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Tautomeric Cyclic Thiones

Part II.* Tautomerism, Acidity and Electronic Spectra of Thioamides of the Oxadiazole, Thiadiazole, and Triazole Groups

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The ultraviolet spectra have been measured for a series of five-membered heterocyclic thioamides, capable of thione-thiol tautomerism, and for their N- and S-methyl derivatives. In all cases it has been found that the thione form must dominate strongly in the tautomeric mixture. LCAO-MO calculations indicate that the thione form has the higher π electron stabilization. Reasonable linear correlations between calculated and experimental transition energies are obtained, whereas the relation between calculated charge distributions and experimental pK_a values is less satisfactory.

It is well known [1] that the equilibrium between cyclic thioamides (Ia) and the tautomeric imidothiol forms (Ib) is well on the thioamide side even in cases where the thioamide forms part of a conjugated five- or six-

Ia Ib

membered ring, where the form (Ib) could be expected to profit from an aromatic π electron system. A similar relation is found among the corresponding amides,[2] whereas in heterocyclic amines the form with the substituent attached to the ring with a single bond is found to be the more stable one.[3] In a previous work [4] it was found that LCAO-calculations with the ω-method could qualitatively reproduce the tautomeric ratios in aminoheterocycles, and that the ultraviolet spectra were reproduced semiquantitatively, whereas the acidity constants showed no good relation to the calculated molecular quantities. In the present work a similar comparison is made with the compounds (II—VII).

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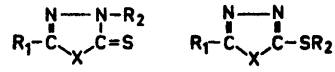
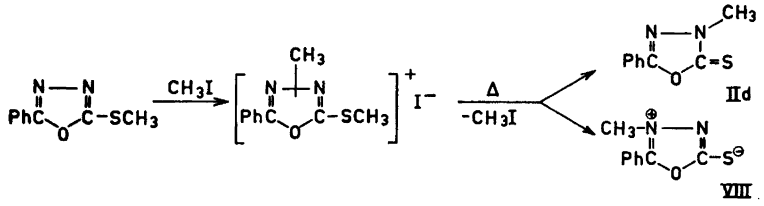


II, IV, VI III, V, VII

a, $R_1 = CH_3$, $R_2 = H$
b, $R_1 = R_2 = CH_3$
c, $R_1 = Ph$, $R_2 = H$
d, $R_1 = Ph$, $R_2 = CH_3$

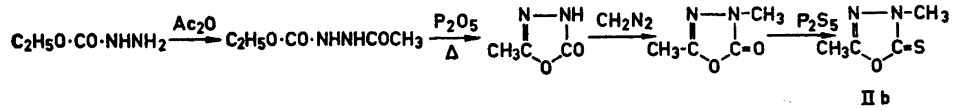
II, III, X = O; IV, V, X = S; VI, VII, X = N–CH_3.

The free acids are all available and were in general prepared by literature methods. The S-methyl derivatives (III, V, and VII) could in general be obtained by methylation of the anions, but cyclization of an open-chain S-methyl derivative was used in one case. The N-methyl derivatives have been less readily available. The triazole derivatives (VIb) and (VId) were obtained by cyclization of 2,4-dimethylthiosemicarbazide with acylating agents. 2-Phenyl-4-methyl-1,3,4-thiadiazolin-5-thione (IVd) was obtained in reasonable yield together with the S-methyl derivative by reaction of the corresponding acid with diazomethane. In the corresponding reaction 2-phenyl-1,3,4-oxadiazolin-5-thione gave a low yield of the N-methyl derivative (IId) together with much S-methyl derivative, whereas with 2-methyl-oxadiazolin-5-thione (IIa) and 2-methyl-thiadiazolin-5-thione (IVa) only S-methyl derivatives were obtained. A different method has been employed by Duffin *et al.*[5] They showed that heating of N,S-dimethyltriazolium iodides in pyridine could in some cases produce N-methyltriazolinethiones. This reaction gave a reasonable yield of (IId) together with the betaine, anhydro-2-phenyl-3-methyl-5-mercapto-1,3,4-oxadiazolium hydroxide, (VIII):



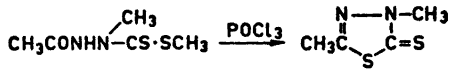
IId VIII

However, when this reaction was applied to the methiodides of (IIIb) and (Vb), no definable products were obtained. The N-methyl derivative (IIb) was obtained by the reaction sequence:

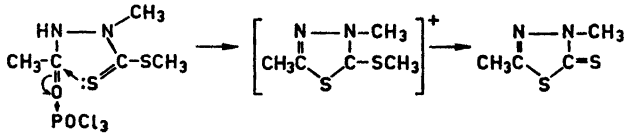


IIb

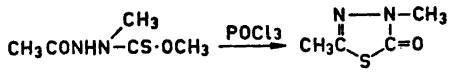
The N-methyl derivative (IVb) was formed by cyclization of methyl 2-methyl-3-acetyl-dithiocarbazate with phosphorus oxychloride:



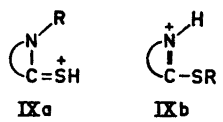
This reaction probably proceeds *via* a thiadiazolium ion, and phosphorus oxychloride can be expected to act as a catalyst by coordinating with the oxygen atom of the acetyl group, thus facilitating the attack of the thiocarbonyl sulphur atom:



An alternative mechanism with the methylthio group acting as the nucleophile is less probable, since the reaction with the corresponding thioncarbazate leads to 3,5-dimethyl-1,3,4-thiadiazolin-2(3)-one:



Tautomeric ratios. The best method for estimation of large tautomeric ratios of basic heterocyclic compounds depends on the determination of the acidity constants of the conjugate acids of the tautomeric compound and of the derivatives with methyl groups instead of the mobile hydrogen atom R_2 in all possible positions.[6] However, this method is not applicable in the present case, since it requires that the protons in the conjugate acids are attached only to the atoms involved in the tautomeric change (IXa and b). In the 1,2-



IXa IXb

diazoles treated here we have at least on additional nitrogen atom, which can accept a proton and confuse the issue. Instead, we have used comparisons of the ultraviolet spectra of the free acids and their N- and S-methyl derivatives. Due to the strong chromophoric properties of the thiocarbonyl group, the thione forms as a rule absorb at considerably longer wavelengths than the thiol forms, and therefore it is easy to estimate that the thione forms must dominate strongly in all the cases investigated (Fig. 1).

A theoretical calculation of the tautomeric ratio requires an evaluation of the difference in free energy between the tautomeric molecules. This difference can be separated in internal energy and entropy terms, and the internal energy can be regarded as a sum of π-electron, σ-electron, and lone pair terms.

As a first approximation, the difference in σ-electron and lone pair energy can be ascribed to changes in the $-NH-\overset{|}{C}=S \rightleftharpoons -N=\overset{|}{C}-SH$ system, since the σ-bonds in the remainder of the molecule must be considerably less

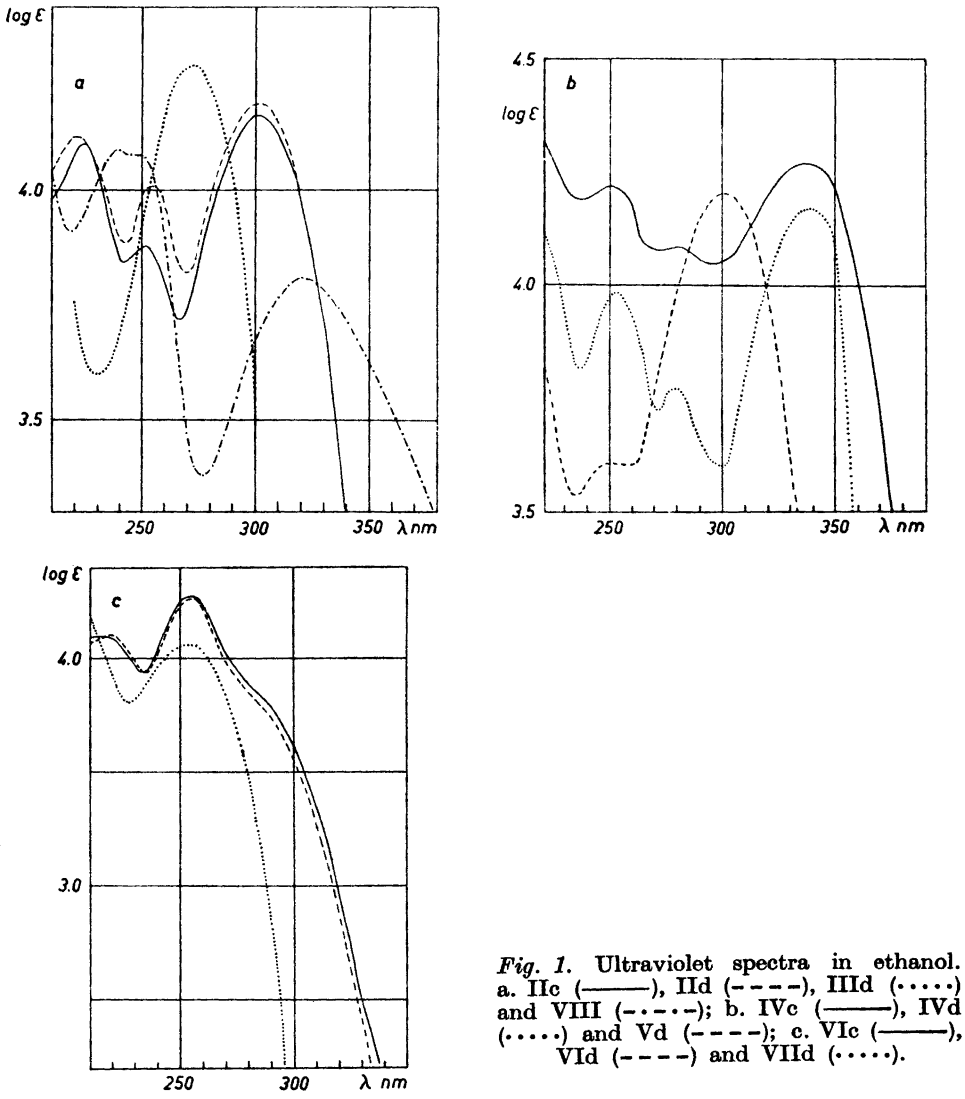


Fig. 1. Ultraviolet spectra in ethanol. a. IIc (———), IId (– – – –), IIId (·····) and VIII (–·–·–); b. IVc (———), IVd (·····) and Vd (– – – –); c. VIc (———), VId (– – – –) and VIId (·····).

affected by the tautomeric change. During the transformation from the thion to the thiol form the following changes occur:

1) An N—H bond is broken
2) an S—H bond is formed
3) a C—N bond is shortened
4) a C—S bond is lengthened
5) a lone pair disappears from a sulphur atom, and
6) a lone pair appears on a nitrogen atom

The state of hybridization of the sulphur atom is not precisely known, but according to Coulson and Altmann [7] a difference in hybridization does not lead to a considerable difference in energy. The terms 1) and 2) can be evaluated with the aid of bond energy values. Cottrell [8] gives 84.3 kcal/mole for N-H bonds and 87.7 kcal/mole for S-H bonds, which should give the thiol form a stabilization of 3.4 kcal. The terms 3) and 4) have been approximatively evaluated for the σ components by assuming that the bond length — bond energy relation can be described by the harmonic potential function $w = w_0 + 0.5\ k\ (r-r_0)^2$.[7] All σ bonds in a conjugated system are regarded as being compressed from the optimal state, which occurs when no π bonds exist. Therefore, the term 3) leads to a destabilization and 4) to a stabilization of the thiol form. However, use of reasonable force constants and bond length changes show that these terms are small and of similar magnitude (Table 1). The changes in π electron energy following the changes 3) and 4) should be accounted for in the LCAO-calculations.

Table 1. Compression energies in the thione-thiol transformation.

X	$k_{CX} \times 10^5$ dyn/cm	r_{CX} Å (single)	r_{CX} Å (thione)	r_{CX} Å (thiol)	ΔE kcal/mole
N	4.9	1.46	1.39	1.32	0.52
S	3.1	1.80	1.68	1.75	0.27

Table 2.

Atom (h)	Parameter set			
	1	2	3	4
C	0	0	0	0
$\dot{N}$	0.5	0.5	0.5	0.5
$\ddot{N}$	1.5	1.5	1.5	1.5
$\ddot{O}$	2.5	2.5	—	—
$\dot{S}$ (in C = S)	0.5	0.5	0.5	0.5
$\ddot{S}$ ($3p$)	1	1	1	1
$\ddot{S}$ (pd^2, ring)	—	—	0	−0.5
Bond (k)				
C—C	0.75	0.75	0.75	0.75
C—N	0.8	0.7	0.8	0.8
N—N	0.6	0.55	0.6	0.6
C—O	0.7	0.6	0.7	0.7
C—S (ring)	0.6	0.4	0.6	0.6
C—S (exocycl.)	0.4	0.4	0.4	0.4
pd^2—pd^2	—	—	0.7	0.7

Table 3. All energy values are given in units of β.

System	Parameter set	Total π energy	ΔE_π	HOMO	LFMO	$\Delta E_{\pi\to\pi^*}$
IIa,b	1	13.890		0.252	−0.818	1.070
			0.238			
IIIa,b	1	13.652		0.804	−0.979	1.783
IIa,b	2	13.318		0.355	−0.707	1.062
			0.374			
IIIa,b	2	12.944		0.738	−0.803	1.541
IIc,d	1	22.118		0.249	−0.701	0.950
			0.244			
IIIc,d	1	21.874		0.674	−0.680	1.354
IIc,d	2	21.568		0.345	−0.615	0.960
			0.358			
IIIc,d	2	21.210		0.612	−0.592	1.194
IVa,b	1	11.086		0.158	−0.886	1.044
			0.228			
Va,b	1	10.858		0.777	−1.063	1.840
IVa,b	2	10.292		0.331	−0.696	1.027
			0.384			
Va,b	2	9.908		0.729	−0.778	1.507
IVa,b	3	10.884		0.272	−0.500	0.772
			0.232			
Va,b	3	10.652		0.870	−0.745	1.615
IVa,b	4	9.886		0.170	−0.644	0.814
			1.164			
Va,b	4	8.722		0.497	−0.953	1.450
IVc,d	1	19.304		0.156	−0.730	0.886
			0.222			
Vc,d	1	19.082		0.652	−0.721	1.373
IVc,d	2	18.542		0.323	−0.606	0.929
			0.382			
Vc,d	2	18.160		0.451	−0.582	1.177
IVc,d	3	19.112		0.267	−0.496	0.763
			0.234			
Vc,d	3	18.878		0.736	−0.635	1.371
IVc,d	4	18.116		0.169	−0.622	0.791
			0.954			
Vc,d	4	17.162		0.482	−0.453	0.954
VIa,b	1	12.336		0.108	−0.944	1.052
			0.194			
VIIa,b	1	12.142		0.767	−1.197	1.964
VIa,b	2	11.710		0.212	−0.820	1.032
			0.320			
VIIa,b	2	11.390		0.698	−0.998	1.696
VIc,d	1	20.552		0.108	−0.750	0.858
			0.196			
VIIc,d	1	20.356		0.643	−0.761	1.407
VIc,d	2	19.946		0.209	−0.671	0.880
			0.320			
VIIc,d	2	19.626		0.581	−0.680	1.261
X	1	5.326		0.433	−0.663	1.099
			0.284			
XI	1	5.042		0.925	−1.022	1.947
X	2	5.188		0.509	−0.594	1.103
			0.428			
XI	2	4.760		0.883	−0.880	1.763

The lone pair energies are often [9] given the same values as the Coulomb integrals of the atoms in question. This has also been made here to account for the terms 5) and 6). These values and the π electron energies, π electron distributions, and mobile bond orders have been obtained by the modified ω-method devised by Janssen,[10] which also takes bond order changes into account. The Coulomb integrals for $\dot{S}$ and $\dot{N}$ used to evaluate the terms 5) and 6) are those obtained in the final iteration. Four sets of parameters have been used (Table 2), which are rather similar to set 3 in Ref. 10. In this work three different models for the sulphur atom in the 1,3,4-thiadiazole ring have been tried, *viz.* the $3p\pi$ (sets 1 and 2), the $3pd^2$ according to Longuet-Higgins[11] (set 3) and the $3pd^2$ according to Kikuchi[12] with an element of electropositivity in the $3pd^2$ orbitals (set 4). The π electron energy values are found in

Table 4. Lone pair energies, E_n, in units of β. $\Delta E_n = E_{n,S} - E_{n,N}$.

System	Parameter set	Atom	E_n	ΔE_n
IIa,b	1	S	0.018	
IIIa,b	1	N	0.302	−0.284
IIa,b	2	S	0.088	
IIIa,b	2	N	0.292	−0.204
IIc,d	1	S	0.020	
IIIc,d	1	N	0.305	−0.285
IIc,d	2	S	0.089	
IIIc,d	2	N	0.301	−0.212
IVa,b	1	S	−0.032	
Va,b	1	N	0.278	−0.310
IVa,b	2	S	0.086	
Va,b	2	N	0.295	−0.209
IVa,b	3	S	0.064	
Va,b	3	N	0.362	−0.298
IVa,b	4	S	0.014	
Va,b	4	N	0.317	−0.303
IVc,d	1	S	−0.030	
Vc,d	1	N	0.282	−0.312
IVc,d	2	S	0.087	
Vc,d	2	N	0.298	−0.211
IVc,d	3	S	0.066	
Vc,d	3	N	0.363	−0.297
IVc,d	4	S	0.015	
Vc,d	4	N	0.334	−0.319
VIa,b	1	S	−0.071	
VIIa,b	1	N	0.264	−0.335
VIa,b	2	S	0.004	
VIIa,b	2	N	0.262	−0.258
VIc,d	1	S	−0.069	
VIIc,d	1	N	0.268	−0.337
VIc,d	2	S	0.005	
VIIc,d	2	N	0.267	−0.262
X	1	S	0.121	
XI	1	N	0.340	−0.219
X	2	S	0.168	
XI	2	N	0.324	−0.156

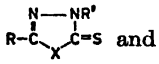
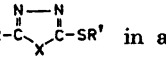
X XI

Table 3, the lone pair energies in Table 4, and π electron distributions and mobile bond orders in Fig. 3. The simple thioamide and imidothiol systems (X) and (XI) are also included.

It appears that in all cases the most stable isomer has also the highest π electron stabilization. However, the lone pair energies, which are the same in the first iteration, come out with rather different values in the final iteration. The nitrogen lone pairs are in all cases more stable than the sulphur lone pairs, the difference increasing in the series X = O, S, N, *i.e.* with increasing electron donating capacity of the third ring heteroatom. This is to be expected, since the thiocarbonyl group is more polarisable than the azomethine group. It can also be seen in Tables 3 and 4 that with sets 1 and 3 the thiol form is favoured by the sum of π electron and lone pair energies, whereas with sets 2 and 4 the thione form is favoured. This rather delicate balance depending on a small shift in parameter values makes a reliable estimation of the stabilization energies difficult, even if it is probable that the differences in lone pair energies are somewhat exaggerated. Still, the larger π electron stabilization of the thione forms should be observed since it indicates, as will be discussed further in connection with the charge diagrams, that the conjugated thioamide resonance is more important than the aromatic resonance in the systems studied here.

Ultraviolet spectra. The ultraviolet spectra of the compounds studied in the present work are found in Table 5. The correlation between experimental and calculated exitation energies (parameter set 2) is shown in Fig. 2. It appears that the linear correlation is not too bad, particularly with regard to the diver-

Table. 5

Ultraviolet spectra of  and  in absolute ethanol.

R	R′	X = O		X = S		X = NCH_3	
		λ_{max} nm	ε	λ_{max} nm	ε	λ_{max} nm	ε
CH_3	H	262	14.200	309	13.700	253	15.600
CH_3	CH_3(N)	263	15.800	306.5	11.000	253	15.100
CH_3	CH_3(S)	219.5	8.360	269	8.780	211	7.690
Ph	H	303	14.500	337	18.400	280 (Sh)[a]	8.000
Ph	CH_3(N)	301.5	15.500	339	14.800	280 (Sh)[b]	8.200
Ph	CH_3(S)	272	18.600	301	16.000	254	11.600

[a] Maximum at 254.5 with ε: 18 800.
[b] Maximum at 254.5 with ε: 18 400.

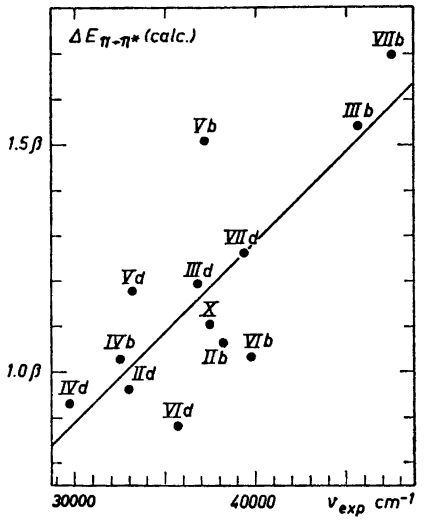
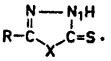


Fig. 2. Relation between calculated and experimental transition energies (parameter set 2).

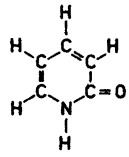
sity of the systems investigated. The correlation coefficient with set 1 is 0.726 and with set 2 0.883. For the thiadiazolinethiones both the Longuet-Higgins (set 3) and the Kikuchi (set 4) models give far lower transition energies than the $3p\pi$ model, whereas for the thiadiazolethiols the Longuet-Higgins model gives too high and the Kikuchi model too low transition energies. In some cases the points are far out of the line, and there appears to be no advantage with the use of these models for the systems here under study.

Table 6. pK_a values in water and q_{N_1} (formal charge) values for  .

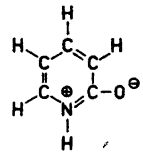
R	X	Parameter set	q_{N_1}	pK_a
CH_3	O	1	0.245	5.01
		2	0.207	
Ph	O	1	0.250	4.27
		2	0.219	
CH_3	S	1	0.240	4.90
		2	0.204	
		3	0.254	
		4	0.247	
Ph	S	1	0.243	4.98
		2	0.208	
		3	0.257	
		4	0.251	
CH_3	NCH_3	1	0.241	8.19
		2	0.204	
Ph	NCH_3	1	0.243	7.66
		2	0.207	

Acidity constants. The pK_a values of the acids (II), (IV) and (VI) in water are found in Table 6 together with the calculated π electron charges on the NH nitrogen atoms. It is obvious that the differences in charge are too small to explain the pK_a differences. Application of the Longuet-Higgins treatment [13] with the present charge and pK_a differences leads to a β value of about 400 kcal/mole, which probably is about one order of magnitude too high. However, the strongest acid also has the highest positive charge, and the weakest acids have among the lowest charges, which at least is in the expected direction. Furthermore it can be mentioned that thioacetamide with q_N: 0.207 (set 1) and 0.166 (set 2) has pK_a: 13.4.[14]

Charge distribution and bond orders. Arndt [15,16] has pointed out that 2- and 4-pyridones and -quinolones must be regarded as mesomeric compounds with the limiting structures (XII) and (XIII). Structure (XIII) expresses the



XII



XIII

aromatic character of these compounds. It has long been realized that simple amides and thioamides show a similar resonance, and in Ref. 10 it was shown that the polarities of these compounds could be described by the calculation method used here. It is apparent in the molecular diagrams (Fig. 3) that a considerable proportion of the thioamide character is preserved in the cyclic thiones, even if the enhanced polarity indicates a larger contribution in the cyclic than in the open-chain compounds of the structures corresponding to (XIII), in harmony with Arndt's theory. On the whole, however, a comparison between the simple structures (X) and (XI) and the cyclic analogues seems to indicate that the thioamide resonance is more important than the aromatic resonance to determine the stability of the cyclic thione form. Even in simple thioamides quite a strong resonance stabilization must exist, since Loewenstein *et al.* [17] using NMR found barriers to internal rotation around the carbon-nitrogen bond in simple thioformamides as high as 24—36 kcal/mole.

HMO treatment. In some of these calculations (parameter set 2) the results of the first calculations, (the HMO results) have also been investigated. The π electron energies favour the thione form rather uniformly by 0.66 β, and the lone pair energies favour the thiol form by about 0.4 β. Thus, in this case the results are in just as good accord with expectations as the results of the ω-calculations. The same can be said about the pK_a—q_N relations. The q_N values from the HMO calculations are about 0.05 electronic units higher than those from the ω-calculations, but the values fall in the same order, and the differences are almost constant. On the other hand, the spectral data are much better represented by the ω-energies. The HMO strongly underestimates the

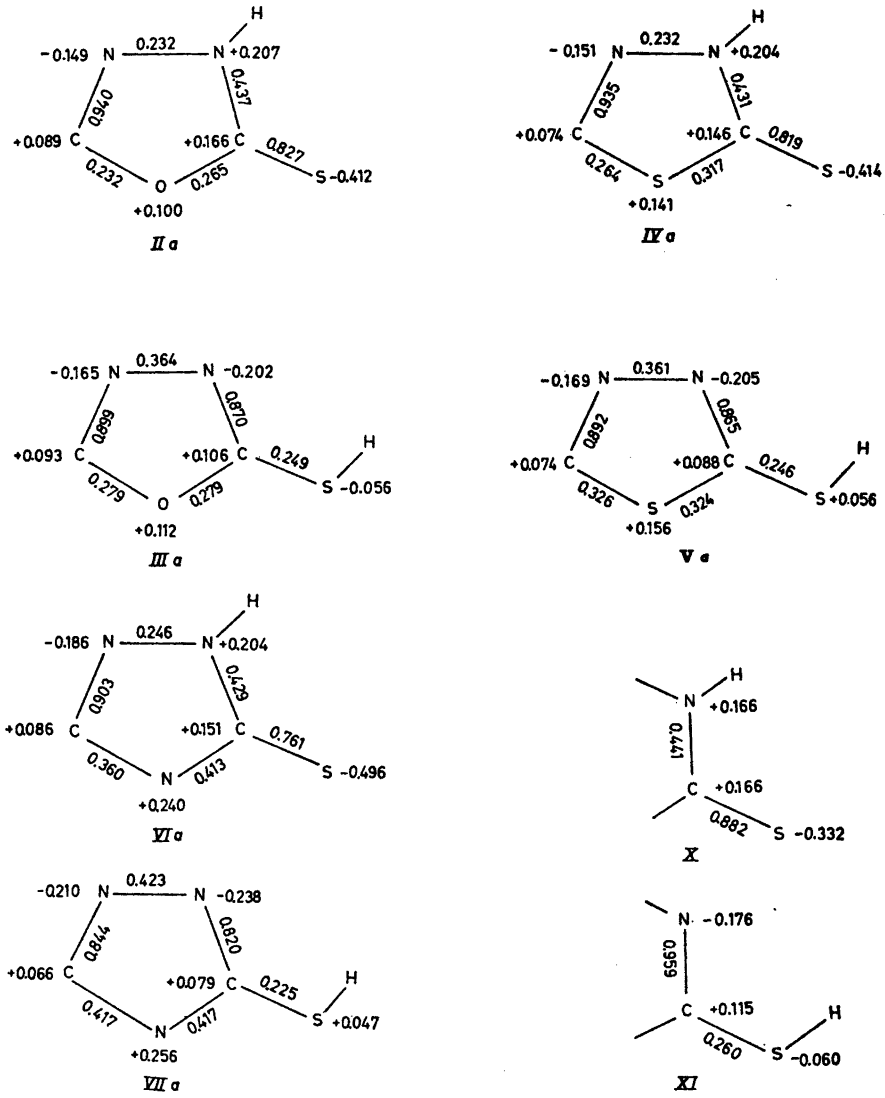


Fig. 3. Molecular diagrams (parameter set 2).

differences between thione and thiol forms for the methyl derivatives, and for the phenyl derivatives the values fall in the wrong order. Thus, the use of the more elaborate calculation method seems to be justified in the present case.

EXPERIMENTAL

2-Methyl-1,3,4-oxadiazolin-5-thione (IIa). Acethydrazide (14.8 g) and carbon disulphide (20 ml) were refiuxed in pyridine (100 ml) for 2 h. The solvent was evaporated, and the residue was dissolved in water (50 ml). Addition of conc. HCl (50 ml) precipitated 2,5-dimercapto-1,3,4-thiadiazole (3.0 g, 10 % yield). The mother liquor was continuously extracted with ether, the ether extract was evaporated, and the crystalline residue (12.5 g, 54 % yield) was purified by repeated recrystallizations from carbon tetrachloride, colourless plates, m.p. 77—78° (Ref. 18, 78°).

2,4-Dimethyl-1,3,4-oxadiazolin-5-thione (IIb). Acetic anhydride (20 ml) was added to a solution of ethyl carbazate (21 g) in toluene (50 ml). When the initial vigorous reaction had subsided, the mixture was refluxed for 15 min and then evaporated. The solid residue of *ethyl 3-acetylcarbazate* (29.4 g, 100 % yield) crystallized from chloroform-light petroleum (b.p. 80—100°) as colourless prisms, m.p. 86—87°. (Found: C 40.9; H 6.92; N 19.4. $C_5H_{10}N_2O_3$ (146.15) requires C 41.1; H 6.85; N 19.2). Attempted cyclizations by heating with phosphorus oxychloride or by vacuum sublimation did not give the desired result. When an intimate mixture of the acetyl derivative and phosphorus pentoxide in the proportion 2:1 was kept at 130—150° and 10 min in a sublimation apparatus, a sublimate of *2-methyl-1,3,4-oxadiazolin-5(4)-one* was obtained, m.p.110—111° (Ref. 19 112°). The optimal quantity of reactants seemed to be determined by the capacity of the cooling surface. Under the best conditions a yield of 70 % could be obtained, but this decreased when the charge was increased. The oxadiazolinone (4.8 g) was added to a solution of diazomethane (2.6 g) in ether (50 ml). Nitrogen gas was evolved, and on distillation *2,4-dimethyl-1,3,4-oxadiazolin-5-one* (3.5 g, 68 % yield) was obtained as a colourless liquid, b.p.$_{16}$ 80—82°, $n_D^{21.5}$ 1.446. (Found: C 41.8; H 5.51; N 24.5. $C_4H_6N_2O_2$ (114.11) requires C 42.1; H 5.26; N 24.6). ν_{CO}: 1782 cm^{-1}. This product, 2.0 g, was heated to 150° with 1.5 g of phosphorus pentasulphide for 0.5 h. Distillation at 14 mm gave a fraction at 84—86°, mostly consisting of starting material, and then at 4 mm there was obtained a colourless fraction, b.p. 100—101°, consisting of the desired oxadiazolinthione (IIb) (1.1. g, 48 % yield), n_D^{20} 1.556, m.p. 47—48°. (Found: C 36.6; H 4.50; N 21.7; S 24.2. $C_4H_6N_2OS$ (130.17) requires C 36.9; H 4. 65; N 21.5; S 24.6).

2-Methyl-5-methylthio-1,3,4-oxadiazole (IIIb) was prepared according to Hoggarth.[18] The same product was formed when the oxadiazolinthione (IIa) reacted with diazomethane. Under these conditions no N-methyl derivative was formed.

2-Phenyl-1,3,4-oxadiazolin-5-thione (IIc) was prepared according to Hoggarth.[18]

2-Phenyl-4-methyl-1,3,4-oxadiazolin-5-thione (IId). The thione (IIc, 1.8 g) was added to diazomethane (0.6 g) in ether (100 ml). After evaporation the residue was extracted with light petroleum (b.p. 40—60°), which left undissolved a crystalline product (0.05 g, 3 % yield), m.p. 124—125°. (Found: C 56.4; H 4.35; N 14.4; S 16.5. $C_9H_8N_2OS$ (192.23) requires C 56.2; H 4.19; N 14.6; S 16.7). The petroleum extract on evaporation gave *2-phenyl-5-methylthio-1,3,4-oxadiazole* (IIId, 1.7 g, 89 % yield), identical with the product described by Hoggarth.[18] This product (7.3 g) was refluxed with methyl iodide (23 g) for 3 days. The solid product (2.8 g, 22 % yield), m.p. 154—156°, was found to be 2-phenyl-4 (or 3)-methyl-5-methylthio-1,3,4-oxadiazolium iodide. (Found: C 36.4; H 3.22; N 8.46; S 9.65; I 37.6. $C_{10}H_{11}IN_2OS$ (332.15) requires C 36.2; H 3.33; N 8.44; S 9.72; I 38.2). Evaporation of the mother liquor gave a semi-solid residue. Extraction with light petroleum gave a solid residue (2.2 g, 30 % yield) of the N-methyl derivative (IId), which crystallized from ethanol as colourless rods, m.p. 124—126°, undepressed on admixture with the product described above.

The methiodide (3.1 g) and pyridine (10 ml) were refluxed for 1 h. The solution was poured into N acetic acid (100 ml), and a crystalline deposit (1.5 g, 84 % yield) was formed, consisting of a mixture of (IId) and (VIII). Crystallization from ethanol gave the latter as colourless needles (0.3 g), m.p. 227—229°. (Found: C 56.1; H 4.23; N 14.7; S 16.7. $C_9H_8N_2OS$ (192.23) requires C 56.2; H 4.19; N 14.6; S 16.7). The mother liquor was evaporated, and the residue was recrystallized from a small volume of ethanol. Colourless rods (0.5 g) were obtained, m.p. 124—126°, undepressed on admixture with (IId).

2-Methyl-1,3,4-thiadiazolin-5-thione (IVa) was prepared according to the method described by Goerdeler *et al.*[20] for 1,3,4-thiadiazolin-5-thione. A 74 % yield was obtained of a colourless product, which crystallized from ethanol as colourless rods, m.p. 186—187°. (Found: C 27.5; H 3.0; N 21.0; S 48.4. $C_3H_4N_2S_2$ requires C 27.3; H 3.05; N 21.2; S 48.5).

2,4-Dimethyl-1,3,4-thiadiazolin-5-thione (IVb). Methyl 2-methyldithiocarbazate[22] (4.4 g) and acetic anhydride (3.15 g) were refluxed in toluene (50 ml) for 15 min. After evaporation, a solid residue was obtained, which crystallized from toluene — heptane as colourless plates (4.8 g, 83 % yield), m.p. 86—87°. (Found: C 33.9; H 5.55; N 15.9; S 36.1. $C_5H_{10}N_2OS_2$ (178.28) requires C 33.7; H 5.65; N 15.7; S 36.0).

This acetyl derivative (4.5 g) and phosphorus oxychloride (25 ml) were refluxed for 90 min. The remaining phosphorus oxychloride was distilled off in a vacuum, and the residue was dissolved in water (25 ml). Solid sodium acetate was added until pH rose to about 4 when a colourless crystalline product separated (1.24 g, 34% yield), which crystallized from light petroleum (b.p. 40—60°) at −30° as colourless rods, m.p. 52—53°. (Found: C 33.1; H 4.12; N 19.2; S 43.6. $C_4H_6N_2S_2$ (146.22) requires C 32.9; H 4.14; N 19.2; S 43.9).

2-Methyl-5-methylthio-1,3,4-thiadiazole (Vb). Methyl 3-acetyldithiocarbazate[18] (28 g) and phosphorus pentasulphide (20 g) were refluxed in dry benzene (300 ml) for 12 h. After filtration and evaporation the residue was distilled, b.p.$_4$ 102—112°. The product (10.8 g, 43 % yield) crystallized partly on standing, and after several recrystallizations from light petroleum (b.p. 40—60°) at −30° colourless rhombic plates were obtained, m.p. 35—35.5°. (Found: C 32.9; H 4.20; N 19.1; S 43.6. $C_4H_6N_2S_2$ (146.22) requires C 32.9; H 4.14; N 19.2; S 43.9).

2,4-Dimethyl-1,3,4-thiadiazolin-5-one. Methylhydrazinium hydrogen sulphate (6.3 g) was dissolved in 1.35 N NaOH (100 ml), and O-methyl S-carboxymethylthionthiolcarbonate[21] (7.6 g) was added. A small amount of oil separated, and the mixture was extracted with ether (5 × 25 ml). The combined ether extracts were dried and evaporated, and the remaining colourless liquid (4.5 g, 83 % yield) was dissolved in toluene (25 ml). Acetic anhydride (4 ml) was added, and after refluxing for 15 min the mixture was evaporated. The solid residue, *methyl 2-methyl-3-acetyl-thioncarbazate*, crystallized from toluene-heptane as colourless rods (5.1 g, 84 % yield), m.p. 94—95.° (Found: C 37.3; H 6.11; N 17.3; S 20.0. $C_5H_{10}N_2O_2S$ (162.21) requires C 37.0; H 6.21; N 17.3; S 19.8).

This product (4.8 g) and phosphorus oxychloride (30 ml) were refluxed for 2 h. The remaining phosphorus oxychloride was distilled off in a vacuum, and the residue was dissolved in water (15 ml). Solid sodium acetate was added until pH rose to about 4, when a colourless oil separated. The mixture was extracted with ether (3 × 50 ml), the combined extracts were washed with N sodium carbonate solution followed by water, dried and evaporated. The remaining colourless liquid was distilled, b.p.$_{14}$ 90—91°, n_D^{20} 1.518 (1.66 g, 43 % yield). (Found: C 37.2; H 4.86; N 21.3; S 24.6. $C_4H_6N_2OS$(130.17) requires C 36.9; H 4.65; N 21.5; S 24.6). $\nu_{C=O}$ 1784 cm^{-1}.

2-Phenyl-1,3,4-thiadiazolin-5-thione (IVc) and *2-phenyl-5-methylthio-1,3,4-thiadiazole (Vd)* were prepared according to Young and Wood.[23]

2-Phenyl-4-methyl-1,3,4-thiadiazolin-5-thione (IVd). The thione (IVc, 3.9 g) was added to a solution of diazomethane (1.0 g) in ether (50 ml). When the evolution of gas had ceased, the solution was evaporated, and the semisolid residue was subjected to chromatography on alumina. Light petroleum (b.p. 80—100°) eluted a pale yellow solid (1.85 g, 44 % yield), which crystallized from ethanol as pale yellow rods, m.p.123—124°. (Found. C 52.1; H 3.99; N 13.4; S 30.4. $C_9H_8N_2S_2$ (208.29) requires C 51.9; H 3.87; N 13.5; S 30.8). Continued elution with benzene-light petroleum (1:1) gave the S-methyl derivative (1.6 g, 38 % yield).

3,4-Dimethyl-1,2,4-triazolin-5-thione (VIa) was prepared according to Kröger *et al.*[24]

1,3,4-Trimethyl-1,2,4-triazolin-5-thione (VIb) was prepared mainly according to Kröger *et al.*[24] These authors give the m.p. 82°, whereas we after two recrystallizations

from 1-propanol found 105—105.5°. (According to a private communication from Dr. Kröger, the lower m.p. is probably due to a printing error).

3,4-Dimethyl-5-methylthio-1,2,4-triazole (VIIb). The hydroiodide was prepared according to Kröger *et al.*[24] and the free base was liberated by treatment with a solution of sodium hydrogen carbonate. After evaporation the residue was extracted with chloroform, and the residue, after evaporating the chloroform solution (57 % yield), was recrystallized from carbon tetrachloride-light petroleum, colourless plates, m.p. 43—47° (Ref. 5, 55—57°). In spite of the low m.p., satisfactory analytical figures were obtained. (Found: N 28.6; S 22.2. $C_5H_9N_3S$ (143.21) requires N 29.3; S 22.4).

3-Phenyl-4-methyl-1,2,4-triazolin-5-thione (VIc) was prepared according to Young and Oates.[25]

3-Phenyl-1,4-dimethyl-1,2,4-triazolin-5-thione (VId). Benzoyl chloride (2.5 ml) was added dropwise to a solution of 2,4-dimethylthiosemicarbazide [26] (2.4 g) in chloroform (25 ml). A colourless precipitate was formed (3.4 g, 74 % yield), which crystallized from absolute ethanol as colourless rods, m.p. 184—185°, consisting of *1-benzoyl-2,4-dimethylthiosemicarbazide.* (Found: C 53.7; H 5.54; N 18.7; S 14.4. $C_{10}H_{13}N_3OS$ (223.28) requires C 53.8; H 5.87; N 18.8; S 14.4). This benzoyl derivative (1.1 g) was refluxed for 4.5 h in N sodium hydrogen carbonate solution (50 ml). On cooling, a colourless precipitate was formed (0.55 g, 54 % yield), which crystallized from absolute ethanol as rectangular plates, m.p. 135.5—136°. (Found C 58.6; H 5.34; N 20.4; S 15.7. $C_{10}H_{11}N_3S$ (205.27) requires C 58.5; H 5.40; N 20.5; S 15.6).

3-Phenyl-4-methyl-5-methylthio-1,2,4-triazole (VIId) was prepared according to Hoggarth.[27]

The ultraviolet spectra were recorded in absolute ethanol solution with a Beckman DU spectrophotometer with photomultiplier attachment. The pK_a determinations were performed in water by titration with standard NaOH in a thermostated vessel (25.0°C), and the pH values were recorded with a glass electrode. A stream of carbon dioxide-free air was passed through the solution. Since the concentration of acid was of the order 4×10^{-3} M, it was not regarded as necessary to apply activity correction to get thermodynamic pK values. In some cases the acids were too slightly soluble for this method. They were then dissolved in an excess of standard NaOH, and the solution was re-titrated with standard acid until precipitation occurred. In some cases the values obtained by these methods were checked by photometric methods, and a good agreement was obtained. The LCAO calculations were performed as described in Ref. 10.

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