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The Development of Synthetic Routes to 1,1,*n*,*n*-Tetramethyl[*n*](2,11)teropyrenophanes

Kiran Sagar Unikela[+],[a] Bradley L. Merner[+],[a] Parisa Ghods Ghasemabadi,[a] C. Chad Warford,[a] Christopher S. Qiu,[a] Louise N. Dawe,[b] Yuming Zhao[a] and Graham J. Bodwell*[a]

Dedicated to the memory of Prof. Sho Ito

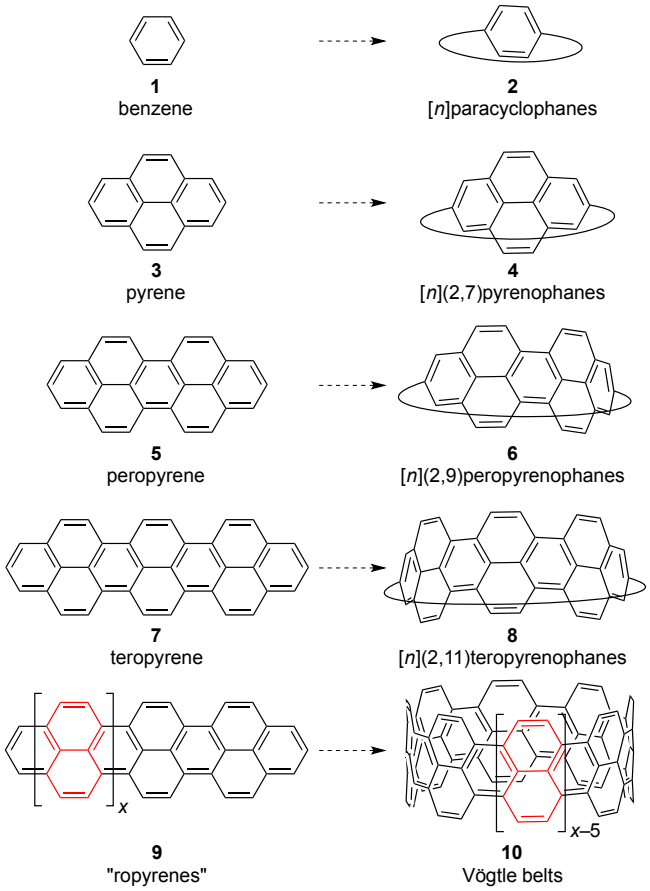
Abstract: A concise synthetic approach to 1,1,*n*,*n*-tetramethyl[*n*](2,11)teropyrenophanes has been developed. It involves the construction of triply-bridged pyrenophanes, during which the three bridges are installed successively using Friedel-Crafts alkylation, Wurtz coupling and McMurry reactions. At the same time, the innate regiochemical preferences of pyrene toward electrophilic aromatic substitution are relied upon to control the substitution pattern. A cyclodehydrogenation reaction is then employed to generate the teropyrene system directly in a nonplanar conformation. The crystal structure of 1,1,7,7-tetramethyl-[7](2,11)teropyrenophane was determined and the teropyrene system was found to have an end-to-end bend angle of 177.9°.

Introduction

Virtually any aromatic system can be distorted from its lowest-energy geometry, whether planar or nonplanar, by incorporating it into an [*n*]cyclophane (a cyclophane consisting of just one aromatic unit and one bridge).[1] The changes in structure are accompanied by an increase in strain energy (SE) as well as changes in the chemical and physical properties of the aromatic system. Of course, many other types of cyclophanes can have distorted aromatic systems, but [*n*]cyclophanes offer the best opportunities to investigate how the properties of an aromatic system change with incremental changes in structure because complications arising from intramolecular π-π interactions are absent.

Benzene (**1**) is by far the most common aromatic system to have been incorporated into cyclophanes. Indeed, it has been "bent and battered" for several decades.[2] The greatest distortion of benzene from planarity can be achieved through bridging two positions that are maximally separated, *i.e*. the 1 and 4 positions. The resulting [*n*]paracyclophanes (**2**) have been subjects of interest for a long time and the most distorted benzene ring reported to date is a kinetically stabilized [4]paracyclophane derivative (α+ß = 72.5°).[3] The development of new methods for the synthesis of highly distorted benzene rings is still being actively pursued.[4]

Benzene (**1**) is the first member of numerous series of polynuclear aromatic hydrocarbons (PAH). One such series propagates through the successive linear annulation of a phenalene unit. This series moves from benzene (**1**) to pyrene (**3**), peropyrene (**5**), teropyrene (**7**) and so on (Scheme 1). Until very recently,[5] this series of armchair-edged graphene nanoribbons (GNR) does not appear to been given a name. Chalifoux and co-workers suggested the name "pyrenacenes" and this nicely reflects the pyenoid (*K*-region-containing) nature of the individual members, but we suggest the term "ropyrenes" because it is consistent with the way that a closely related series of PAH, the rylenes, is named after the common ending of the individual compound names (per*ylene*, ter*rylene*, quater*rylene*...).



Scheme 1. The ropyrene series of PAHs and some [*n*]cyclophanes derived from them.

[a] K. S. Unikela, B. L. Merner, P. Ghods Ghasemabadi, C. C. Warford, C. S. Qiu, Prof. Dr. Y. Zhao, Prof. Dr. G. J. Bodwell
Chemistry Department
Memorial University of Newfoundland
283 Prince Philip Drive, St. John's, NL, Canada, A1E 5V7
E-mail: gbodwell@mun.ca
http://gbodwell.wordpress.com
[b] Prof. Dr. L. N. Dawe
Department of Chemistry and Biochemistry
Wilfrid Laurier University
Science Building, 75 University Ave. W., Waterloo, ON, Canada, N2L 3C5
[+] These authors contributed equally to this work.

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Bridging the ropyrenes at the two most remote positions gives rise to the [*n*](2,7)pyrenophanes (**4**), the [*n*](2,9)peropyrenophanes (**6**), the [*n*](2,11)teropyrenophanes (**8**) and so on. If the amount of bend per benzene ring is held constant, the growing PAH in this series of cyclophanes describes an increasingly large part of an aromatic belt. Ultimately, the PAH wraps around onto itself to afford aromatic belts **10** of the type first described by Vögtle.[6]

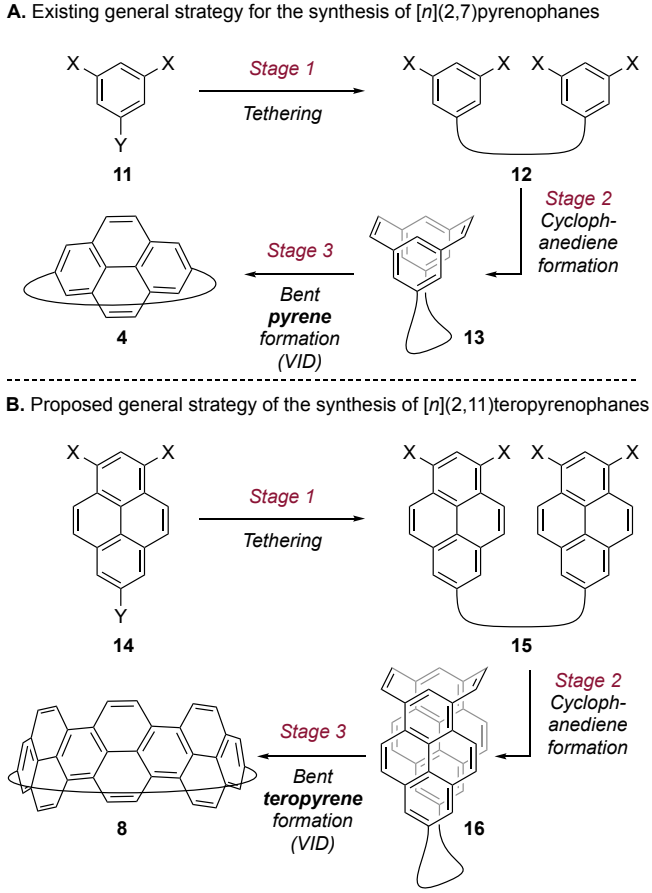
The [*n*]cyclophanes derived from the ropyrenes ([*n*]ropyrenophanes) are interesting for reasons beyond the opportunities they offer to address fundamental questions. For example, enlarging the aromatic systems synthetically has the potential to provide access to bent nanographenes that may be quite soluble due to the nonplanar nature of the extended pi-systems. Capitalizing on these opportunities requires the development of reliable, general synthetic strategies to the respective [*n*]cyclophanes. We recently communicated two related synthetic approaches to the synthesis of some 1,1,*n*,*n*-tetramethyl[*n*](2,11)teropyrenophanes[7] and we now report the full details of the development of a general approach to these systems.

Results and Discussion

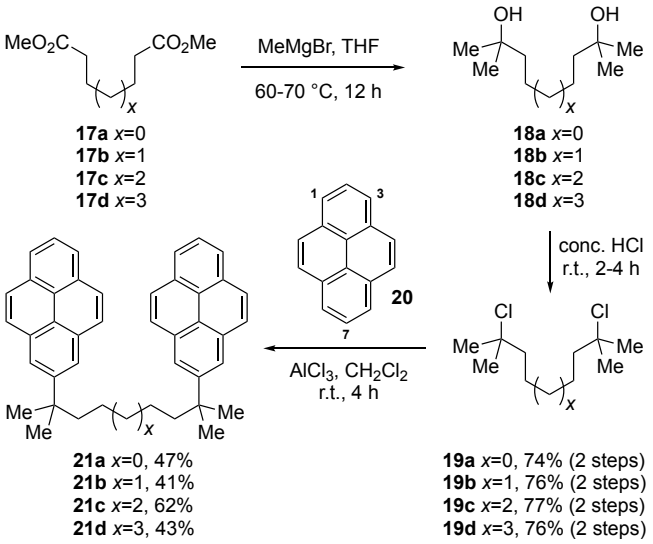
Our group has reported the synthesis of a variety of [*n*](2,7)pyrenophanes (**4**),[8] other (2,7)pyrenophanes[9] and (1,6)pyrenophanes[10] using a common synthetic strategy (Scheme 2A). Key elements of this strategy are 1) tethering two appropriately functionalized benzenes (**11**), 2) conversion of the tethered bis(arene) **12** into a tethered [2.2]metacyclophanediene (**13**) and 3) a valence isomerization / dehydrogenation (VID) reaction in which the pyrene system of **4** is formed in a nonplanar conformation.

To gain access to [*n*](2,11)teropyrenophanes (**8**), it was envisaged that an analogous strategy starting with an appropriately substituted pyrene **14** and proceeding through **15** and **16** could be adopted (Scheme 2B). In this case, the final step results in the formation of a nonplanar teropyrene system from an [*n*.2.2](7,1,3)pyrenophane **16**.

Upon considering the well-understood, but rather limited chemistry of pyrene,[11] it became immediately apparent that the synthesis of suitable 1,3,7-trisubstituted pyrenes as starting materials would be more complicated than those of the 1,3,5-trisubstituted benzenes that were employed in the synthesis of the [*n*](2,7)pyrenophanes (**4**). Instead, the known selectivity of the Friedel-Crafts reaction of *tert*-butyl chloride for the 2 and 7 positions of pyrene was envisioned as a means to achieve the tethering of two pyrene systems in the desired fashion before introducing further substituents. Furthermore, the bulky *tert*-alkyl substitutents were expected to sterically disfavor subsequent substitution reactions at the two adjacent positions of each pyrene unit and thus enable regioselective functionalization at the other end of the pyrene units (*cf.* electrophilic aromatic substitution reactions of 2-*t*-butylpyrene).[12]



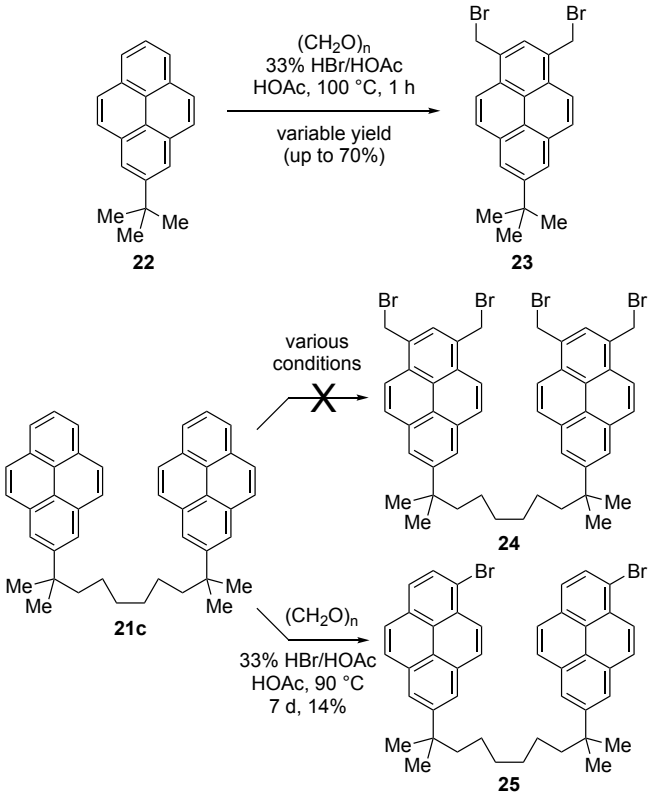
Scheme 2. General strategies for the synthesis of [*n*](2,7)pyrenophanes (**4**) and [*n*](2,11)teropyrenophanes (**8**).



Scheme 3. Synthesis of dipyren-2-ylalkanes **21a-d**.

A series of dipyren-2-ylalkanes **21a-d** was synthesized by way of a three-step sequence starting from diesters **17a-d** (Scheme 3). Grignard reaction of **17a-d** with MeMgBr afforded diols **18a-d**, which were then converted into the corresponding dichlorides **19a-d** upon treatment with concentrated aqueous HCl. Friedel-Crafts alkylation of pyrene (**20**) with dichlorides **19a-d** afforded the desired dipyren-2-ylalkanes **21a-d** in moderate yield. An excess (5.0 equivalents) of pyrene was used in these reactions to minimize overalkylation. In the case of **21a**, linear oligomers were observed by LCMS analysis of the crude reaction mixture, but none could be isolated in pure form.

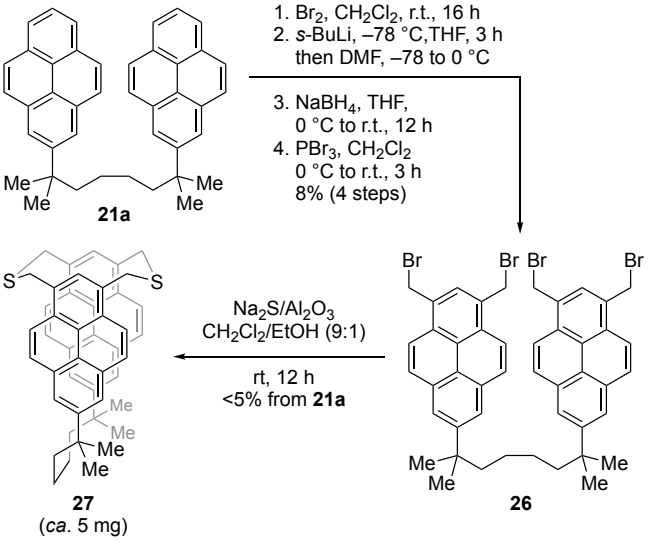
At this stage, the intention was to simultaneously introduce four functional groups through electrophilic aromatic substitution reactions to afford cyclization precursors corresponding to **15**, which could then be advanced through the usual (thiacyclophane-based) pathway[7–9,13] to **16** (Scheme 2B). The most expedient way forward appeared to be fourfold bromomethylation of **21a**-**d**, which would immediately set the stage for dithiacyclophane formation. To find optimal reaction conditions for such bromomethylation reactions, a model study was carried out on 2-*t*-butylpyrene (**22**) (Scheme 4A).[12a,14] Although a 70% yield of dibromide **23** was obtained in one experiment, it proved to be difficult to reproduce this result. The main concern at this point was the somewhat harsh conditions required for the bromomethylation, which might lead to overreaction, ring bromination, or self-alkylation by the newly-installed and active (bromomethyl)pyrene units. Nevertheless, one of the dipyrenylalkanes (**21c**) was selected and several attempts were made to convert it into the corresponding tetrabromide **24** (Scheme 4B). In no case was any of the desired product obtained, but rather complex mixtures of products that included varying amounts of the starting material **21c**. The only pure product isolated from any of these reactions was dibromide **25** (14%), a product of ring bromination and not bromomethylation.



Scheme 4. Model bromomethylation reaction of **22** and attempted synthesis of tetrabromide **24**.

With the knowledge that 2-*tert*-butylpyrene (**22**) undergoes dibromination very selectively at the positions away from the *tert*-butyl group,[12a] the possibility of conducting fourfold bromination of **21a** was then investigated (Scheme 5). The crude product obtained from this reaction was poorly soluble, which made purification and characterization problematic. However, it could be taken in crude form through a sequence of lithiation/formylation, reduction and bromination to afford tetrabromide **26**, albeit in just 8% yield over 4 steps. The purity and solubility of this compound was rather low, but it was nevertheless subjected to a reaction with Na_2S/Al_2O_3[15] to afford a small amount (<5 mg) of dithiacyclophane **27**, which was also impure (^{1}H NMR analysis) and sparingly soluble.

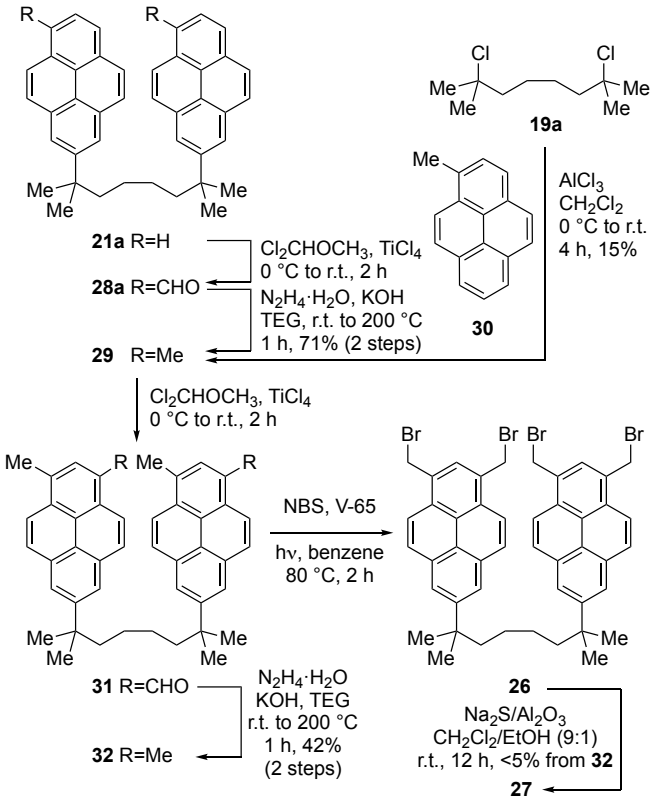
Rieche formylation was then investigated as a means to introduce four functional groups, but reaction of **21a** under standard Rieche formylation conditions gave only dialdehyde **28** in 88% yield (Scheme 6). Increasing the temperature, the reaction time, or the number of equivalents of the reagents used did not result in formylation at the other two available positions of **21a**, but rather lower isolated yields of the same dialdehyde (**28**). Switching to a more powerful Lewis acid ($AlCl_3$) resulted in an increase in the extent of the formylation, but the resulting mixture of di-, tri- and tetraaldehydes was not easily separated. Tether cleavage, presumably via a retro-Friedel–Crafts alkylation reaction, also occurred as evidenced by the isolation of 1-formylpyrene as a byproduct.



Scheme 5. Low-yielding synthesis of dithiacyclophane **27**.

The ease with which dialdehyde **28** could be obtained prompted the investigation of a multistep synthesis of tetrabromide **26,** following an approach that had been reported by Yamato and co-workers for the synthesis of 1,3-bis(bromomethyl)-7-*t*-butylpyrene (Scheme 6).[16] Accordingly, dipyrenylalkane **21a** was subjected to Rieche formylation conditions and the crude dialdehyde **28**, Wolff-Kishner reduction of which afforded hydrocarbon **29** (71%, 2 steps). This compound was also accessible through the Friedel-Crafts alkylation of 1-methylpyrene (**30**)[16] with dichloride **19a**, but the yield was just 15%. Repetition of the formylation/reduction sequence furnished hydrocarbon **32** (42%, 2 steps) *via* dialdehyde **31**. Benzylic bromination of **33** using Yamato's optimized conditions (benzene as solvent and V-65 as the initiator) gave a mixture of products from which a small amount (<15%) of impure tetrabromide **26** was isolated. Attempted purification by either column chromatography or crystallization led to product losses and/or a decrease in purity. As such, the crude product was reacted directly with Na_2S/Al_2O_3[15] to

generate dithiacyclophane **27**. Again, only a small quantity (<5 mg) of **27** was obtained and the level of purity (^{1}H NMR analysis) was unsatisfactory.

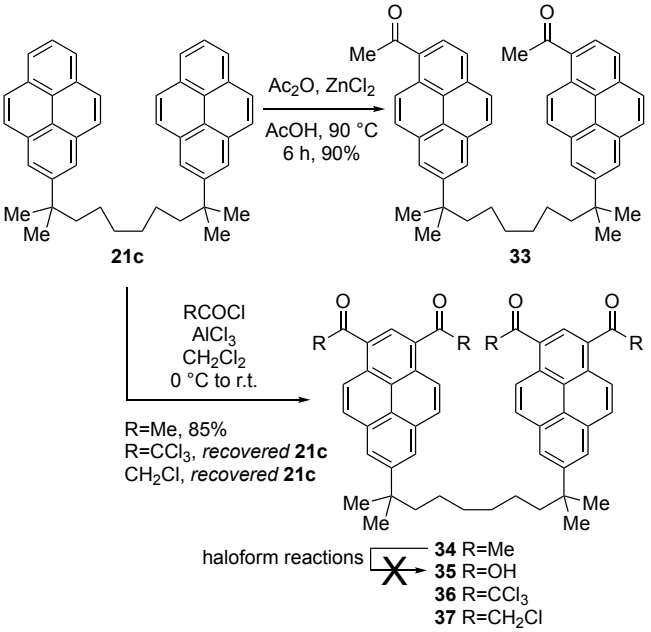


Scheme 6. A second low-yielding synthesis of dithiacyclophane **27**.

In a final attempt to tetrafunctionalize the dipyrenylalkanes **21a**-**d**, the use of Friedel-Crafts acylation was explored. Akin to the Rieche formylation of **21a**, reaction of **21c** with $Ac_2O/ZnCl_2$ at elevated temperature resulted in efficient monoacylation of each pyrene system to afford diketone **33** in 90% yield (Scheme 7). Upon moving to a more reactive acylating system, $AcCl/AlCl_3$, the desired fourfold acylation of **21c** was found to occur under relatively mild conditions to afford tetraketone **34** in 85% yield. Although the simultaneous introduction of four functional groups was successful, each of the acetyl groups in **34** contained one more carbon atom than required. Consequently, haloform reactions (Br_2/KOH, NaOCl, and I_2/KIO_3) were attempted in an effort to generate tetraacid **35**, which was expected to be a reasonable synthetic precursor to tetrabromide **24**. However, in all cases, the starting material was recovered, possibly due to its poor solubility under the conditions that were employed.

As an alternative to the haloform reaction, the direct synthesis of tetrakis(trichloroacetyl)-functionalized compound **36** was investigated. Accordingly, **21c** was subjected to Friedel-Crafts acylation conditions with trichloroacetyl chloride/$AlCl_3$. However, the reaction did not proceed to any appreciable extent. The same result was obtained when a less bulky acid chloride, chloroacetyl chloride, was employed.

The fourfold functionalization-based approaches that had been pursued to this point were in keeping with the general strategy (Scheme 2B), in which a tetrafunctionalized system **15** is slated for conversion into cyclophanediene **16**. This implies simultaneous formation of the two short bridges. Having been unable to capitalize on any of the fourfold functionalization approaches, the possibility of forming the two short bridges in a consecutive fashion was then investigated.



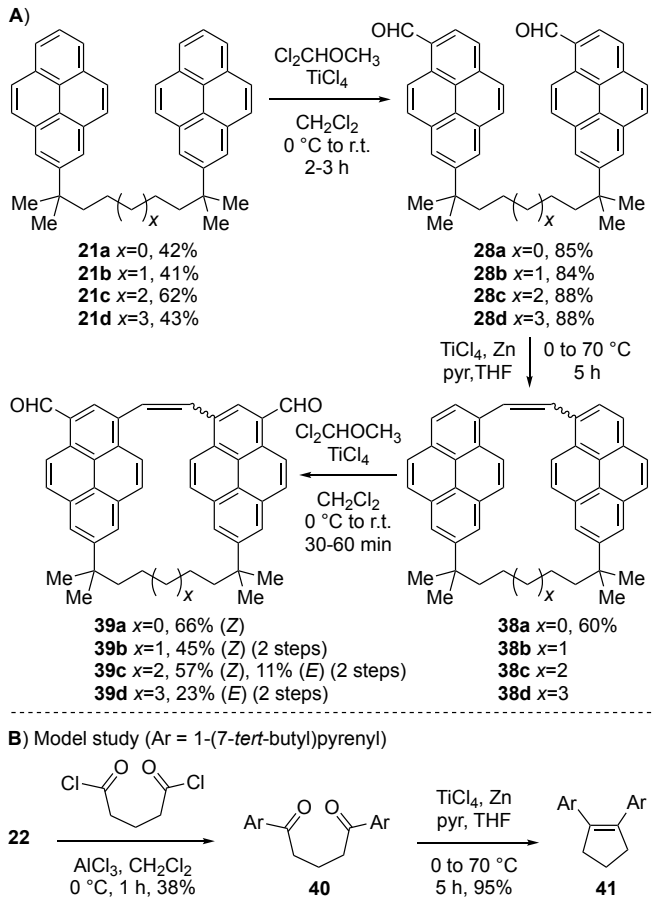
Scheme 7. Friedel-Crafts acylation reactions of **21c**.

The Rieche formylation, which had been found to be a very effective method for the monofunctionalization of each pyrene system of **21a**, was then applied to the full series of dipyrenylalkanes **21a**-**d** to easily afford dialdehydes **28a**-**d** (84-88%, Scheme 8A). Instead of pursuing the standard thiacyclophane approach, which would require several synthetic steps for the formation of each bridge, the possibility of directly converting the dialdehydes **28a**-**d** into the corresponding [*n*.2]cyclophanes **29a**-**d** was investigated. Indeed, ample precedent existed for the use of the McMurry reaction in the synthesis of low-strain cyclophanes.[17]

Before proceeding, a short model study on the McMurry reaction of pyrene aldehydes and ketones was conducted. For example, diketone **40** was synthesized by a Friedel–Crafts acylation reaction of 2-*tert*-butylpyrene (**22**) with glutaroyl dichloride. Several different sets of McMurry reaction conditions were screened for the conversion of **40** into diarylcyclopentene **41** and it was found that the Lenoir variant[18] was best suited for this reaction, affording **41** in 95% yield (Scheme 8B).

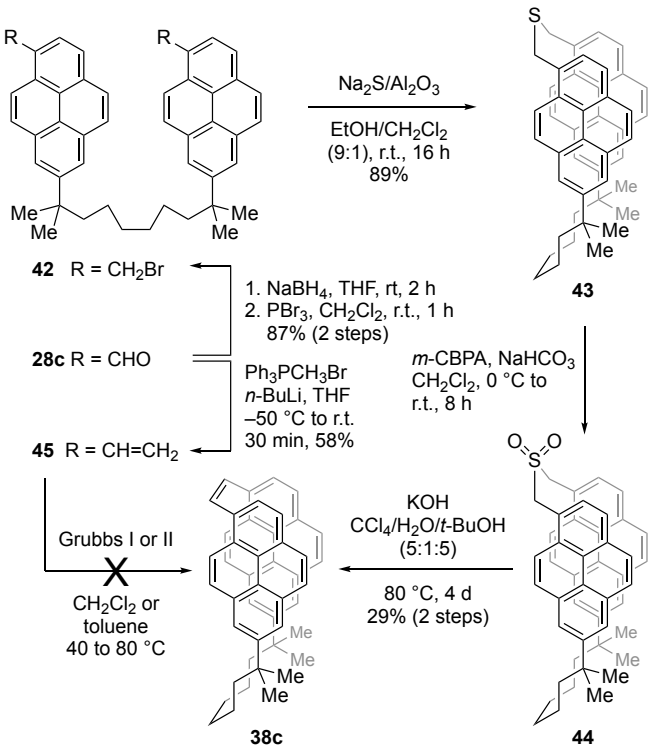
The dialdehydes **28a**-**d** were then subjected to these reaction conditions and the outcome of the reaction depended heavily on the length of the tether. In the case of **28d**, reductive coupling occurred to afford [9.2](7,1)pyrenophane **38d** as a single diastereomer, which was formylated to give dialdehyde **39d** (23% over 2 steps). The next lower homologue, **28c**, also underwent reductive coupling, but resulted in the formation of **38c** as a chromatographically inseparable mixture of diastereomers. Rieche formylation of this mixture delivered a separable mixture of (*E*)-**39c** and (*Z*)-**39c** (11% and 57%, respectively over 2 steps). The ^{1}H NMR spectrum of the minor product (11%) was virtually identical to that of **39d**. On the other

hand, the ^{1}H NMR spectrum of the major product (57%) very closely resembled those of **39a** and **39b**, which were obtained in good yield from the McMurry reactions and subsequent formylations of **28a** and **28b**. The assignment of configuration of the newly-formed double bonds in **39a**-**d** was not obvious from ^{1}H NMR analysis, but based on the geometric characteristics of (*E*)-configured and (*Z*)-configured alkenes, it seemed very likely that **39d** and the minor isomer of **39c** were (*E*)-configured, while **39a**, **39b** and the major isomer of **39c** were (*Z*)-configured. Whereas the level of strain in the (*Z*)-isomers of **39a**-**d** would not be expected to be affected significantly by the length of the long bridge, the (*E*)-isomers would be expected to become increasingly strained as the long bridge of the cyclophanes decreases in length. These configurational assignments for **39a**-**d** were ultimately confirmed by their subsequent reactivity.



Scheme 8. A) Synthesis of pyrenophanedialdehydes **40a**-**d** and **B**) synthesis of dipyrenylcyclopentene **41**.

Before proceeding with the formation of the second short bridge, other options for the conversion of dialdehyde **28c** into cyclophane **38c** were explored (Scheme 9). Reduction of **28c** using $NaBH_4$ followed by bromination of the resulting diol with PBr_3 furnished dibromide **42** (87%, 2 steps). Upon treatment of **42** with Na_2S/Al_2O_3, [8.3]thiacyclophane **43** was obtained in 89% yield. Contraction of the 3-atom thioether bridge to a 2-atom vinylene bridge was achieved by first oxidizing the thioether to the corresponding sulfone, followed by a Ramberg-Bäcklund reaction to give **38c** in 29% yield over 2 steps. Although the yield is low, this adds to the small set of examples of the use of the Ramberg-Bäcklund reaction in realm of cyclophane chemistry.[17,19] The overall yield of **38c** from **28c** using this 5-step protocol was 22%, and is significantly lower than that of a direct McMurry reaction (68% yield). Finally, the use of ring-closing metathesis (RCM) was investigated. Dialdehyde **28c** was olefinated using a Wittig reaction to afford diene **45** (58%), but all attempts to employ a RCM reaction in the synthesis of **38c** were unsuccessful. The application of ring-closing metathesis (RCM) in the synthesis of cyclophanes is well-documented,[17] but its use for installing olefin bridges with any significant strain has been very limited. Thus, the inability to generate **38c** is not surprising.

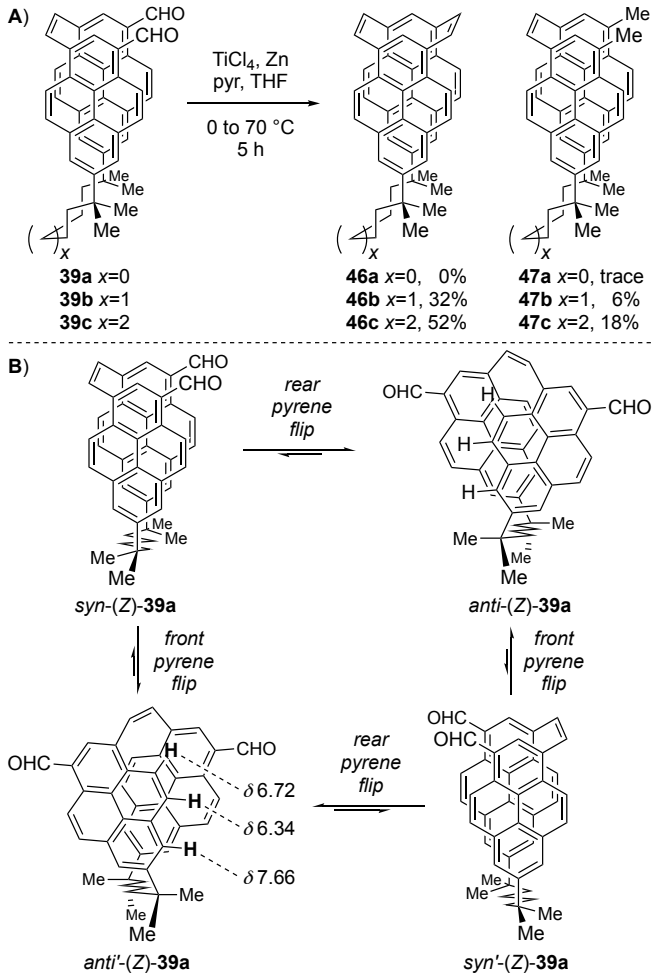


Scheme 9. Alternative synthesis of pyrenophane **38c**.

A (*Z*)-configured alkene is necessary for the formation of the next two-carbon bridge, so progress could only be made with (*Z*)-**39a**-**c**. As before, the most direct route to a new vinylene bridge was the intramolecular McMurry reaction. The literature precedent suggested, however, that this might be problematic.[17] Of the numerous prior attempts to use the McMurry reaction to construct a [2.2]metacyclophane system, the best reported yield was just 4.3%.[20] Nevertheless, the McMurry reactions were performed and (comparatively) excellent yields of **46b** (32%) and **46c** (52%) were obtained (Scheme 10A). In contrast, the reaction leading to **46a** afforded none of the desired product, but rather traces the reduction product **47a** (TLC analysis). More substantial amounts of the corresponding reduction products **47b** (6%) and **47c** (18%) were obtained.

The remarkable success of the McMurry reactions leading to **46b** and **46c** may be due to the fact that the aromatic systems bearing the aldehyde groups in **39b** and **39c** are connected by two bridges instead of one. By analogy to Diels-Alder reactions, the McMurry reactions of **39b** and **39c** are transannular in nature, whereas the prior singly-bridged examples leading to simple [2.2]metacyclophanes[17] are merely intramolecular. This being

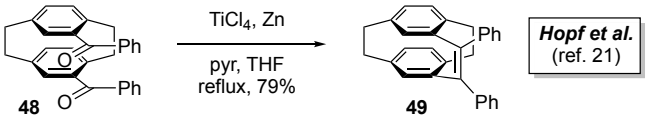
the case, a significant entropic advantage would be expected for the reactions of **39b** and **39c**. Of course, the same argument could be made for **39a**, so the failure of its transannular McMurry reaction to deliver **46a** implies that other effects come into play.



Scheme 10. **A**) Synthesis of pyrenophanedienes **46b**-**c** and **B**) conformational ring flip of pyrenophane **39a**.

A clue that the conformational behavior of **39a**-**c** is important came from a previously reported transannular McMurry reaction,[21] in which *pseudo-gem*-dibenzoyl[2.2]paracyclophane (**48**) afforded triply-bridged cyclophane **49** in 79% yield (Scheme 11). The excellent yield can be attributed to the conformational rigidity of the [2.2]paracyclophane system, which enforces proximity of the two reacting carbonyl groups. Pyrenophanes **39a**-**c** are much more flexible than **48** by virtue of having one long bridge (6-8 atoms). Thus, from the outset, the yields for **46a**-**c** might be expected to be lower than for **49** (79%). The observation that this is indeed the case for **46b** (32%) and **46c** (52%), but drastically so for **46a** (0%) prompted a closer look at the conformational behavior of **39a**-**c**.

Many [*m.n*]cyclophanes, of which **39a**-**c** are examples, are conformationally mobile. The most common processes in such systems are ring flips that interconvert *syn* and *anti* conformers and bridge flips that occur within discrete *syn* and *anti* conformers. The former processes typically have higher energy barriers than the latter and can often be observed experimentally, usually by ^{1}H NMR analysis.[22]



Scheme 11. Hopf's transannular McMurry reaction of **48** to give triply-bridged cyclophane **49**.

For **39a**-**c**, inspection of molecular models suggested that that low-strain *syn* and *anti* conformers are available, and that each of these arene conformers has two or more bridge conformers in the long bridge. The room temperature ^{1}H NMR spectra of **39a**-**c** immediately revealed a marked difference between **39a** and **39b**-**c**. The aromatic protons for **39b** appear within similar ranges: δ 9.1–7.4 ppm for **39b** and δ 9.2–7.3 ppm for **39c** (Figure 1). These ranges are comparable to those for the corresponding protons in **28a**-**c** (δ 9.1–7.7 ppm). In sharp contrast, the aromatic protons for **39a** span a much larger range (δ 9.4–6.3 ppm), especially at the high-field end. Clearly, **39a** has a different conformation preference in solution than **39b**-**c**.

The anomalously high-field-shifted signals in the spectrum of **39a** were determined (COSY, NOESY) to be those for the aryl protons located on the edge of the pyrene system across from the one bearing the formyl group (Scheme 10B). In the *anti* conformations of **39a**-**c**, these protons lie over the opposite pyrene system and would therefore be expected to be strongly shielded. It can therefore be concluded that **39a** has a much more highly populated *anti*-conformation than do **39b**-**c**. In these conformations, it is evident that the two formyl groups are much too far away from one another to undergo reductive coupling. Furthermore, the broadness in the spectra of **39b**-**c** shows that *syn*-*anti* interconversions occur reasonably quickly at room temperature, which means that the reactive *syn* conformer can be readily repopulated as the McMurry reactions proceed (at 66 °C).

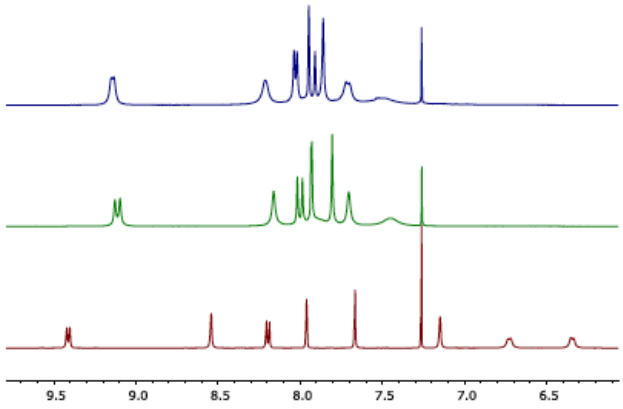


Figure 1. Aromatic region of the ^{1}H NMR spectra of pyrenophanedialdehydes **39a** (red), **39b** (green) and **39c** (blue).

To further understand the anomalous behavior of **39a** in the McMurry reaction, the relative energies of *syn* and *anti* conformers of **39a**-**c** were calculated at the B3LYP/6-31G(d) level of theory (Table 1). Calculations were performed for compounds in the gas phase, in $CHCl_3$ (NMR solvent) and in

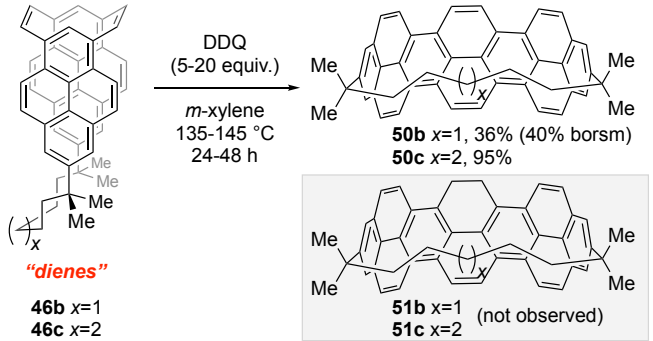
THF (solvent for the McMurry reactions). The results are fully consistent with the observed behavior. In the gas phase, **39a** was calculated to favor the *anti* conformation by 3.87 kcal/mol and **39b** was calculated to favor the *syn* conformation by –0.89 kcal/mol, whereas **39c** showed a slight preference (0.30 kcal/mol) for the *anti* conformation. Upon moving to solution phase, the calculated ΔG values all moved toward the *syn* conformation by 0.58-0.88 kcal/mol, which had the effect of moving the preference of **39c** from *anti* to *syn*. The ΔG values for **39a**-**c** in THF correspond to *anti*:*syn* ratios at 66 °C (boiling point of the solvent of the McMurry reaction) of 85:1, 1:9.4 and 1:1.9, respectively. Thus, the very strong preference for the *anti* conformation in **39a** is responsible for the failure of the intramolecular McMurry reaction.

Table 1. Calculated ΔG values (kcal/mol) for the *anti*-to-*syn* isomerization for **39a**-**c**.[a]

Compound	Gas Phase	$CHCl_3$ Solution	THF Solution
39a	3.87	3.18	2.99
39b	–0.89	–1.47	–1.51
39c	0.30	–0.35	–0.42

[a] Calculations were performed at the B3LYP/6-31G(d) level of theory at standard conditions.

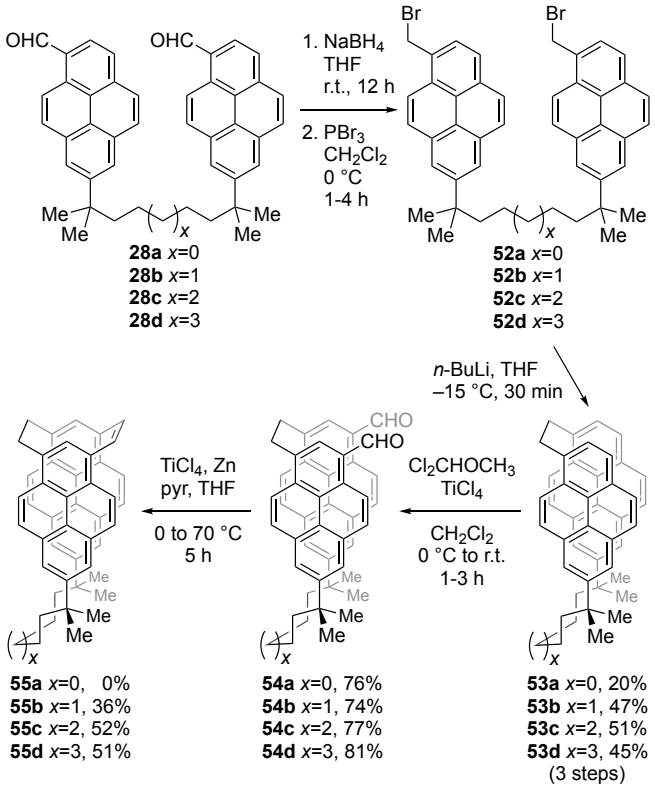
With cyclophanedienes **46b** and **46c** in hand, work aimed at their conversion into the desired (2,11)teropyreneophanes was initiated (Scheme 12). Numerous metacyclophanedienes **13** have been successfully converted into the corresponding (2,7)pyrenophanes **4** upon heating in benzene in the presence of DDQ, so **46c** was subjected to these conditions. After 48 hours, the reaction had stalled and only partial conversion (*ca.* 10%) of **46c** to **50c** was observed (^{1}H NMR analysis). A similar result was obtained when toluene was used as the solvent. Complete consumption of the starting material was achieved upon heating **46c** in *m*-xylene at 135-145 °C for 24-48 hours, whereby a 95% yield of **50c** was obtained.



Scheme 12. Synthesis of teropyrenophanes **50b**-**c** from dienes **46b**-**c**.

In the case of the next smaller homolog, **46b**, the reaction was slower and that the product **50b** showed signs of instability under the conditions of its formation (TLC analysis). It was therefore necessary to carefully monitor the reaction so as to balance the sluggish consumption of **46b** against prolonged exposure of the more strained teropyrene system in **50b** to the harsh reaction conditions. The best result was obtained when the DDQ was added in 4 to 5 portions (total = 20 equiv.) over a 12-hour period. This resulted in the isolation of **50b** in 36% yield along with unreacted **46b** (10%). The separation of **50b** from **46b** could be easily achieved using column chromatography (10% EtOAc/hexanes, R_f=0.27 and 0.60, respectively), which is noteworthy because the use of dichloromethane/hexanes mixtures gave only narrow separation. Additionally, unlike what has been observed in the synthesis of some of the less strained [*n*](2,7)pyrenophanes,[8c] no dihydroteropyrenophanes (**51b**-**c**) were observed in the syntheses of **50b** and **50c** (Scheme 12). This is very likely due to the much harsher reaction conditions.

The "double McMurry" approach to **50b** and **50c** has the advantage of brevity (8 steps from diesters **17b** and **17c**), but is limited in scope to just these two teropyrenophanes. For the next lower homolog **50a**, the synthesis foundered at the second McMurry reaction (conversion of **39a** to **46a**). In the case of the next higher homolog **50d**, the synthesis came to an end at the first McMurry reaction (*E*-configured olefin bridge, **39d**). To address both the stereochemistry problem during the formation of the first two-carbon bridge and possibly also the conformational problem during the formation of the second 2-carbon bridge, a different method for forming the first two-carbon bridge was sought. Although the standard thiacyclophane approach was a candidate, its multistep nature was seen as a disadvantage, especially where the bridges were to be formed one after the other. A direct C–C bond-forming reaction was preferable and the Wurtz coupling was identified as a promising alternative. Although it has not been a mainstay in cyclophane synthesis, the Wurtz coupling does have ample precedent, even for the generation of moderately strained cyclophanes such as [2.2]metacyclophanes.[23]



Scheme 13. Synthesis of [*n*.2.2](7,1,3)pyrenophanes **55a-d**.

To prepare for intramolecular Wurtz coupling reactions, dialdehydes **28a**-**d** were reduced with $NaBH_4$ and the resulting

crude diols (not shown) were converted into the corresponding dibromides **52a**-**d** upon reaction with PBr_3 (Scheme 13). Purification of these dibromides by column chromatography was problematic due to slow hydrolysis of the bromomethyl groups back to hydroxymethyl groups. For this reason, the crude dibromides **45a**-**d** were used in the next step, in which they were reacted with *n*-BuLi to induce intramolecular Wurtz coupling. This afforded [*n*.2](7,1)pyrenophanes **53a**-**d** (20-51%, 3 steps from **28a**-**d**).

Rieche formylation of **53a-d** occurred with high regioselectivity to afford dialdehydes **54a-d** (74-81%), which were subjected to McMurry reaction conditions to afford the [*n*.2.2](7,1,3)pyrenophanes **55b-d** (36-51%). The yields of these McMurry reactions are comparable to those of the second McMurry reactions in the double-McMurry strategy (Scheme 10A). The successful synthesis of **55d** is important because it demonstrates that the presence of a saturated 2-carbon bridge can indeed provide entry to direct precursors to larger teropyrenophanes. On the other hand, it did not enable the formation of the smallest cyclophane-monoene **55a**.

In contrast to what was observed for dialdehydes **39a**-**c**, where only the smallest member of the series **39a** had a highly popoulated *anti* conformation, the ^{1}H NMR spectra of dialdehydes **54a**-**d** pointed toward highly populated *anti* conformations for the first three members of the series **54a**-**c** and a less populated *anti* conformation for the highest homologue **54d** (Figure 2). Nevertheless, the spectrum of **54a**, which is the only one that failed to undergo intramolecular McMurry reaction, is markedly different from the others in that the high-field signals are sharp. This is consistent with a higher *anti–anti'* energy barrier and thus a less accessible *syn* conformation (through which intramolecular McMurry reaction could occur). While this argument holds loosely for the anomalous reactivity of **54a** compared to **54b**-**d**, it should be noted that the spectra of **54c** (successful intramolecular McMurry reaction) and **39a** (unsuccessful intramolecular McMurry reaction) closely resemble one another. Thus the situation is not cut-and-dried and a separate, more detailed study of the conformational behaviour of these systems is warranted.

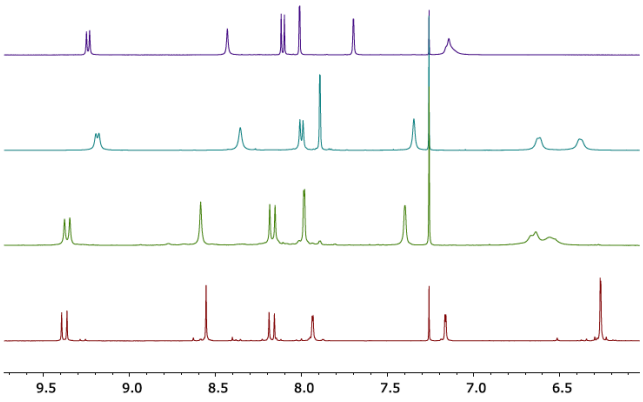


Figure 2. Aromatic region of the ^{1}H NMR spectra of pyrenophanedialdehydes **54a** (red), **54b** (green), **54c** (blue) and **54d** (purple).

Calculations revealed an even stronger preference for the *anti* conformation of **54a** (5.16 kcal/mol in THF, 2120:1 at 66 °C) than for **39a** (2.99 kcal/mol in THF) (Table 2), which is fully consistent with the observation that **55a** was not generated in the McMurry reaction of **54a**. Dialdehydes **54b** and **54c** were calculated to have less pronounced preferences for the *anti* conformation (1.08 and 2.05 kcal/mol, respectively), but not to the extent that the reactive *syn* conformation is not significantly populated under the conditions of the McMurry reaction. At 66 °C in THF, the *syn* conformers of **54b** and **54c** are calculated to be the minor components of 5:1 and 21:1 *anti*:*syn* mixtures and the broadness in their ^{1}H NMR spectra shows that *syn-anti* interconversions take place at a meaningful rate at room temperature. Upon moving to **54d**, the calculations find a somewhat stronger preference for the *anti* conformation (47:1 at 66 °C), which contrasts the observation of lower field aromatic signals in the ^{1}H NMR that speak to a more favoured *syn* conformation. It is possible that a lower energy bridge conformation in the long bridge than the linear one that was employed may now be available. Although a more detailed study of the conformational behaviour of **54d** might prove to be useful, it is clear from the NMR spectrum that **54d** has a more highly populated *syn* conformation in solution than its lower homologs and that *syn-anti* interconversions occur relatively quickly.

Table 2. Calculated ΔG values (kcal/mol) for the *anti*-to-*syn* isomerization for **54a**-**c**.[a]

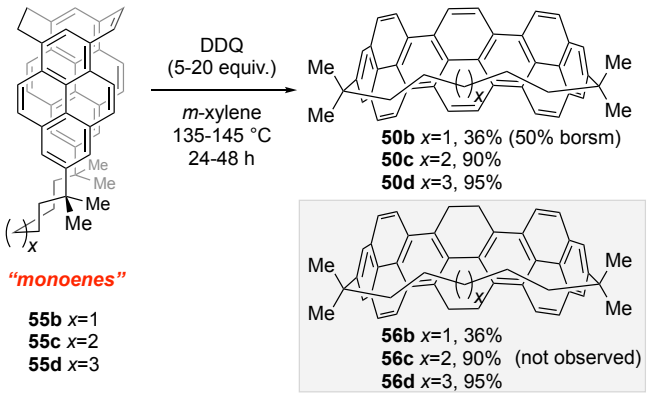
Compound	Gas Phase	$CHCl_3$ Solution	THF Solution
54a	6.00	5.37	5.16
54b	2.29	1.38	1.08
54c	3.12	2.23	2.05
54d	3.01	2.67	2.60

[a] Calculations were performed at the B3LYP/6-31G(d) level of theory at standard conditions.

Any concerns regarding the performance of the VID reaction on a cyclophane-monoene system were quickly allayed upon treatment of **55b-d** with DDQ in *m*-xylene, which brought about the formation of the (2,11)teropyrenophanes **50b**-**d** (Scheme 14). As before, no dihydroteropyrenophanes (*e.g.* **51b**-**c**) or tetrahydroteropyrenophanes (*e.g.* **56b**-**d**) were observed (TLC, LCMS, ^{1}H NMR analysis), which confirmed that the more extensive dehydrogenation involved in these reactions was not an issue. Similar to what was observed during the reactions of dienes **46b** and **46c**, the conversions of **55c** to **50c** and **55d** to **50d** were high-yielding, while the reaction of **55b** leading to the most strained teropyrenophane **50b** (36%, 50% borsm) was considerably more sluggish and required a larger excess of DDQ (20 equiv. instead of 4 equiv.). Reminiscent of **46b**, full consumption of **55b** could not be accomplished, but its chromatographic separation from **55b** was trivially easy using flash chromatography with 10% EtOAc/hexanes as the eluent.

Crystals of **50b** were grown over a period of several weeks from a −15 °C solution in 2% ethyl acetate/hexanes. Due to the very small size of the crystals, synchrotron radiation was needed to collect a dataset from which a solution could be obtained (Figure 3). The end-to-end bend angle (θ_{tot})[7a,7b] for the teropyrene system in **50b** is 177.9°, which is in excellent agreement with the calculated value (B3LYP/cc-pVTZ) of 178.7° and just shy of the 180° angle that corresponds to half a turn. The corresponding angles for **50b**[7b] and **50c**[7b] are 167.0° and 154.3°, respectively. As in the case of **50c** and **50d**, the shape of the bent teropyrene system in **50b** is semielliptical rather than

semicircular. In other words, there is more bend in the central part of the teropyrene system than there is at the ends. To quantify this, the middle pyrene subunit in the teropyrene framework has a bend angle (θ)[7a,7b,8d] of 102.3°, whereas the two terminal pyrene subunits have bend angles of 72.6° and 73.6°, respectively. Of course, all of these values are a few degrees larger than the corresponding values in **50c**. The distance between the bridgehead carbons in **50b** (8.08 Å) is substantially shorter than the corresponding distance in **50c** (9.10 Å) and virtually identical to the distance across [6]CPP (8.09 Å).[24] The aromatic bond lengths are not significantly different from those of **50c** and the same is true for the bridging C–C bond lengths. The C–C–C bond angles at the homobenzylic positions of **50b** are enlarged: 118.6°, 117.7°. By comparison, the largest bond angle in the bridge of **50c** is 118.2° and the largest angle in 1,7-dioxa[7](2,7)pyrenophane is 117.6°.[8b] The ß angles[27] at the two ends of the teropyrene system are relatively small at 4.6° and 4.9°.



Scheme 14. Synthesis of teropyrenophanes **50b-d** from monoenes **55b-d**

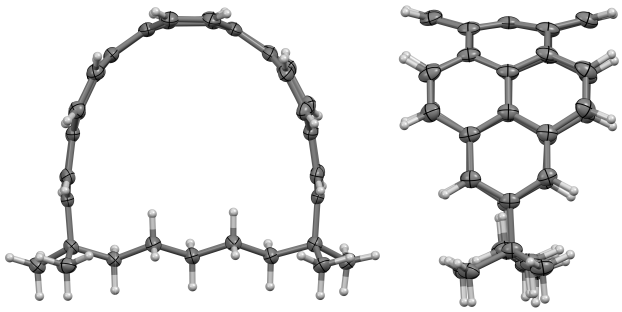


Figure 3. Two views of the asymmetric unit of **50b** with 50% probability displacement ellipsoids. Lattice solvent omitted for clarity. **Crystal Data** for **50b:** $C_{51}H_{46}O_2$ (M =690.88): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 13.3674(19) Å, b = 14.539(2) Å, c = 18.602(3) Å, V = 3615.2(9) Å^3, Z = 4, T = 150(2) K, μ(synchrotron) = 0.091 mm^{-1}, $Dcalc$ = 1.269 g/mm^3, 40734 reflections measured (5.818 ≤ 2Θ ≤ 59.562), 7961 unique (R_{int} = 0.1336) which were used in all calculations. The final R_1 was 0.0811 (I > 2σ(I)) and wR_2 was 0.2034 (all data). CCDC #1842836.

In the crystal, molecules of **50b** are arranged in an alternating up-down fashion along a two-fold screw axis that is parallel to the *b* axis (Figure 4). This creates columns with small channels, which are filled with disordered solvent molecules (Figure S2.) Adjacent columns are rotated by about 90° with respect to one another such that each teropyrene system has a close π-π contact with two other teropyrene systems (3.338(5) Å – 3.393(5) Å (Figure 3).

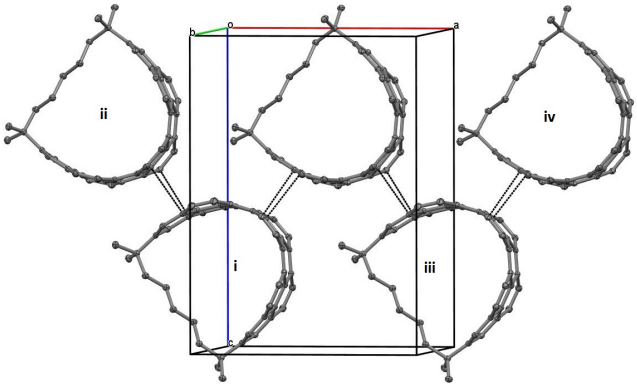


Figure 4. Chain-like arrangement of molecules parallel to the b-axis (coincident with a 2-fold screw axis i = -1/2+x, 1.5-y, 1-z; ii = -1+x, y, z; iii = 1/2 +x, 1.5-y, 1-z; iv = 1+x, y, z. 30% probability ellipsoids, hydrogen atoms and lattice solvent omitted for clarity.

The knowledge that the teropyrene system can be bent almost through a half turn under relatively mild conditions is cause for optimism that the same methodology can be used to generate larger segments of Vögtle belts and ultimately complete Vögtle belts.

Conclusions

Work that was initially aimed at the direct extension of a general strategy for the synthesis of a variety of (2,7)pyrenophanes to the synthesis of [*n*](2,11)teropyrenophanes evolved into the development of a new and relatively short synthetic sequence to a series of 1,1,*n*,*n*-tetramethyl[*n*](2,11)teropyrenophanes **50b-d**. The new strategy exploits Friedel-Crafts alkylation, Wurtz coupling and McMurry reactions to construct the three bridges of triply-bridged pyrenophanes **55b-d**, which can be converted into the corresponding teropyrenophanes upon treatment with DDQ. The use of the Wurtz coupling instead of an initial McMurry reaction proved to be effective in the synthesis of the highest (2,11)teropyrenophane homologue **50d**, as it avoided the issue of the double bond geometry. Neither approach was able to deliver the direct precursors to [6](2,11)teropyrenophane **50a**, i.e. **46a** and **55a**. Even if they did, there is no guarantee that they would have enabled the synthesis of the more highly strained **50a**, especially in light of the fact that the generation of **50b** was troublesome. The diene-based teropyrenophane precursors **50b-c** did not offer any advantage over the monoene-based precursors **55b-d**. This knowledge will guide future synthetic efforts towards more ambitious and challenging targets, such as carbon nanobelts,[25] which have been problematic to synthesize using our earlier dithiacyclophane-based approach.[26] A crystal structure was obtained for the smallest member of the series **50b** and the end-to-end bend of the teropyrene system is just 2° shy of 180°. Efforts aimed at the synthesis of more highly strained teropyrenophanes, *e.g.* **50a**, and the use of **50b-d** as starting points for the synthesis of pi-extended cyclophanes are underway in our laboratory.

Experimental Section

Experimental procedures and characterization data are given below only for compounds that have not been reported earlier.[7a-b]

General Experimental All reactions were performed under an atmosphere of nitrogen. Experiments involving moisture-sensitive compounds were carried out using anhydrous solvents and oven-dried (120 °C) glassware. Solvents for these reactions were dried and distilled according to standard procedures. All other solvents and chemicals were used as received. Solvents were removed under reduced pressure using a rotary evaporator. Chromatographic separations were achieved using Silicycle silica gel 60, particle size 40–63 μm. Column dimensions are recorded as height×diameter. Thin-layer chromatography was performed using precoated plastic-backed POLYGRAM® SIL G/UV254 silca gel plates, layer thickness 200 μm. Compounds were visualized using a UV lamp (254 and 365 nm). Melting points were measured using a Fisher-Johns apparatus and are uncorrected. ^{1}H (500.133 MHz) and ^{13}C (125.77 MHz) NMR spectra were recorded on a Bruker Avance 500 MHz spectrometer using $CDCl_3$ solutions. Chemical shifts are relative to internal standards: Me_4Si (δ_H=0.00 ppm), $CHCl_3$ (δ_H=7.26 ppm) and $CDCl_3$ (δ_C=77.23 ppm). Low-resolution and high-resolution mass spectra were obtained using an Agilent 1100 series LC/MSD instrument and a Waters Micromass GCT PremierTM instrument.

2,7-Dimethyl-2,7-octanediol (**18a**): A solution of dimethyl adipate (**17a**) (10.4 g, 59.7 mmol) in anhydrous THF (100 mL) was added dropwise over a period of 30 min to a stirred 0 °C solution of methylmagnesium bromide (3.0 M in Et_2O, 89 mL, 0.27 mol). After the addition was complete, the reaction mixture was heated at reflux for 10 h. The reaction mixture was cooled to room temperature and quenched by the addition of a saturated ammonium chloride solution (100 mL). The layers were separated and the aqueous layer was extracted with ether (2×50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield a white solid, which was recrystallized from heptane to give 2,7-dimethyl-2,7-decanediol (**18a**) as a white powder (8.63 g, 83%): m.p. 61–62 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47–1.49 (m, 4H), 1.41 (bs, 2H), 1.33–1.36 (m, 4H), 1.21 (s, 12H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 71.15, 44.10, 29.30, 25.03; LCMS (APCI-negative) *m/z* (rel. int.) 173.2 (100, $[M–H]^-$); HRMS (CI) calc'd for $C_{10}H_{23}O_2$ $(MH)^+$ 175.1698, found 175.1692.

2,7-Dichloro-2,7-dimethyloctane (**19a**): A mixture of 2,7-dimethyl-2,7-octanediol (**18a**) (6.34 g, 36.4 mmol) and concentrated aqueous HCl solution (100 mL) was stirred at room temperature for 2 h. The reaction mixture was poured into ice water (300 mL) and extracted with dichloromethane (3×50 mL). The combined organic extracts were washed with a saturated solution of sodium bicarbonate (2×50 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to give 2,7-dichloro-2,7-dimethyloctane (**19a**) as a light yellow oil (6.83 g, 89%), which was used without purification: ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.76–1.81 (m, 4 H), 1.54 (s, 12 H), 1.48–1.52 (m, 4 H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 71.15, 46.10, 32.65, 25.38; LCMS (APCI positive) *m/z* 211.1 ($[M+H]^+$). HRMS data could not be obtained for this compound.

2,7-Dimethyl-2,7-di(2-pyrenyl)octane (**21a**): Aluminum chloride (1.25 g, 9.38 mmol) was added to a stirred 0 °C solution of pyrene (**20**) (4.75 g, 23.5 mmol) and 2,7-dichloro-2,7-dimethyloctane (**19a**) (0.97 g, 4.6 mmol) in dichloromethane (40 mL). The resulting slurry was allowed to warm to room temperature and stirred for 4 h. The reaction was poured into ice water (200 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (2×50 mL) and the combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The solid yellow residue was subjected to column chromatography (20×5 cm; 1:9 dichloromethane/hexanes) to yield 2,7-dimethyl-2,7-bis(2-pyrenyl)octane (**21a**) as a white solid (1.17 g, 47%): R_f=0.34 (1:9 dichloromethane / hexanes); m.p. 204–205 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, *J*=7.5 Hz, 4H), 8.12 (s, 4H), 8.07–7.98 (m, 10H), 1.73–1.70 (m, 4H), 1.47 (s, 12H), 1.03–1.00 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 148.18, 131.32, 131.27, 128.12, 127.54, 125.93, 125.10, 125.00, 123.29, 123.18, 45.54, 38.73, 30.35, 27.89; LCMS (APCI-positive) *m/z* (rel. int.) 545 (10), 544 (48), 543 (100, $[M+H]^+$), 369 (65); HRMS (EI) calc'd for $C_{42}H_{38}$ $[M]^+$ 542.2974, found 542.2970.

1,3-Bis(bromomethyl)-7-*tert*-butylpyrene (**23**): 33% HBr in acetic acid (1.73 mL) was added to a stirred room temperature solution of 2-*tert*-butylpyrene (**22**) (0.318 g, 1.23 mmol) and paraformaldehyde (0.295 g, 9.86 mmol) in glacial acetic acid (10 mL). The reaction mixture was heated at 100 °C for 1 h and then poured into water (100 mL). The resulting mixture was extracted with dichloromethane (3×20 mL) and the combined organic extracts were washed with a saturated solution of sodium bicarbonate (2×50 mL), washed with water (50 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was preadsorbed on silica gel and subjected to column chromatography (20×3 cm, 1:1 dichloromethane / hexanes) to afford 1,3-bis(bromomethyl)-7-*tert*-butylpyrene (**23**) as a yellow solid (0.382 g, 70%): R_f=0.45 (1:1 dichloromethane / hexanes); m.p. 227–229 °C (1:1 dichloromethane / hexanes; Lit.[17] m.p. 229–231 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 2H), 8.27 (d, *J*=9.1 Hz, 2H), 8.20 (d, *J*=9.1 Hz, 2H), 7.95 (s, 1H), 5.12 (s, 4H), 1.58 (s, 9H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 150.14, 131.04, 130.44, 129.88, 129.25, 126.72, 125.89, 123.89, 123.11, 122.84, 35.47, 32.14, 31.89; LCMS (APCI-positive) *m/z* (rel. int.) 445 (49, $[M+H]^+$) , 443 (100, $[M+H]^+$), 441 (51, $[M+H]^+$); HRMS (EI) calc'd for $C_{42}H_{38}{}^{79}Br_2$ $[M]^+$ 441.9932, found 441.9938.

2,7-Dimethyl-2,7-di(6-bromopyren-2-yl)octane (**25**): 33% HBr in acetic acid (0.50 mL, 2.8 mmol) was added to a stirred solution of **21c** (0.110 g, 0.192 mmol) and 1,3,5-trioxane (0.057 g, 1.9 mmol) in glacial acetic acid (5 mL) at room temperature. The reaction was heated at 100 °C for 1 h, cooled to room temperature and then poured into ice water (30 mL). The resulting solution was extracted with dichloromethane (3×20 mL) and the combined organic extracts were washed with water (50 mL), washed a saturated solution of sodium bicarbonate (50 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was pre-adsorbed onto silica gel and subjected to column chromatography (20×3 cm; 10% dichloromethane/hexanes) to afford **25** as a beige solid (0.020 g, 14%): m.p. 178.9–180.2 °C (dichloromethane); R_f=0.21 (2% dichloromethane/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J*=9.1 Hz, 2H), 8.14 (d, *J*=8.1 Hz, 2H), 8.10–8.07 (m, 4H), 8.06 (d, *J*=9.3 Hz, 2H), 7.97 (d, *J*=9.00 Hz, 2H), 7.93 (d, *J*=8.2 Hz, 4H), 1.74–1.69 (m, 4H), 1.43 (s, 12H), 1.09–1.14 (m, 4H) , 0.98–0.89 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.57, 131.07, 130.89, 130.75, 130.56, 129.78, 129.59, 129.36, 127.01, 125.87, 125.43, 123.70, 123.50, 122.36, 119.79, 114.73, 45.13, 38.37, 30.15, 24.83; HRMS (APPI) calc'd for $C_{44}H_{40}{}^{79}Br_2$ $[M]^+$ 726.1505, found 726.1497.

2,7-Bis(6-formylpyren-2-yl)-2,7-dimethyloctane (**28a**)**:** Titanium(IV) chloride (1.40 g, 7.38 mmol) was added to a stirred 0 °C solution of 2,7-dimethyl-2,7-bis(2-pyrenyl)decane (**21a**) (1.59 g, 2.94 mmol) and dichloromethyl methyl ether (0.848 g, 7.38 mmol) in dichloromethane (30 mL). The ice bath was removed and stirring was continued at room temperature for 2 h. The reaction mixture was poured into ice water (150 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (2×30 mL) and the combined organic extracts were washed with a saturated solution of sodium bicarbonate (40 mL), washed with brine (40 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield a brown solid. The resulting solid was subjected to column chromatography (20×3 cm; dichloromethane) to yield 2,7-bis(6-formylpyren-2-yl)-2,7-dimethyloctane (**28**) as a bright yellow solid (1.53 g, 87%): m.p. 129–131 °C (dichloromethane); R_f=0.23 (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.71 (s, 2H), 9.28 (d, *J*=9.0 Hz, 2H), 8.29 (d, *J*=7.8 Hz, 2H), 8.17–8.13 (m, 6H), 8.10 (d, *J*=7.6 Hz, 2H), 8.05 (d, *J*=8.9 Hz, 2H), 7.93 (d, *J*=8.9 Hz, 2H), 1.75–1.73 (m, 4H), 1.50 (s, 12H), 1.05–1.02 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 193.20, 148.54, 135.44 131.18, 131.11, 131.01, 130.95, 130.89, 130.34, 127.38, 127.11, 125.03, 124.74, 124.62, 124.43, 122.98, 122.69, 45.31,

38.46, 29.56, 25.82; LCMS (APCI-positive, *m/z* (rel. int.)) 601 (11), 600 (49), 599 (100, $[M+H]^+$), 571 (18); HRMS (EI) calc'd for $C_{44}H_{38}O_2$ $[M]^+$ 598.2872, found 598.2870.

2,7-Bis(6-methylpyren-2-yl)-2,7-dimethyloctane (**29**)**:** A 50% solution of hydrazine hydrate (0.314 g, 3.14 mmol) and powdered potassium hydroxide (0.156 g, 2.78 mmol) were added to a suspension of 2,7-bis(6-formylpyren-2-yl)-2,7-dimethyloctane (**28**) (0.625 g, 1.05 mmol) in triethylene glycol (30 mL). The reaction mixture was heated at 200 °C for 1 h, cooled to room temperature and poured into ice water (100 mL). The resulting mixture was extracted with dichloromethane (3×40 mL). The combined organic extracts were washed with 1 M HCl (50 mL), a saturated solution of sodium bicarbonate (50 mL), brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The solid orange residue was subjected to column chromatography (30×4 cm, 1:5 dichloromethane / hexanes) to afford 2,7-bis(6-methylpyren-2-yl)-2,7-dimethyloctane (**29**) as a white solid (0.466 g, 82%): m.p. 210–212 °C (dichloromethane); R_f=0.32 (1:9 dichloromethane / hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J*=9.5 Hz, 2H), 8.05–8.02 (m, 6H), 8.00 (d, *J*=9.3 Hz, 2H), 7.94 (d, *J*=9.4 Hz, 2H), 7.89 (d, *J*=8.9 Hz, 2H), 7.80 (d, *J*=7.4 Hz, 2H), 2.94 (s, 6H), 1.73–1.71 (m, 4H), 1.47 (s, 12H), 1.03–1.01 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 148.79, 132.40, 132.06, 131.24, 130.63, 128.14, 125.73, 124.76, 124.51, 122.95, 122.63, 122.40, 122.36, 122.18, 122.03, 45.22, 38.66, 29.76, 26.06, 20.08 (19 of 20 expected signals observed); LCMS (APCI-positive) *m/z* (rel. int.) 573 (13), 572 (52), 571 (100, $[M+H]^+$), 355 (15); HRMS (EI) calc'd for $C_{44}H_{42}$ $[M]^+$ 570.3287, found 570.3281.

Alternative procedure for 2,7-bis(6-methylpyren-2-yl)-2,7-dimethyloctane (**29**)**:** Aluminum chloride (0.489 g, 3.68 mmol) was added to a stirred 0 °C solution of 1-methylpyrene (**30**) (0.831 g, 3.84 mmol) and 2,7-dichloro-2,7-dimethyloctane (**19a**) (0.368 g, 1.75 mmol) in dichloromethane (20 mL). The resulting slurry was allowed to warm to room temperature and stirred for 4 h. The reaction mixture was poured into ice water (100 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (2×20 mL) and the combined organic extracts were washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The solid orange residue was subjected to column chromatography (25×3 cm; 1:9 dichloromethane/hexanes) to yield 2,7-bis(6-methylpyren-2-yl)-2,7-dimethyloctane (**29**) as a white solid (0.148 g, 15%).

2,7-Dimethyl-2,7-bis(6,8-dimethylpyren-2-yl)octane (**32**)**:** Titanium(IV) chloride (0.372 g, 1.96 mmol) was added to a stirred 0 °C solution of 2,7-bis(6-methylpyren-2-yl)-2,7-dimethyloctane (**29**) (0.418 g, 0.733 mmol) and dichloromethyl methyl ether (0.216 g, 1.88 mmol) in dichloromethane (25 mL). The ice bath was removed and the resulting mixture was stirred at room temperature for 2 h. The reaction mixture was poured into ice water (100 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (2×25 mL) and the combined organic extracts were washed with a saturated solution of sodium bicarbonate (40 mL), washed with brine (40 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 2,7-bis(6-formyl-8-methylpyren-2-yl)-2,7-dimethyloctane (**31**) as a light brown solid. This material was suspended in triethylene glycol (20 mL) and hydrazine hydrate (0.566 g, 2.21 mmol) and powdered potassium hydroxide (0.19 g, 2.09 mmol) were added. The reaction was heated at 200 °C for 1 h, cooled to room temperature and poured into ice water (100 mL). The resulting solution was extracted with dichloromethane (3×30 mL). The combined organic extracts were washed with 1 M HCl solution (30 mL), washed with a saturated solution of sodium bicarbonate (30 mL), washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The solid orange residue was subjected to column chromatography (25×3 cm, 1:5 dichloromethane / hexanes) to afford 2,7-bis(1,3-dimethylpyren-7-yl)-2,7-dimethyloctane (**32**) as a white solid (0.184 g, 42%): m.p. 227–230 °C (dichloromethane); R_f=0.27 (1:9 dichloromethane/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, *J*=9.1 Hz, 4H), 8.04 (s, 4H), 7.96 (d, *J*=9.1 Hz, 4H), 7.71 (s, 2H), 2.94 (s, 12H), 1.75–1.72 (m, 4H), 1.49 (s, 12H), 1.04–1.02 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 148.23, 131.70, 131.20, 129.91, 127.76, 126.55, 125.21, 123.73, 123.71, 122.64, 45.31, 38.28, 29.90, 19.80 (14 of 15 expected signals observed) LCMS (APCI-positive) *m/z* (rel. int.) 601 (14), 600 (54), 599 (100, $[M+H]^+$), 355 (15); HRMS (EI) calc'd for $C_{46}H_{46}$ $[M]^+$ 598.3600, found 598.3591.

2,9-Bis(6-acetylpyren-2-yl)-2,9-dimethyldecane (**33**): Acetic anhydride (0.934 g, 9.09 mmol) was added to a stirred solution of 2,9-bis(2-pyrenyl)-2,9-dimethyldecane (**21c**) (0.863 g, 1.52 mmol) and zinc chloride (0.405 g, 2.98 mmol) in glacial acetic acid (20 mL). The reaction mixture was heated at 90 °C for 6 h, cooled to room temperature and poured into ice water (100 mL). The resulting mixture was extracted with dichloromethane (3×30 mL). The combined organic extracts were washed with a saturated solution of sodium bicarbonate (2×50 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The brown residue was subjected to chromatography (30×3 cm, dichloromethane) to afford 2,9-bis(6-acetylpyren-2-yl)-2,9-dimethyldecane (**33**) as a bright yellow solid (0.894 g, 90%): m.p. 218–221 °C (dichloromethane); R_f=0.38 (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (d, *J*=9.3 Hz, 2H), 8.23 (d, *J*=7.4 Hz, 2H), 8.12–8.09 (m, 6H), 8.01 (d, *J*=8.7 Hz, 2H), 7.99 (d, *J*=8.1 Hz, 2H), 7.90 (d, *J*=8.9 Hz, 2H) 2.83 (s, 6H), 1.75–1.72 (m, 4H), 1.47 (s, 12H), 1.10–1,08 (m, 4H), 0.99–0.94 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.14, 148.33, 133.91, 131.63, 130.86, 130.29, 130.03, 129.92, 129.36, 126.95, 126.85, 124.94, 124.85, 124.23, 123.91, 123.74, 122.46, 44.99, 38.22, 30.45, 30.03, 29.41, 24.72; LCMS (APCI-positive) *m/z* (rel. int.) 657 (11), 656 (55), 655 (100, $[M+H]^+$); HRMS (EI) calc'd for $C_{48}H_{46}O_2$ $[M]^+$ 654.3498, found 654.3492.

2,9-Bis(6,8-diacetylpyren-2-yl)-2,9-dimethyldecane (**34**): Aluminum chloride (3.97 g, 29.8 mmol) was added to a stirred 0 °C solution of acetyl chloride (1.11 g, 14.2 mmol) and 2,9-bis(2-pyrenyl)-2,9-dimethyldecane (**21c**) (1.93 g, 3.38 mmol) in dichloromethane (40 mL). The resulting mixture was allowed to slowly warm to room temperature and stirred for 4 h. The reaction mixture was poured into ice water (200 mL) and dichloromethane (50 mL) was added. The layers were separated and the aqueous layer was extracted with dichloromethane (2×50 mL). The combined organic extracts were washed with a saturated solution of sodium bicarbonate (50 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The yellow residue was recrystallized from acetone to afford 2,9-bis(6,8-diacetylpyren-2-yl)-2,9-dimethyldecane (**34**) as a bright yellow solid (2.11 g, 85%): m.p. 211–212 °C (acetone); R_f=0.25 (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (d, *J*=9.0 Hz, 4H), 8.68 (s, 2H), 8.22 (d, *J*=9.0 Hz, 4H), 8.19 (s, 4H), 2.94 (s, 12H), 1.78–1.75 (m, 4H), 1.48 (s, 12H), 1.12–1.10 (m, 4H), 1.02–0.98 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 201.85, 149.29, 132.40, 132.06, 131.24, 130.63, 128.14, 125.73, 124.76, 122.51, 45.22, 38.66, 30.89, 30.33, 29.76, 25.06 (16 of 17 expected signals observed); LCMS (APCI-positive) *m/z* (rel. int.) 741 (13), 740 (56), 739 (100, $[M+H]^+$); HRMS (EI) calc'd for $C_{52}H_{50}O_4$ $[M]^+$ 738.3709, found 738.3700.

(*Z*)-1,1,6,6-Tetramethyl[6.2](7,1)pyrenophane-17-ene (38a): Titanium(IV) chloride (0.55 mL, 5.0 mmol) was added slowly to a stirred slurry of zinc dust (660 mg, 9.9 mmol) in anhydrous THF (35 mL) at room temperature under a nitrogen atmosphere and the resulting brownish black slurry was heated at reflux for 1 h, during which time a dark black colour persisted (the loss of this colour indicates that the McMurry reaction will fail completely). Pyridine (0.68 mL, 8.4 mmol) was added by syringe and stirring was continued at reflux for a further 10 min. 2,7-Bis(6-formylpyren-2-yl)-2,7-dimethyloctane (**28a**) (350 mg, 0.6 mmol) in THF (65 mL) was then added slowly over 10 min and the reaction mixture was heated at reflux for a further 4 h. The hot reaction mixture was poured into chloroform (100 mL) and the solvents were removed under reduced pressure. The residue was adsorbed onto silica gel and subjected to column chromatography (20×3.5 cm, 1:9 chloroform / hexanes) to afford (*Z*)-1,1,6,6-tetramethyl[6.2](7,1)pyrenophane-17-ene (**38a**) as a yellow solid (200 mg, 60%): R_f=0.28 (3:17 chloroform / hexanes); m.p. 254.6–255.5 °C (1:9 chloroform / hexanes), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J*=7.9 Hz, 2H), 8.10 (d, *J*=7.9 Hz, 2H), 8.06 (d, *J*=8.8 Hz, 2H), 7.97 (d, *J*=8.8 Hz, 2H), 7.85 (d, *J*=1.8 Hz, 2H), 7.58 (s,

2H), 7.10 (d, *J*=1.8 Hz, 2H), 6.72 (d, *J*=9.2 Hz, 2H), 6.22 (d, *J*=9.2 Hz, 2H), 1.60 (br s, 2H), 1.38 (br s, 6H), 1.26 (br s, 8H), 0.81 (br s, 2H) –0.01 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.44, 133.32, 131.27, 130.68, 130.37, 130.05, 128.00, 127.78, 127.26, 126.93, 125.23, 125.09, 124.58, 124.44, 122.77, 122.31, 122.12, 46.02, 38.26, 30.88, 27.85, 26.35; LCMS (CI-(+)) *m/z* (rel. int.) 570 (3), 569 (13), 568 (48), 567 (100, $[M+H]^+$); HRMS (APPI) calc'd for $C_{44}H_{38}$ $[M]^+$ 566.2974, found 566.2945.

(*Z*)-11,20-Diformyl-1,1,6,6-tetramethyl[6.2](7,1)pyrenophane-17-ene (39a): To a stirred 0 °C solution of (*Z*)-1,1,6,6-tetramethyl[6,2](7.1)pyrenophane-17-ene (**38a**) (80 mg, 0.14 mmol) and dichloromethyl methyl ether (0.03 mL, 0.4 mmol) in dichloromethane (7 mL) was added titanium(IV) chloride (0.04 mL, 0.4 mmol). The ice bath was removed and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was poured into ice-cold water (20 mL) and the organic layer was separated. The aqueous layer was extracted with dichloromethane (2×15 mL) and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was subjected to column chromatography (10.0×2.5 cm, dichloromethane) to afford (*Z*)-11,20-diformyl-1,1,6,6-tetramethyl[6.2](7,1)pyrenophane-17-ene (**39a**) as a bright yellow solid (58 mg, 66%): R_f=0.30 (dichloromethane); m.p. >300 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.88 (s, 2H), 9.41 (br d, *J*=9.2 Hz, 2H), 8.54 (br s, 2H), 8.19 (d, *J*=9.2 Hz, 2H), 7.96 (s, 2H), 7.66 (s, 2H), 7.15 (br s, 2H), 7.12 (br d, *J*=8.0 Hz, 2H), 6.34 (br d, *J*=8.3 Hz, 2H), 1.66 (br s, 2H), 1.35 (br s, 6H), 1.25 (br s, 8H), 0.71 (br s, 2H), 0.07 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.14, 147.37, 132.37, 132.37, 131.32, 130.97, 129.99, 129.53, 129.44, 128.35, 126.82, 124.64, 124.62, 124.52, 124.00, 122.39, 121.39, 45.58, 38.05, 29.95, 28.00, 26.14 (22 of 23 expected signals observed); LC-MS (CI-(+)) *m/z* (rel. int.) 625 (18), 624 (35), 623 (100, $[M+H]^+$); HRMS (APPI) calcd for $C_{46}H_{38}O_2$ ($[M]^+$) 622.2872, found 622.2876.

1,5-Bis(7-*tert*-butylpyren-1-yl)-1,5-pentanedione (**40**): Aluminum chloride (3.20 g, 24.0 mmol) was added to a stirred 0 °C solution of glutaryl dichloride (0.99 g, 5.9 mmol) and 2-*tert*-butylpyrene (**22**) (3.02 g, 11.7 mmol) in dichloromethane (20 mL). After 1 h, the reaction mixture was poured into ice water (100 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (3×30 mL) and the combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The brown residue was subjected to column chromatography (45×4 cm; dichloromethane) to yield 1,5-bis(7-*tert*-butylpyren-1-yl)-1,5-pentanedione (**40**) as a pale yellow solid (1.36 g, 38%): m.p. 231–233 °C (dichloromethane); R_f=0.35 (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (d, *J*=9.4 Hz, 2H), 8.33 (d, *J*=8.0 Hz, 2H), 8.29 (br s, 4H), 8.18 (d, *J*=9.4 Hz, 2H), 8.13 (d, *J*=8.9 Hz, 2H), 8.09 (d, *J*=8.0 Hz, 2H), 7.99 (d, *J*=8.9 Hz, 2H), 3.46 (t, *J*=7.0 Hz, 4H), 2.49 (quint, *J*=7.0 Hz, 2H), 1.60 (s, 18H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 204.65, 149.79, 133.83, 132.18, 131.14, 130.60, 129.89, 129.78, 129.39, 127.09, 126.24, 125.12, 124.86, 124.03, 123.79, 123.44, 122.75, 41.25, 35.45, 32.10, 20.51; LCMS (APCI-positive) *m/z* (rel. int.) 615 (13), 614 (51), 613 (100, $[M+H]^+$), 355 (12); HRMS (EI) calc'd for $C_{45}H_{40}O_2$ $[M]^+$ 612.3028, found 612.3018. Also obtained from this reaction was 6-(7-*tert*-butylpyren-1-yl)-3,4-dihydro-2*H*-pyran-2-one as a light brown oil (1.45 g, 35%): R_f = 0.32 (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J*=9.3 Hz, 1H), 8.27 (s, 2H), 8.13–8.08 (m, 3H), 8.04–8.01 (m, 2H), 5.71 (t, *J*=4.7 Hz, 1H), 2.91–2.88 (m, 2H), 2.70–2.66 (m, 2H), 1.59 (s, 9H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 169.14, 151.96, 149.59, 131.94, 131.35, 130.82, 128.80, 128.65, 128.56, 128.35, 127.32, 126.51, 124.96, 124.57, 124.49, 123.16, 123.09, 122.93, 101.44, 36.48, 32.16, 28.81, 20.04; IR (neat) ν = 3102, 2953, 2889, 1752, 1594, 1546, 1460; LCMS (APCI-positive) *m/z* (rel. int.) 388 (27), 387 (100, $[M+Na]^+$), 356 (17), 355 (62, $[M+H]^+$); HRMS (EI) calc'd for $C_{25}H_{22}O_2$ $[M]^+$ 354.1620, found 354.1622.

1,2-Bis(7-tert-butylpyren-1-yl)cyclopentene (**41**): Titanium(IV) chloride (1.34 g, 7.22 mmol) was added to a stirred 0 °C slurry of zinc dust (0.461 g, 7.05 mmol) in THF (45 mL). After the addition was complete, the reaction mixture was heated at 70 °C for 1 h, at which point a dark black color persisted. Pyridine (0.2 mL) was added to the mixture and after 10 min a solution of 1,5-bis(7-*tert*-butylpyren-1-yl)-1,5-pentanedione (**40**) (0.540 g, 0.882 mmol) in THF (20 mL) was added. The reaction mixture was heated at 70 ºC for a further 2 h and then poured without significant cooling into chloroform (50 mL). The resulting mixture was concentrated under reduced pressure and adsorbed onto silica gel in preparation for column chromatography. Aqueous work-up for this reaction is not recommended as layer separation can be problematic and the yields are typically lower. The preadsorbed sample was subjected to column chromatography (20×3.5 cm; 1:9 dichloromethane / hexanes) to yield 1,2-bis(7-*tert*-butylpyren-1-yl)cyclopentene (**41**) as a light green oil (0.487 g, 95%): R_f = 0.34 (1:9 dichloromethane / hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, *J*=9.2 Hz, 2H), 8.22 (d, *J*=1.8 Hz, 2H), 8.18 (d, *J*=1.8 Hz, 2H), 8.04 (d, *J*=9.2 Hz, 2H), 7.94 (d, *J*=8.9 Hz, 2H), 7.87–7.85 (m, 4H), 7.80 (d, *J*=7.9 Hz, 2H), 3.43 (t, *J*=7.4 Hz, 4H) 2.57 (quint, *J*=7.4 Hz, 2H), 1.60 (s, 18H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 148.93, 141.49, 134.64, 131.28, 130.92, 130.01, 128.48, 127.19, 127.15, 126.53, 125.55, 125.53, 124.54, 123.26, 122.18, 122.11, 122.09 41.24, 35.32, 32.10, 24.33; LCMS (APCI-positive) *m/z* (rel. int.) 583 (11), 582 (49), 581 (100, $[M+H]^+$); HRMS (EI) calc'd for $C_{45}H_{40}$ $[M]^+$ 580.3130, found 580.3129.

1,1,8,8-Tetramethyl-20-thia[8.3](7,1)pyrenophane (43): Na_2S/Al_2O_3 (0.198 g, 0.497 mmol) was added in three equal portions to a stirred room temperature solution of 2,9-bis(6-(bromomethyl)pyren-2-yl)-2,9-dimethyldecane (**42**) (0.250 g, 0.331 mmol) in 1:9 (v/v) EtOH/dichloromethane (75 mL) over a 20 min period. The resulting slurry was stirred vigorously for 12 h and then was suction filtered. The filtrate was concentrated under reduced pressure and the residue was subjected to column chromatography (25×3 cm; 2:5 dichloromethane / hexanes) to yield **43** as a light yellow oil (0.184 g, 89%); R_f=0.62 (2:5 dichloromethane / hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 2H), 8.01 (d, *J*=7.9 Hz, 2H), 7.98–7.94 (m, 24), 7.96 (d, *J*=7.7 Hz, 2H), 7.71 (s, 2H) 6.82 (s, 4H), 4.41 (s, 4H), 1.73–1.69 (m, 4H) 1.54 (s, 12H), 1.20–1.17 (m, 4H), 0.91–0.87 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 146.94, 131.33, 131.08, 130.99, 130.41, 128.80, 127.78, 127.63, 127.34, 127.28, 125.42, 123.97, 123.36, 122.95, 122.88, 122.85, 45.36, 38.36, 34.13, 30.30, 30.11, 24.05; LCMS (APCI-positive), *m/z* (rel. int.) 631 (12), 630 (51), 629 (100, $[M+H]^+$); HRMS (EI) calc'd for $C_{46}H_{44}S$ $[M]^+$ 628.3164, found 628.3162.

1,1,8,8-Tetramethyl-20-thia[8.3](7,1)pyrenophane-*S*,*S*-dioxide (44): 3-Chloroperoxybenzoic acid (0.066 g, 0.381 mmol) and sodium bicarbonate (0.107 g, 1.27 mmol) were added to a stirred 0 °C solution of thiacyclophane **43** (0.080 g, 0.127 mmol) in dichloromethane (6 mL). The reaction mixture was allowed to warm slowly to room temperature and then stirred for 12 h. The reaction mixture was poured into water (20 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (2×20 mL). The combined organic extracts were washed with water (20 mL), washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to give an orange residue, which was directly subjected to chromatography (15×2 cm, dichloromethane) to afford **44** as a light orange oil (0.042 g, 50%); R_f=0.28 (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16–8.13 (m, 4H), 8.09 (d, *J*=1.4 Hz, 2H), 8.06 (d, *J*=8.9 Hz, 2H), 8.01 (d, *J*=8.9 Hz, 2H), 7.63 (d, *J*=1.4 Hz, 2H), 6.80 (d, *J*=9.3 Hz, 2H), 6.62 (d, *J*=9.3 Hz, 2H), 5.07 (s, 4H), 1.70–1.67 (m, 4H), 1.46 (s, 12H), 1.16–1.14 (m, 4H), 0.81–0.78 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 147.57, 132.25, 131.22, 130.58, 130.41, 129.05, 128.95, 128.38, 127.28, 125.34, 125.03, 123.97, 123.79, 122.72, 122.42, 121.60, 56.71, 45.51, 38.63, 30.43, 30.18, 24.20; LCMS (APCI-positive), *m/z* (rel. int.) 663 (11), 662 (49), 661 (100, $[M+H]^+$); HRMS (EI) calc'd for $C_{46}H_{44}SO_2$ 660.3062 ($[M]^+$), found 660.3058.

(*Z*)-1,1,8,8-Tetramethyl[8.2](7,1)pyrenophanemonoene (*Z*)-38c: Potassium hydroxide (0.048 g, 1.21 mmol) was added to a stirred room temperature solution of sulfone **44** (0.040 g, 0.061 mmol) in a mixture of carbon tetrachloride (2.5 mL), water (1 mL) and *tert*-butanol (2.5 mL). The resulting mixture was heated at 80 °C for 4 d, until all of the starting material had been consumed (TLC analysis). The reaction was cooled to room temperature, poured into water (25 mL) and extracted with dichloromethane (3×15 mL). The combined organic extracts were

washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to give an orange residue, which was adsorbed onto silica gel in preparation for column chromatography. Chromatography (15×1.5 cm, 1:5 dichloromethane / hexanes) afforded (*Z*)-**38c** as a bright yellow oil (0.021 g, 58%): R_f=0.52 (1:5 dichloromethane / hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J*=7.8 Hz, 2H), 7.89 (d, *J*=7.8 Hz, 2H), 7.86–7.84 (m, 4H), 7.81 (d, *J*=8.9 Hz, 2H), 7.73 (s, 2H), 7.65 (bs (poorly resolved doublet), 2H), 7.52 (s, 2H), 7.10 (poorly resolved doublet, 2H), 1.61–1.58 (m, 4H), 1.40 (s, 12H), 1.02–1.00 (m, 4H), 0.49–0.46 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 146.36, 133.38, 131.01, 130.32, 130.00, 127.77, 127.43, 127.24, 127.04, 126.06, 125.28, 125.54, 124.22, 122.80, 122.61, 122.49, 46.42, 38.18, 30.75, 24.42 (20 of 22 expected signals observed) LCMS (APCI-positive), *m/z* (rel. int.) 597 (12), 596 (53), 595 (100, $[M+H]^+$); HRMS (EI) calc'd for $C_{46}H_{42}$ 594.3287 ($[M]^+$), found 594.3281.

2,9-Dimethyl-2,9-bis(6-vinylpyren-2-yl)decane (**45**): A solution of *n*-butyllithium (1.0 M in hexanes, 0.28 mL, 0.28 mmol) was added to methyltriphenylphosphonium bromide (0.101 g, 0.283 mmol) in THF (5 mL) at –50 °C. The reaction mixture was maintained at –50 °C for 15 min and then a solution of 2,9-bis(6-formylpyren-2-yl)-2,9-dimethyldecane (**28c**) (0.050 g, 0.080 mmol) in THF (10 mL) was added. The cold bath was removed and the reaction was stirred at room temperature for 30 min. The solvent was concentrated under reduced pressure and the resulting oily yellow residue was taken up into dichloromethane (20 mL), washed with a 1 M HCl solution (10 mL), washed with a saturated sodium bicarbonate solution (20 mL), washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to give a white foam, which was adsorbed onto silica gel in preparation for chromatography. Column chromatography (15×2 cm, 1:9 dichloromethane / hexanes) afforded 2,9-bis(6-vinylpyren-2-yl)-2,9-dimethyldecane (**45**) as a light yellow oil (0.029 g, 58%); R_f=0.37 (1:9 dichloromethane / hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J*=9.3 Hz, 2H), 8.15 (d, *J*=8.0 Hz, 2H), 8.09 (d, *J*=8.0 Hz, 2H), 8.07 (s, 4H), 8.03 (d, *J*=9.3 Hz, 2H), 7.97–7.95 (m, 4H), 7.79 (dd, *J*=17.3, 11.0 Hz, 2H), 5.98 (dd, *J*=17.3, 1.1 Hz, 2H), 5.61 (dd, *J*=11.0, 1.1 Hz, 2H), 1.79–1.76 (m, 4H), 1.49 (s, 12H), 1.15–1.12 (m, 4H), 1.04–1.00 (m, 4H); ^{13}C NMR (125.77 MHz, $CDCl_3$) δ 147.97, 134.49, 132.33, 131.43, 131.01, 130.82, 128.20, 128.03, 127.72, 127.40, 125.14, 125.00, 123.47, 123.32, 123.29, 123.06, 123.01, 117.09, 45.25, 38.38, 30.29, 29.67, 24.96; LCMS (APCI-positive) *m/z* (rel. int.) 625 (12), 624 (51), 623 ($[M+H]^+$, 100); HRMS (EI) calc'd for $C_{48}H_{46}$ 622.3600 ($[M]^+$), found 622.3603.

1,1,6,6-Tetramethyl[6.2](7,1)pyrenophane (**53a**): Sodium borohydride (0.265 g, 7.02 mmol) was added to a stirred solution of 2,7-bis(6-formylpyren-2-yl)-2,7-dimethyloctane (**28a**) (0.602 g, 1.01 mmol) in THF (100 mL). The reaction mixture was stirred at room temperature for 12 h and then cooled to 0 °C. The reaction mixture was neutralized using a 5.0 M aqueous HCl solution. Most of the THF was removed under reduced pressure. Dichloromethane (300 mL) was added to the resulting mixture. The layers were separated and the aqueous layer was extracted with dichloromethane (2×100 mL). The combined organic layers were washed with brine (70 mL), dried over Na_2SO_4, gravity filtered and concentrated under reduced pressure to afford 2,7-dimethyl-2,7-bis(6-(hydroxymethyl)pyren-2-yl)octane as a fluffy white solid (0.500 g): R_f = 0.10 (50% ethyl acetate / hexanes); R_f = 0.10 (50% ethyl acetate / hexanes); m.p. 102.8–103.5 °C (dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, *J*=9.3 Hz, 2H), 8.11–7.96 (m, 12H), 5.36 (s, 4H), 1.93 (s, 2H), 1.72–1.70 (m, 4H), 1.47(s, 12H), 1.03–1.00 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.72, 133.59, 131.13, 130.53, 128.63, 127.72, 127.15, 125.73, 124.48, 123.19, 123.07, 122.94, 122.79, 63.91, 45.07, 38.21, 29.75, 29.44, 25.60; HRMS (APPI) for $C_{44}H_{41}O$ 585.3152 ($[M+H–H_2O]^+$), found 585.3166. The crude diol (0.500 g, 0.83 mmol) was dissolved in dichloromethane (50 mL) and the solution was cooled to 0 °C. Phosphorus tribromide (0.033 g, 1.21 mmol) was added and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was poured into ice-cold water and the layers of the resulting mixture were separated. The aqueous layer was extracted with dichloromethane (2×10 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4, gravity filtered and concentrated under reduced pressure to afford 2,7-bis(6-(hydroxymethyl)pyren-2-yl)octane (**52a**) (0.326 g) as a pale yellow solid: R_f=0.60 (1:4 ethyl acetate / hexanes); m.p. 258.0–259.4 °C (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J*=9.2 Hz, 2H), 8.14 (d, *J*=9.0 Hz, 2H), 8.13 (d, *J*=1.2 Hz, 2H), 8.10 (d, *J*=1.7 Hz, 2H), 8.06 (d, *J*=7.8 Hz, 2H), 7.99 (d, *J*=8.8 Hz, 2H), 7.97 (d, *J*=7.7 Hz, 2H), 7.96 (d, *J*=8.9 Hz, 2H), 5.25 (s, 4H), 1.77–1.68 (m, 4H), 1.49 (s, 12H), 1.04–0.98 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.35, 132.14, 131.32, 130.88, 130.70, 129.24, 128.80, 128.61, 127.69, 127.44, 125.39, 124.96, 123.82, 123.79, 123.15, 122.99, 45.46, 38.55, 32.66, 29.76, 25.95; HRMS (APPI) calcd for $C_{44}H_{40}{}^{79}Br_2$ 726.1497 ($[M]^+$), found 726.1513. Crude dibromide **52a** (0.326 g, 0.449 mmol) was dissolved in anhydrous THF (30 mL) and the solution was cooled to 0 °C under a nitrogen atmosphere. BuLi (1.05 M, 0.42 mL, 0.45 mmol) was added dropwise over a period of 20 min. The reaction mixture was then quenched with ice-cold water (10 mL) and most of the THF was removed under reduced pressure. Dichloromethane (30 mL) was added to the resulting mixture. The layers were separatedand the aqueous layer was extracted with dichloromethane (2×5 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The pale yellow residue was subjected to column chromatography (4.0×20 cm, 1:8 chloroform / hexanes) to afford 1,1,6,6-tetramethyl[6.2](7,1)pyrenophane (**53a**) (0.120 g, 20% over three steps) as a fluffy white solid: R_f=0.32 (1:3 dichloromethane / hexanes); m.p. 210.1–212.8 °C (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J*=7.7 Hz, 2H), 8.10 (d, *J*=7.7 Hz, 2H), 8.06 (d, *J*=8.8 Hz, 2H), 7.94 (d, *J*=8.8 Hz, 2H), 7.82 (d, *J*=1.7 Hz, 2H), 7.09 (d, *J*=1.7 Hz, 2H), 6.16 (d, *J*=9.2 Hz, 2H), 6.12 (d, *J*=9.2 Hz, 2H), 3.86–3.72 (AA'BB' spectrum, 4H), 1.70–1.63 (m, 2H), 1.38 (s, 6H), 1.40–1.32 (m, 2H), 1.24 (s, 6H), 0.92–0.88 (m, 2H), 0.26–0.15 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.37, 136.76, 130.73, 130.41, 130.30, 130.06, 127.75, 127.23, 127.19, 125.33, 124.93, 124.66, 122.93, 122.45, 122.31, 121.67, 45.77, 38.43, 37.01, 31.47, 28.16, 26.66; HRMS (APPI) calculated for $C_{44}H_{40}$ *m/z* = 568.3130 ($[M]^+$), found 568.3145.

11,20-Diformyl-1,1,6,6-tetramethyl[6.2](7,1)pyrenophane (**54a**): 1,1,6,6-Tetramethyl[6.2](7,1)pyrenophane (**53a**) (0.119 g, 0.209 mmol) was dissolved in dichloromethane (20 mL) and the solution was cooled to 0 °C under a nitrogen atmosphere. Titanium(IV) chloride (0.79 g, 4.2 mmol) and dichloromethyl methyl ether (0.48 g, 4.2 mmol) were added and the resulting deep purple solution was stirred at room temperature for 4 h. The reaction mixture was then slowly poured (*exothermic*) into ice-cold water (20 mL) and the layers were separated. The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The yellow residue was subjected to column chromatography (12×7 cm; 40% dichloromethane / hexanes) to afford 11,20-diformyl-1,1,6,6-tetramethyl[6.2](7,1)pyrenophane (**54a**) (0.095 g, 76%) as a yellow solid: R_f = 0.13 (dichloromethane); m.p. >300 °C (dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.95 (s, 2H), 9.38 (d, *J*=9.2 Hz, 2H), 8.56 (s, 2H), 8.17 (d, *J*=9.5 Hz, 2H), 7.93 (d, *J*=1.8 Hz, 2H), 7.16 (d, *J*=1.8 Hz, 2H), 6.28 (d, *J*=9.2 Hz, 2H), 6.25 (d, *J*=9.2 Hz, 2H), 3.95–3.86 (AA'BB' half-spectrum, 2H), 3.82–3.73 (AA'BB' half-spectrum, 2H), 1.77–1.68 (m, 2H), 1.45–1.38 (m, 2H), 1.36 (s, 6H), 1.24 (s, 6H), 0.88–0.78 (m, 2H), 0.30–0.20 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.47, 147.51, 136.02, 134.85, 132.92, 130.06, 130.01, 129.84, 128.13, 127.72, 124.96, 124.42, 123.79, 122.46, 122.43, 121.72, 121.52, 45.54, 38.44, 36.61, 30.71, 28.89, 26.66; HRMS (APPI) calculated for $C_{46}H_{41}O_2$ 625.3029 ($[M+H]^+$), found 625.3039.

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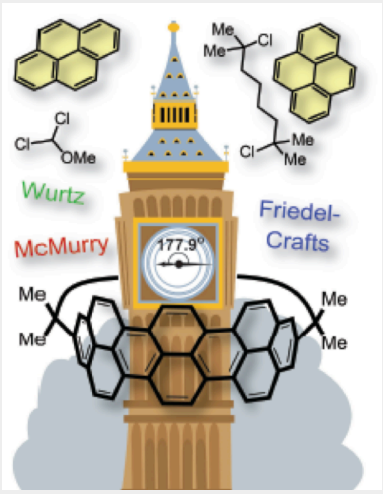
Entry for the Table of Contents (Please choose one layout)

Cyclophanes

FULL PAPER

***BIG BEND* chimes in – this is not second hand news!** Every minute detail of the synthesis of a striking series of 1,1,*n*,*n*-tetramethyl[*n*](2,11)teropyrenophanes (*n*=7–9) is described. The end-to-end bend in the teropyrene system clocks in at as much as 177.9°.



*Kiran Sagar Unikela, Bradley L. Merner, Parisa Ghods Ghasemabadi, C. Chad Warford, Christopher Qiu, Louise N. Dawe, Yuming Zhao, Graham J. Bodwell**

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The Development of Synthetic Routes to 1,1,*n*,*n*-Tetramethyl[*n*](2,11)teropyrenophanes