Structure Determination of Some 5,6-Dihydropyrrolo-[1,2-*a*][3,1,6]benzothiadiazocines

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The conformation of compounds **1** and **2** has been determined in the solid state by X-ray crystallography and in solution by nmr spectroscopy. MM2 and molecular dynamics calculations were used to determine the conformation of compound **2** *in vacuo* and in solution.

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In an earlier paper the synthesis of several derivatives of the novel 5,6-dihydropyrrolo[1,2-*a*][3,1,6]benzothiadiazocine ring system was reported [1]. We now wish to present the conformation of compounds **1** and **2** determined in the solid state by X-ray crystallography, and in solution by nmr spectroscopy. For compound **2** the conformation *in vacuo* and in solution has been studied by MM2 and molecular dynamics calculations. The nmr spectral data of compound **3** are also used in our discussion.

Description of the Structures.

The heterocycles studied are 5,6,8-tricyclic systems. In molecule **1** the 8-membered ring can be described as a slightly twisted "boat" where atoms C(11a), C(7a), C(5), S(4) are approximately coplanar (max deviation 0.029 Å), while atoms N(7), C(6), C(3a), and N lie below this plane at distances -1.11, -1.17, -1.19 and -0.97 Å respectively. The deviation from the "boat" conformation is more pronounced in compound **2**. In this case atoms N(7), C(6), C(3a), N and C(5) are more or less coplanar (deviations of 0.15, -0.17, 0.16, -0.14 and 0.13 Å) while atoms C(7a), C(11a), and S(4) lie below the plane at distances -0.89, -1.06 and -0.74 Å respectively. This distorted conformation is achieved by rotation around the bond C(5)-C(6) resulting in an almost staggered configuration of the ethylene group. Molecule **2** has acquired an "extended" conformation with a distance N-C(21) of 9.34(1) Å, stabilised by intermolecular interactions. The angles between the 6-membered ring of the tosyl group and the two other aromatic rings of **2** are 162 and 55° with the 6-membered and the 5-membered ring respectively. The geometries of the aromatic rings are unremarkable. Tables 1 and 2 contain some selected bond lengths, bond angles and torsional angles for the two compounds. ORTEP views of the two molecules are presented in Figures 1 and 2.

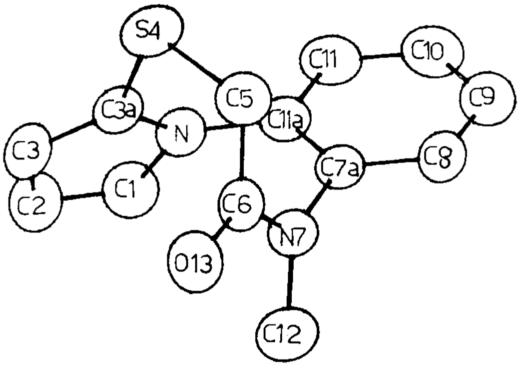


Figure 1. ORTEP view of molecule **1**.

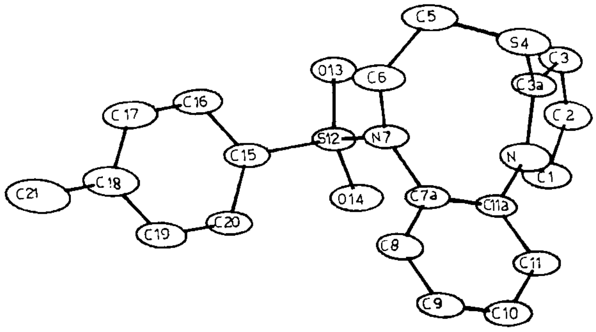


Figure 2. ORTEP view of molecule **2**.

NMR Spectral Analysis.

The pyrrole proton data, of all compounds, were assigned by their typical intra-pyrrole coupling constants. A

Table 1

Selected Bond Lengths (Å) for Compounds **1** and **2**

Bond	Length/Å **1**	 **2**
C(3a)-S(4)	1.736(2)	1.746(4)
S(4)-C(5)	1.830(2)	1.819(8)
C(5)-C(6)	1.502(3)	1.514(7)
C(6)-N(7)	1.355(3)	1.473(4)
N(7)-C(7a)	1.431(2)	1.435(6)
C(11a)-N	1.427(3)	
C(6)-O(13)	1.228(2)	
N(7)-C(12)	1.456(3)	
S(12)-O(13)		1.427(2)
S(12)-O(14)		1.429(2)
S(12)-C(15)		1.761(6)
C(18)-C(21)		1.495(11)

comparison of the proton data (Table 4) of compounds **1** and **3** shows that three of the four benzene protons resonate at ≈7.5 ppm while the fourth resonates at 7.4 ppm. The pattern of coupling constants of this latter resonance indicates that it arises from a proton with only one *ortho* coupling, H(8) or H(11). We used the NOE difference experiment to show that irradiation of the methyl group at position(7), in compound **1** gave a positive enhancement of the signal at 7.37 ppm. We therefore assign this resonance to proton H(8) based on the X-ray data which gave a distance of 3.28 Å between this proton and the methyl carbon which we have taken as an approximate centre of rotation of the methyl protons when the compound is in solution. In contrast, the inter-atomic distance between this methyl carbon and proton H(11) is 5.13 Å. This spectrum

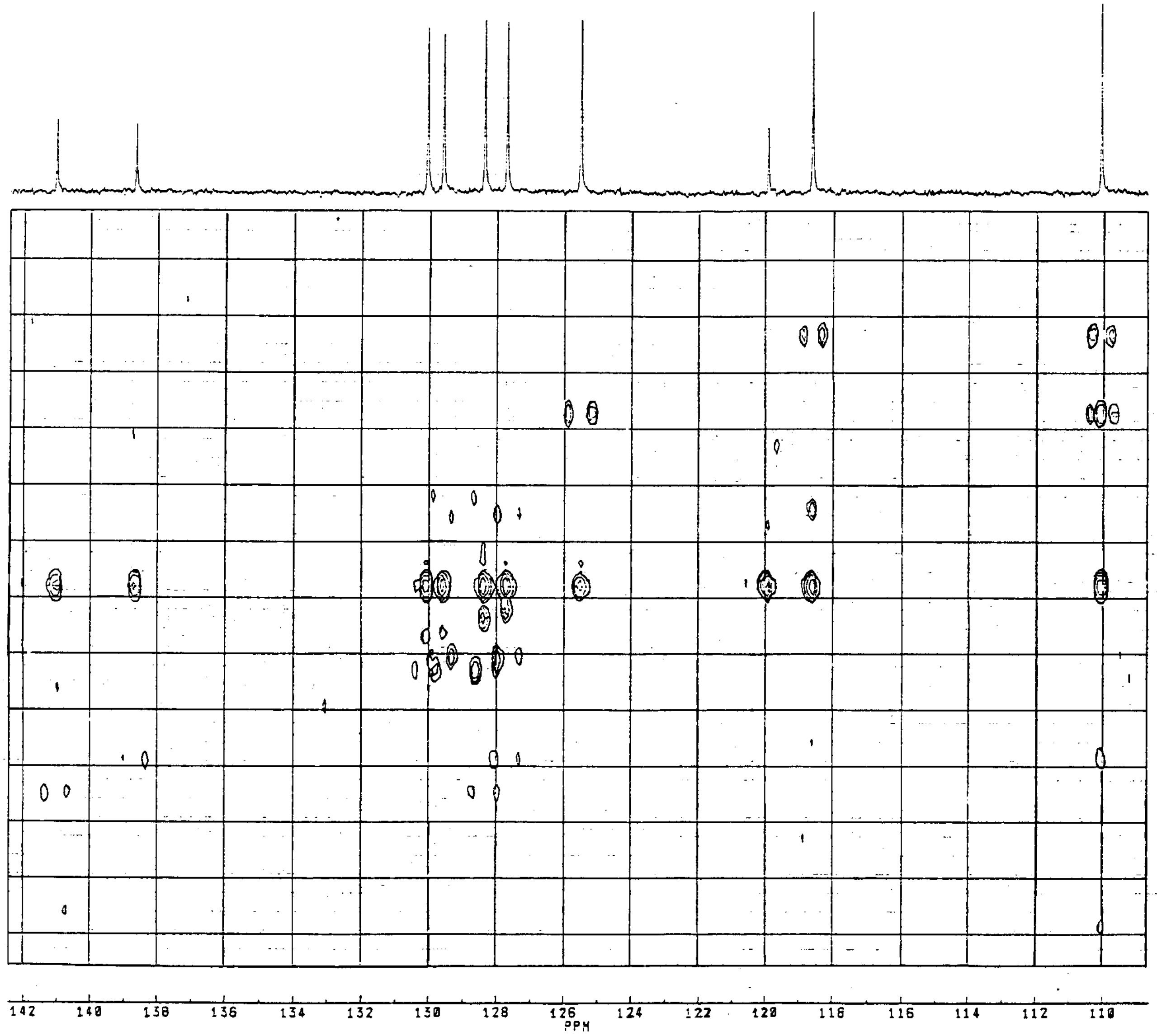


Figure 3. 2D-INADEQUATE spectrum of compound **1** in a saturated solution of deuteriochloroform showing the C-C connectivity of the aromatic regions of the compound.

Table 2

Selected Bond Angles (°) for Compounds **1** and **2**

Bond	Angle/° **1**	**2**
N-C(3a)-S(4)	122.5(2)	123.2(2)
C(3a)-S(4)-C(5)	104.0(1)	103.8(3)
S(4)-C(5)-C(6)	112.1(1)	114.2(4)
C(5)-C(6)-N(7)	116.7(2)	112.3(4)
C(6)-N(7)-C(7a)	123.5(2)	119.0(4)
N(7)-C(7a)-C(8)	120.0(2)	120.6(5)
N(7)-C(7a)-C(11a)	120.1(2)	120.1(2)
C(7a)-C(11a)-C(11)	120.6(2)	120.4(3)
C(7a)-C(11a)-N	118.8(2)	120.8(4)
C(11a)-N-C(3a)	124.8(2)	127.0(3)
S(4)-C(3a)-C(3)	129.7(2)	129.6(2)
C(5)-C(6)-O(13)	120.7(2)	–
O(13)-C(6)-N(7)	122.6(2)	–
C(6)-N(7)-C(12)	118.8(2)	–
C(12)-N(7)-C(7a)	116.8(2)	–
N(7)-S(12)-O(13)	–	107.1(2)
N(7)-S(12)-O(14)	–	106.5(2)
O(13)-S(12)-C(15)	–	106.9(2)
O(14)-S(12)-C(15)	–	109.5(2)
S(12)-C(15)-C(16)	–	120.3(3)
S(12)-C(15)-C(20)	–	119.4(4)
C(17)-C(18)-C(21)	–	121.1(6)
C(19)-C(18)-C(21)	–	120.3(3)

Table 3

Selected Torsional Angles for Compounds **1** and **2**

Compound **1**

Atom1	Atom2	Atom3	Atom4	Angle
C(8)	C(7a)	N(7)	C(12)	-84.5(3)
C(8)	C(7a)	N(7)	C(6)	106.4(2)
C(7a)	N(7)	C(6)	O(13)	174.3(2)
C(7a)	N(7)	C(6)	C(5)	-6.2(3)
N(7)	C(6)	C(5)	S(4)	83.9(2)
C(6)	C(5)	S(4)	C(3a)	-15.8(2)
C(5)	S(4)	C(3a)	C(3)	116.9(2)
C(5)	S(4)	C(3a)	N	-71.1(2)
S(4)	C(3a)	N	C(11a)	19.3(3)
C(3a)	N	C(11a)	C(7a)	60.2(3)
C(3a)	N	C(11a)	C(11)	-121.0(2)

Compound **2**

Atom1	Atom2	Atom3	Atom4	Angle
C(8)	C(7a)	N(7)	S(12)	-166.7(7)
C(8)	C(7a)	N(7)	C(6)	76.1(7)
C(7a)	N(7)	C(6)	C(5)	99.6(5)
N(7)	C(6)	C(5)	S(4)	-57.8(5)
C(6)	C(5)	S(4)	C(3a)	77.1(3)
C(5)	S(4)	C(3a)	C(3)	98.9(7)
C(5)	S(4)	C(3a)	N	-91.0(6)
S(4)	C(3a)	N	C(11a)	11(1)
C(3a)	N	C(11a)	C(7a)	57.7(8)
C(3a)	N	C(11a)	C(11)	-125.0(6)
O(14)	S(12)	C(15)	C(16)	-141.0(4)
O(13)	S(12)	C(15)	C(20)	171.7(3)
H(5b)	C(5)	C(6)	H(6a)	67(2)
H(5a)	C(5)	C(6)	H(6b)	-175(2)

Table 4

Proton Chemical Shifts in ppm

Proton	Compound **1** [a]	**2** [a]	**3** [b]
(1)	6.86	6.96	6.84
(2)	6.26	6.33	6.26
(3)	6.54	6.60	6.56
(5a)	3.2	2.82	3.22
(5b)	3.54	2.55	3.53
(6a)	–	4.41	–
(6b)	–	3.32	–
(8)	7.37 [c]	7.1 [c]	7.37 [c]
(9)	7.56	7.38	7.53
(10)	7.56	7.48	7.53
(11)	7.56	7.36	7.53
	2.84 [d]	–	–
(13), (17)	–	7.36	–
(14), (15)	–	7.21	–
(18)	–	2.38	–

[a] 13 mg/ml. [b] Benzene chemical shifts quoted as centre of multiplet. [c] 15 mg/ml. [d] Methyl.

Table 5

Proton-proton coupling Constants

Proton	Compound **1**	**2** [a]	**3**
(1)-(2)	2.96	2.98	2.96
(1)-(3)	1.71	1.81	1.72
(2)-(3)	3.61	3.61	3.62
(5a)-(5b)	-10.05	-14.22	-10.42
(5a)-(6a)	–	3.64	–
(5a)-(6b)	–	12.74	–
(5b)-(6a)	–	1.71	–
(5b)-(6b)	–	2.80	–
(6a)-(6b)	–	-14.91	–
(7)-(5a)	–	–	1.36 [b]

[a] RMS error = 0.02 Hz. [b] Long range coupling measured in DMSO-d_6.

also shows a positive, though slight, enhancement of the pyrrole proton H(1), which from X-ray data, has an interatomic distance of 3.97 Å to the methyl carbon. Further structural information can be deduced from the analogous but aromatic pyrrolo[1,2-*a*]quinoxaline **4** which shows a marked downfield shift of protons H(1) and H(9) [2] when compared to the equivalent H(1) and H(11) protons of compounds **1-3** described in this paper. The deshielding of the pyrroloquinoxaline protons is caused by the Van der Waals interaction arising from the close proximity of these protons in the planar compound. The absence of such deshielding in compounds **1-3** indicates that the benzene and pyrrole rings are not in the same plane. The benzene proton signals for compound **2** are more dispersed than for compounds **1** and **3**, this is caused by the influence of the tosyl group at position(7) of the former, and consequently the assumption that the most upfield of these signals arises from H(8) for this compound may not be justi-

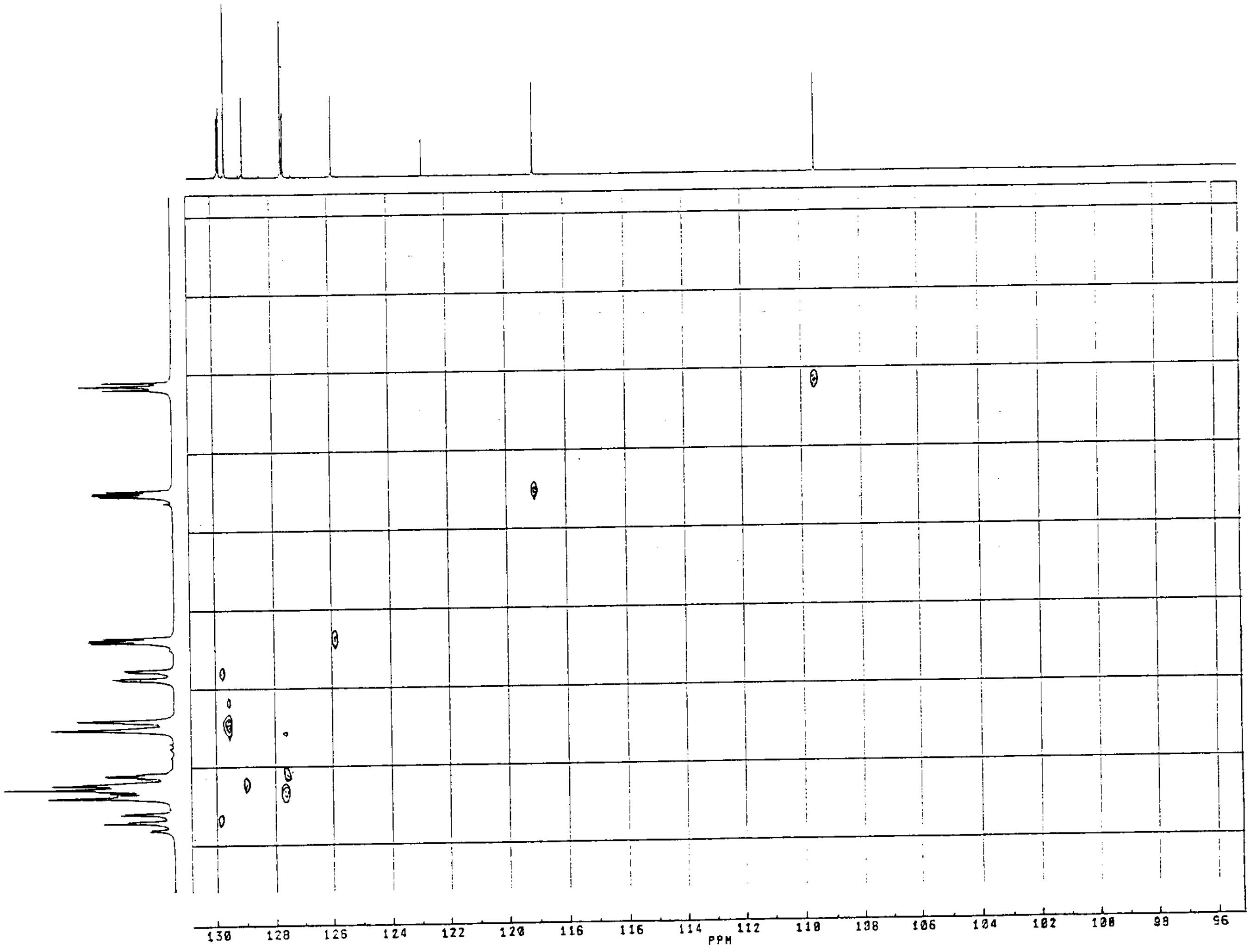


Figure 4. C-H correlation spectrum of compound **2** in a saturated solution of deuteriochloroform showing the correlation between the aromatic carbon and protons.

fied. However, analysis of quaternary carbon coupling assigns the upfield benzene signal at 7.1 ppm in deuteriochloroform to H(8) *vide-infra*. This shielding effect on H(8) is expected to arise from the conjugation of the lone-pair of electrons from N(7) which is greater on C(8), hence H(8), than on C(11). Homonuclear decoupling of H(8) revealed that the most downfield benzene signal in compound **2** arises from proton H(10) because it retained both of the *ortho* couplings during the experiment.

For the same compound the two most downfield signals in the aliphatic region were assigned to the geminal protons H(6a) and H(6b) since this pair of protons is adjacent to the more electronegative N(7). This is supported by quaternary long-range couplings discussed later.

The cmr analysis (Tables 6 and 7) on all of the compounds was achieved by several techniques. Where possible, carbons bonded to assigned protons with discrete signals were assigned by selective decoupling. This technique was particularly useful for assignment of C(8) in all the compounds. However, for compounds **1** and **3** where the remaining benzene proton signals coincided, assignment was achieved in compound **1** by carbon-carbon connectivity using the 2D-INADEQUATE pulse sequence. The 2-D spectrum (Figure 3) of compound **1** shows the C(8) signal at 128.6 ppm (previously assigned) to be connected to the downfield doublet (in the cluster of the four protonated benzene signals) arising from C(9) at 130.2 ppm. Similarly, connectivity is shown between the signal from C(8) and the signal at 141.3 ppm from the quaternary C(7a). The doublets arising from signals at 127.9 and 129.7 ppm show connectivity, and we have assigned the signal at 127.9 ppm to C(11) because the spectrum also shows connection to the remaining benzene quaternary C(11a) signal at 139 ppm, thus the signal at 129.7 ppm is assigned to C(10).

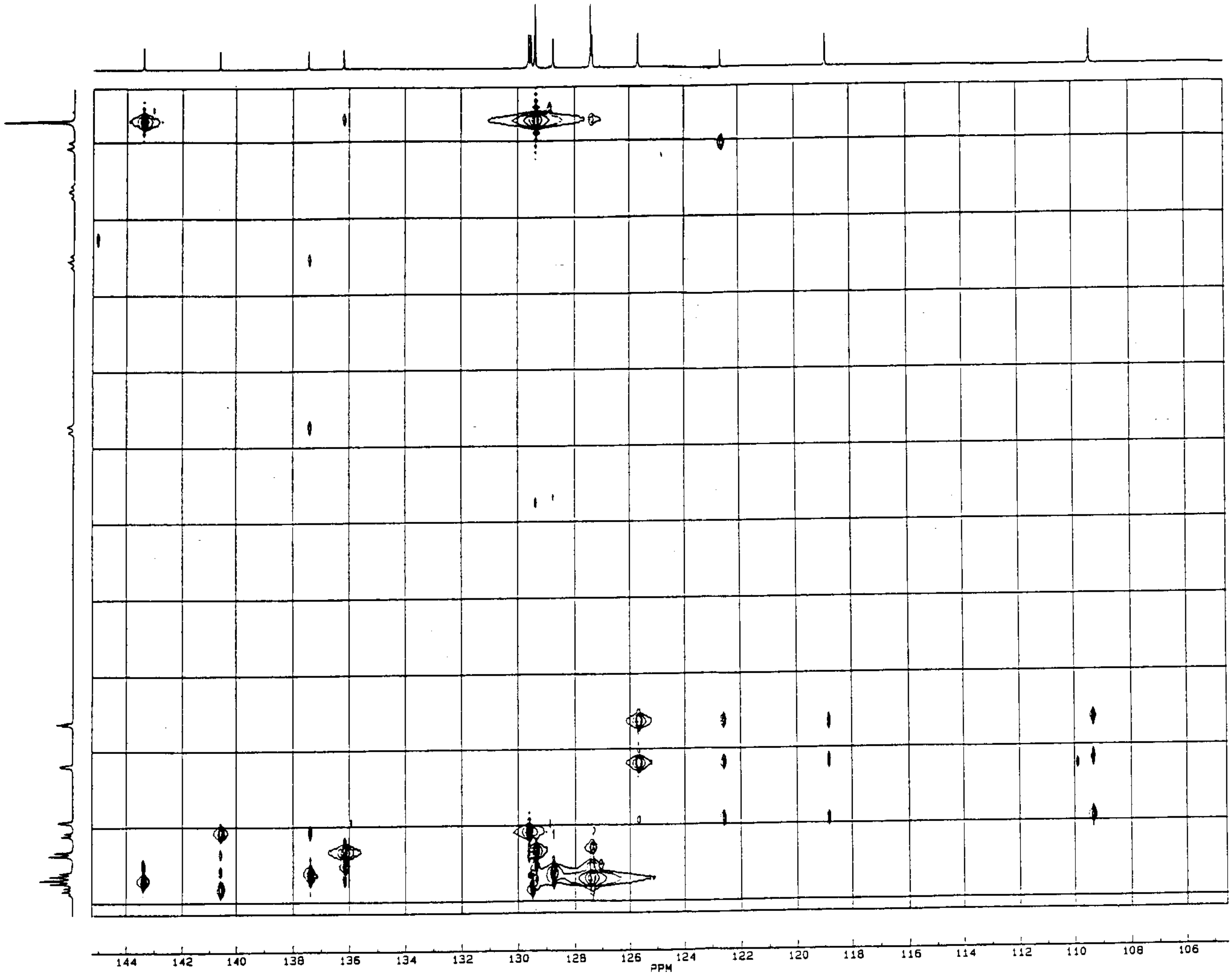


Figure 5. C-H long range coupled correlation spectrum of compound **2** showing the aromatic carbon region correlated with the aromatic and aliphatic proton region.

There is no connectivity shown between the signals of C(9) and C(10), however, this is probably due to the proximity of these signals.

Complete assignment of the benzene carbons in compound **3** was not achieved because of the proximity of signals arising from C(8), C(9) and C(10). Only C(8), by selective decoupling, and C(11) by analogy to compound **1**, have been assigned. The assignment of benzene the quaternary carbons in compound **3** is also uncertain.

Carbon assignment of compound **2** has been achieved by carbon-proton shift correlation through one-bond (Figure 4) and long-range (Figure 5) coupling constants. The benzene C(8) and C(10) are close in chemical shift but can be assigned because of the better dispersed proton signals of H(8) and H(10). On the other hand, C(9) and C(10) give rise to better dispersed signals but the assignment is uncertain because of the proximity of the corresponding proton signals which are also obscured by the downfield signal from the tosyl protons. By analogy with compound **1**, we assign C(11) to the resonance at 127.7 ppm, also, in support of this assignment we ascribe C(9) to the resonance at 128.9 because the signal arising from this carbon in the carbon-proton coupled spectrum gives rise to a simple double-doublet. It has been shown by Günther *et al* [3] that this pattern is associated with the terminal pair of carbons in naphthaline type structures even though the proton spectra are non-first order. Carbon-proton coupled spectra of the quarternary carbon resonances have been obtained for all the compounds thus these coupling constants greatly assist in acquiring structural information. However, it was not possible to make an unambiguous assignment of these carbons in compound **2**, we therefore used the 2—D experiment for the carbon-proton correlation through long-range coupling constants [4]. In this

Table 6

Carbon Chemical Shifts

Proton	Compound **1** [a]	 **2** [a]	 **3** [b]
(1)	125.67	125.9	126.2
(2)	110.30	109.6	110.3
(3)	118.90	119.1	119.1
(3a)	120.23	122.9	119.9
(5)	35.65	38.2	34.3
(6)	167.34	54.5	170.2
(7a)	141.34	137.8	139.9 [e]
(8)	128.56	129.8 [d]	129.6
(9)	130.19	128.9	129.8 [c]
(10)	129.74	129.9 [d]	129.4 [c]
(11)	127.95	127.7	127.7
(11a)	138.98	140.9	134.2 [e]
	36.95 [f]	–	–
(12)	–	136.6	–
(13), (17)	–	127.8	–
(14), (16)	–	129.5	–
(15)	–	143.6	–
(18)	–	21.6	–

[a] 13 mg/ml. [b] 15 mg/ml. [c], [d], [e] pairs of assignments may be reversed. [f] Methyl.

Table 7

Carbon-proton Coupling Constants

Compound **1** [a]

Carbon	H(1)	H(2)	H(3)	H(5a)	H(5b)
(3a)	6.6	6.6	9.0	4.5	0.5
(5)	–	–	–	145.1	142.7

Compound **2** [b]

Carbon	H(1)	H(2)	H(3)	H(5a)	H(5b)	H(6a)	H(6b)
(3a)	6.2	6.2	9.2	9.2	3.0	–	–
(5)	–	–	–	146.2	136.2	3.0 [c]	
(6)	–	–	–	3.5 [c]	136.7	141.6	
(7a)	–	–	–	–	–	3.2	3.2

Compound **3** [a]

Carbon	H(1)	H(2)	H(3)	H(5a)	H(5b)
(3a)	6.4	6.4	8.6	4.9	1.2

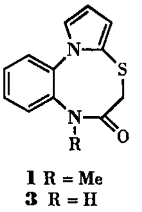
[a] Saturated solution in DMSO-d_6. [b] Saturated solution in deuteriochloroform. [c] Assignments may be reversed.

Table 8

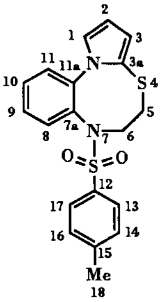
Crystal Data and Intensity Collection Data for Compounds **1** and **2**

		1	**2**
Formula		$C_{13}H_{12}N_2OS$	$C_{19}H_{18}N_2O_2S_2$
MW		244.32	370.49
Space group		$P2_1/c$	C2/c
Cell dimensions	a, Å	12.528(3)	29.950(4)
	b, Å	11.148(2)	7.754(2)
	c. Å	8.889(2)	25.819(4)
	β, °	107.66(2)	143.76(2)
V, A^3		1183.01	3544.81
Z		4	8
dx, gcm^{-3}		1.371	1.388
Total reflections		2249	3361
Significant reflections (l > 3σ(I))		1907	2284
Refined parameters		190	226
R		0.044	0.045
Rw		0.058	0.049
G.O.F		1.3	1.2

experiment, the most intense peaks arose from coupling constants of approximately 4 to 10 Hz (optimised at 5.8 Hz) which covers the range for three bond coupling in the benzene and tosyl ring. Identification of the tosyl quaternary carbons, C(12) and C(15), is shown by C(15) at 143 ppm being correlated to the methyl protons and, through the three-bond coupling, to the proton pair H(13) and H(17), identified in the cluster centered at 7.4 ppm. C(12) at 135.3 ppm shows correlation through the three-bond coupling to the tosyl proton signal centered at 7.2 ppm which arises from protons H(14) and H(16). Of the two benzene quaternaries, C(7a) is distinguished from C(11a) by coupling through N(7) to H(6a) and H(6b). C(7a) also shows a strong signal which arises from the three-bond couplings to the benzene H(9) and H(11) which resonate in the cluster centered at 7.4 ppm. It follows that the two three-bond couplings of the remaining quaternary carbon C(11a) at 140.9 ppm, must be assigned to H(8) and H(10). The pyrrolic quaternary C(3a) resonates at 122.9 ppm and the correlation spectrum shows the expected coupling constants to the three pyrrolic protons, however, it also shows there is an additional coupling constant between C(3a) to one of the methylene protons of C(5). Information for the conformation of compounds **1** and **3** is limited from the proton data (Table 5) as there is only one methylene pair of protons in the aliphatic ring. However, for compound **3** there is a long-range coupling at 1.4 Hz through four-bonds to the methyl proton H(5b), this suggests co-planarity of the five atoms H(7), N(7), C(6), C(5) and H(5a), which form a W path. From the X-ray data of compound **1** the above atoms are also approximately co-planar (maximum deviation -0.05, 0.02, 0.02, -0.03 and 0.29 Å respectively), if one equates the orientation of the N-H bond with the N-Me bond.



1 R = Me
3 R = H



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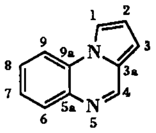

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Karplus equation [5] with the H-nmr data from the methylene protons at positions(5) and (6), the three-bond coupling constants of compound suggested the approximate dihedral angles to be H(5a)-C(5)-C(6)-H(6a) -40°, H(5b)-C(5)-C(6)-H(6a) 80°, and H(5b)-C(5)-C(6)-H(6b) -50°.

From the X-ray data the corresponding dihedral angles were calculated to be H(5a)-C(5)-C(6)-H(6a) -57.4°, H(5b)-C(5)-C(6)-H(6a) 67° and H(5b)-C(5)-C(6)-H(6b) -57°. We therefore conclude that the conformation of the 8-membered ring in compound **2** in solution shows a slight deviation from the X-ray conformation probably due to distortion in the "boat" conformation as discussed in the MM2 and molecular dynamics section.

Comparison of the carbon-proton coupled spectra (Table 7) of C(3a) between compounds **1** and **3** shows only slight differences in the coupling constants to the methylene protons which suggests that there is only a small pertubation between the two structures. This proton coupled spectrum of C(3a) in compound **1** shows an eleven line multiplet which contains 5 couplings of 9, 6.6, 6.6, 4.5, and 0.5 Hz. The latter coupling was estimated from measurement of the line width as it could not be resolved. However, comparison with the same type of spectrum of the compound dissolved in deuteriochloroform where this coupling was resolved, it was shown to be 0.6 Hz. The pyrrolic proton couplings to C(3a) are easily identified as the three largest coupling constants leaving the two minor couplings of 4.5 and 0.5 Hz identified as the three-bond couplings across the sulfur to H(5a) and H(5b). The X-ray data gave the dihedral angle, C(3a)-S(4)-C(5)-H(5a), as -133° and the dihedral angle C(3a)-S(4)-C(5)-H(5b), as 113°. From the Karplus relationship, we assign J(C3a,-H5a) coupling as 4.5 Hz and J(C3a,H5b) as ~0.5 Hz.

Similarly, for compound **2**, the X-ray data gave dihedral angle, C(3a)-S(4)-C(5)-H(5a) as -48° and the C(3a)-S(4)-C(5)-H(5b) dihedral angle as -166°. We, therefore, assign the J(C3a,H5a) coupling as 3.0 Hz and the J(C3a,H5b) coupling as 9.2 Hz.

Long-range coupling between the benzene quaternary carbon, C(7a), and the two methylene protons H(6) and H(6a), gave additional information.

The fully proton coupled spectrum shows a broad multiplet but selective irradiation at very low power reduces the multiplet to a triplet composed of two equal couplings of 3.2 Hz. X-ray data gave the dihedral angles C(7a)-N(7)-C(6)-H(6a) and C(7a)-N(7)-C(6)-H(6b) as -142° and -25° respectively.

Molecular Mechanics and Molecular Dynamics Calculations for Compound 2.

Strain-energy calculations were performed using the Chem3D Plus V.3 [6] package which contained a module for MM2 (molecular mechanics version 2) [7]. The MM2 parameters used are described at [6] with two modifications from the default Chem3D Plus values a) setting the quartic stretching constant to zero and b) the cutoff distances to 40 Å in order to reproduce MM2 energies. Some MM2 parameters were obtained from Leonard *et al.* [9] while a few related to sulfur-nitrogen part of the 8-membered ring were derived using the procedures described by Kao *et al.* [8]. The results of energy-minimization '*in vacuo*' produced a structure where the tosyl group was away from the three fused-ring system. Overall there is reasonable agreement between the energy-minimized '*in vacuo*' structure and the X-ray results. Furthermore a calculation was performed using the X-rays structure measurements. The energy for both cases was practically the same.

In order to investigate the solvent effect the energy minimized '*in vacuo*' molecule was put in a 'bath' enveloped by 35 deuteriochloroform molecules. Subsequently a molecular dynamics (MD) computation was initiated consisting of a series of integration steps which occurred at a fixed interval of 1 femtosecond (10^{-15} sec). Target temperature was set at 308 K. 2000 steps were required for a slow rise to the desired temperature (heating rate 1.0 Kcal/-atom/picosecond). Subsequently the system was left to compute an isoenthalpic trajectory for 15 picoseconds setting the heating/cooling rate to zero. The MD study points to an important feature, namely that the tosyl group folds towards the three-ring system. The distance of the carbon atom of the methyl group from the nitrogen of the pyrrolic ring during the 15 picoseconds MD is on average 5.5 Å while the initial structure and the X-ray results show an ex-

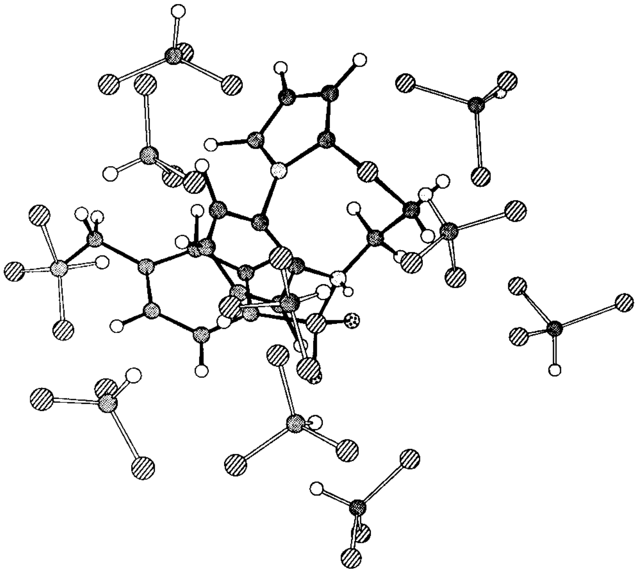

Figure 6. Preferred sites of the molecule **2** accessible to the solvent molecules.

tended structure of 9.1 Å. The nmr study does not provide conclusive evidence for the extent of the folding.

In addition, at certain intervals during the equilibrium period of the MD study a number of configurations were taken and energy-minimized after removing the solvent molecules. All structures obtained this way, remained folded and two of them were providing a better MM2 energy minimum by 2 kcal/mol.

The effect of the solvent was more pronounced for the C(3a)-S(4)-C(5)-C(6) part of the 8-membered ring. The corresponding dihedral angle varies considerably (±40 degrees). Hence the "boat" conformation of the 8-membered ring is subject to substantial distortion. The parts of the 8-membered ring which are connected to the benzene and pyrrole were showing much less mobility (±15 degrees). The C(6)-N(7)-N-C(3a) dihedral angle indicates a distortion from planarity around 25 degrees. The C(3a)-S(4)-C(5)-H(5a) dihedral angle has a value -150°, and the C(3a)-S(4)-C(5)-H(5b) 110°, while the C(7a)-N(7)-C(6)-H(6a) is -170° and the C(7a)-N(7)-C(6)-H(6b) is -60°.

Figure 6 shows the preferred sides of the molecule **2** that are accessible from the solvent molecules.

Figure 7 depicts a folded structure taken from the MD trajectory and energy-minimized.

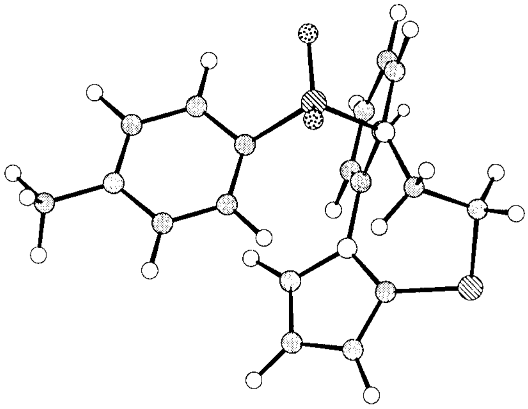

Figure 7. Folded structure of molecule 2 taken from the MD trajectory and energy minimized.

EXPERIMENTAL

Crystal and Molecular Structure Determination of **1** and **2**.

Crystals were obtained by recrystallisation from aqueous ethanol (compound **1**) and propan-2-ol (compound **2**) solutions.

The X-ray data were collected at room temperature in the ω-2θ scan mode ($\theta \leq 70$) on an Enraf Nonius CAD4 diffractometer equipped with graphite monochromator and Cu-target X-ray tube (λ = 1.5418 Å). Intensity data were corrected for Lorentz and polarization effects. The absorption was disregarded. Cell dimensions together with other experimental parameters are indicated in Table 8. Only reflections with I $> 3\sigma$(I) were retained for

Table 9

Positional Parameters for Compounds 1 and 2

(standard deviations in parentheses)

Compound **1**

Atom	x	y	z
N	0.1238(1)	0.6178(2)	0.2486(2)
C(1)	0.0753(2)	0.5063(2)	0.2254(3)
C(2)	0.9803(2)	0.5093(2)	0.2699(3)
C(3)	0.9714(2)	0.6259(2)	0.3254(3)
C(3a)	0.0607(2)	0.6915(2)	0.3138(2)
S(4)	0.0896(1)	0.8430(1)	0.3486(1)
C(5)	0.2191(2)	0.8452(2)	0.5142(3)
C(6)	0.2427(2)	0.7261(2)	0.5967(2)
N(7)	0.2953(1)	0.6430(2)	0.5333(2)
C(7a)	0.3187(2)	0.6594(2)	0.3868(2)
C(8)	0.4278(2)	0.6821(2)	0.3861(3)
C(9)	0.4513(2)	0.6882(2)	0.2435(3)
C(10)	0.3670(2)	0.6711(2)	0.1025(3)
C(11)	0.2580(2)	0.6509(2)	0.1028(3)
C(11a)	0.2346(2)	0.6438(2)	0.2450(2)
C(12)	0.3119(3)	0.5231(3)	0.6011(4)
O(13)	0.2156(1)	0.7071(2)	0.7162(2)
H(1)	0.106(2)	0.444(3)	0.177(3)
H(2)	-0.066(2)	0.435(3)	0.268(3)
H(3)	-0.083(2)	0.650(3)	0.369(3)
H(5a)	0.212(2)	0.897(3)	0.584(3)
H(5b)	0.276(3)	0.873(3)	0.492(3)
H(9)	0.528(2)	0.704(3)	0.239(3)
H(10)	0.393(2)	0.678(3)	0.010(3)
H(11)	0.191(2)	0.635(2)	0.002(2)
H(12a)	0.386(2)	0.538(2)	0.717(3)
H(12b)	0.351(2)	0.477(3)	0.568(3)
H(12c)	0.240(2)	0.499(3)	0.596(3)

Compound **2**

Atom	x	y	z
N	0.5860(1)	0.0998(4)	0.2619(2)
C(1)	0.6023(2)	-0.0683(4)	0.2905(2)
C(2)	0.6704(2)	-0.0699(5)	0.3785(2)
C(3)	0.6965(2)	0.0994(5)	0.4053(2)
C(3a)	0.6448(2)	0.2049(5)	0.3336(2)
S(4)	0.6412(2)	0.4299(1)	0.3280(1)
C(5)	0.6812(2)	0.4823(5)	0.3024(3)
C(6)	0.6279(2)	0.4533(5)	0.2075(2)
N(7)	0.6009(1)	0.2739(4)	0.1795(2)
C(7a)	0.5276(2)	0.2327(4)	0.1310(2)
C(8)	0.4628(2)	0.2755(5)	0.0428(2)
C(9)	0.3920(2)	0.2337(5)	-0.0037(2)
C(10)	0.3857(2)	0.1523(5)	0.0372(2)
C(11)	0.4501(2)	0.1120(4)	0.1260(2)
C(11a)	0.5207(2)	0.1513(4)	0.1723(2)
S(12)	0.6467(1)	0.1381(1)	0.1860(1)
O(13)	0.7251(1)	0.1616(3)	0.2697(1)
O(14)	0.6126(1)	-0.0268(3)	0.1620(2)
C(15)	0.6312(2)	0.2052(4)	0.1071(2)
C(16)	0.6872(2)	0.2890(5)	0.1326(2)
C(17)	0.6737(2)	0.3436(5)	0.0698(3)
C(18)	0.6048(2)	0.3164(4)	-0.0183(2)
C(19)	0.5484(2)	0.2327(4)	-0.0432(2)
C(20)	0.5610(2)	0.1756(4)	0.0184(2)
C(21)	0.5906(3)	0.3748(6)	-0.0859(3)

Table 9 (continued)

Atom	x	y	z
H(1)	0.566(1)	-0.165(1)	0.247(1)
H(2)	0.699(1)	-0.179(1)	0.416(1)
H(3)	0.742(1)	0.152(1)	0.466(1)
H(5b)	0.691(1)	0.604(1)	0.312(1)
H(5a)	0.735(1)	0.402(1)	0.351(1)
H(6a)	0.655(1)	0.477(1)	0.203(1)
H(6b)	0.581(1)	0.537(1)	0.164(1)
H(8)	0.469(1)	0.329(1)	0.017(1)
H(9)	0.346(1)	0.256(1)	-0.069(1)
H(10)	0.338(1)	0.126(1)	0.009(1)
H(11)	0.449(1)	0.062(1)	0.158(1)
H(16)	0.729(1)	0.307(1)	0.187(1)
H(17)	0.711(1)	0.413(1)	0.087(1)
H(19)	0.496(1)	0.207(1)	-0.112(1)
H(20)	0.520 (1)	0.118(1)	0.002(1)
H(21a)	0.631(1)	0.443(1)	-0.061(1)
H(21b)	0.545(1)	0.454(1)	-0.135(1)
H(21c)	0.570(1)	-0.287(1)	0.372(1)

the solution of the structures using the SDP software package [10]. E-maps revealed all non hydrogen atoms, and the hydrogen atoms appeared on difference maps. Refined parameters were calculated [11] by using anisotropic thermal parameters for non hydrogen atoms and isotropic factors for hydrogen atoms. Atomic positional parameters are listed in Table 9.

With the exception of ^{15}N spectra which were recorded on a Brüker 250 MHz spectrometer at 25.3 MHz, all spectra were recorded on a Brüker AM 360 spectrometer, the carbon resonance being 90.56 MHz.

Carbon and proton chemical shifts were referenced to TMS at the concentrations given in the tables. However, the deuteriochloroform (or DMSO-d_6) solvent resonance was used as a reference for 2-D and 1-D carbon-proton coupled spectra. For the proton coupled spectra of the quaternary carbons, compounds **1** and **3** had to be dissolved in DMSO-d_6 in order to achieve the required solubility. It was, however, possible to dissolve enough of compound **1** in deuteriochloroform for a comparison of these coupling constants in a different solvent.

Quaternary carbon signal enhancement was achieved by using the DEPT pulse sequence [12] which was modified for lows power selective decoupling of the benzene protons in order to observe coupling between these carbons and the aliphatic protons.

The digital resolution for the proton spectra was 0.06 Hz/pt while that for the carbon spectra with proton coupling was 0.25 Hz/pt. Proton-proton and carbon-proton coupling constants that were used for structural determination were calculated using the Brüker PANIC programme, based on the LAOCOON 3 programme, run on the ASPECT 3000 computer. RMS error values were 0.2 Hz for proton-proton couplings and 0.17 Hz for carbon-proton couplings.

REFERENCES AND NOTES

[1] G. W. H. Cheeseman, A. A. Hawi and G. Varvounis, *J. Heterocyclic Chem.*, **22**, 423 (1985).

[2] M. L. Heffernan and G. M. Irvine, *Austr. J. Chem.*, **29**, 837 (1976).

[3] H. Günther, H. Schmickler and G. Jikeli, *J. Magn. Reson.*, **11**, 344 (1973).

[4] H. Kessler, C. Griensinger, J. Zarbock and H. R. Loosli, *J. Magn. Reson.*, **57**, 331 (1984).

[5] M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963).

[6] Chem3D Plus version 3.0, The Molecular Modeling System software package, Cambridge Scientific Computing, Cambridge, MA, 1991.

[7] N. L. Allinger MM2(77) Quantum Chemistry Program Exchange (QCPE) Department of Chemistry, Bloomington, Indiana 47405, Program 395.

[8] J. Kao and D. Leister, *J. Am. Chem. Soc.*, **110**, 7286 (1988).

[9] J. M. Leonard and W. P. Ashman, *J. Comp. Chem.*, **11**, 952 (1990).

[10] SDP: Structure Determination Package, Enraf Nonius, Delft, The Netherlands, 1977.

[11] G. M. Sheldrick, SHELX 76, Program for Crystal Structure Determination, University of Cabridge, U.K., 1976.

[12] M. R. Bendell and D. T. Pegg, *J. Magn. Reson.*, **53**, 272 (1983).