Synthesis and reactions of a new 1,1-disubstituted cyclopentadiene

Pelayo Camps* and Tània Gómez

Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmacia, Universitat de Barcelona, Av. Diagonal 643, E-08028, Barcelona, Spain
E-mail: camps@ub.edu

Dedicated to Prof. Julio Alvarez-Builla on the occasion of his 65th anniversary

DOI: http://dx.doi.org/10.3998/ark.5550190.0012.310

Abstract
The synthesis and several synthetic transformations of methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate are described.

Keywords: Methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate, norbornenes, norbornadienes, Diels-Alder reaction, (2-iodoethyl)(phenyl)iodonium triflate

Introduction

For several years, we have been working on the generation, trapping and dimerization of highly pyramidalized alkenes containing the skeleton of tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene, as very reactive species for the fast elaboration of complex polycyclic compounds.1 These pyramidalized alkenes are usually generated by deiodination of double bridgehead 1,2-diiodo precursors with molten sodium in boiling 1,4-dioxane or t-BuLi in THF. In connection with this work, we planned the preparation of a conveniently functionalized 1,1-disubstituted cyclopenta-2,4-diene, to study different model transformations, specially a simple introduction of a 1,2-diidoethylene functionality.

Results and Discussions

In this study, we chose methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate 5 as the 1,1-disubstituted cyclopenta-2,4-diene, whose ester function opens the way for different transformations, apart from those derived from the presence of the diene substructure. Diene 5 was obtained as shown in Scheme 1 from methyl 1-benzyl-2-oxocyclopentanecarboxylate 1.2
Following a procedure described for a related case, keto ester 1 was reacted with trimethylsilyl triflate to give the corresponding silylated enol ether 2, which was directly oxidized by bubbling oxygen through a vigorously stirred DMSO solution in the presence of Pd(OAc)$_2$ as the catalyst to give the known enone 3 in 82% yield of chromatographed product. NaBH$_4$ reduction of 3 in the presence of CeCl$_3$·7H$_2$O following the Luche procedure, gave the known allylic alcohol 4, which was subjected as such to acid catalyzed dehydration to give cyclopentadiene 5 in 66% yield of chromatographed product (Scheme 1).

Scheme 1. Preparation of methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate 5. (i) CF$_3$SO$_3$SiMe$_3$, Et$_3$N, CH$_2$Cl$_2$, rt, 30 min. (ii) Pd(OAc)$_2$, O$_2$, DMSO, rt, 24 h, 3 (82% from 1). (iii) NaBH$_4$, CeCl$_3$·7H$_2$O, MeOH, rt, 1 h. (iv) p-TsOH·H$_2$O, benzene, reflux, 18 h, 5 (66% from 3).

Diene 5 is a relatively stable compound that slowly dimerizes at room temperature to give after 4 months a unique stereoisomeric dimer 6 in 58% yield (Scheme 2), still remaining some diene 5. The structure and relative configuration of this dimer were fully established through NMR data: $^1$H/$^1$H homocorrelation (COSY and NOESY) and $^1$H/$^{13}$C heterocorrelation experiments ($^1$H/$^{13}$C gHSQC and gHMBC sequences). Formation of this stereoisomer requires approaching of both components from the side of the less bulky methoxycarbonyl substituent. The stereochemistry of 6 coincides with that established by other means for the dimer obtained from a related compound, methyl 1-methylcyclopenta-2,4-diene-1-carboxylate.

Diene 5 participated without problems in standard Diels-Alder reactions. Thus, reaction of crude diene 5 with maleic anhydride or cis-1,2-bis-(phenylsulfonyl)ethylene gave the corresponding endo-adducts 7 and 8, respectively (Scheme 2). In both cases, only endo-adducts derived from the addition of the dienophile to the diene from the side of the less bulky methoxycarbonyl group were detected. Formation of the exo-adducts must be disfavored by the steric interaction among the 7-syn substituent and the 2-exo and 3-exo substituents. This type of interaction must be the responsible for the fact that no reaction took place among diene 5 and trans-1,2-bis-(phenylsulfonyl)ethylene, after 60 h in refluxing toluene. In the corresponding adduct, one of the phenylsulfonyl groups will be in an exo-position, thus being very close to the syn-substituent at position 7.
**Cis-1,2-Bis(phenylsulfonyl)ethylene** has been used as an acetylene equivalent in Diels–Alder reactions, when combined with the reductive desulfonylation of the cycloadduct with 2% sodium amalgam. This reduction is usually performed in MeOH in the presence of monosodium phosphate. When we reacted adduct 8 with 2% sodium amalgam under the above conditions, we could isolate slightly impure cyclopropanated compound 11 and a mixture of 11 and the expected diene 10 in low yields. Since compound 11 contains two hydrogen atoms more than diene 10, we considered that these hydrogen atoms must come from the protic medium. When the above reaction was carried out in an aprotic solvent (1,4-dioxane) in the absence of any hydrogen source, diene 10 was isolated in 53% yield (Scheme 2). Diene 10 could not be obtained from anhydride 7 by hydrolysis followed by reaction with Pb(OAc)₄, anhydride 7 being the only product recovered in the last reaction.

**Scheme 2.** Reactions from methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate 5. (i) Rt, 120 d, 6 (58%). (ii) Maleic anhydride, toluene, reflux, 4 h, 7 (90% from 3). (iii) *cis*-1,2-bis(phenylsulfonyl)ethylene, toluene, 100 °C, 15 h, 8 (61% from 3). (iv) (2-iodoethynyl) (phenyl)iodonium triflate (14), MeCN, rt, 20 h, 9 (79% from 3). (v) Na(Hg) 2%, 1,4-dioxane, rt, 18 h, 10 (53%). (vi) Na(Hg) 2%, NaH₂PO₄·2H₂O, MeOH, rt, 24 h, 11 (about 25%), mixture 10 and 11 (about 35%). (vii) NaI, CuI, MeCN, –40 °C to rt, overnight, 12 (46%). (viii) Aqueous NaOH, CH₂Cl₂, rt, 18 h, 12 (35%), 13 (23%).
Scheme 3. Preparation of (2-iodoethynyl)(phenyl)iodonium triflate 14. (i) (a) n-BuLi, THF, –78 °C, (b) I₂, 16 (96%). (ii) Iodosobenzenediacetate, CF₃SO₃H, 14 (46%).

For the preparation of compound 12 we first synthesized the novel (2-iodoethynyl)-(phenyl)iodonium triflate 14, by using a procedure similar to that used for the preparation of [(2-trimethylsilyl)ethynyl](phenyl)iodonium triflate.⁸ Thus, iodination of (trimethylsilyl)-acetylene 15 by reaction with n-BuLi and iodine in THF, as described,⁹ gave 1-iodo-2-(trimethylsilyl)acetylene 16. Reaction of compound 16 with iodosobenzene diacetate (IBDA) and triflic acid gave the crude iodonium triflate 14, as light brown solid containing some acetic acid (Scheme 3). After crystallization from MeCN/CH₂Cl₂ 1:3, triflate 14 was obtained in 46% yield, as white solid, quite stable in a dry argon atmosphere at 5 °C. This procedure is more simple than that described for the preparation of (2-chloroethynyl)(phenyl)iodonium triflate,¹⁰ which implies reaction of (2-chloroethynyl)tributylstannane with (cyano)(phenyl)iodonium triflate, both not commercially available.

Reaction of crude diene 5 with the triflate 14 in MeCN at room temperature for 20 h gave the expected Diels-Alder adduct 9 in 79% yield. Reaction of 9 with NaI/CuI in MeCN, following the procedure described by Stang et al.¹¹ in related cases, gave diiodide 12 in 46% yield (Scheme 2). The stereochemistry of both compounds was clearly established as for 6 on the basis of the different NMR data, especially the ¹H/¹H NOESY experiments, thus showing that the addition of triflate 14 to the diene 5 had taken place, as in the precedent cases, by the less hindered methoxycarbonyl face. Worthy of note, reaction of the iodonium triflate 9 with aqueous sodium hydroxide gave a mixture of the volatile iodosobenzene (traces), diiodide 12 (35%) and iodoketone 13 (23%). These facts suggest competition of the nucleophilic attack of the hydroxide ion to the ipso phenyl and the 2-norbornadiene positions. The enol, initially formed by substitution of the phenyliodonium group by hydroxide, would then tautomerize to the more stable 3-endo-iodoketone 13.

1,2-Diiodoethylene derivatives related to 12 have been prepared through Diels-Alder reactions using bis[phenyl][(trifluoromethyl)sulfonyl]oxy]iodo]acetylene¹² as the dienophile, followed by reaction of the adducts with NaI/CuI.¹¹ However, this dienophile is much less stable and more difficult to prepare than 14.
Conclusions

In conclusion we have prepared methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate and studied its Diels-Alder reactions with maleic anhydride, cis-1,2-bis(phenylsulfonyl)ethylene and (2-iodoethynyl)(phenyl)iodonium triflate, and further transformations of the obtained adducts. Of special interest is the adduct with the above iodonium triflate, that has been transformed into methyl 1-benzyl-2,3-diiodonorbornadiene-7-carboxylate. Work is in progress to apply the described methodologies for the preparation of more complex polycyclic compounds.

Experimental Section

General. Melting points were determined with a MFB 595010 M Gallenkamp melting point apparatus. \(^1\)H NMR spectra were recorded on Varian Gemini-300 (300 MHz), Varian Mercury-400 (400 MHz), or Varian VXR-500 (500 MHz) spectrometers. \(^13\)C NMR spectra were recorded on Varian Mercury-400 (100.6 MHz), or Varian VXR-500 (125.8 MHz) spectrometers. The \(^1\)H/\(^1\)H homocorrelation spectra (COSY and NOESY) and the one bond and long range \(^1\)H/\(^13\)C heterocorrelation spectra (gHSQC and gHMBC, respectively) were performed on a Varian VXR-500 spectrometer. Chemical shifts are given in \(\delta\) scale and the coupling constants in Hz. IR spectra were registered on a FTIR Perkin–Elmer Spectrum RX1 spectrometer usually with the attenuated total reflectance (ATR) technique. High resolution MS spectra were performed in a LC/MSD-TOF spectrometer at the Serveis Científico-Tècnics of the University of Barcelona. The elemental analyses were determined in a Carlo Erba model 1106 equipment at the IIQAB (CSIC) of Barcelona, Spain. For the column chromatography, silica gel 60 AC (35–70 \(\mu\)M, SDS, ref. 2000027) was used. Thin-layer chromatography (TLC) was performed on aluminum-backed sheets with silica gel 60 F\(_{254}\) (Merck, ref. 1.05554) and spots were visualized with UV light, a 1% aqueous solution of KMnO\(_4\) or by placing the sheets in an iodine atmosphere.

Methyl rac-1-benzyl-2-oxocyclopent-3-enecarboxylate (3). To a cold (0 \(^\circ\)C) solution of keto ester 1 (614 mg, 2.64 mmol) and anhydrous Et\(_3\)N (1.8 mL, 1.33 g, 13.2 mmol) in anhydrous CH\(_2\)Cl\(_2\) (4.5 mL), trimethylsilyl trifluoromethanesulfonate (0.72 mL, 880 mg, 4.0 mmol) was added dropwise and the mixture was stirred at room temperature for 30 min. The mixture was cooled to 0 \(^\circ\)C and a saturated solution of NaHCO\(_3\) (3 mL) was added. The organic phase was separated, dried (anhydrous Na\(_2\)SO\(_4\)) and concentrated to dryness in vacuo. The residue was taken in hexane (5 mL) and was washed with water (3 mL). The dried organic phase (anhydrous Na\(_2\)SO\(_4\)) was concentrated in vacuo to give methyl 1-benzyl-2-(trimethylsilyloxy)ciclopent-2-enecarboxylate 2 (750 mg) as yellow oil, that was used as such in the next step. \(R_f = 0.41\) (silica gel, 10 cm, hexane / EtOAc 7:3). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 0.23 (s, 9H, Si(CH\(_3\))\(_3\)), 1.62–1.72 (m, 1H) and 1.84–1.92 (m, 1H) (5-H\(_{cis}\) and 5-H\(_{trans}\)), 2.07–2.25 (complex signal, 2H, 4-H\(_{cis}\)
and 4-H\textsubscript{trans}), 3.01 (d, \textit{J} = 13.5 Hz, 1H) and 3.12 (d, \textit{J} = 13.5 Hz, 1H) (CH\textsubscript{2}-Ph), 3.70 (s, 3H, OCH\textsubscript{3}), 4.62 (t, \textit{J} = 2.4 Hz, 1H, 3-H), 7.18–7.23 (complex signal, 5H, Ar-H).

To a solution of the above trimethylsilyl ether \textit{2} (750 mg) in anhydrous DMSO (4.6 mL), Pd(OAc)\textsubscript{2} (30 mg, 0.13 mmol) was added and the red-brown mixture was vigorously stirred for 24 h while oxygen was being bubbled through the mixture via a syringe. The mixture was diluted with EtOAc (10 mL) and was washed with water (8 mL). The aqueous phase was extracted with EtOAc (2×10 mL) and the combined organic phase and extracts were washed with brine (2×8 mL), dried (anhydrous Na\textsubscript{2}SO\textsubscript{4}) and concentrated in vacuo to give a brown oily residue (605 mg). Column chromatography of the above residue (silica gel, 35–70 \textmu m, 12 g, hexane / EtOAc mixtures) gave in order of elution, starting keto ester \textit{1} (57 mg, hexane / EtOAc 99:1) and enone \textit{3} (496 mg, 82%, hexane / EtOAc 95:5) as colorless oil, \textit{R}\textsubscript{f} = 0.29 (silica gel, 10 cm, hexane / EtOAc 7:3). The \textit{1H} NMR spectrum is concordant with that described.\textsuperscript{4}

**Methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate** (\textit{5}). To a cold (0 °C) solution of enone \textit{3} (382 mg, 1.66 mmol) and CeCl\textsubscript{3}·7H\textsubscript{2}O (803 mg, 2.16 mmol) in MeOH (15 mL), NaBH\textsubscript{4} (246 mg, 6.5 mmol) was added and the solution was stirred at room temperature for 1 h. A saturated aqueous solution of Na\textsubscript{2}SO\textsubscript{4} (10 mL) was added and the mixture was extracted with CH\textsubscript{2}Cl\textsubscript{2} (3×50 mL). The combined organic phases were dried (anhydrous Na\textsubscript{2}SO\textsubscript{4}) and concentrated in vacuo to give crude \textit{5}, as colorless oil, \textit{R}\textsubscript{f} = 0.18 (silica gel, 9 cm, hexane / EtOAc 7:3). \textit{1H} NMR (300 MHz, CDCl\textsubscript{3}) \textit{\delta} 1.72 (broad s, 1H, OH), 4.16 (dq, \textit{J} = 17.3 Hz, \textit{J}' = 2.0 Hz, 1H) and 2.78 (dd, \textit{J} = 17.3 Hz, \textit{J}' = 2.0 Hz, 1H) (5-H\textsubscript{cis} and 5-H\textsubscript{trans}), 2.88 (d, \textit{J} = 13.8 Hz, 1H) and 3.32 (d, \textit{J} = 13.8 Hz, 1H) (CH\textsubscript{2}-Ph), 3.64 (s, 3H, OCH\textsubscript{3}), 5.00 (m, 1H, 2-H), 5.82 (dq, \textit{J} = 5.7 Hz, \textit{J}' = 2.1 Hz, 1H, 4-H), 5.95 (ddt, \textit{J} = 5.7 Hz, \textit{J}' = 1.2 Hz, \textit{J}'' = 2.4 Hz, 1H, 3-H), 7.10–7.14 (m, 2H) and 7.18–7.29 (complex signal, 3H) (Ar-H).

To a solution of alcohol \textit{4} (639 mg, 2.75 mmol) in benzene (60 mL), \textit{p}-TsOH·H\textsubscript{2}O (27 mg, 0.14 mmol) was added and the solution was heated under reflux for 18 h with azeotropic elimination of water with a Dean-Stark equipment. Then, the solution was allowed to cool to room temperature and was treated with saturated aqueous solution of NaHCO\textsubscript{3} (12 mL). The organic phase was separated and the aqueous one was extracted with diethyl ether (1×20 mL and 2×15 mL). The combined organic phase and extracts were washed with water (2×15 mL) and brine (2×15 mL), dried (anhydrous Na\textsubscript{2}SO\textsubscript{4}) and concentrated in vacuo to give crude \textit{5}, as brown oil (587 mg, quantitative yield). Column chromatography of the above oil (silica gel, 35–70 \textmu m, 12 g, hexane / EtOAc mixtures) gave, on elution with hexane / EtOAc 99:1, diene \textit{5} (387 mg, 66%) as a clear brown oil, \textit{R}\textsubscript{f} = 0.36 (silica gel, 10 cm, hexane / AcOEt 9:1). IR (NaCl): \textit{v} 3061, 3028, 2950, 2925, 2854, 1728 (C=O st), 1602, 1495, 1453, 1434, 1369, 1308, 1257, 1218, 1081, 1041, 792, 775, 763, 732, 716, 701 cm\textsuperscript{-1}. \textit{1H} NMR (400 MHz, CDCl\textsubscript{3}) \textit{\delta} 3.12 (s, 2H, CH\textsubscript{2}-Ph), 3.60 (s, 3H, OCH\textsubscript{3}), 6.32 (m, 2H, 3(4)-H), 6.43 (m, 2H, 2(5)-H), 7.14–7.17 (m, 2H) and 7.20–7.26 (complex signal, 3H) (Ar-H). \textit{13C} NMR (100.6 MHz, CDCl\textsubscript{3}) \textit{\delta} 40.8 (CH\textsubscript{2}, CH\textsubscript{2}-Ph), 52.2 (CH\textsubscript{3}, OCH\textsubscript{3}), 67.8 (C, C1), 126.6 (CH, Ar-C4), 127.8 [CH, Ar-C3(5)], 129.7 [CH, Ar-C2(6)], 131.8 [CH, C3(4)], 137.5 (C, Ar-C1), 138.4 [CH, C2(5)], 172.0 (C, COOMe). HRMS (ESI-TOF):

Dimethyl (1RS,3aRS,4SR,7RS,7aRS,8RS)-1,8-dibenzyl-3a,7a-tetrahydro-1H-4,7-methanoindene-1,8-dicarboxylate (6). A sample of crude diene 5 (106 mg, 0.23 mmol) was kept at room temperature for 4 months. The product thus formed was subjected to column chromatography (silica gel, 35–70 µm, 10 g, hexane / EtOAc mixtures). On elution with hexane / EtOAc 99:1, diene 5 (14 mg) was isolated and on elution with hexane / EtOAc 98:2, dimer 6 (75 mg) was obtained as light yellow solid. Crystallization from MeOH (1.5 mL) gave pure 6 (62 mg, 58% from 3), as white solid, mp 144–145 °C, Rf = 0.31 (silica gel, 10 cm, hexane / EtOAc 8:2). IR (ATR): ν 3081, 3025, 3001, 2951, 2929, 2850, 1723 (C=O st), 1492, 1441, 1324, 1303, 1266, 1227, 1189, 1104, 1088, 1079, 1057, 1041, 1024, 951, 781, 769, 754, 741, 723, 714, 697, 602 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 2.67 (d, J = 13.0 Hz, 1H, 1-CH₃-Ph), 2.81 (dd, J = 8.0 Hz, J' = 3.5 Hz, 1H, 7a-H), 2.90 (d, J = 14.0 Hz, 1H, 8-CH₂-Ph), 2.95 (m, 1H, 4-H), 2.98 (d, J = 14.0 Hz, 1H, 8-CH₂-Ph), 3.14 (d, J = 13.0 Hz, 1H, 1-CH₃-Ph), 3.30 (m, 1H, 7-H), 3.34 (m, 1H, 3a-H), 3.60 (s, 3H, 8-COOCH₃), 3.62 (s, 3H, 1-COOCH₃), 5.43 (dd, J = 6.0 Hz, J' = 2.0 Hz, 1H, 3-H), 5.56 (dd, J = 6.0 Hz, J' = 2.0 Hz, 1H, 2-H), 5.72 (ddd, J = 6.0 Hz, J’ = 3.0 Hz, J” = 1.5 Hz, 1H, 6-H), 5.89 (dd, J’ = 6.0 Hz, J” = 3.0 Hz, 1H, 5-H), 6.94 (dm, J = 8.5 Hz, 2H, 8-CH₂-Ar-2(6)-H], 6.98 [ddm, J = 8.0 Hz, J’ = 2.0 Hz, 2H, 1-CH₂-Ar-2(6)-H], 7.15–7.24 [m, 6H, 1-CH₂-Ar-3(5)-H, 8-CH₂-Ar-3(5)-H, 1-CH₂-Ar-4-H and 8-CH₂-Ar-4-H]. ¹³C NMR (125.8 MHz, CDCl₃): δ 37.5 (CH₂, 8-CH₂-Ph), 49.6 (CH₂, 1-CH₂-Ph), 50.3 (CH, C4), 50.7 (CH, C7a), 51.2 (CH₃, 8-COOCH₃), 51.4 (CH₃, 1-COOCH₃), 51.5 (CH, C3a), 51.9 (CH, C7), 61.9 (C, C1), 75.6 (C, C8), 126.3 (CH, 8-CH₂-Ar-C4), 126.6 (CH, 1-CH₂-Ar-C4), 127.9 (CH, 1-CH₂-Ar-C3(5)], 128.0 [CH, 8-CH₂-Ar-C3(5)], 129.1 [CH, 8-CH₂-Ar-C2(6)], 129.8 [CH, 1-CH₂-Ar-C2(6)], 129.9 (CH, C6), 132.1 (CH, C3), 134.5 (CH, C5), 135.0 (CH, C2), 136.9 (C, 1-CH₂-Ar-C1), 138.6 (C, 8-CH₂-Ar-C1), 174.7 (C, 8-COOCH₃), 175.5 (C, 1-COOCH₃). HRMS (ESI–TOF): calcd. for [C₂₈H₂₈O₄+H]+: 429.2060. Found: 429.2059. Calcd. for [C₂₈H₂₈O₄+NH₄]+: 446.2326. Found: 446.2320. Anal. calcd. for C₂₈H₂₈O₄: C, 78.48; H, 6.59. Found: C, 78.31; H, 6.55.

(1R,2S,3R,4S,7r)-7-Benzyl-7-methoxycarboxylic bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride (7). A solution of crude diene 5 (221 mg, 1.03 mmol) and maleic anhydride (152 mg, 1.55 mmol) in anhydrous toluene (4 mL) was heated under reflux for 4 h. The solution was allowed to cool to room temperature and concentrated in vacuo to give a brown viscous oil that was subjected to column chromatography (silica gel, 35–70 µm, 12 g, hexane / EtOAc mixtures). On elution with hexane / EtOAc 95:5, anhydride 7 (289 mg, 90%, from enone 3) was obtained as brown solid. Crystallization of the above product from toluene / pentane 5:6 (1.1 mL), provided the analytical sample of 7 as white solid (146 mg, 45%), mp 145–146 °C, Rf = 0.87 (silica gel, 10 cm, CH₂Cl₂ / MeOH 8:2). IR (KBr): ν 3448, 3018, 2963, 2938, 1855, 1776 and 1739 (C=O st), 1442, 1328, 1295, 1260, 1237, 1225, 1204, 1129, 1090, 1063, 1044, 930, 912, 759, 700, 670, 625 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 2.98 (s, 2H, CH₂-Ph), 3.55 [m, 2H, 1(4)-H], 3.62 (s, 3H, OCH₃), 3.66 (dd, J = 3.0 Hz, J’ = 1.5 Hz, 2H, 2(3)-H), 6.41 [t, J = 2.0 Hz, 2H, 5(6)-H], 6.92 (ddm, J = 7.6 Hz, J’ = 2.0 Hz, 2H, Ar-Hortho), 7.22–7.29 (complex signal, 3H, Ar-Hmeta and Ar-
**H_{para}**). $^{13}$C NMR (100.6 MHz, CDCl$_3$): $\delta$ 36.2 (CH$_2$, CH$_2$-Ph), 45.8 [CH, C2(3)], 50.3 [CH, C1(4)], 52.0 (CH$_3$, OCH$_3$), 77.8 (C, C7), 127.1 (CH, Ar-C4), 128.4 [CH, Ar-C3(5)], 128.8 [CH, Ar-C2(6)], 133.9 [CH, C5(6)], 136.8 (C, Ar-C1), 170.4 [C, (2-3)-COO], 172.7 (C, COOMe). HRMS (ESI-TOF): calcd. for [C$_{18}$H$_{16}$O$_5$+H]$^+$: 313.1071. Found: 313.1077. Calcd. for [C$_{18}$H$_{16}$O$_5$+Na]$^+$: 335.0890. Found: 335.0891. Anal. calcd. for C$_{18}$H$_{16}$O$_5$: C, 69.22; H, 5.16. Found: C, 68.88; H, 5.24.

**Methyl (1R,4S,5S,6R,7S)-7-benzyl-5,6-bis(phenylsulfonyl)bicyclo[2.2.1]hepta-2-ene-7-carboxylate (8).** A solution of crude diene 5 (296 mg, 1.38 mmol) and cis-1,2-bis(phenylsulfonyl)ethylene (468 mg, 1.52 mmols) in anhydrous toluene (5 mL) was heated to 100 °C for 15 h. The solution was allowed to cool to room temperature and concentrated in vacuo to give a brown viscous oil that was subjected to column chromatography (silica gel, 35–70 µm, 50 g, hexane / EtOAc mixtures). In order of elution, dimer 6 (85 mg), starting disulfone (140 mg) and adduct 8 as light brown solid (438 mg, 61% from enone 3), were obtained. The analytical sample of adduct 8 (232 mg) was obtained, as white solid, by crystallization of a sample of the above product (340 mg) from CH$_2$Cl$_2$ / MeOH 4:5 (0.9 mL), mp 236–237 °C. $R_f = 0.15$ (silica gel, 10 cm, hexane / EtOAc 6:4). IR (ATR): ν 3001, 2945, 1726 (C=O st), 1584, 1449, 1337, 1325 (SO$_2$ st), 1293, 1238, 1200, 1149 (SO$_2$ st), 1083, 759, 744, 722, 700, 689, 660, 611, 601, 590, 578 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.88 (s, 2H, CH$_2$-Ph), 3.25 [broad s, 2H, 1(4)-H], 3.46 (s, 3H, OCH$_3$), 4.15 (t, $J = 1.4$ Hz, 2H, 5(6)-H), 6.71 [t, $J = 2.0$ Hz, 2H, 2(3)-H], 6.81–6.84 (dm, $J = 7.5$ Hz, 2H, Ar-H$_{ortho}$ benzyl), 7.16–7.21 (complex signal, 3H, Ar-H$_{meta}$ and Ar-H$_{para}$ benzyl), 7.55 (tm, $J = 7.5$ Hz, 4H, Ar-H$_{meta}$ -SO$_2$Ph), 7.63–7.67 (tm, $J = 7.5$ Hz, 2H, Ar-H$_{para}$ -SO$_2$Ph), 7.96-7.98 (dm, $J = 7.5$ Hz, 4H, Ar-H$_{ortho}$ -SO$_2$Ph). $^{13}$C NMR (100.6 MHz, CDCl$_3$): $\delta$ 35.2 (CH$_2$, CH$_2$-Ph), 51.9 (CH$_3$, OCH$_3$), 52.3 [CH, C1(4)], 70.0 [CH, C5(6)], 71.5 (C, C7), 127.0 (CH, Ar-C4 benzyl), 128.3 [CH, Ar-C3(5) benzyl], 128.5 [CH, Ar-C2(6), SO$_2$Ph], 128.8 (CH, Ar-C2(6) benzyl), 129.0 (CH, Ar-C4 -SO$_2$Ph), 132.9 [CH, C3(3)], 133.7 (CH, Ar-C3(5) -SO$_2$Ph), 136.5 (C, Ar-C1 benzyl), 140.9 (C, Ar-C1 -SO$_2$Ph), 172.6 (C, COOme). HRMS (ESI-TOF): calcd. for [C$_{28}$H$_{26}$O$_{6}$S$_2$+H]$^+$: 523.1244. Found: 523.1238. Calcd. for [C$_{28}$H$_{26}$O$_{6}$S$_2$+NaH]$^+$: 540.1509. Found: 540.1500. Anal. calcd. for C$_{28}$H$_{26}$O$_{6}$S$_2$: C, 64.35; H, 5.01. Found: C, 64.09; H, 4.85.

**Methyl 7-benzylbicyclo[2.2.1]hepta-2,5-diene-7-carboxylate (10).** To a well stirred suspension of compound 8 (735 mg, 1.41 mmol) in anhydrous 1,4-dioxane (15 mL) under an Ar atmosphere, 2% sodium amalgam (12.9 g, 11.3 mmol) was added portionwise within 1 h and then, the mixture was vigorously stirred for 20 h at room temperature. The organic phase was separated and the residue was washed with EtOAc (2×4 mL). The combined organic phase and washings were concentrated in vacuo and the obtained brown oily residue was subjected to column chromatography (silica gel, 35–70 µm, 25 g, hexane / EtOAc mixtures). On elution with hexane / EtOAc 99:1, compound 10 (178 mg, 53%) was isolated as yellow oil. $R_f = 0.66$ (silica gel, 10 cm, hexane / EtOAc 8:2). IR (ATR): ν 3071, 3040, 3000, 2948, 1726 (C=O st), 1496, 1457, 1433, 1318, 1277, 1228, 1200, 1171, 1099, 1083, 1035, 733, 700, 656, 602, 576 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.02 (s, 2H, CH$_2$-Ph), 3.43 (s, 3H, OCH$_3$), 3.64 [quint, $J = 2.0$ Hz, 2H,
1(4-H), 6.73 [t, J = 2.0 Hz, 2H, 2(3)-H], 6.77 [t, J = 2.0 Hz, 2H, 5(6)-H], 6.98 (dm, J = 8.5 Hz, 2H, Ar-H$_{ortho}$), 7.19 (tm, J = 7.5 Hz, 1H, Ar-H$_{para}$), 7.25 (m, 2H, Ar-H$_{meta}$). $^{13}$C NMR (100.6 MHz, CDCl$_3$): δ 39.0 (CH$_2$, CH$_3$-Ph), 51.0 (CH$_3$, OCH$_3$), 55.0 [CH, C1(4)], 96.1 (C, C7), 126.3 (CH, Ar-C$_{para}$), 128.0 (CH, Ar-C$_{meta}$), 128.9 (CH, Ar-C$_{ortho}$), 138.4 (C, Ar-C$_{ips}$), 141.0 [CH, C5(6)], 143.1 [CH, C2(3)], 174.9 (C, COO). HRMS (ESI-TOF): calcd. for [C$_{16}$H$_{16}$O$_2$+H]$^+$: 241.1223. Found: 241.1231. Calcd. for [C$_{16}$H$_{18}$O$_2$+NH$_4$]$^+$: 258.1489. Found: 258.1492. Anal. calcd. for C$_{16}$H$_{16}$O$_2$: C, 79.97; H, 6.71. Found: C, 79.91; H, 6.82.

**Reduction of disulfone (9) with 2% Na(Hg) in methanol: formation of methyl (1RS,2rs,3SR,6SR)-3-benzyltricyclo[2.2.1.0$^{2,6}$]heptane-3-carboxylate (11) and diene (10).** To a well stirred suspension of compound 8 (190 mg, 0.36 mmol) and NaH$_2$PO$_4$·H$_2$O (727 mg, 5.27 mmol) in MeOH (15 mL) under an Ar atmosphere, 2% sodium amalgam (3.34 g, 2.9 mmol) was added portionwise within 1 h and then, the mixture was vigorously stirred for 20 h at room temperature. The organic phase was separated and the residue was washed with MeOH (2×2 mL). The combined organic phase and washings were concentrated in vacuo and the gray solid residue was subjected to column chromatography (silica gel, 35–70 μm, 10 g, hexane / EtOAc mixtures). In order of elution, slightly impure compound 11 (21 mg, about 25%) and a mixture of diene 10 and compound 11 (31 mg) were isolated. NMR data of compound 11: $^1$H NMR (500 MHz, CDCl$_3$): δ 1.21–1.39 (complex signal, 6H, 1-H, 2-H, 5-H$_{endo}$, 6-H, 7-H$_{exo}$, 7-H$_{endo}$), 1.89 (dm, J = 11.2 Hz, 1H, 5-H$_{exo}$), 2.06 (broad s, 1H, 4-H), 2.68 (d, J = 13.2 Hz, 1H) and 2.91 (d, J = 13.2 Hz, 1H) (CH$_2$-Ph), 3.51 (s, 3H, OCH$_3$), 7.10 (dm, J = 8.0 Hz, 2H, Ar-H$_{ortho}$), 7.19 (tm, J = 7.0 Hz, 1H, Ar-H$_{para}$), 7.25 (m, 2H, Ar-H$_{meta}$). $^{13}$C NMR (100.6 MHz, CDCl$_3$): δ 11.3 (CH) and 11.8 (CH) (C1 and C6), 16.9 (CH, C2), 31.2 (CH$_2$, C5), 32.7 (CH$_2$, C7), 37.0 (CH, C4), 39.0 (CH$_2$, CH$_2$-Ph), 51.1 (CH$_3$, OCH$_3$), 60.9 (C, C3), 126.3 (CH, Ar-C$_{para}$), 128.1 (CH, Ar-C$_{meta}$), 129.3 (CH, Ar-C$_{ortho}$), 138.5 (C, Ar-C$_{ips}$), 175.8 (C, COO). HRMS (ESI-TOF): calcd. for [C$_{16}$H$_{18}$O$_2$+H]$^+$: 243.1380. Found: 243.1387.

**(1RS,4SR,7SR)-[7-Benzyl-3-iodo-7-(methoxycarbonyl)bicyclo[2.2.1.0$^{2,6}$]hepta-2,5-dien-2-yl]-(phenyl)dionium triflate (9).** To a solution of crude diene 5 (272 mg, 1.27 mmol) in anhydrous MeCN (1 mL), 2-(iodoethyl)phenylidonium triflate 14 (426 mg, 0.85 mmol) was added portionwise over 30 min and the mixture was vigorously stirred at room temperature for 20 h. More crude diene 5 (100 mg, 0.47 mmol) was added and the mixture was stirred for 2 d. The solvent was eliminated in vacuo and the solid residue (816 mg) was crystallized from CH$_2$Cl$_2$ / Et$_2$O (1:5) (4.8 mL) to give adduct 9 (478 mg, 79%) as light brown solid, mp 161–162 °C. IR (ATR): ν 3084, 2944, 1726 (C=O st), 1604, 1567, 1537, 1443, 1315, 1285, 1232, 1200, 1163, 1146, 1099, 1087, 1025, 990, 757, 735, 706, 633, 597 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): δ 2.94 (d, J = 14.0 Hz, 1H) and 3.03 (d, J = 14.0 Hz, 1H) (CH$_2$-Ph), 3.19 (s, 3H, OCH$_3$), 3.90 (dt, J = 1.0 Hz, J$''$ = 2.5 Hz, 1H, 4-H), 4.03 (dt, J = 1.0 Hz, J$''$ = 2.5 Hz, 1H, 1-H), 6.81 (ddd, J = 5.5 Hz, J$''$ = 3.0 Hz, J$'''$ = 1.0 Hz, 1H, 5-H), 6.83–6.87 (complex signal, 3H, 6-H and Ar-H$_{ortho}$ benzyl), 7.19–7.27 (complex signal, 3H, Ar-H$_{para}$ and Ar-H$_{meta}$ benzyl), 7.48 (m, 2H, Ar-H$_{meta}$ phenylidonium), 7.65 (tm, J = 7.5 Hz, 1H, Ar-H$_{para}$ phenylidonium), 7.98 (dm, J = 7.0 Hz, 2H, Ar-H$_{ortho}$ phenylidonium). $^{13}$C NMR (125.8 MHz, CDCl$_3$): δ 38.5 (CH$_2$, CH$_2$-Ph), 51.7 (CH$_3$,
OCH3), 64.8 (CH, C1), 67.9 (CH, C4), 96.3 (C, C7), 113.0 (C, Ar-C1 phenyliodonium), 120.1 (CF3, q, J = 320 Hz, CF3SO3), 127.2 (CH, Ar-C4 benzyl), 128.4 (C, C3), 128.5 [CH, Ar-C3(5) benzyl], 128.8 [CH, Ar-C2(6)], 130.3 (C, C2), 132.0 [CH, Ar-C3(5) phenyliodonium], 132.8 (CH, Ar-C4 phenyliodonium), 135.9 (C, Ar-C1 benzyl), 136.3 [CH, Ar-C2(6) phenyliodonium], 137.0 (CH, C5), 140.5 (CH, C6), 172.1 (C, COOMe). HRMS (ESI-TOF): calcd. for [C23H19F3I2O5S – CF3SO3]+: 568.9469. Found: 568.9463. Anal. calcd. for C23H19F3I2O5S: C, 38.46; H, 2.67; I, 35.34; F, 8.74. Found: C, 38.93; H, 2.73; I, 35.86; F, 8.30.

Methyl (1R,4S,7s)-7-benzyl-2,3-diiodobicyclo[2.2.1]hepta-2,5-diene-7-carboxylate (12). To a cold (−35 to −40 °C) and vigorously stirred suspension of NaI (254 mg, 1.63 mmol) and Cul (311 mg, 1.63 mmols) in anhydrous MeCN (20 mL), triflate 9 (1.17 g, 1.63 mmol) was added. The mixture was allowed to heat to room temperature and was stirred overnight at this temperature. The mixture was filtered and the filtrate was concentrated in vacuo to give a solid residue (1.98 g) that was subjected to column chromatography (silica gel, 35–70 µm, 80 g, hexane / EtOAc mixtures) to give diiodide 12 as light yellow solid (372 mg, 46%) on elution with hexane / EtOAc 98:2. An analytical sample of 12 (98 mg) was obtained as light yellow solid by crystallization of a part of the above product (130 mg) from MeOH (0.6 mL), mp 105.5–106.5 °C. IR (ATR): ν 3031, 3001, 2946, 1718 (C=O st), 1493, 1453, 1349, 1426, 1316, 1275, 1232, 1201, 1097, 1086, 1033, 1020, 731, 703, 623, 590 cm−1. 1H NMR (500 MHz, CDCl3): δ 2.98 (s, 2H, CH2-Ph), 3.51 (s, 3H, OCH3), 3.76 [t, J = 2.0 Hz, 2H, 1(4)-H], 6.85 [t, J = 2.0 Hz, 2H, 5(6)-H], 6.93 (m, 2H, Ar-Hortho), 7.19–7.26 (complex signal, 3H, Ar-Hpara and Ar-Hmeta). 13C NMR (125.8 MHz, CDCl3): δ 38.7 (CH2, CH2-Ph), 51.5 (CH3, OCH3), 66.7 [CH, C1(4)], 94.9 (C, C7), 114.6 [CH, C2(3)], 126.8 (CH, Ar-C4), 128.3 [CH, Ar-C3(5)], 128.9 [CH, Ar-C2(6)], 137.0 (C, Ar-C1), 138.8 [CH, C5(6)], 172.9 (C, COOMe). HRMS (ESI-TOF): calcd. for [C16H14I2O2+H]+: 492.9156. Found: 492.9153 Anal. calcd. for C16H14I2O2: C, 39.05; H, 2.87; I, 51.58. Found: C, 39.48; H, 2.86; I, 51.84.

Reaction of triflate (9) with aqueous NaOH: isolation of diiodide (12) and methyl (1RS,4SR,5SR,7RS)-7-benzyl-5-ido-6-oxobicyclo[2.2.1]hepta-5-ene-7-carboxylate (13). To a solution of triflate 9 (710 mg, 0.99 mmol) in CH2Cl2 (10 mL), aqueous 1N NaOH (4 mL) was added and the mixture was vigorously stirred at room temperature for 18 h. The organic phase was separated and the aqueous one was extracted with CH2Cl2 (3×3 mL). The combined organic phase and extracts were dried (anhydrous Na2SO4) and concentrated in vacuo to give a brown oily residue (509 mg) that was subjected to column chromatography (silica gel, 35–70 µm, 25 g, hexane / EtOAc mixtures). In order of elution, iodobenzene (12 mg, hexane), diiodide 12 (170 mg, 35%, hexane / EtOAc 99:1) and impure iodo ketone 13 (127 mg, hexane / EtOAc 95:5) were isolated. The above iodo ketone 13 was subjected to a new column chromatography (silica gel, 35–70 µm, 25 g, pentane / EtOAc mixtures) to give pure product 13 (86 mg, 23%, pentane / EtOAc 97:3) as light yellow solid, mp 101–102 °C. IR (ATR): ν 2948, 2922, 2852, 1754, 1728 (C=O st), 1454, 1315, 1238, 1196, 1085, 1035, 909, 736, 701 cm−1. 1H NMR (500 MHz, CDCl3): δ 3.14 (d, J = 13.5 Hz, 1H) and 3.31 (d, J = 13.5 Hz, 1H) (CH2-Ph), 3.35 (dd, J = 3.0 Hz, J' = 1.5 Hz, 1H, 1-H), 3.51 (m, 1H, 4-H), 3.59 (s, 3H, OCH3), 4.45 (d, J = 3.0 Hz, 1H, 5-Hexo), 6.26 (m,
1H, 2-H), 6.62 (dd, J = 6.0 Hz, J' = 3.0 Hz, 1H, 3-H), 6.96 (m, 2H, Ar-H_{ortho} Ph), 7.20–7.28 (complex signal, 3H, Ar-H_{para} and Ar-H_{meta}). $^{13}$C NMR (125.8 MHz, CDCl$_3$): δ 18.8 (CH, C5), 36.8 (CH$_2$, CH$_2$-Ph), 52.3 (CH$_3$, OCH$_3$), 52.8 (CH, C4), 58.1 (CH, C1), 73.5 (C, C7), 127.1 (CH, Ar-C4), 128.5 [CH, Ar-C3(5)], 128.9 [CH, Ar-C2(6)], 129.1 (CH, C2), 136.5 (C, Ar-C1), 144.0 (CH, C3), 173.2 (C, COOMe), 204.8 (C, C6). HRMS (ESI-TOF): calcd. for [C$_{16}$H$_{15}$IO$_3$+H]$^+$: 383.0139. Found: 383.0130. Calcd. for [C$_{16}$H$_{15}$IO$_3$+NH$_4$]$^+$: 400.0404. Found: 400.0401.

Acknowledgements

Financial support from Ministerio de Ciencia e Innovación (CTQ2008-03768) and Comissionat per a Universitats i Recerca (2005-SGR-00180) is gratefully acknowledged.

References