Tetrahedron Vol. 38, No. 5, pp. 665 to 672, 1982
Printed in Great Britain.

0040-4020/82/050665-08$03.00/0
Pergamon Press Ltd.

SYNTHESIS, SPECTRAL PROPERTIES AND CONFORMATIONAL PREFERENCES OF MACROCYCLIC COMPOUNDS CONTAINING 2,5-DITHIO-1,3,4-THIADIAZOLE SUBUNITS

F. BOTTINO and S. PAPPALARDO*
Istituto Dipartimentale di Chimica e Chimica Industriale dell'Università di Catania, Viale A. Doria 6, 95125 Catania, Italy

(*Received in UK 4 August* 1981)

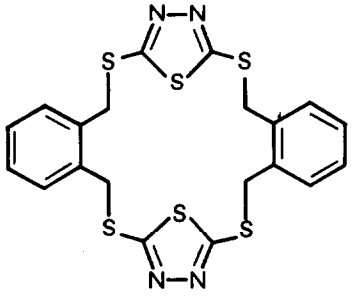
Abstract—The syntheses of macrocycles **1–6**, containing 2,5 - dithio - 1,3,4 - thiadiazole subunits connected by 1,2-, 1,3- and 1,4-bis(methylene)benzenes, as well as of the appropriate open-chain model compounds **7–12** are described. Structure proofs were afforded by their mass and ^{1}H NMR spectra. Different decomposition processes upon electron-impact are ascertained for compounds **1–12**, depending on the position of the bridges and *ortho* substitution; therefore, the mass spectra can provide a sensitive diagnostic tool for structure elucidation of positional isomers. The NMR spectral data of macrocycles **1–6**, coupled with those of the corresponding open-chain derivatives **7–12**, indicate that the preferred conformations are determined primarily by the size and shape of their ring systems. Furthermore, variable-temperature NMR studies on intraannularly methyl substituted macrocycles **3** and **6** provide evidence that the 20-membered mesityl derivative **3** adopt the saddle-shape conformation (IV) (the energy barrier for the restricted rotation of methylene bridges is found to be $\Delta G^{\neq}$ = 13.8 kcal/mole at +5°), while the duryl groups in the 22-membered macrocycle **6** are free rotating even at −60°.

Recently, a rapidly growing interest has been focused on the construction of synthetic macrocyclic compounds containing heterocyclic subunits, because these compounds have been shown to possess unique chemical and biochemical properties.[1]

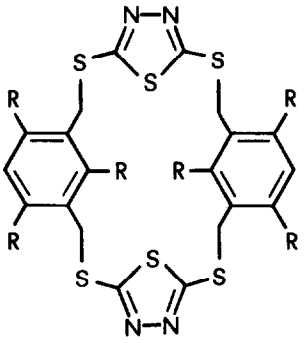
In view of the biological[2] and analytical[2,3] interest in 1,3,4-thiadiazole sulphur derivatives, as well as the limited examples of 1,3,4-thiadiazole inclusion in a macrocyclic framework,[4] we herein describe the synthesis and characterization of macrocycles **1–6**, containing 2,5 - dithio - 1,3,4 - thiadiazole subunits connected by 1,2-, 1,3- and 1,4-bis(methylene)benzenes, respectively, as well as of their open-chain counterparts **7–12**.

As easily recognized from inspection of Scheme 1, the molecular design of these macrocycles was directed to provide 18-, 20- and 22-membered macrocycles with the purpose both to obtain different sizes and shapes of the central hole, and to evaluate possible steric hindrance effects of intraannular substituents.

The structural characterization of compounds **1–12** has been achieved by their mass and ^{1}H NMR spectra. Owing to the lack of information about the electron-impact mass spectral fragmentation of 1,3,4-thiadiazole sulphur derivatives,[5] the mass spectra are of particular interest; furthermore, they can provide a sensitive diag-

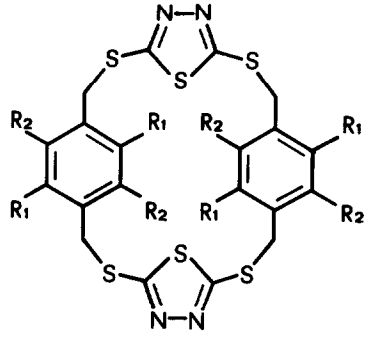


1



2 R = H

3 R = Me

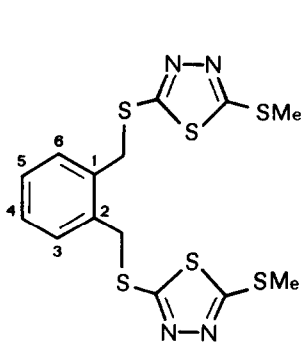


4 $R_1 = R_2 = H$

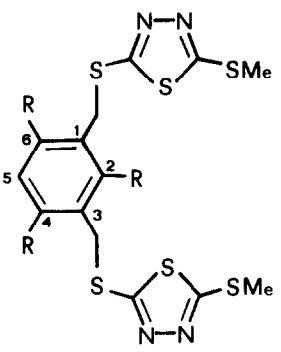
5 $R_1 = H$; $R_2 = Me$

6 $R_1 = R_2 = Me$

Scheme 1.

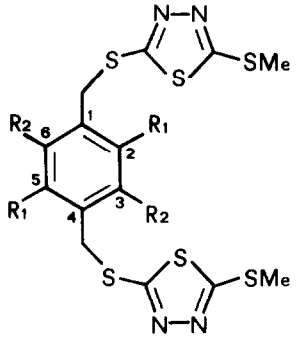


7



8 R = H

9 R = Me



10 $R_1 = R_2 = H$

11 $R_1 = H$; $R_2 = Me$

12 $R_1 = R_2 = Me$

nostic tool for structure elucidation of positional isomers. The conformation and conformation mobility of macrocycles **1–6** were also deduced by comparison of their ^1H NMR spectra with those of open-chain model compounds **7–12**, and by variable-temperature NMR analysis.

Further work on related macrocyclic compounds is in progress in this laboratory.

RESULTS AND DISCUSSION

Syntheses. Macrocycles **1–6** were prepared through nucleophilic displacement reactions starting from the dipotassium salt of 2,5 - dimercapto - 1,3,4 - thiadiazole and the appropriate bis(halomethyl)benzene derivatives in boiling ethanol, under high dilution conditions.

The open-chain model compounds **7–12** were obtained by coupling the sodium salt of 2-mercapto-5-methyl-thio-1,3,4-thiadiazole with the appropriate bis(halomethyl)benzene derivatives in dimethylformamide (DMF) at 80°.

The analytical and physical properties, and the ^1H NMR spectral parameters of compounds **1–12** are shown in Table 1. Further structural proofs were afforded by their mass spectra.

Macrocycles **1–6** are colourless crystalline materials, reasonably soluble in organic solvents. The yields vary from 4% for **1** to 36% for **4**. The higher yields observed for the 22-membered macrocycles **4–6** are a direct consequence of increased ring size and diminished steric hindrance effects. On the other hand, excellent yields (75–95%) were observed for open-chain compounds **7–12**. They show good solubility in common solvents, with the exception of the sparingly soluble duryl derivative **12**, which dissolves in hot DMF, dimethylsulphoxide, and *o*-dichlorobenzene.

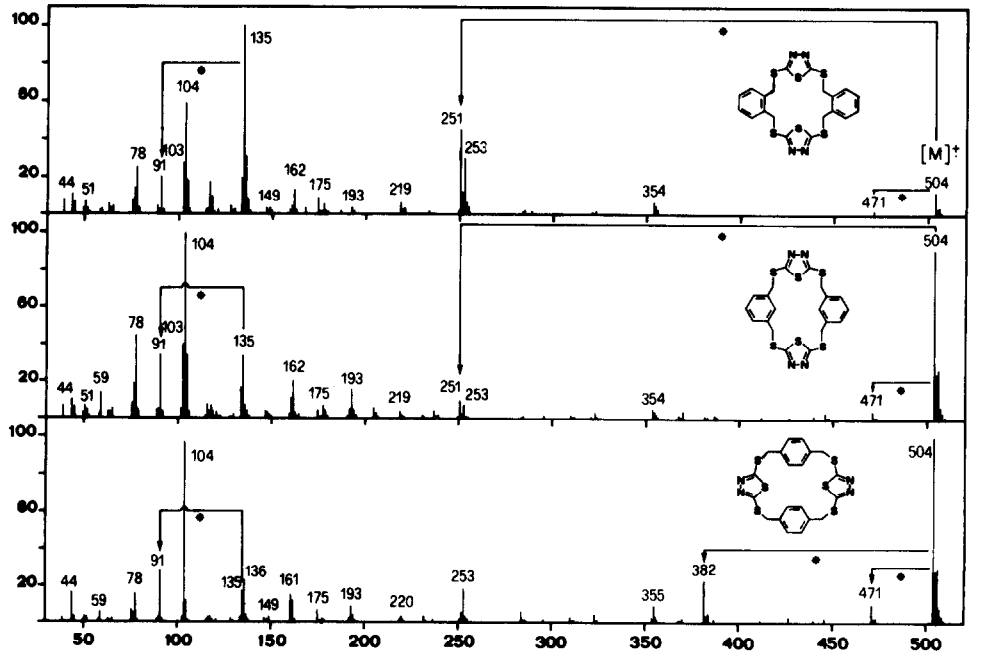


Fig. 1. The mass spectra (70 eV) of the isomeric macrocycles **1**, **2** and **4**.

Table 1. Analytical and physical properties, and ^{1}H NMR spectral parameters (δ ppm) in $CDCl_3$ of compounds 1–12[a]

Compound	M.p. (°C)	Yield, %	Formula (MW)	Nitrogen, % Calcd	Nitrogen, % Found	C-1,H	C-2,H	C-3,H	C-4,H	C-5,H	C-6,H	SCH_3
1	236-238	4	$C_{20}H_{16}N_4S_6$ (504.77)	11.10	10.84	4.94	4.94	7.47	7.47	7.47	7.47	-
2	240-242	15	$C_{20}H_{16}N_4S_6$ (504.77)	11.10	11.25	4.32	7.15[b]	4.32	7.26[b]	7.26[b]	7.26[b]	-
3	273-275	6	$C_{26}H_{28}N_4S_6$ (588.94)	9.51	9.77	4.45[b]	1.62	4.45[b]	2.42	7.00	2.42	-
4	243-244	36	$C_{20}H_{16}N_4S_6$ (504.77)	11.10	10.91	4.43	7.40	7.40	4.43	7.40	7.40	-
5	256-258	28	$C_{24}H_{24}N_4S_6$ (560.88)	9.99	10.24	4.47[c]	7.17[c]	2.27[c]	4.47[c]	7.17[c]	2.27[c]	-
6	290	23	$C_{28}H_{32}N_4S_6$ (616.99)	9.08	8.96	4.66	2.23	2.23	4.66	2.23	2.23	-
						4.44[d]	2.10[d]	2.10[d]	4.44[d]	2.10[d]	2.10[d]	-
7	oil	75	$C_{14}H_{14}N_4S_6$ (430.69)	13.01	12.78	4.76	4.76	7.47[e]	7.47[e]	7.47[e]	7.47[e]	2.80
8	oil	80	$C_{14}H_{14}N_4S_6$ (430.69)	13.01	12.95	4.52	7.54[b]	4.52	7.43[b]	7.43[b]	7.43[b]	2.79
9	136-137	89	$C_{17}H_{20}N_4S_6$ (472.77)	11.85	11.95	4.68	2.51	4.68	2.43	7.01	2.43	2.83
10	124-126	86	$C_{14}H_{14}N_4S_6$ (430.69)	13.01	13.15	4.53	7.48	7.48	4.53	7.48	7.48	2.81
11	147-148	92	$C_{16}H_{18}N_4S_6$ (458.75)	12.21	12.36	4.55	7.27	2.40	4.55	7.27	2.40	2.82
						4.58[c]	7.38[c]	2.35[c]	4.58[c]	7.38[c]	2.35[c]	2.80[c]
12	215-219	95	$C_{18}H_{22}N_4S_6$ (486.80)	11.51	11.29	4.60[d]	2.25[d]	2.25[d]	4.60[d]	2.25[d]	2.25[d]	2.63[d]

[a] Unless otherwise stated, the signals appear as singlets. [b] Broad singlét. [c] In $DMSO_{d6}$. [d] In o-dichlorobenzene. [e] Center of a complex symmetrical multiplet.

Table 2. The mass spectra (70 eV) of macrocycles 3, 5 and 6, and of model compounds 7–12

Compound	m/e (rel. intensity)[a]
3	588(6), 555(3), 439(3), 354(4), 295(9), 294(4), 293(7), 262(3), 261(7), 204(5), 179(3), 178(4), 177(10), 176(8), 175(4), 163(5), 162(4), 161(3), 160(3), 150(4), 149(3), 148(17), 147(73), 146(45), 145(72), 144(3), 135(4), 134(13), 133(21), 132(6), 131(21), 130(13), 129(10), 128(8), 119(8), 118 (3), 117(10), 116(8), 115(13), 107(8), 106(13), 105(21), 104(5), 103(5), 97(5), 95(4), 93(5), 92(4), 91(25), 85(4), 84(5), 83(8), 82(5), 81(7), 79(7), 78(11), 77(14), 76(10), 74(5), 73(18), 71(6), 70 (8), 69(12), 68(5), 67(10), 66(4), 65(8), 64(5), 63(5), 60(4), 59(41), 58(6), 57(14), 56(15), 55 (27), 54(5), 53(9), 52(4), 51(11), 50(7), 46(5), 45(7), 44(100), 43(21), 42(17), 41(37), 40(7), 39 (23).
5	562(8), 561(8), 560(25), 528(3), 527(8), 410(4), 409(3), 281(6), 280(4), 279(4), 261(3), 190(4), 189(3), 164(5), 163(7), 149(4), 148(3), 133(15), 132(100), 131(7), 129(17), 119(9), 118(5), 117 (19), 116(4), 115(8), 105(3), 91(12), 77(3), 76(3), 59(7), 44(5), 41(3), 39(4).
6	616(6), 585(3), 584(4), 583(11), 309(7), 308(4), 307(6), 275(4), 191(6), 190(4), 177(5), 176(3), 162(5), 161(36), 160(100), 159(13), 158(4), 147(6), 146(4), 145(28), 144(4), 133(4), 131(3), 130(7), 129(7), 128(5), 119(3), 117(3), 115(4), 105(7), 91(6), 77(3), 76(5), 59(15), 44(17), 42(8), 41(4)..
7	430(0.4), 269(8), 268(22), 267(50), 266(95), 265(16), 253(3), 235(4),234(3), 233(18), 219(5), 191(5), 190(4), 178(3), 166(6), 165(3), 164(30), 162(13), 161(4), 147(3),137(6), 136(16), 135(100), 134(19), 133(4), 131(28), 128(5), 119(3), 118(28), 117(11), 116(3), 115(4), 105(22), 104(38), 103 (32), 102(4), 93(4), 91(34), 90(3), 89(4), 88(14), 85(3), 79(4), 78(18), 77(13), 76(13), 74(6), 73 (20), 72(9), 65(4), 64(6), 63(4), 59(19), 58(8), 51(6), 47(15), 46(14), 45(18), 44(10), 39(5).

8 430(6), 270(3), 269(15), 268(20), 267(100), 266(15), 234(3), 233(3), 219(4),193(3), 190(4), 178 (3), 166(3), 164(22), 162(9), 161(5), 151(3), 149(5), 148(3), 147(3), 136(3), 135(21), 134(6), 121 (5), 118(11), 117(8), 116(4), 105(16), 104(30), 103(12), 91(20), 90(4), 89(3), 88(9), 78(12), 77(7), 76(8), 74(3), 73(7), 72(3), 65(3), 64(5), 59(13), 58(5), 51(3), 47(8), 46(8), 45(12), 44(6), 39(3).

9 472(1.1), 311(4), 310(8), 309(25), 308(17), 275(5), 177(4), 165(3), 164(14), 147(15), 146(21), 145(100), 131(8), 130(6), 129(4), 128(3), 117(3), 116(3), 115(5), 105(5), 91(8), 88(5), 76(4), 73 (4), 59(6), 47(4), 46(4), 45(6), 44(3).

10 430(6), 269(13), 268(24), 267(100), 266(54), 234(13), 190(3), 164(10), 162(4), 161(5), 136(3), 135(14), 117(6), 105(7), 104(31), 103(7), 91(20), 88(4), 78(6), 77(3), 76(5), 73(4), 59(7), 47(4), 46(4), 45(6), 44(4).

11 460(6), 459(5), 458(21), 298(3), 297(15), 296(26), 295(100), 294(58), 262(5), 261(5), 247(4), 190(4), 189(4), 164(21), 163(17), 162(3), 149(3), 148(6), 145(5), 133(22), 132(49), 131(22), 119 (11), 118(5), 117(19), 116(6), 115(9), 105(4), 91(17), 88(8), 77(3), 76(7), 73(6), 72(3), 64(4), 59(9), 58(4), 47(6), 46(7), 45(10), 44(6), 39(3).

12 486(2.3), 325(9), 324(15), 323(60), 322(27), 290(3), 289(15), 218(4), 191(3), 190(17), 189(3), 177(6), 176(7), 175(4), 174(15), 166(5), 165(8), 164(38), 162(6), 161(44), 160(91), 159(100), 158 (30), 147(12), 146(7), 145(43), 144(8), 143(6), 133(5), 132(3), 131(8), 130(15), 129(17), 128(11), 127(3), 119(7), 117(7), 116(4), 115(10), 105(15), 103(3), 91(30), 90(3), 88(21), 79(4), 77(7), 76 (15), 74(4), 73(11), 72(5), 65(4), 64(8), 59(23), 58(8), 53(4), 51(3), 48(4), 47(14), 46(15), 45 (20), 44(10), 41(6), 39(5).

---

[a] Unless mentioned in the text, peaks with relative intensities less than 3% are discarded.

Mass spectra. The mass spectra of the isomeric parent macrocycles **1**, **2** and **4** are shown in Fig. 1, while those of the remaining compounds **3** and **5–12** are listed in Table 2.

The electron-impact induced mass spectral fragmentation of macrocycles **1–6** may occur as a multistep reaction through different mechanisms, depending on the substitution pattern and the position of the bridges. For instance, the decomposition process of macrocycle **1** is strongly affected by a prominent *ortho* effect.[6] The first step probably involves the macroring opening (rate determining step), which may proceed *via* a 6-membered cyclic transition state by a benzylic hydrogen transfer to the opposing sulphur bridged atom, as shown in Scheme 2. The rearranged molecular ion subsequently might undergo the cleavage of the CH_2–S bond (fast step) to generate either the $[M/2-1]^+$ ion or the $[M/2+1]^+$ ion at *m/e* 251 and 253, respectively. Such a mechanism is verified both by the fact that the molecular ion suffers the loss of a SH radical (characteristic of all macrocycles investigated)[7] and by the presence in the mass spectrum of a metastable peak at about *m/e* 125, supporting the suggestion that the $[M/2-1]^+$ ion is formed directly from the molecular ion. The $[M/2-1]^+$ ion then decomposes to give the fragments at *m/e* 219, 193, 175 and 135 (base peak) by loss of S, SCN, CS_2 and $(SCN)_2$, respectively, from the heteroaromatic portion, and the fragment at *m/e* 103 by cleavage of the CH_2–S bond. On the other hand, the "alternative" $[M/2+1]^+$ ion gives rise to the fragments at *m/e* 162 and 104 by loss of $HCNS_2$ or cleavage of the CH_2–S bond, respectively.

Alternatively, different macroring opening mechanisms can be envisaged for the isomeric macrocycles **2** and **4**, which may involve a 5-membered cyclic transition state by a benzylic hydrogen transfer to the nitrogen atom of the adjacent 1,3,4-thiadiazole ring. As a consequence, different intensities of the main peaks are observed (e.g. the $[M/2-1]^+$ ion is almost absent in macrocycle **4**, as well as the fragment at *m/e* 103; in addition, in the high mass range an intense peak at *m/e* 382, arising from the molecular ion by direct loss of a thiobenzaldehyde molecule, is present), which allow a differentiation of the three positional isomers to be performed.

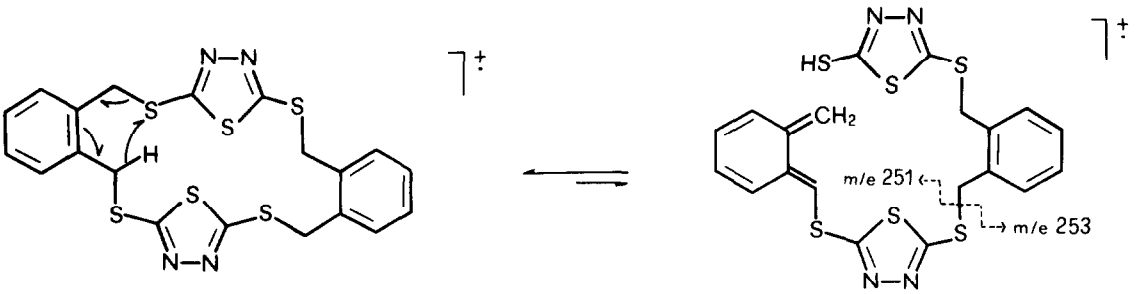
The decomposition process upon electron-impact of polymethylated macrocycles **3**, **5** and **6** is very similar to that of macrocycle **1**. The macroring opening may occur *via* a 6-membered cyclic transition state by a methyl hydrogen transfer to the adjacent bridged sulphur atom. The rearranged molecular ion subsequently undergoes the fission of the CH_2–S bond to give both $[M/2-1]^+$ and $[M/2+1]^+$ ions. The peak at *m/e* 44 (CS) is the base peak in **3**, while in **5** and **6** the base peak is due to the *para* quinoid forms of the hydrocarbon portion of the molecules (peaks at *m/e* 132 ($C_{10}H_{12}$) and 160 ($C_{12}H_{16}$), respectively).

The open-chain derivatives **7–12** give molecular ions which are easily recognized, with the exception of compounds **7** and **9**, for which very weak parent peaks are observed (Table 2). Two main consecutive (and competing) decomposition paths of the molecular ion are observed: (i) the cleavage of the CH_2–S bond to give the ion A (verified in most cases by the appropriate metastable peaks) and (ii) the subsequent ejection of a molecule of 2 - mercapto - 5 - methylthio - 1,3,4 - thiadiazole, through the above mentioned 5- or 6-membered McLafferty rearrangements, to give the ion B. The fragmentation pattern relative to compound **9** is shown in Scheme 3. Due to the competition of paths (i) and (ii), the ion A is always accompanied by the ion (A − 1), which is particularly intense (95% rel. intensity) in **7**. Compounds **8**, **10** and **11** suffer the loss of a SH radical from the ion A, while in compounds **7**, **9** and **12** the SH radical is lost from the (A − 1) ion. The ion A reaches the base peak in **8**, **10** and **11**, while in the *ortho*-disubstituted mesityl and duryl derivatives **9** and **12**, the ion B represents the base peak. In compound **7**, the base peak is the ion at *m/e* 135.

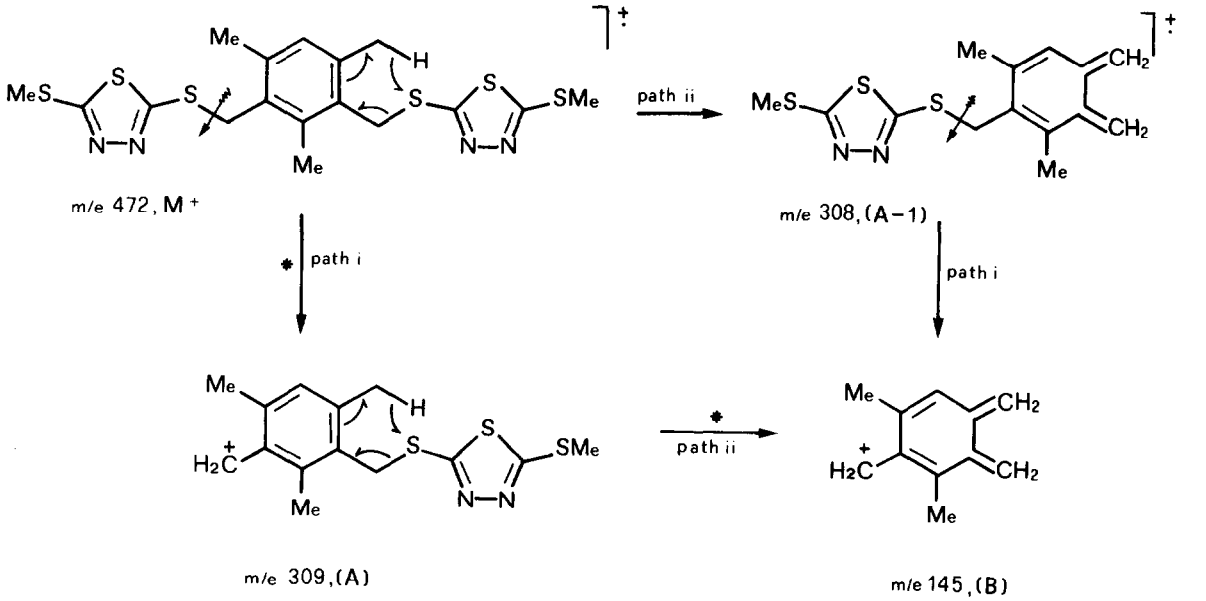
A further feature of the mass spectra of compounds **7–12** is the presence in the low mass range of intense peaks at *m/e* 88 ($C_2H_4N_2S$), 76 (CS_2), 73 (CHN_2S), 59 (C_2H_3S) and 45 (CHS), characteristic of the electron-impact fragmentation of 2-mercapto - 5 - methylthio - 1,3,4 - thiadiazole (*m/e* 164).[8]

^1H NMR spectra. The spectral parameters of compounds **1–12** are listed in Table 1. The ^1H NMR spectra of the compounds investigated consisted of four types of signals corresponding to methyl, methylthio, methylene and aromatic protons. The peak assignments to the respective protons followed in a straightforward manner from the position of the signals and integration.

The conformation and conformational mobility of macrocycles **1–6** could be deduced by NMR spectral data and by VT-NMR analysis. The inspection of a model of macrocycle **1** reveals that the 18-membered ring system may adopt the syn conformation (I) as well as the anti conformation (II), shown in Fig. 2; on the other hand, a quasi planar conformation appears to be energetically disfavoured, because of repulsive interaction between non bonded atoms. A comparison of the ^1H NMR spectra of compounds **1** and **7** shows that the absorption of the aromatic protons in **1** is coincident with that observed in model compound **7**. Whereas the aromatic protons would experience a significant diamagnetic shielding from the opposing phenyl ring only in the syn conformation (I), the present data seem to



Scheme 2.



Scheme 3.

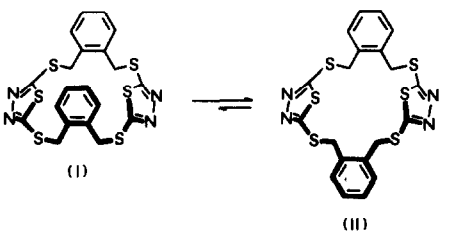


Fig. 2. Possible syn (I) and anti (II) conformations of the 18-membered macrocycle **1**.

indicate that macrocycle **1** exists preferentially in the anti conformation (II). Unfortunately, a VT-NMR study of **1** was precluded by its scarce solubility in suitable solvents.

When a model of the 20-membered macrocycles **2** and **3** is examined, three possible symmetrical conformations, shown in Fig. 3, become apparent: the basket conformation (III), the saddle-shape conformation (IV), and the crown-like conformation (V). The significant upfield shift (0.39 ppm) observed for the intraannular aryl protons in **2** with respect to the corresponding proton in model compound **8** suggests for this ring system the saddle-shape conformation (IV). This conclusion is in agreement with previous ^{1}H NMR[4a,9] and X-ray[10] investigations on related 16- and 20-membered sulphur bridged metacyclophanes.

Further evidence in favour of the saddle-shape conformation (IV) was provided by the ^{1}H NMR spectra of the hexamethyl derivative **3**. Due to the proximity of the 2-positioned methyl group to the adjacent 1,3,4-thiadiazole ring, these protons are considerably shielded (0.89 ppm) with respect to those of model compound **9**. Moreover, a VT-NMR study shows that the absorptions of methyl groups in **3** are unaffected in a wide temperature range, indicating that the molecule is frozen in the saddle-shape conformation (IV). However, the methylene protons in **3** depend on the temperature. At elevated temperatures, they appear as a sharp singlet, but upon reducing the temperature, the methylene region underwent a striking change (Fig. 4): the singlet at δ4.45 broadened ($T_c = +5°$) and finally at $-25°$ was split into an AB system ($\delta_A = 4.14$ ppm, $\delta_B = 4.63$ ppm; $J_{AB} = 14.4$ Hz). On the basis of the coalescence temperature and $\Delta\nu$, the energy barrier for the restricted rotation of the methylene bridges, calculated using the method of Calder and Garratt,[11] was ascertained to be $\Delta G_c^{\neq} = 13.8$ kcal/mole.

Finally, two possible conformations can be considered for the 22-membered ring system: the chair-like conformation (VI), and the boat-like conformation (VII), according to whether the pairs of CH_2–S links attached to a benzene ring are all *trans* or all *cis*, respectively (Fig. 5). Within these skeletal conformations, further conformations can arise if the phenylene groups are not free to rotate.

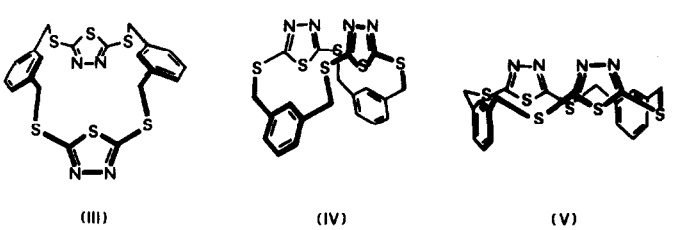


Fig. 3. Possible basket (III), saddle (IV) and crown (V) conformations of the 20-membered macrocycles **2** and **3**.

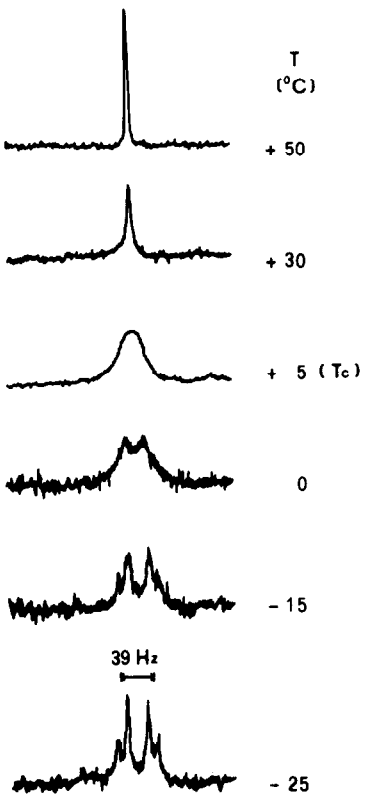
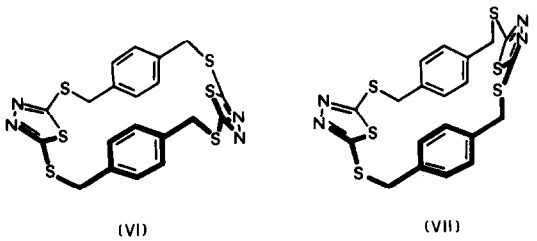


Fig. 4. The methylene region in the 80 MHz ^{1}H NMR spectra ($CDCl_3$) of macrocycle **3** at various temperatures.



(VI) (VII)

Fig. 5. Possible chair (VI) and boat (VII) conformations of the 22-membered macrocycles **4–6**.

The small shielding observed for the aromatic protons in macrocycles **4** (0.08 ppm) and **5** (0.21 ppm), and for the methyl groups in macrocycles **5** (0.08 ppm) and **6** (0.15 ppm) with respect to the corresponding protons in model compounds **10–12**, do not appear to indicate a particular conformational preference for the 22-membered ring system. Accordingly, no splitting of the signal of methyl groups occurred in the low temperature spectra ($CDCl_3$) of macrocycle **6** even at −60°, indicating that the duryl groups are free to rotate.

The results obtained show therefore that the preferred conformation of each ring system is determined primarily by its size and shape.

EXPERIMENTAL

Materials and analytical procedures. 2,5 - Dimercapto - 1,3,4 - thiadiazole and 2,5-bis(chloromethyl) *p*-xylene were commercial products (from EGA), used without purification. Isomeric α,α'-dibromoxylenes were prepared by bromination of the pure xylenes with NBS in CCl_4. Bis(chloromethyl)mesitylene,[12] bis(chloromethyl)durene,[13] and 2 - mercapto - 5 - methylthio - 1,3,4 - thiadiazole[4a] were prepared according to literature procedures. Melting points are uncorrected, and were determined on a Kofler apparatus. Elemental analyses were obtained commercially. The low resolution mass spectra were taken by direct insertion into the ion source of a LKB 9000S instrument under the following conditions: ionization energy, 70 eV; source temperature, 270–290°; trap 60 μA; evaporation temperature, 200–220° for macrocycles **1–6**, and 140–170° for open-chain derivatives **7–12**. ^{1}H NMR spectra were recorded on a Varian EM 360 instrument. VT-NMR experiments were carried out on a Bruker WP-80 spectrometer. Unless otherwise stated, chemical shifts are in parts per million (δ) from internal TMS for $CDCl_3$ solutions. The concentrations used were approximately 15 mg/0.5 ml.

General procedure for the synthesis of macrocycles **1–6**. 2,5 - Dimercapto - 1,3,4 - thiadiazole (1.5 g, 0.01 mole) and KOH (1.12 g, 0.02 mole) in EtOH (100 ml) and the appropriate bis(halomethyl)benzene derivative (0.01 mole) in EtOH–benzene 1:1 mixture (100 ml) were dropped separately but synchronously from two dropping funnels into boiling EtOH (1 l.) over 3 h, under mechanical stirring. The mixture was heated at reflux under stirring for an additional 20 h, and cooled. Removal of the solvent *in vacuo* left a residue, which was extracted with $CHCl_3$, dried (Na_2SO_4), and concentrated to leave the desired macrocycle. The crude product was then recrystallized from DMF to constant mp (Table 1).

General procedure for the synthesis of open-chain model compounds **7–12**. To a solution of bis(halomethyl)benzene derivative (0.01 mole) in DMF (10 ml) was added an aqueous solution of the sodium salt of 2 - mercapto - 5 - methylthio - 1,3,4 - thiadiazole (0.02 mole), in one portion. A white precipitate formed immediately. The mixture was kept at 80° for 1 h under magnetic stirring. After cooling, water was added and the precipitate filtered, dried and recrystallized from ethyl acetate. The sparingly soluble duryl derivative **12** recrystallized from the stipulated solvents, while compounds **7** and **8** were obtained as dense oils, which partly crystallize on standing.

Acknowledgements—The authors gratefully acknowledge partial support of this work by the Ministero della Pubblica Istruzione, as well as Prof. P. Finocchiaro for VT-NMR experiments, and Dr. A. Corsaro and S. Occhipinti for recording the mass spectra.

REFERENCES

[1]G. R. Newkome, J. D. Sauer, J. M. Roper and D. C. Hager, *Chem. Rev.* **77**, 513 (1977).
[2]J. Sandström, *Adv. Heterocyclic Chem.* **9**, 165 (1968) and references cited therein.
[3]S. Gregorowicz and Z. Klima, *Coll. Czech. Chem. Commun.* **33**, 3880 (1968); Y. R. Rao, *Indian J. Chem.* **7**, 836 (1969); M. R. Gajendragad and U. Agarwala, *Indian J. Chem.* **13**, 1331 (1975); *Austral. J. Chem.* **28**, 763 (1975); *J. Inorg. Nuclear Chem.* **37**, 2429 (1975).
[4a]F. Bottino and S. Pappalardo, *Org. Magn. Reson.* **16**, 1 (1981); [b]V. F. Borodkin and N. A. Kolesnikov, *Khim. geterotsikl. Soedinenii* 194 (1971); *Chem. Abstr.* **75**, 35981w (1971); [c]N. A. Kolesnikov, V. E. Maizlish and V. F. Borodkin, *URSS Pat.* 505,654 (March 1976); *Chem. Abstr.* **85**, 78136y (1976).
[5]C. S. Barnes, R. J. Goldsack and R. P. Rao, *Org. Mass Spectrom.* **5**, 317 (1971).
[6]H. Schwarz, *Top. Curr. Chem.* **73**, 231 (1978).
[7]P. Brown and C. Djerassi, *Angew. Chem. Int. Ed. Engl.* **6**, 477 (1967).
[8]F. Bottins, S. Caccamese and S. Pappalardo, *Org. Mass Spectrom.* submitted for publication.
[9]G. Ronsisvalle, F. Bottino and S. Pappalardo, *Org. Magn. Reson.* **14**, 344 (1980); F. Bottino, S. Pappalardo and G. Ronsisvalle, *Gazzetta Chim. Ital.* in press.
[10]N. Bresciani-Pahor, M. Calligaris, L. Randaccio, F. Bottino and S. Pappalardo, *Gazzetta Chim. Ital.* **110**, 227 (1980).
[11]I. C. Calder and P. J. Garratt, *J. Chem. Soc.* (*B*) 660 (1967).
[12]R. C. Fuson and N. Rabjohn, *Organic Synth.* **25**, 65 (1945).
[13]R. R. Aitken, G. M. Badger and J. W. Cook, *J. Chem. Soc.* 331 (1950).