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Synthesis and Conformational Behaviour of Ditosyldiaza[2.2]orthometacyclophanes*

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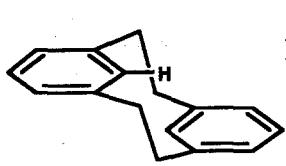
Summary. The N,N′-ditosyl-diaza[2.2]orthometacyclophanes **5a, b** were synthesized from N,N-ditosyl-metaphenylenediamine by reaction with (*Z*)-1,4-dichlorobutene and 1,2-bis-bromomethylbenzene, respectively. Low temperature NMR studies showed that the compound **5b** exists as a 1:1 mixture of chair and boat form of the strained (*E,Z*)-diazanonadiene ring. At room temperature all corresponding resonances are averaged on the NMR time scale (including all four ethylene bridge protons). Going to lower temperatures, in a first step the methylene bridge inversion is frozen (giving two *exo* H and two *endo* H, $\Delta G^{\neq}$ ca. 52 kJ mol^{-1}). In a second step the chair and boat form can be observed separately ($\Delta G^{\neq}$ ca. 43.5 kJ mol^{-1} for the chair/boat flip). The assignments were confirmed by 2D NMR experiments.

Keywords. Dihetero[2.2]orthometacyclophane; Dynamic NMR spectroscopy; Conformational analysis; Ring interconversion of 9-membered ring.

Synthese und konformatives Verhalten von Ditosyl-diaza[2.2]orthometacyclophanen

Zusammenfassung. Die N,N′-Ditosyl-diaza[2.2]orthometacyclophane **5a, b** wurden aus N,N-Ditosyl-metaphenylendiamin durch Umsetzung mit (*Z*)-1,4-Dichlorbuten bzw. 1,2-Bisbrommethylbenzol gewonnen. Tieftemperatur-NMR-Untersuchungen ergaben, daß **5b** als 1:1 Mischung einer Sessel- und einer Bootkonformation des gespannten *E,Z*-Diazanonadienringes vorliegt. Bei Raumtemperatur ist die zugehörige Ringinversion schnell in der NMR-Zeitskala, die entsprechenden Protonen in beiden Konformeren, auch die aller CH_2-Brückenprotonen, ergeben gemittelte Signale. Bei tiefen Temperaturen wird zunächst die Inversion der Methylenbrücken eingefroren (Signale für zwei *exo*- und zwei *endo*-CH_2-Protonen werden erhalten, $\Delta G^{\neq}$ ca. 52 kJ mol^{-1}). Bei weiterer Temperatursenkung können nach Einfrieren eines zweiten dynamischen Prozesses Sessel- und Bootkonformer anhand von getrennten Signalsätzen identifiziert werden (die freie Aktivierungsenthalpie für den zugehörigen Sessel-Boot-Flip beträgt $\Delta G^{\neq}$ ca. 43.5 kJ mol^{-1}). Die Zuordnung der ^{1}H- und ^{13}C-NMR-Resonanzen wurde mit Hilfe von zweidimensionalen NMR-Experimenten gesichert.

* Dedicated to Prof. Dr. E. L. Eliel on the occasion of his 70th anniversary



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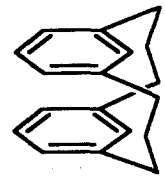

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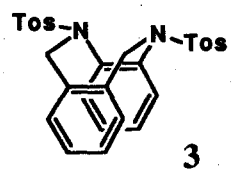

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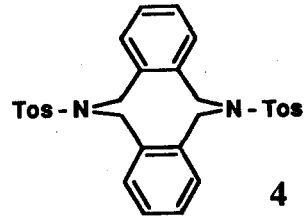

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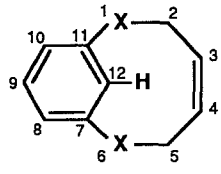

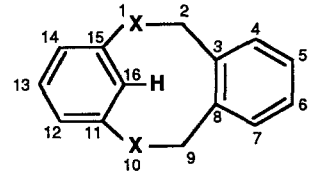

5 a X = N-Tos **5 b**

6 a X = CH_2 **6 b**

Introduction

The stereochemistry of medium-sized rings generally [1] and the cyclophanes especially [2] is of continuous interest. Often, the preferred conformations of very similar compounds are completely different. To find acceptable reasons for this behaviour is the starting point for detailed spectroscopical and theoretical studies.

The [2.2]metacyclophanes [3], for example, as well as several 1,10-diheteroanalogues [4] prefer conformations where the two phenyl rings are anti to each other forming a chair-like arrangement (**1**); in the corresponding [3.3]metacyclophane and the latter's 2,11-diheteroanalogues, however, they are in *syn* position with an overall boat-like geometry (**2**) [5].

Completely reversed results were obtained in a variety of dihetero-orthocyclophanes studied by us. The dihetero[2.2]orthocyclophanes (1,4-diheterocines) **3**, characterized by an 8-membered central ring system, prefer the *syn* conformers (twisted boat conformations) [6], the 10-membered dihetero[3.3]orthocyclophanes, on the other hand, prefer mostly the *anti* conformers **4** (chair conformation) [7].

In the present paper our interest was concentrated on the investigation of the corresponding interconversional process(es) and preferred conformers of the [2.2]orthometacyclophanes **5** with a 9-membered central ring. These compounds are extremely strained [8].

The synthesis of some unsymmetrical dihetero[3.3]orthometacyclophanes has already been published [9]. The carbocyclic [2.2]orthometacyclophane **6 b** has also been synthesized and the conformational equilibrium at ambient temperature has been assigned to a mixture of the *syn*/*anti* conformers (ratio 4 : 1) [10].

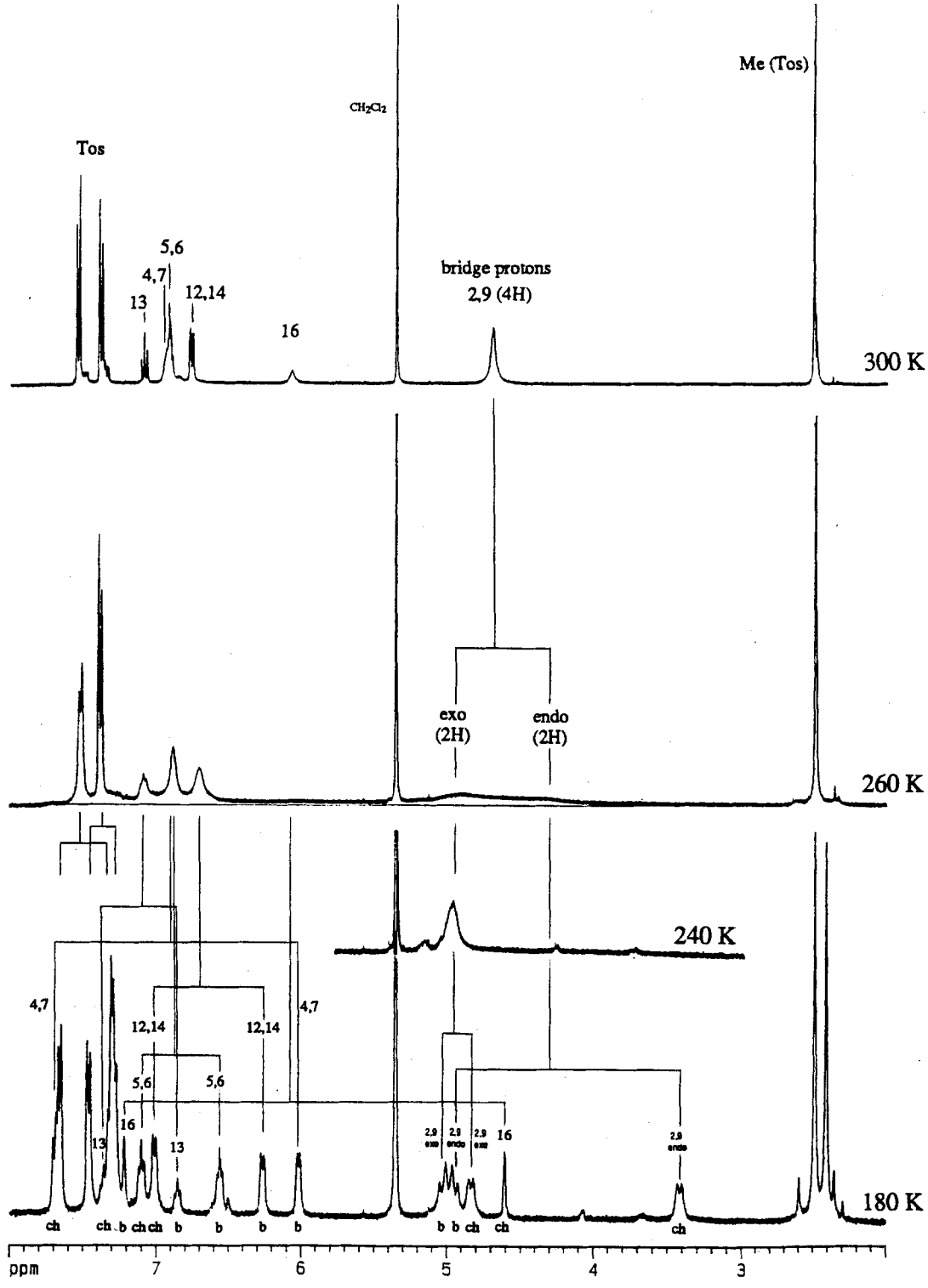

Fig. 1. ^{1}H-NMR spectra of **5b** at 300, 260, and 180 K with an insert at 240 K for the bridge protons. The correlation lines indicate corresponding protons for the chair and boat form. Additional weak signals are caused by impurities (the impurities show a relative increase at low temperatures due to partial precipitation of pure **5b** in the course of the measurement)

Results and Discussion

Synthesis

The N,N′-ditosyl-diaza[2.2]metacyclophanes **5** have been prepared by reaction of N,N′-ditosyl-metaphenylenediamine and (*Z*)-1,4-dichloro-2-butene (for **5a**) or 1,2-bis-bromomethylbenzene (for **5b**) in Cs_2CO_3/acetone, taking advantage of the so-called "cesium effect" [11]. The yields obtained for **5a**, **b** were generally better than 50%, however, diminished dramatically by application of sodium ethanolate/ethanol or potassium carbonate/toluene [12]. Intermolecular cyclization in order to form aza-crown ethers [13] was prevented by means of the voluminous *para*-toluene sulfonyl groups.

Conformational Analysis

The ^{1}H-NMR spectrum of **5b** showed immediately that a time averaged equilibrium of conformers was present in solution (Fig. 1). On the one hand clear assignable resonances for only *one* C_s symmetric species were observed, on the other hand a significant line broadening for the aromatic H-(C-16), the 4 methylene bridge protons H-(C-2,9), and the H-(C-4,7) signal indicate some dynamic process(es).

All protons of the *meta* substituted ring are clearly separated (Tab. 1). The chemical shift of the proton at position 16 is found at rather high field (6.04 ppm) which is obviously due to a ring current effect. The 4/7 dublet and the 5/6 triplet of the other, *ortho* substituted ring overlap in the region of 6.85 − 6.95 ppm. Nevertheless a clear assignment of chemical shifts was possible in the C,H-COSY plot: the triplet for H-(C-5,6) appears rather sharp, whereas the dublet for H-(C-4,7) is obviously the very broad signal at somewhat lower field (compare Fig. 2). The C,H-COSY experiment also allowed unambiguous ^{13}C assignments for all =CH-

Table 1. ^{1}H and ^{13}C chemical shifts of **5a** and **5b** at 300 K (CD_2Cl_2, δ/ppm relative to internal *TMS*)

5a	^{1}H	^{13}C	**5b**	^{1}H	^{13}C
2/5	4.03	46.6	2/9	4.65	51.5
3/4	5.16	128.0	3/8	–	133.5
–	–	–	4/7	6.92	129.9
–	–	–	5/6	6.87	128.1
7/11	–	139.1	11/15	–	139.4
8/10	6.75	127.0	12/14	6.79	127.4
9	7.05	129.4	13	7.04	129.1
12	6.35	134.3	16	6.04	135.2
Tosyl substituents					
1′	–	135.3	1′	–	135.3
2′/6′	7.42	127.4	2′/6′	7.50	128.1
3′/5′	7.33	130.2	3′/5′	7.35	130.0
4′	–	144.0	4′	–	144.3
Me	2.45	21.7	Me	2.47	21.7

type resonances and a clear discrimination between some signals arising from impurities which could not be eliminated even after repeated crystallization of **5b**. These impurities are not very much, but sharp contamination signals in the aromatic region of the ^{13}C-NMR spectrum and are of the same intensity as the aromatic =CH- signals which are unusually small due to the dynamic process(es) in solution. Fig. 2 shows the aromatic region of the C,H-COSY spectrum.

The quarternary carbon atoms C(1′) and C(4′) (of tosyl substituents), C(3,8), C(11,15) (of **5b**) and C(11,15) (of **5a**) were assigned unequivocally from C,H-COSY experiments optimized for long range C,H couplings (Fig. 3). Especially for C(1′) and C(4′) of the tosyl rests, different assignments have been published. The following connectivities are characteristic:

tosyl substituents:	H-(C-3′,C-5′)	–	methyl (^{13}C)
	methyl (^{1}H)	–	C(3′,5′) and C(4′), respectively
	H-(C-3′,C-5′)	–	C(1′)
	H-(C-2′,C-6′)	–	C(4′)
9-membered ring	H-(C-13)	–	C(11,15)
	H-(C-4,C-5,C-6,C-7)	–	C(3,8)

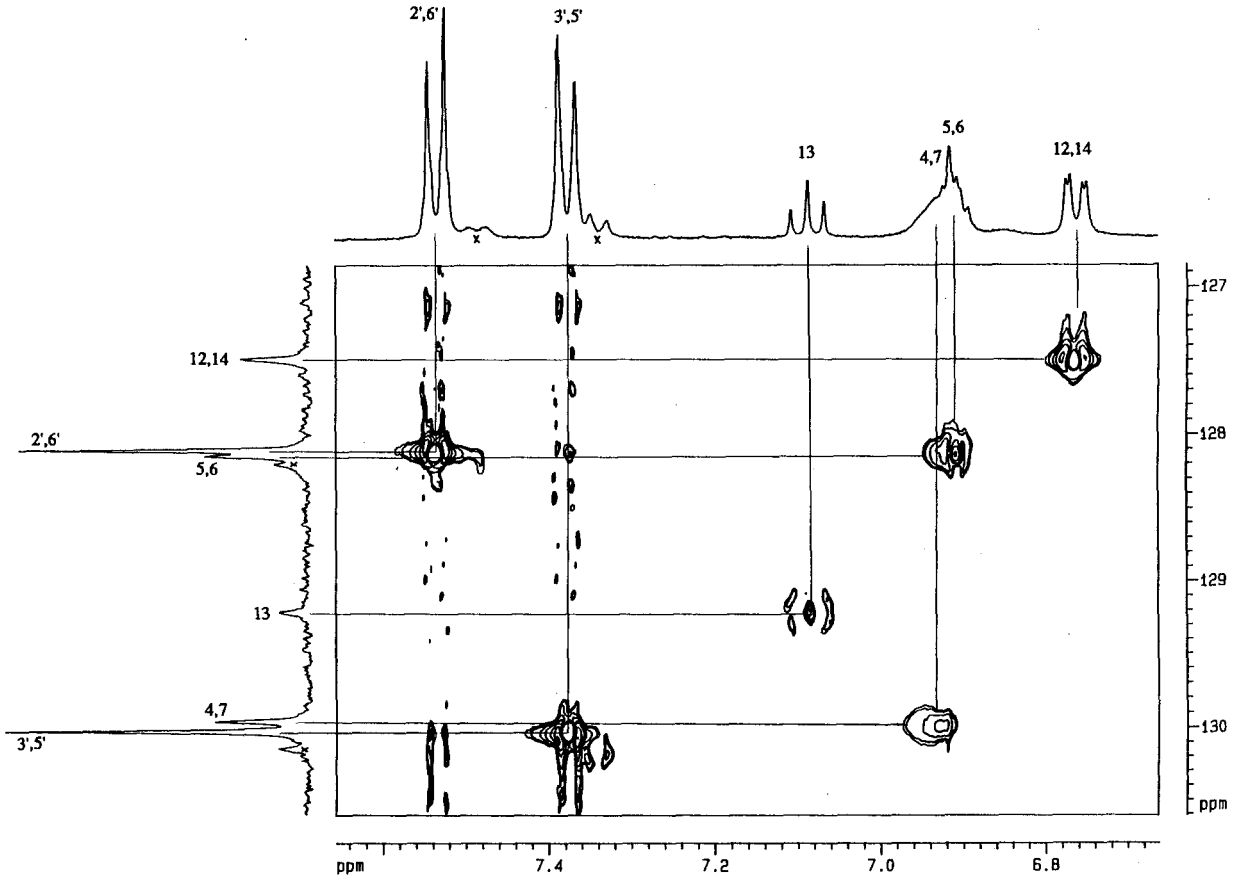

Fig. 2. Aromatic region of the reverse detected C,H-COSY spectrum of **5b** at 300 K (x ... impurities)

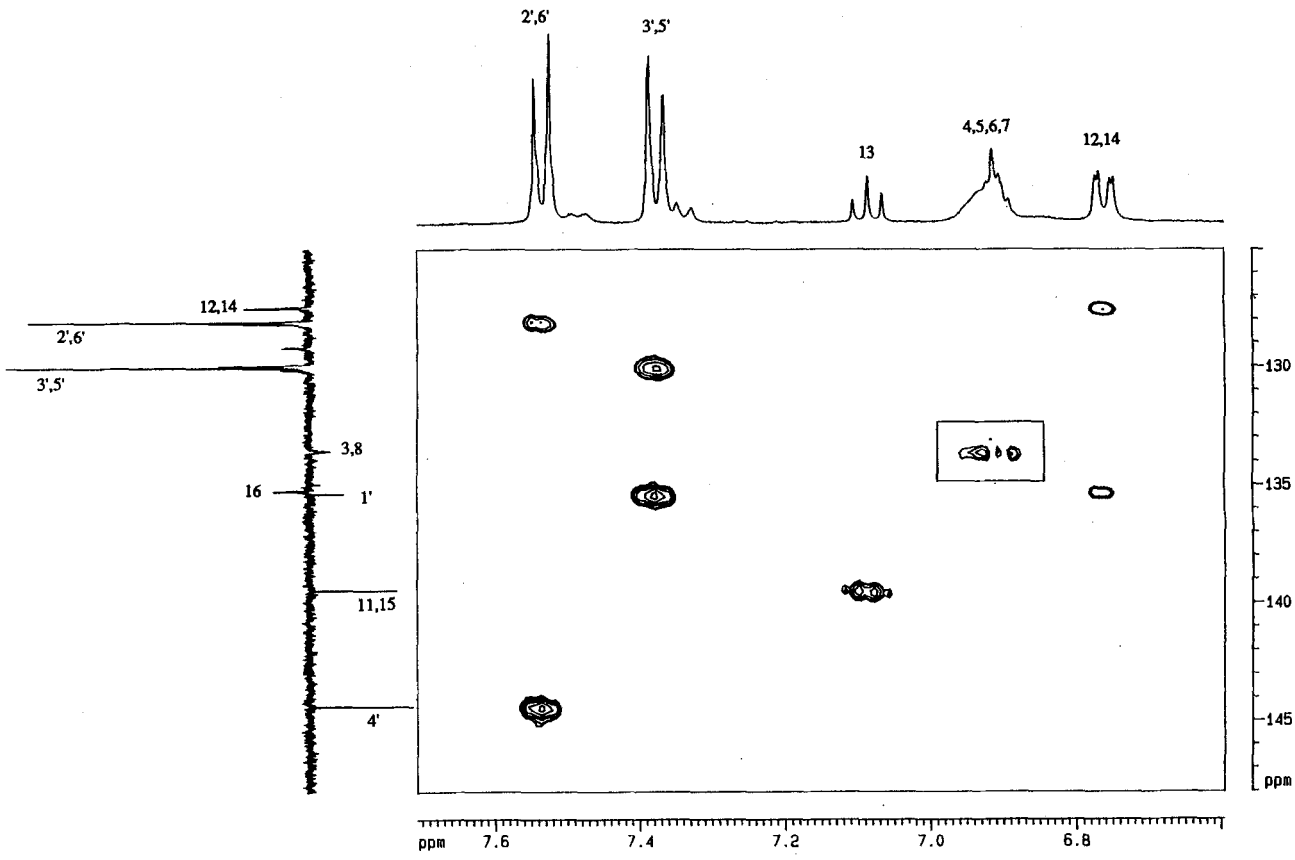

Fig. 3. Aromatic region of the reverse detected C,H-COSY spectrum of **5b** at 300 K, optimized for long-range couplings. The insert (at increased sensitivity) shows the broad cross-peak resulting from the connectivity H-(C-4,5,6,7) – C(3,8). The cross-peak at position H-(C-2′,6′) – C(2′,6′) is not due to an ill suppressed direct C,H connectivity but originates from the interactions of H-(C-2′) with C(6′) and H-(C-6′) with C(2′), respectively. The same principle applies to the cross-peaks at positions H-(C-3′,5′) – C(3′,5′) and H-(C-12,14) – C(12,14)

The ^{1}H- and ^{13}C-NMR spectra of compound **5a** were assigned accordingly (see Table 1).

Figure 1 shows some interesting steps of the temperature dependency of the ^{1}H-NMR in CD_2Cl_2 in the range of 300 – 180 K. All lines broaden at lower temperatures, the broadening of H-(C-16) and the methylene bridge protons being dramatic. The spectrum at 260 K is of special interest. Here two (broad) resonances, each with the intensity of two protons, can be observed. The only reasonable explanation is that the flexibility of the $-N-CH_2-$-bridge is already restricted at that temperature. The average species observed on the NMR time scale is still of C_s symmetry, but the 2-H_{endo}/9-H_{endo} (ca. 4.3 ppm, 2 H, very broad, pointing towards the interior of the central 9-ring system) and the 2-H_{exo}/9-H_{exo} (ca. 4.9 ppm, 2 H, broad, *exo* to the 9-ring system) show up separately. One should note that the aromatic protons are broadened but still of unchanged shift compared to 300 K. One should also note that the *exo* protons sharpen again (insert 240 K in Fig. 1)

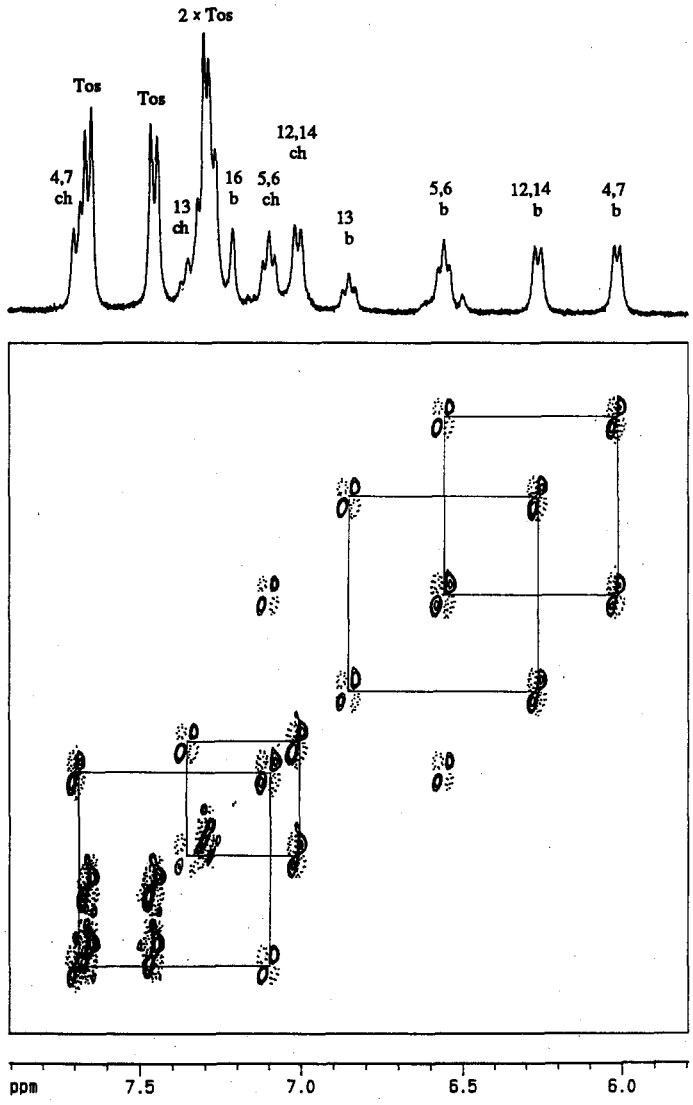

Fig. 4. Aromatic region of the double quantum filtered H,H-COSY spectrum of **5b** at 180 K. For the cross-peak connecting H-5,6(ch) with H-5,6(b) cf. text

which indicates clearly that only the methylene bridge is involved in this first step in freezing out conformers. The *endo* signal does not sharpen any more but this is due to the large shift difference for the corresponding resonances in the conformers of the second step. The coalescence temperature for step one is ca. 270 K with a $\Delta\nu$ of ca. 240 Hz which corresponds to an activation barrier of $\Delta G^{\neq} = 52\,\mathrm{kJ\,mol^{-1}}$.

At ca. 230 K most resonances are so broad that they already disappear in the underground noise. Exceptions with lower coalescence temperatures are one aromatic tosyl resonance (coalescence ca. 200 K), the 2/9 *exo* bridge protons (coalescence at 215 K) and the tosyl methyl group (coalescence at ca. 205 K) which have small $\Delta\nu$ for the newly appearing pair of conformers ($\Delta\nu = 16$ Hz, 64 Hz, and 28 Hz, respectively). Taking into account several exchanging pairs of protons, an

Table 2. ^1H chemical shifts of the boat and chair conformers of compound **5b** at 190 K (CD_2Cl_2, δ/ppm relative to internal *TMS*)

Conformer	Proton-No.					
	2/9	4/7	5/6	12/14	13	16
Boat	4.97 (*exo*) 4.92 (*endo*)	7.66	7.07	6.24	6.83	7.18
Chair	4.81 (*exo*) 3.40 (*endo*)	5.99	6.64	6.98	7.32	4.59

Table 3. Selected values of the force field (PCMODEL [15]) geometries of orthometa[2.2]cyclophane (**6b**) and the 1,10-diazaanalogue **5b**; *exo* and *endo* (due to N-inversion) refers to the position of the two tosyl groups relative to the parent systems; in the case of the *exo/endo* geometries two values are given if there is a significant difference for both sides of the molecule

	6b		**5b**					
	Boat	Chair	Boat			Chair		
			endo/endo	*exo/endo*	*exo/exo*	*endo/endo*	*exo/endo*	*exo/exo*
Out of plane angle (*mesa* substituted ring) [°]								
C16	18.4	18.7	19.8	18.5/19.8	19.2	19.6	18.5/22.7	20.2
C13	5.6	4.6	4.9	3.9/ 5.4	4.9	5.5	4.3/7.4	4.7
Out of plane angle (*ortho* substituted ring) [°]								
	<1	<1	<1	<1	<1	<1	<1	<1
Bond length [Å]								
C1–C2	1.55	1.55	1.49	1.49	1.48	1.48	1.49	1.49
C2–C3	1.52	1.52	1.52	1.53	1.53	1.53	1.52	1.52
C3–C8	1.42	1.42	1.42	1.42	1.42	1.42	1.42	1.42
Bond angles [°]								
C1–C2–C3	114	115	114	114	113	118	117	116
C2–C3–C8	126	126	126	126	126	126	125	126
C2–C1–C15	109	107	114	114	114	113	114	113
C1–C15–C16	117	116	115	113	114	115	115	113
Angle between the two aromatic systems [°]								
	59	166	70	61	62	171	159	159
Distance between H-(C16) and the closest methylene bridge proton [Å]								
	2.29	3.52	2.63	2.22/2.26	2.26	3.45	3.39/3.40	3.37
Calculated energies [kcal/mol]								
	45.98	46.87	86.05	87.24	88.51	90.73	90.81	91.76

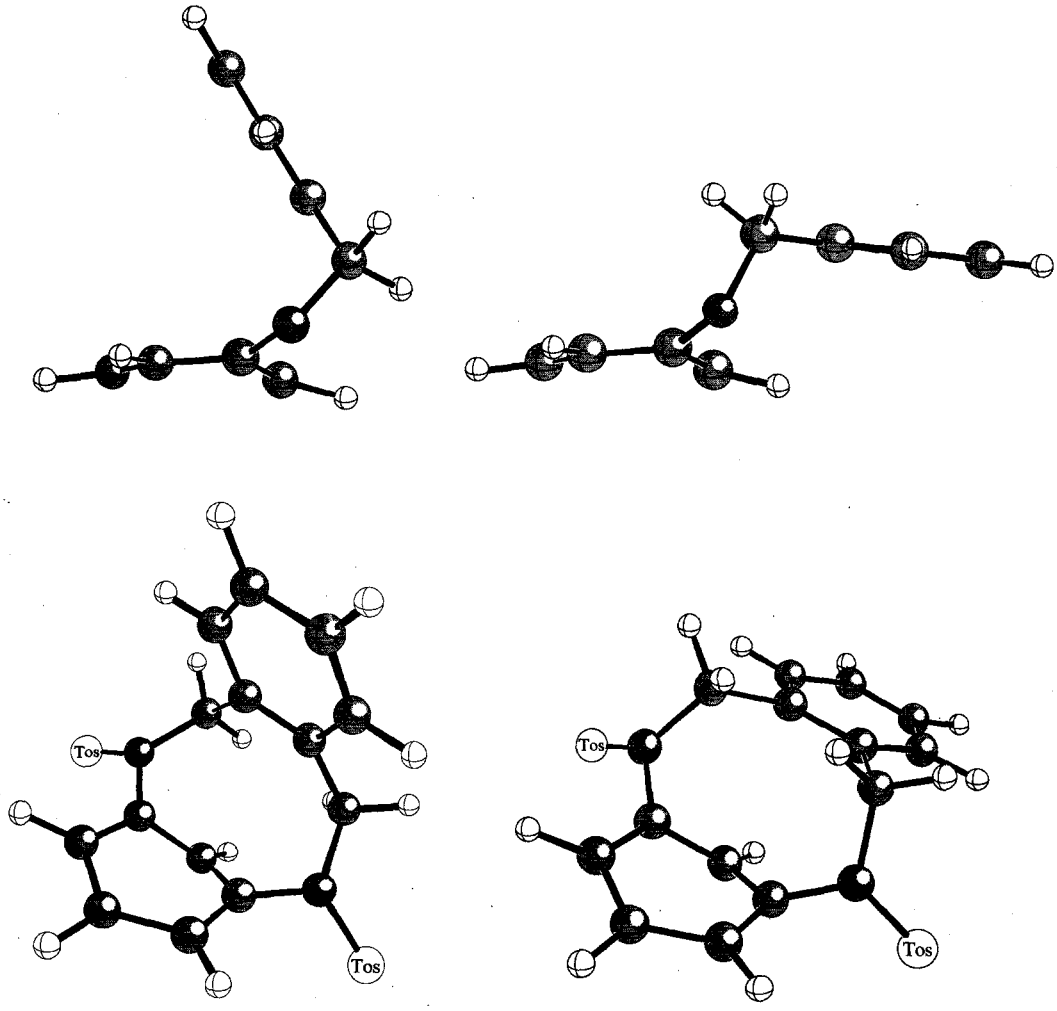

Fig. 5. 5b boat and **5b** chair in different views. Ball & Stick presentation [17] for the PCMODEL [15] geometries; for sake of clarity the tosyl moieties are either omitted completely or symbolized by a simple circle

average barrier of $\Delta G^{\neq} = 43.5 \pm 2\,\mathrm{kJ\,mol^{-1}}$ is obtained for this second step which must be the flip of the aromatic moieties between a chair arrangement and a boat like geometry. This explains also the rather large differences between the chemical shifts for most protons of the two conformers: the drastic change of the orientations of the aromatic rings relative to each other must result in very different positions of protons in the corresponding ring current fields.

The spectrum at 180 K is already very clear and allows a straightforward assignment of resonances using the chemical shifts of corresponding signals together with the original averaged shifts at 260 K (compare the correlations marked in Fig. 1). The assignments are supported by the clear triplet, dublet or singlet type of resonances and correct integrals. As a final proof for the connectivity within the single conformers, a H,H-COSY spectrum was recorded at 180 K. Figure 4 shows the aromatic part of **5b**. The cross peaks for directly coupling aromatic

protons being in full agreement with all other arguments. The partially obscured resonances for H-(C-4,7) chair or H-(C-13) chair show up clearly in the 2D plot.

The cross-peak connecting protons 5 and 6 of the boat conformer with the respective protons of the chair-type conformer obviously does not fit in the assignment pattern given above. It originates either from an exchange phenomenon due to a residual mobility of the *ortho*-substituted aromatic ring or from a dipolar interaction rendered possible by stacking of the two conformers at low temperatures. The appearance of cross peaks caused by coherence transfer pathways generated by mechanisms other than scalar coupling in DQF-COSY spectra at very low temperatures has been observed by several authors and is treated theoretically in detail in Ref. [14].

The decision which set of resonances belongs to the chair conformer and which one to the boat is based on shift arguments due to the ring current effects expected for the two conformers. The same arguments were already used in the corresponding [2.2]orthometacyclophane **6b** [10], however, the trends are even more clear in the 1,10-diazacompound **5b**. Three signals show a dramatic difference in the shift values for the conformers: (i) H-(C-4,7) with a $\Delta\delta$ of 1.67 ppm (only 0.47 in the corresponding compound **6b** [10]), (ii) the C-2/9 *endo* H of the methylene bridge with $\Delta\delta = 1.52$ ppm (1.31 for **6b**), and (iii) especially the H-(C-16) singlet with $\Delta\delta = 2.59$ ppm (0.71 for **6b**). The shift differences are influenced strongly by the ring current effect of the relative benzene ring orientations. However, the relative position of the tosyl moiety and the lone pair at nitrogen may play an important role too.

The tosyl signals were not assigned to the boat and chair conformers because this is of no influence on the conformational conclusions drawn. Final assignments of the ^{1}H chemical shifts to the boat/chair conformers – based on low temperature COSY and ring current arguments – are given in Table 2.

Force field calculations were used to obtain reasonable models for both conformers. In the calculations, the position of the tosyl groups has to be assumed either *exo* or *endo* towards the rest of the molecule. In the experimentally observable molecule, an average structure due to fast nitrogen inversion is most likely, because the barrier for this process is expected to be very low. The results for the diazaorthometacyclophane part of the molecule are not affected by this problem – the characteristic geometrical parameters are almost independent from the configuration of the lone pair and the tosyl substituent at N (compare Table 3).

The resulting structures are shown in Fig. 5 in different views. On can see clearly that:

(i) in the boat form, H-(C-4,7) of the *ortho* substituted ring are directly above the plane of the other ring which results in a strong shielding and a significant upfield shift ($\Delta\delta = 1.67$ ppm);

(ii) in the chair form the C2/C9 *endo* protons point towards the interior of the 9-ring; as a consequence they are in the shielding area of the ring current of the *meta* substituted ring giving an upfield shift ($\Delta\delta = 1.52$ ppm) (the corresponding *exo* protons of the chair as well as all C2/C9 protons of the boat show a normal chemical shift for benzylic protons next to a nitrogen);

(iii) most spectacular is the very high upfield shift for the aromatic proton at C(16) of the chair conformer [H-(C-16) at 4.59 ppm!] due to the close position over the other aromatic ring system.

As already observed for the boat form of **6b**, the *aromatic* resonances for the boat conformer are generally shifted towards higher field because of the opposite second aromatic ring; in the chair form only one aromatic proton (16-H) is above the other ring, the remaining protons are far off (comp. Figs. 1 and 5).

Inspection of Fig. 5 shows that (in contrary to the practically planar *ortho* substituted aromatic ring) the *meta* substituted ring is not planar at all: the out of plane angles for C(16) and C(13) are found to be 19° and 5° (the plane of C11 – C12 – C14 – C15 taken as reference). The values are practically equal for the boat and the chair conformer. In Ref. [10] corresponding values of 14° and 6° are given for a MMX 87 force field calculation of **6b**. We have used a somewhat simplified version of the same type (PCMODEL for an Apple Macintosh [15]). Molecules **5b** and **6b** were minimized with PCMODEL for direct comparison. As far as **6b** is concerned, the resulting geometrical parameters are rather comparable with the data mentioned in Ref. [10]. The energy difference for **6b** was found to be 0.9 kcal mol^{-1} in favour of the boat form which is consistent with the observed 4 : 1 ratio for boat **6b** : chair **6b**.

The exact numerical values for the minimum energies are usually not too significant and the ΔH found for boat **5b** : chair **5b** of ca. 4 kcal/mol in favour of the boat form deviates from the experimental value of $\Delta H \sim 0$ kcal/mol. The N-tosyl part of **5b** is not easy to simulate due to the additional nitrogen inversion; we have tried to use Allinger's MM2 and MAX, but the parametrization was not suited for the sulfonamide function in **5b**. However, the PCMODEL results seem to be rather reasonable and show the same trend as described in Ref. [10] for **6b**.

The bonds C1 – C2, C2 – C3, and C3 – C8 are elongated, the angles C1 – C2 – C3 and C2 – C3 – C8 at the *ortho* aromatic moiety are widened up, and the angles C2 – C1 – C15 and C1 – C15 – C16 at the *meta* substituted branch of the molecules show smaller values than the normal ones. Details of the force field results for **5b**, and **6b** are listed in Table 3.

The barriers between the chair and boat (or *anti* and *syn* [10]) conformers for **5b** and **5a** and their non-aza (all CH) analogs **6b** and **6a** also deserve some comments. In Ref. [10] the activation barrier for **6b** was estimated to be somewhere in the range of 90 – 95 kJ mol^{-1}. The barrier for the corresponding compound with substitution of the *meta* substituted benzene ring with the more flexible (3*Z*)-ethene unit gave an experimental value of $\Delta G^{\neq} = 69$ kJ mol^{-1} [16]. The value found for **5b** (the diaza analog of **6b**) is 43.5 kJ mol^{-1}, the value for the corresponding *Z*-olefinic diaza compound **5a** should be of interest as well.

For compound **5a** the coalescence temperature could not be reached. The ^{1}H-NMR spectrum of **5a** at 300 K (Table 1) is characterized by very sharp resonances which show only small broadening effects upon cooling down. At ca. 210 K all resonances of the cyclononadiene ring system show a broadness which is comparable with the shape of the corresponding resonances for **5b** at 300 K. The singlet between the *meta* substituted nitrogen [H-(C-16) in **5b**, H-(C-12) in **5a**] is already very flat, the olefinic protons H-(C-3,4), the methylene bridge protons (positions 2/9 in **5b**, 2/5 in **5a**), and the aromatic dublet of the *meta* substituted ring [H-(C-12,14) in **5b**, H-(C-8,10) in **5a**] are also significantly broadened. All these lines get indeed very broad after further lowering of the temperature [the aromatic H-(C-12) disappearing in the underground], however, at a temperature of 180 K all lines are still in the fast exchange range. Assuming comparable $\Delta\delta$ as for **5b** (e.g. for the

endo methylene proton which should suffer a similar influence due to the magnetic an isotropy of the aromatic *meta* substituted ring) one arrives at $\Delta G^{\neq} = < 30\,kJ\,mol^{-1}$. An estimated value in the range of $20-25\,kJ\,mol^{-1}$ might be reasonable.

Even if we avoid any speculation concerning the exact numerical values of the barriers for **5a** and **6b**, a comparison within the series of related nonadienes **5a,b**, **6a,b** is rather interesting: the most rigid structure is the tricyclic non-aza compound **6b** with two benzene rings ($\Delta G^{\neq} > 85\,kJ\,mol^{-1}$). Substitution of $-$N*Tos*- for $-CH_2-$ and ethene for the *ortho*-substituted aromatic ring enhances the flexibility of the cyclononadiene system considerably. The contribution of $-$N*Tos*- to the flexibility of the system is more pronounced than the introduction of the *cis* olefinic bridge: $\Delta G^{\neq} = 69\,kJ\,mol^{-1}$ for **6a** and $\Delta G^{\neq} = 43.5\,kJ\,mol^{-1}$ for the diaza compound **5b**. The very low $\Delta G^{\neq} < 30\,kJ\,mol^{-1}$ for the olefinic diaza compound **5a** completes the series of increasing flexible cyclononadienes.

Experimental Part

The melting points given were determined using a Boetius melting point apparatus; they are uncorrected. The mass spectra (70 eV) were obtained using a mass spectrometer CH 6 (Varian MAT) by direct evaporation.

Reaction of N,N'-ditosyl-metaphenylenediamine and 1,4-dihalides

2 g (4.8 mmol) of N,N'-ditosyl-metaphenylenediamine and 1.6 g (5 mmol) of Cs_2CO_3 were dissolved in 150 ml of absolute acetone and heated at reflux. At the boiling temperature slowly (over 4 h) 5 mmol of the corresponding 1,4-dihalide, dissolved in 100 ml of absolute acetone was added and the mixture stirred for another 12 h while heated. Then, after removing the solvent under reduced pressure and crystallization of the oily residue from a small amount of benzene, the solid product was heated with 30 ml of 2 *N* aqueous NaOH solution at reflux. Finally, the substance was cleaned by washing with a small amount of water/acetone and recrystallized from toluene (**5a**) or benzene (**5b**).

N,N'-Ditosyl-1,6-diaza-3,4-dehydro[6]metacyclophane (**5a**)

From N,N'-Ditosyl-metaphenylenediamine and (*Z*)-1,4-dichloro-2-butene; yield 1.05 g (46%), m.p. 281–283°C (from toluene). MS [70 eV, *m/z* (Rel. int.)]: 468 (M^+, 21), 416 (29), 369 (4), 313 (47), 263 (14), 246 (31), 187 (100), 156 (46), 155 (39%). $C_{24}H_{24}N_2O_4S_2$ (468.5): calc. C 61.52, H 5.16, N 5.97, S 13.68; found: C 61.19, H 5.10, N 5.68, S 13.52.

N,N'-Ditosyl-1,10-diaza[2.2]orthometacyclophane (**5b**)

From N,N'-Ditosyl-metaphenylenediamine and 1,2-bis-bromomethylbenzene; yield 1.20 g (46%), m.p. 291–293°C (from benzene). $C_{28}H_{26}N_2O_4S_2$ (518): calc. C 64.84, H 5.05, N 5.40, S 12.36; found: C 64.58, H 5.02, N 5.11, S 12.45.

NMR-Measurements

NMR measurements were performed in 5 mm tubes in CD_2Cl_2 solutions on a Bruker AM 400 WB NMR spectrometer operating at 9.4 T and equipped with an inverse probe for the proton-detected heteronuclear experiments. Sample concentrations were about 20 m*M*. All 2D spectra with the ex-

ception of the long-range C,H-COSY experiment were recorded in the phase-sensitive mode using the TPPI method [18]. Measurement times were about 14 hours for the long-range C,H-COSY experiment and about 4 hours for the other 2D experiments. Data were processed on a satellite station (Bruker Aspect X 32) using the UXNMR software [19]. Signal to noise improvement was achieved by submitting the processed data to the AURELIA algorithm [20]. No symmetrization procedure was applied to the COSY spectrum.

1D ^{1}H experiments: sweep width, 4 kHz; size, 32 k data points; spectra were recorded in 10 K-steps from 300 to 180 K; the temperature was adjusted and kept constant by the variable temperature equipment of the spectrometer (VT 1000); no correction was applied to the meter reading.

J-modulated 1D ^{13}C experiment (SEFT [21]): temperature, 300 K; sweep width, 25 kHz; size, 64 k data points; relaxation delay, 3 s; pulse width (90°), 5.1 μs; filter function, exponential weighting; line broadening factor, 2 Hz.

Double-quantum filtered H,H-COSY [18]: temperature, 180 K; sweep width, 2 kHz; size, 2 k data points in ω_2, 256 experiments in ω_1 (16 scans); relaxation delay, 2.5 s; pulse width (90°), 12.2 μs; zero filling, 1 k data points (real) in ω_1; filter function, sine bell squared shifted by $\pi/3$ rad in both dimensions.

Reverse C,H-COSY with BIRD sequence and GARP1 decoupling [22]: temperature, 300 K; sweep width, 15 kHz in ω_1, 2 kHz in ω_2; size, 2 k data points in ω_2, 256 experiments in ω_1 (32 scans); relaxation delay, 1 s; BIRD delay, 0.3 s; pulse width (90°), 10.9 μs (^{1}H), 8.6 μs (^{13}C hard), 55 μs (^{13}C soft); zero filling, 1 k data points (real) in ω_1; filter function, sine bell squared shifted by $\pi/2$ rad in both dimensions.

Long-range reverse C,H-COSY with *J*-filter [23]: temperature, 300 K; sweep width, 15 kHz in ω_2, 2 kHz in ω_1; size, 2 k data points in ω_2, 512 experiments in ω_1 (96 scans); relaxation delay, 1 s; pulse width (90°), 10.9 μs (^{1}H), 8.6 μs (^{13}C); *J*-filter delay, 3.57 ms (optimized for suppression of one-bond C,H couplings); delay for evolution of long range couplings, 66 ms (optimized for $J = 7.5$ Hz); zero filling, 1 k data points (real) in ω_1; filter function, sine bell squared shifted by $\pi/2$ rad in both dimensions; magnitude representation.

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References

[1] Glass R. S. (1988) Conformational Analysis of Medium-Sized Heterocycles, VCH Publishers
[2] Vögtle F. (1990) Cyclophan-Chemie, Verlag B. G. Teubner Stuttgart
[3] Misumi S., Otsubo T. (1978) Acc. Chem. Res. 11: 251; Vögtle F., Neumann P. (1972) Angew. Chem. **84**: 75
[4] Vögtle F., Neumann P. (1970) Tetrahedron Lett.: 115; Vögtle F., Meurer K., Mannschreck A., Stühler G., Puff H., Roloff A., Sievers R. (1983) Chem. Ber. **116**: 2630; Meurer K., Vögtle F., Mannschreck A., Stühler G., Puff H., Roloff A. (1984) J. Org. Chem. **B**: 3484
[5] Otsuba T., Kitasawa M., Misumi S. (1979) Bull. Chem. Soc. Jpn. **52**: 1515; Rossa L., Vögtle F. (1977) J. Chem. Res., Synop.: 164; Semmelhack M. F., Harrison J. J., Young D. C., Gutierrez A., Rafii S., Clardy J. (1985) J. Am. Chem. Soc. **107**: 7508; Anker W., Bushnell G. W., Mitchell R. H. (1979) Can. J. Chem. **57**: 3080
[6] Kleinpeter E., Gäbler M., Schroth W. (1988) Mh. Chem. **119**: 233; Kleinpeter E., Schroth W. (1989) Z. Chem. **29**: 62; Kleinpeter E., Hartmann J., Werner B., Schroth W. (1990) Magn. Reson. Chem. **28**: 423
[7] Kleinpeter E., Hartmann J., Schroth W. (1990) Magn. Reson. Chem. **28**: 628; Schroth W., Hartmann J., paper on further synthetic details in preparation

[8] Extremely strained metacyclophanes: [4] pyrrolophane: Patterson J. M., Brash J., Drenchko P. (1962) J. Org. Chem. **27**: 1652; [5] metacyclophane: van Straten J. W., de Wolf W. H., Bickelhaupt F. (1977) Tetrahedron Lett.: 4667; Dewar isomer of [4] metacyclophane: Turckenburg L. A. M., van Straten J. W., de Wolf W. H., Bickelhaupt F. (1980) J. Am. Chem. Soc. **102**: 3256
[9] Bodwell G. J., Ernst L., Hopf H., Jones P. G., McNally J. P., Schomburg D. (1990) Chem. Ber. **123**: 2381
[10] Bodwell G. J., Ernst L., Haenel M. W., Hopf H. (1989) Angew. Chem. **101**: 509
[11] Klieser B., Rossa L., Vögtle F. (1984) Kontakte (E. Merck)
[12] In the case of the corresponding [2.2]orthocyclophanes of type 1 (X = N-tosyl), synthesized from N,N'-ditosyl-orthophenylendiamine and (*Z*)-1,4-dichloro-2-butene or 1,2-bis-bromomethyl-benzene, yields between 70% and 80% were obtained; Schroth W., Streckenbach B. (1963) Z. Chem. **3**: 288
[13] Stetter H. (1953) Chem. Ber. **86**: 197
[14] Wimperis S., Bodenhausen G. (1989) Mol. Phys. **66**: 897
[15] Molecular Modeling Software PCMODEL (1990) Serene Software, Bloomington, IN
[16] Goodman J. L., Benson J. A. (1985) J. Am. Chem. Soc. **107**: 5424
[17] Müller N., Falk A. (1989) Ball & Stick Program for Apple Macintosh
[18] Marion D., Wüthrich K. (1983) Biochem. Biophys. Res. Commun. **113**: 967; Rance M., Sorensen O. W., Bodenhausen G., Wagner G., Ernst R. R., Wüthrich K. (1983) Biochem. Biophys. Res. Commun. **117**: 479
[19] Fa. Bruker Analytische Meßtechnik GmbH, Karlsruhe, FRG, software release 10/90
[20] Neidig K. P., Kalbitzer H. R. (1990) J. Magn. Reson. **88**: 155
[21] Brown D. W., Nakashima T. T., Rabenstein D. L. (1981) J. Magn. Reson. **45**: 302
[22] Bax A., Subramanian S. (1986) J. Magn. Reson. **67**: 565
[23] Bax A., Summers M. F. (1986) J. Am. Chem. Soc. **108**: 2093

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