

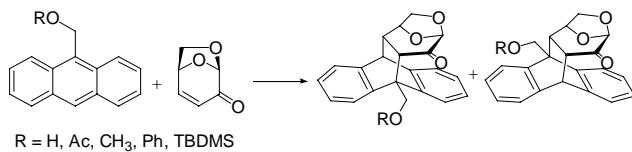
Microwave assisted regioselective cycloaddition reactions between 9-substituted anthracenes and levoglucosenone

Ariel M. Sarotti,[†] Madeleine M. Joullié,^{*,‡} Rolando A. Spanevello[†] and Alejandra G. Suárez ^{*,†}

[†]Instituto de Química Orgánica de Síntesis, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario – CONICET Suipacha 531, S2002LRK Rosario, Argentina

[‡]Department of Chemistry, University of Pennsylvania, 231 S. 34th Street, Philadelphia, PA 19104 USA.

asuarez@fboiy.unr.edu.ar



General

The microwave heating was performed in a CEM-Discover® System using a 10 mL pressure-rated reaction vials. The melting points were taken on a Leitz Wetzlar Microscope Heating Stage Model 350 apparatus and are uncorrected. Optical rotations were recorded with a Jasco DIP 1000 polarimeter. Infrared spectra were obtained on an IRPrestige-21 Fourier Transform Spectrophotometer Shimadzu. High resolution mass spectra (HRMS) were obtained on a Micromass AutoSpec. Nuclear magnetic resonance spectra were recorded on a Bruker AC-200, a Bruker Avance-300 or a Bruker AMX-500 spectrometers with tetramethylsilane as internal standard and deuteriochloroform as solvent. The NMR assignments were corroborated by NOE measurements, H,H- and H,C-correlations.

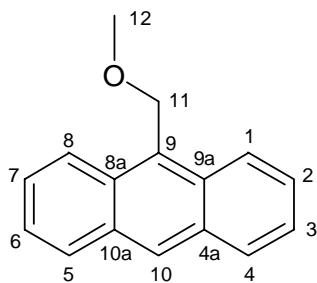
The reactions were monitored by thin layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F254) that were developed using UV light and anisaldehyde-sulfuric acid-acetic acid with subsequent heating. Flash column chromatography were performed using Merck silica gel 60H, by gradient elution created by mixtures of hexanes and increasing amounts of ethyl acetate.

Levoglucosenone (**1**)

Levoglucosenone was synthesized according to the procedure described in literature.¹

9-(Methoxymethyl)anthracene (**3a**)

This compound was prepared by a modification of the published procedure.² Anthracen-9-ylmethanol 97% (6.09 g, 28.38 mmol) was dried azeotropically with dry benzene and dissolved in THF (96 mL) under argon. This solution was cooled at 0 °C and NaH (60%, 3.51 g, 87.83 mmol) was incorporated and stirred for 20 minutes. Methyl iodide (4.4 mL, 70.71 mmol) and tetrabutyl ammonium iodide (1.04 g, 2.82 mmol) were added, the final solution was stirred for 40 minutes and allowed to reach room temperature. This solution was cooled at 0 °C and carefully added methanol (5 mL) and diluted with AcOEt (1 L). The organic phase was washed with water (2 x 100 mL), brine (100 mL), dried (Na₂SO₄) and concentrated. The residual solid was purified by flash chromatography to afford **3a** (6.06 g, 27.25 mmol, 96%).



3a

Yellow crystalline solid; mp 91–92 °C (hexane/ethyl acetate); IR (KBr) 2977, 2924, 1623, 1447, 1344, 1188, 1087, 940, 894, 738, 729 cm⁻¹; ¹H NMR (CDCl₃) δ 8.42 (s, 1 H, H-10), 8.36 (d, *J*=8.8 Hz, 2 H, H-1 and H-8), 7.98 (d, *J*=8.4 Hz, 2 H, H-4 and H-5), 7.56–7.40 (m, 4 H, H-2, H-3, H-6 and H-7), 5.40 (s, 2 H, H-11), 3.51 (s, 3 H, H-12); ¹³C

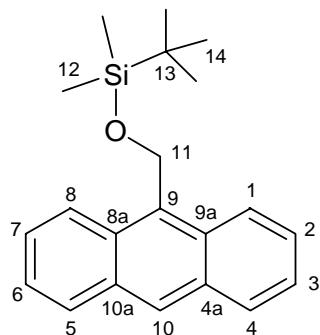
¹ Witczak, Z. J., Ed. *Levoglucosenone and Levoglucosans: Chemistry and Applications*; ATL Press: Mount Prospect, 1994, Chapter 2 (Morin, C.).

² Zimmerman, C.; Mohr, M.; Zippe, H.; Eichberger, R.; Schnabel, W. *J. Photochem. Photobiol. A* **1999**, 125, 47.

NMR (CDCl_3) δ 131.3 (C, C-9), 130.8 (C, C-4a and C-10a), 128.8 (CH, C-4 and C-5), 128.5 (C, C-8a and C-9a), 128.2 (CH, C-10), 126.0 (CH, C-1 and C-8), 124.8 (CH, C-2 and C-7), 124.1 (CH, C-3 and C-6), 66.4 (CH₂, C-11), 58.1 (CH₃, C-12).

(Anthracen-9-ylmethoxy)(tert-butyl)dimethylsilane (3b)

Anthracen-9-ylmethanol 97% (4.45 g, 20.73 mmol) was dissolved in dry THF (125 mL) under argon and dry triethylamine (8.56 mL, 61.53 mmol), DMAP (0.26 g, 2.08 mmol) and TBDMSCl 97 % (8.13 g, 52.32 mmol) were added in this order. The solution was stirred for 40 hours at room temperature and diluted with AcOEt (1 L). The organic phase was washed with water (1 x 280 mL), NaHCO₃ 5 % (1 x 280 mL), NH₄Cl sat (1 x 280 mL) and brine (1 x 280 mL), dried (Na₂SO₄) and concentrated. The residual solid was purified by flash chromatography to afford **3b** (6.53 g, 20.25 mmol, 98%).

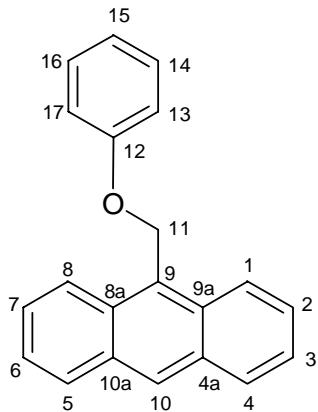


3b

Pale green crystalline solid; mp 115-116 °C (hexane); IR (KBr) 3062, 2956, 2950, 2853, 1461, 1345, 1251, 1072, 1036, 833, 779 cm⁻¹; ¹H NMR (CDCl_3) δ 8.40 (s, 1 H, H-10), 8.38 (d, $J=8.0$ Hz, 2 H, H-1 and H-8), 7.98 (d, $J=8.0$ Hz, 2 H, H-4 and H-5), 7.56-7.40 (m, 4 H, H-2, H-3, H-6 and H-7), 5.64 (s, 2 H, H-11), 0.91 (s, 9 H, H-14), 0.10 (s, 6 H, H-12); ¹³C NMR (CDCl_3) δ 131.4 (C, C-9), 130.2 (C, C-8a and C-9a), 128.8 (CH, C-4 and C-5), 128.8 (C, C-4a and C-10a), 127.7 (CH, C-10), 125.7 (CH, C-1 and C-8), 124.7 (CH, C-2 and C-7), 124.4 (CH, C-3 and C-6), 57.8 (CH₂, C-11), 25.9 (CH₃, C-14), 18.3 (C, C-13), -5.1 (CH₃, C-12).

9-(Phenoxymethyl)anthracene (3c)

Anthracen-9-ylmethanol 97% (2.81 g, 13.07 mmol) was dried azeotropically with dry benzene and dissolved in dry CH₂Cl₂ (200 mL) under argon. This solution was cooled at 0 °C and NEt₃ (2.20 mL, 15.79 mmol) and MsCl (1.23 mL, 15.89 mmol) were added in this order and the reaction stirred for 5 minutes. The solution was diluted with CH₂Cl₂ (200 mL) and washed with water (100 mL), brine (100 mL), dried (Na₂SO₄) and concentrated. The residual solid was dried azeotropically with dry benzene and dissolved in dry acetone (360 mL). Phenol (4.68 g, 49.8 mmol) and anhydrous K₂CO₃ (6.90 g, 49.9 mmol) were incorporated and the solution was stirred at reflux for 24 hours under argon. The solvent was evaporated under reduced pressure. Water (300 mL) and CH₂Cl₂ (300 mL) were added. The aqueous phase was extracted with CH₂Cl₂ (3 x 100 mL). The organic phase was washed with saturated Na₂CO₃ (2 x 150 mL), brine (2 x 150 mL), dried (Na₂SO₄) and concentrated. The residual solid was purified by flash chromatography to afford **3c** (3.38 g, 11.89 mmol, 91%).

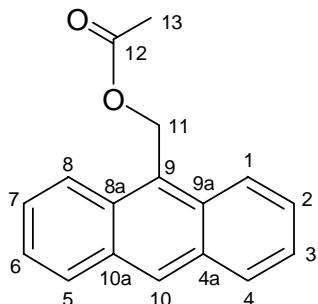


3c

Orange solid; mp 117-118 °C (EtOH); IR (KBr) 3031, 2886, 1597, 1585, 1494, 1476, 1236, 989, 879, 731 cm⁻¹; ¹H NMR (CDCl₃) δ 8.49 (s, 1 H, H-10), 8.29-8.24 (m, 2 H, H-1 and H-8), 8.04-7.99 (m, 2 H, H-4 and H-5), 7.55-7.00 (m, 9 H, H-2, H-3, H-6, H-7, H-13, H-14, H-15, H-16 and H-17), 5.92 (s, 2 H, H-11); ¹³C NMR (CDCl₃) δ 159.1 (C, C-12), 131.4 (C, C-9), 130.9 (C, C-4a and C-10a), 129.5 (CH, C-4 and C-5), 129.0 (CH, C-1 and C-8), 128.9 (C, C-8a and C-9a), 126.8 (CH, C-14 and C-16), 126.4 (CH, C-2 and C-7), 124.9 (CH, C-3 and C-6), 123.9 (CH, C-10), 121.1 (CH, C-15), 114.7 (CH, C-13 and C-17), 62.5 (CH₂, C-11).

Anthracen-9-ylmethanol (3d)

Anthracen-9-ylmethanol 97% (1.08 g, 5.03 mmol) was dissolved in dry CH₂Cl₂ (44 mL) under argon. The solution was cooled at 0 °C and dry pyridine (2.04 mL, 25.22 mmol), DMAP (63 mg, 0.50 mmol) and Ac₂O (1.46 mL, 15.47 mmol) were added in this order. The solution was stirred for 1 hour at 0 °C. The solvent was evaporated under reduced pressure and the crude was dissolved with AcOEt (400 mL). The organic phase was washed with saturated CuSO₄ (3 x 100 mL) and brine (2 x 100 mL), dried (Na₂SO₄) and concentrated. The residual solid was purified by flash chromatography to afford **3d** (1.15 g, 4.59 mmol, 91%).



3d

Pale yellow crystalline solid; mp 115-116 °C (hexane); IR (KBr) 3058, 3001, 2921, 1725 (C=O), 1447, 1380, 1250, 1027, 890, 738 cm⁻¹; ¹H NMR (CDCl₃) δ 8.48 (s, 1 H, H-10), 8.32 (d, J=8.8 Hz, 2 H, H-1 and H-8), 8.01 (d, J=8.4 Hz, 2 H, H-4 and H-5), 7.59-7.45 (m, 4 H, H-2, H-3, H-6 and H-7), 6.13 (s, 2 H, H-11), 2.07 (s, 3 H, H-13); ¹³C NMR (CDCl₃) δ 171.2 (C, C-12), 131.3 (C, C-9), 130.9 (C, C-4a and C-10a), 129.1 (CH, C-10), 129.0 (CH, C-4 and C-5), 126.5 (CH, C-3 and C-6), 126.1 (C, C-8a and C-

9a), 125.0 (CH, C-2 and C-7), 123.8 (CH, C-1 and C-8), 58.7 (CH₂, C-11), 20.9 (CH₃, C-13).

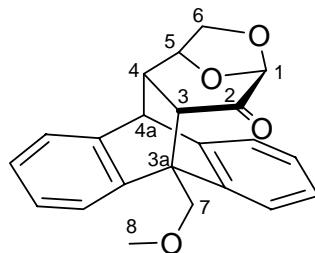
General procedure for the cycloaddition reaction of levoglucosenone and 9-substituted anthracenes. Thermal conditions.

Levoglucosenone and the corresponding diene (2.7 equiv) were dissolved in toluene (*c* 0.23M) and stirred at reflux for the time indicated in Table 1. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography.

General procedure for the cycloaddition reaction of levoglucosenone and 9-substituted anthracenes. Microwave conditions.

Levoglucosenone (80 mg, 0.63 mmol) and the corresponding diene in the amount indicated in Tables 2-4 were placed in a 10 mL vial and dissolved in the corresponding solvent (0.46 mL) and heated for the time and power indicated in Tables 2-4. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography.

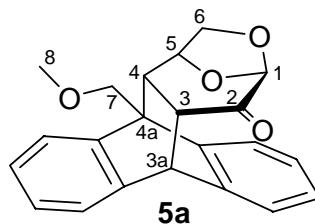
Diels-Alder Product 4a



4a

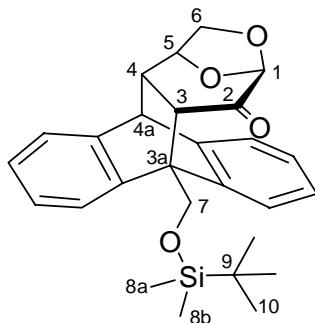
White crystalline solid; mp 251-252 °C (hexane/chloroform); [α]²⁹_D -43.8 (*c* 0.88, CHCl₃); IR (KBr) 3069, 2927, 1719 (C=O), 1464, 1457, 1115, 993, 921, 770 cm⁻¹; ¹H NMR (CDCl₃) δ 7.51-7.00 (m, 8 H, aromatics), 4.89 (d, *J*_{gem}=9.5 Hz, 1 H, H-7), 4.77 (d, *J*_{5-6exo}=4.9 Hz, 1 H, H-5), 4.62 (d, *J*_{gem}=9.5 Hz, 1 H, H-7), 4.54 (s, 1 H, H-1), 4.27 (s, 1 H, H-4a), 3.76-3.61 (m, 5 H, H-6 *endo*, H-6 *exo* and H-8), 3.10 (d, *J*₃₋₄=9.7 Hz, 1 H, H-3), 2.24 (d, *J*₃₋₄=9.7 Hz, 1 H, H-4); ¹³C NMR (CDCl₃) δ 199.1 (C, C-2), 145.2 (C, aromatic), 141.3 (C, aromatic), 140.9 (C, aromatic), 140.6 (C, aromatic), 126.2 (CH, aromatic), 126.0 (CH, 2 C, aromatic), 125.8 (CH, aromatic), 125.0 (CH, aromatic), 124.2 (CH, aromatic), 122.0 (CH, aromatic), 121.3 (CH, aromatic), 99.8 (CH, C-1), 77.1 (CH, C-5), 70.5 (CH₂, C-7), 68.7 (CH₂, C-6), 59.0 (CH₃, C-8), 50.3 (CH, C-4a), 49.8 (C, C-3a), 44.7 (CH, C-4), 44.0 (CH, C-3); HRMS calc. for C₂₂H₂₀O₄Na [M+Na]⁺ 371.1259. Found 371.1266.

Diels-Alder Product 5a



White crystalline solid; mp 236-237 °C (hexane/chloroform); $[\alpha]^{14}_D$ -127.7 (*c* 0.92, CHCl₃); IR (KBr) 3062, 2969, 1735 (C=O), 1457, 1118, 1108, 983, 746 cm⁻¹; ¹H NMR (CDCl₃) δ 7.36-7.03 (m, 8 H, aromatics), 4.88 (d, *J*_{5-6exo}=5.4 Hz, 1 H, H-5), 4.84 (d, *J*_{3-3a}=3.4 Hz, 1 H, H-3a), 4.69 (d, *J*_{gem}=9.9 Hz, 1 H, H-7), 4.64 (s, 1 H, H-1), 4.62 (d, *J*_{gem}=9.9 Hz, 1 H, H-7), 3.84 (dd, *J*_{gem}=7.2 Hz, *J*_{5-6exo}=5.4 Hz, 1 H, H-6 *exo*), 3.72-3.68 (m, 4 H, H-6 *endo* and H-8), 2.99 (dd, *J*₃₋₄=9.9 Hz, *J*_{3-3a}=3.4 Hz, 1 H, H-3), 2.42 (d, *J*₃₋₄=9.9 Hz, 1 H, H-4); ¹³C NMR (CDCl₃) δ 199.0 (C, C-2), 144.5 (C, aromatic), 141.5 (C, aromatic), 141.2 (C, aromatic), 140.3 (C, aromatic), 126.2 (CH, aromatic), 125.9 (CH, 3C, aromatic), 124.9 (CH, aromatic), 124.0 (CH, aromatic), 121.8 (CH, aromatic), 121.4 (CH, aromatic), 99.4 (CH, C-1), 72.7 (CH, C-5), 70.4 (CH₂, C-7), 69.4 (CH₂, C-6), 59.5 (CH₃, C-8), 47.7 (C, C-4a), 46.3 (CH, C-3a), 45.4 (CH, C-4), 43.7 (CH, C-3); HRMS calc. for C₂₂H₂₀O₄ [M]⁺ 348.1362. Found 348.1374.

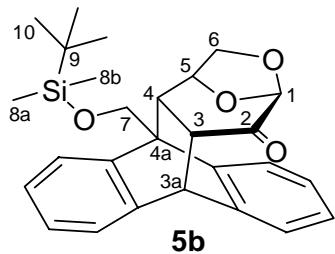
Diels-Alder Product 4b



4b

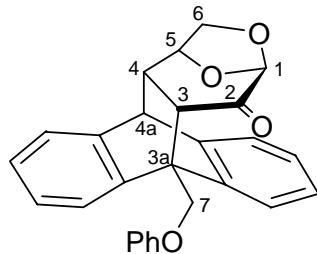
Pale yellow oil; $[\alpha]^{21}_D$ -31.1 (*c* 1.41, CHCl₃); IR (film) 3072, 3023, 2955, 2856, 1724 (C=O), 1457, 1255, 1107, 833, 765 cm⁻¹; ¹H NMR (CDCl₃) δ 7.65-6.98 (m, 8 H, aromatics), 5.28 (d, *J*_{gem}=10.1 Hz, 1 H, H-7), 4.85-4.80 (m, 2 H, H-7 y H-5), 4.55 (s, 1 H, H-1), 4.28 (d, *J*_{4-4a}=1.5 Hz, 1 H, H-4a), 3.78 (dd, *J*_{gem}=7.2 Hz, *J*_{5-6exo}=5.2 Hz, 1 H, H-6 *exo*), 3.72 (dd, *J*_{gem}=7.2 Hz, *J*_{5-6endo}=1.3 Hz, 1 H, H-6 *endo*), 3.16 (d, *J*₃₋₄=9.7 Hz, 1 H, H-3), 2.32 (dd, *J*₃₋₄=9.7 Hz, *J*_{4-4a}=1.5 Hz, 1 H, H-4), 0.96 (s, 9 H, H-10), 0.32 (s, 3 H, H-8a), 0.24 (s, 3 H, H-8b); ¹³C NMR (CDCl₃) δ 198.8 (C, C-2), 145.6 (C, aromatic), 141.6 (C, aromatic), 141.1 (C, aromatic), 140.8 (C, aromatic), 126.0 (CH, aromatic), 125.7 (CH, aromatic), 125.6 (CH, 2 C, aromatic), 124.9 (CH, aromatic), 124.7 (CH, aromatic), 121.9 (CH, aromatic), 121.3 (CH, aromatic), 99.9 (CH, C-1), 77.3 (CH, C-5), 68.7 (CH₂, C-6), 61.2 (CH₂, C-7), 50.8 (C, C-3a), 50.4 (CH, C-4a), 44.8 (CH, C-4), 43.0 (CH, C-3), 25.8 (CH₃, C-10), 18.3 (C, C-9), -5.4 (CH₃, C-8a), -5.6 (CH₃, C-8b); HRMS calc. for C₂₇H₃₂O₄SiNa [M+Na]⁺ 471.1968. Found 471.1827.

Diels-Alder Product 5b



Pale yellow solid; mp 162-163 °C (hexane); $[\alpha]^{28}_D$ -76.8 (*c* 0.64, CHCl₃); IR (KBr) 3005, 2951, 1726 (C=O), 1471, 1257, 1142, 1108, 990, 835, 772 cm⁻¹; ¹H NMR (CDCl₃) δ 7.45-7.32 (m, 2 H, aromatics), 7.20-7.03 (m, 6 H, aromatics), 4.94 (s, 2 H, H-7), 4.88 (d, *J*_{5-6_{exo}}=5.2 Hz, 1 H, H-5), 4.84 (d, *J*_{3-3a}=3.4 Hz, 1 H, H-3a), 4.65 (s, 1 H, H-1), 3.80 (dd, *J*_{gem}=7.1 Hz, *J*_{5-6_{exo}}=5.2 Hz, 1 H, H-6 *exo*), 3.68 (dd, *J*_{gem}=7.1 Hz, *J*_{5-6_{endo}}=1.1 Hz, 1 H, H-6 *endo*), 3.01 (dd, *J*₃₋₄=10.1 Hz, *J*_{3-3a}=3.4 Hz, 1 H, H-3), 2.51 (d, *J*₃₋₄=10.1 Hz, 1 H, H-4), 0.94 (s, 9 H, H-10), 0.33 (s, 3 H, H-8a), 0.25 (s, 3 H, H-8b); ¹³C NMR (CDCl₃) δ 199.1 (C, C-2), 144.4 (C, aromatic), 141.7 (C, aromatic), 141.3 (C, aromatic), 140.5 (C, aromatic), 126.0 (CH, aromatic), 125.8 (CH, aromatic), 125.7 (CH, 2 C, aromatic), 124.8 (CH, aromatic), 123.9 (CH, aromatic), 122.1 (CH, aromatic), 121.2 (CH, aromatic), 99.4 (CH, C-1), 72.8 (CH, C-5), 69.3 (CH₂, C-6), 60.1 (CH₂, C-7), 48.4 (C, C-4a), 46.3 (CH, C-3a), 45.3 (CH, C-4), 43.0 (CH, C-3), 25.6 (CH₃, C-10), 17.9 (C, C-9), -5.6 (CH₃, C-8a), -5.8 (CH₃, C-8b); HRMS calc. for C₂₇H₃₂O₄SiNa [M+Na]⁺ 471.1968. Found 471.1960.

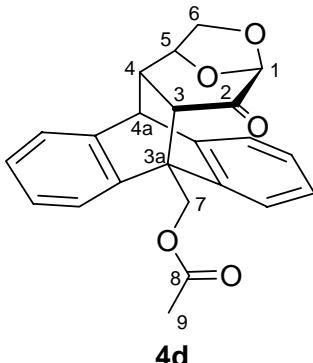
Diels-Alder Product 4c



4c

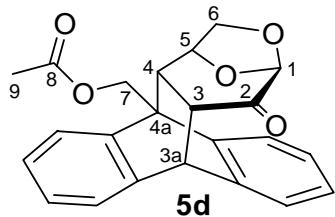
White crystalline solid; mp 249-250 °C (hexane/chloroform); $[\alpha]^{19}_D$ -64.1 (*c* 0.88, CHCl₃); IR (KBr) 3068, 3040, 2969, 2899, 1717 (C=O), 1599, 1497, 1464, 1241, 1115, 750 cm⁻¹; ¹H NMR (CDCl₃) δ 7.47-7.00 (m, 13 H, aromatics), 5.56 (d, *J*_{gem}=9.3 Hz, 1 H, H-7), 5.23 (d, *J*_{gem}=9.3 Hz, 1 H, H-7), 4.83 (d, *J*_{5-6_{exo}}=4.3 Hz, 1 H, H-5), 4.57 (s, 1 H, H-1), 4.35 (d, *J*_{4-4a}=1.5 Hz, 1 H, H-4a), 3.78 (dd, *J*_{gem}=7.3 Hz, *J*_{5-6_{exo}}=4.3 Hz, 1 H, H-6 *exo*), 3.71 (dd, *J*_{gem}=7.3 Hz, *J*_{5-6_{endo}}=1.0 Hz, 1 H, H-6 *endo*), 3.25 (d, *J*₃₋₄=9.7 Hz, 1 H, H-3), 2.37 (dd, *J*₃₋₄=9.7 Hz, *J*_{4-4a}=1.5 Hz, 1 H, H-4); ¹³C NMR (CDCl₃) δ 198.8 (C, C-2), 158.6 (C, aromatic), 145.1 (C, aromatic), 140.8 (C, aromatic), 140.7 (C, aromatic), 140.1 (C, aromatic), 129.5 (CH, 2C, aromatic), 126.4 (CH, aromatic), 126.1 (CH, aromatic), 126.0 (CH, aromatic), 125.9 (CH, aromatic), 125.1 (CH, aromatic), 124.2 (CH, aromatic), 122.2 (CH, aromatic), 121.6 (CH, aromatic), 121.1 (CH, aromatic), 114.9 (CH, 2C, aromatic), 99.7 (CH, C-1), 77.1 (CH, C-5), 68.8 (CH₂, C-6), 66.2 (CH₂, C-7), 50.3 (CH, C-4a), 49.6 (C, C-3a), 44.8 (CH, C-4), 44.3 (CH, C-3); HRMS calc. for C₂₇H₂₂O₄ [M]⁺ 410.1518. Found 410.1500.

Diels-Alder Product 4d



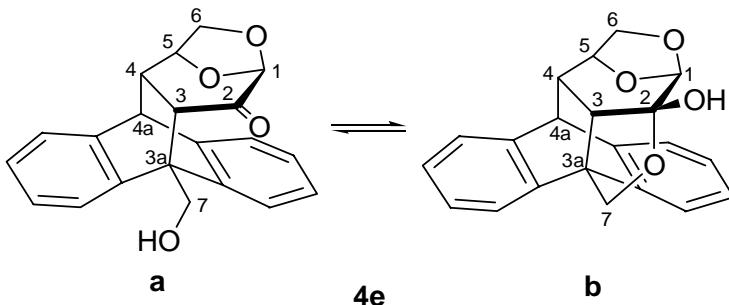
White crystalline solid; mp 241-242 °C (hexane/chloroform); $[\alpha]^{23}_D$ -51.9 (*c* 0.86, CHCl₃); IR (KBr) 3069, 3011, 2961, 2909, 1734 (C=O), 1719 (C=O), 1458, 1366, 1236, 1121, 993, 901, 764, 739 cm⁻¹; ¹H NMR (CDCl₃) δ 7.44-7.07 (m, 8 H, aromatics), 5.63 (d, *J*_{gem}=11.5 Hz, 1 H, H-7), 5.33 (d, *J*_{gem}=11.5 Hz, 1 H, H-7), 4.82 (d, *J*_{5-6exo}=4.7 Hz, 1 H, H-5), 4.57 (s, 1 H, H-1), 4.35 (d, *J*_{4-4a}=1.3 Hz, 1 H, H-4a), 3.78 (dd, *J*_{gem}=7.3 Hz, *J*_{5-6exo}=4.7 Hz, 1 H, H-6 *exo*), 3.70 (dd, *J*_{gem}=7.3 Hz, *J*_{5-6endo}=1.0 Hz, 1 H, H-6 *endo*), 3.11 (d, *J*₃₋₄=9.7 Hz, 1 H, H-3), 2.34 (dd, *J*₃₋₄=9.7 Hz, *J*_{4-4a}=1.3 Hz, 1 H, H-4), 2.17 (s, 3 H, H-9); ¹³C NMR (CDCl₃) δ 198.5 (C, C-2), 170.8 (C, C-8), 144.9 (C, aromatic), 140.6 (C, 2C, aromatics), 139.5 (C, aromatic), 126.5 (CH, aromatic), 126.3 (CH, aromatic), 126.0 (CH, 2C, aromatics), 125.1 (CH, aromatic), 123.2 (CH, aromatic), 122.5 (CH, aromatic), 121.3 (CH, aromatic), 99.5 (CH, C-1), 77.0 (CH, C-5), 68.8 (CH₂, C-6), 63.0 (CH₂, C-7), 50.1 (CH, C-4a), 48.5 (C, C-3a), 44.3 (CH, C-4), 44.0 (CH, C-3), 20.9 (CH₃, C-9); HRMS calc. for C₂₃H₂₁O₅ [M+H]⁺ 377.1389. Found 377.1374.

Diels-Alder Product 5d



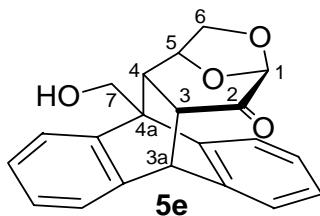
Colorless oil; $[\alpha]^{25}_D$ -79.3 (*c* 1.45, CHCl₃); IR (film) 3072, 2967, 2902, 1739 (C=O), 1458, 1234, 1117, 1043, 751 cm⁻¹; ¹H NMR (CDCl₃) δ 7.40-7.09 (m, 8 H, aromatics), 5.41 (s, 2 H, H-7), 4.87 (d, *J*_{3-3a}=3.3 Hz, 1 H, H-3a), 4.84 (d, *J*_{5-6exo}=5.3 Hz, 1 H, H-5), 4.65 (s, 1 H, H-1), 3.83 (dd, *J*_{gem}=7.3 Hz, *J*_{5-6exo}=5.3 Hz, 1 H, H-6exo), 3.68 (dd, *J*_{gem}=7.3 Hz, *J*_{5-6endo}=1.0 Hz, 1 H, H-6endo), 3.02 (dd, *J*₃₋₄=10.0 Hz, *J*_{3-3a}=3.3 Hz, 1 H, H-3), 2.39 (d, *J*₃₋₄=10.0 Hz, 1 H, H-4), 2.19 (s, 3 H, H-9); ¹³C NMR (CDCl₃) δ 198.4 (C, C-2), 170.8 (C, C-8), 143.2 (C, aromatic), 141.6 (C, aromatic), 140.8 (C, aromatic), 139.4 (C, aromatic), 126.4 (CH, aromatic), 126.3 (CH, aromatic), 126.2 (CH, aromatic), 126.1 (CH, aromatic), 125.0 (CH, aromatic), 124.1 (CH, aromatic), 121.5 (CH, 2 C, aromatic), 99.3 (CH, C-1), 72.3 (CH, C-5), 69.3 (CH₂, C-6), 62.1 (CH₂, C-7), 47.1 (C, C-4a), 46.4 (CH, C-3a), 45.7 (CH, C-3), 43.8 (CH, C-4), 20.8 (CH₃, C-9); HRMS calc. for C₂₃H₂₀O₅ [M]⁺ 376.1311. Found 376.1292.

Diels-Alder Product 4e



Colorless oil; IR (film) 3442, 3040, 2958, 1725 (C=O), 1457, 1245, 1118, 1083, 1045, 993, 749 cm⁻¹; ¹H NMR (CDCl₃) δ 7.67-6.99 (m, aromatics of **a** and **b**), 5.06 (d, *J*_{gem}=9.2 Hz, H-7 of **b**), 4.90 (d, *J*_{gem}=12.3 Hz, H-7 of **a**), 4.82 (d, *J*_{gem}=12.3 Hz, H-7 of **a**), 4.74 (d, *J*=9.2 Hz, H-7 of **b**), 4.74 (broad s, H-5 of **a** and H-1 of **b**), 4.62 (s, H-1 of **a**), 4.38 (d, *J*_{4-4a}=4.1 Hz, H-4a of **b**), 4.33 (d, *J*_{4-4a}=1.9 Hz, H-4a of **a**), 4.21 (d, *J*_{5-6exo}=5.4 Hz, H-5 of **b**), 3.77-3.54 (m, H-6 of **a** and **b**), 3.08 (d, *J*₃₋₄=9.9 Hz, H-3 of **a**), 2.47 (d, *J*₃₋₄=10.3 Hz, H-3 of **b**), 2.34-2.24 (m, H-4 of **a** and **b**); ¹³C NMR (CDCl₃) δ 201.3 (C, C-2 of **a**), 144.6 (C, aromatic of **a** and **b**), 143.8 (C, aromatic of **a** and **b**), 142.2 (C, aromatic of **a** and **b**), 141.4 (C, aromatic of **a** and **b**), 140.8 (C, aromatic of **a** and **b**), 139.9 (C, aromatic of **a** and **b**), 126.5 (CH, aromatic of **a** and **b**), 126.0 (CH, aromatic of **a** and **b**), 125.6 (CH, aromatic of **a** and **b**), 125.4 (CH, aromatic of **a** and **b**), 124.8 (CH, aromatic of **a** and **b**), 124.5 (CH, aromatic of **a** and **b**), 123.7 (CH, aromatic of **a** and **b**), 123.3 (CH, aromatic of **a** and **b**), 122.8 (CH, aromatic of **a** and **b**), 122.2 (CH, aromatic of **a** and **b**), 120.9 (CH, aromatic of **a** and **b**), 118.5 (CH, aromatic of **a** and **b**), 99.8 (CH, C-1 of **a**), 98.8 (CH, C-1 of **b**), 98.8 (C, C-2 of **b**), 76.8 (CH, C-5 of **a**), 73.5 (CH, C-5 of **b**), 69.7 (CH₂, C-6 of **b**), 69.0 (CH₂, C-6 of **a**), 65.7 (CH₂, C-7 of **b**), 60.6 (CH₂, C-7 of **a**), 56.3 (CH, C-4a of **b**), 56.2 (C, C-3a of **b**), 50.9 (C, C-3a of **a**), 50.2 (CH, C-4a of **a**), 50.0 (CH, C-4 of **b**), 44.6 (CH, C-4 of **a**), 42.5 (CH, C-3 of **a**), 37.7 (CH, C-3 of **b**); HRMS calc. for C₂₁H₁₉O₄ [M+H]⁺ 335.1283. Found 335.1276.

Diels-Alder Product 5e



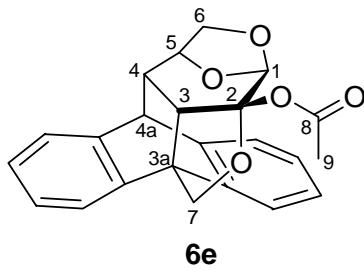
Colorless oil; $[\alpha]^{25}_D$ -76.7 (*c* 1.02, CHCl₃); IR (film) 3511, 3023, 2967, 2900, 1724 (C=O), 1458, 1118, 985, 751 cm⁻¹; ¹H NMR (CDCl₃) δ 7.50-7.05 (m, 8 H, aromatics), 4.99 (d, *J*_{gem}=11.1 Hz, 1 H, H-7), 4.96 (d, *J*_{5-6exo}=5.5 Hz, 1 H, H-5), 4.91 (d, *J*_{gem}=11.1 Hz, 1 H, H-7), 4.85 (d, *J*_{3-3a}=3.3 Hz, 1 H, H-3a), 4.64 (s, 1 H, H-1), 3.80 (dd, *J*_{5-6exo}=5.5 Hz, *J*_{gem}=7.4 Hz, 1 H, H-6exo), 3.67 (dd, *J*_{gem}=7.4 Hz, *J*_{5-6endo}=1.1 Hz, 1 H, H-6endo), 2.99 (dd, *J*₃₋₄=10.0 Hz, *J*_{3-3a}=3.3 Hz, 1 H, H-3), 2.43 (d, *J*₃₋₄=10.0 Hz, 1 H, H-4), 2.21 (broad s, 1 H, OH); ¹³C NMR (CDCl₃) δ 199.2 (C, C-2), 144.0 (C, aromatic), 141.7 (C, aromatic), 141.2 (C, aromatic), 140.3 (C, aromatic), 126.2 (CH, aromatic), 126.0 (CH, 2C, aromatics), 125.9 (CH, aromatic), 124.8 (CH, aromatic), 124.2 (CH, aromatic), 121.5 (CH, aromatic), 121.4 (CH, aromatic), 99.3 (CH, C-1), 72.5 (CH, C-5), 69.3

(CH₂, C-6), 60.1 (CH₂, C-7), 48.3 (C, C-4a), 46.3 (CH, C-3a), 45.4 (CH, C-3), 43.2 (CH, C-4).

Acetylation of **4e**

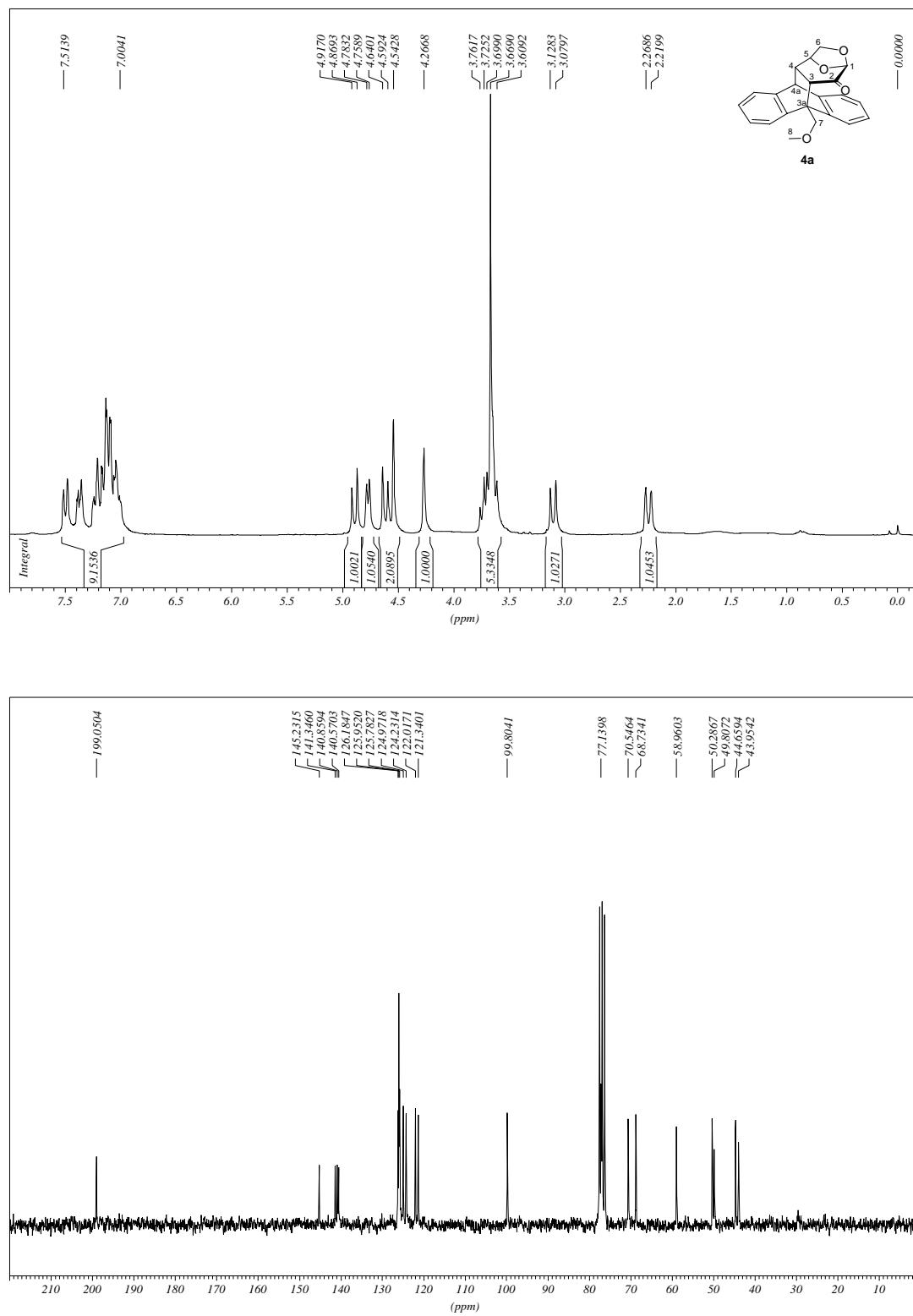
The *ortho* adduct **4e** (105 mg, 0.314 mmol) (as a mixture of the free carbonyl compound and the corresponding hemiketal derivative) was dissolved in dry CH₂Cl₂ (2.5 mL) under argon. The solution was cooled at 0 °C and dry pyridine (0.36 mL, 4.45 mmol), DMAP (3.9 mg, 0.03 mmol) and Ac₂O (0.28 mL, 2.94 mmol) were added in this order. The solution was stirred for 1 hour at 0 °C. The solvent was evaporated under reduced pressure and the crude was dissolved with AcOEt (100 mL). The organic phase was washed with saturated CuSO₄ (3 x 100 mL) and brine (2 x 100 mL), dried (Na₂SO₄) and concentrated. The residual solid was purified by flash chromatography to afford **4d** (59.1 mg, 0.157 mmol, 50%) and **6e** (32.9 mg, 0.087 mmol, 28%).

Acetylated Diels-Alder Product **6e**

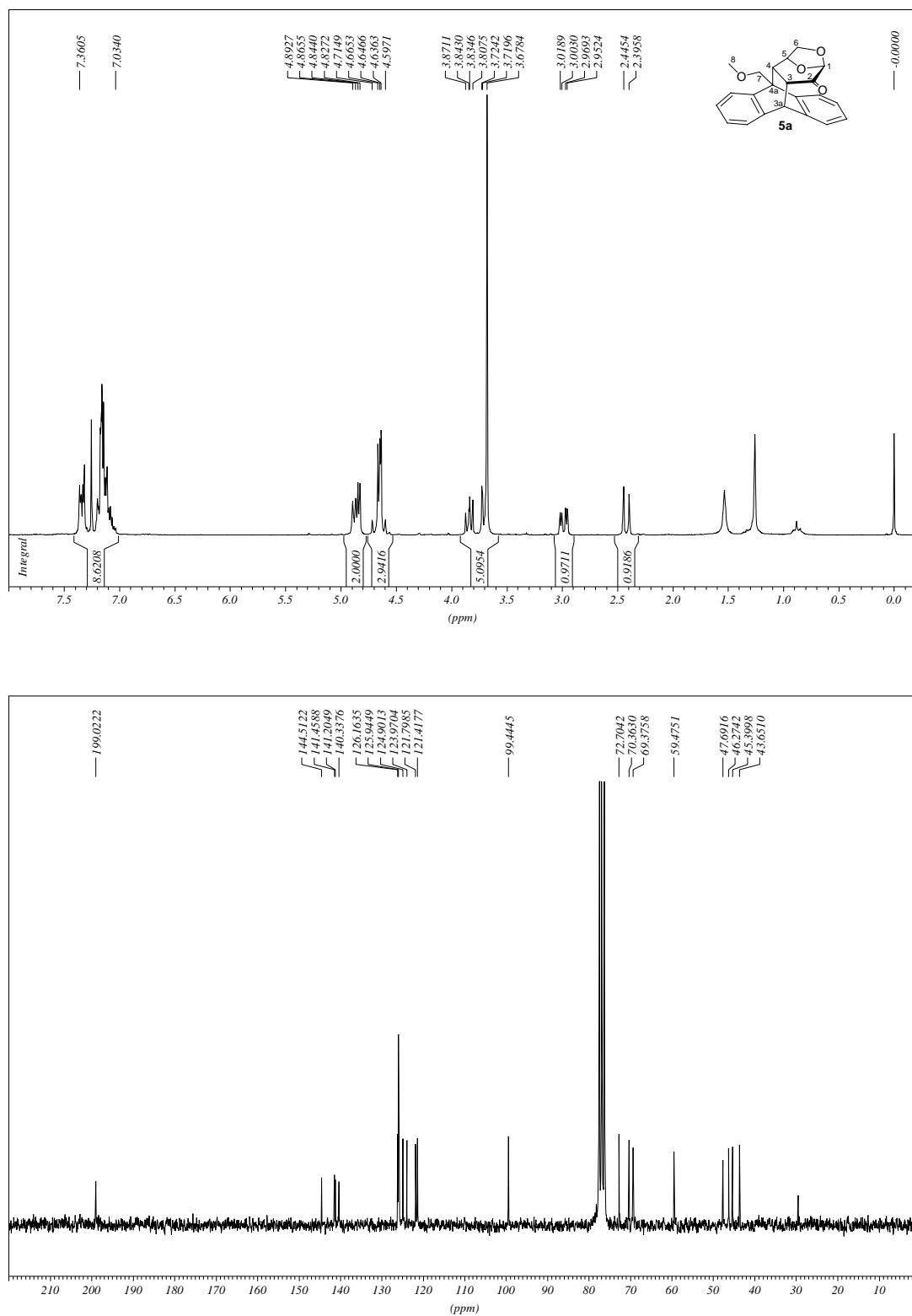


White solid; mp 238-239 °C (hexane/chloroform); $[\alpha]^{16}_D -35.6$ (*c* 0.56, CHCl₃); IR (KBr) 3015, 2959, 1744 (C=O), 1450, 1364, 1244, 1234, 1215, 1001, 959, 758 cm⁻¹; ¹H NMR (CDCl₃) δ 7.39-7.03 (m, 8 H, aromatics), 5.44 (s, 1 H, H-1), 5.16 (d, *J*_{gem}=9.1 Hz, 1 H, H-7), 4.68 (d, *J*_{gem}=9.1 Hz, 1 H, H-7), 4.40 (d, *J*_{4-4a}=4.0 Hz, 1 H, H-4a), 4.22 (dd, *J*_{5-6exo}=5.8 Hz, *J*_{5-6endo}=1.3 Hz, 1 H, H-5), 3.68 (dd, *J*_{gem}=7.3 Hz, *J*_{5-6exo}=5.8 Hz, 1 H, H-6exo), 3.55 (dd, *J*_{gem}=7.3 Hz, *J*_{5-6endo}=1.3 Hz, 1 H, H-6endo), 2.60 (d, *J*₃₋₄=10.3 Hz, 1 H, H-3), 2.35 (dd, *J*₃₋₄=10.3 Hz, *J*_{4-4a}=4.0 Hz, 1 H, H-4), 2.01 (s, 3 H, H-9); ¹³C NMR (CDCl₃) δ 169.7 (C, C-8), 144.2 (C, aromatic), 141.4 (C, aromatic), 141.2 (C, aromatic), 140.1 (C, aromatic), 126.2 (CH, aromatic), 126.0 (CH, aromatic), 125.9 (CH, aromatic), 125.7 (CH, aromatic), 124.6 (CH, aromatic), 123.8 (CH, aromatic), 122.2 (CH, aromatic), 118.6 (CH, aromatic), 103.7 (C, C-2), 98.9 (CH, C-1), 73.5 (CH, C-5), 69.7 (CH₂, C-6), 66.8 (CH₂, C-7), 55.2 (C, C-3a), 54.9 (CH, C-4a), 49.9 (CH, C-4), 37.9 (CH, C-3), 21.4 (CH₃, C-9).

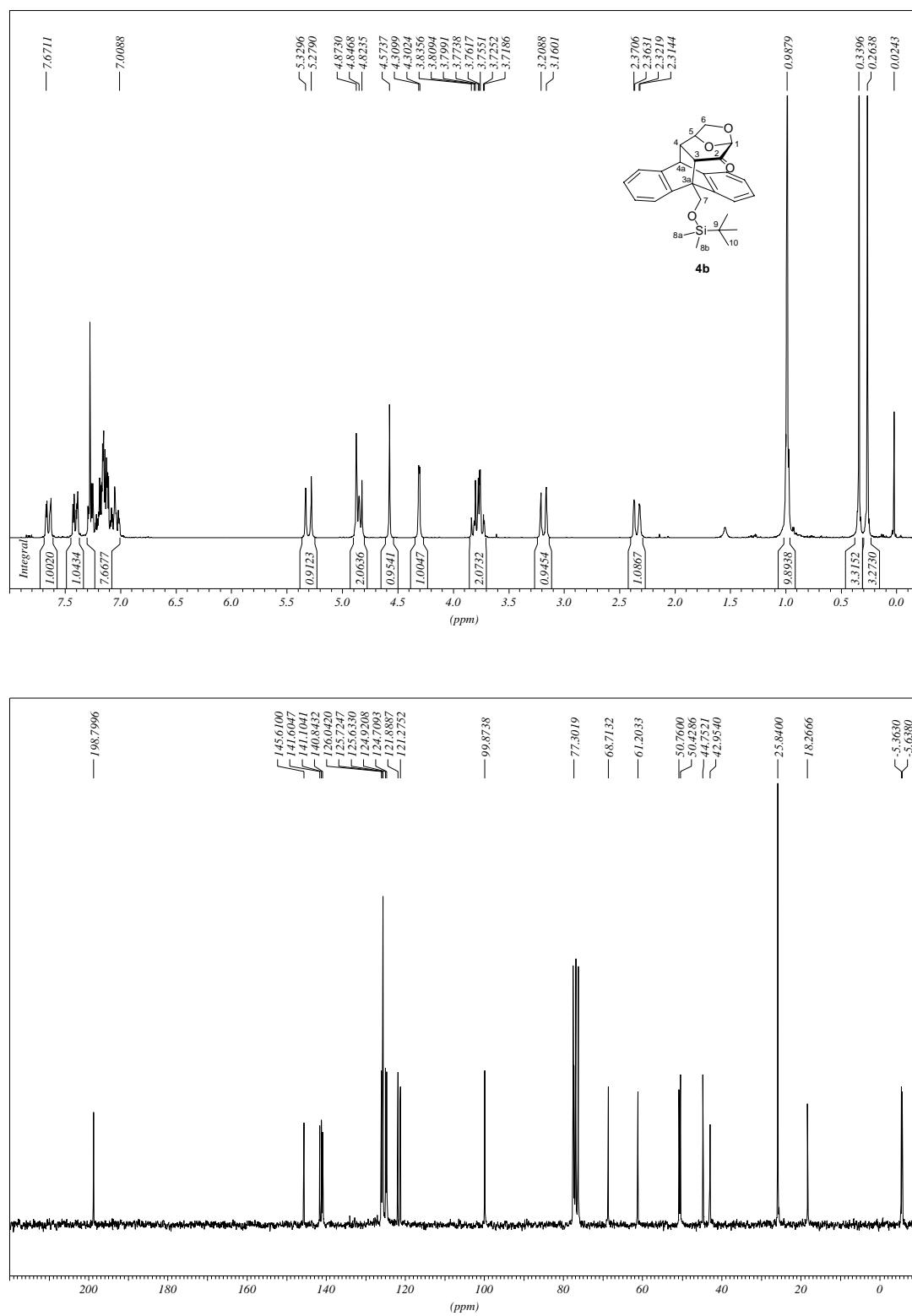
¹H and ¹³C NMR Spectra of **4a**



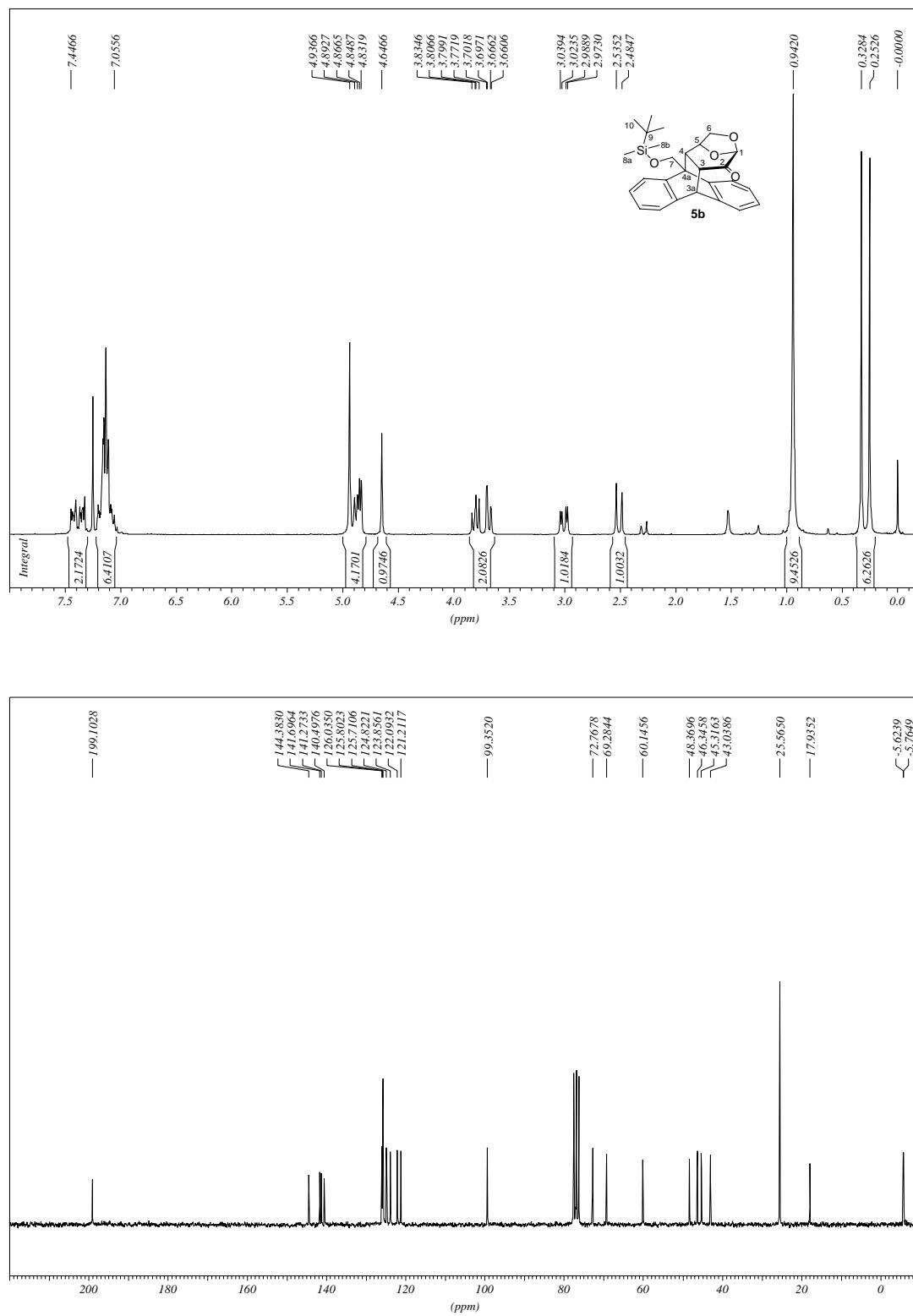
¹H and ¹³C NMR Spectra of **5a**



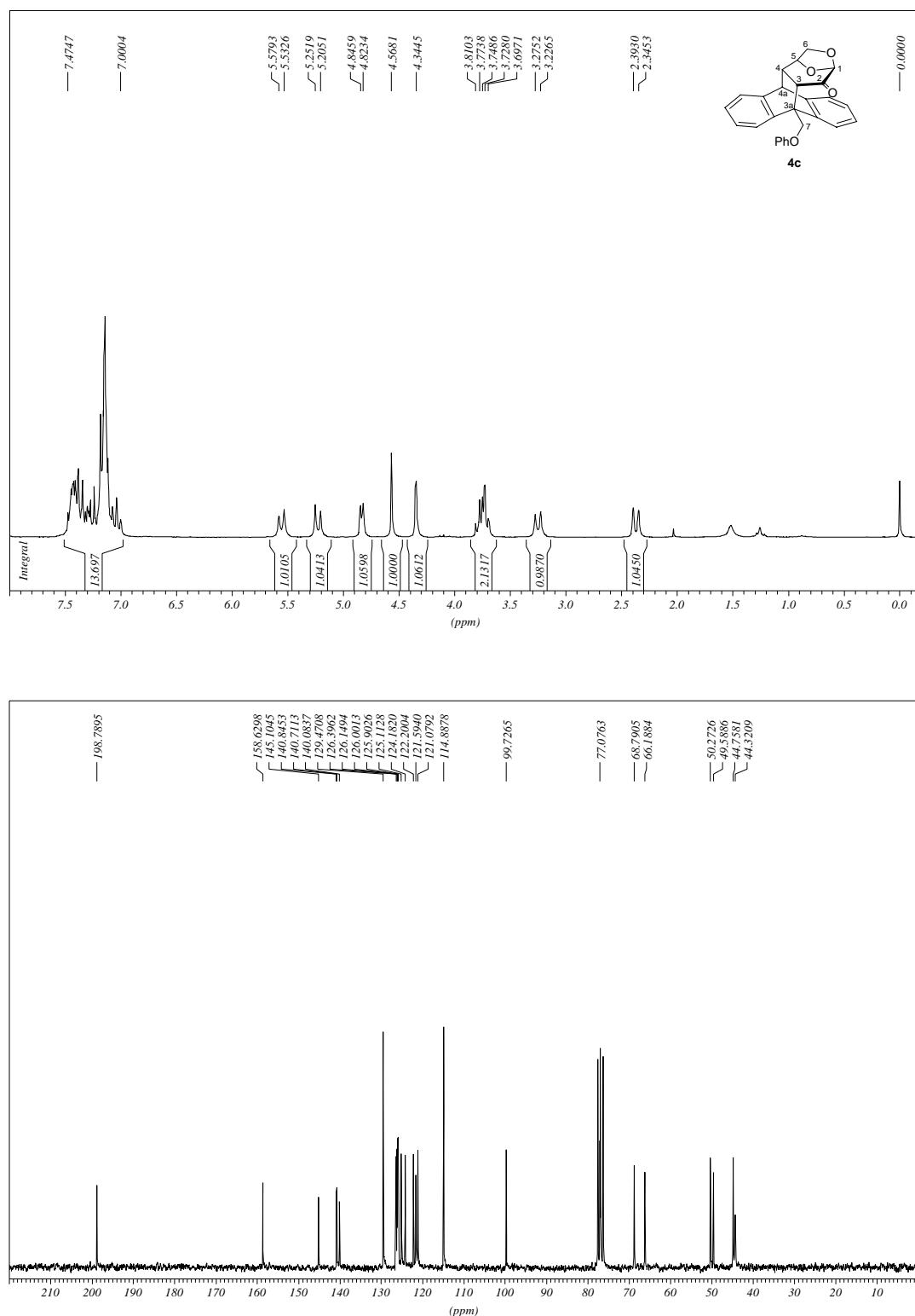
¹H and ¹³C NMR Spectra of **4b**



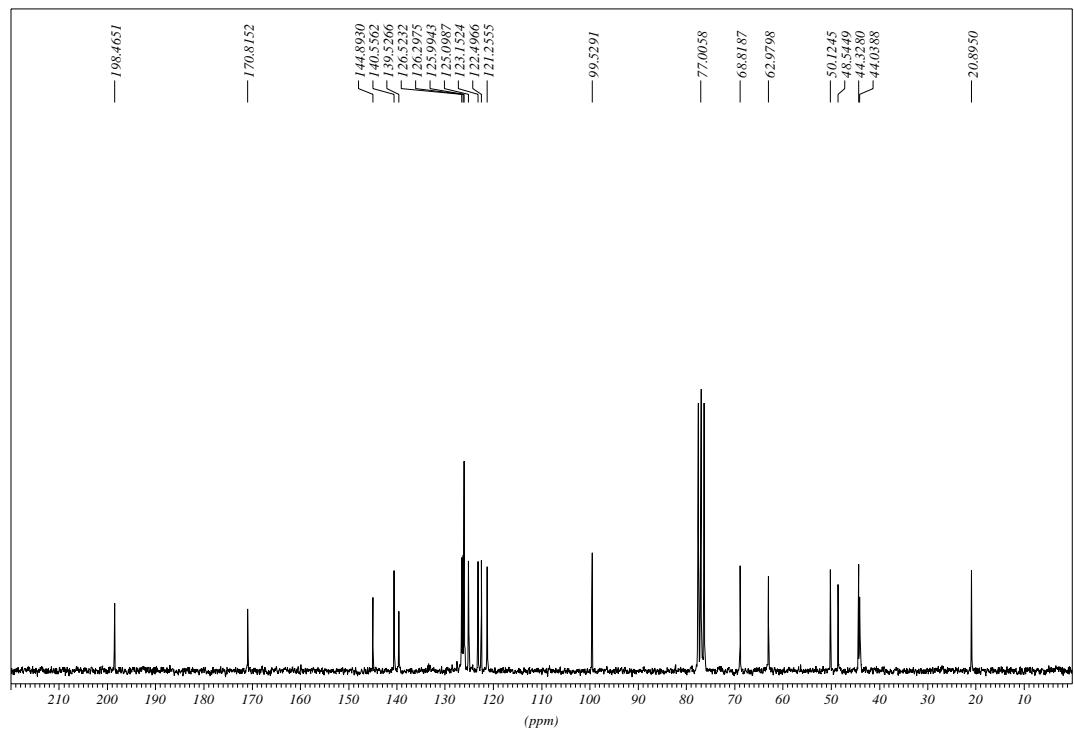
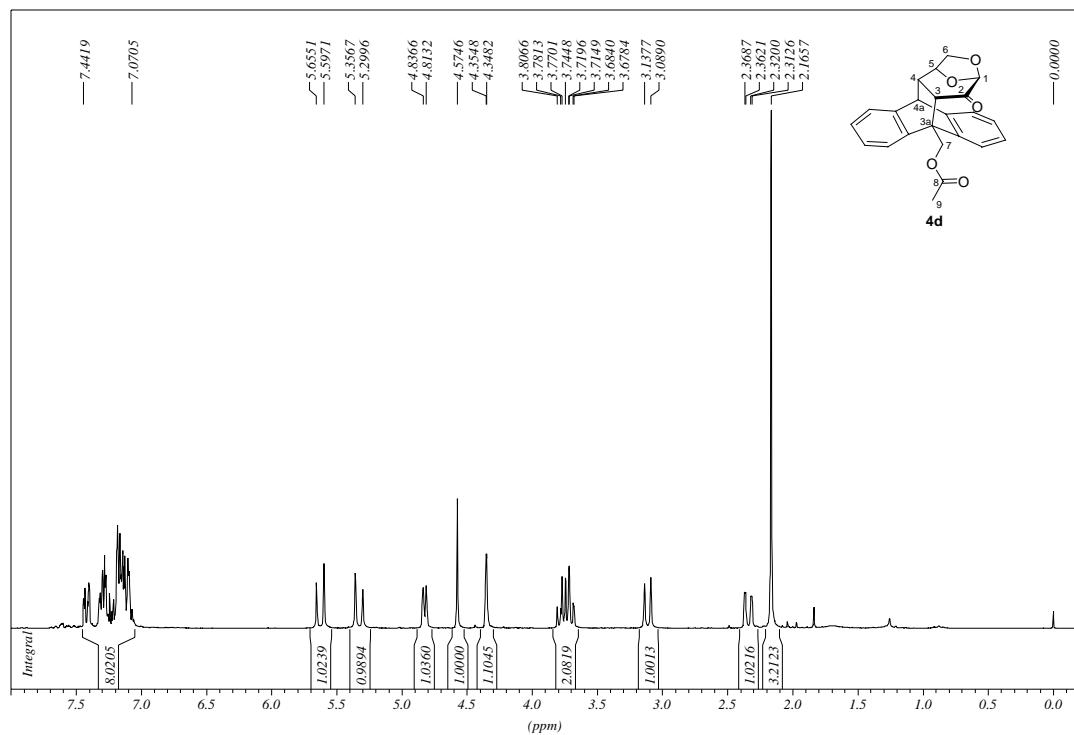
¹H and ¹³C NMR Spectra of **5b**



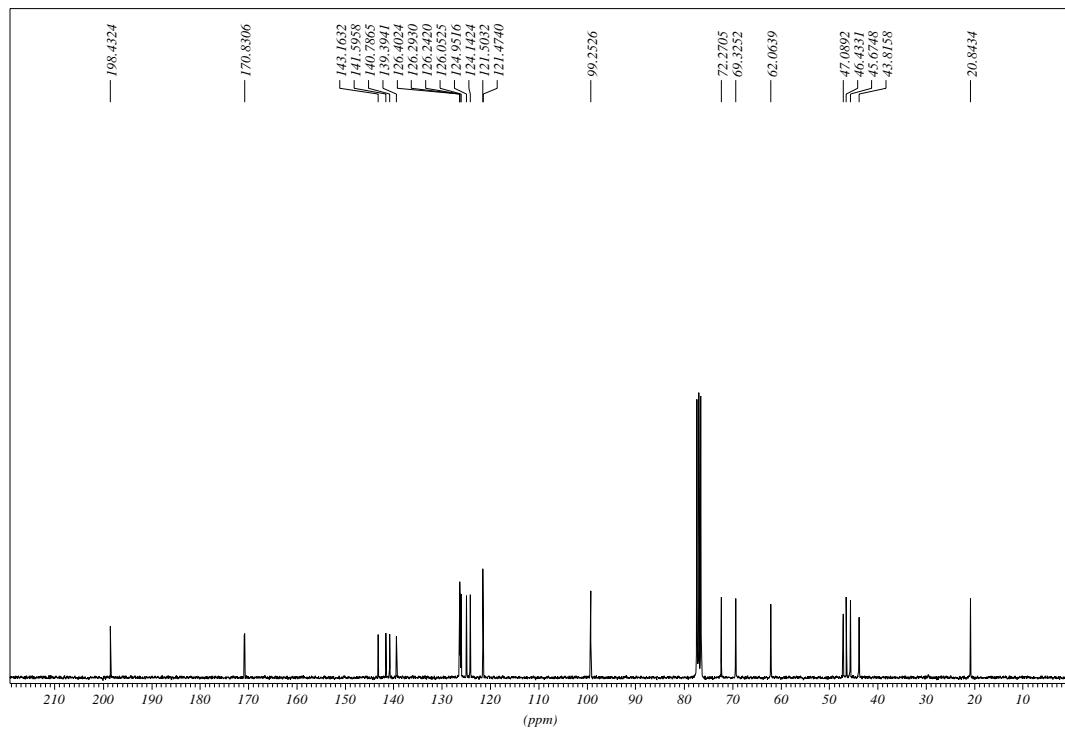
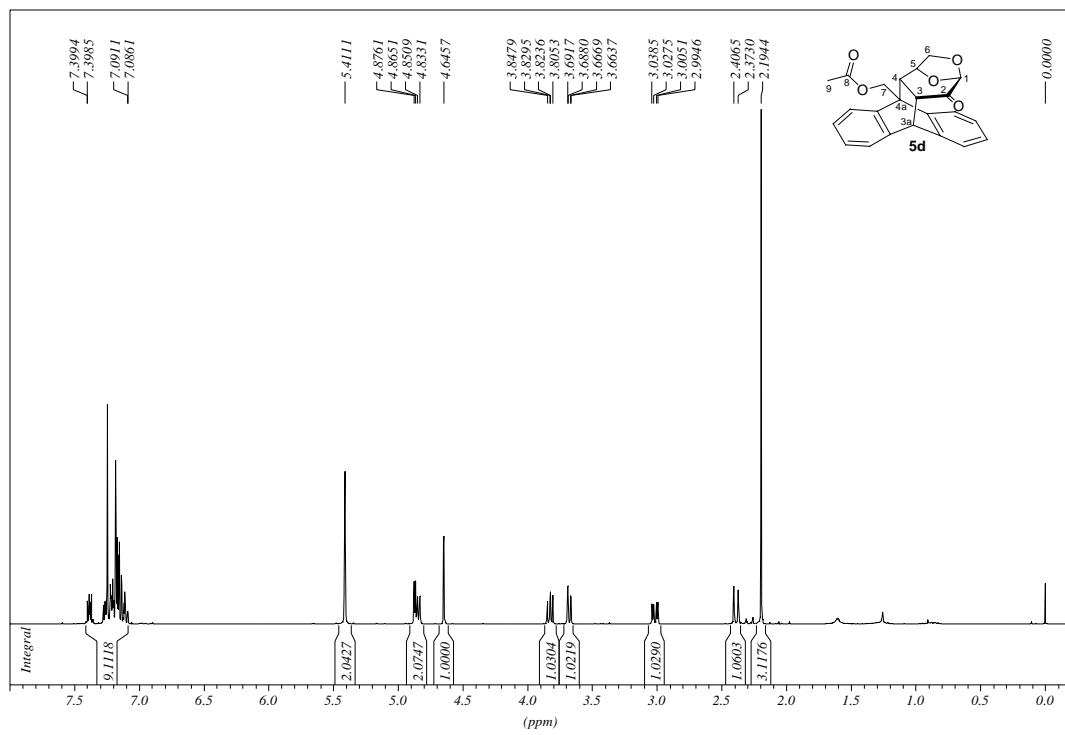
¹H and ¹³C NMR Spectra of **4c**



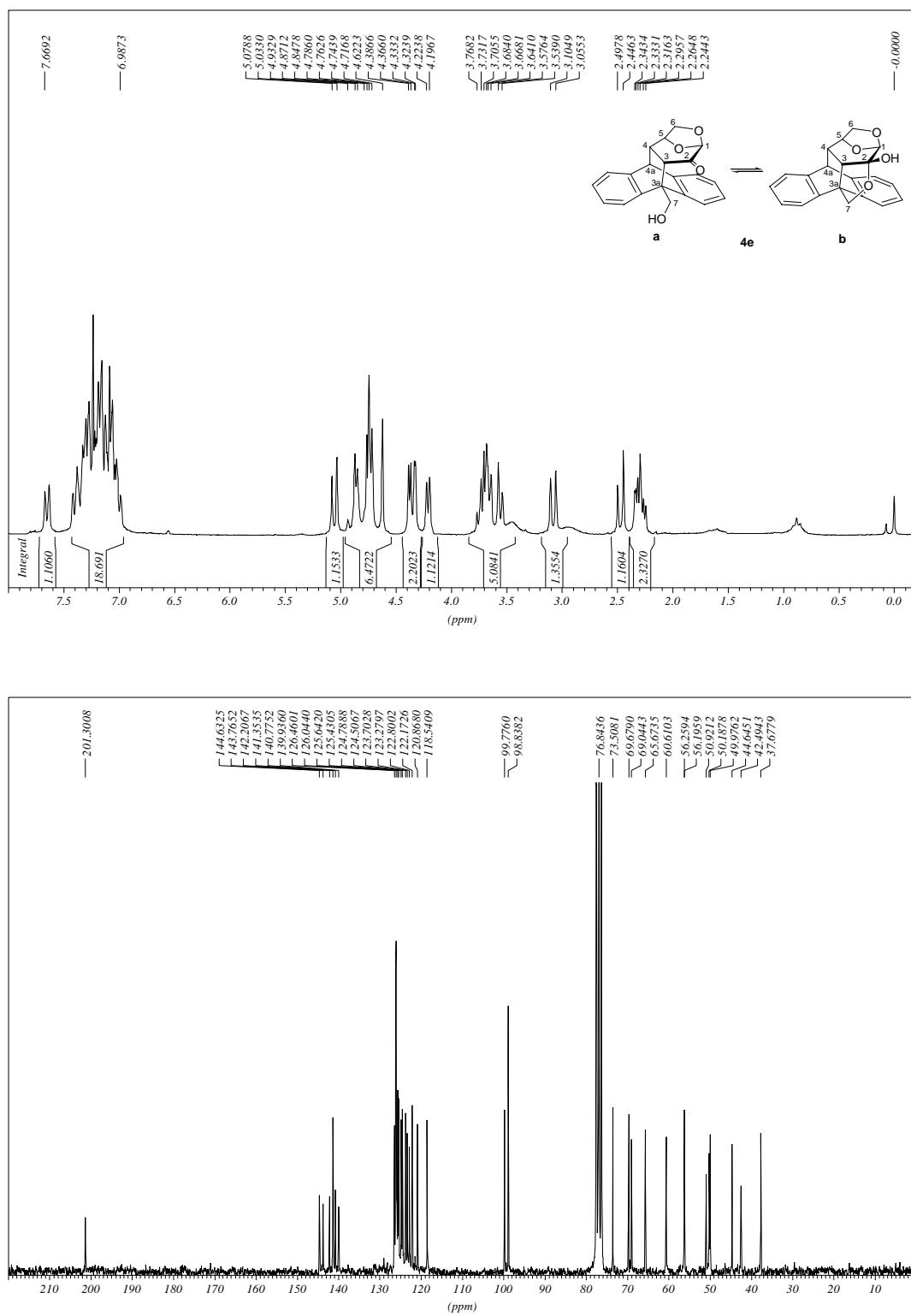
¹H and ¹³C NMR Spectra of **4d**



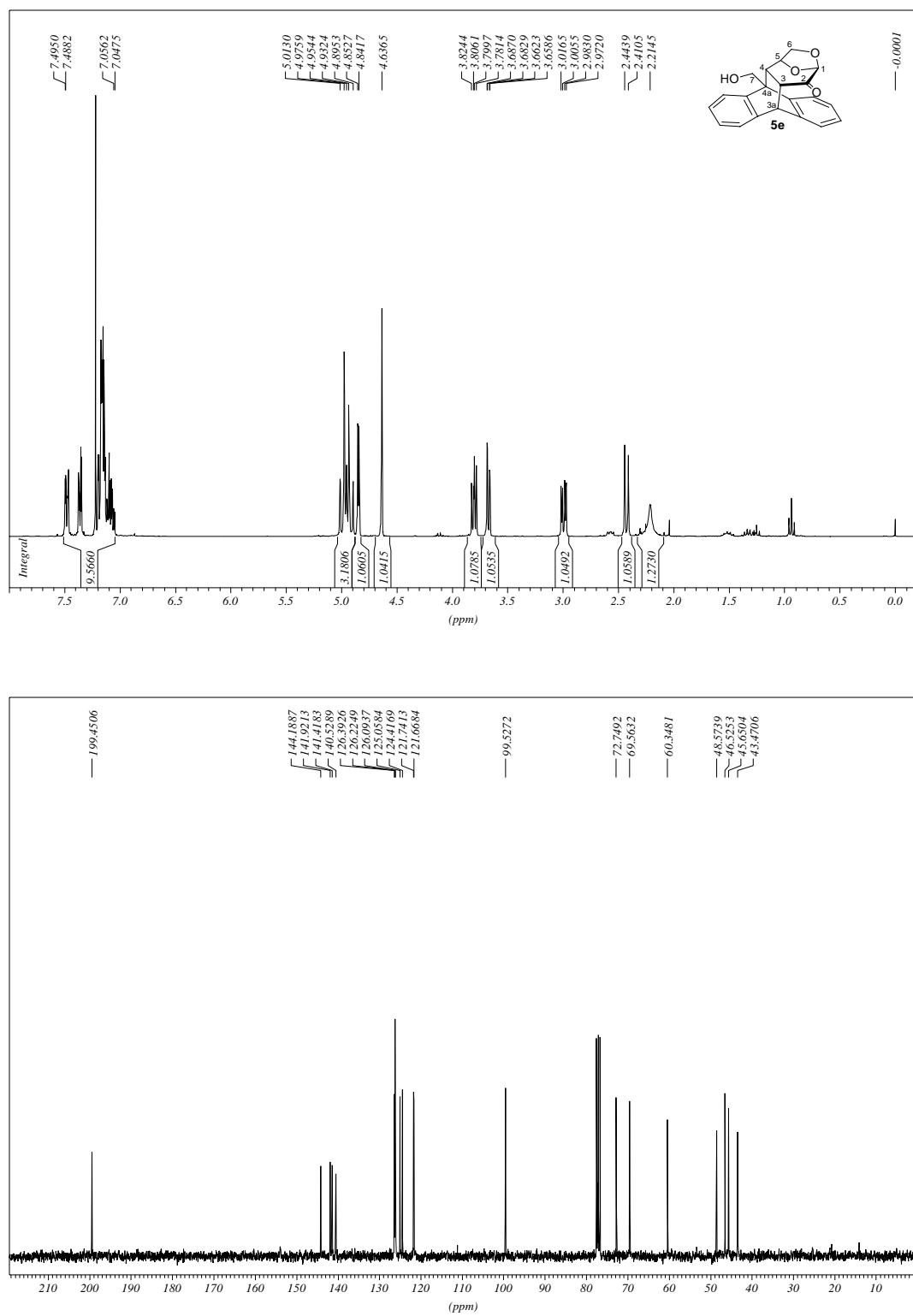
¹H and ¹³C NMR Spectra of **5d**



¹H and ¹³C NMR Spectra of 4e



¹H and ¹³C NMR Spectra of **5e**



¹H and ¹³C NMR Spectra of **6e**

