Benzoannelated *cis,cis,cis,trans*-[5.5.5.6]Fenestranes: Syntheses, Base Lability, and Flattened Molecular Structure of Strained Epimers of the all-*cis* Series

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Abstract: Tribenzofenestranes possessing the strained *cis,cis,cis,trans*-[5.5.5.6]-fenestrane skeleton have been synthesized from *cis*-2,6-diphenylspiro[cyclohexane-1,2′-indane]-1′,3′-diols by twofold cyclodehydration, in striking analogy to the strategy used previously to construct the stereoisomeric all-*cis*-tribenzo[5.5.5.6]fenestranes from the corresponding *trans*-diphenylspirodiols. In this manner, both of the parent hydrocarbons, all-*cis*-tribenzo[5.5.5.6]fenestrane **3** and *cis,cis,cis,trans*-tribenzo[5.5.5.6]fenestrane **4**, have been made accessible from the spirodiketones **5** and **6**, respectively. The C6-functionalized derivatives of **4**—*cis,cis,cis,trans*-fenestranol **9** and *cis,cis,cis,trans*-fenestranone **12**—were prepared through *cis*-diphenylspirotriol **8** and *cis*-diphenyldispiroacetaldiol **11**, by using the same strategy. The *cis,cis,-cis,trans*-[5.5.5.6]fenestrane framework readily epimerizes to the more stable all-*cis* isomers under basic conditions, but is stable under neutral or acidic conditions. For example, *cis,cis,cis,trans*-fenestranone **12** yielded all-*cis* fenestrane **3** under Wolff–Kishner conditions, but *cis,cis,cis,trans*-isomer **4** under Clemmensen conditions. Epimerization was also circumvented by radical-induced desulfurization of fenestrane dithiolane **15** with nBu$_3$SnH/AIBN, producing **4** in excellent yields. A single-crystal X-ray structure analysis of **4** revealed that, in accordance with force field and semi-empirical MO calculations, the extra strain of the benzoannelated *cis,cis,cis,trans*-[5.5.5.6]fenestratriene framework [E_{strain}(**4**) − E_{strain}(**3**) = 46 kJ mol^{-1}] is due both to the almost perfect boat conformation of the six-membered ring and to considerable bond angle widening at the central, non-bridged C4b–C15d–C11b unit (121°). H/D exchange experiments with the *cis,cis,cis,trans* hydrocarbon **4** under basic conditions demonstrated that the strain-induced epimerization to **3** occurs through direct deprotonation of the "epimeric" benzylic bridgehead C7a–H bond, which was found to be more acidic than the two C–H bonds at the benzhydrylic bridgeheads.

Keywords: C–H acidity · cyclodehydration · fenestranes · polycycles · strained molecules

Introduction

The carbon framework of [*m.n.o.p*]fenestranes is defined not only by the characteristic mutual fusion of their four rings along all of the four neopentane C–C bonds in a "*tetrafuso*"-tetracyclic framework,[1] but also by the stereochemistry of its four peripheral bridgehead atoms.[2] Given the numerous possibilities offered by varying the ring sizes and the relative configuration of the bridgeheads, major areas of the potential of fenestrane chemistry[3] remain unexplored experimentally.[4] As far as the strained stereoisomers of the most stable all-*cis* fenestranes are concerned, a few small-ring *cis,cis,cis,trans* isomers of the [4.5.5.5]fenestrane series are known, synthesized by photoinduced [2 + 2] cycloaddition or by Claisen rearrangement of suitable precursors.[5–7] However, except for a particular polycondensed derivative reported recently,[8] no normal ring [*m.n.o.p*]fenestranes (*m*, *n*, *o*, *p* = 5 and/or 6) containing a *trans*-fused bicyclic subunit are known experimentally to date.[9] However, extensive computational work has been published on stereoisomeric [5.5.5.5]fenestranes[2, 3] and also on [6.6.6.6]fenestranes,[1] demonstrating that the strain of the *trans*-bicyclo[3.3.0]octane (*fuso*-diquinane) unit[10] and even of the *trans*-bicyclo[4.3.0]nonane (hydrindane) unit,[11] respectively, is considerably increased by merging them into a *cis,cis,cis,trans*-fenestrane skeleton. Moreover, the calculations point to a sizeable increase in the non-bridged C–C–C bond angles at the central bridgehead atom of the [5.5.5.5]- (and smaller) fenestrane cores.

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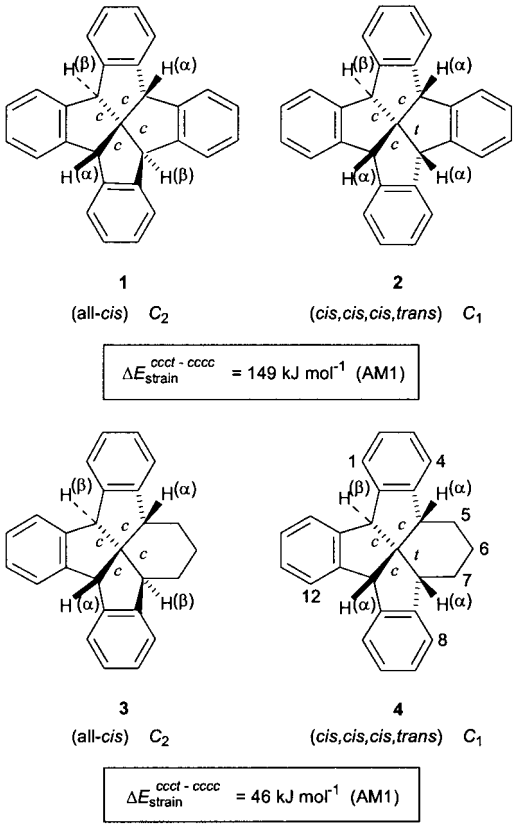
Therefore, fenestranes bearing at least one *trans* fusion at the neopentane core have been of considerable interest in the context of the planar tetracoordinate carbon problem.[12, 13]

Benzoannelated fenestranes[3a] have been shown to be versatile substrates for exploration of the stereochemistry of the *tetrafuso*-tetracyclic framework.[14, 15] A particularly challenging goal in the [5.5.5.5]fenestrane series is a strained stereoisomer of all-*cis*-[5.5.5.5]fenestrindane (**1**),[14d, 17] in the form of its *cis,cis,cis,trans*-isomer **2** (dubbed "epi-fenestrindane"[3a]). Semi-empirical calculations[3a] suggest a considerable increase of strain ($\Delta E_{strain} = 148.5$ kJ mol^{-1}) associated with epimerization of one of the peripheral bridgeheads of **1**, thus generating **2**. This parallels the value calculated for the corresponding [5.5.5.5]fenestratetraenes ($\Delta E_{strain} = 150.2$ kJ mol^{-1}) and significantly exceeds the increase in strain previously calculated for the epimerization of a bridgehead in the *saturated* [5.5.5.5]fenestranes ($\Delta E_{strain} \approx 79.9$ kJ mol^{-1}).[2, 3a, 3d] In this paper, we report on the first examples of [5.5.5.6]fenestranes possessing a *trans*-fused central C–C bond, including *cis,cis,cis,trans*-tribenzo[5.5.5.6]fenestrane **4**



and several C6-functionalized derivatives.[16] The solid-state molecular structure of **4** demonstrates some detailed features of this strained hydrocarbon framework, and H/D exchange experiments have revealed the enhanced acidity of the epimeric bridgehead C–H bond. Although the *trans*-hydrindene unit in **4**, a stereoisomer of the known all-*cis*-[5.5.5.6]fenestrane (**3**),[14d, 17] is certainly less strained than the related diquinene unit in **2**, the amplification of strain induced by its incorporation into a [5.5.5.6]fenestrane framework will become obvious.

Abstract in German: *Tribenzofenestrane mit dem gespannten cis,cis,cis,trans-[5.5.5.6]Fenestran-Gerüst lassen sich aus cis-2,6-Diphenylspiro[cyclohexan-1,2′-indan]-1′,3′-diolen durch zweifache Cyclodehydrierung synthetisieren – in überraschend einfacher Analogie zu der Strategie, die sich beim Aufbau der stereoisomeren all-cis-Tribenzo[5.5.5.6]fenestrane aus den entsprechenden trans-Diphenylspirodiolen bewährt hat. So sind beide Grundkörper, das all-cis-Tribenzo[5.5.5.6]-fenestran **3** und das cis,cis,cis,trans-Tribenzo[5.5.5.6]fenestran **4**, aus den entsprechenden Spirodiketonen **5** bzw. **6** zugänglich. Auf diese Weise lassen sich auch C6-funktionalisierte Derivate von **4**, wie das cis,cis,cis,trans-Fenestranol **9** und das cis,cis,cis,trans-Fenestranon **12**, über das cis-Diphenylspirotriol **8** bzw. das cis-Diphenyldispiroacetaldiol **11** darstellen. Cis,cis,cis,trans-[5.5.5.6]Fenestrane epimerisieren unter basischen Bedingungen leicht zu den thermodynamisch stabileren all-cis Isomeren; im neutralen oder sauren Milieu sind sie jedoch beständig. So führt die Wolff–Kishner-Reaktion von cis,cis,cis,trans-Fenestranon **12** zum all-cis-Fenestran **3**, während die Clemmensen-Reduktion das cis,cis,cis,trans Isomer **4** ergibt. Die Epimerisierung läßt sich auch durch Radikal-induzierte Desulfurierung des Fenestran-Dithiolans **15** mit nBu_3SnH/AIBN umgehen, wobei **4** in hoher Ausbeute entsteht. Die Einkristall-Röntgenstrukturanalyse von **4** belegt in Übereinstimmung mit Kraftfeld- und semiempirischen MO-Rechnungen die erhöhte Spannung des benzoannellierten cis,cis,cis,trans-[5.5.5.6]Fenestratrien-Gerüstes* [E_{strain}(**4**) − E_{strain}(**3**) = 46 kJ mol^{-1}], *die durch die nahezu ideale Boot-Konformation des sechsgliedrigen Ringes und die beträchtliche Aufweitung des nicht überbrückten Winkels C4b-C15d-C11b = 121° am zentralen Kohlenstoff-Atom hervorgerufen wird. H/D-Austauschexperimente mit dem cis,cis,cis,trans-Kohlenwasserstoff **4** unter basischen Bedingungen zeigen, dass die Spannungs-induzierte Epimerisierung zu **3** durch direkte Deprotonierung des „epimeren" benzylischen Brückenkopfs C7a–H erfolgt, der weitaus acider ist als die C–H-Bindungen an den beiden benzhydrylischen Brückenköpfen.*

Results and Discussion

Synthesis and conformation of C6-functionalized *cis*,*cis*,*cis*,-*trans*-tribenzo[5.5.5.6]fenestranes: Synthetic access to *cis,cis,-cis,trans*-[5.5.5.6]fenestranes is simple. It is, in fact, perplexingly simple, since it follows the same strategy as the synthesis of the corresponding all-*cis* isomers, which was based on the stereochemistry of spirotriketone **5** (Scheme 1).[14d, 17, 18] Whereas the spatial orientation of both of the phenyl groups in **5** appeared to be essential to achieve the single-step construction of the all-*cis* fenestrane skeleton of **7**, use of the *cis*-isomer **6** for this purpose seemed to be impossible since, in this case, both of the phenyl groups point towards the same oxo-functionalized position (C-1 *or* C-3) of the indane moiety. In fact, *trans*-spirotriones such as **5** are, in general, the products of kinetic control[19, 20] and formation of the more thermodynamically stable *cis*-diarylspirotriones such as **6** has to be prevented carefully. This prerequisite being fulfilled, the twofold cyclodehydration of appropriate *trans*-2,6-diphenyl-

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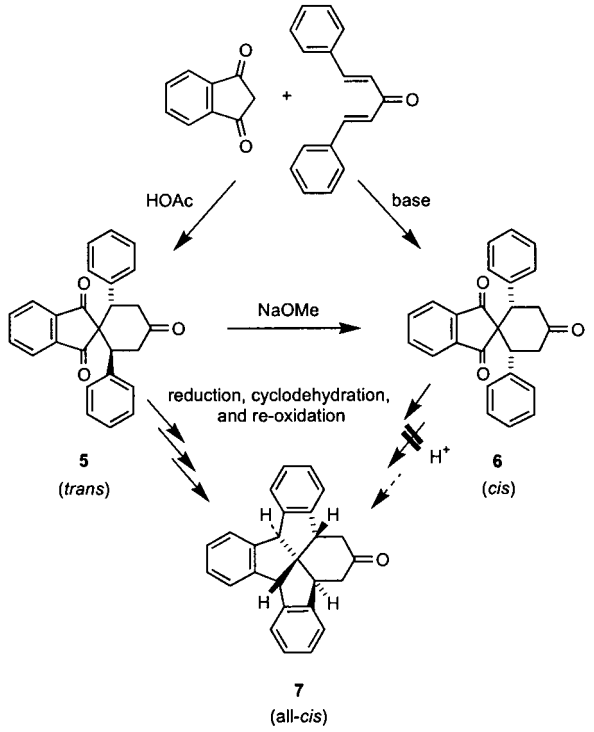
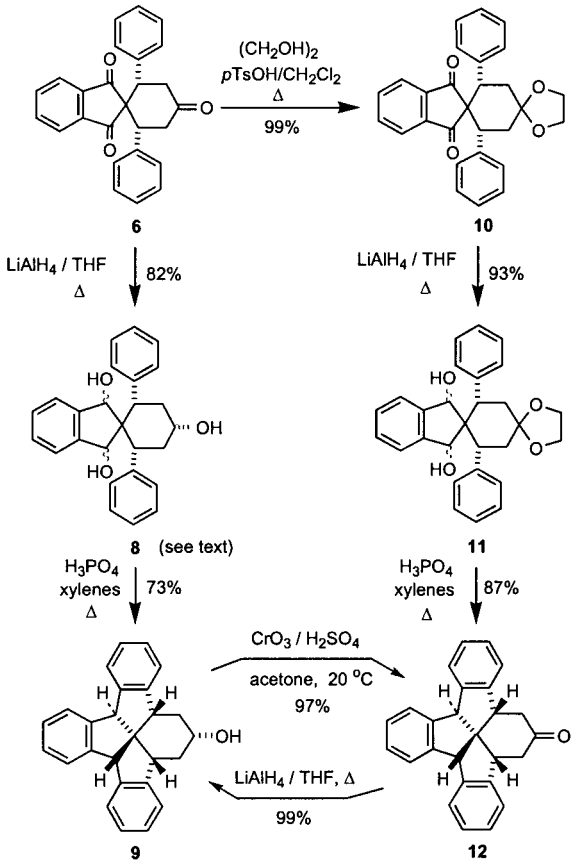


Scheme 1. Construction of the all-*cis*-tribenzo[5.5.5.6]fenestrane framework, with the *trans*-diaryl stereochemistry of **5** as a prerequisite.

spiro[cyclohexan-1,2′-indane]-1′,3′-diols derived from **5** proved to be highly efficient (yield $>90\,\%$).[3a, 17, 21]

We have now discovered that the *cis*-diphenylspirotriketone **6** and related compounds represent excellent starting materials for the synthesis of strained *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestranes such as **4**. As shown in Scheme 2, spirotriketone **6** may be reduced directly to a mixture of spirotriols **8**, which, under acid catalysis and with a limited reaction time, give fenestranol **9** in 73 % isolated yield. Interestingly, this compound represents the 6β-alcohol (see below); the epimeric 6α-fenestranol was observed in very minor amounts but not isolated. Oxidation with CrO_3/H_2SO_4 converted fenestranol **9** into the *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestranone **12** in good yield. It is noteworthy that the triols **8** were found to be much more sensitive to decomposition (presumably by further elimination of water and subsequent oligomerization) than the corresponding all-*cis* fenestranol, which essentially persists under the relatively harsh cyclodehydration conditions.[17] Therefore, the alternative route via ethylene acetal **10** and dispiroindanediol **11**—formed as a mixture of stereoisomers—and final cyclodehydration with concomitant hydrolysis proved to be more convenient. In this way, fenestrane ketone **12** was obtained from **6** in an overall yield of 80 %. In fact, the efficiencies of both sequences **6** → **12** proved to be similar, and also about the same as those of the analogous syntheses of the all-*cis* isomer of **12**.[17]

Spectroscopic analysis of the new tribenzofenestranes **9** and **12** unequivocally confirmed their structures. In particular, the benzhydrylic protons of ketone **12** were evident as two distinct singlet resonances in its ^{1}H NMR spectrum, in contrast to the identical benzhydryl resonances of the all-*cis* stereoisomer **7**. Clearly, formal inversion of the relative configuration at C7a



Scheme 2. Construction of the *cis*,*cis*,*cis*,*trans*-fenestrane framework.

reduces the C_2 molecular symmetry of **7** to C_1 in the case of **12**. The same reduction of symmetry holds for the parent hydrocarbons **3** (C_2) and **4** (C_1), as well as for other derivatives of **4** possessing no additional stereogenic center at C6, such as 1,3-dithiolanes **15** and **16**, as is again reflected by NMR spectroscopy (see below and Experimental Section).

It is also remarkable that reduction of **12** with lithium aluminum hydride (Scheme 2) produces the same single diastereomeric fenestranol, **9**, that was obtained by cyclodehydration of spirotriol **8**. This finding indicates that steric shielding at the diastereofacial sides of the carbonyl group in **12** is more different than presumed for a half-chair conformation of the cyclohexanone ring, as was found to be present in **7**.[17] In fact, force field and semi-empirical MO calculations[22] on fenestranol **9** and fenestranone **12** suggest that the most stable conformers adopt nearly ideal boat conformations (Figure 1). In the case of fenestranone **12**, one of the lateral indane units efficiently suppresses the hydride transfer to the β side of the carbonyl group and steric approach control results in preferential hydride attack at the α side, thus exclusively generating the 6β-fenestranol with an axial hydroxy group (Figure 1, part b). Analysis of the vicinal ^{1}H,^{1}H coupling in **9** clearly corroborates the boat conformation (Figure 1, part c). Among others, the small coupling constants of $J_{H(4b\alpha),H(5\alpha)} \approx J_{H(5\alpha),H(6\alpha)} \approx 0$ Hz and the extremely large value of $J_{H(7\beta),H(7a\alpha)} = 14.0$ Hz are indicative of this conformation. The fact that the axial hydroxy group in **9** persists in the thermodynamically less favorable axial (6β)

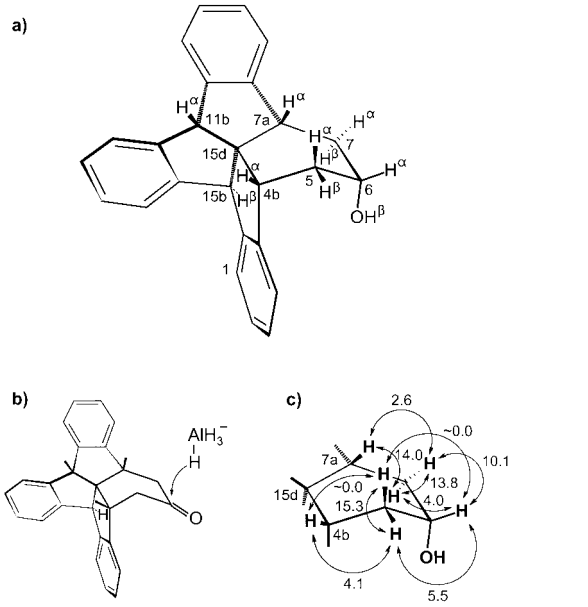
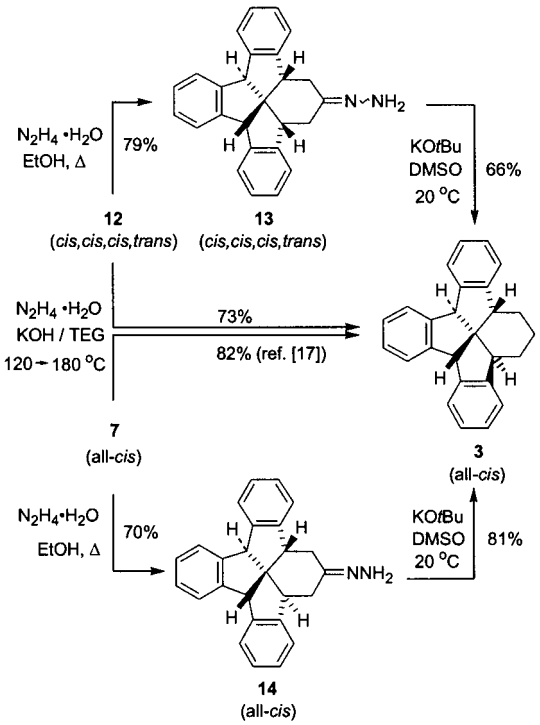


Figure 1. a) Stereoview of fenestranol **9**, b) its formation by stereocontrolled attack of AlH_4^- at **8**, c) $^1H,^1H$ coupling within the cyclohexane ring of **9**.

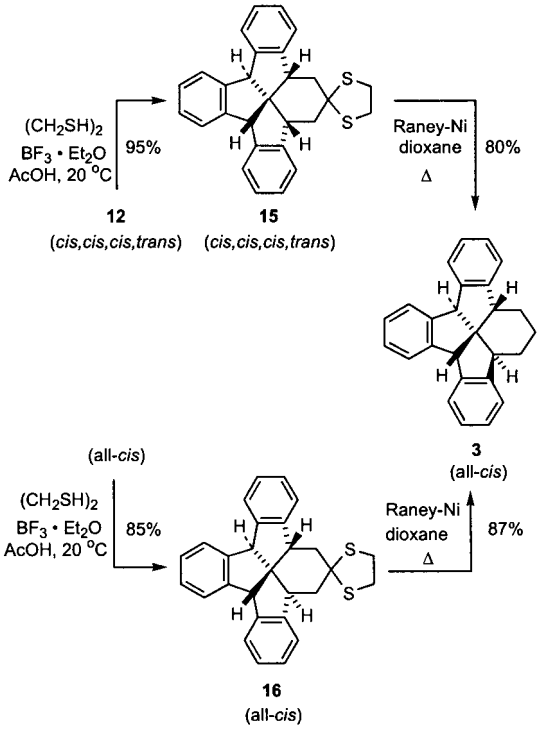
orientation[23] under the relatively harsh acidic conditions points to the equatorial position of the cyclohexanol functionality in the precursor spirotriol **8** (cf. Scheme 2). Thus, the C4–OH functionality in the spirotriols **8** probably survives the cyclodehydration process and is translated into the axial position at C6 of fenestranol **9** without intermediate acid-induced epimerization. The boat conformation of the cyclohexane ring in the *cis*,*cis*,*cis*,*trans*-tribenzo[5.5.5.6]fenestranes suggested by ^1H NMR spectroscopy and by calculations was confirmed by single-crystal X-ray analysis of the parent hydrocarbon **4** (see below).

Reduction of the base-labile *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestrane derivatives: First attempts to remove the carbonyl functionality from the *cis*,*cis*,*cis*,*trans*-fenestrane framework of **12** by Wolff–Kishner reduction failed (Scheme 3). Instead of the desired *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestrane **4**, the all-*cis* isomer **3** was formed exclusively. The sensitivity of the methine group at the C7a bridgehead toward base-catalyzed epimerization has also been revealed by reduction of hydrazone **13** at low temperature.[24] This hydrazone was obtained from the *cis*,*cis*,*cis*,*trans*-fenestrane ketone **12** without epimerization of the fenestrane skeleton, as shown by a control experiment starting from the all-*cis*-[5.5.5.6]fenestrane ketone (**7**), which furnished a different hydrazone, **14**. The latter compound was found to exhibit distinct physical and spectroscopic properties and the all-*cis* stereochemistry can be assigned to it unambiguously. As expected, reduction of **14** also furnished the all-*cis* fenestrane **3**.

The all-*cis* stereoisomer **3** was also obtained in high yield from dithioacetalization of the *cis*,*cis*,*cis*,*trans*- and the all-*cis*-[5.5.5.6]fenestranones **12** and **7**—which yielded the two corresponding diastereomeric spirofenestranes **15** and **16**—and subsequent reduction with neutral Raney nickel[25a] (Scheme 4). These results may be considered advantageous,



Scheme 3. Reduction of the stereoisomeric ketones **7** and **12** through their hydrazones and concomitant epimerization of the *cis*,*cis*,*cis*,*trans*-isomer **13** to the all-*cis* fenestrane **3**.



Scheme 4. Reduction of the stereoisomeric ketones **7** and **12** through their dithioacetals and concomitant epimerization of the *cis*,*cis*,*cis*,*trans*-isomer **15** to the all *cis*-fenestrane **3**.

since both of the sequences furnish the all-*cis*-[5.5.5.6]fenestrane framework of **3** in good overall yields, rendering control over the stereochemistry of the starting spirotriketones superfluous when the all-*cis* fenestrane skeleton is to be constructed. Apparently, however, either the strained *cis*,*cis*,-

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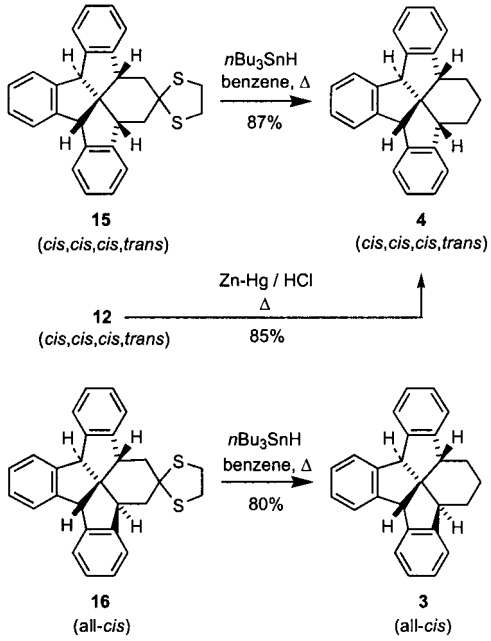
cis,trans-fenestrane skeleton of fenestranone **12** or its derivatives **13** and **15** are too labile to persist under the basic reaction conditions so far used in attempting to generate hydrocarbon **4**.[25b]

A straightforward procedure that did allow us to reduce the carbonyl group of **12** consisted of the radical-induced reduction of the 1,3-dithiolane **15** with Bu_3SnH and AIBN in benzene[26] (Scheme 5). In this case, no epimerization took

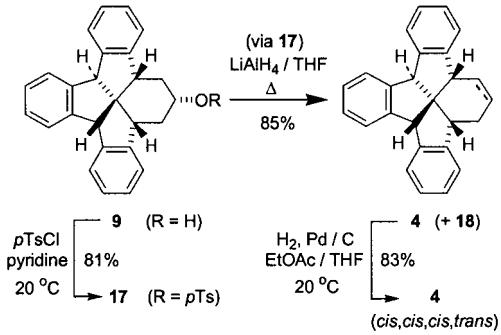


Scheme 5. Synthesis of **4** with retention of the *cis,cis,cis,trans* stereochemistry.

place and the *cis,cis,cis,trans*-fenestrane **4** was obtained in good yield. Not surprisingly, the stereoisomeric dithiolane **16** could also be reduced in a straightforward manner using this method. Thus, non-basic conditions and the presence of mild radicals do not induce epimerization of the strained *cis,cis,cis,-trans*-fenestrane skeleton. In further agreement with these findings, the strongly acidic media present during the Clemmensen reduction of **12** also allowed a highly efficient, albeit tedious, conversion to the *cis,-cis,cis,trans*-hydrocarbon **4** without epimerization (Scheme 5).

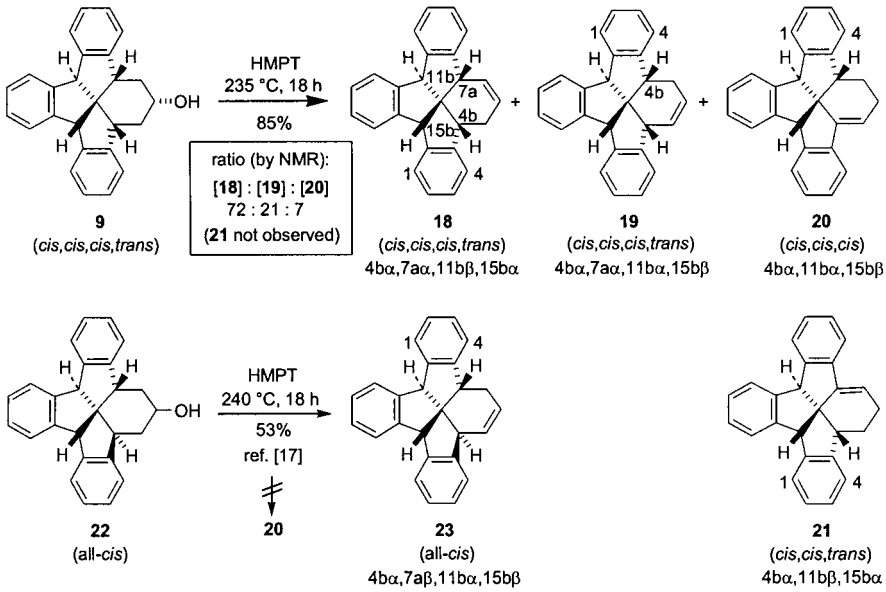
A classical alternative to the 1,3-dithiolane reduction involved the reduction of the tosylate **17**, which was easily prepared from fenestranol **9** (Scheme 6). When **17** was subjected to $LiAlH_4$ reduction in tetrahydrofuran, *cis,cis,cis,-trans*-[5.5.5.6]fenestrane **4** was formed as the major product; however, the fenestrene **18** (see below for further evidence) was also generated, as shown by mass spectrometry and ^1H NMR spectroscopy. Attempts to separate this from **4** by chromatography failed, but hydrogenation of the mixture over palladium on charcoal[25b] accomplished this alternative, five-step synthesis of *cis,cis,cis,-trans*-tribenzo[5.5.5.6]fenestrane **4** from *cis*-diphenylspirotriketone **6** in good overall yield.

In view of the presence of additional unsaturation in *cis,cis,cis,trans*-tribenzo[5.5.5.6]fenestrenes such as **18**, it appeared interesting to perform a directed 1,2-elimination of



Scheme 6. Synthesis of **4** by reduction of **9**, via tosylhydrazone **17**.

water from *cis,cis,cis,trans*-fenestranol **9**. As reported earlier, the corresponding C_2-symmetrical all-*cis* fenestranol **22**, on being heated in a dipolar aprotic solvent (HMPT), is converted to the all-*cis*-tribenzo[5.5.5.6]fenestrene **23** (Scheme 7, bottom).[17] Similar treatment of the C_1-symmetrical fenestranol **9** produced a mixture of the three isomeric [5.5.5.6]fenestranes **18**, **19**, and **20** in a ratio of 72:21:7, by ^1H NMR spectroscopy (Scheme 7, top). Column chromatography and additional HPLC yielded the pure isomers in a ratio of 82:12:6 and enabled structure elucidation to be accomplished. Remarkably, neither the *cis,cis,trans*-fused bridgehead olefin **21** nor the all-*cis* isomer **23** were formed.



Scheme 7. Formation of tribenzo[5.5.5.6]fenestrenes. (Note that atom numbering depends on the position of the double bond.)

The major isomers **18** and **19** both represented Δ(6,7) isomers, possessing the unperturbated *cis*,*cis*,*cis*,*trans* fusion pattern in the [5.5.5.6]fenestrane framework. According to force field and semi-empirical MO calculations (Table 1),[22] **18** and **19** have similar strain energies, with a slight preference

Table 1. Flattening of the geometry at the central carbon atom and relative strain energies of the isomeric tribenzo[5.5.5.6]fenestrenes (by AM1 and PM3 calculations).

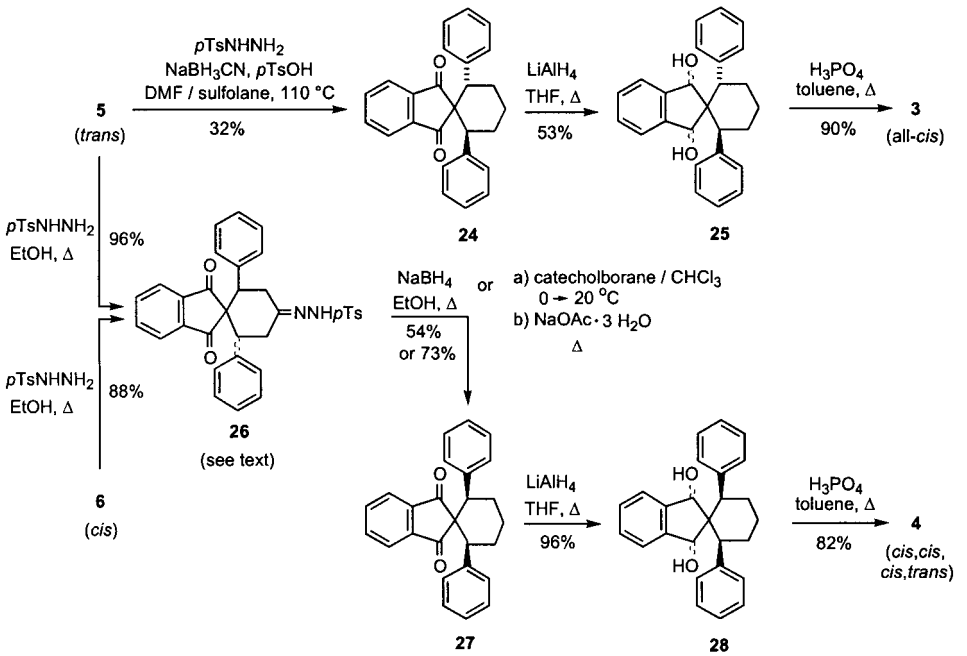
Compound	Upper non-bridged C-C-C angle [°][a]		Lower non-bridged C-C-C angle [°][a]		ΔE_{strain} [kJ mol^{-1}]	
	AM1	PM3	AM1	PM3	AM1	PM3
18	119.3	120.7	119.7	117.9	+62.8	+60.7
19	120.6	120.7	117.1	117.2	+66.9	+65.7
20	115.5	115.5	112.5	112.2	0	0
21	126.0	124.9	124.8	125.7	+141.0	+136.8
23	110.9	110.2	110.3	109.2	+2.9	+6.7

[a] C-C-C bond angles at C15d opened to the top and bottom, respectively, of the structures shown in Scheme 7.

($\Delta E_{strain} = -4.2$ kJ mol^{-1}) for isomer **18**, with the double bond remote from the epimeric, strain-inducing bridgehead C4b. The relative yields of **18** and **19** apparently reflect their relative stabilities. However, the minor isomer **20**, as the Δ(7,7a) isomer—that is, a bridgehead olefin—was calculated to be considerably more stable than **18** ($\Delta E_{strain} = -62.8$ kJ mol^{-1}). Obviously, removal of the proton at the strain-inducing bridgehead in the course of a formal 1,2-H shift in **19** is thermodynamically favorable, since it releases the strain energy from the *cis*,*cis*,*cis*,*trans*-fenestrane skeleton. In turn, the bridgehead olefin **21**, featuring both a Δ(7,7a) double bond and the strain-inducing bridgehead C4b was calculated to be the least stable isomer [$\Delta E_{strain} = +138.1$ kJ mol^{-1}] and, accordingly, this isomer was not formed. Thus, it is remarkable that the most stable isomer within the series of *cis*,*cis*,*cis*,*trans*-[5.5.5.6]tribenzofenestrenes is the bridgehead olefin **19**, which, according to the calculations, is even slightly less strained than the all-*cis*-[5.5.5.6]tribenzofenestrene **23**. As well as the relative strain energies of the five [5.5.5.6]fenestrenes, the unbridged C–C–C bond angles at the central carbon atoms C15d of these olefins have been calculated (Table 1). These geometrical parameters are discussed below, together with those relating to the saturated tribenzo[5.5.5.6]fenestrane **4**.

A straighforward synthesis of *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestrane 4: We have also developed an independent synthesis of **4**, which allowed us to circumvent the formation of stereochemically labile C6-functionalized *cis*,*cis*,*cis*,*trans*-tribenzofenestrane intermediates. To this end, the cyclohexanone functionality of spirotriketone **6** had to be removed prior to the cyclodehydration step, to furnish the target hydrocarbon **4** directly. The same strategy has been used previously by Ten Hoeve and Wynberg in their attempts to synthesize [6.6.6.6]- and [5.6.6.6]fenestranes.[27] We first tested this route in experiments aimed at the conversion of *trans*-spirotriketone **5** into all-*cis*-[5.5.5.6]fenestrane **3** (Scheme 8). Ironically, this approach turned out to be non-trivial for the low-strain, all-*cis*-fenestrane series. Treatment of **5** with *p*-toluenesulfonyl hydrazide in ethanol followed by reduction of the tosylhydrazone furnished *cis*-diphenylspirodiketone **27** in high yield. The same spirodiketone was obtained, using the same method but starting from the *cis*-diphenylspirotriketone **6**. In analogy to the partial *trans* → *cis* isomerization previously reported to occur during the conversion of the corresponding di(5-methylfuryl)spirotriketone,[27] we assume that epimerization occurs in the first step—formation of the *cis*-diphenyl tosylhydrazone **26**—although the stereochemistry of this compound could not be determined unequivocally. However, all attempts to suppress the *trans* → *cis* isomerization in the stepwise reduction of **5** via an isolated tosylhydrazone failed.[28]

Retention of the *trans* orientation in the desired *trans*-diphenylspirodione **24** was eventually achieved in a one-pot procedure, by treating **5** with *p*-toluenesulfonyl hydrazide, sodium cyanoborohydride, and *p*-toluenesulfonic acid in dimethylformamide/sulfolane[29] (Scheme 8). Subsequent reduction of **24** to the corresponding spirodiols **25**, which were obtained as a mixture of stereoisomers, followed by cyclodehydration, furnished the all-*cis*-tetrabenzo[5.5.5.6]fenes-



Scheme 8. Directed syntheses of all-*cis*- and *cis*,*cis*,*cis*,*trans*-fenestranes **3** and **4**, featuring prevention of epimerization.

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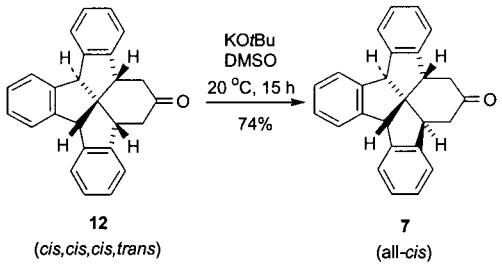
trane **3** in excellent yield. Selective reduction of *cis*-diphenylspirotriketone **6** was achieved through tosylhydrazone **26** (see above), by treatment with sodium borohydride in methanol, or, alternatively, with catecholborane in trichloromethane, giving the *cis*-diphenylspirodione **27** in good yield. Subsequent reduction with lithium aluminum hydride furnished spirodiol **28**, again as a mixture of diastereomers. As expected, in analogy with the behavior of the C4-functionalized *cis*-diphenylspirodiols **8** and **11** (Scheme 2), cyclodehydration of **28** furnished the *cis*,*cis*,*cis*,*trans*-tribenzo[5.5.5.6]fenestrane **4** in excellent yield and with perfect stereospecificity. In view of our original expectation that the *trans* orientation of the phenyl groups would be a conditio sine qua non, it is worth noting (and also amusing) that the overall yields of the stereochemically analogous four-step sequences **5** → **3** and **6** → **4** are almost the same (30 and 28%, respectively).

Mechanism of the base-induced *cis*,*cis*,*cis*,*trans* → all-*cis* epimerization: Because of the facile epimerization occurring during the reduction of fenestranone **12** and its derivatives under basic conditions, we first suspected that the functional group at C6 might be responsible for this effect. For example, α-deprotonation at C7 might induce a transitory heterolytic cleavage of the C7a–C15d bond, which could give rise to epimerization. Alternatively, the formation of a $\Delta(6,7)$ double bond through enolization might contribute by allylic activation of the bridgehead C7a–H bond. In fact, we found that the *cis*,*cis*,*cis*,*trans*-fenestranone **12** could be epimerized to the all-*cis* isomer **7** by treatment with potassium *tert*-butoxide in DMSO at ambient temperature (Scheme 9). This conversion

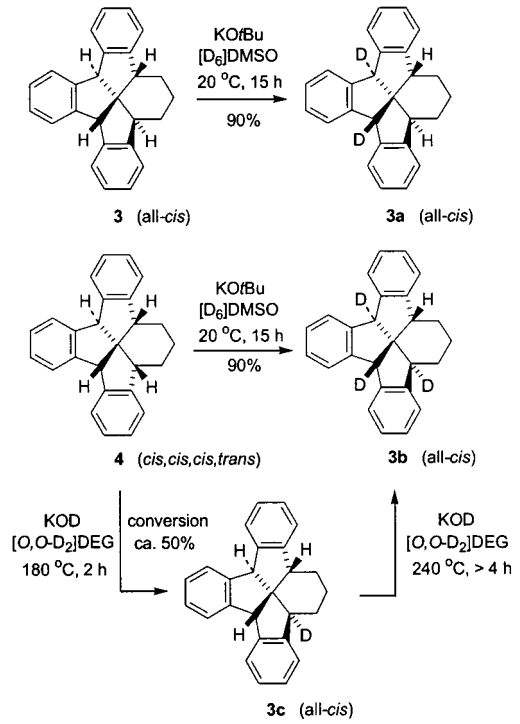


Scheme 9. Directed epimerization of *cis*,*cis*,*cis*,*trans*-fenestranone **12**.

has proven to be an important tool in the synthesis of benzoannelated all-*cis*-fenestranes when the *trans*-diarylspirotriketones are not accessible (cf. Scheme 1).[30] However, the aforementioned assumptions do not explain all of the observations reported above. We therefore subjected the *cis*,*cis*,*cis*,*trans*-fenestrane hydrocarbon **4** itself (obtained by the independent syntheses described above) to the basic conditions existing during Wolff–Kishner and modified Wolff–Kishner reductions.

In fact, when **4** was dissolved in a solution of potassium *tert*-butoxide in dimethyl sulfoxide at ambient temperature, the all-*cis*-tribenzo[5.5.5.6]fenestrane **3** was formed and isolated in almost quantitative yield. Thus, the strained hydrocarbon **4** proved to be sufficiently acidic to undergo epimerization after its formation from the respective *cis*,*cis*,*cis*,*trans*-fenestrane derivatives.

Next, we treated both the all-*cis*- and the *cis*,*cis*,*cis*,*trans*-fenestranes **3** and **4** with potassium *tert*-butoxide in [D_6]dimethyl sulfoxide at ambient temperature (Scheme 10). Starting from **3**, all-*cis*-[11b,15b-D_2]tribenzo[5.5.5.6]fenestrane **3a**,



Scheme 10. Selective H/D exchange in isomeric fenestranes.

with two deuterium atoms in the benzhydrylic positions (D content >97% as determined by ^{1}H NMR spectroscopy), was isolated after 2 h in >90% yield. The same treatment of the *cis*,*cis*,*cis*,*trans* isomer **4** furnished another isotopomer of **3**, all-*cis*-[7a,11b,15b-D_3]tribenzo-[5.5.5.6]fenestrane (**3b**), again exhibiting complete deuterium incorporation at the two benzhydrylic bridgeheads but also at one of the benzylic positions. Obviously, base-induced epimerization of the benzylic bridgehead C7a–H of the strained isomer **4** is faster than the deprotonation/reprotonation sequence involving the benzhydrylic C–H bonds of the relatively unstrained all-*cis* isomer **3**.

This result was clearly confirmed when the *cis*,*cis*,*cis*,*trans*-fenestrane **4** was allowed to react with the weaker base potassium deuteroxide in [*O*,*O*-D_2]-diethylene glycol at 180 °C; that is, under classical Wolff–Kishner conditions. After 3 h, only one of the benzylic bridgehead C–H bonds had incorporated deuterium, while none of the benzhydrylic ones had, and all-*cis*-[7a-D]tribenzo[5.5.5.6]fenestrane **3c** was isolated as the sole all-*cis* isotopomer, with an isotopic purity of >95% (^{1}H NMR), along with unreacted **4**. Forcing conditions (240 °C, >4 h) were required to convert the all-*cis*-[D_1] isotopomer **3c** into **3b** (Scheme 10).[31] Thus, H/D exchange experiments had clearly demonstrated that the C–H bond at the epimeric bridgehead C7a of the strained *cis*,*cis*,*cis*,*trans*-fenestrane **4** is considerably more kinetically acidic not only than those at the benzhydrylic bridgeheads in the same stereoisomer but also than the benzhydrylic C–H bonds of the low-strain all-*cis*-fenestrane **3**.

Molecular structure of *cis*,*cis*,*cis*,*trans*-tribenzo[5.5.5.6]fenestrane 4: Attempts to obtain single crystals from the all-*cis*-tribenzo[5.5.5.6]fenestrane **3** were not successful; fortunately, however, the *cis*,*cis*,*cis*,*trans*-isomer **4** furnished beautiful crystals upon recrystallization from *n*-hexane/ethyl acetate. Pertinent crystallographic data and selected geometrical data are given in Table 2, Table 3, and Table 4.[32] Figure 2 illustrates the solid-state molecular structure of **4** as viewed from the upper (α) face of the fenestrane core; that is, with three bridgehead hydrogens pointing above the plane.

The solid-state molecular structure of **4** clearly confirms both the relative configurations at the four peripheral bridgeheads of the [5.5.5.6]fenestratriene framework and the boat conformation deduced above for the corresponding fenestranol **9**. In fact, the cyclohexane boat in **4** is fused into the angular triindane skeleton in such a way as to impose a rigid and nearly perfect boat conformation.[33] As the most remarkable geometrical parameter, the unbridged C–C–C bond angles at the central carbon atom C15d of **4** are considerably increased. In particular, ∢C4b-C15d-C11b is opened to 120.8(1)°, whereas the other angle, ∢C7a-C15d-C15b, is widened to 115.5(1)° only (Table 3). These values may be compared to those of the corresponding angles in fenestrindane **1** (116.5°)[14d] and its derivative bearing four bromine atoms at the bridgehead positions (121.4°).[3a, 34]

Table 2. Crystal data and structure refinement for *cis*,*cis*,*cis*,*trans*-tribenzo[5.5.5.6]fenestrane **4** (*4bα*,*7aα*,*11bα*,*15bβ*)-5,6,7,7a,11b,15b-hexahydro-4b*H*-dibenzo[2,3:4,5]pentaleno[1,6-*jk*]fluorene.

empirical formula	$C_{26}H_{22}$
formula weight	334.44
T [K]	203(2)
λ [Å]	0.71073
crystal system	monoclinic
space group	$P2(1)/c$
unit cell dimensions	$a = 9.066(1)$ Å
	$b = 19.600(2)$ Å
	$c = 9.930(3)$ Å
	$\alpha = 90°$
	$\beta = 102.79(2)°$
	$\gamma = 90°$
V [Å^3]	1720.7(6)
Z	4
ρ_{calcd} [Mg m^{-3}]	1.291
absorption coefficient [mm^{-1}]	0.073
$F(000)$	712
crystal size [mm^3]	$0.23 \times 0.60 \times 0.25$
θ range for data collection	2.08 to 26.99°
index ranges	$-1 \le h \le 11$,
	$-25 \le k \le 1$,
	$-12 \le l \le 12$
reflections collected	4718
independent reflections	3755 [R(int) = 0.0154]
completeness to $\theta = 26.99°$	99.9%
absorption correction	none
refinement method	full-matrix,
	least-squares on F^2
data/restraints/parameters	3755/0/236
Goodness-of-fit on F^2	1.056
final R indices [$I > 2\sigma(I)$]	$R1 = 0.0451$, $wR2 = 0.1070$
R indices (all data)	$R1 = 0.0764$, $wR2 = 0.1334$
extinction coefficient	0.0159(18)
largest diff. peak and hole	0.253 and −0.181 e Å^{-3}

Table 3. Flattening of the geometry at the central carbon atom and relative strain energies of stereoisomeric tribenzo[5.5.5.6]fenestranes **3** and **4**.

Compound	Method	∢C4b-C15d-C11b [°]	∢C7a-C15d-C15b [°]	ΔE_{strain} [kJ mol^{-1}]
4	X-ray	120.8	115.5	–
4	AM1	119.4	117.8	+49.8
	PM3	120.0	116.5	+43.5
	MM+	118.7	115.8	+38.1
3	AM1	110.2	111.7	0
	PM3	108.8	111.1	0
	MM+	109.3	112.9	0

Table 4. C–C Bond distances [pm] and C–C–C bond angles [°] at the peripheral bridgeheads of *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestrane **4**, as determined by single-crystal X-ray structure analysis. The data for the "strained" bridgehead C7a are given in italics.

Bond distances [pm]		Bond angles [°]	
C4b–C15d	156.6(2)	C4a-C4b-C5	111.3(1)
C4b–C4a	151.1(2)	C4a-C4b-C15d	105.2(1)
C4b–C5	155.5(3)	C5-C4b-C15d	107.8(1)
C7a–C15d	*153.9*(2)	*C7-C7a-C7b*	*122.4*(*1*)
C7a–C7	*151.1*(2)	*C7-C7a-C15d*	*114.0*(*1*)
C7a–C7b	*149.7*(2)	*C7b-C7a-C15d*	*104.1*(*1*)
C11b–C15d	156.8(2)	C11a-C11b-C1c	107.8(1)
C11b–C11a	152.8(2)	C11a-C11b-C15d	102.6(1)
C11b–C11c	150.8(2)	C11c-C11b-C15d	105.7(1)
C15b–C15d	157.9(2)	C15a-C15b-C15c	111.3(1)
C15b–C15a	151.6(2)	C15a-C15b-C15d	105.3(1)
C15b–C15c	150.9(2)	C15c-C15b-C15d	105.7(1)

Hence, taking both angles into account, the *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestrane skeleton of **4** is more flattened than the all-*cis*-[5.5.5.5] congeners such as **1**, but significantly less than the sterically overcrowded fourfold bridgehead derivatives in that series.

Unfortunately, experimental data for the all-*cis*-tribenzo[5.5.5.6]fenestrane **3** are lacking, because the crystals obtained were not suitable for X-ray analysis. However, as also shown in Table 3, semi-empirical and force field calculations satisfactorily reproduced the widening effects found for **4**, PM3 calculations affording the closest agreement in this case. On this basis, computation also allowed us to predict that the all-*cis*-tribenzo[5.5.5.6]fenestrane **3** would be much less flattened than the *cis*,*cis*,*cis*,*trans*-isomer **4**, the unbridged angles of the former isomer being opened by 15 – 17° less than those of the latter.

It may be noted that the carbon triad C4a-C15d-C11b comprising the strongly widened angle does not contain the strain-inducing bridgehead C7a, an observation that may appear counterintuitive. Obviously, the extra strain induced by the attachment of the trimethylene unit at the β position of C7a, rather than at its α position as in **3**, gives rise to bending of the C4b bridgehead more "downwards" to the fenestrane mean plane than bending of the C7a bridgehead "upwards" to it.

A more detailed analysis of the geometry of the neopentane core of **4** reveals that the *cis*,*cis*,*cis*,*trans* configuration gives rise to a significant decrease in the sp^3 character of the

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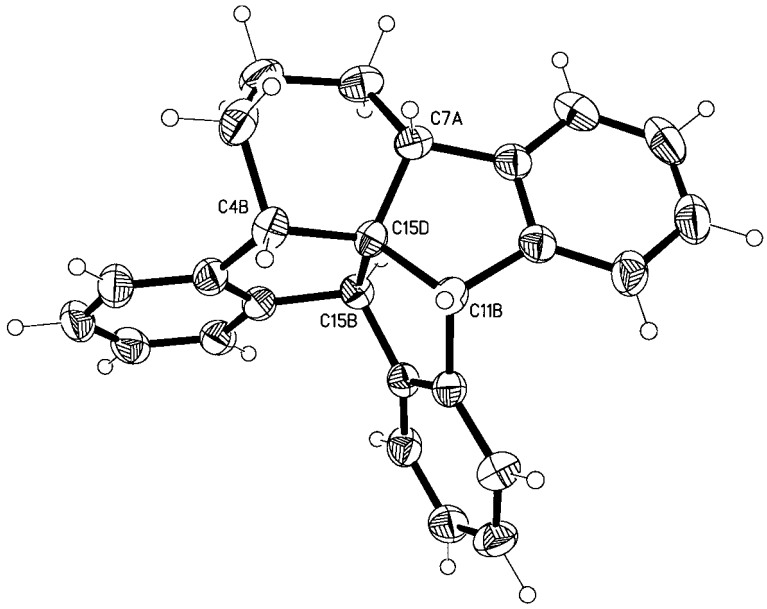

Figure 2. X-ray molecular structure (ORTEP plot) of *cis*,*cis*,*cis*,*trans*-fenestrane **4**.

strained bridgehead carbon atom C7a. This is most evident from the data collected in Table 4. In particular, the average of the C-C-C bond angles at C7a, namely 113.5(1)°, is significantly larger than the mean of the corresponding angles at the other peripheral bridgehead positions, namely 108.1(1)° for C4b, 105.3(1)° for C11b, and 107.4(1)° for C15b. As expected, effects on the C–C bond distances within the fenestrane core are only minor; however, one slight but significant effect may be noted. Among the four central C–C bonds, those involving the peripheral bridgeheads possessing "normal" configuration, namely C4b–C15d, C11b–C15d, and C15b–C15d, have virtually the same lengths, ranging from 156.6(2) to 157.9(2) pm. In contrast, the bond connecting the strained bridgehead to the central one and thus involving the *trans* ring junction, C7a–C15d, is significantly shortened: to 153.9(2) pm. The two lateral C–C bonds at the strained bridgehead C7a are also shorter than the respective C–C bonds at the other benzylic bridgehead C4b: 151.1(2) pm versus 155.5(3) pm and 149.7(2) pm versus 151.1(2) pm. All these observations suggest that the hybridization of the C7a atom is of partial sp^2 character.

Also on the basis of the compatibility of the experimental and computational data, the flattening effects in the tribenzo[5.5.5.6]fenestrenes **18**–**21** and **23** may be ascertained by semi-empirical calculation. The data obtained by AM1 and PM3 calculations (Table 1) clearly reflect the correlation of strain with the flattening at the central carbon atom and suggest that, according to the calculations, the synthetically accessible fenestrenes **18** and **19** are actually somewhat more flattened than fenestrane **4**. The much more highly strained isomer **21**, which was not observed in the experiments, was calculated to be considerably more flattened than the former *cis*,*cis*,*cis*,*trans* isomers. Interestingly, the similarity of strain in the stereoisomeric bridgehead olefins **20** and **23** is not reflected in the size of the unbridged angles at the central carbon atom.

Conclusion

The directed synthesis of benzoannelated *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestranes has been achieved by simple condensation strategies involving acid-catalyzed, twofold cyclodehydration. The base-lability of these strained stereoisomers of the previously described all-*cis*-[5.5.5.6]fenestranes is remarkable; it gives rise to facile epimerization of the C–H bond of the "inverted" benzylic bridgehead, generating the all-*cis*-[5.5.5.6]fenestrane skeleton. The kinetic C–H acidity of this bridgehead is higher than that of the benzhydrylic bridgeheads, and epimerization occurs through a simple deprotonation/reprotonation mechanism at the benzylic bridgehead. Experimental and computational analysis of the stereochemistry of the *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestrane framework has demonstrated the increased sp^2 character of the carbon atom at the inverted bridgehead and the limited but significant flattening of the coordination of the central carbon atom. It is obvious from the results presented here that attempts to construct the highly strained *cis*,*cis*,*cis*,*trans*-[5.5.5.5]fenestranes, such as "epi-fenestrindane" **2**, will have to cope with the paradox that benzoannelation of fenestranes has opened a viable route to these interesting polycyclic hydrocarbons but that it also increases their chemical lability in the strained *cis*,*cis*,*cis*,*trans*-fused stereoisomers. Thus, experimental efforts to convert benzoannelated *cis*,*cis*,*cis*,*trans*-[5.5.5.6]fenestranes to the *cis*,*cis*,*cis*,*trans*-[5.5.5.5]fenestrane congeners represents a true challenge.

Experimental Section

General procedures: Melting points (uncorrected) Electrothermal melting point apparatus. IR spectra: Perkin–Elmer model IR 841. ^{1}H,^{13}C NMR, ^{1}H,^{1}H COSY, and ^{1}H,^{1}H NOESY measurements: Bruker AM 250; TMS (as internal standard) and Bruker DRX 500 (solvent used as internal standard). ^{13}C NMR spectra were recorded as broad-band decoupled in combination with the DEPT or APT technique, respectively. MS and exact mass measurements: VG Autospec, Fisons, electronic ionization (EI, 70 eV). Perfluorokerosene (PFK) was used as a reference for exact mass measurements. Combustion analyses: Perkin–Elmer 240. TLC: silica gel (Kieselgel 60 F_{254}) on aluminum foils (Merck). Column chromatography: silica gel (Kieselgel 60, 0.063–0.200 mm, Merck and Machery–Nagel).

***cis*-2,6-Diphenyl-1′,3′-dihydrospiro[cyclohexane-1,2′-[2*H*]indene]-1′,3′,4-triol (8)**: A solution of spirotriketone **6** (20.0 g, 52.5 mmol) in dry tetrahydrofuran (200 mL) was added over 3 h to a stirred suspension of lithium aluminum hydride (4.2 g, 110 mmol) in dry THF (500 mL). The mixture was then heated to reflux for 15 h. The major part of the solvent was then distilled off and replaced by diethyl ether (200 mL). The mixture was cooled with ice/water, hydrolyzed carefully by adding water, and extracted several times with diethyl ether. The combined organic layers

were dried with sodium sulfate and the solvent was evaporated to give an oily residue from which a colorless precipitate (16.6 g, 82%) formed upon addition of chloroform. This material constitutes a mixture of isomers and may be used directly for cyclodehydration. Repeated crystallization from chloroform gave a mixture of isomers (m.p. 238–240 °C), from which the major isomer (ca. 90%) could be identified by NMR spectroscopy: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.39–7.13 (m, 7H), 7.03–6.73 (m, 6H), 6.65–6.63 (m, 1H), 5.41 (s, 1H), 4.78 (d, J = 8.1 Hz, 1H), 4.09 (dd, J = 5.0, 10.8 Hz, 1H), 3.39 (dd, J = 3.6, 13.7 Hz, 1H), 3.36 (dd, J = 2.9, 13.7 Hz, 1H), 3.05–2.90 (m, 1H), 2.79 (br s, 1H, -OH), 2.78–2.63 (m, 1H), 2.38–2.24 (m, 1H), 2.24 (br s, 1H, -OH), 2.04–1.97 (m, 1H), 1.77 (br s, 1H, -OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 143.2, 142.0, 141.7, 141.3, 130.2, 128.4, 127.6, 127.2, 126.9, 125.4, 121.4, 120.9, 75.2, 74.6, 70.9, 62.6, 48.1, 46.9, 41.0, 38.7; IR (KBr): $\tilde{\nu}$ = 3542, 3390, 2876, 1493, 1031, 746 cm^{-1}; MS (EI, 70 eV): m/z (%): 386 (16) $[M]^+$, 368 (61), 350 (52), 332 (7), 290 (57), 220 (100), 147 (84), 105 (57), 91 (91); elemental analysis calcd (%) for $C_{26}H_{26}O_3$ (386.50): C 80.80, H 6.72; found: C 80.77, H 6.78.

(*4bα*,*7aα*,*11baα*,*15bβ*)-5,6,7,7a,11b,15b-Hexahydro-4*H*-dibenzo[2,3:4,5]-pentaleno[1,6-*jk*]fluorene-6*β*-ol (9)

a) By cyclodehydration of **8**: A suspension of spirotriol **8** (20.0 g, 51.6 mmol) in xylene (80 mL) and orthophosphoric acid (85%, 4.0 mL) was stirred vigorously and heated to reflux temperature for 3 h in a reaction vessel equipped with a water separator. The hot solution was carefully decanted from the oily, brown residue and the solvent was distilled off. The crude product was recrystallized from ethyl acetate to yield pure **9** (31.2 g, 73%) as a colorless solid. M.p. 228–240 °C (decomp), ^{1}H NMR and ^{1}H,^{1}H-COSY (250 MHz, $CDCl_3$), ^{1}H,^{1}H-NOESY and ^{1}H,^{13}C-COSY (500 MHz, $CDCl_3$): δ = 7.49–7.44 (m, 4H), 7.29–6.99 (m, 8H), 4.44 (s, 1H), 4.40 (s, 1H), 4.27 (ddd, J = 10.1, 5.5, 4.0 Hz, 1H), 3.84 (d, J = 4.1 Hz, 1H), 3.50 (dd, J = 14.0, 2.6 Hz, 1H), 2.95 (ddd, J = 13.8, 10.1, 2.6 Hz, 1H), 2.56 (ddd, J = 15.3, 5.5, 4.1 Hz, 1H), 2.28 (d, J = 15.3 Hz, 1H), 1.42 (ddd, J = 14.0, 13.8, 4.0 Hz, 1H), 0.95 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 147.5, 145.8, 144.5, 144.4, 142.6, 127.8, 127.6, 126.9, 126.8, 126.7, 126.4, 125.5, 125.3, 124.5, 123.8, 123.4, 120.9, 68.1, 67.8, 58.8, 56.8, 46.3, 44.4, 36.9, 31.6; IR (KBr): $\tilde{\nu}$ = 3567, 2890, 1472, 1453, 1446, 1074, 770, 756 cm^{-1}; MS (EI, 70 eV): m/z (%): 350 (95) $[M]^+$, 332 (100), 303 (62), 291 (72), 215 (42), 91 (24); elemental analysis calcd (%) for $C_{26}H_{22}O$ (382.46): C 89.11, H 6.33; found: C 89.18, H 6.55.

b) By reduction of **12**: A mixture of fenestranone **12** (1.00 g, 2.88 mmol) and lithium aluminum hydride (0.10 g, 2.60 mmol) in THF (350 mL) was refluxed for 6 h. The reaction mixture was cooled with ice/water, carefully hydrolyzed with water, and extracted several times with diethyl ether. The combined organic layers were dried with sodium sulfate and the solvent was evaporated to give pure **9** (1.00 g, 99%) as a colorless solid. M.p. 231–239 °C (decomp).

***cis*-3′,5′-Diphenyldispiro[1,3-dioxolane-2,1′-cyclohexane-4′,2″-[2*H*]-indene]-1″,3″-dione (10)**: In a reaction vessel equipped with a water separator containing freshly dried molecular sieves (4 Å, 15 g), a solution of spirotriketone **6** (10.2 g, 26.8 mmol), ethylene glycol (1.86 g, 30.0 mmol), and *p*-toluenesulfonic acid (50 mg) in dichloromethane (150 mL) was heated to reflux for 15 h. The solution was washed with aqueous sodium bicarbonate and water and dried with sodium sulfate, and the solvent was evaporated to yield dispiroacetal **10** (11.2 g, 99%) as a colorless powder. M.p. 262–263 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.54–7.51 (m, 1H), 7.45–7.31 (m, 3H), 7.04–6.86 (m, 10H), 4.04 (s, 4H), 3.78 (dd, J = 3.3, 13.8 Hz, 2H), 3.09, (quasi-t, J = 13.5 Hz, 2H), 1.94 (dd, J = 2.0, 13.0 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 203.4, 203.2, 142.8, 142.1, 139.1, 134.8, 134.7, 128.5, 128.1, 127.0, 122.1, 121.8, 108.6, 64.7, 64.6, 62.6, 46.8, 36.4; IR (KBr): $\tilde{\nu}$ = 2889, 1741, 1696, 1255, 1145, 1073, 765 cm^{-1}; MS (EI, 70 eV): m/z (%): 424 (2) $[M]^+$, 364 (1), 320 (13), 233 (7), 175 (100), 86 (56); elemental analysis calcd (%) for $C_{28}H_{24}O_4$ (424.50): C 79.23, H 5.70; found: C 79.35, H 5.94.

***cis*-3′,5′-Diphenyl-1″,3″-dihydrodispiro[1,3-dioxolane-2,1′-cyclohexane-4′,2″-[2*H*]indene]-1″,3″-diol (11)**: A solution of dispiroacetal **10** (11.2 g, 26.4 mmol) in dry tetrahydrofuran (350 mL) was added to a suspension of lithium aluminum hydride (2.0 g, 53.0 mmol) in dry THF (100 mL) and the mixture was heated to reflux for 4 h. The major part of the solvent (ca. 300 mL) was distilled off and replaced with diethyl ether (150 mL). The mixture was carefully hydrolyzed by addition of water and extracted several times with diethyl ether. The combined extracts were dried with sodium sulfate and the solvent was distilled off to give crude dispirodiole **11** (10.5 g, 93%) as a colorless mixture of two isomers (m.p. 245–248 °C). Repeated recrystallization from ethyl acetate furnished a mixture of isomers (m.p. 252–254 °C), from which the major isomer (ca. 90%) could be identified by NMR spectroscopy: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.55–7.52 (m, 2H), 7.22–7.09 (m, 4H), 6.97–6.74 (m, 8H), 5.66 (d, J = 10.0 Hz, 1H), 5.54 (d, J = 9.0 Hz, 1H), 4.04–3.93 (m, 4H), 3.67 (dt, J = 3.3, 13.8 Hz, 2H), 3.00 (quasi-t, $J \approx$ 13.3 Hz, 1H), 2.62 (quasi-t, $J \approx$ 13.8 Hz, 1H), 2.17 (dt, J = 2.6, 13.1 Hz, 1H), 2.14 (d, J = 9.0 Hz, 1H, OH), 1.90 (dt, J = 3.1, 13.7 Hz, 1H), 1.11 (d, J = 10.0 Hz, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 144.5, 143.2, 142.1, 141.6, 131.1, 129.2, 128.8, 127.8, 127.5, 127.4, 126.3, 126.0, 124.5, 122.0, 108.7, 77.8, 77.1, 64.6, 64.5, 58.0, 47.1, 46.3, 40.0, 38.0; IR (KBr): $\tilde{\nu}$ = 3464, 2934, 2900, 1148, 1090, 1017, 749, 699 cm^{-1}; MS (EI, 70 eV): m/z (%): 428 (11) $[M]^+$, 410 (23), 392 (3), 366 (14), 348 (11), 237 (100), 220 (55), 191 (37), 104 (51), 91 (55), 87 (77); elemental analysis calcd (%) for $C_{28}H_{28}O_4$ (428.53): C 78.48, H 6.59; found: C 78.66, H 6.50.

(*4bα*,*7aα*,*11baα*,*15bβ*)-4b,5,7,7a,11b,15b-Hexahydro-6*H*-dibenzo-[2,3:4,5]pentaleno[1,6-*jk*]fluorene-6-one (12)

a) By oxidation of fenestranol **9**: A suspension of fenestranol **9** (300 mg, 86 μmol) in freshly distilled acetone (10 mL) was added slowly to a stirred solution of an excess of chromium trioxide (120 mg, 1.20 mmol) in 2 N sulfuric acid (5.0 mL). The mixture was stirred at ambient temperature until TLC (*n*-hexane/ethyl acetate 3:1) indicated the absence of starting material (ca. 4 h). In some cases, additional reagent and prolongation of the reaction time were necessary. The solid phase was filtered by suction, washed several times with water and dried in vacuo to give crude fenestrane ketone **12** (290 mg, 97%) as a colorless solid (m.p. 290–294 °C). Recrystallization from ethyl acetate gave a sample of m.p. 293–296 °C.

b) By cyclodehydration of dispirodiol **11**: In a reaction vessel equipped with a water separator, dispirodiole **11** (10.4 g, 24.3 mmol) and orthophosphoric acid (85%, 16 mL) in toluene (600 mL) were heated to reflux for 15 h. The hot solution was carefully decanted from the oily brown residue, and the solvent was then distilled off and the residue recrystallized from ethyl acetate to yield fenestrane ketone **12** (7.33 g, 87%) as a colorless powder. M.p. 293–297 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.50–7.47 (m, 1H), 7.41–7.38 (m, 1H), 7.21–7.02 (m, 10H), 4.58 (s, 1H), 4.43 (s, 1H), 4.28 (dd, J = 3.4, 14.6 Hz, 1H), 4.06 (d, J = 5.1 Hz, 1H), 3.38 (dd, J = 6.2, 15.1 Hz, 1H), 2.94 (dd, J = 3.6, 18.6 Hz, 1H), 2.70 (dd, J = 1.8, 15.1 Hz, 1H), 2.27 (dd, J = 14.8, 18.6 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 145.7, 145.1, 144.8, 144.0, 143.8, 141.1, 127.9, 127.8, 127.3, 127.2, 127.1, 126.7, 125.6, 125.1, 124.5, 123.3, 123.2, 121.0, 67.3, 58.8, 56.8, 47.2, 47.0, 44.4, 37.9; IR (KBr): $\tilde{\nu}$ = 2962, 2901, 1715, 1471, 760, 752, 746 cm^{-1}; MS (EI, 70 eV): m/z (%): 348 (100) $[M]^+$, 305 (37), 290 (39); elemental analysis calcd (%) for $C_{26}H_{20}O$ (348.45): C 89.62, H 5.79; found: C 89.69, H 6.04.

(*4bα*,*7aα*,*11baα*,*15bβ*)-4b,5,7,7a,11b,15b-Hexahydro-6*H*-dibenzo-[2,3:4,5]pentaleno[1,6-*jk*]fluorene-6-one hydrazone (13): A solution of fenestrane ketone **12** (1.00 g, 2.87 mmol) and hydrazine hydrate (180 mg, 3.59 mmol) in ethanol (70 mL) was heated to reflux temperature for 5 h. The mixture was cooled at −15 °C overnight. The resulting product was filtered by suction and recrystallized from ethanol to give hydrazone **13** (0.82 g, 79%) as colorless crystals. M.p. 174–179 °C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47–7.46 (m, 1H), 7.36–7.35 (m, 1H), 7.19–7.10 (m, 8H), 7.06–7.03 (m, 2H), 4.74 (br s, 2H, -NH), 4.53 (s, 1H), 4.36 (s, 1H), 4.09 (dd, J = 3.5, 13.9 Hz, 1H), 3.93 (d, J = 4.8 Hz, 1H), 3.27 (dd, J = 5.1, 14.5 Hz, 1H), 2.92 (dd, J = 3.1, 17.1 Hz, 1H), 2.61 (dd, J = 14.6, 1.6 Hz, 1H), 2.15 (quasi-t, J = 14.9, 16.2 Hz, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 151.2, 146.0, 145.7, 144.9, 144.1, 141.6, 127.5, 127.3, 127.0, 126.9, 126.8, 126.5, 125.5, 125.0, 124.5, 123.2, 122.8, 120.9, 67.4, 59.0, 56.4, 45.9, 45.7, 39.2, 24.0; IR (KBr): $\tilde{\nu}$ = 3392, 3069, 3023, 2956, 2892, 1473, 1454, 757 cm^{-1}; MS (EI, 70 eV): m/z (%): 362 (100) $[M]^+$, 346 (47), 345 (21), 331 (46), 305 (61), 289 (55); exact mass measurement (EI-MS): m/z: calcd for $[M]^+$ 362.1783; found: 362.1783.

(*4bα*,*7aβ*,*11baα*,*15bβ*)-4b,5,7,7a,11b,15b-Hexahydro-6*H*-dibenzo-[2,3:4,5]pentaleno[1,6-*jk*]fluorene-6-one hydrazone (14): A solution of fenestrane ketone **7** (1.00 g, 2.87 mmol) and hydrazine hydrate (180 mg, 3.59 mmol) in ethanol (70 mL) was heated to reflux temperature for 5 h. The product precipitated over 15 h on standing at −15 °C. It was filtered by suction, washed with a little ethanol, and then recrystallized from ethanol to give hydrazone **13** (0.73 g, 70%) as a colorless solid. M.p. 337–341 °C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.31 (m, 4H), 7.26–7.17

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(m, 8H), 5.00 (br s, 2H, -NH), 4.48 (s, 1H), 4.47 (s, 1H), 3.58 (t, $J = 6.8$ Hz, 1H), 3.49 (t, $J = 7.1$ Hz, 1H), 2.70–2.57 (m, 4H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 143.6, 143.1, 142.6, 142.4, 142.2, 141.9, 127.4, 127.2, 126.9, 125.3, 125.2, 124.7, 124.6, 124.3, 123.9, 123.8, 67.0, 59.8, 59.0, 58.7, 57.9, 37.5, 35.8$; IR (KBr): $\tilde{\nu} = 3072, 3023, 2881, 1650, 1476, 1457, 1443, 754, 738, 638\ cm^{-1}$; MS (EI, 70 eV): m/z (%): 362 (10) $[M]^+$, 346 (91), 332 (98), 305 (78), 303 (89), 291 (100), 290 (75), 289 (86), 215 (41); exact mass measurement (EI-MS): m/z: calcd for $[M]^+$ 362.1783; found: 362.1790.

(*4b′α*,*7a′α*,*11b′α*,*15b′β*)-4b′,5′,7′,7a′,11b′,15b′-1,3-Dithiolane-2,6′-hexahydro-6′*H*-dibenzo[2′,3′:4′,5′]pentaleno[1′,6′-*jk*]fluorene (15): A mixture of fenestrane ketone **12** (500 mg, 1.44 mmol), 1,2-ethanedithiol (0.50 mL, 5.94 mmol), $BF_3 \cdot Et_2O$ (50% BF_3, 0.5 mL), and acetic acid (5 mL) was stirred at ambient temperature for 2 h. The crude product was separated by filtration, washed with ethanol, and recrystallized from ethyl acetate to give dithiolane **15** (579 mg, 95%) as a colorless powder. M.p. 268–269 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.46–7.45$ (m, 2H), 7.29–7.23 (m, 3H), 7.15–7.00 (m, 7H), 4.42 (s, 1H), 4.34 (s, 1H), 3.89 (d, $J = 4.1$ Hz, 1H), 3.76 (d, $J = 13.1$ Hz, 1H), 3.29–3.23 (m, 3H), 3.10–3.06 (m, 2H), 2.99–2.96 (dd, $J = 2.2$, 13.9 Hz, 1H), 2.67 (dd, $J = 1.8$, 15.0 Hz, 1H), 2.26 (t, $J = 13.6$ Hz, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 145.8$, 144.9, 144.4, 144.2, 142.3, 127.7, 126.9, 126.79, 126.75, 126.5, 125.5, 124.5, 123.3, 121.0, 67.5, 64.1, 58.3, 57.3, 45.6, 45.4, 44.1, 42.7, 41.6, 36.2; IR (KBr): $\tilde{\nu} = 2913$, 1484, 1477, 1466, 1455, 1445, 1431, 762, 743, 733 cm^{-1}; MS (EI, 70 eV): m/z (%): 424 (8) $[M]^+$, 363 (17), 331 (100), 289 (19), 215 (13); exact mass measurement (EI-MS): m/z: calcd for $[M]^+$ 424.1320; found: 424.1325; elemental analysis calcd (%) for $C_{28}H_{24}S_2$ (424.62): C 79.20, H 5.70; found: C 79.10, H 5.60.

(*4b′α*,*7aβ*,*11b′α*,*15bβ*)-4b′,5′,7′,7a′,11b′,15b′-1,3-Dithiolane-2,6′-pentahydro-6′*H*-dibenzo[2′,3′:4′,5′]pentaleno[1′,6′-*jk*]fluorene (16): A mixture of fenestrane ketone **7** (500 mg, 5.94 mmol), 1,2-ethanedithiol (0.50 mL, 5.94 mmol), $BF_3 \cdot Et_2O$ (50% BF_3, 0.5 mL), and acetic acid (5 mL) was stirred at ambient temperature for 2 h. The crude product was separated by filtration, washed with ethanol, and recrystallized from ethyl acetate to yield dithiolane **16** (522 mg, 85%) as a colorless powder. M.p. 247–249 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.37–7.31$ (m, 4H), 7.26–7.16 (m, 8H), 4.44 (s, 2H), 3.55 (quasi-t, $J = 6.5$ Hz, 2H), 3.25 (s, 4H), 2.51 (dd, $J = 6.2$, 14.2 Hz, 2H), 2.34 (dd, $J = 7.0$, 14.2 Hz, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 145.4, 143.4, 142.8, 127.3, 127.2, 126.7, 125.0, 124.6, 124.4, 65.8, 64.8, 59.2, 46.0, 43.3, 38.4$; IR (KBr): $\tilde{\nu} = 3021, 2928, 1476, 755\ cm^{-1}$; MS (EI, 70 eV): m/z (%): 424 (34) $[M]^+$, 363 (29), 331 (100), 289 (22), 215 (10); exact mass measurement (EI-MS): m/z: calcd for $[M]^+$ 424.1320; found: 424.1325; elemental analysis calcd (%) for $C_{28}H_{24}S_2$ (424.62): C 79.20, H 5.70; found: C 79.07, H 5.85.

(*4bα*,*7aα*,*11bα*,*15bβ*)-5,6,7,7a,11b,15b-Hexahydro-4b*H*-dibenzo-[2,3:4,5]pentaleno[1,6-*jk*]fluorene-6-yl *para*-toluenesulfonate (17): Fenestranol **9** (1.00 g, 2.86 mmol) and *p*-toluenesulfonyl chloride (2.30 g, 12.00 mmol) were dissolved in dry pyridine (20 mL). The solution was stirred at ambient temperature for 4 h, and then poured into ice/water (75 mL) and extracted several times with dichloromethane. The combined organic layers were washed with hydrochloric acid (10%), aqueous sodium bicarbonate, and water, and then dried over sodium sulfate. Evaporation of the solvent and recrystallization of the residue from *n*-hexane/ethyl acetate 3:1 gave tosylate **17** (1.17 g, 81%) as a colorless solid. M.p. 166–167 °C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.48$ (AA′*BB*′, 2H), 7.42 (d, $J = 7.4$ Hz, 1H), 7.35 (d, $J = 7.4$ Hz, 1H), 7.48 (*AA*′BB′, 2H), 7.27–7.02 (m, 9H), 6.98 (d, $J = 7.2$ Hz, 1H), 5.15 (ddd, $J = 5.2$, 5.7, 10.4 Hz, 1H), 4.37 (s, 1H), 4.35 (s, 1H), 3.80 (d, $J = 4.8$ Hz, 1H), 3.43 (d, $J = 13.9$ Hz, 1H), 2.80 (ddd, $J = 2.7$, 10.5, 10.8 Hz, 1H), 2.49 (dt, $J = 5.5$, 15.9 Hz, 1H), 2.44 (s, 3H), 2.31 (d, $J = 15.8$ Hz, 1H), 1.72 (ddd, $J = 14.1$, 14.0, 6.0 Hz, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 145.9, 144.5, 144.1, 144.0, 141.5, 134.5, 129.4, 127.5, 127,2, 127.0, 126.9, 126.7, 126.4, 125.5, 125.4, 124.5, 123.2, 122.9, 120.8, 67.3, 58.8, 56.8, 45.5, 44.0, 34.2, 27.9, 21.6$; IR (KBr): $\tilde{\nu} = 2894$, 1173, 912, 896, 750 cm^{-1}; MS (EI, 70 eV): m/z (%): 504 (3) $[M]^+$, 334 (100), 332 (51), 215 (35), 91 (45); elemental analysis calcd (%) for $C_{33}H_{28}O_3S$ (504.65): C 78.54, H 5.59; found: C 78.39, H 5.74.

Dehydration of fenestranol 9 with HMPT: A solution of fenestranol **9** (500 mg, 1.43 mmol) in hexamethylphosphorous triamide (25 mL) was stirred and heated at reflux for 18 h. The reaction mixture was allowed to cool and then poured into water (120 mL). The mixture was extracted with *n*-hexane/diethyl ether 10:1, and the organic layer was washed with water and dried with Na_2SO_4. Evaporation of the solvent gave a crude product which contained three isomeric olefins (**18**:**19**:**20**) in the ratio of 21:6:2 (as determined by ^{1}H NMR. Isomer **18** was isolated by column chromatography (*n*-hexane/ethyl acetate 50:1); isomers **19** and **20** were isolated by HPLC (cyclohexane), yielding **18** (197 mg, 593 μmol, 41%), **19** (28 mg, 84 μmol, 6%) and **20** (14 mg, 42 μmol, 3%) as colorless solids.

(*4bα*,*7aα*,*11bβ*,*15bα*)-5,7a,11b,15b-Tetrahydro-4b*H*-dibenzo[2,3:4,5]-pentaleno[1,6-*jk*]fluorene (18): M.p. 222–223 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.45$ (d, $J = 7.4$ Hz, 1H), 7.39 (d, $J = 7.3$ Hz, 1H), 7.26 (d, $J = 7.6$ Hz, 1H), 7.17–7.05 (m, 9H), 5.88 (dd, $J = 9.7$, 1.7 Hz, 1H), 5.81 (dd, $J = 9.6$, 2.6 Hz, 1H), 4.66 (s, 1H), 4.33 (s, 1H), 3.87 (dd, $J = 12.7$, 3.2 Hz, 1H), 2.73 (ddd, $J = 16.4$, 3.4, 3.2 Hz, 1H), 2.39 (ddd, $J = 16.4$, 12.6, 1.9 Hz, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 147.0, 146.3, 146.1, 145.1, 145.0, 142.0, 136.0, 127.9, 126.72, 126.67, 126.6, 126.1, 125.7, 124.9, 124.2, 124.0, 122.8, 120.8, 63.7, 61.3, 55.5, 54.2, 50.6, 23.9$; IR (KBr): $\tilde{\nu} = 3019$, 1471, 1453, 768, 745, 727, 698 cm^{-1}; MS (EI, 70 eV): m/z (%): 332 (100) $[M]^+$, 331 (10), 317 (11), 304 (16), 303 (25), 302 (13), 291 (12), 289 (13); exact mass measurement (EI-MS): m/z: calcd for $[M]^+$ 332.1565; found: 332.1565.

(*4bα*,*7aα*,*11bα*,*15bβ*)-5,7a,11b,15b-Tetrahydro-4b*H*-dibenzo[2,3:4,5]-pentaleno[1,6-*jk*]fluorene (19): M.p. 232 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.52$ (d, $J = 6.9$ Hz, 1H), 7.48–7.46 (m, 1H), 7.44–7.42 (m, 1H), 7.25–7.12 (m, 9H), 6.32 (dd, $J = 7.9$, 2.8 Hz, 1H), 4.57 (s, 1H), 4.49 (s, 1H), 3.78 (d, $J = 3.8$ Hz, 1H), 2.20 (dd, $J = 12.6$, 2.5 Hz, 1H), 2.02 (ddd, $J = 12.0$, 8.2, 3.8 Hz, 1H), 1.81 (tdd, $J = 12.6$, 5.0, 3.8 Hz, 1H), 1.72 (tt, $J = 12.6$, 3.1 Hz, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 145.8, 145.6, 145.1, 144.9, 144.1, 144.0, 140.3, 127.8, 127.3, 127.1, 127.0, 124.9, 124.3, 124.2, 124.0, 121.9, 120.2, 65.7, 63.1, 60.1, 46.4, 28.7, 26.9, 20.8$; IR (KBr): $\tilde{\nu} = 2935$, 1479, 1466, 751, 734, 645 cm^{-1}; MS (EI, 70 eV): m/z (%) 332 (100) $[M]^+$, 331 (7), 317 (12), 304 (12), 303 (25), 302 (15), 291 (14), 289 (16); elemental analysis calcd (%) for $C_{26}H_{20}$ (332.45): C 93.94, H 6.06; found: C 93.59, H 6.27.

(*4bα*,*11bα*,*15bβ*)-5,6,11b,15b-Tetrahydro-4b*H*-dibenzo[2,3:4,5]pentaleno[1,6-*jk*]fluorene (20): M.p. 202 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.42–7.40$ (m, 2H), 7.29–7.27 (m, 1H), 7.23–7.13 (m, 9H), 6.12 (d, $J = 9.7$, 1H), 5.85 (ddd, $J = 10.0$, 5.0, 2.5 Hz, 1H), 4.51 (s, 1H), 4.36 (s, 1H), 3.76 (s, 1H), 3.25 (t, $J = 7.5$ Hz, 1H), 2.51 (dt, $J = 18.2$, 6.3 Hz, 1H), 2.10 (ddd, $J = 18.2$, 7.5, 2.5 Hz, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 148.0, 146.3, 143.8, 143.7, 142.6, 142.5, 127.6, 127.2, 127.1, 127.0, 126.9, 126.8, 125.5, 124.8, 124.7, 124.6, 124.3, 124.1, 123.4, 65.7, 60.3, 59.3, 45.3, 42.1, 29.2$; IR (KBr): $\tilde{\nu} = 3027$, 1474, 1454, 769, 757, 738, 714 cm^{-1}; MS (EI, 70 eV): m/z (%): 332 (100) $[M]^+$, 331 (7), 317 (14), 304 (11), 303 (23), 302 (12), 291 (15), 289 (15); exact mass measurement (EI-MS): m/z: calcd for $[M]^+$ 332.1565; found: 332.1573.

***trans*-2,6-Diphenylspiro[cyclohexane-1,2′-[2*H*]indene]-1′,3′-dione (24)**: *trans*-Diphenylspirotriketone **5** (4.00 g, 10.5 mmol), *p*-toluenesulfonyl hydrazide (2.68 g, 14.40 mmol), sodium cyanoborohydride (2.43 g, 46.00 mmol), and *p*-toluenesulfonic acid (192 mg) were dissolved in dimethylformamide/sulfolane (1:1, 64 mL) and the mixture was heated to 110 °C for 2.5 h. The hot solution was poured into water (800 mL) with vigorous stirring. The precipitate formed was filtered by suction, washed with water, and dissolved in dichloromethane (200 mL). The organic layer was separated and dried over sodium sulfate. Removal of the solvent gave a product which was purified by column chromatography (silica gel, *n*-hexane/ethyl acetate 3:1) to give *trans*-diphenylspirodiketone **24** (1.24 g, 32%) as a colorless powder. M.p. 169–170 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.51–7.42$ (AA′BB′, 4H), 7.02–6.97 (m, 8H), 6.95–6.92 (m, 2H), 3.64 (dd, $J = 2.9$ Hz, $J = 12.6$, 2H), 2.71–2.62 (m, 2H), 2.10–2.04 (m, 2H), 1.96–1.90 (m, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 203.8, 142.1, 140.6, 134.8, 128.5, 127.8, 126.5, 121.1, 62.9, 44.7, 23.6, 21.0$; IR (KBr): $\tilde{\nu} = 2947, 1732, 1697, 1258, 760, 700\ cm^{-1}$; MS (EI, 70 eV): m/z (%): 366 (79) $[M]^+$, 275 (94), 235 (100), 91 (75); elemental analysis calcd (%) for $C_{26}H_{22}O_2$ (366.46): C 85.22, H 6.05; found: C 85.05, H 6.06.

***trans*-2,6-Diphenylspiro[cyclohexane-1,2′-[2*H*]indene]-1′,3′-diol (25)**: A solution of spirodiketone **24** (720 mg, 1.97 mmol) in tetrahydrofuran (15 mL) was added to a suspension of an excess of lithium aluminum hydride (0.30 g) in dry THF (20 mL), and the mixture was heated at reflux for 18 h. A portion (ca. 20 mL) of the solvent was then removed and replaced by diethyl ether (15 mL). The suspension was carefully hydrolyzed with water, the colorless precipitate was dissolved by adding 2N hydrochloric acid, and the solution was extracted several times with diethyl ether. The combined organic layers were washed with aqueous sodium bicar-

bonate and with water and dried over sodium sulfate. Evaporation of the solvent gave spirodiol **25** (725 mg, 99%) as a colorless powder (m.p. 164–165 °C), which, upon recrystallization from *n*-hexane/ethyl acetate 3:1, was obtained as pure, colorless crystals (700 mg, 96%). M.p. 164–165 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.40-7.38$ (m, 4H), 7.10–7.08 (m, 4H), 7.04–7.03 (m, 2H), 6.89 (br s, 4H), 5.30 (s, 2H), 3.84–3.81 (m, 2H), 2.14–2.08 (m, 2H), 2.04–1.98 (m, 4H), 1.21 (br s, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 144.3$, 142.9, 130.3, 128.0, 127.9, 126.1, 123.6, 78.2, 57.2, 42.5, 29.5, 21.3; IR (KBr): $\tilde{\nu} = 3538$, 3434, 3030, 2924, 1450, 1175, 1015, 759, 707, 696 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 370 (3) $[M]^+$, 352 (88), 334 (17), 237 (52), 147 (100), 117 (54), 91 (91); exact mass measurement (EI): *m*/*z*: calcd for $[M]^+$ 370.1933; found: 370.1934; elemental analysis calcd (%) for $C_{26}H_{26}O_2$ (370.50): C 84.29, H 7.07; found: C 84.12, H, 7.05.

***cis*-2,6-Diphenylspiro[cyclohexane-1,2′-[2*H*]indene]-1′,3′-dione (27)**

a) Tosylhydrazone **26**: A mixture of *trans*-diphenylspirotrione **5** or *cis*-diphenylspirotrione **6** (2.00 g, 5.26 mmol in each case), *p*-toluenesulfonyl hydrazide (1.17 g, 6.31 mmol), and ethanol (40 mL) was heated at reflux for 3 h. The mixture was allowed to cool and then kept at −15 °C overnight. The precipitate was filtered by suction, washed, and recrystallized from ethanol to give a colorless powder (2.52 g, 96%, from **5** and 2.23 g, 88%, from **6**) of m.p. 146–150 °C (decomp).

ba) Reduction of tosylhydrazone **26** with sodium borohydride: Tosylhydrazone **26** (200 mg, 413 μmol) was dissolved in methanol (20 mL). Sodium borohydride (0.5 g) was carefully added in small portions and the mixture was heated at reflux temperature for 15 h. The suspension was allowed to cool, 15 mL of water were added, and the mixture was extracted several times with diethyl ether. The combined extracts were washed with aqueous sodium bisulfate and with water and then dried over sodium sulfate. Evaporation of the solvent and recrystallization of the residue from ethanol gave *cis*-diphenylspirodiketone **27** (82 mg, 54%). M.p. 197–199 °C.

bb) Reduction of tosylhydrazone **26** with catecholborane: Tosylhydrazone **26** (1.60 g, 3.30 mmol) was dissolved in dry chloroform (40 mL) at 0 °C. A solution of catecholborane (1M, 8.0 mL, 8.0 mmol) in tetrahydrofuran was added under argon and the mixture was stirred at ambient temperature for 5 h. Sodium acetate trihydrate (2.18 g, 16.0 mmol) was added and the reaction mixture was heated at gentle reflux for 2 h. The solution was allowed to cool and kept at ambient temperature overnight. The organic layer was washed with water, aqueous sodium bicarbonate, and again with water. The solvent was distilled off and the residue was crystallized from ethanol to give spirodiketone **27** (0.88 g, 73%) as a colorless powder. M.p. 198–199 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.51-7.50$ m, 1H), 7.39-7.31 m, 3H), 7.00–6.99 (m, 4H), 6.95–6.92 (m, 4H), 6.88–6.85 (m, 2H), 3.34 (dd, $J = 3.3$, 13.2 Hz, 2H), 2.75 (dq, $J = 3.7$, 13.2 Hz, 2H), 2.21 (dt, $J = 3.3$, 13.4 Hz, 1H), 1.84 (dq, $J = 3.3$, 13.4 Hz, 2H), 1.76 (dt, $J = 3.7$, 13.1 Hz, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 203.9$, 203.8, 142.9, 141.8, 140.5, 134.7, 134.5, 128.4, 127.9, 126.7, 121.9, 121.7, 63.3, 49.5, 27.3, 26.3; IR (KBr): $\tilde{\nu} =$ 2926, 1733, 1698, 1254, 766, 701 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 366 (65) $[M]^+$, 275 (100), 235 (96), 91 (58); exact mass measurement (EI-MS): *m*/*z*: calcd for $[M]^+$ 366.1620; found: 366.1626.

***cis*-2,6-Diphenylspiro[cyclohexane-1,2′-[2*H*]indene]-1′,3′-diol (28)**: *cis*-Diphenylspirodione **27** (880 mg, 2.40 mmol) was dissolved in dry tetrahydrofuran (20 mL) and the solution was added to a suspension of lithium aluminum hydride (0.40 g, 10.5 mmol) in dry THF (20 mL) and heated to reflux for 24 h. The major part of the solvent was distilled off and replaced with diethyl ether (15 mL). The mixture was carefully hydrolyzed by adding ice/water and extracted several times with diethyl ether. The combined organic layers were dried over sodium sulfate and the solvent was removed. The oily residue was crystallized from ethanol to give spirodiol **28** (471 mg, 53%) as colorless crystals. M.p. 204–205 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.54-7.52$ (m, 2H), 7.22–7.19 (m, 2H), 7.13–7.08 (m, 2H), 6.97–6.95 (m, 1H), 6.90–6.87 (m, 3H), 6.84–6.73 (m, 4H), 5.64 (s, 1H), 5.52 (s, 1H), 3.28 (dt, $J = 13.8$, 13.0 Hz, 2H), 2.69 (dq, $J = 3.8$, 13.0 Hz, 1H), 2.33 (dq, $J =$ 4.2, 13.2 Hz, 1H), 2.12–2.07 (m, 2H), 1.79 (d, $J = 14.2$ Hz, 1H), 1.77–1.68 (m, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 144.6$, 144.4, 143.6, 141.8, 131.0, 128.9, 128.7, 127.73, 127.68, 127.4, 126.1, 126.1, 125.7, 124.5, 121.8, 78.2, 78.0, 58.4, 51.0, 49.7, 31.3, 28.8, 27.6; IR (KBr): $\tilde{\nu} = 3564$, 3443, 2929, 1491, 1453, 1101, 1028, 1010, 759, 747 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 370 (1) $[M]^+$, 352 (74), 334 (4), 237 (58), 147 (100), 117 (37), 91 (62); exact mass measurement (EI-MS): *m*/*z*: calcd for $[M]^+$ 370.1933; found: 370.1926.

***(4ba,7aβ,11ba,15bβ)*-5,6,7,7a,11b,15b-Hexahydro-4b*H*-dibenzo-[2,3:4,5]pentaleno[1,6-*jk*]fluorene (3)**[17]

a) By Wolff–Kishner reduction of fenestranone **12**: A mixture of **12** (140 mg, 400 μmol), triethylene glycol (4.0 mL), hydrazine hydrate (150 μl), and finely powdered potassium hydroxide (100 mg) was stirred and heated at 130 °C for 3 h. The temperature was then slowly raised to 180 °C, while the volatile components were distilled off, and the mixture was kept at this temperature for a further 2 h. The mixture was allowed to cool, the solid residue was dissolved in water and the solution was acidified with hydrochloric acid (10%) and extracted several times with dichloromethane. The combined organic layers were washed with water and dried with sodium sulfate. The solvent was removed and the residue was recrystallized from diethyl ether/tetrahydrofuran 4:1 to give *all-cis*-fenestrane **3** (98 mg, 73%). M.p. 203–207 °C (204–205 °C).[17]

b) By reduction of dithiolane **15** with Raney nickel: Raney nickel, freshly prepared from nickel/aluminum alloy (15.0 g) and washed to pH 7.0, was added to a solution of **15** (580 mg, 1.37 mmol) in 1,4-dioxane (100 mL). The mixture was heated to reflux for 15 h and after cooling to ambient temperature the catalyst was filtered off and washed twice with 25 mL portions of hot 1,4-dioxane. The combined organic solutions were combined, the solvent was evaporated, and the residue was recrystallized from ethanol to give *all-cis*-fenestrane **3** (367 mg, 80%), m.p. 203–205 °C (see above).

c) By reduction of dithiolane **16** with Raney nickel: A solution of **16** (920 mg, 2.17 mmol) was reduced by following the procedure described above for **15**, to give *all-cis*-fenestrane **3** (632 mg, 87%), m.p. 204–205 °C (see above).

d) By reduction of dithiolane **16** with Bu_3SnH:. Azoisobutyronitrile (AIBN, 15 mg) and tri(*n*-butyl)tin hydride (0.40 mL, 1.49 mmol) were added to a solution of **16** (130 mg, 307 μmol) in dry benzene (15 mL) and the mixture was refluxed for 5 h. The solvent was distilled off to give an oily residue, which crystallized within a few hours upon standing. Ethanol (5 mL) was added and the mixture was stirred at ambient temperature overnight, during which most of the by-products, such as bis(tributystannyl)ethanedithiolate and bis[tri-(*n*-butyl)tin] sulfide, dissolved. The remaining organotin compounds were separated by column chromatography (silica gel, *n*-hexane), and subsequent elution with ethyl acetate gave pure **3** (82 mg, 80%), m.p. 202–205 °C (see above).

e) By cyclodehydration of *trans*-diphenylspirodiol **25**: In a reaction vessel equipped with a water separator, spirodiol **25** (300 mg, 811 mmol) and orthophosphoric acid (85%, 1.5 g) were refluxed in toluene (40 mL) for 15 h. The hot solution was carefully decanted from the brownish residue, the solvent was distilled off, and the crude product was recrystallized from ethanol to yield pure *all-cis*-fenestrane **3** (244 mg, 90%), m.p. 204–206 °C (see above).

***(4ba,7aa,11ba,15bβ)*-5,6,7,7a,11b,15b-Hexahydro-4b*H*-dibenzo-[2,3:4,5]pentaleno[1,6-*jk*]fluorene (4)**

a) By reduction of tosylate **17**: A suspension of **17** (0.60 g, 1.19 mmol) and lithium aluminum hydride (150 mg, 3.95 mmol) in dry tetrahydrofuran (90 mL) was heated at reflux for 15 h. The mixture was cooled in ice/water, carefully hydrolyzed by adding aqueous ammonium chloride, and then extracted several times with diethyl ether. The combined organic layers were washed with aqueous sodium thiosulfate (10%) and dried with sodium sulfate. The solvent was distilled off and the residue was recrystallized from *n*-hexane/ethyl acetate 3:1 to yield a colorless solid (337 mg, ca. 85%) which, according to ^{1}H NMR spectroscopy, consisted of a mixture of hydrocarbons **4** (ca. 85%) and olefins (ca. 15%). The mixture (260 mg, 0.78 mmol) was dissolved in dry ethyl acetate/tetrahydrofuran 3:2 (50 mL), palladium on charcoal (10%, 20 mg, Merck) was added, and the mixture was shaken under hydrogen at normal pressure and ambient temperature for 2 d. The catalyst was removed by filtration, the solvent was evaporated, and the oily residue was crystallized from ethanol to give **4** (217 mg, 83%) as colorless needles, m.p. 220–222 °C (see below).

b) By reduction of dithiolane **15** with Bu_3SnH: A solution of **15** (130 mg, 307 μmol) was treated according to the procedure described above for the case of **16**. Workup furnished *ccct*-fenestrane **4** (89 mg, 87%), m.p. 219–221 °C (see below).

c) By Clemmensen reduction of **12**: Conc. hydrochloric acid (0.4 mL) and water (12 mL) were added to zinc (8.00 g, 122.4 mmol) and mercury(II) chloride (0.80 g, 2.95 mmol). This mixture was stirred for 5 min and the

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excess solution was removed. Conc. hydrochloric acid (8 mL) and ketone **12** (0.4 g, 1.15 mmol), suspended in 1,4-dioxane (50 mL), were then added and the solution was heated at reflux for 48 h (more reducing agent and a longer reaction time were sometimes necessary). The solution was cooled to ambient temperature, poured into water (400 mL) and extracted several times with diethyl ether. The organic layer was dried with sodium sulfate, the solvent was distilled off, and the crude product was recrystallized from ethanol to yield **4** (327 mg, 85%), m.p. 220–221 °C (see below).

d) By cyclodehydration of *cis*-diphenylspirodiol **28**: In a reaction vessel equipped with a water separator, spirodiol **28** (300 mg, 811 μmol), orthophosphoric acid (85%, 1.5 g) and toluene (40 mL) were heated at reflux for 24 h. The organic layer was decanted carefully from the oily residue, the solvent was removed in vacuo, and the solid residue was recrystallized from ethanol to give fenestrane **4** (222 mg, 82%) as colorless needles. M.p. 222–223 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.45-7.41$ (m, 2H), 7.20–7.00 (m, 10H), 4.458 (s, 1H), 4.451 (s, 1H), 3.81 (s, 1H), 3.80 (dd, $J = 4.5$ Hz, 1H), 2.37–2.32 (m, 1H), 2.24–2.21 (m, 1H), 1.71–1.68 (m, 1H), 1.59–1.53 (m, 2H), 1.09–1.00 (m, 1H); ^{1}H NMR (500 MHz, C_6D_6): $\delta = 7.30$ (d, $J = 7.4$ Hz, 1H), 7.18–7.16 (m, 1H), 7.08–6.99 (m, 8H), 6.93–6.88 (m, 2H), 4.30 (s, 1H), 4.13 (s, 1H), 3.50 (d, $J = 4.1$ Hz, 1H), 3.49 (dd, $J = 13.2$, 4.7 Hz, 1H), 2.03–1.93 (m, 2H), 1.48–1.40 (m, 2H), 1.35–1.27 (m, 1H), 1.08–0.98 (m, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 146.6$, 146.3, 145.9, 144.8, 144.7, 143.8, 126.9, 126.8, 126.7, 126.6, 126.4, 126.2, 125.1, 124.6, 124.5, 123.2, 122.8, 120.9, 66.8, 59.7, 56.4, 47.0, 45.3, 28.1, 18.3, 15.4; IR (KBr): $\tilde{\nu} = 2922$, 1468, 1453, 754, 741 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 334 (100) $[M]^+$, 305 (34), 291 (34), 257 (24); exact mass measurement (EI-MS): *m*/*z*: calcd for $[M]^+$ 334.1722; found: 334.1722; elemental analysis calcd (%) for $C_{26}H_{22}$ (334.47): C 93.37, H 6.63; found: C 93.26, H 6.54.

Base-induced epimerization of fenestranone 12: A solution of ketone **12** (1.00 g, 2.87 mmol) and potassium *tert*-butoxide (5.0 g) was stirred in DMSO (80 mL) at 20 °C for 15 h. The brownish liquid was then poured into water (500 mL), acidified with 2N hydrochloric acid, and extracted with trichloromethane. The organic extract was washed with water, saturated aqueous sodium bicarbonate, and again with water, dried over sodium sulfate, and concentrated to dryness. The crude product was recrystallized from EtOH/THF to give the all-*cis*-fenestranone **7** (739 mg, 74%) as a colorless solid, m.p. 283–285 °C. The ^{1}H NMR spectrum was found to be identical with that of an authentic sample.

H/D exchange experiments

***(4bα,7aβ,11bα,15bβ)*-11b,15b-Dideutero-5,6,7,7a,11b,15b-hexahydro-4b*H*-dibenzo[2,3:4,5]pentaleno[1,6-*jk*]fluorene (3a)**: A mixture of all-*cis*-fenestrane **3** (20 mg, 60 μmol), KO*t*Bu (100 mg, 1.04 mmol), and [D_6]DMSO (3 mL) was stirred under argon for 24 h at 20 °C. The reaction mixture was then poured into water (50 mL) and extracted with dichloromethane. The organic layer was dried with sodium sulfate and the solvent was removed. The product was purified by column chromatography (*n*-hexane/ethyl acetate 3:1) to yield **3a** (18.4 mg, 90%) as a colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.37-7.32$ (AA′BB′ system, 4H), 7.22–7.15 (m, 8H), 3.17 (t, $J = 6.5$ Hz, 1H), 1.90–1.85 (m, 2H), 1.73–1.69 (m, 2H), 1.46–1.43 (m, 2H); MS (EI, 70 eV): *m*/*z* (%): 337 (100) $[M]^+$, 338 (42), 339 (8).

***(4bα,7aβ,11bα,15bβ)*-7a,11b,15b-Trideutero-5,6,7,7a,11b,15b-hexahydro-4b*H*-dibenzo[2,3:4,5]pentaleno[1,6-*jk*]fluorene (3b)**: This compound was obtained by treating the *cis*,*cis*,*cis*,*trans*-fenestrane **4** with KO*t*Bu and [D_6]DMSO exactly as described above, to yield **3b** (18.3 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.38-7.32$ (AA′BB′ system, 4H), 7.21–7.16 (m, 8H), 3.17 (t, $J = 6.5$ Hz, 1H), 1.91–1.87 (m, 2H), 1.74–1.71 (m, 2H), 1.46–1.44 (m, 2H); MS (EI, 70 eV): *m*/*z* (%): 337 (100) $[M]^+$, 338 (55), 339 (13).

***(4bα,7aβ,11bα,15bβ)*-7a-Deutero-5,6,7,7a,11b,15b-hexahydro-4b*H*-dibenzo[2,3:4,5]pentaleno[1,6-*jk*]fluorene (3c)**: A mixture of **4** (20 mg, 60 μmol), KOD (100 mg, 1.75 mmol), and [*O*,*O*′-D_2]-diethylene glycol (4.0 mL) was stirred under argon and heated at 180 °C for 3 h. The reaction mixture was allowed to cool, then poured into water (50 mL) and extracted with dichloromethane. The organic layer was dried with sodium sulfate and the solvent was removed. The product was purified by column chromatography (*n*-hexane/ethyl acetate 3:1), yielding a mixture (19 mg, 90%) of unreacted **4** and the monodeuterated product **3c** in the ratio of 1.2:1.4 (by ^{1}H NMR) as a colorless solid. ^{1}H NMR of **3c** (500 MHz, $CDCl_3$): $\delta = 7.37-7.32$ (AA′BB′ system, 4H), 7.22–7.15 (m, 8H), 4.37 (s, 2H), 3.17 (t, $J = 6.5$ Hz, 1H), 1.90–1.85 (m, 2H), 1.73–1.69 (m, 2H), 1.46–1.43 (m, 2H).

Crystal structure determination of 4:[32] Diffraction data were collected on a Bruker AXS P4 diffractometer at 203 K with ω scan, using graphite monochromated $Mo_{K\alpha}$ radiation. Pertinent crystallographic data are summarized in Table 2. Three standard reflections were periodically monitored, showing only random deviations. Lp corrections were applied. A total of 4718 reflections were collected in the range $\Theta = 2.08-26.99°$, with $h = -1$ to 11, $k = -25$ to 1, and $l = -12$ to 12, of which 3755 independent reflections ($R_{int} = 0.015$) were used for structure determination. The structure was solved by direct and Fourier methods and refined by full-matrix, least-squares based on F^2 and 236 parameters. All non-hydrogen atoms were refined anisotropically, hydrogen atoms were placed at geometrically calculated positions with $U(H)_{iso} = 1.2\ (C)_{iso}$. Refinement converged smoothly at $R1(I > 2\sigma I) = 0.045$, $wR2$ (all data) = 0.133, $S = 1.056$, max.$(\Delta/\sigma) = 0.000$, min/max height in final DF map −0.18/0.25 e Å^{-3}. Programs used: SHELXTL NT V5.1.[35]

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[32] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-135141. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk)..

[33] The apical atoms of the boat, C5, and C7a, respectively, were found to be 63.4(2) and 66.1(2) pm above its basal mean plane, the four associated C atoms deviating by only ±5.0(2) pm from that plane.

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[35] SHELXTL NT, Version 5.10. Bruker AXS, Inc. Madison, Wisconsin, USA.

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