

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

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

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-iodoethynyl)(phenyl)iodonium triflate

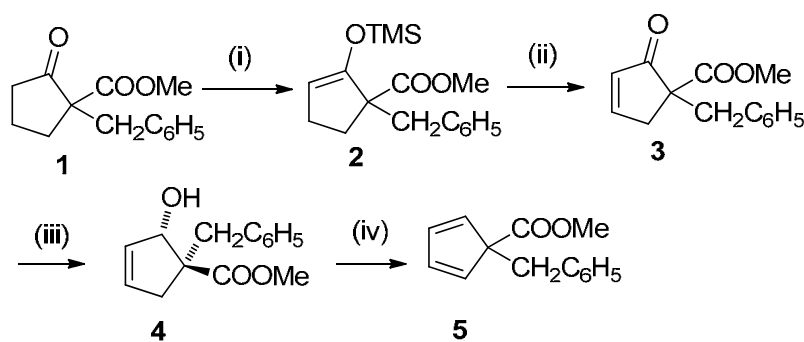
Introduction

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-diiodoethylene 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,³ 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 known⁴ enone **3** in 82% yield of chromatographed product. NaBH₄ reduction of **3** in the presence of CeCl₃·7H₂O following the Luche procedure,^{3,5} gave the known⁴ allylic alcohol **4**, which was subjected as such to acid catalyzed dehydration to give cyclopentadiene **5** in 66% yield of chromatographed product (Scheme 1).



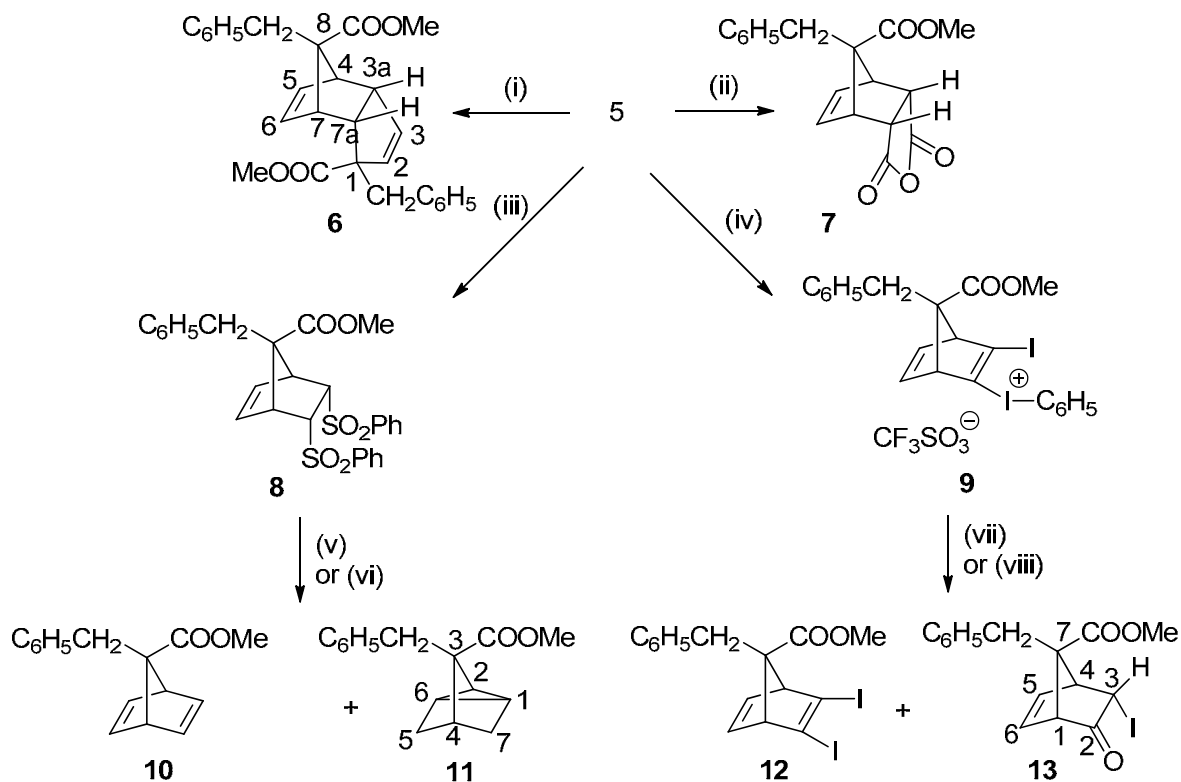
Scheme 1. Preparation of methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate **5**. (i) CF₃SO₃SiMe₃, Et₃N, CH₂Cl₂, rt, 30 min. (ii) Pd(OAc)₂, O₂, DMSO, rt, 24 h, **3** (82% from **1**). (iii) NaBH₄, CeCl₃·7H₂O, MeOH, rt, 1 h. (iv) *p*-TsOH·H₂O, benzene, reflux, 18 h, **5** (66 % from **3**).

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: ¹H/¹H homocorrelation (COSY and NOESY) and ¹H/¹³C heterocorrelation experiments (¹H/¹³C 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.⁶

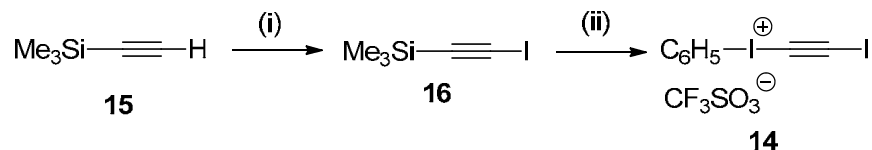
Diene **5** participated without problems in standard Diels-Alder reactions. Thus, reaction of crude diene **5** with maleic anhydride or *cis*-1,2-bis-(phenylsulfonyl)ethylene⁷ gave the corresponding *endo*-adducts **7** and **8**, respectively (Scheme 2). In both cases, only *endo*-adducts derived 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,⁷ 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 $\text{Pb}(\text{OAc})_4$, 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%, $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$, 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, CH_2Cl_2 , 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) I_2 , **16** (96%). (ii) Iodosobenzene diacetate, $\text{CF}_3\text{SO}_3\text{H}$, **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/ CH_2Cl_2 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 $^1\text{H}/^1\text{H}$ 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 iodobenzene (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]bis[(trifluoromethyl)sulfonyl]oxyiodo]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-iodoethyl)(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. ^1H 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 $^1\text{H}/^1\text{H}$ homocorrelation spectra (COSY and NOESY) and the one bond and long range $^1\text{H}/^{13}\text{C}$ heterocorrelation spectra (gHSQC and gHMBC, respectively) were performed on a Varian VXR-500 spectrometer. Chemical shifts are given in δ 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 μm , SDS, ref. 2000027) was used. Thin-layer chromatography (TLC) was performed on aluminum-backed sheets with silica gel 60 F₂₅₄ (Merck, ref. 1.05554) and spots were visualized with UV light, 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 °C) solution of keto ester **1** (614 mg, 2.64 mmol) and anhydrous Et_3N (1.8 mL, 1.33 g, 13.2 mmol) in anhydrous CH_2Cl_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 °C and a saturated solution of NaHCO_3 (3 mL) was added. The organic phase was separated, dried (anhydrous Na_2SO_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_2SO_4) was concentrated in vacuo to give methyl 1-benzyl-2-(trimethylsilyloxy)cyclopent-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). ^1H NMR (300 MHz, CDCl_3) δ 0.23 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 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_{trans}), 3.01 (d, $J = 13.5$ Hz, 1H) and 3.12 (d, $J = 13.5$ Hz, 1H) ($\text{CH}_2\text{-Ph}$), 3.70 (s, 3H, OCH_3), 4.62 (t, $J = 2.4$ Hz, 1H, 3-H), 7.18–7.23 (complex signal, 5H, Ar-H).

To a solution of the above trimethylsilyl ether **2** (750 mg) in anhydrous DMSO (4.6 mL), $\text{Pd}(\text{OAc})_2$ (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_2SO_4) and concentrated in vacuo to give a brown oily residue (605 mg). Column chromatography of the above residue (silica gel, 35–70 μm , 12 g, hexane / EtOAc mixtures) gave in order of elution, starting keto ester **1** (57 mg, hexane / EtOAc 99:1) and enone **3** (496 mg, 82%, hexane / EtOAc 95:5) as colorless oil, $R_f = 0.29$ (silica gel, 10 cm, hexane / EtOAc 7:3). The ^1H NMR spectrum is concordant with that described.⁴

Methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate (5). To a cold (0 °C) solution of enone **3** (382 mg, 1.66 mmol) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (803 mg, 2.16 mmol) in MeOH (15 mL), NaBH_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_2SO_4 (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3×50 mL). The combined organic phases were dried (anhydrous Na_2SO_4) and concentrated in vacuo to give hydroxy ester **4** (384 mg, quantitative yield) as colorless oil, $R_f = 0.18$ (silica gel, 9 cm, hexane / EtOAc 7:3). ^1H NMR (300 MHz, CDCl_3) δ 1.72 (broad s, 1H, OH), 2.47 (dq, $J = 17.3$ Hz, $J' = 2.0$ Hz, 1H) and 2.78 (dd, $J = 17.3$ Hz, $J' = 2.0$ Hz, 1H) (5- H_{cis} and 5- H_{trans}), 2.88 (d, $J = 13.8$ Hz, 1H) and 3.32 (d, $J = 13.8$ Hz, 1H) ($\text{CH}_2\text{-Ph}$), 3.64 (s, 3H, OCH_3), 5.00 (m, 1H, 2-H), 5.82 (dq, $J = 5.7$ Hz, $J' = 2.1$ Hz, 1H, 4-H), 5.95 (ddt, $J = 5.7$ Hz, $J' = 1.2$ Hz, $J'' = 2.4$ 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 **4** (639 mg, 2.75 mmol) in benzene (60 mL), $p\text{-TsOH} \cdot \text{H}_2\text{O}$ (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_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_2SO_4) and concentrated in vacuo to give crude **5**, as brown oil (587 mg, quantitative yield). Column chromatography of the above oil (silica gel, 35–70 μm , 12 g, hexane / EtOAc mixtures) gave, on elution with hexane / EtOAc 99:1, diene **5** (387 mg, 66%) as a clear brown oil, $R_f = 0.36$ (silica gel, 10 cm, hexane / AcOEt 9:1). IR (NaCl): ν 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^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 3.12 (s, 2H, $\text{CH}_2\text{-Ph}$), 3.60 (s, 3H, OCH_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). ^{13}C NMR (100.6 MHz, CDCl_3): δ 40.8 (CH_2 , $\text{CH}_2\text{-Ph}$), 52.2 (CH_3 , OCH_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):

calcd. for $[C_{14}H_{14}O_2+H]^+$: 215.1066. Found: 215.1069. Anal. calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.55; H, 6.97.

Dimethyl (1*RS*,3*aRS*,4*SR*,7*RS*,7*aRS*,8*RS*)-1,8-dibenzyl-3*a*,4,7,7*a*-tetrahydro-1*H*-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 μ m, 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, R_f = 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, $CDCl_3$): δ 2.67 (d, J = 13.0 Hz, 1H, 1- CH_a -Ph), 2.81 (dd, J = 8.0 Hz, J' = 3.5 Hz, 1H, 7*a*-H), 2.90 (d, J = 14.0 Hz, 1H, 8- CH_a -Ph), 2.95 (m, 1H, 4-H), 2.98 (d, J = 14.0 Hz, 1H, 8- CH_b -Ph), 3.14 (d, J = 13.0 Hz, 1H, 1- CH_b -Ph), 3.30 (m, 1H, 7-H), 3.34 (m, 1H, 3*a*-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]. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 37.5 (CH₂, 8-CH₂-Ph), 49.6 (CH₂, 1-CH₂-Ph), 50.3 (CH, C4), 50.7 (CH, C7*a*), 51.2 (CH₃, 8-COOCH₃), 51.4 (CH₃, 1-COOCH₃), 51.5 (CH, C3*a*), 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 $[C_{28}H_{28}O_4+H]^+$: 429.2060. Found: 429.2059. Calcd. for $[C_{28}H_{28}O_4+NH_4]^+$: 446.2326. Found: 446.2320. Anal. calcd. for $C_{28}H_{28}O_4$: C, 78.48; H, 6.59. Found: C, 78.31; H, 6.55.

(1*R*,2*S*,3*R*,4*S*,7*r*)-7-Benzyl-7-methoxycarbonylbicyclo[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 μ m, 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. R_f = 0.87 (silica gel, 10 cm, CH_2Cl_2 / 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, $CDCl_3$): 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-H_{ortho}), 7.22–7.29 (complex signal, 3H, Ar-H_{meta} and Ar-

H_{para}). ^{13}C NMR (100.6 MHz, CDCl_3): δ 36.2 (CH_2 , $\text{CH}_2\text{-Ph}$), 45.8 [CH , $\text{C}2(3)$], 50.3 [CH , $\text{C}1(4)$], 52.0 (CH_3 , OCH_3), 77.8 (C, C7), 127.1 (CH , $\text{Ar-C}4$), 128.4 [CH , $\text{Ar-C}3(5)$], 128.8 [CH , $\text{Ar-C}2(6)$], 133.9 [CH , $\text{C}5(6)$], 136.8 (C, $\text{Ar-C}1$), 170.4 [C, $2(3)\text{-COO}$], 172.7 (C, COOMe). HRMS (ESI-TOF): calcd. for $[\text{C}_{18}\text{H}_{16}\text{O}_5+\text{H}]^+$: 313.1071. Found: 313.1077. Calcd. for $[\text{C}_{18}\text{H}_{16}\text{O}_5+\text{Na}]^+$: 335.0890. Found: 335.0891. Anal. calcd. for $\text{C}_{18}\text{H}_{16}\text{O}_5$: C, 69.22; H, 5.16. Found: C, 68.88; H, 5.24.

Methyl (1*R*,4*S*,5*S*,6*R*,7*S*)-7-benzyl-5,6-bis(phenylsulfonyl)bicyclo[2.2.1]hept-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_2Cl_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} . ^1H NMR (300 MHz, CDCl_3): δ 2.88 (s, 2H, $\text{CH}_2\text{-Ph}$), 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_2Ph), 7.63–7.67 (tm, J = 7.5 Hz, 2H, Ar-H_{para} - SO_2Ph), 7.96–7.98 (dm, J = 7.5 Hz, 4H, Ar-H_{ortho} - SO_2Ph). ^{13}C NMR (100.6 MHz, CDCl_3): δ 35.2 (CH_2 , $\text{CH}_2\text{-Ph}$), 51.9 (CH_3 , OCH_3), 52.3 [CH , $\text{C}1(4)$], 70.0 [CH , $\text{C}5(6)$], 71.5 (C, C7), 127.0 (CH , $\text{Ar-C}4$ benzyl), 128.3 [CH , $\text{Ar-C}3(5)$ benzyl], 128.5 [CH , $\text{Ar-C}2(6)$, SO_2Ph], 128.8 [CH , $\text{Ar-C}2(6)$ benzyl], 129.0 (CH , $\text{Ar-C}4$ - SO_2Ph), 132.9 [CH , $\text{C}2(3)$], 133.7 (CH , $\text{Ar-C}3(5)$ - SO_2Ph), 136.5 (C, $\text{Ar-C}1$ benzyl), 140.9 (C, $\text{Ar-C}1$ - SO_2Ph), 172.6 (C, COOMe). HRMS (ESI-TOF): calcd. for $[\text{C}_{28}\text{H}_{26}\text{O}_6\text{S}_2+\text{H}]^+$: 523.1244. Found: 523.1238. Calcd. for $[\text{C}_{28}\text{H}_{26}\text{O}_6\text{S}_2+\text{NH}_4]^+$: 540.1509. Found: 540.1500. Anal. calcd. for $\text{C}_{28}\text{H}_{26}\text{O}_6\text{S}_2$: 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 \times 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} . ^1H NMR (500 MHz, CDCl_3): δ 3.02 (s, 2H, $\text{CH}_2\text{-Ph}$), 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}). ¹³C NMR (100.6 MHz, CDCl₃): δ 39.0 (CH₂, CH₂-Ph), 51.0 (CH₃, OCH₃), 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_{ipso}), 141.0 [CH, C5(6)], 143.1 [CH, C2(3)], 174.9 (C, COO). HRMS (ESI-TOF): calcd. for [C₁₆H₁₆O₂+H]⁺: 241.1223. Found: 241.1231. Calcd. for [C₁₆H₁₆O₂+NH₄]⁺: 258.1489. Found: 258.1492. Anal. calcd. for C₁₆H₁₆O₂: 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 NaH₂PO₄·H₂O (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 μ m, 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**: ¹H NMR (500 MHz, CDCl₃): 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) (CH₂-Ph), 3.51 (s, 3H, OCH₃), 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}). ¹³C NMR (100.6 MHz, CDCl₃): δ 11.3 (CH) and 11.8 (CH) (C1 and C6), 16.9 (CH, C2), 31.2 (CH₂, C5), 32.7 (CH₂, C7), 37.0 (CH, C4), 39.0 (CH₂, CH₂-Ph), 51.1 (CH₃, OCH₃), 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_{ipso}), 175.8 (C, COO). HRMS (ESI-TOF): calcd. for [C₁₆H₁₈O₂+H]⁺: 243.1380. Found: 243.1378.

(1RS,4SR,7SR)-[7-Benzyl-3-iodo-7-(methoxycarbonyl)bicyclo[2.2.1]hepta-2,5-dien-2-yl]-phenyliodonium triflate (9). To a solution of crude diene **5** (272 mg, 1.27 mmol) in anhydrous MeCN (1 mL), 2-(iodoethynyl)phenyliodonium 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 CH₂Cl₂ / Et₂O (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. ¹H NMR (500 MHz, CDCl₃): δ 2.94 (d, $J = 14.0$ Hz, 1H) and 3.03 (d, $J = 14.0$ Hz, 1H) (CH₂-Ph), 3.19 (s, 3H, OCH₃), 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} phenyliodonium), 7.65 (tm, $J = 7.5$ Hz, 1H, Ar-H_{para} phenyliodonium), 7.98 (dm, $J = 7.0$ Hz, 2H, Ar-H_{ortho} phenyliodonium). ¹³C NMR (125.8 MHz, CDCl₃): δ 38.5 (CH₂, CH₂-Ph), 51.7 (CH₃,

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, 7.94. 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 CuI (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, 1439, 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-H_{ortho}), 7.19–7.26 (complex signal, 3H, Ar-H_{para} and Ar-H_{meta}). 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-iodo-6-oxobicyclo[2.2.1]hept-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-H_{exo}), 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}). ¹³C NMR (125.8 MHz, CDCl₃): δ 18.8 (CH, C5), 36.8 (CH₂, CH₂-Ph), 52.3 (CH₃, OCH₃), 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 [C₁₆H₁₅IO₃+H]⁺: 383.0139. Found: 383.0130. Calcd. for [C₁₆H₁₅IO₃+NH₄]⁺: 400.0404. Found: 400.0401. Anal. calcd. for C₁₆H₁₅IO₃: C, 50.28; H, 3.96; I, 33.20. Found: C, 50.22; H, 4.07; I, 33.12.

(2-Iodoethynyl)(phenyl)iodonium triflate (14). To a cold (0 °C) magnetically stirred solution of iodobenzene diacetate (IBDA, 16.85 g, 52.3 mmol) in anhydrous CH₂Cl₂ (70 mL) under an Ar atmosphere, CF₃SO₃H (8.8 mL, 5.8 g, 99.4 mmol) was added dropwise. Then, the mixture was stirred at 0 °C for 30 min and 1-iodo-2-trimethylsilylacetylene (11.06 g, 49.4 mmol) was added dropwise and the solution was stirred at 0 °C for 2 h, a white precipitate being formed. The solution was decanted from the solid, which was washed three times with anhydrous and cold CH₂Cl₂. The obtained light brown solid (16.35 g) showed to contain acetic acid (molar ratio AcOH/**14** about 1:4 by ¹H NMR) and was crystallized at room temperature from a mixture of MeCN (8 mL) and CH₂Cl₂ (25 mL) to give triflate **14** (11.4 g, 46%) as a white solid. An analytical sample of **14** was obtained by repeating the above crystallization process, mp 96–98 °C. IR (ATR): ν 2106, 1561, 1469, 1446, 1293, 1272, 1212, 1170, 1019, 984, 730, 704, 672, 651, 631 cm⁻¹. ¹H NMR (400 MHz, CD₃CN): δ 7.61 (m, 2H, Ar-H_{meta}), 7.78 (tm, $J = 7.4$ Hz, 1H, Ar-H_{para}), 8.17 (dm, $J = 8.8$ Hz, 2H, Ar-H_{ortho}). ¹³C NMR (100.6 MHz, CD₃CN): δ 30.0 (C, C1), 33.3 (C, C2), 117.7 (C, Ar-C1), 121.5 (CF₃, q, $J = 320$ Hz, CF₃SO₃⁻), 133.7 [CH, Ar-C3(5)], 134.3 (CH, Ar-C4), 136.0 [CH, Ar-C2(6)]. HRMS (ESI-TOF): calcd. for [C₉H₅F₃I₂O₃S – CF₃SO₃]⁺: 354.8475. Found: 354.8472. Anal. calcd. for C₉H₅F₃I₂O₃S: C, 21.45; H, 1.00; I, 50.36; F, 11.31. Found: C, 21.59; H, 0.95; I, 50.52; F, 11.51.

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