A Conformational Analysis of the Six Isomers of Thiobispyridine

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The conformational behaviour of the six isomers of thiobispyridine has been investigated using ab initio STO-3G*//rigid-roto, STO-3G*//STO-3G* and 6-31G**//STO-3G* molecular orbital models. The analysis reveals both the importance of optimising critical structure parameters and the basis set dependence of calculated rotational barrier heights. The most reliable model (6-31G**//STO-3G*) clearly indicates that the minimum energy conformers are not planar and that energy barriers between 30-100 kJ mol^{-1} restrict interconversion to planar structures, thereby preventing conjugation between the p-electrons of the sulfur atom and the π system of both pyridine rings. From the calculated barrier heights, two mechanisms can be employed to explain conformer interconversion about the C-S bond: a disrotatory one-ring flip or a conrotatory two-ring flip mechanism. Where comparisons can be made (*eg.* 2,2'-thiobispyridine), dipole moment calculations are shown to be in good agreement with experiment. Finally, of the six isomers, appropriately substituted 2,2', 2,3'- and 2,4'-thiobispyridines are most prone to a Smiles rearrangment.

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1. Introduction.

The chemistry of the thiobispyridines has been recently reviewed by Summers [1] and it has been indicated that several of these isomers are of importance due to their biological activity. For instance, 2,2'-thiobispyridine shows pronounced activity in various anti-bacterial, anti-fungal and anti-tumour tests, 2,4'-thiobispyridine has been prepared as an analgesic and 4,4'-thiobispyridine (and it's polyhalogenated derivatives) have been patented as bactericides, fungicides, herbicides, nematocides and pesticides. The biological activity of the 2,3'-, 3,3'- and 3,4'-thiobispyridines has not been well characterised.

The theoretical conformational properties of the thiobispyridines are largely unexplored. Structural data on the 2,2'-isomer is available in the literature. From gas phase electron diffraction studies the $R_{C\text{-}S}$ bond length is 1.786 Å with a $\theta_{C\text{-}S\text{-}C}$ interring angle of 104.4° [2,3]. The low R-factors found for a range of dihedral angles indicate a broad potential energy surface for interconversion from one conformer into another. Semi-empirical CNDO/2-CI calculations were used to calculate the electronic transition energies of the 30 lowest singly excited levels [4]. No conclusive preference could be given to any of the three conformations considered in that study, although the best agreement between the CNDO and experimental uv values was obtained with a conformation in which the nitrogen atoms were located anti to each other. In addition, the dipole moment of 2,2'-thiobispyridine has been measured as 3.5 D in benzene solution [5]. Using the EHT-MO and CNDO/2 models [5], it was once again impossible to determine the preferred conformer based on the calculated dipole moments. Similar conclusions can be drawn with respect to the electronic spectrum of 2,2'-thiobispyridine as revealed by ultraviolet photoelectron spectroscopy [6,7]. However, from EHT-MO and CNDO/2 conformational studies on the related 2,2'-sulfonyl bispyridine and its *p*-nitro- and *p,p'*-dinitro-derivatives [8], it was concluded that these molecules prefer a single conformation in which the pyridine ring planes are perpendicular to the C-S-C plane and the nitrogen atoms are located anti to each other.

With the advent of the GAUSSIAN suite of programmes [9-10], ab initio calculations are becoming commonplace on medium-sized molecules. For example, von Nagy-Felsobuki [11-13] and Hofmann *et al.* [14,15] in a series of investigations, used all-electron STO-3G calculations in order to study the conformations of the isomers of bipyridinium dication. More pertinent to this study, Dunne *et al.* [16] have undertaken a comprehensive STO-3G investigation with respected to the related oxybispyridines. Four different conformers for oxybispyridine have been proposed as important in conformational studies and are shown in Figure 1: **A** a planar structure; **B** the "Morino" structure; **C** a structure in which both rings are rotated at various angles to each other relative to the C-O-C plane; **D** the "butterfly" structure with the pyridine rings orthogonal

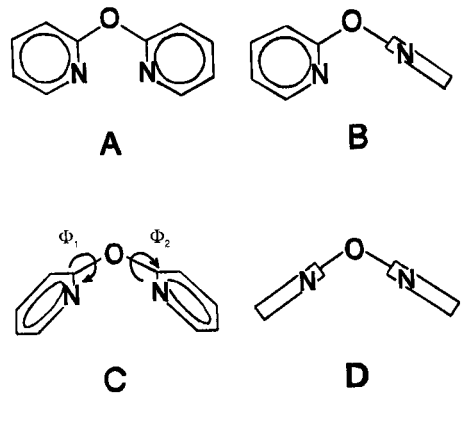

Figure 1. Conformations of 2,2'-oxybispyridine: (A) Planar structure, (B) "Morino" structure, (C) Minimum geometry structure with both rings rotated and denoted by torsional coordinates ($Ø_1$,$Ø_2$), (D) "Butterfly" structure.

to the C-O-C plane. Calculations employing a partial rigid-rotor for all six isomers indicate that the **A** conformers are not the minimum structures, since energy barriers between 70-850 kJ mol^{-1} restrict interconversion to planar structures, thereby preventing conjugation between the *p*-electrons on the oxygen atom and the π system of both pyridine rings. For five of the isomers the minimum energy conformers adopted **C** structures, with the exception (2,4'-oxybispyridine) having a "Morino" structure as it's preferred conformer. However, for the other five isomers the "Morino" structure was within 2.5 kJ mol^{-1} of the minimum. Hence it was concluded that of the three mechanisms used to explain conformer interconversion about the $R_{C\text{-}O}$ bond, the disrotatory one-ring flip mechanism was the most appropriate.

It is the purpose of this study to analyse ab initio conformational structures of the thiobispyridines, thereby extending the previous empirical and semi-empirical work [4-6,8] to all six isomers of thiobispyridine. Moreover, a comprehensive investigation would provide information on: the most likely lowest energy conformer (vis-a-vis structure **A-D**); whether or not the *p*-electrons of the sulfur atom are able to conjugate with both pyridine rings; which of the three possible rotational mechanisms is most viable with respect to conformer interconversion about the $R_{C\text{-}S}$ bond; the conformational dependence of experimental dipole moment measurements; and the possible pathways for intramolecular rearrangements, such as the Smiles rearrangement.

2. Details of the Calculations.

The ab initio electron energies were computed using the LCAO MO SCF restricted Hartree-Fock method within the GAUSSIAN suite of programmes [9,10] using the internal STO-3G* and 6-31G** basis sets. Generally it is found that the STO-3G (s = p) basis set is moderately successful in reproducing experimental geometries of closed-shell molecules [17,18]. However, minimal basis sets are poor in describing anisotropic molecular environments or geometries of hypervalent molecules [18]. Amongst the simplest basis sets constructed to avoid these pitfalls is the STO-3G* representation, which is formed from the STO-3G basis by the addition of a set of five d-type cartesian gaussians [19]. Although trends in barrier heights are often acceptable [16,20] the STO-3G* basis set (like the STO-3G from which it is derived) has been shown to perform inadequately in predicting accurate relative energies of isomers, when compared to more extensive basis sets and experiment [18]. On the other hand, the 6-31G** basis set is a double zeta valence basis set, augmented with six second-order d-type primitive gaussians on the "heavy" atoms and a single set of p-type functions on the hydrogen atoms [21]. The 6-31G** basis set has been shown to give a satisfactory description of relative energies of normal and hypervalent species [18,21,22]. For example, von Nagy-Felsobuki and Kimura [22] using the 6-31G** energies at the 6-31G** optimised geometries (denoted 6-31G**//6-31G**)

Table 1

Optimised Structural Parameters of the Thiobispyidines using the STO-3G*//STO-3G* Model

Conformer	$R_{C\text{-}S}$(/Å)	$\vartheta_{C\text{-}S\text{-}C}$ Angle (/Deg)
	(a) 2,2'-thiobispyidine	
A(0,0)	1.7680	114.1
A (180, 180)	1.7834	123.9
A (0, 180)	1.7697	115.1
B (0, 90)	1.7635	100.2
B (180, 90)	1.7658	103.0
C (343, 123)	1.7623	101.9
D (90, 270)	1.7761	97.7
D (90, 90)	1.7749	97.3
	(b) 2,3'-thiobispyridine	
A(0,0)	1.7670	115.5
A (180, 180)	1.7818	124.1
A (0, 180)	1.7678	115.4
A (180, 0)	1.7814	124.0
B (0, 90)	1.7608	100.9
B (180, 180)	1.7631	103.4
B (90, 0)	1.7639	103.2
B (90, 180)	1.7647	103.1
C (2, 90)	1.7617	100.9
D (90, 270)	1.7723	97.9
D (90, 90)	1.7725	97.8
	(c) 3,3'-thiobispyridine	
A(0,0)	1.7780	124.2
A (180, 180)	1.7805	124.3
A (0, 180)	1.7791	124.2
B (0, 90)	1.7607	103.6
B (180, 90)	1.7616	103.4
C (46, 314)	1.7605	101.7
D (90, 270)	1.7703	98.5
D (90, 90)	1.7703	98.4
	(d) 2,4'-thiobispyridine	
A(0,0)	1.7671	115.3
A (0, 180)	1.7799	123.9
B (0, 90)	1.7631	100.7
B (180, 90)	1.7648	103.1
B (90, 0)	1.7625	103.0
C (342, 121)	1.7619	101.6
D (90, 90)	1.7742	97.5
	(e) 3,4'-thiobispyridine	
A(0,0)	1.7774	124.0
A (180, 0)	1.7795	124.0
B (0, 90)	1.7633	103.5
B (180, 90)	1.7645	103.4
B (90, 0)	1.7607	103.4
C (306, 147)	1.7598	102.0
D (90, 90)	1.7722	98.0
	(f) 4,4'-thiobispyridine	
A(0,0)	1.7770	123.8
B (0, 90)	1.7621	103.3
C (317, 138)	1.7606	102.0
D (90, 90)	1.7733	97.7

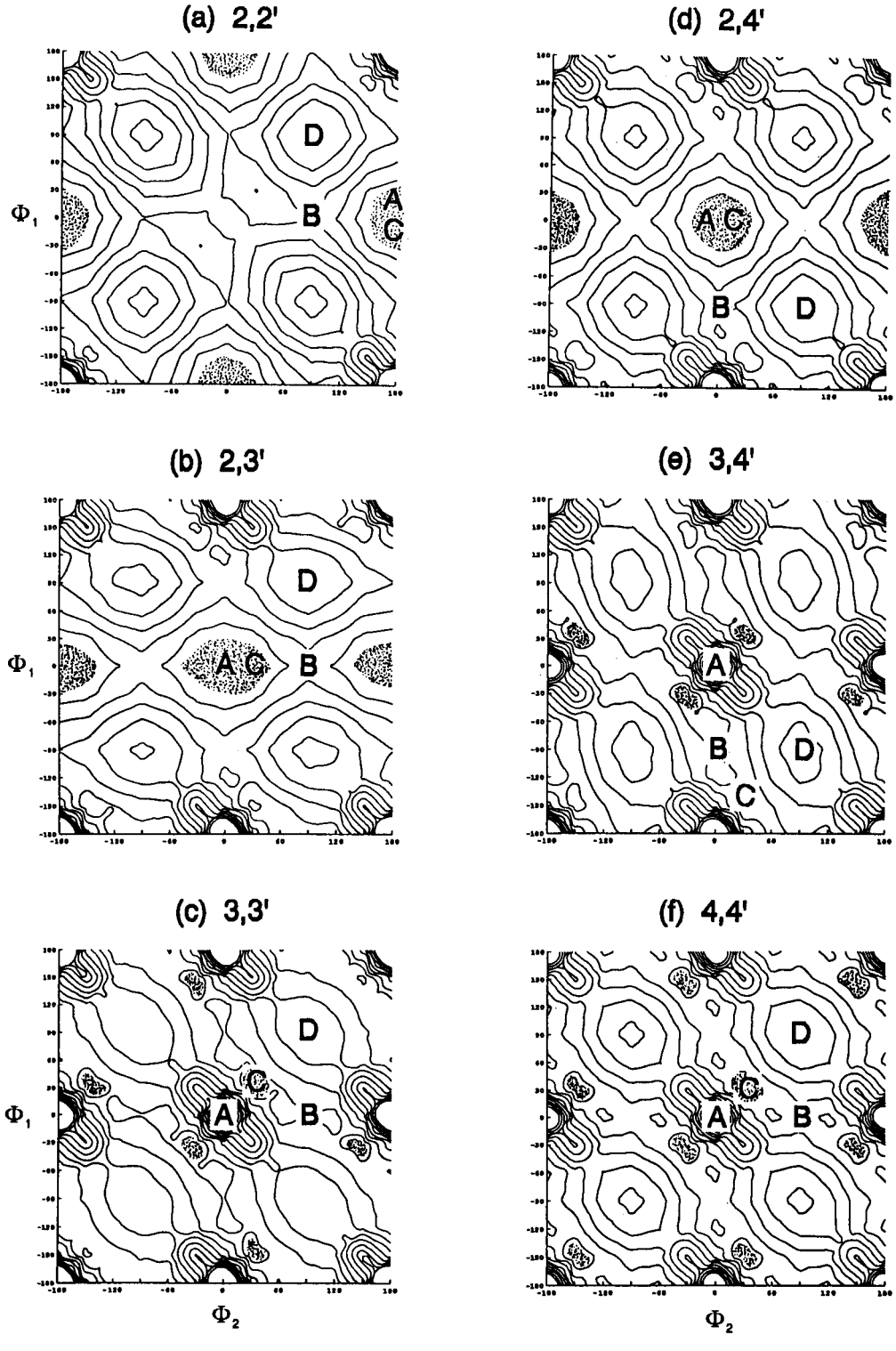

Figure 2. Conformational energy maps of isomers of thiobispyridine: (**a**) 2,2'-thiobispyridine, (**b**) 2,3'-thiobispyridine, (**c**) 3,3'-thiobispyridine, (**d**) 2,4'-thiobispyridine, (**e**) 3,4'-thiobispyridine, (**f**) 4,4'-thiobispyridine. Note: For each isomer the minimum energy conformer is the **C** structure and a contour step size of 5 kj mol^{-1} was used for each succeeding contour. The shaded area represents conformations accessible because of ambient temperature. The structures **A-D** are superimposed on each map.

Table 2

Calculated Barrier Heights for the **A-D** Structures of Thiobispyridines [a]

Conformer	STO-3G*//Rigid-Rotor	STO-3G*//STO-3G*	6-31G**//STO-3G*
	(a) 2,2'-thiobispyridine		
A (0,0)	19.5	47.9	52.0
A (180, 180)	86.4	99.7	81.5
A (0, 180)	0.0	29.9	28.8
B (0, 90)	15.5	0.7	0.0
B (180, 90)	15.7	7.2	1.5
C (343, 123)	0.0	0.0	1.7
D (90, 270)	39.9	21.0	10.8
D (90, 90)	34.2	13.5	0.2
	(b) 2,3'-thiobispyridine		
A (0,0)	0.7	36.8	46.6
A (180, 180)	88.5	105.9	100.3
A (0, 180)	1.2	36.8	46.8
A (180, 0)	82.0	100.5	93.2
B (0, 90)	7.8	0.0	0.1
B (180, 180)	8.2	5.6	1.4
B (90, 0)	12.9	11.1	19.3
B (90, 180)	16.0	12.9	20.9
C (2, 90)	0.0	0.0	0.0
D (90, 270)	29.0	15.4	6.8
D (90, 90)	27.7	13.8	4.6
	(c) 3,3'-thiobispyridine		
A (0,0)	80.0	97.7	98.6
A (180, 180)	90.6	106.2	109.9
A (0, 180)	84.3	101.1	103.1
B (0, 90)	5.0	3.7	9.5
B (180, 90)	7.9	5.0	10.4
C (46, 314)	0.0	0.0	6.5
D (90, 270)	21.1	8.5	1.0
D (90, 90)	20.5	7.7	0.0
	(d) 2,4'-thiobispyridine		
A (0,0)	0.0	31.5	34.0
A (0, 180)	80.6	97.0	82.0
B (0, 90)	13.3	0.5	0.0
B (180, 90)	13.6	6.2	0.9
B (90, 0)	13.0	6.6	5.2
C (342, 121)	0.0	0.0	2.0
D (90, 90)	33.5	14.5	4.0
	(e) 3,4'-thiobispyridine		
A (0,0)	75.9	95.6	90.2
A (180, 0)	80.7	99.8	97.9
B (0, 90)	9.4	8.6	14.2
B (180, 90)	12.2	10.7	15.7
B (90, 0)	3.8	3.1	0.0
C (306, 147)	0.0	0.0	3.1
D (90, 90)	24.9	12.4	3.5
	(f) 4,4'-thiobispyridine		
A (0,0)	72.6	93.6	80.7
B (0, 90)	7.7	4.0	1.3
C (317, 138)	0.0	0.0	0.0
D (90, 90)	28.5	12.8	3.4

[a] All entries in kJ mol^{-1}.

calculated the proton affinities of HCOOH, CH_3COOH, CH_3OH and C_2H_5OH to within ~10 kJ mol^{-1} of the experimental values. The 6-31G** basis set is not commonly used for molecules as electron dense as the thiobispyridines, because of the vast quantity of computer resources required for their use.

A rigid-rotor model was constructed with the inter-ring bond angle $\theta_{C\text{-}S\text{-}C}$ and $R_{C\text{-}S}$ bond lengths fixed at 120° and 1.74 Å respectively in order to generate STO-3G* contour energy maps. These parameters were chosen to model reasonable barrier heights, despite the rigidity forced upon the structure. The geometry of the pyridine ring was essentially that reported by Del Bene [23]. The two-dimensional (ϕ_1, ϕ_2) energy contour plots of the thiobispyridines, generated from a grid comprised on 30° torsional rotations, are presented in Figures 2(a)-(f). The minimum energy conformer for each isomer is labelled **C** on each map, with the minimum **A**, **B** and **D** conformers also marked. The shaded regions represent those conformations accessible at ambient temperature.

Considering the planar (N-inside, N'-inside) conformer as the (0, 0) position, a clockwise rotation of each pyridine moiety (as viewed along the respective inter-ring $R_{S\text{-}C}$ bond) represents a positive rotation. For example, in the case of 2,3'-thiobispyridine, structures **A** (0, 180) and **A** (180, 0) represent the two *trans* conformers of the planar structure. Disrotatory twisting modes are characterised by $(+\phi_1, +\phi_2)$ or $(-\phi_1, -\phi_2)$ torsional combinations, whereas conrotatory modes are identified by $(+\phi_1, -\phi_2)$ or $(-\phi_1, +\phi_2)$ combinations.

To study the effect of structural relaxation upon rotational barrier heights, the inter-ring angles and bond lengths of a select group of conformers were optimised using the Fletcher-Powell algorithm [24]. All possible rotational isomers of the three structures **A**, **B** and **D** (see Figure 1) were optimised in this manner with the results given in Table 1. In the case of the **C** structures, the two twist angles (ϕ_1, ϕ_2) were included in the optimised variable set. The role of basis set dependence on barrier heights was examined using the 6-31G**//STO-3G* model. A comparison of the barrier heights to free rotation generated by STO-3G*//rigid-rotor, STO-3G*//STO-3G* and 6-31G**//STO-3G* models is presented in Table 2.

3. Results and Discussions.

The contour energy maps, given in Figure 2, predict that the minimum energy conformers are either planar or have near-planar structures. In the case of the 2,2'- and 2,4'-isomers, the **A** (0, 0) conformer is the most stable, while the 2,3'-isomer shows a local minimum for this structure. In the case of partial optimised structures of oxybispyridines, Dunne *et al.* [16] showed that the **A** structures lay 70-850 kJ mol^{-1} above the **C** structures and thus it is unlikely that the **A** conformers represent global minimum energy structures. The contour maps also show that, unlike the oxybispyridines [16], very few conformations are accessible to the thiobispyridines at ambient temperature (*i.e.* those structures within 2.5 kJ mol^{-1}). However, the thiobispyridines contain a second row atom and so the minimal basis set without polarisation functions must be considered unreliable (at a rigid-rotor approximation) in predicting the relative isomer energies, since the barrier heights are extremely sensitive to the N-N' and N,H' interactions.

To examine the suitability of the rigid-rotor model, a series of partial geometry optimisations were performed upon all the rotational isomers of the **A-D** conformers. A comparison of the barrier heights between the STO-3G*// rigid-rotor model and those optimised within the STO-3G*//STO-3G* model are given in Table 2 and reveal that in all cases the **A** structures have become destabilised upon optimisation. An examination of the optimised parameters shows that 120° better represents the inter-ring angle of the optimised planar **A** structures than the **B-D** conformers. The energies of the **B**, **C** and **D** structures are lowered more significantly upon optimisation than the **A** structures (up to 50 kJ mol^{-1} in some cases). The trend in energy differences is sensitive to the changes in the inter-ring bond angle upon optimisation. For example, the energies of the **D** structures are lowered to the greatest degree and their optimised angles lie furthest from the 120° of the STO-3G*//rigid-rotor model. For the STO-3G*//STO-3G* model, the minimum energy structures are no longer the **A** structures, but have become psuedo-**B** in character. Hence, the observed stability of the **A** structures within the STO-3G*//rigid-rotor model is due to the artificial constraints embedded in such a model. The number of conformations within 2.5 kJ mol^{-1} of the STO-3G*//STO-3G* minima is still quite small, but importantly some **B** structures are now accessible, opening a low-energy pathway to concerted disrotatory rotation. The non-uniformity of the energy differences between the STO-3G*//rigid-rotor and the STO-3G*//STO-3G* models stresses the importance of optimising critical structure parameters. Hence, the CNDO conformational analysis for the 2,2'-thiobispyridine [4,5] with $R_{C\text{-}S}$ and $\phi_{C\text{-}S\text{-}C}$ fixed at 1.75 Å and 110° respectively is limited by the rigid-rotor approach.

Table 1 shows that for all isomers the planar **A** (180, 180) structures have the longest $R_{C\text{-}S}$ bond length and the largest $\phi_{C\text{-}S\text{-}C}$ bond angle, which indicates the importance of the steric effect of the ortho hydrogens. The *trans* "butterfly" structure (*i.e.* **D** (90, 90)) yields the smallest $\phi_{C\text{-}S\text{-}C}$ inter-ring angle. The **D** structures have the π systems of the pyridine rings overlapping *via* a "through-space" effect and so the $\phi_{C\text{-}S\text{-}C}$ inter-ring angle is reduced. The minimum energy **C** structures have the shortest $R_{C\text{-}S}$ bond length, reflecting the minimisation of steric interaction. For 2,2'-thiobispyridine the STO-3G*//STO-3G* model gives a $R_{C\text{-}S}$ bond length and $\phi_{C\text{-}S\text{-}C}$ inter-ring angle of 1.762 Å and 102° respectively, which is in reasonable agreement with experimental values of 1.786 Å and 104° respectively [2,3]. Thus, it appears that the restriction of con-

Table 3

Calculated Dipole Moments for the **A-D** Structures of Thiobisypridines [a]

Conformer	STO-3G*//Rigid-Rotor	STO-3G*//STO-3G*	6-31G**//STO-3G*
	(**a**) 2,2'-thiobispyridine		
A (0,0)	1.259	1.151	0.143
A (180, 180)	4.062	4.161	6.064
A (0, 180)	2.464	2.799	4.142
B (0, 90)	1.681	1.719	2.868
B (180, 90)	3.799	3.677	5.521
C (343, 123)	2.464	2.407	3.868
D (90, 270)	3.699	3.638	5.131
D (90, 90)	1.824	1.729	3.658
	(**b**) 2,3'-thiobispyridine		
A (0,0)	3.211	3.293	3.052
A (180, 180)	3.776	3.941	5.622
A (0, 180)	3.948	4.242	5.335
A (180, 0)	0.206	0.380	1.464
B (0, 90)	2.632	2.884	3.487
B (180, 180)	2.658	2.379	3.989
B (90, 0)	2.717	2.400	2.394
B (90, 180)	4.564	4.281	5.707
C (2, 90)	2.966	2.864	3.443
D (90, 270)	3.938	3.733	4.807
D (90, 90)	2.070	2.107	2.917
	(**c**) 3,3'-thiobispyridine		
A (0,0)	3.706	3.643	3.186
A (180, 180)	2.458	2.740	4.229
A (0, 180)	1.923	1.759	2.100
B (0, 90)	2.668	2.941	2.481
B (180, 90)	2.791	2.627	3.637
C (46, 314)	3.217	2.883	1.780
D (90, 270)	3.546	3.618	4.217
D (90, 90)	0.117	0.778	0.666
	(**d**) 2,4'-thiobispyridine		
A (0,0)	4.275	4.471	5.124
A (0, 180)	2.341	2.526	3.753
B (0, 90)	3.092	3.419	3.896
B (180, 90)	1.827	1.220	2.853
B (90, 0)	4.147	3.755	4.460
C (342, 121)	4.275	3.590	4.105
D (90, 90)	3.321	3.064	3.772
	(**e**) 3,4'-thiobispyridine		
A (0,0)	3.348	3.216	3.079
A (180, 0)	0.372	0.589	1.761
B (0, 90)	2.717	3.211	2.603
B (180, 90)	0.969	0.948	1.589
B (90, 0)	2.801	2.909	2.845
C (306, 147)	3.163	3.389	3.042
D (90, 90)	2.154	2.497	2.360
	(**f**) 4,4'-thiobispyridine		
A (0,0)	1.759	1.627	0.743
B (0, 90)	1.758	2.382	1.369
C (317, 138)	1.652	2.361	1.224
D (90, 90)	1.217	2.223	1.037

[a] All entries in debye (D).

jugation in these molecules results in the dominance of steric, rather than electronic, effects in the determination of the minimum geometry.

A series of 6-31G** calculations were performed at the STO-3G* optimised geometries (labelled 6-31G**//STO-3G*) of the **A-D** conformers. The barrier heights are given

in Table 2. All barrier heights are reduced for the **B**, **C** and **D** structures, while those of **A** structures remain similar to the STO-3G*//STO-3G* model. The number of conformations accessible at ambient temperature is now more numerous and in particular, the **D** structures have become more stable. It would be anticipated that the 6-31G**//STO-3G* model would yield the most accurate relative isomer energies [18,22]. Hence the most reliable model clearly indicates that the minimum energy conformers are not planar and that energy barriers between 30-100 kJ mol^{-1} restrict interconversion to planar structures.

For the oxybispyridines, Dunne *et al.* [16] have outlined three possible rotational mechanisms for conformer interconversion about the inter-ring bond: a conrotatory rotation of both pyridine rings through structure **A** (0, 0) involving a zero-ring flip; a disrotatory rotation *via* **B** (0, 90) or **B** (90, 0) structures involving a one-ring flip; a conrotatory rotation through the **D** (90, 90) structure involving a two-ring flip. For all isomers of thiobispyridine, the second and third mechanisms are possible since the 6-31G**// STO-3G* model predicts that the barrier heights are within the same order of magnitude as the energy available from the ambient surroundings. However, due to the large barrier heights of the **A** (0, 0) structure, the first mechanism must be considered highly unlikely.

Experimental studies upon the thiobispyridines have focussed on their dipole moments [5]. The accessible conformations have a distinct effect on the magnitude of the measured dipole moment. Table 2 indicates that a range of conformations are available for these molecules at ambient temperature (*i.e.* all conformations along the low energy pathways between **C** and the **B** or **D** structures), whereas Table 3 lists the dipole moments for the **A**-**D** structures calculated using the three models. The STO-3G*//rigid-rotor and STO-3G*//STO-3G* models yield similar results, whereas the 6-31G*//STO-3G* model predicts values differing by up to 2 D from the STO-3G* results. Green [25] has concluded that, at the Hartree-Fock limit, the error associated with the dipole moment of a neutral diatomic molecule with a single sigma bond is of the order 0.1 to 0.2 D, provided a double zeta basis set (augmented with polarisation functions) is employed. The 6-31G** basis set is closer to this criterion, although it is deficient with respect to producing a reliable dipole moment at the Hartree-Fock limit. Furthermore, these molecules are not just sigma bonded. Nevertheless, the 6-31G**//STO-3G* dipole moments are the most accurate calculated to date. The variation of the magnitude of the dipole moments between the accessible conformers for this model is quite marked, suggesting that attempts to interpret experimental dipole moments in terms of a limited set of conformers may provide a nonunique solution. In the study of 2,2'-thiobispyridine, Galasso *et al.* [5] interpreted the experimental dipole moment in terms a superposition of three "butterfly-type" conformers determined from CNDO calculations. The 6-31G**//STO-3G* model for the **C** and **D** (90, 90) structures yields dipole moments of 3.9 and 3.7 D respectively in good agreement with the experimental value [5] of 3.5 D. However, the equally probable **B** structures have dipole moments of 2.9 and 5.5 D, both well removed from the experimental result. Hence, the agreement between the CNDO calculations and experiment seems fortuitous.

The Smiles rearrangement [26] is possible for appropriately substituted oxybispyridines [16], since the **B** (0, 90) structures for all the isomers are within 2.5 kJ mol^{-1} from the minimum energy conformer. The distance between the entering group on one ring and the ipso carbon on the other is at a minimum for the **B** structure and since the ipso carbons are electron deficient sites for all the isomers a nucleophilic attack is readily promoted, thereby facilitating this intramolecular rearrangement. Table 4 lists selected charge distributions using the 6-31G**//STO-3G* model for the **C**, **B** (0, 90) and **D** (90, 90) structures of the thiobispyridines. Unlike the oxybispyridines, the only isomers for which one or both of the ipso carbons are electron deficient sites are 2,2'-, 2,3'- and 2,4'-thiobispyridine. Due to the electropositive nature of the sulfur atom, the proximity of the ipso carbons to the ring nitrogen is the determing factor for the electron deficiency and thus, it is

Table 4

Selected Charge Distributions using 6-31G//STO-3G* Model for the C, B and D Structures fo Thiobispyridine [a]**

Site	2,2'-	2,3'-	3,3'-	2,4'-	3,4'-	4,4'-
			(a) C structure [b]			
q_N	-0.554	-0.562	-0.537	-0.550	-0.537	-0.541
$q_{N'}$	-0.526	-0.549	-0.537	-0.541	-0.547	-0.541
q_C	0.082	0.100	-0.277	0.084	-0.293	-0.172
$q_{C'}$	0.069	-0.262	-0.276	-0.147	-0.152	-0.172
q_S	0.253	0.219	0.240	0.238	0.253	0.265
			(b) B (0, 90) structure			
q_N	-0.563	-0.562	-0.536	-0.560	-0.539	-0.553
$q_{N'}$	-0.505	-0.549	-0.539	-0.538	-0.555	-0.528
q_C	0.107	0.100	-0.225	0.099	-0.328	-0.125
$q_{C'}$	0.062	-0.262	-0.332	-0.158	-0.123	-0.228
q_S	0.235	0.219	0.240	0.226	0.252	0.260
			(c) D (90, 90) structure			
q_N	-0.515	-0.520	-0.542	-0.514	-0.541	-0.535
$q_{N'}$	-0.515	-0.545	-0.542	-0.537	-0.536	-0.535
q_C	0.034	0.051	-0.269	0.045	-0.274	-0.170
$q_{C'}$	0.034	-0.287	-0.269	-0.181	-0.164	-0.170
q_S	0.230	0.214	0.196	0.221	0.203	0.211

[a] All entries in electron units. [b] See Table 1. for definition of the **C** structures.

expected that intramolecular nucleophilic attack will only occur for ipso carbons in the 2 position. To date, Smiles rearrangements have only been observed for substituted 2,2'- and 2,4'-thiobispyridines [27-34], but the calculations suggest that this rearrangement should be also possible for substituted 2,3'-thiobispyridines.

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