

## Molecular Orbital Studies of Thienopyridines and Thienopyridazines. I

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The electronic structures of the six isomers of thienopyridine, and of three isomers of thienopyridazine have been investigated both within the  $\pi$ -electron approximation and by using the CNDO/2 method. Predicted results for bond distances, atomic charges and reactivities are presented and discussed.

The thienopyridines constitute a group of six isomers, some of which have been synthesized quite recently. By now all the isomers are synthesized and described,<sup>1-11</sup> but the experimental information on the chemical and physical properties of the molecules is scarce.

Another group of related molecules are the thienopyridazines. Three of the isomers, the ones included in the study, have recently been synthesized,<sup>12-15</sup> but very little seems to be known about their properties.

The ring-systems discussed in the present paper are interesting from several points of view. They are expected to exhibit some of the properties of benzothiophene which shows certain kinds of biological activity. The thienopyridines are furthermore thieno analogues of isoquinoline and quinoline which are important parts of some alkaloids. In thienopyridine a thiophene unit, characterized as resistant against nucleophilic substitution, but easily undergoing electrophilic substitution is coupled to a pyridine unit exhibiting the opposite characteristics.

Previous theoretical studies of the compounds investigated here are limited to Hückel type calculations on a few of the molecules.<sup>15-17</sup> To our knowledge the molecular structure is not known for any of the compounds included here.

The purpose of the present work is to study the electronic structures of the molecules, and to relate the quantum mechanical predictions to observable molecular properties. In the discussion emphasis is put on an analysis of the trends in the variation of physical and chemical properties by going from one isomer to another. In this first part of the work results for bond distances, atomic charges, and reactivities are presented and discussed.

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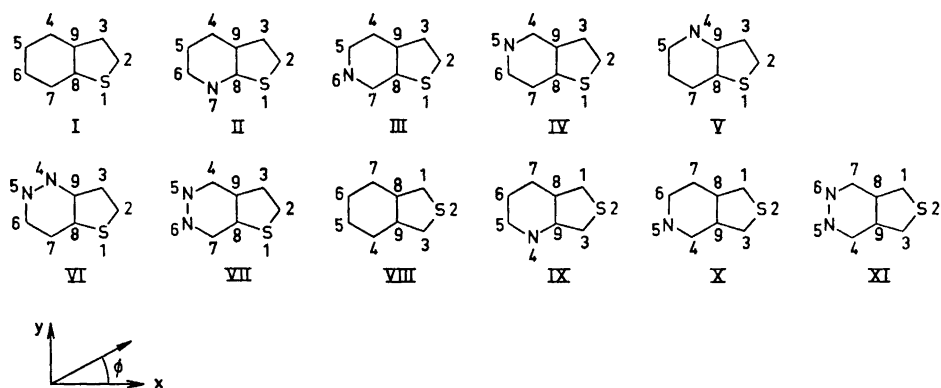


Fig. 1. Labelling of atoms in benzo[b]thiophene (I), thieno[2.3b]pyridine (II), thieno[2.3c]pyridine (III), thieno[3.2c]pyridine (IV), thieno[3.2b]pyridine (V), thieno[3.2c]pyridazine (VI), thieno[2.3d]pyridazine (VII), benzo[c]thiophene (VIII), thieno[3.4b]pyridine (IX), thieno[3.4c]pyridine (X), and thieno[3.4d]pyridazine (XI).

For the purpose of comparison two isomers of benzothiophene have also been included in the investigation. The molecules studied have been divided into two groups. Group A contains the molecules benzo[b]thiophene (I), thieno[2.3b]pyridine (II), thieno[2.3c]pyridine (III), thieno[3.2c]pyridine (IV), thieno[3.2b]pyridine (V), thieno[3.2c]pyridazine (VI), and thieno[2.3d]pyridazine (VII). In group B we have the molecules benzo[c]thiophene (VIII), thieno[3.4b]pyridine (IX), thieno[3.4c]pyridine (X), and thieno[3.4d]pyridazine (XI). The labelling of the molecules and the notation of the atoms are shown in Fig 1.

#### METHODS OF CALCULATION

The molecules have been studied by two different methods of calculation. Molecular ground state properties as well as electrically excited states have been discussed within the  $\pi$ -electron approximation using a recently developed parametrization scheme based on the ZDO approximation.<sup>18,19</sup> Some ground state properties have also been studied by means of the CNDO/2 method treating all valence electrons explicitly.

The molecular ground states have been described by a single determinant wave function whereas configurational mixing including all singly excited configurations has been invoked in the treatment of electronic transitions.

The scheme underlying the approach used in the  $\pi$ -electron calculations has been presented in detail previously. Accordingly only a brief presentation of the formulae needed for the definition of the semi-empirical parameters applied will be given here.

The one-electron one-center parameter  $W_\mu$  is made dependent on the neighbours to atom  $\mu$  through the relation

$$W_\mu = W_\mu^\circ + \sum_v \{ \Delta W_\mu^\circ(v) + \delta_{\mu v}^w (R_{\mu v} - R_{\mu v}^\circ) \}, \quad (1)$$

where  $W_{\mu}^{\circ}$  is a reference value appropriate to atom  $\mu$ ,  $\Delta W_{\mu}^{\circ}(\nu)$  is a correction term characterizing the influence exerted by atom  $\nu$  on atom  $\mu$ , and where the last term in the summation takes care of the corrections due to changes in bond lengths. The sum is limited to the inclusion of the nearest neighbours to atom  $\mu$ .

The core resonance integrals are assumed to obey the linear relations

$$\beta_{\mu\nu} = \beta_{\mu\nu}^{\circ} + \delta_{\mu\nu}^{\beta} (R_{\mu\nu} - R_{\mu\nu}^{\circ}) \quad (2)$$

where  $\beta_{\mu\nu}^{\circ}$  refers to the value of this integral at a given internuclear distance  $R_{\mu\nu}^{\circ}$ .

The two-electron two-center Coulomb integrals for nearest neighbours are estimated by an analogous relation

$$\gamma_{\mu\nu} = \gamma_{\mu\nu}^{\circ} + \delta_{\mu\nu}^{\gamma} (R_{\mu\nu} - R_{\mu\nu}^{\circ}) \quad (3)$$

The two-electron two-center Coulomb integrals for non-nearest neighbours have been estimated by the uniformly charged sphere approximation, and the one-center integrals  $\gamma_{\pi\pi}$  have been taken from previous studies.

The numerical values of the parameters, which have been evaluated previously,<sup>19-22</sup> are collected in Table 1.

Table 1. Semi-empirical parameters applied in the PPP calculations. For definition of symbols, see text. Distances in Å and energies in eV.

Carbon <sup>a</sup>	Sulphur <sup>b</sup>	<sup>c</sup>	Nitrogen <sup>d</sup>
$R_{CC}^{\circ} = 1.397$	$R_{CS}^{\circ} = 1.714$	$R_{CN}^{\circ} = 1.388$	$R_{NN}^{\circ} = 1.33$
$\beta_{CC}^{\circ} = -2.42$	$\beta_{CS}^{\circ} = -1.37$	$\beta_{CN}^{\circ} = -2.72$	$\beta_{NN}^{\circ} = -2.67$
$\delta_{CC}^{\beta} = 3.05$	$\delta_{CS}^{\beta} = 3.05$	$\delta_{CN}^{\beta} = 2.6$	$\delta_{NN}^{\beta} = 3.05$
$\gamma_{CC}^{\circ} = 6.91$	$\gamma_{CS}^{\circ} = 7.28$	$\gamma_{CN}^{\circ} = 7.16$	$\gamma_{NN}^{\circ} = 9.00$
$\delta_{CC}^{\gamma} = -3.99$	$\delta_{CS}^{\gamma} = -3.99$	$\delta_{CN}^{\gamma} = -3.99$	$\delta_{NN}^{\gamma} = -3.99$
$\gamma_{\pi\pi} = 11.97$	$\gamma_{\pi\pi} = 9.58$	$\gamma_{\pi\pi} = 15.44$	
$W_C^{\circ} = -9.84$	$W_S^{\circ} = -10.62$	$W_N^{\circ} = -12.57$	
	$\Delta W_S^{\circ}(C) = 0$	$\Delta W_N^{\circ}(C) = 0.14$	$\Delta W_N^{\circ}(N) = -0.32$
	$\delta_{SC}^W = 9.22$	$\delta_{NC}^W = 5.6$	$\delta_{NN}^W = 9.22$
	$\Delta W_C^{\circ}(S) = -0.70$	$\Delta W_C^{\circ}(N) = 0.03$	
$\Delta W_C^W = 0.07$	$\Delta W_C^W(S) = -0.70$	$\Delta W_C^W(N) = 0.03$	
$\delta_{CC}^W = 9.22$	$\delta_{CS}^W = 9.22$	$\delta_{CN}^W = 5.6$	
$d = 1.47$	$d = 0.84$	$d = 1.20$	

<sup>a</sup> Ref. 19; <sup>b</sup> Ref. 21; <sup>c</sup> Ref. 20; <sup>d</sup> Ref. 22.

In the CNDO/2 calculations we have used the parameter values given by Pople *et al.* in their *spd*-version.<sup>23</sup> Numerical values for the applied parameters are given in Table 2.

Table 2. Numerical values for the parameters in the CNDO/2 method, version *spd*. Energies in eV.

Atomic parameters	H	C	N	S	
$1/2 (I_s + A_s)$	7.18	14.05	19.32	17.65	
$1/2 (I_p + A_p)$		5.57	7.28	6.99	
$1/2 (I_d + A_d)$				0.71	
$-\beta_A$	9	21	25	18.15	
Orbital exponent	1.2	3.25	3.9	5.45	
$\gamma_{AA}$	20.41	16.06	19.28	12.76	
Coulomb integrals between neighbours	CH	CC	CN	NN	CS
$\gamma_{AB}$	11.89	9.72	10.22	10.51	8.07

## RESULTS AND DISCUSSION

1. *Internuclear distances.* The bond distances have been estimated by using the following linear relations between bond lengths and calculated mobile bond order<sup>18,20-22</sup>

$$R_{CC} = 1.517 - 0.18p \quad (4)$$

$$R_{CN} = 1.458 - 0.18p \quad (5)$$

$$R_{CS} = 1.773 - 0.18p \quad (6)$$

$$R_{NN} = 1.453 - 0.18p \quad (7)$$

As the molecular structures of the investigated systems are unknown, we based the numerical evaluation of the matrix elements of the Fock operator on the experimental bond distances in 2-chloroquinoline,<sup>24</sup> thieno[2.3b]thiophene,<sup>25</sup> pyridine,<sup>26</sup> thiophene,<sup>27</sup> and pyridazine.<sup>28</sup> Furthermore theoretically estimated bond distances in isoquinoline<sup>20</sup> and benzo[b]thiophene<sup>21</sup> were used. The obtained bond orders were used to refine the assumed bond distances by means of the relations (4)–(7). This procedure was repeated until selfconsistency was reached. Never more than two cycles were needed. The final bond distances obtained are given in Tables 3 and 4. For labelling of molecules and atoms see Fig. 1.

If we use the molecule benzo[b]thiophene (I) as a reference, we find that the introduction of one or two nitrogen atoms in the phenyl part of the molecule does not lead to any significant changes in the bond distances in its thiophene part. Accordingly, the bond distance variations may be discussed by referring to one molecule in each of the groups A and B. We have chosen the molecules II and IX for this purpose. The bond distances in these molecules are compared to the corresponding ones in pyridine and thiophene in Table 5.

As revealed by the tables the bonds adjacent to the sulphur atom are of the same length. The two C–N bond distances in one and the same molecule are

Table 3. Calculated bond distances for molecules belonging to group A. Distances in Å. For labelling of molecules and atoms, see Fig. 1.

Bond	Molecule						
	I	II	III	IV	V	VI	VII
1-8	1.728	1.727	1.727	1.727	1.727	1.727	1.727
1-2	1.726	1.724	1.724	1.725	1.725	1.725	1.725
2-3	1.354	1.356	1.355	1.356	1.355	1.355	1.355
3-9	1.452	1.451	1.451	1.451	1.452	1.453	1.451
4-9	1.408	1.411	1.409	1.411	1.351	1.352	1.407
4-5	1.391	1.387	1.392	1.331	1.329	1.324	1.337
5-6	1.402	1.408	1.344	1.343	1.408	1.346	1.333
6-7	1.393	1.330	1.332	1.394	1.389	1.392	1.338
7-8	1.404	1.347	1.407	1.404	1.406	1.403	1.403
8-9	1.404	1.404	1.403	1.403	1.405	1.405	1.405

found to be different, the difference being around 0.07 Å in molecule IX. By fusing the pyridine and the thiophene units together, the joint bond is found to be longer than its counterparts in each of the units.

The bond order for the C-C bond 2-3 in molecule II is found to be larger than the corresponding one in benzofuran.<sup>29</sup> It has been suggested that the bond 2-3 in the latter is closest to a double bond.<sup>30</sup>

By the formation of the bicyclic system II bond fixation occurs to a certain degree. The bonds 7-6, 5-4, and 3-2 decrease whereas the bonds 2-1 and 6-5 are elongated. A similar change in bond distances has been noticed in a comparison between pyridine and naphthyridine.<sup>31</sup>

If we compare the calculated results for molecules II and IX, we find a more pronounced bond fixation in the pyridine ring of the latter, but no corresponding change takes place in the thiophene unit. The thiophene ring in IX has in

Table 4. Calculated bond distances for molecules belonging to group B. Distances in Å. For labelling of molecules and atoms, see Fig. 1.

Bond	Molecule			
	VIII	IX	X	XI
1-8	1.379	1.381	1.379	1.379
1-2	1.709	1.707	1.707	1.707
2-3	1.709	1.708	1.708	1.707
3-9	1.379	1.380	1.380	1.379
4-9	1.447	1.446	1.445	1.447
4-5	1.365	1.364	1.368	1.310
5-6	1.437	1.438	1.373	1.365
6-7	1.365	1.307	1.308	1.310
7-8	1.447	1.382	1.448	1.447
8-9	1.441	1.441	1.440	1.439

Table 5. Calculated bond distances in molecules II and IX compared with corresponding bond distances in pyridine and thiophene. Distances in Å.

Bond	Type	Pyridine <sup>a</sup>	Thiophene <sup>a</sup>	II	IX
1-8	C-S			1.727	
1-2	C-S		1.714	1.724	1.708
2-3	C-C		1.362	1.356	
3-9	C-C		1.434	1.451	
4-9	C-C			1.411	1.446
4-5	C-C	1.396		1.387	1.364
5-6	C-C	1.399		1.408	1.348
6-7	C-N	1.338		1.330	1.307
7-8	C-N			1.347	1.382
8-9	C-C			1.404	1.441

<sup>a</sup> For the sake of consistency calculated rather than observed values have been used.

fact a geometry that is more like thiophene itself. It is also worth noticing that whereas the bond distance C-S in II is increased as compared to thiophene the corresponding bond distance in IX is shortened.

A comparison between the experimental bond distances in the molecules 1,2,5-thiadiazole<sup>32</sup> and 2,1,3-benzothiadiazole<sup>33</sup> leads qualitatively to the same results as the comparison made above between thiophene and the molecules in group B.

A qualitative picture of the bond fixation in IX can also be obtained by noticing that it is not possible to draw more than one Kekulé-diagram for the molecule.

2. *Atomic charges.* The  $\pi$ -electron charges obtained by the PPP-approximation, and the  $\sigma$ - and  $\pi$ -electron charges as calculated by the CNDO method are presented in Tables 6 and 7.

The CNDO calculations yield a charge distribution in the  $\sigma$ -skeleton of molecules I and VIII that supports the assumption of an unpolarized core in the PPP-approximation. Introduction of nitrogen atoms in the molecules leads to a less uniform charge distribution. However, both the  $\sigma$ - and the  $\pi$ -electron distributions are found to be distorted comparatively little by the process. The degree of polarization seems to be roughly the same for the  $\sigma$ - and the  $\pi$ -electrons.

The CNDO calculations lead to a net negative charge both of  $\sigma$ - and  $\pi$ -electrons on the nitrogen atoms in all the molecules. The neighbouring carbon atoms have a net positive charge of  $\sigma$ - and  $\pi$ -electrons in all cases except for molecules VI and VII where there is a small negative  $\pi$ -charge on one of the carbons. The positive  $\sigma$ -charges are on the whole larger than the corresponding  $\pi$ -charges. Except for the molecules containing two nitrogen atoms (VI, VII, and XI), this predicted difference seems to be related to the amount of negative  $\sigma$ -charge relative to the amount of negative  $\pi$ -charge on the nitrogen atom.

Table 6. Atomic  $\sigma$ - and  $\pi$ -electron charges for the molecules belonging to group A. For labelling of molecules and atoms, see Fig. 1.

Atom	Method	Molecule							
		I	II	III	IV	V	VI	VII	
1	PPP	1.875	1.875	1.876	1.876	1.876	1.878	1.876	
	CNDO	$\pi^a$	1.868	1.863	1.868	1.864	1.866	1.869	1.860
		$\pi^b$	2.035	2.027	2.036	2.027	2.037	2.033	2.024
		$\sigma$	4.056	4.066	4.044	4.060	4.046	4.045	4.049
2	PPP	1.136	1.140	1.136	1.139	1.136	1.139	1.132	
	CNDO	$\pi$	1.008	1.016	0.990	1.015	0.997	1.003	0.998
		$\sigma$	3.023	3.018	3.032	3.019	3.027	3.024	3.027
3	PPP	0.952	0.949	0.946	0.947	0.945	0.937	0.948	
	CNDO	$\pi$	0.974	0.971	0.985	0.986	0.981	0.972	0.978
		$\sigma$	3.000	2.998	2.998	2.997	3.011	3.010	2.996
4	PPP	1.015	1.011	1.018	0.982	1.091	1.069	0.975	
	CNDO	$\pi$	1.023	0.974	1.054	0.983	1.085	1.066	1.007
		$\sigma$	2.992	3.005	3.000	2.933	4.078	4.026	2.944
5	PPP	1.003	1.002	0.978	1.072	0.960	1.050	1.060	
	CNDO	$\pi$	0.982	1.010	0.951	1.043	0.943	1.013	1.021
		$\sigma$	3.002	3.013	2.940	4.087	2.943	4.045	4.039
6	PPP	1.006	0.970	1.077	0.984	1.004	0.981	1.066	
	CNDO	$\pi$	1.014	0.974	1.079	0.983	1.042	1.004	1.063
		$\sigma$	2.991	2.931	4.070	2.928	3.002	2.939	4.017
7	PPP	0.997	1.074	0.960	0.994	0.992	0.976	0.952	
	CNDO	$\pi$	0.982	1.045	0.941	1.013	0.935	0.961	0.962
		$\sigma$	2.993	4.078	2.937	3.002	3.005	3.013	2.950
8	PPP	1.079	1.053	1.082	1.075	1.073	1.068	1.070	
	CNDO	$\pi$	1.007	0.983	1.032	0.965	1.031	0.983	0.990
		$\sigma$	2.989	2.931	3.002	3.002	2.999	3.016	3.013
9	PPP	0.937	0.927	0.926	0.932	0.922	0.903	0.921	
	CNDO	$\pi$	0.975	1.000	0.934	1.003	0.949	0.965	0.957
		$\sigma$	2.968	2.977	2.978	2.977	2.910	2.920	2.986

<sup>a</sup> Only  $3p_z$  included in the basis.

<sup>b</sup>  $3d_{xz}$  and  $3d_{yz}$  included in the basis.

By the PPP calculations we obtain a positive  $\pi$ -charge on the carbon atoms adjacent to the nitrogens, apart from atoms 8 in molecule II and 6 in molecule X where a small negative charge is found.

The CNDO calculations give slightly different  $\sigma$ - and  $\pi$ -charges on the nitrogen atoms in molecules VI and VII. However, the total net charge is approximately the same on both atoms, and about the same as the net  $\pi$ -electron charge predicted by the PPP method. In the molecules containing one

Table 7. Atomic  $\sigma$ - and  $\pi$ -electron charges for the molecules belonging to group B. For labelling of molecules and atoms, see Fig. 1.

Atom	Method	Molecule			
		VIII	IX	X	XI
1	PPP	1.190	1.911	1.187	1.186
	CNDO $\left\{ \begin{array}{l} \pi \\ \sigma \end{array} \right.$	1.062	1.046	1.085	1.048
		2.997	3.002	2.984	2.999
2	PPP	1.791	1.786	1.786	1.784
	CNDO $\left\{ \begin{array}{l} \pi^a \\ \pi^b \\ \sigma \end{array} \right.$	1.661	1.669	1.654	1.656
		1.921	1.929	1.912	1.907
		4.115	4.104	4.119	4.115
3	PPP	1.190	1.170	1.186	1.186
	CNDO $\left\{ \begin{array}{l} \pi \\ \sigma \end{array} \right.$	1.062	1.082	1.030	1.048
		2.997	3.000	3.009	3.000
4	PPP	0.995	1.082	0.936	0.932
	CNDO $\left\{ \begin{array}{l} \pi \\ \sigma \end{array} \right.$	1.014	1.092	0.951	0.973
		2.998	4.071	2.947	2.955
5	PPP	1.012	0.944	1.086	1.084
	CNDO $\left\{ \begin{array}{l} \pi \\ \sigma \end{array} \right.$	0.992	0.931	1.062	1.054
		2.999	2.947	4.079	4.025
6	PPP	1.012	1.013	1.014	1.084
	CNDO $\left\{ \begin{array}{l} \pi \\ \sigma \end{array} \right.$	0.992	1.018	0.971	1.054
		2.999	3.017	2.936	4.025
7	PPP	0.995	0.983	0.989	0.932
	CNDO $\left\{ \begin{array}{l} \pi \\ \sigma \end{array} \right.$	1.014	0.963	1.048	0.973
		2.998	3.007	3.002	2.955
8	PPP	0.907	0.905	0.909	0.906
	CNDO $\left\{ \begin{array}{l} \pi \\ \sigma \end{array} \right.$	0.971	0.987	0.948	0.972
		2.972	2.982	2.971	2.983
9	PPP	0.907	0.926	0.908	0.906
	CNDO $\left\{ \begin{array}{l} \pi \\ \sigma \end{array} \right.$	0.971	0.952	0.994	0.972
		2.972	2.912	2.983	2.983

<sup>a</sup> Only  $3p_z$  included in the basis.

<sup>b</sup>  $3d_{zx}$  and  $3d_{yz}$  included in the basis.

nitrogen atom the total net charge on the nitrogens as predicted by the CNDO method is up to twice as large as the  $\pi$ -electron charges obtained by the PPP formalism. Furthermore, these latter are of the same order of magnitude as the total net charges on the nitrogen atom in the molecules containing two nitrogens.

The charges on the atoms 1, 2, and 3 do not change significantly from one molecule to another within the same group. For all the molecules belonging to



group A both calculational methods give roughly the same charges on atoms 2 and 3, respectively. By the CNDO calculations we find that for the molecules in group A the atoms 2 and 3 are not far from neutral with respect to both  $\sigma$ - and  $\pi$ -charge. Apart from the nitrogen atoms and the tertiary carbon atoms, atom 2 has the largest total net charge in all the molecules in group A except for II and V. The PPP results indicate that for all the molecules in this group atom 2 has the largest net negative  $\pi$ -electron charge. For most of the molecules it is about twice the charge on the nitrogen atom. This result is not in accordance with reactivity data which indicate that atom 3 should be the most negative one. In this context it might be worth referring to calculations performed on the molecule benzofuran. For this molecule CNDO calculations<sup>30,34</sup> have led to the conclusion that atom 3 has the largest negative charge in accordance with "experimental" charge densities.<sup>35</sup> However, reactivity data and PPP calculations<sup>29</sup> both suggest that atom 2 is the most negative one in this molecule.

For the molecules in group B the total charges on the carbon atoms adjacent to the sulphur atom is larger than the ones on atom 2 in the molecules belonging to group A. This conclusion is valid both for the CNDO and the PPP calculations. Also here the PPP approximation indicates that the largest negative charges are found on the carbon atoms adjacent to sulphur, whereas the CNDO method leads to the result that the nitrogen atoms are the most negative ones.

For the sulphur atom in the molecules belonging to group A we obtain by the CNDO method a positive net  $\sigma$ -charge as well as a positive net  $\pi$ -charge. For the molecules in group B the predicted net  $\sigma$ -charge is negative, whereas the corresponding  $\pi$ -charge is positive.

The PPP calculations lead to a positive  $\pi$ -electron charge on the sulphur atom in all the molecules studied here. The atomic charges on the sulphur atoms in group B are lower than those in group A as calculated by both methods. The  $\pi$ -charge on sulphur in thiophene<sup>21</sup> obtained by PPP calculations is found to have a value between the ones characterizing group A and group B molecules, respectively.

A comparison between the  $\pi$ -electron charges as calculated by the two different approximations leads to the conclusion that the largest discrepancies are found for the atoms 1 and 2. The PPP calculations which give a lower  $\pi$ -electron density on the sulphur atom than the CNDO approximation, lead to a higher density on the neighbouring carbon atoms (atom 1 in group A, and atoms 1 and 3 in group B). This situation may be interpreted in the following way: as only  $3p\pi$  orbitals are included in the atomic orbital basis used in the PPP formalism applied here the possible resonance diagrams for the molecules contain either a neutral or a positively charged sulphur atom. For the MO method too much emphasis is put on ionic configuration leading to a too low  $\pi$ -electron charge on the sulphur atom.

In the CNDO calculations, where also  $3d_{xz}$  and  $3d_{yz}$  orbitals are included in the basis, resonance diagrams containing negatively charged sulphur atoms are possible. The uncertainty characterizing the CNDO/2 method in this context is related to the choice of orbital exponent for the  $d$ -orbital. However, in molecules without pronounced polarizations previous studies indicate that the scaling of the  $d$ -orbitals is not critical for the predicted charges.<sup>36,37</sup>

3. *Reactivities.* The ability of a molecule to undergo different types of chemical reactions, depending on the nature of the perturbing agent, may be empirically expressed in terms of bond orders and certain reactivity indices. These do only refer to the properties of the solution to the ground state problem for the molecule in question, and thus are static in nature.

By using the CNDO results we have calculated the frontier radical density (FRD) index for radical substitution, the frontier orbital density (FOD) index for nucleophilic substitution, and the frontier electron density (FED) index for electrophilic substitution. These are defined by

$$\text{FRD index for atom } \mu = C_{\mu h}^2 + C_{\mu l}^2 \quad (8)$$

$$\text{FOD index for atom } \mu = 2C_{\mu l}^2 \quad (9)$$

$$\text{FED index for atom } \mu = 2C_{\mu h}^2 \quad (10)$$

where  $C_{\mu h}$  is the coefficient in front of the basis orbital centered at atom  $\mu$  in the highest occupied molecular orbital, and  $C_{\mu l}$  is the corresponding coefficient in the lowest vacant orbital.

We have also estimated the free valency indices for the different carbon atoms in the molecules belonging to group B. This index is defined by the relation

$$F_{\mu} = 1.732 - \sum_{\nu} p_{\nu\mu} \quad (11)$$

where  $p_{\mu\nu}$  is the mobil bond order, and where the summation extends over all the nearest neighbours to atom  $\mu$ .

The calculated reactivity indices defined by the relations (8)–(10) are presented in Tables 8 and 9, and the calculated  $F_{\mu}$ -values for the molecules in group B are given in Table 10. Only data referring to carbon atoms are included in the tables.

As revealed by Table 8 the FED index has its largest value for position 3 in all the molecules belonging to group A. CNDO calculations on benzo[b]furan<sup>30</sup> lead to a maximum value of the FED index in position 2. This change of position is in accordance with available reactivity data relating to electrophilic attacks. However, as mentioned in the section above this change is not in agreement with the conclusion based on the atomic charges as predicted by the CNDO method.

The FOD index for the molecules in group A has its largest value in position 2. One would, however, expect the most likely place for nucleophilic substitutions to be one of the neighbouring positions to the nitrogen atom. Experimentally one has observed a nucleophilic substitution *via* an addition to the C–N bond in position 6 in molecule II.<sup>4,5</sup>

The data in Table 9 show that positions 1 and 3 should be the most reactive ones for all the molecules in group B. This should be valid for all the types of reactions considered in the table. Experimentally it has been shown that molecule VIII is more likely to undergo addition reactions than substitution reactions.<sup>33,39</sup> To this kind of reactions bond orders and free valence indices are

Table 8. FRD, FOD, and FED indices for the secondary carbon atoms in the molecules belonging to group A. The figures are based on the CNDO calculation. The indices are defined in the text. For labeling of molecules and atoms, see Fig. 1.

Molecule	I			II			III			IV			V			VI			VII		
Atom	FRD	FOD	FED	FRD	FOD	FED	FRD	FOD	FED	FRD	FOD	FED	FRD	FOD	FED	FRD	FOD	FED	FRD	FOD	FED
2	.229	.403	.056	.223	.398	.048	.220	.411	.029	.211	.344	.079	.230	.429	.031	.216	.375	.057	.196	.345	.047
3	.262	.283	.240	.273	.296	.249	.241	.259	.223	.239	.230	.248	.266	.295	.238	.283	.322	.244	.213	.189	.238
4	.139	.106	.173	.131	.145	.117	.139	.107	.170	.100	.039	.162	—	—	—	—	—	—	.094	.033	.155
5	.067	.058	.075	.054	.032	.077	.085	.065	.105	—	—	—	.044	.016	.072	—	—	—	—	—	—
6	.166	.270	.061	.169	.300	.037	—	—	—	.183	.277	.089	.146	.255	.038	.112	.168	.056	—	—	—
7	.099	.022	.176	—	—	—	.105	.051	.158	.096	.001	.191	.098	.070	.126	.200	.241	.158	.090	.016	.163

Table 9. FRD, FOD, and FED indices for the secondary carbon atoms in the molecules belonging to group B. The figures are based on the CNDO calculations. The indices are defined in the text. For labelling of molecules and atoms, see Fig. 1.

Molecule	VIII			IX			X			XI		
	Atom	FRD	FOD	FED	FRD	FOD	FED	FRD	FOD	FED	FRD	FOD
1	.399	.341	.458	.415	.354	.476	.379	.302	.456	.408	.350	.466
3	.399	.341	.458	.397	.296	.498	.400	.383	.417	.408	.350	.466
4	.235	.202	.268	—	—	—	.234	.245	.222	.206	.191	.220
5	.152	.146	.158	.154	.167	.140	—	—	—	—	—	—
6	.152	.146	.158	.143	.154	.132	.171	.126	.261	—	—	—
7	.235	.202	.268	.229	.247	.211	.222	.165	.280	.206	.191	.220

usually correlated. The free valence indices in Table 10 are in accordance with the observation that molecule VIII undergoes a Diels-Alder reaction<sup>38,39</sup> by addition of maleic anhydride to the positions 1 and 3. The calculated data suggest that the situation should be the same for the remaining molecules in group B.

Table 10. Free valences for the carbon atoms in the molecules belonging to group B. The data are based on the PPP calculations. The free valence index is defined in the text. For labelling of molecules and atoms, see Fig. 1.

Atom	Molecule			
	VIII	IX	X	XI
1	.607	.608	.607	.602
3	.607	.611	.603	.602
4	.495	—	.513	.521
5	.439	.456	—	—
6	.439	.444	.428	—
7	.495	.488	.502	.521
8	.149	.151	.142	.148
9	.149	.134	.153	.148

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