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A comparative study of NMR chemical shifts of sparteine thiolactams and lactams

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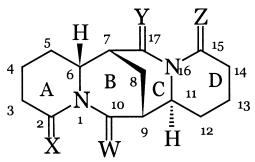
Abstract—The ^{13}C and ^{1}H NMR spectra of the four possible thiolactams of sparteine (**1**) were recorded and the thiolactam group effects were determined. Most of the effects are greater than those of the lactam group in the oxo analogs. A good linear correlation between the ^{13}C chemical shifts of C═S and those of C═O was found. The effects could help in assignment of the spectra and determination of conformation of thiolactams and related thiocarbonyl compounds. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

Quinolizidine alkaloids, containing the sparteine (**1**) or cytisine skeleton[1] are one of the most abundant groups of alkaloids distributed within the *Leguminoseae*, the third largest family of flowering plants.[2] The alkaloids having the sparteine skeleton are very interesting from a stereochemical point of view.[3] These compounds can occur in two conformations, differing in the form of ring C: 1A with the 'boat' conformation and 1B with the 'chair' form.[3,4]

There are four known lactams of sparteine. Two of them, 2-oxosparteine (**2**)[5] and 10-oxosparteine (**3**)[6] were isolated by us from natural sources, while the other two were obtained synthetically.[7,8]

The presence of the lactam groups in the sparteine skeleton causes flattening of the ring comprising the oxo function.[4]



1: X=H_2, W=H_2, Y=H_2, Z=H_2
2: X=O, W=H_2, Y=H_2, Z=H_2
3: X=H_2, W=O, Y=H_2, Z=H_2
4: X=H_2, W=H_2, Y=O, Z=H_2
5: X=H_2, W=H_2, Y=H_2, Z=O
6: X=S, W=H_2, Y=H_2, Z=H_2
7: X=H_2, W=S, Y=H_2, Z=H_2
8: X=H_2, W=H_2, Y=S, Z=H_2
9: X=H_2, W=H_2, Y=H_2, Z=S

In the solid state, ring C in 2-oxosparteine (**2**) has a boat conformation and ring A adopts a distorted half-chair conformation. The A/B configuration is quasi-*trans* and C/D is *trans*.[4] In solution, **2** occurs in conformational equilibrium with dominance of the boat form of ring C (9:1).[3] In 17-oxosparteine (**4**), the lactam group is in ring C which adopts a sofa form both in solution and in the solid state.[9,10] In the solid state, 15-oxosparteine (**5**) is known to exist in a conformation characterised by a half-chair (12α, 13β) ring D with a positive (O)═C–N–C endocyclic torsion angle and ring C in a boat form. In solution, ring C adopts a distorted sofa conformation.[9] In 10-oxosparteine, ring C occurs in the chair form only.[11]

The above-mentioned lactams of sparteine show a very low chemical and biological activity. In contrast to amides, thioamides are very reactive and can be easily transformed into a variety of functional groups.[12] They have been recognised as useful building blocks in organic synthesis and perfect substrates for production of new biologically active substances. In view of the above, we have attempted to transform some of the sparteine lactams into their thioanalogs[13–15] using Lawesson's reagent.[16]

In this paper we wish to discuss the influence of carbonyl and thiocarbonyl groups in the sparteine skeleton on the ^{13}C and ^{1}H NMR spectra.

In the lactam or thiolactam group, there is no possibility of rotation about the N–C bond. Thus, the effect of these groups could be better defined than that of amide or thioamide groups, especially in model compounds having a rigid skeleton. Sparteine (**1**) delivers a skeleton which is not entirely rigid, but the condition is fulfilled quite well in the direct vicinity of the lactam (thiolactam) group. A dependence of the chemical shift of the thiocarbonyl carbon

Keywords: bis-quinolizidine alkaloids; ^{13}C NMR; ^{1}H NMR; conformation; ^{13}C and ^{1}H NMR effects of thiocarbonyl group.

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Table 1. ^{13}C NMR chemical shifts in thionosparteines

C atom	2-Thiono-sparteine (**6**)[13] $CDCl_3$	10-Thiono-sparteine (**7**) $CDCl_3$	15-Thiono-sparteine (**9**)[15] $CDCl_3$	17-Thiono-sparteine (**8**)[14] $CDCl_3$	17-Thiono-sparteine (**8**)[14] C_6C_6
C(2)	201.82	51.97	56.00	57.68	56.96
C(3)	43.01	25.78	25.52	26.15	25.39
C4)	19.29	24.79	24.31	25.66[b]	24.70
C(5)	28.16	29.42	29.52	32.10	31.25
C(6)	64.16	63.6	65.35	66.06	66.44
C(7)	33.69	33.14	32.52	52.88	52.11
C(8)	26.98	22.52	27.29	27.46	26.99
C(9)	36.08	52.41	36.66	36.09	35.49
C(10)	55.12[a]	202.96	61.22	63.66	63.00
C(11)	62.91	60.40	61.12	66.34	65.41
C(12)	32.43	22.29	31.29	34.56	34.32
C(13)	24.59	25.16	18.27	25.63[b]	25.09
C(14)	24.59	18.75	42.22	25.15	24.92
C(15)	55.19[a]	54.27	200.05	52.09	56.06
C(17)	52.23	46.50	49.93	198.72	198.04

[a,b] Signals which can be interchanged.

atom on that of carbonyl carbon atom in the same structure is known quite well[17–19] among others also in the amide/thioamide system,[18] but we could not find any data for other NMR effects of the thiolactam group, i.e. mainly on the neighbouring carbon atoms and protons. Therefore, we decided to collect the results available for the earlier studied thiolactams of sparteine, 2-thionosparteine (**6**),[13] 15-thionosparteine (**9**),[15] and 17-thionosparteine (**8**),[14] and to complete them with the results obtained for 10-thionosparteine (**7**), with the ^1H NMR spectra of **8** and lactams **2** and **5** In $CDCl_3$, to analyse the effects for all sparteine thiolactams.

2. Results and discussion

The values of the ^{13}C NMR chemical shifts of the thiolactams studied are given in Table 1.

The effects of the thiocarbonyl and carbonyl groups on the ^{13}C NMR signals expressed as differences in the ^{13}C chemical shifts between the respective thiolactams and lactams and those obtained for sparteine (**1**), are presented in Table 2.

When comparing the chemical shifts of the carbonyl and thiocarbonyl carbon atoms in the corresponding lactams[7,11,20] and thiolactams[13–15] of sparteine (Table 2) with those of the respective carbon atoms in sparteine (**1**) (in $CDCl_3$), the effect of the carbonyl group is between ca. 110 and 115 ppm, whereas that of the thiocarbonyl is ca. 141 to 145 ppm, and the differences between both effects ($\Delta\delta_{O,S}$) are between 29 and 31 ppm. Kalinowski and Kessler[17] maintain that 'the difference between the chemical shifts found for $^{13}C{=}O$ and $^{13}C{=}S$ ($\Delta\delta_{O,S}$) decreases with increasing donor action of the substituents'. For the pairs of lactams and thiolactams investigated, the respective $\Delta\delta_{O,S}$ differ only up to ~1.9 ppm and it is difficult to find a correct explanation of the difference. It could be the geometry rather than electronic reasons because the maximum $\Delta\delta_{O,S}$ was found for the lactam/thiolactam systems at positions 10 and 17, both in internal rings; the substituents at the lactam

Table 2. Comparison of the ^{13}C effects of thiocarbonyl and carbonyl groups in lactams and thiolactams of sparteine (**1**) (in relation to **1**) in $CDCl_3$

Position	2-Tionosparteine (**6**)/ 2-oxosparteine (**2**)			10-Tionosparteine (**7**)/ 10-oxosparteine (**3**)			15-Tionosparteine (**9**)/ 15-oxosparteine (**5**)			17-Tionosparteine (**8**)/ 17-oxosparteine (**4**)		
	C	C=S	C=O	C	C=S	C=O	C	C=S	C=O	C	C=S	C=O
Thiocarbonyl/carbonyl	C2	145.60	115.2	C10	140.98	110.1	C15	144.64	115.2	C17	145.09	113.4
α to C=S CH_2	C3	17.15	7.2	–			C14	13.23	3.7	–		
α to C=S CH	–			C9	16.22	7.6	–			C7	19.74	11.1
α to N CH_2	C10	−6.86	−15.2	C2	−4.25	−14.0	C17	−3.70	−13.4	C15	−3.32	13.0
α to N CH	C6	−2.32	−5.5	C6	−2.88	−7.5	C11	−3.33	−5.85	C11	1.89	−3.0
β to C=S CH_2/γ to N	C4	−5.44	−5.0	C8	−5.12	−4.9	C13	−6.62	−4.9	C8	−0.20 !	−0.3
β to C=S CH	−			C11	−4.05	5.7	–			C6	−0.42	−1.6
β to N/γ to C=S CH_2	C5	−1.17	−2.5	–			C12	−3.47	−2.1	–		
β to N/γ to C=S CH	–			C7	0	−0.7	–			C9	−0.10	−1.1
β to N CH_2	–			C3	−0.08	−0.9	–			C14	−3.84 !	−1.5
β to N CH_2	–			C5	0.09	−0.5	–			C12	−0.20	−1.2
β to N CH	C7	0.55	−0.7	–			C7	−0.62	−1.0	–		
β to N CH_2	C9	−0.11	−1.3	–			C9	0.47	0.3	–		
γ to N CH_2	C8	−0.66	−0.1	–			C8	−0.35	−0.3	–		
γ to N CH_2	C17	−1.40	0.7	C4	0.06	−0.1	C10	−0.76	−0.5	C13	0.74	0.6
γ to N CH	C11	−1.54	−0.25	–			C6	−1.13	−0.7	–		
γ to C=S/δ to N CH_2	–			C12	−12.47	−12.4	–			C5	+2.77	+1.00
Long distance CH_2	–			C14	−7.24	−7.2	–			C3	+0.29	−0.4

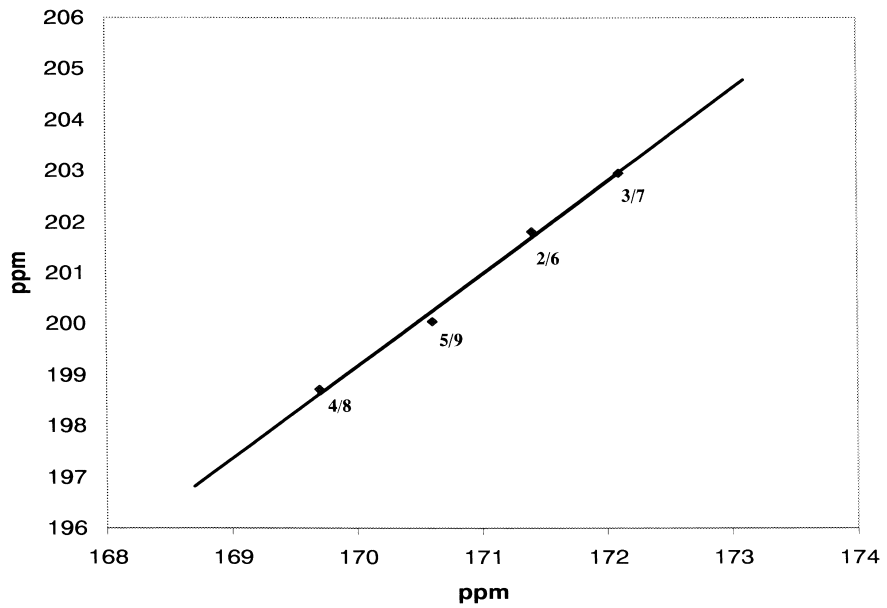

Figure 1. δ ^{13}C═S vs δ ^{13}C═O.

or thiolactam group are the same, they differ only in the geometry (Fig. 1).

Kalinowski and Kessler[17] investigated the relationship between certain ^{13}C═O chemical shifts and the corresponding ^{13}C═S values. The relationship appeared to be linear (Eq. (1)).

$$\delta(C{=}S) = 1.45\ \delta(C{=}O) - 46.5 \quad (1)$$

Katritzky et al.[18] published data for more than 30 pairs of different thiocarbonyl and carbonyl compounds, including those for two pairs of thioamides and amides. The compounds investigated were divided into two groups, and for each of them a specific equation for the ^{13}C═O chemical shifts vs those of ^{13}C═S was derived. The amides/thioamides were included in the group composed of carbamides, thiocarbaminians, thioesters and ketones, and their thio analogues. Statistical analysis of the data for this group led to Eq. (2).

$$\delta(C{=}S) = 1.53\ \delta(C{=}O) - 63.2 \quad (2)$$

Schneider et al.[19] tried to improve a similar equation by introducing partial charge and polarisability terms.

The analysis of our data for thiolactams of sparteine and the literature data for their oxo analogues[7,11,20] led to Eq. (3).

$$\delta(C{=}S) = 1.8086\ \delta(C{=}O) - 108.29 \quad (3)$$

The correlation coefficient obtained is R=0.997 (similar to that in Ref. 17 and better than that in Ref. 18) and the standard deviation is 1.625. The values of the chemical shifts calculated from Equation 3 are very close to the experimental ones (differences vary from 0.01 ppm for 10-thionosparteine/10-oxosparteine to 0.21 ppm for 15-thionosparteine/15-oxosparteine) and are much better than those calculated from Equation 1 and especially from Equation 2. The differences between the values calculated from Equation 2 and the experimental ones for the pairs of thioamides and amides published by Katritzky[18] are 1.63 and 1.96 ppm. When our Equation 3 is applied to the same data, the differences are much smaller (0.84 and 0.70 ppm, respectively). It seems reasonable that also the thioamide/amide systems need a specific equation.

For the same series of relatively rigid sparteine thiolactams, the ^{13}C effects of the C═S group have been determined and compared with the effects of the C═O group on carbon atoms in the related lactams (Table 2). Except for the effects on thiocarbonyl (carbonyl) atoms, the largest are those on carbon atoms at the position α to the C═S group, irrespective of the order of the carbon atom. They are ca. 9–10 ppm greater than the corresponding effects of the C═O group. For the methylene carbon atoms at the α-position to the thiolactam (lactam) nitrogen atom, the effect of the thiocacarbonyl group is negative and amounts to ca. −3 to − 7 ppm and its absolute value is about 9 to 10 ppm lower than that describing the corresponding effects of the C═O group. But when comparing the chemical shifts of the methylene carbon atoms at the α-position to the thiolactam group (both to C═S group and N atom) with those of the corresponding carbon atoms in the lactam analogues, the effect of replacement of oxygen atom by a sulfur atom is almost the same (8.6–9.9 ppm) for the α-carbon atoms to the C═S group as for the α-carbon atoms to N atom (8.3–9.8 ppm).

The effect of the C═S group on the methine carbon atoms at the α-position to thiolactam nitrogen atom is smaller and amounts to ca. −3 ppm, except for 17-thionosparteine (**8**) for which it is positive and small. The absolute value of the C═O effect on the corresponding methine carbon atom is by about 2.5–4.6 ppm larger. Only for 17-oxosparteine (**4**) the effect is negative but the difference in the chemical shifts of this carbon atom between **8** and **4** is ~4.9 ppm.

If the chemical shifts of the carbon atoms at the α-position to the thiolactam or lactam group depended mainly on the heteroatom electronegativity and on the inductive effect, the carbonyl group would be more deshielding than the

thiocarbonyl one. Thus, the real effect of the thiocarbonyl group should be due to the geometry and the size of the group.

The other ^{13}C effects are smaller and even more geometry dependent. Of the β-effects only that on the β-carbon atom to the C═S or C═O group being simultaneously at the γ position to N atom is relatively large and approximately of the same value for both heteroatoms. A very large γ-effect on the C12 and C17 atoms and a long distance effect on the C14 atom in 10-thionosparteine (**7**) and 10-oxosparteine (**3**) is caused by a different conformation of **7** and **3** than that of sparteine (**1**). This could be indicative of the conformation of bis-quinolizidine compounds.

Another value characteristic of the conformation proved to be that of the sum of ^{13}C chemical shifts of all carbon atoms in the molecule.

According to Mikhova et al.,[21] the sum of all ^{13}C chemical shifts $\sum\delta$ is diagnostic for differentiation of sparteine diastereoisomers. The lower the value of $\sum\delta$, the more sterically hindered the isomer.[21,22] It seems reasonable to use the same procedure for the lactams and thiolactams of sparteine when considering their conformation (Table 3).

The lowest value of $\sum\delta$ was found for 10-oxosparteine (**3**), known to occur in the all-chair conformation.[11,23] In this conformation, there is a set of van der Waals repulsion effects of pairs of hydrogen atoms situated close to each other in rings C and D:[24] H8α–H12β, H12β–H17β, and H14β–H17β which are not present in the conformation with a boat (or sofa) conformation of ring C.

The effects are visualised by the ^{13}C high-field shifts for C12, C14, and C17 atoms (22.4 ppm, 18.8 ppm and 46.6 ppm, respectively[11]) caused by the appropriate γ-gauche effects C8–C12, C12–C17 and C14–C17. The same effects are valid in 10-thionosparteine (**7**) in which the chemical shifts of C12, C14 and C17 amount to 22.29, 18.75 and 46.50 ppm, respectively.

The medium values for $\sum\delta$ were obtained for 2-oxosparteine (**2**) and 15-oxosparteine (**5**) and their thionoanalogs, **6** and **9**. Of the two pairs, a little lower values of $\sum\delta$ were found for 2-oxo and 2-thiono derivatives of sparteine, probably because of a small contribution of the conformation with a chair ring C, but the effect can be also affected by e.g. a difference in the geometry of the closest vicinity of the C═O (C═S) bond.

Table 3. The sum of ^{13}C chemical shifts $\sum\delta$ (ppm) in lactams and thiolactams of sparteine in $CDCl_3$

Position of the carbonyl (thiocarbonyl) group	2	10	15	17
Carbonyl compound	709.5[a]	676.4[b]	713.5[c]	730.6[a]
Thiocarbonyl compound	760.25	733.96	761.27	790.23

[a] According to Ref. 20
[b] According to Ref. 11
[c] According to Ref. 7

The highest value of $\sum\delta$ was found for 17-oxosparteine (**4**) and 17-thionosparteine (**8**), less hindered than the other lactams and thiolactams of sparteine. In **4** and **8**, the repulsion of H5α and H17 α protons, present in all other compounds in question, does not occur.

2.1. ^1H NMR spectra

Along with the already published spectra of 2-thionosparteine (**6**) in $CDCl_3$ and C_6D_6,[13] 15-thionosparteine (**9**) in $CDCl_3$,[15] and 17-thionosparteine (**8**) in C_6D_6,[14] the newly recorded spectra of 10-thionosparteine (**7**) and 17-thionosparteine (**8**) in $CDCl_3$ were taken into consideration in a comparative study with the spectra of their oxo analogs **2**, **4** and **5**[25] in C_6D_6 and a spectrum of 10-oxosparteine (aphylline, **3**) in $CDCl_3$.[11] To be able to perform a comparative study for the series, new spectra of **2** and **5** in $CDCl_3$ were also recorded by us. The ^1H chemical shifts of compounds **2**, **5**, **7**, and **8** are presented in Table 4.

To study the thiolactam and lactam effects, proton chemical shifts of sparteine (**1**) in $CDCl_3$[11] and C_6D_6[25] were taken into account. The effects are presented in Tables 5 and 6.

The greatest ^1H deshielding effect is that on the equatorial proton at the α-position to the thiolactam nitrogen atom and at the β-position to the thiocarbonyl group. It amounts to about 3.4–3.6 ppm in C_6D_6 and 3.2–3.3 ppm in $CDCl_3$ solution, except for 15-thionosparteine (**9**), for which it is 2.62 ppm probably for the geometrical reasons. The effect of the C═S group is 1.2–1.6 ppm greater than that of the C═O group.

The other ^1H α-effects are also relatively large. In $CDCl_3$, the equatorial effects of the C═S group are usually by about 0.6–0.8 ppm larger than those of the C═O group, while the axial ones by about 0.2–0.7 ppm larger than those of the C═O group. In benzene solution, the differences in the relative equatorial effects are a little larger than in $CDCl_3$, whereas those of the axial effects—a little smaller.

There are some essential differences in the β and γ-effects measured in chloroform and benzene solutions. In chloroform, most of them are positive, in benzene—negative. It seems reasonable to assume that the main reason is a different kind of interaction of lactams or thiolactams with the two solvents, especially the interaction of the carbonyl or thiocarbonyl group with the aromatic π-electrons of benzene ring.

Some long distance effects are not large and mostly conformation or geometry dependent.

3. Conclusions

Of the two types of NMR methods used here, ^{13}C NMR seems to give more interesting and comprehensive information, especially on the conformation of sparteine thiolactams.

Table 4. ^{1}H Chemical shifts δ (ppm, from TMS) of compounds whose spectra in $CDCl_3$ were recorded for the first time

H atoms	2-Oxosparteine (lupanine, **2**) $CDCl_3$	15-Oxosparteine (**5**) $CDCl_3$	10-Thiono-sparteine (**7**) $CDCl_3$	17-Thiono-sparteine (**8**) $CDCl_3$
2α eq		2.70	5.85	2.72
2β ax		1.97	2.73	1.90
3α ax	2.33	1.49	1.77	1.44[a]
3β eq	2.47	1.57	1.87	1.50[a]
4α eq	1.83	1.72	1.92	1.72
4β ax	1.62	1.22	1.52[b]	1.17
5α ax	1.55	1.34[a]	~1.68[a]	1.82
5β eq	1.76	1.30[a]	~1.68[a]	1.62
6 ax	3.29	1.82	3.41	1.90
7 eq	2.06	1.85	2.03	3.17
8α eq[c]	2.16	1.60	1.84	2.09
8β ax[c]	1.24	1.29	1.63	1.60
9 eq	1.62	1.69	3.04	1.81
10α eq	4.50	2.58		2.79
10β ax	2.51	2.08		2.22
11	1.62	3.55	3.34	3.46
12α eq	1.54	1.92	1.22	1.64
12β ax	1.35	1.54	1.86	1.58
13α ax	1.26	1.67	1.53	1.67
13β eq	1.69	1.77	1.83	1.91
14α eq	1.56[a]	2.42[a]	1.12	1.73
14β ax	1.53[a]	2.35[a]	1.60	1.60
15α ax	1.90		2.85	2.86
15β eq	2.75		2.71	5.84
17α ax	1.93	2.94	3.08[d]	
17β eq	2.82	4.55	2.53[d]	

[a] Second-order fragment.
[b] Determination uncertain.
[c] In ring B.
[d] The signals were assigned on the basis of the long distance coupling of signal at 2.53 ppm with that of H8β.

For a complete series of the four possible sparteine thiolactams, a very well satisfied linear correlation between chemical shifts of C═S and those of C═O in related lactams has been found (Eq. (3)). The correlation coefficient R is 0.997. Equation 3 determined by us is more accurate than a more general Equation 1 published by Kalinowski and Kessler[17] as well as Equation 2 derived by Katritzky et al.[18] for some thiocarbonyl compounds including

Table 5. ^{1}H Effects of thiocarbonyl and carbonyl groups in lactams and thiolactams of sparteine (**1**) in $CDCl_3$

Position	2-Tionosparteine (**6**)/ 2-oxosparteine (**2**)			15-Tionosparteine (**9**)/ 15-oxosparteine (**5**)			10-Tionosparteine (**7**)/ 10-oxosparteine (**3**)			17-Tionosparteine (**8**)	
	H	C═S	C═O	H	C═S	C═O	H	C═S	C═O	H	C═S
α to C═S CH_2 eq	H3β	1.89	1.09	H14α	1.59	0.99	–			–	
α to C═S CH_2 ax	H3α	1.35	0.95	H14β	1.62	0.92	–			–	
α to C═S CH	–			–			H9	1.72	0.87	H7	1.48
α to N CH_2 eq	H10α	3.36	2.12	H17β	2.62	2.01	H2α	3.32	2.11	H15β	3.15
α to N CH_2 ax	H10β	0.87	0.67	H17α	1.29	0.74	H2β	0.94	0.43	H15α	1.00
α to N CH ax	H6	2.20	1.71	H11	1.88	1.72	H6	1.83	1.53	H11	1.63
β to C═S CH_2/γ to N eq	H4α	0.13	0.28	H13β	~0.15	0.22	H8α	−0.07	−0.13	H8β	0.70
β to C═S CH_2/γ to N ax	H4β	0.43	0.54	H13α	~0.55	0.52	H8β	0.73	0.59	H8α	0.18
β to C═S CH	–			–			H11	1.51	1.09	H6	0.32
β to N/γ to C═S CH_2 eq	H5β	0.72	0.64	H12α	0.79	0.71	–			–	
β to N/γ to C═S CH_2 ax	H5α	0.43	0.31	H12β	0.55	0.19	–			–	
β to N/γ to C═S CH	–			–			H7	0.34	0.13	H9	0.49
β to N CH_2 eq	–			–			H3β	0.49	0.12	H14α	0.30
β to N CH_2 ax	–			–			H3α	0.39	−0.10	H14β	0.17
β to N CH_2 eq	–			–			H5β	0.56	0.30	H12α	0.43
β to N CH_2 ax	–			–			H5α	0.44	0.18	H12β	0.25
β to N CH	H7	0.42	0.37	H7	0.31	0.15	–			–	
β to N CH	H9	0.42	0.30	H9	0.50	0.67	–			–	
γ to N CH_2 eq	H8α	0.24	0.25	H8α	−0.35	−0.31	–			–	
γ to N CH_2 ax	H8β	0.46	0.34	H8β	0.52	0.39	–			–	
γ to N CH_2 eq	H17β	0.33	0.28	H10α	0.25	0.20	H4α	0.37	0.17	H13β	0.52
γ to N CH_2 ax	H17α	−0.30	−0.27	H10β	0.28	0.24	H4β	0.44	0.15	H13α	0.36
γ to N CH	H11	0.02	−0.21	H6	0.28	0.24	–			–	
γ to C═S CH_2 eq							H12α	0.01	−0.20	H5α	0.58
γ to C═S CH_2 ax							H12β	0.51	0.36	H5β	0.50

Table 6. The effects of thiocarbonyl and carbonyl groups in lactams and thiolactams of sparteine (**1**) in C_6D_6

Position	2-Tionosparteine (**6**)/ 2-oxosparteine (**2**)			15-Tionosparteine (**9**)/ 15-oxosparteine (**5**)			17-Tionosparteine (**8**)/ 17-oxosparteine (**4**)		
	H	C=S	C=O	H	C=S	C=O	H	C=S	C=O
α to C=S CH_2 eq	H3β	1.94	1.00	H14α		0.86	–		
α to C=S CH_2 ax	H3α	0.99	0.53	H14β		0.60	–		
α to C=S CH	–			–			H7	1.56	0.60
α to N CH_2 eq	H10α	3.60	2.33	H17β		2.28	H15β	3.39	2.35
α to N CH_2 ax	H10β	0.43	0.35	H17α		0.51	H15α	0.37	0.19
α to N CH ax	H6	0.99	1.12	H11		1.17	H11	0.89	0.82
β to C=S CH_2 /γ to N eq	H4α	−0.57	−0.32	H13β		−0.30	H8α	−0.62	−0.60
β to C=S CH_2 /γ to N ax	H4β	−0.07	0.03	H13α		−0.07	H8β	0.14	0.20
β to C=S CH	–			–			H6	0.96	0.05
β to N/γ to C=S CH_2 eq	H5β	−0.02	0.23	H12α		−0.16	–		
β to N/γ to C=S CH_2 ax	H5α	−0.33	−0.30	H12β		−0.42	–		
β to N/γ to C=S CH	–			–			H9	−0.26	−0.20
β to N CH_2 eq	–			–			H14α	−0.30	−0.03
β to N CH_2 ax	–			–			H14β	−0.22	−0.44
β to N CH_2 eq	–			–			H12α	−0.27	−0.24
β to N CH_2 ax	–			–			H12β	0.52	−0.42
β to N CH	H7	−0.31	−0.19	H7		−0.22	–		
β to N CH	H9	−0.06	−0.09	H9		−0.20	–		
γ to N CH_2 eq	H8α	−0.33	−0.20	H8α		−0.95 !	–		
γ to N CH_2 ax	H8β	−0.21	−0.14	H8β		−0.07	–		
γ to N CH_2 eq	H17β	−0.17	−0.12	H10α		−0.24	H13β	−0.28	−0.33
γ to N CH_2 ax	H17α	−0.77	−0.64	H10β		0.51 !	H13α	−0.21	−0.13
γ to N CH	H11	−0.16	−0.41	H6		−0.12	–		

thioamides. Equation 3 is more accurate for the two pairs of thioamides and amides reported by Katritzky[18] than Katritzky's Equation 2.

The knowledge of the ^{13}C NMR effects of the thiolactam group or, more generally, thiocarbonyl group, could be of some help in the spectra assignment. Also the interpretation of the spectra published here was improved having established this effect.

The other important value characteristic of the conformation proved to be that of the sum of ^{13}C chemical shifts of all carbon atoms in the molecule. The smallest is the value for 10-oxo- (**3**) or 10-thionosparteine (**7**) which have the most sterically hindered conformation, that with chair ring C, whereas the largest is the value for 17-oxosparteine (**4**) and 17-thionosparteine (**8**), less hindered than the other lactams and thiolactams of sparteine.

^1H NMR spectra do not deliver as valuable effects as ^{13}C NMR for both assignment of the spectra and geometry or conformation determination of the compounds but they could also be of some help. The ^1H effects of the thiolactam group are generally greater than those of the lactam group, especially the α-effects. It is interesting that the effects are strongly solvent dependent.

The NMR data corroborate the conformation similarity of the corresponding pairs of lactams and thiolactams of sparteine.

Both, the linear correlation between the chemical shifts of C=S and those of C=O in related lactams (Eq. (3)) and the effects of the thiolactam group could be also used in interpretation of the spectra of other classes of thiocarbonyl compounds and in determination of their conformation.

4. Experimental

4.1. General

All melting points were measured on a VEB Wagetechnik Rapido PHMK apparatus and are uncorrected. IR spectra were recorded with a Bruker 113v spectrometer. Gcms analyses were performed and EI mass spectra were recorded on an AMD 402 mass spectrometer.

4.2. NMR spectra

The ^1H and ^{13}C NMR spectra (including $^1H-^1H$ COSY and $^{13}C-^1H$ COSY) were recorded at 293 K on a Varian 300 Mercury spectrometer at 300.13 and 75.462 MHz, respectively. The concentrations were ca 0.15 M. The conditions of the spectra: ^{13}C NMR: number of transients 10000, acquisition time 1.5 s, spectral width 13,718 Hz, number of points 27372, digital resolution 0.50 Hz. ^1H NMR spectra: number of transients 64, acquisition time 3.0 s, the 90° pulse width 8 μs, the 45° pulse width 4 μs, spectral width 9000 Hz, number of points 54016, digital resolution 0.167 Hz per point.

$^1H-^1H$ COSY 90-90: relax. delay 1 s, acquisition time 0.138 s, spectral width 1856.5 Hz, 2D width 1856.5 Hz, 16 repetitions, 256 increments, data processing—sine bell 0.069 s, f_1 data processing sine bell 0.069 s.

$^{13}C-^1H$ COSY: relax. delay 1 s, acquisition time 0.093 s, spectral width 5519.7 Hz, 2D width 1856.5 Hz, 512

repetitions, 256 increments, data processing—sine bell 0.046 s, f_1 data processing sine bell 0.068 s.

The ^1H and $^1H-^1H$ COSY spectra of **2**, **5** and **8** were also recorded with a Bruker Avance 600 spectrometer equipped with a 5 mm TBI ^1H inverse probe head, operating at 600.13 MHz. The concentrations were ca 0.05 M. The conditions of the spectra.

^1H NMR: number of scans 16, acquisition time 6.606 s, 90° pulse width 9 μs, 30° pulse width 3 μs, spectral width 4960.3 Hz, data points 6536, digital resolution 0.076 Hz per point.

$^1H-^1H$ Gs COSY: number of scans 4, acquisition time 0.206 s, spectral width 4960.3 Hz, 1024 repetitions, 512 increments, data processing—sine bell 0.046 s, f_1 data processing sine bell.

Apodization:[26] Lorentzian/Gaussian, LB −1.5, GB 0.25.

4.3. Compounds

4.3.1. (+)-2-Oxosparteine 2. Was isolated from seeds of *Lupinus angustifolius* cv. Mirela according to the procedure described previously.[5] (−)-15-Oxosparteine **5** and (+)-17-oxosparteine **4** were prepared from (−)-sparteinium salt and characterised according to the procedure described previously.[7]

The thiolactam analogues: (+)- 2-thionosparteine **6**,[13] (+)-15-thionosparteine **9**[15] and (+)-17-thionosparteine **8**[14] were obtained from the appropriate lactams according to the methods described previously and were characterised as in Ref. 13–15.

4.3.2. (±)-10-Oxosparteine 3. Was isolated from seeds of *Lupinus mexicanus* according to the procedure described previously.[5] (±)-10-Oxosparteine **3** was contained in the ethyl ether extract. The crude extract was chromatographed on a neutral Al_2O_3 column (1:100) with 150 ml portions of Et_2O, $Et_2O-CH_2Cl_2$ 4:1, $Et_2O-CH_2Cl_2$ 3:1, $Et_2O-CH_2Cl_2$ 3:2 and CH_2Cl_2, collecting fractions of 30 ml each. The fractions $Et_2O-CH_2Cl_2$ (3:1) contained mainly **3** and small amounts of other alkaloids. This mixture was rechromatographed on a column with silica gel (1:75), using mixture of pentane and ethyl ether (1:2). After evaporation (±)-10-oxosparteine **3** was obtained; oil; IR (KBr) 1641 cm^{-1}; ^{13}C NMR ($CDCl_3$)[7] δ 172.1; 59.0; 58.7; 53.9; 43.8; 46.6; 42.2; 32.4; 28.8; 25.4; 25.0; 24.6; 22.7; 22.4; 18.8; *m/z*: 248 (M^+), *m/z*: 136 (100). Anal. calcd for $C_{15}H_{24}N_2O$ (248): C, 72.54, H, 9.74, N, 11.28. Found: C, 72.48, H, 9.70, N, 11.25.

4.3.3. (±)-10-Thionosparteine 7. Lactam **3** (0.032 g, 0.13 mmol) and Lawesson's reagent (0.042 g, 0.10 mmol) were refluxed in toluene (5 ml) for 5 h. The solvent was evaporated at reduced pressure. The excess of Lawesson's reagent was removed on the column filled with 4 g of Al_2O_3 (neutral) using mixture of ethyl ether and dichloromethane (1:1). The solvents were evaporated and the residue was settled in a column with 2 g of neutral Al_2O_3 and eluted with ethyl ether. After evaporation oil was obtained; yield 44%; oil; IR (KBr) 1506 cm^{-1}. ^{13}C NMR ($CDCl_3$) δ 203; 63.6; 60.4; 54.3; 52.4; 52.0; 46.5; 33.1; 29.4; 25.8; 25.2; 24.8; 22.5; 22.3; 18.8; *m/z*: 264 (M^+), *m/z*: 231 (100). Anal. calcd for $C_{15}H_{24}N_2S$ (264): C, 68.13; H, 9.15; N, 10.59. Found: C, 68.07; H, 9.10; N, 10.58.

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