Ph ring as to make a twisted conformation energetically more favoured than the completely planar one. The important role exerted by the non-bonded repulsions between H and S atoms is also apparent by the fact that the preferred geometry predicted for N-protonated 2-phenylthiazole (which has one reasonably small H-H contact as well) has essentially the same angle of twist as the parent compound. Finally, the energetic diagrams of 4- and 5-phenylthiazole provide further arguments in favour of the above observation.

Here, we can explain the different predictions concerning the geometry of 2-phenylthiazole obtained by (a) EH MO theory (twisted form) and (b) SCF π-MO treatment, (in which were included only some of the present non-bonded repulsions, planar form)[4] in terms of the fact that the latter calculations neglected the non-bonded repulsions between hydrogens and lone-pairs. The calculated energy barriers between the preferred geometry and its enantiomer are in every case found to be rather small,

TABLE 1. NET ATOMIC CHARGES

Atom	2-Phenylthiazole NF	2-Phenylthiazole PF	4-Phenylthiazole NF	4-Phenylthiazole PF	5-Phenylthiazole NF	5-Phenylthiazole PF
S	+0·043	+0·216	+0·068	+0·279	+0·055	+0·250
C-2	+0·295	+0·295	+0·230	+0·222	+0·212	+0·211
N	−0·460	−0·153	−0·441	−0·120	−0·407	−0·075
C-4	+0·139	+0·106	+0·205	+0·177	+0·095	+0·035
C-5	−0·065	−0·016	−0·089	−0·063	+0·024	+0·075
H-2			+0·007	+0·062	+0·008	+0·063
H-N		+0·204		+0·208		+0·207
H-4	+0·013	+0·065			+0·018	+0·070
H-5	+0·014	+0·070	+0·018	+0·073		
C-6	+0·031	−0·008	+0·050	+0·018	+0·061	+0·033
C-7	−0·040	−0·007	−0·032	−0·030	−0·049	−0·027
C-8	−0·006	+0·015	−0·009	+0·015	−0·002	+0·015
C-9	−0·022	+0·026	−0·028	+0·013	−0·034	+0·007
C-10	−0·008	+0·015	−0·008	+0·015	−0·002	+0·016
C-11	−0·021	−0·008	−0·046	−0·019	−0·052	−0·032
H-7	+0·014	+0·023	+0·023	+0·011	+0·016	+0·019
H-8	+0·015	+0·045	+0·013	+0·038	+0·015	+0·039
H-9	+0·016	+0·046	+0·013	+0·041	+0·015	+0·040
H-10	+0·017	+0·045	+0·013	+0·039	+0·014	+0·038
H-11	+0·026	+0·021	+0·013	+0·021	+0·013	+0·016

NF and PF stand for neutral and protonated form, respectively. Atom numbering is assumed to be as follows:



especially for 4-phenylthiazole. However, in view of the known failures[11] of EH calculations to account quantitatively for the barrier heights, any conclusions about possible facile interconversion between enantiomers demands adequate experimental information.

Some comments are also worth mentioning regarding the charge distribution obtained by the CNDO/2 method (Table 1). The S atom behaves as a σ electron acceptor and π electron donor and attains a slightly positive charge: overall it acts as electron donor. On the other hand, the tertiary N atom carries a marked negative charge, which leads to the basic properties of these systems. On protonation substantial changes arise in phenylthiazoles in both the σ and π electron distribution. The S atom undergoes an increase of π donor property and a decrease of σ acceptor power, and consequently displays an augmented net positive charge. Meanwhile, the N atom becomes a σ donor but remains a strong π acceptor and still has a slightly negative charge. Almost all of the σ charge is lost to the H atom attached to N. The remaining H atoms all loose some of their electron density, a fact which is consistent with the effects observed in the proton chemical shifts of these compounds.[7a]

A check on the consistency of the calculated charge distribution is provided by the dipole moments, which were evaluated within the framework of the Pople–Segal theory.[20] The calculation yielded a dipole moment of 1·12 D for 2-phenylthiazole (exp.: 1·18 D (cyclohexane) and 1·21 D (CCl_4)),[9] 1·31 D for 4-phenylthiazole (exp.: 1·27 D (cyclohexane) and 1·33 D (CCl_4)),[9] and 1·35 D for 5-phenylthiazole (exp.: 1·89 D (CCl_4)).[9] The close agreement between theory and experiment, especially for 2- and 4-phenylthiazole, is clearly apparent.

The calculated energy values (CNDO) of the highest occupied MO (HOMO) and of the lowest empty MO (LEMO) are the following:

	HOMO	LEMO
2-phenylthiazole	−9·16 eV	0·68 eV
4-phenylthiazole	−9·07	1·10
5-phenylthiazole	−9·03	0·95

On the basis of these estimates it can be inferred that 4- and 5-phenylthiazole should have electron-donating properties remarkably similar and slightly greater than 2-phenylthiazole. This theoretical prediction is consistent with the trend observed both in the half-wave oxidation potentials and in the ionization potentials determined from the charge-transfer band of the complexes.[8] As to the electron accepting properties, these should vary in the order: 4- < 5- < 2-.

REFERENCES

[1] [a] V. Galasso, G. De Alti and A. Bigotto, *Tetrahedron* **27**, 991 (1971); [b] V. Galasso and G. De Alti, *Ibid.* **27**, 4947 (1971); [c] V. Galasso, G. De Alti and A. Bigotto, *Ibid.* **27**, 6151 (1971)

[2] M. J. S. Dewar and A. J. Harget, *Proc. Roy. Soc.* (London) A **315**, 443 (1970)

[3] L. S. Bartell, *J. Chem. Phys.* **32**, 827 (1960)

[4] N. Bodor, M. Farkas and N. Trinajstić, *Croat. Chem. Acta* **43**, 107 (1971)

[5] A. Silberg, I. Simiti, M. Farkas, S. Silberg and H. Mantsch, *Rev. Roumaine Chim.* **7**, 513 (1962): I. Simiti and M. Farkas, *Chem. Ber.* **98**, 3441 (1965): I. Simiti and M. Farkas, *Bull. Soc. Chim. France* 3862 (1968)

[6] R. Arnaud, M. Gelus, J. C. Malet and J. M. Bonnier, *Bull. Soc. Chim. France* 2857 (1966)

[7] [a] G. Vernin, J. P. Aune, H. J. Dou and J. Metzger, *Ibid.* 4523 (1967); [b] G. Vernin, J. C. Poite, J. Metzger, J. P. Aune and H. J. M. Dou, *Ibid.* 1103 (1971); [c] M. Baule, R. Vivaldi, J. C. Poite, H. J. M. Dou, G. Vernin and J. Metzger, *Ibid.* 4310 (1971)

[8] J. M. Bonnier, R. Arnaud and M. Maurey-Mey, *Compt. Rend. Acad. Sci. Ser.* C **267**, 10 (1968)

[9] J. M. Bonnier and R. Arnaud, *Ibid.* **270**, 885 (1970)

[10] R. Hoffmann, *J. Chem. Phys.* **39**, 1397 (1963)

[11] J. R. Hoyland, *Molecular Orbital Studies in Chemical Pharmacology*, p. 31. Edited by L. B. Kier, Springer-Verlag, New York (1970)

[12] B. Tinland, *Theor. Chim. Acta* **11**, 452 (1968)

[13] G. Klopman and B. O'Leary, *Topics in Current Chemistry* **15**, 445 (1970)

[14] R. Hoffmann and J. R. Swenson, *J. Phys. Chem.* **74**, 415 (1970)

[15] R. Hoffmann and A. Imamura, *Biopolymers* **7**, 207 (1969)

[16] J. Hinze and H. H. Jaffé, *J. Am. Chem. Soc.* **84**, 540 (1962)

[17] B. Bak, L. Nygaard, E. J. Pedersen and J. Rastrup-Andersen, *J. Mol. Spectr.* **19**, 283 (1966)

[18] D. T. Clark, *Tetrahedron* **24**, 2663, 4689 (1968)

[19] J. Elguero, private communication

[20] J. A. Pople and C. A. Segal, *J. Chem. Phys.* **44**, 3289 (1966)