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Mixed [2.2]Cyclophanes of Pyrene and Benzene

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An examination of the literature on [2.2]cyclophanes reveals a loose relationship between the relative sizes of the two 'half-cyclophanes' (as measured by the parameter Δd) and the limitations of the dominant general synthetic approaches. Direct coupling methods tend to be successful only for systems with Δd values below 1.0 Å, whereas ring-contraction-based approaches are usually viable for systems with Δd values up to 2.0 Å. For the very few known systems with Δd values greater than 2.0 Å, aromatization-based approaches are the only ones that have been successful. The syntheses of two [2.2]cyclophanes with very large Δd values, [2]paracyclo[2](2,7)pyrenophane (**17**) ($\Delta d = 4.25$ Å) and [2]metacyclo[2](2,7)pyrenophane (**18**) ($\Delta d = 5.04$ Å) are presented here. The syntheses hinge on a valence isomerization/dehydrogenation reaction. The crystallographically determined bend angle, θ, for **18** is 96.1°. Cyclophane **18** undergoes a degenerate conformational flip, the energy barrier for which was determined to be 18.9 kcal mol^{-1} by DNMR.

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Introduction

The [2.2]cyclophanes are comprised of two aromatic units linked by a pair of two-atom bridges. They form not only one of the most populous classes of cyclophanes, but also one of the most thoroughly studied.[1] The majority of work in this area has been conducted on 'symmetrical' cyclophanes, i.e. those consisting of two identical aromatic units with the same substitution pattern. [2.2]Paracyclophane (**1**) and *anti*-[2.2]metacyclophane (**2**) are prime examples. An 'unsymmetrical' [2.2]cyclophane, e.g. [2.2]metaparacyclophane (**8**), consists of two identical aromatic units with different substitution patterns. The term 'mixed' may then be applied to the numerous [2.2]cyclophanes that contain two different aromatic units.

All [2.2]cyclophanes can be viewed as the sum of two xylylene (or xylylene-like) 'half-cyclophane' units (Fig. 1). In most cases, the lowest energy (usually planar) structures of the individual half-cyclophanes are not retained in the [2.2]cyclophane they form. In other words, [2.2]cyclophanes are usually strained to some extent. This is because the formation of single bonds between the respective benzylic carbon atoms of the two half-cyclophanes normally affords a structure in which ideal structural features are precluded. Ultimately, the lowest energy structure of the [2.2]cyclophane reflects a happy medium between a variety of competing energetically unfavourable situations that come into play, e.g. angle strain, torsional strain, pyramidalization of quaternary aromatic carbon atoms, repulsive non-bonding interactions between proximate aromatic pi clouds and diminished aromaticity arising from non-planarity of the aromatic systems.

The strained nature of [2.2]cyclophanes makes them interesting from structural, physical, and chemical viewpoints. Of course, a successful synthesis is required before any of these properties can be studied. Indeed, synthetic challenge is another attractive feature of such systems. Two general approaches to [2.2]cyclophanes have been dominant: the direct coupling approach (D) and the ring-contraction approach (R). In the former case, the [2.2]cyclophane is formed through the direct formation of bonds between the respective benzylic carbon atoms of the two components. This has most often been accomplished through the dimerization of a xyxlene species (typically produced by a Hofmann elimination), cross-coupling of two xylylenes or Wurtz coupling. In this approach, most, if not all, of the strain in the [2.2]cyclophane builds up during the key coupling step. In contrast, the ring-contraction route involves the synthesis of a less strained [3.3]cyclophane (most often a dithia[3.3]cyclophane), which is then subjected to a ring-contraction reaction.[2] In such cases, the strain in the final product is built up over two stages.[3]

In examining the cyclophane literature, it can be seen that the ring-contraction approach generally performs better than the direct coupling approach, not only in terms of yield, but also with respect to the nature of the [2.2]cyclophanes it can be used to synthesize. In this regard, it is interesting to note that limitations of the two major synthetic approaches can be

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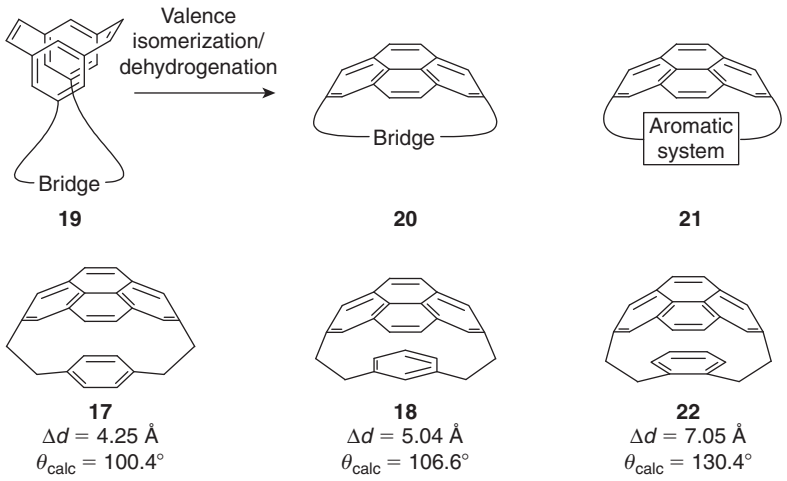


Scheme 1. Elaboration of [*n*](2.7)pyrenophanes into mixed [2.2]cyclophanes of pyrene and benzene.

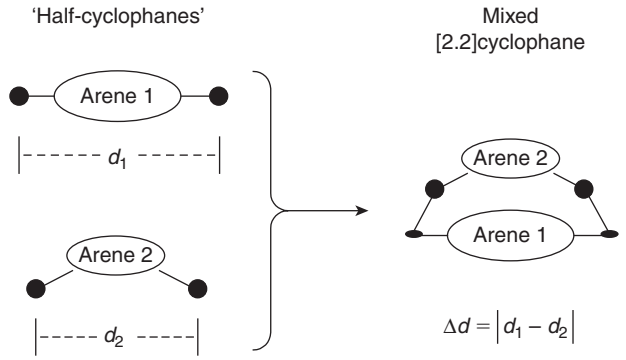


Fig. 1. Definition of the parameter Δd.

expressed loosely in terms of the relative sizes of the two half-cyclophanes that make up a [2.2]cyclophane. A simple measure of size of a half-cyclophane is the distance between the benzylic carbon atoms of the corresponding dimethylarene (d_1 and d_2, Fig. 1, Table in the Accessory Publication). The absolute value of the difference between these two values affords the parameter Δd (Fig. 1).

A selection of [2.2]cyclophanes[4–20] is presented in Table 1 along with their Δd values and their method of formation. The direct coupling approach has generally been successfully applied when the Δd value is small (<1.0 Å). Synthetic expedience often comes at the expense of yield. The ring-contraction approach has the disadvantage of requiring more steps, but is usually superior when it comes to yield, scope, and Δd. [2.2]Cyclophanes with Δd values below ~1.5 Å are typically accessible without much difficulty using the ring-contraction approach and systems with Δd values as high as 2.0 Å, e.g. **15**[18] ($\Delta d = 2.01$ Å), have been synthesized using ring-contraction methodology. Of course, Δd values do not tell the whole story and the limits presented above must be viewed as very fuzzy, i.e. they should be used predictively only as very rough guides. This point is illustrated by the pair of [2.2] cyclophanes **13** ($\Delta d = 1.69$ Å) and **14** ($\Delta d = 1.70$ Å). Although they have essentially the same Δd value, naphthalenophane **13** was synthesized from the corresponding [3.3]dithiacyclophane,[16] but the attempted synthesis of corannulenophane **14** from its dithiacyclophane precursor failed.[17]

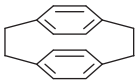
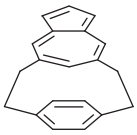
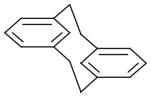
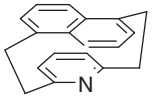
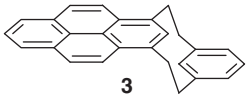
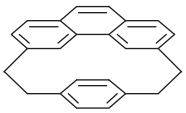
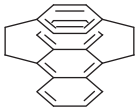
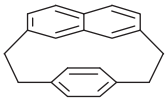
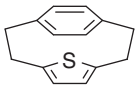
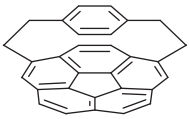
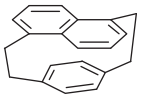
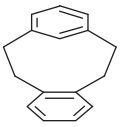
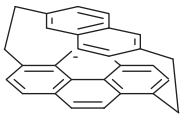
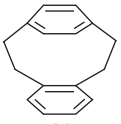
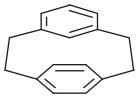
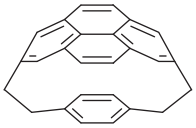
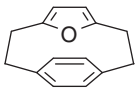
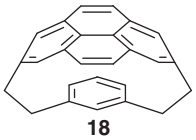
Symmetrical [2.2]cyclophanes are composed of two identical halves, so the value of Δd is necessarily zero. Due to the various factors described above, this does not mean that such cyclophanes are unstrained. Nevertheless, both general approaches have been used successfully to synthesize such systems. Unsymmetrical [2.2]cyclophanes can have larger Δd values than their symmetrical counterparts and such systems are typically more strained. This is exemplified by the series of benzene-based unsymmetrical cyclophanes: [2.2]metaparacyclophane (**8**,[11] $\Delta d = 0.79$ Å), [2.2]orthometacyclophane (**15**,[18] $\Delta d = 2.01$ Å), and [2.2]orthoparacyclophane (**16**,[19] $\Delta d = 3.80$ Å). The first two members of this series were synthesized using a ring-contraction approach, but an attempted synthesis of **16** using an analogous approach failed.[19b] This highly strained system was eventually synthesized, but it required the use of a new general approach (A = aromatization) that relies upon more powerful methodology. This involves the generation of one of the aromatic systems in the final step of the synthesis. As such, the gain of a substantial amount of aromatic stabilization energy[21] counteracts the developing strain as the target cyclophane forms.

Whereas the unsymmetrical [2.2]cyclophanes can boast some significantly strained systems, it is the mixed [2.2]cyclophanes that offer the opportunity for creativity in the design of new strained systems. This simply requires the union of half cyclophanes with substantially different sizes (as defined above). Of course, synthetic methodology that allows this to happen is a necessity.

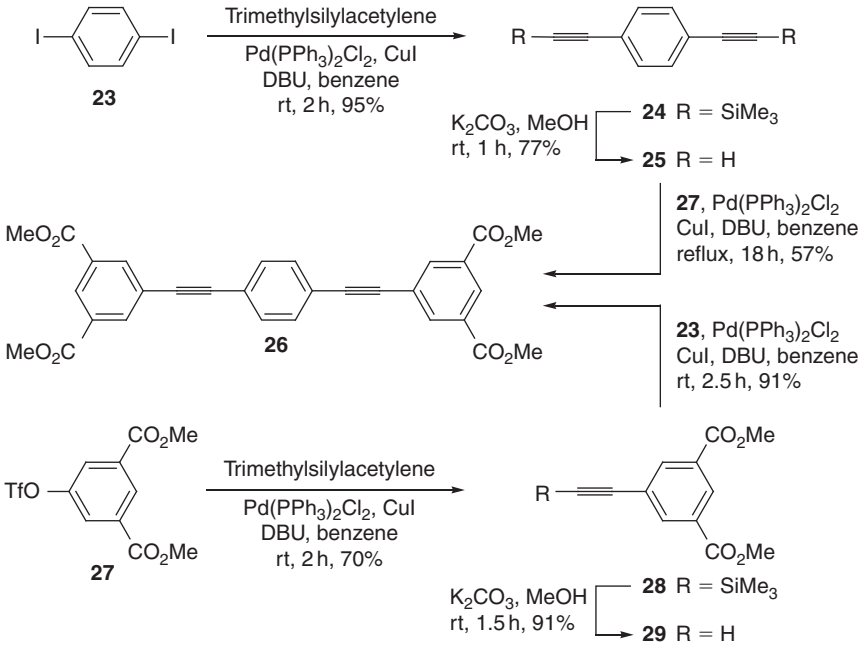
Over the past several years, our group has exploited a valence isomerization/dehydrogenation (VID) reaction to generate a family of [*n*](2,7)pyrenophanes **20** from the corresponding cyclophanedienes **19** (Scheme 1).[20,22] The bridge causes the pyrene system to adopt a non-planar geometry and the degree of distortion from planarity can be described by the angle θ,[22d] which is the smallest angle formed between the planes of atoms defined by C(1)-C(2)-C(3) and C(6)-C(7)-C(8) of the pyrene system. Semiempirical AM1 calculations typically predict larger (4–8°) bend angles (θ_{calc}) than those obtained from crystal structures ($\theta_{X\text{-}ray}$). As such, the AM1-calculated values are quite reliable indicators. The largest value of θ yet observed experimentally is 109.2°.[22b]

Incorporation of an aromatic system into the bridge of **20** affords a class of mixed cyclophane systems **21**, which includes

Table 1. Selected [2.2]cyclophanes, their Δd values and their methods of preparation
D, direct coupling approach; R, ring-contraction approach; A, aromatization-based approach

Entry	Cyclophane	Δ*d* [Å]	Method of preparation	Lit.	Entry	Cyclophane	Δ*d* [Å]	Method of preparation	Lit.
1	 **1**	0.00	D, R	Ref. 4	10	 **10**	0.95	R	Ref. 13
2	 **2**	0.00	D, R	Ref. 5	11	 **11**	1.45	R	Ref. 14
3	 **3**	0.01	R	Ref. 6	12	 **12**	1.52	R	Ref. 15
4	 **4**	0.03	D	Ref. 7	13	 **13**	1.69	R	Ref. 16
5	 **5**	0.46	D	Ref. 8	14	 **14**	1.70	R fails	Ref. 17
6	 **6**	0.58	R	Ref. 9	15	 **15**	2.01	R	Ref. 18
7	 **7**	0.77	R	Ref. 10	16	 **16**	3.80	A	Ref. 19
8	 **8**	0.79	R	Ref. 11	17	 **17**	4.25	A	Ref. 20
9	 **9**	0.92	D	Ref. 12	18	 **18**	5.04	A	This work

three mixed [2.2]cyclophanes of pyrene and benzene: **17**,[20] **18**, and **22** (Scheme 1). To evaluate the viability of these compounds as synthetic targets, parameters such as θ and Δd can be considered. Both parameters suggest that the synthetic challenge is likely to increase in going from **17** ($\Delta d = 4.25$ Å, $\theta_{calc} = 100.4°$, $\theta_{X\text{-}ray} = 89.7°$)[20] to **18** ($\Delta d = 5.04$ Å, $\theta_{calc} = 106.6°$) to **22** ($\Delta d = 7.05$ Å, $\theta_{calc} = 130.4°$). Likewise, both parameters seem to indicate a much larger increase in challenge



Scheme 2. Two synthetic routes to **26**.

(or strain) in going from **18** to **22** than in going from **17** to **18**. The Δd values of **17**, **18**, and **22** are unprecedented for [2.2] cyclophanes, so there is no basis for comparison with other systems. Therefore, the θ_{calc} values were used as grounds for restricting the synthetic work to targets **17** and **18**. The θ_{calc} value for **22** (130.4°) is comparable to that of 1,6-dioxa[6](2,7) pyrenophane ($\theta_{calc} = 132.1°$),[22f] which was previously found to be completely unreactive in the VID reaction.

As a final point, it is worth noting that **17** and **18** are not the only known mixed [2.2]cyclophanes of pyrene and benzene. [2]Metacyclo[2](1,3)pyrenophane (**3**)[6] and several of its derivatives have been reported.[23] However, with Δd values approaching zero, these systems are only of peripheral relevance to the current investigation.

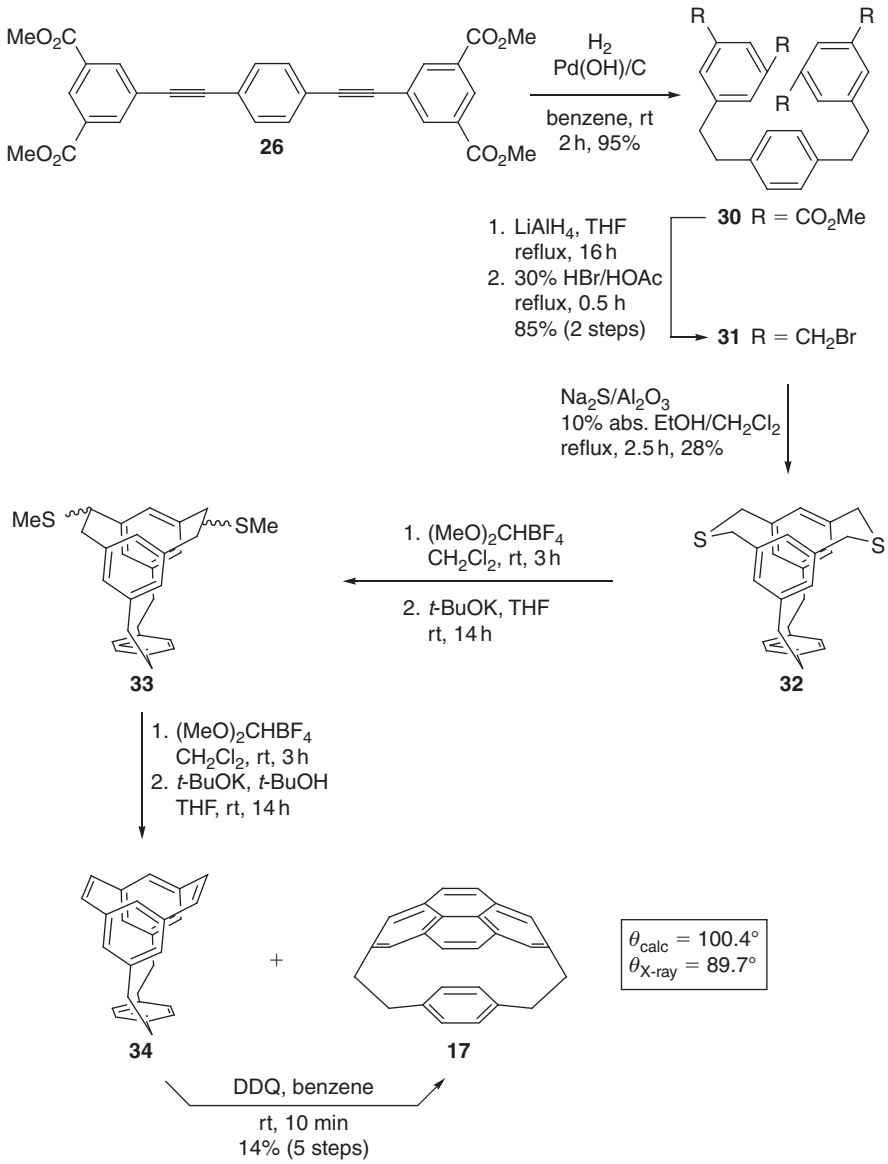
Results and Discussion

For the synthesis of [2]paracyclo[2](2,7)pyrenophane (**17**), two complementary routes starting from 1,4-diiodobenzene (**23**) and triflate **27**[22c] were initially investigated (Scheme 2). In the first of these, Sonogashira coupling of 1,4-diiodobenzene (**23**) with two equivalents of trimethylsilylacetylene gave diyne **24** (95%), which was protodesilylated to yield 1,4-diethynylbenzene **25** (77%). This compound could be conveniently purified on a small scale using sublimation at atmospheric pressure, but explosive decomposition took place when this was attempted with ~4 g of material. Diyne **25** was subjected to Sonogashira coupling using two equivalents of triflate **27** to form tetraester **26** (57%). The low solubility of this diyne complicated its purification and might also have contributed to the relatively low yield.

An alternative route to **26** was then investigated, in which the order of the Sonogashira couplings was reversed (Scheme 2). Starting from triflate **27**, Sonogashira coupling with trimethylsilylacetylene yielded diester **28** (70%). Protodesilylation gave the corresponding terminal alkyne **29** (91%), which was coupled with 1,4-diiodobenzene **23** under Sonogashira conditions to yield diyne **26** in 91% yield (based on 1,4-diiodobenzene). Again, the low solubility of **26** rendered its purification problematic. However, the crude mixture from this Sonogashira coupling was of higher purity than that obtained from the previous route. This, in conjunction with the explosive nature of **25**, made the second approach the preferred one for the production of synthetically useful quantities of **26**.

Since diynetetraester **26** already contains all of the carbon atoms necessary for the synthesis of pyrenophane **17**, the remainder of the synthesis consisted of a series of functional group interconversions and intramolecular carbon-carbon bond-forming reactions (Scheme 3). This commenced with catalytic hydrogenation of the alkyne units in **26** to give tetraester **30** (95%), which revealed the ethano units that would ultimately become the bridges of pyrenophane **17**. The hydrogenation of **26** was somewhat problematic due to its low solubility. Small-scale hydrogenations could be performed using saturated (dilute) solutions of **26** in THF or benzene, but when larger amounts of **30** were required, this method became impractical due to the large volumes of solvent required. For the catalytic hydrogenation of larger quantities of **26**, slow addition of a slurry of **26** in THF to a suspension of catalyst in THF under an atmosphere of hydrogen proved to be the most convenient method (both methods gave **30** in ~95% yield). Tetraester **30** was reacted with excess $LiAlH_4$ in THF to afford the corresponding tetraalcohol, which was reacted in crude form with 30% HBr/HOAc to provide tetrabromide **31** (85%, 2 steps). Attempted conversion of tetrabromide **31** into dithiacyclophane **32** using Na_2S/Al_2O_3 under standard conditions (10% abs. $EtOH/CH_2Cl_2$)[24] afforded the product in less than 3% yield and in low purity (~75% by ^1H NMR analysis). However, when the reaction was performed at reflux temperature, dithiacyclophane **32** was formed in 28% yield. Changing the solvent mixture from CH_2Cl_2/EtOH to $CHCl_3$/EtOH in order to increase the reflux temperature did not further increase the yield.

The difficulty in synthesizing dithiacyclophane **32** was presumably due primarily to the strained nature of the product. An X-ray crystal structure determination (Fig. 2 and Accessory Publication) revealed several non-ideal structural features.



Scheme 3. Synthesis of [2]paracyclo[2](2,7)pyrenophane **17**.

The two trisubstituted benzene rings are boat-shaped, but the distortion from planarity is slight ($\alpha = 2.9°$ and 2.1° at the bow and stern, respectively).[25] The β angles[25] for these rings are also small (1.8–2.5°). More striking is that the smallest angle formed by the average planes of the two trisubstituted rings is 55.8°, which is considerably larger than the angle observed for the parent *syn*-2,11-dithia[3.3]metacyclophane (20.6°).[26] The disubstituted benzene ring is essentially planar ($\alpha = 0.2°$), but the benzylic carbon atoms are bent significantly out of the plane of the benzene ring ($\beta = 8.6°$). Additionally, significantly expanded bond angles are observed at all of the benzylic carbon atoms (116.2(2)° at C(1), 115.1(2)° at C(2), 116.4(3)° at C(9), 113.1(4)° at C(10)). The size and the rigidity of the *p*-phenylene unit is presumably responsible for the splaying of the two trisubstituted benzene rings and the enlargement of the bond angles at the benzylic carbon atoms.

Bridge contraction of dithiacyclophane **32** was accomplished by methylation of the sulfur atoms using Borch reagent, followed by treatment of the resulting bis(methylsulfonium) salt with potassium *tert*-butoxide to induce thia-Stevens rearrangement. This yielded **33** as a mixture of isomers (70% crude from **32**). Methylation of the sulfur atoms in **33** using Borch reagent, followed by Hofmann elimination of the resulting bis(dimethylsulfonium) salts gave a mixture (~1:1 by ^{1}H NMR analysis) of cyclophanediene **34** and the desired [2]paracyclo[2](2,7)pyrenophane **17**. The mixture was converted cleanly to pyrenophane **17** by treatment of the mixture with DDQ in benzene to yield **3** in 14% overall yield from dithiacyclophane **32**.

The formation of **17** during the Hofmann elimination step was somewhat surprising since the formation of pyrenophanes with comparable calculated bend angles (θ) usually requires treatment of the corresponding cyclophanediene with DDQ in hot benzene. The unexpected reactivity of **34** can, as above, be explained by the presence of the rigid *para*-phenylene unit, which forces open the *syn*-[2.2]metacyclophanediene system relative to those present in the precursors to the [*n*](2,7)pyrenophanes. The resulting increase in the inter-ring angle moves the internal C atoms closer to one another and presumably lowers the activation energy to the formation of a bond between them.

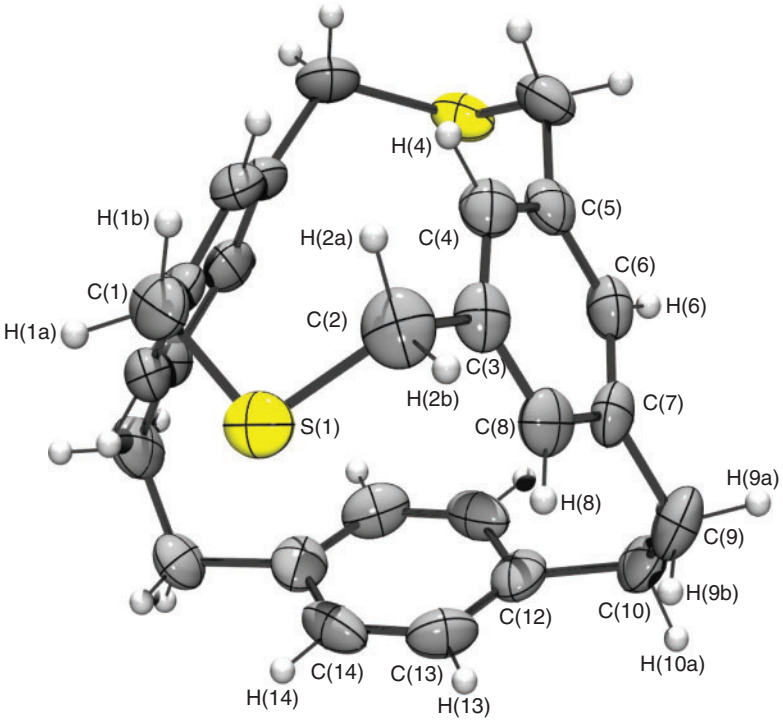


Fig. 2. POV-Ray representation of **32** in the crystal.

At 2%, the overall yield of pyrenophane **17** from triflate **27** is disappointingly low (longest linear sequence: 3% from **17**). This can be traced back to two particular synthetic transformations: the cyclization to furnish strained dithiacyclophane **32** and the often-problematic methylation-Hofmann elimination sequence to form the mixture of **34** and **17**. The crystal structure and ^{1}H NMR spectrum of **17** were discussed in detail in the communication,[20] so they will not be revisited here.

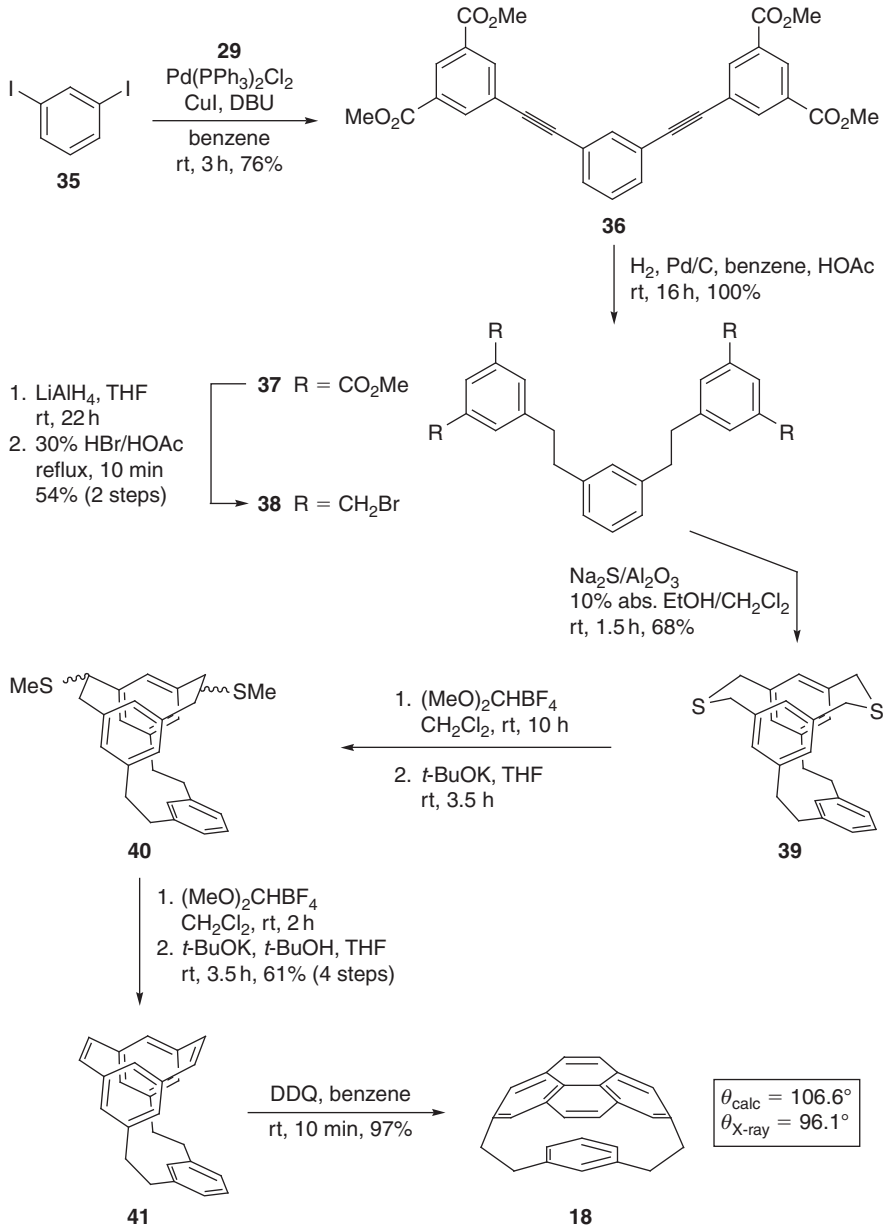
Having successfully synthesized **17**, attention was turned to the isomeric [2]metacyclo[2](2,7)pyrenophane **18**. This was expected to be a more challenging target because the calculated values of θ (106.6°) and Δd (5.04 Å) are both larger than the corresponding values for **17**. As described below, this turned out not to be the case.

The synthetic plan for pyrenophane **18** mirrored that of **17**. Accordingly, it began with Sonogashira coupling of 1,3-diiodobenzene **36** with alkyne **29**, which proceeded in 76% yield to give diyne **36** (Scheme 4). Diyne **36** was found to be more soluble than its constitutional isomer **26**, so it could be purified easily using column chromatography. Catalytic hydrogenation of **36** also proceeded more easily, yielding tetraester **37** in quantitative yield. Reduction of **37** with excess $LiAlH_4$ in THF, followed by treatment of the crude product with 30% HBr/HOAc then afforded tetrabromide **38** in 54% yield. In contrast to the difficulties experienced in the synthesis of dithiacyclophane **32**, reaction of tetrabromide **38** with Na_2S/Al_2O_3 under standard cyclization conditions[24] delivered dithiacyclophane **39** smoothly in 68% yield.

Methylation of the sulfur atoms in the bridges of dithiacyclophane **39** with Borch reagent, followed by treatment of the resulting bis(methylsulfonium) salt with potassium *tert*-butoxide yielded **40** as a mixture of isomers in 88% crude yield from **39**. After treatment of the isomer mixture **40** with Borch reagent to methylate the sulfur atoms, the resulting bis(methylsulfonium) salt was treated with potassium *tert*-butoxide (Hofmann elimination) to form cyclophanediene **41** in 61% yield from dithiacyclophane **39**. Not only is the yield considerably better than that of **34** (and **17**) from **32** (16%), but cyclophanediene **41** was obtained in pure form, i.e. without even trace amounts of pyrenophane **18** (^{1}H NMR analysis). Treatment of a room temperature solution of cyclophanediene **41** in benzene with DDQ resulted in rapid formation of the desired [2]metacyclo[2](2,7)pyrenophane **18** (97%). Without any optimization at all, the overall yield of **18** from 1,3-diiodobenzene **35** is 17% over 10 steps.

The mild conditions for the formation of pyrenophane **18** (and also **17**) are interesting because most other VID reactions leading to pyrenophanes have been conducted using benzene solutions at reflux. Although it may simply be the case that pyrenophanes **17** and **18** are well disposed to VID reaction, it raises the question of whether the VID reactions leading to previously reported pyrenophanes might also proceed at room temperature.

An X-ray crystal structure determination of **18** (crystals from toluene) revealed two independent molecules in the unit cell (Fig. 3, **18a** on the bottom, **18b** on the top). The bend angles are $\theta_{X\text{-ray}} = 96.5°$ for **18a** and $\theta_{X\text{-ray}} = 95.6°$ for **18b**, which are 10.5° (on average) less than the AM1-calculated value ($\theta_{calc} = 106.6°$). As was observed for **17**,[20] this is a little higher than the previously observed differences between calculated and experimentally determined values.[22] The β angles (**18a**: $\beta_{C(17)} = 17.7°$ and $\beta_{C(26)} = 17.6°$; **18b**: $\beta_{C(43)} = 18.4°$ and $\beta_{C(52)} = 17.4°$; average = 17.8°) are even larger than in **17** (16.1–16.3°) and the [*n*](2,7)pyrenophanes (up to 9°). The isolated benzene ring in **18** is, similar to that in **17**, essentially planar ($\alpha < 2.5°$) and the *m*-xyxlene unit is bowed slightly towards the concave face of the pyrene system ($\beta_{\mathbf{18a}C(18)} = 3.9°$, $\beta_{\mathbf{18a}C(25)} = 3.3°$, $\beta_{\mathbf{18b}C(44)} = 7.0°$, $\beta_{\mathbf{18b}C(51)} = 3.6°$). However, in contrast to **17**, the isolated benzene ring in **18** does not lie directly underneath the pyrene system, but rather is slipped to one side. The bridges in **18** exist



Scheme 4. Synthesis of [2]metacyclo[2](2,7)pyrenophane **18**.

in nearly staggered conformations, with a torsional angle around the ethano unit of 51°. This aspect of the structure stands in stark contrast to the nearly eclipsed bridges in **17** and the torsional strain associated with eclipsing may well be a major reason why **18** and its cyclophane precursors (**39**–**41**) were considerably easier to synthesize than their *para*-substituted counterparts (**32**–**34** and **17**).

A final noteworthy feature of the crystal structure of **18** is the presence of several short intermolecular C–H$\cdots\pi$ contacts, which are indicated in Fig. 3. H(48) in molecule **18b** is 2.96 Å from the centroid of the C(4)-C(5)-C(10)-C(11)-C(12)-C(13) ring in molecule **18a** and 3.65 Å from the centroid of the C(3)-C(4)-C(7)-C(8)-C(9)-C(10) ring, also in molecule **18a**. Additionally, H(40) and H(52A) in molecule **18b** are 3.41 and 3.23 Å, respectively, from the centroid of the C(9)-C(10)-C(11)-C(14)-C(15)-C(16) ring in molecule **18a**. It would now appear that 'edge-to-face' C-H$\cdots\pi$ interactions, which are well documented for planar π systems,[27] can also be observed in non-planar aromatic systems. A previously reported compound that also contains two chemically equivalent moieties in the asymmetric unit was also observed to exhibit C-H$\cdots\pi$ interactions in the range of 2.59–2.85 Å.[22l]

The 500 MHz ^{1}H NMR spectrum of pyrenophane **18** showed four signals for the pyrene system instead of the usual two,[22] and four signals were observed for the protons on the ethano bridges. This is consistent with a slow conformational flip of the isolated benzene ring on the NMR time scale that interconverts two degenerate conformers (Fig. 4).

All signals in the ^{1}H NMR spectrum were assigned unambiguously using a variety of standard NMR experiments, including HMQC, HMBC, and NOESY (Fig. 4). The internal proton of the isolated benzene ring in **5** is located in the heart of the shielding cone of the pyrene system, so it appears at very high field (δ 4.18). Coincidentally, this is almost identical to that of the internal proton of *anti*-[2.2]metacyclophane **8**.[28] A smaller shielding effect was observed for the external protons, which

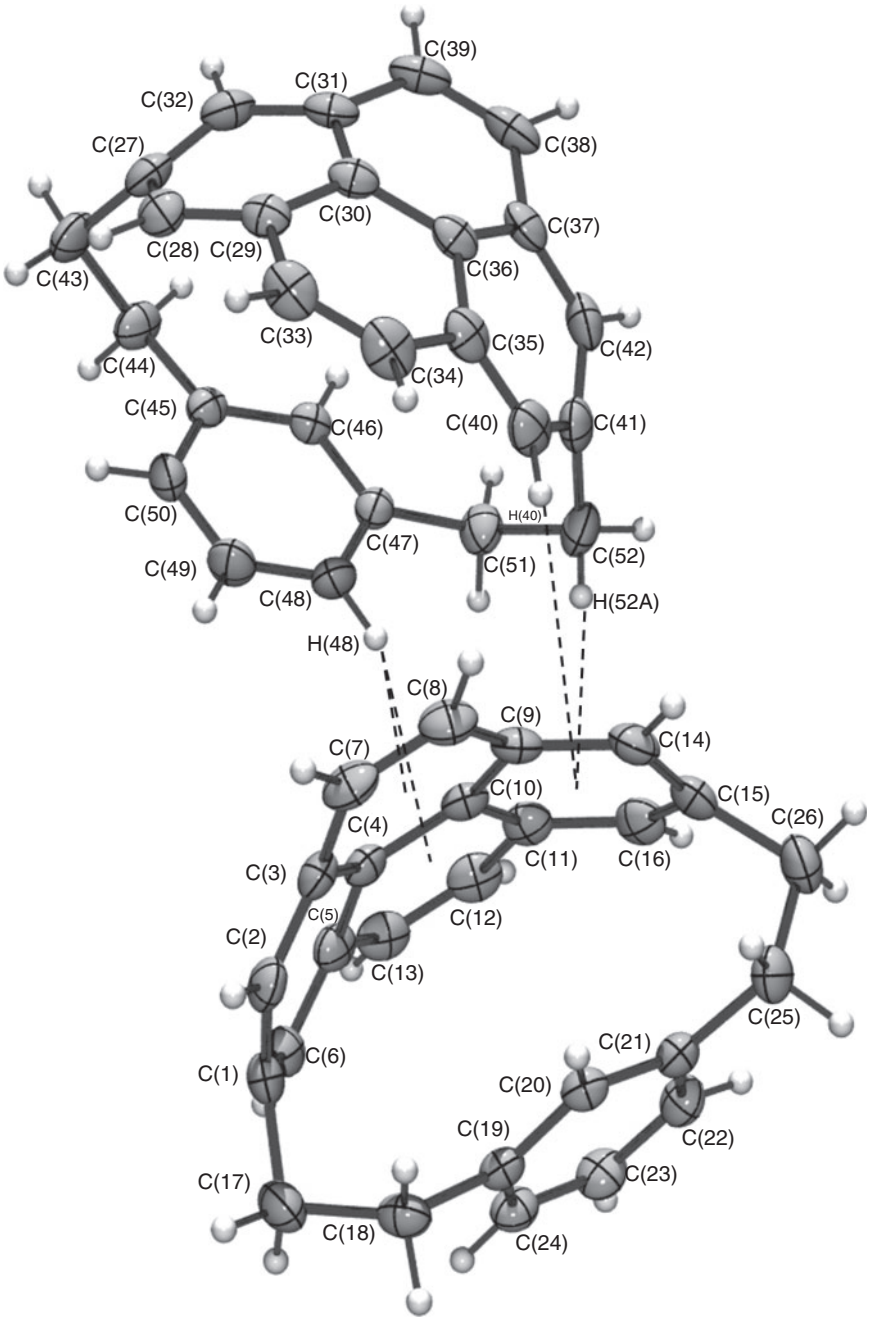
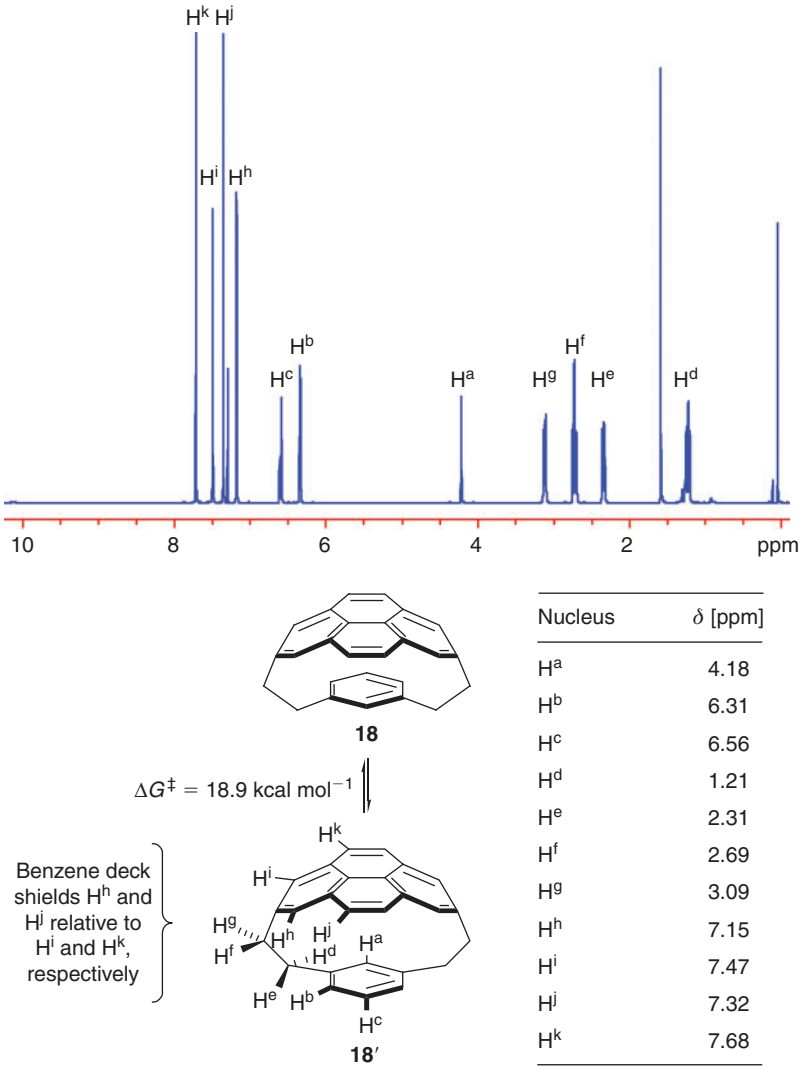


Fig. 3. POV-Ray representation of **18** in the crystal. Short intermolecular C–H$\cdots\pi$ distances are indicated by dashed lines.

appeared as a triplet at δ 6.56 and a doublet at δ 6.31. Being situated underneath one side of the pyrene system, the isolated benzene ring shields the two types of aryl protons that lie above it. Thus H^h (δ 7.15) and H^j (δ 7.32) resonate at higher field than their counterparts H^i (δ 7.47) and H^k (δ 7.68) on the other side of the pyrene system. All four bridge protons are mutually coupled, giving rise to a set of four ddd, one of which (H^d) appears at unusually high field (δ 1.21). Upon examination of a three-dimensional structure of **18** (crystal structure or even simple molecular models), it can be seen that H^d is situated in the shielding zone of the pyrene system.

The energy barrier for the interconversion of **18** and **18′** was determined from a DNMR study. The flipping of the isolated benzene ring results in an exchange in the environments of H^d and H^e, H^f and H^g, H^i and H^h, and H^j and H^k. Although any of these pairs of signals could be used to determine the energy barrier, it proved to be most straightforward to use the signals for H^f and H^g. A DNMR experiment were performed using a solution of [2]metacyclo[2](2,7)pyrenophane **18** in nitrobenzene-d_5. A coalescence temperature of 396.8 K and $\delta_0 = 134.0$ Hz were used to calculate an activation barrier of 18.9 kcal mol^{-1}.[29] Substitution of the pyrene system (the carbon atoms bonded to H^h and H^i are presumably the most reactive sites) would afford diastereomeric products, but an energy barrier of this size would make any room temperature separation problematic and temporary.



Nucleus	δ [ppm]
H^a	4.18
H^b	6.31
H^c	6.56
H^d	1.21
H^e	2.31
H^f	2.69
H^g	3.09
H^h	7.15
H^i	7.47
H^j	7.32
H^k	7.68

Fig. 4. ^{1}H NMR spectrum of **18**, assignments and the ring flipping conformational process.

Conclusions

The VID methodology was found to be very effective in generating two strained mixed [2.2]cyclophanes of pyrene and benzene, pyrenophanes **17** and **18**, under very mild conditions (room temperature). Whereas the synthesis of **17** was problematic at several points, the synthesis of **18** was essentially problem-free. This is contrary to what might have been expected form the predicted values of θ and Δd, which are both significantly larger for **18** than they are for **17**. This serves to illustrate an important point: parameters such as θ and Δd are limited in their predictive value. For a start, they apply to the final targets and not to any of the synthetic precursors. More to the point, they describe a single structural feature, which may not necessarily be an adequate reflection of the strain in a given molecule. This is because the structure of any strained system derives from a compromise between various forms of strain and there is no reason to suggest that the exact position of the middle ground is anything other than case-dependent. In the case at hand, it seems likely that the difference in torsional strain (which is not accounted for in θ and Δd) between the bridges of **17** and **18** plays an important role.

Experimental

Methods and Materials

All chemicals were reagent grade and were used as received. Chromatographic separations were performed on Merck silica gel 60 (particle size 40–63 µm, 230–400 mesh). Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Elemental analyses were performed at the Micro-Analytical Service Laboratory, Department of Chemistry, University of Alberta. Mass spectroscopic (MS) data were obtained on a V. G. Micromass 7070HS instrument. ^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra were obtained on a Bruker AVANCE spectrometer. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were obtained on a General Electric GE 300-NB spectrometer. ^{1}H shifts are relative to internal tetramethylsilane; ^{13}C shifts are relative to the solvent resonance ($CDCl_3$: $\delta = 77.0$). DNMR experiments were recorded on a Bruker DRX-400 pulsed FT spectrometer operating at 400.1 MHz for ^{1}H. Chemical shifts were measured relative to the most downfield nitrobenzene-d_5 peak. All experiments with moisture- or air-sensitive compounds were performed in anhydrous solvents under nitrogen unless otherwise stated.

Solvents were dried and distilled according to standard procedures.

1,4-Bis(trimethylsilylethynyl)benzene ***24***

To a solution of 1,4-diiodobenzene **23** (10.25 g, 31.07 mmol) in degassed benzene (225 mL) under a nitrogen atmosphere, were added $(Ph_3P)_2PdCl_2$ (1.05 g, 1.50 mmol) and CuI (1.00 g, 5.25 mmol), followed after 5 min by trimethylsilylacetylene (7.65 g, 77.9 mmol) and DBU (14.19 g, 93.21 mmol). The reaction mixture was stirred at room temperature for 2 h, washed with saturated aqueous NH_4Cl solution (100 mL), washed with water (2×100 mL), washed with saturated aqueous NaCl solution (100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexanes) to give **24** (7.99 g, 29.5 mmol, 95%) as colourless crystals, mp 118–119°C (hexanes) (lit.[30] 122°C). ν_{max} (nujol)/cm^{-1} 2155 (s), 1492 (m), 1246 (s). δ_H (500 MHz, $CDCl_3$) 7.40 (s, 4H), 0.25 (s, 18H). δ_C (126 MHz, $CDCl_3$) 131.7, 123.1, 104.6, 96.3, −0.1. EI-MS (70 eV) *m/z* [%] 270 (27, M^+), 255 (100).

1,4-Diethynylbenzene ***25***

K_2CO_3 (3.54 g, 25.6 mmol) and 1,4-bis(trimethylsilylethynyl) benzene **24** (2.77 g, 13.3 mmol) were added to methanol (50 mL) and the reaction mixture was stirred for 1 h. The mixture was poured into ice water (100 mL) and filtered under suction. The residue was sublimed at atmospheric pressure (~95°C oil bath; CAUTION: in one instance this procedure led to explosive decomposition of the material) to give **25** (0.99 g, 77%) as colourless plates, mp 94–95°C (sublimes slowly above 76°C) (lit.[30] 95–96°C). δ_H (300 MHz, $CDCl_3$) 7.45 (s, 4H), 3.18 (s, 2H). δ_C (75 MHz, $CDCl_3$) 132.0, 122.5, 82.9, 79.2.

1,4-Bis(3,5-bis(methoxycarbonyl)phenylethynyl) benzene ***26***

Method A. To a solution of triflate **27** (3.22 g, 9.41 mmol) in degassed benzene (80 mL) under a nitrogen atmosphere were added $(Ph_3P)_2PdCl_2$ (0.08 g, 0.1 mmol) and CuI (0.08 g, 0.4 mmol), followed after 5 min by 1,4-diethynylbenzene **25** (0.54 g, 4.3 mmol) and DBU (1.95 g, 12.8 mmol). The reaction mixture was refluxed for 18 h, concentrated under reduced pressure and the residue was taken up in a mixture of $CHCl_3$ (250 mL) and saturated aqueous NH_4Cl solution (100 mL). The layers were separated and aqueous layer was extracted with $CHCl_3$ (100 mL). The combined organic layers were washed with water (2×100 mL), washed with saturated aqueous NaCl solution (100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, chloroform) to give **26** (1.25 g, 57%) as an off-white solid; mp >290°C dec. (chloroform). ν_{max} (nujol)/cm^{-1} 1732 (s), 1247 (m). δ_H (500 MHz, $CDCl_3$) 8.66 (s, 2H), 8.39 (s, 4H), 7.56 (s, 4H), 3.99 (s, 12H). δ_C (126 MHz, $CDCl_3$) 165.6, 136.5, 131.7, 131.1, 130.1, 124.1, 122.9, 90.7, 89.4, 52.5. *m/z* (EI, 70 eV) 510 (M^+, 100%), 479 (10), 224 (10). *m/z* (HRMS-EI, 70 eV). Anal. Calc. for $C_{30}H_{22}O_8$: 510.1313. Found: 510.1334.

Method B. To a solution of 1,4-diiodobenzene **23** (6.03 g, 18.3 mmol) in degassed benzene (400 mL) under a nitrogen atmosphere was added $(Ph_3P)_2PdCl_2$ (0.64 g, 0.91 mmol) and CuI (0.35 g, 1.8 mmol), followed after 5 min by dimethyl 5-ethynylisophtalate **29** (9.98 g, 45.7 mmol) and DBU (8.35 g, 54.8 mmol). The reaction mixture was stirred for 2.5 h, concentrated under reduced pressure and the residue was taken up in a mixture of $CHCl_3$ (1000 mL) and saturated aqueous NH_4Cl solution (500 mL). The layers were separated and the aqueous layer was extracted with $CHCl_3$ (500 mL). The combined organic layers were washed with water (2×500 mL), washed with saturated aqueous NaCl solution (500 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, chloroform) to give **26** (8.51 g, 16.7 mmol, 91%) as an off-white solid.

Dimethyl 5-(Trimethylsilylethynyl)benzene-1,3-dicarboxylate ***28***

To a solution of $(Ph_3P)_2PdCl_2$ (2.57 g, 3.66 mmol) and CuI (1.39 g, 7.30 mmol) in degassed benzene (400 mL) was added triflate **27** (25.07 g, 73.25 mmol), followed after 10 min by a solution of trimethylsilylacetylene (10.07 g, 102.5 mmol) in degassed benzene (200 mL) and DBU (16.70 g, 109.7 mmol). The mixture was stirred under a nitrogen atmosphere for 2 h, concentrated under reduced pressure and the residue was taken up in a mixture of chloroform (250 mL) and saturated NH_4Cl solution (200 mL). The aqueous layer was extracted with chloroform (150 mL). The combined organic layers were washed with water (200 mL), washed with saturated aqueous NaCl solution (200 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 10% ethyl acetate/hexanes) to yield **28** (14.92 g, 51.38 mmol, 70%) as a colourless solid, mp 100–101.5°C. ν_{max} (nujol)/cm^{-1} 2159 (w), 1734 (s), 1593 (w), 1332 (m), 1242 (s). δ_H (500 MHz, $CDCl_3$) 8.61 (s, 1H), 8.30 (s, 2H), 3.96 (s, 6H), 0.27 (s, 9H). δ_C (126 MHz, $CDCl_3$) 165.5, 136.8, 130.8, 130.3, 124.2, 102.7, 96.7, 52.5, −0.22. *m/z* (EI, 70 eV) 290 (M^+, 10%), 275 (100), 259 (9), 201 (10). Anal. Calc. for $C_{15}H_{18}O_4Si$: C 62.04, H 6.25. Found: C 62.23, H 6.36%.

Dimethyl 5-Ethynylisophthalate ***29***

A mixture of dimethyl 5-(trimethylsilylethynyl)benzene-1,3-dicarboxylate **28** (14.92 g, 51.38 mmol), K_2CO_3 (9.23 g, 66.8 mmol), and methanol (650 mL) was stirred under a nitrogen atmosphere for 1.5 h and then poured into water (1000 mL). The resulting mixture was subjected to suction filtration and the solids were washed with water (2×100 mL) and dried under vacuum to afford dimethyl 5-ethynylisophthalate **29** (10.19 g, 46.70 mmol, 91%) as a colourless powder, mp 127–128°C. δ_H (500 MHz, $CDCl_3$) 8.53 (s, 2H), 8.07 (s, 4H), 7.11 (s, 4H), 3.95 (s, 12H), 3.04–2.97 (m, 4H), 2.96–2.89 (s, 4H). δ_C (126 MHz, $CDCl_3$) 166.4, 142.9, 138.9, 133.9, 130.6, 128.6 (2C), 52.3, 37.6, 37.2. *m/z* (EI, 70 eV) 218 (M^+, 50%), 187 (100), 159 (28), 144 (22).

1,4-Bis(2-(3,5-bis(methoxycarbonyl)phenyl)ethyl) benzene ***30***

To a solution of diyne **26** (0.64 g, 1.3 mmol) in degassed benzene (300 mL) was added Pd(OH)/C (Pearlman's catalyst, 0.40 g) and the mixture was stirred vigorously under an atmosphere of hydrogen for 2 h. The flask was purged with nitrogen several times before the contents were filtered through a plug of Celite. The filtrate was concentrated under reduced pressure to afford tetraester **30** (0.62 g, 95%) as a colourless solid, mp 146–147.5°C (chloroform/hexanes). δ_H (500 MHz, $CDCl_3$) 8.56 (s, 2H), 8.10 (s, 4H), 7.14 (s, 4H), 3.98 (s, 8H), 3.04 (m, 4H), 2.96 (m, 4H). δ_C (126 MHz, $CDCl_3$) 166.4, 142.7, 138.8, 133.9, 130.6, 128.5 (2C), 52.3, 37.6, 37.2. *m/z* (EI, 70 eV) 518 (M^+,

6%), 486 (55), 426 (5), 311 (33), 281 (100), 207 (79), 104 (45). Anal. Calc. for $C_{30}H_{30}O_8$: C 69.49, H 5.83. Found: C 69.24, H 5.94%.

*1,4-Bis(2-(3,5-bis(bromomethyl)phenyl)ethyl)benzene **31***

A solution of tetraester **30** (2.16 g, 4.17 mmol) in THF (100 mL) was added dropwise to a well stirred suspension of $LiAlH_4$ (1.90 g, 50.1 mmol) in THF at 0°C under nitrogen. The resulting mixture was stirred at reflux for 16 h, cooled in an ice-bath, and quenched with ethyl acetate (10 mL). The mixture was concentrated under reduced pressure and the residue was suspended in glacial acetic acid (100 mL). 30% HBr/HOAc (10 mL, 50 mmol) was then added and the resulting mixture was heated at reflux for 30 min. After cooling to room temperature, the mixture was poured into water (200 mL) and extracted with CH_2Cl_2 (2×200 mL). The combined organic layers were washed with water (2×150 mL), washed with saturated aqueous $NaHCO_3$ solution (2×150 mL), washed with water (100 mL), washed with saturated aqueous NaCl solution (100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 50% $CHCl_3$/hexanes) to afford tetrabromide **31** (2.33 g, 85%) as a white solid, mp 142.5–143.5°C (hexanes). δ_H (500 MHz, $CDCl_3$) 7.26 (overlapped with solvent, s, 2H), 7.13 (s, 4H), 7.09 (s, 4H), 4.45 (s, 8H), 2.89 (s, 8H). δ_C (126 MHz, $CDCl_3$) 143.1, 138.9, 138.3, 129.3, 128.5, 127.2. *m/z* (EI, 70 eV) 658 (M^+ ($^{81}Br)_2(^{79}Br)_2$, 5%), 497 (17), 417 (27), 381 (100). *m/z* (HRMS-EI, 70 eV). Anal. Calc. for $C_{30}H_{22}(^{79}Br)_4$: 653.8765. Found: 653.8772.

*Belta-2,11-dithia[3.3](1,3)(1,3)[2](5)(1)[2](4)(5)benzeno⟨3⟩phane[31] **32***

To a well stirred, refluxing solution of tetrabromide **31** (2.48 g, 3.77 mmol) in degassed 10% ethanol (abs)/CH_2Cl_2 (825 mL) was added Na_2S/Al_2O_3[24] (7.83 g, 19.4 mmol) in three roughly equal portions over 1 h. After stirring for 1.5 h at reflux temperature, the reaction mixture was cooled to room temperature and suction filtered through a plug of Celite. The filtrate was concentrated under reduced pressure and the residue was subjected to column chromatography (silica gel, 25% $CHCl_3$/hexanes) to afford dithiacyclophane **32** (0.43 g, 28%) as a colourless, foamy solid, mp >280°C. δ_H (500 MHz, $CDCl_3$) 6.96 (br s, 2H), 6.87 (s, 4H), 6.52 (s, 4H), 3.71 (nearly degenerate AB system, 8H), 2.99 (t, *J* 7.0, 4H), 2.86 (t, *J* 6.9, 4H). δ_C (126 MHz, $CDCl_3$) 140.4, 137.2, 137.0, 129.1, 128.7, 128.0, 40.5, 34.9, 32.8. *m/z* (EI, 70 eV) 402 (M^+, 100%), 369 (27), 338 (36). *m/z*(HRMS-EI, 70 eV). Anal. Calc. for $C_{26}H_{26}S_2$: 402.1475. Found: 402.1493.

*Belta[2.2](1,3)(1,3)[2](5)(1)[2](4)(5)benzeno⟨3⟩phane-1,9-diene[31] **34** and [2]Paracyclo[2](2,7)pyrenophane **17***

To a stirred solution of dithiacyclophane **32** (0.60 g, 1.5 mmol) in degassed CH_2Cl_2 (120 mL) under an atmosphere of nitrogen, was added $(MeO)_2CHBF_4$ (1.21 g, 7.47 mmol) and after 3 h the mixture was concentrated under reduced pressure. Ethyl acetate (50 mL) was added to the residue and the mixture was stirred for 5 min before being suction filtered. The beige solid that was collected was washed with ethyl acetate (2×3 mL) and dried under vacuum to yield a bis(sulfonium tetrafluoroborate) salt. This was slurried in degassed THF (120 mL) under nitrogen and *t*-BuOK (0.50 g, 4.5 mmol) was added. The reaction mixture was stirred overnight and saturated aqueous NH_4Cl solution (50 mL) was added. The resulting mixture was concentrated under reduced pressure and the residue was taken up in degassed CH_2Cl_2 (100 mL). The organic solution was washed with saturated aqueous NH_4Cl solution (50 mL), washed with water (50 mL), washed with saturated aqueous NaCl solution (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was passed through a plug of silica gel ($CHCl_3$) and concentration of the filtrate afforded a mixture of bis(methylthio)cyclophane isomers **33** (0.45 g, 70% from **32**) as a foamy, light yellow solid. To a solution of this solid in degassed CH_2Cl_2 (100 mL) was added slowly $(MeO)_2CHBF_4$ (0.85 g, 5.3 mmol) and the mixture was stirred for 3 h under an atmosphere of nitrogen. The mixture was concentrated under reduced pressure and ethyl acetate (15 mL) and methanol (5 mL) were added to the residue. The resulting mixture was stirred for 5 min and then concentrated under reduced pressure to give a brown oil. This oil was stirred in degassed 1:1 *t*-BuOH/THF (100 mL) under nitrogen and *t*-BuOK (0.35 g, 3.1 mmol) was added. After stirring for 16 h, saturated aqueous NH_4Cl solution (20 mL) was added and the mixture was concentrated under reduced pressure. The residue was taken up in degassed CH_2Cl_2 (100 mL) and saturated aqueous NH_4Cl solution (75 mL). The layers were separated and the aqueous layer was extracted with degassed CH_2Cl_2 (50 mL). The combined organic layers were washed with water (100 mL) and saturated aqueous NaCl solution (100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was concentrated under reduced pressure to afford a mixture of cyclophanediene **34** and [2]paracyclo[2](2,7)pyrenophane **17** (0.08 g, 16% from **32**) as a colourless solid. The mixture was dissolved in degassed benzene (25 mL) under nitrogen and DDQ (0.04 g, 0.2 mmol) was added. The mixture was stirred for 10 min at room temperature and then concentrated under reduced pressure. The residue was purified by preparative TLC (silica gel, 60% $CHCl_3$/hexanes) to yield [2]paracyclo[2](2,7)pyrenophane **17** (0.07 g, 14% from **32**) as a colourless solid, which was crystallized from heptane, mp 216–219°C. δ_H (500 MHz, $CDCl_3$) 7.67 (s, 4H), 7.40 (s, 4H), 5.54 (s, 4H), 2.99 (t, *J* 7.3, 4H), 2.32 (t, *J* 7.2, 4H). δ_C (126 MHz, $CDCl_3$) 135.7, 134.2, 131.3, 129.3, 128.6, 128.0, 126.1, 36.5, 33.8. *m/z* (EI, 70 eV) 332 (M^+, 11%), 228 (100). *m/z* (HRMS-EI, 70 eV). Anal. Calc. for $C_{26}H_{20}$: 332.1564. Found: 332.1562.

*1,3-Bis(3,5-bis(methoxycarbonyl)phenylethynyl)benzene **36***

To a solution of $(Ph_3P)_2PdCl_2$ (0.39 g, 0.56 mmol) and CuI (0.39 g, 2.0 mmol) in degassed benzene (250 mL) under nitrogen was added 1,3-diiodobenzene **35** (3.66 g, 11.1 mmol), followed after 5 min by a solution of triflate **29** (5.33 g, 24.4 mmol) in degassed benzene (150 mL) and DBU (4.23 g, 27.8 mmol). The reaction mixture was stirred at room temperature under an atmosphere of nitrogen for 3 h, concentrated under reduced pressure and taken up in a mixture of $CHCl_3$ (200 mL) and saturated aqueous NH_4Cl solution (100 mL). The layers were separated and the aqueous layer was extracted with $CHCl_3$ (150 mL). The combined organic layers were washed with saturated aqueous NH_4Cl solution (100 mL), washed with water (100 mL), washed with saturated aqueous NaCl solution (100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel, 2% EtOAc/$CHCl_3$) to yield **36** (4.31 g, 8.44 mmol, 76%) as a beige solid that was crystallized from EtOH/$CHCl_3$,

mp 176–177.5°C (ethanol/chloroform). ν_{max} (nujol)/cm^{-1} 2216 (w), 1734 (s), 1290 (w), 1249 (m), 1008 (w), 751 (w). δ_H (500.1 MHz, $CDCl_3$) 8.65 (s, 2H), 8.38 (s, 4H), 7.76 (s, 1H), 7.56 (d, *J* 7.9, 2H), 7.04 (t, *J* 7.7, 1H), 3.98 (s, 12H). δ_C (126 MHz, $CDCl_3$) 165.6, 136.5, 134.9, 131.9, 131.0, 130.3, 128.7, 124.1, 123.0, 90.2, 88.1, 52.6. *m/z* (EI, 70 eV) 510 (M^+, 100%), 479 (25), 224 (25). Anal. Calc. for $C_{30}H_{22}O_8$: C 70.58, H 4.34. Found: C 70.10, H 4.19%.

1,3-Bis(2-(3,5-bis(methoxycarbonyl)phenyl)ethyl) benzene ***37***

A mixture of **36** (4.31 g, 8.44 mmol), 20% Pd/C (0.35 g), degassed benzene (700 mL), and acetic acid (0.1 mL) was stirred under a hydrogen atmosphere for 16 h. The reaction mixture was purged with nitrogen for 20 min and then filtered through a plug of $MgSO_4$. The filtrate was concentrated under reduced pressure to yield **37** (4.37 g, 8.44 mmol, 100%) as a colourless oil, which solidified upon standing, mp 150–151.5°C (benzene). δ_H (500.1 MHz, $CDCl_3$) 8.53 (s, 2H), 8.05 (s, 4H), 7.22 (t, *J* 7.4, 1H), 7.04 (d, *J* 7.6, 2H), 6.98 (s, 1H), 3.94 (s, 9H), 2.99 (m, 4H), 2.92 (m, 4H). δ_C (126 MHz, $CDCl_3$) 166.4, 142.6, 141.1, 133.9, 130.6, 128.7, 128.6, 128.5, 126.3, 52.3, 37.6. *m/z* (EI, 70 eV) 518 (M^+, 6%), 486 (83), 311 (22), 281 (100), 207 (50), 177 (10), 104 (17). Anal. Calc. for $C_{30}H_{30}O_8$: C 69.49, H 5.83. Found: C 69.28, H 5.89%.

1,3-Bis(2-(3,5-bis(bromomethyl)phenyl)ethyl)benzene ***38***

A solution of **37** (4.33 g, 8.35 mmol) in dry THF (150 mL) was added over 45 min to a well stirred, 0°C suspension of $LiAlH_4$ (3.80 g, 10.0 mmol) in dry THF (200 mL) under a nitrogen atmosphere. The resulting mixture was stirred at room temperature for 22 h, cooled in an ice-bath, quenched with ethyl acetate (20 mL) and concentrated under reduced pressure. 30% HBr/HOAc (125 mL) was carefully added to the residue and the mixture was heated to reflux, cooled and poured into ice water (300 mL). The resulting mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution (3 × 100 mL), washed with water (100 mL), washed with saturated aqueous NaCl solution (100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel, 50% $CHCl_3$/hexanes) to yield **38** (2.95 g, 4.48 mmol, 54%) as a white solid, mp 109–111.5°C ($CHCl_3$/hexanes). δ_H (500.1 MHz, $CDCl_3$) 7.27 (s, 2H), 7.22 (t, *J* 7.5, 1H), 7.14 (s, 4H), 7.02 (d, *J* 7.5, 2H), 6.94 (s, 1H), 4.45 (s, 8H), 2.89 (s, 8H). δ_C (126 MHz, $CDCl_3$) 143.1, 141.3, 138.4, 129.3, 128.7, 128.5, 127.2, 126.2, 37.6, 37.5, 33.0. *m/z* (EI, 70 eV) 658 (M^+ ($^{81}Br)_2(^{79}Br)_2$, 5%), 577 (3), 497 (59), 417 (87), 381 (100), 335 (29), 219 (43). Anal. Calc. for $C_{26}H_{26}Br_4$: C 47.45, H 3.98. Found: C 47.37, H 3.72%.

Belta-2,11-dithia[3.3](1,3)(1,3)[2](5)(1)[2](3)(5) benzeno⟨3⟩phane[31] ***39***

To a vigorously stirred solution of **38** (2.35 g, 3.57 mmol) in ethanol (abs, 200 mL) and CH_2Cl_2 (1800 mL) was added Na_2S/Al_2O_3 (12.0 g, 4.0 mmol; 3.0 mmol g^{-1}) in three approximately equal portions over 30 min. The reaction mixture was stirred for 1.5 h and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure and the residue was subjected to column chromatography (silica gel, 50% $CHCl_3$/hexanes) to yield **39** (0.98 g, 2.4 mmol, 68%) as a colourless, crystalline solid, mp >218°C dec. ($CHCl_3$/hexanes). δ_H (500.1 MHz, $CDCl_3$) 7.25 (t, *J* 7.6, 1H), 7.10 (s, 2H), 7.06 (d, *J* 7.8, 2H), 6.56 (s, 4H), 6.31 (s, 1H), 3.74 (m, 8H), 2.96 (m, 4H), 2.80 (m, 4H). δ_C (126 MHz, $CDCl_3$) 140.5, 140.3, 136.9, 129.3, 129.0, 128.0, 127.0, 125.9, 39.3, 35.1, 34.2. *m/z* (EI, 70 eV) 402 (M^+, 100%), 369 (23), 338 (25), 217 (14), 119 (29). Anal. Calc. for $C_{26}H_{26}S_2$: C 77.56, H 6.51. Found: C 76.44, H 6.51%.

Belta[2.2](1,3)(1,3)[2](5)(1)[2](3)(5)benzeno⟨3⟩ phane-1,9-diene[31] ***40***

To a well stirred solution of **39** (0.98 g, 2.4 mmol) in CH_2Cl_2 (200 mL) was added Borch reagent (1.18 g, 7.3 mmol) and the mixture was stirred at room temperature for 10 h. The reaction mixture was concentrated under reduced pressure, quenched with ethyl acetate (5 mL) and suction filtered, to yield (after drying under vacuum) a white solid (1.41 g) that was suspended in dry THF (200 mL). KO-*t*-Bu (1.37 g, 12.2 mmol) was added and the mixture was stirred vigorously at room temperature for 3.5 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl solution (5 mL) and the mixture was concentrated under reduced pressure. The residue was taken up in a mixture of CH_2Cl_2 (75 mL) and H_2O (25 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (30 mL) and the combined organic extracts were washed with H_2O (50 mL), washed with saturated aqueous NaCl solution (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was dissolved in $CHCl_3$ and passed through a plug of silica gel to yield isomer mixture **40** (0.92 g, 2.1 mmol, 88% crude from **39**) as a light yellow solid.

To a vigorously-stirred solution of isomer mixture **40** in CH_2Cl_2 (200 mL) was added Borch reagent (1.04 g, 6.4 mmol) dropwise over 5 min. The resulting mixture was stirred at room temperature for 2 h and then concentrated under reduced pressure. Ethyl acetate (5 mL) and methanol (1 mL) were added to the residue and the mixture was again concentrated under reduced pressure. The residue was slurried with THF (200 mL) and HO-*t*-Bu (2 mL) and KO-*t*-Bu (1.20 g, 10.7 mmol) were added. The mixture was stirred vigorously for 3.5 h and the reaction was quenched by the addition of saturated aqueous NH_4Cl solution (5 mL). The reaction mixture was concentrated under reduced pressure and the residue was taken up in CH_2Cl_2 (50 mL) and H_2O (25 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (40 mL). The combined organic extracts were washed with H_2O (25 mL) washed with saturated aqueous NaCl solution (20 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel, 25% $CHCl_3$/hexanes) to yield **41** (0.50 g, 1.4 mmol, 61%) from **39** as a colourless crystalline solid, mp 204–205°C (chloroform/hexanes). δ_H (500.1 MHz, $CDCl_3$) 7.67 (s, 2H), 7.16 (t, *J* 7.5, 1H), 7.11 (s, 4H), 6.96 (d, *J* 7.5, 2H), 6.27 (s, 4H), 5.95 (s, 1H), 2.81 (m, 4H), 2.71 (m, 4H). δ_C (126 MHz, $CDCl_3$) 140.3, 137.1, 135.6, 135.5, 132.6, 131.4, 128.0, 125.6, 125.5, 36.3, 35.5. *m/z* (EI, 70 eV) 334 (M^+, 36%), 229 (100), 215 (67). *m/z* (HR) Anal. Calc. for $C_{26}H_{22}$: 334.1720. Found: 334.1726.

[2]Metacyclo[2](2,7)pyrenophane ***18***

To a solution of **41** (0.26 g, 0.78 mmol) in degassed benzene (20 mL) was added a solution of DDQ (0.19 g, 0.86 mmol) in degassed benzene (5 mL) over 10 min. The reaction mixture was stirred at room temperature for an additional 5 min and concentrated under reduced pressure. The residue was dissolved in $CHCl_3$ and filtered through a plug of silica to yield **18** (0.25 g,

0.75 mmol, 97%) as a crystalline, slightly yellow solid, which was recrystallized from heptane, mp 184–186°C (heptane). δ_H (500.1 MHz, $CDCl_3$) 7.68 (s, 2H), 7.47 (s, 2H), 7.32 (s, 2H), 7.15 (s, 2H), 6.56 (t, *J* 7.5, 1H), 6.31 (d, *J* 7.5, 2H), 4.18 (s, 1H), 3.09 (ddd, *J* 13.0, 5.8, 1.9, 2H), 2.69 (ddd, *J* 13.3, 13.0, 5.3, 2H), 2.31 (ddd, *J* unresolved, 2H), 1.21 (ddd, *J* 13.9, 13.3, 5.8, 2H). δ_C (126 MHz, $CDCl_3$) 137.4, 134.0, 133.0, 131.3, 130.3, 129.8, 129.4, 127.9, 126.2, 126.0, 125.1, 125.1, 38.0, 35.3. *m*/*z* (EI, 70 eV) 332 (M^+, 100%), 317 (10), 228 (97), 213 (8), 202 (7), 166 (17). *m*/*z* (HRMS) Anal. Calc. for $C_{26}H_{20}$: 332.1564. Found: 332.1562.

Accessory Publication

^1H and ^{13}C NMR spectra for compounds **17**, **18**, **24**, **25**, **26**, **28**, **29**, **30**, **31**, **32**, **36**, **37**, **38**, **39**, and **41**; and AM1-calculated values of *d* for a selection of dimethylarenes are available on the Journal's website.

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