

Total Synthesis of (+)-Cytosporolide A via a Biomimetic Hetero-Diels–Alder Reaction

Ken-ichi Takao,* Shuji Noguchi, Shu Sakamoto, Mizuki Kimura, Keisuke Yoshida,
and Kin-ichi Tadano

Supporting Information

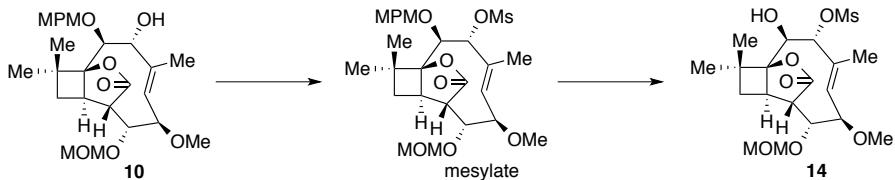
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1. Experimental procedures for new compounds

General methods. Melting points are uncorrected. Specific rotations were measured in a 100 mm cell. ^1H NMR spectra were recorded at 400 or 500 MHz with tetramethylsilane as an internal standard on a JEOL JNM-ECS400 (400 MHz) or a JEOL JNM-ECA500 (500 MHz) spectrometer. ^{13}C NMR spectra were recorded at 125 MHz. High-resolution mass spectra (HRMS) were measured by the ESI mode on a Waters LCT premier XE spectrometer. Thin-layer chromatography (TLC) and preparative TLC were performed on Merck Kieselgel 60 F₂₅₄ plates. The crude reaction mixtures and extracted materials were purified by chromatography on Silica gel 60N (Kanto Chemical), Wakogel C-300 (Wako), or Silica gel 120 (spherical) RP-18 (Kanto Chemical). Combined organic extracts were dried over anhydrous Na₂SO₄. Solvents were removed from the reaction mixture and the combined organic extracts by concentration under reduced pressure using an evaporator with bath at 35–45 °C.

(1*S*,2*S*,3*R*,4*E*,6*R*,7*R*,8*S*,9*R*)-2-Hydroxy-3-(methanesulfonyloxy)-6-methoxy-7-(methoxymethoxy)-4,11,11-trimethyl-12-oxatricyclo[6.3.2.0^{1,9}]tridec-4-en-13-one (14).

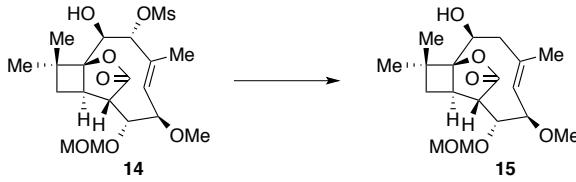


The following reaction was carried out under Ar. To a cooled (0 °C) stirred solution of **10**¹ (467 mg, 0.980 mmol) in pyridine (9 mL) were added Ms_2O (517 mg, 2.97 mmol) and DMAP (362 mg, 2.96 mmol). The mixture was stirred at room temperature for 21 h, and Ms_2O (180 mg, 1.03 mmol) and DMAP (120 mg, 0.982 mmol) were added. After being stirred at room temperature for 23 h, the mixture was diluted with saturated aqueous NaHCO_3 (60 mL) and extracted with EtOAc (50 mL × 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:1) to provide 548 mg (quant.) of mesylate as a colorless oil.¹

To a cooled (0 °C) stirred solution of mesylate (511 mg, 0.921 mmol) in CH_2Cl_2 (15 mL) were added aqueous phosphate buffer (0.5 M aqueous Na_2HPO_4 - NaH_2PO_4 , 1.5 mL) and DDQ (1.05 g, 4.61 mmol). After being stirred at room temperature for 15 h, the mixture was diluted with saturated aqueous NaHCO_3 (250 mL) and extracted with EtOAc (200 mL × 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:5) to provide 417 mg (quant.) of **14** as a colorless oil: TLC R_f 0.23 (EtOAc/hexane, 1:2); $[\alpha]_D^{22} +65.9$ (*c* 1.05, CHCl_3); IR (neat) 3499, 2937, 1760 cm^{-1} ; ¹H NMR (500 MHz, CDCl_3) δ 1.12 (s, 3H), 1.34 (s, 3H), 1.41 (dd, 1H, *J* = 5.6, 12.7 Hz), 1.95 (d, 3H, *J* = 1.4 Hz), 2.18 (dd, 1H, *J* = 9.7, 12.7 Hz), 2.44 (br d, 1H, *J* = 9.2 Hz, OH), 2.75 (ddd, 1H, *J* = 2.5, 5.6, 9.7 Hz), 3.03 (dd, 1H, *J* = 2.5, 3.0 Hz), 3.11 (s, 3H), 3.28 (s, 3H), 3.35 (s, 3H), 4.06 (dd, 1H, *J* = 5.4, 11.7 Hz), 4.16 (dd, 1H, *J* = 8.6, 9.2 Hz), 4.25 (dd, 1H, *J* = 3.0, 5.4 Hz), 4.72 (d, 1H, *J* = 6.9 Hz), 4.83 (d, 1H, *J* = 6.9 Hz), 5.00 (d, 1H, *J* = 8.6 Hz), 5.37 (qd, 1H, *J* = 1.4, 11.7 Hz); ¹³C NMR (125 MHz, CDCl_3) δ 13.5, 24.3, 26.6, 33.4, 38.6, 41.9, 42.5, 55.3, 55.7, 56.7, 72.3, 81.2, 83.8, 87.6, 92.5, 97.1, 126.0, 136.8, 177.6; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{31}\text{O}_9\text{S}$ ($\text{M}+\text{H}$)⁺ *m/z* 435.1689, found 435.1678.

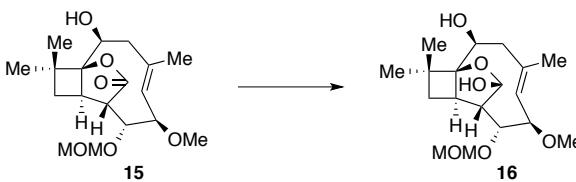
(1*S*,2*S*,4*E*,6*R*,7*R*,8*S*,9*R*)-2-Hydroxy-6-methoxy-7-(methoxymethoxy)-4,11,11-trimethyl-12-oxatricyclo[6.3.2.0^{1,9}]tridec-4-en-13-one (15).

(1) Takao, K.; Hayakawa, N.; Yamada, R.; Yamaguchi, T.; Saegusa, H.; Uchida, M.; Samejima, S.; Tadano, K. *J. Org. Chem.* **2009**, 74, 6452.



The following reaction was carried out under Ar. A solution of catalyst was prepared by mixing Pd₂(dba)₃ and *n*-Bu₃P in degassed 1,4-dioxane at 40 °C for 15 min. To a stirred solution of **14** (190 mg, 0.437 mmol) in degassed 1,4-dioxane (5 mL) were added NaBH₄ (165 mg, 4.37 mmol) and a solution of the premixed catalyst (22 µmol for Pd₂(dba)₃, 44 µmol for *n*-Bu₃P) in 1,4-dioxane (0.50 mL). The mixture was stirred at room temperature for 18 h, quenched with H₂O (10 mL), diluted with saturated brine (50 mL), and extracted with EtOAc (50 mL × 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:5) to provide 106 mg (71%) of an inseparable mixture (*ca.* 7:1) of **15** and its regioisomer as white crystals: mp 146–150 °C; TLC *R*_f 0.25 (EtOAc/hexane, 1:2); [α]_D²³ +127 (*c* 1.19, CHCl₃); IR (neat) 3456, 2935, 1741 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) for **15** δ 1.09 (s, 3H), 1.34 (s, 3H), 1.42 (dd, 1H, *J* = 5.4, 12.6 Hz), 1.62 (br d, 1H, *J* = 8.3 Hz, OH), 1.89 (s, 3H), 2.17 (dd, 1H, *J* = 9.8, 12.6 Hz), 2.41 (t, 1H, *J* = 11.4 Hz), 2.62 (dd, 1H, *J* = 5.6, 11.4 Hz), 2.72 (ddd, 1H, *J* = 2.6, 5.4, 9.8 Hz), 3.02 (t, 1H, *J* = 2.6 Hz), 3.25 (s, 3H), 3.36 (s, 3H), 3.97 (dd, 1H, *J* = 6.0, 11.8 Hz), 4.25 (dd, 1H, *J* = 2.6, 6.0 Hz), 4.26 (m, 1H), 4.72 (d, 1H, *J* = 6.9 Hz), 4.83 (d, 1H, *J* = 6.9 Hz), 5.06 (d, 1H, *J* = 11.8 Hz); ¹³C NMR (125 MHz, CDCl₃) for **15** δ 18.1, 24.6, 26.6, 33.5, 42.4 (2C), 45.5, 55.5, 55.9, 56.2, 69.6, 81.5, 84.2, 93.8, 97.1, 124.6, 138.2, 178.5; HRMS (ESI) calcd for C₁₈H₂₈O₆Na (M+Na)⁺ *m/z* 363.1784, found 363.1782.

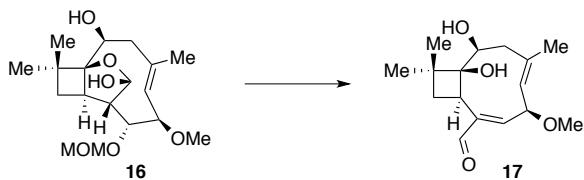
(1*S*,2*S*,4*E*,6*R*,7*R*,8*S*,9*R*,13*R*)-6-Methoxy-7-(methoxymethoxy)-4,11,11-trimethyl-12-oxatricyclo[6.3.2.0^{1,9}]tridec-4-ene-2,13-diol (16).



The following reaction was carried out under Ar. To a cooled (0 °C) stirred solution of a mixture of **15** and its regioisomer (*ca.* 7:1, 88.1 mg, 0.259 mmol) in THF (2 mL) was added DIBALH (1.01 M solution in toluene, 0.51 mL, 0.52 mmol). The mixture was stirred at 0 °C for 15 min, and DIBALH (1.01 M solution in toluene, 0.51 mL, 0.52 mmol) was added. The mixture was stirred at 0 °C for 20 min, and DIBALH (1.01 M solution in toluene, 0.51 mL, 0.52 mmol) was added. After being stirred at 0 °C for 10 min, the mixture was quenched with H₂O (10 mL) and diluted with EtOAc (5 mL). Then potassium sodium (+)-tartrate tetrahydrate (1.32 g) was added

and the mixture was stirred at room temperature for 2 h, diluted with H₂O (10 mL), and extracted with EtOAc (20 mL × 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:5) to provide 53.0 mg (60%) of **16** and a mixture of unreacted **15** and other compounds (43.1 mg), which was treated by the same procedure to provide additional **16** (12.0 mg). In total, 65.0 mg (74% for 2 cycles) of **16** was obtained as a colorless oil: TLC R_f 0.25 (EtOAc/hexane, 2:1); [α]_D²³ +76.5 (*c* 0.770, CHCl₃); IR (neat) 3423, 2933 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 1.18 (s, 3H), 1.27 (s, 3H), 1.57 (dd, 1H, *J* = 6.0, 12.0 Hz), 1.64 (br, 1H, OH), 1.84 (d, 3H, *J* = 1.2 Hz), 1.99 (dd, 1H, *J* = 9.5, 12.0 Hz), 2.41 (t, 1H, *J* = 10.9 Hz), 2.49 (dd, 1H, *J* = 5.2, 10.9 Hz), 2.51–2.56 (m, 2H), 3.29 (s, 3H), 3.40 (s, 3H), 3.51 (br, 1H, OH), 3.93 (dd, 1H, *J* = 2.3, 6.0 Hz), 3.97 (dd, 1H, *J* = 6.0, 11.6 Hz), 4.18 (m, 1H), 4.70 (d, 1H, *J* = 6.9 Hz), 4.77 (d, 1H, *J* = 6.9 Hz), 5.06 (qd, 1H, *J* = 1.2, 11.6 Hz), 5.83 (d, 1H, *J* = 2.3 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 17.5, 24.5, 27.7, 37.9, 39.7, 42.7, 45.8, 55.5, 55.9, 63.9, 70.6, 82.0, 82.1, 95.8, 99.9, 107.5, 123.6, 137.8; HRMS (ESI) calcd for C₁₈H₃₀O₆Na (M+Na)⁺ *m/z* 365.1940, found 365.1942.

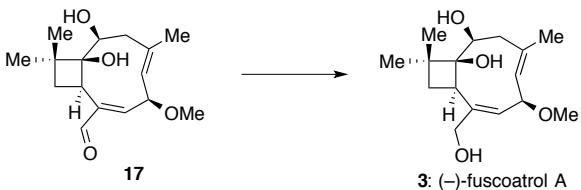
(1*R*,2*E*,4*R*,5*E*,8*S*,9*S*)-8,9-Dihydroxy-6-methoxy-6,10,10-trimethylbicyclo[7.2.0]undeca-2,5-diene-2-carbaldehyde (17).



The following reaction was carried out under Ar. To a cooled (0 °C) stirred solution of **16** (57.8 mg, 0.169 mmol) in THF (10 mL) was added DBU (0.10 mL, 0.68 mmol). The mixture was stirred at 0 °C for 1 h and quenched with saturated aqueous NH₄Cl (10 mL), diluted with H₂O (10 mL), and extracted with EtOAc (30 mL × 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:8) to provide 25.3 mg (54%) of **17** and 29.9 mg of **16**, accompanied by a small amount of by-product, was recovered. The recovered **16** (29.9 mg) was treated by the same procedure to provide additional **17** (5.7 mg). In total, 31.0 mg (66% for 2 cycles) of **17** was obtained as white crystals: mp 109–111 °C; TLC R_f 0.63 (EtOAc/hexane, 2:1); [α]_D²² –220 (*c* 0.660, CHCl₃); IR (neat) 3427, 2955, 1667, 1601 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) ($\beta\alpha/\beta\beta$ conformer = 2:1) for $\beta\alpha$ conformer δ 1.20 (s, 3H), 1.31 (s, 3H), 1.51 (dd, 1H, *J* = 10.5, 12.1 Hz), 1.96 (s, 3H), 2.14 (dd, 1H, *J* = 8.6, 12.1 Hz), 2.40 (dd, 1H, *J* = 4.9, 11.3 Hz), 2.42 (s, 1H, OH), 2.48 (t, 1H, *J* = 11.3 Hz), 3.00 (br dd, 1H, *J* = 8.6, 10.5 Hz), 3.36 (s, 3H), 3.70 (d, 1H, *J* = 1.3 Hz, OH),

4.24 (ddd, 1H, J = 1.3, 4.9, 11.3 Hz), 4.81 (dd, 1H, J = 2.9, 10.4 Hz), 4.92 (d, 1H, J = 10.4 Hz), 6.76 (d, 1H, J = 2.9 Hz), 9.32 (d, 1H, J = 1.0 Hz), for $\beta\beta$ conformer δ 1.11 (s, 3H), 1.34 (s, 3H), 1.43 (dd, 1H, J = 9.2, 10.6 Hz), 1.61 (s, 3H), 1.78 (dd, 1H, J = 10.6, 14.3 Hz), 2.40 (m, 1H), 2.93 (dd, 1H, J = 7.9, 14.3 Hz), 3.23 (br dd, 1H, J = 9.2, 10.6 Hz), 3.37 (s, 3H), 3.89 (d, 1H, J = 1.8 Hz, OH), 4.15 (m, 1H), 4.65 (dd, 1H, J = 2.3, 7.5 Hz), 5.73 (br d, 1H, J = 7.5 Hz), 6.87 (d, 1H, J = 2.3 Hz), 9.40 (d, 1H, J = 1.5 Hz); ^{13}C NMR (125 MHz, CDCl_3) ($\beta\alpha/\beta\beta$ conformer = 2:1) for $\beta\alpha$ conformer δ 17.7, 23.8, 27.5, 33.5, 38.8, 42.1, 45.0, 55.8, 73.9, 77.0, 83.3, 127.1, 135.9, 144.1, 160.8, 196.9, for $\beta\beta$ conformer δ 23.8, 25.1, 25.9, 34.0, 40.1, 44.0 (2C), 56.3, 76.3, 76.5, 84.8, 124.9, 140.6, 144.6, 163.1, 197.3; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{23}\text{O}_4$ ($\text{M}-\text{H}$) $^-$ m/z 279.1596, found 279.1596.

(-)-Fuscoatrol A (3).



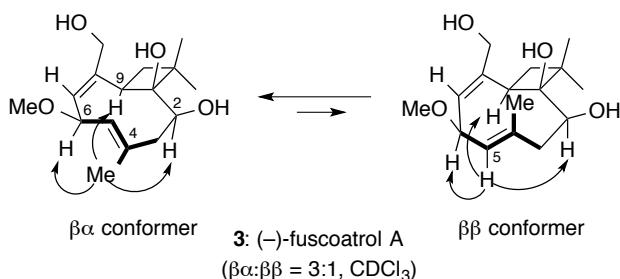
To a cooled (0 °C) stirred solution of **17** (69.1 mg, 0.246 mmol) in MeOH (1 mL) were added CeCl₃·7H₂O (367 mg, 0.984 mmol) and NaBH₄ (37.2 mg, 0.984 mmol). The mixture was stirred at 0 °C for 50 min, and CeCl₃·7H₂O (184 mg, 0.493 mmol) and NaBH₄ (18.6 mg, 0.492 mmol) were added. After being stirred at 0 °C for 40 min, the mixture was quenched with saturated aqueous NH₄Cl (10 mL), diluted with H₂O (20 mL), and extracted with EtOAc (30 mL × 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:6) to provide 60.6 mg (88%) of **3** as white crystals: mp 141–142 °C [lit. mp 144–145 °C]²; TLC *R*_f 0.46 (EtOAc/hexane, 2:1); [α]_D²² –254 (*c* 0.19, CHCl₃) [lit. [α]_D²³ –310 (*c* 0.15, CHCl₃)]²; IR (neat) 3260, 2934 cm^{–1}; ¹H NMR (500 MHz, CDCl₃) (βα/ββ conformer = 3:1) for βα conformer δ 1.10 (s, 3H), 1.29 (s, 3H), 1.62 (dd, 1H, *J* = 10.3, 12.5 Hz), 1.89 (s, 3H), 2.04 (dd, 1H, *J* = 8.4, 12.5 Hz), 2.35 (dd, 1H, *J* = 4.6, 11.1 Hz), 2.53 (t, 1H, *J* = 11.1 Hz), 3.10 (dd, 1H, *J* = 8.4, 10.3 Hz), 3.30 (s, 3H), 3.93 (d, 1H, *J* = 11.1 Hz), 4.22 (m, 1H), 4.34 (d, 1H, *J* = 11.1 Hz), 4.46 (br d, 1H, *J* = 9.8 Hz), 5.14 (d, 1H, *J* = 9.8 Hz), 5.94 (d, 1H, *J* = 1.8 Hz), for ββ conformer δ 1.07 (s, 3H), 1.33 (s, 3H), 1.58 (dd, 1H, *J* = 8.8, 10.9 Hz), 1.77 (s, 3H), 1.77 (dd, 1H, *J* = 10.3, 14.2 Hz), 2.11 (t, 1H, *J* = 10.9 Hz), 2.90 (dd, 1H, *J* = 7.1, 14.2 Hz), 3.22 (dd, 1H, *J* = 8.8, 10.9 Hz), 3.31 (s, 3H), 3.93 (d, 1H, *J* = 10.9 Hz), 4.18–4.26 (m, 2H), 4.30 (br d, 1H, *J* = 7.1 Hz),

(2) Smetanina, O. F.; Kuznetsova, T. A.; Gerasimenko, A. V.; Kalinovsky, A. I.; Pivkin, M. V.; Dmitrenok, P. C.; Elyakov, G. B. *Russ. Chem. Bull.* **2004**, 53, 2643.

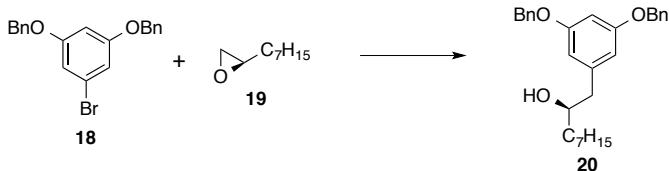
5.64 (br d, 1H, J = 7.1 Hz), 5.97 (br s, 1H); ^{13}C NMR (125 MHz, CDCl_3) ($\beta\alpha/\beta\beta$ conformer = 3:1) for $\beta\alpha$ conformer δ 17.9, 24.8, 27.8, 34.3, 40.4, 41.6, 44.8, 55.7, 67.2, 73.6, 76.2, 82.7, 129.4, 133.7, 137.1, 139.8, for $\beta\beta$ conformer δ 24.2, 25.0, 25.8, 36.0, 39.9, 40.6, 45.4, 56.1, 67.4, 76.2, 76.6, 84.7, 126.1, 134.2, 140.2, 142.6; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{26}\text{O}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$ m/z 305.1729, found 305.1725.

NOE experiment of (-)-fuscoatrol A (3).

When the olefinic methyl group at C-4 of the $\beta\alpha$ conformer (the major conformer) was irradiated, signal enhancements were observed for H-2, H-6, and H-9. On the other hand, NOEs between H-5 and H-2, 6, and 9 were observed in the $\beta\beta$ conformer (the minor conformer).



(2*R*)-1-[3,5-Bis(benzyloxy)phenyl]nonan-2-ol (20).



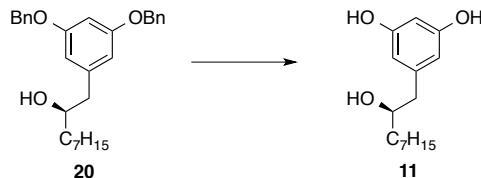
The following reaction was carried out under Ar. To a cooled (-78°C) stirred solution of **18**³ (1.10 g, 2.99 mmol) in THF (15 mL) was added *n*-BuLi (2.69 M solution in hexane, 1.17 mL, 3.15 mmol). The mixture was stirred at -78°C for 30 min, and $\text{BF}_3\cdot\text{OEt}_2$ (0.50 mL, 4.0 mmol) was added. The mixture was stirred at -78°C for 5 min, and **19**⁴ (282 mg, 1.99 mmol) was added. After being stirred at -78°C for 15 min, the mixture was quenched with saturated aqueous NH_4Cl (50 mL), diluted with H_2O (10 mL), and extracted with CH_2Cl_2 (50 mL \times 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:40) to provide 816 mg (95%) of **20** as white crystals: mp 53–55 °C; TLC R_f 0.56 (EtOAc/hexane, 1:5); $[\alpha]_D^{17} -6.8$ (c 1.00, CHCl_3); IR (neat) 3442, 2927, 1594 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 0.89 (t, 3H, J = 6.9 Hz), 1.22–1.41 (m, 9H), 1.41–1.54 (m, 3H), 2.57 (dd, 1H, J = 8.6, 13.4 Hz), 2.77 (dd, 1H, J = 4.0, 13.4 Hz), 3.79 (m, 1H),

(3) Huang, S.; Petersen, T. B.; Lipshutz, B. H. *J. Am. Chem. Soc.* **2010**, *132*, 14021.

(4) Tlais, S. F.; Dudley, G. B. *Org. Lett.* **2010**, *12*, 4698.

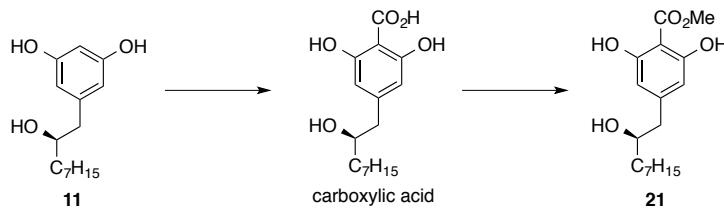
5.03 (s, 4H), 6.48 (d, 2H, J = 2.0 Hz), 6.51 (t, 1H, J = 2.0 Hz), 7.31-7.43 (m, 10H); ^{13}C NMR (125 MHz, CDCl_3) δ 14.3, 22.8, 25.9, 29.5, 29.8, 32.0, 37.0, 44.5, 70.2 (2C), 72.7, 100.3, 108.7 (2C), 127.7 (4C), 128.2 (2C), 128.7 (4C), 137.0 (2C), 141.2, 160.2 (2C); HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{37}\text{O}_3$ ($\text{M}+\text{H}$) $^+$ m/z 433.2743, found 433.2742.

(2*R*)-1-(3,5-Dihydroxyphenyl)nonan-2-ol (11).



To a stirred solution of **20** (1.58 g, 8.28 mmol) in MeOH (15 mL) were added AcOH (0.32 mL, 5.6 mmol) and Pd on carbon (10%, 32.3 mg) under Ar. After the atmosphere was replaced to H_2 , the mixture was stirred at room temperature for 18 h under H_2 . The catalyst was removed by filtration through a pad of Celite and washed well with EtOH. The combined filtrate and washings were concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 2:5) to provide 860 mg (93%) of **11** as white crystals: mp 120–122 °C; TLC R_f 0.44 (EtOAc/hexane, 1:1); $[\alpha]_D^{26} +13.4$ (c 0.775, acetone); IR (neat) 3406, 2928, 1603 cm^{-1} ; ^1H NMR (500 MHz, acetone- d_6) δ 0.87 (t, 3H, J = 6.7 Hz), 1.21-1.42 (m, 9H), 1.42-1.56 (m, 3H), 2.55 (d, 2H, J = 6.8 Hz), 3.36 (d, 1H, J = 5.1 Hz, OH), 3.73 (m, 1H), 6.18 (t, 1H, J = 2.2 Hz), 6.22 (d, 2H, J = 2.2 Hz), 8.01 (br, 2H, OH \times 2); ^{13}C NMR (125 MHz, acetone- d_6) δ 14.4, 23.3, 26.5, 29.4, 30.5, 32.6, 37.7, 45.3, 72.7, 101.2, 108.8 (2C), 142.8, 159.2 (2C); HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{25}\text{O}_3$ ($\text{M}+\text{H}$) $^+$ m/z 253.1804, found 253.1802.

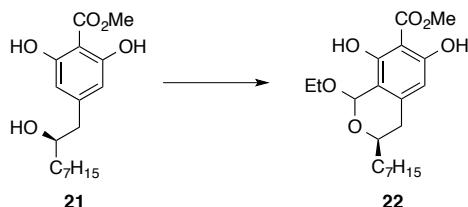
Methyl 2,6-dihydroxy-4-[(2*R*)-2-hydroxynonyl]benzoate (21).



A suspension of KHCO_3 (869 mg, 8.65 mmol) in glycerol (1 mL) was stirred at 60 °C under reduced pressure for 16 h, and then **11** (335 mg, 1.33 mmol) was added at room temperature. After the atmosphere was replaced to CO_2 , the mixture was stirred at 150 °C for 5 h under CO_2 , quenched with 1 M aqueous HCl (100 mL), and extracted with EtOAc (70 mL \times 3). The combined extracts were dried and concentrated under reduced pressure to provide 545 mg of a mixture of carboxylic acid and unreacted **11**, which was used in the next step without further purification.

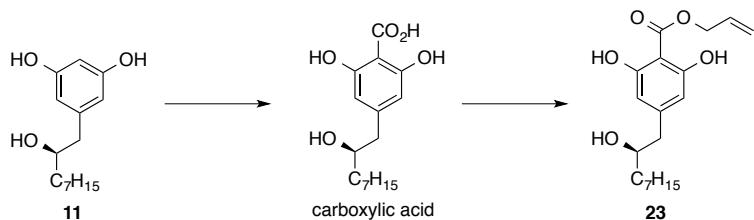
To a cooled (0 °C) stirred solution of the mixture (545 mg) obtained above in DMF (10 mL) were added NaHCO₃ (335 mg, 3.99 mmol) and MeI (0.25 mL, 4.0 mmol). The mixture was stirred at room temperature for 16 h, and NaHCO₃ (222 mg, 2.66 mmol) and MeI (0.17 mL, 2.7 mmol) were added at 0 °C. The mixture was stirred at room temperature for 7 h, and NaHCO₃ (222 mg, 2.66 mmol) and MeI (0.17 mL, 2.7 mmol) were added at 0 °C. After being stirred at room temperature for 15 h, the mixture was quenched with saturated aqueous NH₄Cl (50 mL), quenched with 0.3 M aqueous HCl (30 mL), and extracted with EtOAc (50 mL × 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:6) to provide 252 mg (61%) of **21** and 131 mg (39%) of **11** was recovered. Compound **21** was obtained as white crystals: mp 42–43 °C; TLC R_f 0.71 (EtOAc/hexane, 1:1); $[\alpha]_D^{19} -14.2$ (*c* 0.590, CHCl₃); IR (neat) 3443, 2926, 1672, 1644, 1571 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 0.88 (t, 3H, *J* = 6.9 Hz), 1.21–1.41 (m, 9H), 1.41–1.66 (m, 3H), 2.56 (dd, 1H, *J* = 8.3, 13.5 Hz), 2.71 (dd, 1H, *J* = 4.3, 13.5 Hz), 3.83 (m, 1H), 4.07 (s, 3H), 6.37 (s, 2H), 9.63 (br, 2H, OH×2); ¹³C NMR (125 MHz, CDCl₃) δ 14.2, 22.7, 25.8, 29.4, 29.6, 31.9, 37.1, 44.4, 52.9, 72.2, 98.4, 109.3 (2C), 149.1, 160.8 (2C), 169.9; HRMS (ESI) calcd for C₁₇H₂₇O₅ (M+H)⁺ *m/z* 311.1858, found 311.1859.

Methyl (3*R*)-1-ethoxy-3-heptyl-6,8-dihydroxyisochromane-7-carboxylate (22).



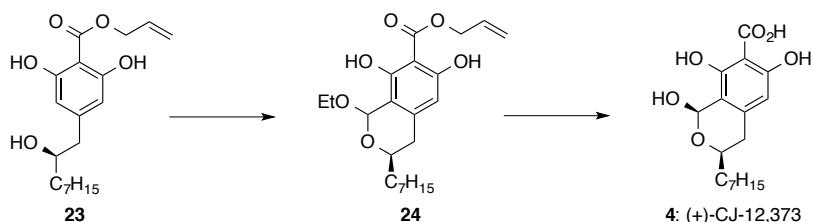
To a cooled (0 °C) stirred solution of **21** (17.3 mg, 55.7 μmol) in (EtO)₃CH (0.69 mL, 4.2 mmol) was added TFA (2.1 μL, 28 μmol). The mixture was stirred at room temperature for 40 min and concentrated under reduced pressure to provide 20.1 mg (quant.) of **22** as a yellow amorphous solid, which was used in the next step without further purification: TLC R_f 0.65 (EtOAc/hexane, 1:2); $[\alpha]_D^{25} +45.0$ (*c* 1.33, CHCl₃); IR (neat) 3440, 2929, 1674, 1644, 1584 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.89 (t, 3H, *J* = 6.9 Hz), 1.22–1.48 (m, 9H), 1.48–1.66 (m, 2H), 1.73 (m, 1H), 2.55–2.65 (m, 2H), 3.73 (m, 1H), 3.92 (m, 1H), 4.05 (s, 3H), 4.16 (m, 1H), 5.68 (s, 1H), 6.24 (s, 1H), 9.52 (br, 1H, OH), 10.02 (br, 1H, OH); ¹³C NMR (125 MHz, CDCl₃) δ 14.2, 15.4, 22.8, 25.6, 29.4, 29.6, 32.0, 34.6, 35.7, 52.9, 63.3, 65.8, 93.8, 98.2, 107.5, 114.5, 145.0, 158.5, 160.0, 170.0; HRMS (ESI) calcd for C₂₀H₃₁O₆ (M+H)⁺ *m/z* 367.2121, found 367.2115.

Allyl 2,6-dihydroxy-4-[(2*R*)-2-hydroxynonyl]benzoate (23).



As described for the preparation of **21**, a mixture of carboxylic acid and unreacted **11** was obtained. To a cooled ($0\text{ }^{\circ}\text{C}$) stirred solution of the obtained mixture (623 mg) in DMF (15 mL) were added NaHCO_3 (529 mg, 6.30 mmol) and allyl bromide (0.54 mL, 4.2 mmol). The mixture was stirred at room temperature for 20 h, and NaHCO_3 (529 mg, 6.30 mmol) and allyl bromide (0.54 mL, 4.2 mmol) were added at $0\text{ }^{\circ}\text{C}$. After being stirred at room temperature for 18 h, the mixture was quenched with saturated aqueous NH_4Cl (50 mL), diluted with 0.3 M aqueous HCl (30 mL), and extracted with EtOAc (50 mL \times 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:10) to provide 360 mg (51%) of **23** and 184 mg (35%) of **11** was recovered. Compound **23** was obtained as white crystals: mp 40–42 $^{\circ}\text{C}$; TLC R_f 0.88 (EtOAc/hexane, 1:1); $[\alpha]_D^{20} -11.9$ (*c* 0.745, CHCl_3); IR (neat) 3451, 2928, 1674, 1644, 1570 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 0.88 (t, 3H, *J* = 7.0 Hz), 1.22–1.41 (m, 9H), 1.41–1.64 (m, 3H), 2.57 (dd, 1H, *J* = 8.6, 13.6 Hz), 2.71 (dd, 1H, *J* = 4.3, 13.6 Hz), 3.83 (m, 1H), 4.97 (td, 2H, *J* = 1.1, 6.1 Hz), 5.41 (qd, 1H, *J* = 1.1, 10.5 Hz), 5.47 (qd, 1H, *J* = 1.1, 17.1 Hz), 6.05 (tdd, 1H, *J* = 6.1, 10.5, 17.1 Hz), 6.37 (s, 2H), 9.70 (br, 2H, OH \times 2); ^{13}C NMR (125 MHz, CDCl_3) δ 14.2, 22.8, 25.8, 29.4, 29.7, 31.9, 37.1, 44.5, 66.9, 72.2, 98.5, 109.3 (2C), 121.2, 130.6, 149.2, 161.0 (2C), 169.3; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{29}\text{O}_5$ ($\text{M}+\text{H}$) $^+$ *m/z* 337.2015, found 337.2007.

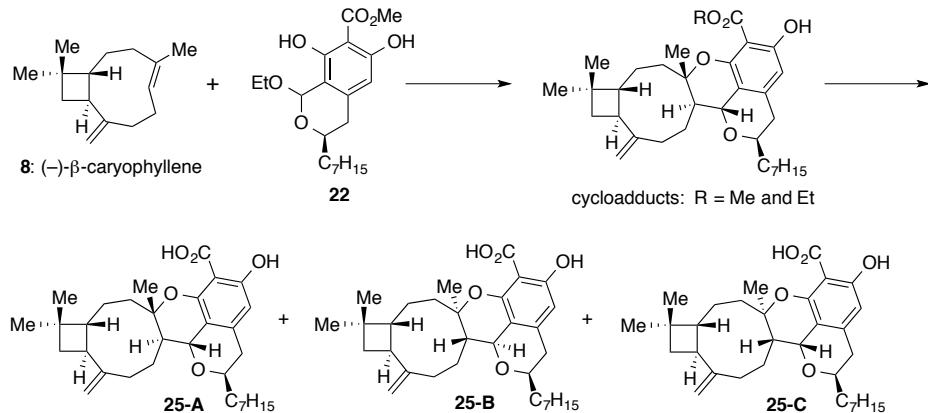
(+)-CJ-12,373 (4).



To a cooled ($0\text{ }^{\circ}\text{C}$) stirred solution of **23** (176 mg, 0.524 mmol) in $(\text{EtO})_3\text{CH}$ (6.5 mL, 24 mmol) was added TFA (20 μL , 0.26 mmol). The mixture was stirred at room temperature for 45 min and concentrated under reduced pressure to provide 210 mg (quant.) of **24**, which was used in the next step without further purification.

The following reaction was carried out under Ar. To a cooled (0 °C) stirred solution of **24** (210 mg) obtained above in THF (4 mL) were added a solution of Pd(PPh₃)₄ (12.1 mg, 10.5 µmol) in THF (1 mL) and pyrrolidine (0.43 mL, 5.2 mmol). The mixture was stirred at room temperature for 10 min, quenched with saturated aqueous NH₄Cl (10 mL), diluted with H₂O (5 mL), and extracted with EtOAc (20 mL × 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (MeOH/CH₂Cl₂, 1:10) to provide 174 mg (quant.) of **4**, which was contaminated by a small amount of impurities but used for the next step. An analytical sample was obtained as white crystals after further purification by PTLC (MeOH/CHCl₃, 1:3): mp 148–150 °C [lit. mp 145 °C]⁵; TLC *R*_f 0.40 (MeOH/CHCl₃, 1:3); [α]_D²⁹ +30.1 (*c* 0.170, MeOH) [lit. [α]_D²⁴ +32.4 (*c* 0.13, MeOH)]⁵; IR (neat) 3438, 2927, 1633, 1589 cm⁻¹; ¹H NMR (500 MHz, CD₃OD) δ 0.90 (t, 3H, *J* = 5.9 Hz), 1.22–1.51 (m, 9H), 1.51–1.64 (m, 3H), 2.47 (dd, 1H, *J* = 11.7, 16.8 Hz), 2.54 (br d, 1H, *J* = 16.8 Hz), 4.04 (m, 1H), 5.49 (s, 1H), 6.08 (s, 1H); ¹³C NMR (125 MHz, CD₃OD) δ 15.2, 24.5, 27.6, 31.3, 31.5, 33.8, 36.1, 37.5, 68.4, 97.9, 103.4, 106.7, 113.6, 142.5, 161.8, 163.6, 179.7; HRMS (ESI) calcd for C₁₇H₂₃O₆ (M–H)[–] *m/z* 323.1495, found 323.1482.

Hetero-Diels–Alder reaction of **8** with **22**. Synthesis of **25-A–C**.



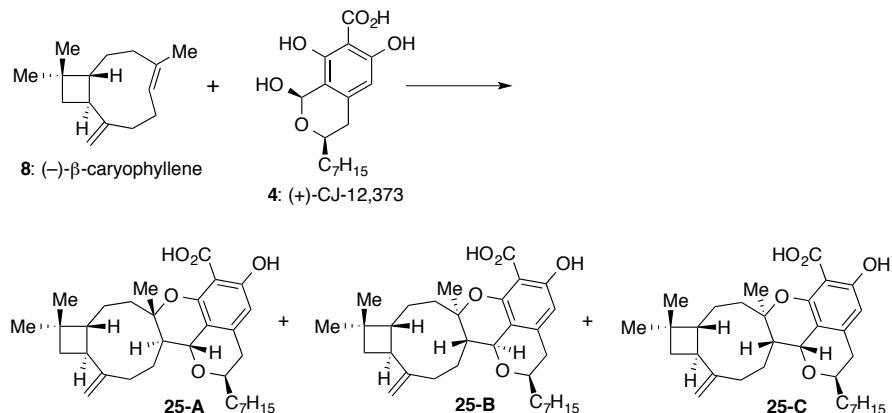
To a stirred solution of **22** (22.9 mg, 60.2 µmol) in toluene (1 mL) was added **8** (22.8 µL, 90.3 µmol). The mixture was stirred at 100 °C for 70 h and concentrated under reduced pressure to provide a mixture of cycloadducts (38.1 mg), which was used in the next step without further purification: TLC *R*_f 0.79 (EtOAc/hexane, 1:4).

To a cooled (0 °C) stirred solution of a mixture of cycloadducts (38.1 mg) obtained above in THF/MeOH (3:2, 4 mL) was added 6 M aqueous NaOH (2.3 mL). The mixture was stirred at 60 °C for 65 h, quenched with 1 M aqueous HCl (15 mL), diluted with H₂O (5 mL), and extracted

(5) Inagaki, T.; Kaneda, K.; Suzuki, Y.; Hirai, H.; Nomura, E.; Sakakibara, T.; Yamauchi, Y.; Huang, L. H.; Norcia, M.; Wondrack, L. M.; Sutcliffe, J. A.; Kojima, N. *J. Antibiot.* **1998**, *51*, 112.

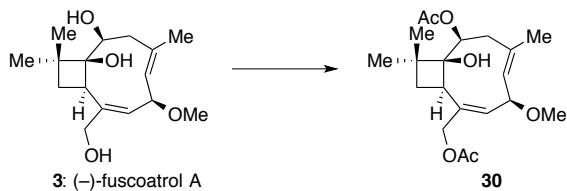
with CH_2Cl_2 (15 mL \times 3). The combined extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:50) to provide 13.5 mg (44% from **22**) of **25-A-C** (**A/B/C** = 3:1:1) as a colorless oil. A mixture of **25-A-C** were partially separated into **25-A/B** and **25-C** by further purification. A mixture of **25-A** and **B** (**A/B** = 3:1) was obtained as a colorless oil: TLC R_f 0.40 (EtOAc/hexane, 1:4); IR (neat) 3418, 3227, 2927, 1694, 1635, 1591 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) for **25-A** δ 0.89 (t, 3H, J = 7.2 Hz), 0.96 (s, 3H), 1.00 (s, 3H), 1.26 (s, 3H), 1.22-1.88 (m, 18H), 1.90-1.98 (m, 2H), 2.10 (ddd, 1H, J = 1.5, 10.6, 14.5 Hz), 2.21 (m, 1H), 2.36 (br dd, 1H, J = 9.8, 14.5 Hz), 2.44-2.64 (m, 2H), 2.51 (dd, 1H, J = 8.9, 16.0 Hz), 2.88 (dd, 1H, J = 5.0, 16.0 Hz), 3.83 (m, 1H), 4.21 (d, 1H, J = 9.8 Hz), 4.81 (s, 1H), 4.87 (s, 1H), 6.49 (s, 1H), 11.30 (br, 1H, CO_2H), 11.96 (s, 1H, OH), for **25-B** δ 0.89 (t, 3H, J = 7.2 Hz), 0.97 (s, 3H), 0.99 (s, 3H), 1.22-1.80 (m, 18H), 1.41 (s, 3H), 1.84 (m, 1H), 1.90-1.98 (m, 2H), 2.04 (m, 1H), 2.18-2.25 (m, 2H), 2.44-2.64 (m, 2H), 2.75 (dd, 1H, J = 4.2, 17.6 Hz), 3.73 (m, 1H), 4.13 (d, 1H, J = 10.6 Hz), 4.87 (s, 1H), 4.92 (s, 1H), 6.39 (s, 1H), 11.43 (br, 1H, CO_2H), 11.82 (s, 1H, OH); ^{13}C NMR (125 MHz, CDCl_3) for **25-A** δ 14.3, 21.6, 22.4, 22.6, 22.8, 25.6, 29.4, 29.6, 29.8, 31.9, 32.6, 33.4, 34.5, 35.8, 38.2, 38.8, 39.5, 40.5, 42.4, 57.6, 68.8, 71.8, 88.3, 98.9, 109.5, 110.2, 112.4, 143.9, 150.4, 155.3, 163.3, 171.1, for **25-B** δ 14.3, 22.0, 22.7, 22.8, 23.0, 25.6, 28.3, 29.6, 29.8, 30.0, 34.5, 36.1, 36.4, 37.3, 38.2, 40.6, 41.0, 41.1, 42.4, 54.6, 73.9, 75.3, 88.8, 98.9, 109.9, 111.4, 112.6, 142.5, 150.8, 151.9, 162.6, 171.0; HRMS (ESI) calcd for $\text{C}_{32}\text{H}_{47}\text{O}_5$ ($\text{M}+\text{H}$) $^+$ m/z 511.3424, found 511.3420. A mixture containing **25-C** as a major component was obtained as a colorless oil: TLC R_f 0.49 (EtOAc/hexane, 1:4); IR (neat) 3418, 3227, 2927, 1694, 1635, 1591 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 0.90 (t, 3H, J = 7.0 Hz), 1.01 (s, 3H), 1.02 (s, 3H), 1.24 (s, 3H), 1.26-1.87 (m, 18H), 1.90-2.20 (m, 4H), 2.28 (m, 1H), 2.46 (m, 1H), 2.51-2.70 (m, 2H), 2.78 (dd, 1H, J = 4.7, 15.6 Hz), 3.55 (m, 1H), 4.18 (d, 1H, J = 6.3 Hz), 4.93 (s, 1H), 4.95 (s, 1H), 6.55 (s, 1H), 11.53 (br, 1H, CO_2H), 11.87 (s, 1H, OH); ^{13}C NMR (125 MHz, CDCl_3) δ 14.3, 22.2, 22.3, 22.8, 23.2, 25.6, 26.5, 29.4, 29.7, 30.4, 32.0, 33.9, 34.5, 35.6, 36.1, 36.5, 38.5, 40.5, 42.4, 53.4, 63.8, 72.2, 86.7, 99.9, 109.5, 110.6, 115.3, 146.0, 149.9, 152.1, 163.3, 171.1; HRMS (ESI) calcd for $\text{C}_{32}\text{H}_{47}\text{O}_5$ ($\text{M}+\text{H}$) $^+$ m/z 511.3424, found 511.3425.

Hetero-Diels–Alder reaction of **8 with **4**. Synthesis of **25-A–C**.**



To a stirred solution of **4** (22.8 mg, 70.3 μ mol) in toluene (1 mL) was added **8** (26.6 μ L, 105 μ mol). The mixture was stirred at 100 °C for 7 h and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:30) to provide 15.9 mg (44% from **4**) of **25-A–C** (**A/B/C** = 7:1:1) as a colorless oil.

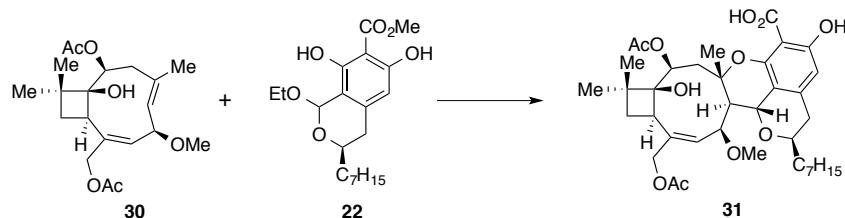
(1*S*,2*S*,4*E*,6*R*,7*E*,9*R*)-2-Acetoxy-8-(acetoxymethyl)-6-methoxy-4,11,11-trimethyl-bicyclo[7.2.0]undeca-4,7-dien-1-ol (30).



To a cooled (0 °C) stirred solution of **3** (7.9 mg, 28 μ mol) in pyridine (0.5 mL) was added Ac₂O (0.5 mL). The mixture was stirred at 40 °C for 18 h and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:6) to provide 11.5 mg (quant.) of **30** as white crystals: mp 112–114 °C; TLC R_f 0.68 (EtOAc/hexane, 1:1); $[\alpha]_D^{24} -184$ (*c* 0.370, CHCl₃); IR (neat) 3500, 2935, 1732 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) ($\beta\alpha/\beta\beta$ conformer = 5:3) for $\beta\alpha$ conformer δ 1.05 (s, 3H), 1.12 (s, 3H), 1.72 (dd, 1H, *J* = 10.7, 13.0 Hz), 1.84 (dd, 1H, *J* = 7.3, 13.0 Hz), 1.95 (s, 3H), 2.06 (s, 3H), 2.12 (s, 3H), 2.40 (dd, 1H, *J* = 4.3, 11.0 Hz), 2.62 (t, 1H, *J* = 11.0 Hz), 2.86 (s, 1H, OH), 3.16 (dd, 1H, *J* = 7.3, 10.7 Hz), 3.30 (s, 3H), 4.52 (d, 1H, *J* = 10.5 Hz), 4.55 (d, 1H, *J* = 12.5 Hz), 4.70 (d, 1H, *J* = 12.5 Hz), 5.25 (d, 1H, *J* = 10.5 Hz), 5.25 (m, 1H), 6.07 (s, 1H), for $\beta\beta$ conformer δ 1.05 (s, 3H), 1.11 (s, 3H), 1.62 (dd, 1H, *J* = 9.0, 11.1 Hz), 1.75 (s, 3H), 1.80 (dd, 1H, *J* = 10.3, 14.0 Hz), 1.92 (t, 1H, *J* = 11.1 Hz), 2.06 (s, 3H), 2.13 (s, 3H), 2.99 (s, 1H, OH), 3.03 (dd, 1H, *J* = 7.6, 14.0 Hz), 3.24 (dd, 1H, *J* = 9.0, 11.1 Hz), 3.31 (s, 3H), 4.34 (d, 1H, *J* = 7.1 Hz), 4.55 (d, 1H, *J* = 12.5 Hz), 4.61 (d, 1H, *J* = 12.5 Hz), 5.25 (m, 1H), 5.76 (d, 1H, *J* = 7.1 Hz), 6.14 (s, 1H); ¹³C NMR (125 MHz, CDCl₃) ($\beta\alpha/\beta\beta$ conformer = 5:3) for $\beta\alpha$

conformer δ 17.8, 21.2, 21.6, 24.1, 27.1, 33.4, 40.3, 40.5, 41.7, 55.7, 68.4, 76.2, 76.3, 81.7, 130.0, 131.5, 133.2, 141.2, 170.2, 170.5, for $\beta\beta$ conformer δ 21.2, 21.5, 23.6, 24.3, 25.1, 35.5, 36.2, 40.5, 45.2, 56.1, 69.3, 76.0, 79.3, 84.2, 126.6, 129.5, 141.9, 142.9, 170.0, 170.2; HRMS (ESI) calcd for $C_{20}H_{31}O_6$ ($M+H$)⁺ *m/z* 367.2121, found 367.2132.

Hetero-Diels–Alder reaction of **30** with **22**. Synthesis of **31**.



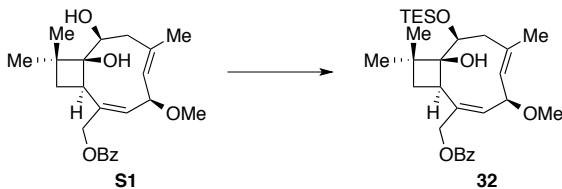
To a stirred solution of **30** (9.8 mg, 27 μ mol) in toluene (0.5 mL) was added **22** (11.3 mg, 32.1 μ mol). The mixture was stirred at 100 °C for 16 h and at 120 °C for 22 h, and **22** (3.3 mg, 9.4 μ mol) was added. After being stirred at 120 °C for 16 h, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:6) to provide 4.0 mg (22%) of **31** and 6.3 mg (64%) of **30** was recovered. Compound **31** was obtained as a pale yellow oil: TLC R_f 0.19 (EtOAc/hexane, 1:1); $[\alpha]_D^{23} +90$ (*c* 0.34, $CHCl_3$); IR (neat) 3478, 3241, 2926, 1731, 1695, 1643, 1591 cm^{-1} ; ¹H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, 3H, *J* = 7.0 Hz), 0.99 (s, 3H), 1.07 (s, 3H), 1.25-1.36 (m, 10H), 1.39 (s, 3H), 1.60 (m, 1H), 1.67 (dd, 1H, *J* = 8.2, 10.6 Hz), 1.69 (br d, 1H, *J* = 17.0 Hz), 1.74 (m, 1H), 2.06 (s, 3H), 2.10 (s, 3H), 2.12 (t, 1H, *J* = 10.6 Hz), 2.52 (dd, 1H, *J* = 4.7, 9.6 Hz), 2.57 (dd, 1H, *J* = 9.1, 15.9 Hz), 2.59 (s, 1H, OH), 2.88 (dd, 1H, *J* = 4.7, 15.9 Hz), 3.10 (dd, 1H, *J* = 8.2, 10.6 Hz), 3.16 (dd, 1H, *J* = 5.8, 17.0 Hz), 3.44 (s, 3H), 3.83 (m, 1H), 4.52 (br d, 1H, *J* = 4.7 Hz), 4.78 (d, 1H, *J* = 13.2 Hz), 4.85 (d, 1H, *J* = 13.2 Hz), 4.94 (d, 1H, *J* = 9.6 Hz), 5.31 (br d, 1H, *J* = 5.8 Hz), 5.78 (br s, 1H), 6.50 (s, 1H), 10.87 (br, 1H, CO_2H), 11.92 (s, 1H, OH); ¹³C NMR (125 MHz, $CDCl_3$) δ 14.2, 21.2, 21.3, 22.7, 22.8, 24.4, 25.3, 25.7, 29.4, 29.7, 32.0, 34.4, 34.6, 35.7, 38.0, 40.6, 43.5, 48.8, 59.0, 62.2, 67.7, 71.2, 72.0, 76.2, 81.8, 86.0, 99.2, 109.8, 111.6, 132.6, 133.9, 143.2, 149.8, 163.1, 169.0, 170.8, 170.9; HRMS (ESI) calcd for $C_{37}H_{53}O_{11}$ ($M+H$)⁺ *m/z* 673.3588, found 673.3609.

(1*S*,2*S*,4*E*,6*R*,7*E*,9*R*)-8-(Bezoyloxymethyl)-6-methoxy-4,11,11-trimethylbicyclo-[7.2.0]undeca-4,7-diene-1,2-diol (**S1**).



To a cooled (0 °C) stirred solution of **3** (19.2 mg, 68.0 µmol) in pyridine (1 mL) was added BzCl (16 µL, 0.14 mmol). The mixture was stirred at 0 °C for 30 min and BzCl (16 µL, 0.14 mmol) was added. After being stirred at 0 °C for 10 min, the mixture was diluted with CH₂Cl₂ (20 mL) and washed with 1 M aqueous HCl (10 mL), saturated aqueous NaHCO₃ (10 mL × 3), and saturated brine (10 mL), respectively. The organic layer was dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:5) to provide 24.9 mg (95%) of **S1** as a colorless oil: TLC *R*_f 0.61 (EtOAc/hexane, 1:1); [α]_D²⁶ -189 (*c* 1.25, CHCl₃); IR (neat) 3478, 2976, 1716 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) (βα/ββ conformer = 5:1) for βα conformer δ 1.11 (s, 3H), 1.29 (s, 3H), 1.71 (dd, 1H, *J* = 10.2, 12.8 Hz), 1.90 (d, 3H, *J* = 1.1 Hz), 1.91 (dd, 1H, *J* = 8.1, 12.8 Hz), 2.40 (dd, 1H, *J* = 4.9, 11.2 Hz), 2.52 (t, 1H, *J* = 11.2 Hz), 2.98 (br, 1H, OH), 3.14 (dd, 1H, *J* = 8.1, 10.2 Hz), 3.28 (s, 3H), 4.21 (dd, 1H, *J* = 4.9, 11.2 Hz), 4.53 (br d, *J* = 10.2 Hz), 4.73 (d, 1H, *J* = 12.9 Hz), 5.06 (d, 1H, *J* = 12.9 Hz), 5.11 (qd, 1H, *J* = 1.1, 10.2 Hz), 6.11 (s, 1H), 7.44-7.47 (m, 2H), 7.58 (m, 1H), 8.03-8.09 (m, 2H), for ββ conformer δ 1.03 (s, 3H), 1.32 (s, 3H), 1.63 (dd, 1H, *J* = 8.6, 11.0 Hz), 1.75 (s, 3H), 1.78 (dd, 1H, *J* = 11.0, 14.6 Hz), 2.03 (t, 1H, *J* = 11.0 Hz), 2.56 (br, 1H, OH), 2.93 (dd, 1H, *J* = 8.6, 14.6 Hz), 3.20 (dd, 1H, *J* = 8.6, 11.0 Hz), 3.31 (s, 3H), 4.23 (m, 1H), 4.37 (br d, 1H, *J* = 7.2 Hz), 4.78 (d, 1H, *J* = 12.6 Hz), 4.95 (d, 1H, *J* = 12.6 Hz), 5.68 (br d, 1H, *J* = 7.4 Hz), 6.21 (br s, 1H), 7.44-7.47 (m, 2H), 7.58 (m, 1H), 8.03-8.09 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) (βα/ββ conformer = 5:1) for βα conformer δ 18.0, 24.3, 27.7, 33.8, 39.6, 41.4, 45.0, 55.7, 68.7, 73.7, 76.4, 82.9, 128.6 (3C), 129.3, 129.8 (2C), 132.3, 133.4, 134.1, 139.8, 166.6, for ββ conformer δ 23.7, 24.7, 25.6, 36.1, 39.9, 40.5, 44.5, 56.1, 69.3, 76.4, 76.7, 85.6, 126.7, 128.5, 129.7 (2C), 130.0 (2C), 130.2, 133.2, 141.9, 142.4, 166.4; HRMS (ESI) calcd for C₂₃H₃₀O₅Na (M+Na)⁺ *m/z* 409.1991, found 409.2006.

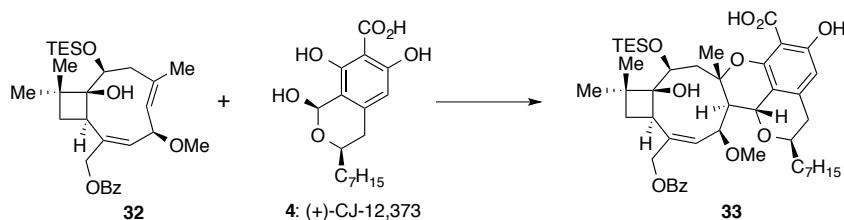
(1S,2S,4E,6R,7E,9R)-8-(Bezoyloxymethyl)-6-methoxy-4,11,11-trimethyl-2-(triethylsilyloxy)bicyclo[7.2.0]undeca-4,7-dien-1-ol (32).



The following reaction was carried out under Ar. To a cooled (0 °C) stirred solution of **S1** (24.9 mg, 64.4 µmol) in CH₂Cl₂ (1 mL) were added Et₃N (36 µL, 0.26 mmol), TESCl (22 µL, 0.13 mmol), and DMAP (2.2 mg, 18 µmol). The mixture was stirred at room temperature for 3 h, and Et₃N (36 µL, 0.26 mmol), TESCl (22 µL, 0.13 mmol), and DMAP (2.2 mg, 18 µmol) were added.

The mixture was stirred at room temperature for 1 h, and Et₃N (36 µL, 0.26 mmol), TESCl (22 µL, 0.13 mmol), and DMAP (4.5 mg, 37 µmol) were added. The mixture was stirred at room temperature for 2 h, and Et₃N (72 µL, 0.52 mmol), TESCl (43 µL, 0.26 mmol), and DMAP (2.2 mg, 18 µmol) were added. After being stirred at room temperature for 16 h, the mixture was quenched with saturated aqueous NH₄Cl (10 mL), diluted with H₂O (10 mL), and extracted with CH₂Cl₂ (15 mL × 3). The combined extracts were washed with saturated aqueous NaHCO₃ (15 mL) and saturated brine (15 mL), respectively. The organic layer was dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane, 1:30) to provide 24.5 mg (87%) of **32** as a colorless oil: TLC *R*_f 0.86 (EtOAc/hexane, 1:1); [α]_D²⁷ −98.4 (*c* 1.23, CHCl₃); IR (neat) 3554, 2955, 1719 cm^{−1}; ¹H NMR (500 MHz, CDCl₃) (βα/ββ conformer = 3:1) for βα conformer δ 0.63 (m, 6H), 0.98 (t, 9H, *J* = 8.0 Hz), 1.06 (s, 3H), 1.20 (s, 3H), 1.66 (dd, 1H, *J* = 10.3, 12.6 Hz), 1.89 (s, 3H), 2.04 (dd, 1H, *J* = 8.5, 12.6 Hz), 2.35 (dd, 1H, *J* = 4.9, 11.2 Hz), 2.52 (t, 1H, *J* = 11.2 Hz), 2.62 (br, 1H, OH), 3.04 (dd, 1H, *J* = 8.5, 10.3 Hz), 3.30 (s, 3H), 4.40 (dd, 1H, *J* = 4.9, 11.2 Hz), 4.53 (br d, *J* = 10.2 Hz), 4.94 (d, 1H, *J* = 12.6 Hz), 5.02 (d, 1H, *J* = 12.6 Hz), 5.18 (d, 1H, *J* = 10.2 Hz), 6.08 (br s, 1H), 7.40–7.44 (m, 2H), 7.54 (m, 1H), 8.04–8.05 (m, 2H), for ββ conformer δ 0.63 (m, 6H), 0.98 (t, 9H, *J* = 8.0 Hz), 0.99 (s, 3H), 1.24 (s, 3H), 1.58 (dd, 1H, *J* = 8.5, 10.9 Hz), 1.75 (s, 3H), 1.75 (dd, 1H, *J* = 10.0, 14.1 Hz), 2.07 (t, 1H, *J* = 10.9 Hz), 2.83 (dd, 1H, *J* = 7.8, 14.1 Hz), 3.08 (m, 1H), 3.31 (s, 3H), 4.30 (dd, 1H, *J* = 7.8, 10.0 Hz), 4.36 (br d, 1H, *J* = 7.1 Hz), 4.92–4.95 (m, 2H), 5.65 (br d, 1H, *J* = 7.1 Hz), 6.14 (br s, 1H), 7.40–7.44 (m, 2H), 7.54 (m, 1H), 8.04–8.05 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) (βα/ββ conformer = 3:1) for βα conformer δ 6.0 (3C), 7.2 (3C), 18.0, 23.9, 27.3, 34.6, 38.4, 40.7, 44.8, 55.8, 69.1, 74.7, 76.6, 83.6, 128.4 (2C), 129.7, 129.8 (2C), 130.3, 132.1, 132.9, 134.3, 138.4, 166.4, for ββ conformer δ 5.8 (3C), 7.2 (3C), 23.2, 23.9, 25.2, 36.5, 40.1, 40.4, 44.0, 56.2, 68.8, 76.4, 77.6, 86.2, 126.3, 129.8 (2C), 130.7 (2C), 130.8, 131.6, 132.9, 140.1, 143.1, 166.4; HRMS (ESI) calcd for C₂₉H₄₄O₅SiK (M+K)⁺ *m/z* 539.2595, found 539.2589.

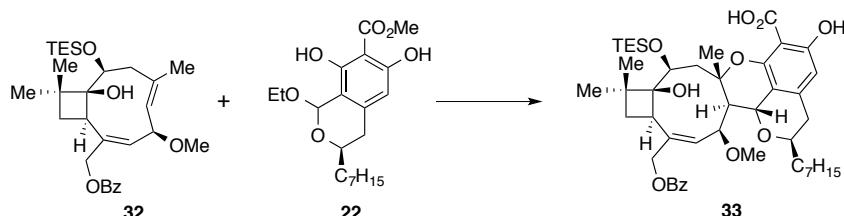
Hetero-Diels–Alder reaction of **32** with **4**. Synthesis of **33**.



To a stirred solution of **32** (15.3 mg, 34.9 µmol) in toluene (1 mL) was added **4** (13.6 mg, 41.9 µmol). The mixture was stirred at 100 °C for 3.5 h, and **4** (13.6 mg, 41.9 µmol) was added.

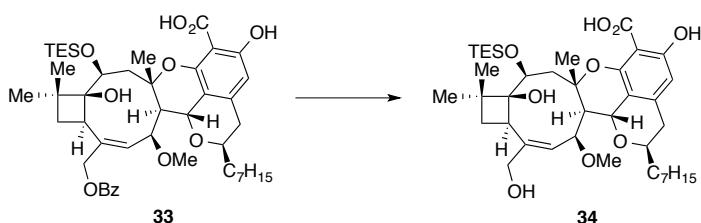
After being stirred at 100 °C for 1.5 h, the mixture was concentrated under reduced pressure. The residue was purified by PTLC (EtOAc/hexane, 1:6) to provide 9.7 mg (35%) of **33** and 4.5 mg (29%) of **32** was recovered. Compound **33** was obtained as a pale yellow oil: TLC R_f 0.69 (EtOAc/hexane, 1:2); $[\alpha]_D^{24} +72$ (*c* 0.49, CHCl₃); IR (neat) 3549, 3229, 2930, 1717, 1698, 1644, 1589 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 0.56-0.68 (m, 6H), 0.87 (t, 3H, *J* = 6.9 Hz), 0.94 (t, 9H, *J* = 7.9 Hz), 1.06 (s, 3H), 1.14 (s, 3H), 1.26-1.35 (m, 10H), 1.41 (s, 3H), 1.58 (m, 1H), 1.64 (d, 1H, *J* = 16.6 Hz), 1.67 (dd, 1H, *J* = 8.2, 10.4 Hz), 1.74 (m, 1H), 2.20 (t, 1H, *J* = 10.4 Hz), 2.57 (dd, 1H, *J* = 4.2, 9.5 Hz), 2.57 (dd, 1H, *J* = 9.1, 15.2 Hz), 2.86 (br s, 1H, OH), 2.90 (dd, 1H, *J* = 4.6, 15.2 Hz), 3.10 (dd, 1H, *J* = 6.9, 16.6 Hz), 3.18 (dd, 1H, *J* = 8.2, 10.4 Hz), 3.40 (s, 3H), 3.83 (m, 1H), 4.13 (d, 1H, *J* = 6.9 Hz), 4.54 (dd, 1H, *J* = 2.0, 4.2 Hz), 4.99 (d, 1H, *J* = 9.5 Hz), 5.13 (d, 1H, *J* = 13.5 Hz), 5.16 (d, 1H, *J* = 13.5 Hz), 5.80 (d, 1H, *J* = 2.0 Hz), 6.54 (s, 1H), 7.44-7.47 (m, 2H), 7.57 (m, 1H), 8.05-8.07 (m, 2H), 11.12 (br, 1H, CO₂H), 11.91 (s, 1H, OH); ¹³C NMR (125 MHz, CDCl₃) δ 6.0 (3C), 7.0 (3C), 14.2, 22.7, 22.8, 24.1, 25.6, 26.5, 29.4, 29.7, 32.0, 34.4, 34.6, 35.9, 37.3, 41.1, 46.2, 48.9, 59.0, 61.9, 67.9, 70.1, 72.0, 76.3, 82.3, 88.2, 99.0, 109.9, 111.9, 128.5 (2C), 129.7 (2C), 130.7, 131.3, 133.0, 135.1, 144.1, 149.9, 163.0, 166.3, 170.4; HRMS (ESI) calcd for C₄₆H₆₅O₁₀Si (M-H)⁻ *m/z* 805.4347, found 805.4380.

Hetero-Diels–Alder reaction of **32** with **22**. Synthesis of **33**.



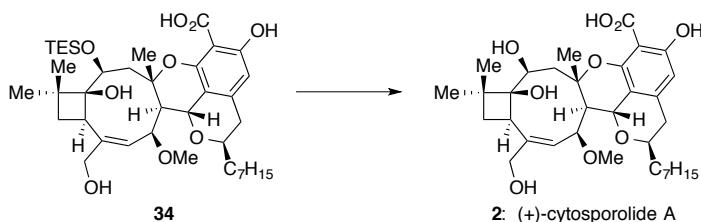
To a stirred solution of **32** (16.7 mg, 38.1 μ mol) in toluene (1 mL) was added **22** (20.4 mg, 57.9 μ mol). The mixture was stirred at 100 °C for 17 h and concentrated under reduced pressure. The residue was purified by PTLC (EtOAc/hexane, 1:6) to provide 6.2 mg (20%) of **33** and 6.2 mg of **32**, accompanied by a small amount of by-product, was recovered. The recovered **32** was treated by the same procedure to provide additional **33** (5.8 mg). In total, 12.0 mg (39% for 2 cycles) of **33** was obtained as a pale yellow oil.

(+)-Cytosporolide A triethylsilyl ether (**34**).



The following reaction was carried out under Ar. To a cooled (-78°C) stirred solution of **33** (6.2 mg, 7.7 μmol) in CH_2Cl_2 (1 mL) was added DIBALH (1.00 M solution in toluene, 31 μL , 31 μmol). The mixture was stirred at -78°C for 20 min, quenched with 1 M aqueous HCl (10 mL), and extracted with EtOAc (20 mL \times 3). The combined extracts were washed with 1 M aqueous HCl (15 mL), dried and concentrated under reduced pressure. The residue was purified by PTLC (EtOAc/hexane, 1:4) to provide 4.7 mg (87%) of **34** as a pale yellow oil: TLC R_f 0.36 (EtOAc/hexane, 1:2); $[\alpha]_D^{25} +55$ (*c* 0.27, CHCl_3); IR (neat) 3241, 2927, 1697, 1644, 1590 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 0.56-0.68 (m, 6H), 0.88 (t, 3H, *J* = 7.0 Hz), 0.94 (t, 9H, *J* = 8.0 Hz), 1.07 (s, 3H), 1.15 (s, 3H), 1.25-1.36 (m, 10H), 1.42 (s, 3H), 1.57-1.64 (m, 2H), 1.64 (d, 1H, *J* = 16.6 Hz), 1.75 (m, 1H), 2.19 (t, 1H, *J* = 10.5 Hz), 2.54 (dd, 1H, *J* = 4.4, 9.6 Hz), 2.58 (dd, 1H, *J* = 8.6, 16.1 Hz), 2.90 (dd, 1H, *J* = 4.6, 16.1 Hz), 3.03 (dd, 1H, *J* = 6.9, 16.6 Hz), 3.24 (dd, 1H, *J* = 8.9, 10.5 Hz), 3.43 (s, 3H), 3.49 (br, 1H, OH), 3.83 (m, 1H), 3.99 (d, 1H, *J* = 10.3 Hz), 4.13 (d, 1H, *J* = 6.9 Hz), 4.16 (d, 1H, *J* = 10.3 Hz), 4.50 (dd, 1H, *J* = 2.0, 4.4 Hz), 4.53 (br, 1H, OH), 4.99 (d, 1H, *J* = 9.6 Hz), 5.82 (d, 1H, *J* = 2.0 Hz), 6.54 (s, 1H), 11.04 (br, 1H, CO_2H), 11.90 (s, 1H, OH); ^{13}C NMR (125 MHz, CDCl_3) δ 5.9 (3C), 7.0 (3C), 14.2, 22.8, 23.0, 24.3, 25.7, 26.6, 29.4, 29.7, 32.0, 33.9, 34.6, 35.9, 38.6, 40.9, 46.3, 49.2, 59.1, 61.9, 65.4, 69.8, 72.0, 76.3, 81.8, 88.1, 99.0, 110.0, 111.8, 133.7, 138.2, 144.0, 149.9, 163.0, 170.3; HRMS (ESI) calcd for $\text{C}_{39}\text{H}_{61}\text{O}_9\text{Si}$ ($\text{M}-\text{H}$) $^-$ *m/z* 701.4085, found 701.4086.

(+)-Cytosporolide A (2).

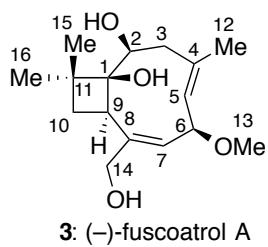


To a cooled (0°C) stirred solution of **34** (6.0 mg, 8.5 μmol) in THF (1 mL) was added HF-pyridine (0.1 mL). The mixture was stirred at room temperature for 15 min, diluted with H_2O (10 mL), and extracted with EtOAc (20 mL \times 3). The combined extracts were washed with saturated brine (20 mL), dried and concentrated under reduced pressure. The residue was purified by ODS column chromatography ($\text{CH}_3\text{CN}/\text{H}_2\text{O}$, 2:1). The obtained product was diluted with EtOAc (20 mL) and washed with 1 M aqueous HCl (10 mL \times 3). The organic layer was dried and concentrated under reduced pressure to provide 3.6 mg (72%) of **2** as a pale yellow oil: TLC R_f 0.20 (EtOAc/hexane, 4:1); $[\alpha]_D^{27} +38$ (*c* 0.33, MeOH) [lit. $[\alpha]_D^{25} +42$ (*c* 0.2, MeOH)]⁶; IR (neat)

(6) Li, Y.; Niu, S.; Sun, B.; Liu, S.; Liu, X.; Che, Y. *Org. Lett.* **2010**, 12, 3144.

3262, 2925, 1693, 1642, 1591 cm⁻¹; ¹H NMR (500 MHz, acetone-d₆) δ 0.87 (t, 3H, *J* = 6.9 Hz), 1.08 (s, 3H), 1.18 (s, 3H), 1.29-1.38 (m, 10H), 1.42 (s, 3H), 1.55 (dd, 1H, *J* = 8.2, 10.7 Hz), 1.65 (m, 1H), 1.72 (dd, 1H, *J* = 1.6, 16.3 Hz), 1.79 (m, 1H), 2.19 (t, 1H, *J* = 10.7 Hz), 2.60 (dd, 1H, *J* = 4.2, 9.8 Hz), 2.66 (dd, 1H, *J* = 9.1, 15.6 Hz), 2.95 (dd, 1H, *J* = 4.8, 15.6 Hz), 3.08 (dd, 1H, *J* = 4.7, 16.3 Hz), 3.20 (dd, 1H, *J* = 8.2, 10.7 Hz), 3.48 (s, 3H), 3.82 (m, 1H), 4.03 (dd, 1H, *J* = 1.6, 4.7 Hz), 4.06 (d, 1H, *J* = 12.6 Hz), 4.29 (d, 1H, *J* = 12.6 Hz), 4.55 (br d, 1H, *J* = 4.2 Hz), 4.67 (br, 1H, OH), 5.02 (d, 1H, *J* = 9.8 Hz), 5.84 (br s, 1H), 6.48 (s, 1H); ¹³C NMR (125 MHz, acetone-d₆) δ 14.4, 23.3, 24.0, 24.5, 25.5, 26.5, 29.3, 29.6, 32.6, 34.3, 34.9, 36.6, 39.3, 41.0, 46.4, 49.7, 59.2, 63.1, 66.1, 70.2, 72.6, 77.4, 81.9, 86.9, 99.9, 109.2, 113.6, 131.5, 138.0, 144.6, 151.3, 163.6, 172.0; HRMS (ESI) calcd for C₃₃H₄₇O₉ (M-H)⁻ *m/z* 587.3220, found 587.3226.

2. Natural product NMR comparison table for (-)-fuscoatrol A (3)



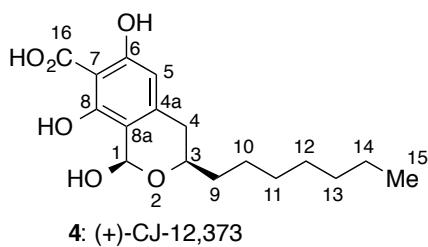
$\beta\alpha$ conformer of (-)-fuscoatrol A (3)

No.	^1H NMR (CDCl_3)		^{13}C NMR (CDCl_3)	
	Synthetic (500 MHz)	Natural ² (500 MHz)	Synthetic (125 MHz)	Natural ² (125 MHz)
1			82.7	82.6
2	4.22 (m)	4.21 (dd, $J = 4.6, 11.1$ Hz)	73.6	73.5
3	2.35 (dd, $J = 4.6, 11.1$ Hz) 2.53 (t, $J = 11.1$ Hz)	2.35 (dd, $J = 4.7, 11.1$ Hz) 2.54 (t, $J = 11.1$ Hz)	44.8	44.7
4			133.7	133.8
5	5.14 (d, $J = 9.8$ Hz)	5.14 (br dd, $J = 1.4, 10.2$ Hz)	129.4	129.3
6	4.46 (br d, $J = 9.8$ Hz)	4.46 (br td, $J = 2.1, 10.2$ Hz)	76.2	76.1
7	5.94 (d, $J = 1.8$ Hz)	5.94 (br d, $J = 2.1$ Hz)	139.8	139.7
8			137.1	137.1
9	3.10 (dd, $J = 8.4, 10.3$ Hz)	3.10 (br t, $J = 9.5$ Hz)	40.4	40.3
10	1.62 (dd, $J = 10.3, 12.5$ Hz) 2.04 (dd, $J = 8.4, 12.5$ Hz)	1.64 (dd, $J = 10.3, 12.3$ Hz) 2.05 (dd, $J = 8.4, 12.3$ Hz)	34.3	34.2
11			41.6	41.5
12	1.89 (s, 3H)	1.89 (d, 3H, $J = 1.3$ Hz)	17.9	17.8
13	3.31 (s, 3H)	3.30 (s, 3H)	55.7	55.6
14	3.93 (d, $J = 11.1$ Hz) 4.34 (d, $J = 11.1$ Hz)	3.93 (d, $J = 11.1$ Hz) 4.34 (br dd, $J = 1.5, 11.0$ Hz)	67.2	67.1
15	1.10 (s, 3H)	1.10 (s, 3H)	24.8	24.7
16	1.29 (s, 3H)	1.29 (s, 3H)	27.8	22.7

$\beta\beta$ conformer of (–)-fuscoatrol A (**3**)

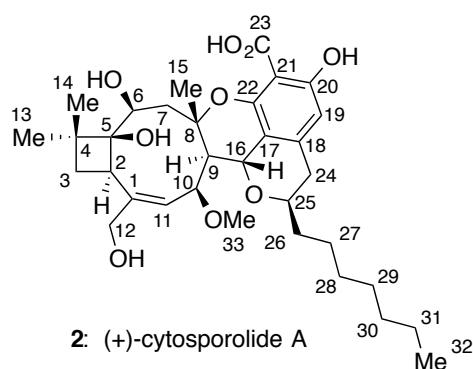
No.	^1H NMR (CDCl_3)		^{13}C NMR (CDCl_3)	
	Synthetic (500 MHz)	Natural ² (500 MHz)	Synthetic (125 MHz)	Natural ² (125 MHz)
1			84.7	84.6
2	4.18-4.26 (m)	4.23 (dd, $J = 7.6, 10.4$ Hz)	76.6	76.5
3	1.77 (dd, $J = 10.3, 14.2$ Hz) 2.90 (dd, $J = 7.1, 14.2$ Hz)	1.78 (dd, $J = 10.4, 14.2$ Hz) 2.91 (dd, $J = 7.0, 14.2$ Hz)	39.9	39.8
4			142.6	142.5
5	5.64 (br d, $J = 7.1$ Hz)	5.64 (td, $J = 1.8, 7.2$ Hz)	126.1	120.6
6	4.30 (br d, $J = 7.1$ Hz)	4.30 (td, $J = 2.1, 7.1$ Hz)	76.2	76.1
7	5.97 (br s)	5.97 (br s)	140.2	140.0
8			134.2	134.1
9	3.22 (dd, $J = 8.8, 10.9$ Hz)	3.21 (br dd, $J = 9.0, 11.2$ Hz)	45.4	45.4
10	1.58 (dd, $J = 8.8, 10.9$ Hz) 2.11 (t, $J = 10.9$ Hz)	1.57 (dd, $J = 8.6, 10.8$ Hz) 2.11 (t, $J = 11.0$ Hz)	36.0	35.9
11			40.6	40.7
12	1.77 (s, 3H)	1.76 (br s, 3H)	25.0	24.9
13	3.30 (s, 3H)	3.31 (s, 3H)	56.1	56.1
14	3.93 (d, $J = 10.9$ Hz) 4.18-4.26 (m)	3.92 (d, $J = 10.8$ Hz) 4.19 (br dd, $J = 3.0, 9.7$ Hz)	67.4	67.2
15	1.07 (s, 3H)	1.07 (s, 3H)	24.2	24.1
16	1.33 (s, 3H)	1.33 (s, 3H)	25.8	25.7

3. Natural product NMR comparison table for (+)-CJ-12,373 (4)



No.	¹ H NMR (CD ₃ OD)		¹³ C NMR (CD ₃ OD)	
	Synthetic (500 MHz)	Natural ⁵ (270 MHz)	Synthetic (125 MHz)	Natural ⁵ (68 MHz)
1	5.49 (s)	5.49 (s)	97.9	98.0
3	4.04 (m)	4.04 (m)	68.4	68.4
4	2.47 (dd, <i>J</i> = 11.7, 16.8 Hz) 2.54 (br d, <i>J</i> = 16.8 Hz)	2.46 (dd, <i>J</i> = 10.6, 16.9 Hz) 2.56 (dd, <i>J</i> = 3.5, 16.9 Hz)	36.1	36.2
4a			142.5	141.8
5	6.08 (s)	6.02 (s)	106.7	106.5
6			163.6	163.6
7			103.4	104.0
8			161.8	161.8
8a			113.6	113.5
9	1.51-1.64 (m, 2H)	1.58 (m, 2H)	37.5	37.5
10	1.22-1.51 (m) 1.51-1.64 (m)	1.3 – 1.4 (m) 1.50 (m)	27.6	27.6
11	1.22-1.51 (m, 2H)	1.3 – 1.4 (m, 2H)	31.5	31.5
12	1.22-1.51 (m, 2H)	1.3 – 1.4 (m, 2H)	31.3	31.2
13	1.22-1.51 (m, 2H)	1.3 – 1.4 (m, 2H)	33.8	33.8
14	1.22-1.51 (m, 2H)	1.3 – 1.4 (m, 2H)	24.5	24.5
15	0.90 (t, 3H, <i>J</i> = 5.9 Hz)	0.90 (t, 3H, <i>J</i> = 6.6 Hz)	15.2	15.2
16			179.7	178.8

4. Natural product NMR comparison table for (+)-cytosporolide A (2)

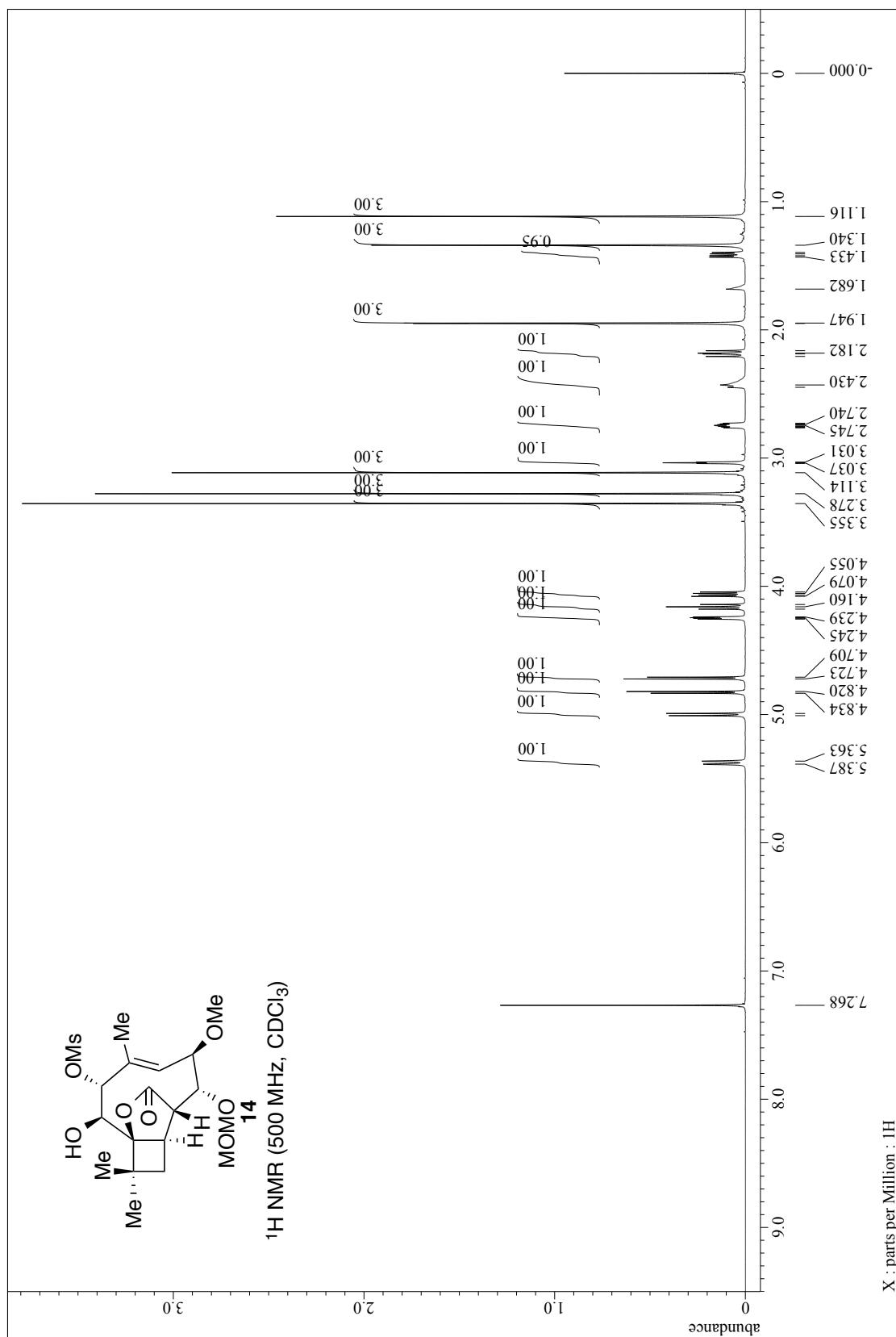


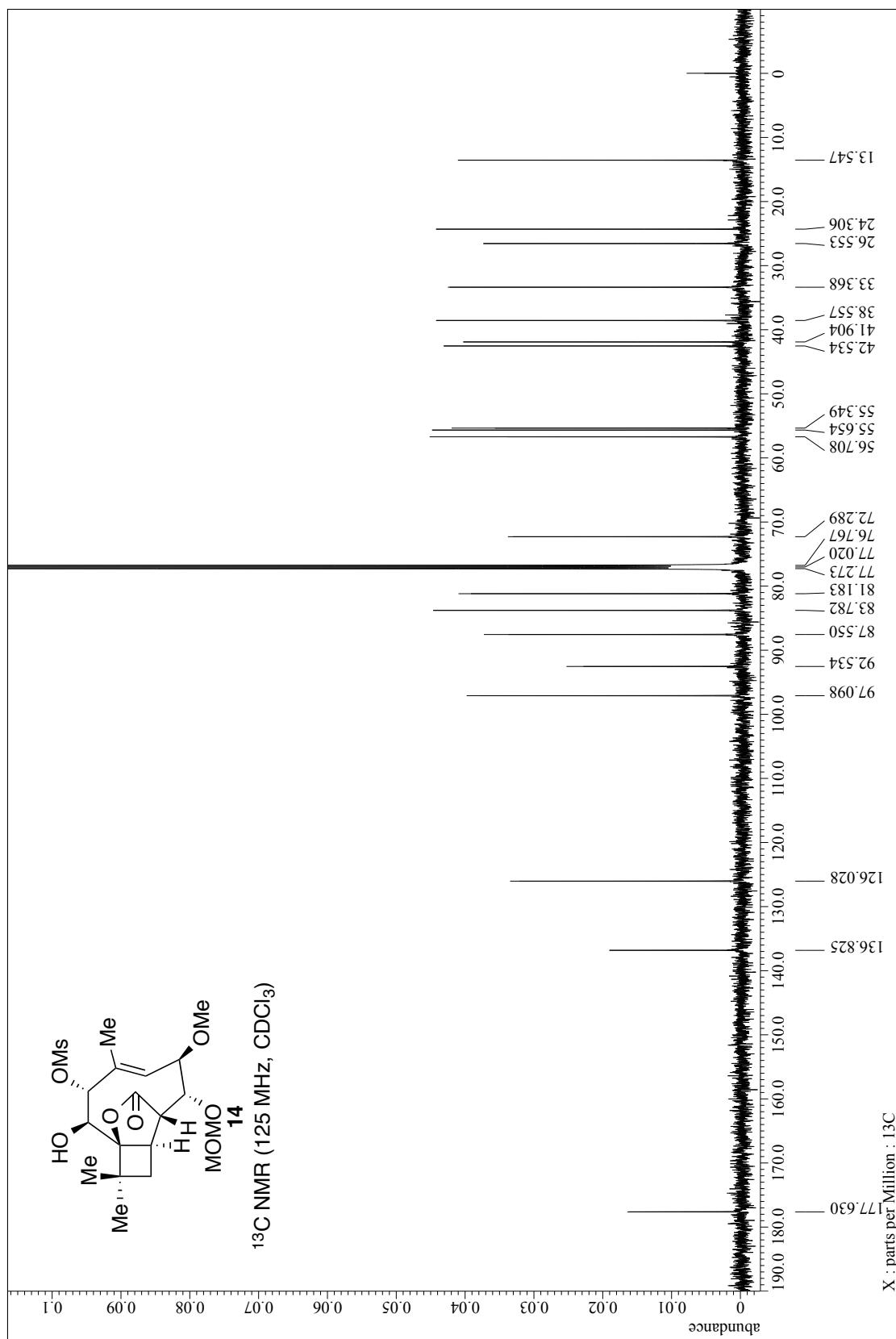
No.	¹ H NMR (acetone-d ₆)		¹³ C NMR (acetone-d ₆)	
	Synthetic (500 MHz)	Natural ⁶ (500 MHz)	Synthetic (125 MHz)	Natural ⁶ (125 MHz)
1			138.0	138.0
2	3.20 (dd, <i>J</i> = 8.2, 10.7 Hz)	3.20 (dd, <i>J</i> = 8.4, 10.6 Hz)	39.3	39.3
3	1.55 (dd, <i>J</i> = 8.2, 10.7 Hz) 2.19 (t, <i>J</i> = 10.7 Hz)	1.55 (dd, <i>J</i> = 8.4, 10.6 Hz) 2.19 (t, <i>J</i> = 10.6 Hz)	34.3	34.2
4			41.0	41.0
5			81.9	81.9
6	4.03 (dd, <i>J</i> = 1.6, 4.7 Hz)	4.03 (d, <i>J</i> = 4.7 Hz)	70.2	70.3
7	1.72 (dd, <i>J</i> = 1.6, 16.3 Hz) 3.08 (dd, <i>J</i> = 4.7, 16.3 Hz)	1.71 (d, <i>J</i> = 16.5 Hz) 3.08 (dd, <i>J</i> = 4.7, 16.5 Hz)	46.4	46.2
8			86.9	87.5
9	2.60 (dd, <i>J</i> = 4.2, 9.8 Hz)	2.60 (dd, <i>J</i> = 4.3, 9.7 Hz)	49.7	49.6
10	4.55 (br d, <i>J</i> = 4.2 Hz)	4.55 (d, <i>J</i> = 4.3 Hz)	77.4	77.4
11	5.84 (br s)	5.83 (s)	131.5	131.5
12	4.06 (d, <i>J</i> = 12.6 Hz) 4.29 (d, <i>J</i> = 12.6 Hz)	4.06 (d, <i>J</i> = 12.6 Hz) 4.29 (d, <i>J</i> = 12.6 Hz)	66.1	66.2
13	1.18 (s, 3H)	1.18 (s, 3H)	24.5	24.5
14	1.08 (s, 3H)	1.07 (s, 3H)	24.0	23.9
15	1.42 (s, 3H)	1.42 (s, 3H)	25.5	25.4
16	5.02 (d, <i>J</i> = 9.8 Hz)	5.02 (d, <i>J</i> = 9.7 Hz)	63.1	63.0
17			113.6	113.5
18			144.6	145.3
19	6.48 (s)	6.48 (s)	109.2	109.4
20			163.6	163.8

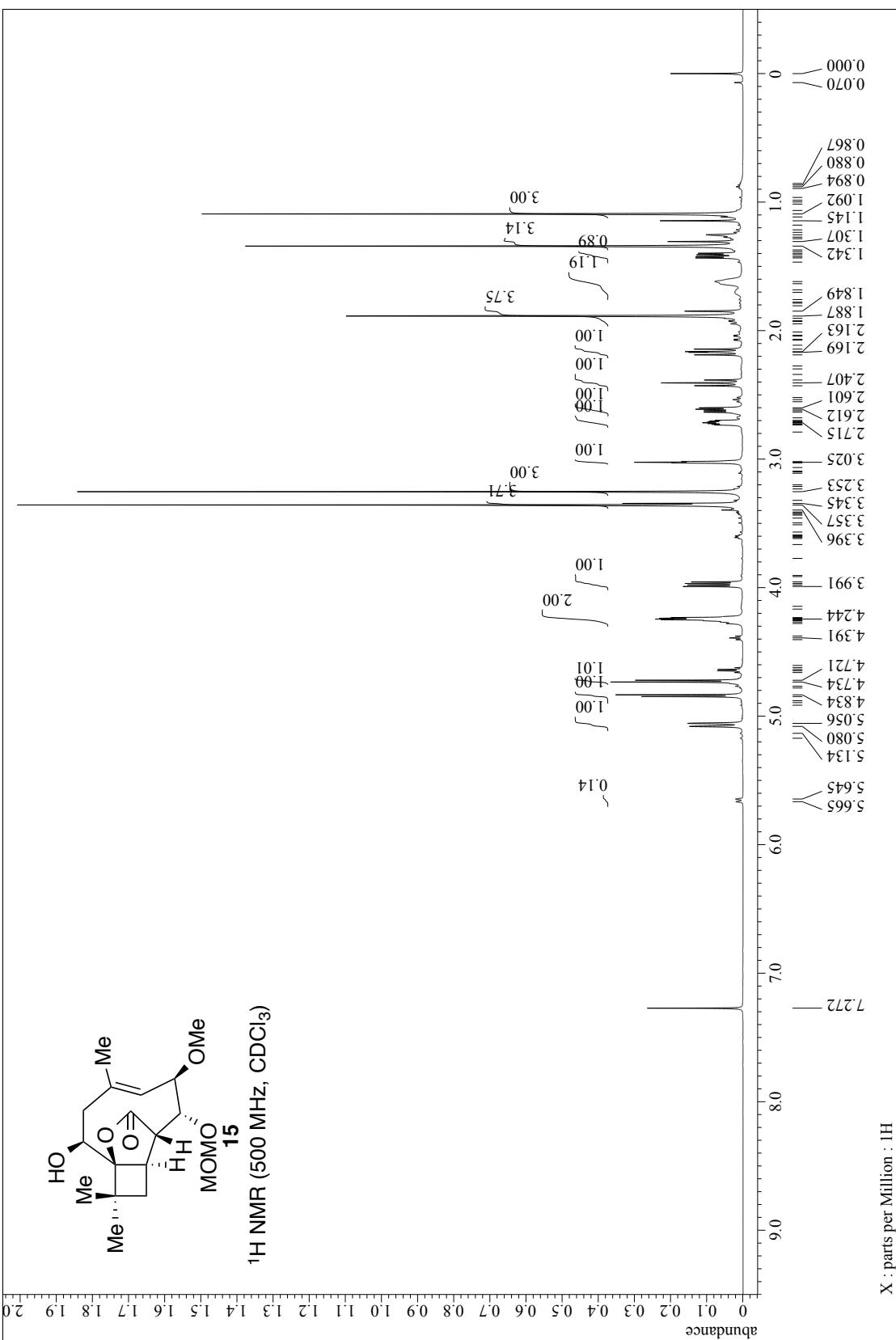
21			99.9	99.2
22			151.3	151.0
23			172.0	171.9
24	2.66 (dd, $J = 9.1, 15.6$ Hz) 2.95 (dd, $J = 4.8, 15.6$ Hz)	2.65 (dd, $J = 9.3, 15.6$ Hz) 2.95 (dd, $J = 4.7, 15.6$ Hz)	34.9	34.9
25	3.82 (m)	3.82 (m)	72.6	72.7
26	1.65 (m) 1.79 (m)	1.64 (m) 1.79 (m)	36.6	36.6
27	1.29-1.38 (m, 2H)	1.29 (m, 2H)	29.3	29.3
28	1.29-1.38 (m, 2H)	1.29 (m, 2H)	29.6	29.6
29	1.29-1.38 (m, 2H)	1.28 (m, 2H) ⁷	26.5	26.4
30	1.29-1.38 (m, 2H)	1.33 (m, 2H)	32.6	32.6
31	1.29-1.38 (m, 2H)	1.30 (m, 2H)	23.3	23.3
32	0.87 (t, 3H, $J = 6.9$ Hz)	0.87 (t, 3H, $J = 6.9$ Hz)	14.4	14.3
33	3.48 (s, 3H)	3.47 (s, 3H)	59.2	59.2
OH-5		4.63 (br s)		
OH-6	4.67 (br)	4.69 (br s)		
OH-20		12.00 (br s)		

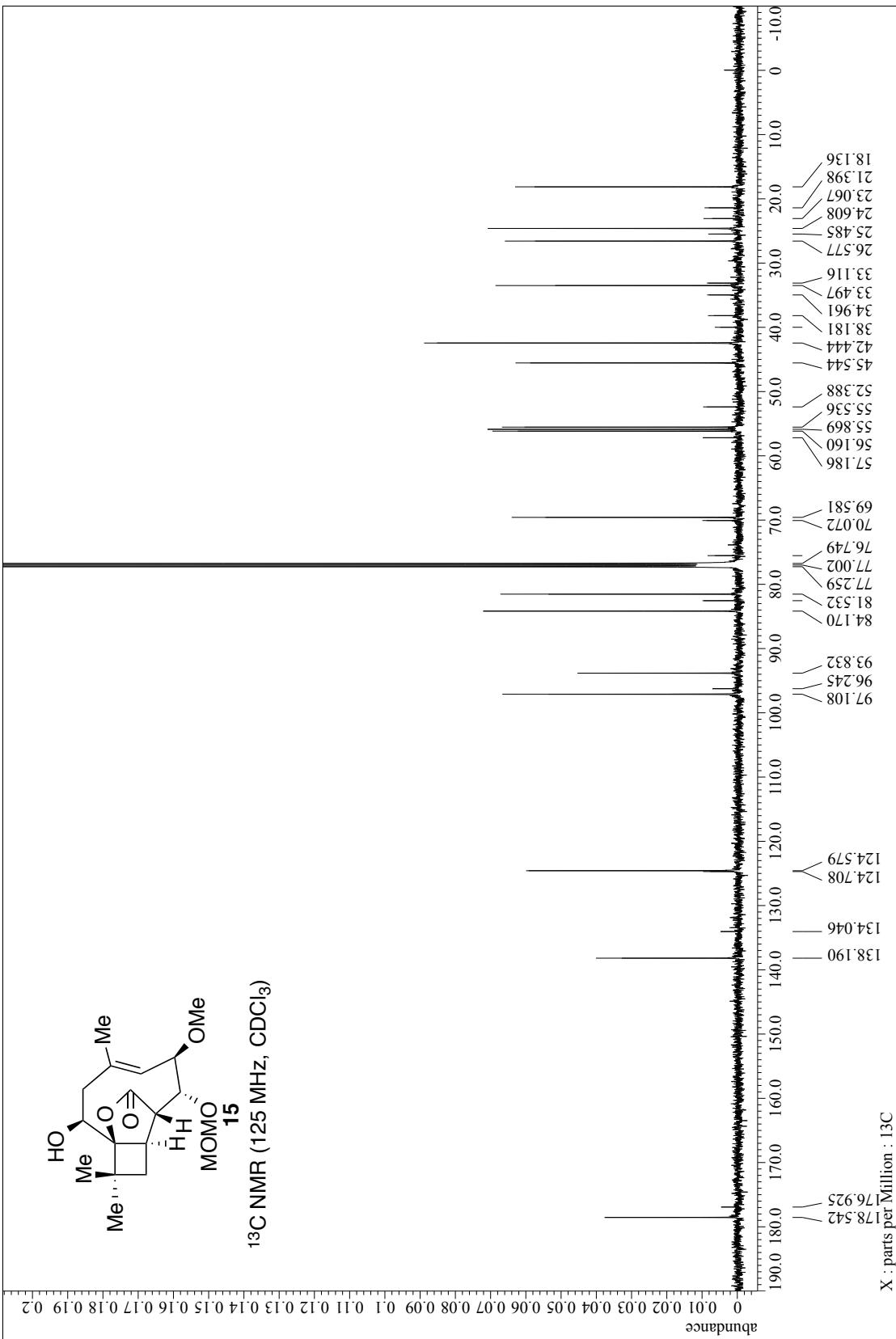
(7) Spence, J. T. J.; George, J. H. *Org. Lett.* **2011**, *13*, 5318.

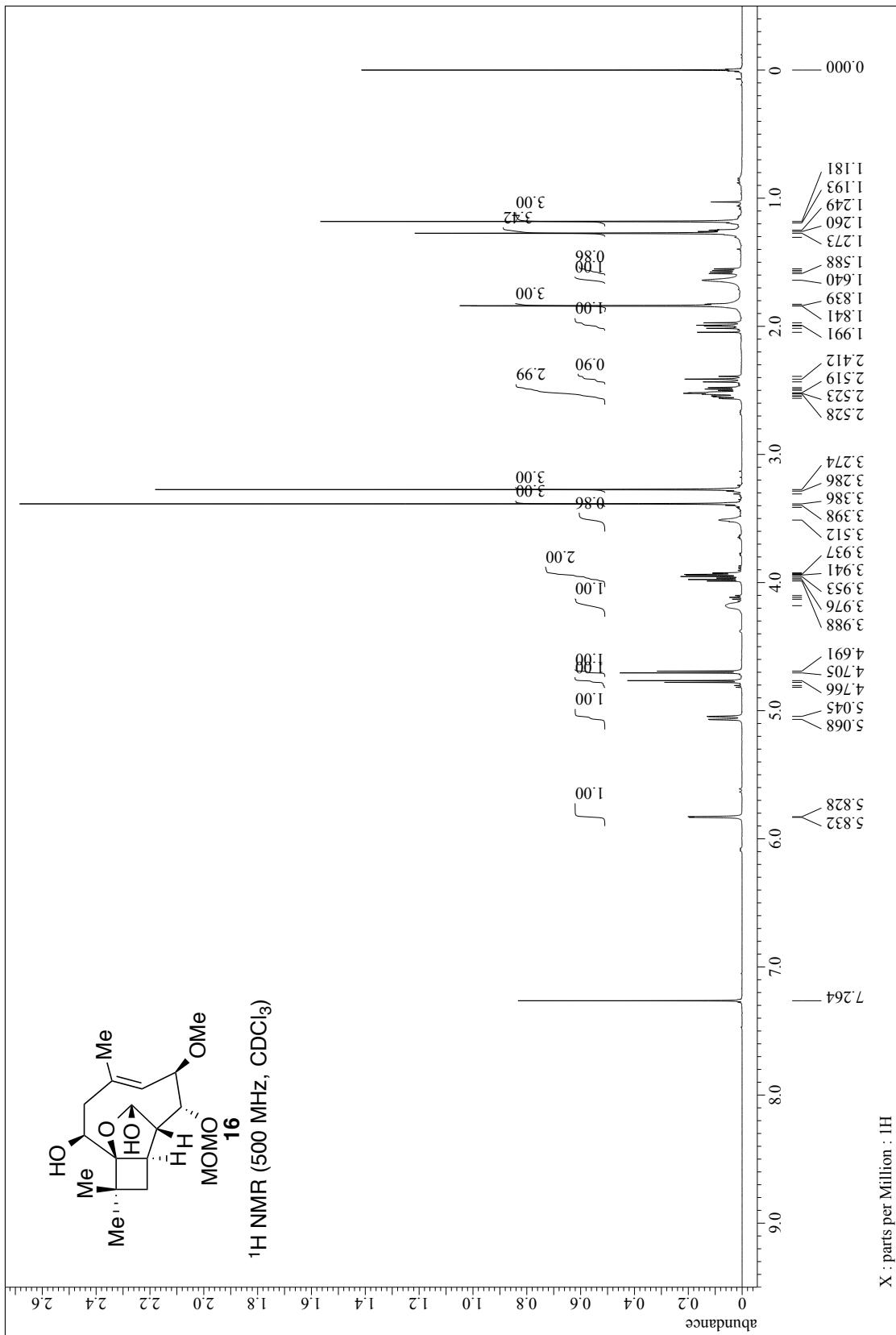
5. ^1H and ^{13}C NMR spectra of new compounds

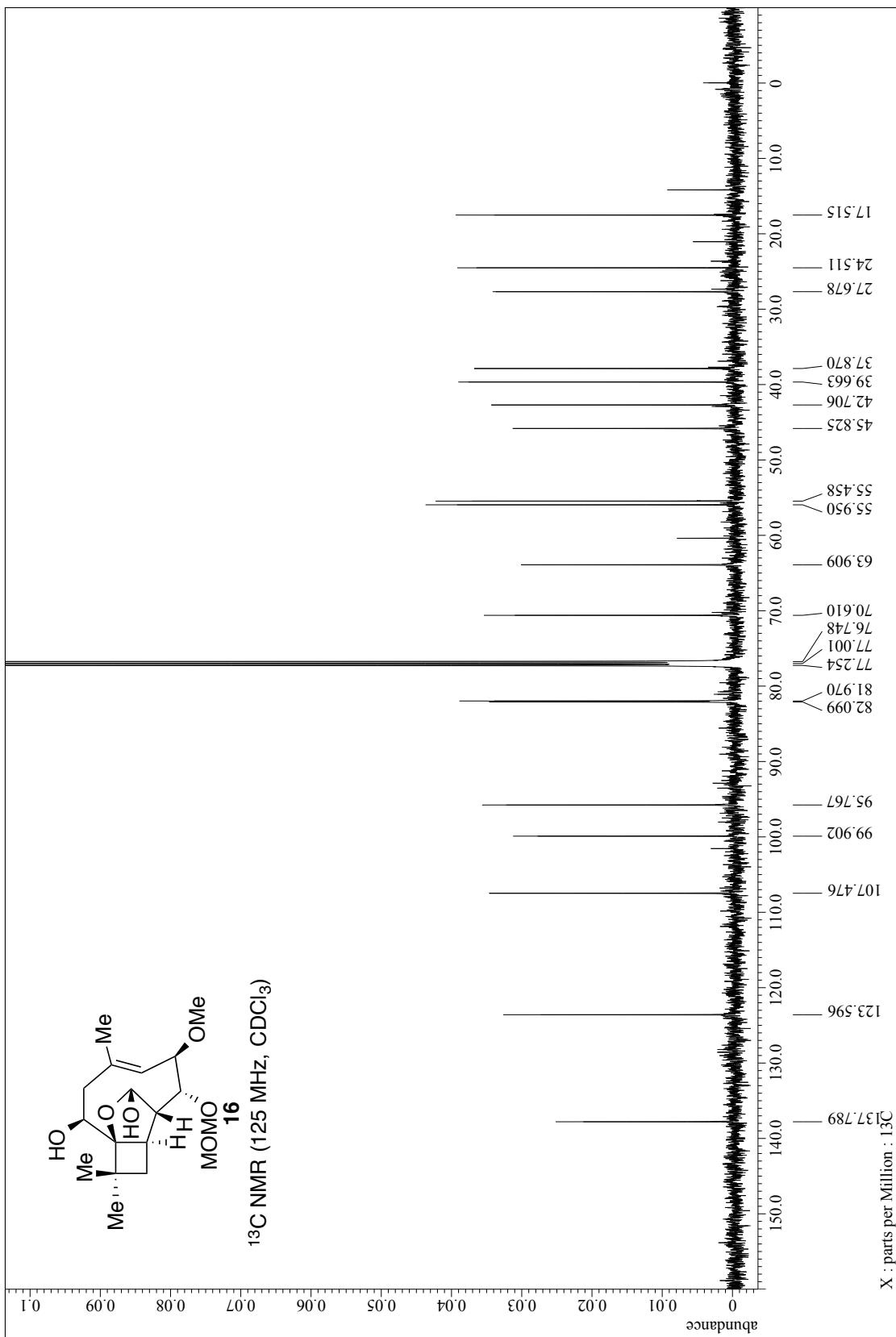


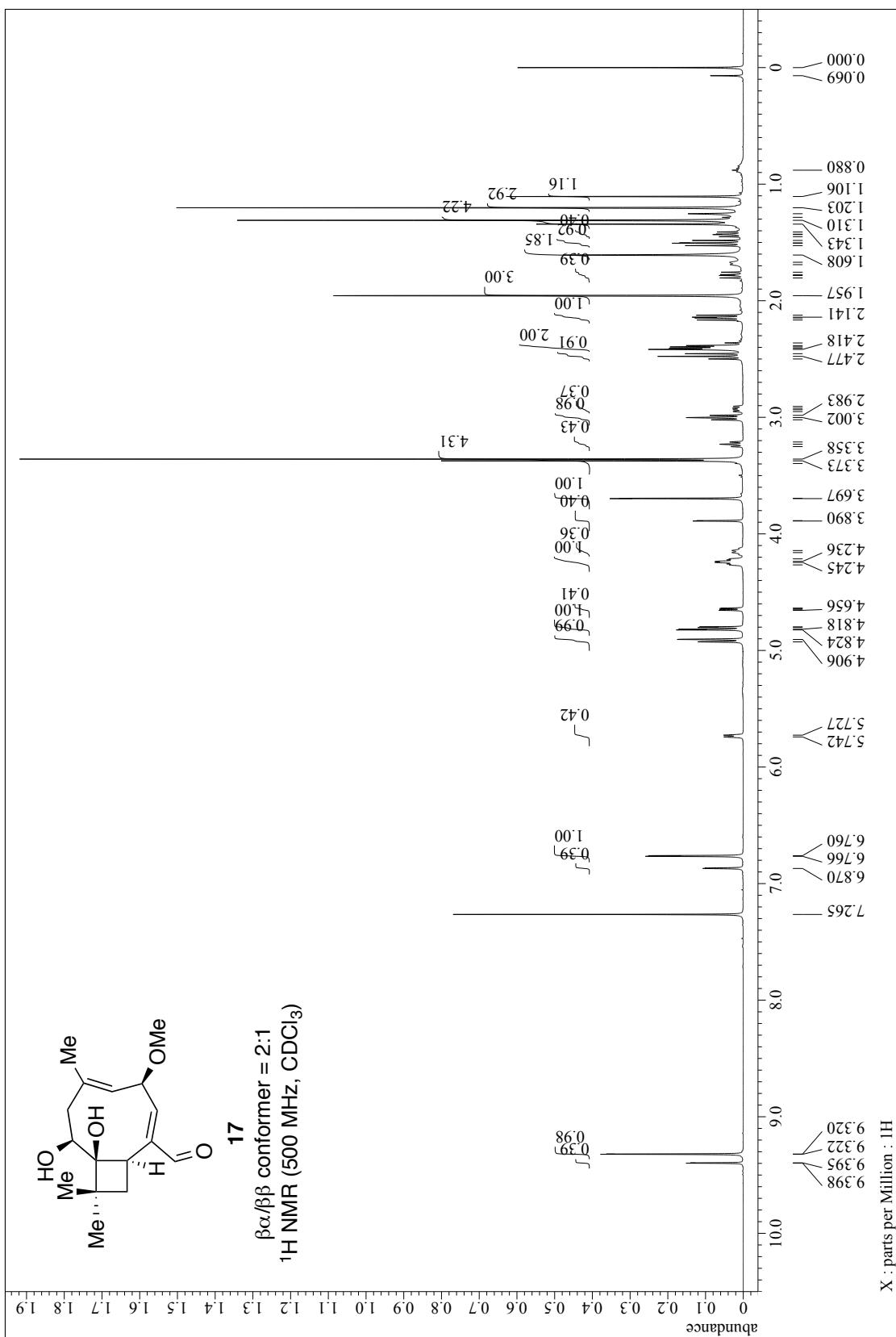


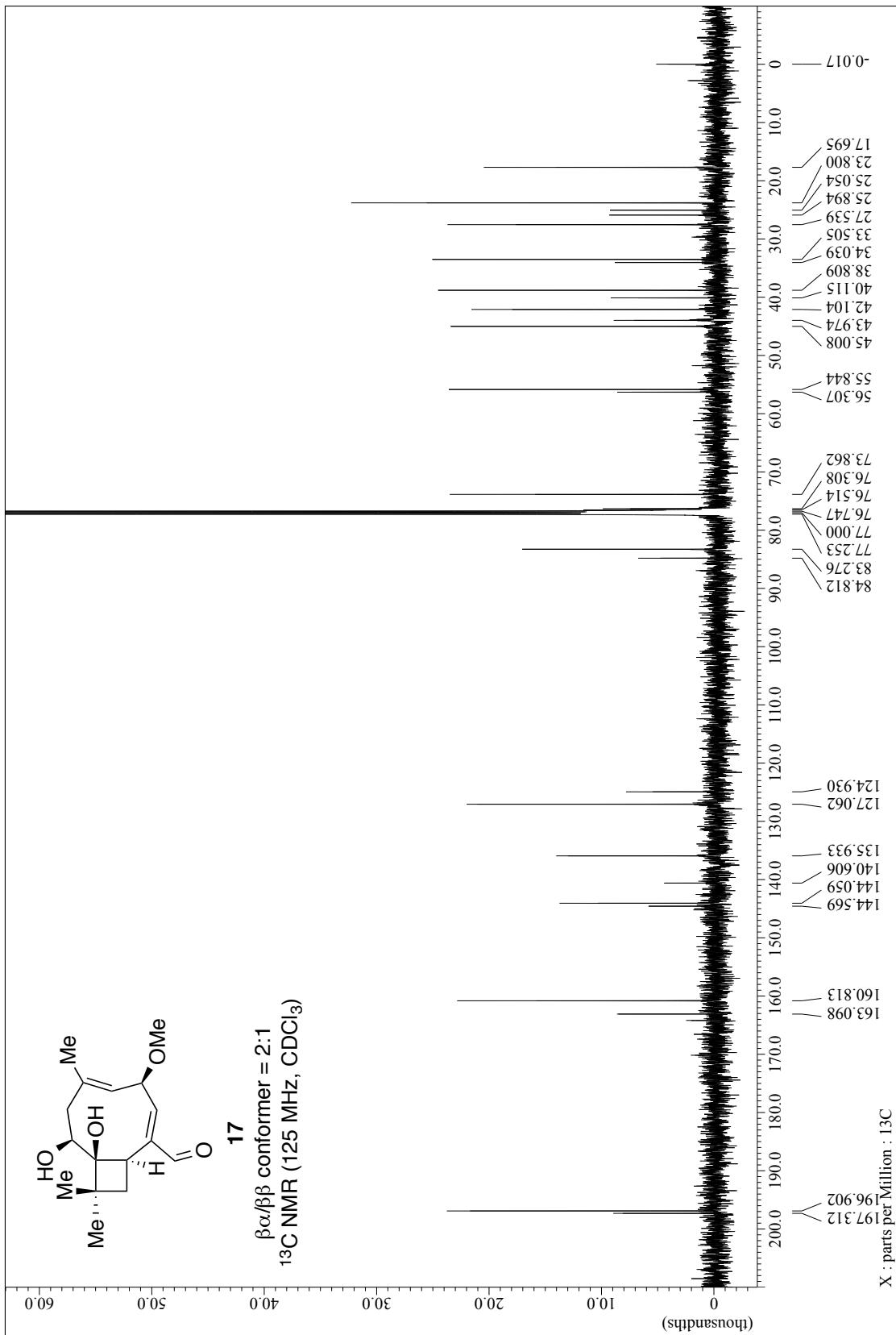


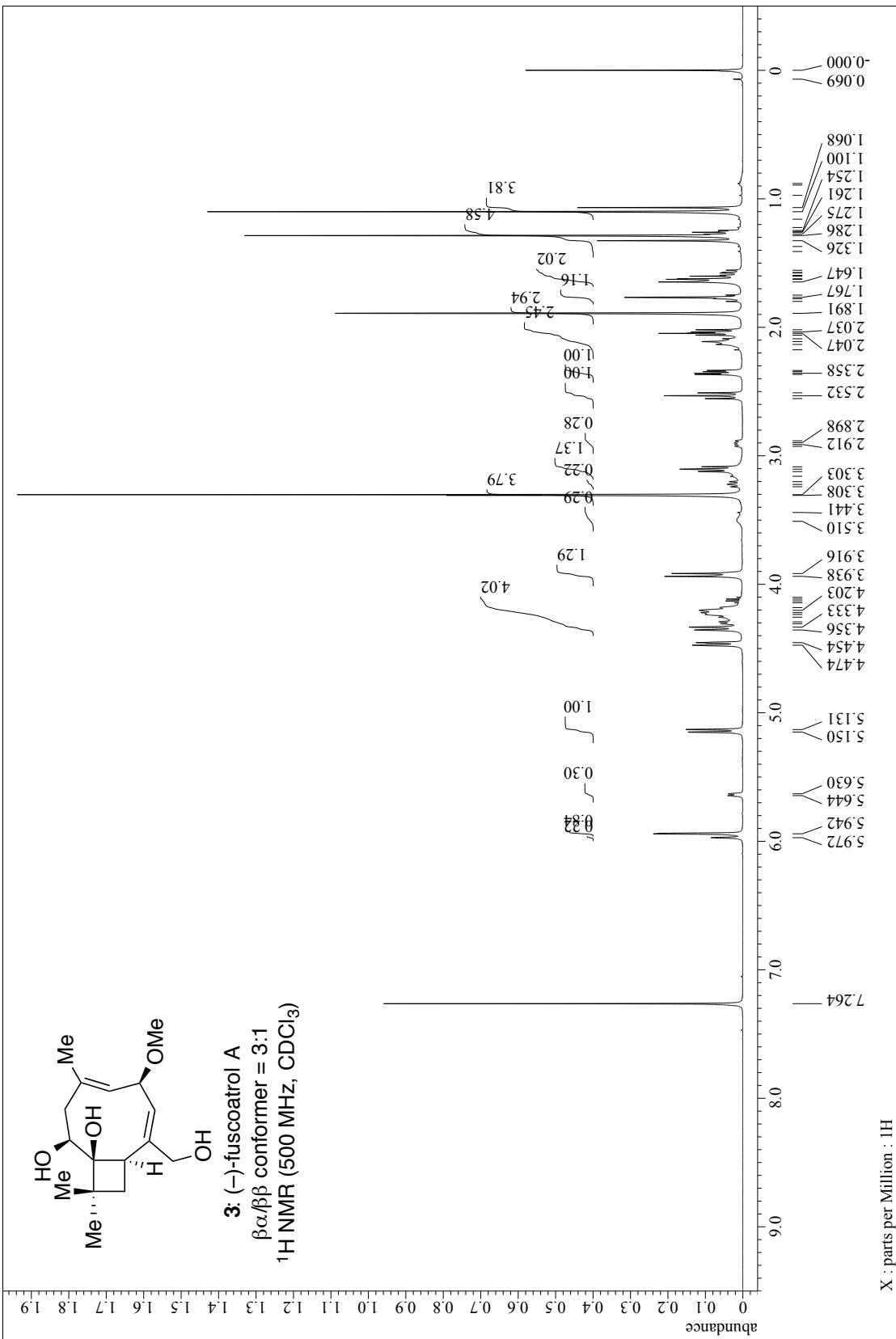


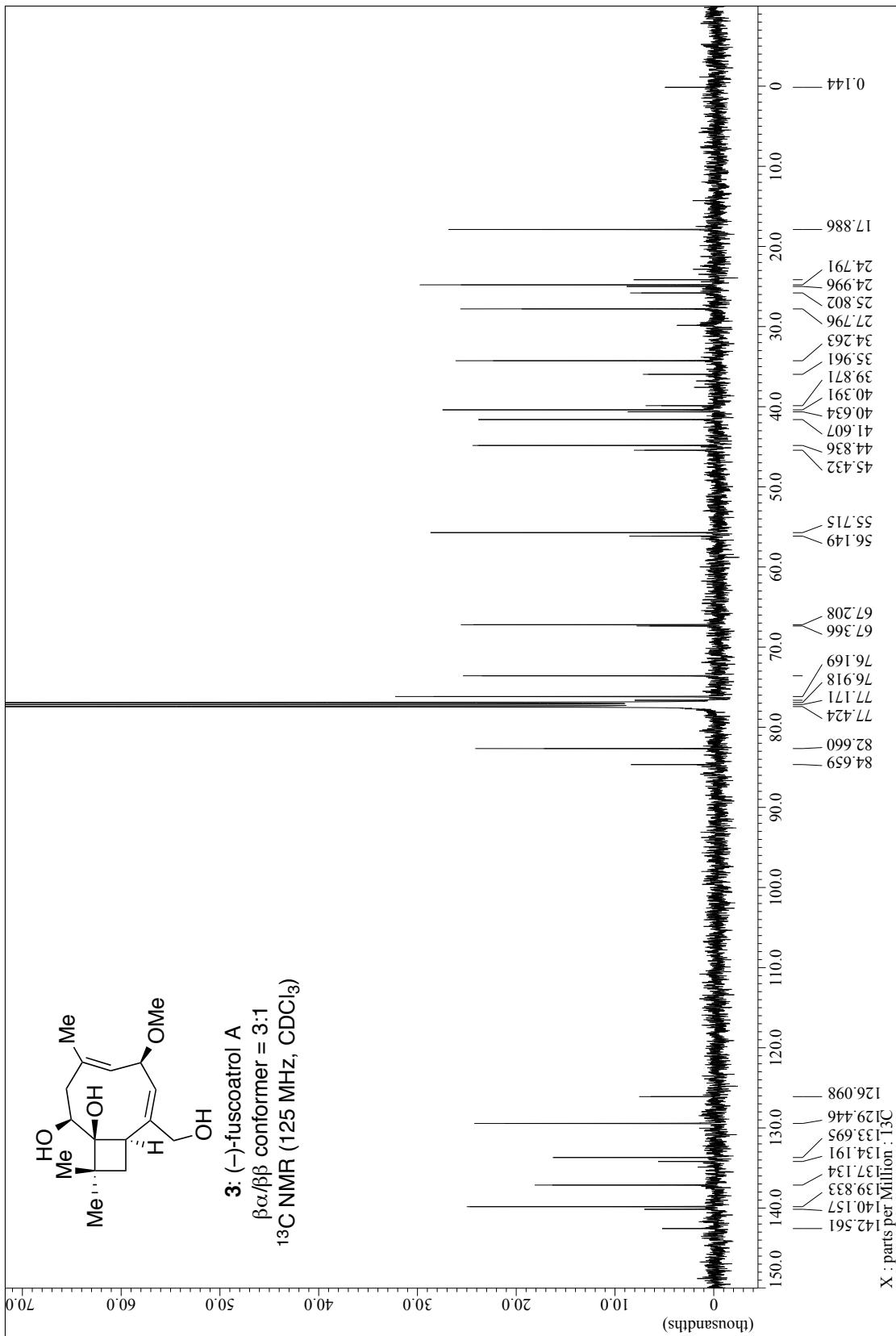


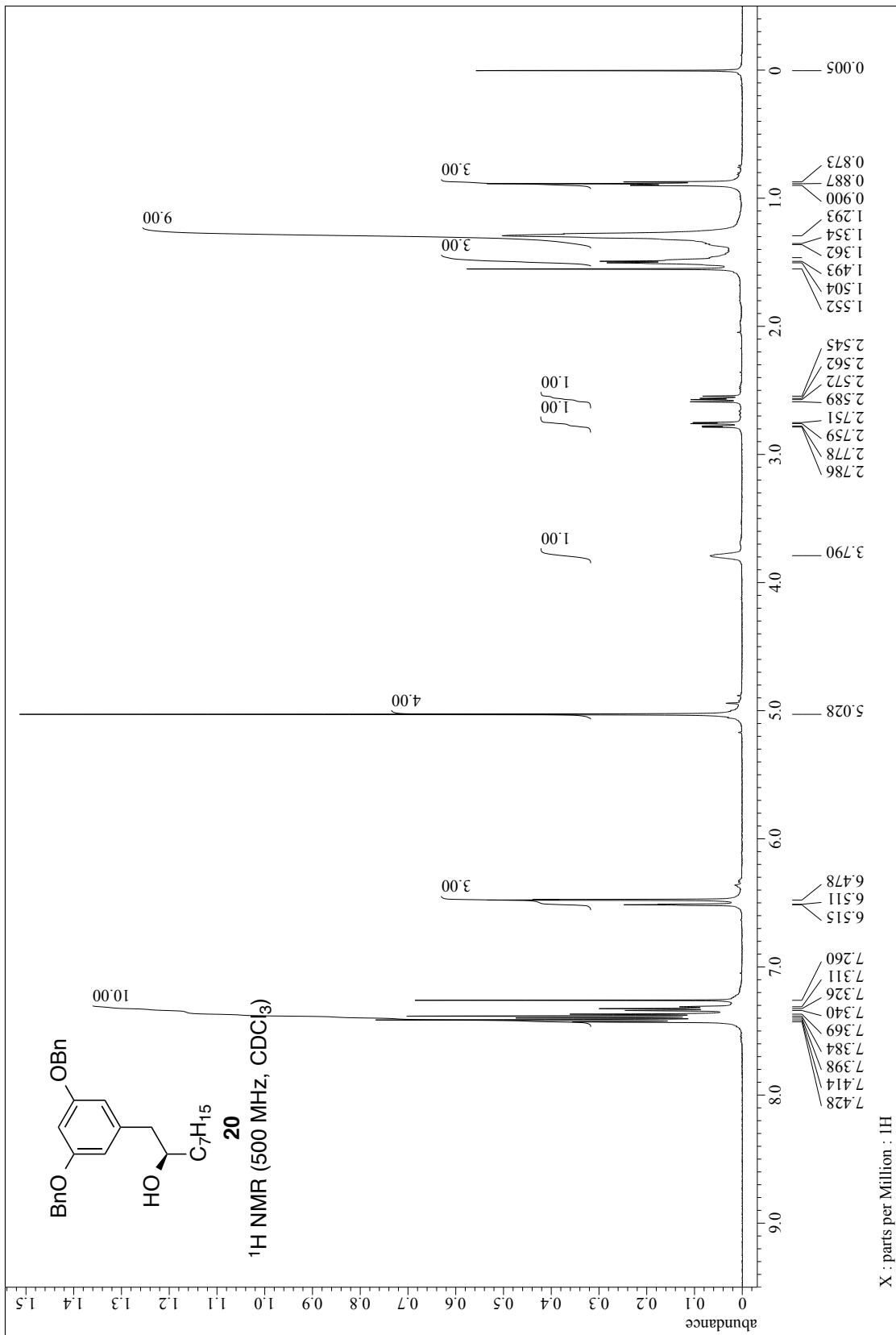


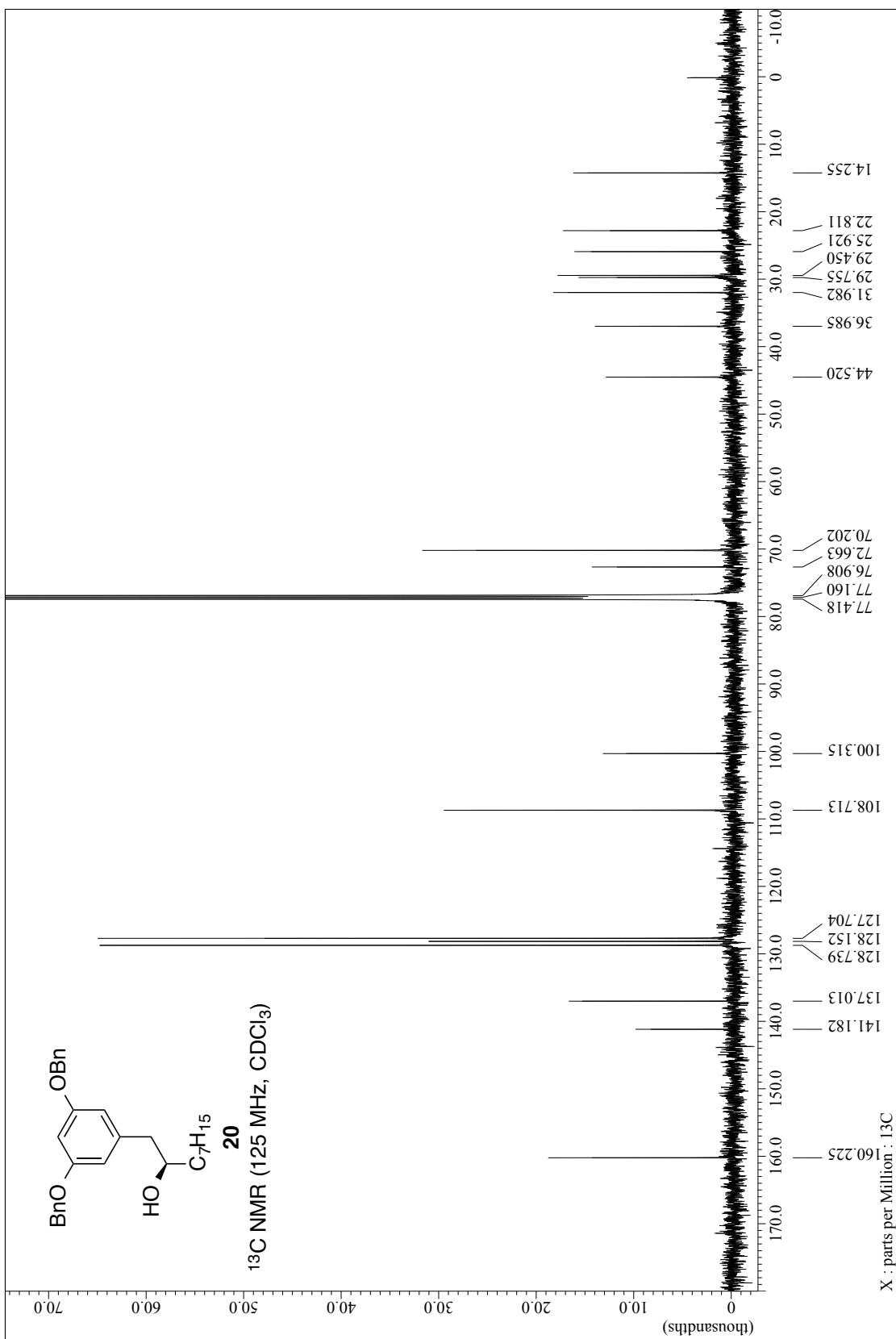


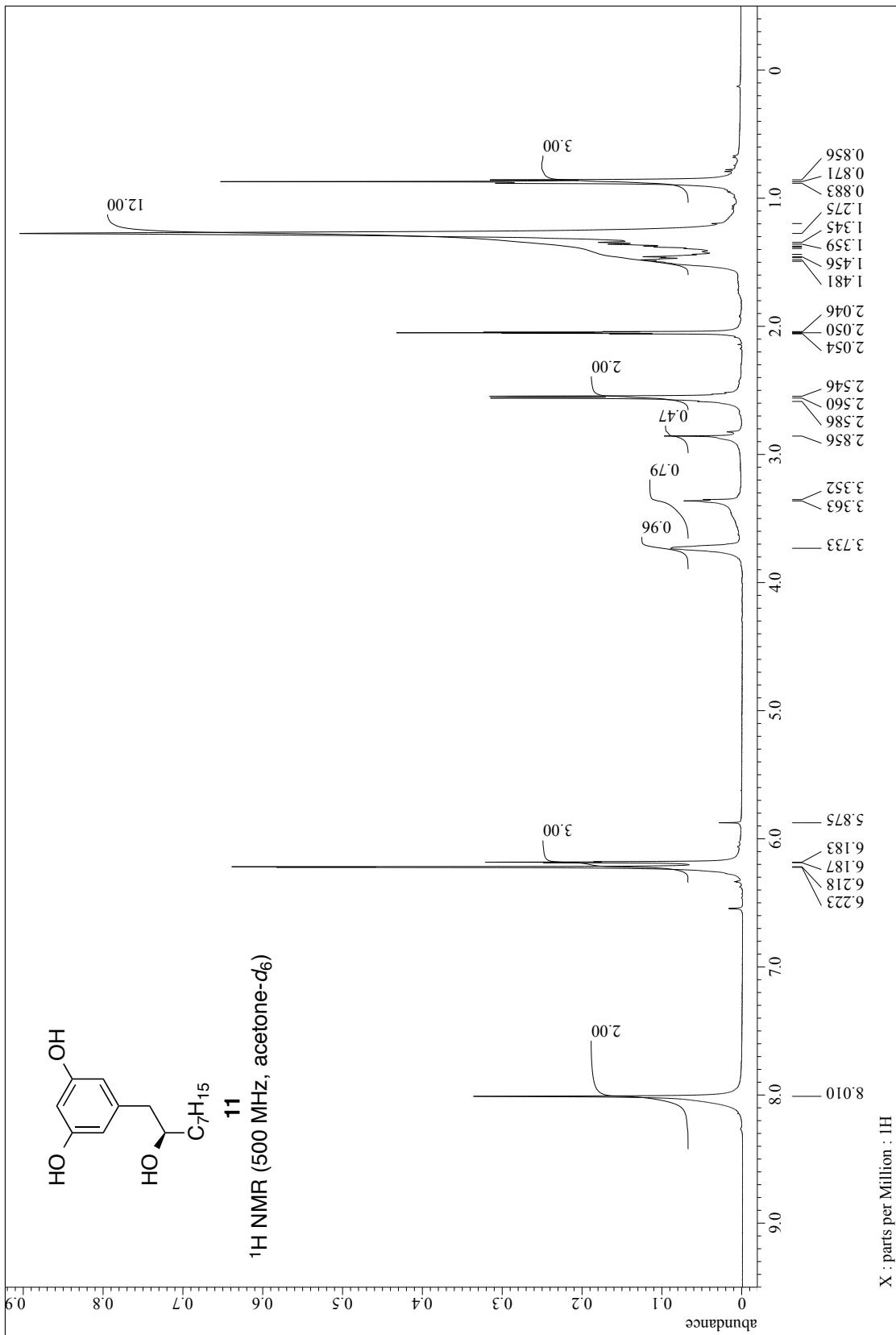


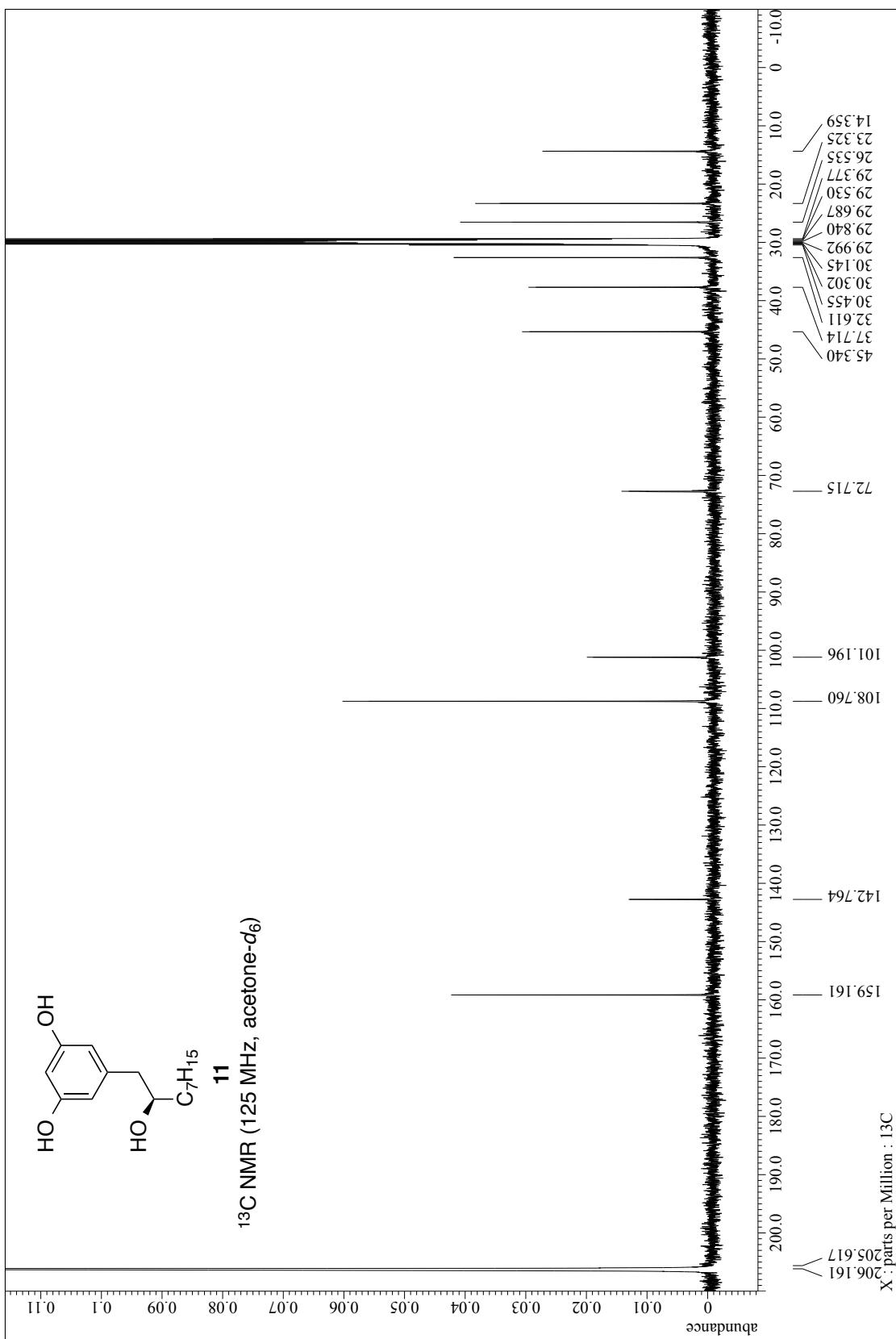


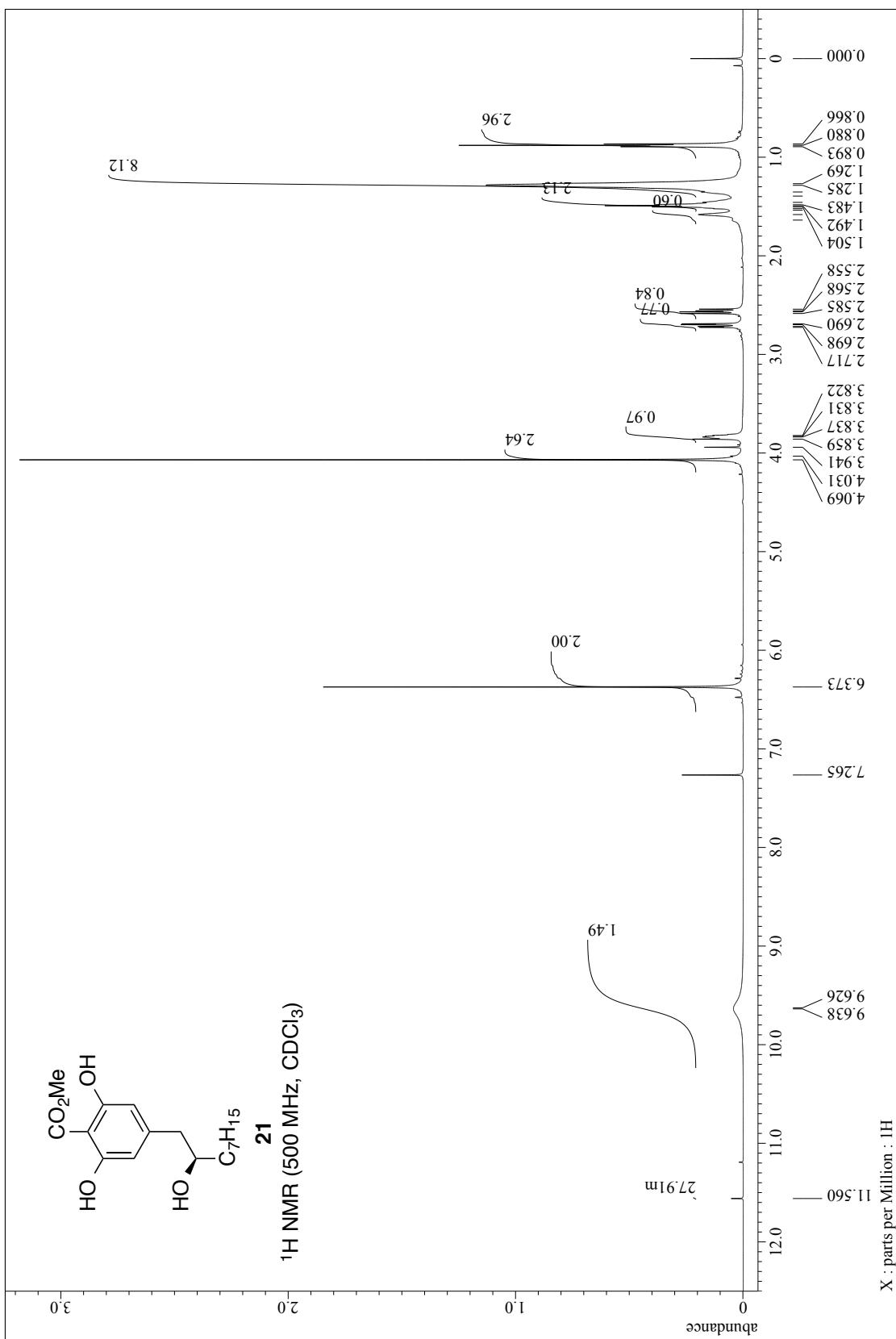


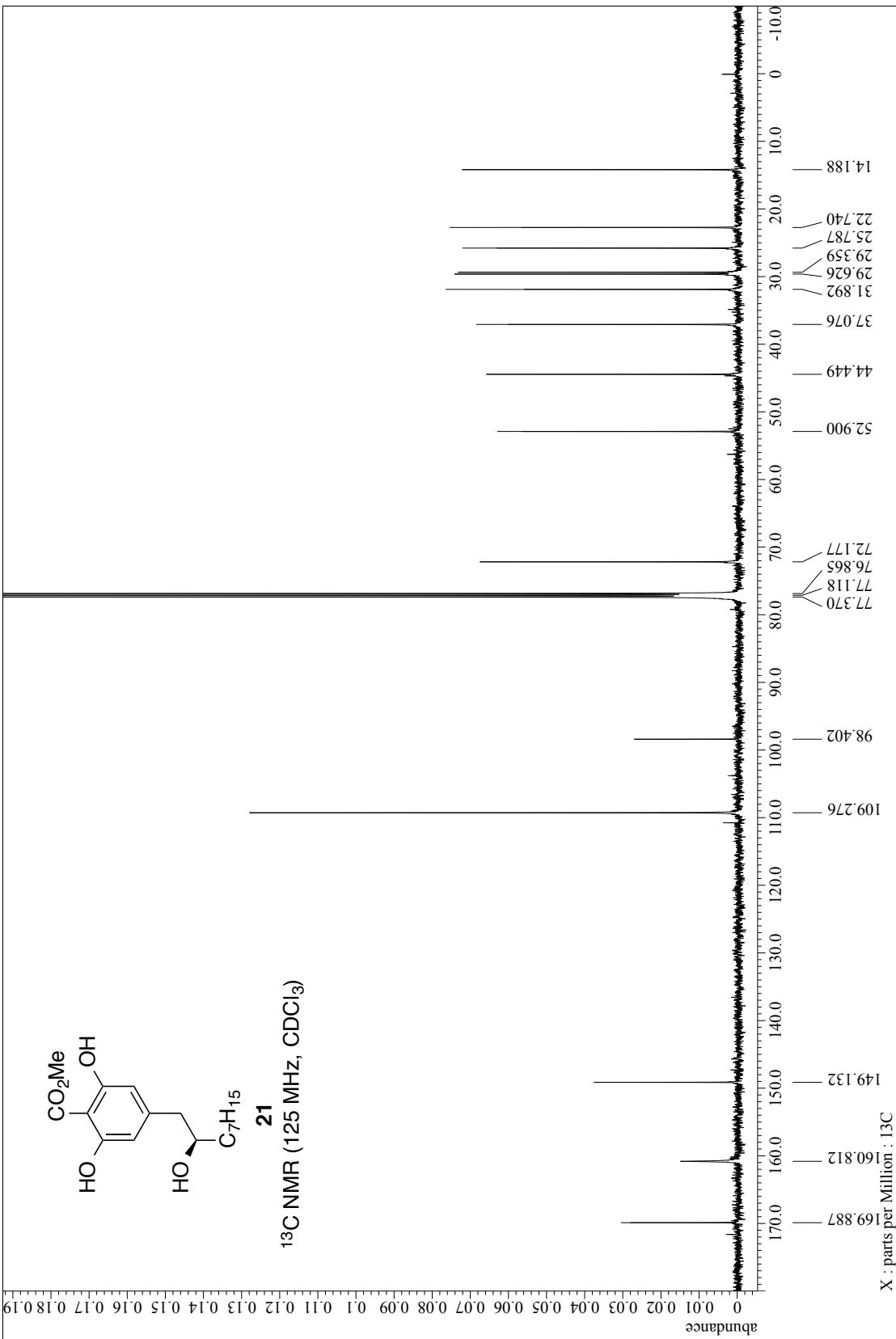


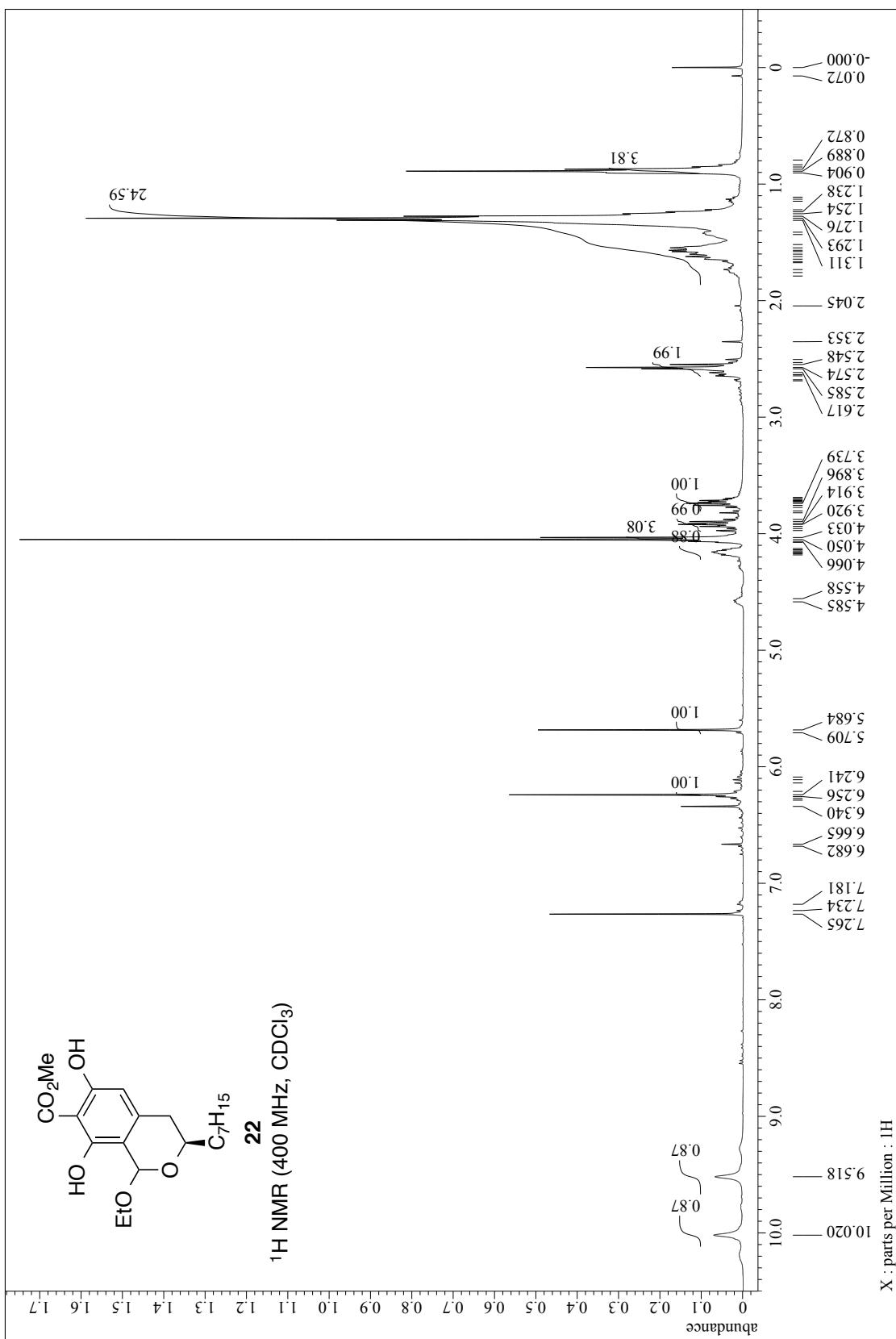


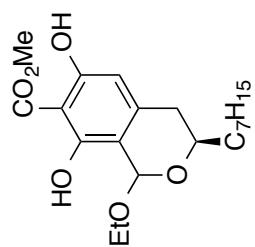
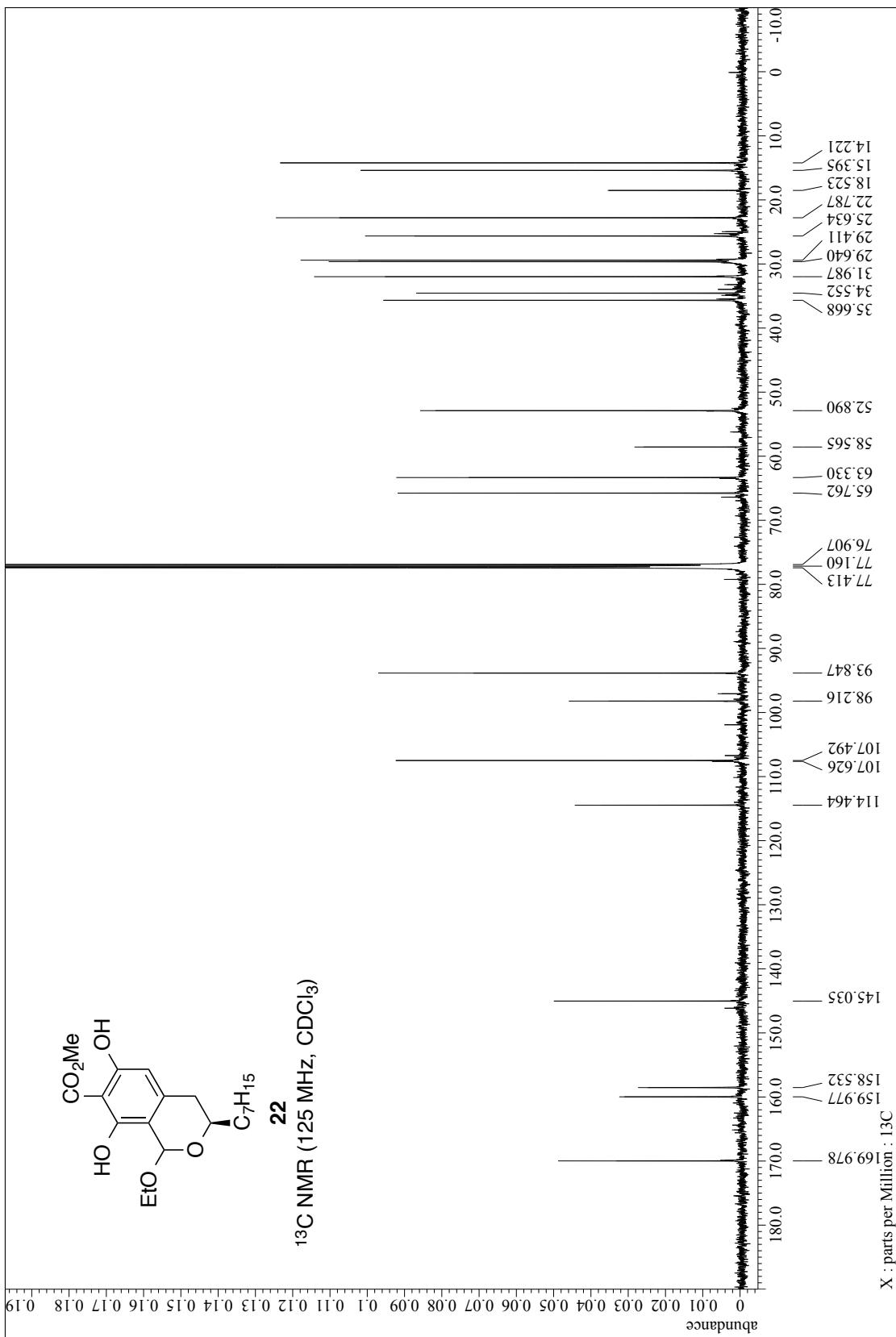


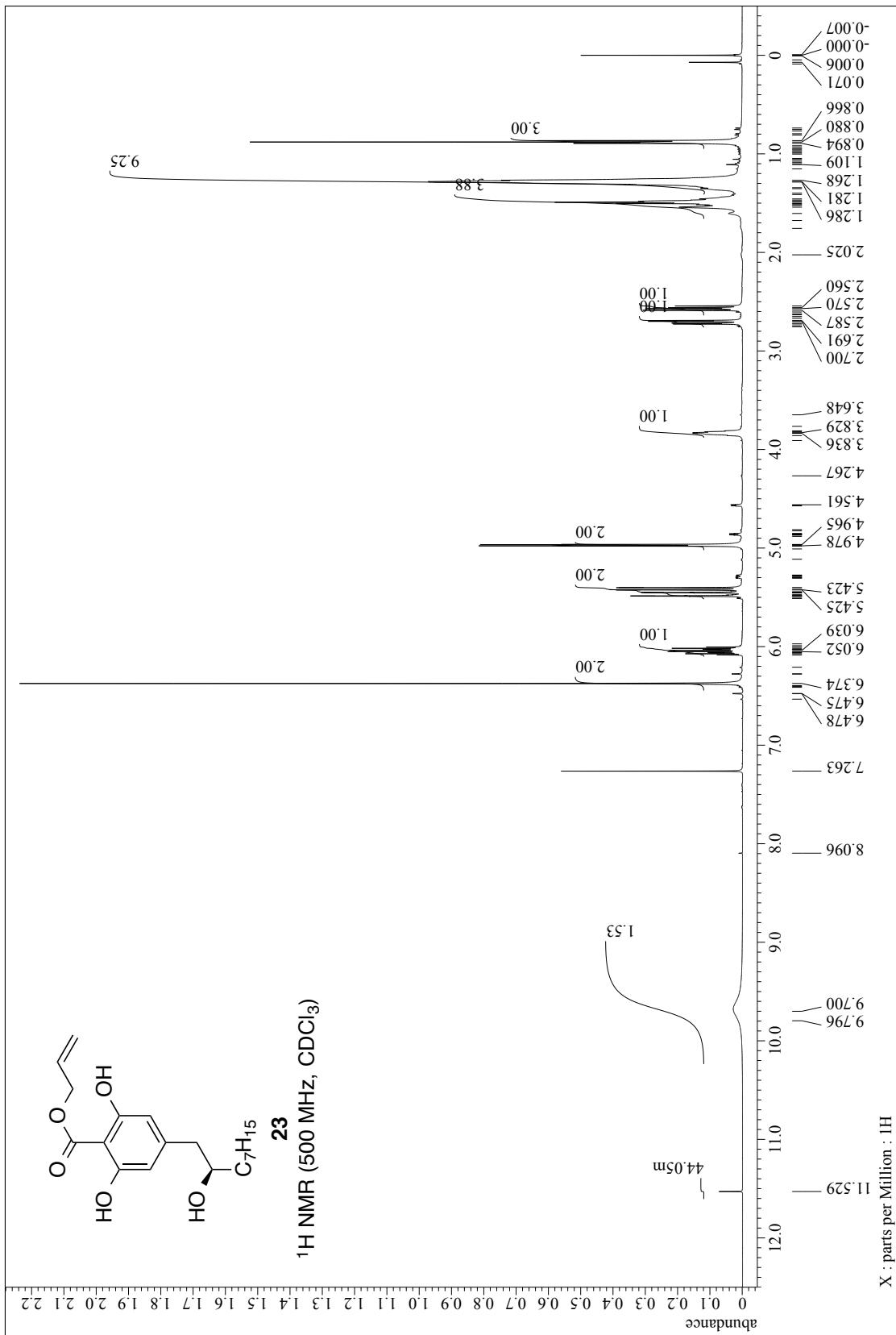


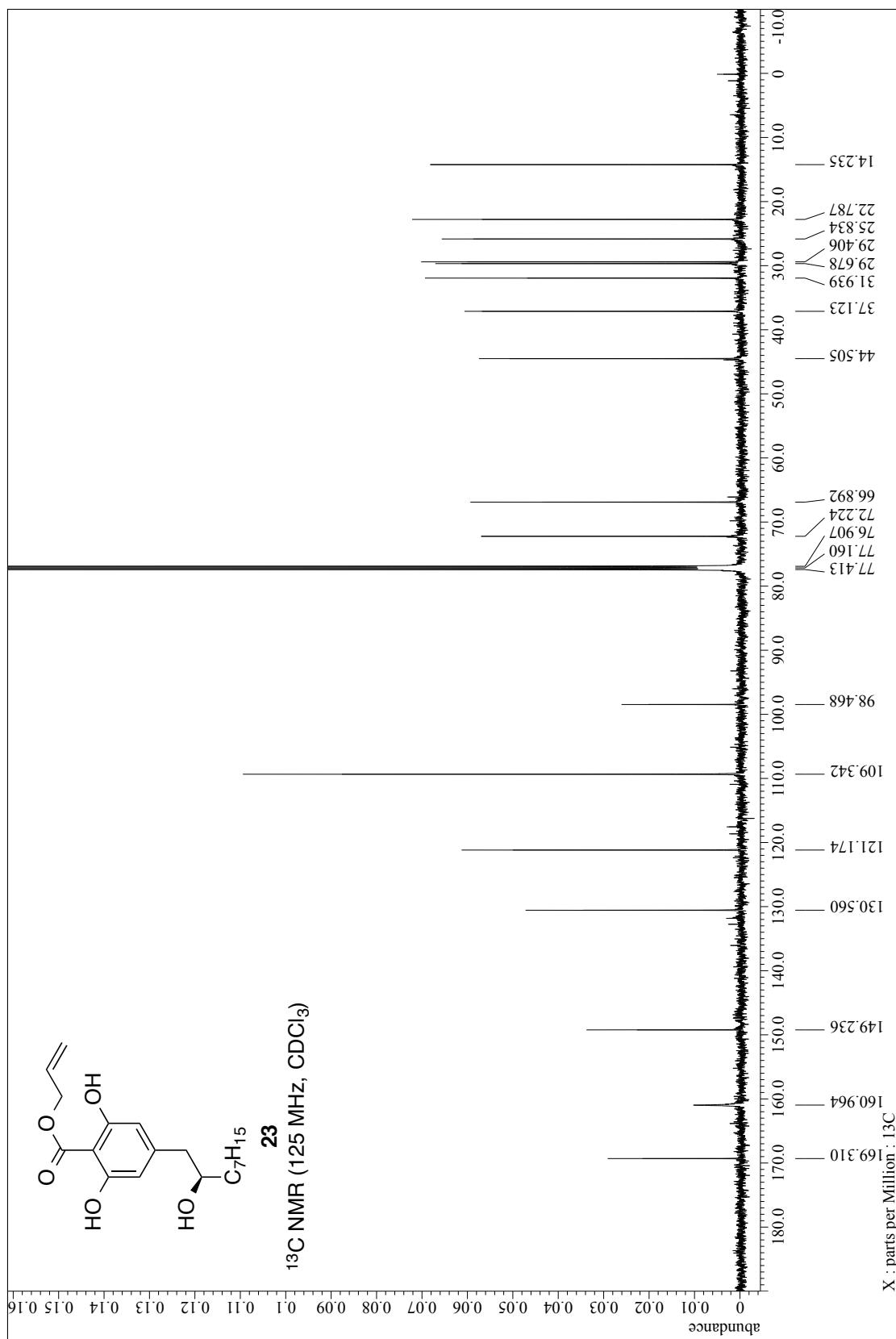


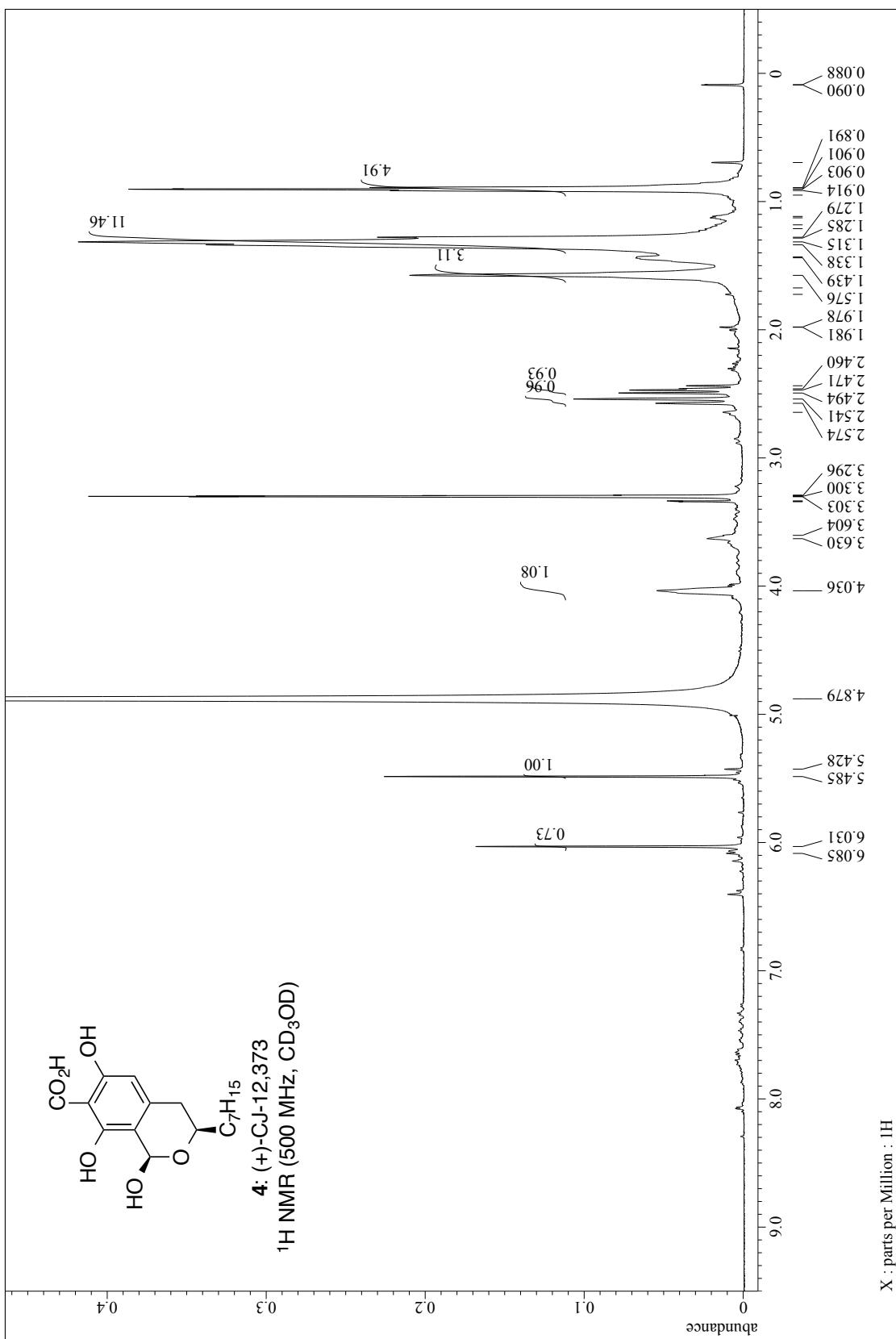


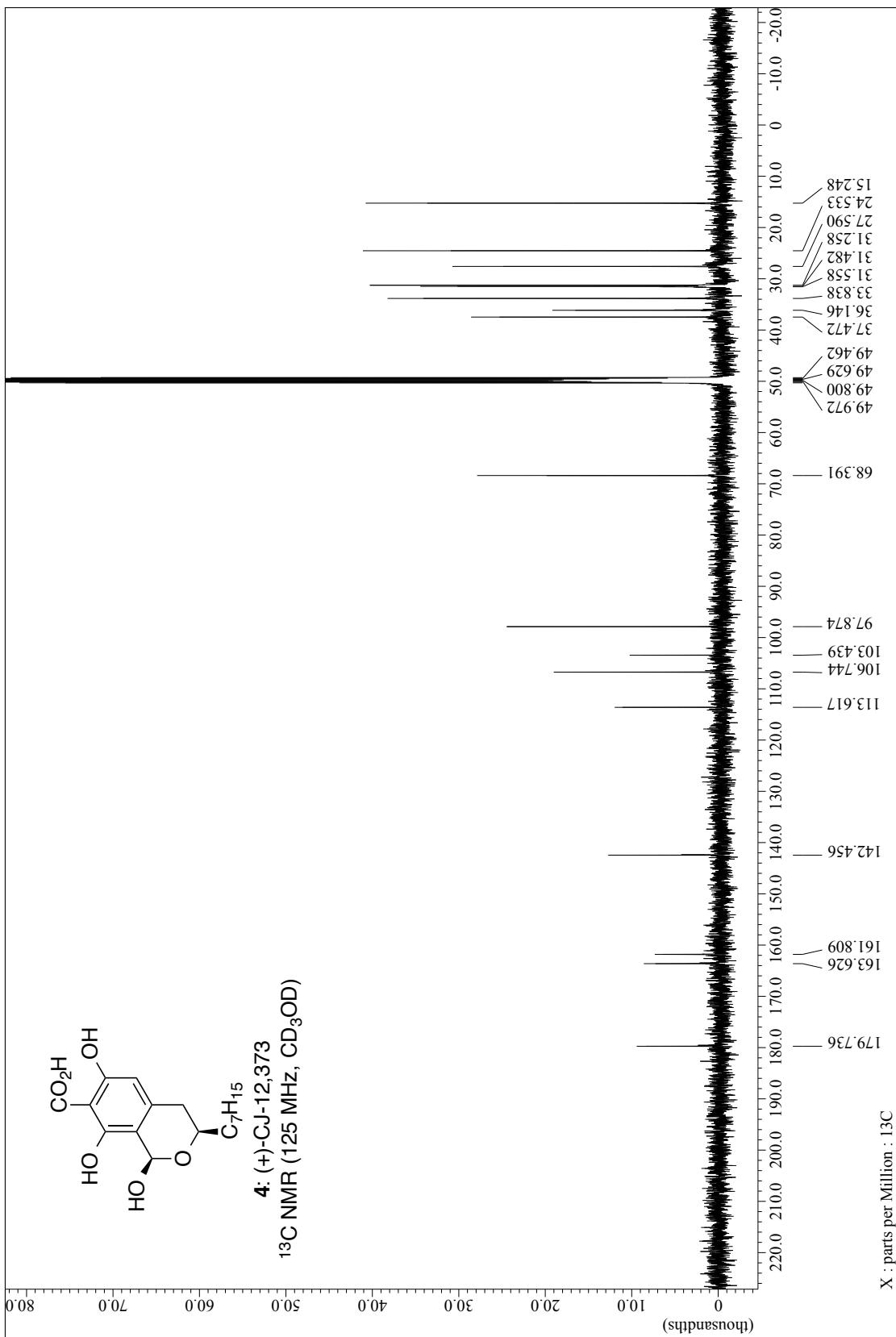


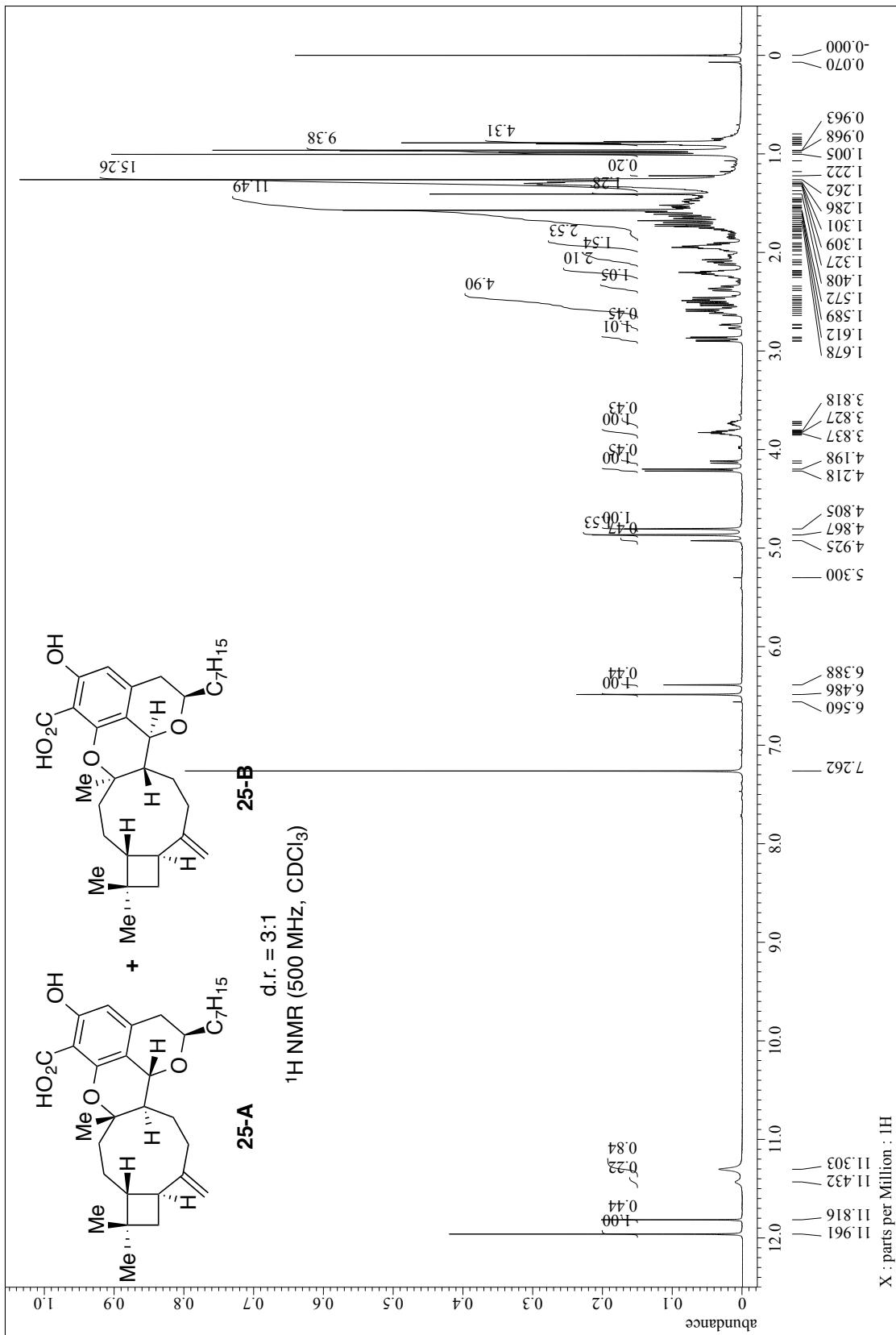


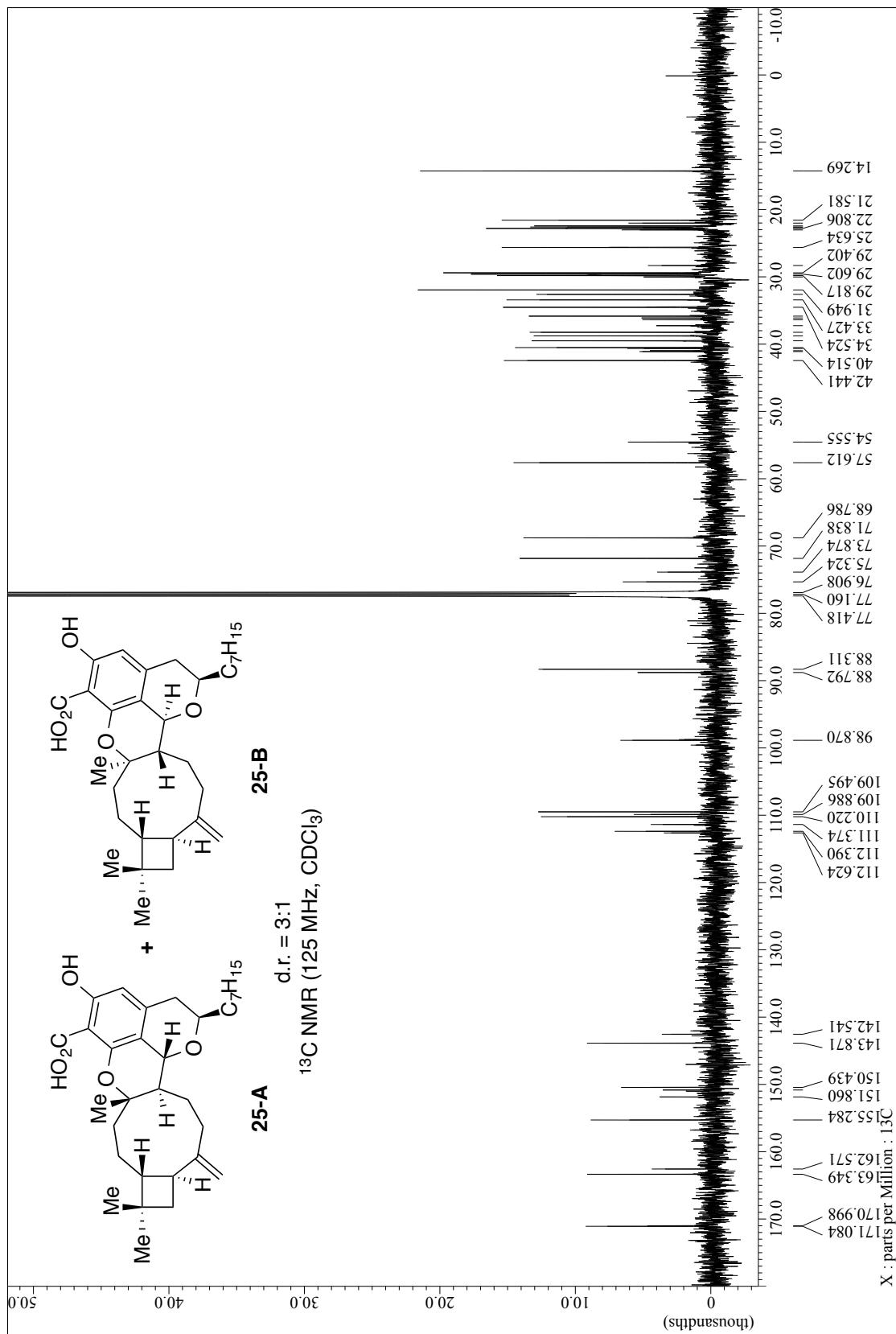


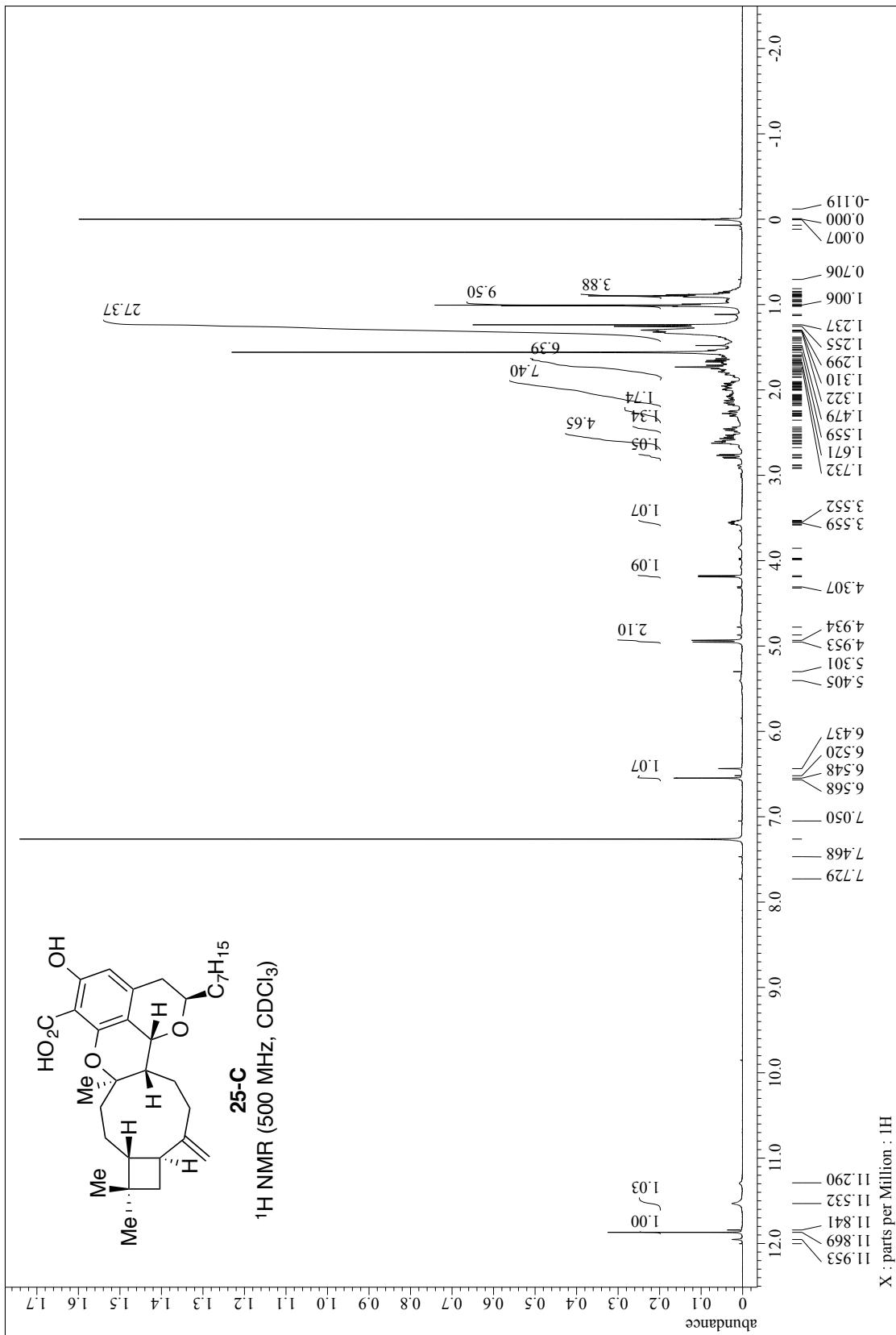


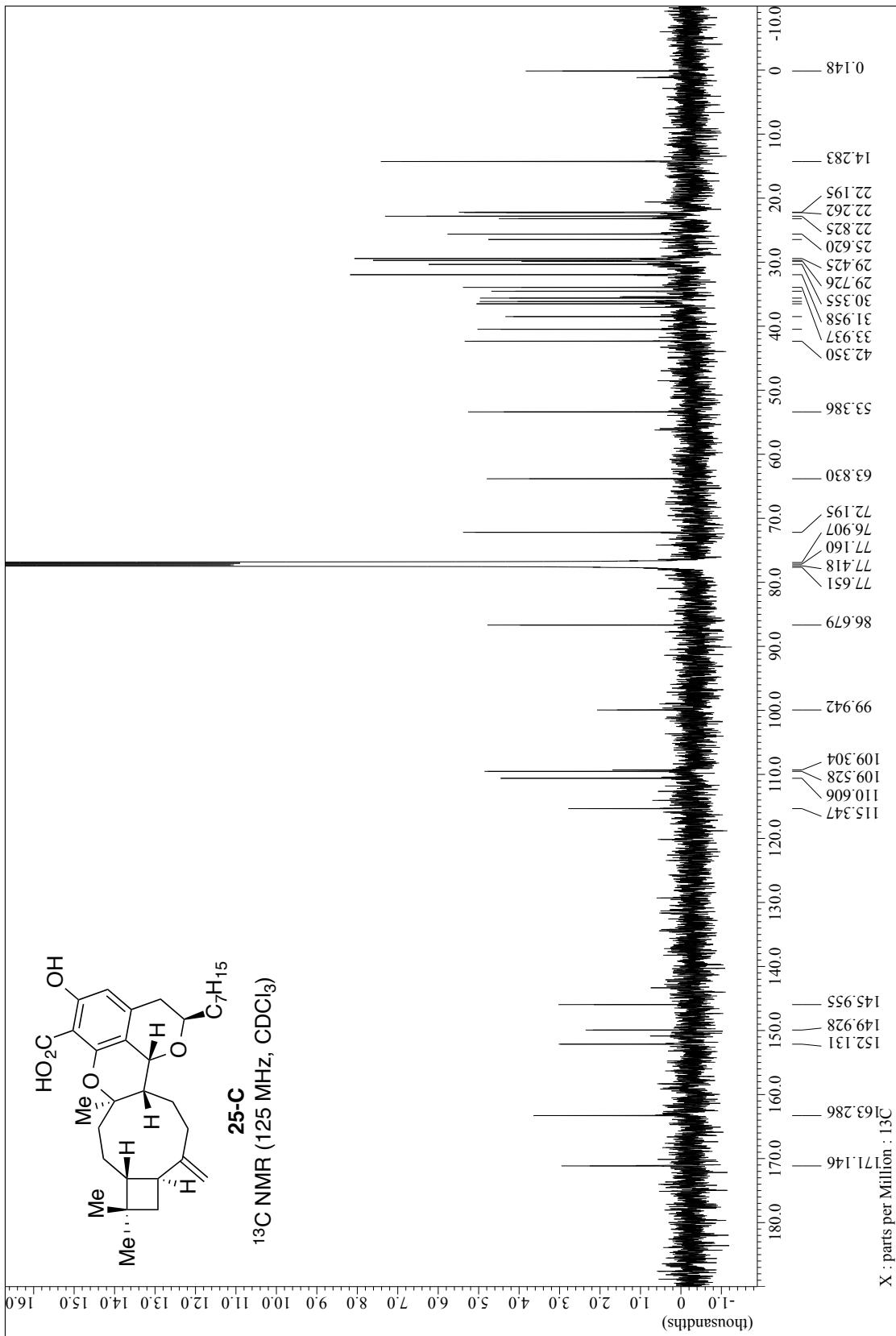


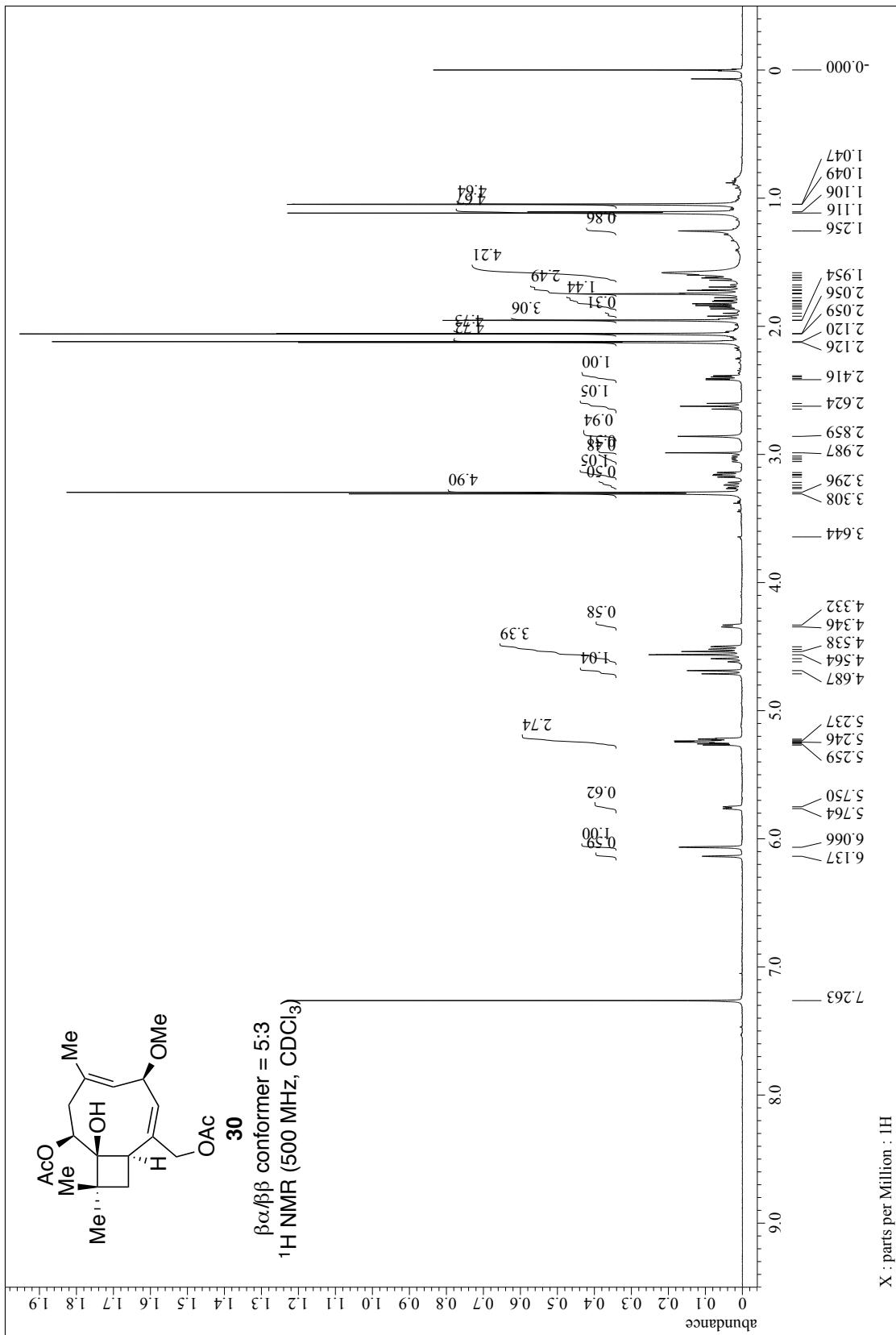


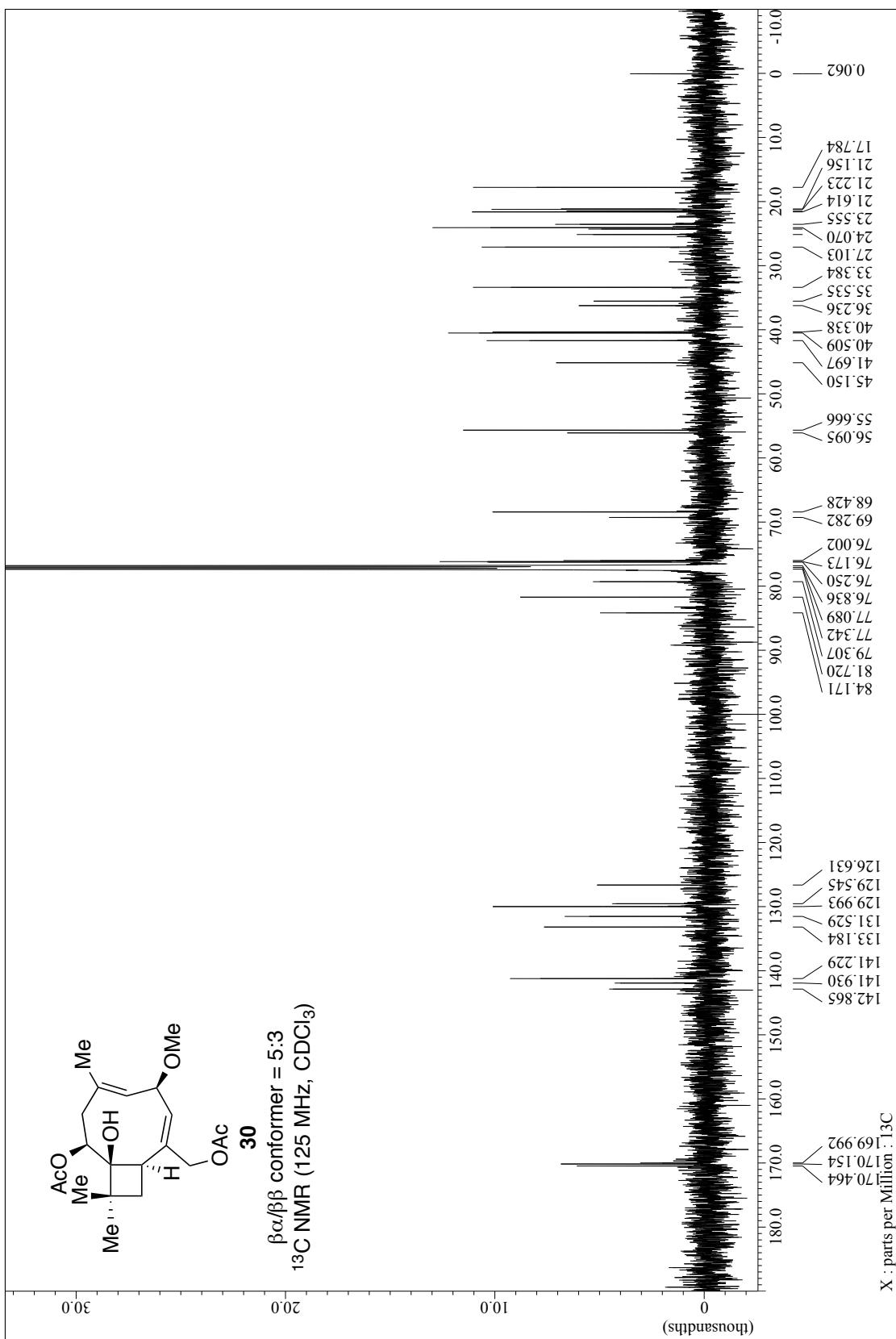


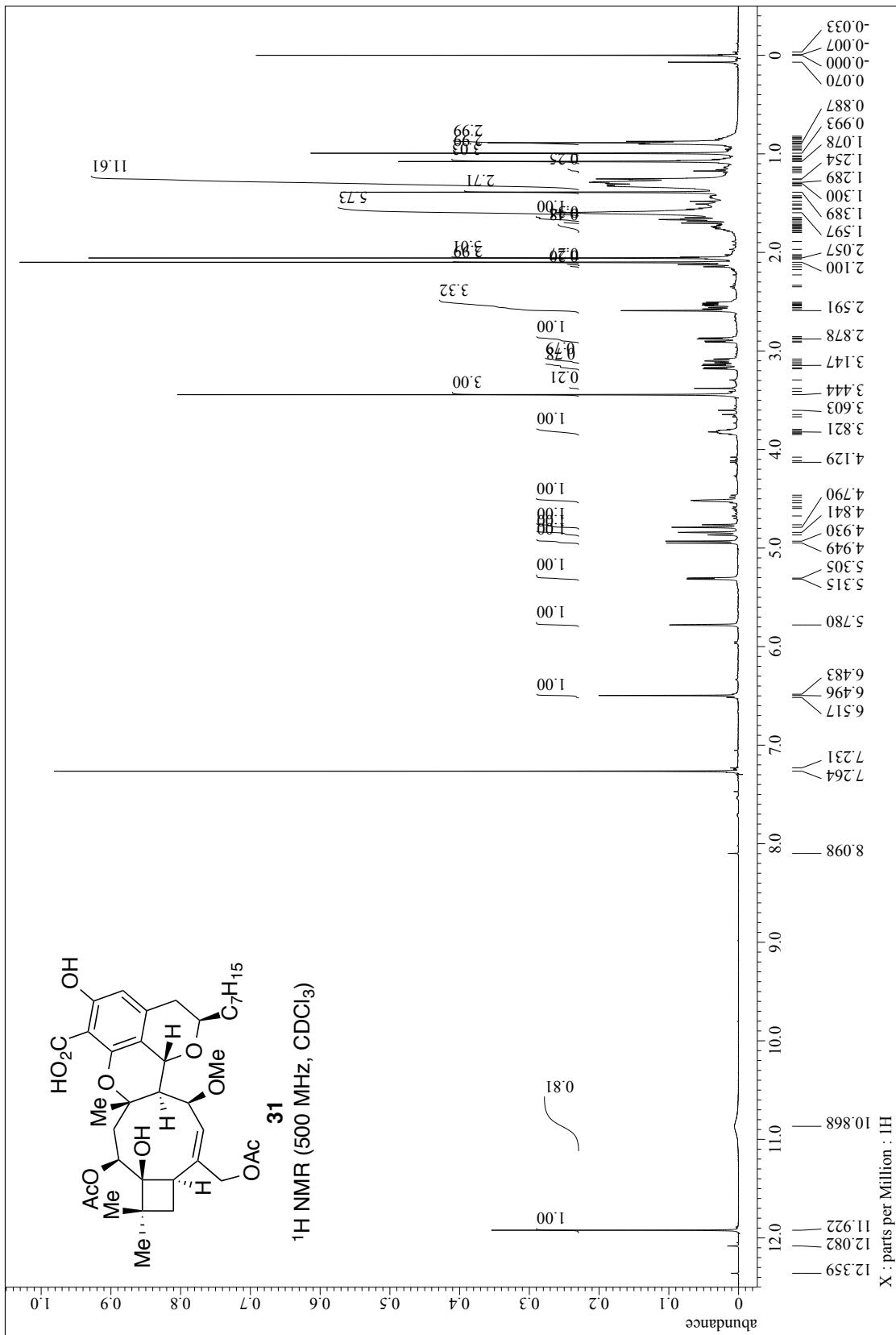


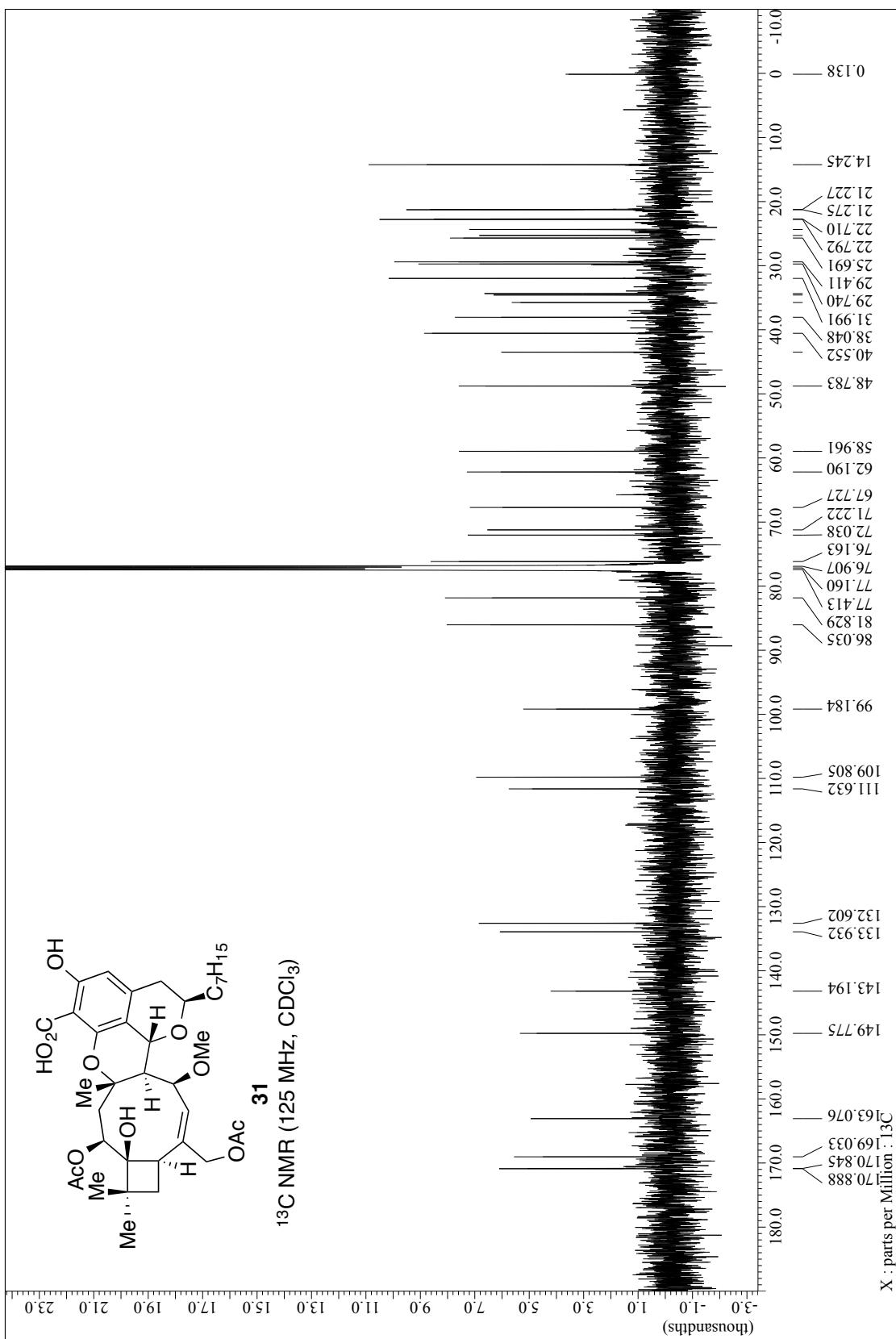


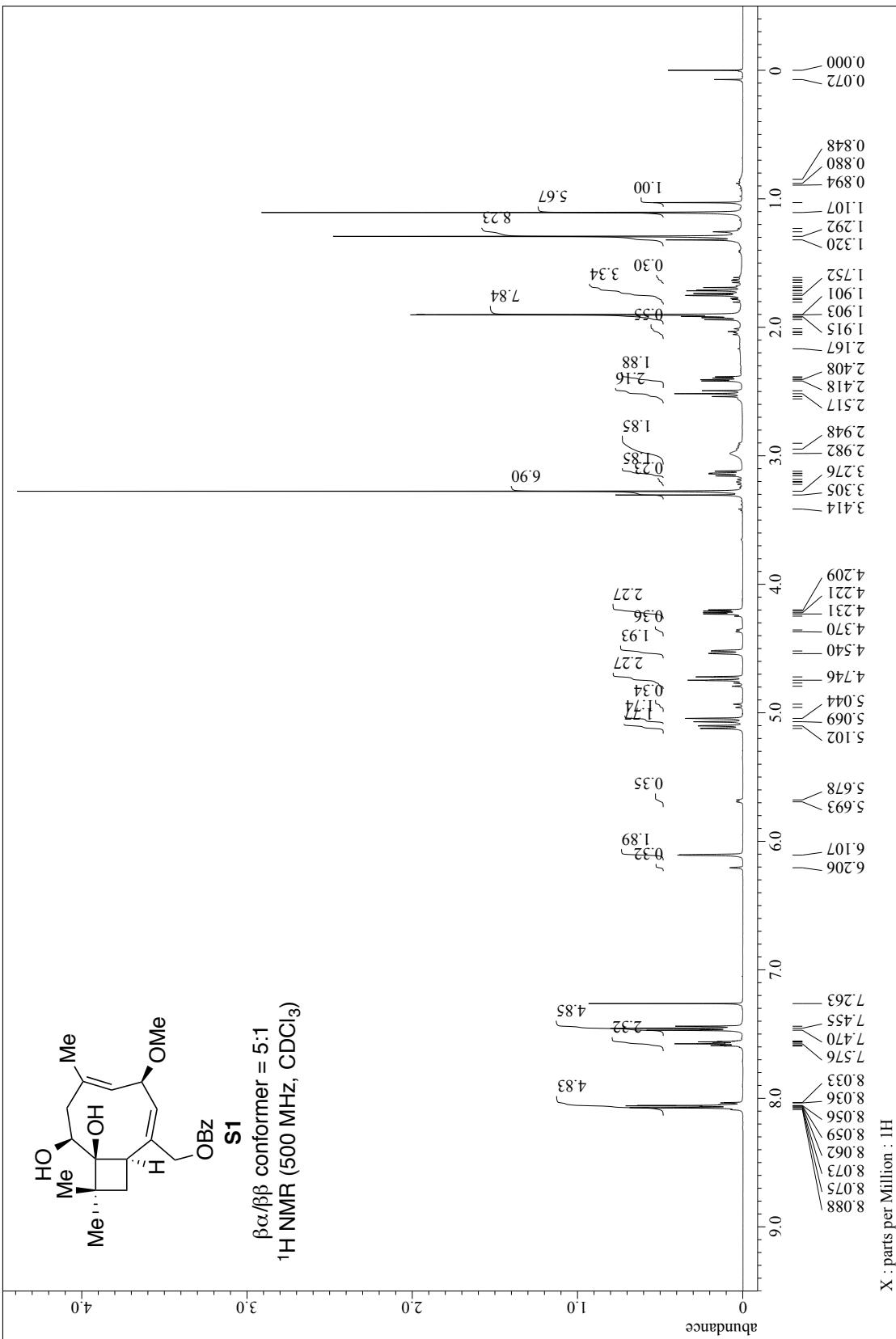


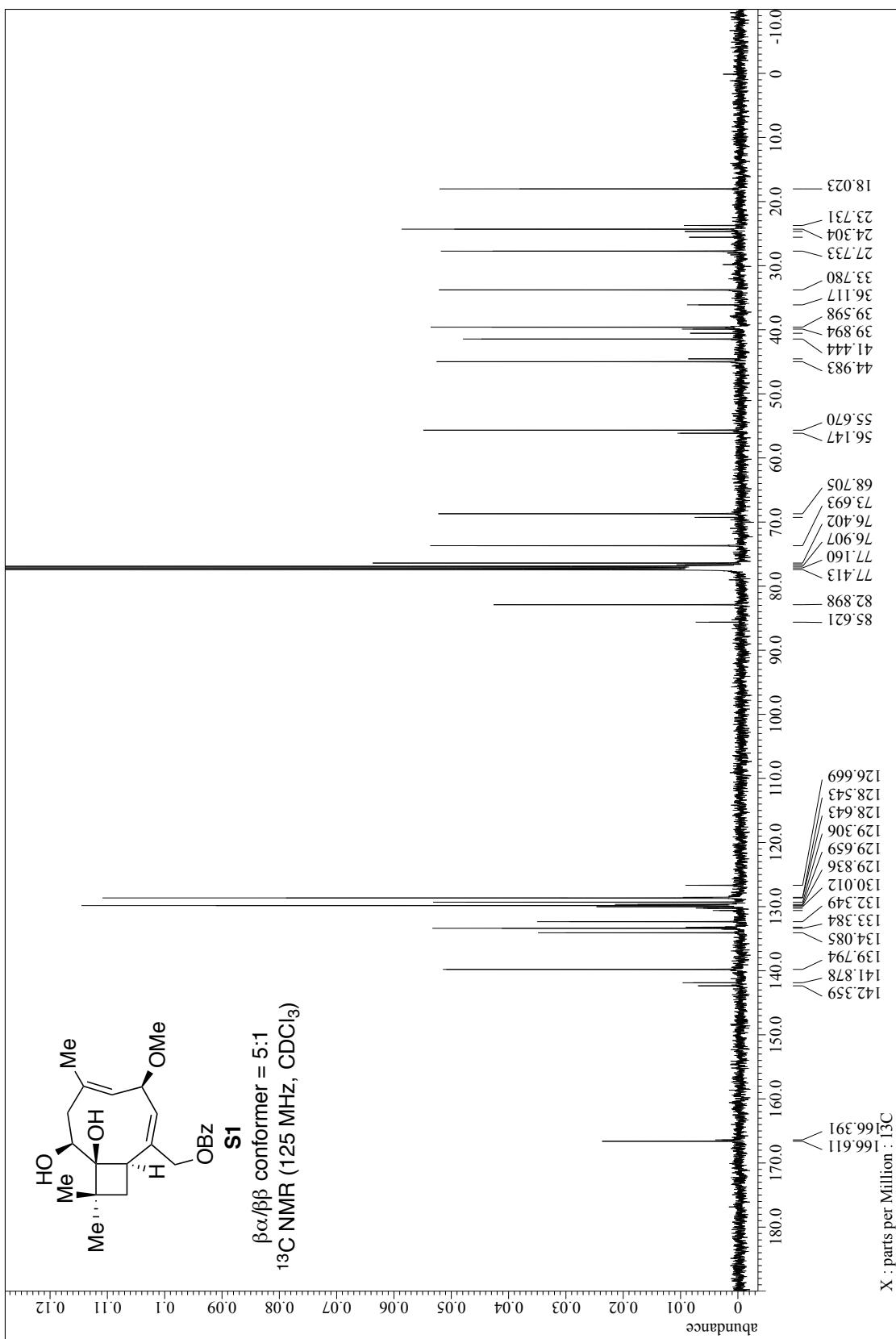


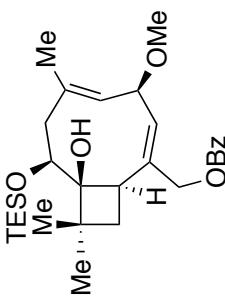
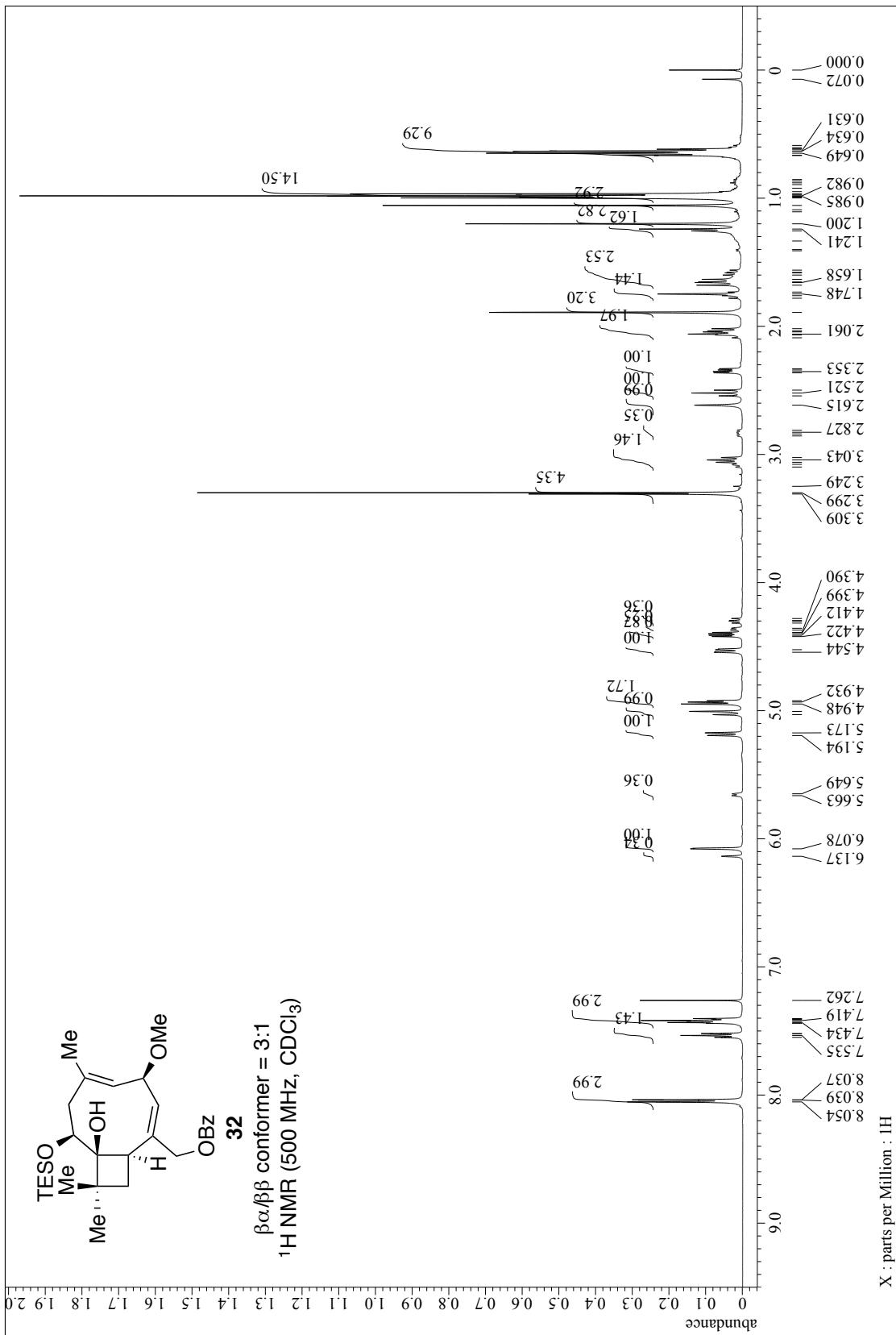












$\beta\alpha/\beta\beta$ conformer = 3:1
 ^1H NMR (500 MHz, CDCl_3)

