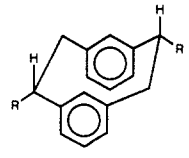
syn-[2.2]Metacyclophane: Isolation, NMR Properties, and Facile Isomerization to *anti*-[2.2]Metacyclophane. A Synthesis Involving Bridge Reactions of Chromium Tricarbonyl Complexed Dithiametacyclophanes

Reginald H. Mitchell,* Thottumkara K. Vinod, and Gordon W. Bushnell

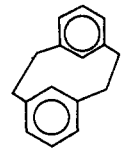
Contribution from the Department of Chemistry, University of Victoria, Victoria, British Columbia, Canada V8W 2Y2. *Received July 11, 1989*

Abstract: Chromium tricarbonyl complexation of 2,11-dithia[3.3]metacyclophane (**11**) holds it in the syn form. Ring contraction using a Stevens rearrangement of the derived mono- or bis(tricarbonylchromium)-complexed sulfonium salts **21** or **39** yields tricarbonylchromium complexed *syn*-[2.2]metacyclophanes with methylthio bridge substituents. Removal of the chromium with Ce(IV) gives free substituted *syn*-[2.2]metacyclophanes, which isomerize to the analogous anti derivatives below 0 °C. The complexed *syn*-phane (η^6-*syn*-2(a)-10(e)-bis(methylthio)[2.2]metacyclophane)tricarbonylchromium(0) (**22**) does not isomerize until about 80 °C, making handling of the complexed phanes easier. Removal of the substituents from **22** to give **35** could not be achieved directly; however, biscomplexation did allow successful isolation of the parent *syn*-[2.2]metacyclophane (**1**) and its mono- and bischromium complexes (**35** and **48**, respectively). Preliminary thermodynamic studies indicate that $\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}_{298}$ for the isomerization of a *syn*- to an *anti*-[2.2]metacyclophane are about 17–18 and 20–21 kcal/mol, respectively, and that chromium tricarbonyl complexation of one of the rings raises these values by about 4 kcal/mol. The ^1H and ^{13}C NMR data of the syn and anti metacyclophanes are compared and discussed relative to the X-ray structures, which are presented for **22** and **28**. The first example of a complexed metacyclophanediene **34**, (η^6-*anti*-[2.2]metacyclophane-1,9-diene)tricarbonylchromium(0), is reported, and interestingly it does not reduce with H_2/catalysts.

Of the 12 possible[1] [2$_n$]cyclophanes only *syn*-[2.2]metacyclophane (**1**) remained unknown at the start of this work.[2] Although *anti*-[2.2]metacyclophane (**2**) was probably first prepared as early as 1899 by Pellegrin[3] in a Wurtz coupling of *m*-xylylene dibromide, it was not rediscovered until 1950.[4] This



1 R=H
3 R=SMe



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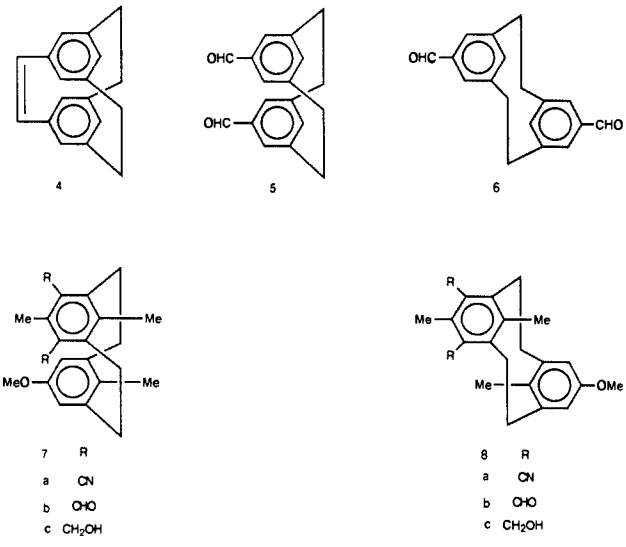
was also the time that Cram[5] began his pioneering studies on paracyclophanes. The intervening almost four decades has seen a fluorishing interest in the properties of cyclophanes and has resulted in the nearly simultaneous appearance of two two-volume books concerning their chemistry.[6,7] It is thus perhaps surprising that such a basic member as **1** would be missing. We thought[8] in 1970 that we had prepared the bridge -SMe substituted derivative of **1**, i.e. **3**, and that during attempts to remove the bridge substituents (Raney nickel or Li/NH_3) the intermediate radical or anions had isomerized, yielding anti products. Since heating a sample of **3** did not cause isomerization, we had no reason at that time to suspect that **1** would readily isomerize to **2**. Two intervening events, however, aroused our suspicions that this might be incorrect. In 1973, Boekelheide and Hollins[9] reported that cleavage at room temperature of the 1,3,5-tris-bridged cyclophane **4** with OsO_4 yielded not the *syn*-cyclophane **5** but the *anti*-cyclophane **6**. They suggested that isomerization of **5** to **6** is facile.



4 5 6

7 R
a CN
b CHO
c CH_2OH

8 R
a CN
b CHO
c CH_2OH

In 1978, Kamp and Boekelheide[10] reported that the *syn*-metacyclophanes with internal methyl groups, **7a–c** all isomerized to the *anti*-cyclophanes **8a–c** on melting (~200 °C). Clearly then there was no reason why **3** should not isomerize. Reinvestigation of **3** has now clearly shown (see below) that no *syn*-[2.2]metacyclophane with internal hydrogen atoms is known and that if **1** is to be synthesized, a route which would yield it at low temperatures is desired. This paper describes the use of arene chromium tricarbonyl complexes to hold metacyclophanes as syn conformers and hence permit the isolation of **1**.

Results and Discussion

Stevens Rearrangement of Salt 9. We first reinvestigated[8b] the Stevens rearrangement of the bissulfonium salt **9**. Reaction of **9** with potassium *tert*-butoxide in THF gave a 94% yield of product

(1) Boekelheide, V. *Top. Curr. Chem.* **1983**, *113*, 87–143.
(2) For preliminary reports, see: Mitchell, R. H.; Vinod, T. K.; Bushnell, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 3340–3341. Mitchell, R. H.; Vinod, T. K.; Bodwell, G. J.; Weerawarna, K. S.; Anker, W.; Williams, R. V.; Bushnell, G. W. *Pure Appl. Chem.* **1986**, *58*, 15–24.
(3) Pellegrin, M. M. *Recl. Trav. Chim. Pays-Bas* **1899**, *18*, 457–465.
(4) Baker, W.; McOmie, J. F. W.; Norman, J. M. *Chem. Ind.* **1950**, 77. Baker, W.; McOmie, J. F. W.; Norman, J. M. *J. Chem. Soc.* **1951**, 1114–1118.
(5) Cram, D. J.; Steinberg, H. *J. Am. Chem. Soc.* **1951**, *73*, 5691–5704.
(6) Keehn, P. M.; Rosenfeld, S. M. *Org. Chem. (N.Y.)* **1983**, *45*, 1–725.
(7) Vogtle, F. *Top. Curr. Chem.* **1983**, *115*, 1–159. Vogtle, F. *Top. Curr. Chem.* **1983**, *113*, 1–185.
(8) (a) Mitchell, R. H.; Boekelheide, V. *J. Am. Chem. Soc.* **1970**, *92*, 3510–3512. (b) Mitchell, R. H.; Boekelheide, V. *J. Am. Chem. Soc.* **1974**, *96*, 1547–1557.
(9) Boekelheide, V.; Hollins, R. A. *J. Am. Chem. Soc.* **1973**, *95*, 3201–3208.
(10) Kamp, D.; Boekelheide, V. *J. Org. Chem.* **1978**, *43*, 3470–3475.

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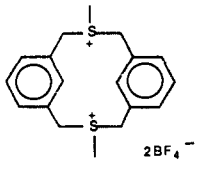
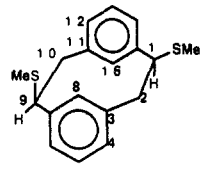
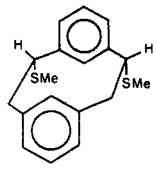
as a mixture of the five isomers **10a–e**, all of which showed the expected MH^+ peaks at *m/e* 301 in their mass spectra (CI). Three of the isomers, **10a–c**, proved to be identical (mp, NMR) with those reported.[8b] The other two isomers, which were extremely difficult to separate from each other by column chromatography, were assigned by use of 250-MHz ^1H NMR (see Table I for details) to the structures **10d** and **10e**, and as the mixture, they



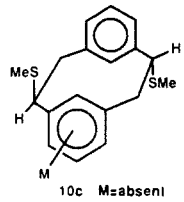
9



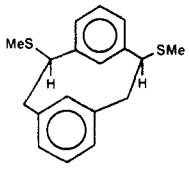
10a



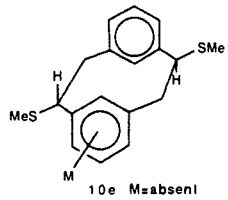
10b



10c M=absent
25 M=Cr(CO)3



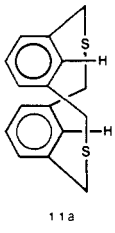
10d



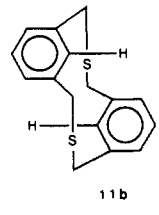
10e M=absent
28 M=Cr(CO)3

are the compound that was erroneously assigned structure **3** previously.[8b] The amounts of the five anti isomers **10a-e** obtained were 38%, 9%, 10%, 14%, and 15%, respectively. No isomer that could be assigned a syn structure was isolated.

***syn*-Cyclophane Routes.** When the original Stevens rearrangement was carried out in 1968–9, it was not known whether the starting dithiacyclophane was syn or anti (**11a** and **11b**, respectively). It was shown by us[11] in 1981 to be predominantly

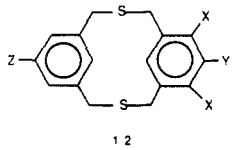


11a



11b

syn. We therefore needed to take advantage of this, and hold the molecule syn during the Stevens rearrangement, such that isomerization to the anti series did not occur. A further observation led us in the right direction in that, in the synthesis of dithiacyclophanes with internal methyl groups, **12**, it has been found



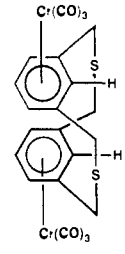
12

X	Y	Z	SYN/ANTI RATIO
H	H	H	1:7
H	NO_2	H	1:1
Br	Me	H	1.3:1
Cl,H	Cl	H	1.8:1
Br	Me	OMe	2.5:1
CN	Me	OMe	10:1

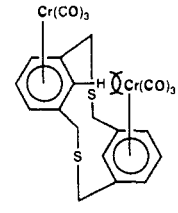
(11) Anker, W.; Bushnell, G. W.; Mitchell, R. H. *Can. J. Chem.* **1979**, *57*, 3080–3087.

by Boekelheide,[10] Vogtle,[12] and ourselves[13] that as electron-withdrawing groups are added to the rings the syn/anti ratio of the products increases. This might be because of charge transfer across the rings in the syn isomer, resulting in some stabilization of it with respect to the anti isomer, or because of removal of electron density from the rings, which reduces the ring repulsion in the syn isomer relative to the anti isomer, which again results in relative stabilization of the former.

An electron-withdrawing group that could be readily removed at the end of the sequence was thus desired. A chromium tricarbonyl complexed arene seemed ideal in that the metal strongly withdraws electrons from the ring, and hence on complexation, the dithiacyclophane **11a** would not be expected to isomerize to the anti series. Moreover the tricarbonylchromium moiety is easily removed by oxidation, conditions which are not used during the conversion of a thiacyclophane to cyclophane. Finally the possibility of using a biscomplex, such as **13** existed, which because of steric interference between the internal hydrogen and the metal in **14** should be even more difficult to isomerize.



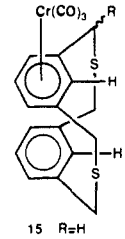
13



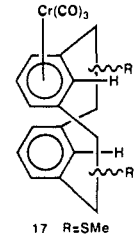
14

The Use of Tricarbonylchromium-Complexed Dithiacyclophanes. No tricarbonylchromium complexes of any simple dithiacyclophanes were known previously. We, therefore, have described their preparation and spectral properties elsewhere.[14] Basically, however, the mono- or biscomplex may be obtained by refluxing the dithiacyclophane with 1.4 or 6 equiv, respectively, of $Cr(CO)_6$ in refluxing *n*-butyl ether.

Although the Stevens rearrangement of the salt **9** was used originally,[8b] an improvement introduced in 1975 was the Wittig rearrangement of the dithiacyclophane itself.[15] Thus in order to avoid having to methylate **15**, the Wittig rearrangement was tried first. Reaction of **15** with either *n*-BuLi or *i*-Pr_2NLi (LDA) at 0 or 50 °C followed by MeI gave, somewhat surprisingly, the bridge-methyl-substituted product **16**, rather than the bridge-contracted product **17**. Evidently, the tricarbonylchromium



15 R=H
16 R=Me

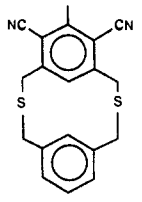


17 R=SMe
35 R=absent

complexation stabilized the intermediate anion sufficiently to stop rearrangement. We have noticed previously that two nitrile groups[16] as in **18** or a pyridine nucleus[17] as in **19** can slow the rearrangement below 50 °C. Use of the slowed Wittig rearrangement has also been made by Davies[18] to functionalize next

(12) Bockmann, K.; Vogtle, F. *Chem. Ber.* **1981**, *114*, 1065–1073.
(13) Mitchell, R. H.; Chaudhary, M.; Kamada, T.; Slowey, P. D.; Williams, R. V. *Tetrahedron* **1986**, *42*, 1741–1744.
(14) Mitchell, R. H.; Vinod, T. K.; Bodwell, G. J.; Bushnell, G. W. *J. Org. Chem.* **1989**, *54*, 5871–5879.
(15) Mitchell, R. H.; Otsubo, T.; Boekelheide, V. *Tetrahedron Lett.* **1975**, *16*, 219–222. Mitchell, R. H. *Heterocycles* **1978**, *11*, 563–586.
(16) (a) Mitchell, R. H.; Mahadevan, R. *Tetrahedron Lett.* **1981**, *22*, 5131–5134. (b) Mahadevan, R. Ph.D. Thesis, University of Victoria, 1981.
(17) Mitchell, R. H.; Zwinkels, J. Unpublished results.

to the complexed arene ring in tricarbonylchromium(0) benzyl ethyl sulfide. Surprisingly no bismethylated product **20** was obtained when excess BuLi or LDA was used, but **20** was obtained in 94% yield when *t*-BuOK was used as the base. The structures



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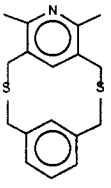

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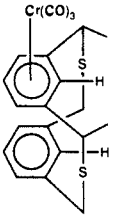
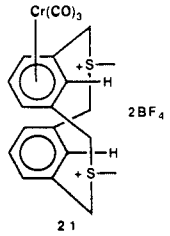
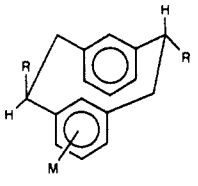


20

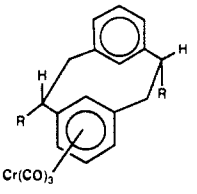
of **16** and **20** were assigned on the basis of their mass and ^{1}H NMR spectra. We hoped that the Stevens rearrangement would be more successful, with neutralization of charge providing the driving force. Thus **15** was converted to its bis(methylsulfonium) salt **21** by using dimethoxycarbonium tetrafluoroborate,[19] $(MeO)_2CHBF_4$, in dichloromethane at 20 °C in 90% yield. Rearrangement of the salt **21** was slow with NaH in THF but rapid with *t*-BuOK in THF and gave an 80% yield of product as a mixture of the two isomers **22** and **23**.



21

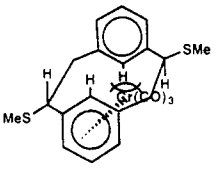


22 M=Cr(CO)$_3$ R=SMe
27 M=absent R=SMe
29 M=absent R=S$^+$Me$_2$BF$_4$



23 R=SMe
24 R=H
32 R=S$^+$Me$_2$BF$_4$

These isomers could be separated by column chromatography to yield 71% of **22**, mp 121–122 °C, and 9% of **23**, mp 160–161 °C. Both gave MH^+ peaks at *m/e* 437 in their mass spectra (CI), and assignment of **22** as syn and **23** as anti was made on the basis of their ^{1}H NMR spectra (see Table I). *anti*-[2.2]Metacyclophanes are normally easily recognized by ^{1}H NMR, since the internal hydrogens are strongly shielded, e.g., δ 4.25 in **2**, because of their placement over the π-cloud of the opposite ring.[20] This is, however, modified somewhat in a metal-complexed cyclophane, since the metal withdraws electron density from the complexed ring, reducing its power to shield protons from the opposite ring. Thus in **24**, H-16 appears at δ 5.45, not as shielded as in the uncomplexed phane, because of the reduced ring current in the complexed ring. On the other hand H-8 appears at δ 2.33, strongly shielded from that in the uncomplexed **2**; in this case, H-8 feels the normal strong shielding of the opposite uncomplexed ring, *and* as well the reduced deshielding of its own aromatic ring, caused by the tricarbonylchromium.[21] In the isomer **23**, H-16 appears at δ 5.95 and H-8 at δ 2.52, and thus it is clearly an anti isomer. Since **22** would be the first authentic *syn*-[2.2]metacyclophane with internal hydrogens, we confirmed its structure in two ways. Firstly, an X-ray crystal structure determination was made. Secondly, we heated **22** to determine if it would isomerize to an anti isomer, which would also therefore prove beyond doubt that it was also syn in solution. Indeed, refluxing **22** in ethanol for 3 h quantitatively isomerized it to **25**. The mass spectrum of **25**, with MH^+ at *m/e* 437, clearly indicated that only an isomerization had taken place. The ^{1}H NMR spectrum showed **25** to be anti, since the internal hydrogens, H-8 and H-16, now appeared at δ 3.44 and 5.92, respectively. Since they are both deshielded from those in **24** (δ 2.33 and 5.45), both –SMe groups must be axial, which is consistent with the uncomplexed ring flipping, converting the equatorial 1-SMe in **22** to the axial 1-SMe in **25**. Had the complexed ring of **22** flipped to give **26**, both –SMe groups would have been equatorial, and sterically H-16 would strongly interfere with the $Cr(CO)_3$ group.



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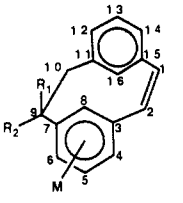
The observed syn to anti ratio of 8:1 for **22**:**23** in the Stevens rearrangement of **21** is a remarkable improvement over the uncomplexed case which yields no syn at all. The fact that **22** could be isolated and did not isomerize until heated gave us hope that indeed **1** could be obtained.

Tricarbonylchromium arenes can be uncomplexed oxidatively,[22] and we chose ceric ammonium nitrate[23] (Ce(IV)) as the reagent of choice. Indeed reaction of **22** with Ce(IV) in MeCN at 20 °C gave a quantitative yield of the previously obtained **10e**. Evidently at 20 °C, any syn isomer **27** first formed isomerizes to anti isomer **10e**. Note that in contrast to **22**, the ring bearing the axial –SMe flips to yield the more stable diequatorial isomer **10e** rather than the diaxial isomer **10c**. Heating **10e** with $Cr(CO)_6$ in *n*-Bu_2O did not return a syn isomer but merely gave the anti isomer **28**; while the syn→anti isomerization is thus facile, the reverse, even in the presence of chromium, is not.

The low-temperature removal of chromium from **22** was investigated next. Reaction of **22** with Ce(IV) in MeCN at –30 °C for 30 min and chromatography of the product at –40 °C on silica gel yielded quantitatively the *syn*-metacyclophane **27** as a white solid. In its ^{1}H NMR spectrum, the internal hydrogens appear at δ 7.05 and 6.76, confirming the presence of one axial and one equatorial –SMe. The other ring protons appear at δ 6.93–6.63, consistent only for the syn structure. When a $CDCl_3$ solution of **27** was warmed to room temperature, **10e** was formed quantitatively. Clearly any chemistry to be attempted on **27** would have to be carried out at low (–30 °C) temperatures. To convert **27** into **1**, the –SMe groups had to be removed. This might be tried reductively or by elimination first to form the alkene and then hydrogenation of this. This latter route was attempted first: methylation of **22** as for **11** gave 86% of the bis-salt **29**. Reaction of **29** with *t*-BuOK in dry THF gave only 22% of the monoene **30**, mp 157–158 °C. Its structure was established by a molecular

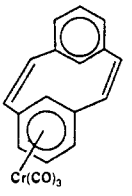


30 M=Cr(CO)$_3$ R$_1$=SMe R$_2$=H
31 M=absent R$_1$=R$_2$=H
33 M=Cr(CO)$_3$ R$_1$=H R$_2$=SMe

ion at *m/e* 388 and later by an X-ray structure. Salt **32** (from **23**) was also reacted with *t*-BuOK/THF and gave **33**. Note that, in the elimination of **29** and **32**, the $-S^+Me_2$ adjacent to the complexed ring was not eliminated. This was true also with KOH, NaOH, NaOMe, *n*-BuLi, and 2,6-di-*tert*-butylphenoxide in ethereal solvents. Presumeably the carbanion at C-9 in **29** and **32** is just too stable and does not allow carbanion formation at C-10 or at the –SMe, which would permit the elimination to proceed. Such a carbanion might also permit a rapid syn to anti isomer-

(18) Davies, S. G.; Holman, N. J.; Laughton, C. A.; Mobbs, B. E. *J. Chem. Soc., Chem. Commun.* **1983**, 1316–1317.
(19) Borch, R. F. *J. Org. Chem.* **1969**, *34*, 627–629.
(20) Mitchell, R. H. *Org. Chem. (N.Y.)* **1983**, *45*, 239–310.
(21) Langer, E.; Lehner, H. *J. Organomet. Chem.* **1979**, *173*, 47–52.
(22) Nicholls, B.; Whiting, M. C. *J. Chem. Soc.* **1959**, 551–556.
(23) Semmelhack, M. F.; Hall, H. T.; Farina, R.; Yoshifuji, M.; Clark, G.; Bargar, T.; Hirotsu, K.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 3535–3545.

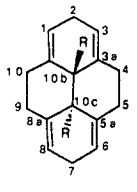
ization by changing the hybridization at the bridge. We thought that presence of a proton source might keep reprotonating the C-9 carbanion and allow the elimination to compete. Indeed, when the solvent was changed from dry THF to a mixture of 1:1 THF/*t*-BuOH, the bis-elimination did proceed and gave 30% of the diene **34**, mp 138–139 °C dec. Unfortunately, still the anti product was formed, even at 0 °C, and at −20 °C the elimination did not proceed.



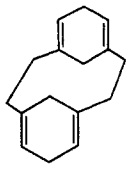
34

The red diene **34** is the first example of a complexed metacyclophanediene. Its structure was assigned on the basis of the mass spectrum molecular ion (MH^+) at *m/e* 341 and its ^1H NMR spectrum, which showed the internal hydrogens at δ 8.48 (H-16) and 5.69 (H-8). H-16 appeared as a triplet, J = 1.0 Hz, which on irradiating collapsed the double doublet at δ 6.91 (H-12,14) to a doublet. The olefinic protons appeared as two doublets at δ 6.60 (H-1,10) and 6.12 (H-2,9). The higher field doublet is assigned to the proton on the complexed ring side (H-2,9), consistent with previous work[24] that has shown complexation of an arene causes an upfield shift of an adjacent sp^2 or sp^3 benzylic proton.

The rapid conformational flip from the syn to anti series that led to **34**, either of the intermediate carbanion or of the diene itself, thus led us to investigate reductive removal of the –SMe substituents. Unfortunately Raney nickel in ethanol requires reflux to remove the –SMe substituents from cyclophanes.[8b] Raney nickel in DMSO is reported[25] to work at room temperature, but failed in the case of **22**, as did sodium amalgam in methanol with NaH_2PO_4 buffer[26] and lithium triethylborohydride (Superhydride).[27] We thus resorted to Li/NH_3, even though we anticipated competing Birch reduction of the aromatic rings might be a problem. Reaction of **22** with 7 equiv of Li in liquid ammonia for only 2 min gave a 40% yield of the isomerized complexed phane **24** and no syn products, even when isolation was carried out at −40 °C. Clearly since **22** does not isomerize to **25** at −40 °C, it seems unlikely that **35** would to **24**, and therefore we believe that the intermediate, probably a carbanionic species adjacent to the complexed ring, is responsible for the facile isomerization. We thus thought it worthwhile to reduce the uncomplexed phane **27**. However, reaction of **27** with either sodium or lithium in liquid ammonia, with workup at 0 or −30 °C, gave about 60% of the hexahydropyrene **36**, mp 196–197 °C. The structure of **36** was assigned on the basis of its mass spectrum molecular ion at *m/e* 210 and its five-line ^{13}C NMR spectrum (compare **37**[28]).



36 R=H
37 R=Me



38

(24) Knox, G. R.; Leppard, D. G.; Pauson, P. L.; Watts, W. E. *J. Organomet. Chem.* **1972**, *34*, 347–352. Deubzer, B.; Fischer, E. O.; Fritz, H. P.; Kriebitzsch, K. N.; Simmons, H. D., Jr.; White, B. R. *Chem. Ber.* **1967**, *100*, 3084–3096. Muller, J.; Goser, P.; Elian, M. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 374–375.

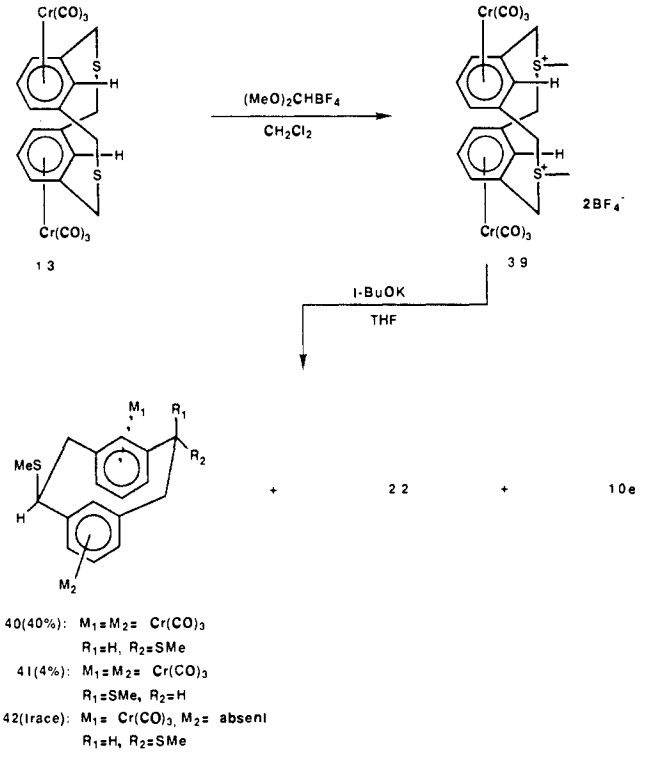
(25) Demoute, J. P.; Hainaut, D.; Toromanoff, E. *C. R. Sceances Acad. Sci. Ser. C* **1973**, *277*, 49–51.

(26) Trost, B. M.; Arnot, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, *17*, 3477–3478.

(27) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1983**, *48*, 3085–3091.

(28) DuVernet, R.; Boekelheide, V. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, *71*, 2961–2964.

Scheme I

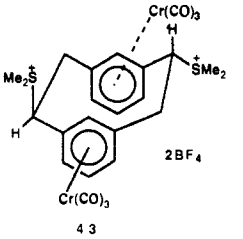


40(40%): $M_1=M_2=$ $Cr(CO)_3$; R_1=H, R_2=SMe
41(4%): $M_1=M_2=$ $Cr(CO)_3$; R_1=SMe, R_2=H
42(trace): $M_1=$ $Cr(CO)_3$, $M_2=$ absent; R_1=H, R_2=SMe

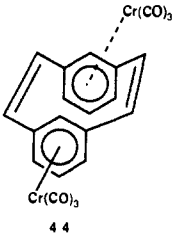
Since *anti*-[2.2]metacyclophane (**2**) on reduction with Na/NH_3 is known[8b,29] to form **38**, *syn*-[2.2]metacyclophane must reduce before isomerization, otherwise **38** should have been formed from it also. The difference in mechanism of reduction of **1** and **2** is perhaps a reflection of the fact that the internal carbons C-8,16 are closer in **1** (2.662 Å) than in **2** (2.689 Å),[30] which could make internal bond formation easier in *syn*-**1**.

Our failure to reduce off the –SMe substituents from the bridges to produce the parent **1**, suggested we would need to completely block isomerization from the syn to the anti series, and thus we decided next to investigate the biscomplexed series.

The Biscomplexed Series. The poorly soluble biscomplex **13** was methylated in refluxing dichloromethane with $(MeO)_2CHBF_4$ as before to give **39**, which on Stevens rearrangement using *t*-BuOK/THF gave a mixture containing 44% of the desired biscomplexed syn isomers **40** and **41** (10:1), together with 18% of the monocomplexed *syn*-phanes **22** and **42** and 10% of uncomplexed *anti*-**10e** (Scheme I). The syn orientation of the rings in **40** is clear from the chemical shifts of the ring protons at δ 4.80–5.72, and the fact that oxidative removal of both chromiums yields the previously obtained **27**. The major isomer **40** was remethylated to give 40% of **43**, which on Hofmann elimination



43



44

using *t*-BuOK in *t*-BuOH/THF (1:1) gave 29% of the red biscomplexed diene **44**, mp 167 °C dec.

This is the first example of a syn diene with internal hydrogens. Its structure was confirmed by a MH^+ peak in its CI mass spectrum at *m/e* 477 and by its ^1H NMR spectrum in which the olefinic protons appear as a sharp singlet at δ 7.01 and the internal

(29) Reiner, J.; Jenny, W. *Helv. Chim. Acta* **1969**, *52*, 1624–1630.

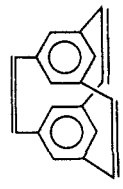
(30) Brown, C. J. *J. Chem. Soc.* **1953**, 3265–3270. Kai, Y.; Yasuoka, N.; Kasai, N. *Acta Crystallogr., Sect. B* **1977**, *33*, 754–762.

Table I. ^{1}H NMR Chemical Shifts (δ) of the Ring Protons of the Syn/Anti (s/a) Pairs of Cyclophanes Studied[a]

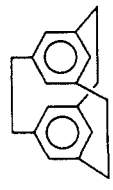
		–SMe									
compd	s/a	1-	9-	H-4	H-5	H-6	H-8	H-12	H-13	H-14	H-16
1	s			6.41	6.62	6.41	6.63	6.41	6.62	6.41	6.63
2	a			7.03	7.27	7.03	4.27	7.03	7.27	7.03	4.27
35	s			4.54	4.91	4.54	4.82	6.60	6.86	6.60	6.90
24	a			5.16	5.47	5.16	2.33	7.13	7.39	7.13	5.45
48	s			4.75	5.12	4.75	5.09	4.75	5.12	4.75	5.09
49	a			5.26	5.56	5.26	3.59	5.26	5.56	5.26	3.59
27	s	eq	ax	6.44[a]	6.61[b]	6.44	7.05	6.38[a]	6.69[b]	6.93	6.76
10a	a	eq	ax	7.09[c]	7.28	7.17[c]	4.87	7.22[c]	7.41	7.66	4.41
10c	a	ax	ax	7.15[d]	7.30	7.21[d]	5.00	7.15[d]	7.30	7.21[d]	5.00
10e	a	eq	eq	7.21	7.44	7.64	4.33	7.21	7.44	7.64	4.33
10d	a	eq	eq′	7.13	7.29	7.13	4.20	7.72	7.56	7.72	4.50
22	s	eq	ax	4.68*	4.68*	4.68*	5.50	6.58	6.94	7.15	6.91
23	a	ax	eq	5.39	5.45	6.01	2.52	7.14	7.39	7.24	5.95
25	a	ax	ax	5.45	5.27	5.54	3.44	7.18	7.38	7.23	5.92
28	a	eq	eq	5.28	5.42	5.96	2.35	7.24	7.49	7.66	5.41

[a] Superscripts indicate which assignments could be reversed; those for **10a** were made by comparison to **10c,d,e** and for **23** by comparison to **25** and **28**. (*) Center of multiplet, 4.64–4.72.

hydrogens as a broad singlet at δ 5.99, with the remaining ring protons at δ 5.15–5.04. Cyclophanenes can normally be easily reduced over platinum, e.g., **45** gives **46**.[9] Surprisingly, however,

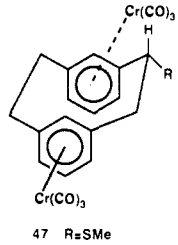


45

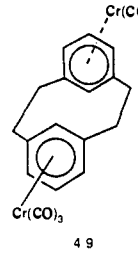


46

44 could not be reduced with either Pt or Pd as catalysts, even after 24 h. Desulfurization of **40** was thus attempted next. Refluxing **40** with W-7 Raney nickel for 8 h in ethanol returned **40** unchanged! At least our hypothesis that syn–anti isomerization would be slowed was correct. We thus tried the more powerful Li/NH_3. The reaction proved to be extremely sensitive to the time that **40** was exposed to the blue solution of solvated electrons. Times over 1 min led to extensive decomplexation and Birch reduction of the rings; however, by quenching with ice after 40 s, a 40% yield of the biscomplexed mono –SMe derivative **47** could be isolated. The mass spectrum molecular ion at *m/e* 527 (MH^+) indicated that only one –SMe had been removed from **40**, and the ^{1}H NMR spectrum indicated that the axial –SMe had gone, since a deshielded internal proton no longer remained, but a deshielded external proton (H-14) did. Subsequent treatment of **47** with Li/NH_3 gave decomplexed Birch-reduced products.



47 R=SMe
48 R=H



49

However, the fact that an axial –SMe had been cleaved cleanly whereas the equatorial –SMe appeared to be the one that was giving the problems was encouraging since the minor isomer **41** was diaxial. Indeed reduction of **41** with Li/NH_3 for 20 s gave a 27% yield of the desired biscomplexed *syn*-cyclophane **48**, mp 198–201 °C. The structure of **48** was assigned from the MH^+ peak at *m/e* 481 and its ^{1}H NMR spectrum, where the internal hydrogens appeared as a singlet at δ 5.09, with the external ring hydrogens at δ 5.12 and 4.75. These can be contrasted to the corresponding anti compound **49** in which the internal hydrogens are at δ 3.59 and the external at δ 5.56 and 5.26. Decomplexation of **48** at –30 °C using Ce(IV) in MeCN gave quantitatively *syn*-[2.2]metacyclophane (**1**) as a white solid, though on one occasion a small amount of the monocomplexed phane **35** was obtained. The structures of **1** and **35** were readily confirmed by warming to 0 and 40 °C, respectively, when clean conversion to the corresponding anti compounds **2** and **24** occurred.

The ^{1}H NMR spectrum of the long awaited **1** showed all its aryl protons shielded above δ 7, with H-8,16 at δ 6.63, H-5,13 at δ 6.62, and H-4,6,12,14 at δ 6.41. The bridge protons appear in two regions 3.20–3.07 (equatorial) and 2.99–2.86 (axial).

Substituted Derivatives of 1. In order to have a substituted derivative of **1** available for comparison in the thermal isomerization studies (below), we synthesized the dimethyl derivative **50** in an analogous manner to **27** as shown in Scheme II. Since **50** and **27** have the same arrangement of methylthio substituents, they could be compared directly as substitutes for the parent cyclophanes.

NMR Properties of the Cyclophanes

The proton chemical shifts of the ring protons for several of the syn–anti pairs of the cyclophanes studied are presented in Table I.

Immediately apparent on examining the data for **1** and **2** and thus comparing a *syn*- to an *anti*-metacyclophane is the extent of the upfield shift of the external protons (H-4,5,6,12,13,14), 0.62–0.65 ppm. This is the consequence of one aromatic ring shielding the other. It is of the same magnitude as the difference between [2.2]paracyclophane and *p*-xylene, 0.57 ppm,[31] but is less than that between **46** and mesitylene, 1.0 ppm.[9] Comparison of the monocomplexes **35** and **24** show that this difference is reduced a little for both the uncomplexed rings (0.56–0.62 ppm) and the complexed rings (0.53 ppm), and this probably reflects the effect of the reduced-ring current of the complexed ring on the opposite uncomplexed ring and of a partial charge transfer from uncomplexed to complexed, which reduces the shielding effect of the uncomplexed ring. For the biscomplexed pair **48**/**49**, the syn/anti difference is reduced further to 0.44–0.51 ppm. This trend is followed in the bridge-substituted examples, but complicated by the less clear multiplets. The internal protons are reversed in chemical shift, with H-8,16 of the *anti*-cyclophane being the most shielded because of protrusion of these protons into the π-cloud of the opposite ring. Interestingly H-8,16 of **1** are only 0.3 ppm shielded from H-3 of *m*-xylene, which is less than might be expected considering that the two rings are inclined at an angle toward each other (molecular mechanics and X-ray data; see below), and it perhaps reflects a superimposed steric deshielding of the two internal hydrogens. In the substituted cases, an axial bridge –SMe deshields the internal proton of the adjacent ring, while an equatorial –SMe deshields the adjacent external ring proton.

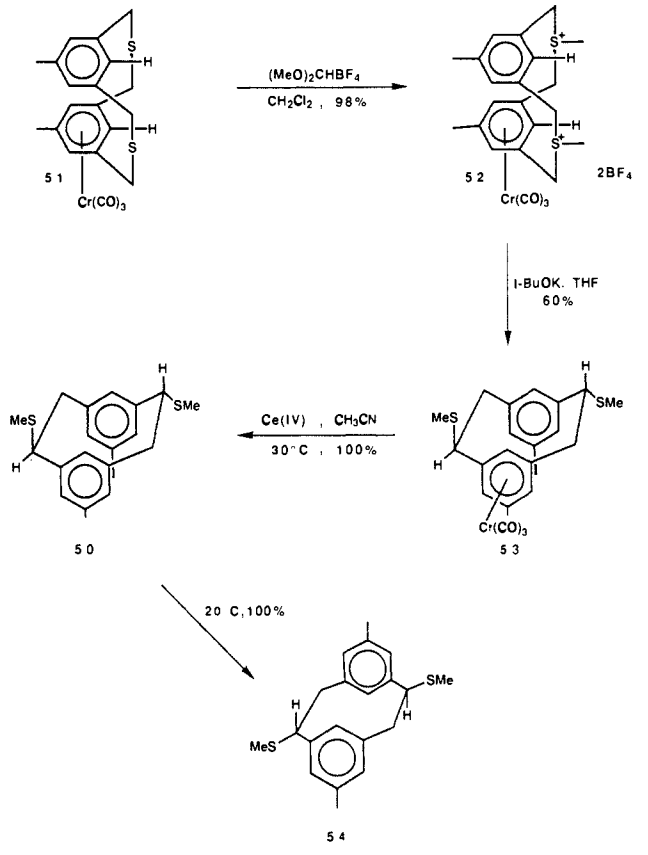
(31) Waugh, J. S.; Fessenden, R. W. *J. Am. Chem. Soc.* **1957**, *79*, 846–849.

Table II. ^{13}C NMR Chemical Shifts (δ) of the Ring Carbons of Several Cyclophanes for Comparison of Syn and Anti Isomers

carbon	2 –[a] anti	10e 1-eq,9-eq[a] anti	10c 1-ax,9-ax[a] anti	10d 1-eq,10-eq[a] anti	10a 1-eq,9-ax[a] anti	27 1-eq,9-ax[a] syn
C-3	138.6	138.4	134.9	138.2	137.1	136.2
C-4	125.1	127.7	127.1	126.4	127.5	127.4
C-5	128.6	129.7	129.1	129.8	128.5	129.1
C-6	125.1	123.8	126.4	126.4	126.2	127.6
C-7	138.6	138.3	134.9	138.2	134.4	134.6
C-8	136.3	136.7	134.8	135.8	134.1	134.5
C-11	138.6	138.4	134.9	137.8	138.4	137.7
C-12	125.1	127.7	127.1	124.6	128.1	128.9
C-13	128.6	129.7	129.1	129.9	129.2	129.3
C-14	125.1	123.8	126.4	124.6	123.8	123.8
C-15	138.6	138.3	134.9	137.8	138.4	137.8
C-16	136.3	136.7	134.8	137.8	137.2	138.1

[a] –SMe.

Scheme II



The complexation shift for H-4 in the syn series ($\delta_1 - \delta_{35}$) is 1.87 ppm and is exactly the same as in the anti series ($\delta_2 - \delta_{24}$), with that for H-5 being 1.71 and 1.80 ppm, respectively. The carbonyl groups thus orientate themselves primarily over the carbons bearing the bridge carbons and C-5,H-5.[14] The internal proton H-8 of **22** is of note, appearing exceptionally downfield at δ 5.50 (compare H-8 of **27** at δ 7.05 and the normal complexation shift of about 1.9 ppm). This is possibly because deformation of the cyclophane ring causes C-8 and hence H-8 to be bent outward toward the $-Cr(CO)_3$. The chemical shift range of the internal "aromatic" protons from δ 2.33 to 7.05 in these examples is in our opinion impressive!

Sato[32] has identified an interesting anomaly in the ^{13}C NMR spectrum of *anti*-[2.2]metacyclophane, in which C-8,16 appear more deshielded at δ 136.3 than would be expected by about 6–7 ppm. The major cause of this downfield shift has been attributed to a decrease in electron density at these carbons because of compression of the p orbitals, which appears to maximize when the two p orbitals are brought together along the same orbital axis.

(32) Takemura, T.; Sato, T. *Can. J. Chem.* **1976**, *54*, 3412–3418.

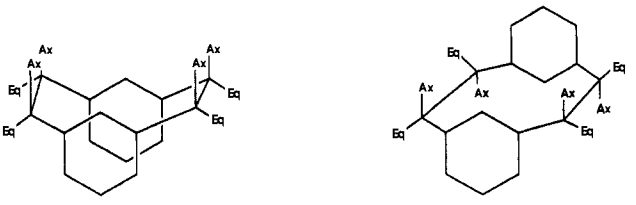
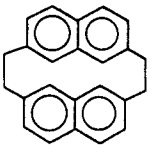


Figure 1. A projection to show the eclipsed nature of the bridges in *syn*-[2.2]metacyclophanes, relative to the staggered bridges in the anti isomers.

An upfield shift of about 3 ppm occurs for the connected atoms (C-3,7,11,15). Indeed protons H-8,16 are also shifted upfield by about 3 ppm, but this is usually attributed to the ring-current effect of the opposite ring even though part of it may arise by induced polarization. We noted above that the internal protons of *syn*-[2.2]metacyclophane are also somewhat shielded, and although we have not been able to obtain a ^{13}C NMR of the parent **1**, we have of the bridge-substituted derivative **27**, and indeed the C-8,16 resonances are also observed deshielded by about the same amount, indicating that these carbons are also compressed. This is confirmed by X-ray data (see below). The relevant ^{13}C NMR data are given in Table II. The shifts observed in the symmetrically substituted compounds **10e,c,d** were used to assign the shifts in the equatorial–axial isomer **10a**, and also for **27**. The resonances for C-8,16 are unambiguous, since their intensities are much greater than for the quaternary carbons close by. A resonance adjacent to an equatorial –SMe, e.g., C-14, is also unambiguous, since it is the most shielded of the aryl carbons. Other carbons with very similar chemical shifts, e.g., C-11,C-15 of **27**, may of course be reversed. It is of note that both C-8 and C-16 of **27** are slightly more deshielded than those in **10a**, which is not the case in the analogous naphthalenophanes **55**, in which the syn (δ 127) is less deshielded than the anti (δ 131),[33] However, the anti isomer's internal carbons are less deshielded than those of **2**, and its internal hydrogens are less shielded than those of **2** as well; thus the distortions in the larger framework of **55** may be more spread out.



55a Syn
55b Anti

Twisting of the Bridge. One of the contributors to the difference in stability between the *syn*- and *anti*-metacyclophanes is the fact that in *syn*-metacyclophane **1** the bridge protons are eclipsed, whereas in *anti*-metacyclophane **2** they are staggered (Figure 1).

(33) Sato, T.; Matsui, H.; Komaki, R. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2051–2054.

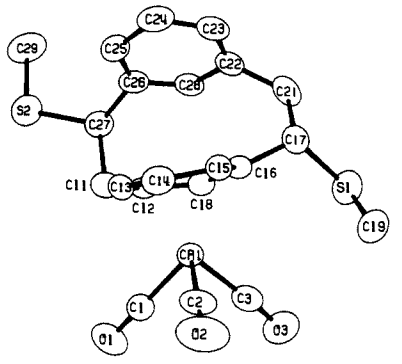


Figure 2. An ORTEP drawing of syn-complex **22**.

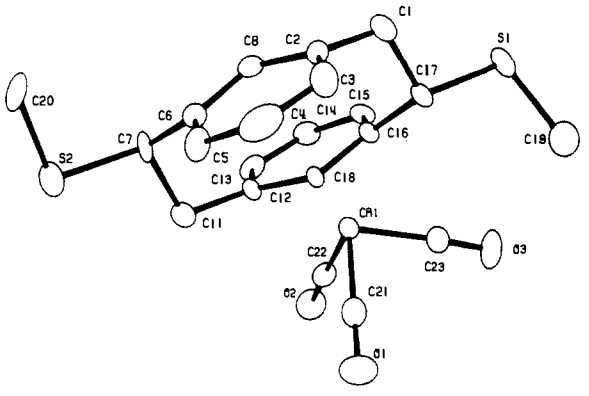


Figure 3. An ORTEP drawing of anti-complex **28**.

In the anti isomers the coupling constant between the 1,2-diaxial hydrogens should therefore be large, whereas coupling between adjacent (1,2-) diequatorial or equatorial–axial hydrogens should be small. In contrast, in the syn isomers, diaxial and diequatorial couplings should be large and axial–equatorial couplings small. While the anti isomers display the expected coupling constant pattern, the syn isomers do not. The axial–axial and equatorial–equatorial couplings are smaller than would be expected, and the equatorial–axial couplings are much larger than would be expected, especially that for $J(9_{eq}-10_{ax})$. This suggests that the bridges twist in the syn isomer, with the 9–10 bridge (bearing the axial –SMe) twisting more than the 1–2 bridge (with the equatorial –SMe). This was also found to be the case in the crystal state (below).

Structural Features of Syn-Complex 22 and Anti-Complex 28

X-ray structure determinations were carried out on the syn-complex **22** and anti-complex **28**. ORTEP drawings are given in Figures 2 and 3, respectively. The interdeck distance between the centers of the two rings in **22** is 3.19 Å, which is only 0.10 Å longer than that in [2.2]paracyclophane.[34] The closest distance between the two rings in **22** is the distance between the two internal carbon atoms C-8 and C-16 (ORTEP, C-18,C-28) and is only 2.662 Å, which is *shorter* by 0.12 Å than the shortest distance between the rings in [2.2]paracyclophane, and almost identical with the C-8,C-16 distance in the *anti*-[2.2]metacyclophane **28** (2.624 Å) and to **2** itself (2.633 Å).[30b] The characteristic boat-type deformation of the rings in the anti isomer **2**[30b] is observed in the case of the syn isomer **22** as well. The "bow" atom C-8 (ORTEP, C-18) is 0.085 Å outside the plane defined by C-11,12,14,15 (ORTEP, C-22,23,25,26). The corresponding value for C-16 (ORTEP, C-28) is 0.073 Å, and the exterior atoms C-5 and C-13 (ORTEP, C-15 and C-24) are about 0.06 Å outside the above planes. The corresponding values for these four atoms in **28** are 0.071, 0.069, 0.049, and 0.044 Å and in **2** for C-8 and C-5 are 0.143 and 0.042 Å.[30a] The nonplanarity of the complexed ring causes significant variations in the Cr–C bond lengths (range 2.176–2.343 Å). Thus while the overall structure of **28** is very similar to that of **2**, the presence of the $-Cr(CO)_3$ group does appear to reduce the out of plane deformations of C-8 and C-16 by a small amount and increase those of C-5 and C-13. Possibly, the –SMe groups also have some effect.

The torsional angles about the two ethano bridges of **22** were calculated and showed that a twist had indeed occurred on the C-9–C-10 bridge as predicted from the coupling constant analysis above. Whereas the dihedral angle between H-11 and H-27 in **28** is 3°, that between H-17 and $H\text{-}21_{eq}$ in **22** has opened to 35°. The mean planes of the two aromatic rings of **22** are inclined at an angle of 28.8° to each other, which is greater than in the *syn*-[3.3]cyclophane **11a** (20.6°).[11] Tables of fractional atomic coordinates, isotropic thermal parameters, bonded atomic distances, bond angles, mean planes and torsion angles, and intermolecular distances, as well as the structure determination details, are given in the supplementary material.

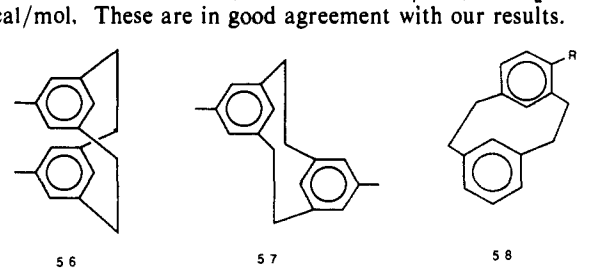
Table III. Rates of Isomerization and Thermochemical Data for the Isomerization of *syn*-[2.2]Metacyclophanes to *anti*-[2.2]Metacyclophanes

	1 → 2	**27 → 10e**	**50 → 54**	**22 → 25**
protons monitored	H-4,6,12,14	H-6	H-6	–SMe
T_1 (°C)	10	0	10	57
k_1 (min^{-1}) [±] $\times 10^4$	21.2 [1.0]	1.33 [.23]	8.05 [.56]	7.32 [.19]
T_2 (°C)	20	7	17	67
k_2 (min^{-1}) [±] $\times 10^4$	72.3 [3.2]	3.69 [.27]	21.53 [.20]	20.94 [.34]
T_3 (°C)	30	34	39	77
k_3 (min^{-1}) [±] $\times 10^4$	182.4 [7.6]	57.0 [1.6]	193 [10]	54.0 [1.3]
ΔH (kcal/mol) [±]	17.8 [1.1]	17.5 [0.9]	18.4 [1.0]	22.3 [0.1]
ΔS (cal K^{-1} mol^{-1}) [±]	−7.7 [3.8]	−11.6 [3.1]	−7.6 [3.5]	−5.6 [1.2]
ΔG (kcal/mol)	20.1	21.0	20.6	23.9
E_a (kcal/mol) [~±0.4]	18.4	18.1	18.9	22.8

Isomerization of the *syn*- to *anti*-[2.2]Metacyclophanes

Despite the very limited quantities of material available, we felt it was sufficiently important to estimate the barrier to isomerization, even if only a few runs could be attempted. Since isomerization occurred at ambient temperatures, the *syn*-cyclophanes **1**, **27**, **50**, and complex **22** were prepared and purified at low temperatures, dissolved in $CDCl_3$, and placed in the NMR probe, at whichever temperature was to be studied. The rate of reaction was then obtained from the integrals for the peaks corresponding to the protons indicated in Table III. Only enough material was available for three duplicate runs on each compound, and thus the results are not as accurate as a more comprehensive study might produce: However, they leave no doubt that $\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}_{298}$ for the isomerization of *syn*-[2.2]metacyclophanes to *anti*-[2.2]metacyclophanes are about 17–18 and 20–21 kcal/mol, respectively, and that chromium tricarbonyl complexation of one of the arene rings raises these values by about 4 kcal/mol. This "complexation stabilization" of the syn isomer relative to the anti isomer is presumeably a summation of the reduced repulsion between the syn rings on complexation, some charge-transfer stabilization in the complexed syn isomer, and increased strain in the transition state for the isomerization of the complexed syn isomer relative to the uncomplexed one.

Very recently, Ito[35] has synthesized the dimethyl-*syn*-cyclophane **56** (compound **50** without bridge substituents) and studied its isomerization to **57**. He found at 298 K $\Delta H^{\ddagger}$ = 19.4 kcal/mol, $\Delta S^{\ddagger}$ = −8.7 cal K^{-1} mol^{-1}, $\Delta G^{\ddagger}$ = 22.6 kcal/mol, and E_a = 20.0 kcal/mol. These are in good agreement with our results.



56 57 58

(34) Keehn, P. *Org. Chem.* (*N.Y.*) **1983**, *45*, 69–238.

(35) Fujise, Y.; Nakasato, Y.; Ito, S. *Tetrahedron Lett.* **1986**, *27*, 2907–2908.

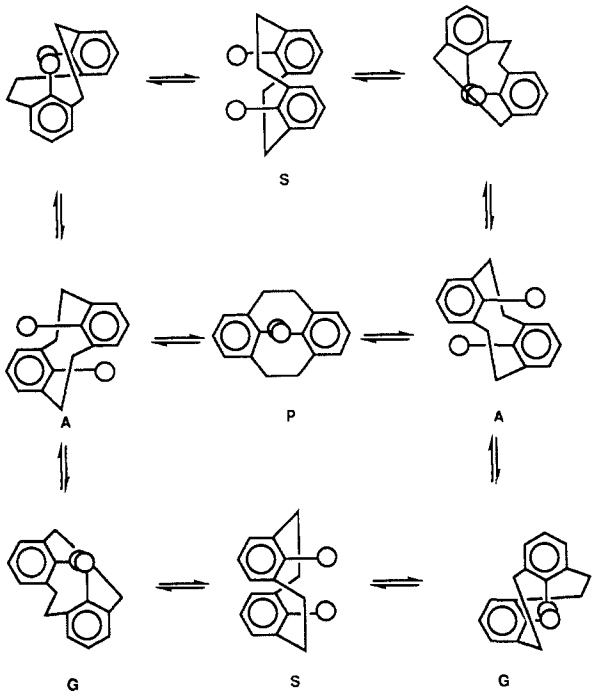


Figure 4. Possible isomerization pathways in the [2.2]metacyclophanes.

E_a for the isomerization of anti→anti, A→A′, Figure 4, has been estimated[36] at 28.4 kcal/mol, by studying the rates of racemization (ring inversion) of the optically active anti derivatives **58**. The difference, E_a(anti) − E_a(syn) or $\Delta H^{\ddagger}$(anti) − $\Delta H^{\ddagger}$(syn) = ~10 kcal/mol, suggests that ΔH° for syn→anti is of this order. Molecular mechanics calculations (MM2+PI) by us[37] and by Ito[36] suggest the difference in strain energies between **1** and **2** is 6–7 kcal/mol; however, such calculations do not take into account the through space π–π interaction between the syn rings of **1**, and thus this difference is almost certainly underestimated. The actual mechanism of isomerization (Figure 4) of either A→A′, S→S′, or S→A is not known. The conversion A→A′ could proceed through a near planar form P, or through an angular form G to the syn S, on through G′ to A′. Similarly S→A could proceed through G without involvement of P. We have tried using molecular mechanics to drive the C1–2–3–4 dihedral angle of **1** to simulate S→G and find the strain energy increases by about 20–30 kcal/mol over the maximum, not inconsistent with the above results. However a more sophisticated approach is required to determine the appropriate pathways with any precision, and we hope that this work will act as encouragement.

Experimental Section

General conditions are given in the supplementary material.

Stevens Rearrangement of *syn*-2,11-Dithia[3.3]metacyclophane Bis(methylsulfonium) Tetrafluoroborate 9. Potassium *tert*-butoxide (1.41 g, 12,6 mmol) was added to a stirred suspension of the sulfonium salt **9**[8b] (2.00 g, 4.20 mmol) in dry THF (125 mL) at 20 °C under N_2. After 5–8 min, water, aqueous HCl, and CH_2Cl_2 were added. The organic layer was separated, dried, and evaporated to yield the crude product (1.2 g, 95%) as a yellow oil. This was preadsorbed onto and chromatographed over silica gel with use of pentane as eluant. Eluted first was 1(e),10(e)-bis(methylthio)[2.2]metacyclophane **10d** (0.17 g, 14%) as colorless needles: mp 156–157 °C; ^{1}H NMR δ 7.72 (d, J = 7.8 Hz, 2 H, H-12,14), 7.56 (t, J = 7.8 Hz, 1 H, H-13), 7.29 (t, J = 8 Hz, 1 H, H-5), 7.13 (d, J = 8 Hz, 2 H, H-4,6), 4.50 (s, 1 H, H-16), 4.20 (s, 1 H, H-8), 3.34–3.23 (m, 4 H, H-1,2_{eq},9_{eq},10), 2.15 (s, 6 H, $-SCH_3$), 2.22–2.07 (m, H-2_{ax},9_{ax}); ^{13}C NMR δ 138.2–124.6 (see Table II), 57.2 (C-1,10), 47.5 (C-2,9), 15.5 ($-SCH_3$); MS (CI) MH^+ at m/e 301 (40), 205 (100). Anal. Calcd for $C_{18}H_{20}S_2$: C, 71.93; H, 6.71. Found: C, 71.83; H, 6.75.

Eluted next was 1(e),9(e)-bis(methylthio)[2.2]metacyclophane **10e** (0.19 g, 15%) as white needles from hexane: mp 162–165 °C; ^{1}H NMR δ 7.64 (dd, J = 7.7, 1.1 Hz, 2 H, H-6,14), 7.44 (t, J = 7.5 Hz, 2 H, H-5,13), 7.21 (dd, J = 7.4, 1.1 Hz, 2 H, H-4,12), 4.33 (d, J = 1.1 Hz, 2 H, H-8,16), 3.36–3.27 (m, 4 H, H-1,2_{eq},9,10_{eq}), 2.13 (s, 6 H, $-SCH_3$), 2.18–2.01 (m, 2 H, H-2_{ax},10_{ax}); ^{13}C NMR δ 138.4–123.8 (see Table II), 57.4 (C-1,9), 47.1 (C-2,10), 15.5 ($-SCH_3$); MS (CI) MH^+ at m/e 301 (4), 205 (100). Anal. Calcd for $C_{18}H_{20}S_2$: C, 71.93; H, 6.71. Found: C, 71.51; H, 6.74.

Eluted thirdly was 1(e),9(a)-bis(methylthio)[2.2]metacyclophane **10a** (0.48 g, 38%) as white needles from cyclohexane: mp 132–133 °C (lit.[8b] mp 132–133 °C); ^{1}H NMR δ 7.66 (d, J = 7.5 Hz, 1 H, H-14), 7.41 (t, J = 7.6 Hz, 1 H, H-13), 7.28 (t, J = 7.4 Hz, 1 H, H-5), 7.22 (d, J = 7.6 Hz, 1 H, H-12), 7.17 (d, J = 7.4 Hz, 1 H, H-6), 7.09 (d, J = 7.4 Hz, 1 H, H-4), 4.87 (s, 1 H, H-8), 4.41 (s, 1 H, H-16), 4.35 (dd, J = 4.8, 2.4 Hz, 1 H, H-9), 3.36–3.20 (m, 3 H, H-1,2_{eq},10_{eq}), 2.56 (dd, J = 13.0, 4.9 Hz, 1 H, H-10_{ax}), 2.18–2.13 (m, 1 H, H-2_{ax}), 2.14 (s, 3 H, $-SCH_3$), 1.93 (s, 3 H, $-SCH_3$); ^{13}C NMR δ 138.4–123.8 (see Table II), 57.3 (C-1), 55.3 (C-9), 47.1 (C-2), 44.8 (C-10), 15.5, 15.1 ($-SCH_3$); MS (CI) MH^+ at m/e 301 (28), 205 (100).

Eluted next was 1(a),9(a)-bis(methylthio)[2.2]metacyclophane **10c** (0.125 g, 10%) as colorless crystals from cyclohexane: mp 219–220 °C (lit.[8b] mp 219–220 °C); ^{1}H NMR δ 7.30 (t, J = 7.7 Hz, 2 H, H-5,13), 7.21 (d, J = 7.4 Hz, 2 H, H-6,14), 7.15 (d, J = 7.2 Hz, 2 H, H-4,12), 5.00 (s, 2 H, H-8,16), 4.37 (dd, J = 4.7, 2.5 Hz, 2 H, H-1,9), 3.23 (dd, J = 12.9, 2.5 Hz, 2 H, H-2_{eq},10_{eq}), 2.64 (dd, J = 12.9, 4.6 Hz, 2 H, H-2_{ax},10_{ax}), 1.95 (s, 6 H, $-SCH_3$); ^{13}C NMR δ 134.9–126.4 (see Table II), 55.2 (C-1,9), 44.7 (C-2,10), 15.0 ($-SCH_3$); MS (CI) MH^+ at m/e 301 (28), 205 (100).

Eluted finally was 1(a),10(a)-bis(methylthio)[2.2]metacyclophane **10b** (0.11 g, 9%) as white crystals from cyclohexane: mp 214–215 °C (lit.[8b] mp 216–217 °C); ^{1}H NMR δ 7.22–7.02 (m, 6 H, H-4,5,6,12,13,14), 5.50 (s, 1 H, H-16), 4.30 (dd, J = 4.2, 2.8 Hz, 2 H, H-1,10), 4.32 (s, 1 H, H-8), 3.20 (dd, J = 14.0, 2.8 Hz, 2 H, H-2_{eq},9_{eq}), 2.55 (dd, J = 14.0, 4.2 Hz, 2 H, H-2_{ax},9_{ax}), 1.91 (s, 6 H, $-SCH_3$).

Attempted Wittig Rearrangement of Thiacyclophane Complex 15. Preparation of the Bridge Methylated Complex 16, (η^6-*syn*-3-Methyl-2,11-dithia[3.3]metacyclophane)tricarbonylchromium(0). *n*-BuLi (59 mmol) in hexane (0.24 mL) was injected into a deaerated solution of complex **15**[14] (100 mg, 0.25 mmol) in dry THF (20 mL) at 20 °C. After 5 min, methyl iodide (0.18 mL, 0.41 mmol) was added (the red color did *not* decolorize), followed by water, aqueous HCl, and dichloromethane. The aqueous layer was further extracted with dichloromethane, and the combined organic layers were dried and evaporated to an oily residue. This was chromatographed over silica gel with use of dichloromethane/pentane (1:3) as eluant to give the methylated complex **16** (21 mg, 20%), which on recrystallization from dichloromethane gave yellow needles: mp 157–158 °C; ^{1}H NMR δ 7.24–7.00 (m, 4 H, H-14,15,16,18), 5.18-4.79 (m, 4 H, H-5,6,7,9), 3.96 and 3.70 (AB, J = 15.7 Hz, 2 H, H-$10_{ax,eq}$), 3.81 and 3.50 (s, 2 H each, H-$1_{ax,eq}$,$12_{ax,eq}$), 3.66 (q, J = 7.2 Hz, 1 H, H-3), 1.72 (d, J = 7.2 Hz, 3 H, C3CH_3); MS (CI) MH^+ at m/e 423 (100). Anal. Calcd for $C_{20}H_{18}CrO_3S_2$: C, 56.83; H, 4.29. Found: C, 56.68; H, 4.18.

Bismethylation of the Bridge of Complex 15. Preparation of (η^6-*syn*-3,10-Dimethyl-2,11-dithia[3.3]metacyclophane)tricarbonylchromium(0) (20). Potassium *tert*-butoxide (66 mg, 0.58 mmol) was added to a solution of complex **15**[14] (100 mg, 0.25 mmol) in dry THF (20 mL) under N_2. After 5 min, methyl iodide (0.3 mL, excess) was added, followed by water, aqueous HCl, and dichloromethane. The organic layer was separated, dried, and evaporated to an oil. This was chromatographed over silica gel with use of dichloromethane/pentane (1:3) as eluant to give the product **20** (100 mg, 94%), which on recrystallization from dichloromethane/pentane (1:1) gave yellow needles: mp 162–164 °C; ^{1}H NMR δ 7.27 (s, 1 H, H-18), 6.90 (bs, 3 H, H-14,15,16), 5.50 (s, 1 H, H-9), 5.03 (d, J = 6.3 Hz, 2 H, H-5,7), 4.75 (t, J = 6.3 Hz, 1 H, H-6), 3.93 and 3.69 (AB, J = 16.2 Hz, 2 H each, H-$1_{ax,eq}$,$12_{ax,eq}$), 3.62 (q, J = 7.6 Hz, 2 H, H-3,10), 1.70 (d, J = 7.6 Hz, 6 H, $-CH_3$); MS (CI) MH^+ at m/e 437 (45). Anal. Calcd for $C_{21}H_{20}CrO_3S_2$: C, 57.78; H, 4.62. Found: C, 57.55; H, 4.68.

(η^6-*syn*-2,11-Dimethyl-2,11-dithionia[3.3]metacyclophane)tricarbonylchromium(0) Bis(tetrafluoroborate) (21) and Its Stevens Rearrangement to Syn-Complex 22. $(MeO)_2CHBF_4$ (2.21 g, 10.9 mmol, 80% of oil by NMR)[19] was added to a solution of **15**[14] (2.23 g, 5.5 mmol) in well deaerated dichloromethane (200 mL) and stirred under N_2 for 3 h. The dichloromethane was decanted from the yellow precipitate, ethyl acetate (150 mL) was added, and stirring was continued for an additional 2 h. The fine precipitate was then collected and dried under vacuum to give **21** (3.00 g, 90%), mp 280 °C dec. This salt (3.00 g, 4.9 mmol) was then added to a suspension of *t*-BuOK (1.32 g, 11.8 mmol in dry THF (350

(36) Glotzmann, C.; Langer, E.; Lehner, H.; Schlogl, K. *Monatsh. Chem.* **1974**, *105*, 907–916.

(37) Serena Software, Box 3076, Bloomington, IN 47402 supplies this program (QCPE 318) suitable for an IBM-PC.

mL) under N_2. This was stirred for 10 min, during which time the salt went into solution, the mixture was then poured onto ice, and aqueous 2 M HCl (100 mL) was added. The mixture was extracted with ether (3 × 350 mL), and the extract was washed, dried, and evaporated to a yellow oil. This was preadsorbed and chromatographed on silica gel with use of dichloromethane/pentane (1:1) as eluant. After small amounts of pyrene and colorless decomplexed product, the yellow anti isomer **23** (190 mg, 8.9%) was eluted, which gave yellow needles from dichloromethane/pentane: mp 160–161 °C; ^{1}H NMR δ 7.38 (t, J = 7.5 Hz, 1 H, H-13), 7.23 (d, J = 8 Hz, 1 H, H-14), 7.18 (d, J = 7 Hz, 1 H, H-12), 6.01 (d, J = 6.5 Hz, 1 H, H-6), 5.95 (s, 1 H, H-16), 5.45 (t, 1 H, H-5), 5.39 (d, 1 H, H-4), 4.45 (dd, J = 4.1, 2.4 Hz, 1 H, H-1_{eq}), 3.46 (dd, J = 12.0, 2.8 Hz, 1 H, H-9_{ax}), 3.04–2.88 (m, 2 H, H-2_{eq}, H-10_{eq}), 2.52 (s, 1 H, H-8), 2.34 (t, J = 11.8 Hz, H-10_{ax}), 2.22 (s, 3 H, -SCH_3), 2.19–2.14 (m, 1 H, H-2_{ax}), 2.03 (s, 3 H, -SCH_3); ^{13}C NMR δ 233.3 (CO), 137.6 and 137.5 (C-11,15), 135.4 (C-16), 130.2 and 128.2 and 126.9 (C-12,13,14), 110.5 and 104.8 (C-3,7), 96.3 and 95.8 (C-4,5), 90.8 (C-6), 86.9 (C-8), 54.6 and 54.0 (C-1,9), 47.6 (C-10), 42.6 (C-2), 15.4 and 14.9 (SCH_3); MS (CI) MH^+ at m/e 437 (100), 204 (100); IR (KBr) 1960, 1850, 660, 615 cm^{-1}. Anal. Calcd for $C_{21}H_{20}CrO_3S_2$: C, 57.78; H, 4.62. Found: C, 58.14; H, 4.65.

Eluted next was the syn isomer **22**, (η^6-*syn*-2(a),10(e)-bis(methylthio)[2.2]metacyclophane)tricarbonylchromium(0) (1.52 g, 71.1%) as orange crystals from dichloromethane/pentane: mp 121–122 °C; ^{1}H NMR δ 7.15 (d, J = 7.5 Hz, 1 H, H-14), 6.94 (t, J = 7.5 Hz), 1 H, H-13), 6,91 (s, 1 H, H-16), 6.58 (d, J = 7.6 Hz, 1 H, H-12), 5.50 (s, 1 H, H-8), 4.76–4.66 (m, 3 H, H-4,5,6), 4.42 (dd, J = 9,5, 7.3 Hz, 1 H, H-9_{eq}), 3.84 (dd, J = 9.5, 3.9 Hz, 1 H, H-1_{ax}), 3.53 (dd, J = 14.2, 9.5 Hz, 1 H, H-2_{ax}), 3.43 (dd, J = 14,3, 9.5 Hz, 1 H, H-10_{ax}), 2.98 (dd, J = 14.0, 3.9 Hz, 1 H, H-2_{eq}), 2.29 (s, 3 H, -SCH_3), 2.26–2.13 (m, 1 H, H-10_{eq}), 2.17 (s, 3 H, -SCH_3); ^{13}C NMR δ 233.6 (CO), 138.8 (C-16), 138.0 (C-11,15?), 129.9 and 128.6 (C-12,13), 124.9 (C-14), 110.9 and 108.9 (C-3,7), 96.9 and 95.1 and 92.6 (C-4,5,6), 84.5 (C-8), 51.7 (C-1), 49.6 (C-9), 44.3 (C-10), 41.5 (C-2), 16.5 and 16.0 (SCH_3); MS (CI) MH^+ at m/e 437 (1), 301 (31), 205 (100); IR (KBr) 1950, 1860, 660, 620 cm^{-1}; UV (CH_3CN) λ_{max} 333 nm (ϵ_{max} = 10 300). Anal. Calcd for $C_{21}H_{20}CrO_3S_2$: C, 57.78; H, 4.62. Found: C, 57.52; H, 4.65.

Thermal Isomerization of the Syn Chromium Complex 22 to Anti-Complex 25. The syn-complex **22** (100 mg, 0.23 mmol) was refluxed in 100% ethanol (20 mL) under N_2 for 3 h. The solvent was evaporated, and the product was recrystallized from dichloromethane/pentane (1:1) to yield anti-complex **25** (80 mg, 80%) as yellow needles; mp 151–152 °C; ^{1}H NMR δ 7.38 (t, 1 H, H-13), 7.23 (d, 1 H, H-14), 7.18 (d, 1 H, H-12), 5.92 (t, J = 1.8 Hz, 1 H, H-16), 5.54 (d, 1 H, H-6), 5.45 (d, 1 H, H-6), 5.27 (t, 1 H, H-5), 4.42 (dd, J = 4.6, 2.4 Hz, 1 H, H-1_{eq}), 3.82 (dd, J = 4.6, 2.7 Hz, 1 H, H-9_{eq}), 3.45 (dd, J = 13.6, 4.8 Hz, 1 H, H-10_{eq}), 3.44 (s, 1 H, H-8), 2.89–2.82 (m, 2 H, H-2_{eq},10_{ax}), 2.31 (dd, J = 13.6, 4.8 Hz, 1 H, H-2_{ax}), 2.20 (s, 3 H, -SCH_3), 2.03 (s, 3 H, -SCH_3); ^{13}C NMR δ 233.2 (CO), 136.6 and 134.0 (C-11,15), 136.0 (C-16), 129.4 and 128.8 and 127.1 (C-12,13,14), 110.0 and 104.8 (C-3,7), 97.8 and 95.3 and 95.2 (C-4,5,6), 84.7 (C-8), 53,9 (C-1), 52.9 (C-9), 46.1 (C-10), 42.5 (C-2), 16.0 and 14.9 (SCH_3); MS (CI) MH^+ at m/e 437 (20), 205 (100); IR (KBr) 1983, 1960, 1880, 655, 610 cm^{-1}. Anal. Calcd for $C_{21}H_{20}CrO_3S_2$: C, 57.78; H, 4.62. Found: C, 57.34; H, 4.71.

Decomplexation of Syn Chromium Complex 22 at −30 °C, Followed by Isomerization at +20 °C to *anti*-[2.2]Phane 10e. Ceric ammonium nitrate (380 mg, 0.68 mmol) was added to a stirred solution of syn-complex **22** (100 mg, 0.23 mmol) in acetonitrile (20 mL) at −30 °C. After 30 min, the mixture was filtered, and the filtrate was evaporated to a solid residue. This was preadsorbed and chromatographed over silica gel with use of dichloromethane as eluant to give the *anti*-phane **10e** (68 mg 100%) identical with the sample obtained above.

Complexation of *anti*-[2.2]Phane Isomer 10e To Yield (η^6-*anti*-1-(e),10(e)-Bis(methylthio)[2.2]metacyclophane)tricarbonylchromium(0) (28). Chromium hexacarbonyl (80 mg, 0.36 mmol) and anti isomer **10e** (100 mg, 0,33 mmol) were heated under reflux in well deaerated *n*-butyl ether (20 mL) under N_2 for 3–4 h. The solvent was then removed, and the residue was Soxhlet extracted with use of dichloromethane. The extract was evaporated, and the residue was chromatographed over silica gel with use of dichloromethane/pentane (1:1) as eluant to yield complex **28** (100 mg, 70%) as yellow needles from dichloromethane/pentane: mp 180–182 °C; ^{1}H NMR δ 7.66 (d, J = 7.8 Hz, 1 H, H-14), 7.49 (t, J = 7.5 Hz, 1 H, H-13), 7.24 (m, 1 H, H-12), 5.96 (d, J = 6.3 Hz, 1 H, H-6), 5.42 (t, J = ~6.5 Hz, 1 H, H-5), 5.41 (bs, 1 H, H-16), 5.28 (d, J = 6.0 Hz, 1 H, H-4), 3.56 (dd, J = 11.6, 3.0 Hz, 1 H, H-1_{ax}), 3.45 (dd, J = 12.4, 3.4 Hz, 1 H, H-9_{ax}), 3.00 (dd, J = 11.3, 3.2 Hz, 1 H, H-10_{eq}), 2.96, (dd, J = 12.3, 3.3 Hz, 1 H, H-2_{eq}), 2.35 (s, 1 H, H-8), 2.27 (d, J = 12.6 Hz, 1 H, H-10_{ax}), 2.20 (s, 3 H, -SCH_3), 2.15 (s, 3 H, -SCH_3), 1.77 (t, J = 11.7 Hz, 1 H, H-2_{ax}); ^{13}C NMR δ 233.1 (CO), 138.4 (C-16), 137.8 and 136.9 (C-11,15), 131.2 and 128.4 (C-12,13), 124.4 (C-14), 111.1 and 108.0 (C-3,7), 94.8 and 94.0 (C-4,5), 90.4 (C-6), 87.9 (C-8), 56.9 (C-1), 54.9 (C-9), 47.6 (C-10), 44.7 (C-2), 15.5 (SCH_3); MS (CI) MH^+ at m/e (2) 205(100); IR (KBr) 1960, 1850, 660, 615 cm^{-1}. Anal. Calcd for $C_{21}H_{20}CrO_3S_2$: C, 57.78; H, 4.62. Found: C, 57.68; H, 4.69.

Low-Temperature Decomplexation of 22 to *syn*-2(a),10(e)-Bis(methylthio)[2.2]metacyclophane (27). Ceric ammonium nitrate (3.8 g, 6.8 mmol) was added to a stirred solution of syn-complex **22** (1.0 g, 2,3 mmol) in acetonitrile (60 mL) maintained at −30 °C. The mixture was stirred for an additional 30 min and then directly poured on to a column of silica gel maintained below −40 °C. The product was eluted with dichloromethane into a flask maintained at −40 °C. The solvent was removed at −30 °C and gave the product as a white solid (0.69 g, 100%); ^{1}H NMR (−50 °C) δ 7.05 (s, 1 H, H-8), 6.93 (d, J = 7.5 Hz, 1 H, H-14), 6.76 (s, 1 H, H-16), 6.69 and 6.61 (t, J = 7.5 Hz, 1 H each, H-5,13), 6.44 (d, J = 7.5 Hz, 1 H, H-6), 6.44 and 6.38 (d, J = 7.5 Hz, 1 H each, H-4,12), 4.42 (t, J = ~8 Hz, 1 H, H-9_{eq}), 4.24 (dd, J = 9.5, 4.1 Hz, 1 H, H-1_{ax}), 3.75 (dd, J = 14.0, 9.6 Hz, 1 H, H-10_{ax}), 3.37 (dd, J = 14.0, 9,5 Hz, 1 H, H-2_{ax}), 2.82 (dd, J = 13.9, 4.1 Hz, 1 H, H-2_{eq}), 2.35 (dd, J = 14.0, 6.6 Hz, 1 H, H-10_{eq}), 2.15 (s, 3 H, -SCH_3), 2.03 (s, 3 H, -SCH_3); ^{13}C NMR (−50 °C) δ 138.1 (C-16), 137.8 and 137,7 and 136.2 and 134.6 (C-4,5,6,12,13), 123.8 (C-14), 52.5 and 51.9 (C-1,9), 44.0 and 43.2 (C-2,10), 16.3 and 16.0 (SCH_3).

Formation of [(3,4,5,6,7,8)-η^6-*anti*-9(a)-(Methylthio)[2.2]metacyclophan-1-ene]tricarbonylchromium(0) (30) from (η^6-*syn*-1,9-Bis(dimethylthionia)[2.2]metacyclophane)tricarbonylchromium(0) Bis(tetrafluoroborate) (29). Salt **29**: $(MeO)_2CHBF_4$[19] (1.21 g, 6.0 mmol of 80% oil) was added to a stirred solution of complex **22** (1.09 g, 2.5 mmol) in dichloromethane (25 mL). The mixture was stirred under N_2 for a further 6 h. The solvent was then decanted, ethyl acetate was added, and the mixture was stirred for an additional 4 h. The solid product was then collected by filtration and dried to give salt **29** (1.6 g, 100%) as a fine yellow powder: mp 240 °C dec; IR (KBr) 1980, 1910, 1040, 630, 610 cm^{-1}.

Monoene **30**: This salt (320 mg, 0.5 mmol) was suspended in dry THF (50 mL) under N_2, and *t*-BuOK (123 mg, 1.1 mmol) was added. After the mixture was stirred for 10 min, aqueous HCl was added, followed by ether (60 mL). The organic layer was separated, washed, dried, and evaporated. The crude product was then preadsorbed and chromatographed on silica gel with use of dichloromethane/pentane (1:1) as eluant to yield monoene **30** (43 mg, 22%) as red needles from dichloromethane/pentane: mp 157–158 °C; ^{1}H NMR δ 7.35–7.10 (m, 3 H, H-12,13,14), 6.86 (d, J = 10.9 Hz, 1 H, H-1), 6.56 (s, 1 H, H-16), 6.30 (d, J = 10.9 Hz, 1 H, H-2), 5.50–5.36 (m, 3 H, H-4,5,6), 4.60 (s, 1 H, H-8), 3.86 (t, J = 3.5 Hz, 1 H, H-9_{eq}), 3.42 (dd, J = 13.0, 3.3 Hz, 1 H, H-10_{eq}), 2.80 (dd, J = 13.0, 3.7 Hz, 1 H, H-10_{ax}), 2.12 (s, 3 H, -SCH_3); ^{13}C NMR δ 233.1 (CO), 137.3 and 135.6 (C-1,2), 133.4 and 133.3 (C-11,15), 129.8 (C-16), 128.8 and 127.2 (C-12,13), 126.6 (C-14), 111.6 and 106.8 (C-3,7), 95.6 and 94.9 (C-5,6), 91.9 (C-4), 83,9 (C-8), 54.0 (C-9), 47.0 (C-10), 15.1 (SCH_3); MS (EI) $M^{+\cdot}$ at m/e 388 (11), 304 (46), 301 (31), 202 (100); IR (KBr) 1950, 1870, 650 cm^{-1}. Anal. Calcd for $C_{20}H_{16}CrO_3S$: M = 388.0225. Found (MS): 388.0263.

In an identical way, complex **23** was converted to salt **32** and then to monoene **33**.

(η^6-*anti*-[2.2]Metacyclophane-1,9-diene)tricarbonylchromium(0) (34) from Syn Salt 29. *t*-BuOK (170 mg, 1.5 mmol) was added to a suspension of salt **29** (320 mg, 0.5 mmol) in THF (25 mL) and *t*-BuOH (25 mL) under N_2, and the mixture was stirred for 10 min. Then aqueous HCl was added to the mixture, followed by ether (60 mL). The organic layer was separated, washed, dried, and evaporated. The crude product was preadsorbed and chromatographed on silica gel with use of dichloromethane/pentane (1:4) as eluant to yield the diene complex **34** (51 mg, 30%) as red needles from dichloromethane/pentane; mp 138–139 °C dec; ^{1}H NMR δ 8,48 (d, J = 1.0 Hz, 1 H, H-16), 7,30 (t, J = 7.3 Hz, 1 H, H-13), 6.91 (dd, J = 7.3, 1.3 Hz, 2 H, H-12,14), 6.66 (d, J = 11.3 Hz, 2 H, H-1,10), 6.12 (d, J = 11.3 Hz, 2 H, H-2,9), 5.69 (s, 1 H, H-8), 5.61 (t, J = 6.6 Hz, 1 H, H-5), 5.29 (d, J = 6.6 Hz, 2 H, H-4,6); ^{13}C NMR 133.9 (C-11,15), 129.7 (C-16), 127.7 (C-12,14), 127.6 (C-13), 108.7 (C-3,7), 94.5 (C-4,6), 91.3 (C-5), 83.7 (C-8); MS (CI) MH^+ at m/e 341 (100); IR (KBr) 1970, 1890, 1860, 650 cm^{-1}. Anal. Calcd for $C_{19}H_{12}CrO_3$: C, 67.06; H, 3.55. Found: C, 66.86; H, 3.72.

Reductive Removal of the Methylthio Groups from Syn Isomer 22. Formation of Anti-Complexed Phane 24. A solution of syn isomer **22** (100 mg, 0.23 mmol) in THF (6 mL, dried over potassium/benzophenone ketyl) was added to anhydrous ammonia (25 mL), followed by Li (12 mg, 1.6 mmol). After stirring for 2 min, the mixture was poured into water. The mixture was then extracted with ether, and the extract was washed, dried, and evaporated. The residue was chromatographed over silica gel with use of dichloromethane/pentane (1:3) as eluant. Eluted first was *anti*-[2.2]metacyclophane **2** (5 mg, 10%). Eluted next was unreduced

anti product **10e** (14 mg, 21%). Eluted lastly was complexed *anti*-phane **24** (31 mg, 40%), identical with a sample prepared by the method of Langer and Leher;[38] mp 162–163 °C (lit.[38] mp 165 °C); ^{1}H NMR δ 7.39 (t, J = 8.0 Hz, 1 H, H-13), 7.13 (d, J = 8.0 Hz, 2 H, H-12,14), 5.47 (t, J = 3.6 Hz, 1 H, H-5), 5.45 (s, 1 H, H-16), 5.16 (d, J = 6.2 Hz, 2 H, H-4,6), 3.29 (m, 2 H, H-1_{eq},10_{eq}), 2.80 (m, 2 H, H-2_{eq},9_{eq}), 2.37 (m, 2 H, H-1_{ax},10_{ax}), 2.33 (s, 1 H, H-8), 1.90 (m, 2 H, H-2_{ax},9_{ax}); ^{13}C NMR δ 233.4 (CO), 138.7 (C-16), 138.1 (C-11,15), 130.7 (C-13), 126.4 (C-12,14), 113.4 (C-3,7), 94.7 (C-5), 91.6 (C-4,6), 89.8 (C-8), 40.4 (C-1,10), 38.6 (C-2,9).

Reduction of Uncomplexed *syn*-Phane 27 To Give Hexahydropyrene 36. *syn*-Phane **27** (100 mg, 0.33 mmol) in THF (6 mL, freshly distilled from potassium/benzophenone ketyl) at −30 °C was added to anhydrous ammonia (25 mL), followed by sodium (46 mg, 2 mmol). The mixture was stirred for 2 min and was then poured into water. The organic fraction was extracted with ether, dried, and concentrated to yield 4,5,9,10,10b,10c-hexahydropyrene (**36**) (42 mg, 60%): mp 196–197 °C; ^{1}H NMR δ 5.45 (bs, 4 H, H-1,3,6,8), 2.72 (bs, 4 H, H-2,9), 2.45–2.20 and 2.20–1.99 (m, 6 H, H-4,5,9,10,10b,10c); ^{13}C NMR δ 136.7 (C-3a,5a,8a,10a), 116.8 (C-1,3,6,8), 47.3 (C-10b,10c), 35.9 (C-4,5,9,10), 27.2 (C-2,7); IR (KBr) 2900, 1660, 950 cm^{-1}; MS (EI) M$^{+\cdot}$ at m/e 210 (100), 182 (62), 167 (84). Anal. Calcd for $C_{16}H_{18}$: M = 210.1408. Found (MS): M = 210.1460.

(η^6,η^6-*syn*-2,11-Dimethyl-2,11-dithionia[3.3]metacyclophane)bis(tricarbonylchromium(0)) Bis(tetrafluoroborate) (39). $(MeO)_2CHBF_4$ (0.92 g, 4.5 mmol, 80% of oil by NMR)[19] was added to a refluxing solution of **13**[14] (1.0 g, 1.8 mmol) in dichloromethane (70 mL) under N_2. After 3 h of reflux, ethyl acetate (70 mL) was added and reflux continued for a further 1 h. The salt was then collected, washed well with ethyl acetate, and dried under vacuum to yield **39** (1.3 g, 100%) as a yellow powder: mp 270 °C dec; IR (KBr) 1950, 1870, 1080, 1040, 660, 615 cm^{-1}.

Stevens Rearrangement of Sulfonium Salt 39. The salt **39** (1.20 g, 1.60 mmol), directly as prepared above, was added to a stirred suspension of KOBu-*t* (50 mg, 4.5 mmol) in dry THF (125 mL) under N_2 at 20 °C. After 10 min, the reaction mixture was poured into water, acidified with aqueous HCl and then extracted with ether. The organic layer was washed, dried, and evaporated to an orange oil, which was preadsorbed and chromatographed over silica gel with use of dichloromethane/pentane (1:2) as eluant. Eluted first was the uncomplexed *anti*-cyclophane **10e** (50 mg, 10%), identical with sample above. Eluted next was a mixture of the monocomplexed *syn*-phanes **22** and **42**, which could not be separated. Isomer **22** was identified by comparison of its ^{1}H NMR peaks with authentic sample, and **42**, having a deshielded ring proton at δ 5.20 and an internal proton at δ 4.80 was identified by subtraction. Eluted next was the biscomplexed syn isomer **40**, (η^6,η^6-syn-2(a),10-(e)-bis(methylthio)[2.2]metacyclophane)-bis-tricarbonylchromium(0) (370 mg, 40%): dec pt 210 °C; ^{1}H NMR δ 5.72 (s, 1 H, H-8), 5.55 (d, J = 5.1 Hz, 1 H, H-14), 5.14–4.80 (m, 6 H, H-4,5,6,12,13,16), 4.09 (dd, J = 13, 6–7 Hz, 1 H, H-9), 3.92 (dd, J = 13, 7–8 Hz, 1 H, H-1), 3.53 (dd, J = 16, 12 Hz, 1 H, H-2_{eq}), 3.32 (dd, J = 17, 11 Hz, 1 H, H-10_{ax}), 2.56 (dd, J = 17, 5 Hz, 1 H, H-10_{eq}), 2.36 (dd, J = 17, 7 Hz, 1 H, H-2_{ax}), 2.32 (s, 3 H, -SCH_3), 2.25 (s, 3 H, -SCH_3); ^{13}C NMR δ 232.7 and 232.6 (CO), 111.6 and 110.5 and 108.0 and 107.9 (C-3,7,11,15), 96.7 and 95.4 and 95.0 and 94.2 and 92.3 (C-4,5,6,12,13), 91.0 (C-14), 86.1 (C-16), 84.3 (C-8), 49.1 and 49.0 (C-1,9), 42.0 and 41.5 (C-2,10), 16.5 and 16.4 (-SCH_3); MS (Cl), MH$^+$ at m/e 573 (absent), 437 (MH − Cr(CO)$_3$); IR (KBr) 1950, 1870, 650, 600 cm^{-1}. Anal. Calcd for $C_{24}H_{20}Cr_2O_6S_2$: C, 50.35; H, 3.52. Found: C, 50.68; H, 3.69.

Eluted last was the diaxial isomer **41** (36 mg, 4%): dec pt 220 °C; ^{1}H NMR δ 5.59 (s, 2 H, H-8,16), 5.55–4.83 (m, 6 H, H-4,5,6,12,13,14), 3.97–3.32 (m, 4 H, H-$1,2_{eq}$,$9,10_{eq}$), 2.44–2.61 (m, 2 H, H-2_{ax},10_{ax}), 2.32 (s, 6 H, -SCH_3); MS (Cl) MH$^+$ at m/e 573 (<5), 205 (100); IR (KBr) 1970, 1870, 650, 610 cm^{-1}. Anal. Calcd for $C_{24}H_{20}Cr_2O_6S_2$: C, 50.35; H, 3.52. Found: C, 50.67; H, 3.70.

(η^6,η^6-*syn*-2(a),10(e)-Bis(dimethylthionia)[2.2]metacyclophane)bis(tricarbonylchromium)(0)) Bis(tetrafluoroborate) (43). $(MeO)_2CHBF_4$ (0.22 g, 1.1 mmol as 80% of oil by NMR)[19] was added to a stirred, refluxing solution of syn-bis-complex **40**[14] (250 mg, 0.44 mmol) in dichloromethane (25 mL) under N_2. After 6 h, reflux was stopped, and the solvent was decanted away. Ethyl acetate (25 mL) was then added, and the mixture was stirred for a further 4 h. The salt was then collected by filtration as a yellow powder (152 mg, 40%), dec pt 270 °C; IR (KBr) 1960, 1890, 1080, 1030, 650, 610 cm^{-1}.

Hofmann Elimination of Bis(salt) 43 To Give (η^6,η^6-*syn*-[2.2]Metacyclophane-1,9-diene)bis(tricarbonylchromium)(0) (44). KOBu-*t* (57 mg, 0.51 mmol) was added to a stirred suspension of salt **43** (150 mg, 0.17 mmol) in a mixture of THF/HOBu-*t* (1:1, 25 mL) under N_2. After 10 min, aqueous HCl was added, followed by ether (50 mL). The organic layer was washed, dried, concentrated and then preadsorbed and chromatographed over silica gel with use of dichloromethane/pentane (1:1) as eluant to yield diene **44** (24 mg, 29%) as a red solid. Recrystallization from dichloromethane/pentane (1:1) gave red needles: mp 167 °C dec; ^{1}H NMR δ 7.01 (s, 4 H, H-1,2,9,10), 5.98 (s, 2 H, H-8,16) 5.15–5.04 (m, 6 H, H-4,5,6,12,13,14); ^{13}C NMR δ 232.6 (CO), 135.4 (C-1,2,9,10), 106.0 (C-3,7,11,15), 94.8 (C-5,13), 93.5 (C-4,6,12,14), 83.3 (C-8,16); MS (Cl) MH$^+$ at m/e 477 (6), 391 (100), 205 (100). Anal. Calcd for $C_{22}H_{12}Cr_2O_6$: M = 475.944. Found (MS): 475.990.

Reductive removal of *one* -SMe group from bis-complex **40** to yield [η^6,η^6-*syn*-2(e)(methylthio)[2.2]metacyclophane]bis(tricarbonylchromium)(0) (**47**). A solution of **40** (100 mg, 0.18 mmol) in dry THF (8 mL) was added to anhydrous ammonia (25 mL), and Li (9 mg, 7 equiv) was added with stirring. The reaction was quenched 60 s after it turned dark blue by pouring onto ice. It was then extracted with ether. The organic extract was washed, dried, concentrated and then preadsorbed and chromatographed over silica gel with use of dichloromethane/pentane (1:1) as eluant to yield mono -SMe bis-complex **47** (38 mg, 40%): dec pt 220 °C; ^{1}H NMR δ 5.56 (d, J = 6.6 Hz, 1 H, H-14), 5.14–4.71 (m, 7 H, H-4,5,6,8,12,13,16), 4.01 (dd, J = 9.9, 6.5 Hz, 1 H, H-1), 3.56 (dd, J = 14.4, 9.9 Hz, 1 H, H-2_{eq}), 3.01–2.76 (m, 4 H, H-9,10), 2.30 (m, 1 H, H-2_{ax}), 2.27 (s, 3 H, -SCH_3); MS (Cl) MH$^+$ at m/e 527 (6), 391 (100); IR (KBr) 1950, 1875, 650, 610 cm^{-1}. Anal. Calcd for $C_{23}H_{18}Cr_2O_6S$: C, 52.48; H, 3.45. Found: C, 52.66; H, 3.78.

(η^6,η^6-*syn*-[2.2]Metacyclophane)bis(tricarbonylchromium)(0) (48). A solution of diaxial isomer **41** (70 mg, 0.12 mmol) in freshly distilled dry THF (5 mL) was added to anhydrous ammonia (20 mL), and then Li (6 mg, 7 equiv) was added with stirring. The reaction was quenched 20 s after it turned dark blue by pouring onto ice. Ether was added, and the organic extract was washed, dried, concentrated and then preadsorbed and chromatographed over silica gel with use of dichloromethane/pentane (1:1) as eluant. This gave the syn-bis-complexed cyclophane **48** (16 mg, 27%), which on recrystallization from dichloromethane/pentane (1:1) gave yellow crystals: mp 198–200 °C dec; ^{1}H NMR δ 5.12 (t, J = 6.3 Hz, 2 H, H-5,13), 5.09 (s, 2 H, H-8,16), 4.75 (d, J = 6.3 Hz, 4 H, H-4,6,12,14), 3.01–2.77 (m, 8 H, H-1,2,9,10); MS (Cl) MH$^+$ at m/e 345 (MH − Cr(CO)$_3$). Anal. Calcd for $C_{22}H_{16}Cr_2O_6$: M = 479.9757. Found (MS): 479.9740.

Low-Temperature Removal of Chromium from 48 To Give *syn*-[2.2]-Metacyclophane 1. Ceric ammonium nitrate (67 mg, 0.13 mmol) was added to a stirred solution of **48** (10 mg, 0.02 mmol) in acetonitrile (5 mL) at −30 °C. The mixture was stirred at −30 °C for 10 min and then was directly poured over a column of silica gel maintained below −40 °C. The product was eluted with dichloromethane into a flask maintained at −40 °C. Removal of solvent below −30 °C left **1** as a white solid (4 mg, 100%): ^{1}H NMR (−30 °C) δ 6.63 (s, 2 H, H-8,16), 6.62 (t, J = 7.5 Hz, 2 H, H-5,13), 6.41 (d, J = 7.5 Hz, 4 H, H-4,6,12,14), 3.20–3.07 (m, 4 H, H-1_{eq},2_{eq},9_{eq},10_{eq}), 2.99–2.86 (m, 4 H, H-1_{ax},2_{ax},9_{ax},10_{ax}); UV (CH_3CN, −30 °C) λ_{max} 260 nm (ε = 360).

(η^6-*syn*-2,6,11,15-Tetramethyl-2,11-dithionia[3.3]metacyclophane)tricarbonylchromium(0) Bis(tetrafluoroborate) (52). $(MeO)_2CHBF_4$ (1.16 g, 5.7 mmol, as 80% oil by NMR)[19] was added under N_2 to a stirred solution of dimethyl monocomplex **51**[14] (1.0 g, 2.3 mmol) in dichloromethane. After 6 h, the solvent was decanted away, ethyl acetate (60 mL) was added, and the mixture was stirred for a further 4 h. The solid salt was then collected by filtration and dried as a fine yellow powder (**52**) (1.44 g, 98%); dec pt 250 °C; IR (KBr) 1980, 650, 610 cm^{-1}.

Stevens Rearrangement of Salt 52 To Give [η^6-*syn*-6,15-Dimethyl-2-(a),10(e)-bis(methylthio)[2.2]metacyclophane]tricarbonylchromium(0) (53). KOBu-*t* (480 mg, 4.3 mmol) was added to a stirred suspension of salt **52** (1.2 g, 1.9 mmol) in dry THF (125 mL) at 20 °C under N_2. After 10 min, water, aqueous HCl, and dichloromethane were added. The organic layer was separated, washed, dried, and concentrated to a yellow oil (0.85 g, 98%). This was preadsorbed and chromatographed over silica gel with use of dichloromethane/pentane (1:3) as eluant. Eluted first was the desired syn isomer **53** (0.72 g, 60%); mp 132–133 °C; ^{1}H NMR δ 7.00 (s, 1 H, H-16), 6.70 and 6.42 (s, 1 H each, H-12,14), 5.29 (s, 1 H, H-8), 4.63 (s, 2 H, H-4,6), 4.38 (dd, J = 9.6, 6.7 Hz, 1 H, H-9), 3.87 (dd, J = 9.4, 4.5 Hz, 1 H, H-1), 3.51–3.37 (m, 2 H, H-2_{ax},10_{ax}), 2.94 (dd, J = 14.1, 4.5 Hz, 1 H, H-2_{eq}), 2.27–2.11 (m, 1 H, H-10_{eq}), 2.31 (s, 3 H, C-13-CH_3), 2.20 and 2.17 and 1.93 (s, 3 H each, C-5-CH_3 and -SCH_3's); MS (El), M$^{+\cdot}$ at m/e 464 (21), 380 (90), 282 (100); IR (KBr) 1950, 1860, 660, 620 cm^{-1}. Eluted next was an uncharacterized anti isomer (90 mg, 10%), internal hydrogens at δ 5.7 and 3.2.

Low-Temperature Removal of Chromium from 53 To Give *syn*-6,15-Dimethyl-2(a),10(e)-bis(methylthio)[2.2]metacyclophane (50). Ceric ammonium nitrate (1.78 g, 3.3 mmol) was added to a stirred solution of **53** (500 mg, 1.1 mmol) in acetonitrile (30 mL) at −30 °C. After 30 min,

(38) Langer, E.; Lehner, H. *Tetrahedron* **1973**, *29*, 375–383.

the mixture was poured directly over a column of silica gel maintained below -40 °C, and the product was eluted with dichloromethane into a flask held at -40 °C. Removal of solvent below -30 °C gave the dimethyl-*syn*-cyclophane **50** (340 mg, 100%) as a white solid: ^{1}H NMR (-30 °C) δ 6.79, 6.74, 6.50, 6.27, 6.24, 6.19 (6 s, 1 H each, H-4,6,8,12,14,16), 4.37 (dd, J = 9.6, 6.6 Hz, 1 H, H-9), 4.13 (dd, J = 9.5, 3.8 Hz, 1 H, H-1), 3.69 (m, 1 H, H-10$_{ax}$), 3.32 (dd, J = 13.4, 9.5 Hz, 1 H, H-2$_{ax}$), 2.78 (dd, J = 13.6, 3.8 Hz, 1 H, H-2$_{eq}$), 2.35 (m, 1 H, H-10$_{eq}$), 2.19 and 2.08 and 1.95 (s, 3 H each, C-5-CH$_3$, C-13-CH$_3$, and -SCH$_3$'s).

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Supplementary Material Available: General experimental conditions, crystal structure determination (including labeling schemes, tables of fractional atomic coordinates, isotropic thermal parameters, bonded atomic distances, bond angles, mean planes and torsion angles, and intermolecular distances), and X-ray experimental details for syn complex **22** and anti complex **28** (26 pages). Ordering information is given on any current masthead page.

Total Syntheses of (+)- and (-)-Didemnenones A and B. Antiselectivity in the Intramolecular Carbomercuration Reaction[1a]

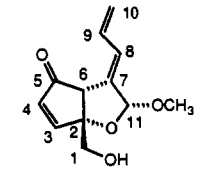
Craig J. Forsyth*,[1b] and Jon Clardy

Contribution from the Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853-1301. *Received August 14, 1989*

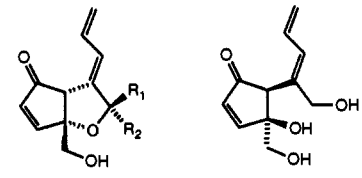
Abstract: Total syntheses of the title compounds were achieved in 11 steps and ca. 7% overall yield from the chiral synthon **10**. In conjunction with previous chiroptical studies, this work allowed the assignment of absolute configurations to didemnenones A-D (**1-4**, respectively), a series of cytotoxic cyclopentanoid marine natural products isolated from the tunicates *Tridemnum* cf. *cyanophorum* and *Didemnum voeltzkowi*. Thus, **1** and **2** were shown to have the 2*R*,6*R* configuration; **3** was shown to have the 2*S*,6*S*, and **4**, most plausibly, the 2*S*,6*R* configurations. Featured in the syntheses are an efficient 1,3 chirality transfer to establish the C2 configuration, one-pot mercuric chloride induced intramolecular cyclization/iodination reactions of an ϵ-alkynyl silyl enol ether to form a *cis*-6-oxabicyclo[3.3.0]oct-3-en-2-one system bearing an exocyclic C8-vinyl iodide and an installation of the C11 oxidation level and diene moiety by sequential SeO_2/*t*-BuOOH oxidation and Pd-mediated vinyl cross-coupling with *n*-$Bu_3SnCHCH_2$. In examining the intramolecular carbomercurations of cyclopentenone silyl enol ethers bearing β-(2-propynyloxy) side chains, an apparently exclusive and unexpected antiselectivity was revealed.

The didemnid tunicates have proven to be a particularly rich source of structurally diverse, biologically potent compounds including the depsipeptides didemnins A-C,[2] heteroaromatic asididemin,[3] and didemnenones A-D.[4] The didemnenones are a series of at least four C_{11} cyclopentanoid natural products that have recently been isolated from the Caribbean tunicate *Tridemnum* cf. *cyanophorum*, didemnenones A (**1**) and B (**2**), and the South Pacific tunicate *Didemnum voeltzkowi*, didemnenones C (**3**) and D (**4**). The didemnenones display a rich abundance and variety of functionality; every carbon atom in these compounds is functionalized. In addition to their intriguing structural features, the broad-range antimicrobial and antileukemic activities displayed by the didemnenones[4] make them ideal synthetic targets. Reported herein are the full details of our synthetic studies on didemnenones A and B,[5] which culminated in their enantioselective total syntheses and the assignment of the absolute configurations to didemnenones A-D depicted in **1-4**.

Isolated along with didemnenones A and B from *T.* cf. *cyanophorum* extracts were the anomeric acetals **5** and **6**, which, rather than being natural products, are believed to have been formed from the inseparable hemiacetals **1** and **2** upon chromatography in the presence of methanol. The structure determination

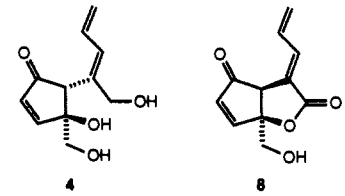


5



1 R_1 = H, R_2 = OH
2 R_1 = OH, R_2 = H
6 R_1 = OCH_3, R_2 = H
7 R_1, R_2 = O

3



4 **8**

of major acetal **5** by X-ray crystallography proved to be instrumental to the elucidation of the relative stereostructures of **1-6** through spectral correlations and chemical interconversions. In particular, allylic oxidations of **1-4** provided pivotal correlations

(1) (a) Taken in part from the Ph.D. Thesis of C.J.F., Cornell University, 1989. (b) Present address: Department of Chemistry, Harvard University, Cambridge, MA 01238.
(2) Rinehart, K. L., Jr.; Gloer, J. B.; Cook, J. C., Jr.; Mizsak, S. A.; Scahill, T. A. *J. Am. Chem. Soc.* **1981**, *103*, 1857-1859.
(3) Kobayashi, J.; Cheng, J.; Nakamura, H.; Ohizumi, Y. *Tetrahedron Lett.* **1988**, *29*, 1177-1180.
(4) Lindquist, N.; Fenical, W.; Sesin, D. F.; Ireland, C. M.; Van Duyne, G. D.; Forsyth, C. J.; Clardy, J. *J. Am. Chem. Soc.* **1988**, *110*, 1308-1309.
(5) Forsyth, C. J.; Clardy, J. *J. Am. Chem. Soc.* **1988**, *110*, 5911-5912.

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