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Alternative syntheses of the D_{2d} symmetric 1,3,5,7-tetraiodotricyclo[3.3.0.0^{3,7}]octane

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Abstract—Three alternative syntheses of 1,3,5,7-tetraiodotricyclo[3.3.0.0^{3,7}]octane are described. Reaction of this tetraiodide with sodium amalgam in the presence of dienes or with molten sodium in boiling 1,4-dioxane in the absence of trapping agents led to very complex mixtures of products, presumably due to competitive 1,2- and 1,3-deiodination reactions.
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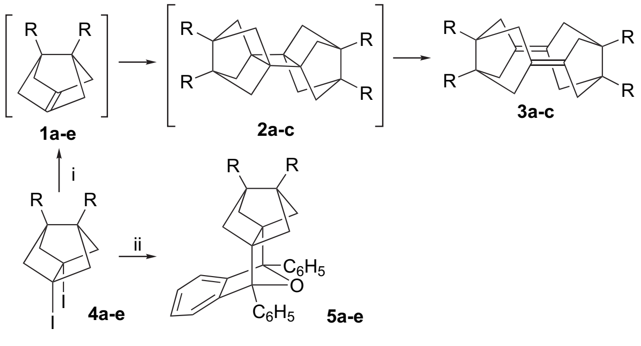
1. Introduction

As a part of our continuing research on pyramidalized alkene chemistry,[1] we have previously described the generation of highly pyramidalized tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene derivatives (**1**) (Scheme 1) by reaction of 1,2-diiodo precursors (**4**) with molten sodium in boiling 1,4-dioxane, sodium amalgam in THF at room temperature or with *t*-BuLi in anhydrous THF at low temperature.[2] All these alkenes were trapped as Diels–Alder adducts with reactive dienes such as 1,3-diphenylisobenzofuran or 11,12-dimethylene-9,10-dihydro-9,10-ethanoanthracene.[3] When the pyramidalized alkenes were generated in the absence of a trapping diene, usually, but not always,[2e] diene dimers (**3**) via cyclobutane dimers (**2**) were obtained.



Scheme 1. Reactivity of highly pyramidalized alkenes **1a**–**e**, where **a**, R=H; **b**, R=Me; **c**, R=–OC(CH$_3$)$_2$O–; **d**, R=–OS(O)$_2$O–; **e**, R=-*o*,*o*′-biphenyl-. (i) Molten sodium, 1,4-dioxane, reflux; (ii) *t*-BuLi, 1,3-diphenylisobenzofuran, THF, −78 °C.

2. Results and discussion

In this article we describe three different syntheses of the D_{2d} symmetric 1,3,5,7-tetraiodotricyclo[3.3.0.0^{3,7}]octane, **6**, a potential precursor of tetraene **12**. Considering our previous experience with derivatives **1**, we reasoned that, as shown in Scheme 2, generation of highly pyramidalized alkene **7**, followed by dimerization to **8**, thermal [2+2] retrocycloaddition to **9**, and further reduction could lead to tetraene **12**. Alternatively, tricyclo[3.3.0.0^{3,7}]oct-1(5),3(7)-diene, **10**, might be generated, which on dimerization might give **11** and after [2+2] retrocycloaddition might lead to the targeted compound **12**. We were aware, however that in the present case, competitive 1,3-deiodination reactions leading to a propellane structure, **13**, could compete with the 1,2-deiodination leading to the pyramidalized alkene **7** (Fig. 1). In fact, UB3LYP/LANL2DZ theoretical calculations predict that propellane **13** is 1.5 kcal mol^{-1} more stable than the highly pyramidalized alkene **7**. In comparing the parent hydrocarbons, UB3LYP/6-31G(d) calculations predict that propellane **14** is 9.0 kcal mol^{-1} more stable than the highly pyramidalized alkene **1a**. However, MP2/6-31G(d) shows that **10** is an energy minimum with pyramidalization angles (Φ=64.1°) and carbon–carbon double bond distance (1.428 Å), quite similar to the previously calculated for alkenes **1a**–**e**.[1a]

We considered of interest to study the possible formation of tetraene **12**, no matter if it took place via the double highly

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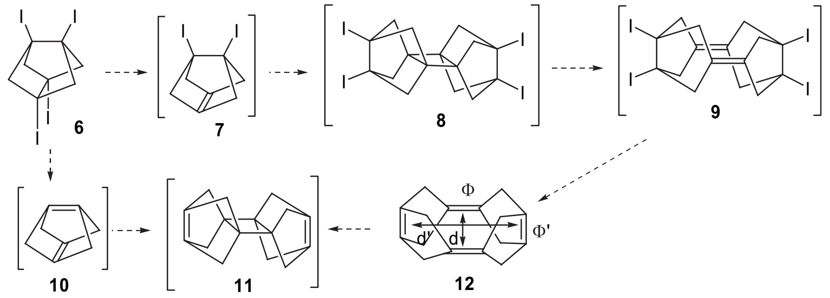


Scheme 2. Possible pathways from **6** to tetraene **12**.

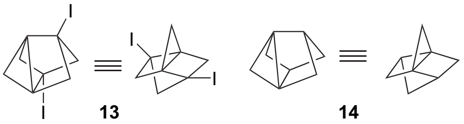
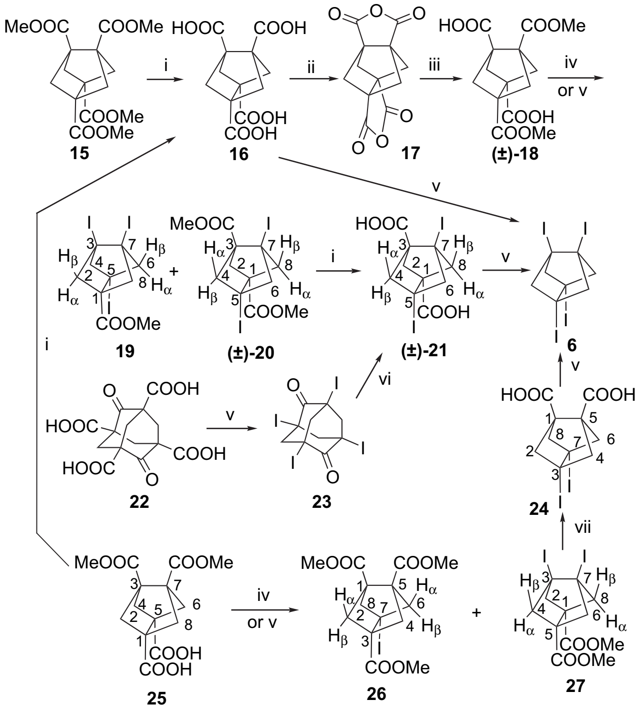


Figure 1. Structures of propellanes **13** and **14**.

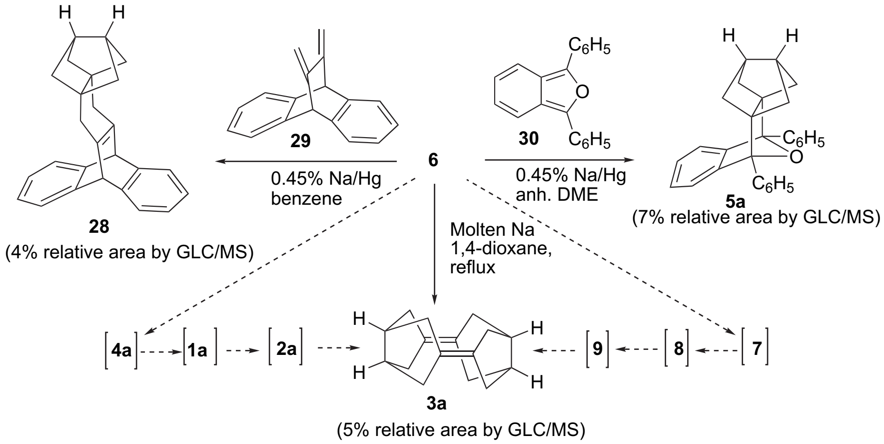
pyramidalized alkene **10** or via the pyramidalized alkene **7**. Tetraene **12**, with its four pyramidalized carbon–carbon double bonds, is a very interesting target. In addition to the pyramidalization-related issues [Φ=26.3° and Φ'=34.1°, as calculated by B3LYP/6-31G(d)], **12** has two pairs of proximal (d=3.619 Å, d'=3.789 Å), parallel double bonds, and π–π orbital interactions are therefore expected to occur.[4] The values of the pyramidalization angles of tetraene **12** suggest that it might be in the limit of isolable pyramidalized alkenes.[1a]

Initially, we used the recently described tetramethyl tricyclo[3.3.0.0^{3,7}]octane-1,3,5,7-tetracarboxylate, **15**, as a potential precursor of tetraiodo derivative **6**.[5] Although, the hydrolysis of tetraester **15** led to **16** in good yield, initial attempts to carry out the iododecarboxylation of tetraacid **16** using the Moriarty modification of the Suárez iododecarboxylation reaction [iodosobenzene diacetate (IBDA), and iodine in benzene or CH_2Cl_2 solution],[6] did not give the expected **6**, most of the starting acid being recovered unchanged. This result was ascribed to the low solubility of tetraacid **16** in both solvents. As an alternative, a stepwise iododecarboxylation reaction was planned. To this end, tetraacid **16** was transformed into bis-anhydride **17** by reaction with acetic anhydride, which on reaction with sodium methoxide in anhydrous methanol gave in good yield diester diacid (±)-**18** (Scheme 3). Iododecarboxylation of (±)-**18** in CH_2Cl_2 provided diiodo diester (±)-**20** in only 16% yield. When diiodo diacid (±)-**21**, obtained in high yield by saponification of (±)-**20**, was subjected to iododecarboxylation, tetraiodo derivative **6** was obtained in 70% yield. While this work was in progress, we found that acetonitrile could be advantageously used as a solvent in the Suárez iododecarboxylation reaction.[2e] When these conditions were applied to diester diacid (±)-**18**, the yield of (±)-**20** rose to 32%. Worthy of note, from this reaction, a small amount (5% yield) of triiodo ester **19** was also isolated, probably formed from the corresponding ester tricarboxylic acid. Moreover, using acetonitrile as a solvent, the direct conversion of tetraacid **16** to **6** was achieved in a modest 15.5% yield. To the best of our knowledge, this is the first time this kind of reaction has been applied to a tetracarboxylic acid. Overall, the direct transformation from **16** to **6** gave a slightly better yield than the five-step sequence going through dianhydride **17** (14.3% yield).



Scheme 3. (i) Concd HCl, AcOH, reflux, **16**: 94% from **15**; 95% from **25**; (±)-**21**: 91%; (ii) Ac_2O, reflux, 77%; (iii) NaOMe, anhyd methanol, reflux, 91%; (iv) IBDA, I_2, CH_2Cl_2, reflux, hν, (±)-**20**: 16%; **26**: 4%; **27**: 16%; (v) IBDA, I_2, acetonitrile, reflux, hν, (±)-**20**: 32%; **19**: 5%; **6**: 15.5% from **16**; 70% from (±)-**21**; 50% from **24**; **23**: 48%; **27**: 49%; (vi) KOH, ethanol, water, reflux, 85.5%; (vii) KOH, methanol, water, reflux, 98%.

As a shorter and higher yielding alternative sequence to tetraiodide **6**, we investigated a second route from the known diester diacid **25**.[5] Double iododecarboxylation of **25** was initially attempted using the Moriarty modification of the Suárez iododecarboxylation reaction in CH_2Cl_2 leading to diiodo diester **27** in 16% yield. Interestingly, iodo triester **26** was also isolated in 4% yield. This compound may arise from partial esterification of **25** by adventitious methyl iodide formed upon iododecarboxylation of acetic acid originated from IBDA. When the reaction was carried out in acetonitrile as the solvent, **27** was isolated in 49% yield. Saponification of **27** gave diacid **24** that on double iododecarboxylation in acetonitrile led to tetraiodo derivative **6**. The overall yield of this second route was 24%.



Scheme 4. Reactions of tetraiodide **6** with sodium amalgam in the presence of dienes **29** and **30** and with molten sodium in boiling 1,4-dioxane.

Unsatisfied with these lengthy and low yield syntheses of tetraiodide **6**, we undertook a third alternative synthesis of this compound from diketo tetraacid **22**, readily obtainable from the well-known Meerwein's ester, a compound easily available in multigram quantities.[7] Fourfold iododecarboxylation of **22** using IBDA and iodine under irradiation in acetonitrile as solvent furnished tetraiodo diketone **23** in 48% (about 84% yield per individual step).

Double Favorskii rearrangement of **23**, under similar conditions to those employed in a related case,[8] gave diiodo diacid (±)-**21** in high yield. Overall, the yield of tetraiodide **6** from diketo tetraacid **22** was 28.7% (11% from Meerwein's ester). Altogether, in spite of the lower yield of the last procedure, it is advantageous over the previous ones due to the availability of the starting Meerwein's ester.

With grams of compound **6** in hand, and in spite of its low solubility in most organic solvents, such as THF or DME, we carried out a preliminary study on the possible generation, trapping, and dimerization of the double highly pyramidalized alkene **10**. Reaction of tetraiodide **6** with *t*-BuLi in anhydrous THF at −78 °C in the presence of 11,12-dimethylene-9,10-dihydro-9,10-ethanoanthracene, **29**, gave a complex mixture of products (GC–MS), most of them derived from the reaction of diene **29** with *t*-BuLi. No product derived from **6** was observed in this mixture. Reaction of **6** with 0.45% sodium amalgam in benzene at room temperature in the presence of diene **29** gave a mixture containing mainly the starting diene and a small amount [4% relative area (r.a.)] of a compound of molecular mass 336, which could correspond to compound **28**. Similarly, reaction of **6** with 0.45% sodium amalgam in anhydrous DME at room temperature in the presence of 1,3-diphenylisobenzofuran, **30**, gave a complex mixture of products, containing mainly (GC–MS), starting diene (12% r.a.), products derived from it, such as 1,3-dihydro-1,3-diphenylisobenzofuran[9] (23% r.a.) and 2-benzoylbenzophenone (8% r.a.),[10] and compound **5a** (7% r.a.). Compound **5a** had been previously obtained by reaction of 1,5-diiodotricyclo[3.3.0.0^{3,7}]octane with *t*-BuLi in the presence of diene **30**.[2b] Also, compound **6** was reacted with molten sodium in boiling 1,4-dioxane in the absence of any trapping agent, thus giving rise to a very complex mixture of products (GC–MS), in which the known compound **3a** was present (5% r.a.).[2b]

These results may be explained by reduction of tetraiodide **6** to the known diiodide **4a**, followed by deiodination to give the highly pyramidalized alkene **1a**, which, as previously described, may be trapped with dienes to give the corresponding Diels–Alder adducts, such as **28** or **5a** or, in the absence of dienes, it may dimerize to give the cyclobutane dimer **2a**, which is then transformed into **3a** (Scheme 4). Alternatively, compound **3a** might be obtained by reduction of tetraiodo dimer **9**, formed as shown in Scheme 2 via the pyramidalized alkene **7** and the corresponding cyclobutane dimer **8**. Similarly, compounds **28** and **5a** could be obtained by reduction of Diels–Alder adducts derived from the highly pyramidalized alkene **7** and dienes **29** and **30**, respectively. We have no evidence in favor of the intermediate formation of the double highly pyramidalized alkene **10**.

The complexity of these reactions could be related to the fact that initial deiodination of **6** could take place in two competitive ways: (i) 1,2-deiodination to give the pyramidalized alkene **7** and (ii) 1,3-deiodination to give propellane **13** (Fig. 1). A study on the reaction of 1,3-diiodotricyclo[3.3.0.0^{3,7}]octane with molten sodium will be published elsewhere.

All of the new compounds herein described were fully characterized by spectroscopic means (IR, ^{1}H, ^{13}C NMR, and MS) and elemental analysis or HRMS. Assignments given for the NMR spectra are based on DEPT, COSY ^{1}H/^{1}H, HETCOR ^{1}H/^{13}C (HSQC and HMBC sequences for one bond and long range heterocorrelations, respectively), and NOESY experiments for selected compounds. Moreover, for tetraiodide **6**, an X-ray diffraction analysis was carried out.[11] Interestingly, **6** has a density of 3.22 g cm^{-3} and a bond length between the vicinal bridgehead carbon atoms of 1.625(7) Å.

3. Conclusions

In conclusion, three different approaches to the D_{2d} symmetric 1,3,5,7-tetraiodotricyclo[3.3.0.0^{3,7}]octane, **6**, have been developed, the key-step being a modified iododecarboxylation procedure, which uses acetonitrile as the solvent and has allowed the tetraiododecarboxylation of tetraacids **16** and **22**, the last one in an acceptable 48% yield. Reactions of **6** with *t*-BuLi at low temperature have the drawback of low solubility of this compound in most organic solvents. Reactions of **6** with sodium amalgam or molten sodium seem to have generated a pyramidalized alkene, probably **1a**, which was trapped as Diels–Alder adducts and dimerized to **3a**. The complexity of these reactions may be understood by taking into account competitive 1,3-deiodination and 1,2-deiodination processes.

4. Computational details

Quantum-mechanical calculations were carried out at the unrestricted Becke's three-parameter hybrid functional with Lee, Yang and Parr correlation functional (UB3LYP) level,[12] using the 6-31G(d) basis set for **12**,[13] and the LANL2DZ basis set for **7** and **13**,[14] or at the restricted Møller–Plesset (MP2) level,[15] using the 6-31G(d) basis set for **10**, as implemented in Gaussian 03 on a Compaq HPC320 computer.[16] Geometry optimizations were undertaken using appropriate symmetry constraints and default convergence limits. The minimum energy nature of the optimized structures was verified from vibrational frequency analysis.

5. Experimental

5.1. 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: ^1H NMR (500 MHz, Varian VXR 500), ^{13}C NMR (75.4 MHz, Varian Gemini 300). ^1H and ^{13}C NMR chemical shifts (δ) are reported in parts per million with respect to internal tetramethylsilane (TMS). The multiplicity of the signals is: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; or their combinations. Assignments given for the NMR spectra are based on DEPT, COSY $^1H/^1H$, HETCOR $^1H/^{13}C$ (HSQC and HMBC sequences for one bond and long range heterocorrelations, respectively) and NOESY experiments for selected compounds. Diastereotopic methylene protons in tricyclo[3.3.0.0^{3,7}]octane derivatives are referred as H_α/H_β as shown in the corresponding structures. IR spectra were recorded on a FT–IR Perkin–Elmer spectrometer, model 1600; only the more intense absorption bands are given. 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 [conditions: 10 psi; initial temperature: 35 °C (2 min); then heating at a rate of 8 °C min^{-1} till 300 °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. HRMS were performed on a Micromass Autospec spectrometer. Neutral aluminum oxide (MN), Brockmann activity 1 or silica gel SDS 60 (35–70 μm) was utilized for the standard and flash column chromatography, respectively. NMR and routine MS spectra were performed at the *Serveis Científico-Tècnics* of the University of Barcelona, while high resolution mass spectra and elemental analyses were carried out at the Mass Spectrometry Laboratory of the University of Santiago de Compostela (Spain) and at the Microanalysis Service of the IIQAB (C.S.I.C, Barcelona, Spain), respectively.

5.2. Tricyclo[3.3.0.0^{3,7}]octane-1,3,5,7-tetracarboxylic acid (16)

5.2.1. From tetramethyl tricyclo[3.3.0.0^{3,7}]octane-1,3,5,7-tetracarboxylate (15). A mixture of tetraester **15** (2.41 g, 7.08 mmol), concd HCl (57 mL), and glacial AcOH (57 mL) was heated under reflux for 15 h. The mixture was allowed to cool to room temperature and the precipitated solid was filtered under vacuum and washed with AcOEt (40 mL) to give tetraacid **16** (1.80 g) as a white solid. The combined filtrate and washings were concentrated in vacuo to give a residue (1.36 g), which was washed with AcOEt (20 mL) to give more tetraacid **16** (98 mg, global yield 94%), mp>300 °C (dec); IR (KBr) ν 3500–2300 (max at 3008, 2910, 2722, 2631, 2563), 1690, 1418, 1316, 1272, 1256 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ: 2.23 [s, 8H, 2(4,6,8)-H_2], 4.96 [br s, 4H, 1(3,5,7)-COO*H*]; ^{13}C NMR (CD_3OD) δ: 53.5 [CH_2, C2(4,6,8)], 59.1 [C, C1(3,5,7)], 174.7 (C, *C*OOH). MS (EI), *m*/*z* (%): 267 [$(M-OH)^+$, 2], 248 [$(M-2H_2O)^{\bullet+}$, 3], 238 [$(M-HCO_2H)^{\bullet+}$, 3], 220 [$(M-HCO_2H-H_2O)^{\bullet+}$, 66], 192 [$(M-2HCO_2H)^{\bullet+}$, 21], 181 (35), 176 (33), 175 [$(M-2HCO_2H-OH)^+$, 24], 150 (27), 149 (39), 148 [$(M-2HCO_2H-CO_2)^{\bullet+}$, 49], 147 (24), 137 (45), 132 (30), 131 (28), 119 (33), 105 (54), 104 (52), 103 (83), 91 (50), 79 (39), 78 (43), 77 (96), 65 (100). Elemental analysis calcd for $C_{12}H_{12}O_8$ (284.22): C 50.71, H 4.26. Found: C 50.51, H 4.30.

5.2.2. From 3,7-bis(methoxycarbonyl)tricyclo[3.3.0.0^{3,7}]-octane-1,5-dicarboxylic acid (25). Following the above procedure, starting from diacid **25** (801 mg, 2.57 mmol), tetraacid **16** (675+18 mg, 95% total yield) was obtained.

5.3. 5,11-Dioxapentacyclo[5.5.1.1^{3,9}.0^{1,9}.0^{3,7}]tetradecane-4,6,10,12-tetrone (17)

A mixture of tetraacid **16** (1.67 g, 5.88 mmol) and Ac_2O (70 mL) was heated under reflux for 2 h. The mixture was allowed to cool to room temperature, concentrated under reduced pressure to give anhydride **17** as a brown solid (1.43 g), which was sublimed at 240–250 °C/1 Torr, providing pure **17** (1.12 g, 77% yield) as a white solid, mp>300 °C (dec); IR (KBr) ν 1835, 1783, 1271, 1248, 939 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ: 2.77 [s, 2(8,13,14)-H_2]; ^{13}C NMR (DMSO-d_6) δ: 50.2 [C, C1(3,7,9)], 58.9 [CH_2, C2(8,13,14)], 168.1 [C, C4(6,10,12)]. MS (EI), *m*/*z* (%): 249 [$(M+H)^+$, 1], 204 [$(M-CO_2)^{\bullet+}$, 95], 176 [$(M-CO_2-CO)^{\bullet+}$, 24], 150 (37), 148 (22), 132 [$(M-2CO_2-CO)^{\bullet+}$, 33], 131 (26), 105 (26), 104 [$(M-2CO_2-2CO)^{\bullet+}$, 96], 103 (69), 92 (31), 91 (30), 78 (90), 77 (54), 63 (45), 52 (65), 51 (100). Elemental analysis calcd for $C_{12}H_8O_6$ (248.19): C 58.07, H 3.25. Found: C 57.75, H 3.25.

5.4. 5,7-Bis(methoxycarbonyl)tricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylic acid [(±)-18]

To a mixture of anhydride **17** (1.08 g, 4.35 mmol) in anhydrous MeOH (70 mL), solid NaOMe (2.35 g, 43.5 mmol) was added and the mixture was heated under reflux for 19 h. The solution was concentrated in vacuo to dryness and the residue was taken in water (50 mL). The aqueous solution was washed with AcOEt (2×9 mL), made acidic with concd HCl (5 mL), and the precipitated solid was filtered, washed with water (3×3 mL), and dried under vacuum to constant weight, to give pure bis-hemiester (±)-**18** (988 mg). The filtrate was extracted with AcOEt (4×30 mL), and the combined organic extracts were dried with anhydrous Na_2SO_4, and concentrated under reduced pressure to give more product (330 mg), which was crystallized from a mixture of AcOEt/*n*-pentane to give pure (±)-**18** (247 mg, total yield 91%), mp 219–221 °C (AcOEt/*n*-pentane); IR (KBr) ν 3700–2400 (max at 3549, 3004, 2958, 2845, 2710, 2640, 2565), 1712, 1443, 1335, 1309, 1281, 1239, 1145, 1089 cm^{-1}; ^{1}H NMR (CD_3OD) δ: 2.19–2.27 [complex signal, 8H, 2-H_2, 4(8)-H_2, and 6-H_2], 3.68 [s, 6H, 5(7)-$COOCH_3$], 4.86 [br s, 2H, 1(3)-COOH]; ^{13}C NMR (CD_3OD) δ: 52.4 [CH_3, 5(7)-COO*C*H_3], 52.9 (CH_2, C6), 53.2 [CH_2, C4(8)], 53.6 (CH_2, C2), 58.6 [C, C1(3)], 59.3 [C, C5(7)], 173.1 [C, 5(7)-*C*$OOCH_3$], 174.3 [C, 1(3)-*C*OOH]. MS (EI), *m*/*z* (%): 313 [$(M+H)^+$, 2], 295 [$(M-OH)^+$, 6], 281 [$(M-CH_3O)^+$, 34], 248 [$(M-2CH_3OH)^{\bullet+}$, 26], 234 [$(M-HCOOCH_3-H_2O)^{\bullet+}$, 100], 220 [$(M-HCOOCH_3-CH_3OH)^{\bullet+}$, 54], 209 (43), 195 (44), 175 (43), 151 (43), 147 (33), 119 (44), 103 (57), 91 (31), 77 (58), 65 (39), 59 [$(COOCH_3)^+$, 52]. Elemental analysis calcd for $C_{14}H_{16}O_8\cdot 0.5H_2O$ (321.28): C 52.34, H 5.33. Found: C 52.28, H 5.19.

5.5. Dimethyl 5,7-diiodotricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylate [(±)-20] and methyl 3,5,7-triiodotricyclo[3.3.0.0^{3,7}]octane-1-carboxylate (19)

A mixture of bis-hemiester (±)-**18** (700 mg, 2.24 mmol), iodine (1.25 g, 4.93 mmol), and iodosobenzene diacetate (IBDA, 1.62 g, 98% content, 4.93 mmol) in anhydrous acetonitrile (50 mL) was irradiated under reflux with a tungsten 100 W lamp in an argon atmosphere for 4 h. More iodine (1.25 g, 4.93 mmol) and IBDA (1.62 g, 4.93 mmol) were added and irradiation under reflux was continued for 20 h more. The resulting solution was concentrated under reduced pressure to dryness, the residue was taken in CH_2Cl_2 (100 mL), and the organic solution was washed with aqueous $Na_2S_2O_3$ solution (10%, 3×50 mL), saturated aqueous $NaHCO_3$ solution (3×50 mL), and brine (2×50 mL). Evaporation of the solvent from the dried organic phase (anhydrous Na_2SO_4) under reduced pressure gave a residue (430 mg), which was subjected to column chromatography [silica gel (21 g), hexane/AcOEt mixture]. On elution with hexane/AcOEt in the ratio of 45:1 (80 mL), triiodo ester **19** (60 mg, 5% yield) was obtained as a white solid. On elution with hexane/AcOEt in the ratio of 30:1 (400 mL), diiodo diester (±)-**20** (337 mg, 32% yield) was obtained as a white solid. The analytical sample of (±)-**20** was obtained by crystallization from AcOEt, mp 154–155 °C; TLC (silica gel), R_f 0.44 [hexane/AcOEt (3:1)]; IR (KBr) ν 1727, 1320, 1269, 1228 cm^{-1}; ^{1}H NMR δ: 2.180 [dt, $J=10.2$ Hz, $J'=2.0$ Hz, 2H, 4(8)-H_β], 2.182 (t, $J=2.0$ Hz, 2H, 2-H_2), 2.54 [dt, $J=10.2$ Hz, $J'=2.0$ Hz, 2H, 4(8)-H_α], 2.55 (t, $J=2.0$ Hz, 2H, 6-H_2), 3.78 [s, 6H, 1(3)-$COOCH_3$]; ^{13}C NMR δ: 28.5 [C, C5(7)], 50.4 (CH_2, C2), 52.2 [CH_3, 1(3)-COO*C*H_3], 60.0 [CH_2, C4(8)], 60.8 [C, C1(3)], 68.7 (CH_2, C6), 169.8 [C, 1(3)-*C*$OOCH_3$]. MS (EI), *m*/*z* (%): 349 [$(M-I)^+$, 6], 317 [$(M-I-CH_3OH)^+$, 38], 289 [$(M-I-HCOOCH_3)^+$, 45], 190 (28), 189 (25), 162 [$(M-HCOOCH_3-2I)^{\bullet+}$, 76], 131 (25), 104 (31), 103 [$(M-HCOOCH_3-2I-COOCH_3)^+$, 100], 102 (45), 91 (33), 78 (36), 77 (75), 59 [$(COOCH_3)^+$, 83]. MS (CI, CH_4), *m*/*z* (%): 477 [$(M+H)^+$, 44], 445 [$(M-CH_3O)^+$, 17], 417 [$(M-COOCH_3)^+$, 15], 350 (18), 349 [$(M-I)^+$, 69], 318 (32), 317 [$(M-I-CH_3OH)^+$, 82], 291 (21), 290 (57), 289 [$(M-I-HCOOCH_3)^+$, 100], 221 [$(M-I-IH)^+$, 46], 191 (35), 190 (48), 189 [$(M-I-IH-CH_3OH)^+$, 48], 163 [$(M-COOCH_3-2I)^+$, 49], 162 (52), 103 [$(M-HCOOCH_3-2I-COOCH_3)^+$, 42]. HRMS calcd for $(C_{12}H_{14}I_2O_4+H)^+$: 476.9060. Found: 476.9071. The analytical sample of **19** was obtained by crystallization from diethyl ether, mp 120–122 °C; IR (KBr) ν 1732, 1314, 1265, 1227 cm^{-1}; ^{1}H NMR δ: 2.31 [m, 2H, 2(8)-H_β], 2.53 [m, 2H, 4(6)-H_α], 2.56 [m, 2H, 2(8)-H_α], 2.65 [m, 2H, 4(6)-H_β], 3.79 [s, 3H, $COOCH_3$]; ^{13}C NMR δ: 27.9 (C, C5), 39.9 [C, C3(7)], 52.3 [CH_3, COO*C*H_3], 60.5 [CH_2, C2(8)], 61.2 (C, C1), 69.1 [CH_2, C4(6)], 168.7 [C, *C*$OOCH_3$]. MS (EI), *m*/*z* (%): 544 ($M^{\bullet+}$, <1), 417 [$(M-I)^+$, 1], 389 [$(M-I-CO)^+$, 2], 357 [$(M-I-HCOOCH_3)^+$, 2], 290 (27), 289 [$(M-I-IH)^+$, 99], 163 (50), 162 [$(M-HI-2I)^{\bullet+}$, 90], 104 (51), 103 [$(M-HCOOCH_3-3I)^+$, 100], 78 (31), 77 (49), 59 [$(COOCH_3)^+$, 25]. HRMS calcd for $(C_{10}H_{11}I_3O_2)^{\bullet+}$: 543.7893. Found: 543.7896. When this reaction was carried out in CH_2Cl_2 as solvent, the yield of (±)-**20** was 16%.

5.6. 5,7-Diiodotricyclo[3.3.0.0^{3,7}]octane-1,3-dicarboxylic acid [(±)-21]

5.6.1. From diiodo diester (±)-20. Hydrolysis of diiodo diester (±)-**20** was carried out as described before for the preparation of tetraacid **16**, from (±)-**20** (357 mg, 0.75 mmol), concd HCl (3 mL), and glacial AcOH (3 mL). Diiodo diacid (±)-**21** (204 mg of precipitated material and 102 mg of extracted product, 91% total yield) was obtained as a white solid, mp>300 °C (dec); IR (KBr) ν 3500–2200 (max at 3456, 3005, 2896, 2718, 2609, 2522), 1698, 1423, 1314, 1271, 1237 cm^{-1}; ^{1}H NMR (CD_3OD) δ: 2.16 (t, $J=2.0$ Hz, 2H, 2-H_2), 2.20 [dt, $J=10.0$ Hz, $J'=2.0$ Hz, 2H, 4(8)-H_β], 2.50 [dt, $J=10.0$ Hz, $J'=2.0$ Hz, 2H, 4(8)-H_α], 2.55 (br s, 2H, 6-H_2), 4.86 [br s, 2H, 1(3)-COOH]; ^{13}C NMR (CD_3OD) δ: 29.3 [C, C5(7)], 51.5 (CH_2, C2), 61.5 [CH_2, C4(8)], 62.4 [C, C1(3)], 70.5 (CH_2, C6), 173.0 [C, 1(3)-COOH]. MS (EI), *m*/*z* (%): 448 ($M^{\bullet+}$, 1), 430 [$(M-H_2O)^{\bullet+}$, 2], 321 [$(M-I)^+$, 4], 303 [$(M-I-H_2O)^+$, 100], 275 [$(M-HCO_2H-I)^+$, 64], 176 [$(M-2I-H_2O)^{\bullet+}$, 39], 175 (23), 149 (32), 148 [$(M-HCO_2H-2I)^{\bullet+}$, 78], 147 (21), 105 (34), 104 (47), 103 (54), 77 (61). Elemental analysis calcd for $C_{10}H_{10}I_2O_4$ (447.99): C 26.81, H 2.25, I 56.65. Found: C 26.80, H 2.07, I 56.26.

5.6.2. From 1,3,5,7-tetraiodoadamantane-2,6-dione (23). Tetraiodo tetrone **23** (9.66 g, 14.5 mmol) was added to a solution of 85% KOH (11.1 g, 168 mmol) in EtOH (30 mL) and water (30 mL) and the mixture was heated under reflux for 4 h. The resulting brown solution was cooled in an ice-bath, made acidic to pH≈1–2 with 5 N HCl (30 mL), with formation of a white solid. The mixture was concentrated to dryness under reduced pressure and the brown residue was dissolved in a mixture of AcOEt (600 mL) and water (150 mL). The organic phase was separated and the aqueous one was extracted with AcOEt (3×100 mL). The combined organic phase and extracts were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure to give an orange residue (6.03 g), which was washed with a small amount of AcOEt to give pure diiodo diacid (±)-**21** (5.54 g, 85.5% yield), as a white solid.

5.7. 1,3,5,7-Tetraiodotricyclo[3.3.0.0^{3,7}]octane (6)

5.7.1. From tetraacid 16. This reaction was carried out in a similar manner to that described for the preparation of diiodo diester (±)-**20**. From **16** (129 mg, 0.45 mmol), iodine [2×(506 mg, 1.99 mmol)], and IBDA [2×(655 mg, 1.99 mmol)] in anhydrous acetonitrile (10 mL), tetraiodo derivative **6** (43 mg, 15.5% yield) was obtained, after washing the obtained yellow solid (71 mg) with diethyl ether, as a white solid very poorly soluble in most of the common organic solvents. When this reaction was carried out in CH_2Cl_2, no tetraiodo compound was isolated, the starting tetraacid being mainly recovered.

5.7.2. From diiodo diacid (±)-21. This reaction was carried out as described for the preparation of diiodo diester (±)-**20**. From (±)-**21** (244 mg, 0.54 mmol), iodine [2×(304 mg, 1.2 mmol)], and IBDA [2×(393 mg, 1.2 mmol)] in anhydrous acetonitrile (11 mL), tetraiodo derivative **6** (230 mg, 70% yield) was obtained, as a white solid.

5.7.3. From diiodo diacid 24. This reaction was carried out in a similar manner to that described for the preparation of diiodo diester (±)-**20**, using a lower excess of iodine (2.5+0.55 equiv) and IBDA (2.5+0.55 equiv). From diiodo diacid **24** (500 mg, 1.11 mmol), after the usual workup, a residue (460 mg) was obtained, which was subjected to column chromatography [flash silica gel (10 g), hexane/AcOEt mixture]. On elution with hexane, tetraiodo compound **6** (340 mg, 50% yield) was obtained as a white solid. The analytical sample was obtained by crystallization from CH_2Cl_2, mp 305–306 °C; IR (KBr) ν 1469, 1263, 1227, 989, 952, 867 cm^{-1}; ^{1}H NMR (300 MHz) δ: 2.64 [s, 2(4,6,8)-H_2]; ^{13}C NMR δ: 39.7 [C, C1(3,5,7)], 69.5 [CH_2, C2(4,6,8)]. MS (EI), *m/z* (%): 612 ($M^{\bullet+}$, 1), 358 [$(M-2I)^{\bullet+}$, 39], 231 [$(M-3I)^+$, 42], 104 [$(M-4I)^{\bullet+}$, 100], 103 (29), 78 (23), 77 (20). Elemental analysis calcd for $C_8H_8I_4$ (611.77): C 15.71, H 1.32, I 82.98. Found: C 15.87, H 1.34, I 83.03.

5.8. 1,3,5,7-Tetraiodoadamantane-2,6-dione (23)

A mixture of 2,6-dioxoadamantane-1,3,5,7-tetracarboxylic acid (**22**) (4.74 g, 13.93 mmol), iodine (15.56 g, 61.3 mmol), and iodosobenzene diacetate (IBDA, 20.14 g, 98% content, 61.3 mmol) in anhydrous acetonitrile (280 mL) was irradiated under reflux with two 100 W tungsten lamps in an argon atmosphere for 4 h. More iodine (15.56 g, 61.3 mmol) and IBDA (20.14 g, 61.3 mmol) were added and irradiation under reflux was continued for 20 h more. The mixture was allowed to cool to room temperature and the solvent was eliminated to dryness under reduced pressure. The residue was taken in AcOEt (450 mL) and the organic solution was washed with aqueous $Na_2S_2O_3$ solution (10%, 3×150 mL), saturated aqueous $NaHCO_3$ solution (3×150 mL), and brine (2×150 mL). Evaporation of the solvent from the dried organic phase (anhydrous Na_2SO_4) under reduced pressure gave a residue from which iodobenzene was distilled off at 100 °C/1–2 Torr. The residue (6.68 g) was taken in AcOEt (250 mL) and the organic solution was dried overnight with P_2O_5 (15 g). The mixture was filtered, the solid material was washed with AcOEt (200 mL), and the solvent was eliminated from the combined filtrate and washing under reduced pressure to give a light orange solid. Washing this solid with a small amount of diethyl ether, tetraiodo dione **23** (4.45 g, 48% yield) was obtained as a white solid. An analytical sample was obtained by sublimation at 220–230 °C/1 Torr, mp 307–308 °C; IR (KBr) ν 1736, 765, 661, 634 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.72 [s, 4(8,9,10)-H_2]; ^{13}C NMR (DMSO-d_6) δ: 46.6 [C, C1(3,5,7)], 62.2 [CH_2, C4(8,9,10)], 193.9 [C, C2(6)]. MS (EI), *m/z* (%): 668 ($M^{\bullet+}$, 6), 541 [$(M-I)^+$, 29], 513 [$(M-I-CO)^+$, 5], 386 [$(M-2I-CO)^{\bullet+}$, 37], 259 [$(M-3I-CO)^+$, 52], 231 [$(M-3I-2CO)^+$, 12], 132 [$(M-4I-CO)^{\bullet+}$, 32], 104 [$(M-4I-2CO)^{\bullet+}$, 100], 103 (76), 78 (82), 77 (74), 63 (45), 52 (44), 51 (86). HRMS calcd for $(C_{10}H_8I_4O_2)^{\bullet+}$: 667.6703. Found: 667.6706.

5.9. Dimethyl 3,7-diiodotricyclo[3.3.0.0^{3,7}]octane-1,5-dicarboxylate (27) and trimethyl 7-iodotricyclo-[3.3.0.0^{3,7}]octane-1,3,5-tricarboxylate (26)

This reaction was carried out as described for the preparation of diiodo diester (±)-**20**. From the known[5] diacid **25** (3.90 g, 12.5 mmol), iodine [2×(6.99 g, 27.5 mmol)], and IBDA [2×(9.03 g, 27.5 mmol)], after the usual workup, a residue (9.19 g) was obtained, which was subjected to column chromatography [flash silica gel (30 g), hexane/AcOEt mixture]. On elution with hexane/AcOEt in the ratio of 80:20, diiodo diester **27** (2.90 g, 49% yield) was obtained as a white solid. An analytical sample was obtained by crystallization from diethyl ether, mp 165.6–166.4 °C; TLC (silica gel), R_f 0.35 [hexane/AcOEt (3:1)]; IR (KBr) ν 1746, 1729 1435, 1304, 1270, 1215, 1131, 1081, 963, 946 cm^{-1}; ^{1}H NMR (300 MHz) δ: 2.48 [s, 8H, 2(4,6,8)-H_α and 2(4,6,8)-H_β], 3.70 [s, 6H, 1(5)-$COOCH_3$]; ^{13}C NMR δ: 41.0 [C, C3(7)], 52.3 [CH_3, 1(5)-COO*C*H$_3$], 58.8 [C, C1(5)], 61.4 [CH_2, C2(4,6,8)], 168.9 [C, 1(5)-*C*OOCH$_3$]. MS (EI), *m/z* (%): 476 ($M^{\bullet+}$, 1), 444 [$(M-CH_3OH)^{\bullet+}$, 14], 317 [$(M-I-CH_3OH)^+$, 23], 289 [$(M-I-HCOOCH_3)^+$, 71], 163 (22), 162 [$(M-HCOOCH_3-2I)^{\bullet+}$, 100], 150 (23), 131 (16), 104 (20), 103 (68), 102 (23), 77 (39), 59 [$(COOCH_3)^+$, 39]. Elemental analysis calcd for $C_{12}H_{14}I_2O_4$ (476.05): C 30.28, H 2.96, I 53.32. Found: C 30.22, H 2.94, I 53.42.

When the above reaction was carried out in a similar way but using CH_2Cl_2 instead of acetonitrile as the solvent, from diacid **25** (189 mg, 0.61 mmol), after the usual workup, a residue (123 mg) was obtained, which was subjected to column chromatography [silica gel (3.5 g), hexane/AcOEt mixture]. On elution with hexane/AcOEt in the ratio of 30:1 (240 mL), diiodo diester **27** (46 mg, 16% yield) was obtained as a white solid. On elution with hexane/AcOEt in the ratio of 10:1 (110 mL), iodo triester **26** (10 mg, 4% yield) was obtained as a white solid. An analytical sample of **26** was obtained by crystallization from diethyl ether, mp 134–135 °C; TLC (silica gel), R_f 0.19 [hexane/AcOEt (3:1)]; IR (KBr) ν 1731, 1437, 1336, 1299, 1272, 1219 cm^{-1}; ^{1}H NMR δ: 2.10 [m, 2H, 2(4)-H_α], 2.36 [m, 2H, 2(4)-H_β], 2.39 [m, 2H, 6(8)-H_β], 2.49 [m, 2H, 6(8)-H_α], 3.70 [s, 6H, 1(5)-$COOCH_3$], 3.80 (s, 3H, 3-$COOCH_3$); ^{13}C NMR (50.3 MHz) δ: 30.0 (C, C7), 51.3 [CH_2, C2(4)], 52.1 (CH_3, 3-COO*C*H_3), 52.2 [CH_3, 1(5)-COO*C*H_3], 58.1 [C, C1(5)], 60.5 (C, C3), 60.9 [CH_2, C6(8)], 170.1 [C, 1(5)-*C*$OOCH_3$], 170.8 (C, 3-*C*$OOCH_3$). MS (EI), *m/z* (%): 377 [$(M-CH_3O)^+$, 11], 348 [$(M-HCO_2CH_3)^{\bullet+}$, 21], 316 [$(M-CH_3OH-HCOOCH_3)^{\bullet+}$, 84], 309 (75), 289 [$(M-COOCH_3-HCOOCH_3)^+$, 18], 277 (29), 221 [$(M-HCOOCH_3-I)^+$, 51], 189 [$(M-HCOOCH_3-CH_3OH-I)^+$, 100], 182 (47), 162 (54), 161 [$(M-2HCOOCH_3-I)^+$, 88], 150 (49), 133 (38), 119 (30), 103 [$(M-HCOOCH_3-2I-COOCH_3)^{\bullet+}$, 75], 91 (34), 77 (64), 59 [$(COOCH_3)^+$, 100]. HRMS calcd for $(C_{14}H_{17}IO_6)^{\bullet+}$: 408.0070. Found: 408.0063. From the aqueous phase, after acidification with 10% HCl (5 mL), extraction with AcOEt (7×10 mL), and concentration of the dried organic extracts, starting diacid **25** (83 mg, 44% yield) was recovered.

5.10. 3,7-Diiodotricyclo[3.3.0.0^{3,7}]octane-1,5-dicarboxylic acid (24)

A mixture of diester **27** (730 mg, 1.53 mmol) and a solution of KOH (10%) in MeOH (9 mL) was heated under reflux for 3 h. Water (7 mL) was added and heating under reflux was continued for 3 h more. The organic solvent was distilled off under reduced pressure and the aqueous phase was made acidic with aqueous HCl (10%, 8 mL). The precipitated solid was filtered, thoroughly washed with water (3×8 mL), and dried with P_2O_5 under reduced pressure to give diiodo diacid **24** (680 mg, 98% yield). The analytical sample was obtained by crystallization from a mixture of AcOEt/*n*-pentane in the ratio of 1:1, mp>280 °C (dec). IR (KBr) 3400−2300 (max at 3092, 2992, 2942, 2713, 2613), 1715 cm^{-1}; ^{1}H NMR (CD_3OD) δ: 2.43 [d, J=9.0 Hz, 4H], 2.49 [d, J=9.0 Hz, 4H, 2(4,6,8)-H_α and 2(4,6,8)-H_β], 4.90 [s, 2H, 1(5)-COOH]; ^{13}C NMR (CD_3OD) δ: 42.3 [C, C3(7)], 60.4 [C, C1(5)], 62.7 [CH_2, C2(4,6,8)], 172.2 [C, 1(5)-COOH]. MS (EI), *m/z* (%): 449 [$(M+H)^+$, 2], 448 ($M^{\bullet+}$, 1), 430 [$(M-H_2O)^{\bullet+}$, 8], 403 [$(M-COOH)^+$, 5], 358 [$(M-2COOH)^{\bullet+}$, 14], 304 (16), 303 [$(M-I-H_2O)^+$, 18], 276 (77), 275 [$(M-I-HCOOH)^+$, 89], 231 [$(M-I-2COOH)^+$, 31], 150 (33), 149 (76), 148 (76), 105 (42), 104 [$(M-2I-2COOH)^{\bullet+}$, 100], 103 (56), 78 (51), 77 (63). Elemental analysis calcd for $C_{10}H_{10}I_2O_4$ (448.00): C 26.81, H 2.25, I 56.65. Found: C 27.19, H 2.32, I 56.13.

5.11. Reaction of tetraiodide 6 with *t*-BuLi in the presence of 11,12-dimethylene-9,10-dihydro-9,10-ethanoanthracene (29)

To a stirred and cold (−78 °C) suspension of tetraiodide **6** (100 mg, 0.163 mmol) and diene **29** (83 mg, 0.36 mmol) in anhydrous THF (5 mL) maintained under an argon atmosphere, a solution of *t*-BuLi in pentane (1.5 M, 0.4 mL, 0.6 mmol) was added dropwise. After stirring for 30 min at −78 °C, the mixture was allowed to heat to room temperature. Methanol (1 mL) and water (5 mL) were added and the mixture was extracted with diethyl ether (3×10 mL). The combined organic phases were dried (anhydrous Na_2SO_4) and concentrated in vacuo to give a yellowish residue (172 mg), which when analyzed by GC–MS showed the presence of four components: (i) starting diene **29** [molecular ion: *m/z*=230, rt 23.2 min, 14.3% relative area (r.a.)]; (ii) product of addition of C_4H_{10} to the starting diene (rt 25.3 min, 29.6% r.a.), MS *m/z* (%): 288 ($M^{\bullet+}$, 46), 232 (50), 231 [$(M-C_4H_9)^+$, 100], 217 (61), 216 (69), 215 (60), 178 [$(C_{14}H_{10})^{\bullet+}$, 46], 57 (20); (iii) product of double addition of C_4H_9 to the starting diene (rt 27.4 min, 46.9% r.a.), MS *m/z* (%): 344 ($M^{\bullet+}$, 24), 288 (13), 232 (29), 231 (94), 178 [$(C_{14}H_{10})^{\bullet+}$, 31], 57 (100); (iv) product of addition of C_4H_9 and C_4H_7O (tetrahydrofuryl) to the starting diene (rt 25.3 min, 9.2% r.a.), MS *m/z* (%): 358 ($M^{\bullet+}$, 5), 274 (5), 231 (7), 178 [$(C_{14}H_{10})^{\bullet+}$, 12], 71 [$(C_4H_7O)^+$, 100].

5.12. Reaction of tetraiodide 6 with 0.45% sodium amalgam in the presence of diene 29

To a mixture of 0.45% sodium amalgam [from Na (97 mg, 4.24 mmol) and Hg (21.6 g, 108 mmol)] and diene **29** (90 mg, 0.39 mmol) in anhydrous benzene (10 mL) kept under an argon atmosphere, solid tetraiodide **6** (100 mg, 0.163 mmol) was added at once and the reaction mixture was stirred overnight at room temperature. The mixture was filtered through a pad of Celite® and the residue was thoroughly washed with AcOEt (3×10 mL). Concentration of the combined filtrate and washings under reduced pressure gave a residue (194 mg) containing inorganic material, which was extracted with CH_2Cl_2 (20 mL). Elimination of the solvent from the extract in vacuo gave a new residue (113 mg), which when analyzed by GC–MS showed the presence of two main components: (i) starting diene **29** (rt 23.2 min, 95% r.a.) and (ii) a product (rt 31.5 min, 4% r.a.), whose MS spectrum is compatible for compound **28**, MS *m/z* (%): 337 (24), 336 ($M^{\bullet+}$, 81), 293 (17), 267 (18), 265 (17), 253 (18), 252 (19), 217 (34), 216 (100), 215 (62), 203 (61), 202 (60), 178 [$(C_{14}H_{10})^{\bullet+}$, 78].

5.13. Reaction of tetraiodide 6 with 0.45% sodium amalgam in the presence of 1,3-diphenylisobenzofuran (30)

To 0.45% sodium amalgam [from Na (600 mg, 26 mmol) and Hg (133 g, 663 mmol)] a solution of diene **30** (650 mg, 2.4 mmol) and tetraiodide **6** (611 mg, 1.0 mmol) in anhydrous 1,2-dimethoxyethane (DME, 65 mL) was added and the reaction mixture was stirred overnight at room temperature, under an argon atmosphere and protected from light. The mixture was filtered through a pad of Celite® and the filtrate was analyzed by GC–MS showing the presence of many components, those with higher r.a. being: (i) dihydro-1,3-diphenylisobenzofuran[9] (rt 23.5 min, 23% r.a.), (ii) 2-benzoylbenzophenone[10] (rt 25.0 min, 8% r.a.), (iii) starting diene **30** (rt 26.6 min, 12% r.a.), and (iv) compound **5a**[2b] (rt 28.5 min, 7% r.a.).

5.14. Reaction of tetraiodide 6 with molten sodium in boiling 1,4-dioxane

Solid tetraiodide **6** (1.22 g, 2.0 mmol) was added to molten sodium (920 mg, 40 mmol) in boiling 1,4-dioxane and the mixture was heated under reflux for 4 h. The mixture was filtered through a pad of Celite® and the residue was washed with Et_2O (3×20 mL). Distillation of the combined filtrate and washings at atmospheric pressure using a 10 cm Vigreux column left a residue (650 mg), still containing 1,4-dioxane, which when analyzed by GC–MS showed the presence of many components, among them: (i) and (ii) products **A** and **B**: diastereomeric 2-(1,4-dioxan-2-yl)-1,4-dioxane (1,4-dioxane dimers)[17] (molecular ions: $m/z=174$, rt's 11.5 and 11.9 min, 9 and 10% r.a.'s, respectively); (iii) product **C** (rt 14.2 min, 36% r.a.), MS m/z (%): 194 ($M^{\bullet+}$, 8), 117 (16), 113 (15), 112 (12), 107 [$(M-C_4H_7O_2)^+$, 12], 91 (29), 87 [$(C_4H_7O_2)^+$, 32], 86 (21), 79 (48), 73 (51), 67 (100); (iv) product **D** (rt 16.4 min, 10% r.a.), MS m/z (%): 214 ($M^{\bullet+}$, 1), 213 (1), 171 (18), 143 (20), 131 (25), 129 (30), 117 (21), 106 (21), 105 (34), 91 (58), 80 (22), 79 (46), 77 (24), 67 (100); (v) compound **3a**[2b] (rt 19.1 min, 5% r.a.), (vi) product **E** (rt 21.4 min, 12% r.a.), MS m/z (%): 280 ($M^{\bullet+}$, 6), 218 (14), 205 (25), 193 [$(M-C_4H_7O_2)^+$, 33], 132 (44), 131 (49), 107 [$(M-C_4H_7O_2-C_4H_6O_2)^+$, 82], 91 (49), 86 (48), 79 (57), 73 (100), 67 (55); (vii) product **F** (rt 23.3 min, 8% r.a.), MS m/z (%): 300 ($M^{\bullet+}$, 1), 259 (10), 213 [$(M-C_4H_7O_2)^+$, 44], 171 (20), 131 (37), 129 (31), 117 (25), 105 (33), 91 (69), 87 (37), 81 (27), 79 (74), 77 (33), 73 (47), 67 (100); (viii) product **G** (rt 25.4 min, 8% r.a.), MS m/z (%): 299 (24), 298 ($M^{\bullet+}$, 87), 143 (23), 129 (24), 117 (26), 115 (22), 107 (25), 106 (28), 105 (27), 93 (26), 91 (78), 87 (40), 79 (59), 77 (41), 73 (100).

5.15. X-ray crystal structure determination of 6[11]

A prismatic crystal (0.1×0.1×0.2 mm) was selected and mounted on a MAR345 diffractometer with an image plate detector. Unit-cell parameters were determined from 9482 reflections ($3<\theta<31°$) and refined by least-squares method. Intensities were collected with graphite monochromatized Mo Kα radiation. Reflections (9891) were measured in the range $3.29\leq\theta\leq31.72°$. Reflections (1945) of which were nonequivalent by symmetry [R_{int}(on I)=0.046]. Reflections (1842) were assumed as observed applying the condition $I>2\sigma(I)$. Lorentz polarization and absorption corrections were made. The structure was solved by direct methods, using SHELXS computer program[18] and refined by full matrix least-squares method with SHELX-97 computer program,[19] using 1945 reflections (very negative intensities were not assumed). The function minimized was $\sum w||F_o|^2-|F_c|^2|^2$, where $w=[\sigma^2(I)+(0.0482P)^2+11.4234P]^{-1}$, and $P=(|F_o|^2+2|F_c|^2)/3$, f, f' and f'' were taken from the literature.[20] All H atoms were located from a difference synthesis and refined with an isotropic temperature factor. The final R(on F) factor was 0.046, $wR(\text{on}|F|^2)=0.114$ and goodness of fit=1.095 for all observed reflections. Number of refined parameters was 73. Max shift/esd=0.00, mean shift/esd=0.00. Max and min peaks in final difference synthesis was 0.732 and -0.753 eÅ^{-3}, respectively. [$C_8H_8I_4$], $M_r=611.74$, orthorhombic, space group $Pnca$, $a=9.7270(10)$, $b=12.2340(10)$, $c=10.6080(10)$, $\alpha=90$, $\beta=90$, $\gamma=90°$, $V=1262.4(2)$ Å^3, $Z=4$, $F(000)=1072$, $\rho_{calcd}=3.219$ g cm^{-3}; crystal dimensions (mm), 0.1×0.1×0.2 mm; μ (Mo Kα) linear absorption coefficient=9.828 mm^{-1}, $T=293(2)$ K, 1945 reflections and 73 parameters were used for the full matrix (Fig. 2).

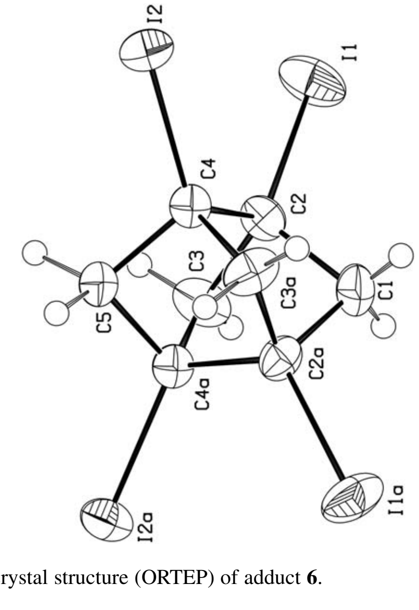


Figure 2. Crystal structure (ORTEP) of adduct **6**.

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References and notes

1. For a very recent review on pyramidalized alkenes see: (a) Vázquez, S.; Camps, P. *Tetrahedron* **2005**, *61*, 5147–5208; See also: (b) Borden, W. T. *Chem. Rev.* **1989**, *89*, 1095–1109.
2. (a) Camps, P.; Font-Bardia, M.; Pérez, F.; Solans, X.; Vázquez, S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 912–914; (b) Camps, P.; Font-Bardia, M.; Pérez, F.; Solà, Ll.; Solans, X.; Vázquez, S. *Tetrahedron Lett.* **1996**, *37*, 8601–8604; (c) Camps, P.; Luque, F. J.; Orozco, M.; Pérez, F.; Vázquez, S. *Tetrahedron Lett.* **1996**, *37*, 8605–8608; (d) Camps, P.; Pujol, X.; Vázquez, S. *Tetrahedron* **2002**, *58*, 10081–10086; (e) Camps, P.; Muñoz, M. R.; Vázquez, S. *J. Org. Chem.* **2005**, *70*, 1945–1948.
3. For the use of 2,5-dimethylfuran or furan as trapping agents, see: Camps, P.; Fernández, J. A.; Font-Bardia, M.; Solans, X.; Vázquez, S. *Tetrahedron* **2005**, *61*, 3593–3603.
4. (a) Gleiter, R.; Schäfer, W. *Acc. Chem. Res.* **1990**, *23*, 369–375; (b) Lange, H.; Schäfer, W.; Gleiter, R.; Camps, P.; Vázquez, S. *J. Org. Chem.* **1998**, *63*, 3478–3480.
5. Ayats, C.; Camps, P.; Duque, M. D.; Font-Bardia, M.; Muñoz, M. R.; Solans, X.; Vázquez, S. *J. Org. Chem.* **2003**, *68*, 8715–8718.
6. (a) Concepción, J. I.; Francisco, C. G.; Freire, R.; Hernández, R.; Salazar, J. A.; Suárez, E. *J. Org. Chem.* **1986**, *51*, 402–404; (b) Moriarty, R. M.; Khosrowshahi, J. S.; Dalecki, T. M. *J. Chem. Soc., Chem. Commun.* **1987**, 675–676.

7. (a) Böttger, O. *Chem. Ber.* **1937**, *70*, 314–325; (b) Newkome, G. R.; Nayak, A.; Behera, R. K.; Moorefield, C. N.; Baker, G. R. *J. Org. Chem.* **1992**, *57*, 358–362.
8. Webster, O. W.; Sommer, L. H. *J. Org. Chem.* **1964**, *29*, 3103–3105.
9. Adams, R.; Gold, M. H. *J. Am. Chem. Soc.* **1940**, *62*, 56–61.
10. Rieche, A.; Schulz, M. *Ann.* **1962**, *653*, 32–45.
11. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 604057. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].
12. (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652; (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789.
13. (a) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939–947; (b) Gordon, M. S.; Binkley, J. S.; Pople, J. A.; Pietro, W. J.; Hehre, W. J. *J. Am. Chem. Soc.* **1982**, *104*, 2797–2803.
14. The LANL2DZ basis set consists of the valence double-zeta D95V basis set for first-row atoms and the Los Alamos effective core potential for I. See: (a) Dunning, T. H., Jr.; Hay, P. J. *Modern Theoretical Chemistry*; Schaefer, H. F., III, Ed.; Plenum: New York, NY, 1976; Vol. 3, pp 1–28; (b) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270–283; (c) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284–298; (d) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299–310.
15. (a) Cremer, D. Møller–Plesset Perturbation Theory. *Encyclopedia of Computational Chemistry*; Schleyer, P. v. R., Ed.; Wiley: Chichester, UK, 1998; Vol. 3, pp 1706–1735; (b) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, NY, 1986; (c) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618–622.
16. Ab initio calculations were carried out using the Gaussian program. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreve, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Rev. B.02*; Gaussian: Pittsburgh, PA, 2003.
17. Watanabe, Y.; Otha, K.; Suyama, S. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2063–2066.
18. Sheldrick, G. M. *A Program for Automatic Solution of Crystal Structures*; University of Göttingen: Germany, 1997.
19. Sheldrick, G. M. *SHELX-97: A Program for Crystal Structure Refinement*; University of Göttingen: Germany, 1997.
20. *International Tables of X-ray Crystallography*; Ibers, J. A., Hamilton, W. C., Eds.; Kynoch: Birmingham, UK, 1974; Vol. IV, pp 99–100 and 149.