Journal of Inclusion Phenomena and Molecular Recognition in Chemistry **15**: 247–258, 1993.

Synthesis of *N,N'*-Ditosyl-8,19-dimethoxy-2,5-diaza-[6.1]-naphthyl-cyclophane: Crystal and Molecular Structure of Its 1:1 Chloroform Solvate

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(Received: 30 October 1992; in final form: 9 February 1993)

Abstract. The title compound, $C_{41}H_{40}N_2O_6S_2$, has been synthesised in good yield and was found to form a 1:1 inclusion compound with $CHCl_3$ and other organic solvents. The crystal and molecular structure of the $CHCl_3$ solvate has been determined by single crystal X-ray analysis and refined to an R-value of 0.034 for 3229 reflections. The compound is monoclinic, space group $P2_1/c$, with $a = 15.316(1)$, $b = 14.515(1)$, $c = 18.720(3)$ Å, $\beta = 101.98(1)°$, and $Z = 4$. One molecule of chloroform is included in the crystal lattice.

Key words. *N*-tosyl-azamacrocycles, cyclophane, clathrate formation, synthetic routes, MS-fragmentation pattern.

Supplementary data relevant to this article have been deposited with the British Library as Supplementary Publication No. SUP 82146 (9 pp.).

1. Introduction

In the last few years we have been active in the synthesis and characterization of *N*-tosyl azamacrocycles that are able to complex transition metals and form clathrates [1]. With the aim of enlarging the cavity, and in order to introduce more rigid 'walls', we felt that suitable derivatives of pamoic acid **1** could be used for producing such macrocycles. In fact, pamoic acid is a cheap, commerical product capable of complexing many metals [2] and can be easily functionalized in order to obtain cyclic structures, with potential inclusion properties.

Therefore, according to the reaction sequences depicted in Scheme 1, pamoic acid (**1**) was transformed to the bisbromomethyl derivative **4**, which in turn can be converted into various azamacrocycles by condensation with appropriate ditosyl amides. In this paper we describe the synthesis of azamacrocycle **5** together with the molecular structure of its inclusion compound with $CHCl_3$ as determined by X-ray diffraction methods.

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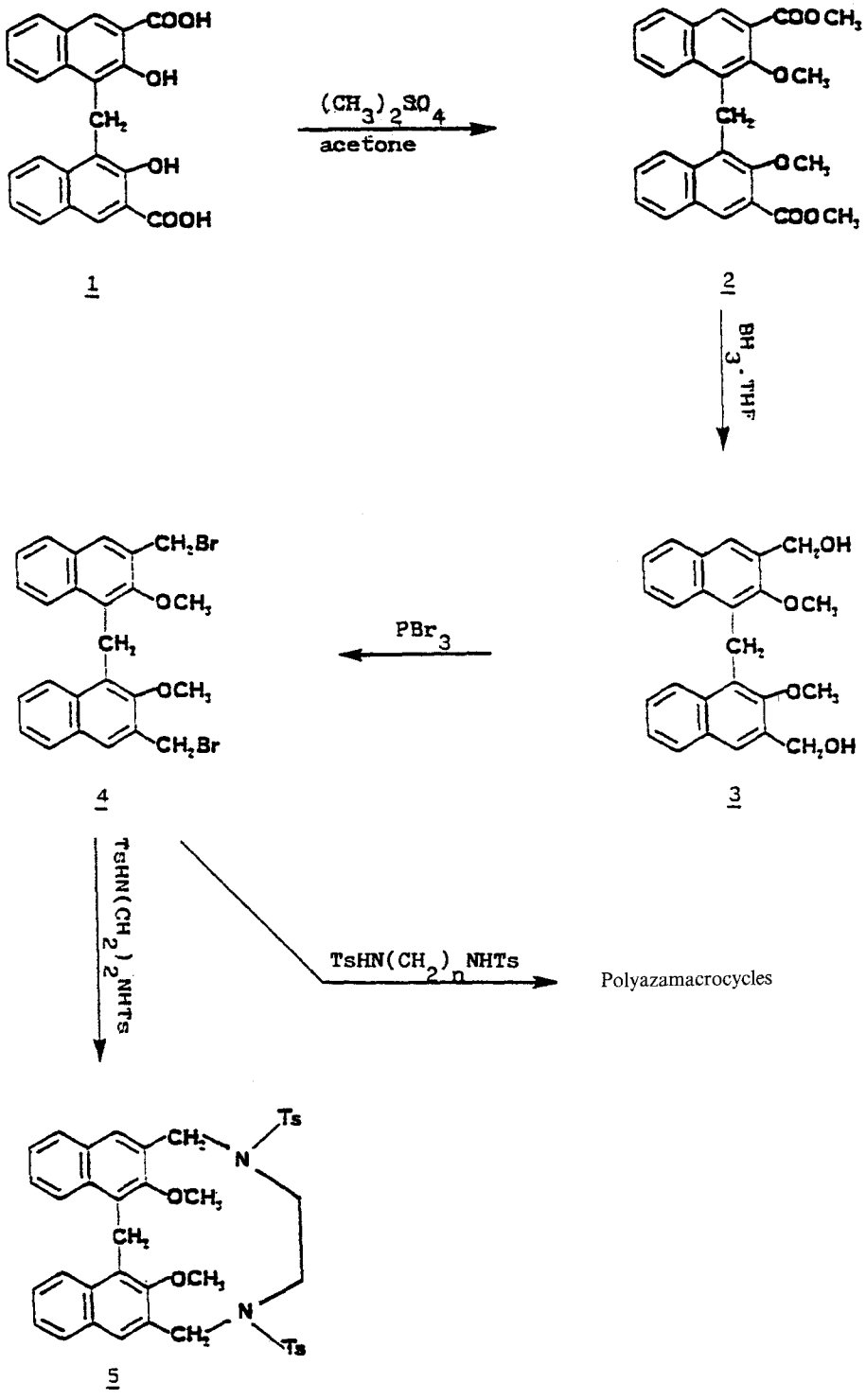

COOH
OH
CH2
OH
COOH
1
(CH3)2SO4
acetone
COOCH3
OCH3
CH2
OCH3
COOCH3
2
BH3.THF
CH2OH
OCH3
CH2
OCH3
CH2OH
3
PBr3
CH2Br
OCH3
CH2
OCH3
CH2Br
4
TsHN(CH2)2NHTs
TsHN(CH2)nNHTs
Polyazamacrocycles
Ts
N
CH2
OCH3
CH2
OCH3
N
CH2
Ts
5

Scheme 1.

2. Experimental

2.1. GENERAL

Pamoic acid, 4,4′-methylenebis(3-hydroxy-2-naphthoic) acid (**1**), solvents and chemicals used were high purity commerical products from Aldrich, which were recrystallized before use. All syntheses were performed under a dry N_2 atmosphere.

^{1}H NMR spectra were recorded in $CDCl_3$ with Me_4Si as an internal standard using a Bruker WP-80 or AC-250 instrument operating at 80 and 250 MHz, respectively.

Mass spectra were obtained using a double focusing Kratos MS 50S instrument equipped with a standard FAB source and a DS 90 data system. 3-Nitro benzyl alcohol was used as matrix.

Melting points were determined on a Büchi 530 melting point apparatus and are uncorrected.

2.2. SYNTHETIC PROCEDURES

*4,4′-Methylenebis(3-methoxy-2-naphthoic) ester (**2**)*

A mixture of 14.01 g (0.036 mol) of **1**, 23.63 g (0.17 mol) of K_2CO_3 and 24.74 g (0.19 mol) of dimethyl sulfate suspended in 1 L of acetone was stirred and refluxed for 24 h. The reaction mixture was then cooled, the solvent evaporated, and the residue treated with 250 mL of NH_3 solution (30%). After 2 h the resulting suspension was acidified with hydrochloric acid (36%), and extracted with CH_2Cl_2.

The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The resulting residue was crystallized from methanol to give 15.2 g (95%) of **2**:m.p. 133°C (lit. 132–133°C) [3]; ^{1}H NMR ($CDCl_3$) δ: 3.82 (*s*, OCH_3, 6H), 3.99 (*s*, $COOCH_3$, 6H), 5.02 (*s*, Ar-CH_2-Ar, 2H), 7.37 (*m*, ArH, 4H), 7.76 (*m*, ArH, 2H), 8.18 (*m*, ArH, 2H), 8.27 (*s*, ArH, 2H); MS (70 eV, 170°C) *m/z* $M^{+\cdot}$444.

*4,4′-Methylenebis(3-methoxy-2-naphthyl alcohol) (**3**)*

BH_3·THF (15 mL, 15 mmol) was added by a syringe to a stirred solution of 1.38 g (3.1 mmol) of the ester **2**, in 100 mL of dry THF under N_2. The mixture was refluxed overnight, cooled, and the excess BH_3 carefully decomposed with water. Water (50 mL) saturated with K_2CO_3 was added, and the resulting mixture was warmed again at ~50°C for 2 h. The mixture was then cooled, extracted with $CHCl_3$, and dried (Na_2SO_4). The solvent was evaporated, and the residual oil chromatographed on silica gel with ethylacetate/cyclohexane (1:1) as the mobile phase. The eluted product was isolated as a foam, which was dried under high vacuum to give 1.16 g (96%) of diol **3**; ^{1}H NMR ($CDCl_3$) δ: 2.38 (*bs*, OH, 2H, exchange with D_2O), 3.82 (*s*, OCH_3, 6H), 4.94 (*s*, Ar—CH_2—Ar + CH_2—OH, 6H), 7.28 (*m*, ArH, 4H), 7.67 (*m*, ArH, 4H), 8.10 (*m*, ArH, 2H).

*4,4′-Methylenebis(3-methoxy-2-naphthyl bromide) (**4**)*

C_6H_6 (100 mL) was added to 2.0 g (5.15 mmol) of diol **3** dissolved in 10 mL of CH_2Cl_2; to this stirred solution 1.5 g (5.55 mmol) of PBr_3 was added and the

mixture was stirred for 3 h. The reaction mixture was then mixed with 100 mL of Et_2O and washed several times with water saturated with K_2CO_3, and then with water. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The resulting solid was recrystallized from ethylacetate/chloroform to give 2.3 g (88%) of **4**: m.p. 195–197°C; ^{1}H NMR ($CDCl_3$) δ: 4.05 (*s*, OCH_3, 6H), 4.81 (*s*, CH_2Br, 4H), 4.96 (*s*, $ArCH_2Ar$, 2H), 7.31 (*m*, ArH, 4H), 7.71 (*m*, ArH, 4H), 8.13 (*m*, ArH, 2H).

Macrocycle ***5***

To a stirred suspension of anhydrous K_2CO_3 (1.6 g, 11.5 mmol) in anhydrous DMF (50 mL) at 80°C was added dropwise and at constant rate, over a period of 7 h, from two different separatory funnels, a solution of *N,N'*-ditosylethylenediamine [4] (0.78 g, 2.1 mmol) and a solution of **4** (1.1 g, 2.1 mmol) in DMF (50 mL in total). After the addition was completed, the reaction mixture was stirred overnight at room temperature. The mixture was then filtered, and the filtrate was concentrated under reduced pressure. The resulting white solid was chromatographed on silica gel with CH_2Cl_2 as the mobile phase. The material from the column was recrystallized from ethylacetate/chloroform to give 0.82 g (54%) of **5**: m.p. 295–298°C; ^{1}H NMR ($CDCl_3$) δ: 2.29 and 3.31 (two *t*, $J = 14$ Hz, NCH_2, 4H), 2.40 (*s*, $TsCH_3$, 6H), 3.06 (*s*, OCH_3, 6H), 3.49 and 4.59 (*AB* quartet, Ar—CH_2—Ar, $J = 12.3$ Hz, 2H), 7.32 (*d*, $J = 8.2$ Hz, TsH, 4H), 7.50 (*m*, ArH, 4H), 7.81 (*m*, ArH, +TsH, 8H), 8.40 (*m*, ArH, 2H). FAB-MS: *m/z* 721 MH^+.

2.3. X-RAY DATA

Intensity data for compound **5** were collected using a crystal of approximate dimensions $0.22 \times 0.28 \times 0.36$ mm^3 on an Enraf-Nonius CAD4 four-circle diffractometer using MoK_α radiation ($\lambda = 0.71069$ Å). Crystal data are as follows: $C_{41}H_{40}N_2O_6S_2 \cdot CHCl_3$, f_w 840.3, monoclinic, $P2_1c$, $a = 15.316(1)$ Å, $b = 14.515(1)$ Å, $c = 18.720(3)$ Å, $\beta = 101.98(1)°$, $V = 4071.0(1.3)$ Å^3, $Z = 4$, $D_x = 1.371$ g/cm^3, $T = 298$ K, μ (MoK_α) $= 3.71$ cm^{-1}.

Lattice parameters were determined by the least-squares method for 24 reflections ($24° < 2\theta < 28°$). 4326 reflections up to $\theta = 22.5°$ were measured in the $\omega - 2\theta$ scan mode. The 3229 independent reflections for which $I/\sigma(I) > 3.0$ were corrected for Lorentz and polarization effects, but not for absorption.

The structure was solved by the direct method and refined by least squares; final refinement was achieved with the SHELXTL [5] program package. Weights of each reflection in refinement (on F) were calculated from $w = 1/[\sigma^2(F_0) + 0.000742F_0^2]$, $\sigma(F_0)$ being the esd, based on counting statistics, for the observed structure factor. Scattering factors were taken from the *International Tables for X-ray Crystallography* [6]. All the H atoms included in the refinement were found from the difference syntheses.

The guest molecules ($CHCl_3$) were located in cavities generated by packing of the host molecules and exhibited statistical disorder with two different orientations.

Refinement resulted in final values of $R = 0.034$, $R' = 0.037$ and $S = 1.12$; in the last cycle $(\Delta/\sigma)_{max} < 0.10$. Final max and min $\Delta\rho$ were 0.2 and $-0.27e$ Å^{-3}, respectively. All calculations were performed on a NOVA-3 computer.

3. Results and Discussion

According to the reaction Scheme I, compound **4**, in principle, could react with bis-tosylamides yielding the 1 : 1 condensation product (**5**) or cyclic compounds with a larger skeleton (2 : 2, 3 : 3, etc.). As discussed in the experimental section, only the 1 : 1 macrocycle was isolated from the reaction mixture, and it was shown to be capable of forming 1 : 1 inclusion compounds with $CHCl_3$, CH_3CN and toluene.

The solid state structure of **5** solvated with $CHCl_3$ was solved by X-ray diffraction techniques and the atomic fractional coordinates are reported in Table I; Tables II and III show bond distances and angles, while selected torsion angles are given in Table IV. The molecular conformation of host **5** and the atomic numbering scheme are illustrated in Figure 1.

The solid-state conformation of **5** is attained through the presence of both anticlinal (112.5°) and synclinal (−73.0°) C—N—C—C torsion angles. The conformation of the macrocycle can be referred to the plane defined by the three atoms N(1), N(2) and C(41): the two naphthyl rings are twisted in the same direction with respect to

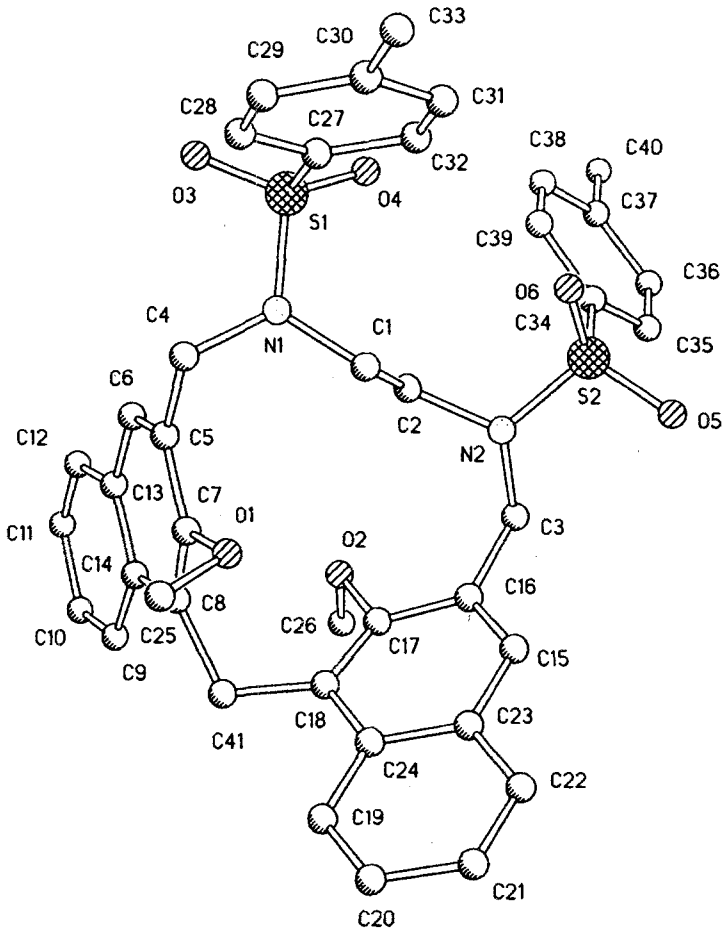


Fig. 1. Perspective view of macrocycle **5** with the atom numbering scheme.

Table I Atom coordinates ($\times 10^4$) and temperature factors ($Å^2 \times 10^3$) for $C_{41}H_{40}N_2O_6S_2 \cdot CHCl_3$

Atom	x	y	z	U
S(1)	2732(1)	3559(1)	3802(1)	44(1)*
S(2)	2250(1)	4127(1)	1123(1)	48(1)*
O(1)	−448(1)	2475(1)	2744(1)	46(1)*
O(2)	−738(1)	4799(1)	1775(1)	42(1)
O(3)	2736(2)	3770(2)	4553(1)	55(1)*
O(4)	3138(1)	4179(2)	3378(1)	54(1)*
O(5)	2047(2)	3948(2)	353(1)	65(1)*
O(6)	2851(2)	3541(2)	1600(1)	60(1)*
N(1)	1691(2)	3463(2)	3392(1)	41(1)*
N(2)	1298(2)	4091(2)	1385(1)	38(1)*
C(1)	1513(2)	3297(2)	2591(2)	39(1)*
C(2)	1341(2)	4201(2)	2182(2)	39(1)*
C(3)	494(2)	4437(2)	882(2)	40(1)*
C(4)	1024(2)	3129(2)	3803(2)	42(1)*
C(5)	70(2)	4491(2)	3898(2)	41(1)*
C(6)	160(2)	3655(2)	3599(2)	36(1)*
C(7)	−562(2)	3313(2)	3069(2)	36(1)*
C(8)	−1331(2)	3809(2)	2823(2)	35(1)*
C(9)	−2246(2)	5182(3)	3034(2)	52(1)*
C(10)	−2321(3)	5987(3)	3385(2)	59(2)*
C(11)	−1611(3)	6321(3)	3908(2)	60(2)*
C(12)	−844(3)	5843(3)	4070(2)	52(1)*
C(13)	−737(2)	5000(2)	3725(2)	40(1)*
C(14)	−1452(2)	4650(2)	3183(2)	38(1)*
C(15)	−448(2)	3054(2)	456(2)	43(1)*
C(16)	−292(2)	3818(2)	892(2)	38(1)*
C(17)	−871(2)	3985(2)	1375(2)	36(1)*
C(18)	−1492(2)	3364(2)	1500(2)	37(1)*
C(19)	−2304(2)	1885(3)	1091(2)	51(1)*
C(20)	−2450(2)	1146(3)	629(2)	56(2)*
C(21)	−1954(2)	1036(2)	87(2)	57(1)*
C(22)	−1321(2)	1665(2)	20(2)	52(1)*
C(23)	−1138(2)	2434(2)	501(2)	41(1)*
C(24)	−1653(2)	2560(2)	1042(2)	39(1)*
C(25)	−868(3)	1722(3)	3013(3)	76(2)*
C(26)	−1349(3)	5509(2)	1487(2)	61(2)*
C(27)	3256(2)	2487(2)	3776(2)	42(1)*
C(28)	3224(2)	1842(3)	4318(2)	52(1)*
C(29)	3652(3)	1017(3)	4306(2)	61(2)*
C(30)	4117(3)	797(3)	3770(3)	67(2)*
C(31)	4135(2)	1450(3)	3234(2)	68(2)*
C(32)	3716(2)	2286(3)	3233(2)	58(2)*
C(33)	4595(3)	−117(3)	3767(3)	105(2)*
C(34)	2685(2)	5254(2)	1254(2)	47(1)*
C(35)	2553(2)	5880(3)	683(2)	55(1)*
C(36)	2909(3)	6751(3)	794(2)	63(2)*
C(37)	3378(2)	7034(3)	1472(2)	60(2)*
C(38)	3505(2)	6397(3)	2039(2)	61(2)*
C(39)	3174(2)	5518(3)	1931(2)	56(1)*
C(40)	3749(3)	7996(3)	1592(3)	86(2)*
C(41)	−1967(2)	3502(2)	2132(2)	44(1)*

Table I (*Continued*).

Atom	*x*	*y*	*z*	*U*	
Cl(1)a	4397(7)	2659(7)	6267(6)	99(2)*	statistically disordered molecules of chloroform
Cl(1)b	4605(9)	2665(9)	6267(7)	166(5)*	
Cl(2)a	4767(3)	4595(4)	6313(3)	144(3)*	
Cl(2)b	5216(3)	4412(4)	6095(3)	121(2)*	
Cl(3)a	5197(6)	3518(6)	5157(6)	200(4)*	
Cl(3)b	5297(5)	2952(5)	5085(5)	167(3)*	
C(42)	4571(3)	3555(4)	5689(3)	108(2)*	

* Equivalent isotropic *U* defined as one third of the trace of the orthogonalised $U(i, j)$ tensor.

Table II. Bond distances (Å) for $C_{41}H_{40}N_2O_6S_2 \cdot CHCl_3$

S(1)—O(3)	1.437(2)	S(1)—O(4)	1.425(3)
S(1)—N(1)	1.626(2)	S(1)—C(27)	1.757(3)
S(2)—O(5)	1.434(2)	S(2)—O(6)	1.424(2)
S(2)—N(2)	1.632(3)	S(2)—C(34)	1.764(4)
O(1)—C(7)	1.386(4)	O(1)—C(25)	1.413(5)
O(2)—C(17)	1.391(4)	O(2)—C(26)	1.421(4)
N(1)—C(1)	1.487(4)	N(1)—C(4)	1.482(5)
N(2)—C(2)	1.489(4)	N(2)—C(3)	1.475(4)
C(1)—C(2)	1.514(5)	C(3)—C(16)	1.506(5)
C(4)—C(6)	1.506(4)	C(5)—C(6)	1.355(5)
C(5)—C(13)	1.418(5)	C(6)—C(7)	1.415(4)
C(7)—C(8)	1.375(4)	C(8)—(14)	1.425(5)
C(8)—C(41)	1.516(4)	C(9)—C(10)	1.357(5)
C(9)—C(14)	1.419(5)	C(10)—C(11)	1.391(5)
C(11)—C(12)	1.343(6)	C(12)—C(13)	1.410(5)
C(13)—C(14)	1.423(4)	C(15)—C(16)	1.368(5)
C(15)—C(23)	1.403(5)	C(16)—C(17)	1.413(5)
C(17)—C(18)	1.365(5)	C(18)—C(24)	1.440(4)
C(18)—C(41)	1.525(5)	C(19)—C(20)	1.367(5)
C(19)—C(24)	1.413(5)	C(20)—C(21)	1.396(6)
C(21)—C(22)	1.356(5)	C(22)—C(23)	1.425(5)
C(23)—C(24)	1.419(5)	C(27)—C(29)	1.388(5)
C(27)—C(32)	1.383(5)	C(28)—C(29)	1.368(5)
C(29)—C(30)	1.382(6)	C(30)—C(31)	1.385(6)
C(30)—C(33)	1.515(6)	C(31)—C(32)	1.374(6)
C(34)—C(35)	1.386(5)	C(34)—C(39)	1.385(5)
C(35)—C(36)	1.375(6)	C(36)—C(37)	1.385(5)
C(37)—C(38)	1.390(6)	C(37)—C(40)	1.506(6)
C(38)—C(39)	1.372(6)	Cl(1)b—C(42)	1.68(1)
Cl(1)a—C(42)	1.75(1)	Cl(2)a—C(42)	1.894(8)
Cl(3)b—C(42)	1.95(1)	Cl(2)b—C(42)	1.669(7)
		Cl(3)a—C(42)	1.52(1)

Table III. Bond angles (deg.) for $C_{41}H_{40}N_2O_6S_2 \cdot CHCl_3$

O(3)—S(1)—O(4)	119.7(1)	O(3)—S(1)—N(1)	106.6(1)
O(4)—S(1)—N(1)	106.8(1)	O(3)—S(1)—C(27)	107.9(1)
O(4)—S(1)—C(27)	106.8(2)	N(1)—S(1)—C(27)	108.7(1)
O(5)—S(2)—O(6)	119.9(2)	O(5)—S(2)—N(2)	105.9(1)
O(6)—S(2)—N(2)	107.1(1)	O(5)—S(2)—C(34)	107.8(2)
O(6)—S(2)—C(34)	106.9(1)	N(2)—S(2)—C(34)	108.8(2)
C(7)—O(1)—C(25)	114.5(3)	C(17)—O(2)—C(26)	113.6(2)
S(1)—N(1)—C(1)	116.5(2)	S(1)—N(1)—C(4)	119.8(2)
C(1)—N(1)—C(4)	118.0(2)	S(2)—N(2)—C(2)	116.2(2)
S(2)—N(2)—C(3)	118.5(2)	C(2)—N(2)—C(3)	117.4(2)
N(1)—C(1)—C(2)	110.2(3)	N(2)—C(2)—C(1)	112.4(3)
N(2)—C(3)—C(16)	110.7(3)	N(1)—C(4)—C(6)	111.5(3)
C(6)—C(5)—C(13)	122.1(3)	C(4)—C(6)—C(5)	120.6(3)
C(4)—C(6)—C(7)	121.2(3)	C(5)—C(6)—C(7)	118.2(3)
O(1)—C(7)—C(6)	117.6(3)	O(1)—C(7)—C(8)	119.4(3)
C(6)—C(7)—C(8)	122.8(3)	C(7)—C(8)—C(14)	118.5(3)
C(7)—C(8)—C(41)	119.0(3)	C(14)—C(8)—C(41)	122.1(3)
C(10)—C(9)—C(14)	121.9(3)	C(9)—C(10)—C(11)	120.6(4)
C(10)—C(11)—C(12)	119.9(4)	C(11)—C(12)—C(13)	121.6(3)
C(5)—C(13)—C(12)	121.7(3)	C(5)—C(13)—C(14)	118.3(3)
C(12)—C(13)—C(14)	119.4(3)	C(8)—C(14)—C(9)	124.3(3)
C(8)—C(14)—C(13)	119.1(3)	C(9)—C(14)—C(13)	116.6(3)
C(16)—C(15)—C(23)	121.6(3)	C(3)—C(16)—C(15)	121.1(3)
C(3)—C(16)—C(17)	121.0(3)	C(15)—C(16)—C(17)	117.8(3)
O(2)—C(17)—C(16)	116.7(3)	O(2)—C(17)—C(18)	119.9(3)
C(16)—C(17)—C(18)	123.3(3)	C(17)—C(18)—C(24)	118.2(3)
C(17)—C(18)—C(41)	120.5(3)	C(24)—C(18)—C(41)	121.2(3)
C(20)—C(19)—C(24)	121.8(4)	C(19)—C(20)—C(21)	120.5(3)
C(20)—C(21)—C(22)	119.8(3)	C(21)—C(22)—C(23)	121.3(3)
C(15)—C(23)—C(22)	121.1(3)	C(15)—C(23)—C(24)	119.8(3)
C(22)—C(23)—C(24)	119.1(3)	C(18)—C(24)—C(19)	124.0(3)
C(18)—C(24)—C(23)	118.5(3)	C(19)—C(24)—C(23)	117.5(3)
S(1)—C(27)—C(28)	119.4(3)	S(1)—C(27)—C(32)	120.8(3)
C(28)—C(27)—C(32)	119.7(3)	C(27)—C(28)—C(29)	119.2(4)
C(28)—C(29)—C(30)	122.4(4)	C(29)—C(30)—C(31)	117.3(4)
C(29)—C(30)—C(33)	121.8(4)	C(31)—C(30)—C(33)	120.9(4)
C(30)—C(31)—C(32)	121.7(4)	C(27)—C(32)—C(31)	119.6(4)
S(2)—C(34)—C(35)	120.7(3)	S(2)—C(34)—C(39)	120.0(3)
C(35)—C(34)—C(39)	119.3(3)	C(34)—C(35)—C(36)	119.7(3)
C(35)—C(36)—C(37)	121.7(4)	C(36)—C(37)—C(38)	117.8(4)
C(36)—C(37)—C(40)	121.3(4)	C(38)—C(37)—C(40)	121.0(4)
C(37)—C(38)—C(39)	121.2(3)	C(34)—C(39)—C(38)	120.3(3)
C(8)—C(41)—C(18)	112.1(3)	Cl(1)b—C(42)—Cl(2)b	110.1(5)
Cl(1)a—C(42)—Cl(2)a	103.6(4)	Cl(1)a—C(42)—Cl(3)a	125.3(6)
Cl(1)b—C(42)—Cl(3)b	94.7(6)	Cl(2)a—C(42)—Cl(3)a	113.1(5)
Cl(2)b—C(42)—Cl(3)b	104.1(4)		

the reference plane in order to impart a helical conformation, with the two methoxy groups pointing in opposite directions, and lying above and below this plane, respectively.

For steric reasons, the methoxy groups are almost perpendicular to the naphthyl rings. Likewise the two tosyl groups are positioned in opposite directions to one

Table IV. Selected torsion angles (deg.) for $C_{41}H_{40}N_2O_6S_2 \cdot CHCl_3$

O(3)—S(1)—N(1)—C(1)	176.6
O(3)—S(1)—N(1)—C(4)	−30.6
O(4)—S(1)—N(1)—C(1)	47.5
O(4)—S(1)—N(1)—C(4)	−159.7
C(27)—S(1)—N(1)—C(1)	−67.4
C(27)—S(1)—N(1)—C(4)	85.4
S(1)—N(1)—C(1)—C(2)	−94.2
C(4)—N(1)—C(1)—C(2)	112.5
N(1)—C(1)—C(2)—N(2)	171.1
C(2)—N(2)—C(3)—C(16)	−73.0
S(1)—N(1)—C(4)—C(6)	139.9
C(1)—N(1)—C(4)—C(6)	−67.7
N(1)—C(4)—C(6)—C(5)	−81.1
N(1)—C(4)—C(6)—C(7)	96.0
C(25)—O(1)—C(7)—C(6)	102.8
C(25)—O(1)—C(7)—C(8)	−82.7
C(4)—C(6)—C(7)—O(1)	0.1
C(4)—C(6)—C(7)—C(8)	−174.2
O(1)—C(7)—C(8)—C(41)	−9.3
C(6)—C(7)—C(8)—C(41)	165.0
C(6)—C(5)—C(13)—C(12)	176.1
C(6)—C(5)—C(13)—C(14)	−4.4
C(41)—C(8)—C(14)—C(9)	13.3
C(41)—C(8)—C(14)—C(13)	−165.8
C(26)—O(2)—C(17)—C(16)	100.8
C(26)—O(2)—C(17)—C(18)	−83.9
O(2)—C(17)—C(18)—C(24)	175.9
O(2)—C(17)—C(18)—C(41)	−7.0
C(41)—C(18)—C(24)—C(19)	5.8
C(41)—C(18)—C(24)—C(23)	−174.9
C(20)—C(19)—C(24)—C(18)	178.1
O(3)—S(1)—C(27)—C(28)	28.7
O(3)—S(1)—C(27)—C(32)	−149.9
O(4)—S(1)—C(27)—C(28)	158.6
O(4)—S(1)—C(27)—C(32)	−20.0
N(1)—S(1)—C(27)—C(28)	−86.5
N(1)—S(1)—C(27)—C(32)	94.9
S(1)—C(27)—C(28)—C(29)	−178.4
C(32)—C(27)—C(28)—C(29)	0.2

another and aligned approximately with the O—CH_3 bond of a methoxy group. This spatial arrangement also seems to be a preferred conformation in solution; in fact, the OCH_3 signals of **5** are dramatically shifted upfield ($\sim$0.8–0.9 ppm) with respect to those of the parent compounds **2**, **3**, or **4**. This effect could be ascribed to the ring-current anisotropy of the tosyl groups which lie above the methoxy groups in **5**.

Such an arrangement generates open cavities, defined by the tosyl and naphthyl rings, which lie above and below the reference N(1)—N(2)—C(41) plane. The phenyl as well as the naphthyl rings are nearly planar, with the bridgehead C(41)

atom slightly bent out of the best plane of the naphthyl rings with an average C(41)—C—C—C dihedral angle of ~166°. The phenyl rings of the tosyl groups are arranged almost perpendicular to the plane defined by the N—S—C_{Ar} atoms, and this geometry would allow a strong conjugative interaction between the π electrons of the aryl rings and the sulphonyl group [7].

The S—N bond lengths are in the region of 1.64 Å, and the pyramidal coordination about N is considerably flattened, with angles ranging from 116.5(2)–119.8(2)°, as is normally found in such compounds [1,8]. The endocyclic aromatic C—C—C angles are at normal values, whereas the valency angle C(8)—C(41)—C(18) is 112.1(3)°. C—C, C—N and C—S bond lengths and angles are normal, as well as the geometry of the sulphonyl group.

The molecular packing is consistent with van der Waals interactions, and generates intermolecular voids of suitable sizes to include the molecule of $CHCl_3$.

Calculations performed on host **5** indicate that the diameter of the internal cavity generated by the 13-membered ring is in the range 3–5 Å between the atomic centres (and correspondingly less considering the van der Waals radii, see Figure 2) whereas the open voids defined by the tosyl and naphthyl rings within the same molecular unit are not large enough to incorporate guest molecules.

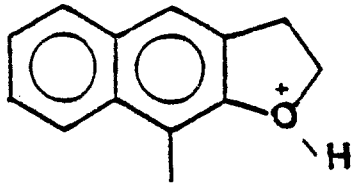
3.1. MASS SPECTRA

The FAB-MS spectrum of macrocycle **5** is rich in interesting and very diagnostic fragmentation pathways.

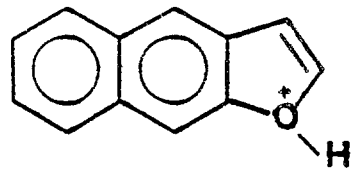
Inspection of Figure 3 reveals that the molecular ion $[MH]^+$ at $m/z = 721$ constitutes the base peak. The fragment ion $[MH - TsH]^+$ at $m/z = 565$ is also intense, probably generated by the loss of *p*-toluenesulfinic acid from the molecular ion. According to Newkome *et al.* [9] this fragment may originate through a five-membered cyclic transition state, by a naphthylic hydrogen transfer to the sulphonyl oxygen. This latter peak is accompanied by the peak at $m/z = 566$, corresponding to $[MH - Ts]^{+\cdot}$, probably owing to the easy loss of a tosyl group (155 a.u.) from the molecular ion.

The peaks at $m/z = 409$ and $m/z = 410$, corresponding to the fragments $[MH - TsH - TsH]^+$ and $[MH - Ts - TsH]^{+\cdot}$ respectively, occur with lower intensities as a consequence of other concomitant decomposition processes.

The region at relatively low masses is characterized by the presence of peaks at $m/z = 185$ and $m/z = 169$ which correspond to the heterocycle structures depicted below and are present in very high intensities.



$m/z = 185$



$m/z = 169$

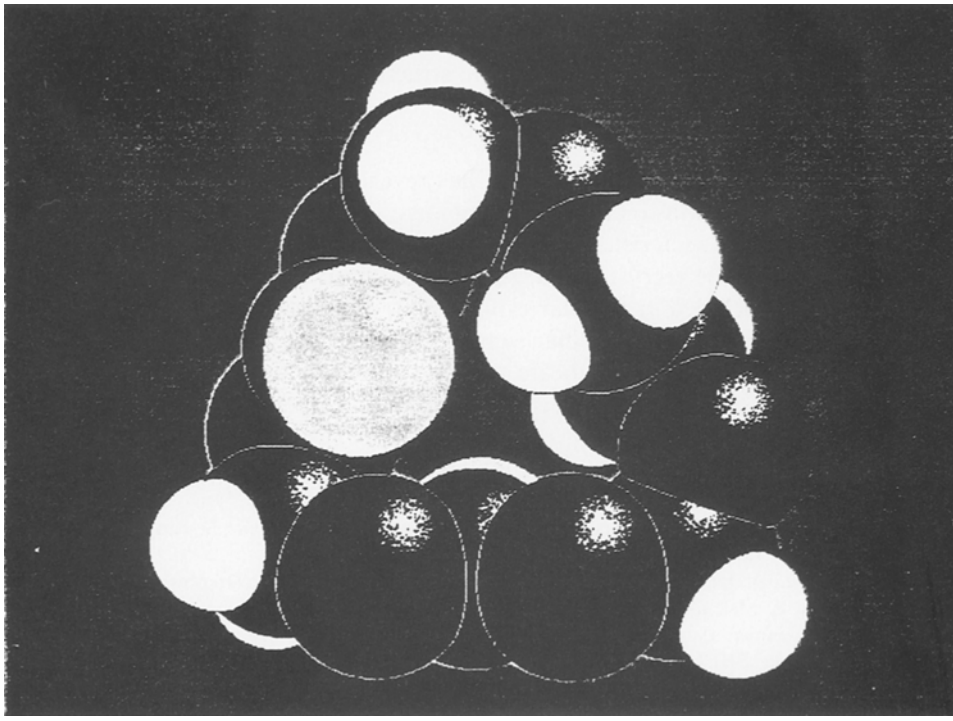


Fig. 2. Space-filling view of **5** projected onto the 'best' plane, showing the central cavity of the molecule (using spheres of various van der Waals radii).

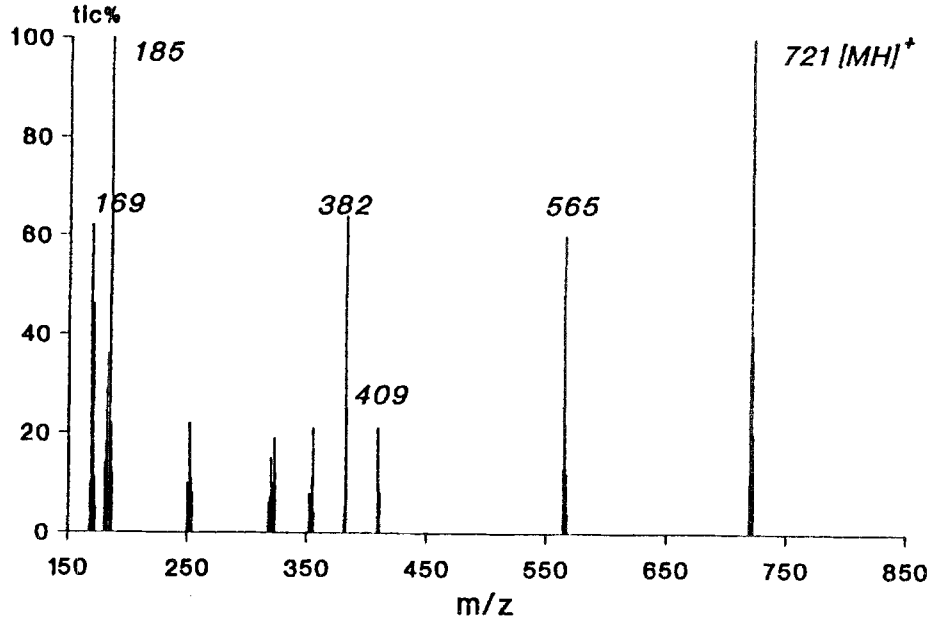


Fig. 3. FAB-MS spectrum of **5**, after subtraction of the contribution from the matrix (2-nitrobenzyl alcohol) and normalized with respect to the peak at 721 Dalton $[MH]^+$.

These fragments may originate from the molecular ion by a loss of the *N,N'*-ditosylethylenediamine bridge on this charged ion and subsequent rearrangement which produces the above mentioned heterocyclic structures [10].

3.2. INCLUSION PROPERTIES OF **5**

Recrystallization of pure **5** from CH_3CN has revealed, by NMR analysis, that the solvent is included in nonstoichiometric amounts, in the cavities of **5**. We therefore decided to investigate such behaviour in greater detail by selecting different solvents from which **5** could be recrystallized. Among the various solvents chosen, toluene was found to be included in a molar ratio of 1:1. The ^1H NMR chemical shifts of this solvated compound do not differ significantly with respect to those of the pure components; this finding may indicate that the adduct is formed only in the solid state, whereas in solution each molecule is free with respect to one another.

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