A study of the *N*-inversion barrier and the circular dichroism spectra of 1-thia-10-aza[2.2]metacyclophane

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The inversion barriers and the excited singlet electronic states of 1-thia-10-aza[2.2]metacyclophane (X = NH **1**) and two isovalent compounds (X = NCH_3 **2**, X = PH **3**) have been calculated with semiempirical AM1 and multireference configuration interaction (MRD-CI) methods. Owing to the inversion at the heteroatom N or P, all compounds investigated exhibit two different minima which are separated energetically by less than 1 kcal mol^{-1}. The inversion barriers are calculated to be 5.5 kcal mol^{-1} (X = NH), 4.5 kcal mol^{-1} (X = NCH_3) and 15.6 kcal mol^{-1} (X = PH), respectively.

Good agreement between the experimental and calculated circular dichroism (CD) spectra is obtained for the X = NH compound (**1**). The various bands can be characterized as separate and coupled $\pi\pi^*$ transitions localized in the aromatic rings and by valence-type excitations involving the lone-pair orbital of the sulfur atom (3p) and/or antibonding σ^*-MOs of C–S bonds. The dominant CD transitions do not change significantly if the nitrogen is replaced by a phosphorus centre.

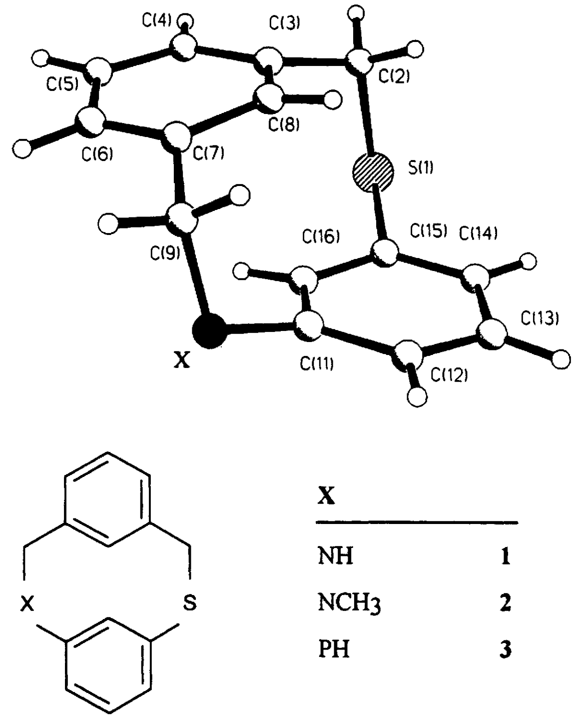
From a comparison of the CD spectra calculated for both inversion minima for X = NH, it is predicted that the energetically lowest lying conformation in solution or in the gas phase is not identical with the conformer found in X-ray studies. This supports earlier conclusions which show that the conformer found in the crystal is favoured by intermolecular hydrogen bondings.

1 Introduction

Hetera[2.2]metacyclophanes have been the subject of long-standing interest in synthetic and physical organic chemistry especially for their chiroptical properties.[1] The isovalent compounds 1-oxa[2.2]metacyclophane and 1-thia[2.2]metacyclophane were first prepared by Vögtle *et al.*[2] and constitute a new family of substances where two inherent achiral benzene chromophores with several low-lying $\pi\pi^*$ states are connected to give helical-chiral structures. In a recent study,[3] the circular dichroism (CD) spectra of these two molecules have been theoretically determined by a newly developed combination of semiempirical AM1[4] and multi-reference single and double excitation configuration interaction (MRD-CI)[5] treatments. Good agreement between calculated and experimental CD data was obtained in the spectral range 300–180 nm and strong contributions of electronic transitions involving the C–S–C chromophore were found.

In this paper our investigations are extended to the isovalent 1-thia-hetera[2.2]metacyclophanes with X = NH (**1**), NCH_3 (**2**) and PH (**3**) (Fig. 1). **1** is the first known hetera[2.2]metacyclophane with an unsubstituted NH moiety in the bridging position. It was obtained by Vögtle and co-workers by hydrolysis of the analogous *N*-trifluoroacetylated [2.2]metacyclophane.[6]

Inspection of molecular models of the compounds shows that two conformers **1a** and **1b** with inverted configurations at the N or P atoms may exist in analogy to those of NH_3 or PH_3 (see Fig. 2). Thus the first aim of this study is the determination of the minimum energy structures of these conformers and their corresponding inversion barriers. This is especially interesting since strongly varying *N*-inversion barriers have been found in saturated heterocycles[7] so that comparison with the strained [2.2]metacyclophane structure gives new insights in stereoelectronic interactions occurring in the phane environment.

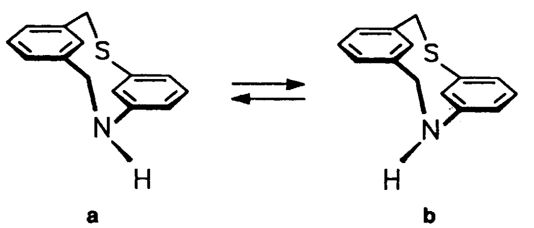


X	
NH	**1**
NCH3	**2**
PH	**3**

Fig. 1

The X-ray data of **1** could prove the existence of **1b** only in the crystal.[6] In the solid state, however, **1b** is energetically stabilized by intermolecular hydrogen bonding so that in solution or gas phase **1a** could be lower in energy. From temperature-dependent NMR experiments no information about the existence of the second conformer could be obtained. This may be attributed, however, to low inversion barriers (*i.e.*, < 8 kcal mol^{-1}) and/or very similar NMR parameters (^1H chemical shifts and coupling constants) of **1a** and **1b**.

In the present study we show that in solution structure **1a** is favoured against structure **1b**. This conclusion is supported by



a **b**

1

Fig. 2 Schematic structures of the two different inversion minima of **1**

the calculation of the total energies of both conformers and by a comparison of experimental and theoretical CD spectra. This shows that experimental CD spectroscopy in combination with theoretical calculations of excitation energies and rotatory strengths (*R*) can give further information about the stability of various conformers in different environments if the CD spectra of the conformers are significantly different. This combination gives new insights into conformational processes which are too fast to be observed on the NMR timescale, but slow enough to be determined in time ranges of optical excitations.

2 Theoretical details

Using a modified version of the MOPAC 6.0 program package[8] all geometries were fully optimized at the AM1-SCF level. Subsequent CI calculations of the CD spectra were undertaken in the standard manner of Buenker and Peyerimhoff[5] using localized molecular orbitals (LMO) of the SCF ground state wavefunction as the molecular basis. The selection of the correlated electrons (28 in all cases) and the calculation of the rotatory strengths (*R*) was performed as described in ref. 3. The minimum energy paths **a** $\longrightarrow$ **b** were calculated by assuming the dihedral angle R–X–C11–C12 (*R* being H or CH_3, X = N or P) as a reaction coordinate. The stationary points found have been properly characterized as saddle points by vibrational analysis (one imaginary frequency).

3 Results and discussion

3.1 Geometries, energies and inversion barriers

Generally, the AM1 optimized structure of **1b** compares well with the experimental X-ray data (see Table 1). The bridging C–C bond lengths, as predicted by the AM1 method, are ≈0.06 Å longer and in the benzene ring, boat type deformation angles α are ≈4° larger than observed experimentally. These differences do not seem alarming because packing forces in the crystal may reduce the internal distances of the atoms.

The geometries of the inverted conformers **1a** and **3a** are very similar in all cases except for the bond angles and dihedral angles at the X-substituted bridge. In both conformers the nuclear geometry causes the lone-pair orbital at X = NR or X = PH to be twisted with respect to the plane of the benzene ring so that only a small conjugative interaction with the π-system occurs. This is of particular importance for the discussion of the excited states (CD spectra, see below). As expected the X = PH compound shows longer bond lengths in the bridge so that a less distorted structure (as in the parent compound [2.2]metacyclophane with C_{2h} symmetry) is obtained (see Table 1). The conformers **b** are found to be 1.3 kcal mol^{-1} (**1**), 0.9 kcal mol^{-1} (**2**) and 0.6 kcal mol^{-1} (**3**) higher in energy than the minima of the corresponding conformers **a**. At first glance this may contradict the experimental finding that only **1b** is observed in the crystal. However, as already discussed in a previous work[6] thermodynamic crystal-packing effects favour structure **1b** due to intermolecular hydrogen bonding.

Table 1 Comparison of the calculated geometric parameters of **1b**[a] with experimental data. The numbering of the atoms refers to Fig. 1. Bond lengths are given in Å, angles in degrees

	X = NH (1)		X = PH (3)
Variable	AM1-SCF	X-ray[b]	AM1-SCF
Bond length			
X–C11	1.43	1.43	1.68
X–C9	1.46	1.51	1.76
C9–C7	1.50	1.51	1.47
C3–C2	1.48	1.50	1.48
S–C2	1.81	1.86	1.80
S–C15	1.71	1.78	1.71
aromatic C–C bonds	1.395–1.404	1.394–1.404	1.371–1.413
Bond angles			
C7–C9–X	114	111	113
C9–X–C11	113	112	103
X–C11–C12	120	123	118
X–C11–C16	121	118	121
S–C2–C3	110	110	113
C15–S–C3	98	99	104
Dihedral angles			
C16–C11–X–C9	−71	−78	−63
C16–C11–X–H	167[a]	169	184
'Boat' type deformation angles			
α (ring 1)[c,d]	4 13	4 9	4 9
a (ring 2)[d,f]	5 11	5 9	4 11
Length of the bridges			
X-bridge[g]	2.93	2.92	3.06
S-bridge[h]	3.13	3.13	3.12

[a] The only significant difference between conformer **1a** and **1b** is the dihedral angle describing the environment of the nitrogen atom, *i.e.*, C16–C11–X–H, which is 52° for **1a**. For **3a** the dihedral angle C16–C11–P–H is 36°. [b] Ref. 6. [c] Angle between the points: midpoint of the straight line between C11 and C15, midpoint of the straight line between C12 and C14, C13. [d] Same as *c* but with atoms C12/C14, C11/C15 and C16. [e] Same as *c* but with atom C7/C3, C4/C6 and C5. [f] Same as *c* but with atoms C4/C6, C7/C3 and C8. [g] Distances between C7 and C11. [h] Distances between C3 and C15.

Table 2 AM1-SCF calculated heats of formation (Δ_fH), energy differences [$\Delta E = \Delta_fH$ (**a**) − Δ_fH (**b**)] and inversion barriers ($\Delta E^‡$) of **1**–**3** in kcal mol^{-1}. For comparison some data for similar compounds are also given. Experimental values[7] are given in parentheses

Compound	Δ_fH (**a**)	ΔE	$\Delta E^‡$
NH_3	−7.3	0.0	4.2 (5.8)
$NH_2(CH_3)$	−2.9	0.0	4.2 (4.8)
$NH(CH_3)_2$	−2.9	0.0	4.6 (4.4)
PH_3	10.2	0.0	32.8 (37.0)
1a	72.6	1.3	5.4 (< 8)
2a	78.5	0.9	4.5
3a	73.5	0.6	15.6
4	−19.6	0.0	5.0 (8.0)

Next we discuss the calculated inversion barriers ($\Delta E^‡$) given in Table 2. For comparison experimental and theoretical AM1 data for some related molecules are also given. The inversion barrier of the seven-membered ring azepine (in the following abbreviated as **4**) is especially of interest because its molecular structure is very similar to the present compounds. The form of the potential energy curve for the inversion calculated at the AM1 level is given in Fig. 3. The reaction coordinate is the dihedral angle *θ* C12–C11–N–H (for the

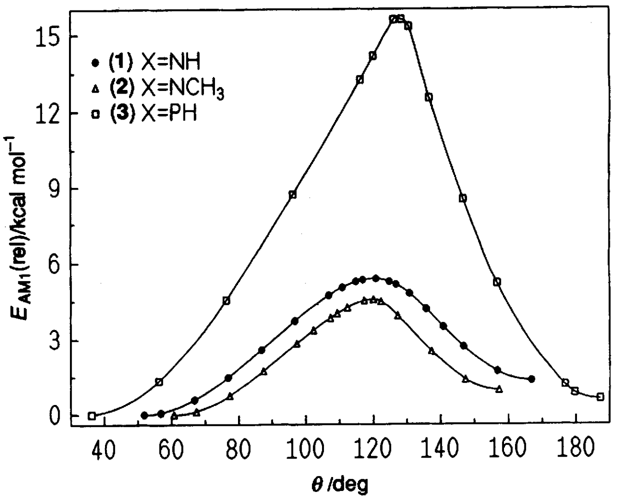


Fig. 3 Energy profile of the inversion motion **a** ⟶ **b** using the AM1 method. As the reaction coordinate the dihedral angle θ = C12–C11–X–R (X = N, P; R = H, CH$_3$) was taken.

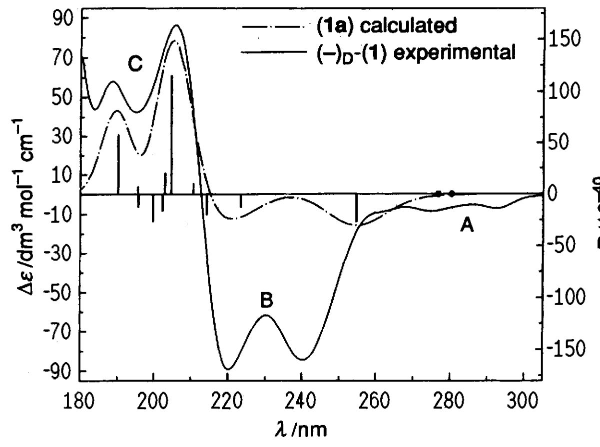


Fig. 4 Comparison of the experimental CD spectra of **1** (——) and the AM1/MRD-CI calculated rotatory strength for **1a** designated by sticks. The CD spectrum of **1** was measured with Jasco J720-spectropolarimeter, solvent hexafluoropropan-2-ol, 0.2 cm cell, $c = 1.3 \times 10^{-4}$ mol dm^{-3}. The filled points indicate the two lowest excited states with near-zero R values. (– – –) Shows the simulated CD spectrum obtained by summing rotatory strength weighted Gaussian curves with Δ_{fwhm} = 0.3 eV for each calculated CD transition. In cgs, R has units of esu cm erg G^{-1}. This corresponds to 3.336×10^{-15} m^3 C^2 s^{-1}.

numbering of the centres see Fig. 1). Along the profile all other geometrical parameters were optimized.

Inspection of Table 2 shows that the calculated barriers ($\Delta E^{\ddagger}$) at the AM1 level compare quite well with experiment, but with a tendency of being a little bit too low especially for PH$_3$. The calculated inversion barriers of **1** and **2** are 5.4 and 4.5 kcal mol^{-1}, respectively. Both are very similar to the inversion barrier found for the seven-membered ring (**4**) and only slightly larger compared with those of NH$_3$ (4.2 kcal mol^{-1}). The lower $\Delta E^{\ddagger}$ value of **2** is in accordance with the lower energy difference ΔE between **a** and **b**. For **3** with X = PH we predict an inversion barrier of 15.6 kcal mol^{-1} which is smaller than for PH$_3$ itself, but much larger than for the N compounds. Obviously in all molecules under consideration the 'free' inversion motion is hindered by the environment (the alkyl bridges and the benzene rings). While the inversion barriers found for the nitrogen compounds are too small to be determined by temperature-dependent NMR spectroscopy, the barrier height calculated for the phosphorus system would be large enough to be indicated by this experimental method. For **1** the calculated data agree with the experimental upper limit of about 8 kcal mol^{-1} so that at room temperature (298 K) a fast reaction **b** $\rightleftharpoons$ **a** and thus an equilibrium mixture of **a** and **b** conformers is to be expected. The equilibrium portions of conformers **a** at 298 K using the AM1 heats of formation are 87% (X = NH), 80% (X = NCH$_3$) and 70% (X = PH) so that all CD spectra in solution (neglecting solvation effects) should be dominated by the **a** conformer.

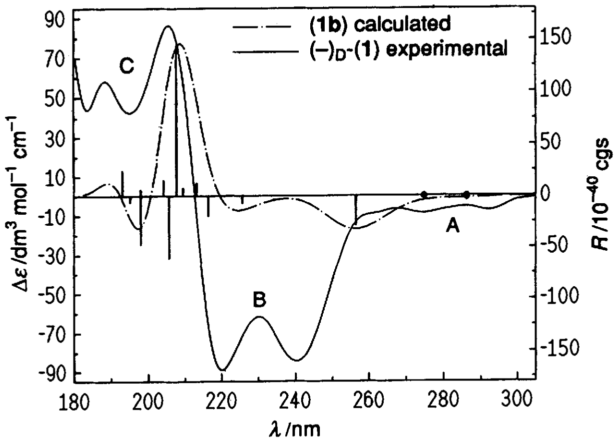


Fig. 5 Comparison of the experimental CD spectra of **1** (——) and the AM1/MRD-CI calculated rotatory strength for **1b** designated by sticks and weighted Gaussian curves (– – –). For more information see Fig. 4.

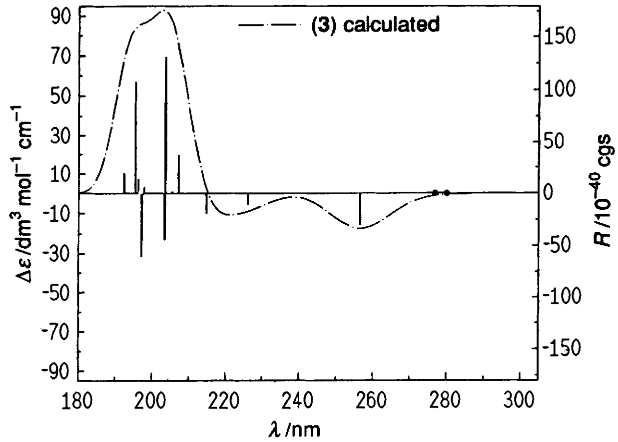


Fig. 6 AM1/MRD-CI calculated rotary strength for **3a** designated by sticks and weighted Gaussian curves (– – –). For more information see Fig. 4.

3.2 CD spectra

The calculated CD spectra of compounds **1a**, **1b** and **3a** are given in Figs. 4–6. For **1a** a characterization of the bands is given in Table 3. Because the nature of the various excitations is very similar in all compounds (see below) the corresponding tables are not shown for the other compounds. For a better comparison the experimental spectra obtained for **1** are given in Figs. 4 and 5.

The characteristic CD bands in the spectrum of **1a** (see Fig. 4) are typical for a variety of (*M*)-1-hetera[2.2]metacyclophanes.[2,9] The lowest energy band (labelled A) shows a very low negative intensity and corresponds to the longest wavelength band in the UV spectra. Between 220 and 250 nm the first intense negative Cotton effect (band B) consisting obviously of at least two transitions is observed. On going to higher energies, a similar intense and structure peak (band C, maxima at 190 and

Table 3 AM1/MRD-CI results of vertical excitation energies (ΔE, experimental band maxima in parentheses) and rotatory strengths R of the 15 lowest excited states of (−)-(*M*)-1-thia-aza[2.2]metacyclophane (**1a**). The state-character in terms of the dominating singly excited configurations in the final wavefunction is given in the last column. Values in parentheses indicate π-MOs of the benzene ring one (S-, X-substituted) or two, respectively. 3p Refers to one of the lone-pair orbitals of the S-atom

ΔE[a]		$R/10^{-40}$ cgs[b]	Band	Excitation type
eV	nm			
4.32	286.8 (290)	−0.33	A	$L_b(1)$
4.38	283.0	−0.47	A	$L_b(2)$
4.77	260.0 (240)	−28.02	B	$3p(S) \longrightarrow \sigma^*(C\text{–}S)$
5.45	227.4 (220)	−13.03	B	$3p(S) \longrightarrow \sigma^*(C\text{–}S)$
5.69	217.9 (220)	−20.31	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
5.79	214.2	10.32	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
5.96	207.9 (200)	121.44	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
6.01	206.2	21.15	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
6.03	205.6	−16.18	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
6.11	202.9	−26.65	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
6.24	198.8	−12.72	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
6.24	198.6	7.36	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
6.27	197.7	0.19	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$
6.42	193.0 (190)	61.15	C	[c] $\pi\pi^*(1)$; $\pi\pi^*(2)$; $3p(S)\pi^*(1)$

[a] The calculated excitation energies are shifted by +1.3 eV. [b] In cgs, R has units of esu cm erg G^{-1}. This corresponds to 3.336×10^{-15} m^3 C^2 s^{-1}. [c] Each state has to be described by a linear combination of various transitions (see the text).

210 nm) is observed which exhibits a positive Cotton effect. Differences between the spectra of **1a** (Fig. 4) and **1b** (Fig. 5) appear only in the higher energy region (above 200 nm). While for **1a** the C band consists of two peaks with positive Cotton effects for **1b**, the second peak of C possesses a small negative Cotton effect.

Comparing our theoretical results with the experimental findings (Figs. 4 and 5), the overall agreement with respect to the excitation energies and intensities of the calculated and experimental CD bands is good, keeping in mind the size and complexity of the molecules investigated. Furthermore, the comparison shows that **1a** is the dominant conformer in solution. This is consistent with our energy data in which **1a** is calculated to be the energetically lower conformer, *i.e.*, it is the main absorbing species under the experimental conditions of the CD measurements.

For **1a** a characterization of the excitations responsible for the various bands can be taken from Table 3. The A-band is formed by two L_b-type transitions localized separately in the two aromatic rings. The calculated R values are very low (but with the correct negative sign[†]) indicating only small perturbations of the L_b-type states which are dipole- and magnetically forbidden in benzene itself. In the region of the B-band of **1a** we found two negative transitions which are characterized by excitations from the lone-pair orbital of the S-atom (*i.e.*, 3p) into antibonding σ*-MOs of the C–S–C fragment. The splitting of the two maxima, however, is calculated slightly too large. The calculated intensity is too low which may be due to vibrational effects and/or environment effects not taken into account in the present model.

The following two intense positive bands (C) at 210 and 190 nm arise due to a large number of electronically excited states. They are composed of strongly electric dipole allowed ππ* transitions in both rings and excitations from the lone-pair orbital of the S-atom (*i.e.*, 3p) into π* of the S,N-substituted ring and the σ*-MOs of the C–S–C fragment.

Next we compare the calculated data of **1a** with those of **1b** (see Figs. 4 and 5). Significant differences of the R values are observed below 200 nm where **1a** shows an intense positive transition absent in **1b**. All other CD transitions are quite comparable in magnitude and excitation energy. The different shape of band C in the spectra of **1a** and **1b** could indicate that the nature of the excitations responsible for that energy region are different in both isomers. From Table 3 it can be seen, however, that for $\Delta E < 220$ nm the energetic spacing of the electronic states is very small. As already described for **1a**, for **1b** the electronic structures of the states are also determined by three different transitions, *e.g.*, ππ* transitions in both rings and excitations from the lone-pair orbital of the S-atom (*i.e.*, 3p) into π* of the *S*,*N*-substituted ring and the σ*-MOs of the C–S–C fragment. Owing to the small energy spacing, large interactions between the various excitations takes place so that each electronic state must be described as a linear combination of various similar important excitations. Because the final linear combination depends strongly on the energetic position of the various transitions small changes in the molecular environment of both benzene rings are sufficient to change the composition of the electronic states and as a consequence lead to different *R*-values. Summarizing, the differences between the two spectra do not result from different types of transition but from the complicated interplay of the various excitations.

As can be seen from Table 3 excitations from the valence shell of the nitrogen centre are not important for the region of the spectra described in the present study. This is consistent with UV data of alkylated amines which show that the first valence excitation appears below 180 nm (6.4 eV).[10] Effects of the nitrogen centre due to conjugative interaction with the π-system of the benzene ring are small because the lone-pair orbital is twisted with respect to the plane of the benzene ring. Therefore it is understandable that differences in the CD spectra to other (*M*)-1-hetera[2.2]metacyclophanes, *e.g.*, 1-thia[2.2]metacyclophane, are very small. Because excitations arising from the nitrogen centre are found to be unimportant the spectrum of **2** is expected to be very similar to that of **1**.

The similarities of the calculated spectrum as stated above are also found if the spectrum of **3a** (X = PH, see Fig. 6) is compared with that of **1a**. Differences between the spectra can be ascribed to some high energy transitions, which are slightly shifted compared with the nitrogen compound, *i.e.*, excitations from the valence shell of the phosphorus centre do not appear. Inspection of UV absorption data of NH_3 and PH_3[10] reveal that excitation out of the lone-pair orbital of the phosphorus atom are only slightly lower in energy compared with NH_3 so that significant participation in the excited states is expected to occur below 180 nm.

4 Conclusions

In the present work the minimum energy structures of several 1-thia-hetera[2.2]metacyclophanes with X = NH **1**, X = NCH_3 **2** and X = PH **3** have been determined. The energy difference and the barrier height between the two conformers with inverted configuration at the X centre were calculated. The CD spectra of the compounds **1a**, **1b** and **3a** were calculated using a newly developed combination of semiempirical AM1[4] and multi-reference single and double excitation configuration interaction (MRD-CI)[5] treatments.[3] From a comparison between experimental and theoretical CD spectra it is shown that structure **1a** is the principal absorbing species under the experimental conditions used. This finding is consistent with our energy data in which **1a** is calculated to be the energetically lower isomer. This seems to conflict with the X-ray data which

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[†] Most of the intensity of the A-band of **1a** is possibly borrowed from higher lying ππ* states by vibronic coupling.

finds only structure **1b** but this apparent contradiction is resolved by results of a previous study in which intermolecular hydrogen bonds were found to favour structure **1b** in the crystalline environment.

A careful analysis of the character of the various bands of the CD spectra shows that differences between the various compounds do not result from different types of excitation process but from the complicated interplay of various excitation types, *e.g.*, $\pi\pi^*$ transitions in both rings and excitations from the lone-pair orbital of the S-atom (*i.e.*, 3p) into π^* of the *S,N*-substituted ring and the σ^*-MOs of the C–S–C fragment. Excitations out of the valence shell of the nitrogen or the phosphorus centre were found to be unimportant for the energy region discussed in the present study.

Furthermore, it was demonstrated that the combination of experimental CD with theoretical calculations can give detailed information about conformational processes that are too fast for the NMR timescale.

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