Monatshefte für Chemie 119, 233—246 (1988)

Monatshefte für Chemie
Chemical Monthly

Intramolecular Flexibility of Heteroanalogous Benzo- and Dibenzo-1,5-cyclooctadienes

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(Received 15 April 1987. Accepted 10 June 1987)

The temperature-variable ^1H and ^{13}C NMR spectra of a series heteroanalogous mono- and dibenzo-1,5-cyclooctadiene derivatives have been obtained, and the present dynamic process discussed in terms of the preferred conformations of the eight-membered ring and the occuring ring interconversional process as well. The boat conformation, which is at − 120 °C still the average of the apparent twist boat conformations, has been identified by dynamic NMR spectroscopy, interconverting via a boat inversional mode. The free energies of activation, $\Delta G_c^{\neq}$, for the latter process have been determined and discussed according to structural variations, the concentration of the samples, present heteroatoms, and solvent influences, respectively. A few chemical shift aspects of more general interest are mentioned.

(Keywords: Mono- and dibenzo-1,5-cyclooctadiene derivatives; Dynamic NMR; Conformational analysis; Ring interconversion of 8-membered rings)

Intramolekulare Beweglichkeit heteroanaloger Benzo- und Dibenzo-1,5-cyclooctadiene

Die ^1H- und ^{13}C-NMR-Spektren einer Reihe heteroanaloger Benzo- und Dibenzo-1,5-cyclooctadiene werden berichtet und der bei Temperaturvariation meßbare dynamische Prozeß hinsichtlich Vorzugskonformationen des 8-Ringes bzw. der Art des vorliegenden Ringinversionsprozesses diskutiert. Die Bootkonformation (bei − 120 °C noch ein schnelles Gleichgewicht der entsprechenden Twist-Boot-Konformationen) wird mittels dynamischer NMR-Spektroskopie nachgewiesen und die 8-Ringinversion über einen Bootinversionscyclus realisierend identifiziert. Hierfür meßbare freie Aktivierungsenthalpien, $\Delta G_c^{\neq}$, werden bezüglich struktureller Einflüsse, der Probenkonzentration, vorhandener Heteroatome und des Lösungsmittels diskutiert. Einige Effekte auf die chemischen Verschiebungen von mehr allgemeinem Charakter werden berichtet.

Introduction

Dynamic NMR investigations of dibenzo-1,5-cyclooctadienes, and some heteroanalogues as well, have displayed the more rigid chair, **C**, and

the more flexible boat, **B**, to be the ground state conformations of the 8-membered ring [1–3]. The twist boat conformation, **TB**, however, due to smallest eclipsing interactions, has been found to be the most stable one, both by variable-temperature ^{1}H NMR studies [3, 4] as well as force field calculations [5, 6]. Beside that, the 8-membered ring was found to interconvert via two mechanisms:

(i) boat-to-chair interconversion [2, 3, 5, 6]:

$$\mathbf{B} \rightleftharpoons \mathbf{TS\text{-}1} \rightleftharpoons \mathbf{C} \rightleftharpoons \mathbf{TS\text{-}1}^{+} \rightleftharpoons \mathbf{B}^{+}, \text{ and}$$

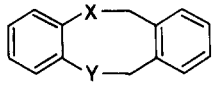
(ii) boat inversion [6, 8]:

$$\mathbf{TB} \rightleftharpoons \mathbf{B} \rightleftharpoons \mathbf{TB}^{+} \rightleftharpoons \mathbf{TS\text{-}2} \rightleftharpoons \mathbf{TB}^{++}.$$

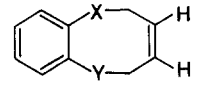
Whereas the structure of the transition state **TS-1** of the boat-to-chair interconversional process is quite clear (extremely unstable structure of six coplanar atoms of the 8-membered ring [2]), different interpretations about the latter one, **TS-2**, have been given (of skew type [6], of folded boat type [2], or any intermediate of these two [3]).

We did prepare some heteroanalogous mono- and dibenzo-1,5-cyclooctadiene derivatives, **1**–**8** [7], and after having these compounds in hand we became interested in the dynamic behaviour and the major ground state conformations of these compounds.

Scheme 1



no.	X	Y
1	-NTos	-NTos
2	-NTos	-O-
3	-S-	-O-
4	-O-	-O-



no.	X	Y
5	-NMes	-NMes
6	-NTos	-NTos
7	-NTos	-O-
8	-O-	-O-

The adequate ^{1}H dynamic NMR study and the discussion of the results in terms of the interconversion of preferred conformations of the 8-membered rings is the major objective of this paper.

Results

The ^{1}H NMR spectra of the studied compounds, **1**–**8**, have been obtained at variable temperatures—Fig. 1 depicts the adequate variations in the spectrum of N,N′-ditosyl-diazocine, **1**; similar effects have been

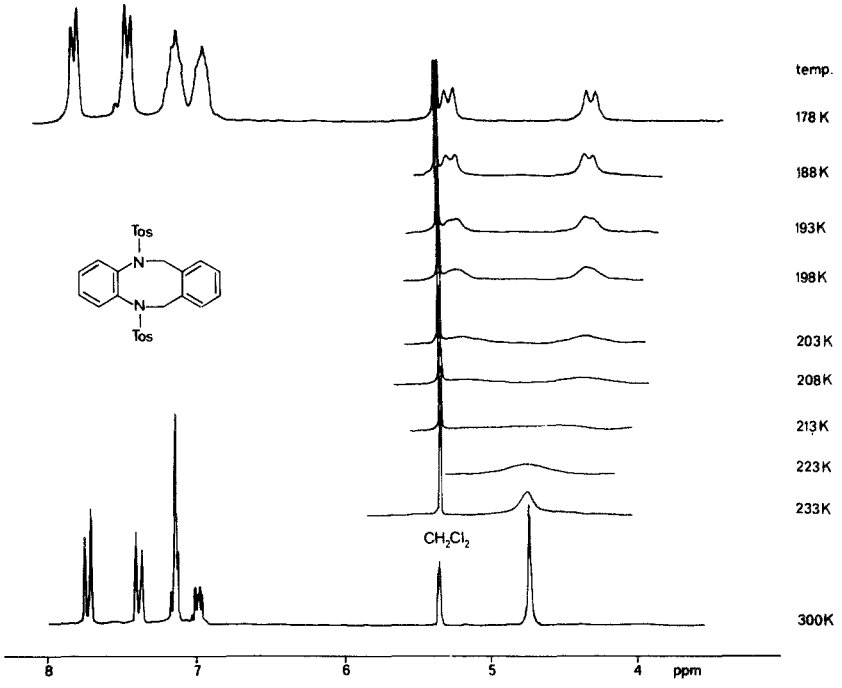


Fig. 1. 200.13 MHz ^{1}H NMR spectrum of N,N′-ditosyl-diazocine (**1**) at variable temperatures

observed in the ^{1}H NMR spectra of **2**, **3**, **5**–**7**. The ^{1}H NMR spectra of the compounds **4** and **8** did not change analogously up to $-120\,^\circ$C.

The room temperature ^{1}H chemical shifts are collected in Table 1; the adequate assignments were rather simple according to the very different and characteristic absorption ranges. A few exceptions and results of more general interest are:

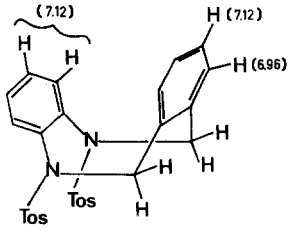
(i) Due to the different heteroatoms in the 8-membered rings, the geminal coupling constants of the adjacent diastereotopic CH_2 protons have been found variable:

$$\begin{array}{ll} \text{—N(tosyl)—CH}_2\text{—} & J_{gem} = 12.0\,\text{Hz} \\ \text{—O—CH}_2\text{—} & J_{gem} = 13.5\,\text{Hz} \\ \text{—S—CH}_2\text{—} & J_{gem} = 11.5\,\text{Hz}, \end{array}$$

but the sequence is different to adequate values in the corresponding 7-membered rings [8].

(ii) One of the four different aromatic protons of compound **1** has been found separated, shifted to higher field (at $\delta = 6.96$ ppm in CD_2Cl_2).

Scheme 2



In searching for the reason therefore, ^1H homonuclear NOE difference spectra [9] have been obtained, resulting both at room temperature as well as at $-100\,°C$ in measurable NOEs for the proton of interest, if the adjacent CH_2 proton(s) have been irradiated (at room temperature: $\delta = 4.77$ ppm; at $-100\,°C$: $\delta = 4.28$ ppm), and inversely. Hereby spatial proximity between studied protons is unequivocally, even if the reason therefore is still less clear—peri-like interactions of the present type result usually in low field effects [4]. The NOE study is depicted in Fig. 2 and the obtained results are discussed (*vide infra*).

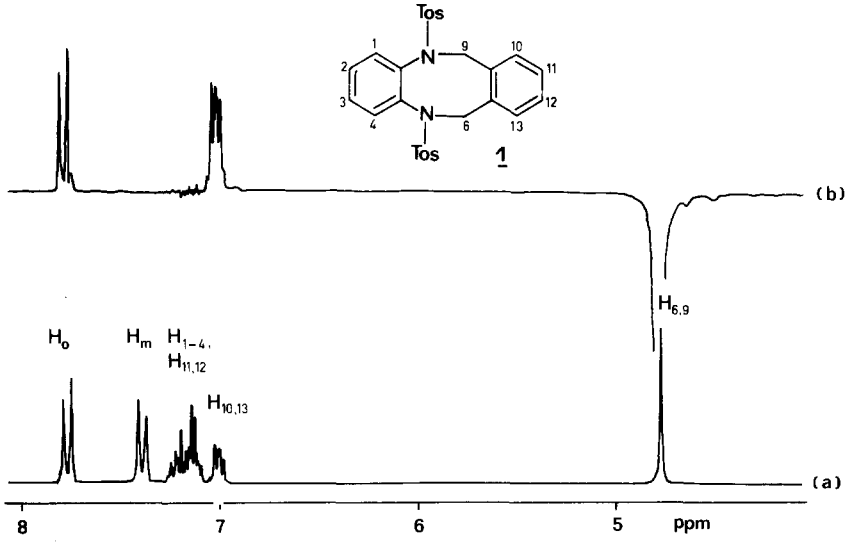
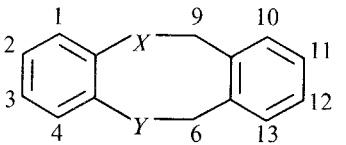


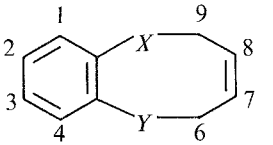
Fig. 2. 200.13 MHz ^1H NMR spectrum of N,N'-ditosyl-diazocine (**1**) (*a*). NOE difference spectrum (irradiation of $H_{6,9}$ at $\delta = 4.72$ ppm) (*b*)

Table 1. ^{1}H *chemical shifts,* δ (ppm), *of the mono- and dibenzo-1,5-cyclooctadiene derivatives,* **1–8**, *at ambient temperature in the solvent* CD_2Cl_2

1–4



5–8

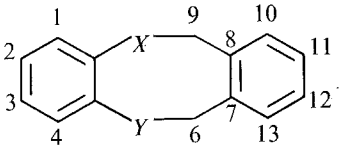


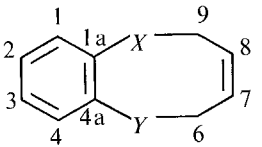
Compound			C^6H_2	C^9H_2	C^7H; C^8H	$C^{10}H$; $C^{13}H$	$C^{11}H$—$C^{12}H$ C^1H—C^4H	Tosyl/ mesyl
No.	*X*	*Y*						
1	N*Tos*	N*Tos*	4.72 (s)		—	6.96 (m)	7.12 (m)	2.45 (s); 7.72 (d); 7.35 (d)
2	N*Tos*	O	5.06 (s)	4.91 (s)[a]	—	6.86–7.28 (m)		2.42 (s); 7.72 (d); 7.25 (d)
3	S	O	5.35 (s)	4.40 (s)	—	6.83–7.27 (m)		—
4	O	O	5.41 (s)		—	6.86–7.28 (m)		—
5	N*Mes*	N*Mes*	4.47 (m)		5.72 (m)	7.33–7.45 (m)		3.08 (s)
6	N*Tos*	N*Tos*	4.22 (m)		5.59 (m)	7.15–7.27 (m)		2.44 (s); 7.68 (d); 7.35 (d)
7	N*Tos*	O	4.77 (d)	4.36 (d)[a]	5.63–5.85 (m)	6.88–7.28 (m)		2.44 (s); 7.48 (d); 7.28 (d)
8	O	O	4.92 (m)		5.90 (m)	6.98 (s)		—

[a] Due to the obtained NOE effect on the ortho tosyl protons

Table 2. ^{13}C *chemical shifts*, δ (ppm), *of the mono- and dibenzo-1,5-cyclooctadiene derivatives*, **1–8**, *at ambient temperature in the solvent* CD_2Cl_2

1–4





5–8

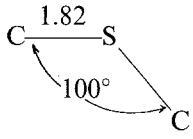
Compound			C-6	C-9	C-1a	C-4a	C-7	C-8	C-1–C-4 C-10–C-13[a]	Tosyl/mesyl
No.	*X*	*Y*								
1	N*Tos*	N*Tos*	53.5		136.8		134.6		127.9; 129.0 129.1; 130.6	21.7 144.5 130.2 128.2; 136.7
2	N*Tos*	O	54.2	74.9	136.1	154.6	131.7	134.4	131.4; 131.0 129.6; 129.2 129.2; 128.9 124.0; 122.6	21.7 129.8 127.9 144.1 136.3
3	S	O	76.7	36.5	129.7	156.8	136.3	137.5	123.1; 127.7 127.5; 127.8 128.4; 129.3 130.7; 130.8	—
4	O	O	75.3		150.0		135.9		122.0; 123.6 128.5; 129.1	—

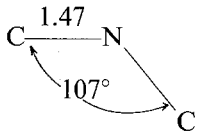
5	N*Mes*	N*Mes*	47.8		136.9		128.9[b]		129.1; 129.8[b]	39.0
6	N*Tos*	N*Tos*	48.2		136.5		129.0[b]		128.9; 128.1[b]	21.7 144.5 130.1; 128.4 136.8
7	N*Tos*	O	68.4	50.1	129.9	154.7	129.4[b]	130.7[b]	123.4; 127.9[b] 122.4; 127.9	21.7 144.5 129.7 136.8; 128.4
8	O	O	69.8		147.1		128.9[b]		123.5; 122.1[b]	—

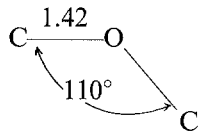
[a] Not assigned; the tentative assignment is adequate for our purpose, since any reversal does not alter the conformational conclusions formulated in the text

[b] Or reversed

(iii) The chemical shift differences of the diastereotopic CH_2 protons, $\Delta\nu$—see Table 3, are determined presumably by their spacial proximity to the neighboured protons and substituents, if present (transannular and peri-like interactions). Obviously because of variations in the geometry of the 8-membered ring due to decreasing bond lengths as well as increasing bond angles in the following manner:





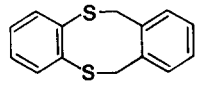


these interactions get less important in the following order:

S—CH_2—	N—CH_2—	O—CH_2
388 Hz (**3**)	193 Hz (**1**)	110 Hz (**2**) all at 200.13 MHz.
	200 Hz (**6**)	127 Hz (**3**)

The presence of the chair conformation, **C**, in measurable amounts [2] in dibenzo-dithiocine (**9**) but its complete absence in compounds **1**–**8** must be of similar reasons.

Scheme 3



9

Also the ^{13}C NMR spectra were run at variable temperatures. Any adequate exchange process, however, except of quite normal low temperature shifts could not be studied; so only the room temperature ^{13}C NMR spectra are given in Table 2.

The free energies of the present dynamic process have been calculated at the coalescence temperature, T_c, using Eq. (1) for the coupled two-site exchange ($J_{AB} \neq 0$) via the *Eyring* equation [10].

$$k_c = \frac{\pi\sqrt{\Delta\nu^2 + 6J_{AB}{}^2}}{\sqrt{2}} \tag{1}$$

Necessary dynamic NMR parameters, obtained from the ^1H NMR spectra of compounds **1**–**8**, and the calculated interconversional barriers, $\Delta G_c^{\neq}$, are given in Table 3.

Table 3. *Dynamic* ^{1}H NMR *parameters and the boat inversional barriers,* $\Delta G_c^{\neq}$, *of mono- and dibenzo-1,5-cyclooctadiene derivatives*

Compound			Solvent	Studied protons	T_c(K)	$\Delta\nu$(Hz)	J_{gem}(Hz)	$\Delta G_c^{\neq}$ (kJ/mol)
No.	*X*	*Y*						
1	N*Tos*	N*Tos*	CD_2Cl_2	N—CH_2—	212	193	12	40.6
2	N*Tos*[a]	O	CD_2Cl_2	O—CH_2—	193	110	12	37.6
3	S	O	CD_2Cl_2	O—CH_2—	180	127	13.5	34.8
				S—CH_2—	188	388	11.5	34.7
			toluene	O—CH_2—	178	102	13.5	34.7
				S—CH_2—	188	405	11.5	34.7
			CD_3OD	O—CH_2—	183	118	13.5	35.5
				S—CH_2—	188	259	11.5	35.3
			acetone	O—CH_2—	185	109	13.5	36.0
				S—CH_2—	190	222	11.5	36.0
4	O	O	CD_2Cl_2/ freon 22	O—CH_2—	< 155	—	—	—
5	N*Mes*	N*Mes*	CD_2Cl_2	N—CH_2—	190	148	12.0	36.6
6	N*Tos*	N*Tos*	CD_2Cl_2/ freon 22	N—CH_2—	175	200	12	33.1
7	N*Tos*[a]	O	CD_2Cl_2/ freon 22	O—CH_2—	155	~ 150	~ 12	~ 29.6
8	O[b]	O	CD_2Cl_2/ freon 22	O—CH_2—	< 150	—	—	—

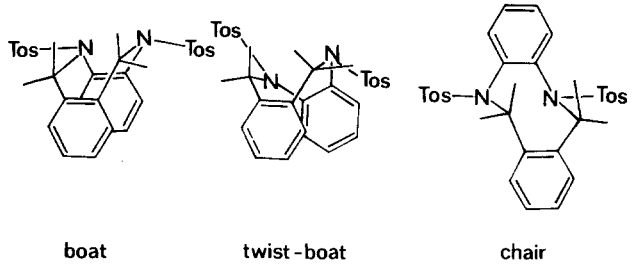
[a] N—CH_2— protons not yet in the slow exchange area at 173 K
[b] The 7,8-dimethyl analogue of **8** has also been investigated with the same result

Discussion

Present Interconversional Process and Preferred Conformations

Due to the present spectroscopical variations contrasted to literature results [1–6], the flexible boat conformation, which is even at − 120 °C still the average of the apparent twist boat conformations, has been assigned to interconvert via a boat inversional mode. The chair conformation however, is probably due to the higher order of eclipsing interactions [3, 6] and due to some other reasons (*vide infra*) destabilized too much to be identified by dynamic NMR spectroscopy (< 5%). These assignments according to both the preferred conformations and the ring interconversional process as well are proved independently by ^{13}C NMR spectroscopy and some other arguments:

Scheme 4



(i) From the ^{13}C NMR spectra we could not get any further information about the absent chair conformation in **1**–**8**.

(ii) But at lowest accessible temperatures, the carbon signals of the 8-membered rings broaden (the resonance lines for **4** disappeared almost at − 117 °C, see Fig. 3) obviously due to a further dynamic process, which we assign to the twist boat/boat—interconversion getting slow at that temperatures. Hereby the designated boat inversional process is supported to be the actual one by dynamic NMR spectroscopy.

(iii) One of the two N-lone pairs in **1**, **4**, and **5**, and the only one in **2**, and **6**, respectively, should be conjugated with the neighboured phenyl ring to enable mesomerism [11], which is impossible in the more rigid chair conformation, but readily possible in the twist boat conformations. So, obviously the twist boat conformations of compounds **1**, **4**, and **5** have one nitrogen atom in-plane (sp^2) and the other one out-of-plane (probably more or less sp^3-hybridized), rapidly interconverting still at − 120 °C.

(iv) The ^1H homonuclear NOE difference experiments (for comp. **1** represented in Fig. 2) indicate readily spacial conditions within the averaged boat conformation: if CH_2 protons are irradiated, both the *ortho*

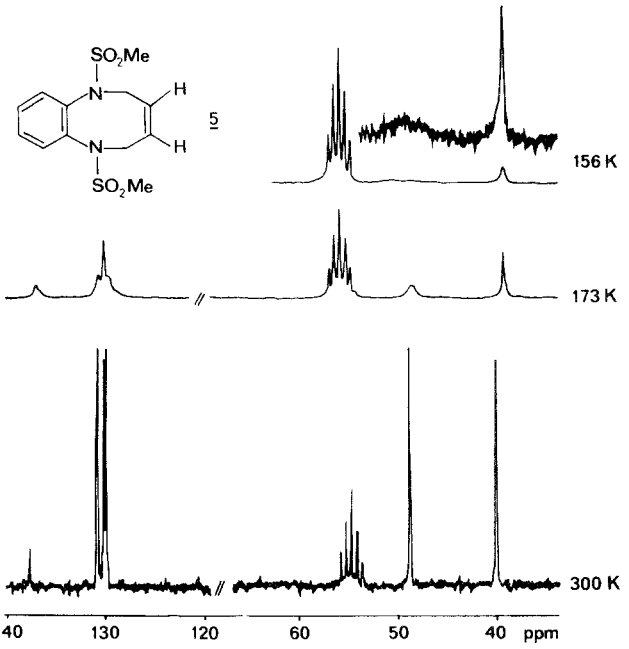


Fig. 3. 50.327 MHz ^{13}C NMR spectrum of compound **5** at variable temperatures

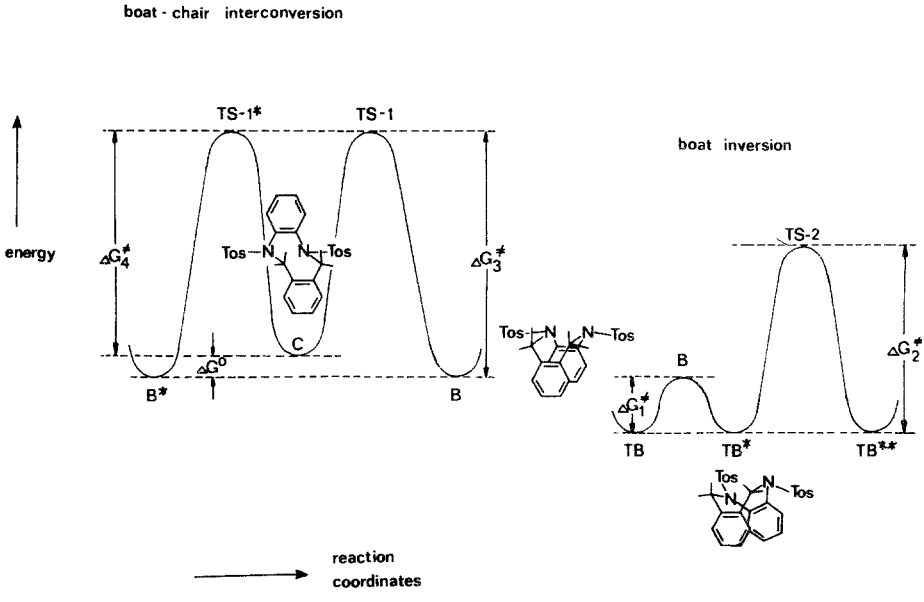


Fig. 4. Ring interconversional pathways of the studied heteroanalogous benzo- and dibenzo-1,5-cyclooctadiene derivatives **1–8**

tosyl protons as well as the pseudo peri protons of the adjacent phenyl ring display the expected NOE effects.

Due to the aforementioned reasons we designate the following reaction coordinates (see Fig. 4) to depict the interconversional pathways of the 8-membered ring in **1**–**8**.

According to the relative free energies of the obtained preferred conformations and transition states as well, the following remarks are notable:

(i) The free energy difference between the chair, **C**, and the boat conformations, **B**, is:

$$\Delta G^{\circ}_{\mathbf{B}\rightarrow\mathbf{C}} > 4.2\,\text{kJ/mol}\ (\mathbf{C} < 5\%\ \text{at}\ -100\,^{\circ}\text{C});$$

due to this aspect the boat-to-chair interconversional process could not be followed in the present dynamic NMR study.

(ii) The free energy of activation of the twist boat/boat interconversion is:

$$\Delta G_1^{\ddagger} < 29\,\text{kJ/mol}\ (T_c < -120\,^{\circ}\text{C});$$

this process could not be investigated with our probe.

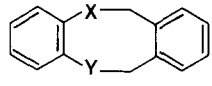
(iii) Only the boat inversional barriers, $\Delta G_2^{\ddagger}$, are detectable for the studied compounds and will be discussed next according to structural variations.

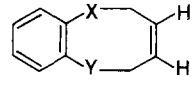
Boat Inversional Barriers

The boat inversional barriers (collected in Table 3) are dependent on the relative free energy of the ground state, **TB**, and the transition state, **TS-2**. Due to structural variations in the studied spezies, these two can be electronically as well as sterically influenced. Within this modell, the following is notable for compounds **1**–**8**:

(i) 6-8-6 systems display larger barriers than 6-8-0 systems due to the extra peri-like destabilization of the transition state, **TS-2**, in the first group of compounds.

Scheme 5





X / Y		
-NTos /-NTos	40.6	33.1
-NTos / -O-	37.6	29.6
-O- / -O-	< 29	< 29

(ii) Within these two series, the NR/NR-compounds (**1** and **6**) display the highest barriers followed by the NR/O—analogues (**2** and **7**); the boat inversional barriers of the O/S- and the O/O-compounds (**3**, **4**, and **8**) are lowest (see Scheme 5). The reason therefore is twice: N-tosyl is obviously stabilizing the ground state electronically (due to mesomerism) and destabilizing the transition state sterically more than the heteroatoms oxygen and sulfur. Hereby the obtained boat inversional barriers get larger than in the relevant compounds.

(iii) In doing that, obviously the mesyl substituent (—SO_2Me) is more successful than its tosyl analogue [—SO_2—C_6H_4—$Me(p)$]. The major contribution to the larger barrier of the mesyl compound (**5**: $\Delta G_c^{\neq}$ = 36.6 kJ/mol; **6**: $\Delta G_c^{\neq}$ = 33.1 kJ/mol) is expected to originate from the steric transition state destabilization due to its higher spacial requirement.

(iv) The pure intramolecular character of the present boat inversional process has been proved by general concentration independence of the obtained free energies of activation.

(v) The boat inversional barriers have been found dependent on the NMR solvent (being investigated with comp. **3**): less polar solvents results in lowest barriers (CD_2Cl_2: 34.8 kJ/mol; toluene: 34.7 kJ/mol), whereas more polar ones increase the obtained $G_c^{\neq}$-values (acetone: 36.0 kJ/mol; methanol: 35.4 kJ/mol). Even when these differences in the boat inversional barrier are small, the tendency is relevant—the boat inversional barriers have been obtained from two independent CH_2 groups (OCH_2 and SCH_2) in one compound **3**. Herefrom we expect the ground state, the twist boat conformations, **TB**, more polar than the relevant transition state, **TS-2**, and the polar solvents stabilizing the former adequately.

Hydrogen bond influences are less important; otherwise effects in methanol are expected more drastic.

Experimental

The ^{13}C NMR spectra were obtained at 50.327 MHz and the ^1H NMR spectra at 200.13 MHz using a BRUKER WP 200 NMR spectrometer. The chemical shift differences $\Delta\nu$ (Hz) in the dynamic NMR spectra were determined by extrapolation to the coalescence temperature, T_c, from the slow exchange area. These values, $\Delta\nu_c$, together with the geminal coupling constants, and T_c have been used to obtain the boat inversional barriers in the usual way [10]. The probe temperature was checked by reference samples (ethylene glycol—high temperatures; methanol—low temperatures); the experimental error is $\pm$ 1–2 °C.

Acknowledgement

We thank Mrs. *R. Mühlpfordt* for experiment assistance.

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