Generation and reactions of an octacyclic hindered pyramidalized alkene.

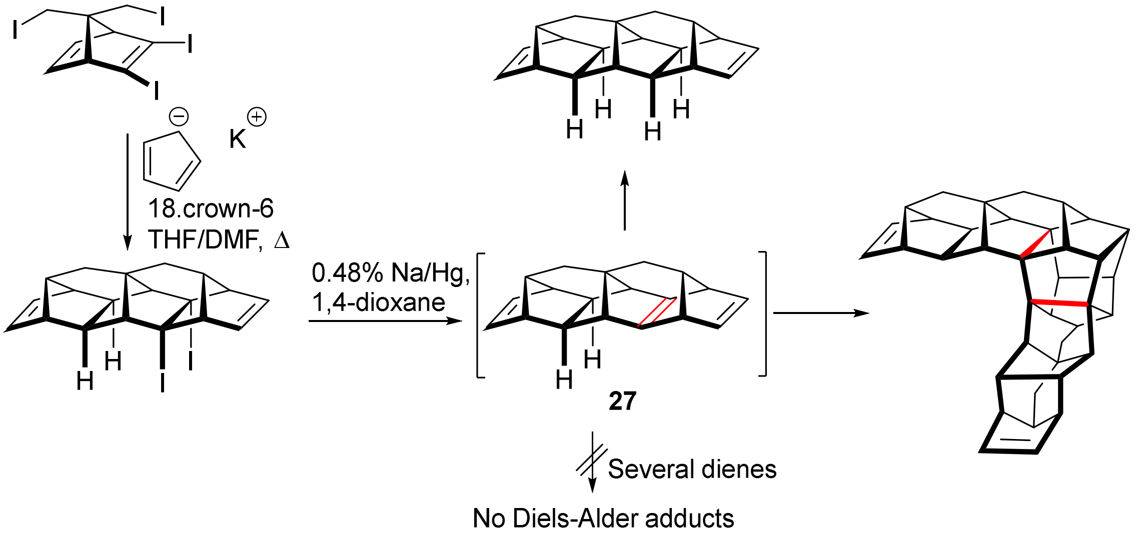
Pelayo Camps,[*,†] David Lozano,[†] Carla Barbaraci,[†] Merce Font-Bardia,[§,ǀ] F. Javier Luque,[‡] Carolina Estarellas[‡]

[†] Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia i Ciències de l'Alimentació, and Institut de Biomedicina (IBUB), Universitat de Barcelona, Av. Joan XXIII 27–31, 08028 Barcelona (Spain).

[§] Departament de Cristal·lografia, Mineralogia i Dipòsits Minerals, Universitat de Barcelona, Martí Franquès s/n, 08028 Barcelona (Spain).

[ǀ] Unitat de Difracció de RX, Centres Científics i Tecnològics de la Universitat de Barcelona (CCiTUB), Solé i Sabarís 1–3, 08028 Barcelona (Spain)

[‡] Departament de Nutrició, Ciències de l'Alimentació i Gastronomia, Universitat de Barcelona, Av. Prat de la Riba 171, 08921 Santa Coloma de Gramenet (Spain) and Institut de Biomedicina (IBUB), Universitat de Barcelona, Av. Joan XXIII 27–31, 08028 Barcelona (Spain).



Abstract. Octacyclo[10.6.1.$0^{1,10}$.$0^{3,7}$.$0^{4,9}$.$0^{8,19}$.$0^{11,16}$.$0^{13,17}$]nonadeca-5,8,14-triene (**27**) a hindered pyramidalized alkene, has been generated from a diiodide precursor. Contrary to the usual behavior of known pyramidalized alkenes, no Diels-Alder adducts were obtained from the present alkene when it was generated by different standard procedures in the presence of different dienes. However, products derived from the reduction, *t*-BuLi addition, condensation with the solvent, or dimerization, were isolated from these reactions, depending on the conditions used to generate it. No [2+2] cross product among this pyramidalized alkene and tricyclo[3.3.1.0^{3,7}]non-3(7)-ene was formed when a mixture of the corresponding precursor diiodides was reacted with sodium amalgam. The analysis of selected geometrical and orbital parameters determined from quantum mechanical calculations indicates that the degree of pyramidalization of this alkene and its higher steric hindrance compared with other polycyclic pyramidalized alkenes may explain its peculiar reactivity.

Introduction

The chemistry of highly pyramidalized alkenes has been the subject of several reviews[1-7] and new highly reactive intermediates of this kind have been recently described.[8-12] In a pyramidalized alkene, the olefinic carbon atoms are rehybridized by admixture of additional *p* character into the original sp^2 σ-orbitals. This makes the geometry around the olefinic carbon atoms non-planar. The π bond is now formed from two *p*-orbitals with some *s*-character. These orbitals are well aligned (torsion angle = 0), but they are not parallel. Consequently, the distance between them increases and the neat overlap decreases, affecting the intrinsic reactivity properties of the pyramidalized double bond.

From a structural point of view, the degree of pyramidalization of *syn*-pyramidalized alkenes belonging to the C_{2v} point group of symmetry (left structure of Figure 1) can be described by the pyramidalization angle (Φ), which corresponds to the angle between the plane containing one of the olefinic carbon atoms and the two substituents attached to it and the elongation of the C=C bond. Its value can be obtained according to the formula given in Figure 1 from the RCC (α) and RCR (β) angles. For alkenes belonging to the C_s point group of symmetry (right structure of Figure 1), the flap or hinge angle (Ψ), corresponding to the dihedral angle among the R_2CCR_2 and R_1CCR_1 planes, or its supplementary angle (ζ), are usually used. While pyramidalized alkenes are generally related to the geometrical strain of the olefinic carbon atoms, it is worth noting that alkene pyramidalization may also occur due to electronic effects.[13]

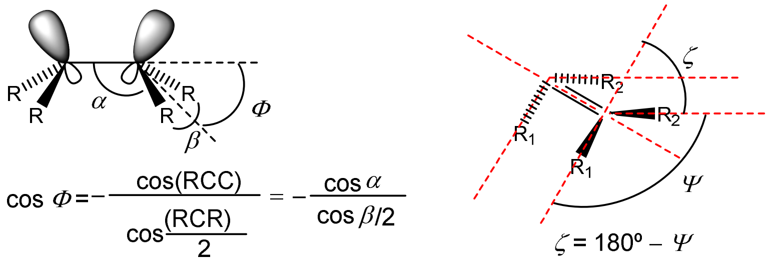


Figure 1. Pyramidalization angle (Φ), flap angle (Ψ), and supplementary flap angle (ζ = 180º − Ψ) in *syn*-pyramidalized alkenes

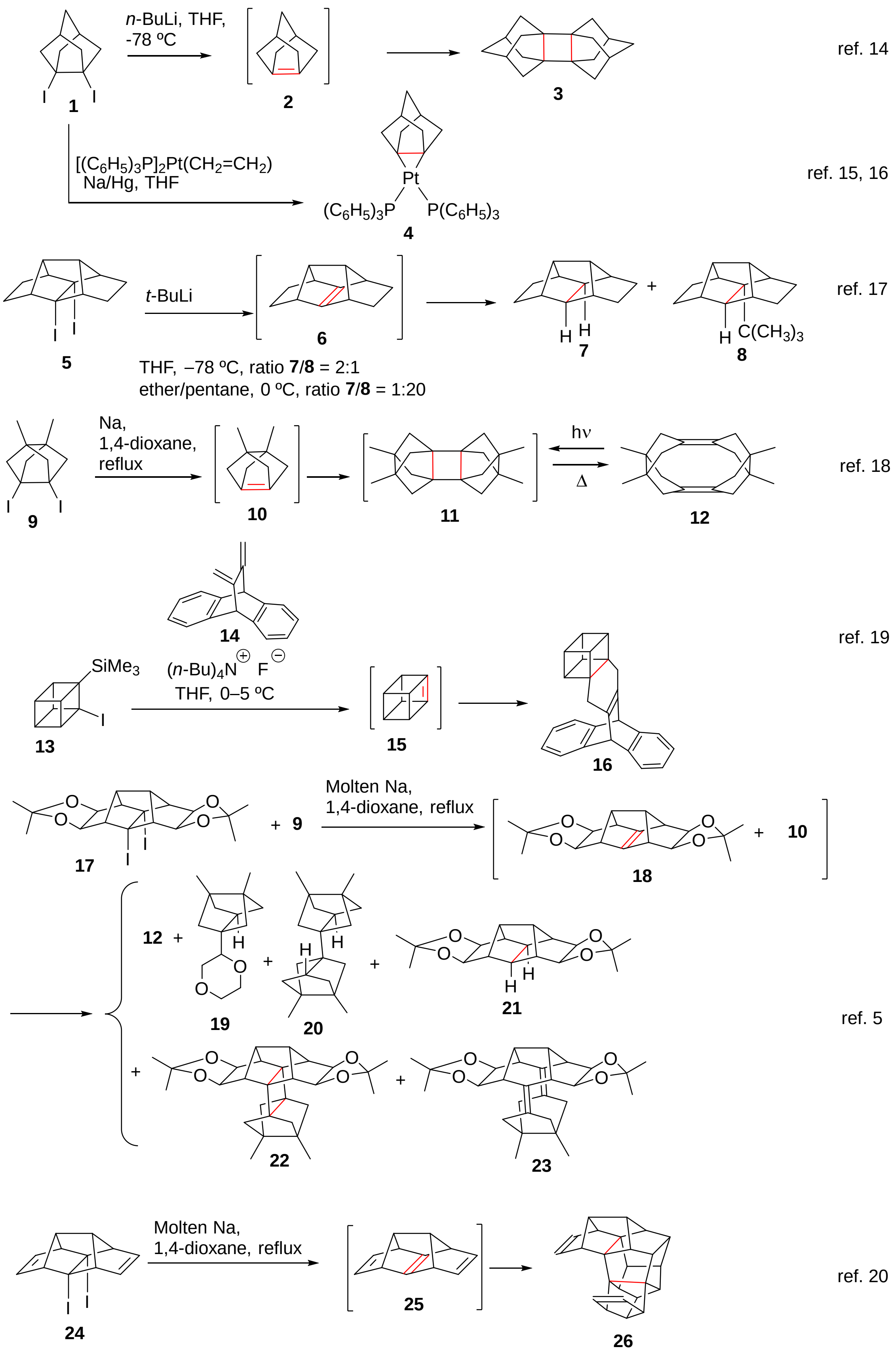
With regard to the synthetic accessibility, the more pyramidalized alkenes are usually generated by reaction of a vicinal double bridgehead diiodide or dibromide with an organolithium reagent in THF, sodium/potassium alloy or sodium amalgam in an ether solvent or molten sodium in boiling 1,4-dioxane. Scheme 1 collects several of the most representative reactions of pyramidalized alkenes.

Borden et al.[14] generated pyramidalized alkene **2** (tricyclo[3.3.1.0^{3,7}]non-3(7)-ene) on reaction of diiodide **1** with *n*-butyllithium in THF at low temperature and isolated the cyclobutane dimer **3** in good yield. Also, reaction of diiodide **1** with liquid sodium amalgam in the presence of ethylene-bis(triphenylphosphine)Pt(0), gives the Pt complex **4** derived from pyramidalized alkene **2**.[15,16]

Paquette, Borden et al.[17] also generated the pyramidalized alkene **6** (a bisethano derivative of bicyclo[3.3.0.0^{3,7}]oct-1(5)-ene**)** on reaction of diiodide **5** with *t*-BuLi in THF, isolating the reduction product **7** and product **8** derived from the addition of *t*-BuLi to alkene **6**. The ratio **7**/**8** was temperature dependent, formation of **8** highly increasing with temperature. Our group generated the pyramidalized alkene **10** from diiodide **9** on reaction with molten sodium in boiling 1,4-dioxane, isolating diene **12** in good yield.[18] This product might be derived from pyramidalized alkene **10** by dimerization to the highly strained cyclobutane derivative **11** followed by a thermal [2+2] retrocycloaddition process. In fact, irradiation of diene **12** gave cyclobutane dimer **11**, which slowly reverted in $CDCl_3$ solution at room temperature to diene **12**.

Lukin and Eaton[19] generated 1,2-dehydrocubane (cubene, **15**), one of the most highly pyramidalized alkenes ever prepared, by reaction of 1-iodo-2-(trimethylsilyl)cubane with fluoride anions. This alkene was trapped as a Diels-Alder adduct (**16**) with diene **14**. In the absence of diene **14**, cubene dimerized to a cyclobutane dimer that experiences different kinds of intramolecular [2+2] retrocycloaddition processes (not shown in Scheme 1). Our group carried out cross coupling reactions among different pyramidalized alkenes with ether or acetal functionalized diiodide precursors. For instance, reaction of a mixture of diiodides **9** and **17** with molten sodium in boiling 1,4-dioxane gave a mixture of the cyclobutane and diene cross products, **22** and **23**, respectively, derived from the corresponding pyramidalized alkenes, **18** and **10**. The diene dimer **12** and other side products, such as **19**, a product of addition of alkene **10** to the solvent, or **20**, a dihydrodimer of **10**, were also isolated.[5]

Scheme 1. **Described procedures to generate pyramidalized alkenes and reaction products.**



When diiodide **24** was reacted with molten sodium in boiling 1,4-dioxane, product **26**, a dimer from a formal [2+2+2+2]-cycloaddition of pyramidalized alkene **25** was isolated in 24% yield.[20] This is the only example of such a kind of dimerization of a pyramidalized alkene.

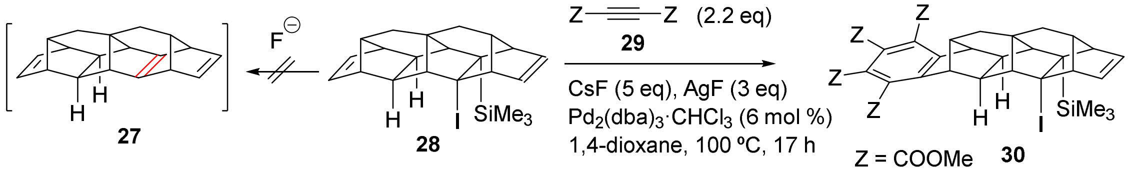
Pyramidalized alkenes show a certain biradical character,[19] and their contribution might be important in reactions, such as the [2+2] and the [2+2+2+2] cyclizations, which are likely to be stepwise biradical processes.

Following our previous efforts,[5,18,20] in this study we report the generation of octacyclo[$10.6.1.0^{1,10}.0^{3,7}.0^{4,9}.0^{8,19}.0^{11,16}.0^{13,17}$]nonadeca-5,8,14-triene (**27**), a hindered pyramidalized alkene, by using standard procedures from a diiodide precursor. Furthermore, we provide an exhaustive characterization of its chemical reactivity, which strikingly was unable to form Diels-Alder adducts in contrast with the usual behavior of pyramidalized alkenes.

Results and Discussion

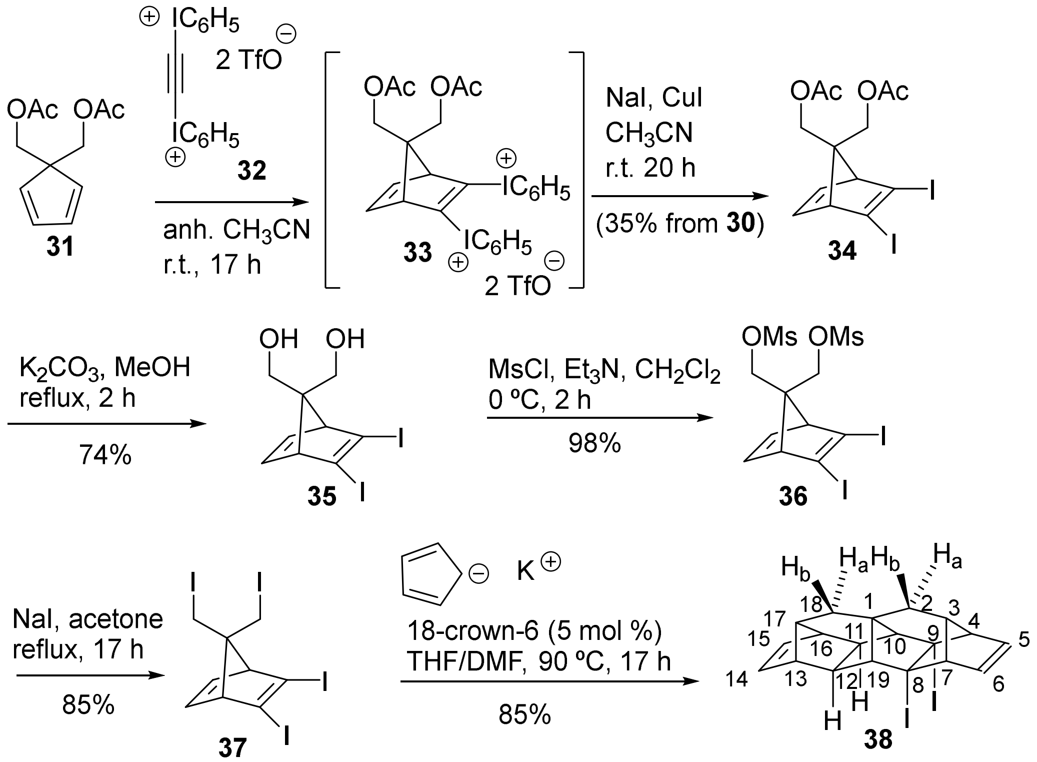
Recently, we have described[21] the preparation of octacycle **28** as a possible precursor of pyramidalized alkene **27** (Scheme 2) by reaction with fluoride anions, following the procedure described by Lukin and Eaton[19] to generate cubene **15**. However, all attempts to generate **27** on reaction with CsF alone or in combination with AgF in the presence of dienes, such as 1,3-diphenylisobenzofuran, tetraphenylcyclopentadienone, furan or anthracene at different temperatures, left the starting compound unchanged. When compound **28** was reacted with dimethyl acetylenedicarboxylate **29**, CsF and AgF in the presence of tris(dibenzylideneacetone)dipalladium(0)·$CHCl_3$ [Pd$(dba)_2$·$CHCl_3$] as catalyst, product **30** was obtained as a result of cocyclotrimerization of **29** and **28**, at the C=C bond further from the iodine and trimethylsilyl groups. In all the reactions, the obtained products always contained the trimethylsilyl group. The lack of reactivity of the trimethylsilyl group towards fluoride anions is likely due to the steric hindrance experienced by this group.

Scheme 2. Attempted generation of 27 from 28.



To solve this problem, we have prepared diiodide **38** according to Scheme 3. 5,5-Bisacetoxymethyl-1,3-cyclopentadiene[22] **31** was reacted with ethyne-1,2-diylbis(phenyl)iodonium ditriflate **32**, prepared as described,[23] and the crude product was directly reacted with an equimolar mixture of NaI and CuI to give the diiodide **34** in 35% yield.

Scheme 3. Preparation of octacycle 38 from cyclopentadiene 31.

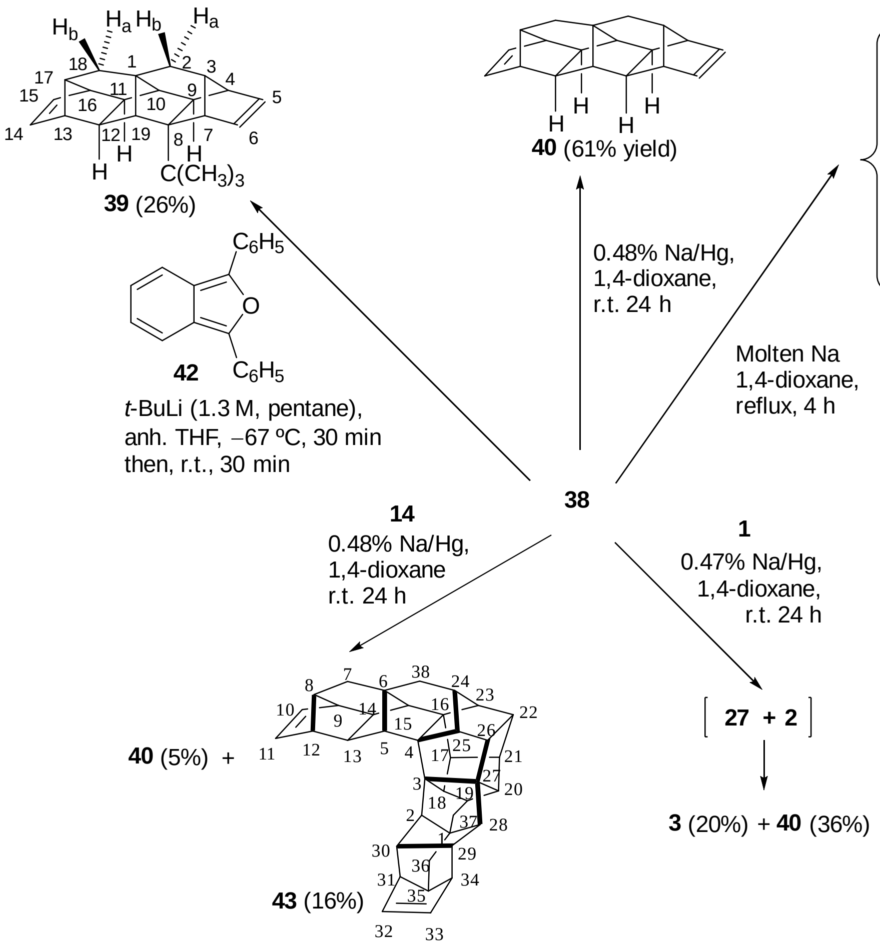


Reaction of **31** with the less electrophilic, but much more readily available dienophile, 2-iodoethynyl(phenyl)iodonium triflate,[24] in acetonitrile at reflux for 64 h, followed by treatment with NaI / CuI did not give the expected diiodide **34**. Reaction of **34** with methanol catalyzed by K_2CO_3 gave in good yield the corresponding diol **35,** which was transformed into the corresponding bismesylate **36** on reaction with MsCl in the presence of Et_3N. Reaction of **36** with NaI in acetone at reflux gave the tetraiodide **37** in good yield. Reaction of **37** with potassium cyclopentadienide in a mixture THF/DMF in the presence of a catalytic amount (5 mol %) of 18-crown-6 gave in high yield the desired octacyclic diiodide **38**. As in the preparation of **28**, this transformation implies a double domino nucleophilic substitution of neopentyl-type iodides by the cyclopentadienide anion followed by a double intramolecular Diels-Alder reaction, with formation of six new C-C bonds and four new cycles apart from those of the cyclopentadienide. Thus, the octacyclic product **38** is formed from the bicyclic precursor **37** in only one step. Although the structure of the symmetric compound **38** (C_s point group) was clearly deduced from the ^{1}H- and ^{13}C-NMR data, it was confirmed by X-ray diffraction analysis. See ORTEP structure of diiodide **38** in the SI.[25]

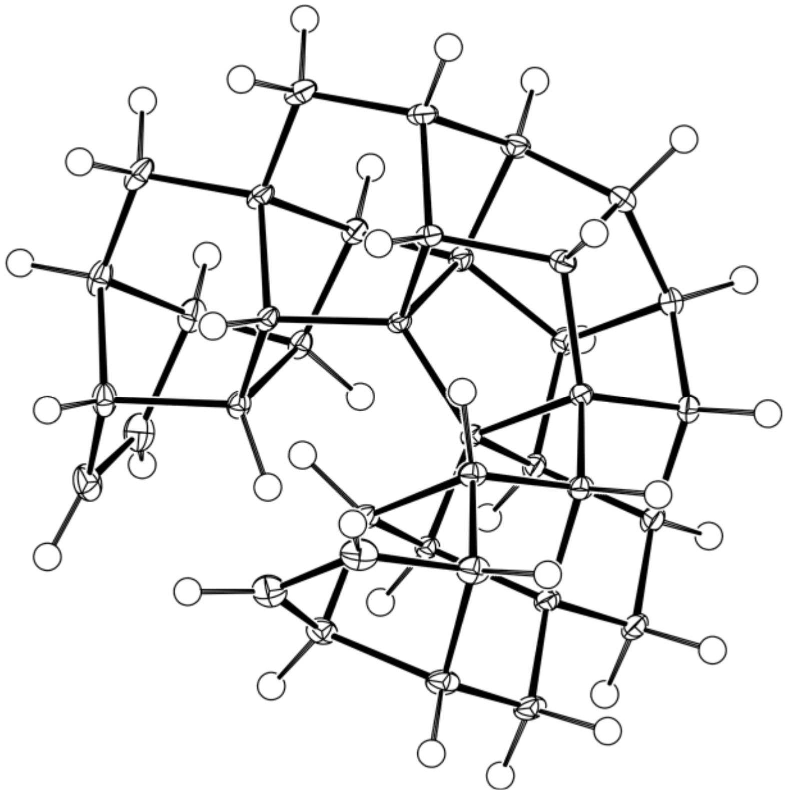
When a cold solution of diiodide **38** and 1,3-diphenylisobenzofuran **42** in THF was treated with a pentane solution of *t*-BuLi, the expected Diels-Alder adduct from the reaction of the pyramidalized alkene **27** and diene **42** was not observed in the crude product by ^{1}H-NMR. After column chromatography, the only isolated product was **39** (26% yield), which must derive from the reaction of **27** with *t*-BuLi followed by protonation during the quenching of the reaction mixture.[17] Similar results were obtained when diene **42** was replaced by anthracene or diene **14** in the above reaction. In both cases, the ^{1}H-NMR spectrum of the crude product did not show the expected signals for the corresponding Diels-Alder adducts and, after column chromatography, the only isolated product was always **39** (Scheme 4).

To solve this problem, a solution of diiodide **38** and diene **14** in 1,4-dioxane was added to an excess of 0.48% sodium amalgam. The ^{1}H-NMR spectrum of the crude product from this reaction did not show the presence of the expected Diels-Alder adduct from pyramidalized alkene **27** and diene **14**. By column chromatography, two hydrocarbon products were isolated, the reduction product **40** (5%) and the [2+2+2+2] dimer **43** (16%). Worthy of note, when a solution of diiodide **38** in 1,4-dioxane was reacted with 0.48% sodium amalgam in the absence of diene **14**, the formation of dimer **43** was not observed. Compound **40** was the only isolated product (61% yield). The structure of **40** was easily deduced from its NMR data, which show the high symmetry of this compound (C_{2v} point group of symmetry) and later confirmed by X-ray diffraction analysis. See ORTEP structure of compound **40** in the SI.[26]

Scheme 4. Transformations of octacycle 38.



In the case of dimer **43**, the structure was first obtained by X-ray diffraction analysis, and the data showed that the unit cell of **43** contains one molecule of each enantiomer (Figure 2).[27]



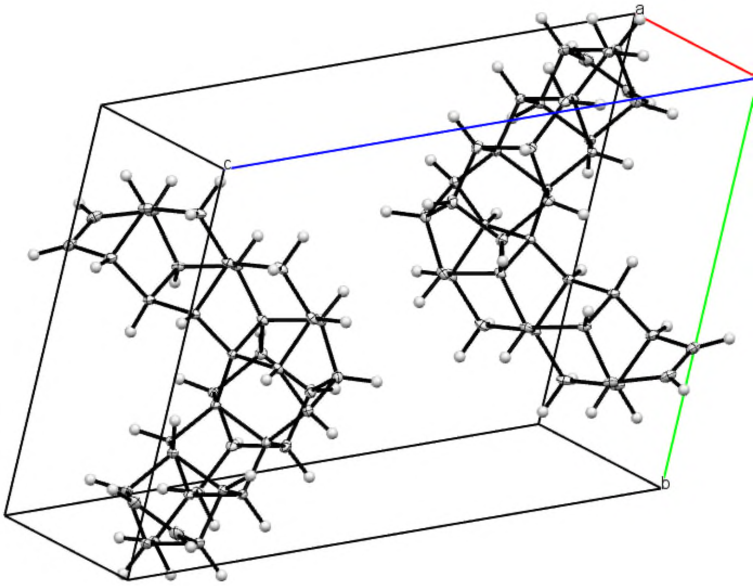


Figure 2. (Top) ORTEP representation of diiodide **43**: ellipsoid contour at 50% probability level. (Bottom) unit cell of dimer **43**.

Keeping in mind the C_2 symmetry point group of **43** and the fact that all signals of the different protons and ^{13}C atoms of **43** appear clearly separated, except for both pairs of methylenic protons, we could fully assign its ^{1}H- and ^{13}C-NMR spectra with the aid of the ^{1}H/^{1}H homocorrelation spectra (COSY and NOESY) and ^{1}H/^{13}C heterocorrelation spectra (sequence gHSQC for one bond correlations and gHMBC for long range correlations). Specially significant to carry out this assignment was the observation of correlations among pairs of protons belonging to different half of the molecule, such as 13(30)-H (δ = 1.70 ppm)/18(25)-H (δ = 1.98 ppm)/, 14(29)-H (δ = 1.63 ppm)/17(26)-H (δ = 2.24–2.29 ppm) and 14(29)-H/18(25)-H (δ = 1.98 ppm) in its ^{1}H/^{1}H NOESY spectrum (Figure 3).

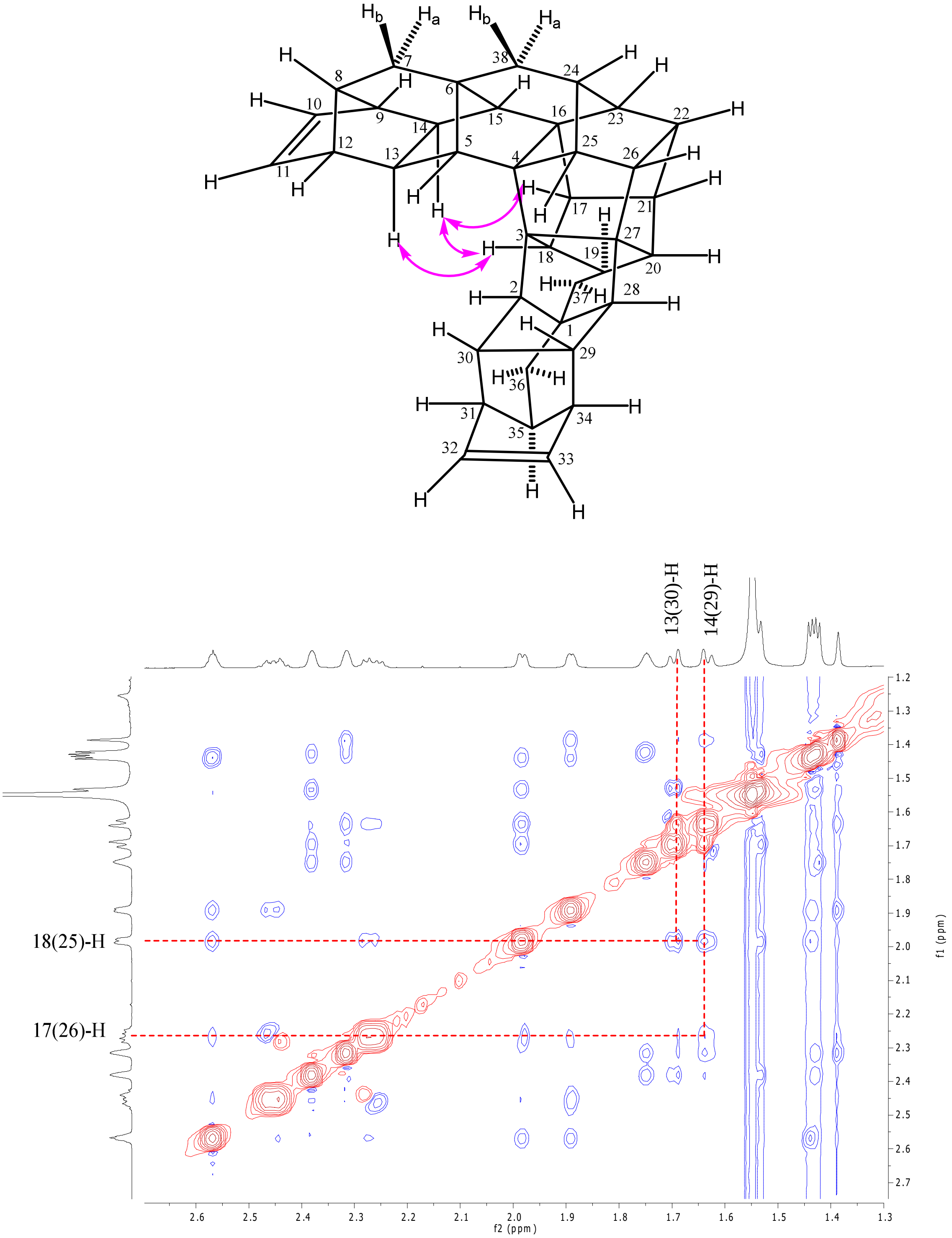


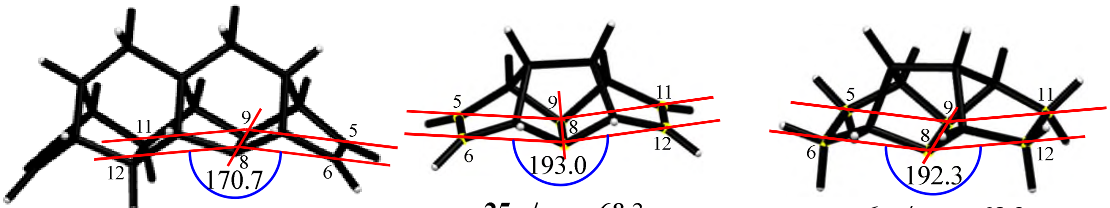
Figure 3. Significant $^{1}H/^{1}H$ correlations among protons of different half of **43** in its NOESY spectrum.

When diiodide **38** was added to molten sodium in boiling 1,4-dioxane, the standard conditions used by our group to obtain dimers from pyramidalized alkenes,[5,18,20] once again no dimer was observed in the crude reaction product (^{1}H-NMR) and, after column chromatography, compounds **40** (55% yield) and **41** (25% yield) were the only isolated products. The last one is a formal addition product of pyramidalized alkene **27** to the solvent.

Pyramidalized alkene **27** contains the tricyclo[3.3.1.0^{3,7}]nonane substructure of **2**. Since pyramidalized alkene **2** dimerizes to a cyclobutane dimer **3**,[14] a cross coupling reaction among the pyramidalized alkenes **27** and **2** might give a cross cyclobutane product. When a solution of diiodides **38** and **1** (ratio **38**/**1** = 1/3) in 1,4-dioxane was reacted with liquid (0.47%) sodium amalgam, the only isolated products were the cyclobutane dimer **3** (20% yield) and the reduction product **40** (36% yield).

Attempted formation of a bis(triphenylphosphine)Pt(0) complex derived from **27** was carried out by reacting a THF solution of **38** and ethylene-bis(triphenylphosphine)Pt(0) with liquid (0.47%) sodium amalgam, following the procedure described by Borden et al.[15,16] to prepare complex **4** from pyramidalized alkene **2** (Scheme 1). However, a complex mixture of products was obtained, from which the expected complex could not be isolated.

The preceding results might be explained by assuming the formation of pyramidalized alkene **27** on reaction of diiodide **38** with *t*-BuLi, sodium amalgam or molten sodium in boiling 1,4-dioxane. Thus, although it does not react with the different studied dienes, it does not experience cross coupling with tricyclo[3.3.1.0^{3,7}]non-3(7)-ene **2**, and it does not form a complex with bis(triphenylphosphine)Pt(0), it reacts however with *t*-BuLi to give the addition product **39**, with 1,4-dioxane to give the reduction product **40** or the addition product **41**, and in only one occasion, dimer **43**, a kind of reactions also observed for other pyramidalized alkenes. On the contrary, pyramidalized alkene **6** (Scheme 1), generated by reaction of diiodide **5** with liquid sodium amalgam, gave in good yields Diels-Alder adducts with many dienes, such as **14** (Scheme 1), 1,3-diphenylisobenzofuran **42**, furan or 2,5-dimethylfuran,[28] as well as a cross coupling product with pyramidalized alkene **10** (see structure on Scheme 1).[29] Moreover, the related pyramidalized alkene **18** from diiodide **17**, also gave cross coupling reaction with pyramidalized alkene **10** (Scheme 1) and a Diels-Alder adduct with 1,3-diphenylisobenzofuran **42**.[5]



27, ψ = 128.0
ζ = 52.0
Biradical = 1.37

25, ϕ = 68.3
ψ = 109.8
ζ = 70.2
Biradical = 1.85

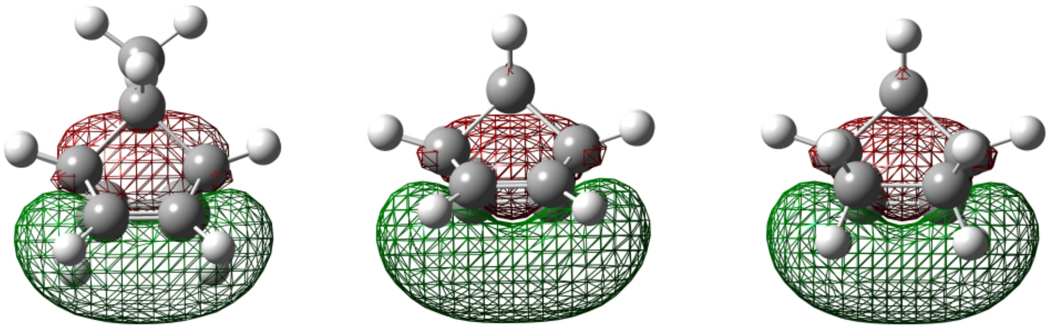
6, ϕ = 68.3
ψ = 109.9
ζ = 70.1
Biradical = 1.51

Figure 4. Calculated structures for pyramidalized alkenes **27**, **25** and **6**: Pyradimalization angles (ϕ), flap angles (ψ), supplementary flap angles (ζ), dihedral angles formed by the shown planes (º) and biradical character (number of unpaired electrons). Numbering of the different carbon atoms correspond to their IUPAC names as bridged polycyclic compounds.

The results herein described can be partly explained on the basis of the lower pyramidalization and greater steric hindrance of alkene **27** compared with the related alkenes **6**, **18** or **25**. Using the optimized geometries of pyramidalized alkenes **27**, **6** and **25** obtained from M06-2X/6-311+G(d)[30,31] calculations (Figure 4), the pyramidalization angle (ϕ) of alkenes **6** and **25**, which contain the substructure of tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene, were calculated to be both equal to 68.3º. Since for symmetry reasons, the pyramidalization angle of alkene **27** is not applicable, comparison will be performed on the basis of their flap (ψ) or complementary flap angles (ζ). The complementary flap angles of alkenes **6** and **25** were calculated to be 70.1º and 70.2º, respectively, quite close to their pyramidalization angles. However, in alkene **27**, a value of 52.0º calculated for the complementary flap angle is indicative of a much lower degree of pyramidalization, in concordance with the fact that this alkene contains the substructure of tricyclo[3.3.1.0^{3,7}]non-3(7)-ene (**2**), for which a pyramidalization angle (ϕ) of 53.7º had been calculated with the B3LYP/6-31G(d) basis set.[5]

The differences in the degree of pyramidalization of alkenes **27**, **6**, and **25** are also reflected in the orbitalic features of the double bond (Figure 5), as revealed from the analysis of the natural bond orbitals (NBO)[32] derived at the CISD/6-31G(d)[33] level. For standard double bonds (i.e., without geometrical strain), the *sp*^{2} hybridization implies a spatial orientation of the π orbital of 90º. In pyramidalized alkenes, however, geometrical distortion introduces a deviation in the angle formed by the atomic hybrid orbital. The results indicate that the deviation angle for alkenes **25** and **6** amounts to

124° and 123°, respectively, while the deviation angle for alkene **27** is 114°. This confirms that the structural stress in alkene **27**, which contains the tricyclo[3.3.1.0^{3,7}]non-3(7)-ene subunit, is lower than in the more reactive alkenes **6** or **25**, which contains the tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene moiety.



27 **25** **6**

Figure 5. Representation of molecular orbitals obtained via CISD/6-31G(d) for alkenes **27**, **25** and **6**.

Furthermore, the biradical character of compounds **27**, **25** and **6** was examined following the method of Takatsuka *et al.*,[34] which relies on the number of unpaired electrons (N_e; Eq. 1) determined from the occupancy of the natural orbitals obtained from broken-symmetry calculations at the UHF/6-31G(d) level.

$$N_e = \sum_i n_i \left(2 - n_i\right) \tag{1}$$

where n_i denotes the occupation number.

The results point out that N_e increases from **27** (1.37) to **6** (1.51) and to **25** (1.85). This can be interpreted from the larger degree of pyramidalization of the double bond in the two latter compounds (see above). Nevertheless, keeping in mind the similar geometrical features of **25** and **6** (see Figure 4), the larger value of N_e determined for alkene **25** compared to compound **6** reveals the contribution played by the double bonds located at the two ends of the molecule (between atoms 5 and 6 as well as 11 and 12; Figure 4). A similar effect can be expected for compound **27** due to the presence of the double bond (between atoms 5 and 6; Figure 4). Indeed, calculations performed for the compound obtained upon saturation of this double bond leads to an estimated N_e value of 1.18. Accordingly, it can be concluded that the geometrical differences introduced by the distinct bridges in the skeleton of these alkenes increase effectively the biradical character of the most strained compounds.

Finally, to evaluate the relative steric hindrance of alkenes **6**, **25** and **27**, the external angles among the planes defined by the atoms C8, C9, C11 and C12, on one hand, and C8, C9, C5 and C6, on the other hand, were calculated (see Figure 6). For alkenes **6** and **25**, which contain the same carbocyclic skeleton, angles of 192.3º and 193.0º were calculated. However, for alkene **27**, the corresponding value was 170.7º. These values show that the external face of the pyramidalized C=C bond in compounds **6** and **25** is much more accessible than in alkene **27**.

Overall, the combination of lower degree of pyramidalization and higher steric hindrance can explain the reactivity observed for the hypothetical pyramidalized alkene **27**. From the obtained results, it may be assumed that alkene **27** might be generated from diiodide **38** under the different reaction conditions studied: a) reaction with *t*-BuLi in THF, since product **39**, derived from the addition of the *t*-butyl group to **27** was obtained; b) reaction with sodium amalgam, since the reduction product **40** and dimer **43** were isolated; c) reaction with molten sodium in boiling 1,4-dioxane, since the reduction product **40** and the product of addition of **27** and the solvent were isolated. The lack of reactivity of **27** towards different dienes, ethylene-bis(triphenylphosphine)Pt(0) or tricyclo[3.3.1.0^{3,7}]non-3(7)-ene **2** (generated simultaneously in situ) can be explained on the basis of the steric hindrance and the possibility of alternative transformations. For instance, in the attempted cross coupling among pyramidalized alkenes **2** and **27**, compound **3**, the cyclobutane dimer of **2**, and the reduction product **40** were the only isolated products. Reasonably, the formation of these products must be faster than the cross coupling of **2** and **27**, mainly due to the steric hindrance of **27**. However, alternative mechanisms to explain these results can not be ruled out.

CONCLUSION

Octacyclic diiodide **38** was prepared from cyclopentadiene **31**, following a synthetic sequence parallel to that previously used to prepare the octacyclic iodo trimethylsilyl derivative **28**. Pyramidalized alkene **27** may be assumed to be generated from diiodide **38** by under the usual conditions utilized to generate most of the pyramidalized alkenes described to date, i.e.: reaction with *t*-BuLi/THF/low temperature, liquid sodium amalgam/1,4-dioxane at room temperature, or molten sodium in boiling 1,4-dioxane. However, **27** could not be trapped with dienes **14** (see Scheme 1), 1,3-diphenylisobenzofuran **42**, or anthracene, no matter the conditions used to generate it. Different products derived from **27** have been isolated from these reactions, among them **39**, on reaction with *t*-BuLi, **40** and **41** on reaction with the solvent 1,4-dioxane, and dimer **43**. At present, however, alternative pathways for the formation of these products not implying the intermediate formation of pyramidalized alkene **27** can not be excluded. From the calculated structures, a lower pyramidalization and a greater steric hindrance of **27** compared with alkenes **6** and **25** was deduced. The combination of these two factors might explain the obtained results. From a synthetic point of view, it is worth noting that the bicyclic tetraiodide **37** is transformed in only two steps into nonadecacycle **43**, via the octacyclic diiodide **38**.

EXPERIMENTAL

General Experimental Methods. Melting points were determined in open capillary tubes with a MFB 595010M Gallenkamp melting point apparatus. All new compounds were fully characterized by their analytical (melting point, elemental analysis and/or accurate mass measurement, spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR) and in the cases of compounds **38**, **40** and **43**, also by X-Ray diffraction analysis. Assignments given for the NMR spectra are based on DEPT, ^{1}H/^{1}H homocorrelations (COSY and NOESY), ^{1}H/^{13}C single quantum correlation (gHSQC sequence) and ^{1}H/^{13}C multiple bond correlation (gHMBC sequence) spectra. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Mercury 400 (400 MHz for ^{1}H and 100.6 MHz for ^{13}C) spectrometer. Unless otherwise stated, the NMR spectra have been performed in $CDCl_3$. Chemical shifts (δ) are reported in parts per million related to internal TMS or $CDCl_3$ for ^{1}H and ^{13}C NMR, respectively. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad; or their combinations. IR spectra were registered on a FTIR Perkin–Elmer Spectrum RX1 spectrometer using the attenuated total reflectance (ATR) technique or a Nicolet Avantar 320 FT-IR spectrometer. Absorption values are given as wavenumbers (cm^{-1}), only significant absorptions are given. The intensity of the absorptions is given as strong (s), medium (m) or weak (w). High resolution mass spectra (HRMS) were carried out at the Mass

Spectrometry Unity of the Centres Científics i Tecnològics of the Universitat de Barcelona (CCiTUB) and are reported as *m/z*. LC/MSD-TOF spectrometer with electrospray ionization (ESI-TOF-MS) from Agilent Technologies was used. Low polar compounds (**37**–**40** and **43**) did not ionized under the usual electrospray ionization conditions used. The elemental analyses were carried out at the IQAC (CSIC) of Barcelona, Spain, in elemental microanalyzers (A5) model Flash 1112 series from Thermofinnigan for (C, H, N) determinations, and in a titroprocessor Methrom model 808 for the halogen determination. Automatized chromatography was carried out on a Combiflash RF 150 psi from Teledyne Isco. For the flash column chromatography, silica gel 60 AC (35–70 μm, SDS, ref. 2000027) was used. The eluents employed are reported as volume/volume percentages. Thin-layer chromatography (TLC) was performed on aluminum-backed sheets with silica gel 60 F254 (Merck, ref. 1.05554) and spots were visualized with UV light or a 1% aqueous solution of $KMnO_4$. X-Ray diffraction analysis of compounds **38, 40** and **43** were performed in a D8 Venture diffractometer at the CCiTUB of the University of Barcelona. The compounds and reagents were purchased to the following companies: DMAD, iodosobenzene diacetate, trimethylsilyl trifluoromethanesulfonate, dicyclopentadiene, KOBu-*t*, silica gel, 30% KH in mineral oil, and CuI were obtained from Sigma-Aldrich, trimethylsilyl cyanide, trimethylsilylacetylene, 1,4-dichloro-2-butene, *t*-BuLi, 1,2-bis(tributylstannyl)ethyne, ethylene-bis(triphenylphosphine)platinum(0), MsCl, 18-crown-6 and NaI from ACROS Organics, CF_3SO_3H from Fluorochem, 1,3-diphenylisobenzofuran from Fluka, anthracene from Merck and iodine from Scharlau chemicals. All of them were used without further purification.

[(1*R*,4*S*)-2,3-Diiodobicyclo[2.2.1]hepta-2,5-diene-7,7-diyl]bis(methylene) diacetate 34. A solution of ethyne-1,2-diylbis(phenyliodonium) ditriflate[23] **32** (2.37 g, 3.25 mmol) in anhydrous acetonitrile (20 mL) was prepared in a 50 mL round-bottomed flask provided with Ar atmosphere and magnetic stirring. The solution was cooled to – 35 °C and a solution of cyclopentadiene **31** (569 mg, 2.71 mmol) in anhydrous CH_3CN (7 mL) was added dropwise and the mixture was stirred at rt for 17 h. The solution was cooled to –35 °C, powdered NaI (828 mg, 5.52 mmol) and CuI (1.05 g, 5.51 mmol) were added and the mixture was stirred at rt for 20 h. The solvent was distilled under reduced pressure, and to eliminate the formed iodobenzene, toluene (10 mL) was added and the solvent and volatiles were distilled off under reduced pressure, repeating this process three more times. The black solid residue (4.03 g) was subjected to automatic column chromatography [35–70 µm silica gel (40 g), hexane / EtOAc mixtures]. On elution with hexane / EtOAc from 85:15 to 80:20 (4 min), diacetate **34** (466 mg, 35% yield) was obtained as light yellow oil. R_f: 0.19 (silica gel, 10 cm, hexane / EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02 (s, 3H, *syn*-CH_3COO), 2.06 (s, 3H, *anti*-CH_3COO), 3.51–3.52 [m, 2H, 1(4)-H], 4.20 (s, 2H, *anti*-CH_2OAc), 4.27 (s, 2H, *syn*-CH_2OAc), 6.81–6.84 ppm [m 2H, 5(6)-H]; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 20.8 (*anti*-*C*H_3COO and *syn*-*C*H_3COO), 64.2 (CH_2, *anti*-*C*H_2OAc), 64.3 (CH_2, *syn*-*C*H_2OAc), 65.6 [CH, C1(4)], 85.6 (C, C7), 113.5 [C, C2(3)], 139.4 [CH, C5(6)], 170.55 (C) and 170.56 ppm (C) (*syn*-CH_3COO and *anti*-CH_3COO); IR (NaCl): $\tilde{\upsilon}$ = 1740 (s), 1243 (s), 1035 cm^{-1} (s); HRMS (ESI-TOF) *m/z*: $[M + NH_4]^+$ Calcd for $C_{13}H_{18}I_2NO_4$ 505.9320; Found 505.9323.

[(1*R*,4*S*)-2,3-Diiodobicyclo[2.2.1]hepta-2,5-diene-7,7-diyl]dimethanol 35. A solution of diacetate **34** (151 mg, 0.31 mmol) in anhydrous MeOH (7.4 mL) was placed in a round-bottomed flask provided with Ar atmosphere, magnetic stirring and reflux condenser. Anhydrous K_2CO_3 (11 mg, 80 µmol) was added and the mixture was heated at reflux for 2 h. The solvent was eliminated under reduced pressure to give a brown solid residue (145 mg) that was subjected to automatic column chromatography (35–70 µm silica gel, 12 g, hexane / EtOAc mixtures) to give diol **35** (93 mg, 74% yield) as a yellowish solid, on elution with hexane / EtOAc from 15:85 to 30:70. The analytical sample of **35** (74 mg) was obtained as white solid by crystallization of the above product from a 1:3 mixture CH_2Cl_2 / pentane (1 mL). R_f = 0.18 (silica gel, 10 cm, hexane / EtOAc 1:1), m.p. 89–90 °C (CH_2Cl_2 / pentane); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13–2.18 (broad s, 1H, *syn*-CH_2O*H*) and 2.26–2.31 (broad s, 1H, *anti*-CH_2O*H*), 3.55 [pseudo t, $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 2.0 Hz, 2H, 1(4)-H], 3.85–3.87 (broad s, 2H, *anti*-C*H*$_2$OH), 3.96–3.98 (broad s, 2H, *syn*-C*H*$_2$OH), 6.82 ppm [pseudo t, $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 2.0 Hz, 2H, 5(6)-H]; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 65.2 [CH, C1(4)], 65.7 (CH_2, *anti*-*C*H_2OH), 66.1 (CH_2, *syn*-*C*H_2OH), 90.3 (C, C7), 114.0 [C, C2(3)], 139.5 ppm [CH, C5(6)]; IR (NaCl): $\tilde{\upsilon}$ = 3100–3600 [broad band, max. at 3342 (s)], 1019 cm^{-1} (s); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_9H_{11}I_2O_2$ 404.8843; Found: 404.8839; elemental analysis calcd (%) for $C_9H_{10}I_2O_2$: C 26.75, H 2.50, I 62.83; found: C 26.94, H 2.43, I 62.66.

[(1*R*,4*S*)-2,3-Diiodobicyclo[2.2.1]hepta-2,5-diene-7,7-diyl]bis(methylene) bismethanesulfonate 36. A solution of diol **35** (199 mg, 0.49 mmol) in anhydrous CH_2Cl_2 (4.5 mL) was prepared in a round-bottomed flask provided with Ar atmosphere and magnetic stirring. Anhydrous Et_3N (0.27 mL, 1.97 mmol) was added dropwise, the solution was cooled to 0 °C (ice-water bath), MsCl (90 μL, 1.18 mmol) was added dropwise and the reaction mixture was stirred at 0 °C for 2 h. Saturated aqueous solution of $NaHCO_3$ (0.5 mL) was added. The aqueous phase was separated and the organic one was washed with more saturated aqueous solution of $NaHCO_3$ (3 × 5 mL). The combined aqueous phases were extracted with CH_2Cl_2 (3 × 5 mL), the combined organic phase and extracts were washed with water (7 mL), dried (anhyd Na_2SO_4) and concd in vacuo to give crude dimesylate **36** (298 mg), which was subjected to automatic column chromatography (35–70 μm silica gel, 12 g, hexane / EtOAc mixtures) to give dimesylate **36** (271 mg, 98% yield) as a yellow oil, on elution with hexane / EtOAc from 65:35 to 10:90. The analytical sample of **36** (203 mg) was obtained as yellow solid by crystallization of the above product from a 1:3 mixture CH_2Cl_2 / pentane (2 mL). R_f = 0.30 (silica gel, 10 cm, hexane / EtOAc 1:1); m.p. 154–155 °C (CH_2Cl_2 / pentane); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.01 (s, 3H) and 3.05 (s, 3H) [*syn*- and *anti*-$CH_2OS(O_2)CH_3$], 3.62 [pseudo t, $^3J_{(H,H)} = {}^4J_{(H,H)} = 2.0$ Hz, 2H, 1(4)-H], 4.41 (s, 2H, *anti*-CH_2OMs), 4.45 (s, 2H, *syn*-CH_2OMs), 6.89 [pseudo t, $^3J_{(H,H)} = {}^4J_{(H,H)} = 2.0$ Hz, 2H, 5(6)-H]; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 37.3 (2 CH_3, CH_3SO_3), 64.9 [CH, C1(4)], 68.7 (CH_2, *anti*-CH_2OMs), 69.3 (CH_2, *syn*-CH_2OMs), 84.7 (C, C7), 113.2 [C, C2(3)], 139.5 [CH, C5(6)]; IR (NaCl): $\tilde{\upsilon}$ = 1355 (s), 1174 (s) cm^{-1} (s); HRMS (ESI-TOF) *m/z*: $[M + NH_4]^+$ Calcd for $C_{11}H_{18}I_2NO_6S_2$ 577.8659; Found: 577.8682; elemental analysis calcd (%) for $C_{11}H_{14}I_2O_6S_2$: C 23.59, H 2.52, I 45.31, S 11.45; found: C 23.83, H 2.51, I 45.34, S 11.32.

(1*R*,4*S*)-2,3-Diiodo-7,7-bis(iodomethyl)bicyclo[2.2.1]hepta-2,5-diene 37. A solution of dimesylate **36** (200 mg, 0.36 mmol) in anhydrous acetone (3.1 mL) was placed in a round-bottomed flask provided with Ar atm, magnetic stirring and reflux condenser. Powdered NaI (550 mg, 3,65 mmol) was added and the reaction mixture was heated to reflux for 17 h. The solvent was evaporated under reduced pressure to give a yellow residue (770 mg) that was subjected to column chromatography (35–70 μm silica gel, 3 g, hexane) to give tetraiodide **37** (190 mg, 85% yield) as a yellow viscous oil. R_f = 0.67 (silica gel, 10 cm, hexane / EtOAc 8:2); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 3.59 [pseudo t, $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 2.0 Hz, 2H, 1(4)-H], 3.65–3.67 (m, 2H, *anti*-C*H*$_2$I), 3.70–3.72 (m, 2H, *syn*-C*H*$_2$I), 6.66 ppm [pseudo t, $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 2.0 Hz, 2H, 5(6)-H]; ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 12.0 (CH$_2$, *syn*-*C*H$_2$I), 12.8 (CH$_2$, *anti*-*C*H$_2$I), 69.1 [CH, C1(4)], 87.5 (C, C7), 113.6 [C, C2(3)], 139.7 ppm [CH, C5(6)]; IR (NaCl): $\tilde{\nu}$ = 1417 (s), 1217 (s), 1197 (s), 734 (s), 639 cm^{-1} (s); elemental analysis calcd (%) for $C_9H_8I_4$·0.1hexane: C 18.23, H 1.50, I 80.27; found: C 18.03, H 1.34, I 80.59.

(1*s*,3*s*,4*R*,7*S*,8*R*,9*S*,10*S*,11*R*,12*S*,13*R*,16*S*,17*s*,19*R*)-8,9-Diiodooctacyclo[10.6.1.0^{1,10}.0^{3,7}.0^{4,9}.0^{8,19}.0^{11,16}.0^{13,17}]nonadeca-5,14-diene 38.

a) Preparation of a potassium cyclopentadienide THF 0.2 M solution. In a 10 mL flask, KH (30% in mineral oil, 134 mg, 1.00 mmol) was washed with anhydrous THF (5 × 5 mL) under an Ar atm. To the washed KH, anhyd THF (5 mL) was added and the suspension was cooled to 0 °C (ice-water bath). Freshly distilled cyclopentadiene (120 µL, 99 mg, 1.5 mmol) was added and the mixture was stirred at this temperature for 10 min. 18-crown-6 (13 mg, 49 µmol, about 5% with respect to KH) was added and the mixture was stirred at 0 °C for 10 min and at rt for 15 min to give a pink suspension.

b) Substitution reaction: In a 25 mL flask provided with magnetic stirring, reflux condenser and Ar atmosphere, a solution of tetraiodide **37** (187 mg, 0.30 mmol) in anhydrous DMF (2.2 mL) was prepared. The solution was cooled to 0 °C (ice-water bath) and then part of the above solution of potassium cyclopentadienide (3.3 mL, 0.66 mmol) was added dropwise. The mixture was stirred at 0 °C for 5 min, at rt for 10 min and then it was heated at 90 °C for 17 h. The mixture was allowed to cool to rt, MeOH (0.1 mL) was added and the mixture was stirred for 10 min. Then, EtOAc (5 mL) and water (5 mL) were added and the organic phase was separated. The aqueous phase was extracted with EtOAc (3 × 8 mL) and the combined organic phases were washed with saturated aqueous solution of $NaHCO_3$ (3 × 8 mL), water (2 × 8 mL) and brine (8 mL), dried (anhydrous Na_2SO_4) and concd in vacuo to give a brown oily residue (213 mg), which was subjected to column chromatography [35–70 µm silica gel (4 g) pentane/EtOAc mixtures] to give on elution with pentane, octacycle **38** (128 mg, 85% yield) as white solid. An analytical sample of **38** (97 mg) was obtained as white solid, by crystallization of the above product from CH_2Cl_2/MeOH 1:3 (2 mL). R_f = 0.62 (silica gel, 10 cm, hexane / EtOAc 9:1); m.p. 236.8–237.5 °C (CH_2Cl_2/MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (d, $^3J_{(H,H)}$ = 2.8 Hz, 2H, 18-H_2), 1.68 (d, $^3J_{(H,H)}$ = 2.8 Hz, 2H, 2-H_2), 1.71–1.74 (m, 1H, 17-H), 1.87 [s, 2H, 10(19)-H], 2.00–2.03 (m, 1H, 3-H), 2.12 [s, 2H, 11(12)-H], 2.41 [pseudo q, $^3J_{(H,H)}$ = $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 1.7 Hz, 2H, 13(16)-H], 3.09 [pseudo q, $^3J_{(H,H)}$ = $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 1.9 Hz, 1H, 4(7)-H], 6.12 [pseudo t, $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 1.8 Hz, 2H, 14(15)-H], 6.25 ppm [pseudo t, $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 1.8 Hz, 2H, 5(6)-H]; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 34.1 (CH_2, C2), 34.9 (CH_2, C18), 43.9 (C, C1), 47.8 [CH, C11(12)], 49.3 [CH, C13(16)], 52.1 (CH, C17), 52.7 (CH, C3), 58.7 [CH, C10(19)], 59.8 [CH, C4(7)], 70.7 [C, C8(9)], 137.2 [CH, C14(15)], 141.5 ppm [CH, C5(6)]; IR (NaCl): $\tilde{\upsilon}$ = 3067 (w), 2954 (m), 2915 cm^{-1} (m); elemental analysis calcd (%) for $C_{19}H_{18}I_2$: C 45.63, H 3.63, I 50.75; found: C 45.40, H 3.64, I 50.62.

Reaction of diiodide 37 with *t*-BuLi in the presence of diene 42: Isolation of (1*R,3*S**,4*S**,7*R**,8*R**,9*S**,10*S**,11*S**,12*R**,13*S**,16*R**,17*R**,19*S**)-8-*t*-butyloctacyclo[10.6.1.0^{1,10}.0^{3,7}.0^{4,9}.0^{8,19}.0^{11,16}.0^{13,17}]nonadeca-5,14-diene 39.** A solution of octacycle **38** (90 mg, 0.18 mmol) and diene **42** (58 mg, 0.22 mmol) in anhydrous THF (2.9 mL) was prepared in a two-necked round-bottomed flask provided with Ar atmosphere, magnetic stirring and low temperature thermometer. The solution was cooled to −67 °C and a solution of *t*-BuLi in pentane (1.7 M, 110 μL, 0.19 mmol) was added dropwise, the color of the solution changed from yellow to dark brown. The mixture was stirred at this temperature for 30 min and it was allowed to heat to rt for 30 min. MeOH (0.15 mL), water (2 mL) and Et_2O (3 mL) were successively added, the organic phase was separated and the aqueous one was extracted with Et_2O (3 × 4 mL). The combined organic phase and extracts were dried (anhydrous Na_2SO_4) and concentrated in vacuo to give a yellow oil (108 mg) that was subjected to column chromatography (35–70 μm silica gel, 3.5 g, pentane / EtOAc mixtures). On elution with pentane, compound **39** (14 mg, 26% yield) was obtained as a grey solid. The analytical sample of **39** (11 mg) was obtained by sublimation in a cold finger (60 °C / about 0.01 Torr for 6 h) as a white solid. R_f = 0.73 (silica gel, 10 cm, hexane / EtOAc 9:1); m.p. 144–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 [s, 9H, $C(CH_3)_3$], 1.37 (overlapped dd, $^2J_{(H,H)}$ = 14,8 Hz, $^3J_{(H,H)}$ = 2.8 Hz, 1H) and 1.39 (overlapped dd, $^2J_{(H,H)}$ = 14.8 Hz, $^3J_{(H,H)}$ = 2.8 Hz, 1H) (18-H_a and 18-H_b), 1.41 (overlapped dd, $^2J_{(H,H)}$ = 14.0 Hz, $^3J_{(H,H)}$ = 2.8 Hz, 1H) and 1.43 (overlapped dd, $^2J_{(H,H)}$ = 14.0 Hz, $^3J_{(H,H)}$ = 2.8 Hz, 1H) (2-

H_a and 2-H_b), 1.50 (s, 1H, 10-H), 1.57 (d, $^3J_{(H,H)}$ = 6.0 Hz, 1H, 11-H), 1.63 (d, $^4J_{(H,H)}$ = 1.6 Hz, 1H, 19-H), 1.68 (s, 1H, 9-H), 1.77–1.81 (complex signal, 2H, 3-H and 17-H), 2.22–2.24 (broad s, 1H, 4-H), 2.27 (d, $^3J_{(H,H)}$ = 6.0 Hz, 1H, 12-H), 2.30 (broad s, 1H, 13-H), 2.38 (broad s, 1H, 16-H), 2.41–2.43 (broad s, 1H, 7-H), 5.95 (dd, $^3J_{(H,H)}$ = 5.6 Hz, $^4J_{(H,H)}$ = 3.2 Hz, 1H, 5-H), 6.03 (overlapped dd, $^3J_{(H,H)}$ = 5.6 Hz, $^4J_{(H,H)}$ = 3.2 Hz, 1H, 15-H), 6.05 (overlapped dd, $^3J_{(H,H)}$ = 5.6 Hz, $^4J_{(H,H)}$ = 3.2 Hz, 1H, 14-H), 6.24 ppm (dd, $^3J_{(H,H)}$ = 5.6 Hz, $^4J_{(H,H)}$ = 3.2 Hz, 1H, 6-H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 33.4 [CH_3, C(CH$_3$)$_3$], 35.9 (CH_2, C18), 36.09 (CH_2, C2), 36.12 [C, C(CH_3)$_3$], 41.8 (C, C1), 44.3 (CH, C12), 45.1 (CH, C11), 47.9 (CH, C9), 49.2 (CH, C13), 49.7 (CH, C16), 52.0 (CH, C4), 52.8 (CH, C17), 53.4 (CH, C7), 54.2 (CH, C10), 57.2 (CH, C19), 58.3 (CH, C3), 61.1 (C, C8), 133.1 (CH, C5), 137.2 (CH, C15), 137.4 (CH, C14), 143.9 ppm (CH, C6). IR (NaCl): $\tilde{\upsilon}$ = 3055 (w), 2934 (s), 2917 (s), 2898 (s), 719 (s), 707 (s), 660 cm^{-1} (s); elemental analysis calcd (%) for $C_{23}H_{28}\cdot 1/4H_2O$: C 89.41, H 9.30; found: C 89.11, H 9.24.

Reaction of diiodide 38 with Na/Hg in the presence of 11,12-dimethylene-9,10-dihydro-9,10-ethanoanthracene 14: Isolation of (3s,4R,7S,8R,9S,10s,11R,12S,13R,16S,17s,19s)-octacyclo[10.6.1.0^{1,10}.0^{3,7}.0^{4,9}.0^{8,19}.0^{11,16}.0^{13,17}]nonadeca-5,14-diene, 40 and (1R*,2S*,3R*,4R*,5S*,6R*,8R*,9R*,12S*,13R*,14S*,15R*,16R*,17R*,18S*,19S*,20R*,21S*,22S*,23R*,24S*,25S*,26R*,27R*,28R*,29S*,30R*,31S*,34R*,35R*)nonadecacyclo[17.17.1.1^{6,24}.0^{1,28}.0^{2,30}.0^{3,18}.0^{3,27}.0^{4,16}.0^{4,25}.0^{5,13}.0^{6,15}.0^{8,12}.0^{9,14}.0^{16,23}.0^{17,21}.0^{20,27}.0^{22,26}.0^{29,34}.0^{31,35}] octatriaconta-10,32-diene 43. Sodium amalgam [0.48% from Hg (11.4 g) and Na (54 mg)] was prepared in a two-necked round-bottomed flask provided with Ar atmosphere and magnetic stirring. A solution of diiodide **38** (90 mg, 0.18 mmol) and diene **14** (50 mg, 0.22 mmol) in anhydrous 1,4-dioxane (1.2 mL) was added at rt and the mixture was stirred at this temperature for 24 h. The solution was decanted from the amalgam and was filtered through a short pad of Celite®, washing the filter with Et_2O (5 × 10 mL). The combined filtrate and washings were concd in vacuo to give a viscous yellow oil (122 mg) which was subjected to column chromatography (35–70 μm silica gel, 4 g, pentane / EtOAc mixtures). On elution with pentane, a mixture of **40** and dimer **43** in a molar ratio **40**/**43** = 1:0.6 (12 mg) and a mixture of unknown products plus anthracene (9 mg) were obtained as grey solids. The mixture of **40** and **43** (12 mg) was sublimed in a cold finger (50 ºC / about 0.01 Torr for 6 h) to give sublimed **40** (2 mg, 5% yield) and a residue that was washed with pentane to give dimer **43** (7 mg, 16% yield) as a white solid. No dimer was present in the pentane washing.

*Analytical and spectroscopic data of **40**:* R_f = 0.64 (silica gel, 10 cm, hexane / EtOAc 9:1); m.p. 133–134 °C (CH_2Cl_2 / MeOH); m.p. 131–132 ºC (sublimed); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38–1.45 [m, 10H, 8(9,11,12)-H, 10(19)-H and 2(18)-H_2], 1.78–1.83 [m, 2H, 3(17)-H], 2.36 [pseudo q, $^3J_{(H,H)}$ = $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 2.0 Hz, 4H, 4(7,13,16)-H], 6.04 ppm [pseudo t, $^3J_{(H,H)}$ = $^4J_{(H,H)}$ = 2.0 Hz, 4H, 5(6,14,15)-H]; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 34.5 [CH_2, C2(18)], 41.7 (C, C1), 46.5 [CH, C8(9,11,12)], 49.5 [CH, C4(7,13,16)], 50.8 [CH, C10(19)], 53.1 [CH, C3(17)], 137.0 ppm [CH, C5(6,14,15)]; IR (NaCl): $\tilde{\upsilon}$ = 3044 (w), 2944 (s), 2834 (m), 705 cm^{-1} (m); elemental analysis calcd (%) for $C_{19}H_{20}$: C 91.88, H 8.12; found: C 91.77, H 8.34.

*Analytical and spectroscopic data of **43***: R_f = 0.64 (silica gel, 10 cm, hexane / EtOAc 9:1); m.p. >300 °C (pentane); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 [s, 2H, 15(28)-H], 1.42 [d, $^3J_{(H,H)}$ = 2.8 Hz, 4H, 7(36)-H_2], 1.44 [d, $^3J_{(H,H)}$ = 2.8 Hz, 4H, 37(38)-H_2], 1.53 [s, 2H, 2(5)-H], 1.63 [d, $^3J_{(H,H)}$ = 6.0 Hz, 2H, 14(29)-H], 1.70 [d, $^3J_{(H,H)}$ = 6.4 Hz, 2H, 13(30)-H], 1.73–1.76 [m, 2H, 8(35)-H], 1.89 [broad d, $^3J_{(H,H)}$ = 2.4 Hz, 2H, 20(23)-H], 1.98 [broad d, $^3J_{(H,H)}$ = 4.0 Hz, 2H, 18(25)-H], 2.24–2.29 [dd, $^3J_{(H,H)}$ = 10.0 Hz, $^3J_{(H,H)}$ = 4.4 Hz, 2H, 17(26-H)], 2.32 [broad s, 2H, 9(34)-H], 2.38 [broad s, 2H, 12(31)-H], 2.43–2.48 [m, 2H, 21(22)-H], 2.55–2.58 [m, 2H, 19(24)-H], 6.04 [dd, $^3J_{(H,H)}$ = 5.6 Hz, $^4J_{(H,H)}$ = 2.8 Hz, 2H, 10(33)-H], 6.08 ppm [dd, $^3J_{(H,H)}$ = 5.4 Hz, $^4J_{(H,H)}$ = 3.0 Hz, 2H, 11(32)-H]; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 34.0 [CH_2, C37(38)], 34.6 [CH_2, C7(35)], 42.2 [CH, C13(30)], 42.5 [CH, C14(29)], 49.2 [C, C1(6)], 49.68 [CH, C9(34)], 49.74 [CH, C12(31)], 50.5 [CH, C17(26)], 52.3 [CH, C21(22)], 53.1 [CH, C8(35)], 53.3 [CH, C19(24)], 54.02 [CH, C2(5)], 54.05 [CH, C15(28)], 57.9 [CH, C20(23)], 59.8 [CH, C18(25)], 65.8 [C, C3(4)], 69.2 [C, C16(27)], 137.0 [CH, C10(33)], 137.1 ppm [CH, C11(32)]; IR (NaCl): $\tilde{\upsilon}$ = 3058 (w), 2938 (s), 2924 cm^{-1} (s); elemental analysis calcd (%) for $C_{38}H_{36}\cdot 1/3H_2O$: C 86.03, H 7.64; found: C 85.81, H 7.32.

Reaction of diiodide 38 with molten sodium in 1,4-dioxane at reflux: Isolation of 39 and the stereoisomeric mixture of 4-[1,4-dioxan-2(R*)-yl]- and 4-[1,4-dioxan-2(S*)-yl]-(1S*,3R*,4R*,7S*,8S*,9R*,10R*,11R*,12S*,13R*,16S*,17S*,19R*)-

octacyclo[10.6.1.$0^{1,10}$.$0^{3,7}$.$0^{4,9}$.$0^{8,19}$.$0^{11,16}$.$0^{13,17}$]nonadeca-5,14-diene 41. In a two-necked round-bottomed flask provided with Ar atmosphere and reflux condenser, sodium (60 mg, 2.6 mmol) and anhydrous 1,4-dioxane (2.5 mL) were placed. The mixture was heated at reflux till the sodium was molten and then diiodide **38** (121 mg, 0.24 mmol) was added at once and the reaction mixture was heated at reflux for 4 h. The formation of a yellow solid was observed. The mixture was allowed to cool to rt, MeOH (0.5 mL) was added and the mixture was stirred for 30 min. The mixture was filtered through a short pad of Celite® washing the filter with Et_2O (3 × 10 mL) and pentane (1 × 10 mL). The combined filtrate and washings were concd in vacuo to give a beige solid (125 mg) that was subjected to column chromatography (35–70 μm silica gel, 4 g, pentane / EtOAc mixtures). On elution with pentane, compound **40** (33 mg, 55% yield) was obtained as white solid. On elution with a mixture of pentane / EtOAc (90:10), the stereoisomeric mixture **41** (20 mg, 25% yield) was isolated as brown solid. The analytical sample of **40** (24 mg) was obtained as white solid by crystallization of the above product (33 mg) from a mixture CH_2Cl_2 / MeOH (1:3, 1.5 mL). The analytical sample of **41** (12 mg) was obtained as white solid by crystallization of the above product (20 mg) from a mixture CH_2Cl_2 / MeOH (1:3, 1.5 mL).

Analytic and spectroscopic data of the stereoisomeric mixture **41***:* R_f = 0.57 (silica gel, 10 cm, hexane / EtOAc 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40–1.60 (complex signal, 8H), 1.76–2.01 (complex signal, 3H), 2.27–2.42 (complex signal, 4H), 3.35–3.75 (complex signal, 7H), 5.98–6.20 ppm (complex signal, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 34.90 (CH_2), 34.97 (CH_2), 35.25 (CH_2), 35.32 (CH_2), 42.2 (CH), 42.4 (CH), 42.55 (C), 45.0 (CH), 45.4 (CH), 48.8 (CH), 49.1 (CH), 49.3 (CH), 49.6 (CH), 49.8 (CH), 50.8 (CH), 50.85 (CH), 51.77 (CH), 51.84 (CH), 52.2 (2 CH), 52.6 (CH), 52.8 (CH), 53.0 (CH), 53.1 (CH), 54.8 (C), 55.2 (CH), 55.6 (CH), 56.1 (C), 66.6 (CH_2), 66.7 (CH_2), 67.6 (2 CH_2), 69.64 (CH_2), 78.6 (CH), 80.7 (CH), 134.7 (CH), 137.0 (CH), 137.1 (2 CH), 137.3 (CH), 137.4 (CH), 137.9 (CH), 138.5 ppm (CH). IR (NaCl): $\tilde{\nu}$ = 3059 (w), 2943 (s), 2924 cm^{-1} (s); HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{23}H_{27}O_2$ 335.2006; Found: 335.2006.

Attempted formation of dimer 43 by reaction of diodide 38 with sodium amalgam in the absence of diene 14: isolation of 40. Sodium amalgam [0.47% from Hg (9.55 g) and Na (45 mg, 1.96 mmol)] was prepared in a two-necked round-bottomed flask provided with Ar atm and magnetic stirring. A solution of diiodide **38** (80 mg, 0.16 mmol) in anhydrous 1,4-dioxane (1.1 mL) was added at rt and the mixture was stirred at this temperature for 24 h. The solution was decanted from the amalgam and was filtered through a short pad of Celite®, washing the filter with Et_2O (5 × 3 mL). The combined filtrate and washings were concentrated in vacuo to give a viscous yellow oil (139 mg) which was subjected to column chromatography (35–70 μm silica gel, 3 g, pentane / EtOAc mixtures). On elution with pentane, **40** (12 mg) as white solid and impure **40** (19 mg) as grey solid were obtained. The second fraction (19 mg) was sublimed (60 °C, about 0.01 Torr) to give pure **40** (12 mg, 61% overall yield).

Attempted cross coupling among pyramidalized alkenes 2 and 27: Isolation of 40 and dimer 3. Sodium amalgam [0.47% from Hg (11.1 g) and Na (50 mg, 2.18 mmol)] was prepared in a two-necked round-bottomed flask provided with Ar atm and magnetic stirring. A solution of diiodide **38** (84 mg, 0.17 mmol) and diiodide **1** (188 mg, 0.50 mmol) in anhydrous 1,4-dioxane (2 mL) was added at once at rt and the mixture was stirred at this temperature for 24 h. The solution was decanted from the amalgam and was filtered through a short pad of Celite®, washing the filter with Et_2O (5 × 4 mL). The combined filtrate and washings were concd in vacuo to give a viscous yellow oil (115 mg) which was subjected to column chromatography (35–70 μm silica gel, 3.5 g, pentane / EtOAc mixtures). On elution with pentane, a mixture of **40** and dimer **3** in a ratio **40** / **3** about 1:2.5 by ^{1}H-NMR (31 mg) as white solid and impure mixture of the above products (14 mg) as grey solid were obtained. The second fraction (14 mg) was sublimed (60 °C, about 0.01 Torr) to give a mixture of **40** and dimer **3** in a ratio **40** / **3** about 1:0.3 by ^{1}H NMR (8 mg) (36% overall yield of **40** and 20% of **3**). The residue of the above sublimation contained mainly dimer **3** (MS, EI).

X-ray crystal-structure determination of compound 38. A colorless prism-like specimen of $C_{19}H_{18}I_2$, approximate dimensions 0.214 mm × 0.226 mm × 0.365 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a D8 Venture system equipped with a Multilayer monochromator and a Mo microfocus (λ = 0.71073 Å). The frames were integrated with the Bruker SAINT software package[35] using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 10601 reflections to a maximum θ angle of 30.53° (0.70 Å resolution), of which 4596 were independent (average redundancy 2.307, completeness = 98.0%, R_{int} = 3.26%, R_{sig} = 6.07%) and 4000 (87.03%) were greater than 2σ(F^2). The final cell constants of *a* = 11.9655(3) Å, *b* = 15.3718(4) Å, *c* = 16.7007(4) Å, volume = 3071.78(13) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). Data were corrected for absorption effects using the multi-scan method (SADABS).[35] The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6280 and 0.7461. The structure was solved and refined using the Bruker SHELXTL Software Package,[36] using the space group P b c a, with Z = 8 for the formula unit, $C_{19}H_{18}I_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 190 variables converged at R1 = 2.53%, for the observed data and wR2 = 7.11% for all data. The goodness-of-fit was 1.040. The largest peak in the final difference electron density synthesis was 0.700 e $Å^{-3}$ and the largest hole was −1.040 e $Å^{-3}$ with an RMS deviation of 0.167 e $Å^{-3}$. On the basis of the final model, the calculated density was 2.163 g cm^{-3} and F(000), 1904 e. For more details, see Table 1 in the Supporting Information.

X-ray crystal-structure determination of compound 40. A colorless prism-like specimen of $C_{19}H_{20}$, approximate dimensions 0.058 mm × 0.103 mm × 0.440 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a D8 Venture system equipped with a multilayer monochromator and a Mo microfocus (λ = 0.71073 Å). The frames were integrated with the Bruker SAINT software package,[35] using a narrow-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 71539 reflections to a maximum θ angle of 30.57° (0.70 Å resolution), of which 7702 were independent (average redundancy 9.288, completeness = 99.2%, R_{int} = 4.49%, R_{sig} = 2.43%) and 6307 (81.89%) were greater than 2σ(F^2). The final cell constants of *a* = 5.9104(4) Å, *b* = 11.1856(8) Å, *c* = 19.9679(14) Å, α = 105.046(2)°, β = 96.566(2)°, γ = 90.113(2)°, volume = 1265.80(15) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). Data were corrected for absorption effects using the multi-scan method (SADABS).[35] The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6714 and 0.7461. The structure was solved and refined using the Bruker SHELXTL Software Package,[36] using the space group P −1, with Z = 4 for the formula unit, $C_{19}H_{20}$. The final anisotropic full-matrix least-squares refinement on

F^2 with 343 variables converged at R1 = 5.45%, for the observed data and wR2 = 17.00% for all data. The goodness-of-fit was 1.044. The largest peak in the final difference electron density synthesis was 0.505 e Å^{-3} and the largest hole was −0.338 e Å^{-3} with an RMS deviation of 0.064 e Å^{-3}. On the basis of the final model, the calculated density was 1.303 g cm^{-3} and F(000), 536 e. For more details, see Table 1 in the Supporting Information.

X-ray crystal-structure determination of compound 43. A colorless plate-like specimen of $C_{38}H_{36}$, approximate dimensions 0.062 mm × 0.204 mm × 0.307 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a D8 Venture system equipped with a multilayer monochromator and a Mo microfocus (λ = 0.71073 Å). The frames were integrated with the Bruker SAINT software package,[35] using a narrow-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 64261 reflections to a maximum θ angle of 30.66° (0.70 Å resolution), of which 7215 were independent (average redundancy 8.907, completeness = 99.4%, R_{int} = 4.19%, R_{sig} = 2.51%) and 5824 (80.72%) were greater than $2\sigma(F^2)$. The final cell constants of a = 7.3827(3) Å, b = 11.4509(5) Å, c = 14.5547(6) Å, α = 77.556(2)°, β = 86.847(2)°, γ = 77.599(2)°, volume = 1173.44(9) Å^3, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). Data were corrected for absorption effects using the multi-scan method (SADABS).[35] The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.7149 and 0.7461. The structure was solved and refined using the Bruker SHELXTL Software Package,[36] using the space group P −1, with Z = 2 for the formula unit, $C_{38}H_{36}$. The final anisotropic full-matrix least-squares refinement on F^2 with 343 variables converged at R1 = 4.45%, for the observed data and wR2 = 12.41% for all data. The goodness-of-fit was 1.018. The largest peak in the final difference electron density synthesis was 0.414 e Å^{-3} and the largest hole was −0.240 e Å^{-3} with an RMS deviation of 0.058 e Å^{-3}. On the basis of the final model, the calculated density was 1.394 g cm^{-3} and F(000), 528 e. For more details, see Table 1 in the Supporting Information.

Computational Methods. Full geometry optimizations were performed with the M06-2X density functional method[30] by using the 6-311+G(d)[31] basis set. The nature of the stationary points was verified by inspection of the vibrational frequencies within the harmonic oscillator-rigid rotor approximation. Molecular Electrostatic Potential analysis was performed from the optimized geometries. The Natural Bond Orbital analysis (NBO)[32] was carried out at CISD/6-31G(d) level of theory,[33] in order to evaluate the orbitals of the pyramidalized double bounds. All DFT computations were carried out using the keyword Integral(Grid=Ultrafine) as implemented in Gaussian09,[37] which was used to carry out these calculations. The biradical character of pyramidalized alkenes was examined following the method of Takatsuka *et al.*,[34] which relies on the number of unpaired electrons determined from the occupancy of the natural orbitals obtained from broken-symmetry calculations at the UHF/6-31G(d) level.

Nomenclature. The complex name of these polycyclic compounds have been obtained by using the POLCYC program.[38]

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: xxxx, It contains copies of the ^{1}H NMR, ^{13}C NMR, DEPT, ^{1}H/^{1}H homocorrelation (NOESY and COSY), ^{1}H/^{13}C heterocorrelation (gHSQC and gHMBC sequences) spectra of all of the new compounds (**34–41** and **43**), ORTEP representations of compounds **38**, **40** and **43**, experimental data of the X-ray crystal-structure determination of compounds **38**, **40** and **43** (Table 1), DFT calculations data of pyramidalized alkenes **6**, **25** and **27** and CIF data of compounds **38**, **40** and **43**.

AUTHOR INFORMATION

Corresponding author:
E.mail: camps@ub.edu
ORCID:
Pelayo Camps 0000-0002-9633-3525
David Lozano: 0000-0003-3348-9781
Carla Barbaraci: 0000-0002-6155-6702
Merce Font-Bardia: 0000-0002-7892-8744
F. Javier Luque: 0000-0002-8049-3567
Carolina Estarellas: 0000-0002-0944-9053

Notes

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