Construction of a quaternary carbon at the carbonyl carbon of the cyclohexane ring

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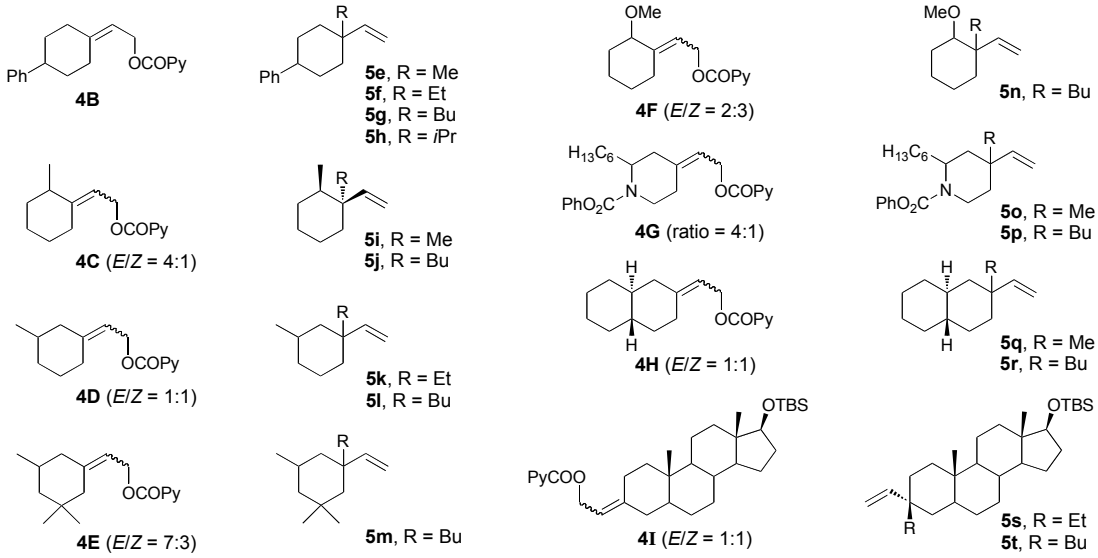
Table S1 Reaction of various types of substrates with copper reagents



Entry	Substrate	Reagent (1.5 equiv)	Additive (equiv)	Major product[a]	**5** : **6**[b]	Stereo-selectivity of **5**[b]	Isolated yield %[c]
1	**4B**	$Me_2CuMgBr$	–	isomer of **5e**	1:99	–	nd
2	**4B**	$Me_2CuMgBr$	$ZnBr_2$ (1.5)	**5e**	95:5	99:1	87
3	**4B**	$Me_2CuMgBr$	ZnI_2 (1.5)	**5e**	100:0	99:1	96
4	**4B**	$Et_2CuMgBr$	–	**5f**	82:18	95:5	nd
5	**4B**	$Et_2CuMgBr$	$ZnBr_2$ (4)	**5f**	100:0	99:1	81
6	**4B**	$Bu_2CuMgBr$	–	**5g**	70:30	100:0	nd
7	**4B**	$Bu_2CuMgBr$	ZnI_2 (1.5)	**5g**	100:0	100:0	88
8	**4B**	$iPr_2CuMgBr$	–	**5h**	0:100	–	*d*
9	**4B**	$iPr_2CuMgBr$	$ZnBr_2$ (4)	**5h**	99:1	100:0	83
10	**4C**	$Me_2CuMgBr$	–	isomer of **5i**	17:83	nd	nd
11	**4C**	$Me_2CuMgBr$	$ZnBr_2$ (4)	**5i**	98:2	95:5	61
12	**4C**	$Bu_2CuMgBr$	–	**5j**	55:45	93:7	nd
13	**4C**	$Bu_2CuMgBr$	$ZnBr_2$ (4)	**5j**	100:0	96:4	76
14	**4D**	$Et_2CuMgBr$	–	**5k**	67:33	93:7	nd
15	**4D**	$Et_2CuMgBr$	ZnI_2 (1.5)	**5k**	99:1	97:3	62
16	**4D**	$Bu_2CuMgBr$	–	**5l**	62:38	95:5	nd
17	**4D**	$Bu_2CuMgBr$	ZnI_2 (1.5)	**5l**	100:0	97:3	79
18	**4E**	$Bu_2CuMgBr$	–	**5m**	72:28	100:0	nd
19	**4E**	$Bu_2CuMgBr$	ZnI_2 (1.5)	**5m**	99:1	100:0	76
20	**4F**	$Bu_2CuMgBr$	–	isomer of **5n**	40:60	100:0	nd
21	**4F**	$Bu_2CuMgBr$	ZnI_2 (1.5)	**5n**	100:0	100:0	70
22	**4G**	$Me_2CuMgBr$	–	**5o**	78:22	98:2	nd
23	**4G**	$Me_2CuMgBr$	ZnI_2 (1.5)	**5o**	98:2	98:2	72
24	**4G**	$Bu_2CuMgBr$	–	isomer of **5p**	19:81	nd	nd
25	**4G**	$Bu_2CuMgBr$	ZnI_2 (1.5)	**5p**	98:2	100:0	84
26	**4H**	$Me_2CuMgBr$	–	isomer of **5q**	25:75	100:0	nd
27	**4H**	$Me_2CuMgBr$	ZnI_2 (1.5)	**5q**	99:1	100:0	76
28	**4H**	$Bu_2CuMgBr$	–	**5r**	nd	nd	*e*
29	**4H**	$Bu_2CuMgBr$	ZnI_2 (1.5)	**5r**	100:0	99:1	96
30	**4I**	$Et_2CuMgBr$	ZnI_2 (1.5)	**5s**	100:0	98:2	87
31	**4I**	$Bu_2CuMgBr$	–	**5t**	88:12	100:0	nd
32	**4I**	$Bu_2CuMgBr$	ZnI_2 (1.5)	**5t**	100:0	100:0	80

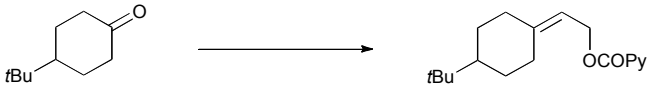
[a] isomer: The corresponding regioisomer **6**. [b] 100: The isomer was not seen in the expanded ^1H NMR spectroscopy. [c] nd: Not determined. [d] The ratio of **5h** : **6h** : alcohol : **4B** = 0:29:61:10. [e] A mixture of **5r** and the regioisomer **6r** were obtained only in <10% yield.

General

Infrared (IR) spectra are reported in wave numbers (cm^{-1}). The ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured in $CDCl_3$ using $SiMe_4$ (δ = 0 ppm) and the center line of $CDCl_3$ triplet (δ = 77.1 ppm) as internal standards, respectively. Signal patterns are indicated as br s, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants *(J)* are given in hertz (Hz). Chemical shifts of carbons accompany plus (for CH and CH_3) and minus (for C and CH_2) signs of APT experiments. After the reactions, organic extracts were concentrated by using a rotary evaporator and the residues were purified by chromatography on silica gel (Kanto, silica gel 60N).

Synthesis of Picolinates

2-(4-*tert*-Butylcyclohexylidene)ethyl Picolinate (4A)



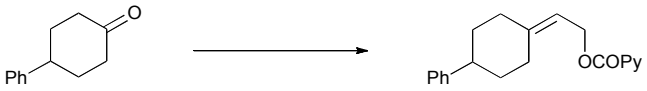
3A **4A**

To a suspension of LiCl (593 mg, 14.0 mmol) in MeCN (10 mL) were added DBU (1.80 mL, 12.0 mmol) and triethyl phosphonoacetate (2.60 mL, 13.0 mmol) at 0 °C. The mixture was stirred at 0 °C for 30 min, and ketone **3A** (1.54 g, 9.98 mmol) was added. The reaction was carried out at room temperature overnight and quenched by addition of saturated $NaHCO_3$. The mixture was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (2.22 g, 99%): ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (s, 9 H), 1.28 (t, *J* = 7 Hz, 3 H), 1.10–1.33 (m, 3 H), 1.76–1.99 (m, 3 H), 2.16 (dt, *J* = 3, 14 Hz, 1 H), 2.31 (dm, *J* = 14 Hz, 1 H), 3.87 (dm, *J* = 14 Hz, 1 H), 4.14 (q, *J* = 7 Hz, 2 H), 5.60 (s, 1 H). The spectrum was identical with the data reported.[1]

To a solution of the above ester (765 mg, 3.64 mmol) in THF (7 mL) was added DIBAL (7.80 mL, 1.03 M in hexane, 8.03 mmol) dropwise at –78 °C. After 1 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed, and 1 N HCl was added. The mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to afford the corresponding alcohol (616 mg), which was used for the next reaction without further purification: ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 9 H), 0.82–1.26 (m, 4 H), 1.75 (tm, *J* = 14 Hz, 1 H), 1.80–1.94 (m, 2 H), 2.02 (tm, *J* = 13 Hz, 1 H), 2.26 (tq, *J* = 14, 3 Hz, 1 H), 2.69 (tq, *J* = 14, 3 Hz, 1 H), 4.09–4.20 (m, 1 H), 5.36 (t, *J* = 7 Hz, 1 H). The spectrum was identical with that reported.[2]

To an ice-cold solution of the above alcohol in CH_2Cl_2 (11 mL) were added picolinic acid (538 mg, 4.37 mmol), DMAP (133 mg, 1.09 mmol) and DCC (976 mg, 4.73 mmol). The mixture was stirred at room temperature for 1 h, diluted with ether, and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4A** (958 mg, 92% from the ester): mp. 55–56 °C; IR (nujol) 1730, 1302, 1135 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 9 H), 0.78–1.29 (m, 3 H), 1.74–1.96 (m, 3 H), 2.06 (tm, *J* = 13 Hz, 1 H), 2.25 (dm, *J* = 13 Hz, 1 H), 2.82 (dm, *J* = 14 Hz, 1 H), 4.95 (d, *J* = 7 Hz, 2 H), 5.46 (t, *J* = 7 Hz, 1 H), 7.47 (ddd, *J* = 8, 5, 1 Hz, 1 H), 7.84 (ddd, *J* = 8, 8, 2 Hz, 1 H), 8.15 (ddd, *J* = 8, 1, 1 Hz, 1 H), 8.77 (dm, *J* = 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.5 (+), 28.2 (–), 28.7 (–), 28.8 (–), 32.4 (–), 36.8 (–), 48.1 (+), 62.2 (–), 114.6 (+), 125.0 (+), 126.7 (+), 136.9 (+), 147.0 (–), 148.3 (–), 149.8 (+), 165.2 (–); HRMS (FAB) calcd for $C_{18}H_{26}NO_2$ [$(M+H)^+$] 288.1964, found 288.1958.

2-(4-Phenylcyclohexylidene)ethyl Picolinate (4B)



3B **4B**

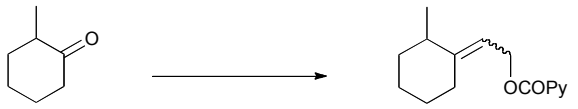
To an ice-cold suspension of LiCl (342 mg, 8.07 mmol) in MeCN (6 mL) were added DBU (1.0 mL, 6.70 mmol) and triethyl phosphonoacetate (1.5 mL, 7.49 mmol). The mixture was stirred 0 °C for 30 min, and a solution of ketone **3B** (987 mg, 5.67 mmol) was added dropwise. The reaction was carried out at 0 °C for 3 h and quenched by addition of saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (1.37 g, 97%): ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7 Hz, 3 H), 1.55–1.72 (m, 2 H), 1.96–2.12 (m, 3 H), 2.27–2.42 (m, 2 H), 2.78 (tt, *J* = 12, 3.5 Hz, 1 H), 3.93–4.02 (m, 1 H), 4.16 (q, *J* = 7 Hz, 2 H), 5.68 (s, 1 H), 7.15–7.34 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4 (+), 29.4 (–), 34.8 (–), 35.6 (–), 37.7 (–), 44.1 (+), 59.6 (–), 113.8 (+), 126.2 (+), 126.8 (+), 128.5 (+), 146.0 (–), 161.9 (–), 166.8 (–). The spectra were identical with those reported.[3]

To a solution of the above ester (632 mg, 2.58 mmol) in THF (5 mL) was added DIBAL (5.5 mL, 1.03 M in hexane, 5.69 mmol) dropwise at –78 °C. After 1 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed, and 1 N HCl was added. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding allylic alcohol (466 mg, 89%): IR (neat) 3331, 1493, 987, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.39–1.65 (m, 3 H), 1.88–2.07 (m, 3 H), 2.16–2.41 (m, 2 H), 2.65–2.84 (m, 2 H), 4.18 (d, *J* = 7 Hz, 2 H), 5.45 (t, *J* = 7

Hz, 1 H), 7.15–7.33 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.6 (–), 35.0 (–), 35.6 (–), 36.8 (–), 44.6 (+), 58.7 (–), 121.1 (+), 126.1 (+), 126.9 (+), 128.4 (+), 143.0 (–), 146.7 (–).

To an ice-cold solution of the above alcohol (439 mg, 2.17 mmol) in CH_2Cl_2 (11 mL) were added picolinic acid (321 mg, 2.61 mmol), DMAP (79.7 mg, 0.65 mmol) and DCC (583 mg, 2.82 mmol). The mixture was stirred at room temperature for 2 h, diluted with Et_2O and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4B** (661 mg, 99%): IR (neat) 1718, 1301, 1127, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45–1.68 (m, 2 H), 1.94–2.09 (m, 3 H), 2.19–2.33 (m, 1 H), 2.34–2.44 (m, 1 H), 2.73 (tt, *J* = 12, 3.5 Hz, 1 H), 2.83–2.88 (m, 1 H), 4.99 (d, *J* = 7.5 Hz, 2 H), 5.56 (t, *J* = 7.5 Hz, 1 H), 7.16–7.33 (m, 5 H), 7.44 (ddd, *J* = 8, 5, 1 Hz, 1 H), 7.86 (ddd, *J* = 8, 8, 2 Hz, 1 H), 8.17 (ddd, *J* = 8, 1, 1 Hz, 1 H), 8.78 (ddd, *J* = 5, 2, 1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.8 (–), 34.8 (–), 35.3 (–), 36.7 (–), 44.4 (+), 62.2 (–), 115.8 (+), 125.2 (+), 126.1 (+), 126.81 (+), 126.85 (+), 128.4 (+), 137.0 (+), 145.8 (–), 146.5 (–), 148.3 (–), 149.9 (+), 165.2 (–); HRMS (FAB) calcd for $C_{20}H_{22}NO_2$ [$(M+H)^+$] 308.1651, found 308.1651.

(*E*)- and (*Z*)-2-(2-Methylcyclohexylidene)ethyl Picolinate (4C)



3C **4C** (*E*/*Z* = 4:1)

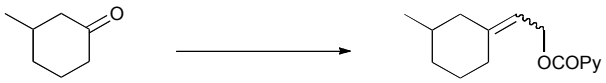
To a suspension of LiCl (297 mg, 7.01 mmol) in MeCN (5 mL) were added DBU (0.90 mL, 6.03 mmol) and triethyl phosphonoacetate (1.30 mL, 6.49 mmol) at 0 °C. The mixture was stirred at 0 °C for 30 min, and ketone **3C** (0.60 mL, 4.97 mmol) was added. The reaction was carried out at room temperature overnight and quenched by addition of saturated $NaHCO_3$. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (647 mg, 71%) as a 4:1 mixture of the *E*/*Z* stereoisomers by ^{1}H NMR spectroscopy. The (*E*)-isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (d, *J* = 7 Hz, 3 H), 1.29 (t, *J* = 7 Hz, 3 H), 1.01–1.92 (m, 5 H), 2.02–2.47 (m, 3 H), 3.54 (dt, *J* = 13, 5 Hz, 1 H), 4.15 (q, *J* = 7 Hz, 2 H), 5.58 (s, 1 H). The (*Z*)-isomer: ^{1}H NMR δ 4.14 (q, *J* = 7 Hz, 2 H), 5.55 (d, *J* = 2 Hz, 1 H).

To a solution of the above ester (647 mg, 3.55 mmol) in THF (7 mL) was added DIBAL (7.60 mL, 1.03 M in hexane, 7.83 mmol) dropwise at –78 °C. After 1 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed, and 1 N HCl was added. The mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to afford the corresponding alcohol as a 4:1 mixture of the *E*/*Z* stereoisomers by ^{1}H NMR spectroscopy. The mixture was used

for the next reaction without further purification. The (*E*)-isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (d, *J* = 7 Hz, 3 H), 0.92–2.18 (m, 8 H), 2.54 (dm, *J* = 14 Hz, 1 H), 4.14–4.23 (m, 1 H), 5.34 (t, *J* = 7 Hz, 1 H). The (*Z*)-isomer: ^{1}H NMR δ 2.84–2.96 (m, 1 H). The signals for the isomers were identical with those reported.[2]

To an ice-cold solution of the above alcohol in CH_2Cl_2 (14 mL) were added picolinic acid (524 mg, 4.26 mmol), DMAP (130 mg, 1.06 mmol) and DCC (952 mg, 4.62 mmol). The mixture was stirred at room temperature for 1 h, diluted with ether and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4C** (756 mg, 87% from the ester) as a 4:1 mixture of the *E*/*Z* stereoisomers by ^{1}H NMR spectroscopy. The (*E*)-isomer: IR (neat) 1739, 1717, 1307, 1289, 1128 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (d, *J* = 7 Hz, 3 H), 0.80–2.20 (m, 8 H), 2.58–2.70 (m, 1 H), 4.91–5.07 (m, 2 H), 5.43 (t, *J* = 7 Hz, 1 H), 7.48 (ddd, *J* = 8, 5, 1.5 Hz, 1 H), 7.84 (ddm, *J* = 8, 8 Hz, 1 H), 8.07 (d, *J* = 8 Hz, 1 H), 8.76 (dm, *J* = 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3 (+), 25.3 (–), 27.9 (–), 28.7 (–), 36.4 (–), 38.4 (+), 62.2 (–), 112.4 (+), 125.0 (+), 126.6 (+), 136.8 (+), 148.1 (–), 149.7 (+), 150.7 (–), 165.0 (–); HRMS (FAB) calcd for $C_{15}H_{20}NO_2$ [$(M+H)^+$] 246.1494, found 246.1497.

(*E*)- and (*Z*)-2-(3-Methylcyclohexylidene)ethyl Picolinate (4D)



3D **4D** (*E*/*Z* = 1:1)

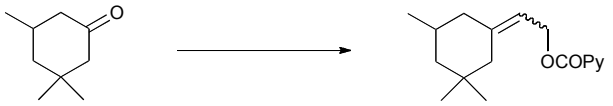
To a suspension of LiCl (297 mg, 7.01 mmol) in MeCN (5 mL) were added DBU (0.90 mL, 6.03 mmol) and triethyl phosphonoacetate (1.30 mL, 6.49 mmol) at 0 °C. The mixture was stirred at 0 °C for 30 min, and ketone **3D** (0.61 mL, 5.00 mmol) was added. The reaction was carried out at room temperature overnight and quenched by addition of saturated $NaHCO_3$. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (801 mg, 88%) as a 1:1 mixture of the stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 and 0.98 (2 d, *J* = 6.5 and 6.5 Hz, 1:1, total 3 H), 1.02–2.30 (m, 11 H), 3.59–3.72 (m, 1 H), 4.14 (q, *J* = 7 Hz, 2 H), 5.60 and 5.61 (2 s, 1:1, total 1 H).

To a solution of the above ester (801 mg, 4.39 mmol) in THF (8 mL) was added DIBAL (9.40 mL, 1.03 M in hexane, 9.68 mmol) dropwise at –78 °C. After 1 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed, and 1 N HCl was added. The mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to afford the corresponding

alcohol, which was used for the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 and 0.94 (2 d, *J* = 7 and 7 Hz, 1:1, total 3 H), 0.87–2.04 (m, 8 H), 2.12–2.23 (m, 1 H), 2.54 (dm, *J* = 10 Hz, 1 H), 4.14 (dm, *J* = 6 Hz, 2 H), 5.36 and 5.39 (2 t, *J* = 6 and 6 Hz, 1:1, total 1 H). The spectrum of the alcohol was identical with that reported.[2]

To an ice-cold solution of the above alcohol (571 mg) in CH_2Cl_2 (16 mL) were added picolinic acid (649 mg, 5.27 mmol), DMAP (161 mg, 1.32 mmol) and DCC (1.18 g, 5.72 mmol). The mixture was stirred at room temperature for 1 h, diluted with ether and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4D** (997 mg, 93% from ester) as a 1:1 mixture of the stereoisomers by ^{1}H NMR spectroscopy. The mixture: IR (neat) 1740, 1718, 1301, 1289, 1246, 1129 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 and 0.95 (2 d, *J* = 6 and 6 Hz, 1:1, total 3 H), 0.83–2.04 (m, 7 H), 2.14–2.26 (m, 1 H), 2.59–2.72 (m, 1 H), 4.94 (d, *J* = 7 Hz, 2 H), 5.42–5.52 (m, 1 H), 7.46 (ddd, *J* = 8, 5, 1 Hz, 1 H), 7.83 (ddd, *J* = 8, 8, 1 Hz, 1 H), 8.14 (d, *J* = 8 Hz, 1 H), 8.76 (d, *J* = 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.0 (+), 22.1 (+), 26.4 (–), 26.8 (–), 28.3 (–), 33.5 (+), 34.0 (+), 34.7 (–), 36.3 (–), 37.0 (–), 45.0 (–), 61.9 (–), 62.0 (–), 115.0 (+), 124.9 (+), 126.6 (+), 136.8 (+), 146.4 (–), 148.1 (–), 149.6 (+), 165.0 (–); HRMS (FAB) calcd for $C_{15}H_{20}NO_2$ [$(M+H)^+$] 246.1494, found 246.1495.

(*E*)- and (*Z*)-2-(3,3,5-Trimethylcyclohexylidene)ethyl Picolinate (4E)



3E **4E** (*E*/*Z* = 7:3)

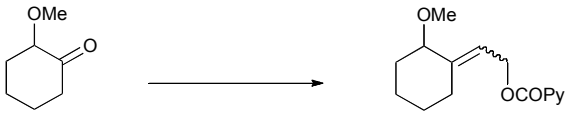
To an ice-cold suspension of LiCl (396 mg, 9.34 mmol) in MeCN (12 mL) were added DBU (1.27 mL, 8.51 mmol) and triethyl phosphonoacetate (1.71 mL, 8.54 mmol). The mixture was stirred 0 °C for 30 min, and a solution of ketone **3E** (990 mg, 7.06 mmol) in MeCN (2 mL) was added dropwise. The reaction was carried out at 0 °C overnight and quenched by addition of saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (1.08 g, 73%) as a 7:3 mixture of the *E*/*Z* stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81 (s, 2.1 H) and 0.83 (s, 0.9 H), 0.93 (d, *J* = 6 Hz, 0.9 H) and 0.96 (d, *J* = 6.5 Hz, 2.1 H), 0.98 (s, 2.1 H) and 1.02 (s, 0.9 H), 1.27 (q, *J* = 7 Hz, 0.9 H) and 1.28 (q, *J* = 7 Hz, 2.1 H), 1.24–2.24 (m, 6 H), 3.58 (ddd, *J* = 13, 3, 2 Hz, 0.3 H) and 3.83 (dddd, *J* = 13, 3, 2, 2 Hz, 0.7 H), 4.08–4.20 (m, 2 H), 5.55–5.58 (m, 0.7 H) and 5.68–5.70 (m, 0.3 H). The *E* and *Z* stereochemistries were assigned to the major and minor isomers by converting the isomers to the known alcohols (see below).

To a solution of the above ester (897 mg, 4.26 mmol) in THF (8.5 mL) was added DIBAL (12.3

mL, 1.04 M in hexane, 12.8 mmol) dropwise at –78 °C. After 1 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed, and 1 N HCl was added. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding alcohol (707 mg, 98%) as a 7:3 mixture of the *E*/*Z* stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80 (s, 3 H), 0.89 (d, *J* = 6 Hz, 0.9 H) and 0.92 (d, *J* = 6.5 Hz, 2.1 H), 0.94 (s, 2.1 H) and 0.98 (s, 0.9 H), 0.86–1.92 (m, 6.7 H), 2.17 (dm, *J* = 11 Hz, 0.3 H), 2.26 (dm, *J* = 13 Hz, 0.3 H), 2.58 (dm, *J* = 13 Hz, 0.7 H), 4.08–4.21 (m, 2 H), 5.34 (tm, *J* = 7 Hz, 0.7 H) and 5.49 (tm, *J* = 7 Hz, 0.3 H). The major and minor signals were identical with the data reported for the *E* and *Z* stereoisomers.[4]

To an ice-cold solution of the above alcohol (702 mg, 4.17 mmol) in CH_2Cl_2 (14 mL) were added picolinic acid (621 mg, 5.05 mmol), DMAP (517 mg, 4.23 mmol) and DCC (1.12 g, 5.43 mmol). The mixture was stirred at room temperature for 2.5 h, diluted with Et_2O and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4E** (1.12 g, 98%): as a 7:3 mixture of the *E*/*Z* stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (s, 2.1 H) and 0.80 (s, 0.9 H), 0.89 (d, *J* = 6.5 Hz, 0.9 H) and 0.93 (d, *J* = 6.5 Hz, 2.1 H), 0.94 (s, 2.1 H) and 0.96 (s, 0.9 H), 0.86–1.94 (m, 5.7 H), 2.20 (dm, *J* = 11 Hz, 0.3 H), 2.38 (dm, *J* = 13 Hz, 0.3 H), 2.71 (dm, *J* = 13 Hz, 0.7 H), 4.87–5.00 (m, 2 H), 5.43 (tm, *J* = 7.5 Hz, 0.7 H) and 5.59 (tm, *J* = 7.5 Hz, 0.3 H), 7.47 (ddm, *J* = 8, 5 Hz, 1 H), 7.84 (ddm, *J* = 8, 8 Hz, 1 H), 8.13 (dm, *J* = 8 Hz, 1 H), 8.77 (dm, *J* = 5 Hz, 1 H); HRMS (FAB) calcd for $C_{17}H_{24}NO_2$ [$(M+H)^+$] 274.1807, found 274.1806.

(*E*)- and (*Z*)-2-(2-Methoxycyclohexylidene)ethyl Picolinate (4F)



3F **4F** (*E*/*Z* = 2:3)

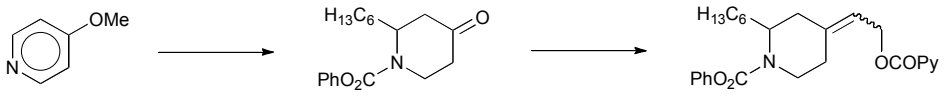
To an ice-cold suspension of LiCl (262 mg, 6.18 mmol) in MeCN (12 mL) were added DBU (0.78 mL, 5.22 mmol) and triethyl phosphonoacetate (1.12 mL, 5.59 mmol). The mixture was stirred 0 °C for 30 min, and a solution of ketone **3F** (554 mg, 4.32 mmol) in MeCN (8 mL) was added dropwise. The reaction was carried out at 0 °C overnight and quenched by addition of saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (811 mg, 95%) as a 2:3 mixture of the *E*/*Z* stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.288 (t, *J*

= 7 Hz, 1.8 H) and 1.293 (t, *J* = 7 Hz, 1.2 H), 1.33–1.97 (m, 5 H), 1.98–2.11 (m, 1 H), 2.46–2.64 (m, 1 H), 3.02–3.12 (m, 0.4 H), 3.23 (s, 1.8 H) and 3.31 (s, 1.2 H), 3.56 (dd, *J* = 10.5, 3.5 Hz, 0.4 H), 4.10–4.21 (m, 2 H), 5.23–5.28 (m, 0.6 H) 5.79 (d, *J* = 2 Hz, 0.6 H) and 5.82 (d, *J* = 0.5 Hz, 0.4 H). The minor and major signals were identical with the data reported for the *E* and *Z* isomers.[5]

To a solution of the above ester (876 mg, 4.42 mmol) in THF (9 mL) was added DIBAL (12.7 mL, 1.04 M in hexane, 13.2 mmol) dropwise at –78 °C. After 2 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed, and 1 N HCl was added. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding alcohol (673 mg, 98%) as a 2:3 mixture by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25–2.38 (m, 9 H), 3.23 (s, 1.8 H) and 3.26 (s, 1.2 H), 3.54–3.59 (m, 0.4 H), 4.11–4.30 (m, 2.6 H), 5.53–5.65 (m, 1 H). The spectrum was identical with the reported data.[5]

To an ice-cold solution of picolinic acid (645 mg, 5.24 mmol) in CH_2Cl_2 (12 mL) were added Et_3N (1.34 mL, 12.9 mmol), DMAP (536 mg, 4.38 mmol) and 2-chloro-1-methylpyridinium iodide (2.20 g, 8.61 mmol). The mixture was stirred at room temperature for 30 min, and a solution of the above alcohol (673 mg, 4.31 mmol) in CH_2Cl_2 (2 mL) was added. The reaction was carried out at room temperature overnight and quenched by addition of saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with 1 N HCl and brine, dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4F** (1.05 g, 93%) as a 2:3 mixture of the *E*/*Z* stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30–2.42 (m, 8 H), 3.247 (s, 1.8 H) and 3.254 (s, 1.2 H), 3.56–3.61 (m, 0.4 H) and 4.27–4.33 (m, 0.6 H), 4.98–5.04 (m, 2 H), 5.64–5.74 (m, 1 H), 7.48 (ddm, *J* = 8, 5 Hz, 1 H), 7.85 (ddd, *J* = 8, 8, 2 Hz, 1 H), 8.15 (dm, *J* = 8 Hz, 1 H), 8.77 (dm, *J* = 5 Hz, 1 H); HRMS (FAB) calcd for $C_{15}H_{20}NO_3$ [$(M+H)^+$] 262.1443, found 262.1442.

(*E*)- and (*Z*)-2-(2-Hexyl-1-(phenoxycarbonyl)piperidin-4-ylidene)ethyl Picolinate (4G)



3G **4G** (ratio = 4:1)

According to the literature procedure[6] $C_6H_{13}MgBr$ (3.07 mL, 0.85 M in THF, 2.60 mmol) and phenyl chloroformate (0.33 mL, 2.63 mmol) were added to a solution of 4-methoxypyridine (258 mg, 2.37 mmol) in THF (24 mL) dropwise at –23 ºC. After 4 h at –23 ºC, the reaction was quenched by addition of 3 N HCl. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over $MgSO_4$ and

concentrated to afford the corresponding enone, which was used for the next reaction without further purification.

A solution of the above enone and 10% Pd/C (75 mg) in MeOH (10 mL) was stirred at room temperature for 3 h under hydrogen, diluted with EtOAc and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to give ketone **3G** (494 mg, 63% from 4-methoxypyridine): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7 Hz, 3 H), 1.18–1.70 (m, 10 H), 2.34–2.47 (m, 2 H), 2.61 (ddd, *J* = 15, 12, 7 Hz, 1 H), 2.71–2.84 (m, 1 H), 3.21–3.50 (m, 1 H), 4.42–4.58 (m, 1 H), 4.77 (br s, 1 H), 7.12 (d, *J* = 8 Hz, 2 H), 7.23 (dd, *J* = 8, 8 Hz, 1 H), 7.39 (dd, *J* = 8, 8 Hz, 2 H).

To an ice-cold suspension of 60% NaH (7.2 mg, 0.18 mmol) in THF (0.7 mL) was added triethyl phosphonoacetate (0.028 mL, 0.14 mmol). The mixture was stirred 0 °C for 10 min, and a solution of ketone **3G** (38.9 mg, 0.128 mmol) in THF (0.8 mL) was added dropwise. The reaction was carried out at 0 °C for 2.5 h and quenched by addition of saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (41 mg, 86%) as a 4:1 mixture of the stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82–0.92 (m, 3 H), 1.1–1.8 (m, 13 H), 2.16–2.69 (m, 3 H), 2.92–3.24 (m, 1 H), 3.75–3.93 (m, 1 H), 4.18 (q, *J* = 7 Hz, 2 H), 4.12–4.38 (m, 1 H), 4.53 (br s, 1 H), 5.74 (s, 0.8 H) and 5.85 (s, 0.2 H), 7.10 (d, *J* = 8 Hz, 2 H), 7.20 (dd, *J* = 8, 8 Hz, 1 H), 7.37 (dd, *J* = 8, 8 Hz, 2 H).

To a solution of the above ester (40 mg, 0.107 mmol) in THF (1 mL) was added DIBAL (0.31 mL, 1.03 M in hexane, 0.32 mmol) dropwise at –78 °C. After 1 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed, and 1 N HCl was added. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding alcohol (34 mg, 95%), which was used for the next reaction without further purification: ^{1}H NMR of the mixture (300 MHz, $CDCl_3$) δ 0.80–0.94 (m, 3 H), 1.1–1.8 (m, 10 H), 2.0–3.2 (m, 8 H), 2.82–3.08 (m, 1 H), 4.06–4.31 (m, 3 H), 4.47 (br s, 1 H), 5.51 (t, *J* = 6.5 Hz, 0.8 H) and 5.65 (t, *J* = 6.5 Hz, 0.2 H), 7.10 (d, *J* = 7.5 Hz, 2 H), 7.20 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.37 (dd, *J* = 7.5, 7.5 Hz, 2 H).

To an ice-cold solution of the above alcohol (291 mg, 0.877 mmol) in CH_2Cl_2 (9 mL) were added picolinic acid (130 mg, 1.06 mmol), DMAP (110 mg, 0.90 mmol) and DCC (240 mg, 1.17 mmol). The mixture was stirred at room temperature for 5 h, diluted with Et_2O, and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4G** (382 mg, 99%) as a 4:1

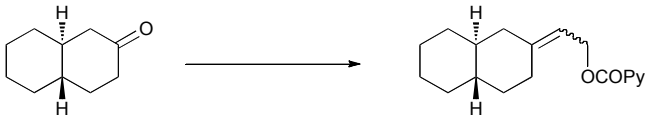
mixture of the stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80–0.94 (m, 3 H), 1.1–3.2 (m, 17 H), 4.21–4.36 (m, 1 H), 4.40–4.64 (m, 1.2 H) and 4.90–5.12 (m, 1.8 H), 5.63 (t, *J* = 6.5 Hz, 0.8 H) and 5.80 (t, *J* = 6.5 Hz, 0.2 H), 7.11 (d, *J* = 7.5 Hz, 2 H), 7.20 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.37 (dd, *J* = 7.5, 7.5 Hz, 2 H), 7.49 (ddm, *J* = 8, 5 Hz, 1 H), 7.86 (ddd, *J* = 8, 8, 2 Hz, 1 H), 8.16 (d, *J* = 8 Hz, 1 H), 8.78 (d, *J* = 5 Hz, 1 H); HRMS (FAB) calcd for $C_{26}H_{33}N_2O_4$ [(M+H)$^+$] 437.2440, found 437.2439.

(4a*R,8a*R**)-Octahydronaphthalen-2(1*H*)-one (3H)**

3H

To a flask containing NH_3 (ca. 25 mL) at –70 °C were added a solution of the octalenone (421 mg, 2.80 mmol) in THF (1 mL), *t*BuOH (0.21 mL, 2.2 mmol) and Li (ca. 170 mg, 24 mg-atom). After 15 min at –70 °C, saturated NH_4Cl was added to the solution with vigorous stirring. The product was extracted with Et_2O several times. The combined extracts were dried over $MgSO_4$ and concentrated to afford a mixture of *trans*-octalone **3H** and the corresponding alcohol. A solution of the mixture in acetone (20 mL) was cooled to 0 °C and Jones reagent (1.4 mL, 4.0 M, 5.6 mmol) was added to the solution. The mixture was stirred for 15 min and the excess reagent was destroyed by addition of *i*PrOH. The mixture was diluted with EtOAc and the solution isolated by decantation was rinsed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to afford octalone **3H** (281 mg, 66%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84–1.48 (m, 7 H), 1.63–1.84 (m, 4 H), 1.90–2.15 (m, 2 H), 2.25–2.44 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6 (–), 26.2 (–), 32.7 (–), 33.7 (–), 34.3 (–), 41.65 (–), 41.70 (+), 43.4 (+), 48.7 (–), 211.8 (–). The ^{13}C NMR spectrum was identical with that reported for the *trans* isomer.[7]

(*E*)- and (Z)-2-((4a*R,8a*R**)-Octahydronaphthalen-2(1*H*)-ylidene)ethyl Picolinate (4H)**



3H **4H** (*E*/*Z* = 1:1)

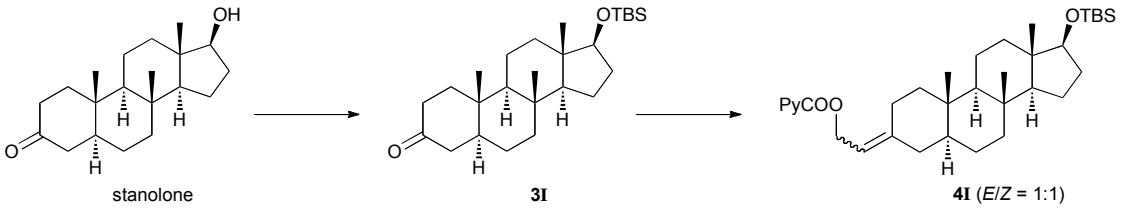
To an ice-cold suspension of LiCl (80 mg, 1.88 mmol) in MeCN (10 mL) were added DBU (0.23 mL, 1.54 mmol) and triethyl phosphonoacetate (0.34 mL, 1.70 mmol). The mixture was stirred 0 °C for 30 min, and a solution of ketone **3H** (196 mg, 1.29 mmol) in MeCN (3 mL) was added dropwise. The reaction was carried out at 0 °C overnight and quenched by addition of saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were

dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (242 mg, 90%) as a 1:1 mixture of the stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84–1.94 (m, 13 H), 1.27 (q, *J* = 7 Hz, 3 H), 2.10–2.31 (m, 2 H), 3.72–3.79 (m, 0.5 H) and 3.81–3.90 (m, 0.5 H), 4.14 (q, *J* = 7 Hz, 2 H), 5.59 (br s, 1 H).

To a solution of the above ester (185 mg, 0.832 mmol) in THF (8 mL) was added DIBAL (2.40 mL, 1.04 M in hexane, 2.47 mmol) dropwise at –78 °C. After 1.5 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed and 1 N HCl was added. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding alcohol, which was used for the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82–2.25 (m, 16 H), 2.46–2.55 (m, 0.5 H) and 2.59–2.69 (m, 0.5 H), 4.14 (d, *J* = 7 Hz, 2 H), 5.39 (tm, *J* = 7 Hz, 1 H).

To an ice-cold solution of the above alcohol in CH_2Cl_2 (8 mL) were added picolinic acid (164 mg, 1.33 mmol), DMAP (104 mg, 0.85 mmol) and DCC (319 mg, 1.54 mmol). The mixture was stirred at room temperature overnight, diluted with Et_2O and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4H** (209 mg, 88% from the ester) as a 1:1 mixture of the stereoisomers by ^{1}H NMR spectroscopy. The mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84–2.30 (m, 15 H), 2.59–2.68 (m, 0.5 H) and 2.63–2.83 (m, 0.5 H), 4.95 (d, *J* = 7 Hz, 2 H), 5.46 (t, *J* = 7 Hz, 1 H), 7.47 (ddd, *J* = 8, 5, 1.5 Hz, 1 H), 7.84 (ddd, *J* = 8, 8, 1.5 Hz, 1 H), 8.14 (dm, *J* = 8 Hz, 1 H), 8.77 (d, *J* = 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3 (–), 26.5 (–), 28.8 (–), 33.4 (–), 33.5 (–), 33.9 (–), 34.2 (–), 34.6 (–), 35.1 (–), 36.2 (–), 36.8 (–), 43.29 (+), 43.35 (+), 44.0 (+), 44.1 (–), 44.6 (+), 62.26 (–), 62.33 (–), 114.9 (+), 115.0 (+), 125.0 (+), 126.8 (+), 137.0 (+), 146.8 (–), 147.0 (–), 148.4 (–), 149.9 (+), 165.3 (+); HRMS (FAB) calcd for $C_{18}H_{24}NO_2$ [$(M+H)^+$] 286.1807, found 286.1806.

(*E*)- and (*Z*)-2-[(10*S*,13*S*,17*S*)-17-(*tert*-Butyldimethylsilyloxy)-10,13-dimethylhexahydro-1*H*-cyclopenta[*a*]phenanthren-3(2*H*,4*H*,10*H*,12*H*,13*H*,14*H*,15*H*,16*H*,17*H*)-ylidene]ethyl Picolinate (4I)



To an ice-cold solution of stanolone (329 mg, 1.13 mmol) in DMF (4 mL) were added imidazole

(369 mg, 5.42 mmol) and TBSCl (508 mg, 3.37 mmol). The mixture was stirred at room temperature overnight and diluted with EtOAc and saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc three times. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish TBS ether **3I** (399 mg, 87%): ^{1}H NMR (300 MHz, $CDCl_3$) δ –0.01 (s, 3 H), 0.00 (s, 3 H), 0.71 (s, 3 H), 0.87 (s, 9 H), 1.01 (s, 3 H), 0.64–1.94 (m, 17 H), 1.97–2.12 (m, 2 H), 2.20–2.46 (m, 3 H), 3.54 (t, *J* = 8 Hz, 1 H). The spectrum was identical with that reported.[8]

To an ice-cold suspension of LiCl (53 mg, 1.25 mmol) in MeCN (1 mL) were added DBU (0.160 mL, 1.07 mmol) and triethyl phosphonoacetate (0.23 mL, 1.15 mmol). The mixture was stirred at 0 °C for 30 min, and **3I** (363 mg, 0.897 mmol) was added. The reaction was carried out at room temperature overnight and quenched by addition of saturated $NaHCO_3$. The resulting mixture was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding ester (415 mg, 97%) as a 1:1 mixture of the stereoisomers by ^{1}H NMR spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$) δ –0.012 (s, 3 H), –0.005 (s, 3 H), 0.56–2.40 (m, 21 H), 0.69 (s, 3 H), 0.86 (s, 9 H), 0.91 (s, 3 H), 1.26 (t, *J* = 7 Hz, 3 H), 3.47 and 3.72 (2 dm, *J* = 15 and 15 Hz, 1:1, total 1 H), 3.53 (t, *J* = 8 Hz, 1 H), 4.13 (q, *J* = 7 Hz, 2 H), 5.64–5.60 (m, 1 H).

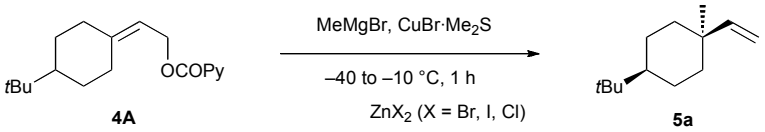
To a solution of the above ester (393 mg, 0.828 mmol) in THF (2 mL) was added DIBAL (1.8 mL, 1.03 M in hexane, 1.85 mmol) dropwise at –78 °C. After 1 h at –78 °C, the reaction was quenched by addition of water. The cooling bath was removed, and 1 N HCl was added. The mixture was extracted with EtOAc three times. The combined extracts were washed with saturated $NaHCO_3$ and brine successively, dried over Na_2SO_4 and concentrated to afford the corresponding alcohol (324 mg), which was used for the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.00 (s, 3 H), 0.06 (s, 3 H), 0.69 (s, 3 H), 0.87 (s, 12 H), 0.56–2.55 (m, 23 H), 3.53 (t, *J* = 8 Hz, 1 H), 4.02–4.24 (m, 2 H), 5.26–5.43 (m, 1 H).

To an ice-cold solution of the above alcohol (324 mg) in CH_2Cl_2 (3 mL) were added picolinic acid (122 mg, 0.991 mmol), DMAP (30 mg, 0.246 mmol) and DCC (222 mg, 1.08 mmol). The mixture was stirred at room temperature for 1 h, diluted with ether and filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish picolinate **4I** (398 mg, 89% from ester) as a 1:1 mixture of the stereoisomers by ^{1}H NMR spectroscopy. The mixture: $[\alpha]_D^{23}$ +15 (*c* 0.72, $CHCl_3$); IR (neat) 1740, 1718, 1302, 1247, 1124, 1094 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ –0.04 (s, 3 H), –0.03 (s, 3 H), 0.66 (s, 3 H), 0.84 (s, 9 H), 0.85 (s, 3 H), 0.52–2.30 (m, 21 H), 2.31 and 2.60 (2d, *J* = 14 and 15 Hz, 1:1, total 1 H), 3.49 (t, *J* = 8 Hz, 1 H), 4.83–4.99 (m, 2 H), 5.36–5.45 (m, 1 H), 7.42 (ddd, *J* = 8, 5, 1

Hz, 1 H), 7.80 (ddd, *J* = 8, 8, 2 Hz, 1 H), 8.11 (dm, *J* = 8 Hz, 1 H), 8.73 (d, *J* = 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.8 (+), –4.5 (+), 11.4 (+), 11.8 (+), 11.9 (+), 18.1 (–), 20.7 (–), 20.8 (–), 23.5 (–), 24.8 (–), 25.9 (+), 28.6 (–), 28.9 (–), 30.9 (–), 31.55 (–), 31.61 (–), 32.5 (–), 35.5 (+), 36.46 (–), 36.49 (–), 37.2 (–), 39.3 (–), 39.4 (–), 39.7 (–), 43.3 (–), 47.4 (+), 48.0 (+), 50.6 (+), 54.5 (+), 54.6 (+), 62.16 (–), 62.20 (–), 81.8 (+), 114.5 (+), 114.7 (+), 125.1 (+), 126.8 (+), 137.0 (+), 146.9 (–), 147.1 (–), 148.3 (–), 149.9 (+), 165.2 (–), 165.3 (–).

General procedure for the Allylation

(1*s*,4*s*)-4-*tert*-Butyl-1-methyl-1-vinylcyclohexane (5a)



4A **5a**

Allylation with $ZnBr_2$ (Table 1, Entry 3): To an ice-cold suspension of CuBr·Me_2S (26.7 mg, 0.130 mmol) and $ZnBr_2$ (28.8 mg, 0.128 mmol) in THF (1 mL) was added MeMgBr (0.28 mL, 0.93 M in THF, 0.260 mmol) slowly. The mixture was stirred at 0 °C for 30 min, cooled to –40 °C and added a solution of picolinate **4A** (24.9 mg, 0.0866 mmol) in THF (1 mL). The mixture was allowed to warm to –10 °C over 1 h and diluted with hexane and saturated NH_4Cl with vigorous stirring. The layers were separated and the aqueous layer was extracted with hexane twice. The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford **5a** (14.7 mg, 94%): IR (neat) 3081, 1364, 910 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.77–1.03 (m, 3 H), 0.83 (s, 9 H), 0.94 (s, 3 H), 1.06–1.30 (m, 4 H), 1.46–1.59 (s, 2 H), 1.67–1.78 (m, 2 H), 4.96 (dm, *J* = 18 Hz, 1 H), 5.02 (dm, *J* = 11 Hz, 1 H), 5.76 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (–), 27.7 (+), 31.5 (+), 32.5 (–), 36.6 (–), 38.5 (–), 48.3 (+), 112.0 (–), 146.3 (+). The stereochemistry was determined as drawn by comparison of the ^{13}C NMR data with that reported.[9]

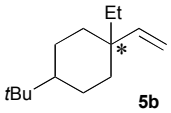
Allylation with ZnI_2 (Table 1, Entry 6): To an ice-cold suspension of CuBr·Me_2S (27.9 mg, 0.136 mmol) and ZnI_2 (43.4 mg, 0.136 mmol) in THF (1 mL) was added MeMgBr (0.29 mL, 1.0 M in THF, 0.27 mmol) slowly. The resulting mixture was stirred at 0 °C for 30 min and cooled to –40 °C. A solution of **4A** (26.0 mg, 0.0905 mmol) in THF (1 mL) was added to the mixture dropwise. The mixture was allowed to warm to –10 °C over 1 h and diluted with hexane and saturated NH_4Cl with vigorous stirring. The product was extracted with hexane and purified as described above to afford **5a** (13.9 mg, 85%).

Allylation with $ZnCl_2$ (Table 1, Entry 7): To an ice-cold suspension of CuBr·Me_2S (37.7 mg, 0.183 mmol) and $ZnCl_2$ (24.2 mg, 0.178 mmol) in THF (1 mL) was added MeMgBr (0.34 mL, 1.06 M in THF, 0.36 mmol) slowly. The resulting mixture was stirred at 0 °C for 30 min and cooled to

–40 °C. A solution of **4A** (34.5 mg, 0120 mmol) in THF (1 mL) was added to the mixture dropwise. The resulting mixture was allowed to warm to –10 °C over 1 h and diluted with hexane and saturated NH_4Cl with vigorous stirring. The product was extracted with hexane and purified as described above to afford **5a** (18.6 mg, 86%).

Allylation Products

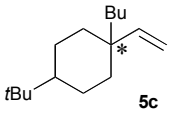
4-*tert*-Butyl-1-ethyl-1-vinylcyclohexane (5b)



5b

Table 1, Entry 11: According to the general procedure a solution of **4A** (36.8 mg, 0.128 mmol) in THF (1 mL) was added to a mixture of EtMgBr (0.38 mL, 1.0 M in THF, 0.38 mmol), $CuBr{\cdot}Me_2S$ (39.5 mg, 0.192 mmol) and ZnI_2 (61.3 mg, 0.192 mmol) in THF (1.5 mL) at –40 °C, and the mixture was allowed to warm to 0 °C over 1 h to afford **5b** (21.5 mg, 86%): IR (neat) 3079, 1639, 1365, 1000, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.76 (t, *J* = 7.5 Hz, 3 H), 0.81 (s, 9 H), 0.73–1.17 (m, 5 H), 1.22 (q, *J* = 7.5 Hz, 2 H), 1.46–1.58 (m, 2 H), 1.73–1.81 (m, 2 H), 4.92 (dd, *J* = 18, 2 Hz, 1 H), 5.14 (dd, *J* = 11, 2 Hz, 1 H), 5.50 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.9 (+), 23.4 (–), 27.7 (+), 32.5 (–), 36.1 (–), 36.9 (–), 40.0 (–), 48.8 (+), 114.0 (–), 144.9 (+).

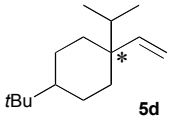
4-*tert*-Butyl-1-butyl-1-vinylcyclohexane (5c)



5c

Table 1, Entry 13: According to the general procedure a solution of **4A** (27.5 mg, 0.0957 mmol) in THF (1.0 mL) was added to a mixture of BuMgBr (0.25 mL, 1.09 M in THF, 0.273 mmol), $CuBr{\cdot}Me_2S$ (29.5 mg, 0.143 mmol) and ZnI_2 (45.8 mg, 0.144 mmol) in THF (1.0 mL) at –40 ºC, and the mixture was warmed to –10 ºC over 1 h to afford **5c** (20.1 mg, 94%): ^1H NMR (300 MHz, $CDCl_3$) δ 0.81 (s, 9 H), 0.80–1.28 (m, 13 H), 1.47–1.58 (m, 3 H), 1.75–1.82 (m, 2 H), 4.92 (dd, *J* = 17.5, 1.5 Hz, 1 H), 5.12 (dd, *J* = 11, 1.5 Hz, 1 H), 5.52 (dd, *J* = 17.5, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 23.4 (–), 23.6 (–), 25.7 (+), 27.7 (+), 32.5 (–), 36.6 (–), 39.8 (–), 44.7 (–), 48.7 (+), 113.7 (–), 145.4 (+).

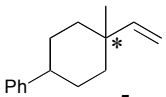
4-*tert*-Butyl-1-isopropyl-1-vinylcyclohexane (5d)



5d

Table 1, Entry 15: According to the general procedure a solution of **4A** (34.4 mg, 0.120 mmol) in THF (1 mL) was added to a mixture of *i*PrMgBr (0.89 mL, 0.81 M in THF, 0.721 mmol), CuBr·Me_2S (73.8 mg, 0.359 mmol) and ZnI_2 (114.6 mg, 0.359 mmol) in THF (1 mL) at –40 ºC, and the mixture was warmed to 0 ºC over 3 h to afford **5d** (23.1 mg, 93%): IR (neat) 3079, 1636, 1365, 911 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.79 (d, *J* = 7 Hz, 6 H), 0.81 (s, 9 H), 0.76–1.20 (m, 6 H), 1.25–1.38 (m, 1 H), 1.48–1.56 (m, 2 H), 1.84–1.92 (m, 2 H), 4.90 (dd, *J* = 18, 2 Hz, 1 H), 5.20 (dd, *J* = 11, 2 Hz, 1 H), 5.46 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.3 (+), 23.5 (–), 27.6 (+), 32.4 (–), 34.2 (–), 39.1 (+), 42.4 (–), 48.6 (+), 115.3 (–), 142.8 (+).

1-Methyl-4-phenyl-1-vinylcyclohexane (5e)

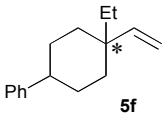


5e

With $ZnBr_2$: According to the general procedure a solution of **4B** (28.8 mg, 0.0937 mmol) in THF (1 mL) was added to a mixture of MeMgBr (0.27 mL, 1.06 M in THF, 0.286 mmol), CuBr·Me_2S (29.5 mg, 0.144 mmol) and $ZnBr_2$ (31.7 mg, 0.141 mmol) in THF (1 mL) at –40 ºC, and the mixture was warmed to 5 ºC over 3 h to afford **5e** (16.4 mg, 87%): IR (neat) 3080, 1636, 910, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (s, 3 H), 1.34–1.47 (m, 2 H), 1.55–1.73 (m, 4 H), 1.77–1.87 (m, 2 H), 2.40–2.52 (m, 1 H), 5.04 (dd, *J* = 17.5, 1.5 Hz, 1 H), 5.09 (dd, *J* = 11, 1.5 Hz, 1 H), 5.84 (dd, *J* = 17.5, 11 Hz, 1 H), 7.14–7.30 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.4 (–), 31.6 (+), 36.4 (–), 38.1 (–), 44.5 (+), 112.5 (–), 125.9 (+), 127.0 (+), 128.3 (+), 146.3 (+), 147.7 (–); HRMS (EI) calcd for $C_{15}H_{20}$ [M^+] 200.1565, found 200.1567.

With ZnI_2: According to the general procedure a solution of **4B** (31.4 mg, 0.102 mmol) in THF (1 mL) was added to a mixture of MeMgBr (0.33 mL, 0.93 M in THF, 0.307 mmol), CuBr·Me_2S (31.1 mg, 0.151 mmol) and ZnI_2 (49.2 mg, 0.154 mmol) in THF (1 mL) at –40 ºC and the mixture was warmed to –5 ºC over 2 h to afford **5e** (19.7 mg, 96%).

1-Ethyl-4-phenyl-1-vinylcyclohexane (5f)

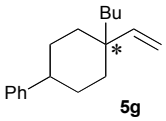


5f

According to the general procedure a solution of **4B** (80 mg, 0.274 mmol) in THF (2 mL) was added to a mixture of EtMgBr (0.95 mL, 0.85 M in THF, 0.81 mmol), CuBr·Me_2S (83.3 mg, 0.405 mmol) and $ZnBr_2$ (243 mg, 1.08 mmol) in THF (5 mL) at –40 °C. The mixture was warmed to 0 °C

over 2 h to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford **5f** (47.5 mg, 81%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, *J* = 7 Hz, 3 H), 1.22–1.42 (m, 4 H), 1.56–1.76 (m, 4 H), 1.82–1.95 (m, 2 H), 2.41–2.54 (m, 1 H), 5.01 (dd, *J* = 18, 2 Hz, 1 H), 5.24 (dd, *J* = 11, 2 Hz, 1 H), 5.60 (dd, *J* = 18, 11 Hz, 1 H), 7.12–7.36 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.9, 30.3, 35.8, 36.9, 39.8, 45.0, 114.5, 125.9, 126.9, 128.3, 144.6, 147.9.

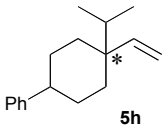
1-Butyl-4-phenyl-1-vinylcyclohexane (5g)



5g

According to the general procedure a solution of **4B** (31.2 mg, 0.102 mmol) in THF (1 mL) was added to a mixture of BuMgBr (0.31 mL, 0.975 M in THF, 0.302 mmol), CuBr·Me_2S (31.2 mg, 0.152 mmol) and ZnI_2 (48.3 mg, 0.151 mmol) in THF (1 mL) at –40 ºC, and the mixture was warmed to –5 ºC over 2 h to afford **5g** (21.6 mg, 88%): IR (neat) 3079, 1451, 1002, 910, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7 Hz, 3 H), 1.19–1.43 (m, 8 H), 1.54–1.72 (m, 4 H), 1.83–1.92 (m, 2 H), 2.39–2.52 (m, 1 H), 4.99 (dd, *J* = 18, 1.5 Hz, 1 H), 5.20 (dd, *J* = 11, 1.5 Hz, 1 H), 5.61 (dd, *J* = 18, 11 Hz, 1 H), 7.13–7.32 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 23.6 (–), 25.7 (–), 30.3 (–), 36.3 (–), 39.7 (–), 44.6 (–), 44.9 (+), 114.2 (–), 125.9 (+), 126.9 (+), 128.3 (+), 145.0 (+), 147.9 (–); HRMS (FAB) calcd for $C_{18}H_{26}$ [M^+] 242.2035, found 242.2041.

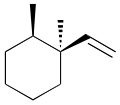
1-Isopropyl-4-phenyl-1-vinylcyclohexane (5h)



5h

According to the general procedure a solution of **4B** (71.0 mg, 0.239 mmol) in THF (1 mL) was added to a mixture of *i*PrMgBr (0.80 mL, 0.90 M in THF, 0.72 mmol), CuBr·Me_2S (74 mg, 0.36 mmol) and $ZnBr_2$ (216 mg, 0.710 mmol) in THF (5 mL) at –40 °C. The resulting mixture was allowed to warm to 0 °C over 2 h to afford **5h** (45.5 mg, 83%): IR (neat) 3027, 912, 756, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (d, *J* = 7 Hz, 3 H), 1.28–1.47 (m, 3 H), 1.52–1.74 (m, 4 H), 1.96 (dm, *J* = 14 Hz, 2 H), 2.43 (tt, *J* = 16, 4 Hz, 1 H), 4.98 (dd, *J* = 18, 2 Hz, 1 H), 5.28 (dd, *J* = 11, 2 Hz, 1 H), 5.55 (dd, *J* = 18, 11 Hz, 1 H), 7.12–7.33 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.2 (+), 30.4 (–), 33.9 (–), 39.1 (+), 42.3 (–), 44.8 (+), 115.8 (–), 125.9 (+), 126.9 (+), 128.3 (+), 142.4 (+), 147.9 (–).

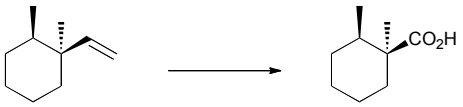
(1*R,2*R**)-1,2-Dimethyl-1-vinylcyclohexane (5i)**



5i

According to the general procedure a solution of **4C** (75 mg, 0.306 mmol) in THF (2 mL) was added to a mixture of MeMgBr (0.93 mL, 1.0 M in THF, 0.93 mmol), $CuBr{\cdot}Me_2S$ (95 mg, 0.462 mmol) and $ZnBr_2$ (276 mg, 1.23 mmol) in THF (6 mL) at –40 °C, and the resulting mixture was warmed to 0 °C over 3 h to afford **5i** (26 mg, 61%): IR (neat) 3075, 1260, 911 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.79 (d, *J* = 7 Hz, 3 H), 0.99 (s, 3 H), 0.70–2.15 (m, 9 H), 4.96 (dd, *J* = 18, 2 Hz, 1 H), 5.04 (dd, *J* = 11, 2 Hz, 1 H), 6.08 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.7 (+), 22.5 (–), 26.6 (–), 27.0 (+), 31.1 (–), 39.5 (–), 39.8 (–), 41.3 (+), 112.8 (–), 142.7 (+).

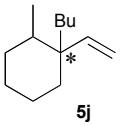
Determination of the stereochemistry of 5i



5i **S1**

To an ice-cold solution of **5i** (25 mg, 0.181 mmol) in H_2O-CCl_4-MeCN (3 : 1 : 1, 1.8 mL) were added $NaIO_4$ (162 mg, 0.76 mmol) and $RuCl_3{\cdot}nH_2O$ (1 mg). After 5 h at 0 °C, the mixture was diluted with Et_2O and aqueous Na_2SO_3. The layers were separated and the aqueous layer was extracted with Et_2O twice. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford acid **S1** (21 mg, 73%): ^1H NMR (300 MHz, $CDCl_3$) δ 084–1.74 (m, 8 H), 1.06 (d, *J* = 7 Hz, 3 H), 1.29 (s, 3 H), 1.96–2.06 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 22.8, 24.5, 25.2, 30.2, 35.2, 39.6, 45.7, 183.3. The ^{13}C NMR spectrum was identical with that reported,[10] thus establishing the relative stereochemistry as drawn above.

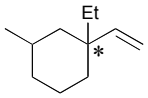
1-Butyl-2-methyl-1-vinylcyclohexane (5j)



5j

According to the general procedure a solution of **4C** (26.5 mg, 0.108 mmol) in THF (1 mL) was added to a mixture of BuMgBr (0.38 mL, 0.85 M in THF, 0.323 mmol), $CuBr{\cdot}Me_2S$ (32.8 mg, 0.160 mmol) and ZnI_2 (52.7 mg, 0.165 mmol) in THF (1 mL) at –40 ºC and the mixture was warmed to –5 ºC over 2.5 h to afford **5j** (14.8 mg, 76%): ^1H NMR (300 MHz, $CDCl_3$) δ 0.81 (d, *J* = 7 Hz, 3 H), 0.89 (d, *J* = 7 Hz, 3 H), 1.09–1.69 (m, 15 H), 4.91 (dd, *J* = 18, 2 Hz, 1 H), 5.10 (dd, *J* = 11, 2 Hz, 1 H), 5.83 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 16.0 (+), 22.2 (–), 23.7 (–), 25.5 (–), 25.9 (–), 31.1 (–), 32.6 (–), 38.8 (–), 39.2 (+), 42.2 (–), 113.5 (–), 142.4 (+).

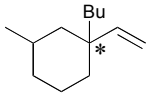
1-Ethyl-3-methyl-1-vinylcyclohexane (5k)



5k

According to the general procedure a solution of **4D** (36.7 mg, 0.150 mmol) in THF (1 mL) was added to a mixture of EtMgBr (0.45 mL, 1.0 M in THF, 0.45 mmol), CuBr·Me_2S (46.3 mg, 0.225 mmol) and ZnI_2 (71.8 mg, 0.225 mmol) in THF (2 mL) at –40 °C. The resulting mixture was allowed to warm to 0 °C over 1 h to afford **5k** (14.2 mg, 62%): IR (neat) 3079, 1458, 1001, 909 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.75 (t, *J* = 7 Hz, 3 H), 0.83 (d, *J* = 6 Hz, 3 H), 0.68–0.94 (m, 3 H), 1.02 (dt, *J* = 5, 13 Hz, 1 H), 1.18–1.75 (m, 7 H), 4.88 (dd, *J* = 18, 2 Hz, 1 H), 5.11 (ddd, *J* = 11, 2, 1 Hz, 1 H), 5.52 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.7 (+), 22.6 (–), 23.2 (+), 28.4 (+), 35.1 (–), 35.6 (–), 37.1 (–), 40.9 (–), 44.8 (–), 113.7 (–), 145.2 (+).

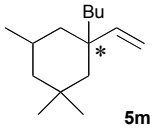
1-Butyl-3-methyl-1-vinylcyclohexane (5l)



5l

According to the general procedure a solution of **4D** (28.7 mg, 0.117 mmol) in THF (1 mL) was added to a mixture of BuMgBr (0.41 mL, 0.85 M in THF, 0.349 mmol), CuBr·Me_2S (36.0 mg, 0.175 mmol) and ZnI_2 (55.1 mg, 0.173 mmol) in THF (1 mL) at –40 ºC, and the mixture was warmed to –5 ºC over 2 h to afford **5l** (16.8 mg, 79%): IR (neat) 3079, 1458, 1001, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.84 (d, *J* = 7 Hz, 3 H), 0.87 (t, *J* = 6.5 Hz, 3 H), 0.69–1.74 (m, 15 H), 4.89 (dd, *J* = 18, 2 Hz, 1 H), 5.10 (dd, *J* = 11, 2 Hz, 1 H), 5.55 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (+), 22.6 (–), 23.2 (+), 23.6 (–), 25.5 (–), 28.4 (+), 35.6 (–), 40.7 (–), 44.9 (–), 45.2 (–), 113.4 (–), 145.7 (+); HRMS (EI) calcd for $C_{13}H_{24}$ [M^+] 180.1878, found 180.1877.

1-Butyl-3,3,5-trimethyl-1-vinylcyclohexane (5m)

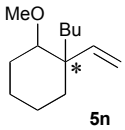


5m

According to the general procedure a solution of **4E** (32.4 mg, 0.119 mmol) in THF (1 mL) was added to a mixture of BuMgBr (0.48 mL, 0.738 M in THF, 0.354 mmol), CuBr·Me_2S (36.6 mg, 0.178 mmol) and ZnI_2 (57.4 mg, 0.180 mmol) in THF (1 mL) at –40 ºC, and the mixture was warmed to –5 ºC over 2 h to afford **5m** (18.7 mg, 76%): IR (neat) 3078, 1458, 1004, 906 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.54–1.36 (m, 22 H), 1.43 (dm, *J* = 14 Hz, 1 H), 1.63–1.78 (m, 1 H), 1.87 (dm, *J* = 14 Hz, 1 H), 4.87 (dd, *J* = 18, 1.5 Hz, 1 H), 4.99 (dd, *J* = 11, 1.5 Hz, 1 H), 5.67 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 23.0 (+), 23.6 (–), 24.6 (+), 25.3 (–), 27.2

(+), 32.1 (–), 34.7 (+), 40.7 (–), 42.2 (–), 46.3 (–), 49.2 (–), 51.3 (–), 111.2 (–), 147.3 (+); HRMS (EI) calcd for $C_{15}H_{28}$ [M^+] 208.2191, found 208.2197.

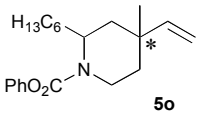
1-Butyl-2-methoxy-1-vinylcyclohexane (5n)



5n

According to the general procedure a solution of **4F** (28.0 mg, 0.107 mmol) in THF (1 mL) was added to a mixture of BuMgBr (0.34 mL, 0.938 M in THF, 0.319 mmol), CuBr·Me_2S (33.0 mg, 0.161 mmol) and ZnI_2 (52.3 mg, 0.164 mmol) in THF (1 mL) at –40 ºC, and the mixture was warmed to 5 ºC over 3 h to afford **5n** (14.6 mg, 70%): IR (neat) 3075, 1104, 909 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7 Hz, 3 H), 1.08–1.86 (m, 14 H), 2.91 (dd, *J* = 9.5, 3.5 Hz, 1 H), 3.33 (s, 3 H), 4.97 (dd, *J* = 18, 2 Hz, 1 H), 5.15 (dd, *J* = 11, 2 Hz, 1 H), 5.85 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 21.5 (–), 23.6 (–), 24.0 (–), 25.5 (–), 26.0 (–), 31.1 (–), 38.1 (–), 45.0 (–), 57.1 (+), 85.6 (+), 113.9 (–), 141.9 (+).

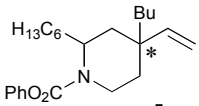
Phenyl 2-Hexyl-4-methyl-4-vinylpiperidine-1-carboxylate (5o)



5o

According to the general procedure a solution of **4G** (47.8 mg, 0.110 mmol) in THF (1 mL) was added to a mixture of MeMgBr (0.31 mL, 1.06 M in THF, 0.329 mmol), CuBr·Me_2S (33.8 mg, 0.164 mmol) and ZnI_2 (52.4 mg, 0.164 mmol) in THF (1 mL) at –40 ºC, and the mixture was warmed to 5 ºC over 3 h to afford **5o** (26.1 mg, 72%): IR (neat) 1718, 1419, 1204,749, 688 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7 Hz, 3 H), 1.00 (s, 3 H), 1.2–2.1 (m, 14 H), 3.03–3.37 (m, 1 H), 4.06 (d, *J* = 13.5 Hz, 1 H), 4.25–4.44 (m, 1 H), 5.03 (d, *J* = 17.5 Hz, 1 H), 5.04 (d, *J* = 11 Hz, 1 H), 5.91 (dd, *J* = 17.5, 11 Hz, 1 H), 7.07–7.39 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (+), 22.7 (–), 26.7 (–), 29.2 (–), 31.9 (–), 32.0 (–), 32.3 (+), 34.6 (–), 34.8 (–), 36.7 (–), 40.6 (–), 52.0 (+), 111.2 (–), 121.8 (+), 125.1 (+), 129.3 (+), 146.8 (+), 151.7 (–); HRMS (FAB) calcd for $C_{21}H_{32}NO_2$ [$(M+H)^+$] 330.2433, found 330.2438.

Phenyl 4-Butyl-2-hexyl-4-vinylpiperidine-1-carboxylate (5p)

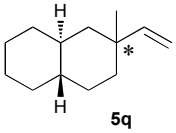


5p

According to the general procedure a solution of **4G** (47.3 mg, 0.108 mmol) in THF (1 mL) was added to a mixture of BuMgBr (0.42 mL, 0.738 M in THF, 0.323 mmol), CuBr·Me_2S (33.4 mg,

0.163 mmol) and ZnI_2 (52.3 mg, 0.164 mmol) in THF (1 mL) at –40 ºC. The mixture was warmed to –5 ºC over 2 h to afford **5p** (34.0 mg, 84%): IR (neat) 1718, 1419, 1204 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7 Hz, 6 H), 1.1–1.9 (m, 19 H), 1.95 (d, *J* = 13.5 Hz, 1 H), 3.00–3.25 (m, 1 H), 4.05 (d, *J* = 13.5 Hz, 1 H), 4.22–4.45 (m, 1 H), 4.98 (dd, *J* = 18, 1 Hz, 1 H), 5.14 (dd, *J* = 11, 1 Hz, 1 H), 5.76 (dd, *J* = 18, 11 Hz, 1 H), 7.06–7.39 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (+), 22.7 (–), 23.3 (–), 25.1 (–), 26.8 (–), 29.2 (–), 31.9 (–), 32.1 (–), 32.6 (–), 36.5 (–), 37.8 (–), 39.9 (–), 45.0 (–), 52.1 (+), 112.7 (–), 121.8 (+), 125.1 (+), 129.3 (+), 145.2 (+), 151.7 (–), 154.0 (–); HRMS (FAB) calcd for $C_{24}H_{38}NO_2$ [$(M+H)^+$] 372.2903, found 372.2900.

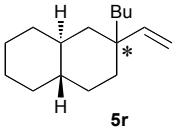
(4a*S,8a*S**)-2-Methyl-2-vinyldecahydronaphthalene (5q)**



5q

According to the general procedure a solution of **4H** (34.1 mg, 0.119 mmol) in THF (1 mL) was added to a mixture of MeMgBr (0.34 mL, 1.06 M in THF, 0.360 mmol), $CuBr{\cdot}Me_2S$ (36.8 mg, 0.179 mmol) and ZnI_2 (57.0 mg, 0.179 mmol) in THF (1 mL) at –40 ºC. The mixture was allowed to warm to –5 ºC over 2 h to afford **5q** (16.2 mg, 76%): IR (neat) 3079, 1448, 909 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 3 H), 0.77–1.73 (m, 16 H), 4.95 (dd, *J* = 17.5, 1.5 Hz, 1 H), 4.99 (dd, *J* = 11, 1.5 Hz, 1 H), 5.79 (dd, *J* = 17.5, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.7 (–), 26.8 (–), 30.3 (–), 31.7 (+), 33.8 (–), 34.3 (–), 37.5 (–), 37.8 (–), 38.9 (+), 43.5 (+), 45.9 (–), 111.8 (–), 147.2 (+).

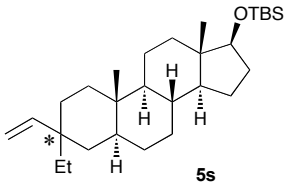
(4a*S,8a*S**)-2-Butyl-2-vinyldecahydronaphthalene (5r)**



5r

According to the general procedure a solution of **4H** (33.3 mg, 0.117 mmol) in THF (1 mL) was added to a mixture of BuMgBr (0.47 mL, 0.738 M in THF, 0.347 mmol), $CuBr{\cdot}Me_2S$ (36.4 mg, 0.177 mmol) and ZnI_2 (55.9 mg, 0.175 mmol) in THF (1 mL) at –40 ºC, and the mixture was warmed to –5 ºC over 2 h to afford **5r** (24.6 mg, 96%): IR (neat) 3078, 1418, 1001, 909 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.77–1.78 (m, 25 H), 4.89 (dd, *J* = 18, 2 Hz, 1 H), 5.10 (dd, *J* = 11, 2 Hz, 1 H), 5.57 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3 (+), 23.6 (–), 25.6 (–), 26.7 (–), 26.8 (–), 30.2 (–), 33.8 (–), 34.3 (–), 35.9 (–), 38.7 (+), 43.9 (+), 44.1 (–), 44.8 (–), 113.4 (–), 145.9 (+); HRMS (EI) calcd for $C_{16}H_{28}$ [M^+] 220.2191, found 220.2185.

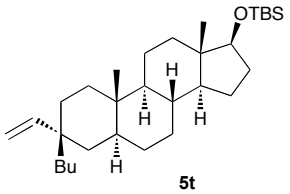
***tert*-Butyl(((10*S*,13*S*,17*S*)-3-ethyl-10,13-dimethyl-3-vinylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)oxy)dimethylsilane (5s)**



5s

According to the general procedure a solution of **4I** (40.7 mg, 0.0757 mmol) in THF (1 mL) was added to a mixture of EtMgBr (0.23 mL, 1.0 M in THF, 0.230 mmol), CuBr·Me_2S (23.3 mg, 0.113 mmol) and ZnI_2 (36.4 mg, 0.114 mmol) in THF (1 mL) at –40 °C. The resulting mixture was allowed to warm to 0 °C over 1 h to give **5s** (29.3 mg, 87%): $[\alpha]_D^{23}$ +23 (*c* 0.53, $CHCl_3$); IR (neat) 3078, 1472, 1255, 1119, 1094, 1081, 909, 835 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ –0.011 (s, 3 H), –0.004 (s, 3 H), 0.67 (s, 3 H), 0.745 (t, *J* = 8 Hz, 3 H), 0.754 (s, 3 H), 0.87 (s, 9 H), 1.20 (q, *J* = 8 Hz, 2 H), 0.54–1.91 (m, 22 H), 3.51 (t, *J* = 8 Hz, 1 H), 4.91 (dd, *J* = 18, 1 Hz, 1 H), 5.12 (dd, *J* = 11, 1 Hz, 1 H), 5.51 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (+), –4.4 (+), 7.8 (+), 11.5 (+), 12.1 (+), 18.2 (–), 20.7 (–), 23.6 (–), 26.0 (+), 28.9 (–), 30.4 (–), 31.0 (–), 31.7 (–), 34.9 (–), 35.7 (+), 36.4 (–), 36.9 (–), 37.3 (–), 39.0 (–), 40.6 (–), 42.1 (+), 43.4 (–), 50.8 (+), 54.9 (+), 82.0 (+), 113.5 (–), 145.6 (+).

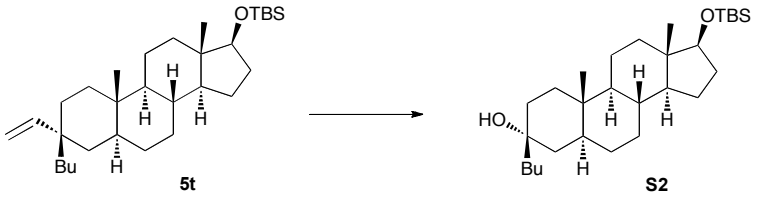
tert-Butyl((3*R*,10*S*,13*S*,17*S*)-3-butyl-10,13-dimethyl-3-vinylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yloxy)dimethylsilane (5t)



5t

According to the general procedure a solution of **4I** (31.0 mg, 0.0576 mmol) in THF (0.7 mL) was added to a mixture of BuMgBr (0.18 mL, 0.96 M in THF, 0.173 mmol), CuBr·Me_2S (17.8 mg, 0.0866 mmol) and ZnI_2 (28.3 mg, 0.0887 mmol) in THF (0.8 mL) at –40 ºC, and the mixture was warmed to –5 ºC over 2 h to afford **5t** (21.7 mg, 80%): IR (neat) 1249, 1087, 909, 834, 774 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ –0.01 (s, 3 H), 0.00 (s, 3 H), 0.67 (s, 3 H), 0.76 (s, 3 H), 0.87 (s, 9 H), 0.54–1.91 (m, 31 H), 3.51 (t, *J* = 8 Hz, 1 H), 4.90 (dd, *J* = 18, 1.5 Hz, 1 H), 5.09 (dd, *J* = 11, 1.5 Hz, 1 H), 5.53 (dd, *J* = 18, 11 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (+), –4.4 (+), 11.5 (+), 12.1 (+), 14.2 (+), 18.2 (–), 20.7 (–), 23.6 (–), 25.6 (–), 26.0 (+), 28.9 (–), 30.97 (–), 31.01 (–), 31.7 (–), 34.9 (–), 35.7 (+), 36.4 (–), 37.3 (–), 39.3 (–), 40.5 (–), 42.1 (+), 43.4 (–), 44.7 (–), 50.8 (+), 54.9 (+), 82.0 (+), 113.2 (–), 146.1 (+); HRMS (EI) calcd for $C_{31}H_{56}OSi$ [M^+] 472.4100, found 472.4094.

Determination of the stereochemistry of 5t



A stream of ozone was bubbled to a solution of **5t** (51.5 mg, 0.109 mmol) in CH_2Cl_2 (3 mL) at –78 °C for 30 min, Ar was bubbled to remove excess O_3, and Me_2S (0.10 mL) was added. The solution was stirred at room temperature for 20 min and diluted with CH_2Cl_2. The solution was washed with brine, dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford the corresponding aldehyde (29.6 mg, 57%).

To a solution of the above aldehyde (29.6 mg, 0.0623 mmol) in CH_2Cl_2 (1 mL) was added *m*CPBA (16.1 mg, 0.0933 mmol). The mixture was stirred at room temperature for 48 h and diluted with saturated NH_4Cl. The product was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated to afford the corresponding formate, which was used for the next reaction without further purification.

To a solution of the above formate in MeOH (1 mL) was added KOH (7 mg, 0.12 mmol). The mixture was stirred at room temperature overnight and diluted with EtOAc. The product was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford alcohol **S2** (10.2 mg, 20% from the aldehyde): ^{1}H NMR (300 MHz, $CDCl_3$) δ –0.073 (s, 3 H), –0.066 (s, 3 H), 0.62 (s, 3 H), 0.67 (s, 3 H), 0.80 (s, 9 H), 0.6–1.9 (m, 32 H), 3.47 (t, J = 8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (+), –4.4 (+), 11.3 (+), 11.5 (+), 14.2 (+), 18.2 (–), 20.7 (–), 23.4 (–), 23.6 (–), 25.4 (–), 26.0 (+), 28.6 (–), 31.0 (–), 31.7 (–), 33.2 (–), 34.0 (–), 35.7 (+), 36.0 (–), 37.3 (–), 40.0 (–), 41.1 (+), 43.4 (–), 44.3 (–), 50.8 (+), 54.6 (+), 71.7 (–), 81.9 (+). The ^{1}H and ^{13}C NMR spectra except APT were consistent with those reported.[8]

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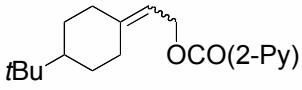
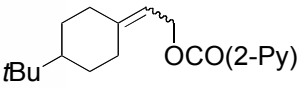


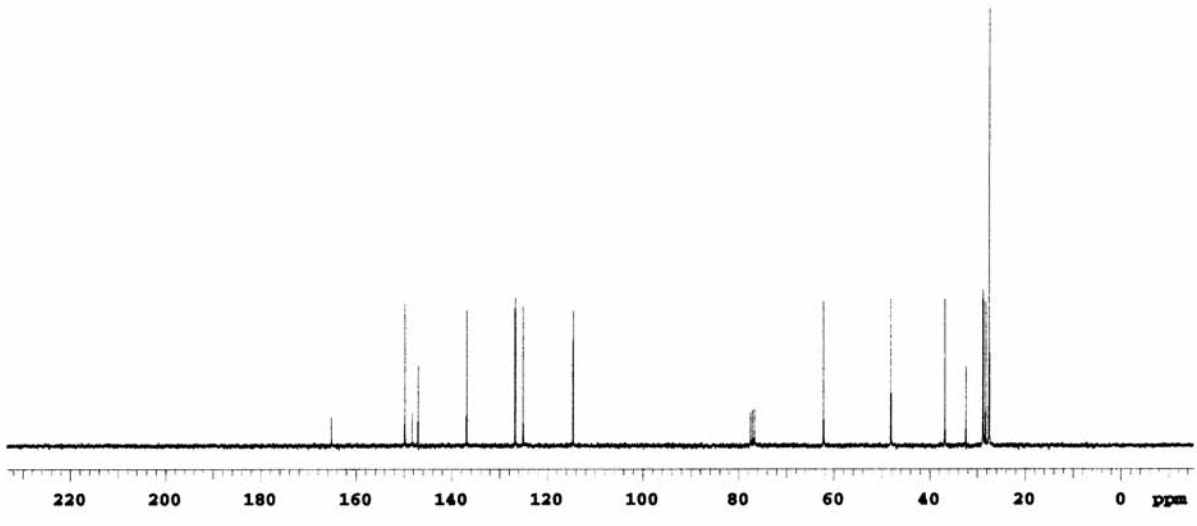
4A

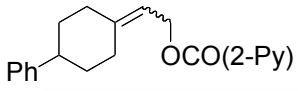
^{1}H NMR (300 MHz, $CDCl_3$)



4A

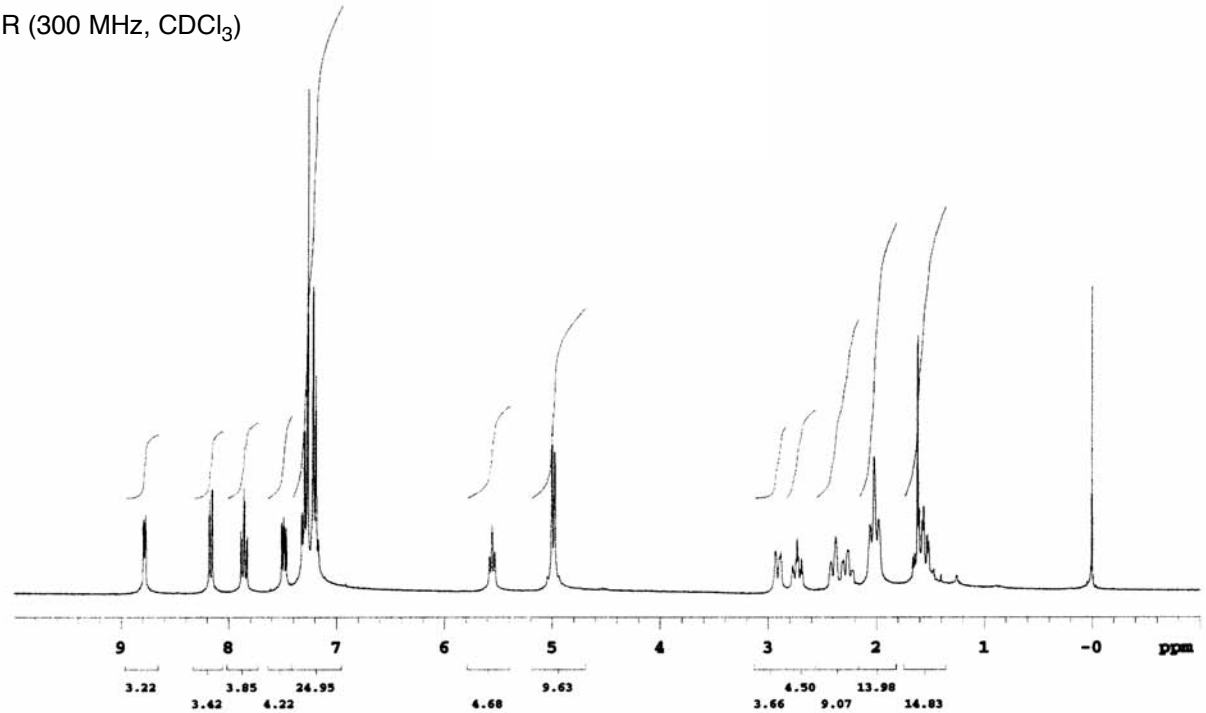
^{13}C NMR (75 MHz, $CDCl_3$)

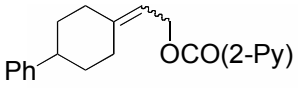




4B

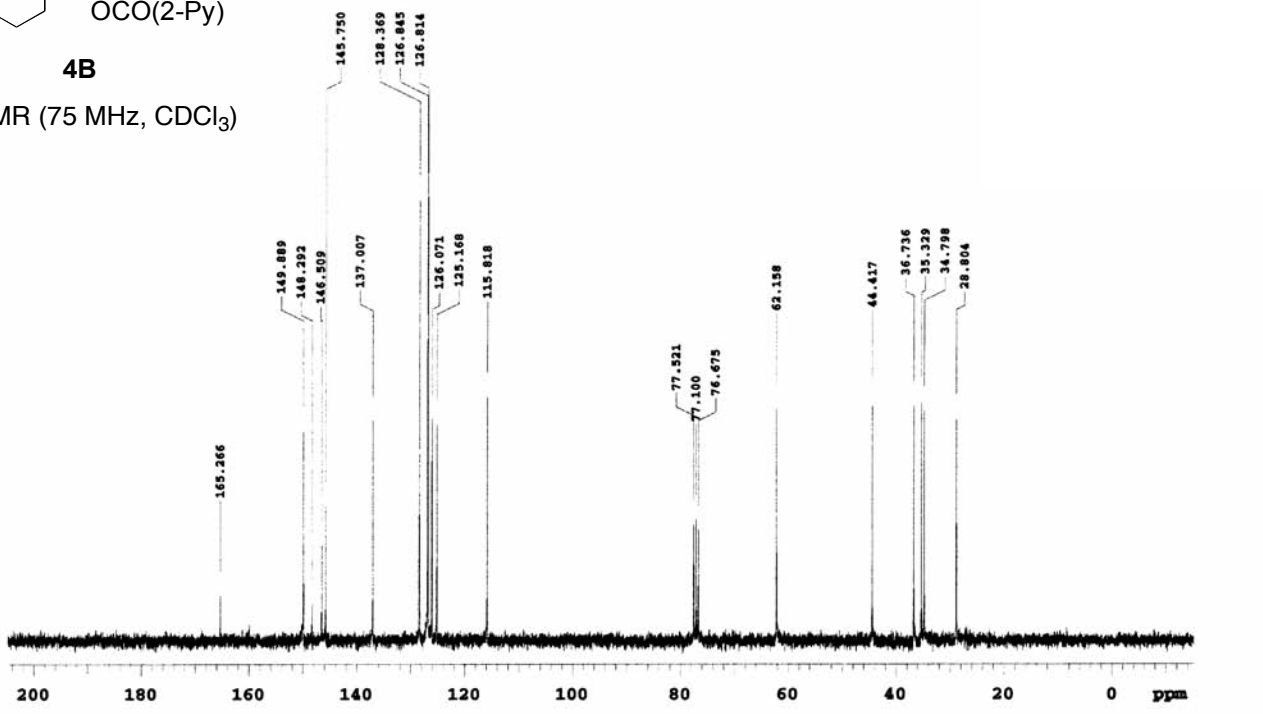
^{1}H NMR (300 MHz, $CDCl_3$)

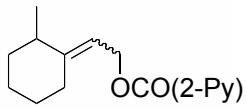




4B

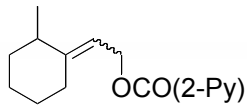
^{13}C NMR (75 MHz, $CDCl_3$)





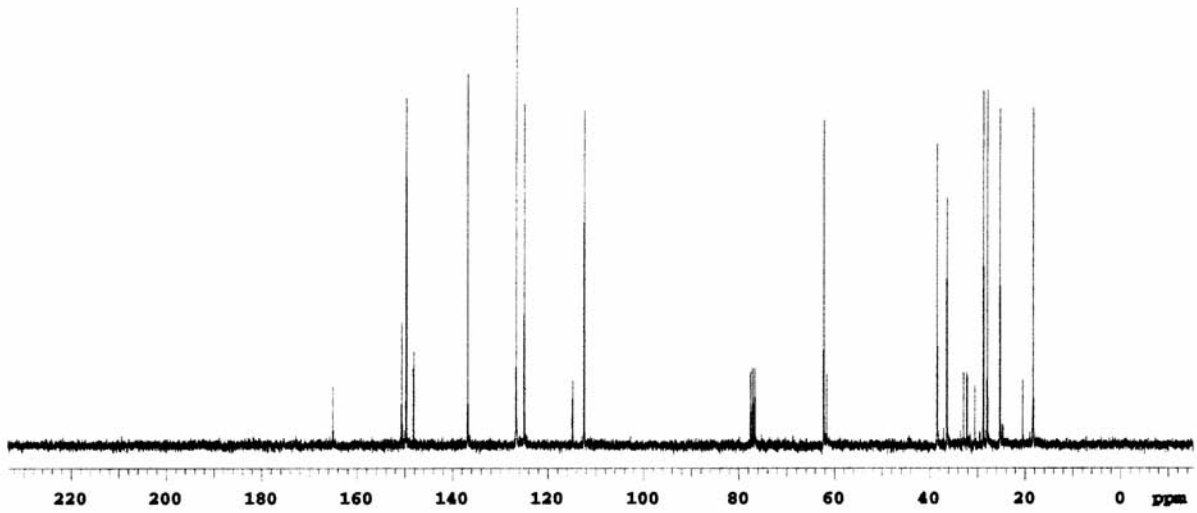
4C

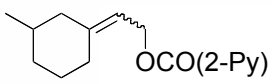
^{1}H NMR (300 MHz, $CDCl_3$)



4C

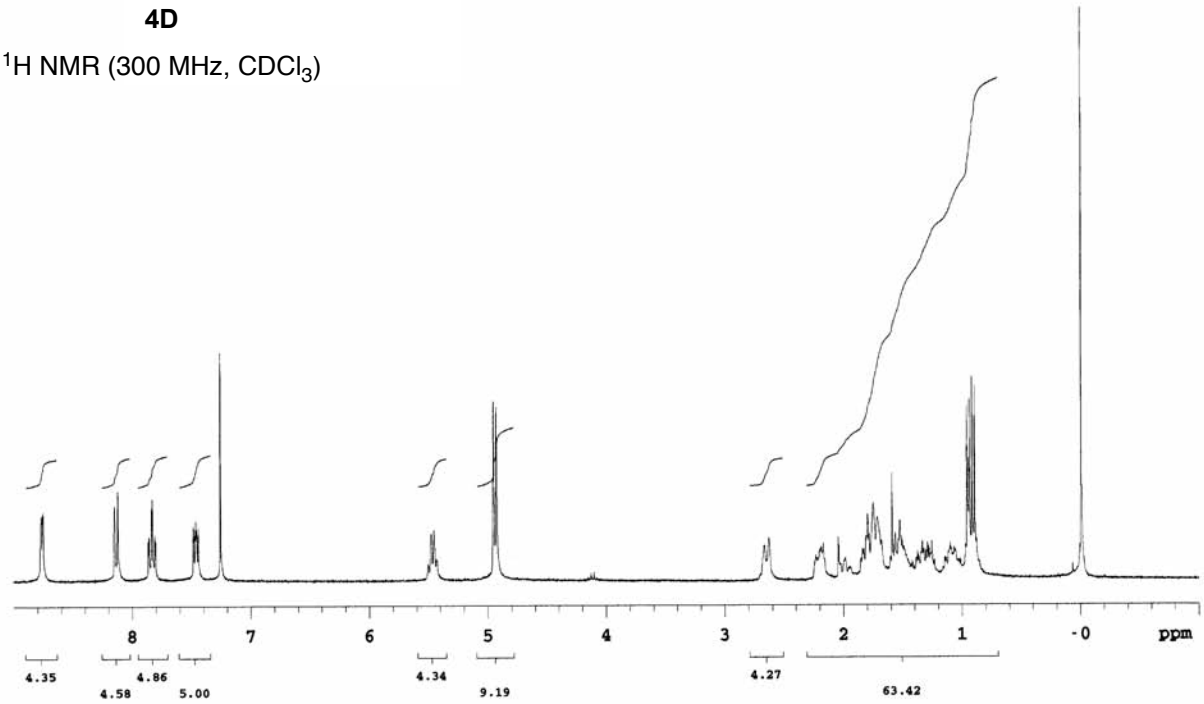
^{13}C NMR (75 MHz, $CDCl_3$)

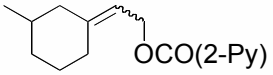




4D

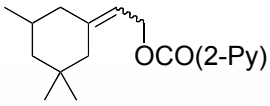
^{1}H NMR (300 MHz, $CDCl_3$)





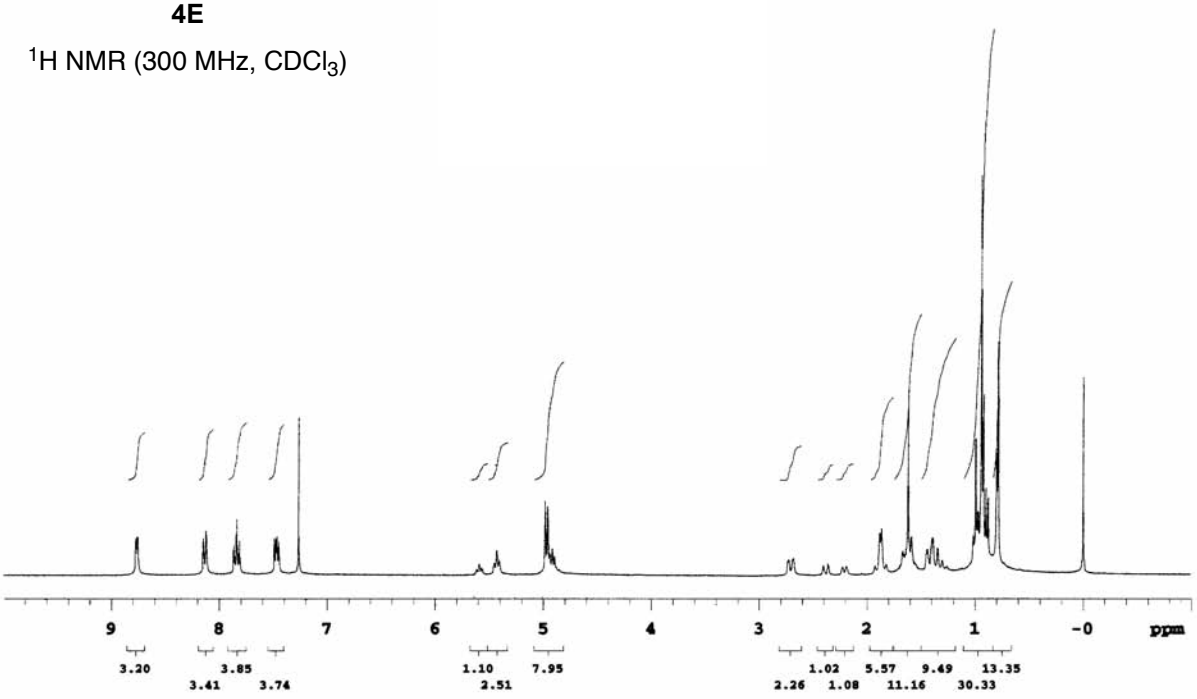
4D

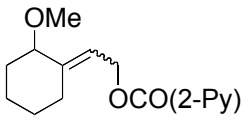
^{13}C NMR (75 MHz, $CDCl_3$)



4E

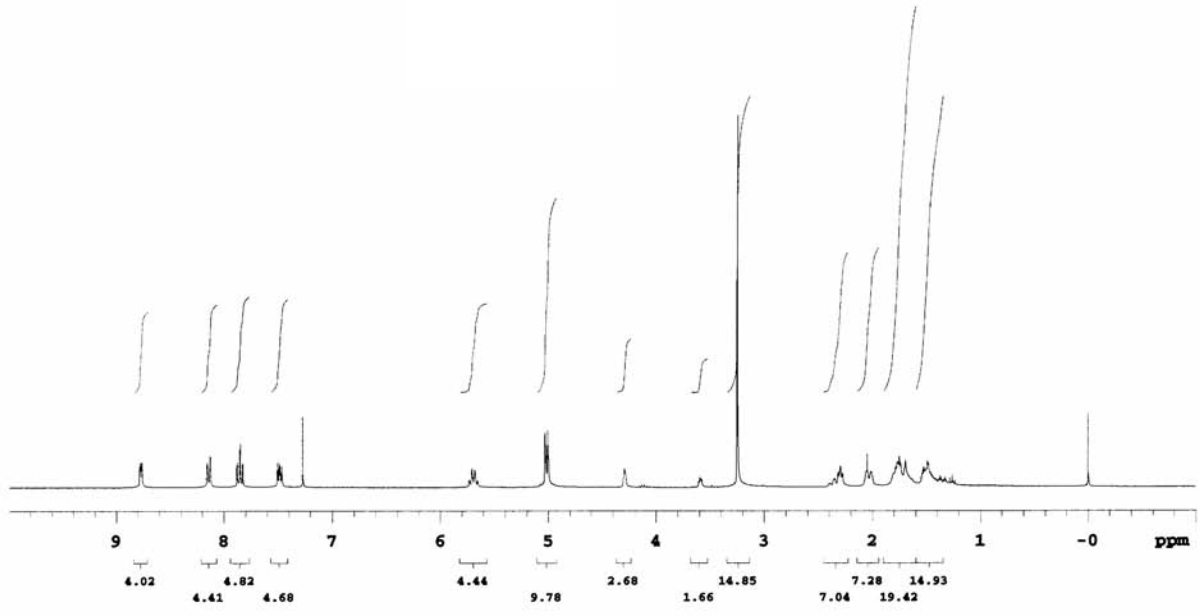
^{1}H NMR (300 MHz, $CDCl_3$)

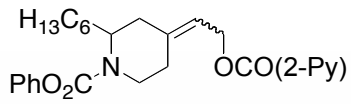




4F

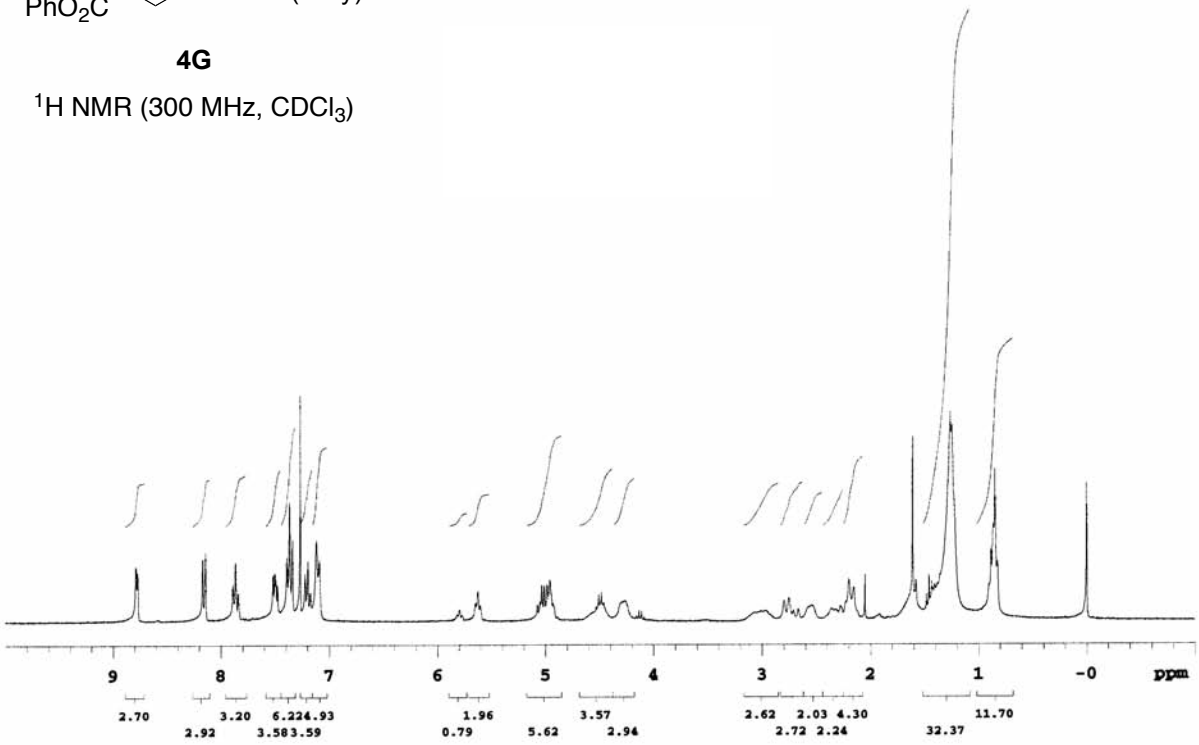
^{1}H NMR (300 MHz, $CDCl_3$)

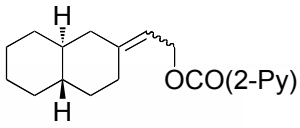




4G

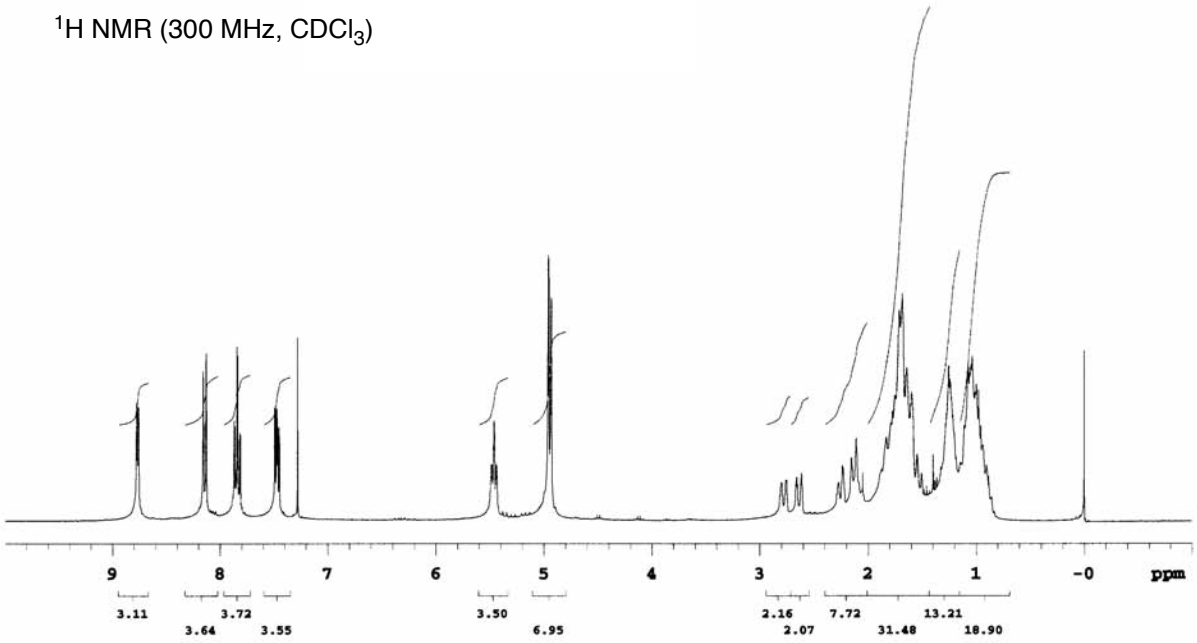
^{1}H NMR (300 MHz, $CDCl_3$)

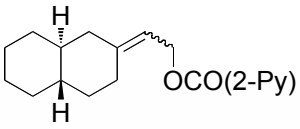




4H

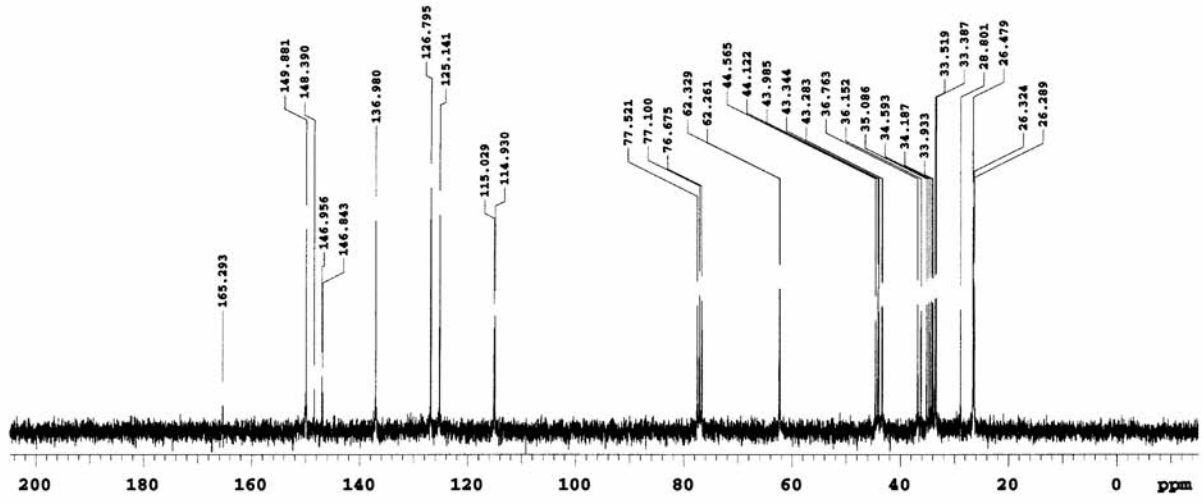
^{1}H NMR (300 MHz, $CDCl_3$)

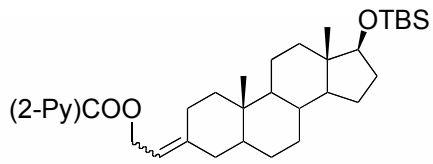




4H

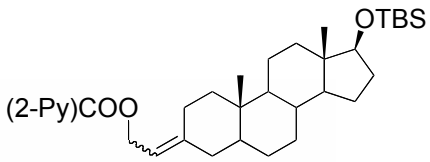
^{13}C NMR (75 MHz, $CDCl_3$)





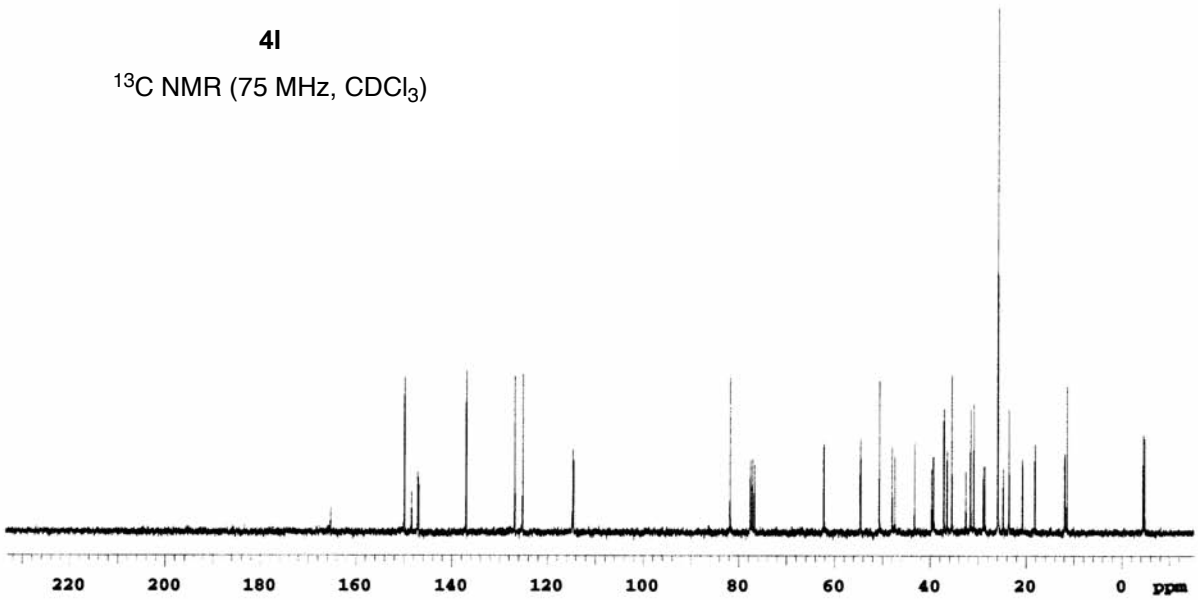
4l

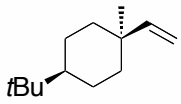
^{1}H NMR (300 MHz, $CDCl_3$)



4l

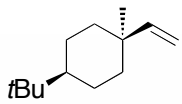
^{13}C NMR (75 MHz, $CDCl_3$)





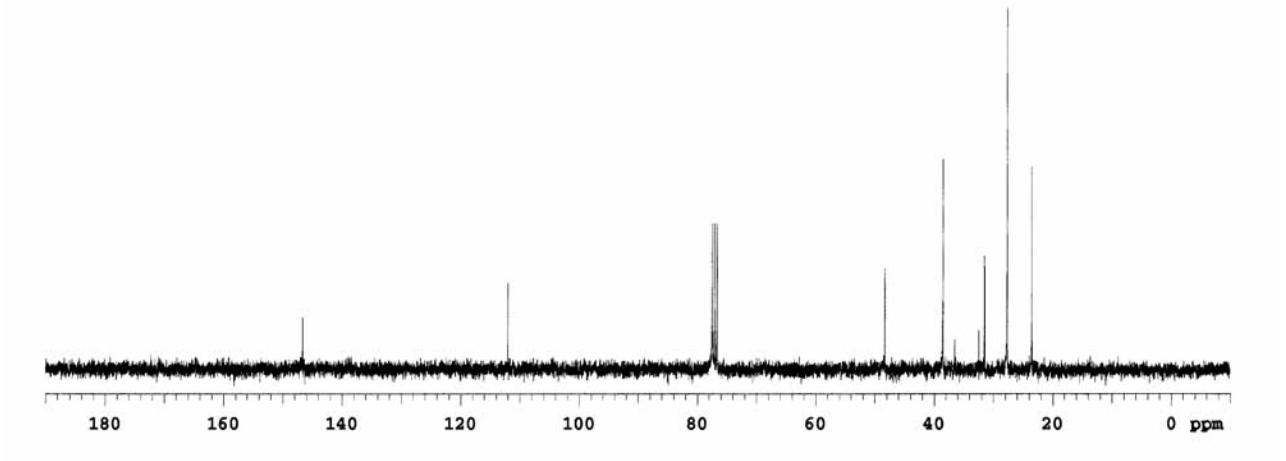
5a

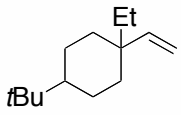
^{1}H NMR (300 MHz, $CDCl_3$)



5a

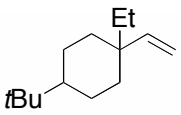
^{13}C NMR (75 MHz, $CDCl_3$)





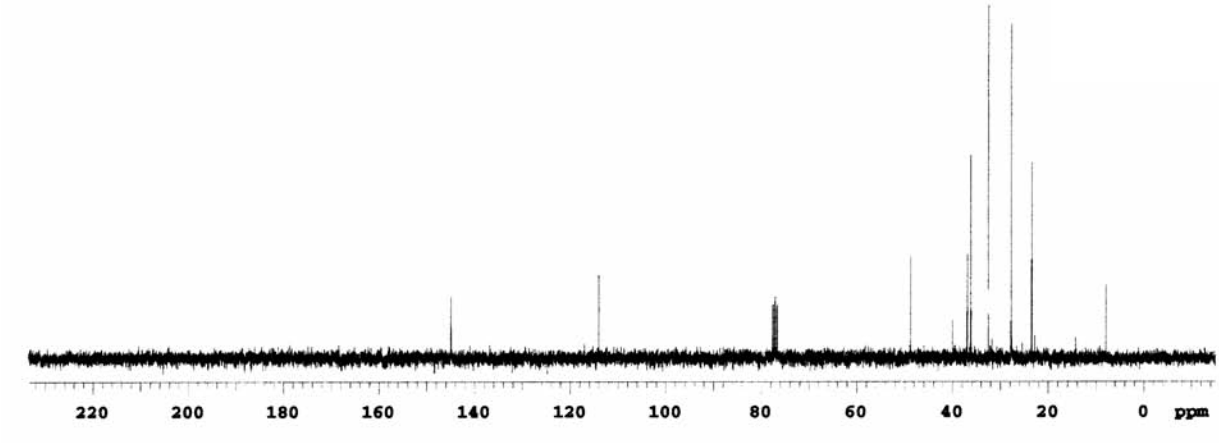
5b

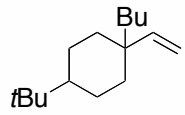
^{1}H NMR (300 MHz, $CDCl_3$)



5b

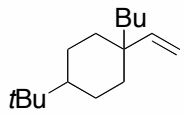
^{13}C NMR (75 MHz, $CDCl_3$)





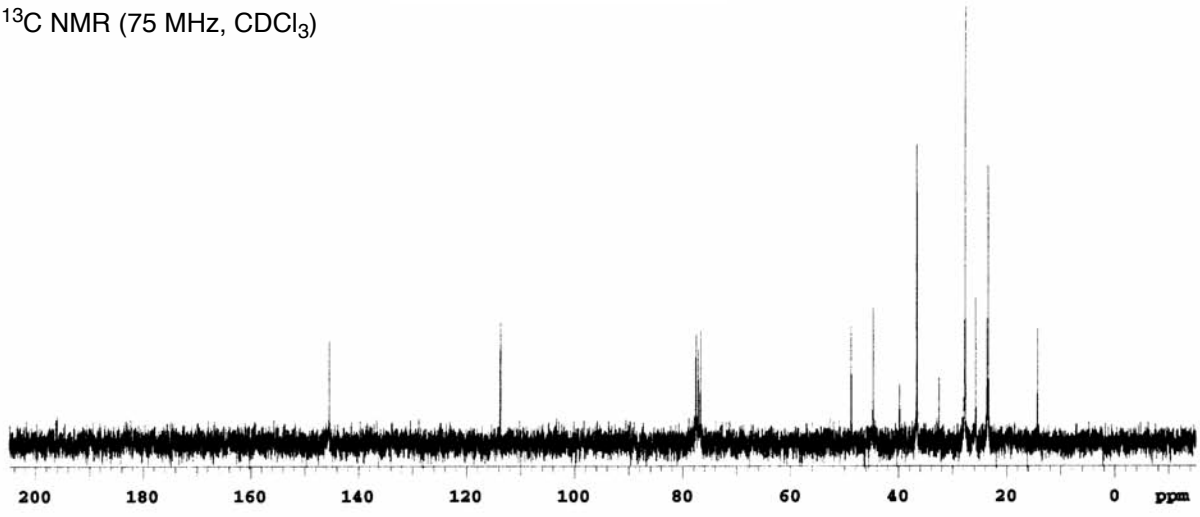
5c

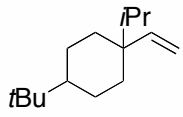
^{1}H NMR (300 MHz, $CDCl_3$)



5c

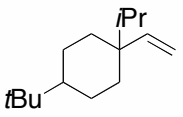
^{13}C NMR (75 MHz, $CDCl_3$)





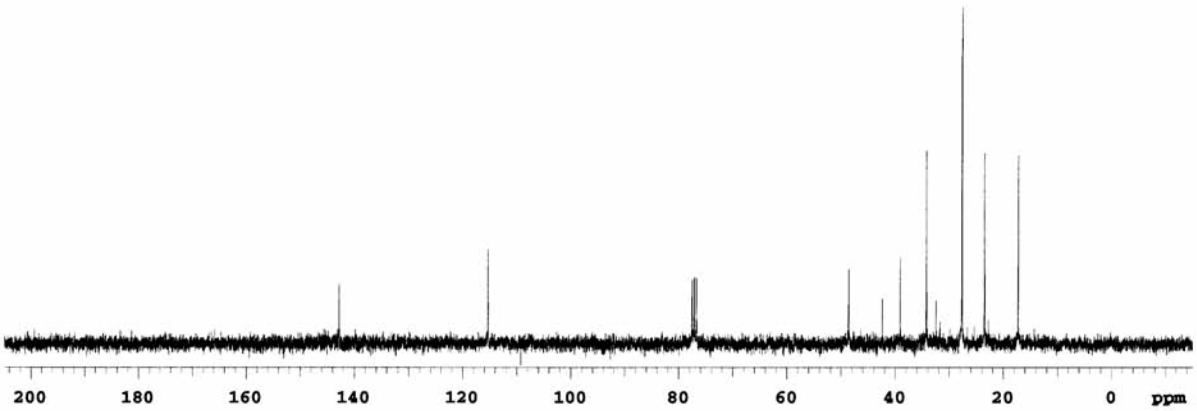
5d

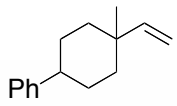
^{1}H NMR (300 MHz, $CDCl_3$)



5d

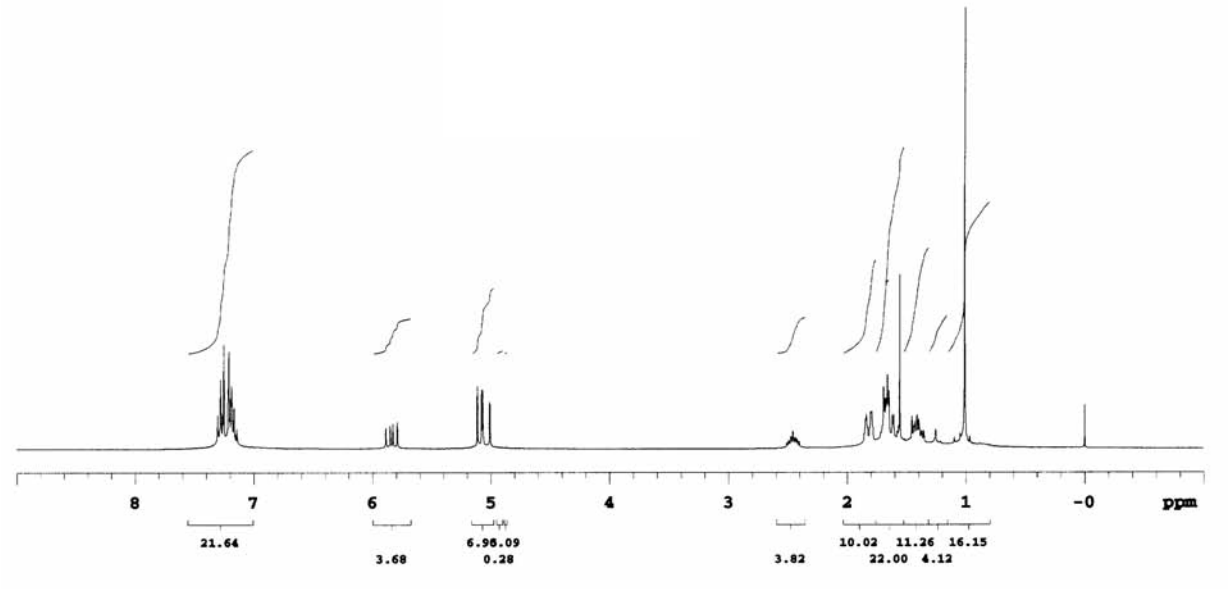
^{13}C NMR (75 MHz, $CDCl_3$)

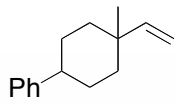




5e

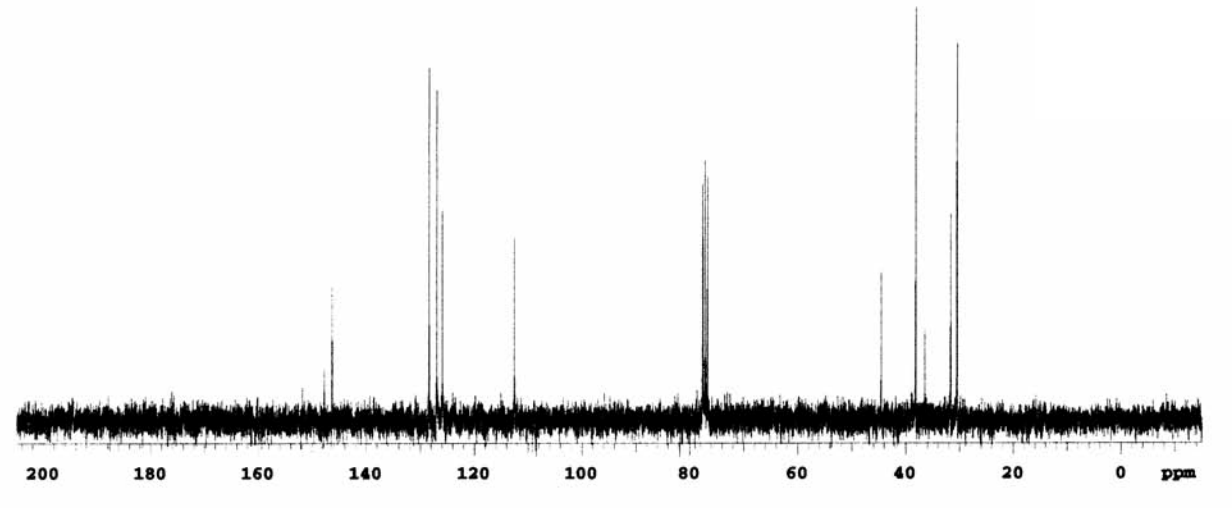
^{1}H NMR (300 MHz, $CDCl_3$)

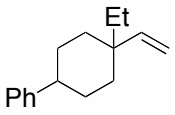




5e

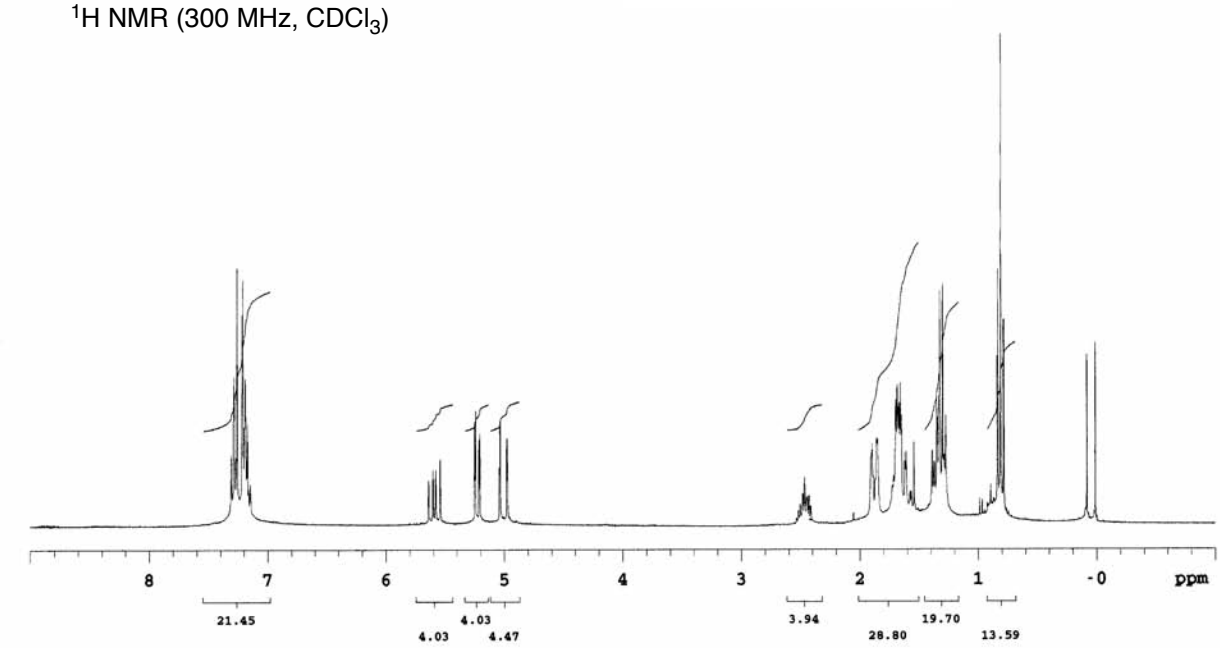
^{13}C NMR (75 MHz, $CDCl_3$)

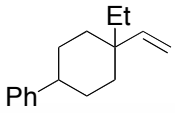




5f

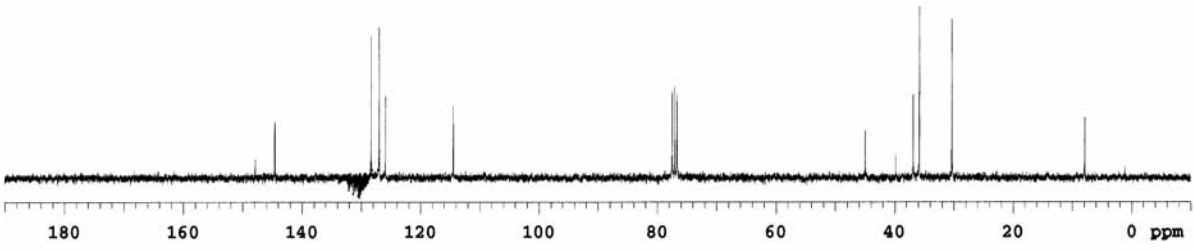
^{1}H NMR (300 MHz, $CDCl_3$)

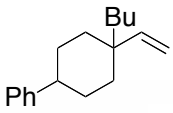




5f

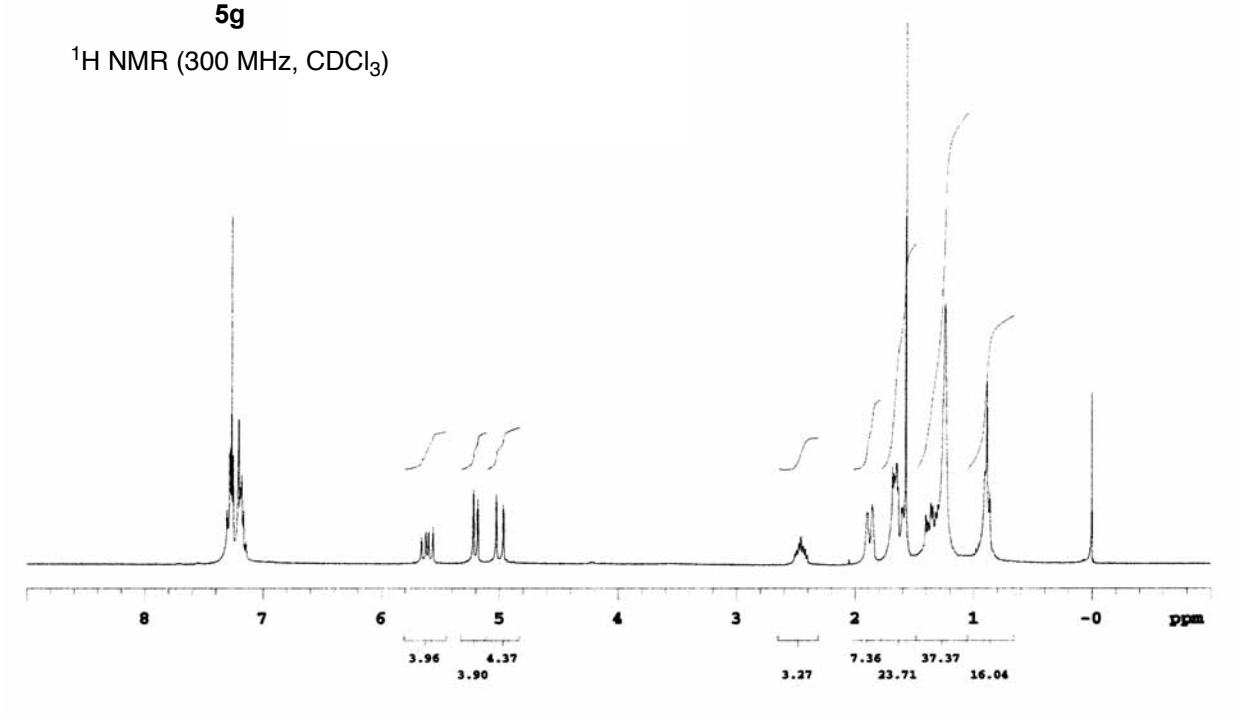
^{13}C NMR (75 MHz, $CDCl_3$)

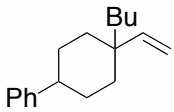




5g

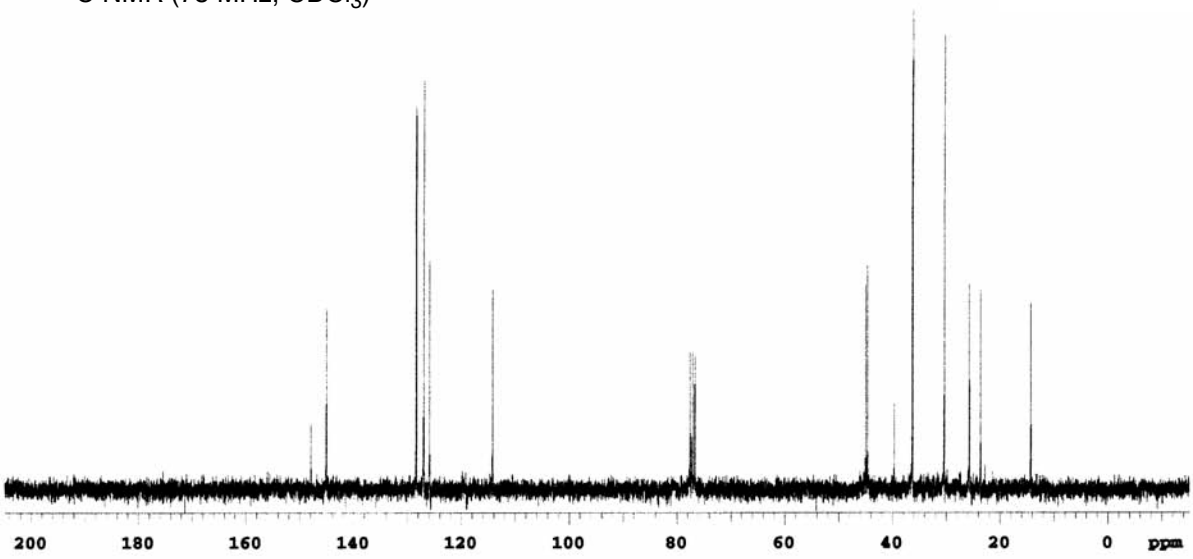
^{1}H NMR (300 MHz, $CDCl_3$)

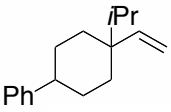




5g

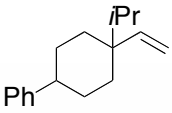
^{13}C NMR (75 MHz, $CDCl_3$)





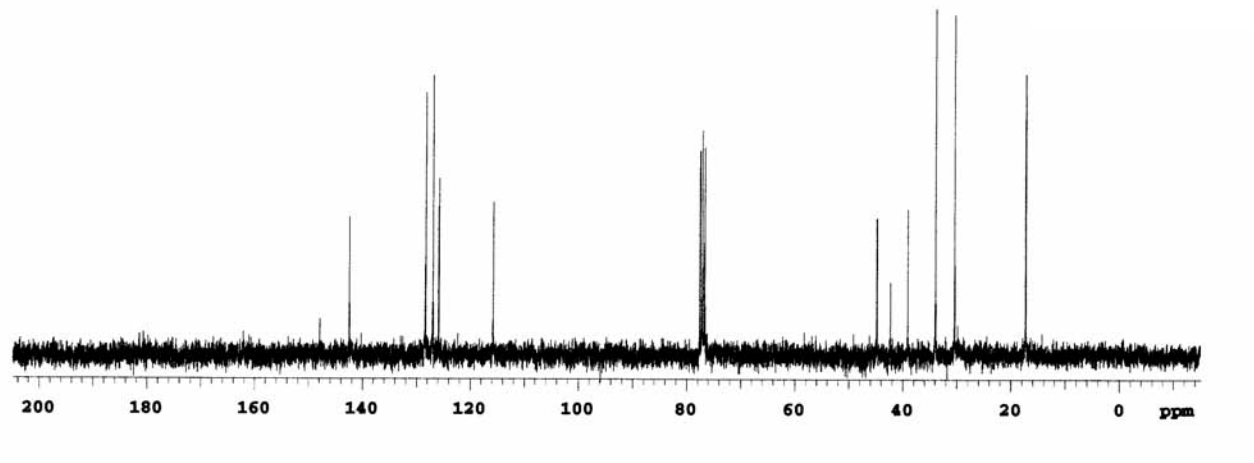
5h

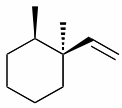
^{1}H NMR (300 MHz, $CDCl_3$)



5h

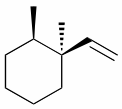
^{13}C NMR (75 MHz, $CDCl_3$)





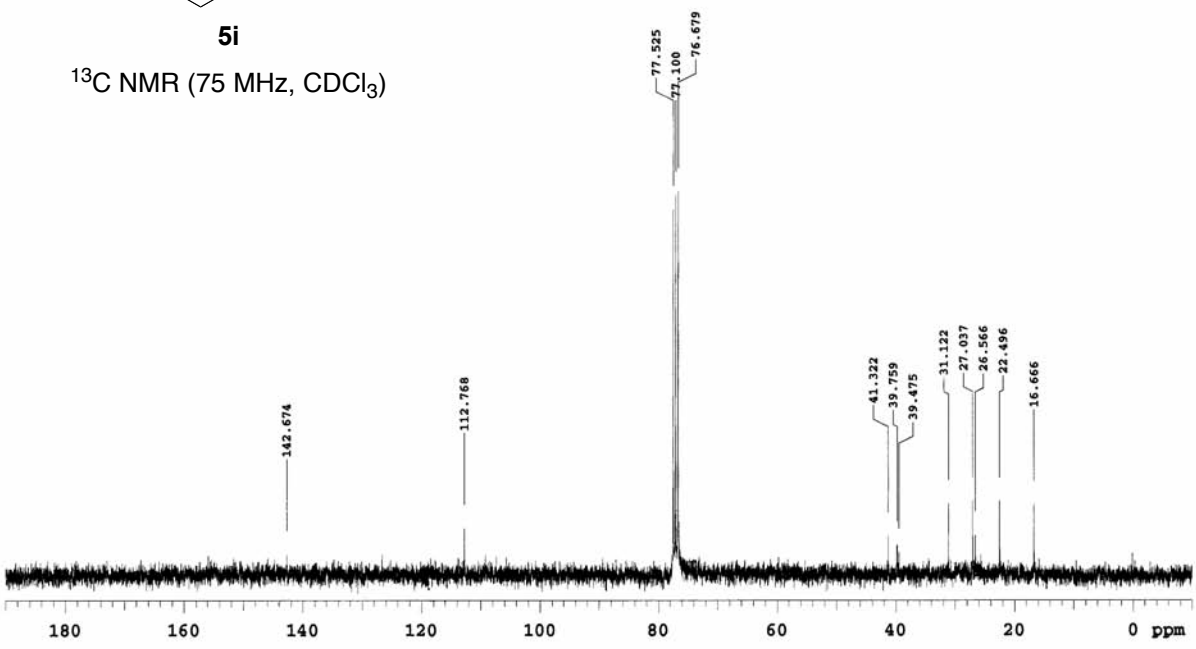
5i

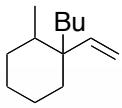
^{1}H NMR (300 MHz, $CDCl_3$)



5i

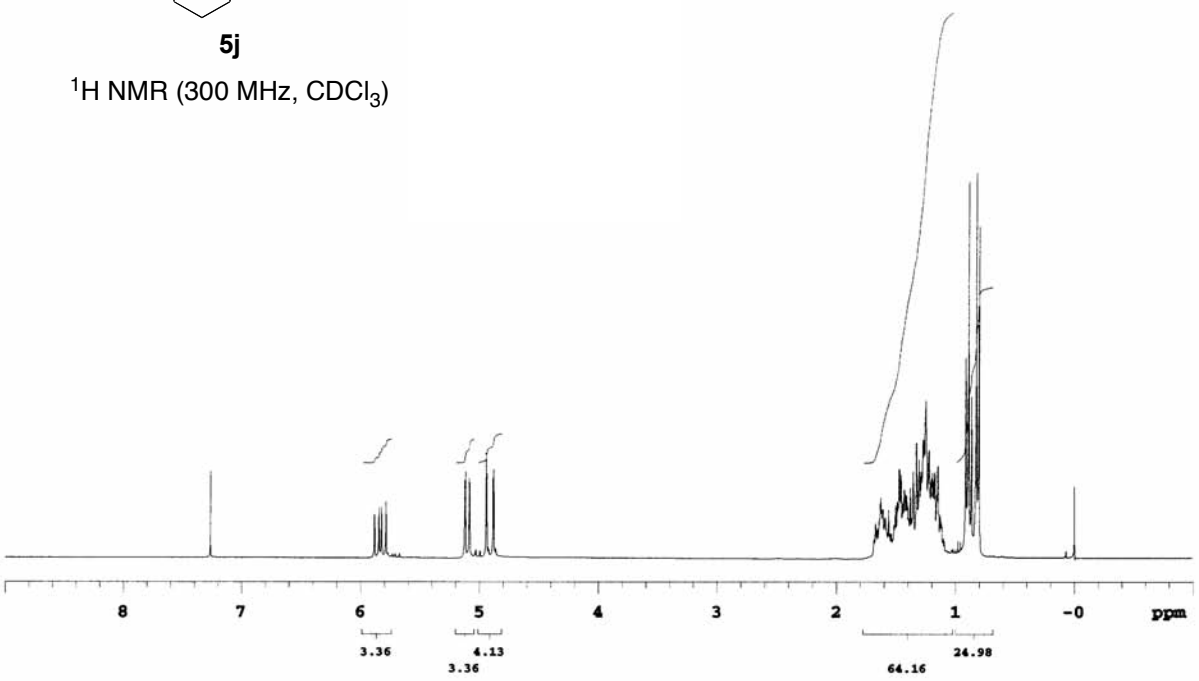
^{13}C NMR (75 MHz, $CDCl_3$)

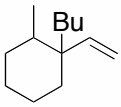




5j

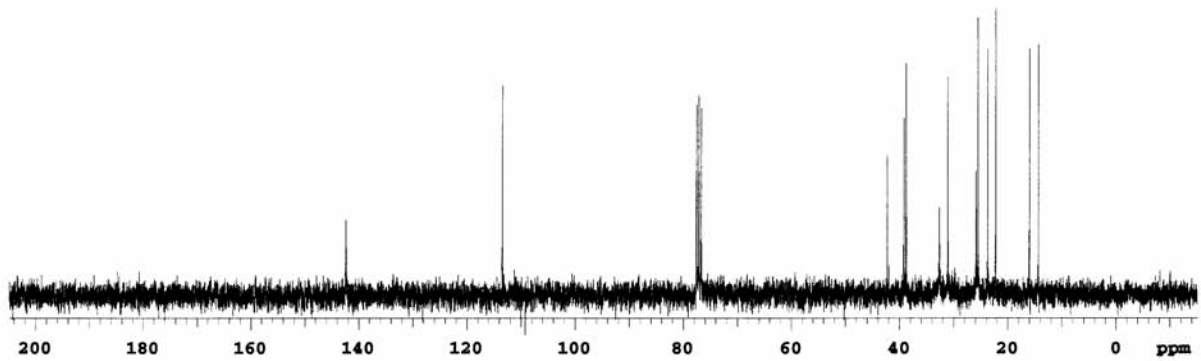
^{1}H NMR (300 MHz, $CDCl_3$)

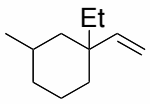




5j

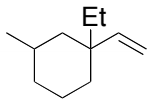
^{13}C NMR (75 MHz, $CDCl_3$)





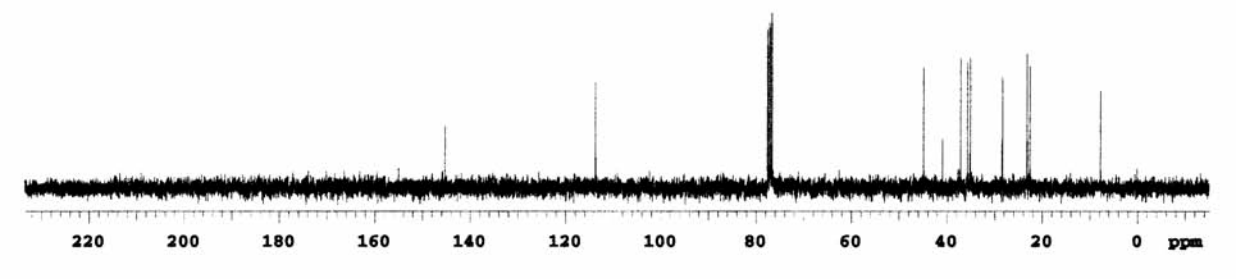
5k

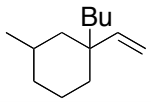
^{1}H NMR (300 MHz, $CDCl_3$)



5k

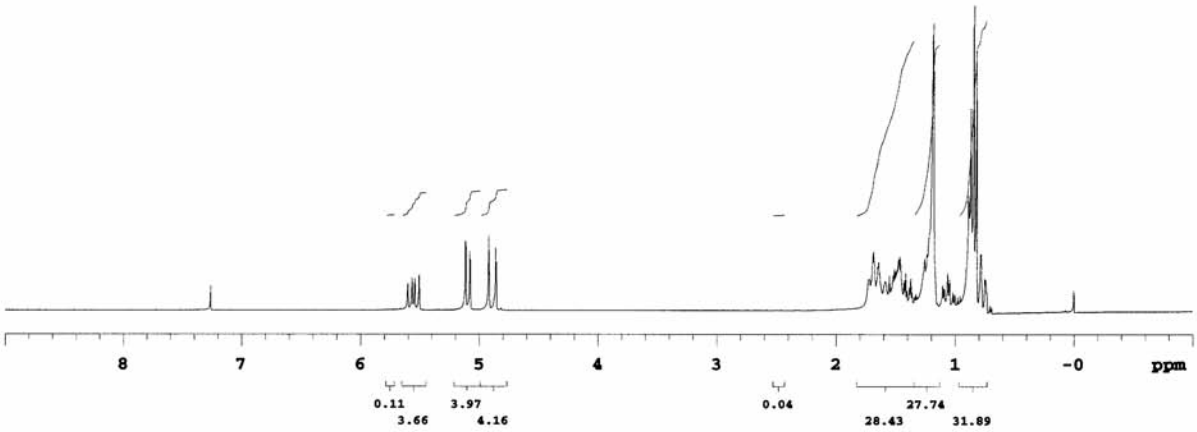
^{13}C NMR (75 MHz, $CDCl_3$)

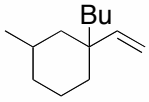




5l

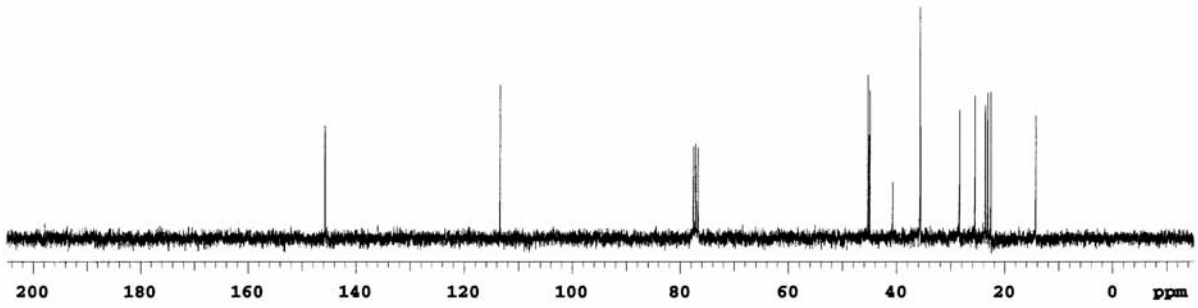
^{1}H NMR (300 MHz, $CDCl_3$)

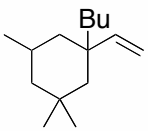




5l

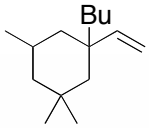
^{13}C NMR (75 MHz, $CDCl_3$)





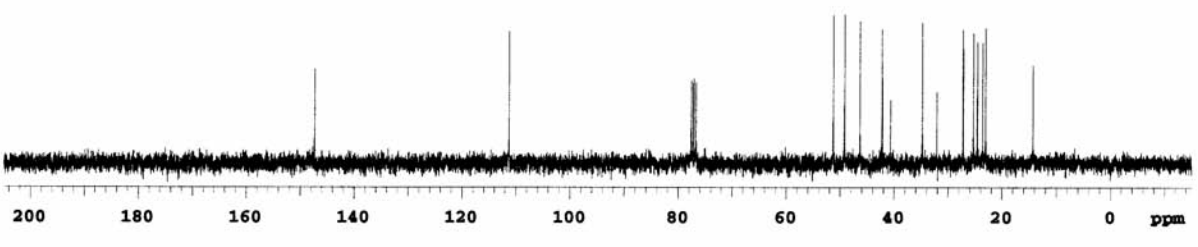
5m

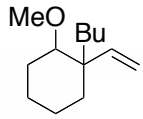
^{1}H NMR (300 MHz, $CDCl_3$)



5m

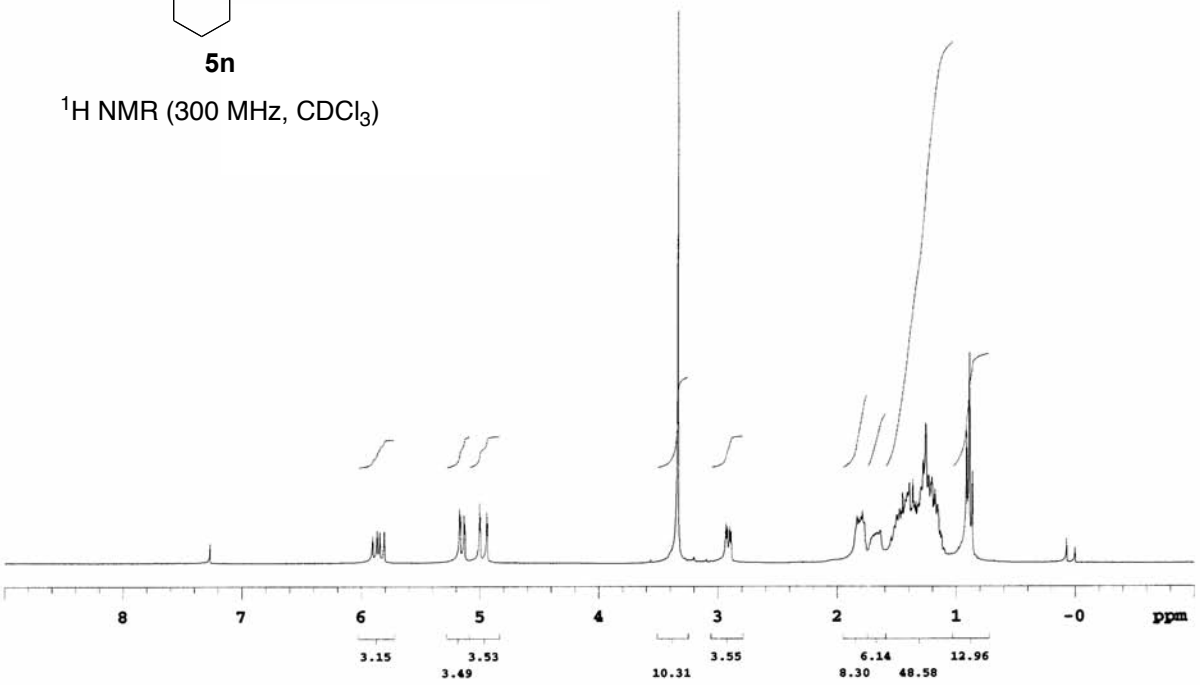
^{13}C NMR (75 MHz, $CDCl_3$)

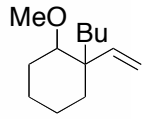




5n

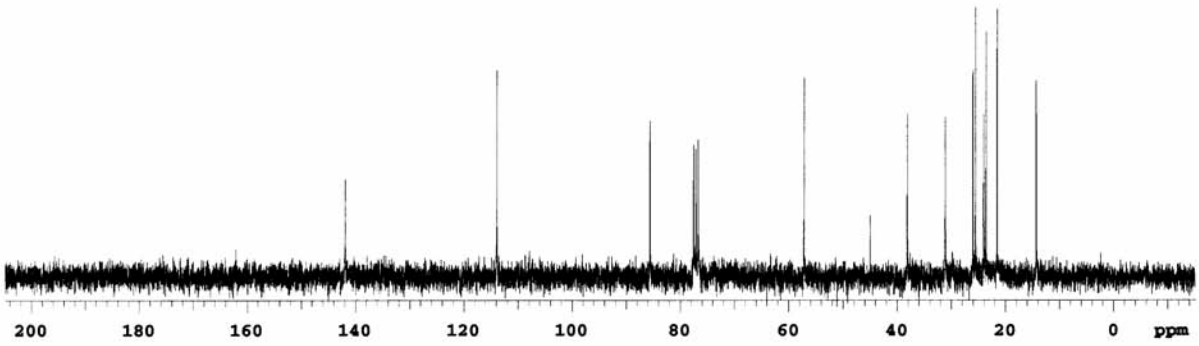
^{1}H NMR (300 MHz, $CDCl_3$)

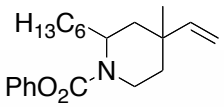




5n

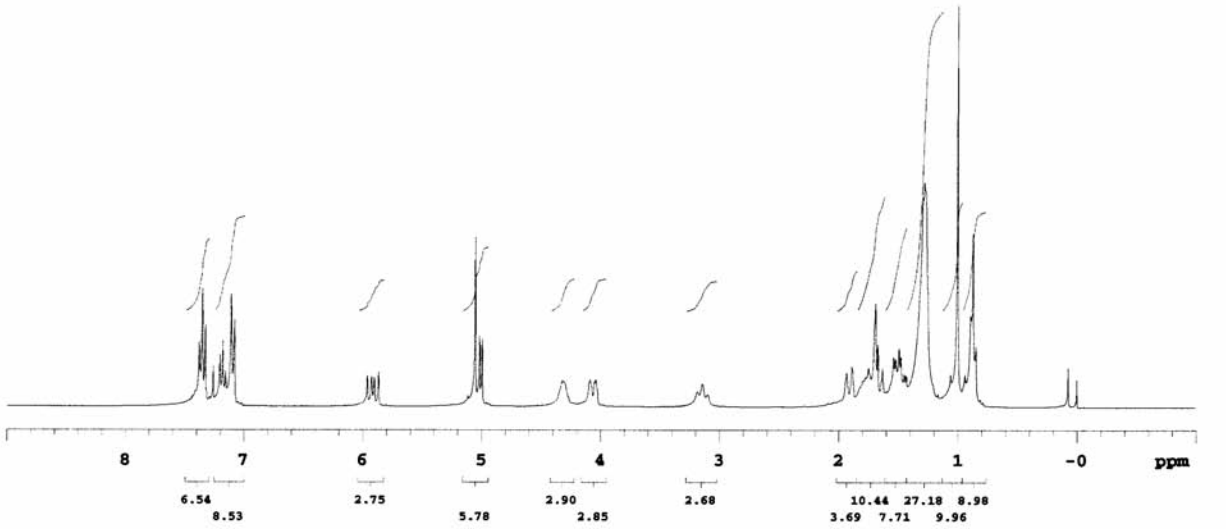
^{13}C NMR (75 MHz, $CDCl_3$)

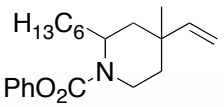




5o

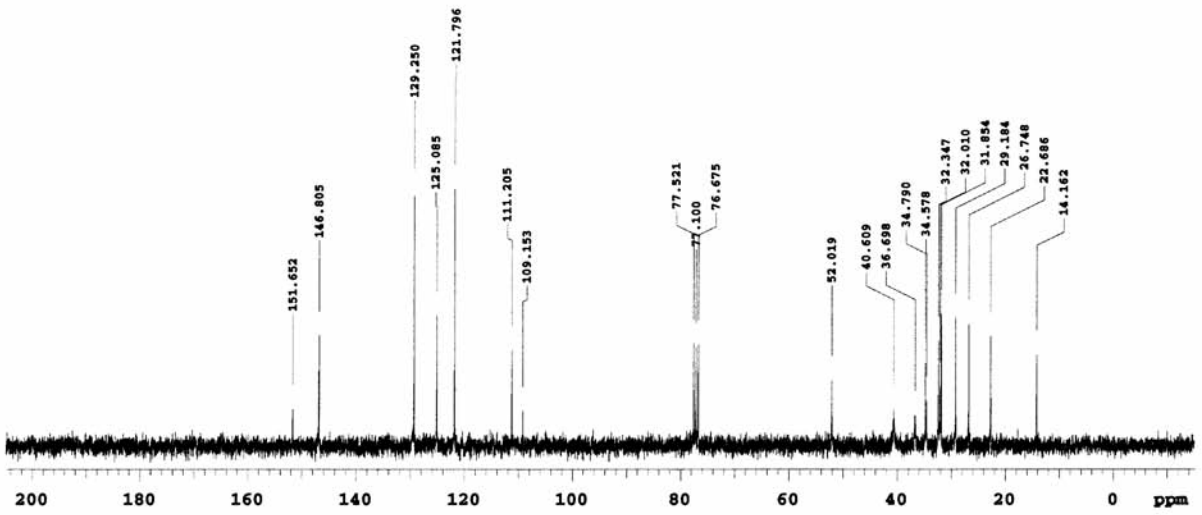
^{1}H NMR (300 MHz, $CDCl_3$)

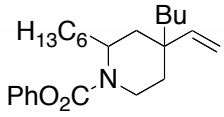




5o

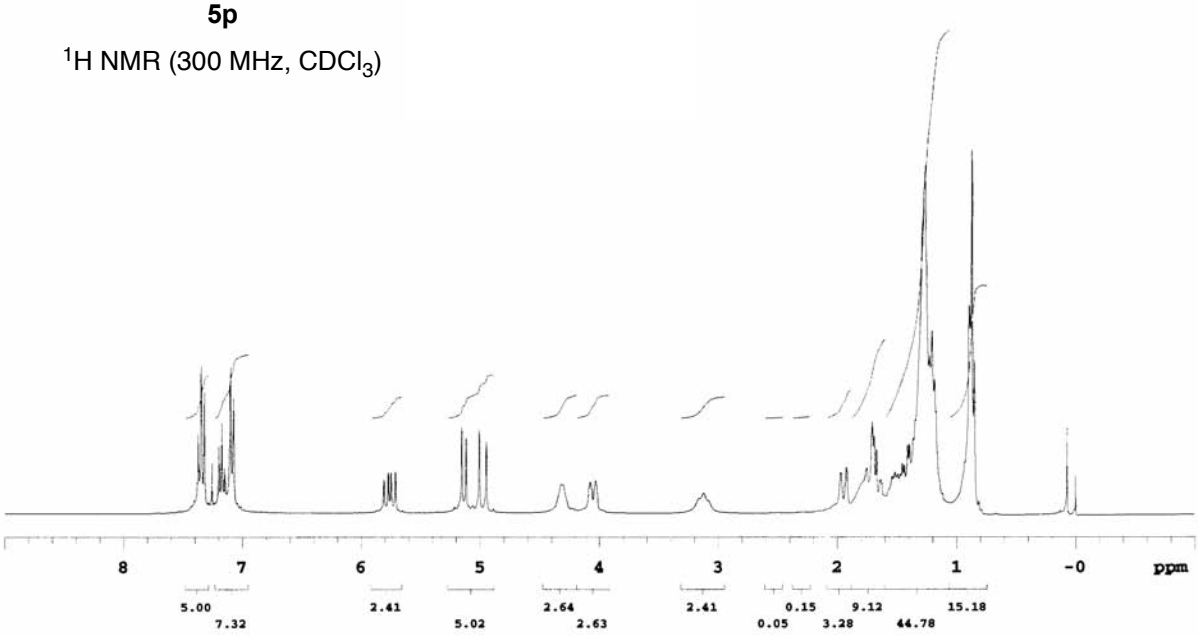
^{13}C NMR (75 MHz, $CDCl_3$)

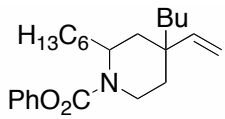




5p

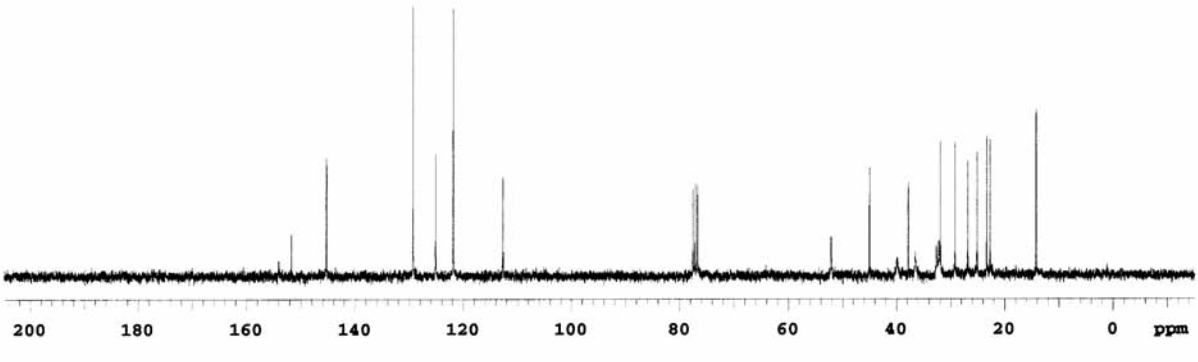
^{1}H NMR (300 MHz, $CDCl_3$)

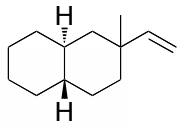




5p

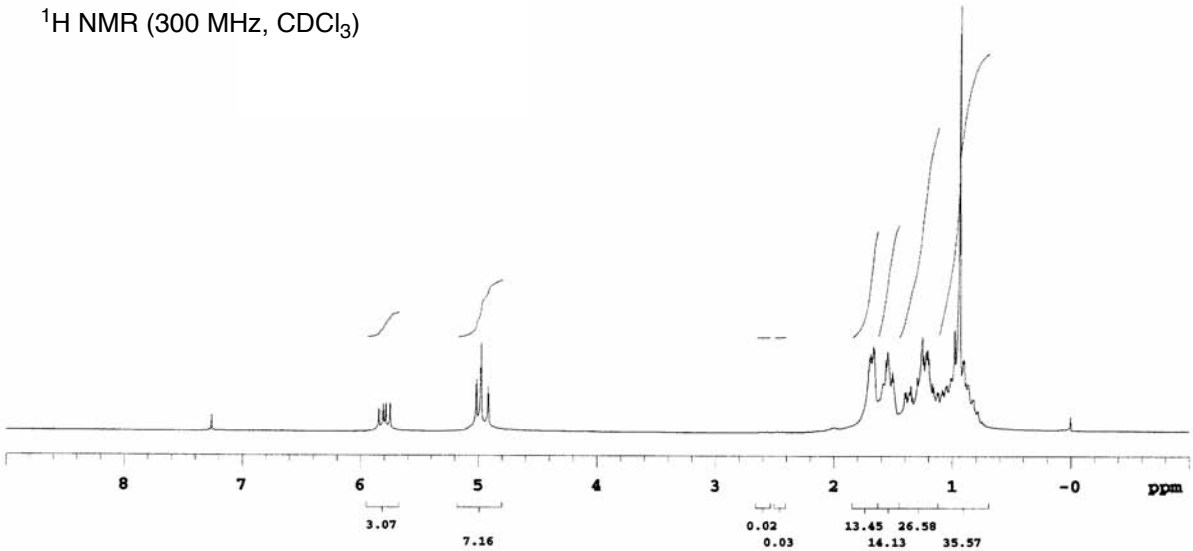
^{13}C NMR (75 MHz, $CDCl_3$)

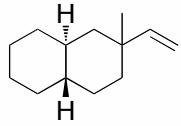




5q

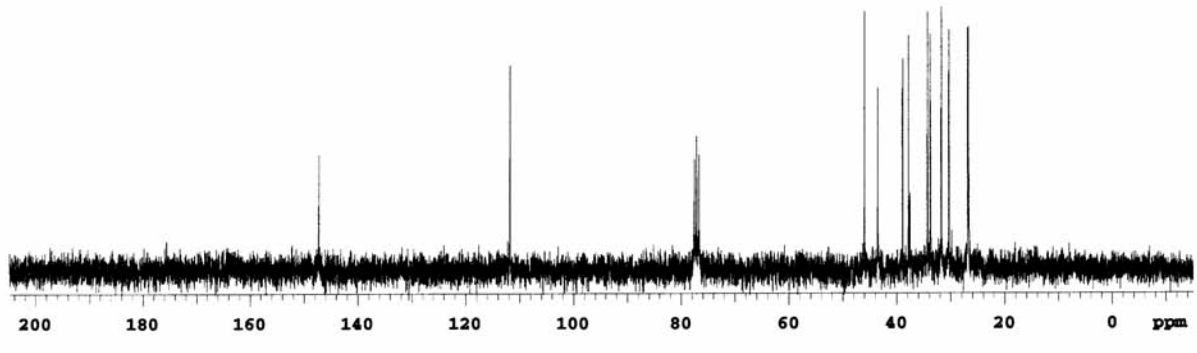
^{1}H NMR (300 MHz, $CDCl_3$)

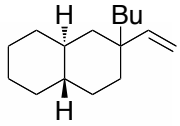




5q

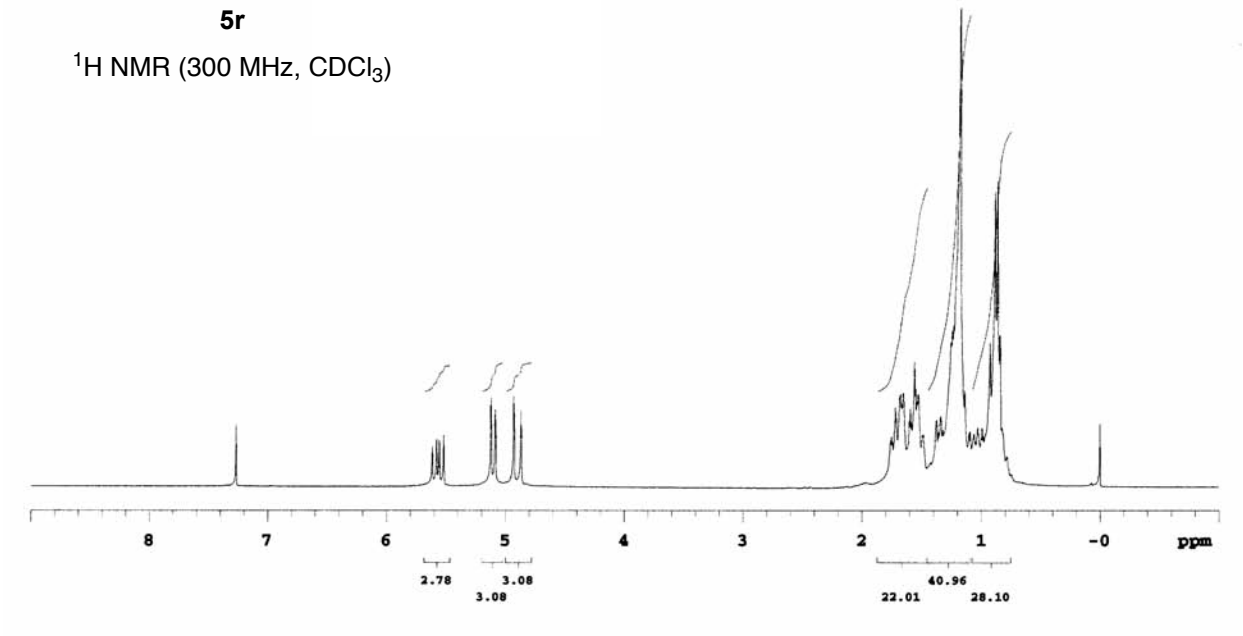
^{13}C NMR (75 MHz, $CDCl_3$)

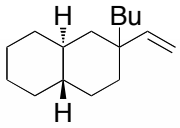




5r

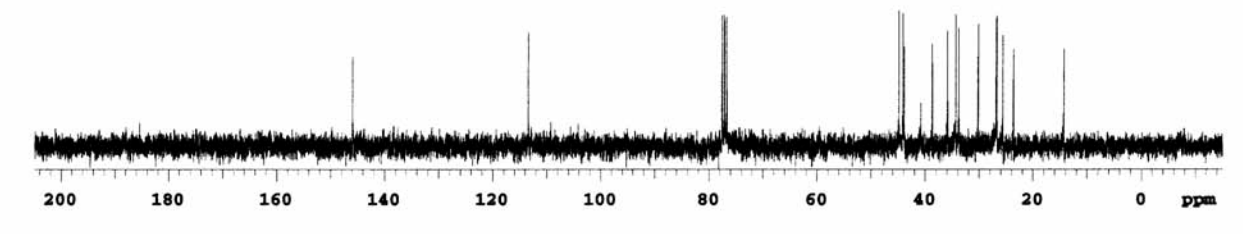
^{1}H NMR (300 MHz, $CDCl_3$)

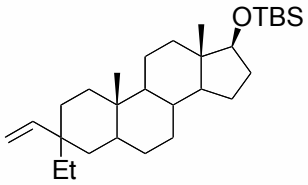




5r

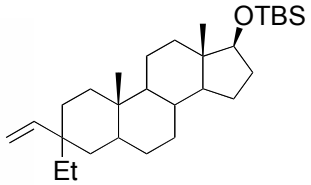
^{13}C NMR (75 MHz, $CDCl_3$)





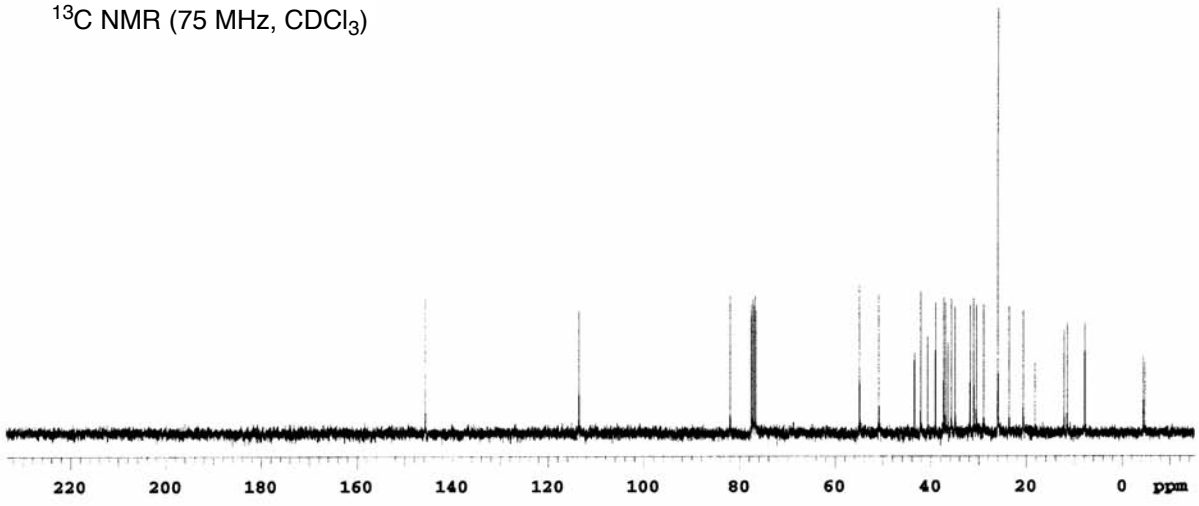
5s

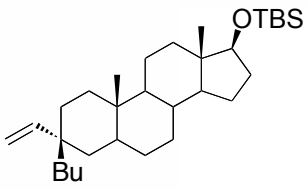
^{1}H NMR (300 MHz, $CDCl_3$)



5s

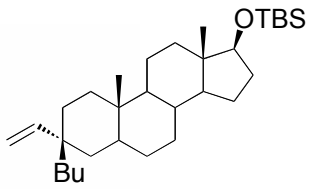
^{13}C NMR (75 MHz, $CDCl_3$)





5t

^{1}H NMR (300 MHz, $CDCl_3$)



5t

^{13}C NMR (75 MHz, $CDCl_3$)