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The Regioselective Generation of Arynes from Polyhalogenobenzenes. An Improved Synthesis of *syn*- and *anti*-1,4,5,8,9,12-Hexahydro-1,4:5,8:9,12-triepoxytriphenylene

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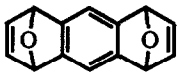
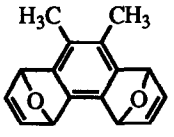
Abstract: *The halogenated benzenes, 1, 2 ,4, 5-tetrabromobenzene* ***6****, hexabromobenzene* ***9****, p-dichlorotetrabromobenzene* ***11****, and 1, 2-dibromo-4, 5-dichlorobenzene* ***12****, were investigated as 1, 3-bis-, 1, 4-bis-, and 1, 3, 5-tris-aryne precursors by using alkyllithiums and alkali metal amides as the metalating reagents. The arynes were trapped in Diels-Alder reactions with furan as the diene. The title compounds* ***3a/b*** *are now readily available in two steps in 7% overall yield from 1, 2, 4, 5-tetrabromobenzene* ***6****.*

INTRODUCTION

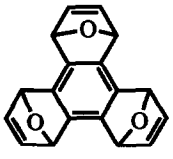
The bisdienophiles **1a/b** and **2a/(±)-2b**, and the trisdienophiles **3a/b**, are useful building blocks for the rapid assembly of molecular collars,[1] snakes,[2] and cages[3,4] by means of their highly diastereoselective[5-7] Diels-Alder reactions with exocyclic diene moieties grafted on to a 7-oxanorbornane skeleton. For example, the molecular cage compound trinacrene **5** [3] can be easily constructed (Scheme 1) from **3a** and Vogel's bisdiene **4**. [8] Compounds **1-3a/b** can all be obtained by trapping furan with the appropriate aryne precursor. Thus, their efficient synthesis is dependent upon the availability of substrates that can behave as 1,3-bis-, 1,4-bis-, and 1,3,5-tris-aryne[9] equivalents.



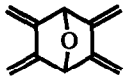
1a *syn*
1b *anti*



2a *syn*
(±)-2b *anti*



3a *syn*
3b *anti*



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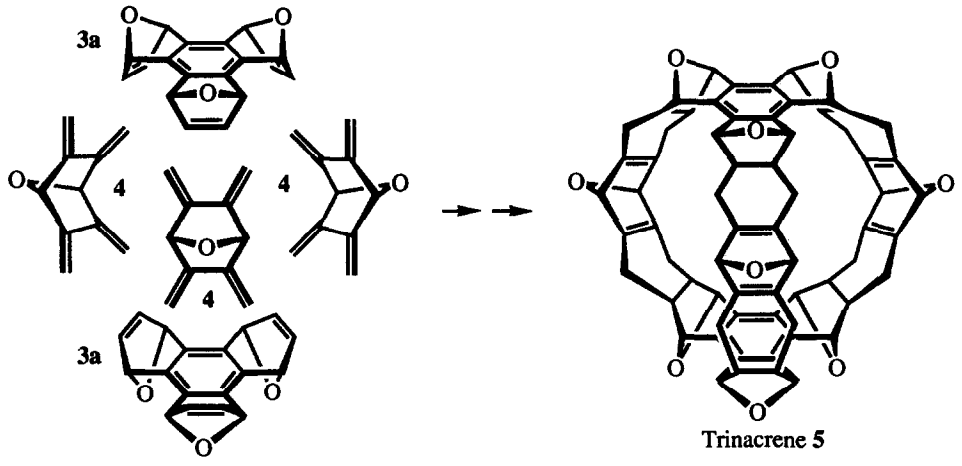
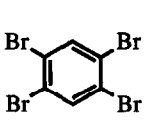
Halogenobenzenes have been used extensively for the generation of arynes,[10-17a] mainly by hydrogen-metal exchange (metalation) on a position *ortho* to the halogen and by halogen-metal exchange,[18,19] always followed by elimination of the halogen salt. The bisdienophiles **1a/b** can be prepared[12,13,16] in good yield by treatment of 1,2,4,5-tetrabromobenzene **6** with two equivalents of *n*-butyllithium at low temperature in the presence of furan. In this case, hydrogen-metal exchange is not observed. This fact accounts for the regioselective formation of linear adducts. Treatment with only one equivalent affords[12,13] the monoadduct **7a**.



Scheme 1

The synthesis of bisdienophiles **2a/(±)-2b** is complicated by the necessity of generating two aryne units which are 1,3-related. This problem has been solved[20,21] by starting from 4,5-dibromo-3,6-diiodo-*o*-xylene **8**. The method takes advantage of the faster rate of halogen-metal exchange for iodine compared to bromine. Regioselective formation of the *p*-dilithioarene directs the regioselective formation of a 1,3-bisaryne, while the remaining positions on the benzene ring are blocked by the methyl groups. The trisdienophiles **3a/b** were first prepared[22a] (6 steps in 0.4% yield overall) from 2,5-dibromoaniline. This method is not suitable[22b] for the preparation of these compounds on a multigram scale. Our synthesis[3] of **3a/b** by low temperature treatment of



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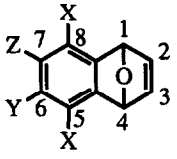

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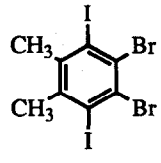
7a X=H, Y=Z=Br
7b X=Y=Z=Br
(±)- **7c** X=Y=Br, Z=H
7d X=Br, Y=Z=H
7e X=Cl, Y=Z=Br
7f X=H, Y=Z=Cl



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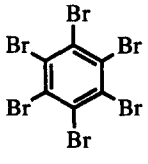

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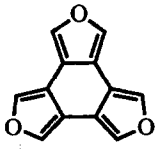

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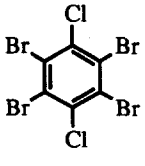

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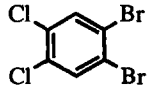


12

hexabromobenzene **9** with one equivalent of *n*-butyllithium in the presence of furan - leading initially to the formation of the monoadduct **7b** - and then subsequent addition of two more equivalents of *n*-butyllithium to the reaction mixture, has the attraction of being a one-pot procedure, but it is also plagued by the low yields (2.4% of *syn* plus *anti*) and by the difficulty of purifying the products.

In considering the further synthetic elaboration of trinacrene **5**, we recognised that a new synthetic strategy for the preparation of the *syn*-trisdienophile **3a** was essential, if this interesting molecular cage compound was to become more than just a structural curiosity. Also, the trisdienophiles **3a/b** are synthetic precursors of benzo[1,2-c:3,4-c':5,6-c"]trisfuran **10**,[22a] whose chemistry is still to be investigated.

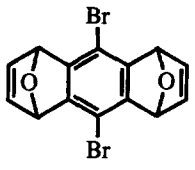
Thus, we decided to screen a range of polyhalogenobenzenes in search of polyaryne equivalents in which the stepwise regioselective generation of the aryne units could be controlled by the nature and/or relative positions of different halogens on the benzene ring, as well as by changing reaction conditions.

Our approach was based on the following simple premises: (1) The relative rate of metal-halogen exchange is higher for bromine than for chlorine, and (2) if the organometallic species can choose whether to eliminate lithium chloride or bromide, then the latter is preferred.[12,14] (3) If a hydrogen atom is available *ortho* to a chlorine atom, then hydrogen-metal exchange will be preferred to chlorine-lithium exchange - but not to bromine-lithium exchange[23,24] - and (4) elimination of lithium chloride will follow. Finally, (5) for those substrates having hydrogen atoms *ortho* to a halogen, arynes can be obtained by the action of a suitable base such as $NaNH_2$ or KNH_2.

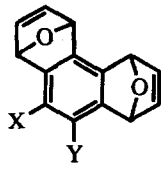
Here, we report on our findings obtained starting with (a) hexabromobenzene **9**, (b) *p*-dichlorotetrabromobenzene **11**, (c) 1,2-dibromo-4,5-dichlorobenzene **12**, and (d) 1,2,4,5-tetrabromobenzene **6**.

RESULTS AND DISCUSSION

(a) *Hexabromobenzene* **9**. Previously, we explained[3] the formation of the trisdienophiles **3a/b** by assuming that the monoadduct **7b** could be partially *para*-dilithiated,[25,26] thus giving 1,3-related arynes upon double elimination of lithium bromide. In order to verify this hypothesis and obtain a better understanding of the reaction mechanism which might enable us to improve the yields of **3a/b**, we treated the monoadduct **7b** with *n*-butyllithium at -78°C in toluene, followed by quenching of the reaction mixture with methanol after 30 min. at this temperature. When one equivalent of *n*-butyllithium was used, the only product isolated was (±)-**7c** (54%). When two equivalents of *n*-butyllithium were used, the major product was still (±)-**7c** (61%), although **7d** (6%) was also formed. Quenching of the reaction mixture after 4.5 h did not improve the yield of **7d** and the presence of furan does not alter the situation. We believe that the isolation of **7d** demonstrates the formation of an *o*-dilithioarene - a 1,3-bisaryne precursor, leading to the formation of the trisdienophiles **3a/b** in the presence of furan.



13a *syn*
13b *anti*



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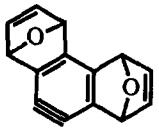
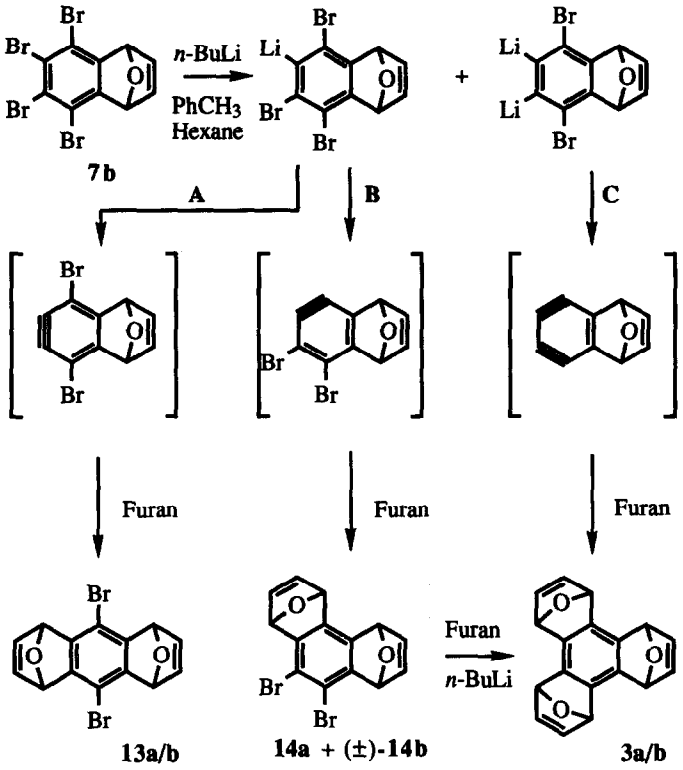
14a	X=Y=Br	*syn*
(±)-**14b**	X=Y=Br	*anti*
(±)-**14c**	X=H, Y=Br	*syn*
(±)-**14d**	X=H, Y=Br	*anti*
(±)-**14e**	X=H, Y=Cl	*syn*
(±)-**14f**	X=H, Y=Cl	*anti*



15a *syn*
(±)-**15b** *anti*

When the monoadduct **7b** was treated with one equivalent of *n*-butyllithium in toluene at -78°C in the presence of furan and the mixture was allowed to warm up to room temperature, the linear bisdienophiles **13a/b** bearing two bromine atoms in the *para* positions were the main products (43%). Minor quantities (<2%) of the angular isomers **14a**/(±)-**14b** were also formed. These latter compounds could contribute to the formation of

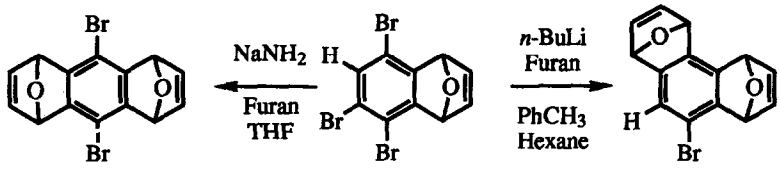
the trisdienophiles **3a/b** by undergoing further lithiation-elimination when another two equivalents of *n*-butyllithium are present. The possible reactions of the monoadduct **7b** in toluene/hexane, when it is treated with an excess of *n*-butyllithium in the presence of furan, are outlined in Scheme 2. The trisdienophiles **3a/b** are obtained in low yield presumably because the favoured reaction pathway is A, almost to the exclusion of pathways B and C. Changing the solvent (diethyl ether or THF) did not affect the outcome.[27] Since halogen-metal exchange normally occurs at the most electropositive halogen, the preferential site of exchange in the monoadduct **7b** is not all that surprising. However, it is remarkable that the formation of a *o*-dilithioarene is preferred to that of a *m*-dilithioarene in which the two carbanionic centres would be further apart.[28]



Note that the bisaryne displayed inside the square brackets along pathway C is no more than a convenient shorthand representing the formation of two successive aryne intermediates.

Scheme 2

The predominant formation of the linear bisdienophiles **13a/b** *via* pathway A indicates the favoured direction of lithium bromide elimination. The structure of the benzene ring in the monoadduct **7c** is probably better represented by the Kekulé structure given in Scheme 3 in which the two fused rings share a single bond. This partial bond fixation - known as the Mills-Nixon effect[29] - could be brought about by the fusion with the strained 2,5-dihydrofuran moiety. This effect would favour pathway A because arynes are more easily formed at a position where the two carbon atoms share a higher double bond character bringing them closer together.[17b] This effect clearly overpowers the one exerted by the bromine atoms. 1,2,4-Tribromobenzene was found to form the aryne exclusively at the 3,4-position.[30]

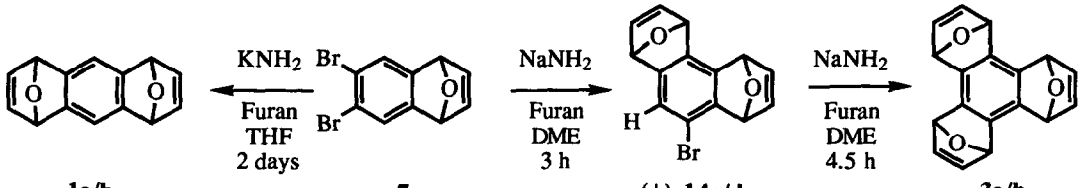


Scheme 3

The quenched product (±)-**7c** is a regioselectively versatile aryne precursor. Its treatment with $NaNH_2$ or KNH_2 leads to the formation of the aryne at the 6,7-bond, whereas treatment of (±)-**7c** with *n*-butyllithium generates the aryne at the 5,6-bond, as indicated (Scheme 3) by the products of furan trapping - namely **13a/b** and (±)-**14c/d**, respectively. Treatment of (±)-**14c/d** with $NaNH_2$ or KNH_2, followed by furan trapping gives the trisdienophiles **3a/b**. Thus, they can be obtained in four steps in 1% overall yield from hexabromobenzene **9**. Although this procedure is less efficient than the one we described previously,[3] the isolation of the products by flash chromatography is easier to perform.

(b) *p-Dichlorotetrabromobenzene* **11**. *p*-Dichlorotetrabromobenzene **11** has been reported[12,14] to be a 1,4-bisaryne equivalent. However, we decided to assess its use as 1,3,5-trisaryne synthon *via* the monoadduct **7e**. In this way, we hoped to promote the exchange of both the bromine atoms and the formation of the *o*-dilithioarene as a result of the stronger inductive electron-withdrawing effect of chlorine compared with bromine. Treatment of **11** with one equivalent of *n*-butyllithium in diethyl ether at -78°C, followed by trapping with furan, afforded (33%) the monoadduct **7e**. Various attempts to improve upon this yield by using different solvents (*e.g.* toluene, THF) and temperatures were unsuccessful. When the monoadduct **7e** was subjected to the lithiation-quenching experiments, the results were almost identical to those obtained with the monoadduct **7b** and so we did not to pursue this route any further.

(c) *1,2-Dibromo-4,5-dichlorobenzene* **12**. 1,2-Dibromo-4,5-dichlorobenzene **12**[14] was readily synthesized from *o*-dichlorobenzene on reaction with bromine and iron. Selective lithium-bromine exchange by treatment of **12** with 1.3 equivalents of *n*-butyllithium in diethyl ether in the presence of furan at -15 °C gave the monoadduct **7f** (42%). When this reaction was conducted at lower temperatures or in different solvents (*e.g.* toluene, THF), the yields of **7f** were considerably lower. Treatment of **7f** with 1.2 equivalents of *n*-butyllithium in THF, followed by addition of furan, gave (12%) the angular adducts (±)-**14e/f**. However, all attempts to obtain the arynes **15a**/(±)-**15b** from (±)-**14e/f** by using an excess of *n*-butyllithium or *t*-butyllithium were fruitless. When **7f** was subjected to dehydrohalogenation with $NaNH_2$ in THF or DME, subsequent trapping with furan gave (±)-**14e/f** (31%), together with small amounts of their corresponding linear isomers. However, this method failed to effect double dehydrohalogenation.



Scheme 4

(d) *1,2,4,5-Tetrabromobenzene* **6**. 1,2,4,5-Tetrabromobenzene **6** has been used extensively as a 1,4-bisaryne equivalent.[12,13] When **6** is treated with only one equivalent of *n*-butyllithium, furan trapping yields[13] the monoadduct **7a**, which was also identified as a potential 1,3-bisaryne equivalent *via* a double dehydrohalogenation. When **7a** was treated with KNH_2 in THF, furan trapping gave only the linear bisdienophiles **1a/b** (69%). However, when the reaction was conducted in DME using $NaNH_2$ as base, the angular bisdienophiles (±)-**14c/d** were the main products present after 3 h. These went on to give the trisdienophiles **3a/b** as the major isolated products after a further 4.5 h (Scheme 4). Minor quantities of the linear bisdienophiles **1a/b**, and their analogues, bearing one bromine atom on the benzene ring, could be isolated. In THF, although the reaction was much slower, the products were identical to those obtained in DME. Clearly, these results can be ascribed to the nature of the base. Probably, KNH_2 is more effective than $NaNH_2$ at promoting an isomerisation, which redistributes the bromine atoms at the various positions on the benzene ring by a process similar to the one observed in the conversion of 1,2,4-tribromobenzene to 1,3,5-tribromobenzene. This type of isomerisation has been referred to[31] as the "halogen dance".

To the best of our knowledge, the reaction of **7a** *with* $NaNH_2$ *constitutes the best and most efficient synthesis of the trisdienophiles* **3a/b** *(10%) and represents a substantial improvement on those previously reported.*[3,22a]

The arynes **15a** and (±)-**15b** are formed with difficulty. In fact, when **7a** is subjected to dehydrohalogenation, the formation of the trisdienophiles **3a/b** is not observed until most of the monoadduct **7a** has been converted into the bisdienophiles (±)-**14c/d**. This behaviour is probably a consequence of the deformation of the benzene ring by the two *o*-fused oxanorbornene systems. This deformation has been clearly demonstrated by an X-ray structural analysis conducted[32] on the *anti*-bisdienophile (±)**2b**, where a pronounced alternation of the bond orders around the benzene ring is observed: The longer bonds are those which are shared with the oxanorbornene skeletons and the one between the substituents X and Y in structural formula **14**. This distortion is not observed in the linear bisdienophiles **1a/b**.[15,33,34] Presumably when three fused 2,5-dihydrofuran skeletons are acting cooperatively, this partial bond fixation must be more pronounced and the benzene rings in the trisdienophiles **3a/b** are probably best described by the Kekulé structure employed in Scheme 4. Unfortunately, X-ray crystal structures of **3a/b** are not yet available. Nonetheless, one is led to question just how much aromatic character their benzene rings have lost.

CONCLUSIONS

The results that we have obtained are in accordance with the premises which formed the basis for our original investigation. The [2,5-a]-fusion of the 2,5-dihydrofuran on to a polyhalogenobenzene ring promotes the formation of a naphth-6-yne rather than a naphth-5-yne. However, it is possible to influence this regioselectivity by appropriate choice of substituents and reaction conditions. The hexahalogenobenzenes **9** and **11** clearly are not very convenient 1,3,5-trisaryne equivalents. However, the tetrahalobenzenes **12** and **6** can be employed as 1,3-bisaryne equivalents. The ability of 1,2,4,5-tetrabromobenzene **6** to behave as 1,3-bis-, 1,4-bis- or 1,3,5-tris-aryne equivalent upon simple changes in the reaction conditions, allows the chemist to dictate the architecture of subsequent annulations onto a benzene ring.

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EXPERIMENTAL

Diethyl ether, toluene, and hexane were dried over sodium wire. Tetrahydrofuran (THF) was distilled from the sodium ketyl of benzophenone. Anhydrous dimethoxyethane (DME) was supplied by Aldrich. All air-sensitive and/or moisture sensitive reactions were conducted under a dry argon atmosphere. KNH_2 and $NaNH_2$ were freshly prepared prior to use. Thin layer chromatography (TLC) was carried out on either glass or

aluminium SiO_2 Carlo Erba Stratocrom SIF 254 or Al_2O_3 Carlo Erba Stratocrom ALF plates. Compounds were visualised with iodine or by examination under UV light. Column chromatography was conducted on Aldrich Si gel 230-400 mesh, 60Å, or Carlo Erba basic Al_2O_3. The *syn* or *anti* configuration of the oxygen atoms for those compounds, which were not characterised by X-ray crystallographic analysis, was assigned on the basis of an analogy with the chromatographic behaviour of the known compounds - the *anti* isomers always being the more chromatographically-mobile. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer in $CDCl_3$ using $(CH_3)_4Si$ as internal standard. Mass spectra were measured by electron impact (EI) on a Finnigan Mat 90 spectrometer operated by Dr. Marcello Saitta. Melting points were determined on a Kofler hot stage apparatus, and are not corrected. No attempt was made to separate pure enantiomers of chiral compounds or to establish if the crystalline products were racemic compounds or racemic mixtures. Elemental analyses were conducted by Redox SNC, 20093 Cologno M. Milan (Italy).

1,2-Dibromo-4,5-dichlorobenzene **12.**[14] A suspension of iron powder (3 g) in *o*-dichlorobenzene (23 ml, 30 g, 0.2 mol) was heated gently, and Br_2 (26.15 ml, 81.6 g, 0.51 mol) was added during 20 min. The mixture was allowed to stand at room temperature overnight. The solid residue was washed with hot water (300 ml), 5% NaOH (300 ml), again with water (300 ml), and dried. The crude product was crystallised several times from toluene to give white crystals (33.92 g, 54%), which were characterised as **12**: m.p. 154-156°C (lit.[14] 150-152°C); ^1H-NMR: δ=7.71 (s, 2H); ^{13}C-NMR: δ=134.4, 132.6, 123.5; MS (EI): m/e (rel. int.), 304 (M^+, 100), 223 (19), 188 (2) 144 (21), 109 (21), 74 (40). $C_6H_2Br_2Cl_2$ requires: C, 23.64; H, 0.66; Br, 52.43; Cl, 23.26. Found: C, 23.69; H, 0.64; Br, 52.34; Cl, 23.34%.

p-Dichlorotetrabromobenzene **11.** A suspension of iron powder (3 g) in *p*-dichlorobenzene (11.8 ml, 14.7 g, 0.1 mol) was heated gently and Br_2 (51.28 ml, 1 mol) was added during 40 min. The mixture was allowed to stand at room temperature overnight. The solid residue was washed with hot water (500 ml), 5% NaOH (300 ml), again with water (500 ml), and dried. The crude product was crystallised several times from toluene to give white crystals (11.7 g, 25.5%), which were characterised as **11**: m.p. 286-290°C (lit.[35] 281°C); ^1H-NMR: no signal; ^{13}C-NMR: δ=126.5; MS (EI): m/e (rel. int. for the highest peak of each isotopic pattern), 462 (M^+, 100), 383 (24), 304 (19), 223 (7), 142 (5), 107 (8), 72 (4). $C_6Br_4Cl_2$ requires: C, 15.58; Br, 69.09; Cl, 15.33. Found: C, 15.65; Br, 68.88; Cl, 15.28%.

5,6,7,8-Tetrabromo-1,4-dihydro-1,4-epoxynaphthalene **7b**. *n*-BuLi (60 mmol: 24 ml of a 2.5 M solution diluted with 60 ml of dry hexane) was added to a suspension of hexabromobenzene **9** (33.0 g, 59.8 mmol) in dry toluene (1800 ml) and furan (90 ml) at -78°C over 4 h, and the mixture was allowed to reach room temperature during 16 h. After careful treatment with water (50 ml), the organic phase was washed with water (3 x 300 ml), dried ($MgSO_4$), and concentrated. Fractional crystallisation from acetone gave unreacted **9** and a white solid (13.7 g, 50%), which was characterised as **7b**: m.p. 154-156°C; ^1H-NMR: δ=7.15 (s, 2H), 5.85 (s, 2H); ^{13}C-NMR: δ=152.5, 142.8, 125.4, 116.9, 85.3; MS (EI): m/e (rel. int. for the highest peak of each isotopic pattern), 460 (M^+, 15), 434 (47), 353 (100), 271 (24), 191 (24), 111 (27). $C_{10}H_4Br_4O$ requires: C, 26.12; H, 0.88; Br, 69.52; O, 3.48. Found: C, 26.09; H, 0.85; Br, 69.28; O, 3.78%.

(±)-5,6,8-Tribromo-1,4-dihydro-1,4-epoxynaphthalene **(±)-7c**. *n*-BuLi (17.2 mmol: 6.9 ml of a 2.5 M solution diluted with 27.8 ml of dry hexane) was added to a solution of 5,6,7,8-tetrabromo-1,4-dihydro-1,4-epoxynaphthalene **7b** (8.0 g, 17.4 mmol) in dry toluene (523 ml) at -78°C over 25 min. The reaction mixture was maintained at this temperature for 30 min. before being quenched with methanol/toluene (3/20 ml). The mixture was allowed to reach room temperature, and then it was washed with water (3 x 200 ml), dried ($MgSO_4$), and concentrated to give a yellow solid (7.25 g). Fractional crystallisation from acetone gave unreacted **7b** and pale yellow crystals 3.57 g (54%), which were characterised as **(±)-7c**: m.p. 144-146°C; ^1H-NMR: δ=7.38 (s, 1H), 7.14 (s, 2H), 5.85 (s, 1H), 5.84 (s, 1H); ^{13}C-NMR: δ=154.2, 151.1, 143.1, 142.5,

132.7, 122.3, 116.3, 113.1, 84.9, 83.7; MS (EI): m/e (rel. int. for the highest peak of each isotopic pattern), 380 (M^+, 9), 354 (35), 273 (100), 193 (15), 113 (28). $C_{10}H_5Br_3O$ requires : C, 31.54; H, 1.32; Br, 62.94; O, 4.2. Found: C, 31.57; H, 1.33; Br 62.87; O, 4.3%.

(±)-5,6,8-Tribromo-1,4-dihydro-1,4-epoxynaphthalene (±)-**7c** *and 5,8-dibromo-1,4-dihydro-1,4-epoxynaphthalene* **7d**. n-BuLi (34.7 mmol: 13.9 ml of a 2.5 M solution diluted in 55.6 ml of dry hexane) was added to a solution of 5,6,7,8-tetrabromo-1,4-dihydro-1,4-epoxynaphthalene **7b** (8.0 g, 17.4 mmol) in dry toluene (523 ml) at -78°C over 50 min. The reaction mixture was maintained at -78°C for 30 min before being quenched with methanol/toluene (6/40 ml). The mixture was allowed to reach room temperature, and then it was washed with water (3 x 200 ml), dried ($MgSO_4$), and concentrated to give a yellow solid (5.64 g). Fractional crystallisation from acetone afforded pale yellow crystals (2.77 g), which were characterised as (±)-**7c**. The composition of the residue from the mother liquor (2.73 g), was analysed by ^{1}H-NMR spectroscopy using authentic (±)-**7c** and a sample of **7d** (independently synthesised) as internal standards. In this way, it was established that the residue was composed of (±)-**7c** (1.27 g) and **7d** (334 mg). The analytical and spectroscopic characteristics of **7d** were as follows: m.p. 95-97°C (lit.[22a] 65-66.5°C); ^{1}H-NMR: δ=7.13 (s, 2H), 6.94 (s, 2H), 5.86 (s, 2H); ^{13}C-NMR: δ=151.9, 142.8, 130.2, 113.1, 83.7; MS (EI): m/e (rel. int.), 300 (M^+, 7), 274 (27), 193 (100), 113 (31). $C_{10}H_6Br_2O$ requires: C, 39.78; H, 2; Br, 52.92; O, 5.3. Found: C, 39.86; H, 1.99; Br, 53.01; O, 5.14%. The yields of (±)-**7c** and **7d** were 61% and 6%, respectively.

syn- and *anti-9,10-Dibromo-1,4,5,8-tetrahydro-1,4,5,8-diepoxyanthracene* **13a** and **13b** and *syn-* and *(±)-anti-9,10-dibromo-1,4,5,8-tetrahydro-1,4,5,8-diepoxyphenantrene* **14a** and (±)-**14b**. *n*-BuLi (12 mmol: 4.8 ml of a 2.5 M solution diluted in 19.2 ml of dry hexane) was added to a suspension of 5,6,7,8-tetrabromo-1,4-dihydro-1,4-epoxynaphthalene **7b** (5.0 g, 10.8 mmol) in dry toluene (325 ml) and furan (16.3 ml) at -78°C over 15 min. The reaction mixture was allowed to reach room temperature overnight. After careful treatment with water (10 ml), the mixture was washed with brine (3 x 100 ml), dried ($MgSO_4$), and concentrated to give a dark solid (4.3 g). Fractional crystallisation from toluene (100 ml) gave white crystals (710 mg), which were characterised as **13b**: m.p. 218°C (dec.); ^{1}H-NMR: δ=7.13 (s, 4H), 5.77 (s, 4H); ^{13}C-NMR: δ=151.1, 143.3, 107.1, 83.5; MS (EI): m/e (rel. int.), 366 (M^+, 18), 340 (14), 314 (41), 235 (46), 233 (100), 152 (87). $C_{14}H_8Br_2O_2$ requires: C, 45.69; H, 2.19; Br, 43.42; O, 8.69. Found: C, 45.80; H, 2.18; Br, 43.58 ; O, 8.44%. The residue from the mother liquor (3.5 g) was subjected to column chromatography (SiO_2, hexane/ethyl acetate 9/1-1/9). The first fraction (1.278 g) to be eluted from the column was subjected to fractional crystallisation from acetone to give two products: **13b** (583 mg) and another crystalline material (439 mg), which was characterised as **13a**: m.p. 208°C; ^{1}H-NMR: δ=7.13 (s, 4H), 5.78 (s, 4H); ^{13}C-NMR: δ= 151.0, 143.3, 107.1, 83.4; MS (EI): m/e (rel. int.), 366 (M^+, 20), 340 (14), 314 (43), 235 (46), 233 (100), 152 (97). $C_{14}H_8Br_2O_2$ requires: C, 45.69; H, 2.19; Br, 43.42; O, 8.69. Found: C, 45.78; H, 2.18; Br 43.65; O, 8.47%. The yields of **13a** and **13b** were 11% and 32%, respectively. The second fraction to be eluted (80 mg, 2%) was a mixture of the angular bisdienophiles **14a**/(±)-**14b**, which were not separated, but were identified on the basis of their spectroscopic data. ^{1}H-NMR: δ=7.05-7.01 (m, 6H), 6.93-6.90 (m, 2H), 5.84 (s, 2H), 5.77 (s, 2H), 5.72 (s, 4H). MS (EI): m/e (rel. int.), 366 (M^+, 3), 314 (14), 288 (12), 233 (39), 152 (100).

(±)-syn- and *(±)-anti-9-Bromo-1,4,5,8-tetrahydro-1,4,5,8-diepoxyphenanthrene* (±)-**14c** and (±)-**14d**. *Method a* . *n*-BuLi (3.1 mmol: 1.26 ml of 2.5 M solution diluted with 5 ml of dry hexane) was added to a solution of (±)-5,6,8-tribromo-1,4-dihydro-1,4-epoxynaphthalene (±)-**7c** (1.0 g, 2.6 mmol) in dry toluene (79 ml) and furan (4 ml) at -78°C, in 10 min. The mixture was allowed to reach room temperature overnight and was then carefully treated with water (5 ml). The organic phase was washed with brine (3 x 50 ml), dried ($MgSO_4$), and concentrated to give a yellow gummy solid, from which some unreacted (±)-**7c** separates upon treatment with acetone. The liquid was concentrated to give a residue (557 mg), which was subjected to column

chromatography (SiO_2, CH_2Cl_2) to afford, in order of elution, (±)-**14d** (130 mg, 17%): m.p. 195-197°C (lit.[22a] 199-202°C); ^{1}H-NMR: δ=7.01 (s, 2H), 6.99-6.91 (m, 3H), 5.79 (s, 1H), 5.74 (s, 1H), 5.70 (m, 1H), 5.62 (m, 1H); ^{13}C-NMR: δ=148.0, 144.8, 142.0, 141.9, 141.8, 141.7, 141.2, 138.5, 120.0, 110.1, 82.6, 81.6, 81.2, 80.1; MS (EI): m/e (rel. int.), 288 (M^+, 13), 262 (9), 236 (28),155(16), 154 (13), 153 (100), 152 (85), 151(12), 150(10); HRMS calculated for $C_{14}H_9{}^{79}BrO_2$ 287.9786, found 287.9767, and (±)-**14c** (120 mg, 16%): m.p.125-130°C (lit.[22a] 125-135°C); ^{1}H-NMR: δ=7.05-7.01 (m, 1H), 6.97-6.85 (m, 4H), 5.85 (m, 1H), 5.76 (m, 1H), 5.73 (m, 1H), 5.62 (m, 1H); ^{13}C-NMR: δ=148.3, 145.1, 142.4, 142.1, 142.0, 141.8, 141.2, 138.5, 119.8, 109.9, 82.4, 81.5, 81.2, 80.1; MS (EI): m/e (rel. int.),288 (M^+, 9), 262 (5), 236 (23), 234 (13), 153 (100), 152 (84), 151 (22), 150 (13). $C_{14}H_9BrO_2$ requires: C, 58.16; H, 3.14; Br, 27.64; O, 11.07. Found: C, 58.22; H, 3.12; Br, 27.92; O, 11.31%.

Method b. 6,7-Dibromo-1,4-dihydro-1,4-epoxynaphthalene **7a** (1.0 g, 3.3 mmol) was added to a suspension of $NaNH_2$ (2.29 g of Na and NH_3) in dry DME (60 ml) and furan (12 ml). The mixture was heated under reflux and the reaction was monitored by TLC and ^{1}H-NMR spectroscopy. After 3 h, the mixture was cooled, treated with water/DME (4/10 ml), and then extracted with chloroform (3 x 75 ml). The extracts were combined, washed with water (3 x 50 ml), dried ($MgSO_4$), and concentrated to give a residue which was subjected to column chromatography (SiO_2, PhMe/Et_2O 9/1). The first product to be eluted from the column was characterised as (±)-**14d** (318 mg, 33%) followed by (±)-**14c** (298 mg, 31%).

6,7-Dichloro-1,4-dihydro-1,4-epoxynaphthalene **7f**. *n*-BuLi (76.2 mmol: 30.48 ml of a 2.5 M solution diluted with 100 ml of dry hexane) was added to a solution of 1,2-dibromo-4,5-dichlorobenzene **12** (18.0 g, 59.3 mmol) in dry diethyl ether (1300 ml) and furan (88 ml) at -15°C over 4 h. The mixture was allowed to reach room temperature overnight. After careful treatment with water (5 ml), the organic phase was washed with water (3 x 200 ml), dried ($MgSO_4$), and concentrated to give a residue which was crystallised from toluene to give white crystals (5.28 g, 42%), which were characterised as **7f**: m.p. 101-102°C; ^{1}H-NMR: δ=7.31 (s, 2H), 7.01 (s, 2H), 5.69 (s, 2H); ^{13}C-NMR: δ=149.4, 142.9, 128.6, 122.6, 81.8; MS (EI): m/e (rel. int.), 212 (M^+, 17), 186 (32), 149 (100), 113 (14). $C_{10}C_{12}H_6O$ requires: C, 56.37; H, 2.84; Cl, 33.28; O, 7.51. Found: C, 56.33; H, 2.83; Cl, 33.20; O, 7.64%.

(±)-syn- and *(±)-anti-9-Chloro-1,4,5,8-tetrahydro-1,4,5,8-diepoxyphenanthrene* (±)-**14e** and (±)-**14f**.

Method a. n-BuLi (7.25 mmol: 2.9 ml of a 2.5 M solution diluted in 4.4 ml of dry hexane) was added to a solution of 6,7-dichloro-1,4-dihydro-1,4-epoxynaphthalene **7f** (1.4 g, 6.6 mmol) in dry THF (200 ml) and furan (10 ml) at -78°C over 10 min. The reaction mixture was allowed to reach room temperature overnight, treated with water/THF (2/10 ml), and concentrated. The residue was suspended in dichloromethane, washed with brine (3 x 40 ml), dried (Na_2SO_4), and concentrated to give a pale yellow solid (1.21 g), which was subjected to column chromatography (Al_2O_3, PhMe/Et_2O 95/5) to give, in order of elution: unreacted **7f**; (±)-**14f** (99 mg, 6%): m.p. 166-168 °C ; ^{1}H-NMR: δ=7.0 (s, 2H), 6.99-6.92 (m, 2H), 6.78 (s, 1H), 5.81 (m, 1H), 5.75 (m, 1H), 5.71 (m, 1H), 5.63 (m, 1H); ^{13}C-NMR: δ=147.8, 142.2, 142.0 141.8, 141.78, 141.73, 140.9, 137.8, 122.4, 117.6, 81.7, 81.0, 80.9, 80.0; MS (EI): m/e (rel. int.), 244 (M^+, 25), 218 (13), 192 (36), 190 (33), 188 (16), 153 (97), 152 (100). HRMS calculated for $C_{14}H_9{}^{35}ClO_2$ 244.0291, found 244.0261; and (±)-**14e** (98 mg, 6%): m.p.114-131°C; ^{1}H-NMR: δ=7.04-6.84 (m, 4H), 6.76 (s, 1H), 5.81 (m, 1H), 5.80 (m, 1H), 5.77 (m, 1H), 5.61 (m, 1H); ^{13}C-NMR: δ=148.2, 142.4, 142.4, 142.1, 141.9, 141.8, 140.9, 137.8, 122.2, 117.4, 81.4, 81, 80.6, 80.1; MS (EI) : m/e (rel. int.), 244 (M^+, 13), 218 (8), 192 (31), 190 (30), 188 (11), 153 (88), 152 (100). HRMS calculated for $C_{14}H_9{}^{35}ClO_2$ 244.0291, found 244.0277.

Method b. Solid $NaNH_2$ (292 mg, 7.5 mmol) was added to a solution of 6,7-dichloro-1,4-dihydro-1,4-epoxynaphthalene **7f** (200 mg, 0.938 mmol) in dry THF (17 ml) and furan (46.9 mmol, 3.4 ml). The reaction mixture was refluxed for one day, before adding more furan (3.4 ml) and $NaNH_2$ (292 mg). After 7 days, the reaction mixture was cooled, treated with water/THF (2/10 ml), and concentrated. The residue was suspended in dichloromethane, washed with brine (3 x 15 ml), dried ($MgSO_4$), concentrated, and subjected to

column chromatography (Al_2O_3, PhMe/Et_2O 95/5), affording (±)-**14f** (38 mg, 16%) followed by (±)-**14e** (35 mg, 15%).

6,7-Dibromo-5,8-dichloro-1,4-dihydro-1,4-epoxynaphthalene **7e**. *n*-BuLi (2.8 mmol: 1.12 ml of a 2.5 M solution diluted in 4.5 ml of dry hexane) was added to a suspension of *p*-dichlorotetrabromobenzene **11** (1.0 g, 2.16 mmol) in dry diethyl ether (100 ml) and furan (3.2 ml) at -78°C during 10 min.. The reaction mixture was allowed to warm up to room temperature overnight. After careful addition of water (3 ml), the organic phase was washed with water (3 x 50 ml), dried ($MgSO_4$), and concentrated to give an oil, which was subjected to column chromatography (Al_2O_3, hexane/toluene 95/5-60/40) to give, besides unreacted **11**, a fraction containing over 90% of **7e** as a white solid (m.p. 146°C, 266 mg, 33%), which was not purified any further: ^{1}H-NMR: δ=7.13 (s, 2H), 5.89 (s, 2H); ^{13}C-NMR: δ=149.5, 142.7, 126.5, 123.9, 83.2; MS (EI): m/e (rel. int.), 368 (M^+, 11), 342 (37), 263 (100), 228 (11), 149 (10).

syn- and *anti-1,4,5,8-Tetrahydro-1,4,5,8-diepoxyanthracene* **1a** and **1b**. 6,7-Dibromo-1,4-dihydro-1,4-epoxynaphthalene **7a** (1.0 g, 3.3 mmol) was added to a suspension of KNH_2 (1.03 g of K and NH_3) in dry THF (56 ml) and furan (11.3 ml). The mixture was heated under reflux for 2 days, cooled, treated with water/THF (2/10 ml), and concentrated. The residue was suspended in dichloromethane, washed with brine (3 x 30 ml), dried ($MgSO_4$), and concentrated. The residue was treated with methanol and the solid obtained was recrystallised from acetone to give **1b** (243 mg, 35%): m.p. 257°C (dec.) (lit.[33] 257°C); ^{1}H-NMR: δ=7.19 (s, 2H), 7.02 (s, 4H), 5.63 (s, 4H); ^{13}C-NMR: δ=147.8, 143.4, 114.0, 82.3; MS (EI): m/e (rel. int.), 210 (M^+, 31), 184 (28), 181 (9), 158 (11), 156 (41), 155 (75), 154 (43), 153 (100), 152 (79). $C_{14}H_{10}O_2$ requires: C, 79.98; H, 4.79; O, 15.22. Found: C, 79.91; H, 4.77; O, 15.32%. The methanol extracts were subjected to column chromatography (SiO_2, hexane/ethyl acetate 3/1) to give **1a**, crystallised from methanol (236 mg, 34%): m.p.193°C (lit.[33] 193°C); ^{1}H-NMR: δ= 7.18 (s, 2H), 7.03 (s, 4H), 5.63 (s, 4H); ^{13}C-NMR: δ= 147.7, 143.5, 113.8, 82.3; MS (EI): m/e (rel.int.), 210 (M^+, 33), 184 (26), 181 (11), 158 (10), 156 (38), 155 (67), 154 (41), 153 (100), 152 (79). $C_{14}H_{10}O_2$ requires: C, 79.98; H, 4.79; O, 15.22. Found: C, 80.02; H, 4.76; O, 15.22%.

syn- and *anti-1,4,5,8,9,12-Hexahydro-1,4:5,8:9,12-triepoxytriphenylene* **3a** and **3b**. 6,7-Dibromo-1,4-dihydro-1,4-epoxynaphthalene **7a** (1.0 g, 3.3 mmol) was added to a suspension of $NaNH_2$ (2.29 g of Na and NH_3) in dry DME (60 ml) and furan (12 ml). The mixture was heated under reflux and the reaction was monitored by TLC and ^{1}H-NMR spectroscopy. After 7.5 h, the mixture was cooled, treated with water/DME (4/10 ml), and extracted with chloroform (3 x 75 ml). The extracts were combined and washed with water (3 x 50 ml), dried ($MgSO_4$), and concentrated to give a solid residue (578 mg). This residue was treated with acetone (5 ml) to give a white precipitate (58 mg), which was characterised as **3b**: m.p.>250°C (lit.[3]>250°C); ^{1}H-NMR: δ=6.92-6.85 (m, 4H), 6.79-6.73 (m, 2H), 5.77-5.72 (m, 2H), 5.71-5.65 (m, 4H); ^{13}C-NMR: δ= 141.1, 140.9, 140.8, 134.6, 134.3, 133.9, 80.0, 79.9; MS (EI): m/e (rel. int.), 276 (M^+, 34), 250 (14), 224 (16), 219 (20), 196 (27), 194 (27), 193 (18), 192 (34), 191 (100), 190 (50), 189 (64), 165 (50), 163 (22), 139 (18). HRMS calculated for $C_{18}H_{12}O_3$ 276.0786, found 276.0777. The acetone extracts were subjected to column chromatography (SiO_2, toluene/diethyl ether/ethyl acetate 60/40/0-60/0/40) to give, in order of elution, **3b** (10 mg) and **3a** (22 mg): m.p.>250°C (lit.[3]>250°C); ^{1}H-NMR: δ=6.78 (s, 6H), 5.73 (s, 6H); ^{13}C-NMR: δ=141.1, 134.2, 79.9; MS (EI): m/e (rel. int.), 276 (M^+, 19), 250 (20), 224 (16), 219 (19), 196 (25), 194 (26), 193 (16), 192 (31), 191 (100), 190 (48), 189 (66), 165 (55), 163 (25), 139 (18). HRMS calculated for $C_{18}H_{12}O_3$ 276.0786, found 276.0753. The combined yields of **3a** and **3b** were 10%.

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