Conformational Analysis of Some Four-carbon 2,2'-Bridged Biphenyls

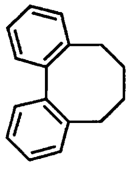
Parviz Rashidi-Ranjbar† and Jan Sandström*
Division of Organic Chemistry 3, Chemical Center, University of Lund, PO Box 124, S-221 00 Lund, Sweden

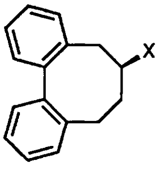
1,2,3,4-Dibenzocyclo-octa-1,3-diene (systematic name: 5,6,7,8-tetrahydrodibenzo[*a,c*]cyclo-octene) and a number of its 6-monosubstituted and *cis*- and *trans*-6,7-disubstituted derivatives have been resolved into enantiomers and diastereoisomers by chiral chromatography. $^3J_{HH}$-values and empirical force-field calculations indicate that the preferred conformation of the cyclo-octadiene ring is a twist boat-chair (TBC) form with twist boat (TB) forms 4–12 kJ mol^{-1} higher in energy. In the TBC form, the C-6 (-7) substituents can be oriented in equatorial (*e*) and axial (*a*) directions. The monosubstituted compounds appear as *e* (major) and *a* forms, the *trans*-disubstituted as *e,e* (major) and *a,a* forms, and the *cis*-disubstituted as enantiomeric *e,a* and *a,e* forms. The *e*–*a*, *e,e*–*a,a* and *e,a*–*a,e* interchanges involve inversion of the biphenyl moiety with barriers in the range 95–102 kJ mol^{-1}, determined by ^{1}H NMR band shape analysis and by following the thermal racemization or epimerization by CD spectroscopy. The free-energy differences between *e* and *a* or *e,e* and *a,a* forms are reproduced by standard MMP2-85 calculations, except for a few compounds, among them the *trans*-disubstituted compounds with halogen substituents. For these, replacement of bond dipoles by atomic charges in the calculations led to more realistic results. The *e,e*–*a,a* equilibrium of the *trans*-dibromo compound is remarkably insensitive to solvent polarity.

The stereochemistry of bridged biaryls has been the subject of extensive research over a long period of time because of interest in the chirality and spectroscopic properties of conformationally restricted biaryls and their possible use in the determination of the absolute configurations of atropisomeric biaryls.[1,2]

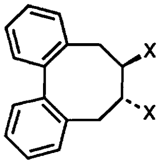
We have recently reported on the stereochemistry of a number of chiral benzo- and naphtho-annellated cyclo-octane derivatives,[3–5] which have been resolved by liquid chromatography with microcrystalline triacetylcellulose as the chiral stationary phase. One of these compounds was 1,2,3,4-dibenzocyclo-octa-1,3-diene, for which a twist boat-chair conformation with C_2 symmetry was proposed, based on empirical force-field calculations.[3] The chirality of this molecule depends on the biphenyl unit as the stereogenic element.[6] Further stereogenic elements may be introduced by substitution in the saturated bridge. One substituent in position 6 or two *trans*-oriented substituents in positions 6 and 7 give the possibility of two diastereoisomeric pairs of enantiomers, with the configurations *RR*–*SS* and *RS*–*SR* for the monosubstituted and *RRR*–*SSS* and *RRS*–*SSR* (in the order C-6, C-7, biphenyl) for the *trans*-disubstituted derivatives. *cis*-6,7-Disubstituted compounds with identical substituents will have these in a *meso* configuration, and their chirality will depend solely on the biphenyl unit, the configuration being *RSR* or *RSS*. It follows from models,[7] and is also proven by an X-ray crystallographic study of the *trans*-6,7-dibromo derivative,[5] that the *RR* (*SS*) and *RRR* (*SSS*) diastereoisomers have the substituents in equatorial orientation [*e* or *e,e*, Figure 1(*a*)], and the *RS* (*SR*) and *RRS* (*SSR*) isomers have the axial [*a* or *a,a*, Figure 1(*b*)] orientation. In the *cis*-6,7-disubstituted compounds the conformations will be *e,a* and *a,e*.

In the present work we will discuss the conformations of 1,2,3,4-dibenzocyclo-octa-1,3-diene (**1**) and a number of its 6-mono- and *cis*- and *trans*-6,7-disubstituted derivatives [(**2**)–(**6**)].

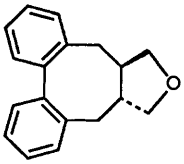

(**1**)



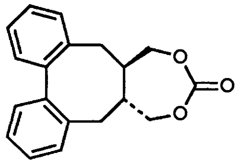
(**2**) **a**; X = Cl
b; X = Br
c; X = OAc
d; X = OH



(**3**) **a**; X = Me
b; X = Cl
c; X = Br
d; X = CO_2H
e; X = CO_2Me
f; X = CH_2OH



(**4**)



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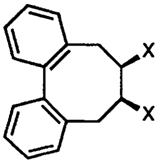

(**6**) **a**; X = Me
b; X = Cl

Experimental

The preparation and enantiomer separation of the compounds studied will be described elsewhere.[8] The NMR spectra at

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† On leave of absence from the Department of Chemistry, Faculty of Science, Tehran University.

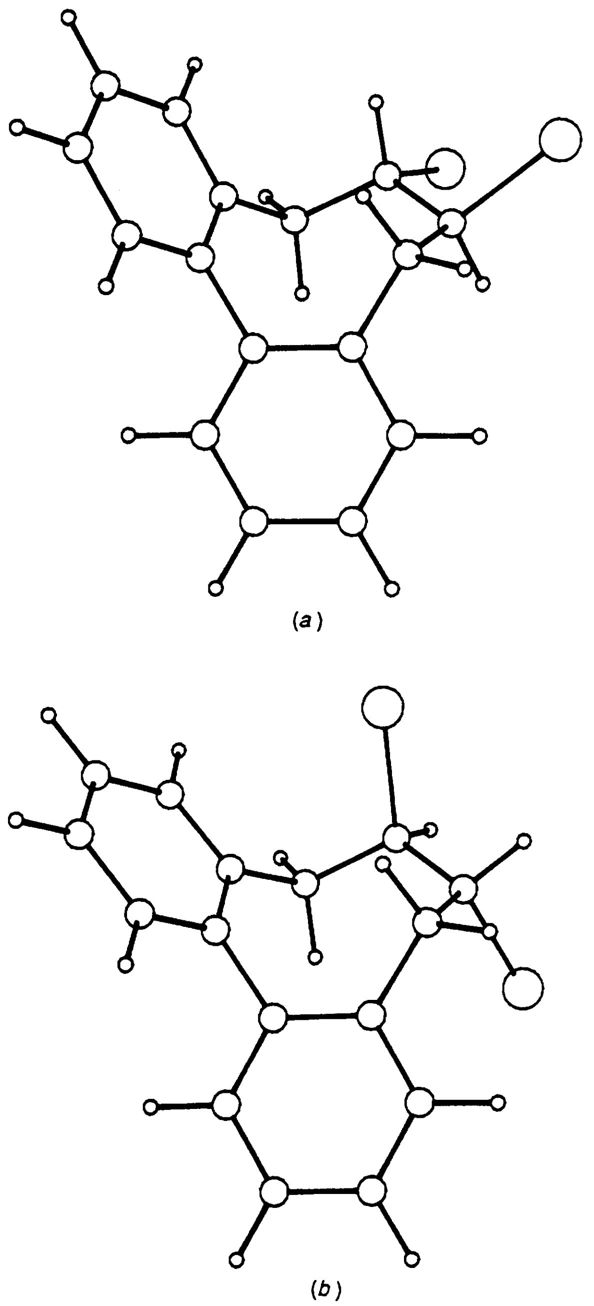

Figure 1. (*a*) Calculated conformation of the *e,e* form of compound (**3c**). (*b*) Calculated conformation of the *a,a* form of compound (**3c**).

ambient and low temperature were recorded with a Varian Model XL-300 spectrometer and the high-temperature spectra with a JEOL Model MH-100 NMR spectrometer. First-order rate constants for *e*⟶*a* and *e,e*⟶*a,a* exchange for compounds (**2b**) and (**3c**) were obtained from exchange-broadened spectra by spectra simulation, using the DNMR5 program.[9] The spectra of the benzylic proton (5-H, 8-H) resonances of compound (**3c**) could be approximated as the AB parts of an ABXX′ system, *i.e.* the exchange was treated as ABXX′ $\rightleftharpoons$ CDYY′.[5] The spin system of compound (**2b**) is more complex, but the 6-H resonances could be simulated as the X (Y) parts in an $A_2BX \rightleftharpoons C_2DY$ system without couplings between A and B or between C and D. The transverse relaxation times (T_2) and free energies of activation were evaluated as described before.[10]

First-order rate constants (k_1) for *e*⟶*a*, *e,e*⟶*a,a*, and *e,a*⟶*a,e* exchange for compounds (**2**), (**3**), and (**6**) respectively, were obtained by monitoring of the intensity of a strong CD band of a pure enantiomer in a water-jacketed cell connected to a circulation thermostat (Haake Model N3 digital thermostat). The CD spectra were recorded with a JASCO Model J-500A spectropolarimeter. For compounds (**2**) and (**3**), the experiment was performed with the minor diastereoisomer in order to obtain the largest change in CD intensity. The values for k_1 were obtained from the observed rate constant k_{obs} and the equilibrium constant K using the equations $k_{\text{obs}} = k_1 + k_{-1}$ and $K = [\text{minor}]/[\text{major}] = k_1/k_{-1}$, where k_{-1} is the rate constant for the reverse reaction. For the racemization of compounds (**6**), these equations reduce to $k_1 = k_{\text{obs}}/2$.

The errors in the computed free-energy barriers are mainly due to errors in the temperature measurements and are estimated to be $< \pm 0.4$ kJ mol^{-1} for the barriers obtained from NMR spectra and $< \pm 0.2$ kJ mol^{-1} for those obtained from CD measurements.

The molecular mechanics calculations were performed with the MMP2-(85) force field,[11,12] using the interactive computer graphics programme MOLBUILD.[13] Incremental driving was performed by changing selected dihedral angles in predetermined steps and by minimizing the energy with respect to all other internal co-ordinates after each step, as described in ref. 11.

Results and Discussion

The unsubstituted hydrocarbon (**1**) is conformationally similar to cyclo-octa-1,3-diene, which has been thoroughly studied by Anet and Yavari by ^{1}H and ^{13}C NMR spectroscopy and by force-field calculations.[14] Two types of minimum-energy conformations were found, the lower one being described as twist boat-chair (TBC) with C_2 symmetry, with two non-symmetrical twist boat (TB) forms only 2.1 kJ mol^{-1} higher in energy. All three forms have enantiomeric counterparts. Force-field calculations on compound (**1**) yield two similar types of minimum-energy conformation, but now the TB forms are 11.8 kJ mol^{-1} above the TBC forms (Figure 2). The ^{1}H and ^{13}C NMR spectra are in agreement with C_2 symmetry and show no exchange broadening in the temperature range +30 to −80 °C, but this alone does not disprove the presence of a small amount of the TB form in rapid equilibrium with the TBC form even at −80 °C. It was considered of interest to study the conformational interconversions in compound (**1**) by force-field calculations. The (−)-TBC–(−)-TB interconversion in (*R*)-(**1**) [the (−) sign refers to the biphenyl dihedral angle] was studied by incremental driving of the 5–6–7–8 dihedral angle (Figure 3) from +50° in the direction of −50°. At −30° a transition state with C_2 symmetry [Figure 4(*a*)] was reached, 30.6 kJ mol^{-1} above the TBC form, and continued rotation led to the (−)-TB form. A transition state with the same energy was reached when the 4–5–6–7 dihedral angle was driven from −82° in the (−)-TBC form towards positive angles. This interconversion occurs with only small changes in the biphenyl dihedral angle. Driving of the 4–5–6–7 dihedral angle in the first TB form from +64° to −64° led to another TB form, (−)-TB′ [Figure 2(*c*)], *via* a boat-like transition state [B, Figure 4(*b*)], 13.3 kJ mol^{-1} above the TB forms.

Inversion of the biphenyl unit was effected by incremental driving of, first, the 1–2–3–4 dihedral angle from −64° to 0° and, thereafter, the 5–6–7–8 dihedral angle from −66° to 0°. The resulting transition state had half-chair conformation [HC, Figure 4(*c*)] and was 110.7 kJ mol^{-1} above the TBC form. Energy minimization after a small increase of the 1–2–3–4 dihedral angle led to the (+)-TB′ form. Similar driving from the

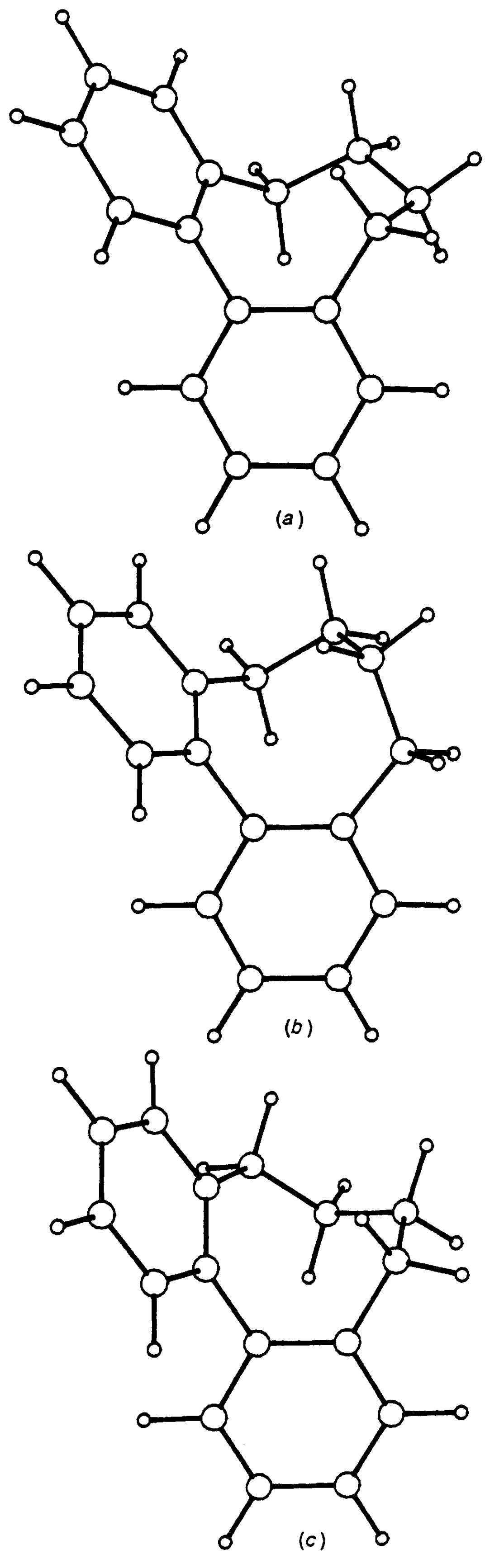

Figure 2. (*a*) Calculated TBC conformation of compound (**1**). (*b*) Calculated TB conformation of compound (**1**). (*c*) Calculated TB′ conformation of compound (**1**).

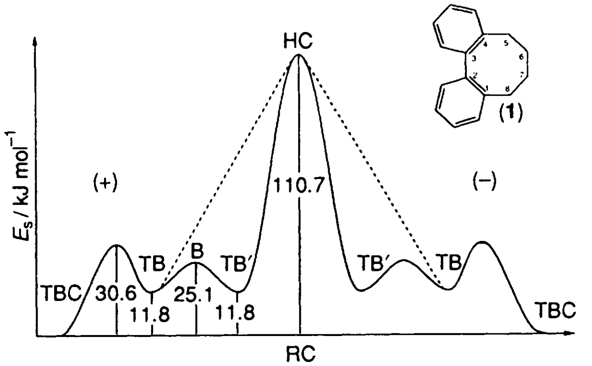

Figure 3. Energy profile for computed conformational interconversions in compound (**1**). E_s = steric energy. RC = reaction co-ordinate. The dihedral angles driven are for TBC $\rightleftharpoons$ TB 5–6–7–8, for TB $\rightleftharpoons$ TB′ 4–5–6–7, and for (+)-TB′-HC-(−)-TB′ or (+)-TB-HC-(−)-TB (dotted line) 1–2–3–4 followed by 5–6–7–8 (see the text).

(−)-TB form led to the same transition state (the dotted line in Figure 3).

As a test of the procedure, the calculations of Anet and Yavari on cyclo-octa-1,3-diene[14] were repeated. These authors used a modified Boyd force field.[15] With the MMP2-(85) force field the following energy differences with respect to the TBC form were obtained (results from ref. 14 in parentheses): TB −0.9 (+2.1); transition state (+)-TBC-(+)-TB (C_2) +40.1 (+38.1); transition state (+)-TB-(+)-TB′ (boat, C_2) +27.8 (+26.4); transition state (+)-TB′-(−)-TB′ (half-chair, C_2) +38.3 (+36.0), all in kJ mol^{-1}. The agreement is quite good, considering the difference in force fields.

Monitoring of the rate of racemization of compound (**1**) at +27 and +41 °C gave the free-energy barrier to ring inversion [(−)-TBC $\longrightarrow$ (+)-TBC] of 97 kJ mol^{-1} (Table 1). This process involves a change of the dihedral angle of the biphenyl unit from *ca.* +60° to −60° or *vice versa.* The same conformations and conformational exchange processes should be valid for the substituted dibenzocyclo-octadienes.

The ^{1}H NMR spectrum of 6-bromo-1,2,3,4-dibenzocyclo-octa-1,3-diene (**2b**) shows resonances of two forms in the ratio 78:22. The 5-H resonances appear as separated AB parts of ABX spectra, and the 6-H resonances as well separated multiplets (nearly quintets). Analysis of the 5-H resonances as AB parts of ABX spectra gave, for the major form, J_{AB} 13.2 and J_{AX} 11.6 Hz, with J_{BX} too small to be resolved. The corresponding coupling constants for the minor form were found to be 13.9, 7.3, and 1.5 Hz (Table 2).

Force-field calculations predict two TBC forms, one with an 'equatorial' and one with an 'axial' C–Br bond. The former is calculated to be 3.1 kJ mol^{-1} lower in energy. The lowest TB form is calculated to be 6.7 kJ mol^{-1} higher in energy than the highest TBC form. The dihedral angles between the C-5–5-H and C-6–6-H bonds are calculated to be 74 and 39° in the TBC form with axial C–Br bond (TBC-*a*) and 167 and 78° in the TBC-*e* form. Use of the equation derived by Haasnoot *et al.*[16] for calculation of vicinal coupling constants gave J_{AX} 7.5, J_{BX} 1.7 Hz for the form with an axial C–Br bond, and J_{AX} 11.7, J_{BX} 1.3 Hz for the equatorial analogue. Here, the labels A, B, and X refer to the same atoms (5-H^a, 5-H^b, and 6-H) in the *e,e* and *a,a* forms. Calculations with the equation recently proposed by Imai and Osawa[17] gave similar results, the most notable difference being slightly higher values for the lower coupling constants. Evidently, the vicinal coupling constants observed for the major conformer (11.6 and *ca.* 0 Hz) agree reasonably well with those expected for the form with an equatorial C–Br bond, and those found for the minor conformer (7.3 and 1.5 Hz) with those expected for the form with an axial C–Br bond. Thus the results of the force-field calculations agree with experimental results.

The calculated vicinal coupling constants for the coupling of 5-H[a] and 5-H[b] with 6-H are for the TB form corresponding to TBC-*e*: J_{AX} 11.7, J_{BX} 4.9 Hz, and for the TB form corresponding to TBC-*a*: J_{AX} 2.0, J_{BX} 5.2 Hz. Based on these results, it may be predicted that a moderate amount of TB form in rapid equilibrium with the TBC-*e* form would not affect J_{AX} but would raise J_{BX}, for which the observed value is lower than that calculated for the pure TBC form. Mixing of some TB form in the TBC-*a* form would lead to larger changes in the coupling constants. Evidently, the results of these calculations speak against the existence of even a moderate fraction of TB forms in equilibrium with the TBC forms.

Above 150 °C exchange broadening was observed in the ^{1}H NMR spectrum, and by simulation of the 6-H resonances in the range +177 to +191 °C, values for $\Delta G^‡$ (major→minor) 98.4–98.7 kJ mol^{-1} (Table 1) and $\Delta G°$ (minor–major) 3.2 kJ mol^{-1} (Table 2) were obtained.

The thermal equilibration (+)-major $\rightleftharpoons$ (−)-minor starting from pure (−)-minor was monitored by CD spectroscopy at +28.0 °C in ethanol and gave $\Delta G^‡$ (major→minor) 97.1 kJ mol^{-1}. The difference from the NMR result [solvent $(CCl_3)_2CO$] may be due to a solvent effect but is also in agreement with an expected negative activation entropy[2] ($\Delta S^‡$ −10 J mol^{-1} K^{-1} without considering the difference in solvent).

The 6-chloro (**2a**), 6-acetoxy (**2c**), and 6-hydroxy (**2d**) analogues behave very much like bromo compound (**2b**), appearing in TBC-*e* (major) and TBC-*a* forms as indicated by NMR spectra and force-field calculations (Table 2).

The stereochemical situation for the *trans*-6,7-disubstituted compound (**3**) is similar to that for the 6-monosubstituted analogues (**2**). Two forms with C_2 symmetry appear in the NMR spectra at ambient temperature. For these, it is possible to evaluate J_{AX} and J_{BX} and also the 6-H, 7-H coupling constants $J_{XX'}$ for the major forms and some of the minor forms (Table 2). $J_{XX'}$ falls in the range 8.3–11.4 Hz for the major forms and 1.7–2.0 Hz for the minor forms, which together with the J_{AX}- and J_{BX}-value confirm the assignment of the major form to the *e,e* conformer and the minor form to the *a,a* conformer. MMP2-(85) calculations on the dibromo compound (**3c**) predict the 6-H, 7-H dihedral angle to be 158° in the TBC-*e,e* form and 68° in the TBC-*a,a* form, and the calculated coupling constants are 9.9 and 1.3 Hz respectively, to be compared with experimental values of 9.5 and 2.0 Hz. Similar calculations for the TB forms give the angle 65° and *J* 1.6 Hz for the form related to TBC-*e,e* and 175° and 10.8 Hz for the form related to TBC-*a,a*. This also speaks against a significant proportion of the TB forms in equilibrium with the TBC forms. The calculations predict the lowest TB form to be 15.5 kJ mol^{-1} above the highest TBC form.

Force-field calculations based on dipole–dipole interactions for compounds (**2**) and (**3**) with one exception (**3c**) predict the TBC-*e* and -*e,e* forms to be lower in energy than the corresponding axial forms, in agreement with experiments, and in most cases the calculated ΔE-values reproduce the experimental $\Delta G°$-values reasonably well (Table 2). The most striking exceptions are compounds (**2c**), (**3b**), (**3c**), and (**3f**). For the first three of these the stability of the axial form is exaggerated, whereas the opposite is found for compound (**3f**). For compounds (**3b**) and (**3c**) one could expect that the dipole–dipole interaction model is inadequate to account for the repulsion between axial halogen atoms and the rather proximate negatively charged aromatic carbon atoms. Replacement of the bond dipoles by monopoles at the atoms in fact led to considerable and (somewhat exaggerated) destabilization of the axial forms (Table 2).

An X-ray crystallographic study of the *e,e* and *a,a* forms of compound (**3c**) showed both forms to adopt TBC geometries in

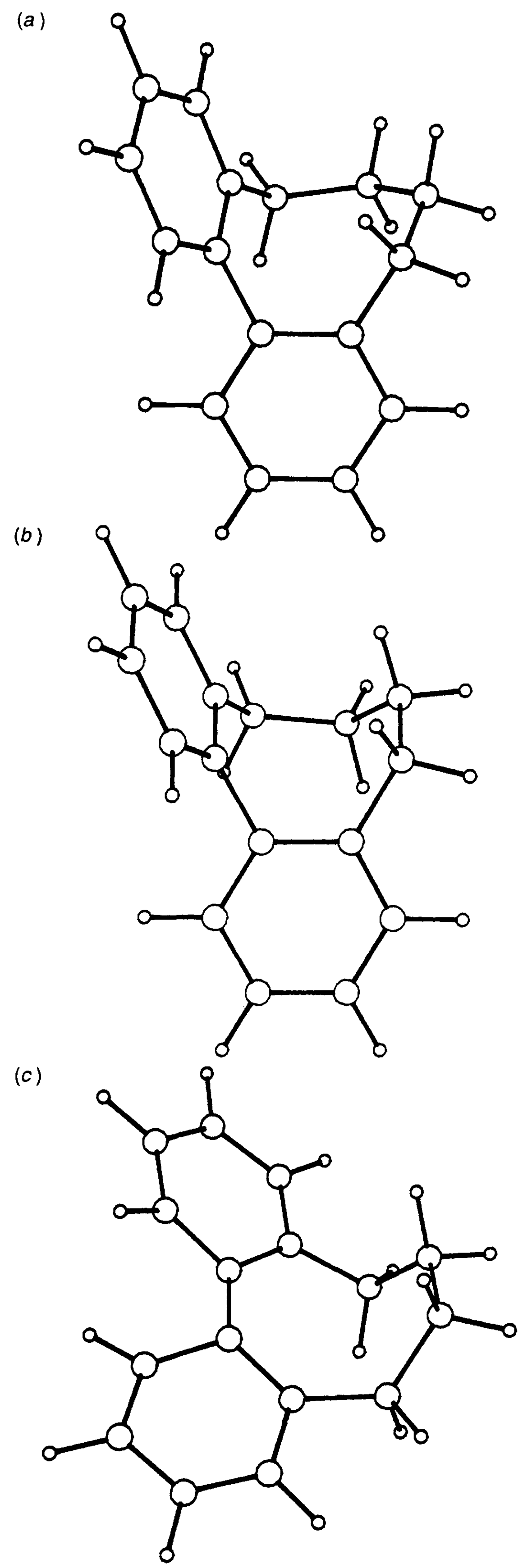

Figure 4. (*a*) Calculated conformation of the TBC–TB transition state of compound (**1**). (*b*) Calculated B conformation of compound (**1**). (*c*) Calculated HC conformation of compound (**1**).

Table 1. Barriers to ring inversion. Solvent for CD, ethanol; for NMR, $(CCl_3)_2CO$.

Compound	Process	Method	T/K	k/s^{-1}	$\Delta G^{\ddagger}_{inv}$/kJ mol^{-1} [a]
(1)	(+)-TBC→(−)-TBC	CD	300.8	0.88×10^{-4}	97.1
			314.2	3.94×10^{-4}	97.6
(2b)	*e*→*a*	CD	302.7	1.71×10^{-4}	96.0
	e→*a*	NMR	455.8	50.0	98.4
			459.2	60.0	98.5
			464.0	75.0	98.7
(2c)	*e*→*a*	CD	301.7	0.49×10^{-4}	98.8
(3c) [b]	*e,e*→*a,a*	CD	298.3	1.18×10^{-4}	95.5
			303.2	1.81×10^{-4}	96.0
	e,e→*a,a*	NMR	459.8	45	99.7
			471.4	75	100.3
(6a)	*e,a*→*a,e*	CD	308.7	5.48×10^{-4}	95.0
			318.7	17.8×10^{-4}	95.0
			328.7	48×10^{-4}	95.4
(6b)	*e,a*→*a,e*	CD	313.7	0.67×10^{-4}	102.0
			323.7	2.24×10^{-4}	102.1
			333.7	6.2×10^{-4}	102.5

[a] Estimated error limits for CD ±0.2 kJ mol^{-1}, for NMR ±0.4 kJ mol^{-1}. [b] From ref. 5.

Table 2. Observed coupling constants (in Hz) and observed $\Delta G°$-values and calculated ΔE-values for the equatorial–axial equilibria (in kJ mol^{-1}) of compounds **(2)**–**(5)**. Solvent $CDCl_3$.

Compound	Conformer	J_{AB}	J_{AX}	J_{BX}	$J_{XX'}$	$\Delta G°$ (maj–min)	ΔE (*e*–*a*)
(2a)	maj (*e*)	−13.3	11.4	1.3		−3.2	−3.0 (−4.1) [a]
	min (*a*)	−13.8	6.9	1.3			
(2b)	maj (*e*)	−13.2	11.6	~0.5		−3.2	−3.1 (−4.8) [a]
	min (*a*)	−13.9	7.3	1.5			
(2c)	maj (*e*)	−12.8	10.9	~0.5		−2.5	−0.8
	min (*a*)	−13.8	7.8	~0.5			
(2d)	maj (*e*)	−12.6	11.0	1.7		−1.4	−1.5
	min (*a*)	−13.4	7.8	~0.5			
(3a)	maj (*e,e*)	−13.4	10.3	~0.5	8.3	−6.5	−5.6
	min (*a,a*)	−13.5	*b*	1.7	*b*		
(3b)	maj (*e,e*)	−14.0	11.6	0.3	9.3	−3.2	−0.1 (−4.4) [a]
	min (*a,a*)	−14.4	6.7	1.2	1.7		
(3c)	maj (*e,e*)	−14.2	11.5	1.6	9.5	−1.5	+0.4 (−3.1)
	min (*a,a*)	−14.2	6.9	1.0	2.0		
(3d)	maj (*e,e*)	−13.4	10.7	~0.5	11.2	−7.6	−5.6
	min (*a,a*)	*b*	*b*	*b*	*b*		
(3e)	maj (*e,e*)	−13.7	10.7	~0.5	11.4	−7.9	−10.8
	min (*a,a*)	*b*	*b*	*b*	*b*		
(3f)	maj (*e,e*)	−13.0	10.6	~0.5	11.0	−4.3	−10.1
	min (*a,a*)	−13.7	6.8	1.7	*b*		
(4)	*e,e*	−13.0	9.6	~0.5	10.4		
(5)	*e,e*	−13.4	9.3	~0.5	10.2		

[a] With monopoles, H–C(sp^3): ±0.058, H–C(sp^2): ±0.119, C–Cl: ±0.169, C–Br: ±0.149, all in units of electronic charge. [b] Invisible either because of too low intensity or because of overlap by reasonances of the major form.

close agreement with those obtained by MM calculations,[5] thus confirming the results from the coupling-constant analysis and the MM calculations.

The *e,e*–*a,a* equilibrium constant for compound **(3c)** was found to be remarkably insensitive to solvent polarity, varying from 0.59 in CD_3OD over 0.47 in $(CD_3)_2CO$ and $CDCl_3$ to 0.46 in C_6D_{12}, all at ambient temperature.

The tetrahydrofuran **(4)** and the cyclic carbonate **(5)** are held rigidly in the TBC forms with equatorial substituents, and the similarity of the coupling constants with those found for the *e* and *e,e* forms of compounds **(2)** and **(3)**, respectively, supports the dominance of the TBC forms for the latter as well.

The *cis*-6,7-disubstituted compounds **(6a)** and **(6b)** exist as single enantiomeric pairs, and their NMR spectra show a complete lack of symmetry elements. MM calculations predict the TBC forms to be the most stable ones, with the TB form 6.6 kJ mol^{-1} higher in energy for the dimethyl compound **(6a)** but only 3.9 kJ mol^{-1} higher for the dichloro compound **(6b)**. The low TBC–TB energy difference for compounds **(6)** may be ascribed to excess of strain in the TBC form due to the presence of one destabilizing axial substituent. The calculated steric energy for the TBC form of compound **(6a)** is 4.4 kJ mol^{-1} higher than that for the *e,e* form of compound **(3a)**, and for the dichloro analogues this difference is 4.9 kJ mol^{-1}.

An analysis of the ^1H NMR spectrum of compound **(6b)** yields coupling constants which agree well with those calculated for the TBC form (Table 3). The observation of a four-bond coupling, J_{DX}, of 1.2 Hz agrees with the W orientation of the intervening bonds found in the calculated geometry (Figure 5).

The inversion barriers summarized in Table 1 fall in the narrow range of 95.0–98.8 kJ mol^{-1} at or near ambient temperature, with the exception of that for the *cis*-dichloro

Table 3. ^{1}H Coupling constants for the *cis*-6,7-disubstituted compounds (**6a**) and (**6b**). For labelling, see Figure 4. Solvent $CDCl_3$.

	R = Me (**6a**)			R = Cl (**6b**)		
Protons	Dihedral angle/°	J_{exp}/Hz	J_{calc}/Hz	Dihedral angle/°	J_{exp}/Hz	J_{calc}/Hz
A–B		−13.7			−14.6	
A–X	−72	1.6	1.5	−75	1.2	1.2
B–X	41	7.4	+6.3	38	8.6	7.2
C–D		−13.3			−14.0	
C–Y	158	9.4	11.2	159	10.1	10.1
D–X					1.2	
D–Y	−87	~0.5	0.6	−85	1.6	0.7
X–Y	50	*a*	+4.1	52	3.5	3.5

[a] Not possible to evaluate.

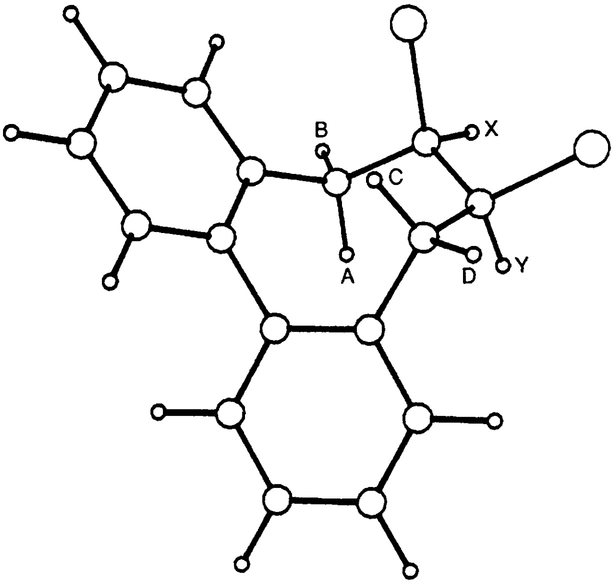

Figure 5. Assignment of protons in the TBC form of compounds (**6**).

compound (**6b**), which is 102 kJ mol^{-1}. As indicated by the force-field calculations, the inversion itinerary probably involves a TBC–TB transformation followed by inversion of the biphenyl unit *via* a half-chair transition state [Figure 4(*c*)] as the rate-determining step. With regard to their high ground-state strain, one should expect compounds (**6a**) and (**6b**) to have the lowest barriers, other things being equal. This is in fact true for compound (**6a**) but not for the dichloro compound (**6b**). The calculated rate-determining step involves a close interaction between the 6,7-substituents for the *cis* (but not for the *trans*) compounds, which would increase the barrier much more for the dichloro than for the dimethyl compound because of the stronger repulsion between eclipsed bond dipoles in the former case. The situation is similar to that for 1,2-dichloroethane and butane in eclipsed and *gauche* orientation. The calculated (MM2-85) energy difference between eclipsed and *gauche* forms is 24.7 kJ mol^{-1} for 1,2-dichloroethane but only 16.2 kJ mol^{-1} for butane. The difference, 8.5 kJ mol^{-1}, is quite similar to the 7 kJ mol^{-1} difference between the inversion barriers for compounds (**6b**) and (**6a**), supporting the hypothesis of a half-chair form as the transition state.

Acknowledgements

We are grateful to the Swedish Natural Science Research Council and the Knut and Alice Wallenberg Foundation for financial support.

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Paper 9/05185F
Received 5*th December* 1989
Accepted 8*th February* 1990