Heteroatom Chemistry
Volume 3, Number 1, 1992

Conformational Study of 1,4-Thiazinan-3-one

Jorma K. Koskimies* and Aija Halonen

Department of Chemistry, University of Helsinki Vuorikatu 20, SF-00100 Helsinki, Finland

Received 24 June 1991.

ABSTRACT

The proton NMR spectra of several 1,4-thiazinan-3-ones were analyzed using LAOCOON. The geminal and vicinal coupling constants indicate that the ring conformation of this heterocycle is a half-chair similar to δ-valerolactam. Molecular mechanics calculations show that the energy of the boat is only slightly higher than that of the half-chair. The conformational equilibria of methyl-substituted compounds were calculated by the coupling constant method. These energies are compared to those obtained by molecular mechanics.

INTRODUCTION

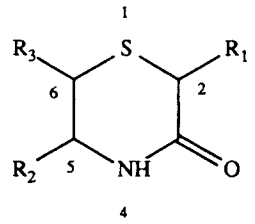
In a previous paper [1] it was reported that 1,4-oxathian-2-one prefers to adopt a somewhat unusual classical boat conformation both in solution as well as in the solid state [2]. Therefore, we decided to investigate the ring conformation of the corresponding lactam 1,4-thiazinan-3-one [4]. In the present study we describe the proton NMR spectra of lactams **1–8** and the conformational conclusions drawn on them (Figure 1).

RESULTS AND DISCUSSION

1,4-thiazinan-3-one (**1**), a not uncommon heterocycle [5,6], has been patented for sedative [7] and calcium-antagonist activity [8] as well as for use as transdermal accelerators [9] and moisturizers in cosmetics [10]. Related compounds show antiinflammatory [11] or antihypertension [12] properties. The NMR spectra or the conformations of thiazinanones have not been described. The conformation of the carbon analogue of δ-valerolactam is believed to be a flattened chair on the basis of experimental [13] and theoretical [14,15] considerations. Because of the strong resonance, the amide moiety of the ring is almost planar, while the rest of the ring is bent out of the plane. In thiazinanone the absence of several gauche C–H interactions, and the long bonds and small bond angle of sulfur, may well lower the energy of the boat so that this conformation will become important in the structure of the compound (Figure 2). Indeed, two X-ray crystal structures exist in which thiazinanone assumes a boat conformation, presumably because of the fused planar 5-member ring [16,17].

MM Calculations

A molecular mechanics (Macromodel MM2) [18] calculation on thiazinanone confirms the previous assumptions. The molecule has two separate conformations, the half-chair being favored by 5.6 kJ/mol with respect to the boat. This corresponds at room temperature to a *ca* 10:1 mixture of chair and boat. The structure with minimum energy is a flattened chair (or half-chair) with the amide moiety nearly planar and the sulfur atom especially deviating from this plane. The amide deviates from plane (torsion angle C1–C2–N–C4 10.3°) because the molecule tries to minimize the angle strain that is the major con-



	R_1	R_2	R_3	
1	H	H	H	
2	Me	H	H	
3	H	Me	H	
4	H	H	Me	
5	Me	Me	H	trans
6	Me	Me	H	cis
7	H	H	Et	
8	Bz	H	H	

FIGURE 1 List of compounds.

This paper is dedicated to Professor Ernest L. Eliel on the occasion of his seventieth birthday.

*To whom correspondence should be addressed.

1042-7163/92/$3.50 + .25

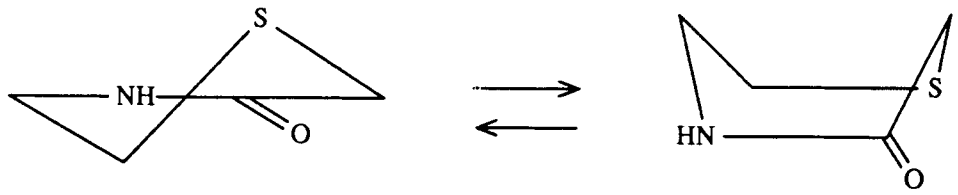


FIGURE 2 Ring conformations of thiazinanone.

tributor to the total steric energy of the molecule. The boat form, on the other hand, has almost a planar amide group (torsion angle C1–C2–N3–C4 4.0°), the increase in energy being due mainly to the torsional component and the van der Waals component. For comparison, the corresponding dihedral angles in the boat forms of the X-ray structures [16,17] are 0.1° and 6.4°. The energies calculated with MacroModel for possible conformations of **1–8** are listed in Table 1. It is obvious that the boat is a minor but significant contributor to the conformational equilibrium in substituted thiazinanones such as **2** and **4**.

NMR Spectra

NMR spectra were obtained in $CDCl_3$ solution using a 200 MHz or a 400 MHz instrument at 24°C. The interpretation of the proton spectra was not possible without resorting to simulation and iterative analysis on the LAOCOON [19] program because the C-5 and C-6 protons gave a second order spectrum with overlapping peaks even on a high field instrument. The pattern for the 5 methylene protons is further complicated by coupling to the nitrogen proton. The chemical shifts and the coupling constants were optimized until the RMS error was less than 0.1 (except for **1**, 0.22) and the probable errors for the iterated parameters were less than 0.1 Hz. From the AA'BB'X spectrum of **1** only the couplings J_{AB} and $J_{AB'}$ could be obtained. An example of a simulated spectrum is depicted in Figure 3.

The Chemical Shifts. The assignments of the chemical shifts were based mainly on the magnitude of vicinal coupling constants: The vicinal protons having a large coupling constant were designated axial (see Table 2). In this way the protons α to nitrogen (C-5) and the protons α to sulfur both have the equatorial hydrogen resonating at a lower field in accordance with the shielding effects reported by Lambert [20]. Of the two C-2 protons the higher field one was assigned equatorial. This is consistent with the known shifts of the methylene protons next to sulfur in a six-member ring [20]. This assignment is supported by the appearance of a long range coupling in 5-methyl-1,4-thiazinan-3-one (**3**) of 1.4 Hz between the equatorial C-6 proton and the high field proton of the C-2 methylene. A planar W-arrangement required by this type of J_5 coupling is more likely to be attained between the two equatorial protons rather than between equatorial and axial.

The Geminal Couplings. The C-2 geminal coupling constants (Table 3) (16.1–16.7 Hz) fall between the corresponding C-3 geminal couplings in 1,4-oxathian-2-ones (14.0–14.9 Hz) [1] and C-3 in δ-valerolactones (17-18 Hz) [21,22]. The value of this constant is useful in determining the conformation of the ring; it is dependent on the angle between the carbonyl bond and CH_2 because of hyperconjugation between the π-system and the CH_2 group. The maximum deviation from the normal value is obtained when the C=O bisects the CH_2 group

TABLE 1 MacroModel Energies (kJ) Calculated for Conformations of **1–8**

Compound	*Chair*		*Boat*	
1	31.6		37.2	
2	*e*: 39.3	*a*: 43.4	*e*: 44.1	*a*: 49.8
3	*e*: 34.6	*a*: 36.3	*e*: 42.9	*a*: 48.3
4	*e*: 35.5	*a*: 39.5	*e*: 39.9	*a*: 40.3
5	*ee*: 42.1	*aa*: 48.1	*ea*: 55.5	*ae*: 55.6
6	*ea*: 43.8	*ae*: 46.6	*ee*: 49.2	
7	*e*: 40.8	*a*: 46.0		
8	*e*: 51.3	*a*: 56.6		

TABLE 2 The Proton Chemical Shifts of Thiazinanones in ppm

Compound	H_{2e}	H_{2a}	H_4	H_{5e}	H_{5a}	H_{6e}	H_{6a}	*Me*
1 90 MHz	3.29		7.29	3.61		2.81		
1 200 MHz	3.29		7.80	3.61		2.82		
2		3.54	6.96	3.64	3.53	2.89	2.86	1.46
3	3.23	3.27	6.89		3.79	2.77	2.51	1.29
4	3.25	3.37	7.03	3.55	3.29		3.19	1.30
5		3.49	6.13		3.77	2.85	2.62	1.47
								1.32
6		3.48	6.13	3.85		2.76	2.62	1.51
								1.26
7	3.25	3.33	6.98	3.58	3.32		2.99	Me 1.63
								CH_2 1.64
								1.63
8		3.67	7.15	3.53	3.47	2.73	2.70	CH_2 2.90
								3.47
								Ph 7.26

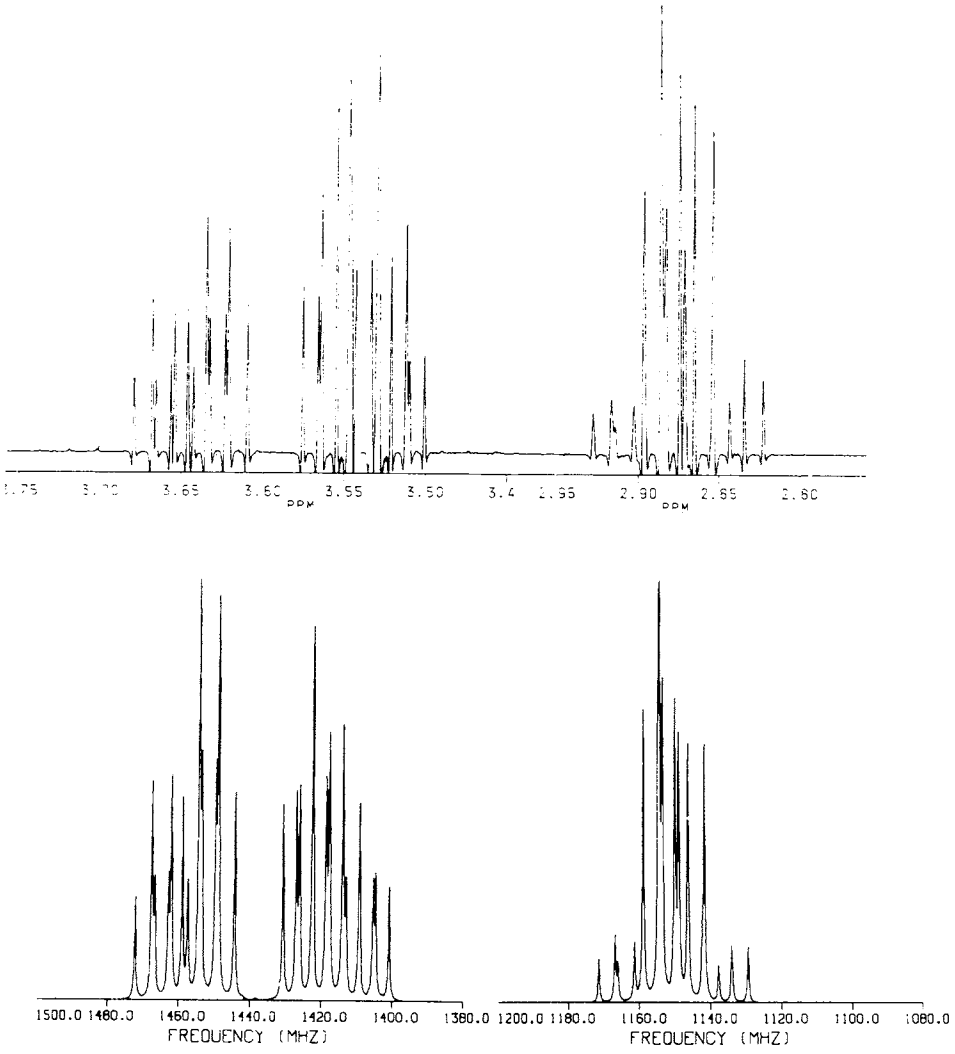


FIGURE 3 The resolution enhanced 400 MHz spectrum of 6 and 5 protons of **2** (top). The 6 protons' multiplet (top left) is overlapped by a quartet resulting from the 2 proton. Below is the simulated spectra.

Table 3 Proton Coupling Constants for Thiazinanones in Hz

Comp	J_{22}	J_{55}	J_{66}	J_{5e6e}	J_{5e6a}	J_{5a6e}	J_{5a6a}	J_{45e}	J_{45a}	J_{Me}	Others
1				7.27	3.86			3.52			
2		13.19	12.41	5.64	4.34	3.90	9.16	4.66	3.74	6.97	
3	16.70		13.30			3.63	9.12		1.99	6.45	J_{2e6e} = 1.36
											J_{2e6a} = −0.27
											J_{6ex} = 1.0
4	16.33	12.91			3.78		9.29	4.62	2.63	6.73	
5			12.36			3.67	9.68		3.25	Me_2 7.00	J_{6e}
										Me_5 6.35	
6			13.75			3.70	9.7		1.61	Me_2 7.15	J_{26} = 1.04
										Me_5 6.97	
7	16.11	13.08			3.85		8.98	4.24	2.80	CH_2 4.39	
										9.71	
										Me 7.34	
8		13.44	12.84	5.23	4.43	4.26	8.75	4.9	3.2	CH_2 9.27	
										4.45	
										14.09	

($J \approx -18$ Hz), whereas close to normal coupling constants ($J \approx -12$ to -13 Hz) are observed when C=O bond is parallel to the H–H axis of CH_2 [23,24].

We estimate the base value for thiazinanone C-2 to be $^2J = -13$ Hz from the value for undistorted cyclohexanones -12 to -13 Hz [24] and -13 for thiane [24]. Accordingly, in thiazinanones the hyperconjugative contribution to the geminal coupling amounts to 13–16.4 = 3.4 Hz. Using Cookson's experimental curve, [24] it may be estimated that this corresponds to the angle of 20° between the C–H and C=O. MM models for chair and boat forms give this angle as 26° and −6° respectively. Thus, the chair model is consistent with the C-2 geminal couplings constant. The C-5 and C-6 geminal coupling constants appear to be normal. The C-5 couplings range from – 12.9 to – 13.2 Hz and are close to what has been observed for piperidines (−11 to −14 Hz) and *N*-acylpiperidines (−13 to −13.2 Hz) [24]. The ^2J of C-6 (12.3–13.7 Hz) falls between the corresponding values for thianes (13.4–15 Hz [24]) or 1,4-oxathiane (13.5 Hz [25]) and for 1,4-oxathianones (11.9–12.4 Hz [1]).

Vicinal Couplings. The vicinal coupling constants (Table 3) between the protons at 5 and 6 are most important in the determination of the ring conformation because of the Karplus relationship. These couplings are remarkably constant regardless of the ring substitution. The puckering or flattening of the ring can be deduced from Lambert's R-value [26]. These parameters vary from 1.88 for the parent compound **1** to 1.61 for the 2-benzyl compound **8** (Table 4). This means that the N–CH_2CH^2–S part of the ring is somewhat flattened compared to cyclohexane (in the parent compound the R-value gives [26] an internal ring N4–C5–C6–S1 dihedral angle, $\Psi = 55.9°$) and is somewhat more flattened in the 2-methyl and 2-benzyl compounds, **2** and **8**. The torsion angle of 55° calculated from the R-value does not agree very well with those obtained from the MM calculation for chair or boat forms of the ring. However, it is closer to the value of 59.4° of the chair model than to the much puckered model for the boat form (67.7°), thus supporting the chair. The largest vicinal coupling constant is around 9 Hz for the compounds studied (**2–8**). (This implies that in **2–8** the substituents have only slight preference for the (pseudo)equatorial position at 2, 5, or 6.) It seems unlikely that the true axial–axial coupling constant of thiazinanone would be as low as 9 Hz. The calculation using the Karplus equation [27] and MM model geometry gives the $J_{aa} = 12$ Hz in both possible conformers. The lower coupling constant observed must arise from averaging methyl equatorial and methyl axial half-chair conformers (ring inversion) and/or methyl equatorial conformer of the boat. Ignoring the contribution of the boat conformations for simplicity, calculation of the conformational energy for 2-methyl from its vicinal coupling constant $J_{56} = 9.16$ and the $J_{aa} = 12.2$ Hz and $J_{ee} = 2.1$ of the half-chair, obtained from the half-chair MM model by the Karplus equation, gives $K = 2.3$ and $\Delta G = 2.1$ kJ/mol. Similarly, roughly equal values are obtained for the conformational energies of 5-methyl (2.6 kJ/mol) and 6-methyl (2.7 kJ/mol) (Table 5). The size of ΔG for 6-methyl proves that the ring conformation is chair since in the boat form this value is expected to be negligible [1].

TABLE 4 R-Values and Corresponding Dihedral Angles Ψ

	R	Ψ
1	1.88	55.9°
2	1.80	55.2°
8	1.61	53.4°

TABLE 5 Conformational Equilibria and Energies (kJ) of Thiazinanones at 24°C

Compound	*K*	ΔG	Δ*H*(MM2)
2	2.32	2.1 ± 0.7	4.2
3	2.88	2.6 ± 0.7	1.7
4	2.94	2.7 ± 0.7	4.0
5	3.90	3.4 ± 0.9	6.0
6	3.90	3.4 ± 4	2.8
7	2.47	2.2 ± 0.8	5.2
8	1.78 (28°C)	1.4 ± 0.8	5.3

The methyl couplings. It has been demonstrated that the vicinal methyl coupling in a 6-member ring is larger for the axial than for the equatorial methyls [1,21,28]. Inspection of the methyl couplings of the two 2,4-dimethyl lactams shows that compound **6** has larger coupling constants both for 2-methyl and 4-methyl, whereas in its isomer, **5**, these coupling constants are similar to monomethyl couplings in compounds **2** and **3**. This in-

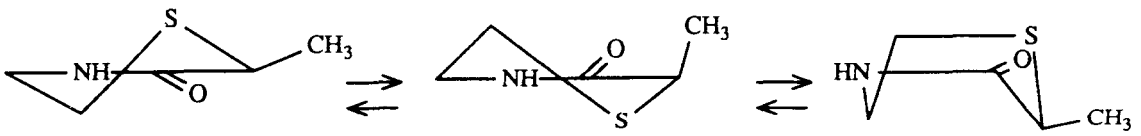


FIGURE 4 Possible conformations of **2**.

dicates that in **6** the methyls have considerable axial character and therefore **6** must be cis and **5** trans, in accordance with the long range coupling data (see below).

The N*H* is coupled to both 5 hydrogens (Table 2). The J_{45e} is between 4.2 – 4.7 Hz while J_{45a} varies more from 1.6 to 3.7 Hz. Obviously, there is a dependence on the dihedral angle between the coupled protons [29]. The dihedral angle in half-chair thiazinanone (from the MacroModel) between the NH and equatorial 5 proton is around 48 degrees, and the observed coupling constant fits well with the value obtained from the Karplus–Conroy curve [30]. The torsional angle between NH and the axial 5 proton, 66°, would indicate a coupling in the range 1.5–4 Hz, which also is observed. However, the significant variation observed in this coupling cannot be from a similar variation in the dihedral angles of the half-chair. The most likely explanation is that there are variable amounts of boat conformation in the conformational equilibria of these compounds, because in the boat form the torsional angles for H–C5–N–H are very different compared to the chair form (e.g., angle H_a–C5–N–H ca. 115°).

Long Range Couplings. In compound **3** the equatorial 6 proton is coupled to the high field signal of the 2 protons (see above). This fact is used in the assignment of the 2 protons. The long range coupling through a planar W-arrangement through sulfur is well known [31]. A similar coupling (J = 1.0 Hz) is clearly visible in compound **6** (Figure 5). Hence the minor isomer of the two 2,5-dimethyl compounds must have the 2-methyl group predominantly pseudoaxial (for the J_{2e5e} to be visible). It follows that compound **6** is *cis* and the major isomer **5** *trans*.

C-13 Spectra. The carbon resonances were assigned on the basis of signal multiplicity and correlation of signals from different compounds (see Table 6). The shift parameters (A_{ik}) for methyl substituents are obtained from:

$$\delta(k) = C_k + \sum_i A_{ik}$$

where $\delta(k)$ is the chemical shift of carbon k, C_k a constant for carbon k, and A_{ik} is the shift increment predicted for carbon k upon introduction of the methyl substituent at carbon i (Table 7). Compared to similar parameters in 1,4-oxathianones [32], the size of α and β parameters would suggest that there is a notable contribution of the axial conformation in the methyls. The small or negligible γ shift parameters would speak for the half-chair rather than for the boat conformation being the dominant conformation [32].

TABLE 6 Carbon-13 Shifts of Thiazinanones (ppm)

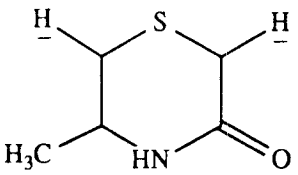
	C-2	C-3	C-5	C-6	Others
1	29.31	168.48	43.88	25.62	
2	35.65	172.54	43.28	26.44	16.41
3	32.18	168.16	50.76	29.25	21.67
4	29.14	168.81	50.60	34.62	18.74
5	35.32	172.33	49.85	32.58	16.74
					21.24
6	37.08	171.83	52.17	32.29	17.77
					22.21
7	29.25	169.53	48.99	42.20	26.65
					12.08
8	43.47	171.5	43.74	26.17	37.52
					i138.5
					o,m 129.66
					128.68
					p 127.11

TABLE 7 C-13 Shift Parameters for Methyl Substituents (see text)

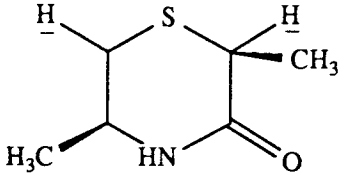
Position	C-2	C-3	C-5	C-6
α	4.89	—	7.29	8.62
β	—	3.73	6.12	5.30
γ	−0.69	−0.07	—	1.95
δ	1.7	0.82	−0.06	—

CONCLUSION

The ring conformation of thiazinanone is a somewhat flattened half-chair, based on the magnitude of the geminal coupling constant at 2 and vicinal couplings. However, the boat form is energetically not very far above the chair (by 5.6 kJ/mol MacroModel calculation) and may be an important contributor to the conformational equilibrium of substituted compounds. That the boat is not the



3 J = 1.4 Hz



6 J = 1.0 Hz

FIGURE 5 Long range coupling ^5J.

predominant conformation is evident from the following considerations: (1) The selective irradiation of the axial proton in compound **3** caused only a 0.5% increase in the signal intensity of the axial 5 proton. (2) The appearance of a long range coupling of ca. 1 Hz between the equatorial 2 and 6 protons in compound **3** and **6** requires chair-like conformation. (3) The conformational equilibria (see below) are explained best if the half-chair is the main conformer.

The conformational equilibria for half-chair obtained by the coupling constant method are clearly not compatible with the enthalpy differences obtained by the molecular mechanics method (Table 5). The expected value for methyl ΔG in these compounds would be a little lower than the energy of one *syn–axial* Me/H interaction (3.8 kJ/mol in cyclohexane). The discrepancy may be attributed at least partly to the large error in the ΔG value. The error arises from the coupling constants J_{ee} and J_{aa} that, in turn, are determined by the geometries produced by MM and the Karplus equation used. If the existence of boat forms that are in the equilibria measured by the coupling constant method is taken into account (see Figure 6) the ΔG values for methyl in half-chair thiazinanone in positions 2, 5, and 6 are $\geq$2.1, $\leq$2.6, and 2.7 kJ/mol. These figures come closer to MM values, though the difference is still significant and cannot be attributed only to the entropy term $T\Delta S$. By making the assumption that $\Delta G_{2\text{-Me}} = \Delta G_{6\text{-Me}}$ (the methyls have similar steric interactions) the chair–boat energy difference in compound **2** can be estimated to be 5.9 kJ/mol. The corresponding value from MM calculations, 4.8 kJ/mol, is fairly close.

The 1,4-thiazinanone ring is conformationally mobile, the main form being a half-chair. In methyl-substituted compounds, the boat energies become so low that, at room temperature, the compounds appear as a mixture of half-chair and boat forms.

EXPERIMENTAL

Thiazinanones (see Table 8) were prepared by two methods: In method A, the reaction of appropriately substituted ethylene imine and ethyl mercaptoacetate gave the δ-amino acid ester, which underwent ring closure to the desired lactam [5,6]. In method B, replacement of acetate by sulfur in the appropriately substituted β-nitroethyl acetate with ethyl mercaptoacetate gave the ester of the δ-nitro acid. Reduction of nitro by iron followed by cyclization gave 1,4-thiazinan-3-one [6]. *trans-* and *cis-*2,6-Dimethyl-1,4-thiazinanone (**5** and **6**) were obtained as a mixture, mp 83–90°, which was not resolved. 2-Benzyl-1,4-thiazinanone (**8**) was prepared by treatment of 1,4-thiazinanone (0.20 g of **1**) with *n*-butyllithium in tetrahydrofuran for 15 min at ca. −30° followed by addition of benzyl bromide. The product was isolated by evaporation, taking it up into ether, washing with water, and drying. After preparative TLC on silica (Merck PSC-Fertigplatten Kieselgel 60 F_{254} Art. 5717) 80 mg (24%) of **8**, an oil, was obtained; high resolution mass spectrum: calculated for $C_{11}H_{13}ONS$: 207.0718; found 207.0719.

The NMR spectra were recorded on Bruker 400

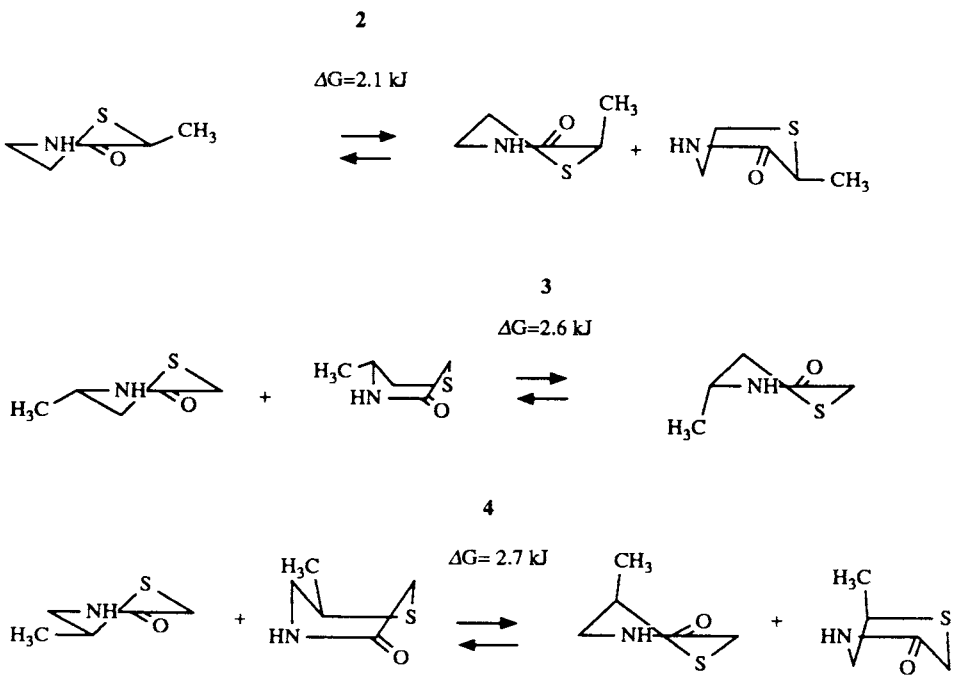


FIGURE 6 The equilibria in **2-4** obtained by the coupling constant method.

TABLE 8 Preparative Data for Thiazinanones **1–8**

Compound	Subst.	Method	Yield%	Mp. (lit.)	Ref.	IR/cm^{-1} [a] C=O	IR/cm^{-1} [a] NH
1	—	A	61	87–91° (90–91°)	5	1665	3190
2	2-Me	A	40	78–79° (75–76°)	6	1670	3220
3	5-Me	A	78	128–30° (128–30°)	6	1660	3180
4	6-Me	B	8	53–57° (58–60°)	6	1665	3180
5,6	3,5-diMe	A	37	83–90° (93–95°)	6	1665	3190
7	6-Et	B	8	35–40° (40–42°)	6	1665	3120
8	2-Bz	C	25	—	—	1660	3375[b]

[a] KBr.
[b] Film.

MHz, Jeol 90 MHz, JEOL GX400, and Varian Gemini 200 MHz instruments in ca. 5–10% $CDCl_3$ solutions. The LAOCOON III program [19] was run on VAX 8800 (VMS) and the calculated spectrum was plotted with DISSPLA VERSION 11.0. MacroModel 3.0 [18] was run on MicroVax as a VMS version.

ACKNOWLEDGMENTS

The authors are grateful to Mr. Bernard Watson and Dr. Alistair Swanson of the Organic Chemistry Department, Leeds University, England, and Mr. Esa Haapaniemi from University of Oulu, for the NMR high field spectra, Mr. Timo Mansikka for preparing compound **8**, and to Mr. Jorma Matikainen for a mass spectrum.

REFERENCES

[1] J. K. Koskimies, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1449.
[2] M. Näsäkkälä, J. K. Koskimies, *J. Chem. Soc., Perkin Trans. 2*, 1986, 671. For NOE experiments see J. Koskimies, T. P. Jauhiainen, T. Ollikainen: *The Conformation of 1,4-Oxathian-2-one revisited*, A paper presented at the 11th National NMR Symposium in Turku, 1988.
[4] These compounds have been called thiomorpholinones, tetrahydrothiazinones; for nomenclature see *Pure and Appl. Chem.*, *55*, 1983, 410.
[5] H. Bestian, *Ann.*, *566*, 1950, 210.
[6] H. Lehr, S. Karlan, M. W. Goldberg, *J. Med. Chem.*, *6*, 1963, 136.
[7] M. W. Goldberg, H. H. Lehr, *USP* 2755278/1956; CA 51:501b.
[8] U. Lerch, R. Henning, J. Kaiser, GP 3714371/1988; CA 110:114848c.
[9] M. Tsuji, T. Inoue, T. Yatani, M. Nakajima, M. Saida, Y. Shimozono, M. Sakai, Jap P 63077865/1986; CA 109:128982h.
[10] G. Lang, J. Maignan, J. L. Leveque, L. Rasseneur, GP 3313581/1983 and 3313582/1983; CA 100:103375p and CA100:56684b.
[11] W. P. Jackson, E. R. Pettipher, Int. Appl. WO 9001929/1990; CA 113:115323b.
[12] J. T. Suh, B. E. Williams, J. W. Skiles, B. Loev, USP 4287203/1981; CA 96:20130c.
[13] C. Romers, E. W. M. Rutten, C. A. A. van Driel, W. W. Sanders, *Acta Cryst.*, *22*, 1967, 893.
[14] A Warshell, M. Levitt, S. Lifson, *J. Mol. Spectrosc.*, *33*, 1970, 84.
[15] L. Treschanke, P. Rademacher, *Theochem.*, *23*, 1985, 35.
[16] N. N. Dhaneswar, S. S. Tavale, T. N. Guru Row, *Acta Cryst.*, *C41*, 1985, 1528.
[17] G. Zanotti, F. Pinnen, G. Lucente, S. Cerrini, E. Gavuzzo, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2647.
[18] W. C. Still, F. Mohamadi, N. G. J. Richards, W. C. Guida, M. Lipton, R. Liskamp, G. Chang, T. Hendrickson, F. DeGunst, W. Hasel, MacroModel V3.0, Department of Chemistry, Columbia University, New York, NY, 10027.
[19] See J. W. Cooper: *Spectroscopic Techniques for Organic Chemists*, Wiley-Interscience, New York, (pp. 339–355) 1980.
[20] J. B. Lambert, J. E. Goldstein, *J. Am. Chem. Soc.*, *99*, 1977, 5689.
[21] F. I. Carroll, G. N. Mitchell, J. T. Blackwell, A Sobti, R. Meck, *J. Org. Chem.*, *39*, 1974, 3890.
[22] H. Ferres, I. K. Hatton, L. J. A. Jennings, A. W. R. Tyrrell, D. J. Williams, *Tetrahedron Lett.*, *24*, 1983, 3769.
[23] M. Barfield, D. M. Grant, *J. Am. Chem. Soc.*, *85*, 1963, 1899.
[24] R. C. Cookson, T. A. Crabb, J. J. Frankel, J. Hudec, *Tetrahedron Suppl.*, *7*, 1966, 355.
[25] J. C. Barnes, G. Hunter, M. W. Lown, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1354.
[26] J. B. Lambert, *Acc. Chem. Res.*, *4*, 1971, 87.
[27] C. A. G. Haasnoot, F. A. A. M. de Leeuw, C. Altona, *Tetrahedron*, *36*, 1980, 2783.
[28] P. Äyräs, *Suomen Kemistil., B46*, 1973, 151.
[29] A. R. Katzritzky, R. E. Reavill, *J. Chem. Soc.*, 1963, 753.
[30] H. Günther: *NMR Spectroscopy*, Wiley, Chichester (p. 107) 1980.
[31] For long-range coupling in dithiane see E. L. Eliel, *Tetrahedron*, *30*, 1974, 1503.
[32] J. Koskimies, *Magn. Res. Chem.*, *24*, 1986, 131.