

Supporting Information

Conia-ene Annulation of the α -Cyano β -TMS-capped Alkynyl Cycloalkanone System and Its Synthetic Application

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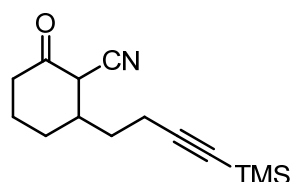
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The General Procedure for 1,4-addition in the Synthesis of Compounds 10, 11, 12, 13, 14, 15, 16, 17 and 18.

The general procedure is illustrated immediately below with compound 11 as a specific example.

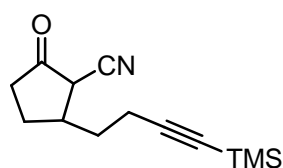
2-Oxo-6-(4-trimethylsilylbut-3-ynyl)-cyclohexanecarbonitrile (11)



To a stirred solution of compound 2 (302 mg, 2.50 mmol) in THF (5 mL) was added freshly prepared (4-buty-1-nyl)trimethylsilane magnesium chloride solution (6.0 mL, 0.92 M in THF, 5.50 mmol) dropwise at -30 °C. After stirring for 10 min at the same temperature, TMSCl (0.95 mL, 7.50 mmol) was introduced in one portion. The resulting mixture was stirred for another 1 h at -30 °C. Saturated NH₄Cl solution (8 mL) was added to quench the reaction. The aqueous layer was separated and extracted with diethyl ether (3 x 15 mL). The combined organic extracts were washed with brine, dried over MgSO₄, filtered and concentrated to give the crude residue, which was purified by flash chromatography on silical gel with EtOAc/*n*-hexane (1:9) to afford compound 11 [476 mg, 77% yield, a mixture of keto isomers in a ratio of 1:2 (*cis* : *trans*)] as a yellow oil.

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2249, 2174, 1728; ¹H NMR (CDCl₃, 600 MHz) major isomer: δ 3.33 (d, *J* = 11.6 Hz, 1H), 2.56-2.52 (m, 1H), 2.38-1.80 (m, 6H), 1.74-1.33 (m, 4 H), 0.08 (s, 9H); minor isomer: δ 3.52 (d, *J* = 4.5 Hz, 1H); ¹³C NMR (CDCl₃, 150 MHz) major isomer: δ 200.0 (C), 115.7 (C), 105.1 (C), 86.0 (C), 49.6 (CH), 42.2 (CH), 40.3 (CH₂), 32.9 (CH₂), 27.0 (CH₂), 24.7 (CH₂), 24.6 (CH₂), 16.8 (CH₂), -0.1 (3 x CH₃); minor isomer: δ 200.9 (C), 115.4 (C), 104.7 (C), 86.2 (C), 47.5 (CH), 40.9 (CH), 38.8 (CH₂), 30.4 (CH₂), 28.8 (CH₂), 17.0 (CH₂), -0.3 (3 x CH₃); HRMS (EI) C₁₄H₂₁NOSi: 247.1392; found: 247.1391.

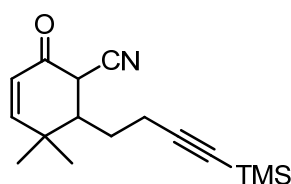
2-Oxo-5-(4-trimethylsilylbut-3-ynyl)-cyclopentanecarbonitrile (10)



A mixture of keto isomers in a ratio of 1:3.2 (*cis* : *trans*) was obtained as a yellow oil (68% yield).

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2244, 2175, 1760; ¹H NMR (CDCl₃, 600 MHz) major isomer: δ 2.92 (d, J = 12.2 Hz, 1H), 2.40-2.27 (m, 5H), 2.05-1.51 (m, 4H), 0.10 (s, 9H); minor isomer: δ 3.39 (d, J = 7.6 Hz, 1H); ¹³C NMR (CDCl₃, 150 MHz) major isomer: δ 205.9 (C), 116.0 (C), 105.1 (C), 86.1 (C), 45.9 (CH), 41.7 (CH), 37.1 (CH₂), 32.7 (CH₂), 27.0 (CH₂), 17.5 (CH₂), -0.1 (3 x CH₃); minor isomer: δ 206.3 (C), 114.2 (C), 105.0 (C), 86.1 (C), 44.2 (CH), 38.5 (CH), 36.1 (CH₂), 29.6 (CH₂), 26.5 (CH₂), 17.9 (CH₂), -0.2 (3 x CH₃); HRMS (EI) C₁₃H₁₉NOSi: 233.1236; found: 233.1231.

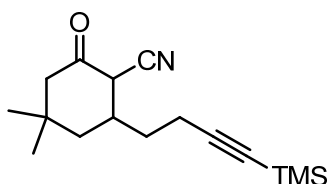
5,5-Dimethyl-2-oxo-6-(4-trimethylsilylbut-3-ynyl)-cyclohex-3-enecarbonitrile (12)



A mixture of keto isomers in a ratio of 1.5:1 (*cis* : *trans*) was obtained as a yellow oil (40% yield).

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2248, 2177, 1694; ¹H NMR (CDCl₃, 600 MHz) major isomer: δ 6.78 (d, J = 10.8 Hz, 1H), 5.98 (d, J = 10.2 Hz, 1H), 3.68 (d, J = 5.4 Hz, 1H), 2.41 (dt, J = 17.3, 5.9 Hz, 1H), 2.30-2.19 (m, 2H), 1.89-1.79 (m, 2H), 1.26 (s, 3H), 1.18 (s, 3H), 0.09 (s, 9H); minor isomer: δ 6.70 (d, J = 10.2 Hz, 1H), 5.94 (d, J = 10.2 Hz, 1H), 3.48 (d, J = 13.2 Hz, 1H); ¹³C NMR (CDCl₃, 150 MHz) major isomer: δ 188.2 (C), 161.1 (CH), 124.0 (CH), 116.1 (C), 104.6 (C), 86.7 (C), 43.5 (CH), 39.0 (CH), 36.2 (C), 28.5 (CH₃), 26.2 (CH₂), 19.4 (CH₂), -0.1 (3 x CH₃); minor isomer: δ 188.9 (C), 162.1 (CH), 124.1 (CH), 116.4 (C), 105.5 (C), 85.7 (C), 44.3 (CH), 43.1 (CH), 36.8 (C), 29.0 (CH₂), 27.2 (CH₃), 21.7 (CH₃), 17.6 (CH₂), -0.1 (3 x CH₃); HRMS (EI) C₁₆H₂₃NOSi: 273.1549; found: 273.1544.

4,4-Dimethyl-2-oxo-6-(4-trimethylsilylbut-3-ynyl)-cyclohexanecarbonitrile (13)

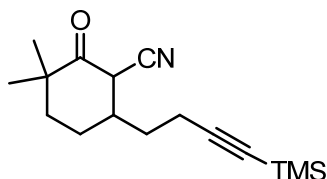


A mixture of keto isomers in a ratio of 1:1 (*cis* : *trans*) was obtained as yellow oil (75% yield).

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2248, 2174, 1731; ¹H NMR (CDCl₃, 600 MHz) *trans* isomer: δ 3.23 (d, J = 12.3 Hz, 1H), 2.64 (d, J = 13.0 Hz, 1H), 2.32-2.25 (m, 3H), 2.18 (s, 2H), 1.66-1.59 (m, 2H), 1.54-1.48 (m, 1H), 1.06 (s, 3H), 0.83 (s, 3H), 0.04 (s,

9H); *cis* isomer: δ 3.34 (d, J = 4.5 Hz, 1H); ^{13}C NMR (CDCl_3 , 150 MHz) major isomer: δ 199.6 (C), 115.2 (C), 104.4 (C), 86.0 (C), 50.9 (CH_2), 46.1 (CH), 40.6 (CH_2), 36.0 (CH), 35.0 (C), 31.5 (CH_3), 31.2 (CH_2), 25.0 (CH_3), 16.7 (CH_2), -0.1 (3 x CH_3); minor isomer: δ 200.6 (C), 115.6 (C), 104.7 (C), 86.3 (C), 53.1 (CH_2), 49.1 (CH), 42.2 (CH_2), 37.4 (CH), 35.6 (C), 32.7 (CH_2), 31.5 (CH_3), 25.3 (CH_3), 16.8 (CH_2), -0.1 (3 x CH_3); HRMS (EI) $\text{C}_{16}\text{H}_{25}\text{NOSi}$: 275.1705; found: 275.1706.

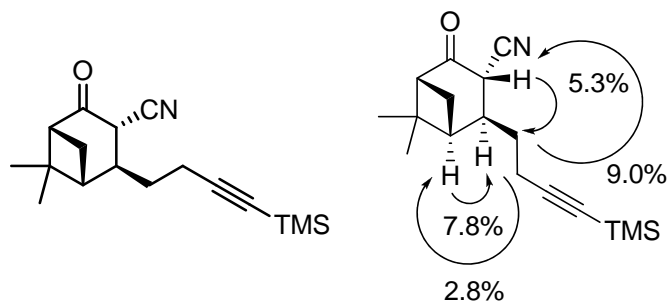
3,3-Dimethyl-2-oxo-6-(4-trimethylsilylbut-3-ynyl)-cyclohexanecarbonitrile (14)



A mixture of keto isomers in a ratio of 1:2.4 (*cis* : *trans*) was obtained as a yellow oil (72% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν_{max} 2249, 2175, 1721; ^1H NMR (CDCl_3 , 400 MHz) major isomer: δ 3.64 (dd, J = 12.8, 2.4 Hz, 1H), 2.34-2.26 (m, 1H), 2.21 (dd, J = 14.8, 7.2 Hz, 1H), 2.02-1.89 (m, 3H), 1.85-1.69 (m, 2H), 1.59-1.45 (m, 2H), 1.09 (s, 3H), 1.02 (s, 3H), 0.02 (s, 9H); minor isomer: δ 3.81 (dd, J = 5.2, 2.4 Hz, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) major isomer: δ 204.1 (C), 116.0 (C), 105.2 (C), 85.7 (C), 46.3 (CH), 44.7 (C), 42.5 (CH), 38.6 (CH_2), 32.8 (CH_2), 25.0 (CH_2), 24.7 (CH_3), 24.0 (CH_3), 16.5 (CH_2), -0.1 (3 x CH_3); minor isomer: δ 204.4 (C), 115.7 (C), 104.8 (C), 85.6 (C), 45.5 (CH), 45.4 (C), 39.9 (CH), 36.5 (CH_2), 28.0 (CH_2), 25.2 (CH_3), 25.1 (CH_3), 22.9 (CH_2), 17.0 (CH_2), -0.2 (3 x CH_3); HRMS (EI) $\text{C}_{16}\text{H}_{25}\text{NOSi}$: 275.1705; found: 275.1703.

(1*R**,3*S**,4*S**,5*R**)-6,6-dimethyl-2-oxo-4-(4-(trimethylsilyl)but-3-ynyl)bicyclo[3.1.1]heptane-3-carbonitrile (15)



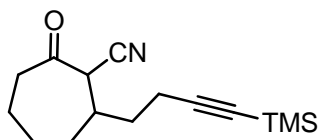
NOE experiment of compound **15**

A single stereoisomer **15** was obtained as a yellow oil (74% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν_{max} 2247, 2175, 1732; ^1H NMR (CDCl_3 , 600 MHz): δ 3.47 (dd, J = 8.0, 3.4 Hz, 1H), 2.69 (t, J = 5.0 Hz, 1H), 2.53-2.27 (m, 4H), 2.22 (t, J = 5.0

Hz, 1 H), 1.88-1.66 (m, 2H), 1.57 (d, $J = 11$ Hz, 1H), 1.36 (s, 3H), 0.87 (s, 3H), 0.09 (s, 9H); ^{13}C NMR (CDCl_3 , 150 MHz): δ 202.0 (C), 117.1 (C), 105.2 (C), 86.3 (C), 56.6 (CH), 43.3 (CH), 42.6 (CH), 42.5 (C), 37.8 (CH), 32.2 (CH_2), 26.0 (CH), 21.9 (CH_2), 21.6 (CH), 17.6 (CH_2), -0.1 (3 x CH_3); HRMS (EI) $\text{C}_{17}\text{H}_{25}\text{NOSi}$: 287.1705; found: 287.1706.

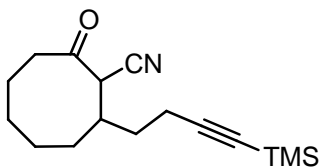
2-Oxo-7-(4-trimethylsilylbut-3-ynyl)-cycloheptanecarbonitrile (16)



A mixture of keto isomers in a ratio of 3.2:1 (*cis* : *trans*) was obtained as a yellow oil (72% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν_{max} 2249, 2175, 1732; ^1H NMR (CDCl_3 , 600 MHz) major isomer: δ 3.69 (d, $J = 3.2$ Hz, 1H), 2.80-2.72 (m, 1H), 2.59-2.57 (m, 1H), 2.34-2.26 (m, 2H), 2.22-2.11 (m, 1H), 1.91-1.80 (m, 4H), 1.72-1.55 (m, 3H), 1.38-1.34 (m, 1H), 0.13 (s, 9H); minor isomer : δ 3.51 (d, $J = 8.4$ Hz, 1H), 2.80-2.72 (m, 1H), 2.59-2.57 (m, 1H), 2.34-2.26 (m, 2H), 2.22-2.11 (m, 1H), 1.91-1.80 (m, 4H), 1.72-1.55 (m, 3H), 1.38-1.34 (m, 1H), 0.13 (s, 9H); ^{13}C NMR (CDCl_3 , 150 MHz) major isomer : δ 202.7 (C), 116.0 (C), 104.8 (C), 86.4 (C), 49.6 (CH), 42.1 (CH_2), 38.4 (CH), 32.7 (CH_2), 32.3 (CH_2), 26.6 (CH_2), 22.9 (CH_2), 17.5 (CH_3), 0.0 (3 x CH_3); minor isomer: δ 202.1 (C), 116.8 (C), 105.0 (C), 86.2 (C), 49.3 (CH), 42.0 (CH_2), 38.1 (CH), 31.9 (CH_2), 31.8 (CH_2), 25.6 (CH_2), 23.6 (CH_2), 17.1 (CH_2), -0.1 (3 x CH_3); HRMS (EI) $\text{C}_{15}\text{H}_{23}\text{NOSi}$: 261.1549; found: 261.1548.

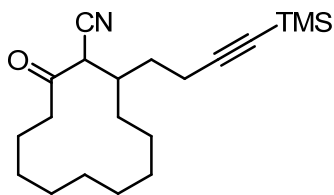
2-Oxo-8-(4-trimethylsilylbut-3-ynyl)-cyclooctanecarbonitrile (17)



A single diastereomer **17** was obtained as a yellow oil (71% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν_{max} 2247, 2173, 1714; ^1H NMR (CDCl_3 , 600 MHz): δ 3.58 (d, $J = 3.2$ Hz, 1H), 2.77-2.74 (m, 1H), 2.56 (td, $J = 12.3, 3.5$ Hz, 1H), 2.35-2.18 (m, 3H), 1.84-1.79 (m, 2H), 1.75-1.68 (m, 2H), 1.63-1.56 (m, 2H), 1.50-1.46 (m, 2H), 1.26-1.19 (m, 1H), 0.98-0.91 (m, 1H), 0.13 (s, 9H); ^{13}C NMR (CDCl_3 , 150 MHz): δ 205.6 (C), 114.9 (C), 104.7 (C), 86.5 (C), 50.0 (CH), 39.1 (CH_2), 34.4 (CH), 32.1 (CH_2), 30.9 (CH_2), 28.7 (CH_2), 25.6 (CH_2), 23.6 (CH_2), 17.1 (CH_2), -0.1 (3 x CH_3); HRMS (EI) $\text{C}_{16}\text{H}_{25}\text{NOSi}$: 275.1705; found: 275.1701.

2-Oxo-12-(4-trimethylsilylbut-3-ynyl)-cyclododecanecarbonitrile (**18**)



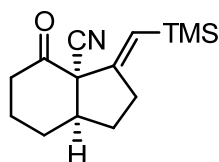
A single diastereomer **18** was obtained as a yellow oil (69% yield).

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2243, 2173, 1721; ¹H NMR (CDCl₃, 400 MHz): δ 3.60 (d, J = 8.0 Hz, 1H), 3.12-3.01 (m, 1H), 2.59-2.28 (m, 4H), 2.15-2.07 (m, 1H), 1.97-1.89 (m, 1H), 1.83-1.19 (m, 16H), 0.02 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz): δ 201.1 (C), 115.2 (C), 104.7 (C), 86.6 (C), 48.5 (CH), 36.7 (CH₂), 34.3 (CH), 29.1 (CH₂), 26.4 (CH₂), 25.9 (CH₂), 23.2 (CH₂), 23.0 (CH₂), 22.5 (CH₂), 22.3 (CH₂), 21.8 (CH₂), 21.0 (CH₂), 17.2 (CH₂), 0.0 (3 x CH₃); HRMS (EI) C₂₀H₃₃NOSi: 331.2331; found: 331.2339.

The General Procedure for ZnI₂ Mediated Cyclization in the Synthesis of Compounds **21**, **23**, **24**, **25**, **26**, **27**, **28**, **29** and **30**.

The general procedure is illustrated immediately below with compound **21** as a specific example.

(3 α R,7 α R,E)-4-oxo-3-((trimethylsilyl)methylene)-octahydro-1H-indene-3 α -carbonitrile (**21**)

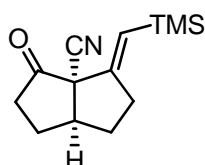


To a stirred solution of compound **11** (371 mg, 1.54 mmol) in toluene (15 mL) was added anhydrous ZnI₂ (478 mg, 1.54 mmol) in one portion at room temperature. The resulting mixture was allowed to stir at reflux for 3 h. After cooling the mixture to room temperature, water (10 mL) was added to quench the reaction. The aqueous layer was separated and extracted with Et₂O (3 x 10 mL). The combined organic extracts were washed with brine, dried over MgSO₄, filtered and concentrated. The crude product thus obtained was purified with flash chromatography on silica gel (EtOAc:*n*-hexane=1:4) to give compound **21** (280 mg, 88% yield) as a white solid, which was recrystallized from EtOAc and CH₂Cl₂ to form a crystalline compound.

mp = 87.0–88.0 °C; IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2238, 1715, 1616; ¹H NMR (CDCl₃, 600 MHz): δ 5.62 (t, J = 2.5 Hz, 1H), 2.79-2.76 (m, 1 H), 2.58-2.54 (m, 2H), 2.45

(ddd, $J = 14.8, 4.5, 1.5$ Hz, 1H), 2.29 (ddd, $J = 14.8, 12.3, 5.3$ Hz, 1H), 2.14-2.07 (m, 1H), 1.98-1.94 (m, 1H), 1.89-1.82 (m, 1H), 1.79-1.70 (m, 2H), 1.40 (tdd, $J = 20.0, 11.0, 3.4$ Hz, 1H), 0.09 (s, 9H); ^{13}C NMR (CDCl_3 , 150 MHz): δ 201.7 (C), 152.8 (C), 128.6 (CH), 118.9 (C), 62.5 (C), 48.9 (CH), 37.6 (CH_2), 29.6 (CH_2), 28.6 (CH_2), 26.2 (CH_2), 23.9 (CH_2), -1.0 (3 x CH_3); HRMS (EI) $\text{C}_{14}\text{H}_{21}\text{NOSi}$: 247.1392; found: 247.1392.

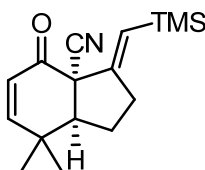
(3 α R,6 α S,E)-3-oxo-4-((trimethylsilyl)methylene)-octahydropentalene-3 α -carbonitrile (23)



Compound **23** was obtained as a white solid (85% yield), which was recrystallized from EtOAc and CH_2Cl_2 to form a crystalline compound.

mp = 57.0–58.0 °C; IR (CH_2Cl_2 cast, cm^{-1}) ν_{max} 2236, 1749, 1616; ^1H NMR (CDCl_3 , 600 MHz): δ 6.04 (t, $J = 2.4$ Hz, 1H), 3.15 (ddd, $J = 7.5, 7.5, 3.3$ Hz, 1H), 2.58-2.54 (m, 1H), 2.50-2.36 (m, 3H), 2.20-2.12 (m, 2H), 1.77 (dtt, $J = 13.3, 4.0, 3.8$ Hz, 1H), 1.64-1.57 (m, 1H), 0.09 (s, 9H); ^{13}C NMR (CDCl_3 , 150 MHz): δ 206.4 (C), 151.8 (C), 129.7 (CH), 118.9 (C), 58.6 (C), 48.3 (CH), 36.6 (CH_2), 30.3 (CH_2), 29.9 (CH_2), 24.2 (CH_2), -0.9 (3 x CH_3); HRMS (EI) $\text{C}_{13}\text{H}_{19}\text{NOSi}$: 233.1236; found: 233.1230.

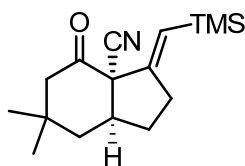
(3 α R,7 α S,E)-7,7-dimethyl-4-oxo-3-((trimethylsilyl)methylene)-2,3,3 α ,4,7,7 α -hexahydro-1H-indene-3 α -carbonitrile (24)



Compound **24** was obtained as a yellow oil (77% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν_{max} 2236, 1691, 1619; ^1H NMR (CDCl_3 , 600 MHz): δ 6.67 (dd, $J = 10.0, 2.0$ Hz, 1H), 6.15 (t, $J = 2.5$ Hz, 1H), 5.96 (d, $J = 10.0$ Hz, 1H), 2.63 (ddd, $J = 12.2, 6.5, 2.0$ Hz, 1H), 2.44 (dtd, $J = 17.2, 9.2, 2.0$ Hz, 1H), 2.37 (dddd, $J = 20.2, 10.1, 8.2, 2.9$ Hz, 1H), 2.01 (dddd, $J = 12.6, 7.3, 6.5, 1.7$ Hz, 1H), 1.62-1.54 (m, 1H), 1.49 (s, 3H), 1.16 (s, 3H), 0.1 (s, 9H); ^{13}C NMR (CDCl_3 , 150 MHz): δ 187.0 (C), 158.5 (CH), 152.9 (C), 129.0 (CH), 124.6 (CH), 120.8 (C), 54.6 (C), 54.4 (CH), 35.1 (C), 29.9 (CH_2), 29.6 (CH_3), 27.6 (CH_2), 27.1 (CH_3), -0.8 (3 x CH_3); HRMS (EI) $\text{C}_{16}\text{H}_{23}\text{NOSi}$: 273.1549; found: 273.1547.

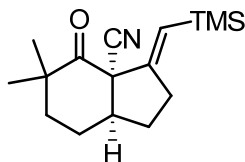
(3 α R,7 α S,E)-6,6-dimethyl-4-oxo-3-((trimethylsilyl)methylene)-octahydro-1*H*-indene-3 α -carbonitrile (**25**)



Compound **25** was obtained as a white solid (86% yield), which was recrystallized from EtOAc and CH₂Cl₂ to form a crystalline compound.

mp = 122.5–124.5 °C; IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2234, 1711, 1615; ¹H NMR (CDCl₃, 600 MHz): δ 5.59 (t, J = 2.5 Hz, 1H), 2.87 (tdd, J = 6.2, 6.1, 5.9 Hz, 1H), 2.66-2.53(m, 2H), 2.24-2.19 (m, 1H), 2.17(d, J = 14.2 Hz, 1H), 2.06 (dd, J = 14.3, 2.7 Hz, 1H), 1.77 (dd, J = 8.0, 5.3 Hz, 1H), 1.52 (ddd, J = 13.7, 5.7, 2.5 Hz, 1H), 1.29 (t, J = 13.4 Hz, 1H), 0.99 (s, 3H), 0.90 (s, 3H), 0.07 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz): δ 202.3 (C), 153.1 (C), 129.0 (CH), 119.0 (C), 61.7 (C), 49.9 (CH₂), 45.3 (CH), 39.8 (CH₂), 34.9 (C), 31.3 (CH₃), 30.0 (CH₂), 28.6 (CH₂), 24.6 (CH₃), -1.1 (3 x CH₃); HRMS (EI) C₁₆H₂₅NOSi: 275.1705; found: 275.1706.

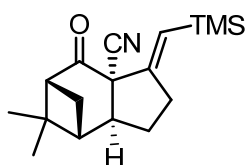
(3 α R,7 α S,E)-5,5-dimethyl-4-oxo-3-((trimethylsilyl)methylene)-octahydro-1*H*-indene-3 α -carbonitrile (**26**)



Compound **26** was obtained as a colorless oil (83% yield).

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2236, 1703, 1616; ¹H NMR (CDCl₃, 600 MHz): δ 5.64 (t, J = 2.5 Hz, 1H), 2.77-2.73 (m, 1H), 2.58-2.49 (m, 2H), 2.08-2.01 (m, 1H), 1.78-1.73 (m, 1H), 1.72-1.68 (m, 1H), 1.64-1.62 (m, 2H), 1.55-1.48 (m, 1H), 1.11 (s, 3H), 0.95 (s, 3H), 0.04 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz): δ 205.5 (C), 152.6 (C), 128.5 (CH), 119.8 (C), 60.5 (C), 48.2 (CH), 44.2 (C), 36.7 (CH₂), 30.1 (CH₂), 28.7 (CH₂), 27.2 (CH₃), 26.5 (CH₃), 22.4 (CH₂), -1.1 (3 x CH₃); HRMS (EI) C₁₆H₂₅NOSi: 275.1705; found: 275.1709.

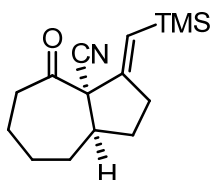
(3 α R,5*R*,7*R*,7 α S,E)-6,6-dimethyl-4-oxo-3-((trimethylsilyl)methylene)-octahydro-5,7-methano-3 α *H*-indene-3 α -carbonitrile (**27**)



Compound **27** was obtained as a white solid (85% yield), which was recrystallized from EtOAc and CH₂Cl₂ to form a crystalline compound.

mp = 79.0–80.0 °C; IR (CH₂Cl₂ cast, cm⁻¹) v_{max} 2235, 1719, 1615; ¹H NMR (CDCl₃, 600 MHz): δ 5.84 (t, *J* = 2.1 Hz, 1H), 2.98 (d, *J* = 8.8 Hz, 1H), 2.64 (td, *J* = 7.9, 2.1 Hz, 2H), 2.60 (t, *J* = 5.5 Hz, 1H), 2.36-2.30 (m, 2H), 2.12-2.09 (m, 1H), 1.72-1.66 (m, 1 H), 1.45 (d, *J* = 11.4 Hz, 1H), 1.31 (s, 3H), 0.94 (s, 3H), 0.03 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz): δ 202.0 (C), 154.4 (C), 126.1 (CH), 120.2 (C), 56.5 (C), 56.2 (CH), 46.8 (CH), 45.2 (CH), 44.8 (C), 31.9 (CH₂), 29.4 (CH₂), 25.8 (CH₃), 22.2 (CH₂), 21.9 (CH₃), -1.0 (3 x CH₃); HRMS (EI) C₁₇H₂₅NOSi: 287.1705; found: 287.1704.

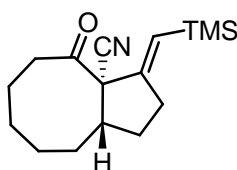
(3α*R*,8α*R*,*E*)-4-oxo-3-((trimethylsilyl)methylene)-decahydroazulene-3α-carbonitrile (28)



Compound **28** was obtained as a yellow oil (80% yield).

IR (CH₂Cl₂ cast, cm⁻¹) v_{max} 2239, 1710, 1620; ¹H NMR (CDCl₃, 600 MHz): δ 5.70 (dd, *J* = 2.9, 1.9 Hz, 1H), 2.86-2.82 (m, 1H), 2.63 (ddd, *J* = 16.4, 11.7, 5.5 Hz, 1H), 2.59-2.54 (m, 1H), 2.37-2.30 (m, 1H), 2.11-1.91 (m, 6H), 1.82-1.76 (m, 1H), 1.66 (dd, *J* = 11.8, 8.0 Hz, 1H), 1.35-1.28 (m, 1H), 0.09 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz): δ 202.2 (C), 152.8 (C), 129.4 (CH), 118.4 (C), 63.1 (C), 49.5 (CH), 42.8 (CH₂), 31.7 (CH₂), 31.5 (CH₂), 30.9 (CH₂), 27.3 (CH₂), 22.5 (CH₂), -0.8 (3 x CH₃); HRMS (EI) C₁₅H₂₃NOSi: 261.1549; found: 261.1552.

(3α*R*,9α*S*,*E*)-4-oxo-3-((trimethylsilyl)methylene)-decahydro-1*H*-cyclopenta[8]annulene-3α-carbonitrile (29)

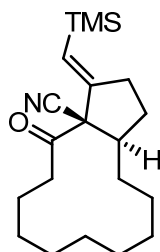


Compound **29** was obtained as a white solid (81% yield), which was recrystallized from EtOAc and CH₂Cl₂ to form a crystalline compound.

mp = 87.0–88.0 °C; IR (CH₂Cl₂ cast, cm⁻¹) v_{max} 2238, 1703, 1613; ¹H NMR (CDCl₃, 600 MHz): δ 5.49 (t, *J* = 2.5 Hz, 1H), 2.81-2.76 (m, 1H), 2.66 (ddd, *J* = 17.6, 8.8, 0.8 Hz, 1H), 2.57 (dt, *J* = 3.3, 9.7 Hz, 1H), 2.50 (dddd, *J* = 17.4, 9.8, 8.0, 2.8 Hz, 1H), 2.26 (ddd, *J* = 11.6, 5.4, 3.3 Hz, 1H), 2.02-1.94 (m, 2H), 1.92-1.84 (m, 2H), 1.79-1.70 (m, 2H), 1.69-1.61 (m, 2H), 1.28-1.21 (m, 1H), 0.99-0.93 (m, 1H), 0.07 (s, 9H); ¹³C

NMR (CDCl₃, 150 MHz): δ 206.7 (C), 152.6 (C), 127.8 (CH), 116.7 (C), 66.3 (C), 45.0 (CH), 37.5 (CH₂), 31.1 (CH₂), 30.8 (CH₂), 30.7 (CH₂), 30.3 (CH₂), 25.7 (CH₂), 25.2 (CH₂), -1.0 (3 x CH₃); HRMS (EI) C₁₆H₂₅NOSi: 275.1705; found: 275.1703.

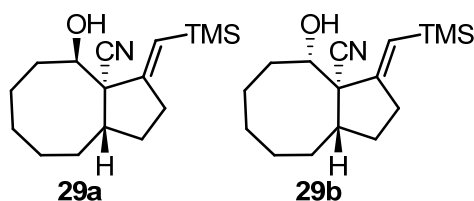
(3 α S,13 α R,E)-4-oxo-3-((trimethylsilyl)methylene)-tetradecahydro-1H-cyclopenta[12]annulene-3 α -carbonitrile (30)



A single diastereomer **30** was obtained as a white solid (78% yield), which was recrystallized from EtOAc and CH₂Cl₂ to form a crystalline compound.

mp = 145.5–147.5 °C; IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2235, 1710, 1613; ¹H NMR (CDCl₃, 600 MHz): δ 5.65 (dd, *J* = 2.9, 1.6 Hz, 1H), 2.79–2.62 (m, 3H), 2.47–2.35 (m, 2H), 2.21–2.10 (m, 1H), 2.08–1.99 (m, 1H), 1.65–1.36 (m, 4H), 1.30–1.08 (m, 12H), 0.06 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz): δ 203.7 (C), 155.6 (C), 129.1 (CH), 117.8 (C), 68.4 (C), 44.5 (CH), 33.8 (CH₂), 32.5 (CH₂), 31.1 (C), 27.3 (CH₂), 26.0 (CH₂), 24.5 (CH₃), 24.0 (CH₂), 23.2 (CH₂), 22.3 (CH₂), 22.2 (CH₂), 21.8 (CH₂), -1.0 (3 x CH₃); HRMS (EI) C₂₀H₃₃NOSi: 331.2331; found: 331.2339.

(3 α R,4R,9 α S,E)-4-hydroxy-3-((trimethylsilyl)methylene)-decahydro-1H-cyclopeanta[8]annulene-3 α -carbonitrile (29a) and (3 α R,4S,9 α S,E)-4-hydroxy-3-((trimethylsilyl)methylene)-decahydro-1H-cyclopenta[8]annulene-3 α -carbonitrile (29b)



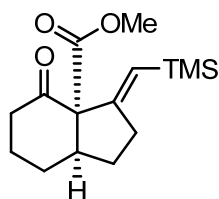
To a stirred solution of compound **29** (45 mg, .016 mmol) in MeOH (4 mL) was added NaBH₄ (6 mg, 0.16 mmol) at 0 °C. The resulting mixture was stirred for 30 min at the same temperature. H₂O (4 mL) was added to quench the reaction. The aqueous layer was separated and extracted with diethyl ether (3 x 10 mL). The combined organic extracts were washed with brine, dried over MgSO₄, filtered and concentrated. The crude product thus obtained was purified with flash chromatography on silica gel (EtOAc:*n*-hexane=1:4) to give compound **29a** (33 mg, 75% yield) as a white solid,

which was recrystallized from EtOAc and CH₂Cl₂ to form a crystalline compound.
mp = 121.0–123.0 °C; IR (CH₂Cl₂ cast, cm⁻¹) v_{max} 3458, 2234, 1624; ¹H NMR (CDCl₃, 600 MHz): δ 5.85 (dd, *J* = 2.0, 1.0 Hz, 1H), 4.14 (dd, *J* = 4.4, 1.6 Hz, 1H), 2.57–2.53 (m, 1H), 2.50 (dd, *J* = 8.8, 7.0 Hz, 1H), 2.12 (dddd, *J* = 17.4, 13.6, 7.2, 3.2 Hz, 1H), 2.09–2.04 (m, 2H), 1.98–1.92 (m, 3H), 1.81–1.75 (m, 2H), 1.73–1.68 (m, 1H), 1.63–1.58 (m, 2H), 1.53–1.46 (m, 2H), 1.37 (tdd, *J* = 12.7, 12.3, 6.9 Hz, 1H), 0.11 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz): δ 162.1 (C), 124.5 (CH), 121.5 (C), 73.9 (CH), 55.9 (C), 38.9 (CH), 35.3 (CH₂), 33.2 (CH₂), 32.4 (CH₂), 29.1 (CH₂), 26.6 (CH₂), 24.2 (CH₂), 17.8 (CH₂), -0.6 (3 x CH₃); HRMS (EI) C₁₆H₂₇NOSi: 277.1862; found: 277.1863.

Further elution gave compound **29b** (7 mg, 15% yield) as a white solid, which was recrystallized from EtOAc and CH₂Cl₂ to form a crystalline compound.

mp = 123–125 °C; IR (CH₂Cl₂ cast, cm⁻¹) v_{max} 3436, 2232, 1622; ¹H NMR (CDCl₃, 600 MHz): δ 5.94 (d, *J* = 2.6 Hz, 1H), 3.28–3.25 (m, 1H), 2.47 (dd, *J* = 14.6, 5.9 Hz, 1H), 2.40–2.38 (m, 1H), 2.17–2.11 (m, 2H), 2.09–2.05 (m, 2H), 2.00–1.95 (m, 1H), 1.94–1.89 (m, 2H), 1.85–1.79 (m, 1H), 1.75–1.70 (m, 1H), 1.66–1.59 (m, 2H), 1.52–1.42 (m, 2H), 1.31 (tdd, *J* = 12.9, 12.3, 6.9 Hz, 1H), 0.12 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz): δ 160.2 (C), 127.5 (CH), 120.3 (C), 76.3 (CH), 43.5 (CH), 35.3 (CH₂), 32.8 (CH₂), 32.7 (CH₂), 31.5 (C), 29.7 (CH₂), 26.2 (CH₂), 24.2 (CH₂), 23.3 (CH₂), -0.4 (3 x CH₃); HRMS (EI) C₁₆H₂₇NOSi: 277.1862; found: 277.1864.

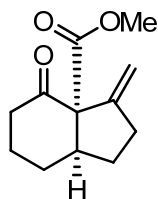
(3α*S*,7α*R*,*E*)-methyl-4-oxo-3-((trimethylsilyl)methylene)octahydro-1*H*-indene-3α-carboxylate (39**)**



A single diastereomer **39** was obtained as a yellow oil (77% yield).

IR (CH₂Cl₂ cast, cm⁻¹) v_{max} 2900, 1738, 1717, 1247, 839; ¹H NMR (CDCl₃, 400 MHz): δ 5.40 (t, *J* = 2.8 Hz, 1H), 3.71 (s, 3H), 2.98–2.92 (m, 1H), 2.49–2.42 (m, 2H), 2.35–2.31 (m, 2H), 1.95–1.88 (m, 1H), 1.82–1.75 (m, 2H), 1.70–1.56 (m, 2H), 1.55–1.40 (m, 1H), 0.09 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz): δ 206.4 (C), 171.2 (C), 155.3 (C), 125.8 (CH), 74.5 (C), 52.4 (CH₃), 46.8 (CH₂), 39.0 (CH₂), 29.4 (CH₂), 28.6 (CH₂), 26.2 (CH₂), 23.9 (CH₂), -0.9 (3 x CH₃); HRMS (EI) C₁₅H₂₄O₃Si: 280.1495; found: 280.1504.

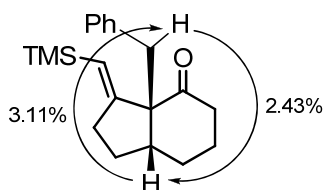
(3α*S*,7α*R*)-methyl 3-methylene-4-oxooctahydro-1*H*-indene-3α-carboxylate (40**)**



A single diastereomer **40** was obtained as a yellow oil (71% yield).

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 2949, 1732, 1716, 1434, 1229, 1045, 898; ¹H NMR (CDCl₃, 400 MHz): δ 5.21 (t, J = 2.0 Hz, 1H), 4.95 (t, J = 2.4 Hz, 1H), 3.73 (s, 3H), 3.04-2.97 (m, 1H), 2.51-2.31 (m, 4H), 1.96-1.80 (m, 3 H), 1.71-1.62 (m, 1 H), 1.56-1.47 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ 205.8 (C), 171.0 (C), 147.8 (C), 111.7 (CH₂), 71.7 (C), 52.5 (CH₃), 47.5 (CH₂), 39.1 (CH₂), 29.5 (CH₂), 28.0 (CH₂), 25.8 (CH₂), 23.7 (CH₂); HRMS (EI) C₁₂H₁₆O₃: 208.1099; found: 208.1094.

(3 α R,7 α R,E)-3 α -benzyl-3-((trimethylsilyl)methylene)hexahydro-1*H*-inden-4(2*H*)-one (**41**)

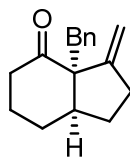


To a solution of naphthalene (130 mg, 1.01 mmol) in THF (5 mL), were added lithium metal (7 mg, 1.01 mmol) in small pieces. The reaction mixture was stirred at room temperature under an argon atmosphere until lithium metal was completely dissolved (~3 h). In another flask, a solution of **21** (50 mg, 0.20 mmol) in THF (5 mL) at -45 °C under an argon atmosphere was added previously prepared solution of lithium naphthalenide (~2 mL) until the solution become dark green color. After stirring the mixture for 30 min at -45 °C, BnBr (0.1 mL, 0.71 mmol) was added by syringe and maintained for 2 h at the same temperature. The reaction mixture was allowed to roomtemperature and stirred for another 1 h, then diluted with water and aqueous NH₄Cl solution and extracted with EtOAc (3 X 10 mL). The combined organic layer was dried with MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane: 0.1/0.9) to afford **41** (55 mg, 87% yield) as a colorless oil.

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 3027, 2950, 1700, 1607, 1453, 1247, 848; ¹H NMR (400 MHz, CDCl₃): δ 7.28-7.15 (m, 5H), 5.31 (t, J = 2.4 Hz, 1H), 3.47 (d, J = 14.0 Hz, 1H), 2.60-2.53 (m, 1H), 2.47 (d, J = 14.0 Hz, 1H), 2.29-2.17 (m, 3H), 1.96-1.77 (m, 2H), 1.65-1.55 (m, 3H), 1.42-1.35 (m, 2H), 0.12 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 211.6 (CO), 162.8 (C), 139.4 (C), 130.5 (CH), 128.4 (CH), 126.2 (CH), 121.4 (CH), 68.1 (C), 44.1 (CH), 41.1 (CH₂), 39.5 (CH₂), 29.5 (CH₂), 29.4 (CH₂), 28.8 (CH₂), 23.6

(CH₂), -0.4 (3 x CH₃); HRMS (EI) C₂₀H₂₈OSi: 312.1909; found: 312.1905.

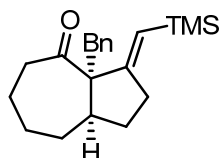
(3*αR*,7*αR*)-3*α*-benzyl-3-methylenehexahydro-1*H*-inden-4(2*H*)-one (42)



To a solution of naphthalene (183 mg, 1.43 mmol) in THF (5 mL), were added lithium metal (10 mg, 1.43 mmol) in small pieces. The reaction mixture was stirred at room temperature under an argon atmosphere until lithium metal was completely dissolved (~3 h). In another flask, a solution of **35** (50 mg, 0.29 mmol) in THF (5 mL) at -45 °C under an argon atmosphere was added previously prepared solution of lithium naphthalenide (~2 mL) until the solution become dark green color. After stirring the mixture for 30 min at -45 °C, BnBr (0.1 mL, 1.00 mmol) was added by syringe and maintained for 2 h at the same temperature. The reaction mixture was allowed to roomtemperature and stirred for another 1 h, then diluted with water and aqueous NH₄Cl solution and extracted with EtOAc (3 X 10 mL). The combined organic layer was dried with MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane: 0.1/0.9) to afford **42** (41 mg, 58% yield) as a colorless oil.

IR (CH₂Cl₂ cast, cm⁻¹) ν_{\max} 3027, 2934, 1700, 1453, 1141, 895, 703; ¹H NMR (400 MHz, CDCl₃): δ 7.28-7.15 (m, 5H), 5.03 (t, *J* = 2.2 Hz, 1H), 5.03 (t, *J* = 2.2 Hz, 1H), 3.58 (d, *J* = 14.0 Hz, 1H), 2.60-2.54 (m, 1H), 2.50 (d, *J* = 14.0 Hz, 1H), 2.35-2.21 (m, 3H), 1.97-1.88 (m, 1H), 1.83-1.75 (m, 1H), 1.67-1.52 (m, 3H), 1.44-1.35 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃): δ 211.6 (CO), 154.6 (C), 139.3 (C), 130.5 (CH), 128.3 (CH), 126.3 (CH), 108.4 (CH), 65.5 (C), 44.5 (CH), 41.2 (CH₂), 39.3 (CH₂), 29.5 (CH₂), 29.0 (CH₂), 28.5 (CH₂), 23.4 (CH₂); HRMS (EI) C₁₇H₂₀O: 240.1514; found: 240.1513.

(3*αR*,8*αR*,*E*)-3*α*-benzyl-3-((trimethylsilyl)methylene)octahydroazulen-4(5*H*)-one (43)

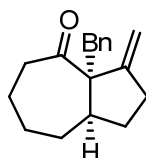


To a solution of naphthalene (123 mg, 0.96 mmol) in THF (5 mL), were added lithium metal (7 mg, 0.96 mmol) in small pieces. The reaction mixture was stirred at room temperature under an argon atmosphere until lithium metal was completely dissolved

(~3 h). In another flask, a solution of **28** (50 mg, 0.19 mmol) in THF (5 mL) at $-45\text{ }^{\circ}\text{C}$ under an argon atmosphere was added previously prepared solution of lithium naphthalenide (~2 mL) until the solution become dark green color. After stirring the mixture for 30 min at $-45\text{ }^{\circ}\text{C}$, BnBr (0.08 mL, 0.67 mmol) was added by syringe and maintained for 2 h at the same temperature. The reaction mixture was allowed to roomtemperature and stirred for another 1 h, then diluted with water and aqueous NH_4Cl solution and extracted with EtOAc (3 X 10 mL). The combined organic layer was dried with MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane: 0.2/0.9) to afford **43** (40 mg, 64% yield) as a colorless oil.

IR (CH_2Cl_2 cast, cm^{-1}) ν_{max} 3028, 2951, 1694, 1452, 1247, 841, 702; ^1H NMR (400 MHz, CDCl_3): δ 7.28-7.15 (m, 5H), 5.31 (dd, $J = 2.4$ and 2.8 Hz, 1H), 3.07 (d, $J = 13.6$ Hz, 1H), 2.92 (d, $J = 13.6$ Hz, 1H), 2.54-2.31 (m, 3H), 1.96-1.53 (m, 8H), 1.38-1.26 (m, 2H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 211.0 (CO), 163.5 (C), 139.2 (C), 131.3 (CH), 127.9 (CH), 126.2 (CH), 122.8 (CH), 68.5 (C), 42.6 (CH), 41.9 (CH_2), 41.0 (CH_2), 34.1 (CH_2), 29.2 (CH_2), 28.1 (CH_2), 26.5 (CH_2), 23.8 (CH_2), -0.3 (3 x CH_3); HRMS (EI) $\text{C}_{21}\text{H}_{30}\text{OSi}$: 326.2066; found: 326.2068.

(3 α R,8 α R)-3 α -benzyl-3-methyleneoctahydroazulen-4(5H)-one (**44**)

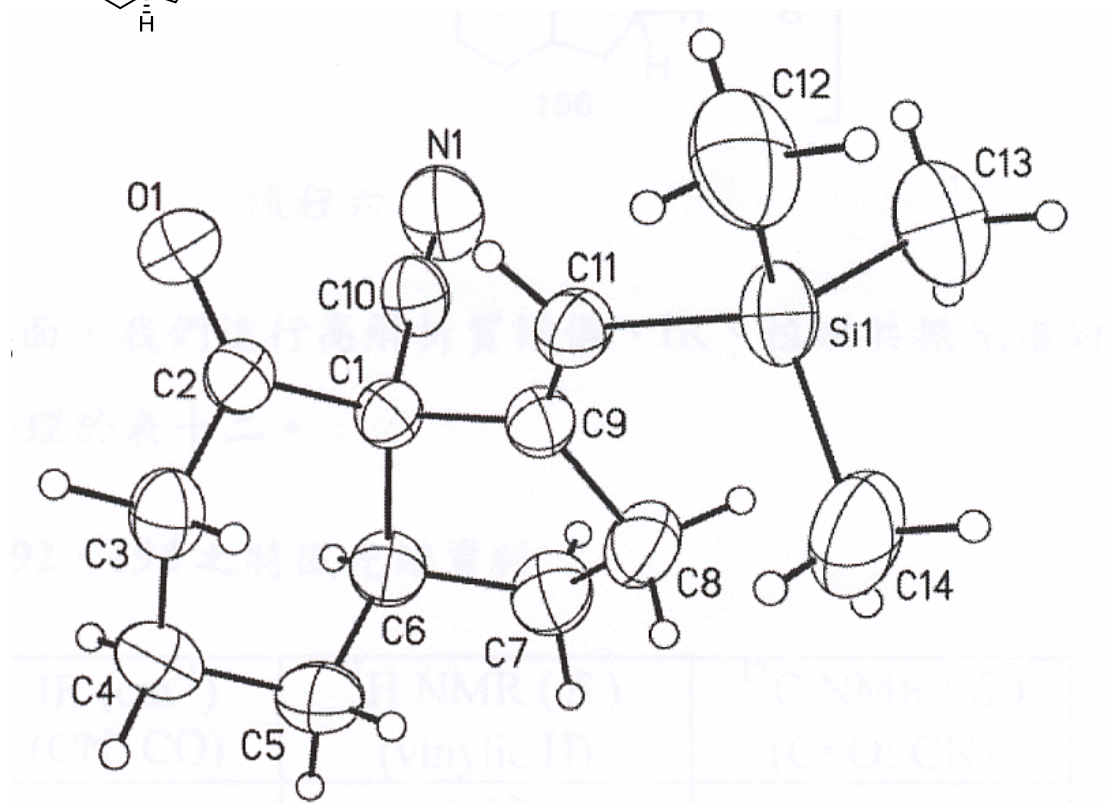
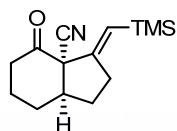


To a solution of naphthalene (85 mg, 0.66 mmol) in THF (2.5 mL), were added lithium metal (5 mg, 0.66 mmol) in small pieces. The reaction mixture was stirred at room temperature under an argon atmosphere until lithium metal was completely dissolved (~3 h). In another flask, a solution of **36** (25 mg, 0.13 mmol) in THF (2.5 mL) at $-45\text{ }^{\circ}\text{C}$ under an argon atmosphere was added previously prepared solution of lithium naphthalenide (~2 mL) until the solution become dark green color. After stirring the mixture for 30 min at $-45\text{ }^{\circ}\text{C}$, BnBr (0.06 mL, 0.46 mmol) was added by syringe and maintained for 2 h at the same temperature. The reaction mixture was allowed to roomtemperature and stirred for another 1 h, then diluted with water and aqueous NH_4Cl solution and extracted with EtOAc (3 X 10 mL). The combined organic layer was dried with MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/*n*-hexane: 0.1/0.9) to afford **44** (13.4 mg, 38% yield) as a colorless oil.

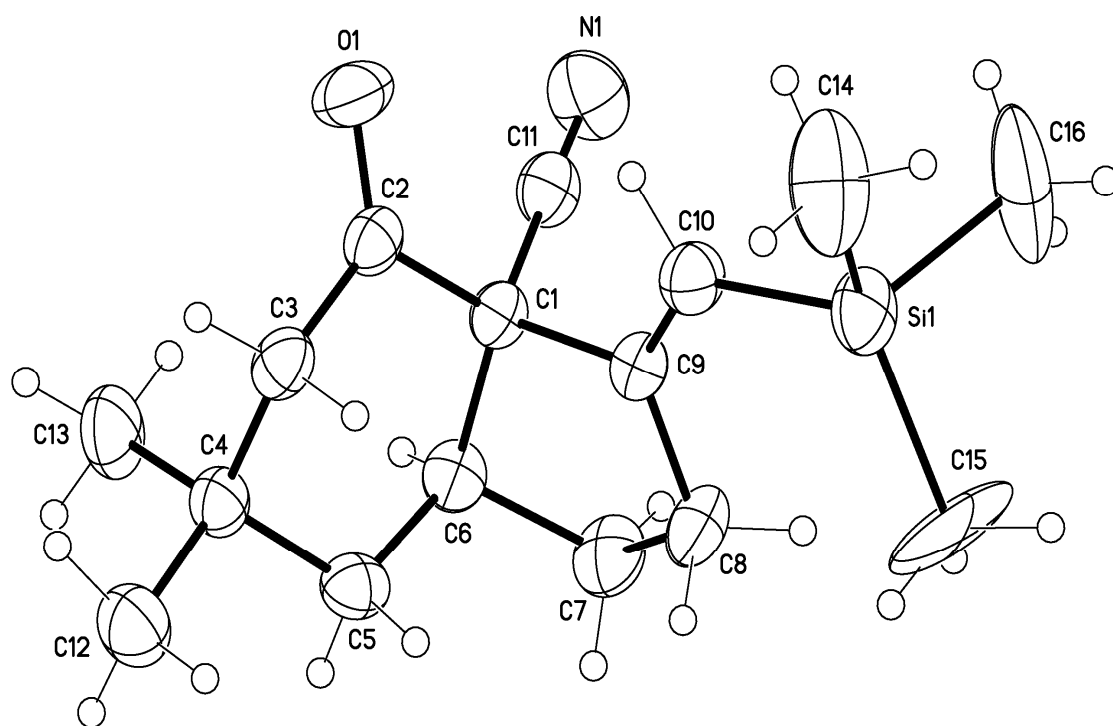
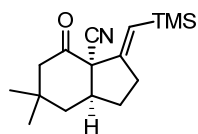
IR (CH_2Cl_2 cast, cm^{-1}) ν_{max} 3027, 2927, 1693, 1453, 702; ^1H NMR (400 MHz, CDCl_3): δ 7.29-7.15 (m, 5H), 5.09 (s, 1H), 4.77 (s, 1H), 3.01 (d, $J = 13.6$ Hz, 1H), 2.97 (d, $J =$

13.6 Hz, 1H), 2.55-2.61 (m, 4H), 2.01-1.41 (m, 6H), 1.39-1.16 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 211.0 (CO), 154.6 (C), 138.7 (C), 130.9 (CH), 127.8 (CH), 126.1 (CH), 109.0 (CH), 65.8 (C), 42.7 (CH), 42.3 (CH_2), 41.8 (CH_2), 34.2 (CH_2), 29.1 (CH_2), 28.4 (CH_2), 26.3 (CH_2), 24.1 (CH_2); HRMS (EI) $\text{C}_{18}\text{H}_{22}\text{O}$: 254.1671; found: 254.1657.

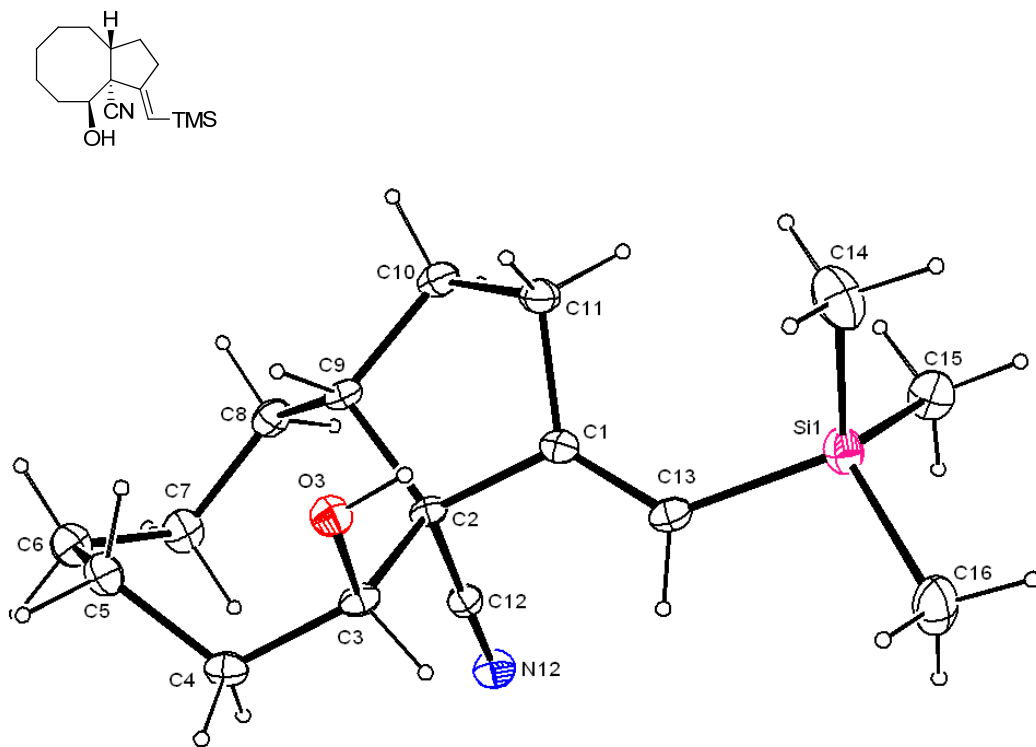
The X-ray analysis of compound **21** (CCDC 765390)



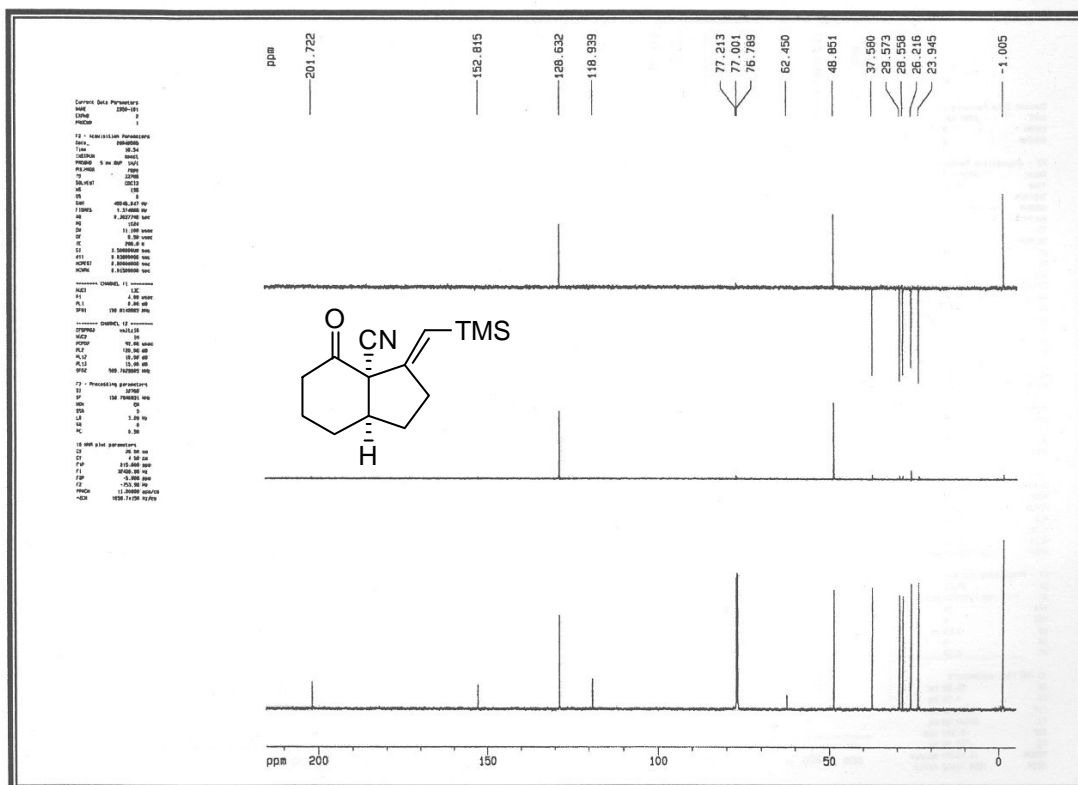
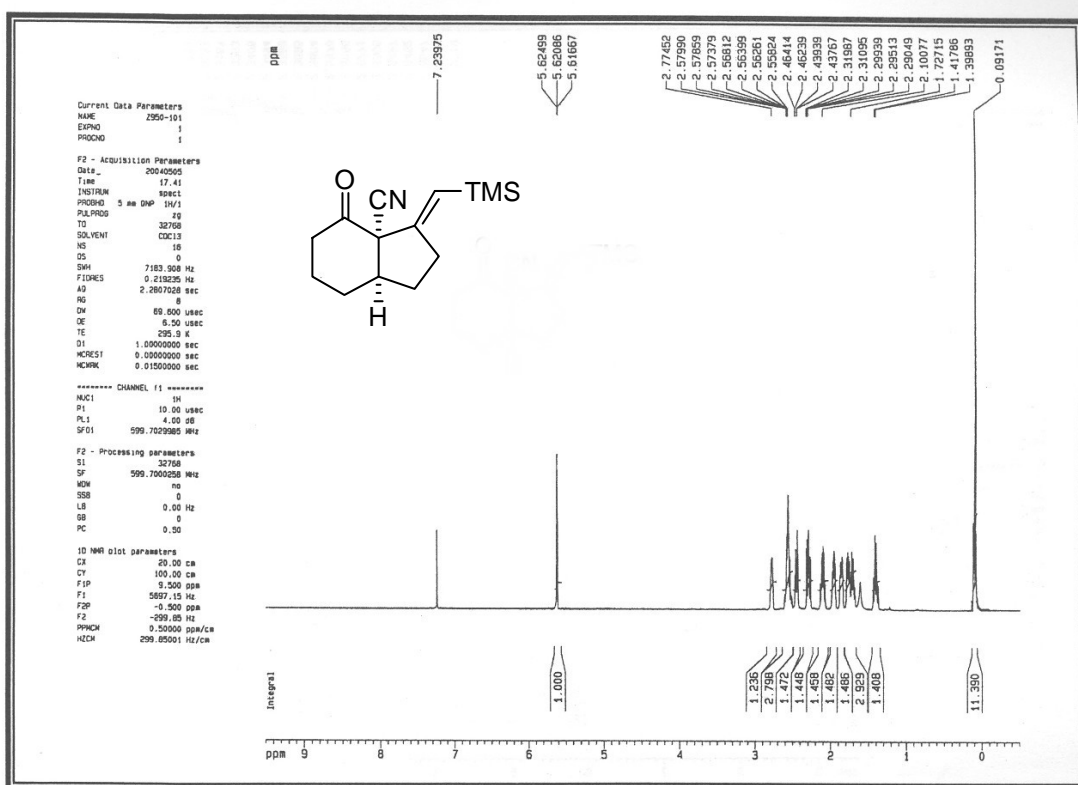
The X-ray analysis of compound **25** (CCDC 765388)



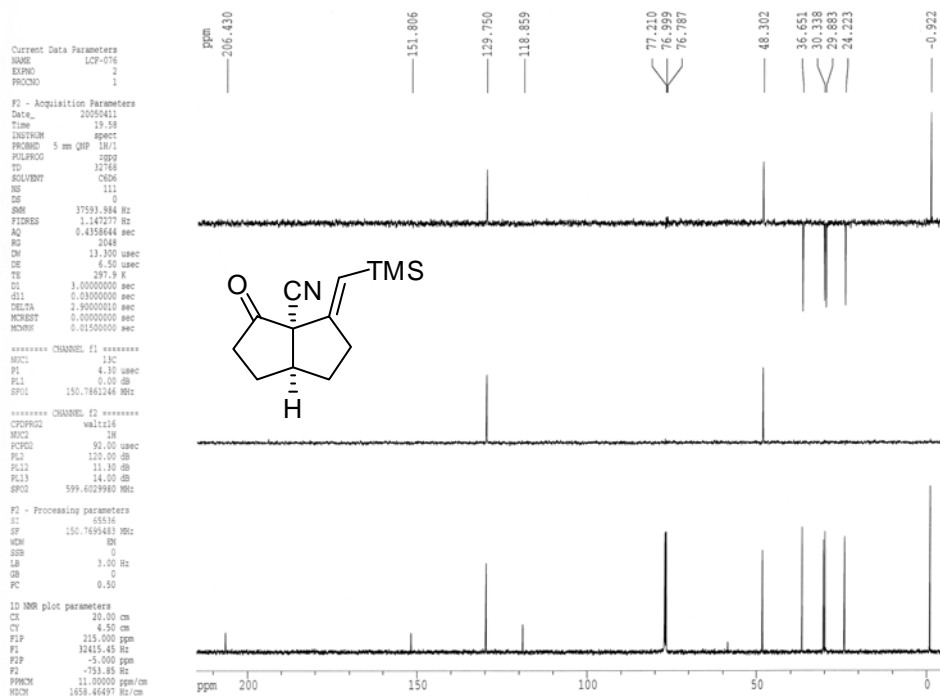
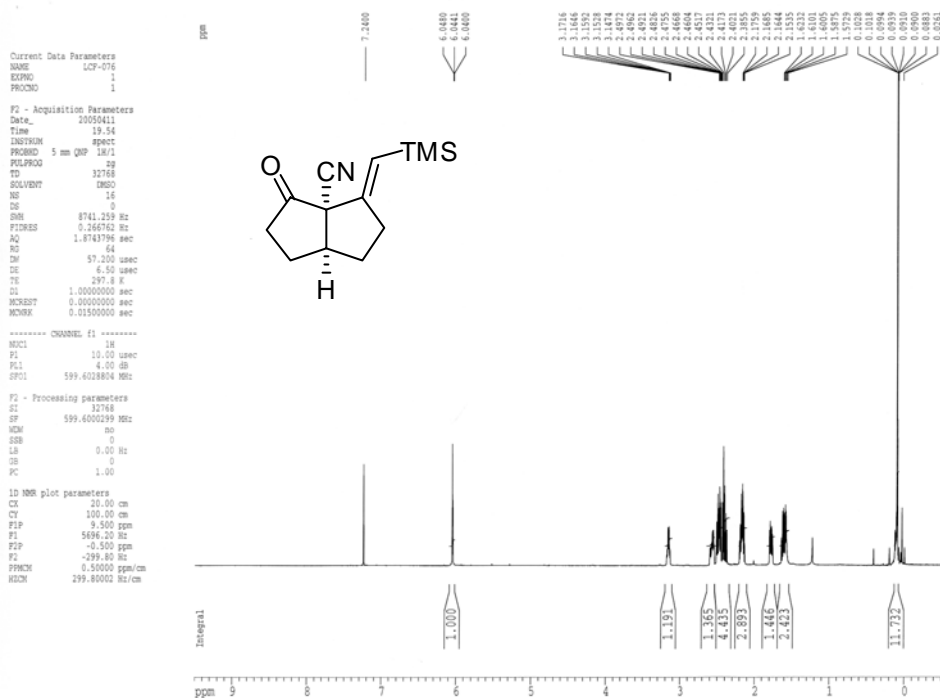
The X-ray analysis of compound **29a** (CCDC 765389)



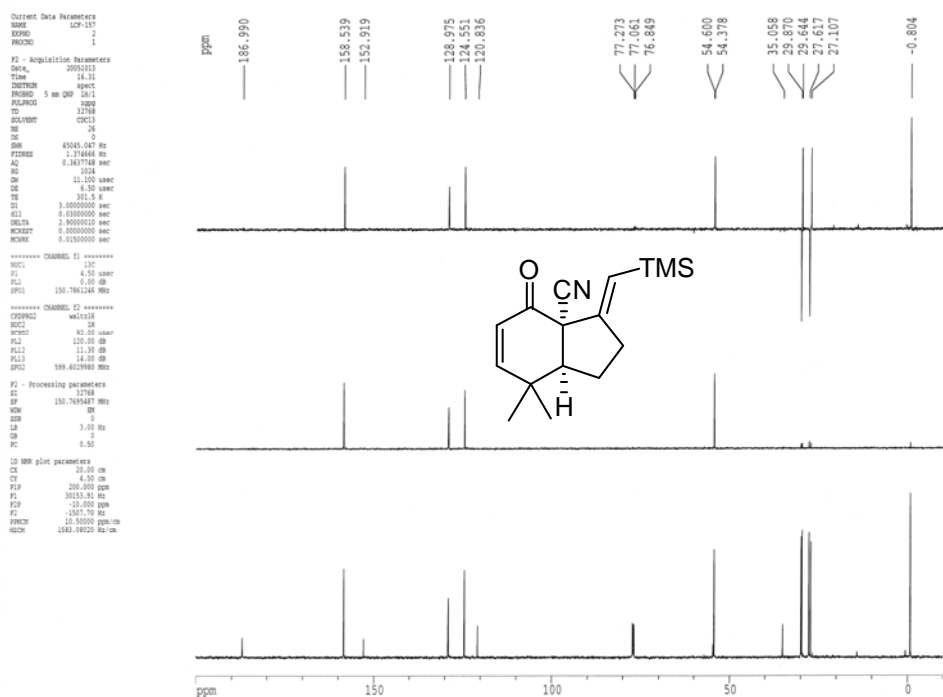
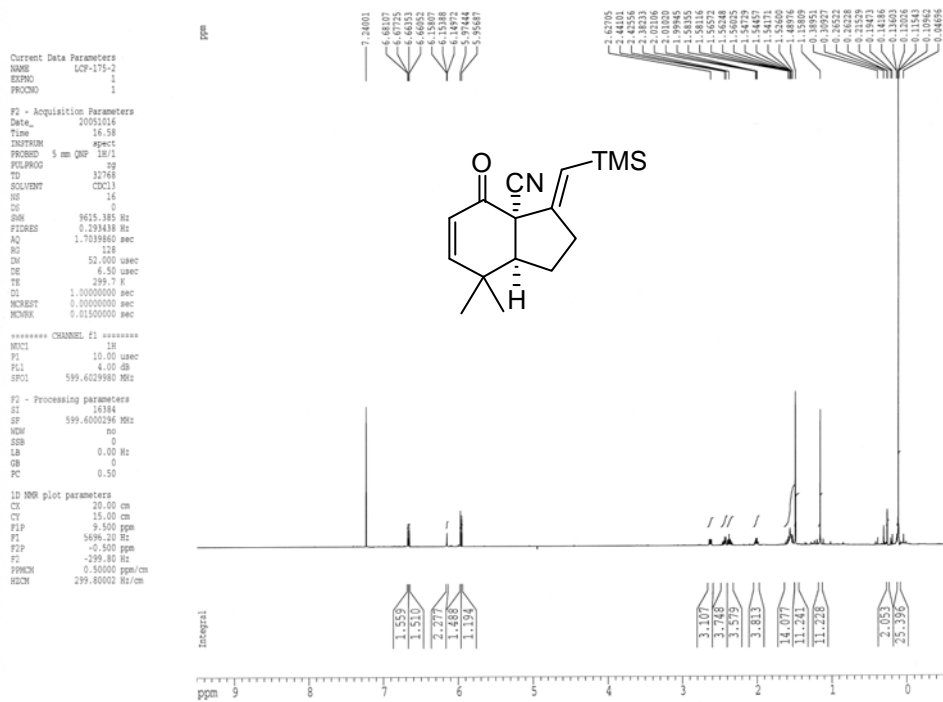
¹H and ¹³C NMR spectra for compound 21



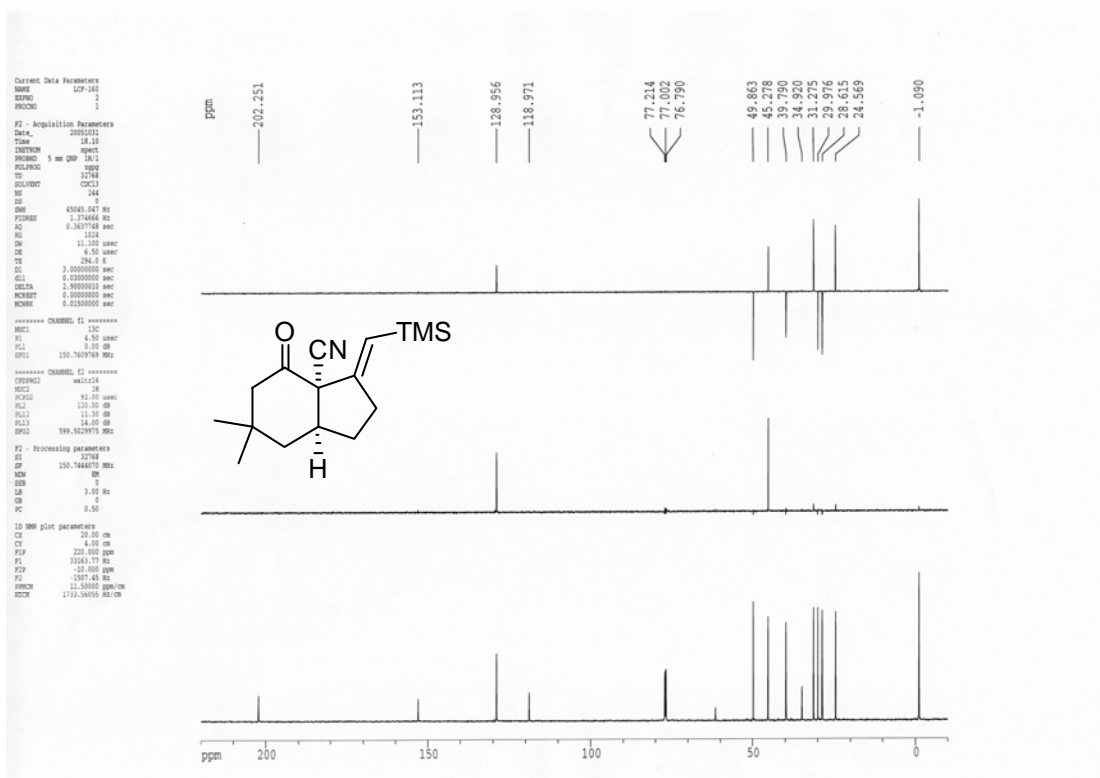
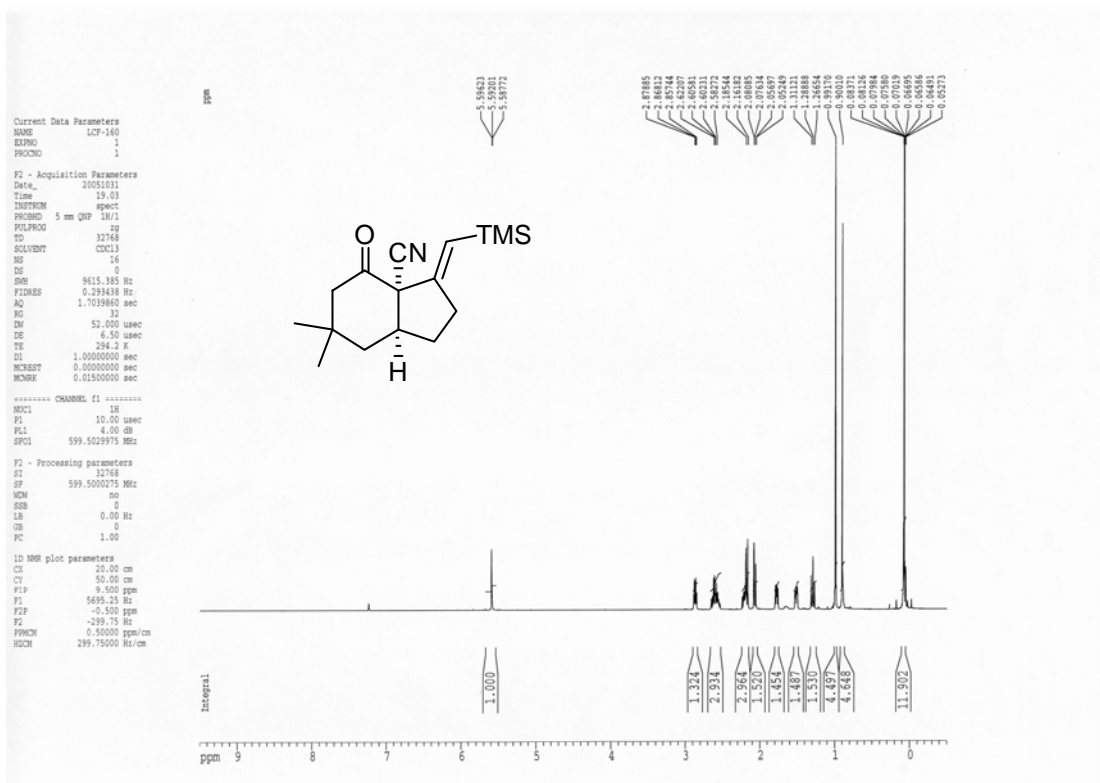
¹H and ¹³C NMR spectra for compound 23



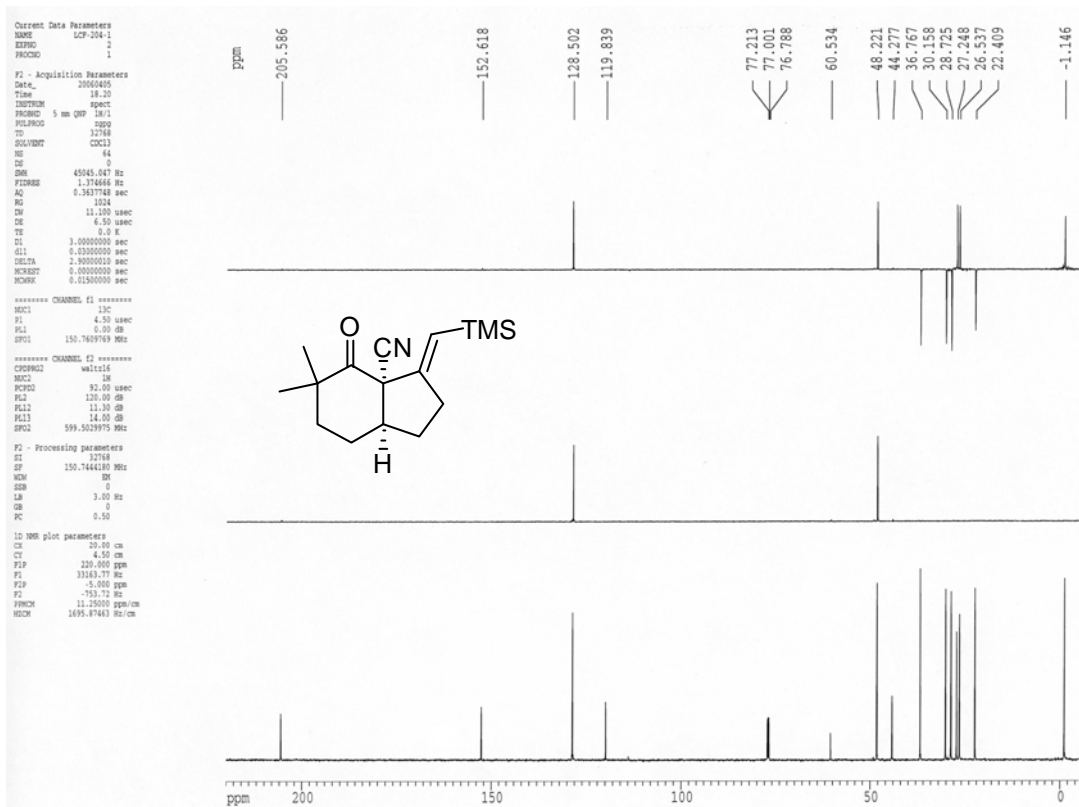
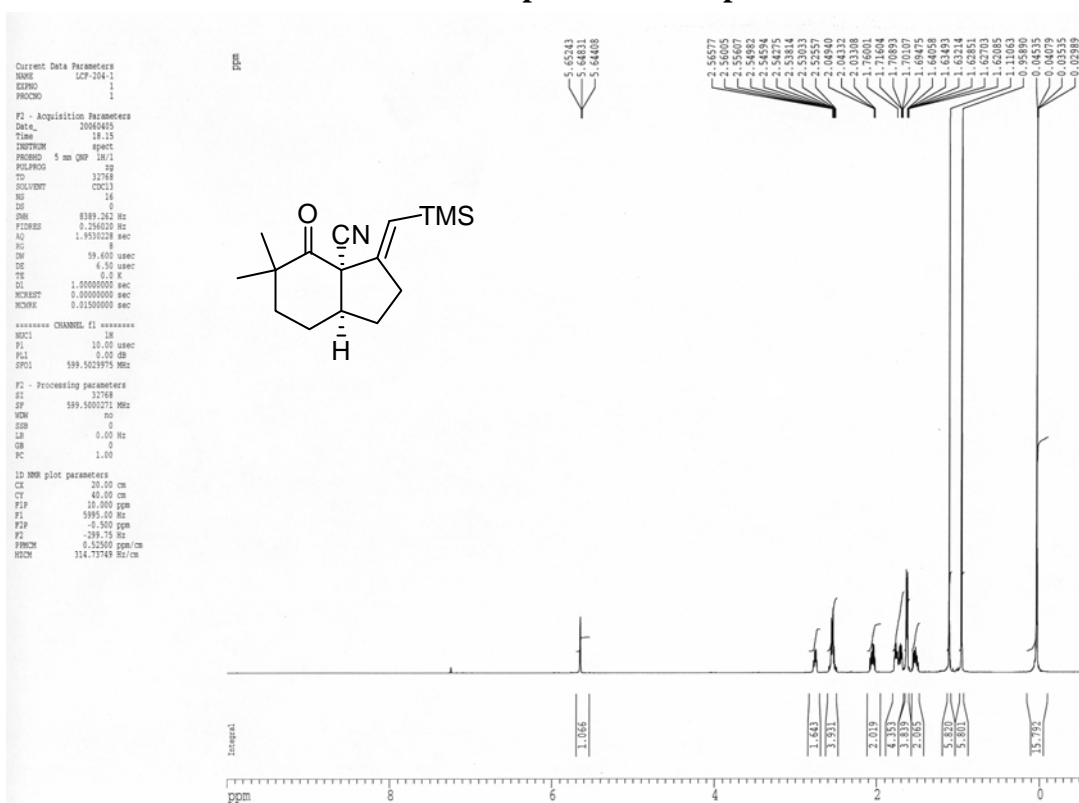
¹H and ¹³C NMR spectra for compound 24



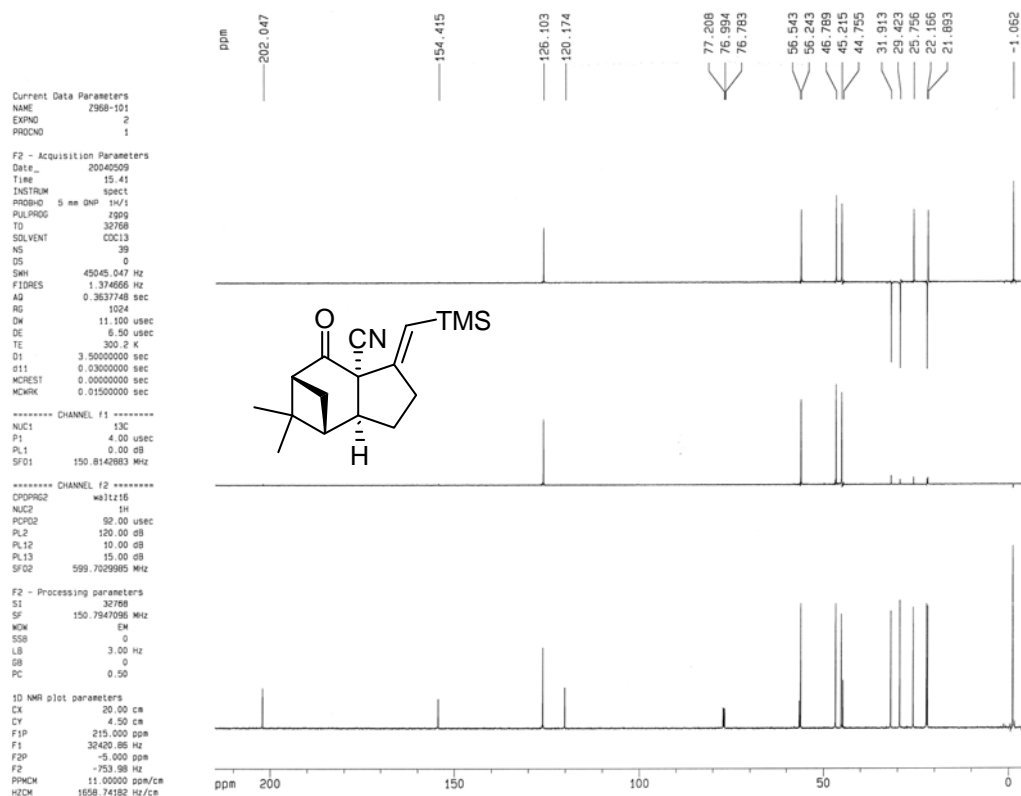
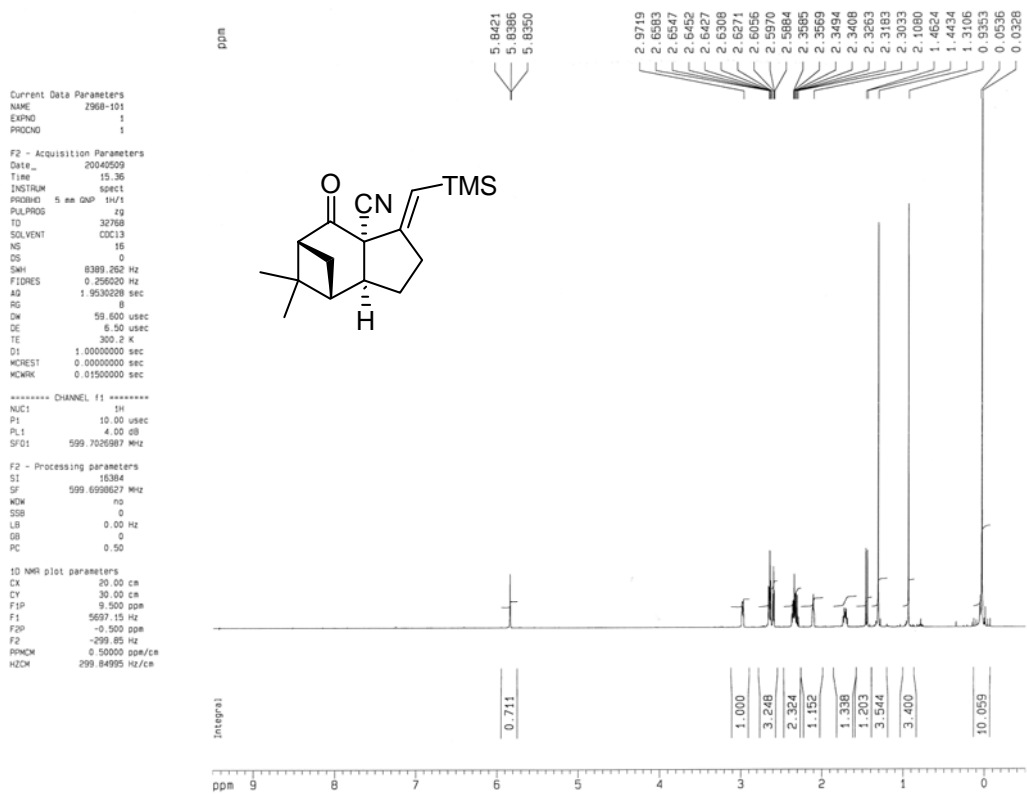
¹H and ¹³C NMR spectra for compound 25



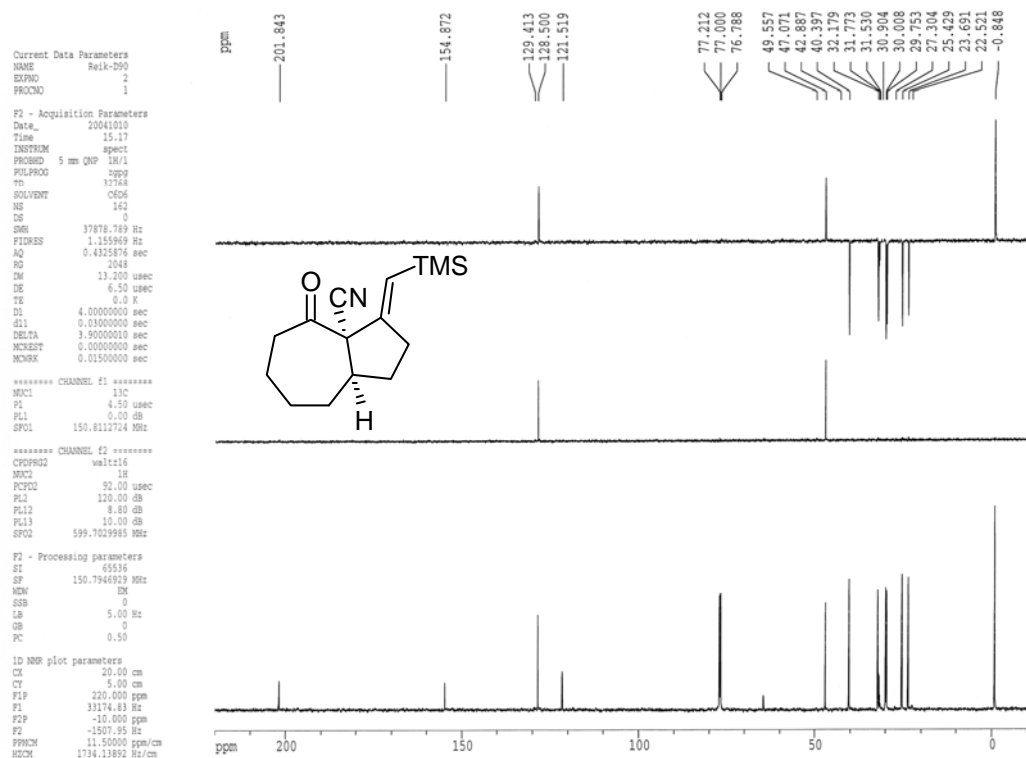
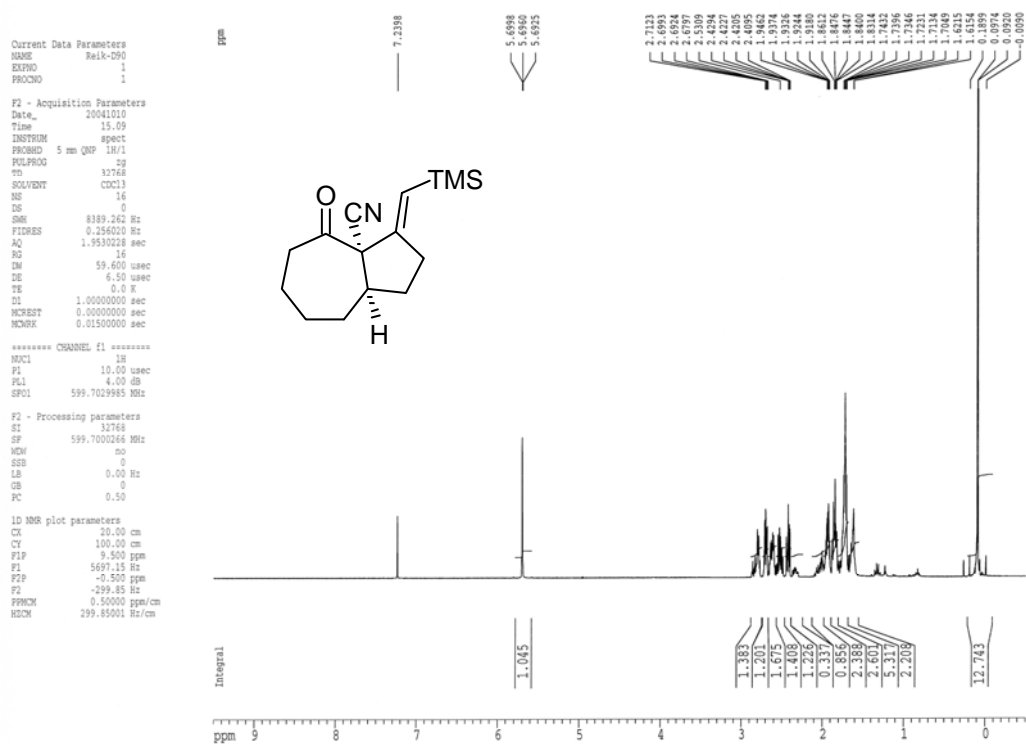
¹H and ¹³C NMR spectra for compound 26



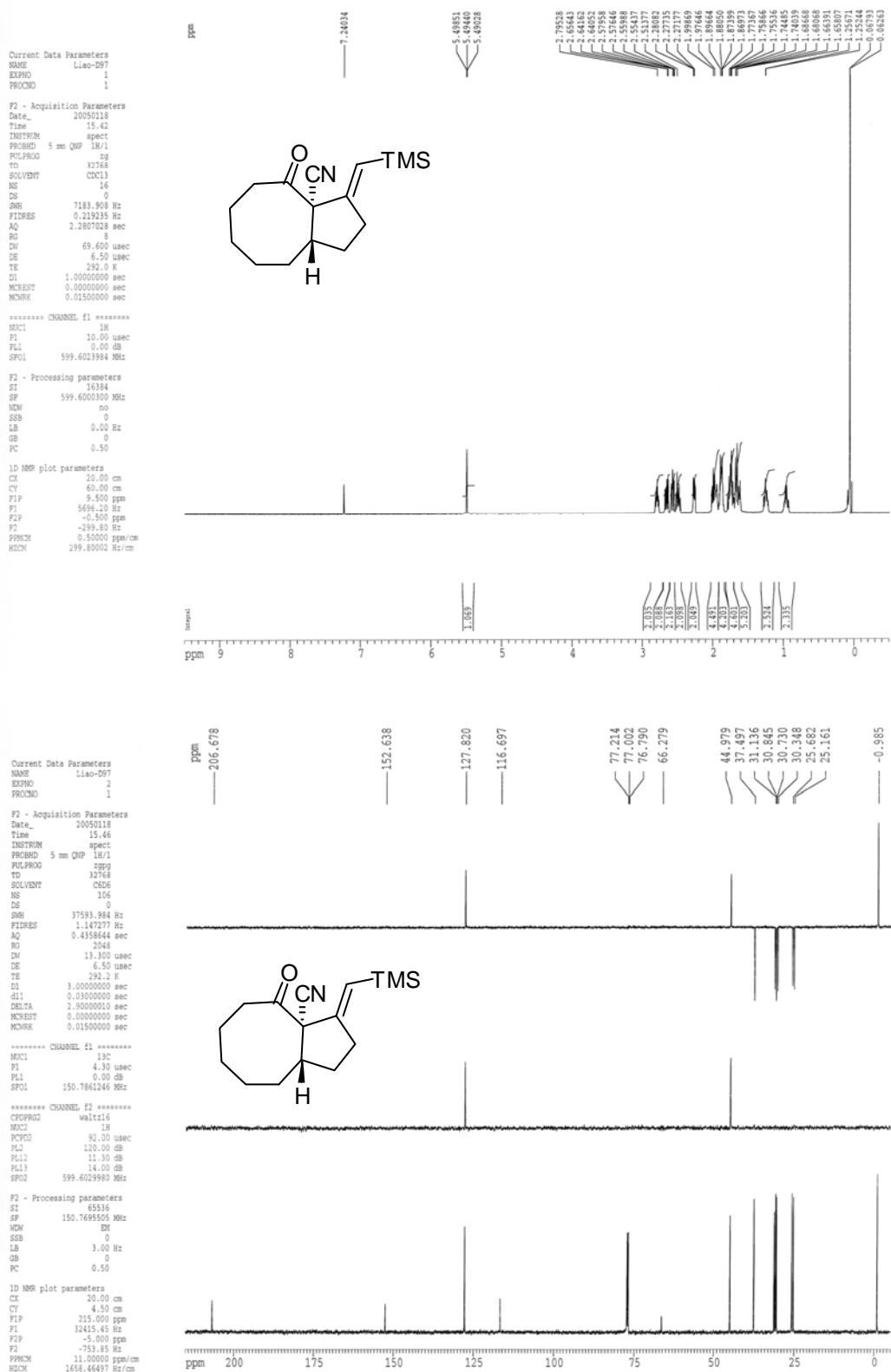
¹H and ¹³C NMR spectra for compound 27



¹H and ¹³C NMR spectra for compound 28



¹H and ¹³C NMR spectra for compound 29



¹H and ¹³C NMR spectra for compound 30

