Generation and Reactions of an Octacyclic Hindered Pyramidalized Alkene

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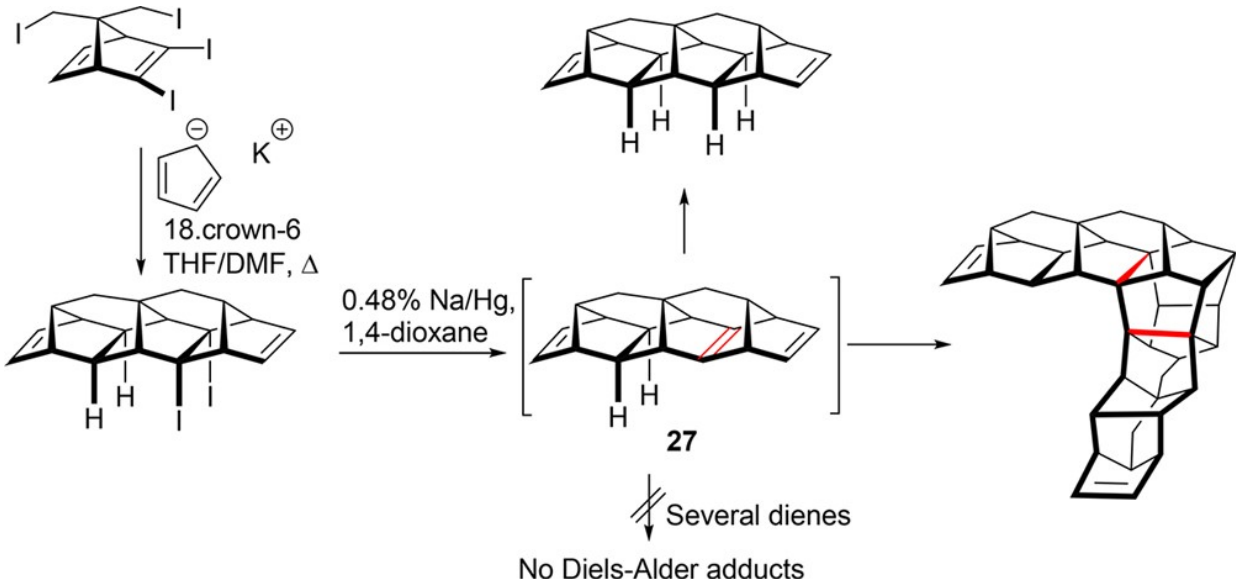
ABSTRACT:

Octacyclo[10.6.1.01,10.03,7.04,9.08,19.011,16.013,17]-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[3.3.1.03,7]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 an admixture of additional p-character into the original sp2 σ-orbitals. This makes the geometry around the olefinic carbon atoms nonplanar. 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 C2v 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 Cs point group of symmetry (right structure of Figure 1), the flap or hinge angle (Ψ), corresponding to the dihedral angle among the R2CCR2 and R1CCR1 planes, or its supplementary angle (ζ) is 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

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- [3.3.1.03,7]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 ethylenebis(triphenylphosphine)Pt(0) gives the Pt complex 4 derived from pyramidalized alkene 2.15,16 Paquette and Borden et al.17 also generated the pyramidalized alkene 6 (a bisethano derivative of bicyclo[3.3.0.03,7]-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, the 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 CDCl3 solution at room temperature to diene 12.

Lukin and Eaton19 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

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[10.6.1.01,10.03,7.04,9.08,19.011,16.013,17]- 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 described21 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 Eaton19 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)·CHCl3 [Pd(dba)2· CHCl3] 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 toward fluoride anions is likely due to the steric hindrance experienced by this group.

To solve this problem, we have prepared diiodide 38 according to Scheme 3. 5,5-Bisacetoxymethyl-1,3-cyclopentadiene22 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.

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 K2CO3 gave in good yield the corresponding diol 35, which was transformed into the corresponding bismesylate 36 on reaction with MsCl in the presence of Et3N. 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 (Cs point group) was clearly deduced from the 1H and 13C NMR data, it was confirmed by X-ray diffraction analysis (see the 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 1H 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 1H 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 1H 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 (C2v point group of symmetry), and later confirmed by X-ray diffraction analysis (see ORTEP structure of compound 40 in the SI).26

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

Keeping in mind the C2 symmetry point group of 43 and the fact that all signals of the different protons and 13C atoms of 43 appear clearly separated, except for both pairs of methylenic protons, we could fully assign its 1H and 13C NMR spectra with the aid of the 1H/1H homocorrelation spectra (COSY and NOESY) and 1H/13C heterocorrelation spectra (sequence gHSQC for one-bond correlations and gHMBC for long-range correlations). Especially significant to carry out this assignment was the observation of correlations among pairs of protons belonging to a 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 1H/1H NOESY spectrum (Figure 3).

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 (1H 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[3.3.1.03,7]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[3.3.1.03,7]non-3(7)-ene 2, and it does not form a complex with bis(triphenylphosphine)Pt(0); however, it reacts 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, on only one occasion, dimer 43, a kind of reaction 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 crosscoupling reaction with pyramidalized alkene 10 (Scheme 1) and a Diels−Alder adduct with 1,3-diphenylisobenzofuran 42.5 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[3.3.0.03,7]oct-1(5)-ene, were calculated to both be equal to 68.3°. Since for symmetry reasons the pyramidalization angle of alkene 27 is not applicable, a comparison will be performed on the basis of their flap (ψ) or supplementary flap angles (ζ). The supplementary flap angles of alkenes 6 and 25 were calculated to be 70.1° and 70.2°, respectively, quite close to their pyramidalization angles. However, in alkene 27, a value of 52.0° calculated for the supplementary flap angle is indicative of a much lower degree of pyramidalization, in concordance with the fact that this alkene contains the substructure of tricyclo[3.3.1.03,7]non-3(7)-ene (2), for which a pyramidalization angle (ϕ) of 53.7° had been calculated with the B3LYP/6-31G(d) basis set.5 The differences in the degrees 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 (NBOs)32 derived at the CISD/ 6-31G(d)33 level. For standard double bonds (i.e., without geometrical strain), the sp2 hybridization implies a spatial orientation of the π orbital of 90°. 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[3.3.1.03,7]non-3(7)-ene subunit, is lower than in the more reactive alkenes 6 or 25, which contain the tricyclo[3.3.0.03,7]oct-1(5)-ene moiety. 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 (Ne; eq 1) determined from the occupancy of the natural orbitals obtained from broken-symmetry calculations at the UHF/6-31G(d) level.

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

where ni denotes the occupation number.

The results point out that Ne 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 Ne 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 lead to an estimated Ne 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 4). For alkenes 6 and 25, which contain the same carbocyclic skeleton, angles of 192.3° and 193.0° were calculated. However, for alkene 27, the corresponding value was 170.7°. 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 a 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; and (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 toward different dienes, ethylene-bis(triphenylphosphine)Pt(0), or tricyclo[3.3.1.03,7]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.

CONCLUSIONS

Octacyclic diiodide 38 was prepared from cyclopentadiene 31, following a synthetic sequence parallel to that previously used to prepare the octacyclic iodotrimethylsilyl derivative 28. Pyramidalized alkene 27 may be assumed to be generated from diiodide 38 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 were 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 SECTION

General Experimental Methods. Melting points were determined in open capillary tubes with an MFB 595010M Gallenkamp melting point apparatus. All new compounds were fully characterized by their analytical (melting point, elemental analysis, and/or accurate mass measurement) and spectroscopic data (IR, 1H NMR, and 13C 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, 1H/1H homocorrelations (COSY and NOESY), 1H/13C single-quantum correlation (gHSQC sequence), and 1H/13C multiplebond correlation (gHMBC sequence) spectra. 1H and 13C NMR spectra were recorded on a Varian Mercury 400 (400 MHz for 1H and 100.6 MHz for 13C) spectrometer. Unless otherwise stated, the NMR spectra have been performed in CDCl3. Chemical shifts (δ) are reported in parts per million related to internal TMS or CDCl3 for 1H and 13C NMR, respectively. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; or their combinations. IR spectra were registered on an FTIR Perkin−Elmer Spectrum RX1 spectrometer using the attenuated total reflectance (ATR) technique or a Nicolet Avantar 320 FTIR spectrometer. Absorption values are given as wavenumbers (cm−1), and 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 Cientifí cs i Tecnologȉ ics of the Universitat de Barcelona (CCiTUB) and are reported as m/z. An LC/MSD-TOF spectrometer with electrospray ionization (ESI-TOF-MS) from Agilent Technologies was used. Low polar compounds (37−40 and 43) did not ionize under the usual electrospray ionization conditions used. The elemental analyses were carried out at the IQAC (CSIC) of Barcelona, Spain, in elemental microanalyzer (A5) model Flash 1112 series from Thermofinnigan for (C, H, N) determinations and in a titroprocessor Methrom model 808 for the halogen determination. Automated 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 KMnO4. X-ray diffraction analyses 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 from 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; CF3SO3H from Fluorochem; 1,3-diphenylisobenzofuran from Fluka; anthracene from Merck; and iodine from Scharlau Chemicals. All of them were used without further purification.

[(1R,4S)-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) ditriflate23 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 CH3CN (7 mL) was added dropwise

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. 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. Rf: 0.19 (silica gel, 10 cm, hexane/EtOAc 8:2). 1H NMR (400 MHz, CDCl3): δ = 2.02 (s, 3H, syn-CH3COO), 2.06 (s, 3H, anti-CH3COO), 3.51−3.52 [m, 2H, 1(4)-H], 4.20 (s, 2H, anti- CH2OAc), 4.27 (s, 2H, syn-CH2OAc), 6.81−6.84 ppm [m, 2H, 5(6)-H]. 13C NMR (100.6 MHz, CDCl3): δ = 20.8 (anti-CH3COO and syn-CH3COO), 64.2 (CH2, anti-CH2OAc), 64.3 (CH2, syn-CH2OAc), 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-CH3COO and anti-CH3COO); IR (NaCl): ῡ= 1740 (s), 1243 (s), 1035 cm−1 (s). HRMS (ESI-TOF) m/z: [M + NH4]+ calcd for C13H18I2NO4 505.9320; found 505.9323.

[(1R,4S)-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 K2CO3 (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 CH2Cl2/pentane (1 mL). Rf = 0.18 (silica gel, 10 cm, hexane/EtOAc 1:1), mp 89−90 °C (CH2Cl2/pentane). 1H NMR (400 MHz, CDCl3): δ = 2.13−2.18 (broad s, 1H, syn-CH2OH) and 2.26−2.31 (broad s, 1H, anti-CH2OH), 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−CH2OH), 3.96−3.98 (broad s, 2H, syn−CH2OH), 6.82 ppm [pseudo t, 3J(H,H) = 4J(H,H) = 2.0 Hz, 2H, 5(6)-H]. 13C NMR (100.6 MHz, CDCl3): δ = 65.2 [CH, C1(4)], 65.7 (CH2, anti-CH2OH), 66.1 (CH2, syn-CH2OH), 90.3 (C, C7), 114.0 [C, C2(3)], 139.5 ppm [CH, C5(6)]. IR (NaCl): ῡ = 3100−3600 [broad band, max. at 3342 (s)], 1019 cm−1 (s). HRMS (ESI-TOF) m/z: [M + H]+ Calcd for C9H11I2O2 404.8843; Found: 404.8839. Elemental analysis calcd (%) for C9H10I2O2: C 26.75, H 2.50, I 62.83; found: C 26.94, H 2.43, I 62.66.

[(1R,4S)-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 CH2Cl2 (4.5 mL) was prepared in a round-bottomed flask provided with Ar atmosphere and magnetic stirring. Anhydrous Et3N (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 NaHCO3 (0.5 mL) was added. The aqueous phase was separated, and the organic one was washed with more saturated aqueous solution of NaHCO3 (3 × 5 mL). The combined aqueous phases were extracted with CH2Cl2 (3 × 5 mL), and the combined organic phase and extracts were washed with water (7 mL), dried (anhydrous Na2SO4), and concentrated in vacuo to give crude dimesylate 36 (298 mg), which was subjected to automatic column chromatography (35−70 µm of 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 of CH2Cl2/pentane (2 mL). Rf = 0.30 (silica gel, 10 cm, hexane/EtOAc 1:1); mp 154−155 °C (CH2Cl2/pentane). 1H NMR (400 MHz, CDCl3) δ: 3.01 (s, 3H) and 3.05 (s, 3H) [syn- and anti-CH2OS(O2)CH3], 3.62 [pseudo t, 3J(H,H) = 4J(H,H) = 2.0 Hz, 2H, 1(4)-H], 4.41 (s, 2H, anti-CH2OMs), 4.45 (s, 2H, syn-CH2OMs), 6.89 [pseudo t, 3J(H,H) = 4J(H,H) = 2.0 Hz, 2H, 5(6)-H]. 13C NMR (100.6 MHz, CDCl3) δ: 37.3 (2 CH3, CH3SO3), 64.9 [CH, C1(4)], 68.7 (CH2, anti-CH2OMs), 69.3 (CH2, syn-CH2OMs), 84.7 (C, C7), 113.2 [C, C2(3)], 139.5 [CH, C5(6)]. IR (NaCl): ῡ= 1355 (s), 1174 (s) cm−1 (s). HRMS (ESI-TOF) m/z: [M + NH4]+calcd for C11H18I2NO6S2 577.8659; found: 577.8682. Elemental analysis calcd (%) for C11H14I2O6S2: 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.

(1R,4S)-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 atmosphere, 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. Rf = 0.67 (silica gel, 10 cm, hexane/EtOAc 8:2). 1H NMR (400 MHz, CDCl3): 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-CH2I), 3.70−3.72 (m, 2H, syn-CH2I), 6.66 ppm [pseudo t, 3J(H,H) = 4J(H,H) = 2.0 Hz, 2H, 5(6)-H]. 13C NMR (100.6 MHz, CDCl3): δ = 12.0 (CH2, syn-CH2I), 12.8 (CH2, anti-CH2I), 69.1 [CH, C1(4)], 87.5 (C, C7), 113.6 [C, C2(3)], 139.7 ppm [CH, C5(6)]. IR (NaCl): ῡ = 1417 (s), 1217 (s), 1197 (s), 734 (s), 639 cm−1 (s). Elemental analysis calcd (%) for C9H8I4·0.1 hexane: C 18.23, H 1.50, I 80.27; found: C 18.03, H 1.34, I 80.59.

(1s,3s,4R,7S,8R,9S,10S,11R,12S,13R,16S,17s,19R)-8,9-Diiodooctacyclo[10.6.1.01,10.03,7.04,9.08,19.011,16.013,17]nonadeca-5,14-diene 38. 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 atmosphere. To the washed KH,

anhydrous 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.

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 and 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 NaHCO3 (3 × 8 mL), water (2 × 8 mL), and brine (8 mL), dried (anhydrous Na2SO4) and concentrated 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 CH2Cl2/MeOH 1:3 (2 mL). Rf = 0.62 (silica gel, 10 cm, hexane/EtOAc 9:1); mp 236.8−237.5 °C (CH2Cl2/MeOH). 1H NMR (400 MHz, CDCl3): δ = 1.39 (d, 3J(H,H) = 2.8 Hz, 2H, 18-H2), 1.68 (d, 3J(H,H) = 2.8 Hz, 2H, 2-H2), 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]. 13C NMR (100.6 MHz, CDCl3): δ = 34.1 (CH2, C2), 34.9 (CH2, 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 C19H18I2: C 45.63, H 3.63, I 50.75; found: C 45.40, H 3.64,

Reaction of Diiodide 37 with t-BuLi in the Presence of Diene 42: Isolation of (1R*,3S*,4S*,7R*,8R*,9S*,10S*,11S*,12R*, 13S*,16R*,17R*,19S*)-8-t-butyloctacyclo[10.6.1.01,10.03,7.04,9 .08,19.011,16.013,17]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 lowtemperature 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 Et2O (3 mL) were successively added, and the organic phase was separated. The aqueous one was extracted with Et2O (3 × 4 mL). The combined organic phase and

extracts were dried (anhydrous Na2SO4) 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 gray solid. The analytical sample of 39 (11 mg) was obtained by sublimation in a coldfinger (60 °C/about 0.01 Torr for 6 h) as a white solid. Rf = 0.73 (silica gel, 10 cm, hexane/EtOAc 9:1); mp 144−145 °C. 1H NMR (400 MHz, CDCl3): δ = 0.96 [s, 9H, C(CH3)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-Ha and 18-Hb), 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-Ha and 2-Hb), 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). 13C NMR (100.6 MHz, CDCl3): δ = 33.4 [CH3, C(CH3)3], 35.9 (CH2, C18), 36.09 (CH2, C2), 36.12 [C, C(CH3)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): ῡ=3055 (w), 2934 (s), 2917 (s), 2898 (s), 719 (s), 707 (s), 660 cm−1 (s). Elemental analysis calcd (%) for C23H28·1/4H2O: 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[10.6.1.01,10.03,7.04,9.08,19.011,16.013,17]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[17.17.1.16,24.01,28.02,30.03,18.03,27.04,16.04,25.05,13 .06,15.08,12.09,14.016,23.017,21.020,27.022,26.029,34.031,35] 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 Et2O (5 × 10 mL). The combined filtrate and washings were concentrated 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 gray solids. The mixture of 40 and 43 (12 mg) was sublimed in

a coldfinger (50 °C/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. Rf = 0.64 (silica gel, 10 cm, hexane/EtOAc 9:1); mp 133−134 °C (CH2Cl2/MeOH); mp 131−132 °C (sublimed). 1H NMR (400 MHz, CDCl3): δ = 1.38−1.45 [m, 10H, 8(9,11,12)-H, 10(19)-H and 2(18)-H2], 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]. 13C NMR (100.6 MHz, CDCl3): δ = 34.5 [CH2, 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 C19H20: C 91.88, H 8.12; found: C 91.77, H 8.34.

Analytical and Spectroscopic Data of 43. Rf = 0.64 (silica gel, 10 cm, hexane/EtOAc 9:1); mp > 300 °C pentane). 1H NMR (400 MHz, CDCl3): δ = 1.39 [s, 2H, 15(28)-H], 1.42 [d, 3J(H,H) = 2.8 Hz, 4H, 7(36)-H2], 1.44 [d, 3J(H,H) = 2.8 Hz, 4H, 37(38)-H2], 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]. 13C NMR (100.6 MHz, CDCl3): δ = 34.0 [CH2, C37(38)], 34.6 [CH2, 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 C38H36·1/3H2O: 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[10.6.1.01,10.03,7.04,9.08,19.011,16.013,17]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 until the sodium was molten. 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 Et2O (3 × 10 mL) and pentane (1 × 10 mL). The combined filtrate and washings were concentrated 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 a brown solid. The analytical sample of 40 (24 mg) was obtained as a white solid by crystallization of the above product (33 mg) from a mixture CH2Cl2/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 CH2Cl2/MeOH (1:3, 1.5 mL).

Analytic and Spectroscopic Data of the Stereoisomeric Mixture 41. Rf = 0.57 (silica gel, 10 cm, hexane/EtOAc 9:1). 1H NMR (400 MHz, CDCl3): 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). 13C NMR (100.6 MHz, CDCl3): δ = 34.90 (CH2), 34.97 (CH2), 35.25 (CH2), 35.32 (CH2), 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 (CH2), 66.7 (CH2), 67.6 (2 CH2), 69.64 (CH2), 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): $\tilde{\upsilon}$= 3059 (w), 2943 (s), 2924 cm−1 (s). HRMS (ESI-TOF) m/z: [M + H]+ calcd for C23H27O2 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 atmosphere 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 Et2O (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 gray 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 atmosphere 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 Et2O (5 × 4 mL). The combined filtrate and washings were concentrated 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 1H NMR (31 mg) as white solid and impure mixture of the above products (14 mg) as gray 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

532 40/3 of about 1:0.3 by 1H NMR (8 mg) (36% overall yield of 40 and 20% of 3). The residue of the
533 above sublimation contained mainly dimer 3 (MS, EI).
534 X-ray Crystal-Structure Determination of Compound 38. A colorless prism-like specimen of C19H18I2,
535 approximate dimensions 0.214 mm × 0.226 mm × 0.365 mm, was used for the X-ray crystallographic
536 analysis. The X-ray intensity data were measured on a D8 Venture system equipped with a Multilayer
537 monochromator and a Mo microfocus (λ = 0.71073 Å). The frames were integrated with the Bruker
538 SAINT software package35 using a narrow-frame algorithm. The integration of the data using an
539 orthorhombic unit cell yielded a total of 10601 reflections to a maximum θ angle of 30.53° (0.70 Å
540 resolution), of which 4596 were independent (average redundancy 2.307, completeness = 98.0%, Rint =
541 3.26%, Rsig = 6.07%) and 4000 (87.03%) were greater than 2σ(F2). The final cell constants of a =
542 11.9655(3) Å, b = 15.3718(4) Å, and c = 16.7007(4) Å and volume = 3071.78(13) Å3 are based upon
543 the refinement of the XYZ-centroids of reflections above 20σ(I). Data were corrected for absorption
544 effects using the multiscan method (SADABS).35 The calculated minimum and maximum transmission
545 coefficients (based on crystal size) are 0.6280 and 0.7461. The structure was solved and refined using
546 the Bruker SHELXTL Software Package,36 using the space group Pbca, with Z = 8 for the formula unit,
547 C19H18I2. The final anisotropic full-matrix least-squares refinement on F2 with 190 variables
548 converged at R1 = 2.53%, for the observed data, and wR2 = 7.11% for all data. The goodness-of-fit was
549 1.040. The largest peak in the final difference electron density synthesis was 0.700 e Å−3, and the
550 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,
551 the calculated density was 2.163 g cm−3 and F(000), 1904 e. For more details, see Table 1 in the
552 Supporting Information. X-ray Crystal-Structure Determination of Compound 40. A colorless prism-like
553 specimen of C19H20, with approximate dimensions of 0.058 mm × 0.103 mm × 0.440 mm, was used
554 for the X-ray crystallographic analysis. The X-ray intensity data were measured on a D8 Venture system
555 equipped with a multilayer monochromator and a Mo microfocus (ë= 0.71073 Å). The frames were
556 integrated with the Bruker SAINT software package,35 using a narrow-frame algorithm. The integration
557 of the data using a triclinic unit cell yielded a total of 71539 reflections to a maximum θ angle of 30.57°
558 (0.70 Å resolution), of which 7702 were independent (average redundancy 9.288, completeness =
559 99.2%, Rint = 4.49%, Rsig = 2.43%) and 6307 (81.89%) were greater than 2σ(F2). The final cell
560 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 =
561 90.113(2)°, and volume = 1265.80(15) Å3 are based upon the refinement of the XYZ-centroids of
562 reflections above 20σ(I). Data were corrected for absorption effects using the multiscan method
563 (SADABS).35 The calculated minimum and maximum transmission coefficients (based on crystal size)
564 are 0.6714 and 0.7461. The structure was solved and refined using the Bruker SHELXTL Software
565 Package,36 using the space group P−1, with Z = 4 for the formula unit, C19H20. The final anisotropic
566 full-matrix least-squares refinement on F2 with 343 variables converged at R1 = 5.45%, for the observed
567 data, and wR2 = 17.00% for all data. The goodness-of-fit was 1.044. The largest peak in the final
568 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 C38H36, with 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%, Rint = 4.19%, Rsig = 2.51%) and 5824 (80.72%) were greater than 2σ(F2). 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)°, and γ = 77.599(2)° and volume = 1173.44(9) Å3 are based upon the refinement of the XYZ-centroids of reflections above 20σ(I). Data were corrected for absorption effects using the multiscan 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, C38H36. The final anisotropic full-matrix least-squares refinement on F2 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 method30 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 the 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.

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(25) CCDC 1818504 for compound 38. See Supporting Information for details.

(26) CCDC 1818505 for compound 40. See Supporting Information for details.

(27) CCDC 1818506 for compound 43. See Supporting Information for details.

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Legends to figures

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

Scheme 1 Described Procedures to Generate Pyramidalized Alkenes and Reaction Products

Scheme 2. Attempted Generation of 27 from 28

Scheme 3 Preparation of Octacycle 38 from Cyclopentadiene 31

Scheme 4 Transformations of Octacycle 38

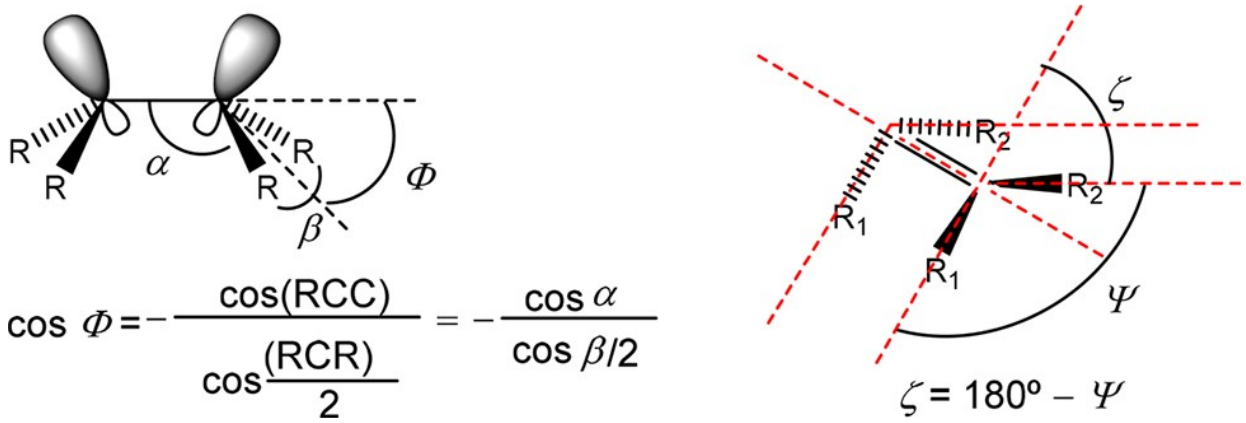
Figure.2 (Top) ORTEP representation of diiodide 43: ellipsoid contour at 50% probability level. (Bottom) Unit cell of dimer 43.

Figure.3 Significant 1H/1H correlations among protons of a different half of 43 in its NOESY spectrum.

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

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

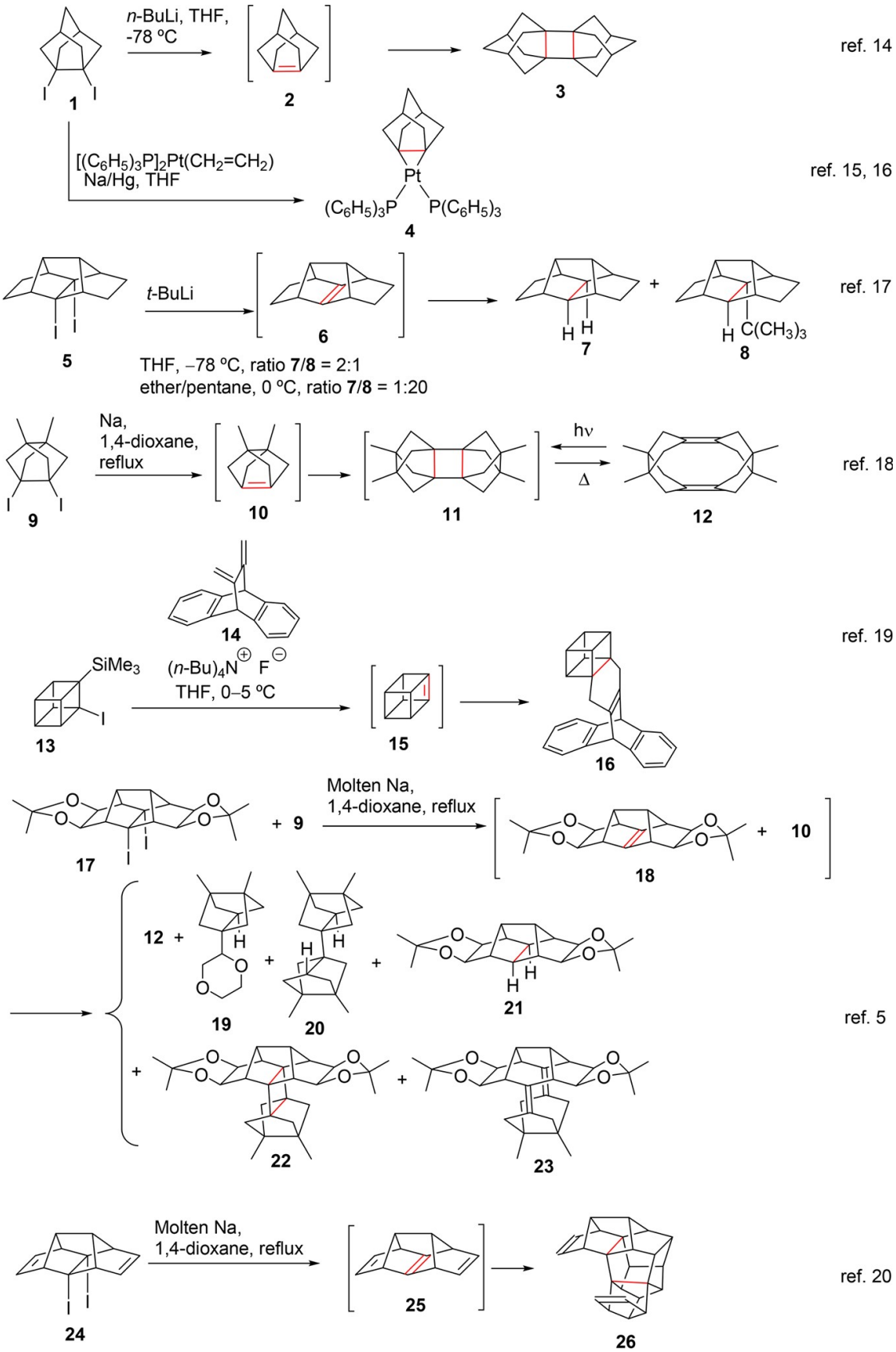
FIGURE 1



$$\cos\Phi = -\frac{\cos(RCC)}{\cos\frac{(RCR)}{2}} = -\frac{\cos\alpha}{\cos\beta/2}$$

$$\zeta = 180^{o} - \Psi$$

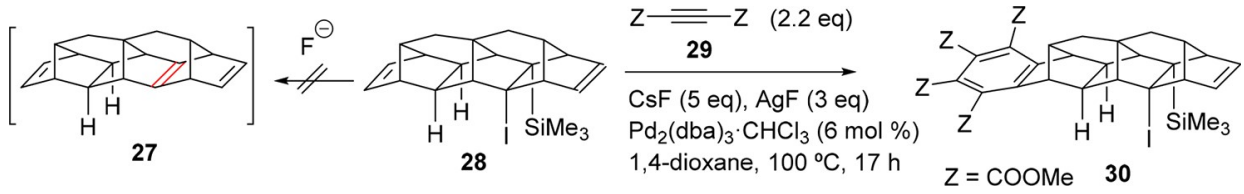
SCHEME 1


n-BuLi, THF, -78 ºC
1
2
3
ref. 14
[(C6H5)3P]2Pt(CH2=CH2)
Na/Hg, THF
Pt
(C6H5)3P
P(C6H5)3
4
ref. 15, 16
t-BuLi
5
6
7
8
THF, –78 ºC, ratio 7/8 = 2:1
ether/pentane, 0 ºC, ratio 7/8 = 1:20
ref. 17
Na,
1,4-dioxane,
reflux
9
10
11
12
hν
Δ
ref. 18
14
SiMe3
(n-Bu)4N F
THF, 0–5 ºC
13
15
16
ref. 19
17
+ 9
Molten Na,
1,4-dioxane, reflux
18
+ 10
12 +
19
20
21
22
23
ref. 5
Molten Na,
1,4-dioxane, reflux
24
25
26
ref. 20

716 **SCHEME 2**

717

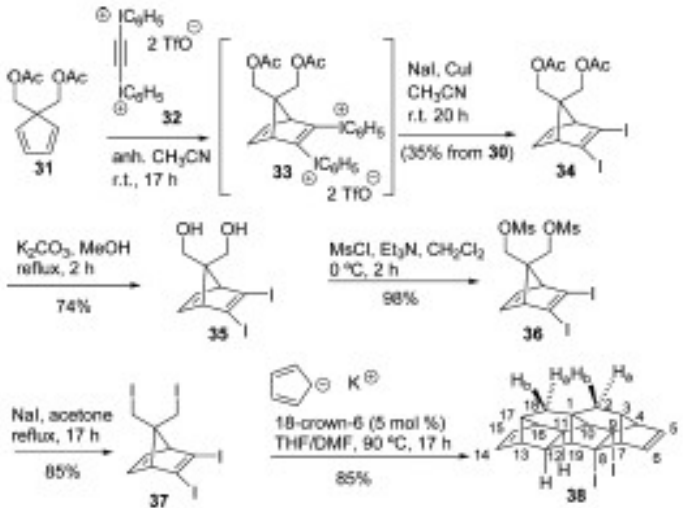
718



719

720

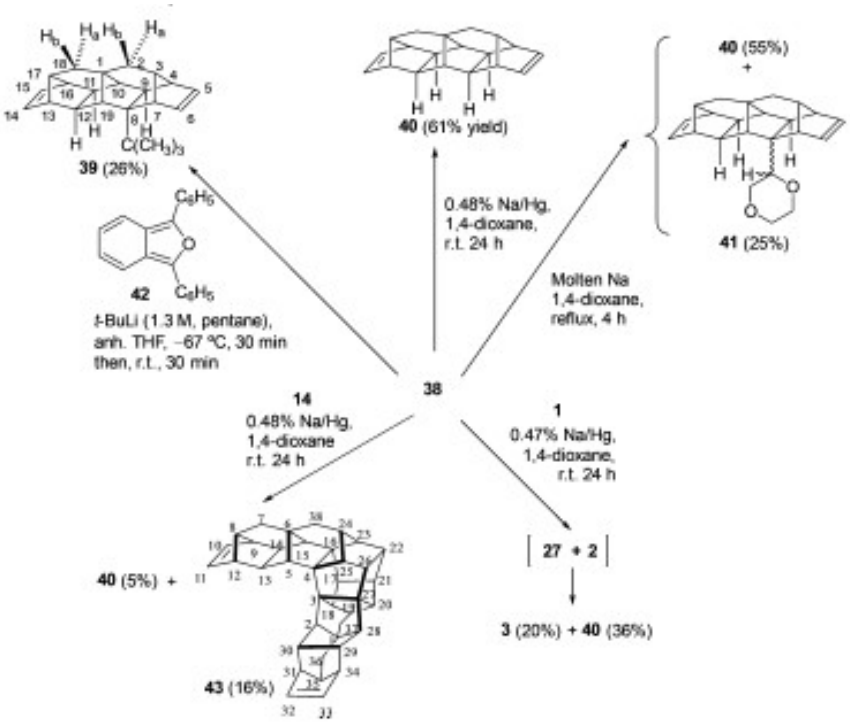
SCHEME 3


OAc OAc
31
2 TfO
32
anh. CH3CN
r.t., 17 h
33
NaI, CuI
CH3CN
r.t. 20 h
(35% from 30)
34
K2CO3, MeOH
reflux, 2 h
74%
35
MsCl, Et3N, CH2Cl2
0 °C, 2 h
98%
36
NaI, acetone
reflux, 17 h
85%
37
18-crown-6 (5 mol %)
THF/DMF, 90 °C, 17 h
85%
38

726 **SCHEME 4**

727

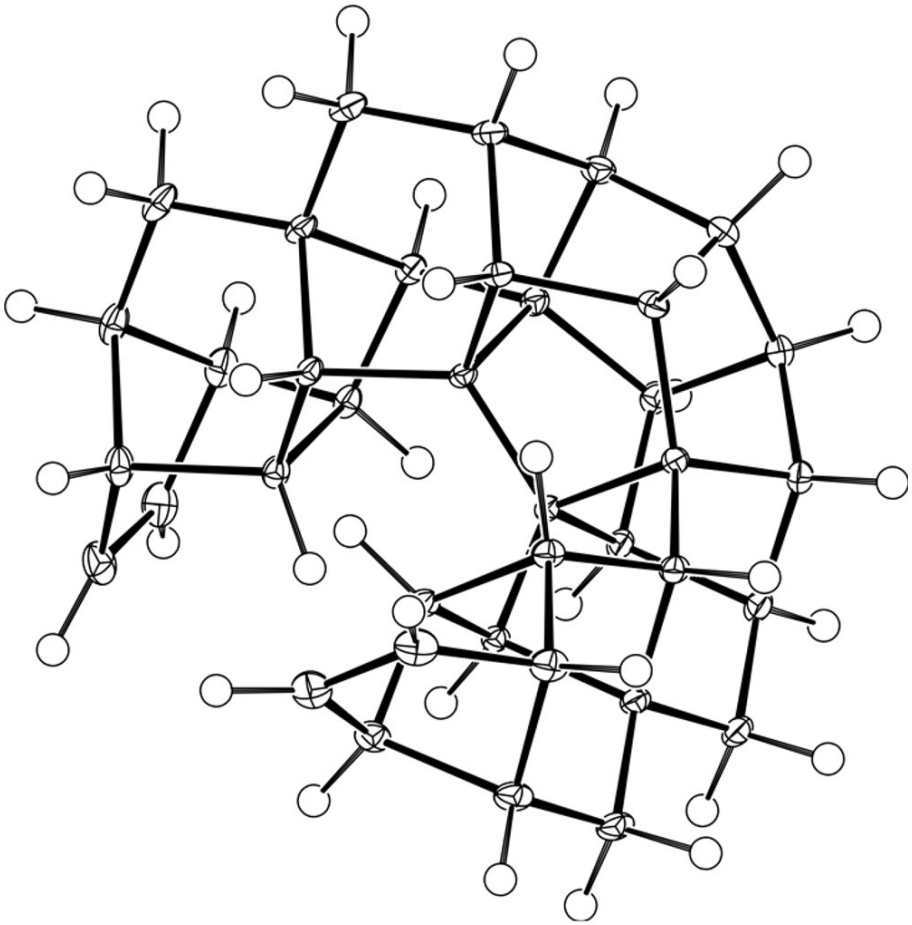
728

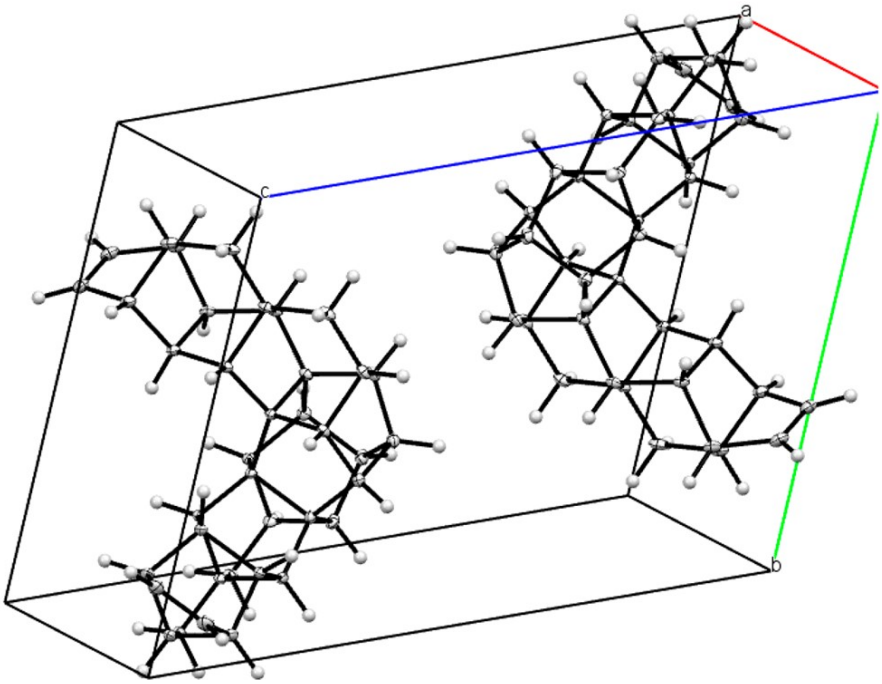


729

730

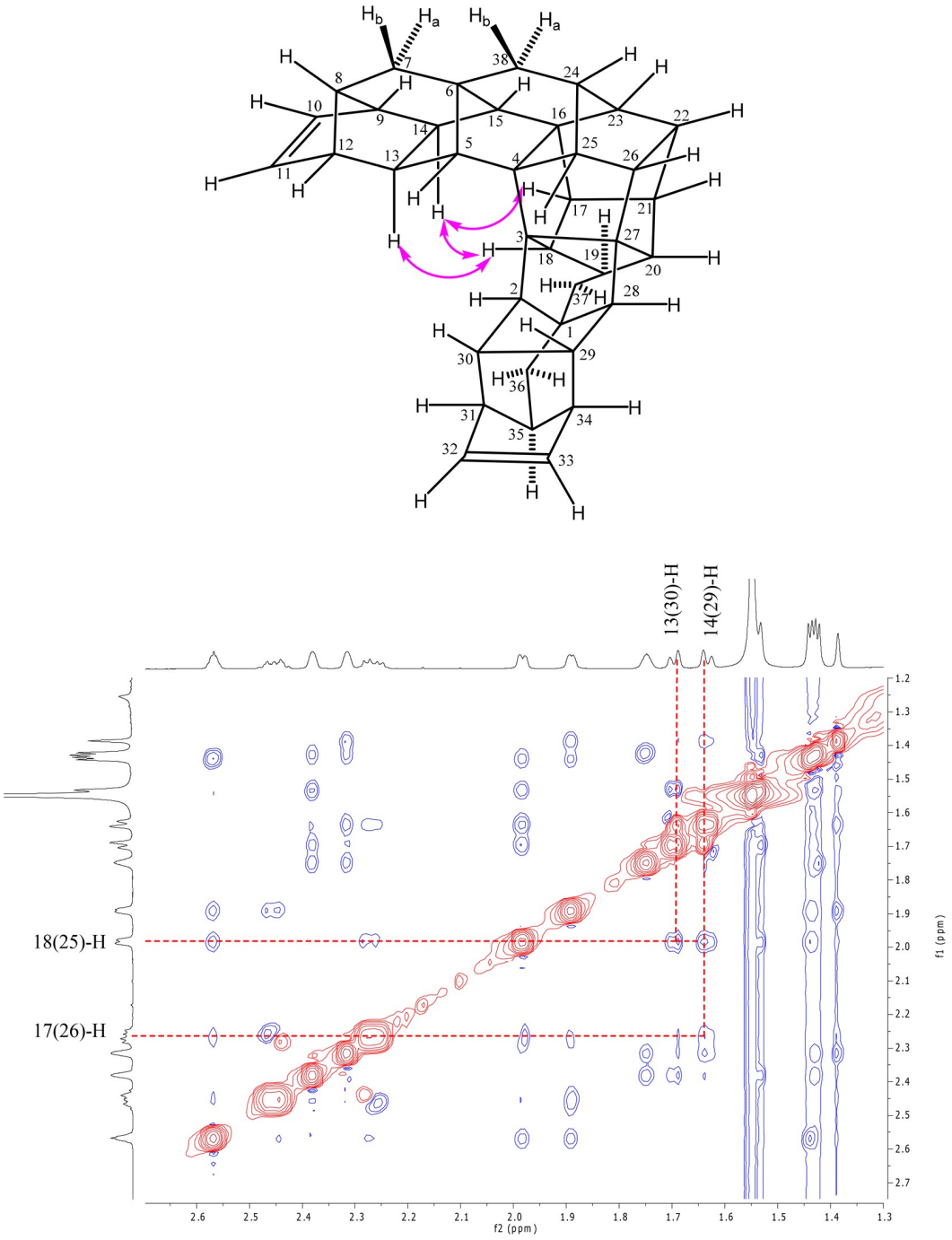
FIGURE 2





735 **FIGURE 3**

736



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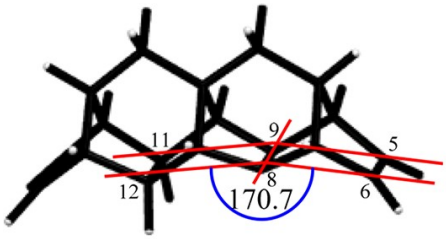
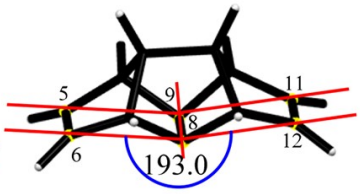
742

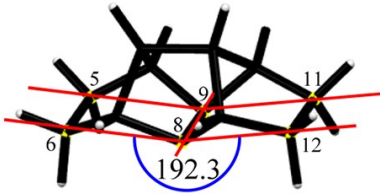
FIGURE 4



27, ψ = 128.0
ζ = 52.0
Biradical = 1.37

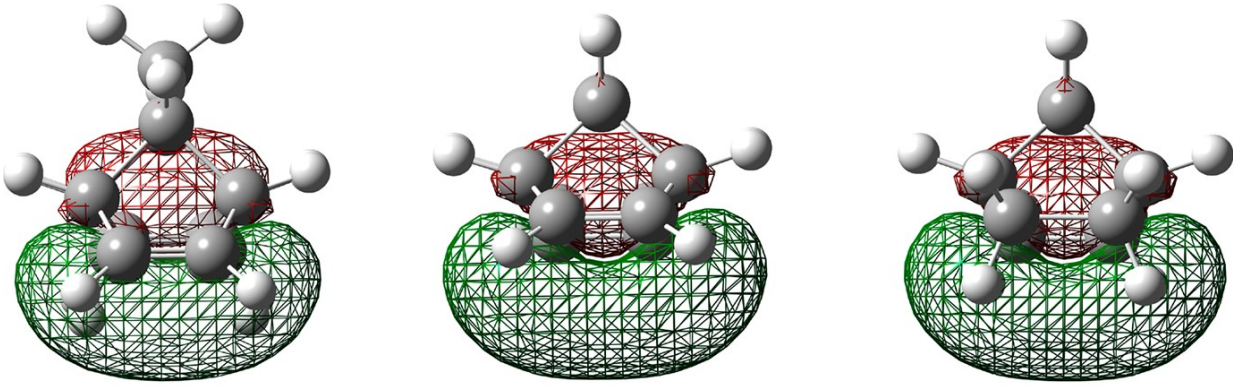


25, ϕ = 68.3
ψ = 109.8
ζ = 70.2
Biradical = 1.85



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

FIGURE 5



27 **25** **6**