Mimicking Polyolefin Carbocyclization Reactions: Gold-Catalyzed Intramolecular Phenoxycyclization of 1,5-Enynes

Supporting Information

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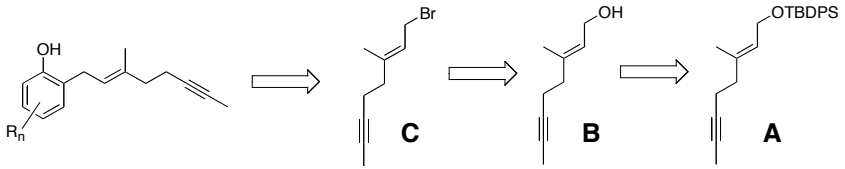
General information

PPh_3AuNTf_2.1/2 C_7H_8 was purchased from Aldrich. All manipulations were carried out under an argon atmosphere. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker AV 300 instrument. All signals were expressed as ppm (δ) and internally referenced to residual protio solvent signals. Coupling constants (J) are reported in Hz and refer to apparent peak multiplicities. Mass spectrometry analyses (direct introduction by chemical ionization with ammoniac or electrospray) were performed at the Ecole Nationale Supérieure de Chimie de Paris. High resolution mass spectra were performed at the Ecole Normale Supérieure (Paris) and University Pierre and Marie Curie (Paris).

Substrate synthesis

Enyne-substituted phenols **1a-j** were prepared in a three steps procedure starting from the known enyne[1] **A** according to the following retrosynthetic route:



(E)-3-methyloct-2-en-6-yn-1-ol B

Enyne **A** (3.58 mmol) was dissolved in anhydrous THF (20 mL) at room temperature and tetra-*n*-butylammonium fluoride (4.32 mmol, 1M in THF) was added. The reaction mixture was stirred for 1h at room temperature then quenched with water, extracted with ethyl acetate (3×30 mL), dried on $MgSO_4$, filtered and the volatiles removed under reduced pressure. Column chromatography (petroleum ether 30-60/ethyl acetate: 75/25) gave alcohol **B** as a yellow oil (79% yield).

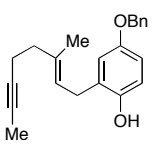
(E)-1-bromo-3-methyloct-2-en-6-yne C

Alcohol **B** (2.76 mmol) was dissolved in anhydrous Et_2O (20 mL) at 0°C and PBr_3 (3.31 mmol) was then added slowly. The reaction mixture was stirred at 0°C for 30 min then quenched with saturated aqueous $NaHCO_3$ (20 mL) and extracted with Et_2O (3×30 mL). The collected organic phases are washed with saturated aqueous $NaHCO_3$ (30 mL), water (30 mL), brine (30 mL) and dried on $MgSO_4$. The volatiles were removed under reduced pressure to give crude bromide **B** as a colorless oil (quantitative yield). The crude product was used for the next step without further purification.

General procedure for the phenol *ortho*-alkylation[2]

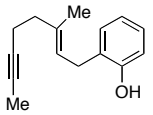
A phenol derivative was dissolved in anhydrous toluene at room temperature and NaH (1.1 equiv.) was added portionwise. After stirring for 15 min, allylic bromide **C** was added and the solution stirred for 2-5 h. The reaction mixture was then treated with 0.5 M HCl and extracted with di*iso*propylether. The organic layer was washed with sat. $NaHCO_3$, dried over $MgSO_4$ and the volatiles were removed under reduced pressure. The product was purified by column chromatography on silica gel using the solvent mixture indicated for TLC as the eluent.

(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4-benzyloxyphenol 1a



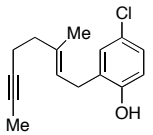
TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.18. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.74-1.76 (m, 6H), 2.21-2.29 (m, 4H), 3.34 (d, J = 7.1 Hz, 2H), 4.99 (s, 2H), 5.36 (dq, J = 7.2, 1.4 Hz, 1H), 6.72-6.78 (m, 3H), 7.30-7.44 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.9, 17.6, 30.0, 38.8, 70.7, 76.5, 78.4, 113.2, 116.6, 116.9, 122.6, 127.5, 127.8, 128.2, 128.5, 137.0, 137.4, 148.5, 152.9. CI-MS (NH_3) m/z 338 $[M+NH_4]^+$, 320 $[M+H]^+$. HRMS (CI-NH_3) calculated for $C_{22}H_{28}O_2N$: 338.2120; found: 338.2136.

(E)-2-(3'-methyloct-2'-en-6'-ynyl)-phenol 1b



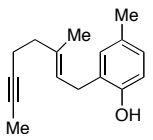
TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.31. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.77 (s, 6H), 2.20-2.34 (m, 4H), 3.39 (d, J = 7.2 Hz, 2H), 5.21 (br s, 1H), 5.40 (dq, J = 7.2, 1.2 Hz, 1H), 6.80-6.90 (m, 2H), 7.09-7.15 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.8, 17.6, 29.8, 38.8, 76.5, 78.4, 115.9, 120.8, 122.9, 126.9, 127.5, 129.9, 136.9, 154.4. CI-MS (NH_3) m/z 232 $[M+NH_4]^+$, 215 $[M+H]^+$. HRMS (ESI) calculated for $C_{16}H_{20}O_2Na$: 253.1199; found: 253.1198.

(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4-chlorophenol 1c



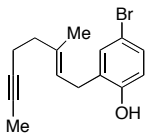
TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.24. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.77 (t, J = 2.4 Hz, 3H), 1.78 (s, 3H), 2.22-2.33 (m, 4H), 3.34 (d, J = 7.2 Hz, 2H), 5.23 (br s, 1H), 5.35 (tq, J = 7.2, 1.3 Hz, 1H), 6.73 (d, J = 8.4 Hz, 1H), 7.03-7.10 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.9, 17.5, 29.6, 38.7, 76.7, 78.2, 117.2, 121.9, 125.4, 127.2, 128.7, 129.6, 137.8, 153.0. CI-MS (NH_3) m/z 266 $[M+NH_4]^+$, 249 $[M+H]^+$.

(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4-methylphenol 1d



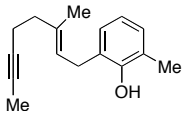
TLC (cyclohexane/ethyl acetate: 95/5) R_f = 0.15. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.76 (s, 3H), 1.77 (s, 3H), 2.20-2.31 (m, 7H), 3.35 (d, J = 7.2 Hz, 2H), 5.01 (br s, 1H), 5.38 (tq, J = 7.2, 1.2 Hz, 1H), 6.71 (dd, J = 6.6, 1.8 Hz, 1H), 6.90-6.93 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.9, 17.6, 20.5, 29.9, 38.8, 78.4, 115.9, 123.0, 126.6, 127.9, 129.9, 130.5, 136.7, 152.2. ESI-MS m/z 227 $[M-H]^-$. HRMS calculated for $C_{16}H_{20}O_2Na$: 267.1356; found: 267, 1352.

(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4-bromophenol 1e



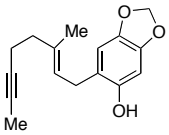
TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.25. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.76 (s, 3H), 1.77 (s, 3H), 2.19-2.33 (m, 4H), 3.34 (d, J = 7.2 Hz, 2H), 5.18 (br s, 1H), 5.35 (tq, J = 7.2, 1.3 Hz, 1H), 6.69 (d, J = 8.3 Hz, 1H), 7.18-7.24 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.5, 15.9, 17.5, 29.6, 38.7, 76.6, 78.2, 112.7, 117.7, 121.9, 129.2, 130.2, 132.5, 137.8, 153.6. CI-MS (NH_3) m/z 310 $[M(^{79}Br)+NH_4]^+$, 293 $[M(^{79}Br)+H]^+$. HRMS calculated for $C_{15}H_{17}O^{81}Br$: 294.0444; found: 294.0453.

(E)-2-(3'-methyloct-2'-en-6'-ynyl)-6-methylphenol 1f



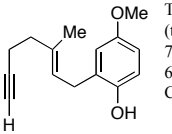
TLC (cyclohexane/ethyl acetate: 95/5) R_f = 0.30. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.78 (t, J = 2.4 Hz, 3H), 1.80 (d, J = 1.2 Hz,, 3H), 2.23-2.33 (m, 7H), 3.38 (d, J = 7.2 Hz, 2H), 5.24 (s, 1H), 5.40 (tq, J = 7.2, 1.2 Hz, 1H), 6.77 (t, J = 7.4 Hz, 2H), 6.99 (t, J = 8.1 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.8, 15.9, 17.5, 30.4, 38.8, 76.5, 78.2, 120.2, 123.1, 124.5, 126.1, 127.6, 129.1, 137.2, 152.9. CI-MS (NH_3) m/z 246 $[M+NH_4]^+$, 229 $[M+H]^+$. HRMS calculated for $C_{16}H_{21}O$: 229.1592; found: 229.1588.

(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4,5-(methylenedioxy)phenol 1g



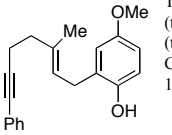
TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.22. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.76 (d, J = 1.0 Hz,, 3H), 1.78 (t, J = 2.4 Hz, 3H), 2.18-2.31 (m, 4H), 3.27 (d, J = 7.2 Hz, 2H), 4.89 (br s, 1H), 5.33 (tq, J = 7.2, 1.2 Hz, 1H), 5.87 (s, 2H), 6.42 (s, 1H), 6.62 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.7, 17.5, 29.6, 38.8, 67.2, 78.3, 98.8, 100.9, 109.2, 118.6, 123.0, 137.0, 141.3, 146.4, 148.9. CI-MS (NH_3) m/z 276 $[M+NH_4]^+$, 259 $[M+H]^+$. HRMS (EI) calculated for $C_{16}H_{18}O_3N$: 258.1256; found: 258.1254.

(E)-2-(3'-methylhept-2'-en-6'-ynyl)-4-methoxyphenol 1h



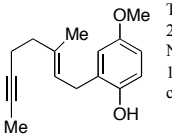
TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.19. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.58 (s, 3H), 1.99 (t, J = 2.5 Hz, 1H), 2.20-2.38 (m, 4H), 3.35 (d, J = 7.2 Hz, 2H), 3.75 (s, 3H), 4.95 (br s, 1H), 5.40 (t, J = 7.2 Hz, 1H), 6.62-6.75 (m, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 15.9, 17.3, 29.3, 29.6, 38.2, 55.7, 69.0, 83.9, 112.0, 115.8, 116.4, 123.0, 128.1, 136.2, 148.1, 153.7. HRMS (ESI) calculated for $C_{15}H_{18}O_2Na$: 253.1199; found: 253.1197.

(E)-2-(3'-methyl-7'-phenylhept-2'-en-6'-ynyl)-4-methoxyphenol 1i



TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.11. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.82 (s, 3H), 2.36 (t, J = 7.2 Hz, 2H), 2.56 (t, J = 7.2 Hz, 2H), 3.37 (d, J = 7.2 Hz, 2H), 3.73 (s, 3H), 4.76 (br s, 1H), 5.46 (t, J = 7.2 Hz, 1H), 6.62-6.71 (m, 3H), 7.23-7.29 (m, 3H), 7.34-7.39 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.1, 18.5, 28.0, 29.8, 38.5, 55.7, 81.3, 89.5, 112.0, 115.6, 116.4, 123.0, 123.8, 127.5, 128.1, 131.6 136.5, 148.1, 153.7. HRMS (ESI) calculated for $C_{21}H_{22}O_2Na$: 329.1512; found: 329.1512.

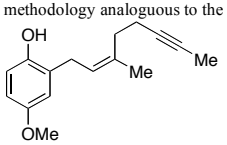
(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4-methoxyphenol (E)-1j



TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.18. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.28 (s, 6H), 2.17-2.32 (m, 4H), 3.35 (d, J = 7.2 Hz, 2H), 3.75 (s, 3H), 5.37 (t, J = 7.2 Hz, 1H), 6.63-6.76 (m, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.9, 17.3, 17.6, 30.1, 38.8, 55.7, 76.6, 78.3, 112.0, 115.8, 116.6, 122.7, 128.1, 137.0, 148.3, 153.7. CI-MS (NH_3) m/z 262 $[M+NH_4]^+$, 245 $[M+H]^+$. HRMS (CI-NH_3) calculated for $C_{16}H_{21}O_2$: 245.1542; found: 245.1537.

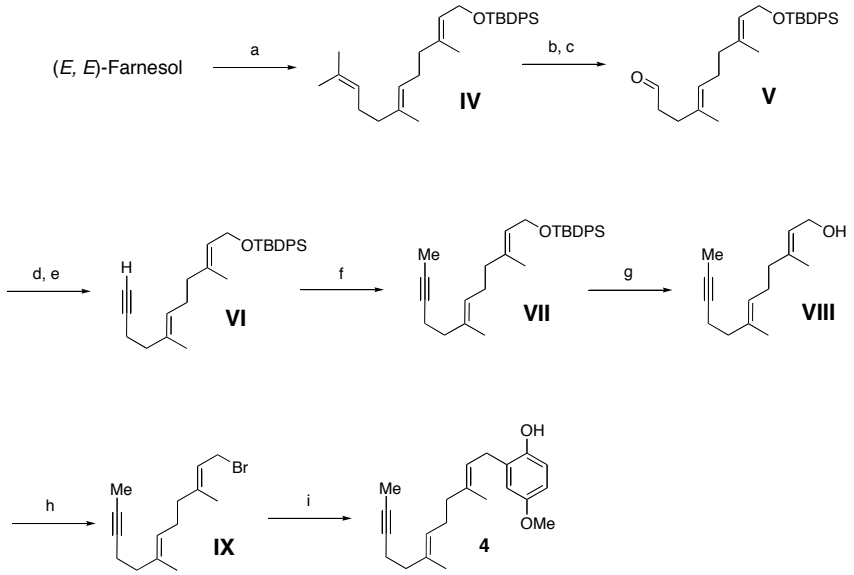
(Z)-2-(3'-methyloct-2'-en-6'-ynyl)-4-methoxyphenol (*Z*)-1j

(Z)-1-bromo-3-methyloct-2-en-6-yne used in this synthesis has been prepared in a 8 steps sequence starting from nerol by a methodology analoguous to the one used for **C**.



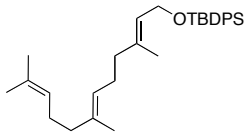
TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.17. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.75-1.78 (m, 6H), 2.25-2.40 (m, 4H), 3.37 (d, J = 7.1 Hz, 2H), 3.75 (s, 3H), 4.81 (br s, 1H), 5.36 (t, J = 7.1 Hz, 1H), 6.62-6.75 (m, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.5, 17.3, 23.1, 29.6, 31.2, 55.7, 76.2, 78.6, 112.0, 115.8, 116.2, 123.6, 128.1, 136.8, 148.1, 153.6. HRMS (CI-NH_3) calculated for $C_{16}H_{20}O_2Na$: 267.1356; found: 267.1354.

Enyne-substituted phenol **4** was prepared in a 9 steps procedure starting from commercially available (*E*, *E*)-farnesol according to the following route:



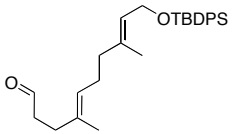
Reaction conditions : a) *tert*-BuPh_2SiCl, imidazole, DMF, 0°C to RT, 99%. b) *m*-CPBA, $CHCl_3$, 0°C; c) H_5IO_6, 0°C, Et_2O/THF, 25% over two steps d) CBr_4, PPh_3, Zn, CH_2Cl_2, 0°C to RT; e) *n*-BuLi, Et_2O, 0°C, 87% over two steps. f) *n*-BuLi, excess CH_3I, THF, -78°C to RT, 97%. g) *n*-Bu_4NF, THF, RT, 84%. h) PBr_3, Et_2O, 0°C, 97%. i) 4-methoxyphenol, NaH, toluene, RT, 61%.

***tert*-Butyl-diphenyl-(3,7,11-trimethyl-dodeca-2,6,10-trienyloxy)-silane IV**



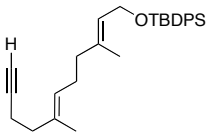
^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.05 (s, 9H), 1.44 (s, 3H), 1.60 (s, 6H), 1.68 (s, 3H), 1.95-2.08 (m, 8H), 4.22 (d, J = 6.3 Hz, 2H), 5.08-5.13 (m, 2H), 5.38 (t, J = 6.3 Hz, 1H), 7.34-7.42 (m, 6H), 7.67-7.72 (m, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.0, 16.3, 17.7, 19.2, 25.7, 26.3, 26.7, 26.8, 39.5, 39.7, 61.2, 124.0, 124.4, 126.6, 127.7, 129.5, 134.1, 134.8, 135.1, 135.6, 137.1. HRMS (ESI) calculated for $C_{31}H_{44}ONaSi$: 483.3054; found: 483.3048.

10-(*tert*-Butyl-diphenyl-silanyloxy)-4,8-dimethyl-deca-4,8-dienal V



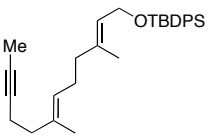
TLC (cyclohexane/ethyl acetate: 90/10) R_f = 0.57. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.04 (s, 9H), 1.43 (s, 3H), 1.61 (s, 3H), 1.96-2.10 (m, 4H), 2.28-2.33 (m, 2H), 2.47-2.53 (m, 2H), 4.22 (d, J = 6.3 Hz, 2H), 5.14 (t, J = 7.0 Hz, 1H), 5.37 (t, J = 6.3 Hz, 1H), 7.34-7.42 (m, 6H), 7.67-7.71 (m, 4H), 9.73 (t, J = 1.9 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.8, 16.9, 26.8, 27.5, 32.4, 39.9, 42.8, 61.8, 124.9, 125.8, 128.2, 130.1, 133.8, 134.7, 136.2, 137.4, 203.3. HRMS (ESI) calculated for $C_{29}H_{42}O_3NaSi$: 489.2795; found: 489.2791.

***tert*-Butyl-(3,7-dimethyl-undeca-2,6-dien-10-ynyloxy)-diphenyl-silane VI**



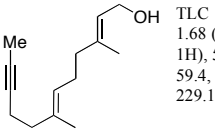
TLC (cyclohexane/ethyl acetate: 98/2) R_f = 0.59. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.04 (s, 9H), 1.43 (s, 3H), 1.61 (s, 3H), 1.94 (t, J = 2.3 Hz, 1H), 1.98-2.10 (m, 4H), 2.17-2.28 (m, 4H), 4.22 (d, J = 6.3 Hz, 2H), 5.18 (t, J = 5.5 Hz, 1H), 5.37 (t, J = 5.6 Hz, 1H), 7.35-7.42 (m, 6H), 7.67-7.71 (m, 4H). HRMS (ESI) calculated for $C_{29}H_{38}O_3NaSi$: 485.2482; found: 485.2476.

tert-Butyl-(3,7-dimethyl-dodeca-2,6-dien-10-ynyloxy)-diphenyl-silane VII



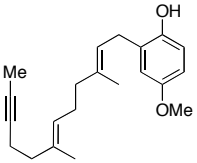
TLC (cyclohexane/ethyl acetate: 98/2) R_f = 0.70. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.04 (s, 9H), 1.43 (s, 3H), 1.60 (s, 3H), 1.77 (t, J = 2.2 Hz, 3H), 1.98-2.22 (m, 8H), 4.22 (d, J = 6.2 Hz, 2H), 5.15 (t, J = 6.2 Hz, 1H), 5.38 (t, J = 6.3 Hz, 1H), 7.34-7.42 (m, 6H), 7.67-7.71 (m, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.5, 15.8, 16.3, 18.0, 19.2, 26.3, 26.8, 39.1, 39.4, 61.1, 75.7, 79.1, 124.1, 125.0, 127.6, 129.5, 134.1, 135.6, 136.9. HRMS (ESI) calculated for $C_{29}H_{38}O_3NaSi$: 485.2482; found: 485.2476.

3,7-Dimethyl-dodeca-2,6-dien-10-yn-1-ol VIII



TLC (cyclohexane/ethyl acetate: 80/20) R_f = 0.31. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.60 (s, 3H), 1.68 (s, 3H), 1.77 (t, J = 2.2 Hz, 3H), 2.02-2.23 (m, 8H), 4.14 (d, J = 6.9 Hz, 2H), 5.15 (t, J = 6.1 Hz, 1H), 5.41 (t, J = 6.1 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.8, 16.2, 18.0, 26.2, 39.0, 39.4, 59.4, 75.6, 79.1, 123.4, 124.7, 134.1, 139.6. HRMS (ESI) calculated for $C_{14}H_{22}ONa$: 229.1563; found: 229.1561.

2-(3,7-Dimethyl-dodeca-2,6-dien-10-ynyl)-4-methoxy-phenol 4

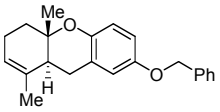


TLC (cyclohexane/ethyl acetate: 98/2) R_f = 0.27. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.59 (s, 3H), 1.76 (s, 6H), 2.06-2.22 (m, 8H), 3.32 (d, J = 7.2 Hz, 2H), 3.75 (s, 3H), 4.75 (br s, 1H), 5.13 (t, J = 5.8 Hz, 1H), 5.30 (t, J = 6.0 Hz, 1H), 6.63-6.76 (m, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 3.4, 15.9, 16.2, 17.9, 26.4, 29.9, 39.0, 39.6, 55.7, 75.6, 79.1, 112.0, 115.7, 116.3, 121.5, 124.6, 128.0, 134.3, 138.4, 148.3, 153.7. HRMS calculated for $C_{21}H_{28}O_3Na$: 351.1931; found: 351.1928.

Cyclization reaction

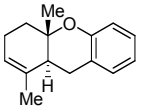
In a typical experiment, enyne **1** (0.15 mmol) was placed in a Shlenk tube under Ar and distilled Et_2O (0.5 M) was added. PPh_3AuNTf_2.1/2 C_7H_8 (0.0015 mmol) was added and the reaction mixture was stirred at room temperature until completion of the reaction. The crude reaction mixture was then filtered on a pad of silica using 20 mL AcOEt and the solvents removed under reduced pressure. The product was purified by column chromatography on silica gel using the solvent mixture indicated for TLC as the eluent.

7-Benzyloxy-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2a



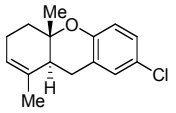
TLC (cyclohexane/ethyl acetate: 99/1) R_f = 0.13. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.12 (s, 3H), 1.74 (s, 3H), 1.81-1.97 (m, 2H), 2.15-2.22 (m, 2H), 2.85 (q, J = 10.6 Hz, 1H), 5.02 (s, 2H), 5.41 (br s, 2H), 6.75-6.83 (m, 3H), 7.33-7.46 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.4, 19.9, 24.1, 26.3, 35.5, 41.9, 70.7, 75.8, 114.7, 115.6, 117.8, 121.6, 123.0, 127.5, 127.8, 128.5, 133.5, 137.5, 147.9, 152.3. CI-MS (NH_3) m/z 338 $[M+NH_4]^+$. HRMS (ESI) calculated for $C_{22}H_{24}O_2Na$: 343.1669; found: 343.1667.

1,4a-Dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2b



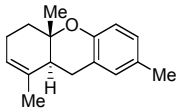
TLC (cyclohexane/ethyl acetate: 99/1) R_f = 0.31. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.13 (s, 3H), 1.75 (s, 3H), 1.80-1.98 (m, 2H), 2.19-2.23 (m, 2H), 2.50-2.64 (m, 2H), 2.89 (q, J = 10.7 Hz, 1H), 5.41 (br s, 1H), 6.81-6.88 (m, 2H), 7.09-7.16 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.6, 19.9, 22.0, 24.1, 25.9, 35.5, 36.8, 41.9, 76.0, 117.4, 119.7, 121.5, 122.5, 127.5, 129.9, 133.6, 153.7. CI-MS (NH_3) m/z 215 $[M+H]^+$. HRMS (ESI) calculated for $C_{15}H_{18}O_2Na$: 253.1199; found: 253.1198.

7-Chloro-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2c



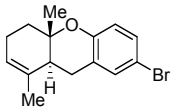
TLC (cyclohexane/ethyl acetate: 99/1) R_f = 0.36. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.09 (s, 3H), 1.72 (s, 3H), 1.83 (ddd, J = 17.3, 8.7, 5.6 Hz, 1H), 1.93 (dd, J = 9.1, 4.1, 1.7 Hz, 1H), 2.15-2.25 (m, 2H), 2.45-2.54 (m, 2H), 3.63 (q, J = 8.2 Hz, 1H), 5.40 (br s, 1H), 6.75 (d, J = 6.3 Hz, 1H), 7.04-7.07 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.5, 19.8, 24.0, 25.8, 30.3, 35.3, 41.6, 76.6, 118.7, 121.8, 124.1, 124.5, 127.6, 129.5, 133.2, 152.4. CI-MS (NH_3) m/z 248 $[M(^{35}Cl)]^+$. HRMS (CI-CH_4) calculated for $C_{15}H_{18}O^{35}Cl$: 249.1046; found: 249.1044.

1,4a,7-Trimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2d



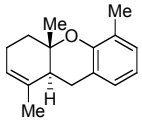
TLC (cyclohexane/ethyl acetate: 99/1) R_f = 0.20. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.11 (s, 3H), 1.73 (s, 3H), 1.79-1.96 (m, 2H), 2.14-2.24 (m, 2H), 2.27 (s, 3H), 2.44-2.55 (m; 2H), 2.84 (q, J = 10.5 Hz, 1H), 5.39 (br s, 1H), 6.73 (d, J = 8.4 Hz, 1H), 6.83-6.86 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.5, 19.9, 20.5, 24.1, 25.9, 35.5, 42.0, 75.9, 117.1, 121.5, 122.1, 128.1, 128.8, 130.2, 133.6, 151.4. CI-MS (NH_3) m/z 246 $[M+NH_4]^+$, 229 $[M+H]^+$. HRMS (ESI) calculated for $C_{16}H_{20}O_2Na$: 267.1356; found: 267, 1353.

7-Bromo-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2e



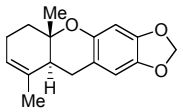
TLC (cyclohexane/ethyl acetate: 98/2) R_f = 0.55. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.09 (s, 3H), 1.71 (s, 3H), 1.73-1.95 (m, 2H), 2.15-2.20 (m, 2H), 2.42-2.55 (m; 2H), 2.84 (q, J = 10.7 Hz, 1H), 5.40 (s, 1H), 6.70 (d, J = 8.5 Hz, 1H), 7.17-7.22 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.5, 19.8, 24.0, 25.8, 35.3, 41.6, 76.5, 111.7, 119.2, 121.7, 124.6, 130.3, 132.3, 133.1, 152.8. CI-MS (NH_3) m/z 294 $[M(^{81}Br)^{\bullet}]^+$. HRMS (EI) calculated for $C_{15}H_{17}O^{79}Br$: 292.0463; found: 292.0466.

1,4a,5-Trimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2f



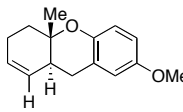
TLC (cyclohexane/ethyl acetate: 99/1) R_f = 0.69. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.08 (s, 3H), 1.72 (s, 3H), 1.78-1.98 (m, 2H), 2.18-2.23 (m, 7H), 2.46-2.58 (m; 2H), 2.86 (q, J = 10.6 Hz, 1H), 5.39 (s, 1H), 6.74 (t, J = 7.4 Hz, 2H), 6.96 (dd, J = 11.0, 7.3 Hz, 1H), ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.1, 16.8, 19.9, 24.1, 26.0, 35.5, 41.9, 75.7, 119.0, 121.4, 121.8, 126.4, 127.3, 128.4, 133.8, 151.9. CI-MS (NH_3) m/z 229 $[M+H]^+$. HRMS (CI-NH_3) calculated for $C_{16}H_{21}O$: 229.1592; found: 229.1591.

6,7-(Methylenedioxy)-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2g



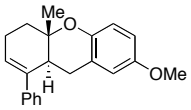
TLC (cyclohexane/ethyl acetate: 99/1) R_f = 0.12. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.08 (s, 3H), 1.71 (s, 3H), 1.75-1.95 (m, 2H), 2.14-2.21 (m, 2H), 2.36-2.52 (m; 2H), 3.00 (q, J = 9.3 Hz, 1H), 5.38 (s, 1H), 5.85 (d, J = 1.5 Hz, 1H), 5.87 (d, J = 1.5 Hz, 1H), 6.37 (s, 1H), 6.54 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.2, 19.8, 24.1, 26.1, 35.4, 41.9, 75.9, 99.0, 100.7, 108.4, 113.7, 121.5, 133.5, 141.0, 146.6, 148.1. CI-MS (NH_3) m/z 259 $[M+H]^+$. HRMS (CI-NH_3) calculated for $C_{16}H_{19}O_3$: 259.1334; found: 259.1335.

7-Methoxy-4a-methyl-4,4a,9,9a-tetrahydro-3H-xanthene 2h



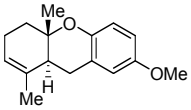
TLC (cyclohexane/ethyl acetate: 98/2) R_f = 0.24. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.09 (s, 3H), 1.80-1.98 (m, 2H), 2.20-2.31 (m, 2H), 2.45-2.58 (m, 2H), 2.69 (dd, J = 12.5, 2.3 Hz, 1H), 3.75 (s, 3H), 5.47 (d, J = 9.8 Hz, 1H), 5.64-5.70 (m, 1H), 6.63 (d, J = 2.9 Hz, 1H), 6.70 (dd, J = 8.9, 2.9 Hz, 1H), 6.76 (d, J = 8.9 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 22.0, 23.4, 25.8, 28.7, 30.6, 41.8, 55.7, 75.8, 113.3, 113.6, 116.9, 121.1, 121.2, 134.9, 147.9, 152.8. HRMS (ESI) calculated for $C_{15}H_{20}O_3Na$: 271.1305; found: 271.1304.

7-Methoxy-4a-methyl-1-phenyl-4,4a,9,9a-tetrahydro-3H-xanthene 2i



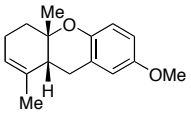
TLC (cyclohexane/ethyl acetate: 98/2) R_f = 0.30. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.19 (s, 3H), 1.97-2.06 (m, 2H), 2.22 (dd, *J* = 16.6, 13.8 Hz, 1H), 2.36-2.44 (m, 2H), 2.70 (dd, *J* = 16.6, 5.2 Hz, 1H), 3.00-3.11 (m, 1H), 3.70 (s, 3H), 5.71-5.75 (m, 1H), 6.52 (d, *J* = 2.8 Hz, 1H), 6.65-6.80 (m, 2H), 7.20-7.37 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 16.4, 24.6, 27.2, 35.1, 40.5, 55.6, 75.9, 113.8, 114.1, 117.8, 123.2, 126.0, 126.8, 127.4, 128.0, 139.8, 141.2, 147.4, 153.0. HRMS (ESI) calculated for $C_{21}H_{22}O_2Na$: 329.1512; found: 329.1510.

7-Methoxy-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene (*trans*)-2j



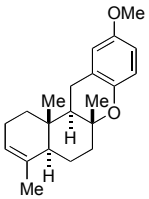
TLC (cyclohexane/ethyl acetate: 98/2) R_f = 0.13. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.09 (s, 3H), 1.70 (s, 3H), 1.80-1.95 (m, 2H), 2.17-2.22 (m, 2H), 2.43-2.55 (m, 2H), 2.85 (q, *J* = 10.8 Hz, 1H), 3.76 (s, 3H), 5.39 (br s, 1H), 6.64-6.77 (m, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 15.3, 18.9, 23.1, 25.3, 34.5, 40.9, 54.7, 74.8, 112.6, 113.4, 116.8, 120.6, 122.0, 132.5, 146.6, 151.9. CI-MS (NH_3) m/z 245 $[M+H]^+$. HRMS (CI-CH_4) calculated for $C_{16}H_{21}O_2$: 245.1542; found: 245.1543.

7-Methoxy-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene (*cis*)-2j



TLC (cyclohexane/ethyl acetate: 98/2) R_f = 0.24. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 1.10 (s, 3H), 1.54-1.63 (m, 1H), 1.72 (s, 3H) 1.83-1.92 (m, 1H), 1.98-2.18 (m, 3H), 2.61 (dd, *J* = 16.5, 8.4 Hz, 1H), 3.00 (dd, *J* = 16.5, 5.7 Hz, 1H), 3.74 (s, 3H), 5.35 (br s, 1H), 6.58 (d, *J* = 2.8 Hz, 1H), 6.65-6.74 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) : δ = 22.0, 23.4, 25.8, 28.7, 30.6, 41.8, 55.7, 75.8, 113.3, 113.6, 116.9, 121.1, 121.2, 134.9, 147.9, 152.8. HRMS (ESI) calculated for $C_{16}H_{20}O_2Na$: 267.1355; found: 267.1356.

7-Methoxy-4,6a,12b-trimethyl-1,4a,5,6,6a,12,12a,12b-octahydro-2H-benzo[a]xanthene 5



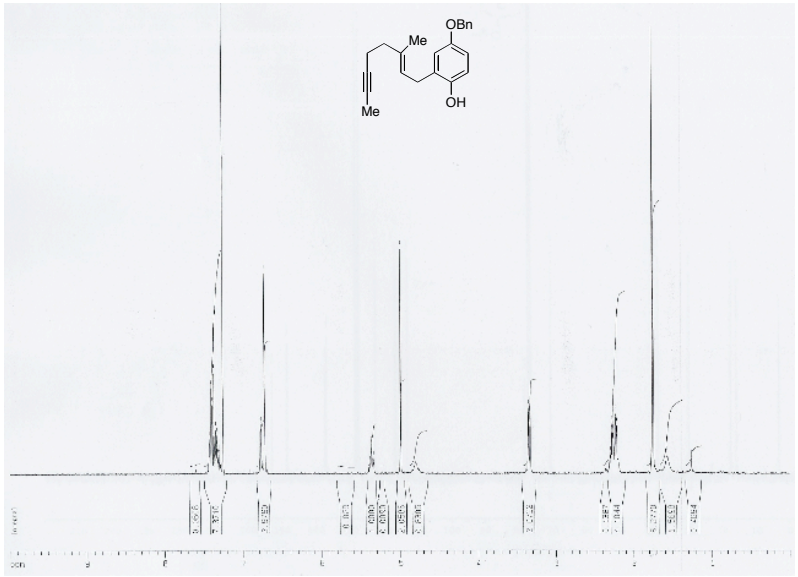
TLC (cyclohexane/ethyl acetate: 99/1) R_f = 0.55. ^{1}H-NMR (300 MHz, $CDCl_3$) : δ = 0.80 (s, 3H), 1.21-1.32 (m, 5H), 1.60-1.82 (m, 9H), 2.03-2.11 (m, 2H), 2.58-2.78 (m, 2H), 3.75 (s, 3H), 5.32 (s, 1H), 6.61-6.72 (m, 3H). ^{13}C-NMR (75 MHz, C_6D_6) : δ = 11.6, 21.3, 21.7, 22.9, 23.4, 35.0, 35.3, 40.8, 48.7, 49.6, 55.2, 76.3, 113.3, 114.9, 118.0, 120.6, 123.1, 134.2, 148.0, 153.7. HRMS (ESI) calculated for $C_{21}H_{28}O_2Na$: 335.1982; found: 335.1979.

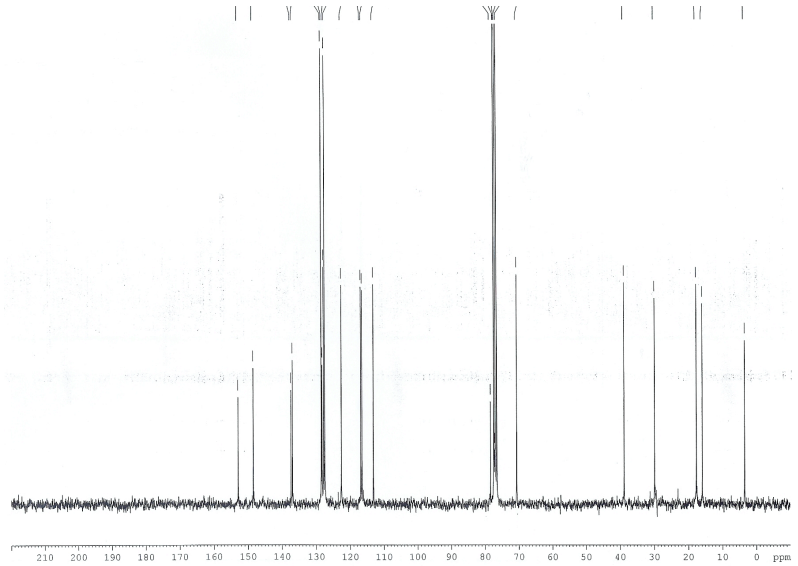
References

(1) Mohr, P. J.; Halcomb, R. L. *J. Am. Chem. Soc.* **2003**, *125*, 1712.

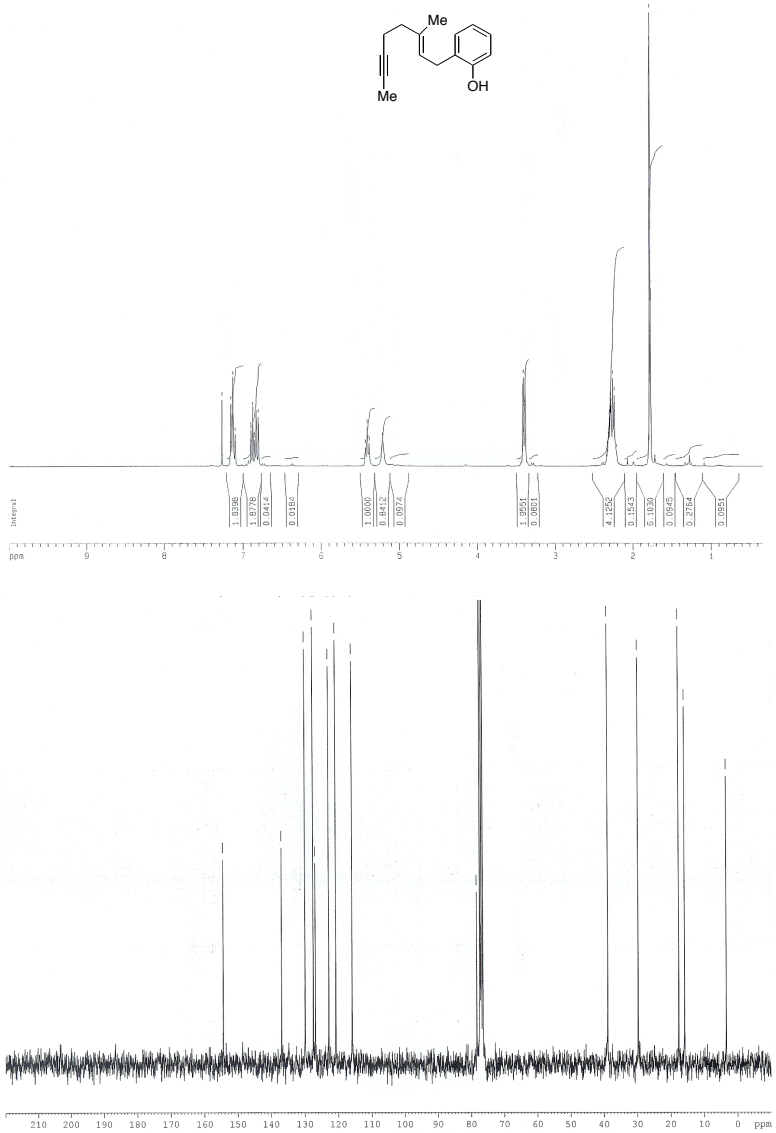
(2) Uto, Y.; Ae, S.; Koyama, D.; Sakakibara, M.; Otomo, N.; Otsuki, M.; Nagasawa, H.; Kirk, K. L.; Hori, H. *Bioorg. Med. Chem.* **2006**, *14*, 5721.

(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4-benzyloxyphenol 1a

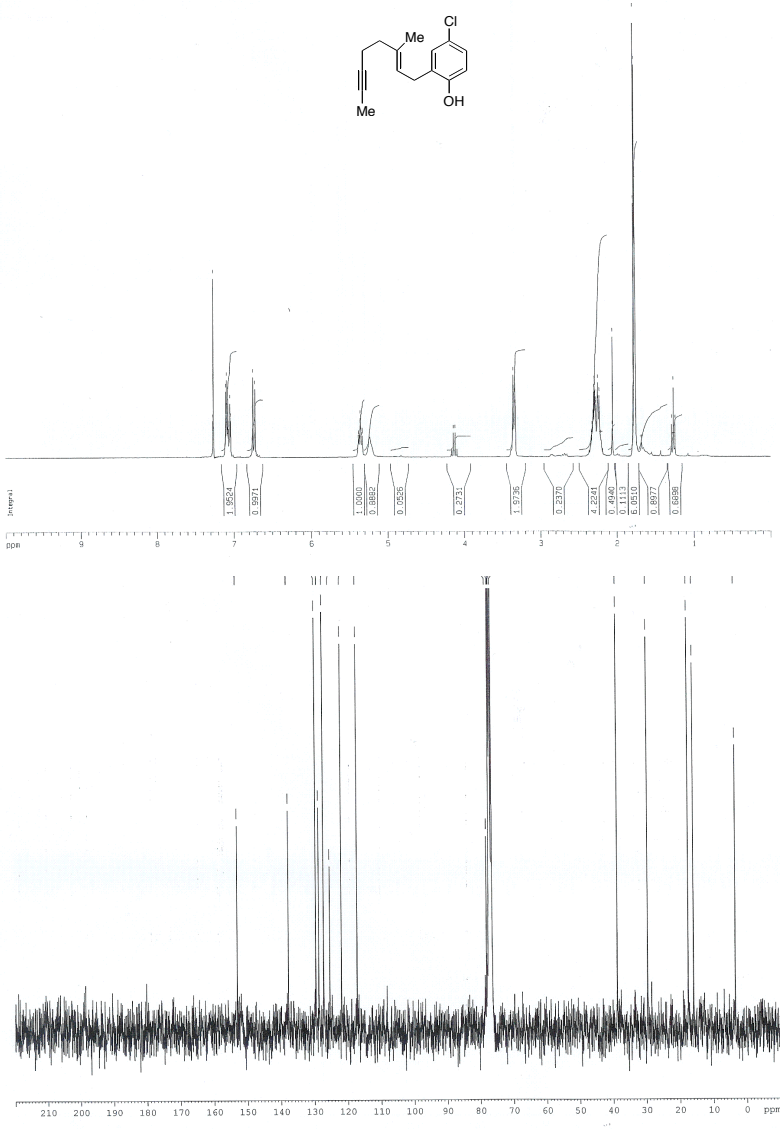




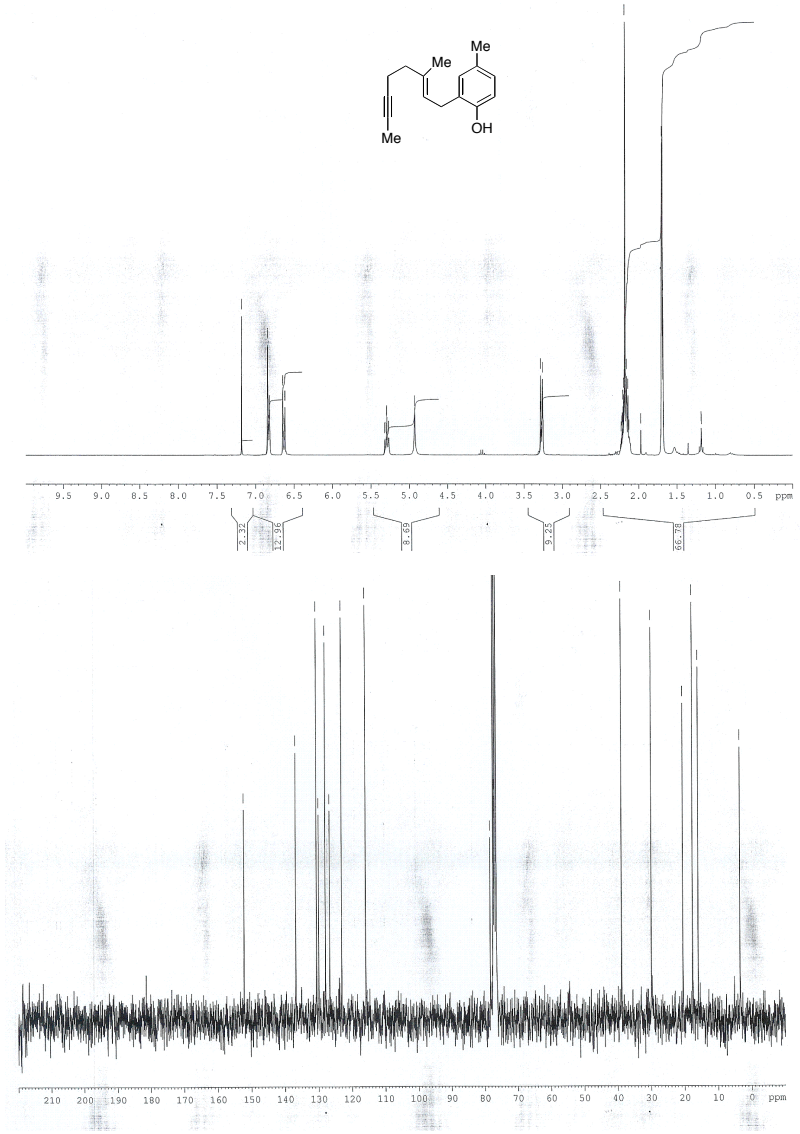
(E)-2-(3'-methyloct-2'-en-6'-ynyl)-phenol 1b



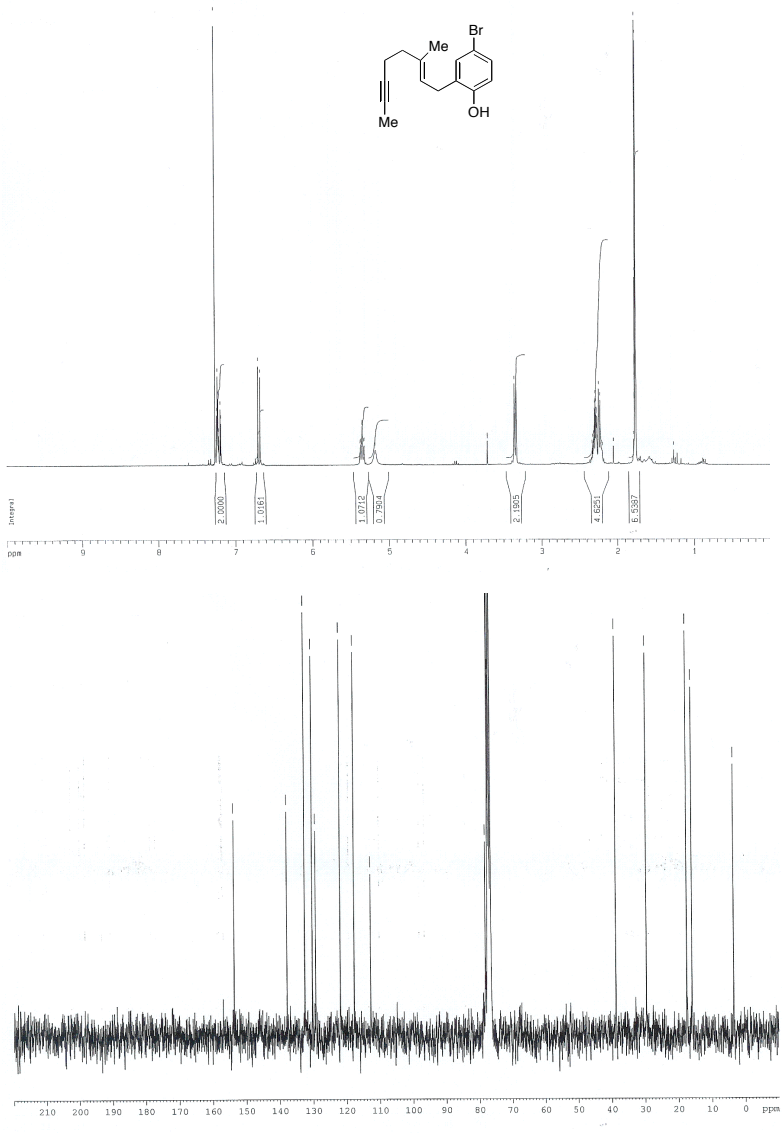
(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4-chlorophenol 1c



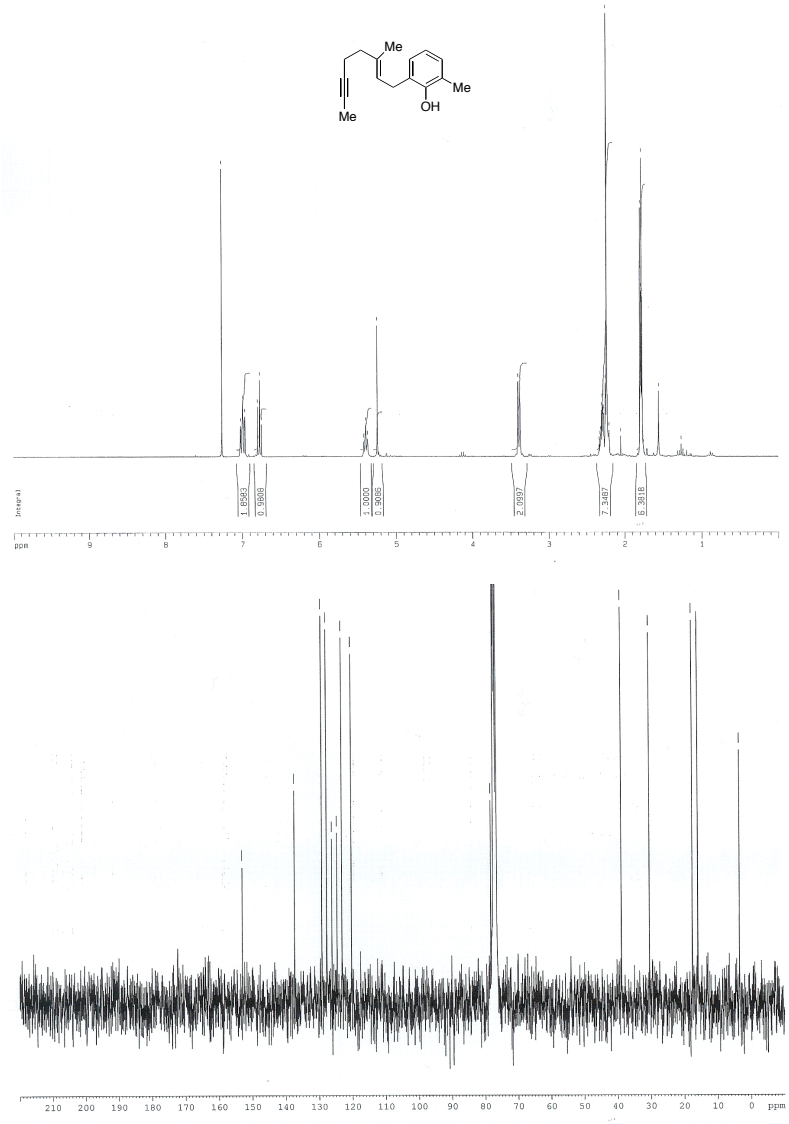
(E)-2-(3’-methyloct-2’-en-6’-ynyl)-4-methylphenol 1d



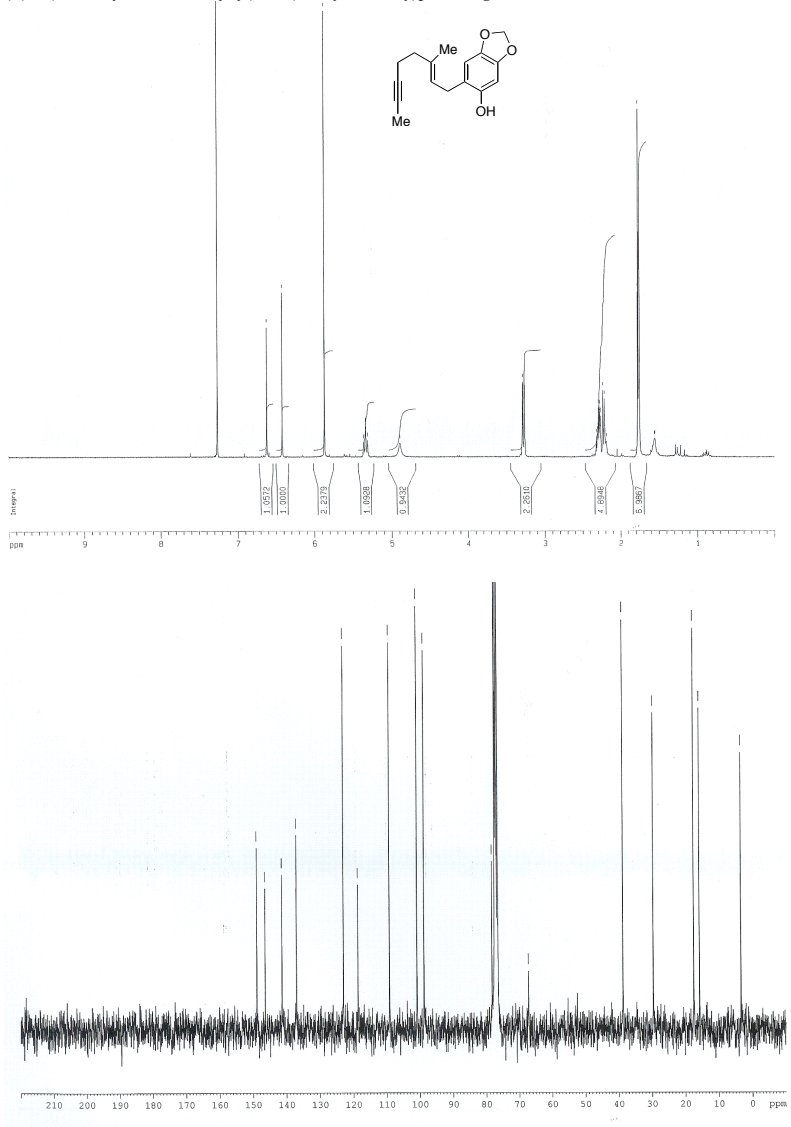
(E)-2-(3’-methyloct-2’-en-6’-ynyl)-4-bromophenol 1e



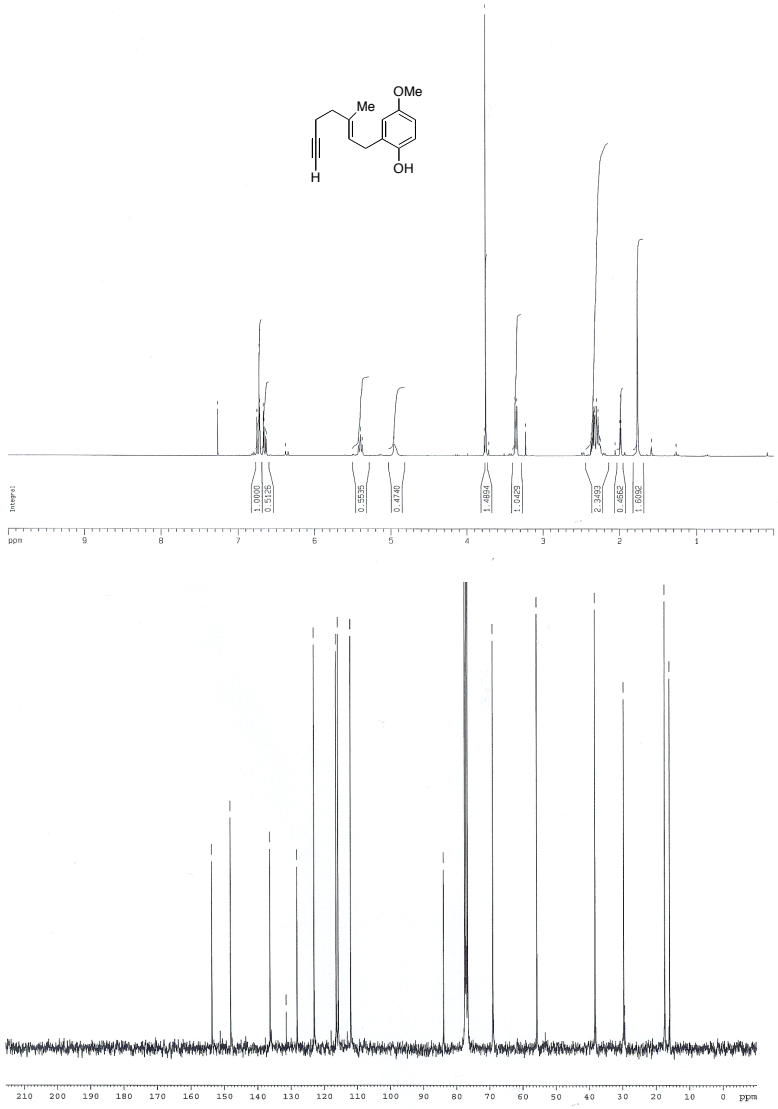
(E)-2-(3'-methyloct-2'-en-6'-ynyl)-6-methylphenol 1f



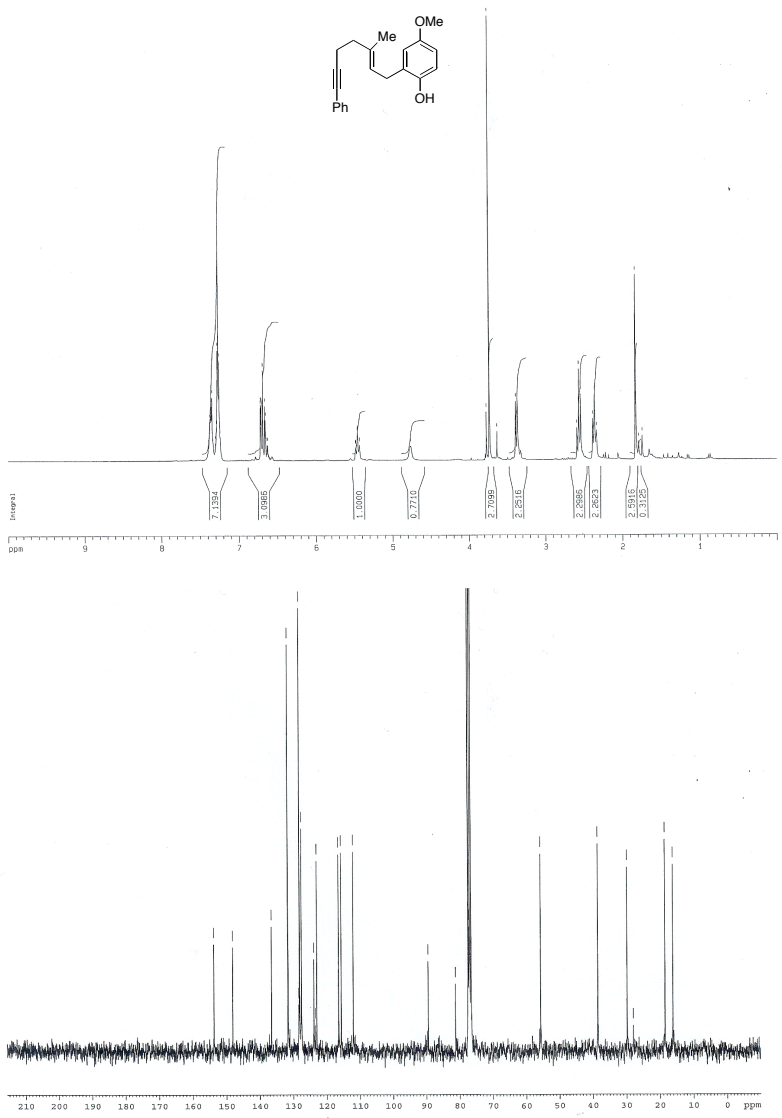
(E)-2-(3'-methyloct-2'-en-6'-ynyl)-4,5-(methylenedioxy)phenol 1g



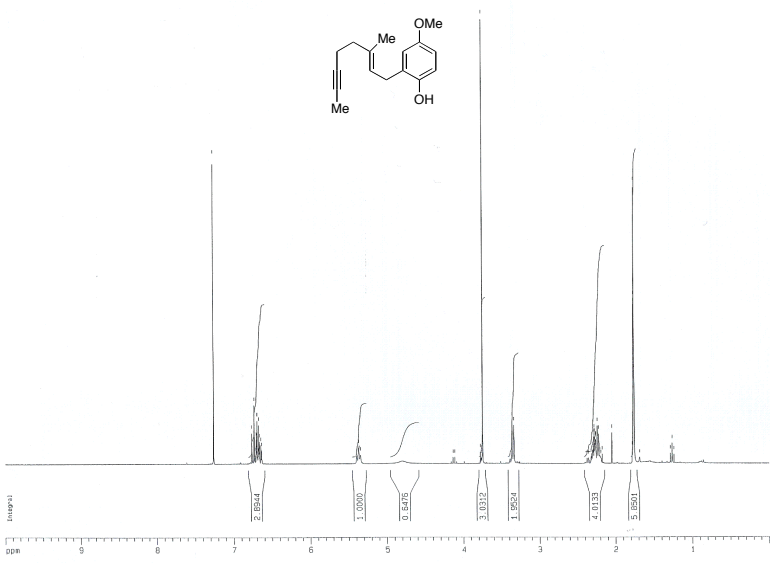
(E)-2-(3'-methylhept-2'-en-6'-ynyl)-4-methoxyphenol 1h

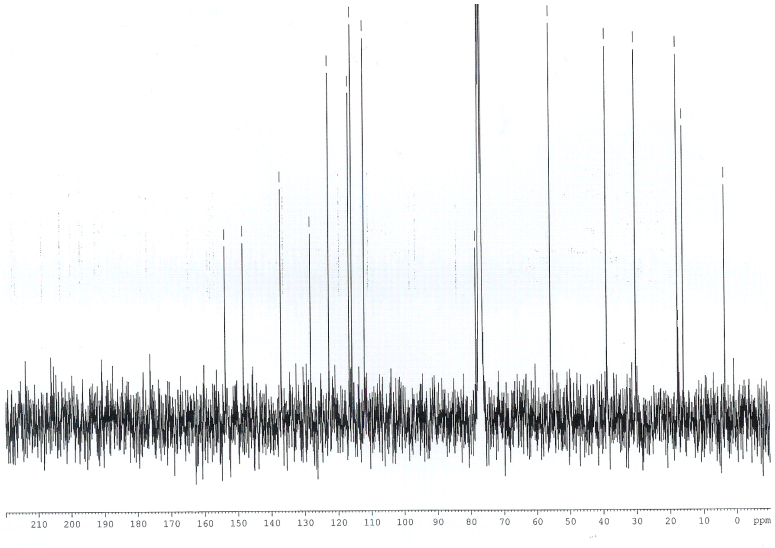


(E)-2-(3'-methyl-7'-phenylhept-2'-en-6'-ynyl)-4-methoxyphenol 1i

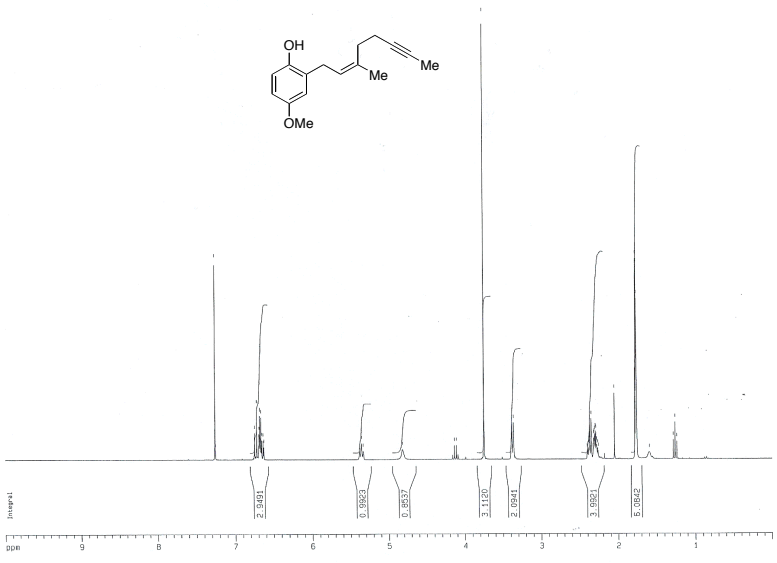


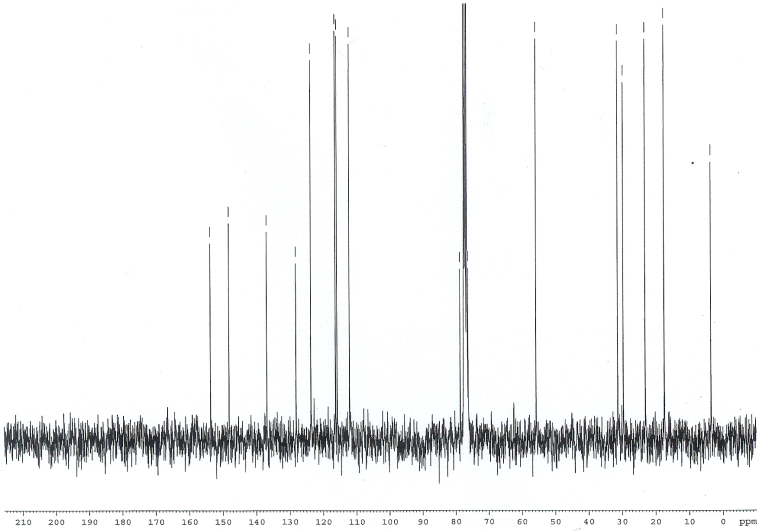
(E)-2-(3’-methyloct-2’-en-6’-ynyl)-4-methoxyphenol (E)-1j



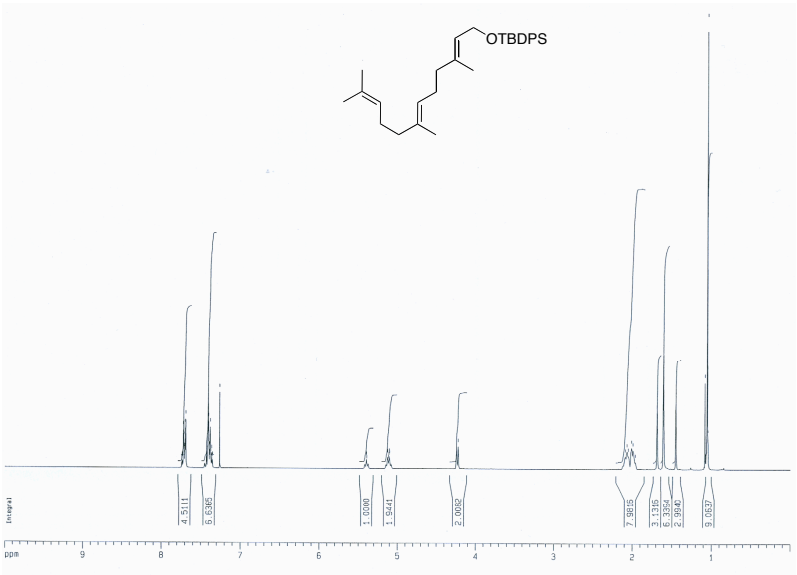


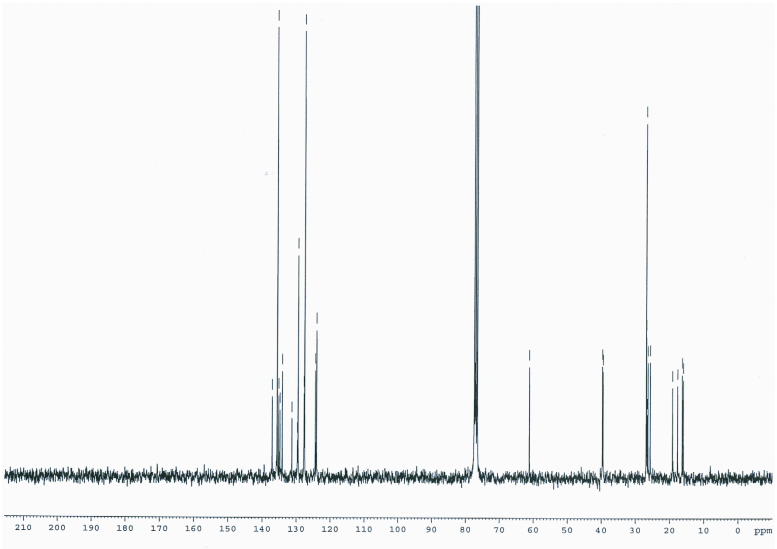
(Z)-2-(3’-methyloct-2’-en-6’-ynyl)-4-methoxyphenol (*Z*)-1j



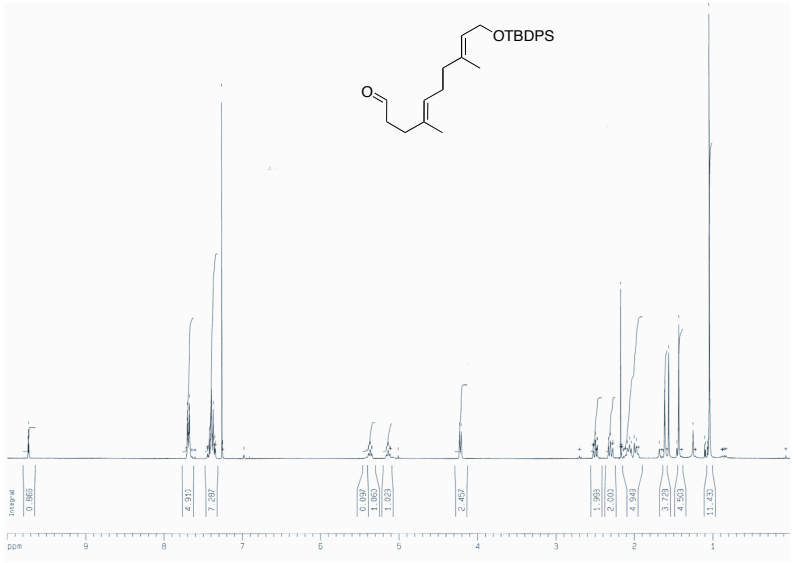


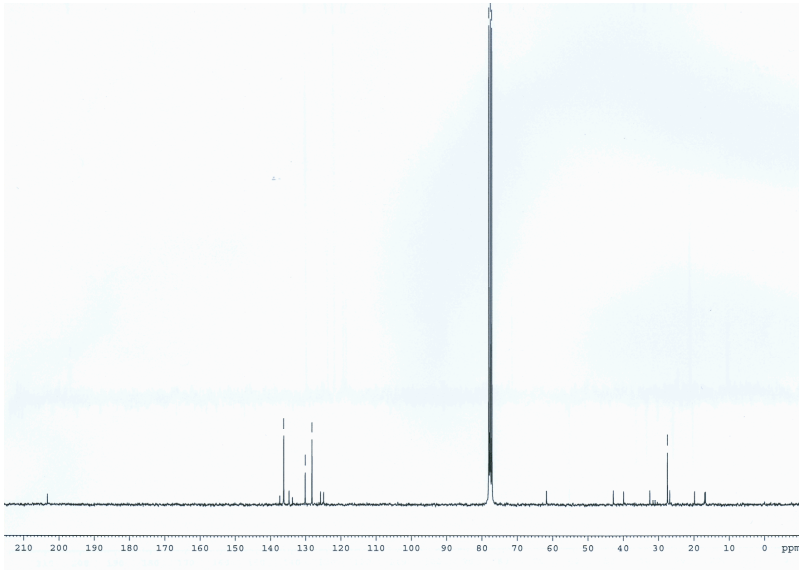
***tert*-Butyl-diphenyl-(3,7,11-trimethyl-dodeca-2,6,10-trienyloxy)-silane IV**



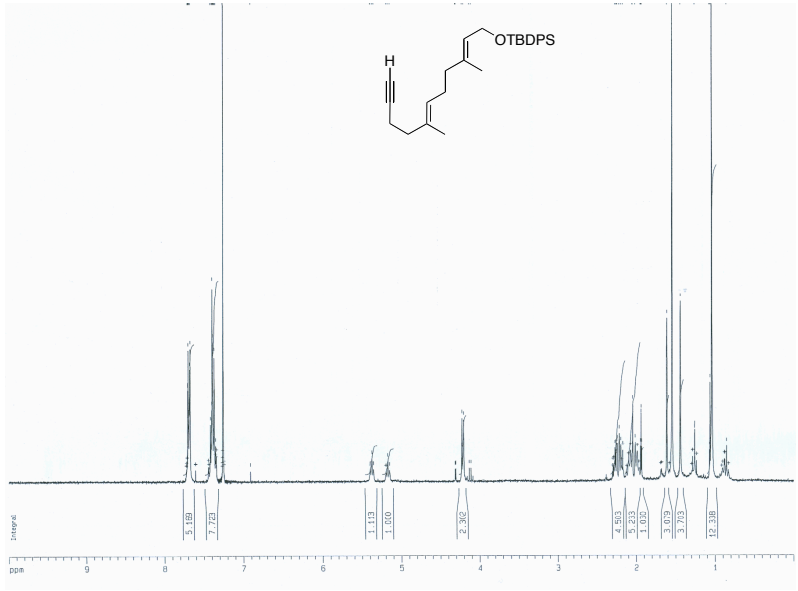


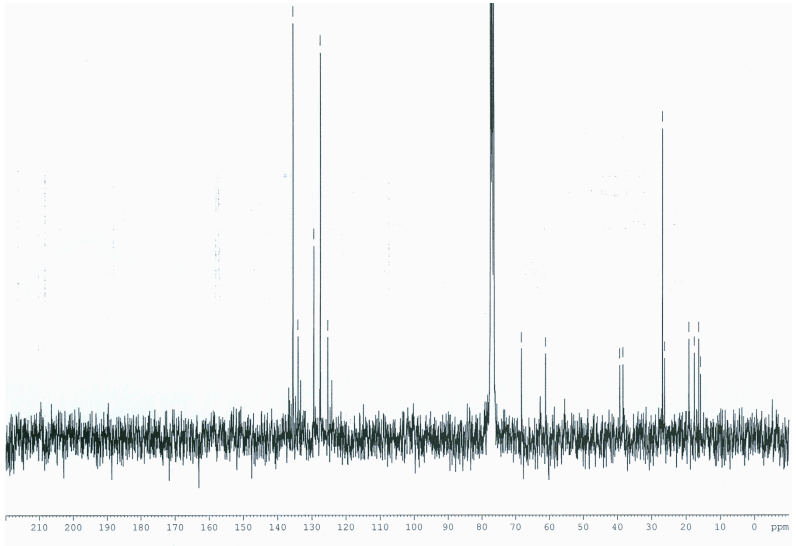
10-(*tert*-Butyl-diphenyl-silanyloxy)-4,8-dimethyl-deca-4,8-dienal V



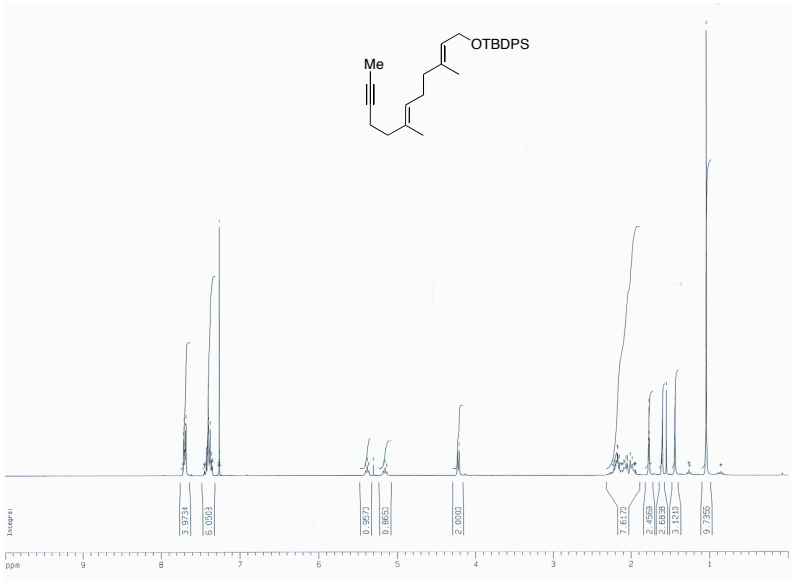


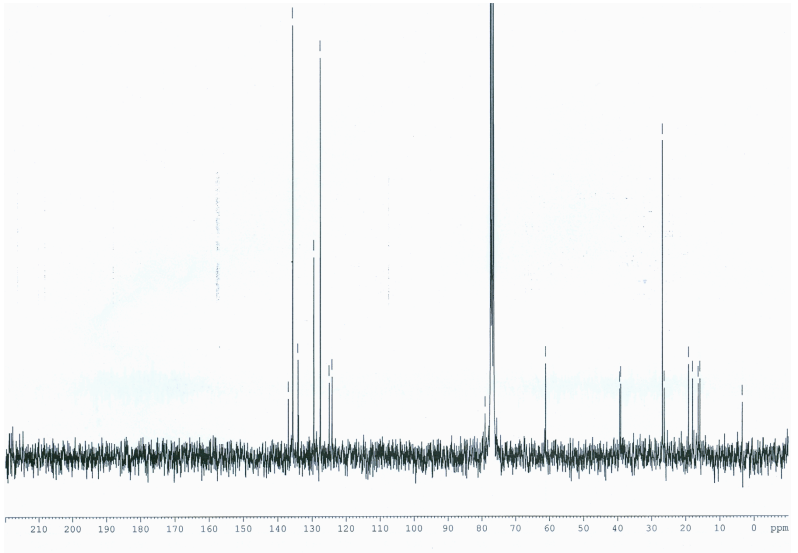
***tert*-Butyl-(3,7-dimethyl-undeca-2,6-dien-10-ynyloxy)-diphenyl-silane VI**



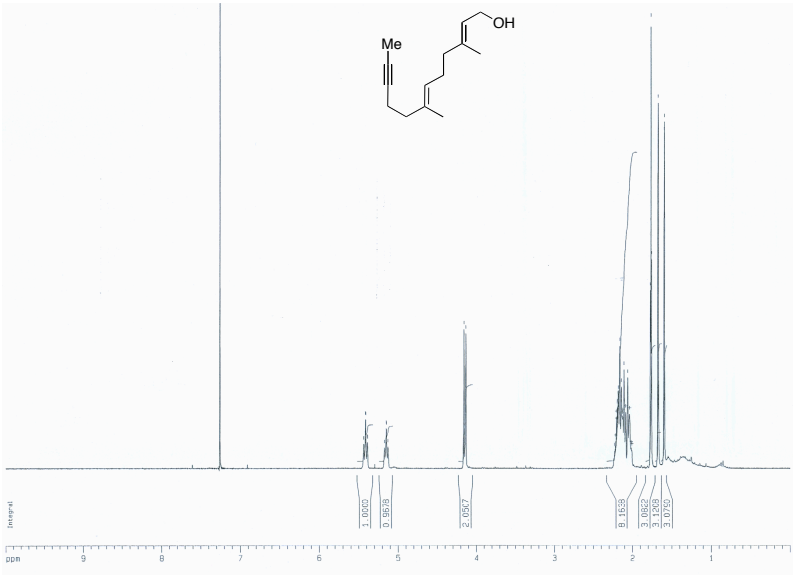


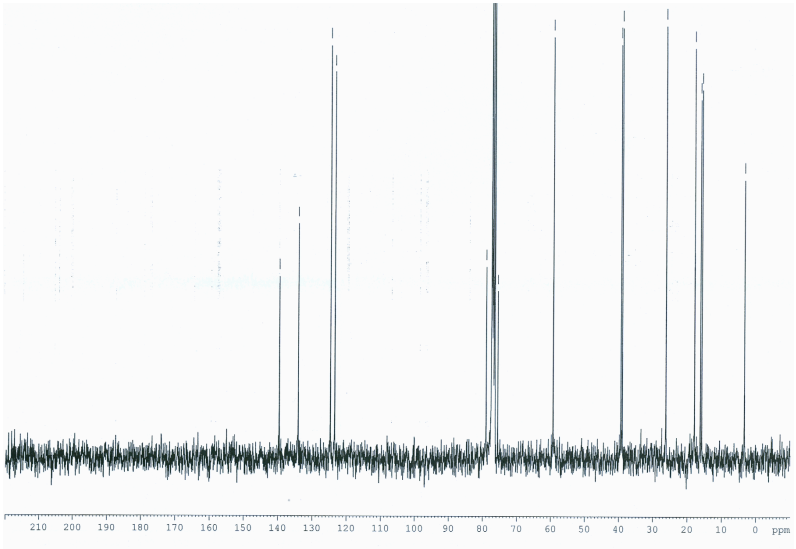
***tert*-Butyl-(3,7-dimethyl-dodeca-2,6-dien-10-ynyloxy)-diphenyl-silane VII**



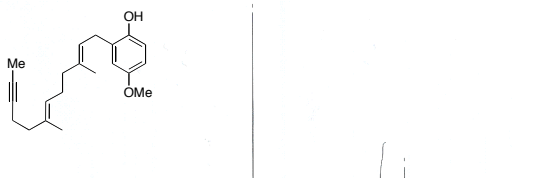


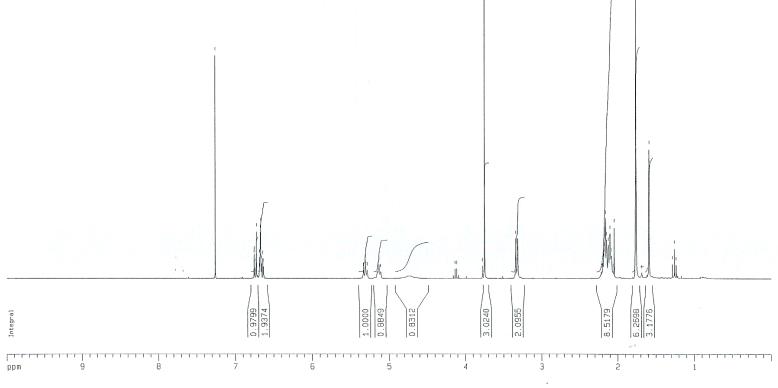
3,7-Dimethyl-dodeca-2,6-dien-10-yn-1-ol VIII

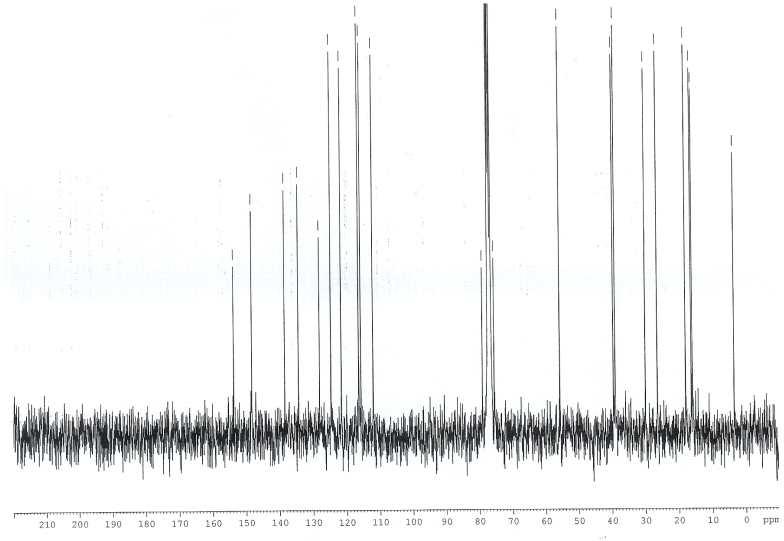




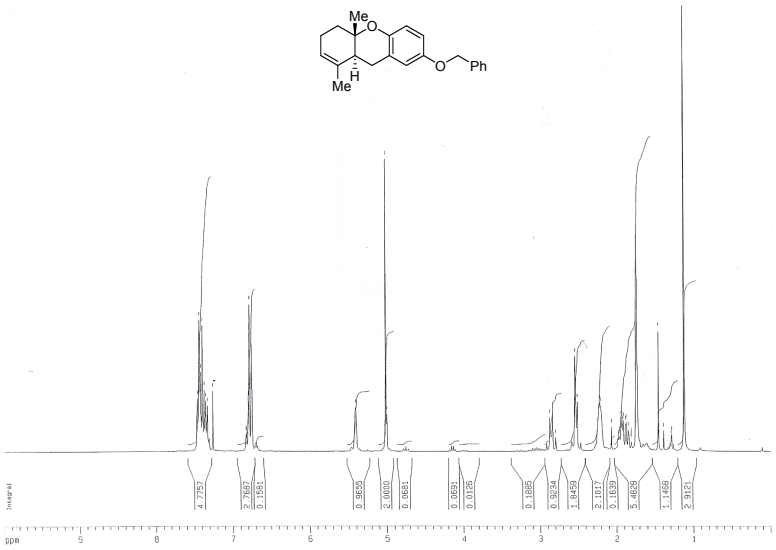
2-(3,7-Dimethyl-dodeca-2,6-dien-10-ynyl)-4-methoxy-phenol 4

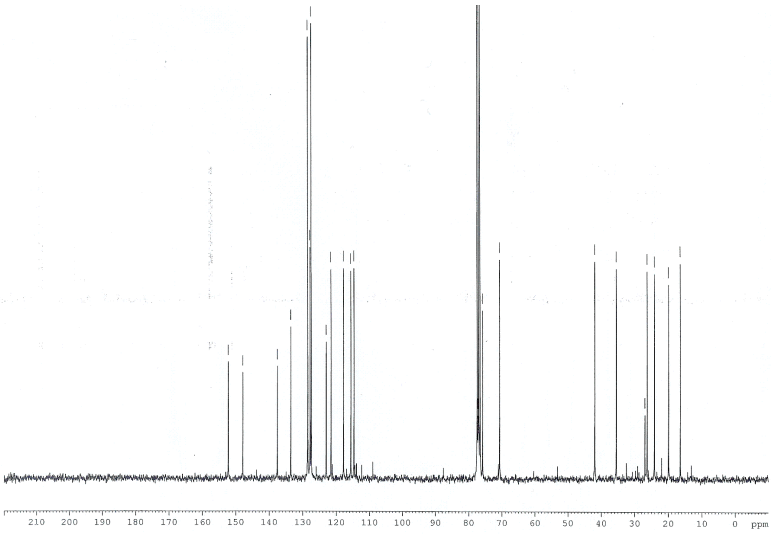




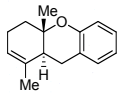


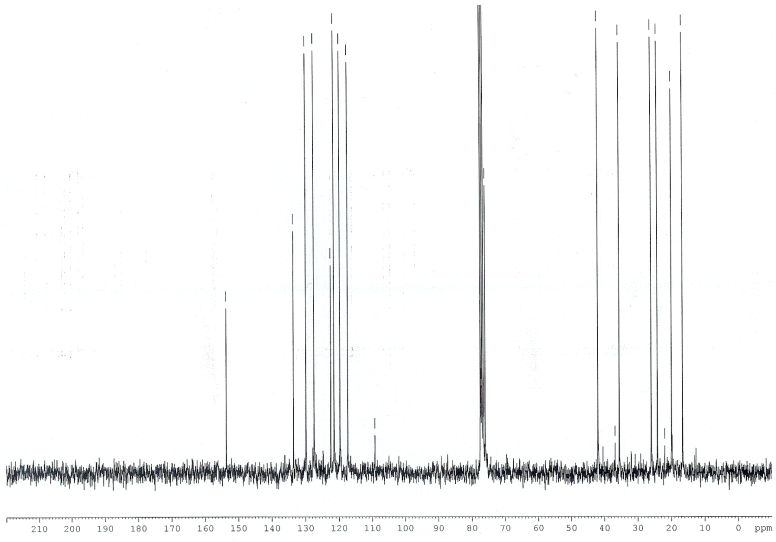
7-Benzyloxy-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2a



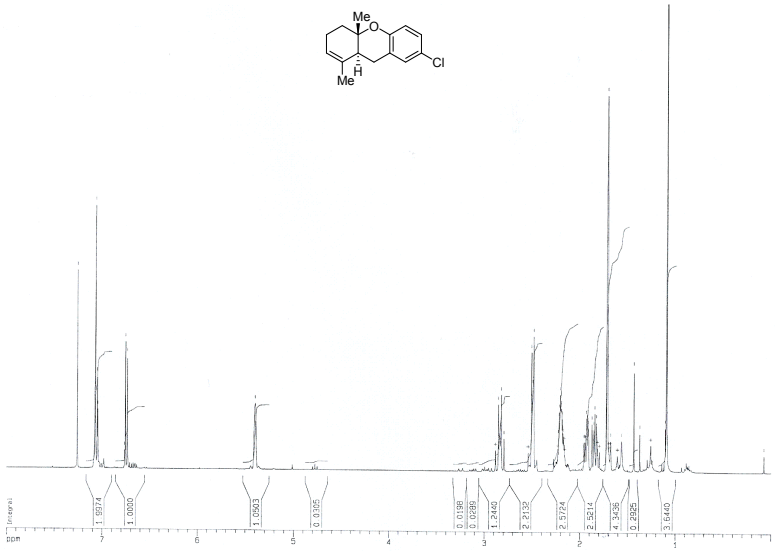


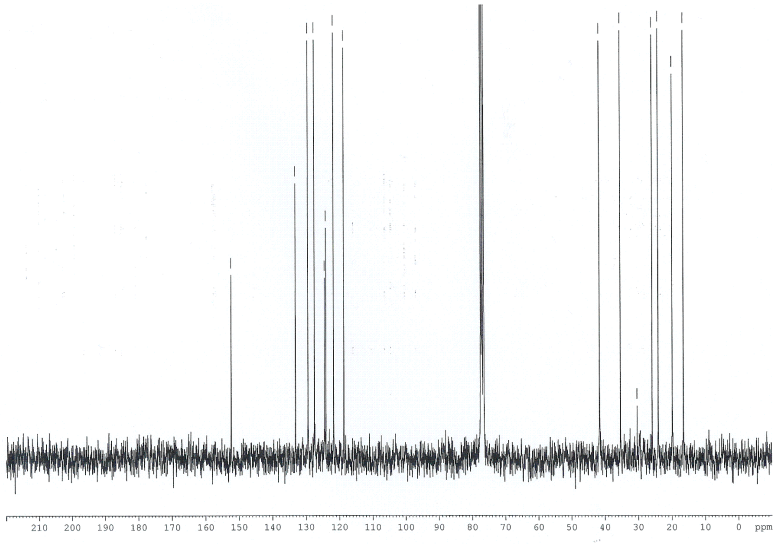
1,4a-Dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2b



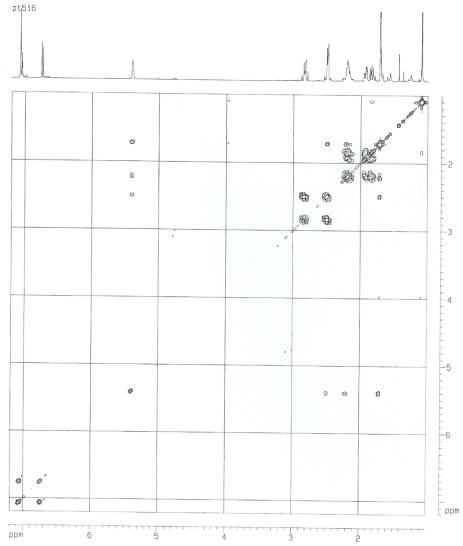


7-Chloro-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2c

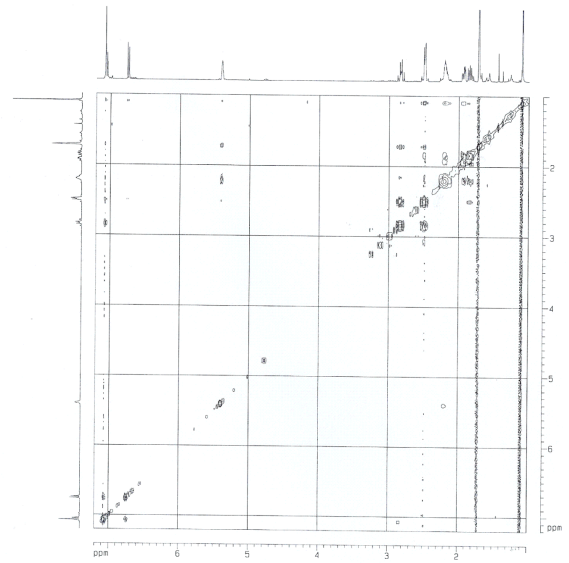




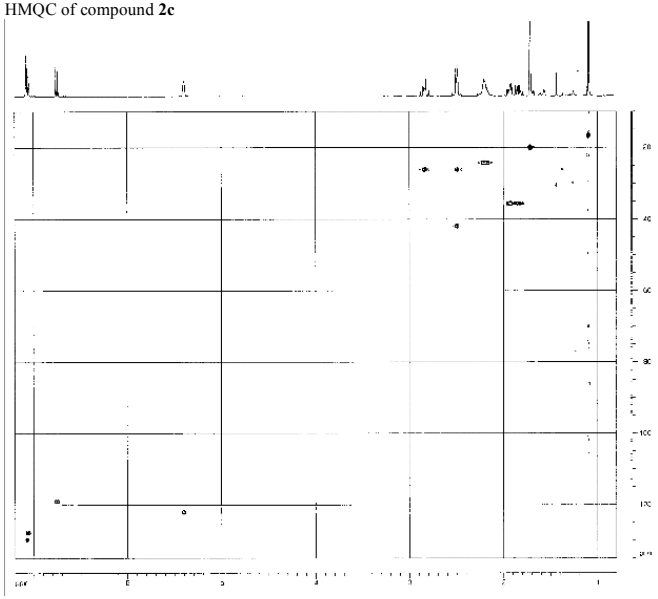
COSY of compound **2c**



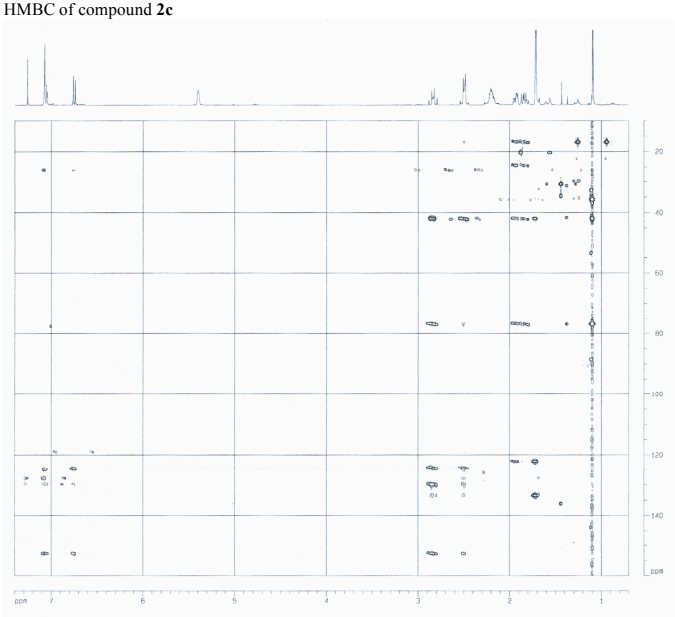
NOESY of compound **2c**



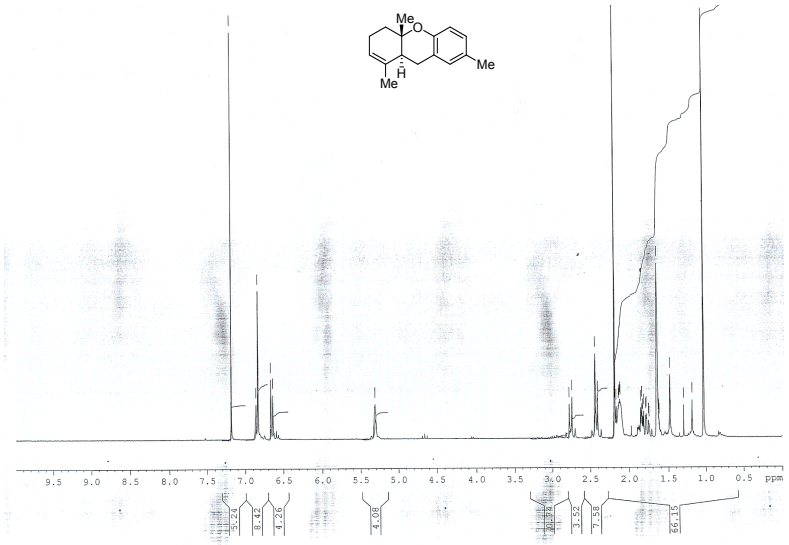
HMQC of compound **2c**

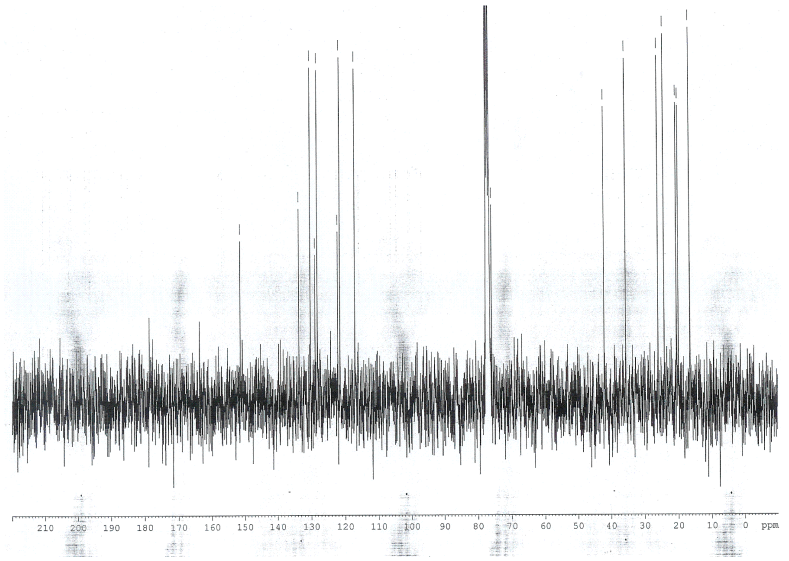


HMBC of compound **2c**

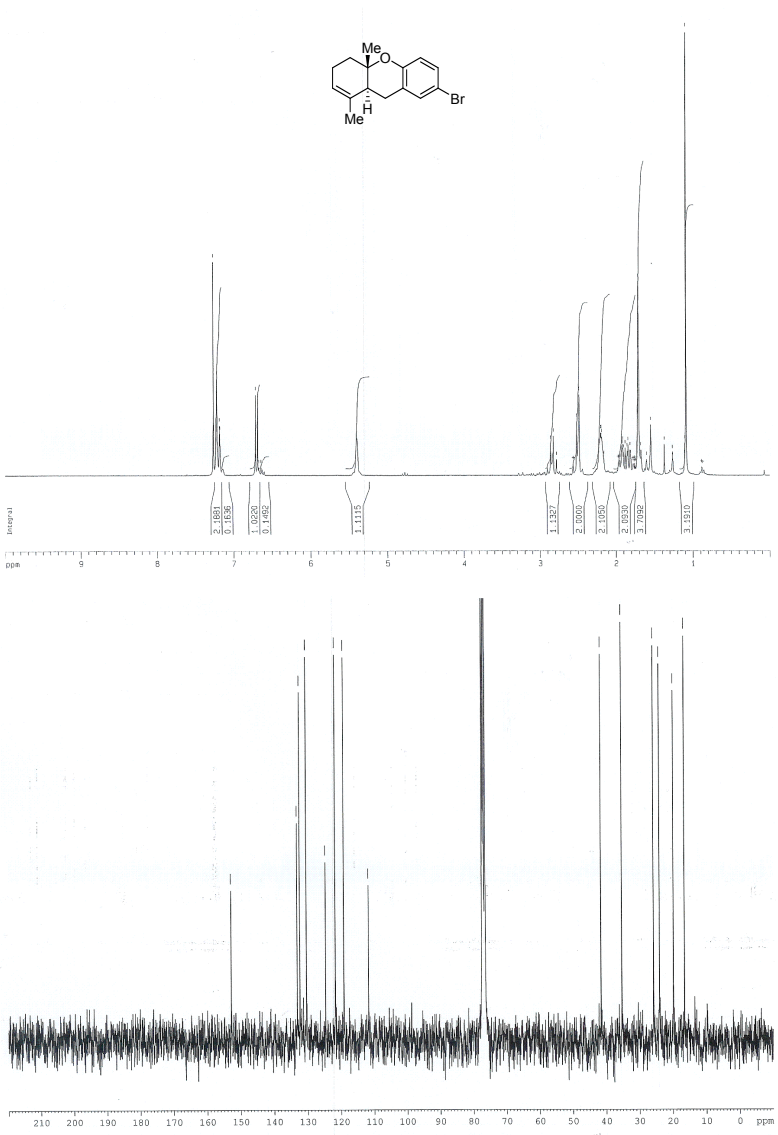


1,4a,7-Trimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2d

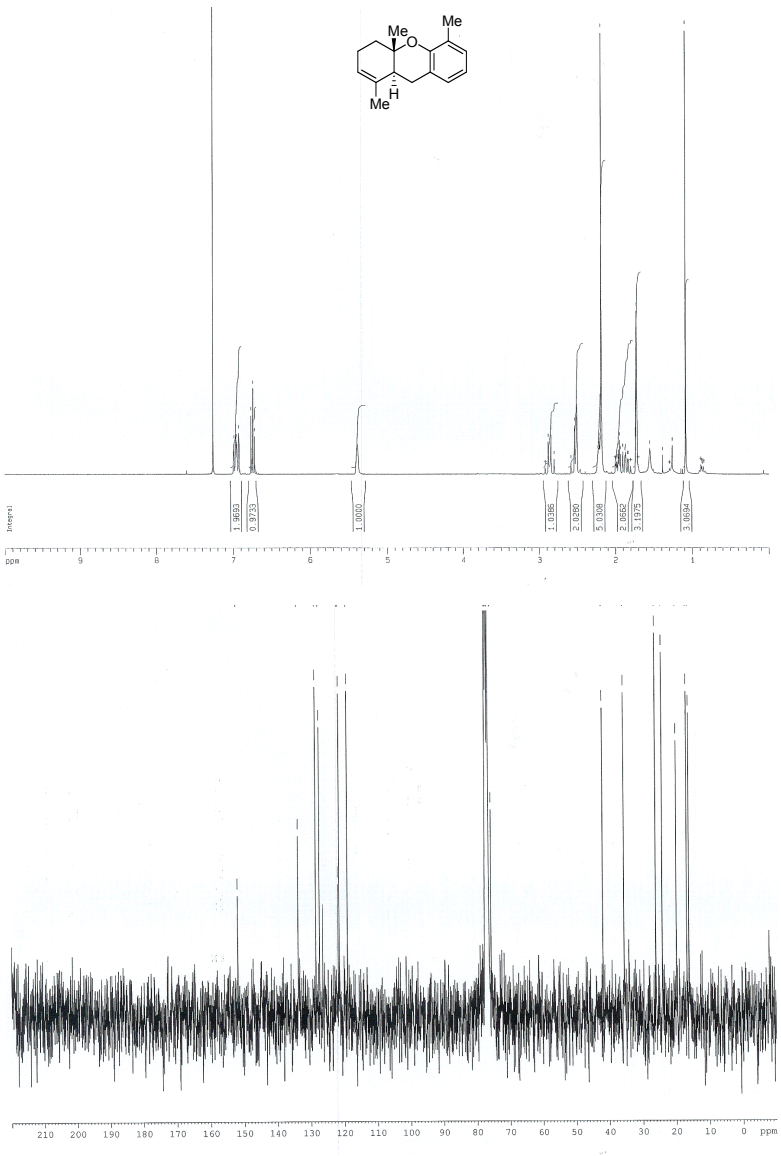




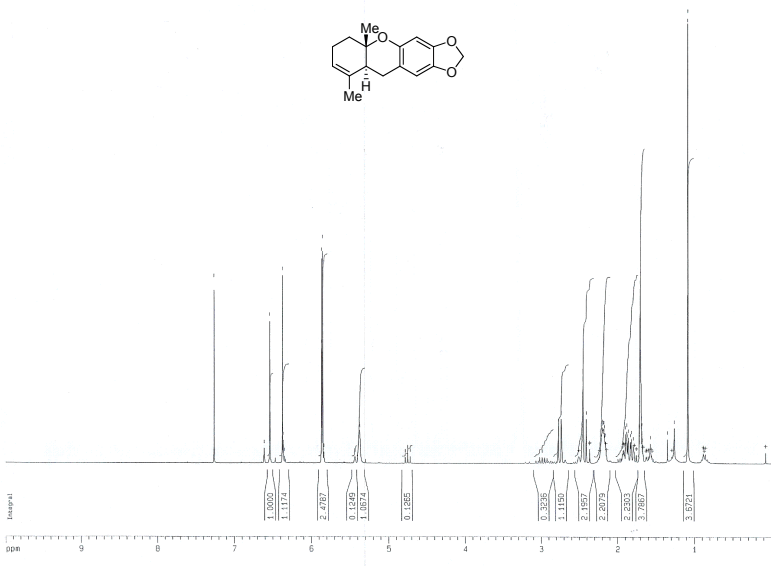
7-Bromo-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2e

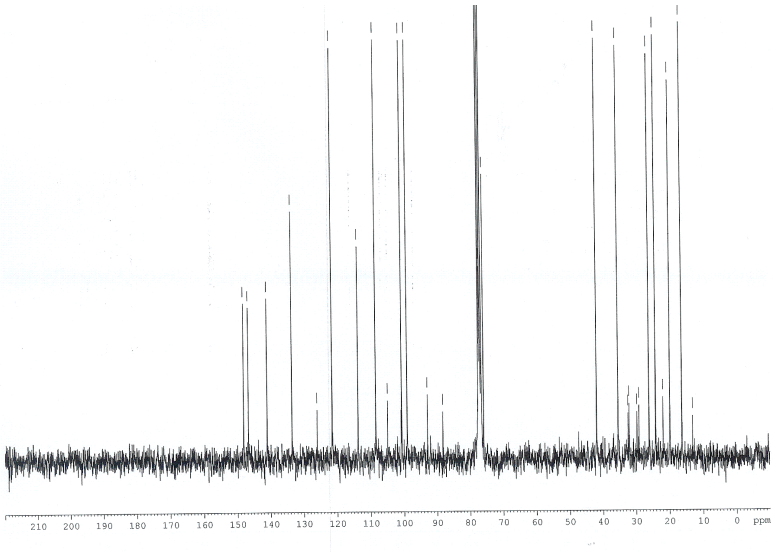


1,4a,5-Trimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2f

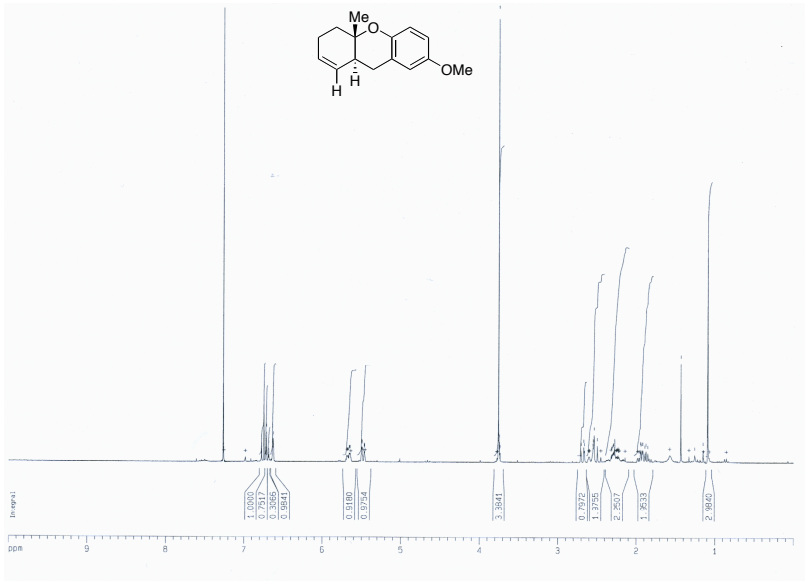


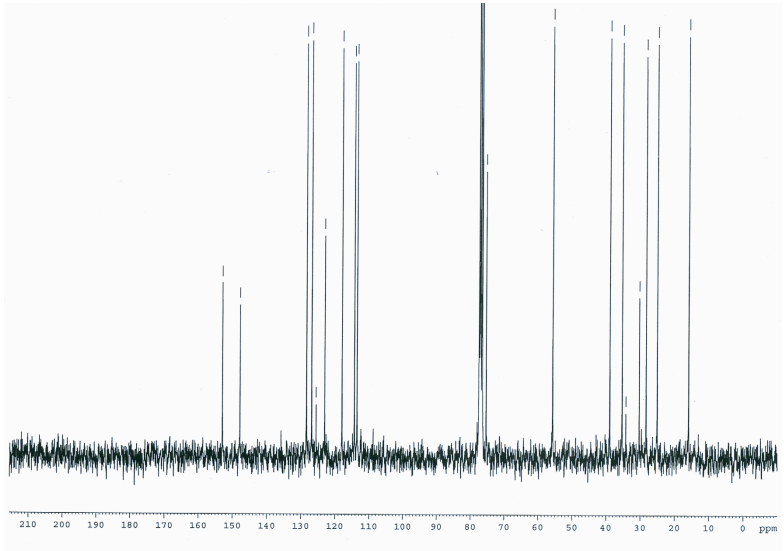
6,7-(Methylenedioxy)-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene 2g



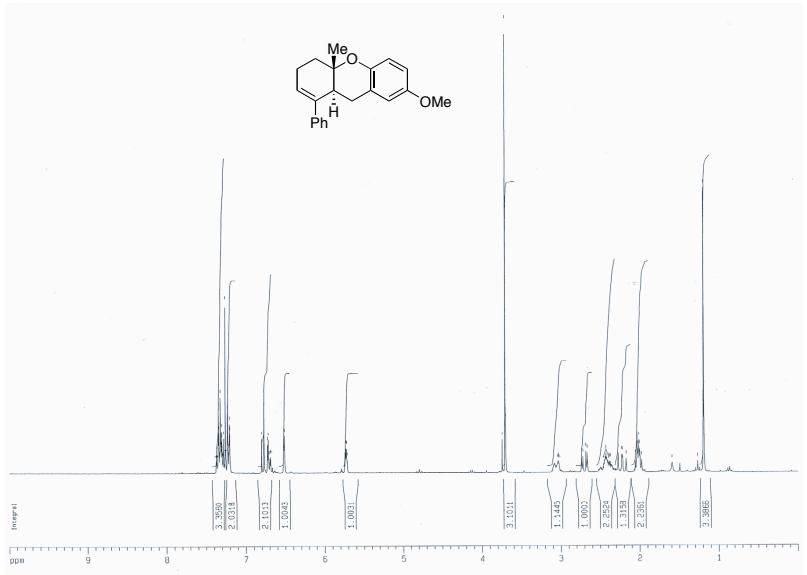


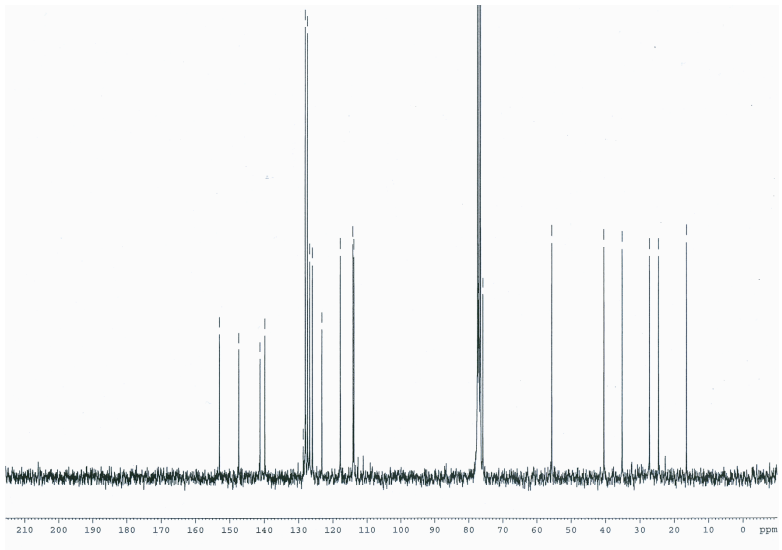
7-Methoxy-4a-methyl-4,4a,9,9a-tetrahydro-3H-xanthene 2h



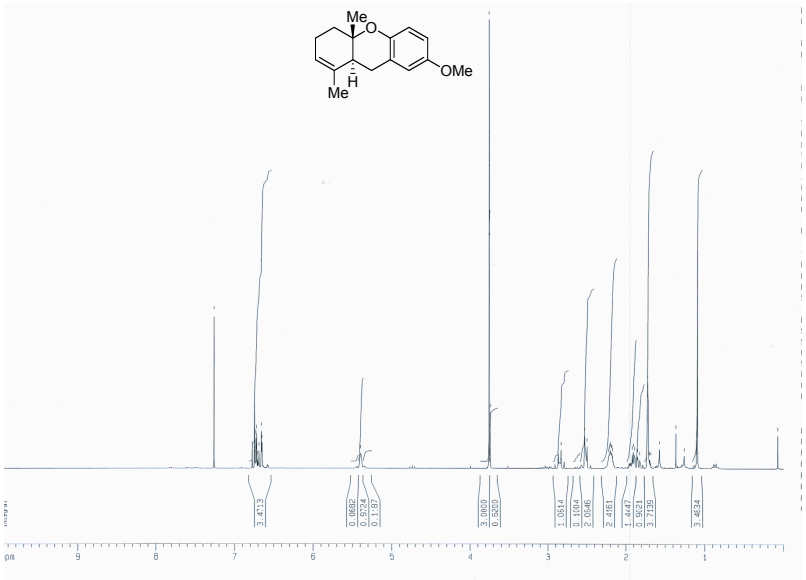


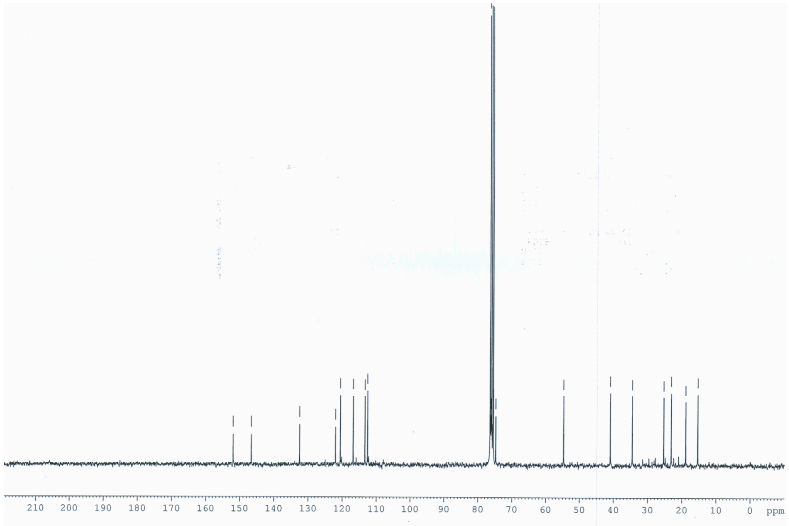
7-Methoxy-4a-methyl-1-phenyl-4,4a,9,9a-tetrahydro-3H-xanthene 2i



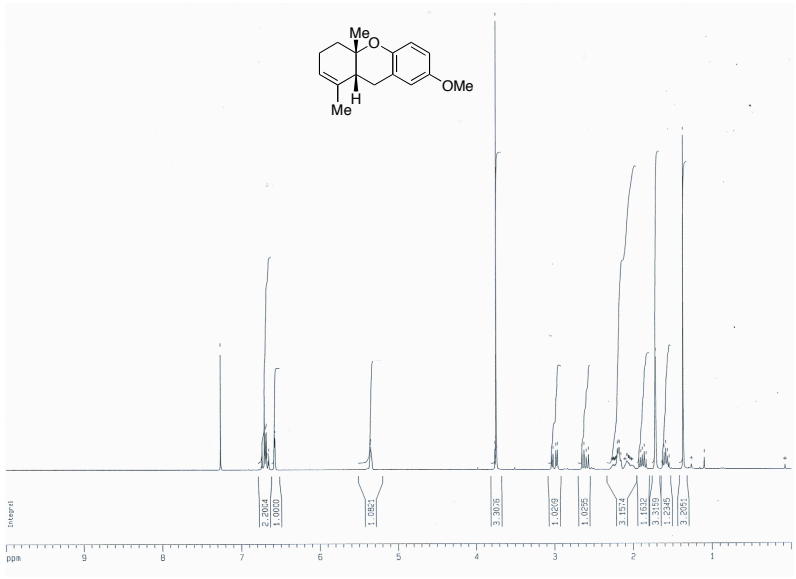


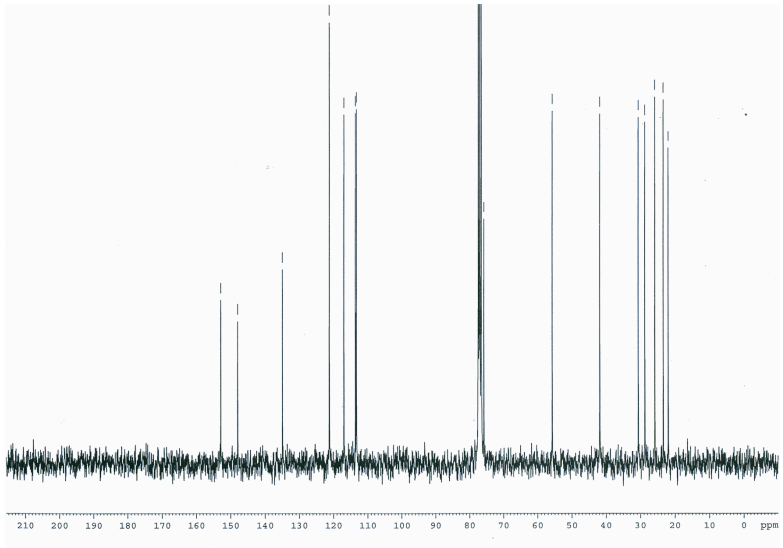
7-Methoxy-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene (*trans*)-2j



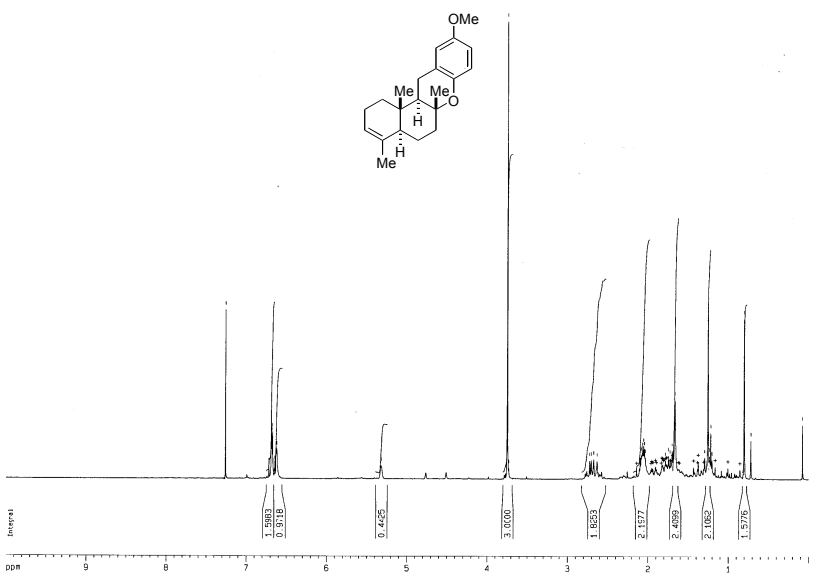


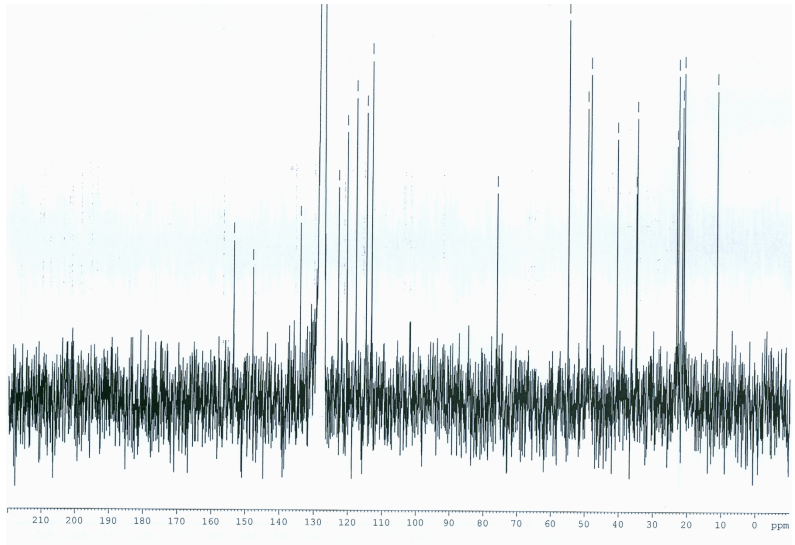
7-Methoxy-1,4a-dimethyl-4,4a,9,9a-tetrahydro-3H-xanthene (*cis*)-2j





7-Methoxy-4,6a,12b-trimethyl-1,4a,5,6,6a,12,12a,12b-octahydro-2H-benzo[a]xanthene 5





NOESY of compound **5**