Pergamon

Tetrahedron 58 (2002) 10081–10086

TETRAHEDRON

Synthesis and reactivity of a new functionalized and highly pyramidalized alkene containing the bisnoradamantane skeleton

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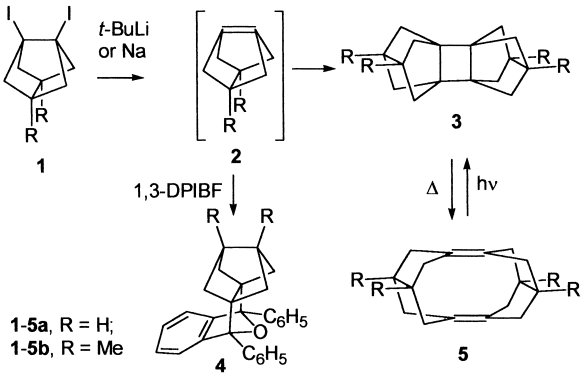
Received 16 July 2002; accepted 4 October 2002

Abstract—The generation and trapping of the highly pyramidalized 3,7-isopropylidenedioxytricyclo[3.3.0.0^{3,7}]oct-1(5)-ene **16** containing ketal functions is reported. Its dimerization followed by a [2+2] retrocycloaddition reaction allows a straightforward access to functionalized polycyclic compounds. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Earlier, we described the synthesis of the unfunctionalized highly pyramidalized alkenes **2a** and **2b** (Scheme 1), their trapping with dienes and its dimerization in the absence of any trapping agent.[1] When deiodination was carried out at room temperature cyclobutane dimers **3** were isolated, while working under refluxing 1,4-dioxane diene dimers **5** were obtained. Dienes **5** were transformed photochemically to cyclobutanes **3** on irradiation in the absence of any photosensitizer and the cyclobutane compounds **3** were converted back into dienes **5** on heating.

The thermal conversion of cyclobutane **3b** to diene **5b** could be cleanly followed by differential scanning calorimetry (DSC). The conversion of cyclobutane **3a** to diene **5a** was shown to be faster than the previous one (^{1}H NMR spectroscopy), a fact that was in accord with theoretical calculations on the relative stability of these pairs of compounds. In fact, cyclobutane **3a** was obtained at best as a mixture containing **3a** and **5a** in the ratio of 4:1. Later on, we described the first cross coupling reactions between two highly pyramidalized alkenes (**2a/7a** and **2b/7a**)[2] and a similar cross coupling reaction[3] implying for the first time a functionalized and highly pyramidalized alkene (**2b/7b**). In the last case, the corresponding cyclobutane cross product (**8c**) was quite thermally stable, although it could be fully transformed into the corresponding diene **9c** which on irradiation gave back the cyclobutane product (Scheme 2). Further manipulation of the functional groups in **8c** led to the dienetetrone **11**, via the cyclobutane derivative **10**.[3]



Scheme 1. Synthesis, chemical trapping and dimerization of highly pyramidalized alkenes **2a**,**b**.

In continuing our interest on the synthesis of functionalized and highly pyramidalized alkenes as useful intermediates in organic synthesis, we describe herein the synthesis, trapping and dimerization of 3,7-isopropylidenedioxytricyclo[3.3.0.0^{3,7}]oct-1(5)-ene **16** (Scheme 3).

2. Results and discussion

The preparation of **16** was planned from the diiodo derivative **15**, whose synthesis was envisioned from the known pinacol **12**,[4] in which the 2,2′-biphenylene subunit represents two latent carboxyl functions. Ketalization of pinacol **12** was carried out in a standard way by reaction with 2,2-dimethoxypropane under *p*-TsOH catalysis. For the conversion of the 2,2′-biphenylene subunit into two carboxyl groups we used ruthenium tetroxide generated from a catalytic amount of $RuCl_3 \cdot H_2O$ and an excess of an aqueous solution of NaClO (13%, from Fluka) in a

Keywords: cyclobutane; bisnoradamantane skeleton; pyramidalized alkenes.

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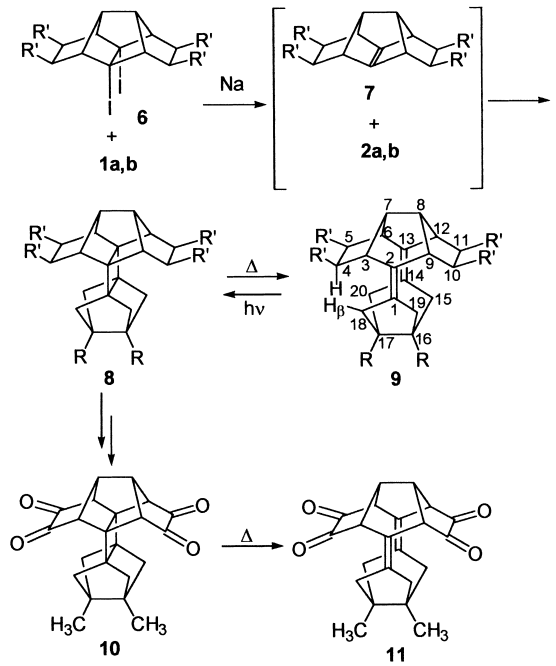
PII: S0040-4020(02)01323-6

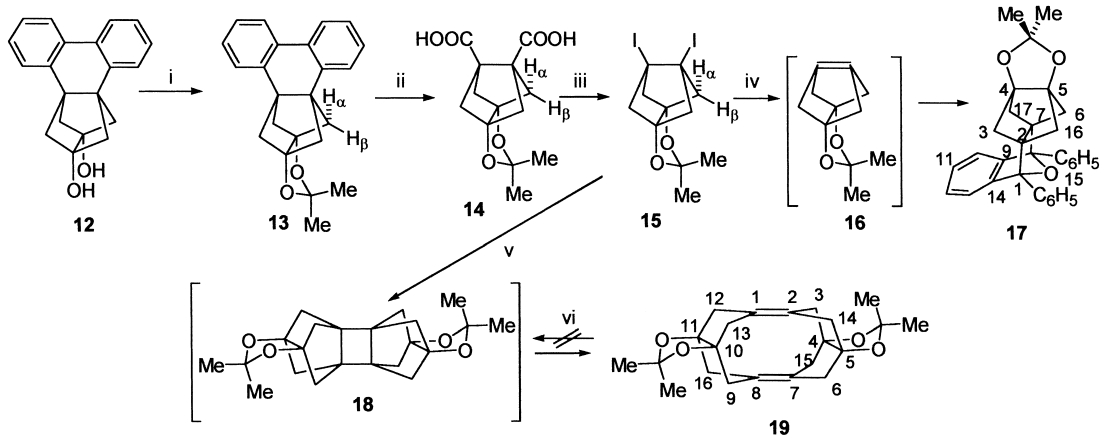


Scheme 2. Cross-coupling of highly pyramidalized alkenes leading to tetrasecododecahedradienes.

into account the Sharpless related procedure.[6] In this way, diacid **14** could be obtained in 68% yield of crystallized product. Worthy of note, in a run in which oxidation was not complete for unknown reasons, we isolated acid **20** in 25% yield instead of diacid **14** (Scheme 4). Compound **20** was converted into **14** in 68% yield, on further oxidation under similar conditions.

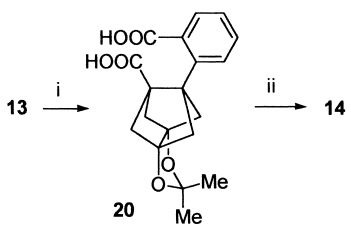
Compound **20**, might be an intermediate in the conversion of **13** to **14**, formed by oxidation of only one of the phenyl rings. It is interesting the fact that the phenyl ring of **20** is oxidized by this procedure in spite of having an electron-withdrawing substituent.[7] To the best of our knowledge, this is the first time a biphenylene group has been used as two latent carboxyl groups.

Iododecarboxylation of **14** was carried out as usual by reaction with iodosobenzene diacetate and iodine in CH_2Cl_2, following the Moriarty modification[8] of the Suárez procedure.[9] In this way, diiodo compound **15** was obtained as a white solid in 49% yield. Reaction of **15** with *t*-BuLi in the presence of 1,3-diphenylisobenzofuran (1,3-DPIBF) gave in good yield compound **17**, the Diels–Alder adduct derived from the expected highly pyramidalized alkene **16** and the 1,3-DPIBF, as the diene. When compound **15** was reacted with melted sodium in boiling 1,4-dioxane, diene dimer **19** was obtained in 63% yield. No cyclobutane dimer



Scheme 3. (i) 2,2-Dimethoxypropane, *p*-TsOH, 4 Å molecular sieves, $CHCl_3$, reflux, 3 h, 69%; (ii) $RuCl_3{\cdot}H_2O$, NaOCl, $CH_3CN/CH_2Cl_2/H_2O$, room temperature, 60 h, 68%; (iii) I_2, iodosobenzene diacetate, CH_2Cl_2, *hν*, 4 h, 49%; (iv) *t*-BuLi, 1,3-diphenylisobenzofuran, −78°C, 30 min, 61%; (v) Na, 1,4-dioxane, reflux, 4 h, 63%; (vi) *hν*, cyclohexane, 6 h.

two-phase system, using a mixture of acetonitrile/CH_2Cl_2 as the organic phase. This procedure is an improved modification of the Wolfe method,[5] in which the solvent (CCl_4) is replaced by CH_2Cl_2 and acetonitrile is also added taking



Scheme 4. (i) $RuCl_3{\cdot}H_2O$, aqueous 5.4% NaOCl, $CH_3CN/CH_2Cl_2/H_2O$, room temperature, 60 h, 25%; (ii) $RuCl_3{\cdot}H_2O$, aqueous 4.25% NaOCl, $CH_3CN/CH_2Cl_2/H_2O$, room temperature, 60 h, 68%.

was observed in this reaction. Moreover, when compound **19** was irradiated with a 300 W tungsten lamp in cyclohexane, contrary to all of the previously studied dienes (**5a**, **5b**, **9a**–**9c**), no cyclobutane derivative **18** was ever observed.

This different behavior can be understood taking into account the relative enthalpies of reaction and strain energies calculated (MM2[10]) for the conversion of the cyclobutane derivatives into the corresponding dienes (Table 1). Since, we had previously carried out different ab initio calculations (including MP2/6-31G* and B3LYP/6-31G*) on cyclobutanes **3b** and **10** and dienes **5b** and **11** which gave comparable results to the MM2 method and to the experimental values,[1c,3b] we did not perform ab initio calculations in the cases of **18** and **19**. As can be seen

Table 1. Molecular mechanics (MM2) data [enthalpies of reaction (ΔH_r, kcal/mol), strain energy differences (ΔE_{str}, kcal/mol)] calculated for the conversion of cyclobutane derivatives **3a**,**b**, **8c**, **10** and **18** to dienes **5a**,**b**, **9c**, **11** and **19**, respectively

Transformation	ΔH_r (diene−cyclobutane)	ΔE_{str} (diene−cyclobutane)
3a→5a	−46.1	−84.2
3b→5b	−43.2[a,b]	−81.2
8c→9c	−21.0	−59.1
10→11	−36.2[b,c]	−74.3
18→19	−57.1	−95.2

[a] The experimental value obtained by DSC in dynamic experiments was −45.6±1.1 kcal/mol.[1b]
[b] Different ab initio methods, including MP2/6-31G* and B3LYP/6-31G*, gave comparable results.[1c,3b]
[c] The experimental value obtained by DSC in dynamic experiments was −30.7±1.4 kcal/mol.[3b]

from Table 1, the conversion of **18** to **19** (ΔH_r=−57.1 kcal/mol) is by far the most exothermic of these processes. The closest more exothermic process corresponds to the conversion of **3a** to **5a** (ΔH_r=−46.1 kcal/mol) and as we previously stated,[1c] pure cyclobutane derivative **3a** could not be obtained because of its easy opening to **5a**. The rest of the cyclobutane derivatives collected in Table 1 (**3b**, **8c** and **10**) showed to be stable compounds that were converted into the corresponding dienes (**5b**, **9c** and **11**) on heating. As a rule, the more exothermic is the reaction the faster it is, what suggests product-like transition states.

As can be seen from Table 1, the strain energy associated with these transformations (ΔE_{str}) is the main responsible for the enthalpy differences (ΔH_r). The main contribution to ΔE_{str} in these reactions is due to the opening of the cyclobutane ring while other contributions can account for the observed ΔE_{str} differences. For instance, we explained the relative high stability of cyclobutane **8c** taking into account the strain energy involved in its conversion to the more spherical diene **9c**. The strain energy due to the approach of the 4H/18H$_\beta$, 5H/20H$_\beta$, 10H/19H$_\beta$ and 11H/15H$_\beta$ pairs of protons in the opened compound may partially compensate the strain release associated with the opening of the cyclobutane. The absence in **11** of the 4(5,10,11)-H protons due to the sp^2 hybridized C4(5,10,11) carbon atoms, reduces the strain energy associated with the conversion of **10** to **11**, making this a faster reaction.[3a] The absence in **3a**, **3b** and **18** of the substituted ethylene bridges, present in the above compounds, further reduces the strain energies associated with their conversion to the corresponding dienes, all these transformations being faster than the previous ones. We also explained the greater stability of **3b** as compared with **3a** on the basis of the increased crowding around the C4–C5 (C10–C11) bonds in passing from **3b** to **5b** due to the shortening of these bonds. The experimental C4–C5 (C10–C11) bond length in **3b** is 1.649(4) Å and the corresponding length in **5b** is 1.622(4) Å (X-ray).[1b] The shortening of these bonds (0.027 Å) in going from **3b** to **5b** is close to the value calculated by MM2 (0.020 Å). A similar shortening of these bonds were also calculated for the conversion of **3a** to **5a** (0.025 Å). Obviously, the strain increase associated with the shortening of these bonds, should be higher in the conversion of **3b** to **5b**, due to the presence of the methyl groups on these carbon atoms, making this process less exothermic and **3b** more stable.

Table 2. Molecular mechanics (MM2) data [distances between the olefinic carbon atoms (d, Å), angle of pyramidalization (Φ, degrees), strain energy (E_{str}, kcal/mol) and strain energy differences (OSE)] calculated for compound **19** and its mono-(**19**+H$_2$) and di-hydrogenated (**19**+2H$_2$) products

Parameter	**19**	**19**+H$_2$	**19**+2H$_2$
d_{C1-C8}	2.91	3.28	3.73
Φ	11.1	10.7	–
E_{str}	46.8	59.0	68.3
OSE [**19**−(**19**+H$_2$)]	12.2		
OSE [(**19**+H$_2$)−(**19**+2H$_2$)]		9.3	

Worthy of note, the calculated shortening of the C4–C5 (C10–C11) bonds in passing from **18** to **19** was only 0.006 Å. This fact must be related to the presence of the ketal rings in these compounds, altogether explaining the lower strain energy increase in the conversion of **18** to **19** and the relative instability of **18**, which could not be detected.

The calculated pyramidalization angle (Φ) of **16** (62.6°, B3LYP/6-31G*)[11] is similar to those previously calculated for the related alkenes **2a**, **2b**, **7a** and **7b**.[2] Also, diene **19** is a slightly pyramidalized (Φ=11.1°, MM2[10]) and hyperstable alkene[12] (see Table 2) as it was the case for dienes **5a**, **5b**, **9a**–**9c**.[3b,13]

All of the new compounds herein described have been fully characterized on the basis of their spectral data (IR, ^{1}H- and ^{13}C NMR, COSY ^{1}H/^{1}H, COSY ^{1}H/^{13}C and MS spectra) and elemental analyses.

In conclusion, the functionalized and highly pyramidalized alkene **16** has been generated, trapped as the Diels–Alder adduct **17** and dimerized to diene **19**. A key-step of this synthesis consists of the use of the 2,2′-biphenylene group as two latent carboxyl groups, this transformation being carried out by RuO_4 oxidation using a catalytic amount of $RuCl_3{\cdot}H_2O$ and excess of NaClO in an improved two-phase system (acetonitrile–CH_2Cl_2/H_2O).

Work is in progress to use the developed methodology for the generation and trapping of reactive intermediates having two highly pyramidalized double bonds.

3. Experimental

3.1. General

Melting points were determined with a MFB 595010 M Gallenkamp melting point apparatus. Unless otherwise stated, NMR spectra were recorded in $CDCl_3$ in the following spectrometers: ^{1}H NMR (500 MHz, Varian VXR 500), ^{13}C NMR (75.4 MHz, Varian Gemini 300). ^{1}H and ^{13}C NMR chemical shifts (δ) are reported in ppm with respect to internal tetramethylsilane (TMS). The multiplicity of the signals is: s, singulet; d, doublet; t, triplet; m, multiplet. Assignments given for the NMR spectra are based on DEPT, COSY ^{1}H/^{1}H, HETCOR ^{1}H/^{13}C (HMQC sequence) experiments. IR spectra were recorded on a FT/IR Perkin–Elmer spectrometer, model 1600. Routine

MS spectra were taken on a Hewlett-Packard 5988A spectrometer, the sample was introduced directly or through a gas chromatograph, Hewlett-Packard model 5890 Series II, equipped with a 30-meter HP-5 (5% diphenyl–95% dimethyl-polysiloxane) column [10 psi, initial temperature: 100°C (2 min), then heating at a rate of 10 °C/min till 250°C, then isothermic] and the electron impact technique (70 eV). Only significant ions are given: those with higher relative abundance, except for the ions with higher *m/z* values. Neutral aluminum oxide MN and silica gel SDS 60 (60–200 μm) were usually used for the standard column chromatography. NMR and routine MS spectra were performed at the Serveis Científico-Tècnics of the University of Barcelona, while elemental analyses were carried out at the Microanalysis Service of the IIQAB (CID, CSIC), Barcelona, Spain. Systematic names for **17** and **19** were obtained with the POLCYC program.[14]

3.1.1. 1,5-(2,2′-Biphenylene)-3,7-(isopropylidenedioxy)-tricyclo[3.3.0.0^{3,7}]octane (13). To a solution of 3,7-(2,2′-biphenylene)tricyclo[3.3.0.0^{3,7}]octane-1,5-diol (**12**)[4] (3.49 g, 12.0 mmol) in $CHCl_3$ (230 mL), 4 Å molecular sieves (20 g), 2,2-dimethoxypropane (6.5 mL) and *p*-toluenesulfonic acid monohydrate (120 mg) were added and the mixture was heated under reflux for 3 h. The mixture was allowed to cool to room temperature and filtered and the filtrate was concentrated in vacuo to give crude **13** (3.51 g). Crystallization of the above solid (isopropanol) gave pure **13** as a white solid (2.73 g, 69% yield), mp 195.5–196.5°C (isopropanol). IR (KBr) 3065, 2989, 2940, 2891, 1496, 1442, 1373, 1277, 1258, 1227, 1202, 1164, 1120, 991, 971, 848, 763, 728 cm^{-1}. ^{1}H NMR 1.63 (s, 6H, $C(CH_3)_2$), 2.32 (d, J=6.8 Hz, 4H) and 2.38 (d, J=6.8 Hz, 4H) [2(4,6,8)-H_α and 2(4,6,8)-H_β], 7.21–7.25 [m, 6H, 3′(3″)-H, 4′(4″)-H and 5′(5″)-H], 7.87–7.91 [m, 2H, 6′(6″)-H]. ^{13}C NMR 28.6 [CH_3, (CH_3)$_2$C], 46.9 [C, C1(5)], 56.9 [CH_2, C2(4,6,8)], 88.6 [C, C3(7)], 120.0 [C, $(CH_3)_2C$], 123.0 (CH), 126.9 (CH), 127.3 (CH) and 128.1 (CH) (Ar-CH), 130.6 (C) and 136.2 (C) (Ar-C). MS (EI), *m/z* (%): 330 (M$^{\cdot+}$, 11), 272 [(M−C_3H_6O)$^{\cdot+}$, 10], 232 (40), 229 (32), 215 (24), 204 (25), 203 (38), 202 (35), 98 (30), 59 (100). Anal. calcd for $C_{23}H_{22}O_2$: C 83.60, H 6.72. Found C 83.85, H 6.77.

3.1.2. 3,7-(Isopropylidenedioxy)tricyclo[3.3.0.0^{3,7}]-octane-1,5-dicarboxylic acid (14). To a solution of **13** (0.29 g, 0.88 mmol) in CH_2Cl_2 (6 mL), acetonitrile (6 mL) and H_2O (12 mL), $RuCl_3{\cdot}H_2O$ (12 mg, 0.053 mmol) was added and then aqueous NaOCl (31 mL, 13% aqueous solution, approx. 54 mmol, approximately double than the maximum theoretical amount) was added dropwise. The flask was stopped and the mixture was vigorously stirred at room temperature for 60 h. The organic layer was separated and the aqueous phase was washed with CH_2Cl_2 (4×10 mL), cooled (ice-bath), made acidic (pH 2–3) with 2N HCl (5 mL) and extracted with ethyl acetate (4×15 mL). The combined ethyl acetate extracts were dried (Na_2SO_4), filtered and concentrated in vacuo to give pure **14** as a white solid (0.16 g, 68% yield). An analytical sample of **14** was obtained by crystallization, mp 230°C (hexane/ethyl acetate). IR (KBr) 3400–2500 (max. at 3195, 2982, 2937, 2902, 2686, 2581, OH st, CH st), 1739, 1713 and 1679 (CO st), 1487, 1409, 1373, 1290, 1266, 1238, 1205, 1180, 1165, 1150, 1133, 1119, 1089, 1023, 965, 890, 857, 827, 767, 709 cm^{-1}. ^{1}H NMR (CD_3OD) 1.50 [s, 6H, $C(CH_3)_2$], 2.03 [d, J=7.0 Hz, 4H, 2(4,6,8)-H_β], 2.32 [d, J=7.0 Hz, 4H, 2(4,6,8)-H_α], 4.87 (broad s, 2H, mobile H). ^{13}C NMR (CD_3OD) 28.6 [CH_3, (CH_3)$_2$C], 52.8 [CH_2, C2(4,6,8)], 55.6 [C, C1(5)], 90.2 [C, C3(7)], 122.2 [C, $(CH_3)_2C$], 174.7 (C, COOH). MS (EI), *m/z* (%): 268 (M$^{\cdot+}$, 1), 253 [(M−CH_3)$^+$, 8], 210 [(M−C_3H_6O)$^{\cdot+}$, 50], 192 [(M−C_3H_6O−H_2O)$^{\cdot+}$, 53], 165 [(M−C_3H_6O−COOH)$^{\cdot+}$, 25], 164 (35), 146 (38), 119 (31), 91 (100), 59 (89). Anal. calcd for $C_{13}H_{16}O_6{\cdot}1/2H_2O$: C 56.31, H 6.18. Found C 56.37, H 6.08. The same yield was obtained by using 4.25% aqueous NaOCl.

3.1.3. 5-(2-Hydroxycarbonylphenyl)-3,7-(isopropylidenedioxy)tricyclo[3.3.0.0^{3,7}]octane-1-carboxylic acid (20). To a solution of **13** (660 mg, 2.0 mmol) in CH_2Cl_2 (14 mL), acetonitrile (14 mL) and H_2O (24 mL), $RuCl_3{\cdot}H_2O$ (24 mg, 0.11 mmol) was added, and then, aqueous NaOCl (195 mL, 5.4% aqueous solution, approx. 142 mmol) was added dropwise. The flask was stopped and the mixture was vigorously stirred at room temperature for 60 h. After a working-up similar to that described in Section 3.1.2, an oily residue was obtained which was dissolved in $CHCl_3$ (5 mL) and treated with cyclohexylamine (2 mL). The obtained solid was filtered, taken in water (5 mL) and the solution was made acidic with 1N HCl. The aqueous solution was extracted with ethyl acetate (3×5 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated in vacuo to give **20** as a white solid (170 mg, 25% yield). An analytical sample of **20** was obtained by crystallization, mp 204–205°C (dec.) (hexane/ethyl acetate, 1:1). IR (KBr) 3500-2400 (max. at 3147, 3065, 3002, 2951, 2901, 2623, 2590, OH st and CH st), 1735 and 1703 (CO st), 1488, 1434, 1379, 1335, 1288, 1249, 1211, 1164, 1125, 1080, 1050, 994, 972, 845, 797, 756, 725, 641 cm^{-1}. ^{1}H NMR (CD_3OD) 1.52 (s, 3H) and 1.54 (s, 3H)[$C(CH_3)_2$], 2.00 [dd, J=7.8 Hz, J'=3.8 Hz, 2H, 4(6)-H_β], 2.12 [dd, J=8.0 Hz, J'=3.5 Hz, 2H, 2(8)-H_β], 2.57 [d, J=8.0 Hz, 2H, 2(8)-H_α], 2.77 [d, J=7.5 Hz, 2H, 4(6)-H_α], 4.87 (s, 2H, mobile H), 7.27 (dt, J=1.3 Hz, J'=7.5 Hz, 1H, Ar-4-H), 7.42 (dt, J=1.5 Hz, J'=7.5 Hz, 1H, Ar-5-H), 7.47 (dd, J=1.0 Hz, J'=8.0 Hz, 1H, Ar-6-H), 7.58 (dd, J=1.3 Hz, J'=7.8 Hz, 1H, Ar-3-H). ^{13}C NMR (CD_3OD) 28.8 [CH_3, (CH_3)$_2$C], 52.9 [CH_2, C2(8)], 54.1 [CH_2, C4(6)], 56.5 (C, C1), 58.3 (C, C5), 90.0 [C, C3(7)], 121.6 [C, $(CH_3)_2C$], 127.6 (CH, Ar-C4), 130.3 (CH, Ar-C3), 130.8 (CH, Ar-C6), 131.6 (CH, Ar-C5), 134.2 (C, Ar-C2), 140.4 (C, Ar-C1), 173.2 (C, Ar-COOH), 175.9 (C, 1-*C*OOH). MS (EI), *m/z* (%): 329 [(M−CH_3)$^+$, 58], 326 [(M−H_2O)$^+$, 16], 269 [(M−C_3H_8O−OH)$^+$, 69], 268 [(M−C_3H_8O−H_2O)$^{\cdot+}$, 31], 251 (47), 223 (42), 165 (54), 115 (51), 69 (60), 59 (57), 57 (79), 55 (100). Anal. calcd for $C_{19}H_{20}O_6{\cdot}1/2H_2O$: C 64.58, H 5.99. Found C 64.67, H 5.91.

3.1.4. Oxidation of 20 to 14. To a solution of **20**·$1/2H_2O$ (120 mg, 0.35 mmol) in CH_2Cl_2 (3 mL), acetonitrile (3 mL) and H_2O (5 mL), $RuCl_3{\cdot}H_2O$ (5 mg, 0.022 mmol) was added, and then aqueous NaOCl (40 mL, 4.25% aqueous solution, approx. 23 mmol) was added dropwise. The flask was stopped and the mixture was vigorously stirred at room temperature for 60 h. The organic layer was separated and the aqueous phase was washed with CH_2Cl_2 (4×10 mL), cooled (ice-bath), made acidic (pH 2–3) with 2N HCl

(2 mL) and extracted with ethyl acetate (4×15 mL). The combined ethyl acetate extracts were dried (Na_2SO_4), filtered and concentrated in vacuo to give **14** (64 mg, 68% yield).

3.1.5. 1,5-Diiodo-3,7-(isopropylidenedioxy)tricyclo [3.3.0.0^{3,7}]octane (15). A suspension of diacid **14** (2.0 g, 7.46 mmol), iodosobenzene diacetate (5.3 g, 16.4 mmol) and iodine (4.17 g, 16.4 mmol) in anhydrous CH_2Cl_2 (100 mL) was irradiated under reflux with a 60 W tungsten lamp for 4 h. The mixture was allowed to cool to room temperature, more iodosobenzene diacetate (5.3 g, 16.4 mmol) and iodine (4.17 g, 16.4 mmol) were added and irradiation under reflux was continued for 18 h more. The cold (room temperature) solution was washed with 10% aqueous solution of sodium thiosulfate (3×30 mL), saturated $NaHCO_3$ aqueous solution (3×30 mL) and brine (2×30 mL), dried (Na_2SO_4), filtered and concentrated in vacuo to give a residue (3.7 g) which was submitted to column chromatography (silica gel, hexane/ethyl acetate mixtures). On elution with hexane/ethyl acetate mixture in the ratio of 96:4, pure **15** (1.57 g, 49% yield) was obtained as a white solid. An analytical sample of **15** was obtained by crystallization, mp 157–158°C (hexane). IR (KBr) 2985, 2940, 2896, 1474, 1374, 1273, 1238, 1202, 1158, 1109, 1059, 980, 899, 851, 821, 797, 752, 679 cm^{-1}. ^{1}H NMR 1.49 [s, 6H, C(CH$_3$)$_2$], 2.26 [d, J=7.5 Hz, 4H, 2(4,6,8)-H$_\beta$], 2.66 [d, J=7.5 Hz, 4H, 2(4,6,8)-H$_\alpha$]. ^{13}C NMR 28.4 [CH$_3$, C(*C*H$_3$)$_2$], 38.7 [C, C1(5)], 61.3 [CH$_2$, C2(4,6,8)], 88.5 [C, C3(7)], 121.4 [C, *C*(CH$_3$)$_2$]. GC/MS (IE), t_r=22.9 min, m/z (%): 417 [(M−CH$_3$)$^+$, 1], 305 [(M−I)$^+$, 97], 247 [(M−I−C$_3$H$_6$O)$^+$, 13], 178 [(M−2I)$^{\cdot+}$, 11], 120 [(M−2I−C$_3$H$_6$O)$^{\cdot+}$, 72], 92 (70), 91 (100). Anal. calcd for $C_{11}H_{14}I_2O_2$: C 30.58, H 3.27, I 58.75. Found C 30.86, H 3.27, I 58.61. In different runs, the yields were in the range 49–53%.

3.1.6. 4,5-Isopropylidenedioxy-1,8-diphenyl-15-oxahexacyclo[6.6.1.1^{2,5}.1^{4,7}.0^{2,7}.0^{9,14}]heptadeca-9,11,13-triene (17). A mixture of **15** (203 mg, 0.47 mmol) and 1,3-diphenylisobenzofuran (152 mg, 0.56 mmol) in anhydrous THF (7.5 mL) was cooled to −78°C and a solution of *t*-butyllithium (1.5 M in pentane, 535 μL, 0.8 mmol) was added dropwise. After stirring for 30 min at this temperature, methanol (2 mL) and water (10 mL) were added and the mixture was extracted with diethyl ether (3×10 mL). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo to give a residue (266 mg), which was submitted to column chromatography (silica gel, mixture of hexane/ethyl acetate in the ratio of 96:4) to give pure **17** (128 mg, 61% yield). The analytical sample was obtained by crystallization, mp 186–187°C (hexane). IR (KBr) 3060, 3032, 2990, 2938, 2889, 1601, 1498, 1474, 1453, 1371, 1348, 1305, 1265, 1246, 1210, 1194, 1155, 979, 886, 859, 764, 743, 717, 697, 678 cm^{-1}. ^{1}H NMR 1.36 [dd, J=3.5 Hz, J'=7.5 Hz, 2H, 3(17)-H$_{syn}$], 1.46 [s, 6H, C(CH$_3$)$_2$], 1.85 [d, J=8.0 Hz, 2H, 6(16)-H$_{anti}$], 1.98 [dd, J=3.5 Hz, J'=7.8 Hz, 2H, 6(16)-H$_{syn}$], 2.03 [d, J=8.0 Hz, 2H, 3(17)-H$_{anti}$], 6.95 [dd, J=3.0 Hz, J'=5.5 Hz, 2H, 11(12)-H], 7.12 [dd, J=3.0 Hz, J'=5.5 Hz, 2H, 10(13)-H], 7.37 [tt, J=7.5 Hz, J'=1.5 Hz, 2H, Ar-H$_{para}$], 7.46 [pseudo t, J=7.5 Hz, 4H, Ar-H$_{meta}$], 7.61 [dd, J=8.5, J'=1.5 Hz, 4H, Ar-H$_{ortho}$]. ^{13}C NMR 28.2 [CH$_3$, (*C*H$_3$)$_2$C], 50.2 [CH$_2$, C6(16)], 50.9 [CH, C3(17)], 59.6 [C, C2(7)], 87.9 [C, C1(8)], 88.8 (C) and 89.4 (C) (C4 and C5), 119.4 [C, *C*(CH$_3$)$_2$], 120.0 [CH, C11(12)], 125.6 [CH, Ar-C$_{ortho}$], 126.9 [CH, C10(13)], 127.6 (CH, Ar-C$_{para}$), 128.4 (CH, Ar-C$_{meta}$), 137.4 (C, Ar-C$_{ipso}$), 146.4 [C, C9(14)]. GC/MS (EI), t_r=36.9 min, m/z (%): 448 (M$^{\cdot+}$, 2), 390 [(M−C$_3$H$_6$O)$^{\cdot+}$, 14], 362 [(M−C$_3$H$_6$O−CO)$^{\cdot+}$, 23], 334 (26), 306 (22), 285 (27), 271 (27), 270 [(C$_{20}$H$_{14}$O)$^{\cdot+}$, 100], 105 (C$_6$H$_5$CO$^+$, 94), 77 (61). Anal. calcd for $C_{31}H_{28}O_3$: C 83.01, H 6.29. Found C 82.99, H 6.37.

3.1.7. 4,5:10,11-Bis(isopropylidenedioxy)pentacyclo [8.2.1.1^{2,5}.1^{4,7}.1^{8,11}]hexadeca-1,7-diene (19). A mixture of freshly cut sodium (460 mg, 20 mmol) in anhydrous 1,4-dioxane (20 mL) was heated under reflux until sodium melted. Then, diiodide **15** (864 mg, 2.0 mmol) was added and the mixture was heated under reflux for 4 h. The resulting suspension was allowed to warm to room temperature and filtered through Celite®. The solid material was washed with $CHCl_3$ (3×10 mL) and the combined organic phases were concentrated in vacuo to give a residue (359 mg). Column chromatography (neutral aluminum oxide, hexane/$CHCl_3$ mixtures) of the above residue furnished, on elution with a mixture hexane/$CHCl_3$ in the ratio of 65:35, pure **19** as a white solid, (225 mg, 63% yield). The analytical sample of **19** was obtained by crystallization, mp >330°C ($CHCl_3$). IR (KBr) 2977, 2931, 2916, 2885, 2855, 1456, 1371, 1311, 1274, 1228, 1208, 1150, 1098, 994, 912, 895, 845, 749, 702, 654 cm^{-1}. ^{1}H NMR (300 MHz) 1.52 [s, 12H, C(CH$_3$)$_2$], 2.47 (d, J=12.5 Hz, 8H) and 3.05 (d, J=12.5 Hz, 8H) [3(6,9,12,13,14,15,16)-H$_\alpha$ and 3(6,9,12,13,14,15,16)-H$_\beta$]. ^{13}C NMR 29.6 [CH$_3$, C(*C*H$_3$)$_2$], 46.1 [CH$_2$, C3(6,9,12,13,14,15,16)], 89.6 [C, C4(5,10,11)], 117.9 [C, *C*(CH$_3$)$_2$], 135.9 [C, C1(2,7,8)]. GC/MS (EI), t_r=29.9 min, m/z (%): 357 [(M+H)$^+$, 18], 356 (M$^{\cdot+}$, 70), 341 [(M−CH$_3$)$^+$, 40], 298 [(M−C$_3$H$_8$O)$^{\cdot+}$, 10], 240 [(M−2C$_3$H$_8$O)$^{\cdot+}$, 47], 212 (49), 184 (76), 170 (48), 169 (100), 155 (43), 141 (47), 129 (43), 128 (45), 91 (64), 77 (44). Anal. calcd for $C_{22}H_{28}O_4$: C 74.13, H 7.92. Found C 74.00, H 7.96.

Acknowledgements

Financial support from Comissionat per a Universitats i Recerca of the Generalitat de Catalunya (project 2001-SGR-00085) is gratefully acknowledged. S. V. thanks to the Ministerio de Ciencia y Tecnología for a fellowship (Programa Ramón y Cajal). We thank the Serveis Científico-Tècnics of the University of Barcelona and particularly Dr M. Feliz and Dr A. Linares for recording the NMR spectra, the Centre de Supercomputació de Catalunya (CESCA) for computational facilities and Ms P. Domènech from the IIQAB (CSIC, Barcelona, Spain) for carrying out the elemental analyses.

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