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PROTONATION STUDIES ON ISOMERIC TETRAFLUORO-2,11-DITHIA[3·3]CYCLOPHANES, TETRAFLUORO[2·2]*METAPARA*CYCLOPHANE AND THEIR CORRESPONDING NON-FLUORINATED ANALOGS. COMPARISON WITH FLUORINATED AND NON-FLUORINATED[2·2]CYCLOPHANES: A STABLE ION AND SEMI-EMPIRICAL (AM1, PM3) INVESTIGATION

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Protonation of tetrafluoro-2,11-dithia[3·3]*para*cyclophane and tetrafluoro-2,11-dithia[3·3]*metapara*cyclophane in high-acidity super acid media, namely $FSO_3H.SbF_5$ (1:1) 'magic acid'–SO_2ClF, gave their corresponding acidic disulfonium ions. Additional ring protonation to give a disulfonium–monoarenium trication was not observed. With the non-fluorinated 2,11-dithia[3·3]cyclophanes, the disulfonium ions can be ring protonated in equilibrium to give a dynamic disulfonium–monoarenium trication. Tetrafluoro[2·2]-*metapara*cyclophane is monoprotonated at the *meta* ring and gives a complex mixture of conformational isomers. Multinuclear magnetic resonance data on the cyclophane precursors and their derived cations are compared and analysed. The energies, conformations and charge distributions of the isometric fluorinated and non-fluorinated [2·2]- and dithia[3·3]cyclophanes were calculated by the AM1 and PM3 methods, respectively. In all but one case the cyclophane arenium ions predicted by theory to be energetically most favoured are those observed in solution under stable ion conditions. In agreement with experiment, the instabilities of *S,S,C*-cyclophane trications are also theoretically predicted.

INTRODUCTION

Synthetic design, structure analysis, conformational dynamics, transannular interactions and guest–host chemistry of cyclophanes represent topical research areas of great current activity.[1,2]

The concepts of intramolecular interactions in facially disposed fixed cyclophanes and transannular substituent effects in these systems were recognized early in the pioneering work of Cram and co-workers.[3,8] Filler and co-workers[9] showed that in conformationally rigid, small cyclophanes, fluorination of one deck leads to a remarkable deactivation of the opposite deck in typical Friedel–Crafts reactions. We showed previously[10] that despite such deactivation, under appropriate conditions tetrafluoro- (**1**) and octafluoro[2·2]paracyclophane (**2**) are both monoprotonated in superacids to give persistent arenium ions **1**-H^+ and **2**-H^+ (Figure 1). Monoprotonation of [2·2]paracyclophane (**3**) to **3**-H^+ and [2·2]metaparacyclophane(**4**) to **4**-H^+ had already been shown by Hefelfinger and Cram,[11] and diarenium ion formation, $\mathbf{3} \rightarrow \mathbf{3}\text{-}H_2^{+2}$. at very low temperatures was demonstrated by Hopf *et al.*[12]

The isomeric dithia[3·3]cyclophanes **5**–**7** (Figure 2) are important as precursors to a host of cyclophanes

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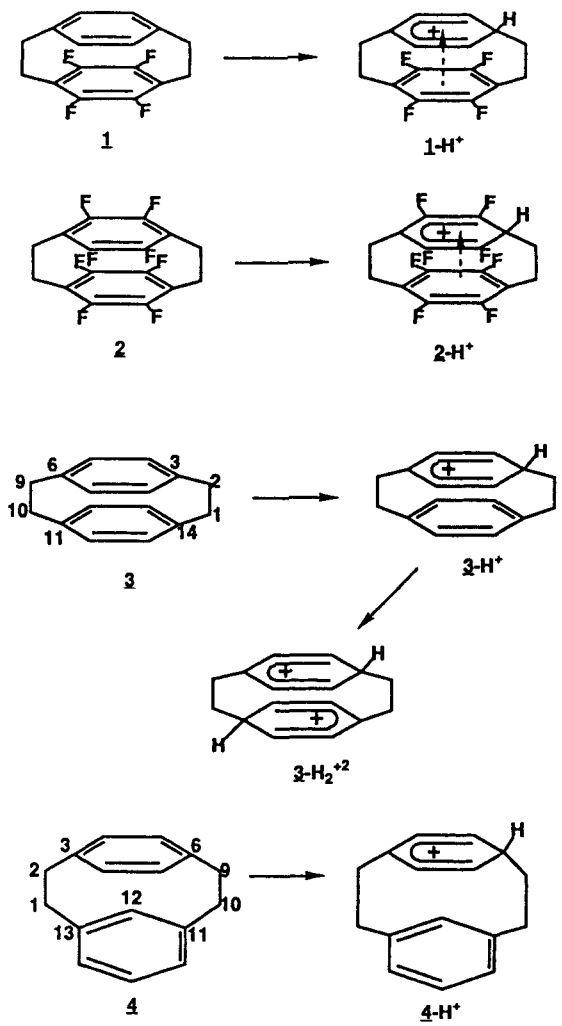


Figure 1. Superacid protonations of cyclophanes **1**, **2**, **3** and **4**

formed by classical photoextrusion reactions. Their corresponding disulfonium ions serve as precursors to cyclophane 1,9-dienes (by Stevens rearrangement and Hofmann elimination).[13–15] However, the chemistry of dithiacyclophanes toward superelectrophiles is rather obscure. It is known that disulfonium ions of methylation (with Meerwein salts) of dithia[3·3]cyclophanes are readily formed and isolated, but NMR data on these systems are scarce.[13–15] It seems unclear to what extent the electrophilic reactivities of the cyclophane π systems are perturbed in the disulfonium ions. The energies and conformations of the resulting supercharged ions are not available. Would generation of disulfonium monoarenium trications be possible with isomeric dithia[3·3]cyclophanes in superacid media? With fluor-

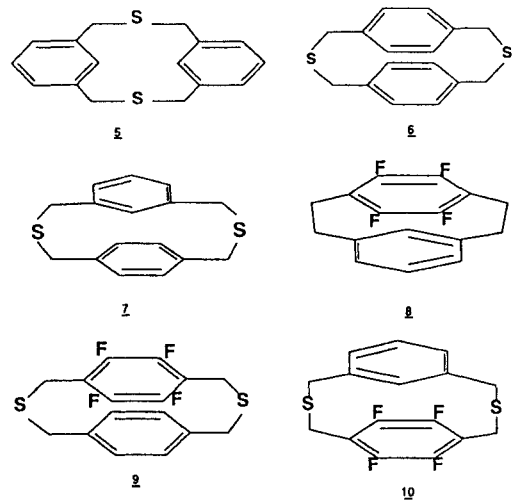


Figure 2. Fluorinated and non-fluorinated [2·2]- and dithia[3·3]cyclophanes

inated cyclophanes **1** and **8**, introduction of a sulfur bridge, viz. dithia[3·3]cyclophanes **9** and **10**, might diminish (or cancel) the imposed transannular deactivation. Could this in turn facilitate the formation of supercharged ions?

All of the six possible isomers of dithia[3·3]-cyclophanes have been synthesized and their preferred conformations determined.[16] The parent *metameta* isomer **5** was shown by Anker *et al.*[17] to have a *syn* conformation in the solid state and predominantly also in solution. Vögtle *et al.*[18] showed that intraannular substitution can alter the *syn*/*anti* conformational preference in [2·2]*meta*cyclophanes.

In this study, we explored the protonations of fluorinated dithia[3·3]cyclophanes **9** and **10**, their non-fluorinated analogs **6** and **7** and the fluorinated [2·2]*meta*paracyclophane **8** (Figure 2) under stable ion conditions and compared their NMR data with those of the arenium ions of **1**–**4** (Figure 1). To obtain further insight into the relative stabilities of disulfonium ions and mono- and diarenium ions of cyclophanes, their heats of formation, conformations and charge distribution, we also carried out semi-empirical (PM3 and AM1) studies on the mono- and diprotonation of isomeric [2·2]cyclophanes and examined the di- and triprotonation of their corresponding dithia[3·3]-cyclophanes.

RESULTS AND DISCUSSION

Comparative NMR studies of the cyclophane substrates (Figure 3)

Although multinuclear magnetic resonance data on **9**,

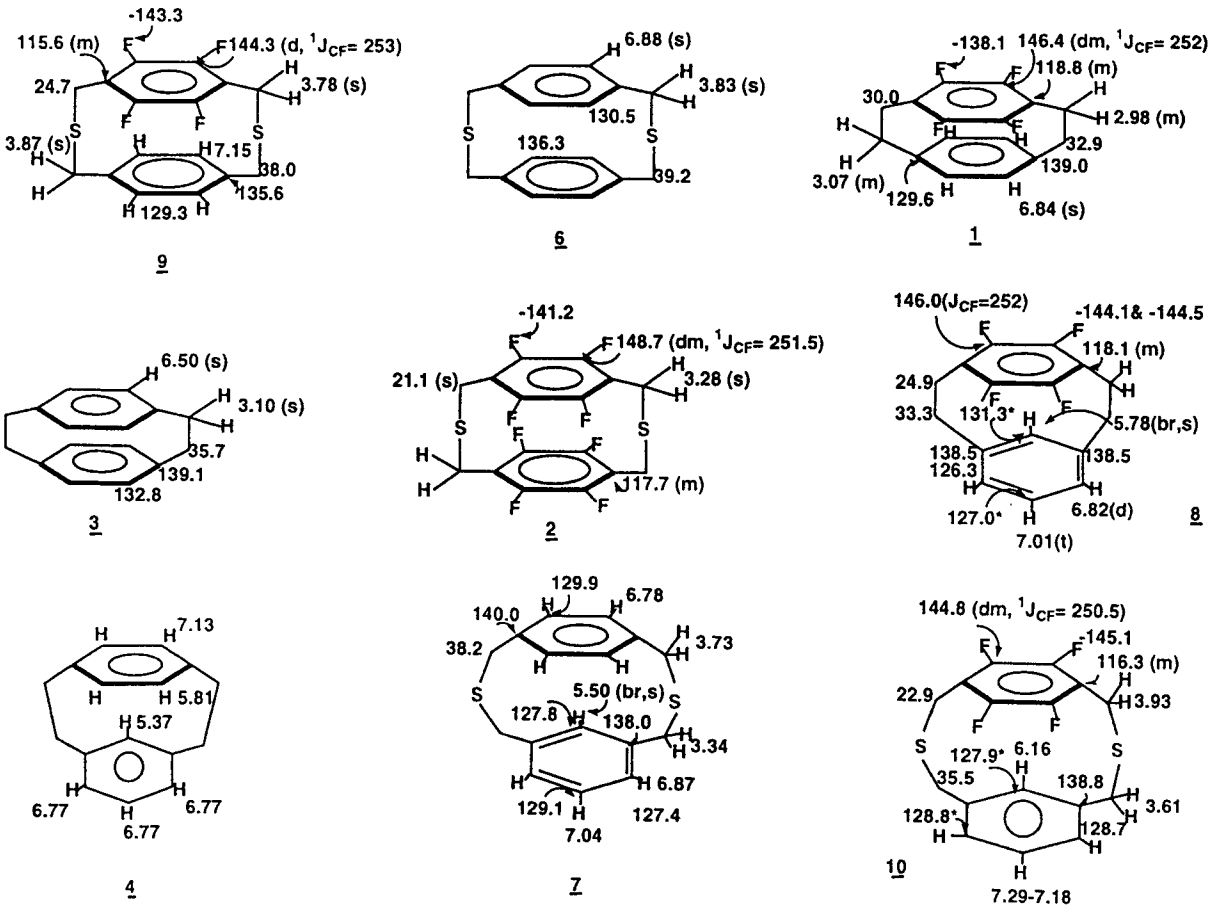


Figure 3. Multinuclear magnetic resonance data for the cyclophane substrates (asterisks indicate interchangeable assignments)

10 and **8** were previously reported by Filler *et al.*,[19] their specific assignments in comparison with the non-fluorinated dithia analogs **6** and **7** and the fluorinated and non-fluorinated [2·2]cyclophanes **1**–**4** were not addressed. Therefore, we began by comparing the NMR data of the cyclophane substrates.

The aromatic protons in **9** are deshielded by 0·27 ppm as compared with **6**. The same comparison between **1** and **3** gives a deshielding of 0·34 ppm for the tetrafluoro[2·2]*para*cyclophane. If, as suggested previously,[9] this is a manifestation of transannular π-electron flow into the fluorinated ring, it can be concluded that the sulfur bridge has diminished this effect but has not removed it. In **9**, the methylene bridge protons bonded to the tetrafluorobenzene ring are slightly more shielded relative to the CH_2 groups adjacent to the non-fluorinated deck. The positions of the latter are very close to the values found in **6**.

In the ^{13}C NMR spectrum of **9**, the *ipso* carbons of the fluorinated deck are more shielded relative to those of the opposite deck and appear as a multiplet owing to fluorine coupling. The bridge carbons adjacent to the fluorinated deck are also shielded. These trends, which are also clearly observable with tetrafluoro- and octafluoro[2·2]*para*cyclophanes **1** and **2** in comparison with **3**, may reflect the importance of resonance forms with fluoronium ion character. The position of the CF carbon doublet in **9** is close to those of **1** (and **2**). The fluorines in **9** are *ca* 5 ppm more shielded relative to those in **1**. The ^{13}C resonances of the non-fluorinated deck in **9** are very close to those of **6**.

In [2·2]*metaparacyclophane* **4** with a stepped *anti* conformation,[20] the anisotropically shielded internal hydrogen is at 5·37 ppm.[11] In the tetrafluoro[2·2]-*metaparacyclophane* **8** this hydrogen is more deshielded and appears at 5·78 ppm. With the larger dithia[3·3]cyclophanes **7** (also with preferred stepped *anti* conformation)[20] and **10**, the internal hydrogen appears at 5·50 and 6·15 ppm, respectively. Thus the anisotropic shielding has diminished by 0·13 and

0·38 ppm, respectively, in the non-fluoro versus the fluoro derivatives on introduction of the sulfur bridge. It might be suggested that the attractive $\pi-\pi$ interaction between the fluorinated and non-fluorinated rings in **8** may contribute to a more effective shielding, giving a larger $\Delta\delta_{1_H}$ when the bridge is elongated. Alternatively, the downfield shift of the internal hydrogen in **8** and **10** (as compared with **4** and **7**) may stem from interaction with the fluorines. If so, the relative orientation of the internal hydrogen and the inner fluorines must be more favourable in the [3·3]cyclophane skeleton.

A similar shielding of the *ipso* carbons of the fluorinated deck and its bridging methylenes relative to these carbons in the opposite deck is seen with **10**, and a similar feature is observed for **8**. In **8**, a slight non-equivalence of the fluorines is observed whereas little overall difference is seen in the fluorine positions between **8** and **10**.

Superacid protonations (Figure 4)

Protonation of **9**

Slow addition of a slurry of **9** in SO_2 to a homogeneous solution of $FSO_3H.SbF_5$ (1:1)–SO_2 at dry-ice–acetone temperature gave a yellow solution on mixing, implying sulfur rather than ring protonation. The ^1H NMR spectrum (at $-68\,^{\circ}C$) exhibited two broad singlets at 7·34 and 7·23 ppm (1H each) for the SH^+ protons. The SH^+ absorptions were more deshielded as compared with typical dialkylsulfonium ions (5·80–6·52 ppm).[21] The ring protons appeared as a deshielded singlet at 7·72 ($\Delta\delta = 0{\cdot}57$). This value is only slightly shielded relative to the *ortho* hydrogens of the arenium ion moiety in **1**-H^+ (Figure 5) Thus, under these conditions, an NMR-observable arenium ion (a trication) was not detected. Similarly to **1**-H^+, the disulfonium ion **9**-H_2^{2+} exhibited

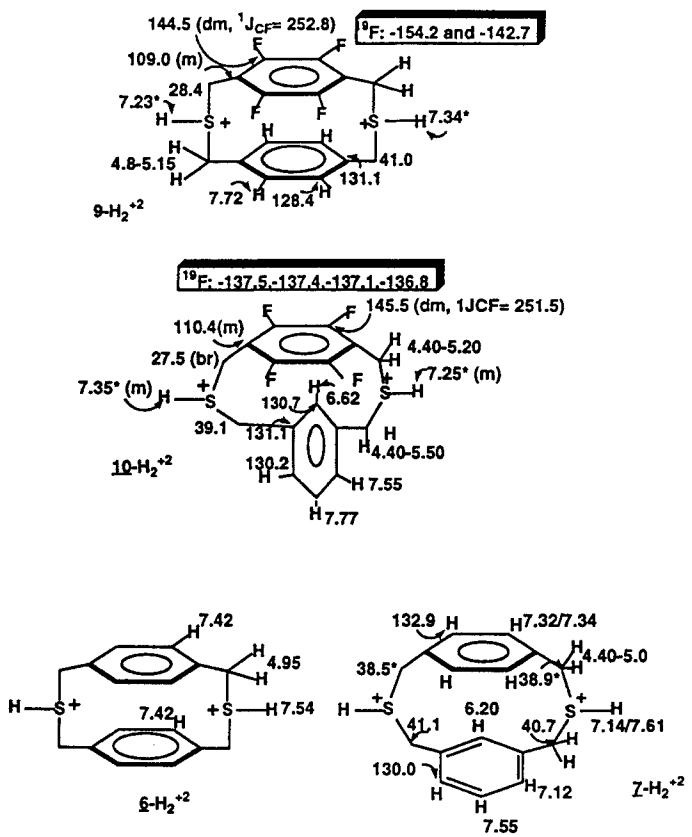


Figure 4. Multinuclear magnetic resonance data for the protonated cyclophanes (asterisks indicate interchangeable assignments)

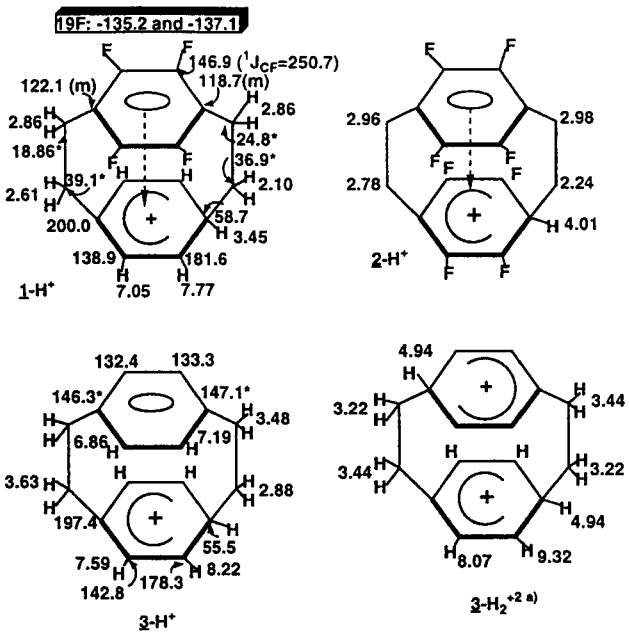


Figure 5. Comparison of the NMR data for the mono- and diprotonated **1**, **2** and **3**. [a]Taken from Ref. 12

two fluorine absorptions in close proximity. The methylene bridge hydrogen were deshielded, as expected, forming a complex multiplet between 4·80 and 5·15 ppm. Both types of the bridging methylene carbons were deshielded in the disulfonium ion, and exhibited long-range coupling to SH (5–6 Hz). Whereas the CF carbon resonances were almost unchanged in the disulfonium ion, the *ipso* carbons were more shielded in the disulfonium ion. Quenching of the dication furnished intact **9**(^{1}H NMR).

Protonation of **10**

Low-temperature reaction of **10** in SO_2 with 'magic acid'–SO_2 similarly gave a yellow solution indicative of sulfur protonation, **10** → **10**-H_2^{2+}. The ^{1}H NMR spectrum exhibited the SH^+ protons as non-equivalent multiplets at 7·25 and 7·35 ppm (2H). The diagnostic internal hydrogen peak moved from 6·16 ppm in the precursor to 6·62 ppm in the disulfonium ion. The remaining aromatic protons were also deshielded and appeared as a doublet at 7·55 (2H) and a distorted triplet at 7·77 (1H). Clearly, ring protonation to form a trication was not observed. The methylene bridge protons were deshielded, and deshielding of the bridge carbons and shielding of the *ipso* carbons were apparent in the ^{13}C NMR spectrum of **10**-H_2^{2+} (recorded at −54 °C), whereas the CF carbon peaks were almost unchanged. The ^{19}F NMR spectrum (at −60 °C) showed four different singlet fluorine resonances. Except for line narrowing due to a decrease in viscosity, the ^{1}H spectrum was virtually unchanged up to −35 °C. Quenching of the ion solution returned the structurally intact **10** (^{1}H NMR).

In an attempt to bring about ring protonation of the disulfonium ion, **10** was dissolved in the highest acidity superacid $HF.SbF_5$ (1:1)–SO_2ClF at dry-ice–acetone temperature. A yellow–orange solution resulted when the sample temperature was allowed to rise to *ca* −68 °C with vigorous mixing. The ^{1}H NMR spectrum (recorded at −68 °C) indicated only the disulfonium ion and not the arenium ion.

Protonation of non-fluorinated [3·3]cyclophanes **6** *and* **7** *(Figure 4)*

Low-temperature reaction of **6** in SO_2 with 'magic acid' in the same solvent gave a red solution on mixing. The ^{1}H NMR spectrum (at −68 °C) exhibited the SH protons as a broad singlet at 7·54 ppm (2H). The aromatic protons gave rise to a deshielded singlet at 7·42 ($\Delta\delta = 0{\cdot}54$). Thus, despite the red color, a persistent arenium ion was not observed by NMR under these conditions. It seems reasonable to suggest that the disulfonium–monoarenium trication was a contributing species in a rapid equilibrium. Indeed, quenching of the

ion solution furnished a 2:1 mixture of **3** and **4** (^{1}H NMR). Compound **4** is formed from **3** by *ipso* protonation and skeletal rearrangement. The diagnostic internal hydrogen of **4** appeared at 5·30 ppm in the crude mixture resulting from ion quenching.

Similar low-temperature protonation of **7** in 'magic acid'–SO_2 initially gave a yellow–brown solution at dry-ice–acetone temperature, which on vigorous mixing and with a rise in temperature (*ca* −60 °C) irreversibly turned pale red. The ^{1}H NMR spectrum of this solution showed the SH protons as two singlets at 7·61 and 7·14 ppm and the bridging methylene protons as a deshielded complex between 4·40 and 5·0 ppm. The originally equivalent ring hydrogens of the para ring became slightly non-equivalent in the disulfonium ion and their resonances appeared in the 7·32–7·34 region, considerably deshielded relative to **7**. The internal hydrogen peak of the meta ring moved from 5·30 to 6·20 ppm (a 7 Hz doublet). The remaining aromatic protons of the meta ring were also deshielded. Deshielding of the bridge carbons was also detectable in the carbon spectrum of **7**-H_2^{2+}. In the aromatic region, 11 absorptions were seen between 130 and 133 ppm.

The ^{1}H NMR spectrum of the yellow–brown sample which was kept at dry-ice–acetone temperature (*ca* −75 °C) showed it to be identical with the pale red sample formed at higher temperatures (*ca* −60 °C) discussed above. Thus, whereas a persistent trication was not observed, ring protonation apparently occurred in a rapid equilibrium. Similar observations were made in $HF.SbF_5$ (1:1)–SO_2ClF.

Protonation of **8**

The low-temperature reaction of the fluorinated [2·2]cyclophane **8** with 'magic acid' in SO_2 solvent at dry-ice–acetone temperature gave a deep-red solution on mixing. Its ^{1}H NMR spectrum (at −70 °C) was complex and was consistent with a mixture of arenium ions whose conformational interconversion was slow on the NMR time scale. Ring protonation was clearly evident based on the presence of broad absorptions between 4·75 and 5·15 ppm. In the ^{13}C spectrum, a major sp^2(C) absorption at 48 ppm and a minor one at 52 ppm were detectable. The aromatic region in the ^{1}H NMR spectrum is widely spread between 6·60 and 9·90 ppm. The relative integrals pointed to monoprotonation at the *ipso* position of the *meta* ring. The ^{1}H NMR spectrum was unchanged down to −40 °C, and conformational averaging (coalescence of resonances) did not occur. The fluorine spectrum of the monocation showed two slightly broad resonances which had not shifted noticeably relative to the precursor.

Comparative discussion of superacid prontonations

Protonation of the facially fluorinated and non-fluorinated dithia[3·3]cyclophanes **9** and **10** led in all cases to the formation of persistent acidic disulfonium ions; persistent disulfonium monoarenium ions were not observed, either in 'magic acid' or in $HF.SbF_5$ (1:1) at dry-ice–acetone temperature. Since **1** is monoprotonated under these conditions, it must be concluded that the SH^+ bridge exerts a considerable deactivation on the aromatic rings.

Comparison of the NMR data for **1**-H^+ (Figure 5) and **9**-H_2^{2+} (Figure 4) is instructive. The fluorines, the *ipso* carbons and the CF carbons of the fluorinated deck in **1**-H^+ are more deshielded relative to these positions in the disulfonium species, despite the proximity of the SH^+ linkage to the fluorinated deck in the disulfonium ion. The deshielding of the fluorinated ring in **1**-H^+ relative to **9**-H_2^{2+} taken together with shielding of the arenium ion protons in **1**-H^+ as compared with **3**-H^+ provide complementary evidence in support of transannular π-electron drain into the arenium ion by the proximal fluorinated deck in **1**. Comparison of the chemical shift of the *ortho* hydrogens of the arenium ions in **3**-H^+ and **1**-H^+ (as discussed previously)[10] showed a noticeable shielding of the arenium ion of the fluorinated cyclophane. Diprotonation, **3**-$H^+ \rightarrow$ **3**-H_2^{2+} (Figure 5), on the other hand, led to substantial deshielding of the arenium ion protons.

With the more reactive non-fluorinated dithia[3·3]-cyclophanes **6** and **7**, equilibrium ring protonation at low temperature can be inferred from both the distinct color of the ion solutions (yellow → red) and a considerably more deshielded inner proton in the case of **7**-H^+. With the fluorinated [3·3]cyclophanes, ring protonation at higher temperature may be inferred from skeletal rearrangement which was observed on quenching of **6**-H_2^{2+}.

Hefelfinger and Cram[11] demonstrated that the non-fluorinated **4** is monoprotonated at the *ipso* carbon of the *para* ring in FSO_3H–SO_2ClF (Figure 1). In this lower acidity superacid, the persistent arenium ion is observable only at very low temperatures (*ca* −98 °C).[11] We find that the same cation can be observed at −75 °C in 'magic acid'–SO_2 (or SO_2ClF).

With the less reactive **8**, ring protonation at the *ipso* position of the *meta* ring is suggested, but the NMR spectra are complicated owing to the presence of a mixture of conformationally isomeric arenium ions, unlike the rigid fluorinated **2** which gives a single arenium ion that remains static on the NMR time scale even at −60 °C.

Semi-empirical calculations on isomeric [2·2]cyclophanes and the dithia[3·3]cyclophanes

To provide further insight into the energetics, conformational aspects and charge distribution of [2·2]- and dithia[3·3]cyclophanes and for comparison with our solution studies in superacids, we calculated these pro-

Table 1. Calculated and experimental geometry of cyclophanes[a]

Compound		D_1	D_2	D_3	D_4	D_5	D_6	θ	φ	ω
[2·2] *Para*cyclophane	Exp.	1·387	1·384	1·512	1·562	2·778	3·093	12·6	113·7	
	AM1s	1·394	1·403	1·491	1·555	2·608	2·946	13·6	110·7	
	AM1	1·405	1·408	1·520	1·587	2·572	2·826	10·2	108·9	
[2·2] *Metapara*cyclophane	Exp.					2·7	3·0	14·0	112·0	107·0
	AM1	1·393	1·403	1·489	1·540	2·733	2·908	15·3	113·0	109·2

[a] Distances in Å, angles in degrees.

perties for [2·2]cyclophanes **3**, **4**, **1** and **8** by the AM1 method and for [3·3]cyclophanes **6**, **7**, **9** and **10** by the PM3 method.

Structural/conformational features

In Table 1 are compared the calculated distances (Å) and angles of the neutral *para-* and *metapara-*cyclophanes with those obtained from x-ray diffraction studies.[1] The x-ray data for the *metapara*cyclophane are preliminary and incomplete, but the agreement in both cases is reasonably good. The *para*cyclophane calculation was carried out twice, once with some symmetry restrictions (AM1s) and once without. The geometric variables are coded as shown in Figure 6.

Mono- and diprotonation of these cyclophanes are predicted by AM1 to cause several changes in their geometries, mainly in the shape, deviation from planarity and separation of the two rings. We have chosen two distances and four angles, defined in Figures 7 and 8, to show these changes. The changes in these parameters on protonation are given for the two cyclophanes in Table 2. The calculated ring conformation and deviation from planarity (θ) vary with the site of protonation as follows.

[2·2] Paracyclophane. Protonation at the *ipso* position of one ring (C-3) causes that ring to change from a shallow boat with $\theta = 13·6°$ to a shallow chair with $\theta = 12·6°$. The unprotonated ring remains a boat with $\theta = 12·6°$. The bridging angle (θ) is essentially unchanged at 110·3° on the unprotonated side of the molecule but increases to 112·5° on the protonated side. Little change is seen in the other dimensions also. The lengths of the bridge segments, D_4, are 1·546 Å on both sides, and the lengths of segments D_3 are 1·490 Å on the unprotonated side and 1·488 and 1·530 Å on the protonated side. The dimensions of the unprotonated ring, D_1 and D_2, are 1·395 and 1·406 Å, respectively.

Diprotonation at the *ipso* positions in both rings (C-3 and C-11) flattens both rings considerably. The value of θ is halved to 4·9°, and the rings adopt a slightly twisted chair conformation. The separation of the rings

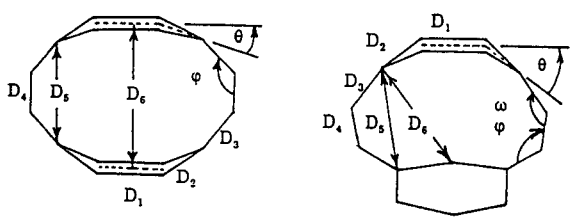
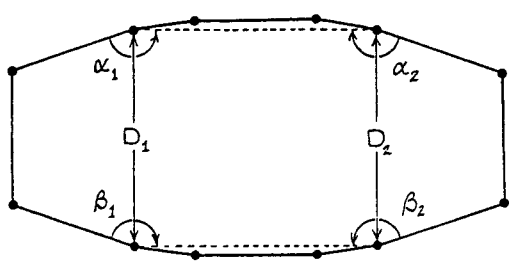
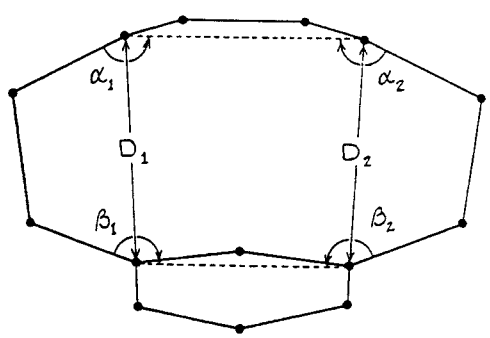


Figure 6. Geometrical variables examined in the calculations



D1: 2.572Å α1: 161.1° β1: 161.1°
D2: 2.572Å α2: 161.1° β2: 161.1°

Figure 7. Geometrical variables examined in the calculations



D1: 2.733Å α1: 152.5° β1: 147.5°
D2: 2.733Å α2: 152.3° β2: 147.6°

Figure 8. Geometrical variables examined in the calculations

Table 2. Changes in geometry of cyclophanes on protonation[a]

Compound	Proton location	ΔD_1	ΔD_2	$\Delta\alpha_1$	$\Delta\alpha_2$	$\Delta\beta_1$	$\Delta\beta_2$
[2·2] *Para*cyclophane	C-3	+0·133	+0·010	−11·3	+4·1	+1·3	−4·7
	C-3, C-11	+0·177	+0·335	+8·0	−24·1	−14·9	+4·9
[2·2] *Metapara*cyclophane	C-11	+0·199	−0·046	+2·0	−0·8	−9·6	+3·3
	C-12	−0·008	−0·008	+0·7	+0·9	−1·0	−0·9
	C-3	0·253	−0·062	−18·9	+9·6	−0·6	−0·9
	C-3, C-11	+0·217	+0·301	+11·1	−23·2	−14·1	+2·1

[a] Distances in Å, angles n degrees.

also increases, though the values of D_4, at 1·540 and 1·538 Å, are similar to those in the monoprotonated species.

[2·2] Metaparacyclophane. The calculated θ in the para ring of the neutral compound is 15·3°. The *meta* ring is puckered only very slightly across the points of attachment to the ethylene bridges but adopts a half-boat ($\theta = 6·6°$) conformation in the perpendicular direction, curving away from the *para* ring. Protonation in the *meta* ring increases θ in the *para* ring by about 1° and increases the planarity of the *meta* ring, making it a very shallow twisted boat. Protonation in the *ipso* position of the *para* ring (C-3) causes it to adopt a half-boat configuration with $\theta = 16·0°$.

The ring configurations in the C-3, C-11-diprotonated molecule are essentially as they were in the corresponding monoprotonated species.

[3.3] Dithiacyclophanes. The phenyl rings in both of the neutral dithiacyclophanes are within 3° of planarity. However, examination of the optimized geometry of the dithia[3.3]paracyclophane **6** and its disulfonium ion **6**-H_2^{2+} (Table 3) reveals that diprotonation increases the strain by spreading the C—S—S angles (δ) by 6·2°. This in turn increases the deviation of the benzene rings from planarity by 3·4°, despite the fact that the CS bonds also increase in length by 0·028 Å, and the ends of the opposing rings move further apart by 0·30 Å.

Table 3. Calculated geometries for the neutral and *S,S*-diprotonated dithia[3·3]cyclophane

Compound	d_{C-S} (Å)	δ_{CSC} (°)	θ_{plan} (°)[a]	$d_{ring-ring}$ (Å)[b]
6	1·828	102·9	2·9	3·150
6 H_2^{2+}	1·856	109·1	6·3	3·453

[a] Deviation of benzene ring from planarity.
[b] Distance between opposing rings measured between *ipso* positions.

Energies and charges

The $\Delta\Delta H_f^\circ$ value for *ipso* (C-3) protonation of [2·2] *para*cyclophane, **3**, is calculated to be 174·6 kcal mol^{-1} (181·0 kcal mol^{-1} for PM3) (1 kcal = 4·184 kJ), whereas that of [2·2] *metapara*cyclophane, **4**, is 181·6, 171·9 and 168·3 for protonation on C-11, C-12 and C-3, respectively (Figure 9). The predicted preference for protonation at the *ipso* position of the *para* ring in **4** is consistent with stable ion studies.[11]

As expected, tetrafluorination in one ring of the cyclophanes increases the energy gap between the protonated and unprotonated forms. The difference is about 8 kcal mol^{-1} when protonation is on the unfluorinated ring and about 9–15 kcal mol^{-1} for protonation on the fluorinated ring. $\Delta\Delta H_f^\circ$ for monoprotonation of the *para*cyclophane **1**, in the *ipso* position of the unfluorinated ring (C-3) is 182·0 kcal mol^{-1} (190·6 kcal mol^{-1} for PM3). That for protonation in the fluorinated ring (C-11) is 189·8 kcal mol^{-1}. Again, this is consistent with solution observations.[10] The $\Delta\Delta H_f^\circ$ values for monoprotonation on the tetrafluorinated metaparacyclophane **8**, at C-11, -12 and -3 are 189·3, 180·5 and 183·7 kcal mol^{-1}, respectively.

Not surprisingly, monoprotonation of the dithia-[3·3]cyclophanes **6**, **7**, **9** and **10** is calculated to be more favorable at sulfur than at the ring carbons, although the difference is nearly 16 kcal mol^{-1} less for the *metapara*cyclophanes **7** and **10** than for the *para* isomers **6** and **9** [$\Delta\Delta H_{f(C-S)}^\circ = 17·7(7)$ vs 33·5(6) kcal mol^{-1}] (Figure 9).

Similarly, protonation of the monosulfonium ion is favored to occur on the second sulfur rather than at a ring carbon by 51·9 kcal mol^{-1} for **6** and 35·7 kcal mol^{-1} for **7**. Hence, as in the monoprotonation case, the *metapara*cyclophane is less resistant to *C*-protonation than the *para* isomer by about 16 kcal mol^{-1}. The difference is clearly due to an increase in strain caused by ring protonation at the *para* ring, because $\Delta\Delta H_f^\circ$ for monoprotonation at sulfur is identical for the [3·3] *metapara* and [3·3] *parapara* isomers, within the limits of the calculation.

To attempt to clarify the effect of the cyclophane

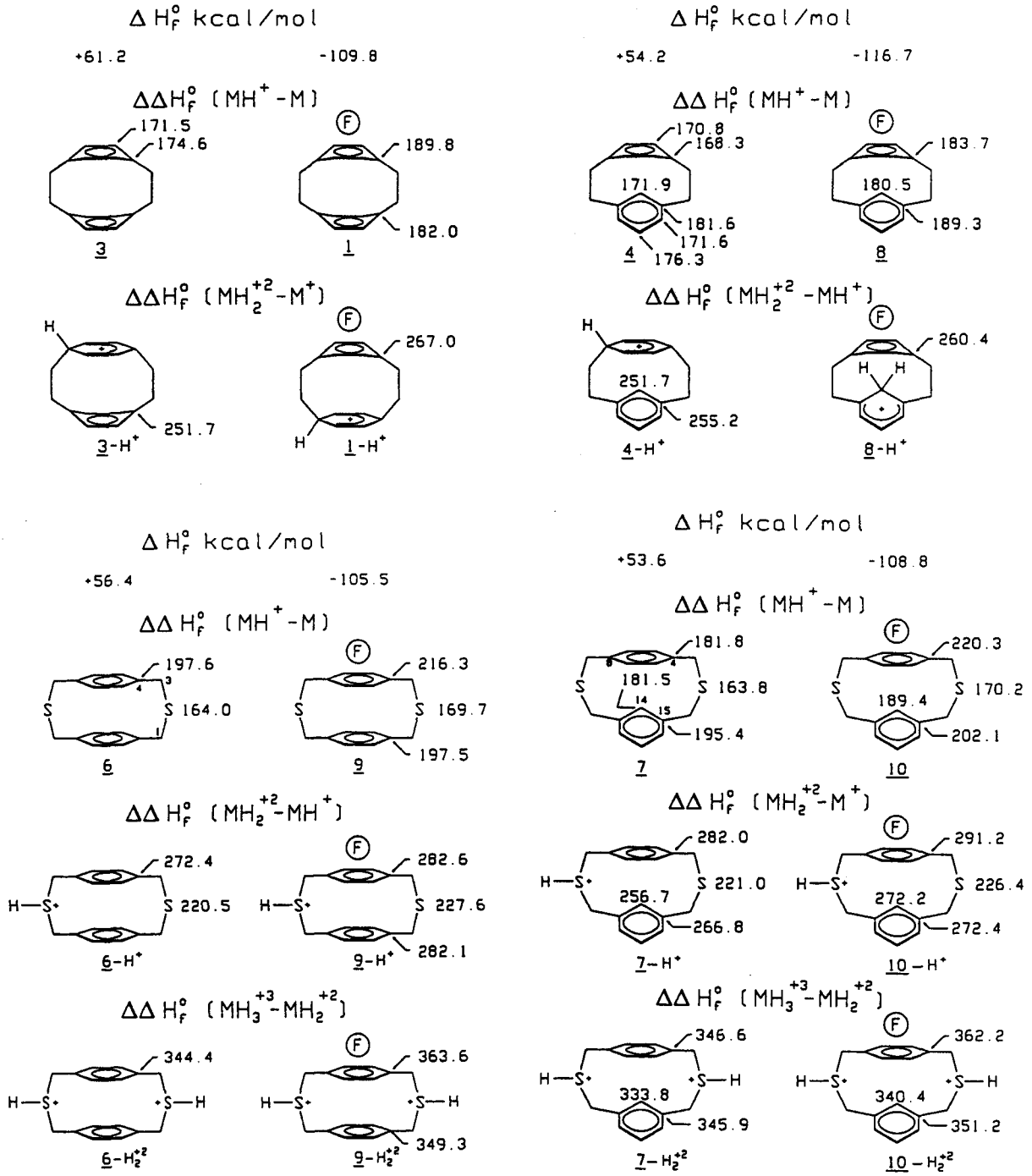


Figure 9. Calculated relative stabilities ($\Delta\Delta H_f^\circ$) for for [2·2]- and dithia[3·3]cyclophane cations

system on the observed energies, we carried out PM3 calculations on the monocyclic model compounds 1,3- and 1,4-bis(thiomethoxymethyl)benzene, **11** and **12** (Figure 10). $\Delta\Delta H_f^\circ$ for *S,S*-diprotonation is 379·2 kcal mol^{-1} for **11** and 278·8 kcal mol^{-1} for **12**, both slightly less than 5 kcal mol^{-1} than that for **6** and **7**. Hence the ring deformation in the cyclophanes does not appear to play a major role in determining the ease of protonation on the sulfurs.

In agreement with our solution NMR results, further protonation of the disulfonium dications to form the *S,S,C*-triprotonated cyclophanes is calculated to be endothermic by 333·8–362·2 kcal mol^{-1} (Figure 9). Here the energy of protonation on the *ipso* carbon is, within 2 kcal mol^{-1}, the same for the *metapara*- and *para*cyclophane. Protonation on C-14 of the *metapara* isomer is about 10 kcal mol^{-1} less endothermic. This may be attributed to the greater stability of the resulting cyclohexadienylic cation when the ends of the conjugated system are tertiary rather than secondary.

Tetrafluorination on one ring of the dithia[3·3]*para*cyclophane **9** makes mono-, di- and triprotonation more endothermic by about 6 kcal mol^{-1} per proton added than it is for the corresponding non-fluorinated systems.

The pattern observed in the computed charges (Figure 11, calculated charges for fluorinated and non-fluorinated [2·2]- and dithia[3·3]-cyclophanes; not shown – supplementary material, available on request) is typical for calculations on unsolvated species. That is, charge is delocalized mainly via the polarizabilities of the bonds, with the attached protons bearing most of the positive charge, particularly in carbocations. In the benzenium ions, the most positive carbon is that *para* to the site of protonation; the *ortho* carbons are slightly positive and the *meta* carbons negative. Calculated charges are a particularly unreliable indicator for the site of protonation in the dithia[3·3]cyclophanes. These compounds are diprotonated exclusively on the sulfurs which exhibit the least negative charges in the molecule.

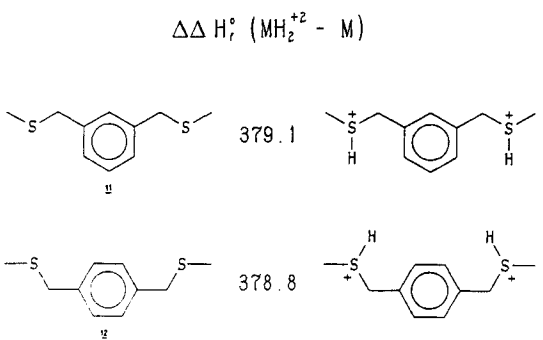


Figure 10. $\Delta\Delta H_f^\circ$ for protonation of the open models **11** and **12**

Heats of formation calculated for the mono- and diprotonated systems definitely show the preference for *S*- over *C*-protonation and provide an explanation for the disulfonium ion's inability to protonate further. The calculated ring-carbon charges for the disulfonium ions differ little from those in the neutral molecules, except that the *ipso* carbons are predicted to be more negative.

In [2·2]*para*cyclophane, **3**, both the calculated relative energies of the monoprotonated species and the calculated total charges predict ring protonation on the unsubstituted position, rather than on the *ipso* position as is observed. Visual inspection of the optimized structure of the *ortho*-protonated ion, however, reveals that, in strong contrast to the *ipso*-protonated species, there is essentially no relaxation of the puckering of the phenyl ring relative to that in the neutral molecule. It is not clear why the relief of strain is not reflected in a lower ΔH_f° for the *ipso*-protonated ion, but the difference between the two ions is only 3·1 kcal mol^{-1}, and specific solvation effects may well reverse their order of stability.

The calculated charges in the *ipso*-protonated paracyclophane again suggest that further protonation in the remaining neutral ring should not take place at an *ipso* position. However, in agreement with the location of attack of the second proton observed in solution,[12] the neutral ring's *ipso* carbon having the most negative charge is that opposite the site of initial protonation.

In the tetrafluorinated ring of **1**, the *ortho* positions are positively charged, and the *ipso* carbons have a higher negative charge than those of the non-fluorinated ring, but are less negative than the *ortho* positions of the non-fluorinated ring.

EXPERIMENTAL

The syntheses of and the analytical data for tetrafluorodithia[3·3]*para*cyclophane (**9**) tetrafluorodithia[3·3]-*metapara*cyclophane (**10**), tetrafluoro[2·2]*metapara*-cyclophane (**8**) and the fluorinated [2·2]*para*-cyclophanes **1** and **2** have been reported previously by Filler *et al.*[19]

The superacid solutions were freshly prepared from freshly distilled FSO_3H (Linde) and SbF_5 (Aldrich). $HF.SbF_5$ (1:1) was purchased from Aldrich. Anhydrous SO_2 (Linde) and SO_2ClF (Aldrich) were used as received.

The NMR spectra were collected on a GN 300 MHz wide-bore instrument. For the ambient spectra, $CDCl_3$ was used as the solvent. The spectra were referenced relative to internal $CDCl_3$ for ^1H and ^{13}C spectra and relative to external $CFCl_3$ for the fluorine spectra. For the low-temperature stable-ion studies, the probe was cooled to *ca* −74 °C while shimming with an acetone-d_6 sample. The freshly prepared cold ion solutions in 5 mm NMR tubes were inserted into the precooled probe. The ^1H and ^{13}C spectra were recorded

first; then the sample was ejected and kept at dry-ice–acetone temperature while the probe was changed after thawing to room temperature. The fluorine probe was subsequently cooled while shimming on an acetone-d_6–$CFCl_3$ (1:1, vv) sample which also served as the external reference.

General procedure for stable ion generation. All operations were carried out under a dry nitrogen atmosphere. Typically, *ca* 20 mg of the cyclophane were charged into a 10 mm NMR tube, cooled in a dry-ic–acetone bath and cold SO_2 or SO_2ClF (*ca* 0.5 ml) was added to form a slurry. The super acid (*ca* 1 ml) was charged into a second cooled 5 mm NMR tube and diluted with SO_2 or SO_2ClF (*ca* 1 ml) with mixing. The resulting clear homogeneous sample was poured directly into the cold sample of cyclophane at dry-ice–acetone temperature with efficient vortex mixing.

AM1 calculations. Semi-empirical calculations were carried out on the cyclophanes and dithiacyclophanes using MOPAC 5·0. Because this version of MOPAC has no sulfur parameters for AM1, PM3 was used for the dithia[3·3]cyclophanes, while AM1 was used for the [2·2]cyclophanes. For two of the cyclophanes, **3** and **1**, a PM3 calculation was performed on the neutral hydrocarbon and the *ipso*-protonated form as a comparison with the AM1 calculation. Initial geometries were calculated using PC-MODEL (Version 4, Serena Software).

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REFERENCES

1. P. M. Kehn and S. M. Rosenfeld (Eds.), *Cyclophanes*, Academic Press, New York (1983).
2. F. Diederich, *Cyclophanes*, Royal Society of Chemistry, Cambridge (1991).
3. D. J. Cram and J. M. Cram, *Acc. Chem. Res.* **4**, 204 (1971).
4. M. G. Siegel, C. L. Liotta and D. J. Cram, *J. Am. Chem. Soc.* **104**, 1387 (1982).
5. H. J. Reich and D. J. Cram, *J. Am. Chem. Soc.* **91**, 3527 (1969).
6. M. Sheehan and D. J. Cram, *J. Am. Chem. Soc.* **91**, 3553 (1969).
7. H. J. Reich and D. J. Cram, *J. Am. Chem. Soc.* **91**, 3505 (1969).
8. H. J. Reich and D. J. Cram, *J. Am. Chem. Soc.* **91**, 3534 (1969).
9. (a) R. Filler, G. L. Cantrell and E. W. Choe, *J. Org. Chem.* **52**, 511 (1987); (b) R. Filler and J. E. Gadomski, *J. Fluorine. Chem.* **47**, 175 (1990).
10. K. Laali and R. Filler, *J. Fluorine. Chem.* **43**, 415 (1989).
11. D. J. Hefelfinger and D. J. Cram, *J. Am. Chem. Soc.* **93**, 4754 (1971).
12. H. Hoff, J. H. Shim and H. Volz, *Angew. Chem., Int. Ed. Engl.* **26**, 564 (1987).
13. R. M. Mitchell and V. Boekelheide, *J. Am. Chem. Soc.* **96**, 1547 (1974).
14. V. Boekelheide, P. M. Anderson and T. A. Hylton, *J. Am. Chem. Soc.* **96**, 1558 (1974).
15. V. Boekelheide, K. Galuszko and K. S. Szeto, *J. Am. Chem. Soc.* **96**, 1578 (1974).
16. G. J. Bodwell, L. Ernst, H. Hopf, P. G. Jones, J. P. McNally and D. Schomburg, *Chem. Ber.* **123**, 2380 (1990), and references cited therein.
17. W. Anker, G. W. Bushnell and R. H. Mitchell, *Can. J. Chem.* **57**, 3080 (1979).
18. F. Vogtle, W. Wieder and H. Forster, *Tetrahedron Lett.* 4361 (1974).
19. R. Filler, G. L. Cantrell, D. Wolanin and S. M. Naqvi, *J. Fluorine Chem.* **30**, 399 (1986).
20. R. H. Mitchell, in *Cyclophanes*, edited by P. M. Kehn and S. M. Rosenfeld, Vol. 1, Chapt. 4. Academic Press, New York (1983).
21. G. A Olah, G. K S. Prakash and J. Sommer, in *Superacids*, Chapt. 4. Wiley, New York (985).