Increased Efficiency in Cross-Metathesis Reactions of Sterically-Hindered Olefins

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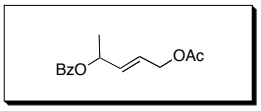
GENERAL INFORMATION

NMR spectra were recorded on an Oxford 300 MHz NMR spectrometer running Varian VNMR software. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) with reference to internal solvent for ^{1}H NMR and ^{13}C NMR spectra. Chemical shifts are reported in parts per million (ppm) downfield from H_3PO_4 for ^{31}P NMR spectra. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), septet (sept), multiplet (m), and broad (br). Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Visualization was performed with standard potassium permanganate stains or UV light. Flash column chromatography of organic compounds was performed using silica gel 60 (230-400 mesh). All glassware was either oven dried or flame dried, and reactions were done under an atmosphere of argon unless otherwise noted. All organic solvents were dried by passage through solvent purification columns containing activated alumina. All commercial chemicals were used as obtained.

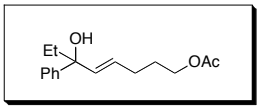
GENERAL CROSS METATHESIS PROCEDURE

A 10 mL 2-neck round bottom flask was charged with a stir bar and outfitted with a reflux condenser and a septum. The apparatus was flame-dried under active vacuum, and then allowed to cool to ambient temperature under a positive pressure of argon. The flask was then charged the catalyst (0.025 mmol) as a solid. Dry, degassed CH_2Cl_2 (2.0 mL) was then added via syringe. The substrates (0.5 mmol of limiting olefin reagent) were then added simultaneously via syringe to the stirring solution. The septum was replaced with a glass stopper, and the solution was heated to reflux for the indicated amount of time. After cooling to ambient temperature, ethyl vinyl ether (0.5 mL) was

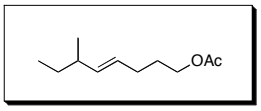
added via syringe, and the solution was stirred for an addition 10 minutes. After concentration under reduced pressure, the resulting crude oil was purified by silica gel chromatography (2 x 10 cm).



Chromatography eluent: 9:1 hexanes:ethyl acetate. Spectral data were consistent with literature values.[1]

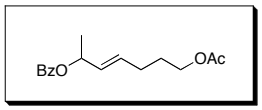


Chromatography eluent: 1:2.5→1:1 diethyl ether:pentane. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38-7.44 (2H, m), 7.30-7.36 (2H, m), 7.20-7.26 (1H, m), 5.81 (1H, dt, *J* = 15, 1 Hz), 5.63 (1H, dt, *J* = 15, 7 Hz), 4.05 (2H, t, *J* = 7 Hz), 2.13 (2H, q, *J* = 9 Hz), 2.03 (3H, s), 1.90 (2H, m), 1.72 (2H, m), 0.82 (3H, t, *J* = 7 Hz). ^{13}C{^{1}H} NMR (75.41 MHz, $CDCl_3$): δ 171.17, 145.92, 128.20, 128.07, 127.73, 126.62, 125.48, 76.69, 63.86, 35.08, 28.64, 28.19, 20.97, 7.95. HR-MS (FAB^+) Calculated for $C_{16}H_{22}O_3Na$, 285.1467; found, 285.1458.

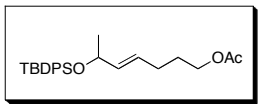


Chromatography eluent: 20:1 hexanes:ethyl acetate. . ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.33 (2H, m), 4.07 (2H, t, *J* = 6 Hz), 2.06 (3H, s), 2.00 (1H, m), 1.70 (m, 2H), 1.29 (m, 4H), 0.98 (3H, d, *J* = 7 Hz), 0.86, (3H, q, *J* = 8 Hz) ^{13}C{^{1}H} NMR (75.41 MHz, $CDCl_3$): δ 171.34, 137.50, 127.14, 64.19, 38.56, 29.95, 29.03, 28.74, 21.16, 20.54, 11.93. HR-MS (FAB^+) Calculated for $C_{11}H_{20}O_2$, 184.1463; found, 184.1462.

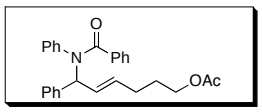
[1] Blackwell, H. E.; O'Leary, D. J.; Chatterjee, A. K.; Washenfelder, R. A.; Bussmann, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 58-71.



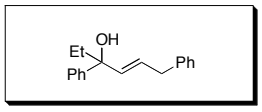
Chromatography eluent: 10:1 hexanes:ethyl acetate. . ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02-8.06 (2H, m), 7.52-7.58 (1H, m), 7.40-7.46 (2H, m), 5.72-5.82 (1H, m), 5.52-5.66 (1H, m), 4.06 (2H, t, *J* = 7 Hz), 2.13 (2H, q, *J* = 8 Hz), 2.03 (3H, s), 1.68-1.78 (3H, m), 1.4 (3H, d, *J* = 6 Hz). ^{13}C{^{1}H} NMR (75.41 MHz, $CDCl_3$): δ 171.33, 166.04, 132.98, 131.95, 130.96, 130.68, 129.76, 128.49, 71.69, 64.04, 28.76, 28.10, 21.17, 20.70. HR-MS (FAB^+) Calculated for $C_{16}H_{20}O_4$, 276.1362; found, 276.1367.



Chromatography eluent: 20:1 hexanes:ethyl acetate. . ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.70 (4H, m), 7.32-7.44 (6H, m), 5.3-5.6 (2H, m), 4.27 (1H, quint, *J* = 6Hz), 4.01 (2H, t, *J* = 8 Hz), 2.06 (3H, s), 1.97-2.02 (2H, m), 1.58-1.65 (2H, m), 1.15 (3H, d, *J* = 6 Hz), 1.06 (9H, s). ^{13}C{^{1}H} NMR (75.41 MHz, $CDCl_3$): δ 136.14, 136.07, 135.48, 134.60, 129.69, 129.63, 128.15, 127.66, 127.57, 70.38, 64.15, 31.81, 28.54, 28.32, 27.2, 25.50, 24.69, 22.87, 21.22, 19.44, 14.34. HR-MS (FAB^+) Calculated for $C_{25}H_{33}SiO_3$, 409.2199; found, 409.2186.

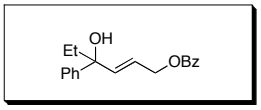


Chromatography eluent: 4:1 hexanes:ethyl acetate. . ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26-7.38 (7H, m), 7.06-7.18 (6H, m), 6.74-6.78 (2H, m), 6.57 (1H, d, *J* = 8 Hz), 5.85-5.95 (1H, m), 5.70-5.80 (1H, m), 4.05 (2H, t, *J* = 6 Hz), 2.17 (2H, q, *J* = 8 Hz), 2.03 (3H, s), 1.72 (2H, quint, *J* = 7 Hz). ^{13}C{^{1}H} NMR (75.41 MHz, $CDCl_3$): δ 171.32, 170.59, 141.20, 140.65, 136.74, 134.82, 130.12, 129.50, 128.70, 128.63, 128.52, 128.08, 127.93, 127.82, 127.72, 127.53, 127.27, 64.00, 62.26, 29.03, 28.14, 21.19. HR-MS (FAB^+) Calculated for $C_{27}H_{28}NO_3$, 414.2069; found, 414.2071.

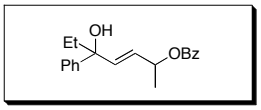


Chromatography eluent: 10:1 hexanes:ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.2-7.5 (10H, m), 5.87-5.93 (2H, m), 3.45 (2H, d, *J* = 5Hz), 1.96 (2H, q,

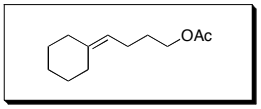
J = 7 Hz), 0.87 (t, *J* = 7 Hz). $^{13}C\{^{1}H\}$ NMR (75.41 MHz, $CDCl_3$): δ 146.07, 140.04, 137.80, 128.72, 128.61, 128.26, 128.00, 126.82, 126.26, 125.69, 76.96, 38.90, 35.28, 8.20. HR-MS (FAB^+) Calculated for $C_{18}H_{19}O$, 251.1436; found, 251.1427.



Chromatography eluent: 10:1 hexanes:ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02-8.08 (2H, m), 7.52-7.60 (1H, m), 7.40-7.46 (4H, m), 7.32-7.38 (2H, m), 7.22-7.38 (1H, m), 6.20 (1H, dt, *J* = 16, 2 Hz), 5.97 (1H, dt, *J* = 16, 6 Hz), 4.86 (2H, d, *J* = 6 Hz), 1.97 (2H, m), 1.93 (1H, br s), 0.85 (3H, t, *J* = 7 Hz). $^{13}C\{^{1}H\}$ NMR (75.41 MHz, $CDCl_3$): δ 166.53, 145.31, 140.60, 133.19, 130.38, 129.84, 128.57, 128.47, 127.15, 125.64, 122.91, 76.85, 65.15, 35.08, 8.09. HR-MS (FAB^+) Calculated for $C_{19}H_{19}O_3$, 295.1334; found, 295.1333.

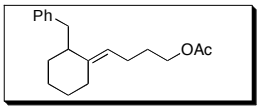


Product isolated as an unassigned 3:2 mixture of diastereomers. Chromatography eluent: 9:1 hexanes:ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02-8.08 (2H, m), 7.52-7.58 (1H, m), 7.40-7.48 (4H, m), 7.30-7.38 (2H, m), 7.22-7.28 (1H, m), 6.18 (0.4H, dd, *J* = 1,4 Hz), 6.12 (0.6H, dd, *J* = 1,4 Hz), 5.62-5.72 (1H, m), 1.94 (m, 2H), 1.46 (3H, app t, *J* = 8 Hz), 0.84 (3H, t, *J* = 8 Hz). $^{13}C\{^{1}H\}$ NMR (75.41 MHz, $CDCl_3$): δ 166.00, 145.55, 145.50, 138.29, 137.90, 133.03, 130.78, 129.76, 128.49, 128.40, 128.32, 127.05, 125.71, 125.63, 76.71, 71.39, 71.32, 35.22, 35.17, 31.77, 22.84, 20.78, 20.70, 14.32, 8.13, 8.08. HR-MS (FAB^+) Calculated for $C_{20}H_{21}O_3$, 309.1491; found, 309.1496.

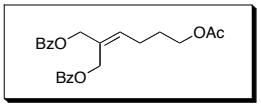


Chromatography eluent: 20:1 pentane:diethyl ether. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.04 (1H, t, *J* = 7 Hz), 4.04 (2H, t, *J* = 7 Hz), 2.1 (6H, m), 2.04 (3H, s), 1.65 (2H, quint, *J* = 8 Hz), 1.5 (6H, m). $^{13}C\{^{1}H\}$ NMR (75.41 MHz, $CDCl_3$): δ 171.39,

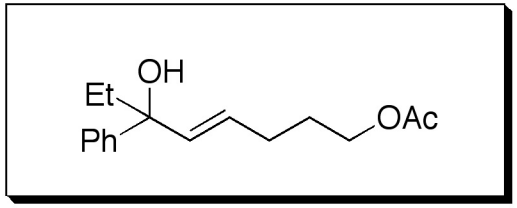
140.97, 119.91, 64.21, 37.34, 29.09, 28.83, 28.80, 28.04, 27.97, 27.07, 23.49, 21.18. HR-MS (FAB^+) Calculated for $C_{12}H_{20}O_2$, 196.1463; found, 196.1463.



Chromatography eluent: 20:1 pentane:diethyl ether. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.12-7.24 (5H, m), 5.00 (1H, t, *J* = 7 Hz), 3.99 (2H, t, *J* = 7 Hz), 2.90 (1H, dd, *J* = 13, 5 Hz), 2.57 (1H, dd, *J* = 13, 8 Hz), 2.24-2.36 (2H, m), 2.06 (3H, s), 2.00-2.10 (3H, m), 1.5-1.7 (8H, m). $^{13}C\{^1H\}$ NMR (75.41 MHz, $CDCl_3$): δ 171.44, 143.06, 141.76, 129.29, 128.27, 125.80, 119.61, 64.22, 46.22, 46.33, 39.07, 32.98, 29.10, 28.33, 27.27, 24.19, 23.54, 21.25. HR-MS (FAB^+) Calculated for $C_{19}H_{26}O_2$, 286.1933; found, 286.1940.



Chromatography eluent: 6:1 hexanes:ethyl acetate. . ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95-8.04 (4H, m), 7.55 (2H, t, *J* = 8Hz), 7.40 (4H, t, *J* = 8Hz), 5.94 (1H, t, *J* = 8Hz), 5.01 (2H, 2), 4.94 (2H, s), 4.11 (2H, t, *J* = 6Hz), 2.38 (2H, q, *J* = 8 Hz), 2.04 (3H, s), 1.80 (2H, quint, *J* = 7Hz), . $^{13}C\{^1H\}$ NMR (75.41 MHz, $CDCl_3$): δ 171.24, 166.54, 166.54, 135.70, 133.20, 133.15, 130.36, 130.18, 130.03, 129.77, 128.52, 128.50, 67.42, 63.70, 60.54, 28.31, 24.50, 21.08. HR-MS (FAB^+) Calculated for $C_{23}H_{23}O_6$, 395.1495; found, 395.1498.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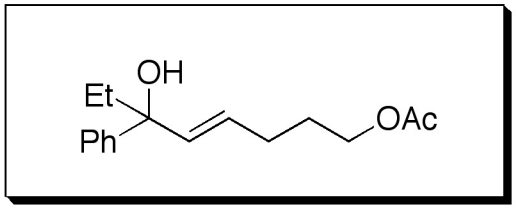
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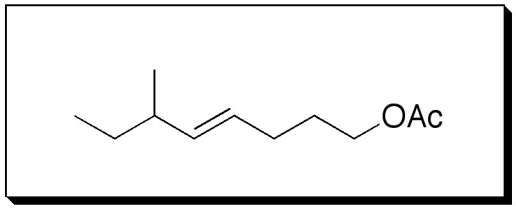
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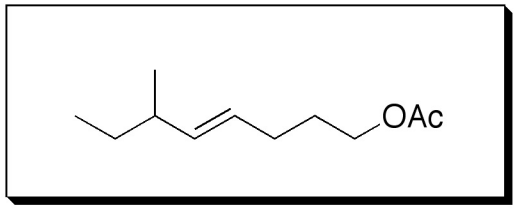

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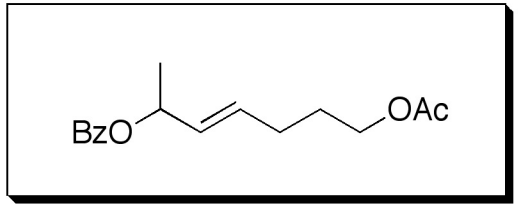
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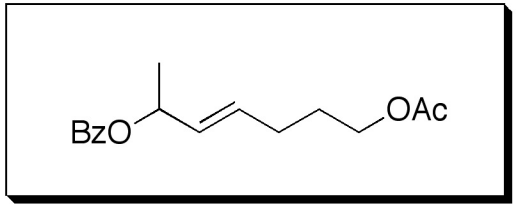
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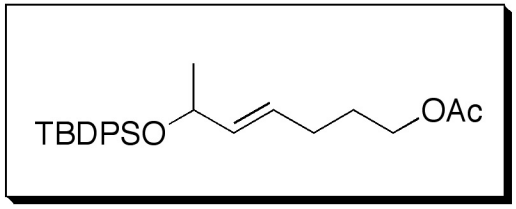
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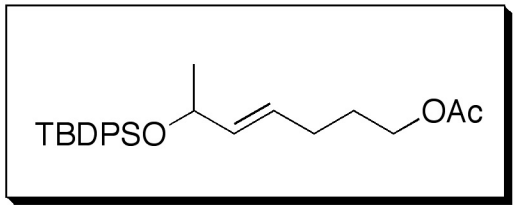
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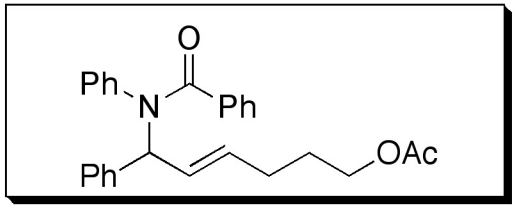
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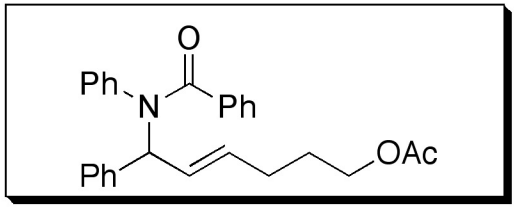
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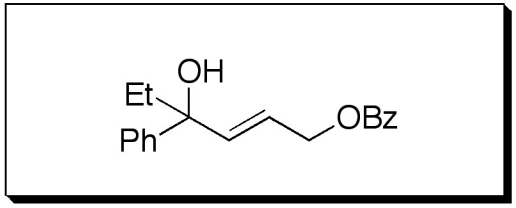
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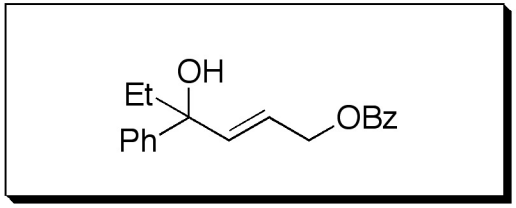
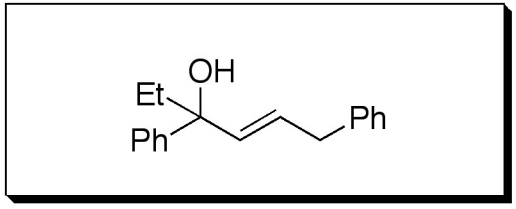
3.17
3.11

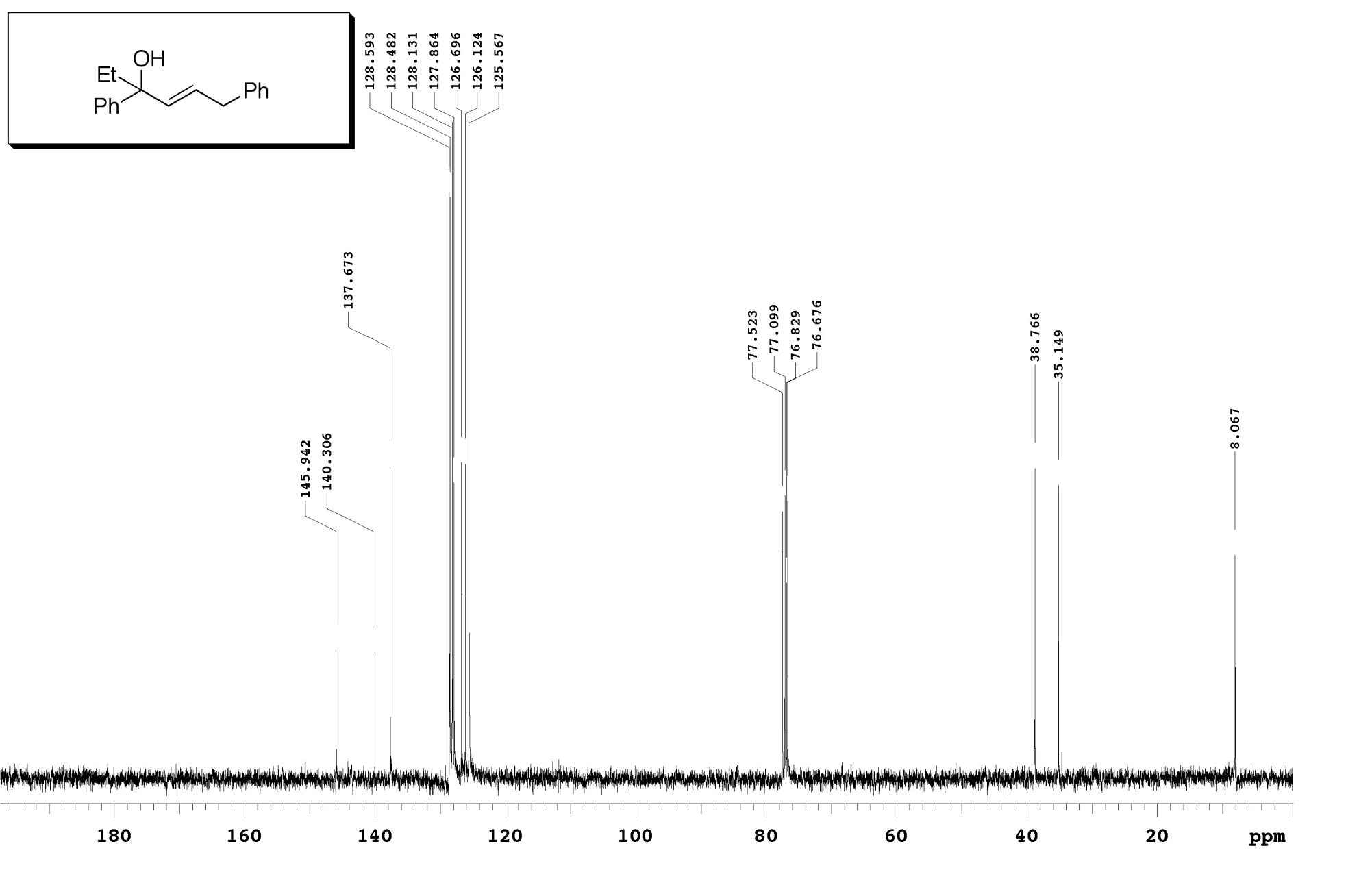


166.318
145.100
140.389
132.978
130.172
129.633
128.358
128.267
126.940
125.431
122.698
77.448
77.023
76.642
76.598
64.945
34.872
7.880

180
160
140
120
100
80
60
40
20
ppm


OH
Et
Ph
Ph

9
8
7
6
5
4
3
2
1
ppm
11.00
1.93
2.00
1.81
3.31


OH
Et
Ph
Ph
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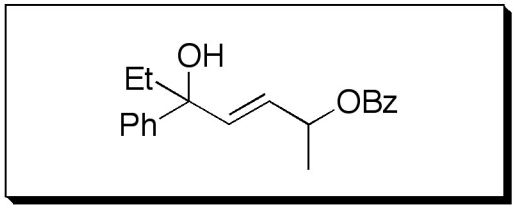
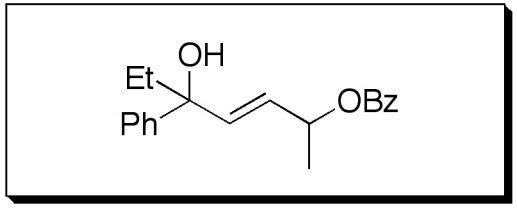
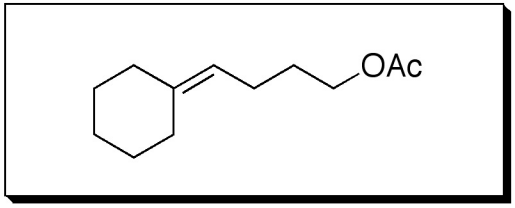
128.482
128.131
127.864
126.696
126.124
125.567
137.673
145.942
140.306
77.523
77.099
76.829
76.676
38.766
35.149
8.067
180
160
140
120
100
80
60
40
20
ppm


OH
Et
Ph
OBz

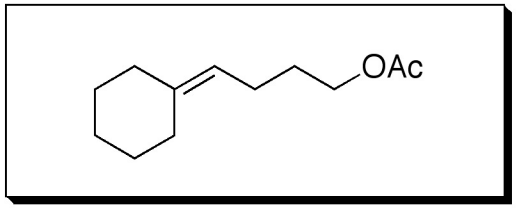
9
8
7
6
5
4
3
2
1
ppm
2.00
4.20
1.05
2.09
1.12
0.64
0.43
1.06
1.07
2.07
3.50
3.62


OH
Et
Ph
OBz

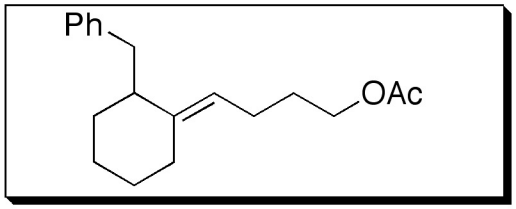
129.581
128.318
128.219
128.139
126.872
125.537
125.449
132.851
130.642
130.600
138.105
137.727
145.377
145.327
165.832
77.477
77.054
76.630
76.535
71.212
71.144
35.038
34.992
31.596
22.664
20.600
20.528
7.952
7.899
180
160
140
120
100
80
60
40
20
ppm


OAc

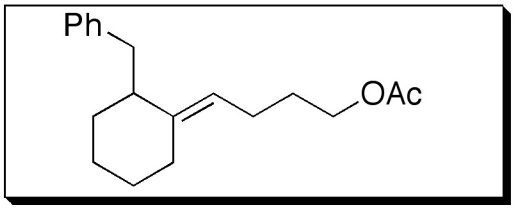
9
8
7
6
5
4
3
2
1
ppm
1.00
2.20
5.94
3.32
2.36
6.76


OAc

77.655
77.234
76.808
64.205
37.335
29.087
28.832
28.802
27.974
27.074
23.493
21.181
119.909
140.973
171.390
220
200
180
160
140
120
100
80
60
40
20
0
ppm

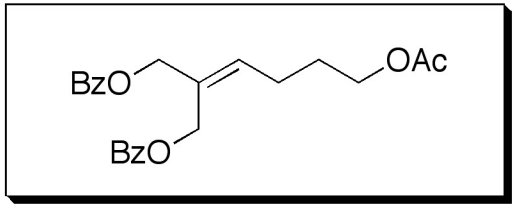

Ph
OAc

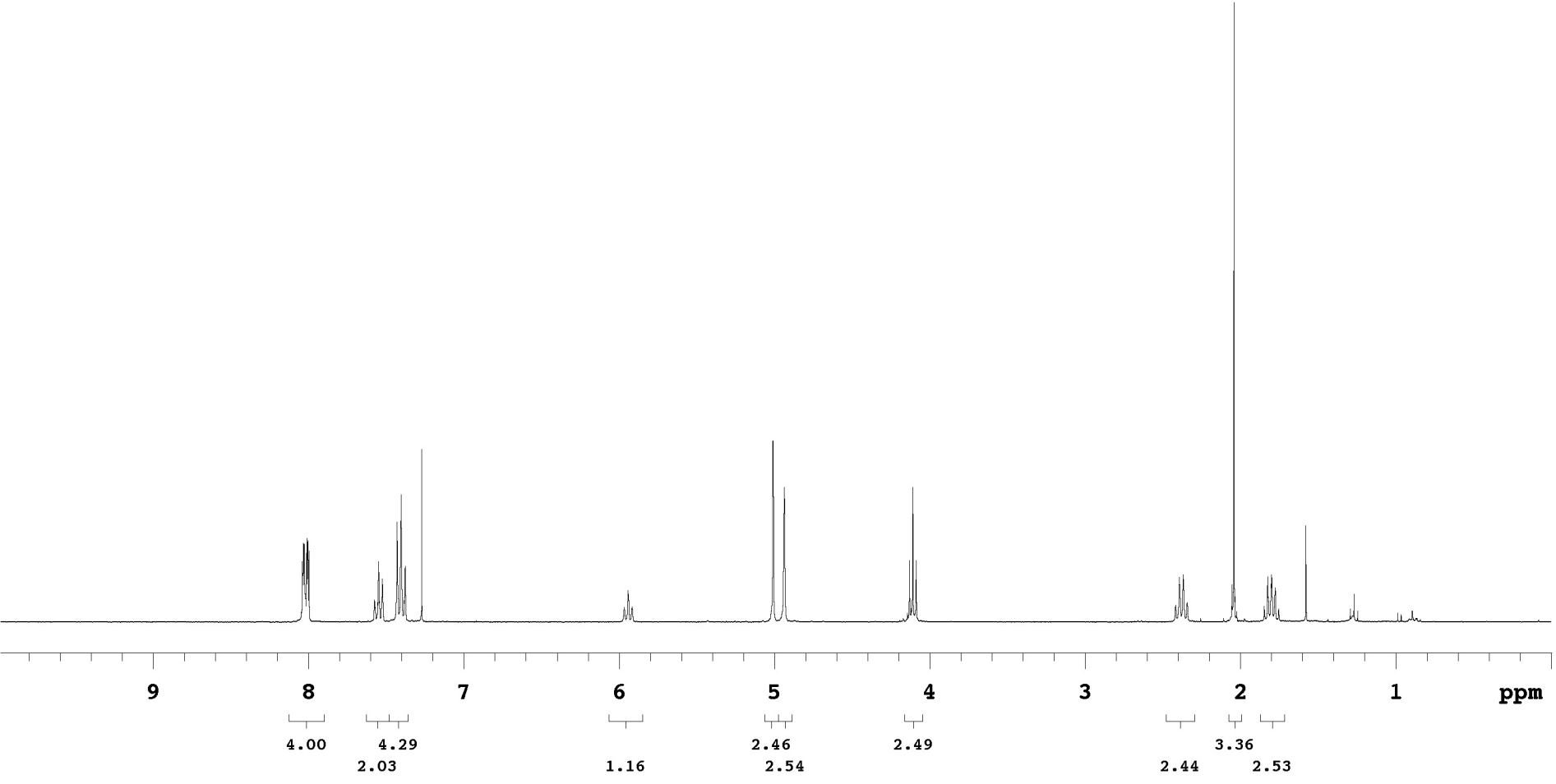
9
8
7
6
5
4
3
2
1
ppm
4.59
1.00
1.97
1.10
1.00
2.44
6.23
8.46

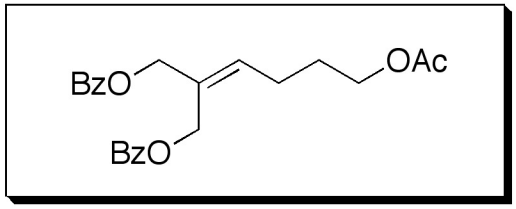


171.220
142.836
141.535
129.069
128.047
125.578
119.390
77.433
77.210
77.009
76.587
63.996
46.104
38.851
32.759
28.883
28.106
27.051
23.970
23.322
21.025

200 180 160 140 120 100 80 60 40 20 0 ppm


BzO
OAc
BzO


9
8
7
6
5
4
3
2
1
ppm
4.00
4.29
2.03
1.16
2.46
2.54
2.49
2.44
3.36
2.53


BzO
OAc
BzO

130.028
129.773
128.524
128.497
135.700
133.202
133.145
130.358
130.179
171.237
166.537
166.408
77.651
77.226
76.801
67.419
63.695
60.536
28.309
24.501
21.084
180
160
140
120
100
80
60
40
20
ppm