

Molecular Orbital Studies of the Thienopyrazines

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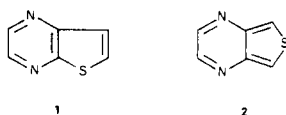
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The calculated reactivity indices and bond lengths for thieno[2,3-*b*]- and thieno[3,4-*b*]-pyrazine are reported.

J. Heterocyclic Chem., **13**, 581 (1976).

Until the recent disclosure (1) of the preparation of thieno[2,3-*b*]pyrazine (**1**) this heterocycle had been reported (2) only as a constituent of several polycyclic molecular arrays. In view of the isoelectronic and isosteric relationships between **1** and quinoxaline, a knowledge of the properties of **1** (1) becomes quite significant to the direction and design of future studies involving **1**. To this end the molecular orbital calculations for **1** have been performed and are presented here. For comparative purposes similar data for the unknown (3) thieno[3,4-*b*]pyrazine molecule (**2**) have also been determined and are discussed below. The methods employed for these calculations have been discussed in detail elsewhere (4):

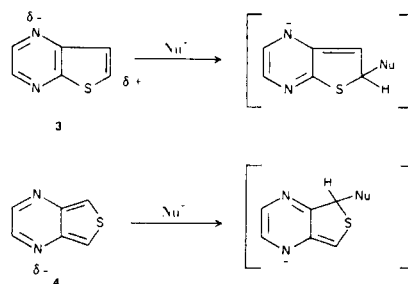


Reactivities.

The ability of a molecule to undergo different types of chemical reactions, which are dependent on the nature of the reacting agent, may be expressed by various reactivity indices. Such easily attainable (4) indices are the frontier radical density (FRD), an index for radical substitution; the frontier orbital density (FOD), an index for nucleophilic substitution; and the frontier electron density (FED), an index for electrophilic substitution. These results for **1** and **2** are presented in Table I.

As revealed by the FRD and FED indices, both **1** and **2** should undergo free radical reactions and electrophilic substitutions at C-3 in the former and C-1 and C-3 in the latter. This is not surprising in view of the calculated and experimental results which have been reported for related

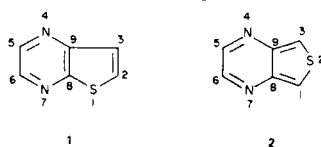
thieno[2,3-*b*]-, thieno[3,2-*b*]-, thieno[3,4-*b*]- and thieno[3,4-*c*]pyridines (4,5,6). On the other hand, the FOD index indicated that nucleophilic substitution will occur at C-2 in **1** and C-1 and C-3 in **2**. It is noteworthy that the carbons adjacent to the ring nitrogens have a lower FOD than those next to the sulfur atom. However, similar data have been accrued for thieno[2,3-*b*]- and thieno[3,2-*b*]pyridine (4) and may be rationalized as being due to the extended vinylogous relationships of C-2 in **1** and C-1 and C-3 in **2** with the pyrazine ring nitrogens. This, in turn, would imply that a polarized species (*i.e.*, **3** and **4**) is prevalent for **1** and **2** under nucleophilic reaction conditions and that H-2 in **1** and H-1/H-3 in **2** should be sufficiently acidic to react with an appropriate base.



Bond Lengths.

Table II presents the calculated bond distances for **1** and **2**. It is obvious from this data that the bonding situation is close to that for the structurally related thienopyridines and suggests that a certain amount of bond fixation exists in the pyrazine portion of **1**. A similar picture unfolds for the thienopyridines (4) and is certainly a manifestation of the electronic requirements imposed by a fused thiophene moiety. On the other hand, the

Table I

Reactivity Indices for Compounds **1** and **2**(8)

Reactivity Indices

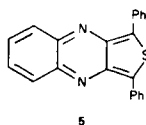
Atom	Molecule 1			Atom	Molecule 2		
	FRD	FOD	FED		FRD	FOD	FED
2	0.208	0.387	0.028	1	0.382	0.281	0.482
3	0.261	0.281	0.240	3	0.382	0.281	0.482
4	0.194	0.280	0.108	4	0.281	0.291	0.271
5	0.041	---	0.081	5	0.152	0.177	0.127
6	0.164	0.305	0.022	6	0.152	0.177	0.127
7	0.149	0.177	0.120	7	0.281	0.291	0.271
8	0.029	0.058	---	8	0.028	0.024	0.032
9	0.125	0.229	0.021	9	0.028	0.024	0.032

Table II

Comparison of Calculated Bond Distances in Å for Thieno[2,3-*b*]pyridine (**1**) and Thieno[3,2-*b*]pyridine (**2**) with Thieno[2,3-*b*]pyrazine and Thieno[3,4-*b*]pyridine (**3**) with Thieno[3,4-*b*]pyrazine (**4**)

Bond					
1-8	1.727 Å	1.727 Å	1.727 Å	1.381 Å	1.384 Å
1-2	1.724	1.725	1.725	1.707	1.706
2-3	1.356	1.355	1.355	1.708	1.706
3-9	1.451	1.452	1.452	1.380	1.384
4-9	1.411	1.351	1.351	1.446	1.378
4-5	1.387	1.329	1.328	1.364	1.310
5-6	1.408	1.408	1.411	1.438	1.433
6-7	1.330	1.389	1.329	1.307	1.310
7-8	1.347	1.406	1.347	1.382	1.378
8-9	1.404	1.405	1.406	1.441	1.442

bonding fixation situation for **2** is more pronounced, as with thieno[3,4-*b*]pyridine (**4**), and indicates that the C-1 and C-3 of its thiophene portion should behave as the termini of a *s*-butadiene fragment. This expectation is corroborated by the reported (7) Diels-Alder reaction of 1,3-diphenylthieno[3,4-*b*]quinoxaline (**5**) with *N*-phenylmaleimide.



REFERENCES AND NOTES

- (1) S. W. Schneller, F. W. Clough, and L. E. Hardee, *J. Heterocyclic Chem.*, **13**, 273 (1976).
- (2) For example, see S. W. Schneller and F. W. Clough, *J. Heterocyclic Chem.*, **12**, 513 (1975); W. F. Gray, I. H. Pomerantz, and R. D. Ross, *ibid.*, **9**, 707 (1972); M. Goto, A. Sakurai, K. Ohta, and H. Yamakami, *Tetrahedron Letters*, 4507 (1967); A. Sakurai and M. Goto, *ibid.*, 2941 (1968).
- (3) Substituted derivatives of **2** are known: (a) 2,3-Diphenyl-5-methylthieno[3,4-*b*]pyrazine: S. Nishimura, A. Sakumoto, and E. Imoto, *Nippon Kagaku Zasshi*, **82**, 1540 (1961); *Chem. Abstr.*, **57**, 15051 (1962); (b) 2,3-Diphenyl-5-(ω -carboxypropyl)thieno[3,4-*b*]pyrazine: S. Nishimura and E. Imoto, *Nippon Kagaku Zasshi*, **82**, 1680 (1961); *Chem. Abstr.*, **59**, 1619 (1963); (c) 2,3-

Dihydroxy- and 2,3-diphenylthieno[3,4-*b*]pyrazine: R. Motoyama and E. Imoto, *Nippon Kagaku Zasshi*, **78**, 793 (1957); *Chem. Abstr.*, **54**, 22560 (1960); See reference 8 for proper atom numbering of **2**.

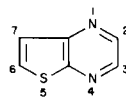
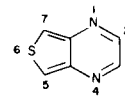
(4) A. Helland and P. N. Skancke, *Acta Chem. Scand.*, **26**, 2601 (1972).

(5a) Thieno[2,3-*b*]pyridine: L. H. Klemm, C. E. Klopfenstein, R. Zell, D. R. McCoy, and R. A. Klemm, *J. Org. Chem.*, **34**, 347 (1969); (b) Thieno[3,2-*b*]pyridine: L. H. Klemm, R. Zell, I. T. Barnish, R. A. Klemm, C. E. Klopfenstein, and D. R. McCoy, *J. Heterocyclic Chem.*, **7**, 373 (1970); (c) Thieno[3,4-*b*]- and thieno[3,4-*c*]pyridine: L. H. Klemm, W. O. Johnson, and D. V. White, *ibid.*, **9**, 843 (1972).

(6) See S. W. Schneller, *Int. J. Sulfur Chem.*, **B**, **7**, 309 (1972).

(7) M. J. Haddadin, N. C. Chelhot, and M. Pieridou, *J. Org. Chem.*, **39**, 3278 (1974).

(8) The correct atom numbering and ring orientations for ring systems **1** and **2** are indicated below with structures *i* and *ii*. The alternatives (i.e., **1** and **2**) employed herein are to simplify molecular orbital data comparisons with the related thienopyridine molecules.

*i**ii*