Supporting Information

Antarafacial Mediation of Oxygen Delivery By a Phenylsulfinyl Group in the Epoxidation of Proximal Double Bonds: Intramolecular Trapping of an Early Pummerer Intermediate with Stereoelectronic Control

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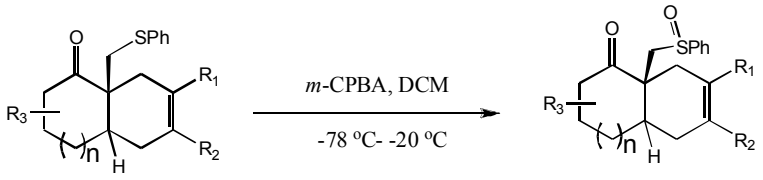
General Methods

Unless mentioned otherwise, all non-aqueous reactions were carried out in vacuum-flame-dried glasswares under a balloon-pressure of argon; reagents were commercially available and used as received; anhydrous solvents were purchased as the highest grade from Sigma-Aldrich, or passed through a solvent-purification system, or purified as following: THF was distilled from Na/benzophenone, CH_2Cl_2 was distilled from CaH_2. Reactions were monitored by thin-layer chromatography on Merck silica gel 60-F254 coated 0.25 mm plates. Flash column chromatography was performed using RediSep® pre-packed disposable silica gel columns (normal phase, 230-400 mesh) from Teledyne Isco. And prep-TLC was performed on Merck silica gel 60-F254 coated 0.50 or 1 mm

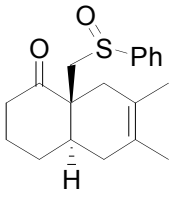
plates. Yields were reported as isolated, spectroscopically pure compounds. And NMR spectra were obtained on Bruker DRX 300, or 400 MHz, or Bruker DMX 500 MHz spectrometers. $CDCl_3$, dried by standing over K_2CO_3, was used and chemical shifts were referenced on residual solvent peaks (TMS: δ = 0.0 ppm, CD_2Cl_2: δ = 5.34 ppm for ^1H NMR and $CDCl_3$: δ = 77.00 ppm, CD_2Cl_2: 35.80 ppm for ^{13}C NMR). Abbreviations for ^1H NMR: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, or br = broad. IR spectra were obtained on a Perkin-Elmer Paragon 1000 FTIR spectrometer. And high resolution mass spectra were acquired from Columbia University Mass Spectral Core facility on a JEOL HX110 spectrometer or from Memorial Sloan-Kettering Cancer Center on a Perkin-Elmer Sciex API 100 in ionspray mode.

Procedures:

General procedure for the preparation of sulfoxides:

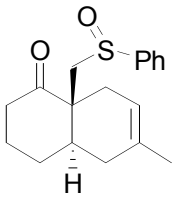


To a stirred solution of sulfide[1] (1 eq.) in DCM (0.1 M) at −78 °C was added *m*-CPBA (1.2 eq., 77% purity) in one portion. The resulting mixture was warmed to −20 °C over 2 hours, and then quenched with saturated $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (aq.). The mixture was extracted with DCM, washed with saturated $NaHCO_3$ (aq.), dried over anhydrous $MgSO_4$, filtered and concentrated at reduced pressure. Chromatography of the residue gave the sulfoxide as a mixture of diastereoisomers.



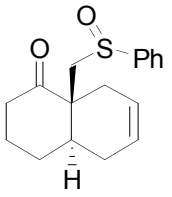
2

Sulfoxide **2** was prepared by following above general procedure as a mixture of diastereoisomers in 70% yield (Chromatography with Hexane/Ethyl Acetate = 2:1 to 1:1). HRMS (FAB+) calcd for $C_{19}H_{25}O_2S$ (M+H): 317.1575, found 317.1562.



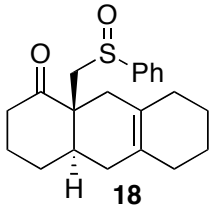
11

Sulfoxide **11** was prepared by following above general procedure as a mixture of diastereoisomers in 65% yield (Chromatography with Hexane/Ethyl Acetate = 2:1). HRMS (FAB+) calcd for $C_{18}H_{23}O_2S$ (M+H): 303.1418, found 303.1430.



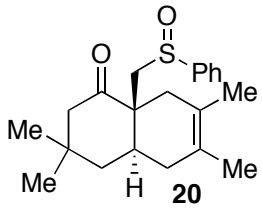
16

Sulfoxide **16** was prepared by following above general procedure as a mixture of diastereoisomers in 97% yield (Chromatography with Hexane/Ethyl Acetate = 2:1). HRMS (FAB+) calcd for $C_{17}H_{21}O_2S$ (M+H): 289.1262, found 289.1273.



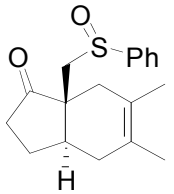
18

Sulfoxide **18** was prepared by following above general procedure as a mixture of diastereoisomers in 57% yield (Chromatography with Hexane/Ethyl Acetate = 2:1). HRMS (FAB+) calcd for $C_{21}H_{27}O_2S$ (M+H): 343.1732, found 343.1744.



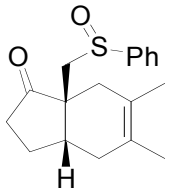
20

Sulfoxide **20** was prepared by following above general procedure as a mixture of diastereoisomers in 77% yield (Chromatography with Hexane/Ethyl Acetate = 4:1). HRMS (FAB+) calcd for $C_{21}H_{29}O_2S$ (M+H): 345.1888, found 345.1874.



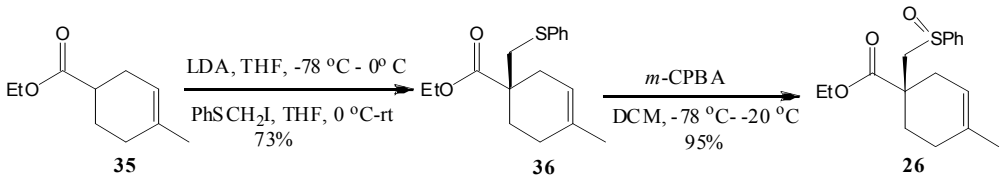
22

Sulfoxide **22** was prepared by following above general procedure as a mixture of diastereoisomers in 62% yield (Chromatography with Hexane/Ethyl Acetate = 2:1 to 1:1). HRMS (FAB+) calcd for $C_{18}H_{23}O_2S$ (M+H): 303.1419, found 303.1418.



24

Sulfoxide **24** was prepared by following above general procedure as a mixture of diastereoisomers in 74% yield (Chromatography with Hexane/Ethyl Acetate = 2:1). HRMS (FAB+) calcd for $C_{18}H_{23}O_2S$ (M+H): 303.1419, found 303.1412.

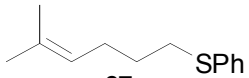


To lithium diisopropylamide (2.6 mmol, prepared from *n*-BuLi (1.04 mL, 2.5 M in hexane) and diisopropylamine (3.0 mmol, 0.42 mL) in THF at 0 °C) in THF (10 mL) at −78 °C was added ester **35**[2] (0.336 g, 2.0 mmol) in THF (3 mL) slowly. The resulting mixture was warmed to 0 °C within 1 h and then kept at this temperature for another 0.5 h. To the mixture at −78 °C was added iodomethylphenylsulfide (1.000 g, 4.0 mmol) in THF (2 mL). The mixture was stirred and warmed to rt overnight. The reaction mixture was quenched with 10 mL water and extracted with EtOAc, dried over anhydrous $MgSO_4$, filtered and concentrated at reduced pressure. Chromatography of the residue (hexane/EA = 100:1) afforded the desired product **36** (0.423 g, 73%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.35 (m, 2H), 7.27−7.23 (m, 2H), 7.18−7.14 (m, 1H), 5.31−5.29 (m, 1H), 4.00−3.95 (q, *J* = 7.2 Hz, 2H), 3.24−3.21 (d, *J* = 12.4 Hz, 1H),

3.20−3.17 (d, J = 12.4 Hz, 1H), 2.54−2.50 (m, 1H), 2.01−1.87 (m, 5H), 1.62 (d, J = 1.2 Hz, 3H), 1.17−1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 136.9, 133.1, 130.0, 128.7, 126.1, 118.4, 60.5, 45.6, 41.5, 32.8, 29.2, 27.1, 23.2, 14.0; IR (NaCl, cm^{-1}): 2964, 2926, 1727, 1529, 1350; HRMS (FAB+) calcd for $C_{17}H_{22}O_2S$ (M+): 290.1341, found 290.1349.

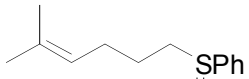
Sulfoxide **26** was prepared by following above general procedure as a mixture of diastereoisomers in 95% yield (Chromatography with Hexane/Ethyl Acetate = 4:1). HRMS (FAB+) calcd for $C_{17}H_{23}O_3S$ (M+H): 307.1368, found 307.1382.



37

Sulfide **37** was prepared by the procedure reported by Myles.[3]

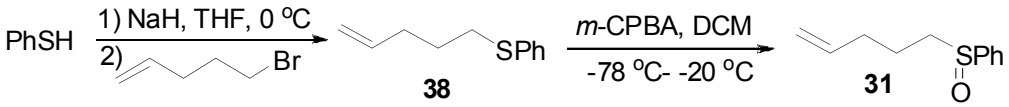
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.13 (m, 5H), 5.11−5.06 (m, 1H), 2.92−2.88 (t, J = 7.2 Hz, 2H), 2.14−2.08 (m, 2H), 1.71−1.64 (m, 2H), 1.68 (d, J = 0.8 Hz, 3H), 1.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 132.5, 128.9, 128.7, 125.6, 123.3, 33.0, 29.2, 27.0, 25.6, 17.7; IR (NaCl, cm^{-1}): 2965, 2926, 2854, 1584, 1480, 1438, 736, 690; HRMS (FAB+) calcd for $C_{13}H_{18}S$ (M+): 206.1129, found 206.1136.



28

Sulfoxide **28** was prepared by the above general procedure as a colorless oil in 87% yield (Chromatography with Hexane/Ethyl Acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.60 (m, 2H), 7.55−7.44 (m, 3H), 5.05−5.01 (m, 1H), 2.80−2.76 (t, *J* = 7.6 Hz, 2H), 2.13−2.07 (q, *J* = 7.2 Hz, 2H), 1.83−1.75 (tt, *J* = 15.0, 7.4 Hz, 1H), 1.68 (d, *J* = 0.8 Hz, 3H), 1.71–1.60 (m, 1H), 1.58 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 133.1, 130.8, 129.1, 123.9, 122.5, 56.6, 26.7, 25.6, 22.1, 17.7; IR (NaCl, cm^{-1}): 2965, 2925, 2854, 1443, 1046, 748, 692; HRMS (FAB+) calcd for $C_{13}H_{19}OS$ (M+H): 223.1157, found 223.1158.

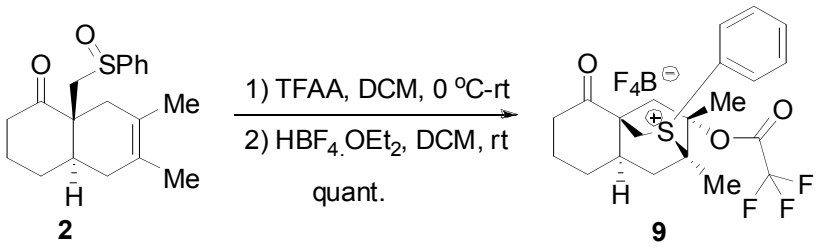


To a solution of thiophenol (0.550 g, 5.00 mmol) in THF (20 mL) at 0 °C was added NaH (0.240 g, 6.00 mmol, 60% in mineral oil). The mixture was stirred at 0 °C for 10 minutes and then 4-Peten-1-bromide (1.118 g, 7.50 mmol) was added. The resultant mixture was stirred at rt for 10 hours and then quenched with 10 mL water. The mixture was extracted with EtOAc, dried over anhydrous $MgSO_4$, filtered and concentrated at reduced pressure. Chromatography of the residue (hexane) afforded the desired product **38** (0.822 g, 92%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.25 (m, 4H), 7.18−7.14 (m, 1H), 5.83−5.72 (m, 1H), 5.06−4.97 (m, 2H), 2.93−2.90 (t, *J* = 7.2 Hz, 2H), 2.21−2.16 (m, 2H), 1.77−1.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 136.6, 128.9, 128.8, 125.7, 115.3, 32.8, 32.6, 28.2; IR (NaCl, cm^{-1}): 3075, 2930, 1640, 1584, 1480, 1438, 913, 737, 690; HRMS (FAB+) calcd for $C_{11}H_{14}S$ (M+): 178.0816, found 178.0820.

Sulfoxide **31** was prepared by the above general procedure as a colorless oil in 87% yield (Chromatography with Hexane/Ethyl Acetate = 4:1).

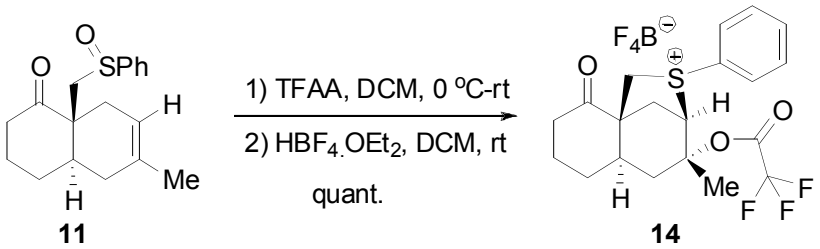
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.59 (m, 2H), 7.55−7.48 (m, 3H), 5.79−5.66 (m, 1H), 5.05−4.98 (m, 2H), 2.82−2.77 (ddd, *J* = 9.0, 6.4, 2.6 Hz, 2H), 2.21−2.14 (m, 2H), 1.93−1.83 (m, 1H), 1.79−1.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 136.8, 130.9, 129.2, 124.0, 116.0, 56.4, 32.4, 21.2; IR (NaCl, cm^{-1}): 3060, 2933, 1640, 1443, 1044, 784, 692; HRMS (FAB+) calcd for $C_{11}H_{15}OS$ (M+H): 195.0844, found 195.0844.



To a solution of sulfoxide **2a** (0.064 g, 0.20 mmol) in DCM (4 mL) at 0 °C was added TFAA (0.126 g, 0.60 mmol) dropwise. The mixture was stirred at 0 °C for 0.5 h and rt for another 0.5 h. To the mixture was added $HBF_4.OEt_2$ (0.194 g, 1.2 mmol). The color of solution turned red then brown. The mixture was stirred at rt for 12 h, then quenched with water. The mixture was extracted with DCM and organic extract was concentrated at reduced pressure. The residue was dissolved in DCM (5 mL) and concentrated for two times to provide compound **9** as an off-white solid with quantitative yield, m.p. 177−179 °C (decomp.). The sample for characterization and single crystal preparation was obtained by recrystallization in DCM at 0 °C.

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.02−8.00 (m, 2H), 7.96−7.93 (m, 1H), 7.88−7.84 (m, 2H), 4.43−4.39 (dd, *J* = 13.2, 3.2 Hz, 1H), 3.68−3.64 (d, *J* = 13.2 Hz, 1H), 3.05−3.00 (dd,

J = 17.6, 3.2 Hz, 1H), 2.74−2.67 (td, *J* = 14.2, 6.1 Hz, 1H), 2.50−2.36 (m, 3H), 2.27−2.07 (m, 4H), 2.05 (s, 3H), 1.99−1.91 (m, 1H), 1.69 (m, 1H), 1.13 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 206.5, 155.1 (O=C-CF3), 154.7 (O=C-CF3), 136.6, 133.2, 132.2, 115.8 (O=C-CF3), 115.2, 112.9 (O=C-CF3), 86.8, 62.5, 44.7, 39.3, 39.1, 37.5, 37.2, 30.9, 27.4, 25.0, 21.0, 17.0; IR (NaCl, cm^{-1}): 2954, 1786, 1708, 1163, 1133, 1053, 1030, 739, 681; HRMS (FAB+) calcd for $C_{21}H_{24}O_3F_3S$ (M-BF_4): 413.1398, found 413.1390.



To a solution of sulfoxide **2b** (0.119 g, 0.394 mmol) in DCM (4 mL) at 0 °C was added TFAA (0.248 g, 1.18 mmol) dropwise. The mixture was stirred at 0 °C for 0.5 h and rt for another 0.5 h. To the mixture was added $HBF_4.OEt_2$ (0.383 g, 2.36 mmol). The color of solution turned red then brown. The mixture was stirred at rt for 12 h, then quenched with water. The mixture was extracted with DCM and organic extract was concentrated at reduced pressure. The residue was dissolved in DCM (5 mL) and concentrated for two times to provide compound **13** as an off-white solid with quantitative yield, m.p. 183−185 °C (decomp.). The sample for characterization and single crystal preparation was obtained by recrystallization with DCM/diethyl ether.

^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.82−7.80 (m, 3H), 7.74−7.71 (m, 2H), 4.90−4.87 (d, *J* = 14.0 Hz, 1H), 4.82−4.80 (dd, *J* = 4.8, 2.0 Hz, 1H), 3.46−3.42 (d, *J* = 14.0 Hz, 1H), 3.00−2.95 (dd, *J* = 14.8, 5.2 Hz, 1H), 2.60−2.56 (m, 1H), 2.52−2.43 (m, 2H), 2.41−2.37

(d, J = 14.8 Hz, 1H), 2.19−2.14 (m, 2H), 1.95 (s, 3H), 1.94−1.84 (m, 1H), 1.81−1.75 (m, 3H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ 205.4, 156.3 (O=C-CF3), 155.9 (O=C-CF3), 135.5, 132.1, 129.9, 123.4, 115.7 (O=C-CF3), 112.9(O=C-CF3), 84.8, 66.1, 59.9, 47.3, 41.1, 40.9, 37.9, 36.6, 26.8, 25.3, 22.9; IR (NaCl, cm^{-1}): 2941, 2873, 1785, 1716, 1226, 1169, 1147, 1056, 750; HRMS (FAB+) calcd for $C_{20}H_{22}O_3F_3S$ (M-BF_4): 399.1242, found 399.1253.

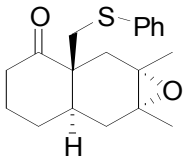
Epoxidation Reaction Procedures:

Procedure A:

To a solution of sulfoxide (0.1 mmol) in DCM (1 mL) at 0 °C was added TFAA (0.3 mmol) dropwise. The resulting mixture was stirred at 0 °C for 0.5 h and rt for additional 0.5 h. Then to the mixture was added 1 mL saturated aqueous $NaHCO_3$. The biphasic mixture was stirred at rt for 4 h and extracted with DCM and organic extract was concentrated at reduced pressure. Chromatography of the residue gave the corresponding epoxide.

Procedure B:

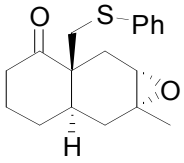
To a solution of sulfoxide (0.1 mmol) in DCM (1 mL) at −78 °C was added TFAA (0.3 mmol) dropwise. The resulting mixture was slowly warmed to rt for within 12 h. Then to the mixture was added 1 mL saturated aqueous $NaHCO_3$. The biphasic mixture was stirred at rt for 4 h and extracted with DCM and organic extract was concentrated at reduced pressure. Chromatography of the residue gave the corresponding epoxide.



4

The epoxide **4** was synthesized by **procedure A** in 0.1 mmol scale. After chromatography (Hexanes/Ethyl Acetate = 4:1), the epoxide **4** was obtained as a colorless oil (30 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.36 (m, 2H), 7.32−7.28 (m, 2H), 7.26−7.23 (m, 1H), 3.32−3.28 (dd, *J* = 12.2, 2.0 Hz, 1H), 2.99−2.96 (d, *J* = 12.2 Hz, 1H), 2.37−2.32 (m, 1H), 2.25−2.22 (m, 1H), 2.19−2.15 (dd, *J* = 16.0, 2.4 Hz, 1H), 2.11−2.07 (d, *J* = 16.0 Hz, 1H), 1.98−1.94 (m, 2H), 1.85−1.78 (m, 1H), 1.73−1.66 (dd, *J* = 14.4, 12.1 Hz, 1H), 1.65−1.50 (m, 3H), 1.30 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.6, 136.6, 130.8, 129.1, 126.9, 61.0, 60.6, 50.6, 39.4, 38.8, 35.9, 35.1, 34.7, 26.8, 26.19, 21.8, 19.1; IR (NaCl, cm^{-1}): 2927, 2862, 1707, 1437, 1163, 742, 691; HRMS (FAB+) calcd for $C_{19}H_{25}O_2S$ (M+H): 317.1575, found 317.1573.

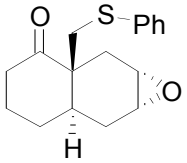


15

The epoxide **15** was synthesized by **procedure A** in 0.1 mmol scale. After chromatography (Hexanes/Ethyl Acetate = 8:1), the epoxide **15** was obtained as a white solid (21 mg, 70%), m.p. 68−70 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.34 (m, 2H), 7.32−7.28 (m, 2H), 7.24−7.22 (m, 1H), 3.29−3.26 (dd, *J* = 12.0, 2.4 Hz, 1H), 3.06−3.03 (d, *J* = 12.0 Hz, 1H), 2.95−2.93 (d,

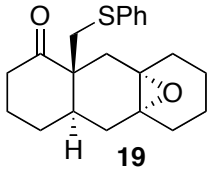
J = 5.6 Hz, 1H), 2.43−2.22 (m, 3H), 2.16−2.12 (dd, *J* = 16.4, 2.4 Hz, 1H), 1.99−1.94 (m, 2H), 1.85−1.76 (td, *J* = 11.4, 5.7 Hz, 1H), 1.73−1.69 (dd, *J* = 14.1, 12.0 Hz, 1H), 1.67−1.50 (m, 3H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.4, 136.0, 130.2, 129.1, 126.7, 57.3, 56.7, 49.7, 39.1, 38.9, 35.7, 33.3, 28.5, 27.1, 26.1, 22.8; IR (NaCl, cm^{-1}): 2926, 2862, 1705, 1436, 740, 690; HRMS (FAB+) calcd for $C_{18}H_{23}O_2S$ (M+H): 303.1419, found 303.1416.



17

The epoxide **17** was synthesized by **procedure B** in 0.1 mmol scale. After chromatography (Hexanes/Ethyl Acetate = 4:1), the epoxide **17** was obtained as a colorless oil (10 mg, 35%).

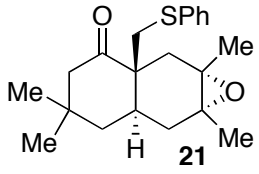
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.33 (m, 2H), 7.31−7.28 (m, 2H), 7.25−7.20 (m, 1H), 3.31−3.27 (dd, *J* = 12.0, 2.4 Hz, 1H), 3.18 (d, *J* = 3.6 Hz, 1H), 3.11−3.08 (d, *J* = 12.0Hz, 1H), 3.12−3.10 (m, 1H), 2.45−2.36 (m, 1H), 2.32 (dd, *J* = 16.4, 5.9 Hz, 1H), 2.27 (m, 1H), 2.17−2.12 (m, 1H), 2.10 (m, 1H), 2.03−1.95 (m, 1H), 1.82−1.75 (m, 2H), 1.68−1.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.4, 136.0, 130.4, 129.1, 126.8, 51.2, 50.0, 49.5, 39.0, 38.2, 35.6, 28.2, 27.8, 27.3, 26.2; IR (NaCl, cm^{-1}): 2926, 2859, 1706, 1437, 740, 691; HRMS (FAB+) calcd for $C_{17}H_{21}O_2S$ (M+H): 289.1262, found 289.1259.



19

The epoxide **19** was synthesized by **procedure A** in 0.1 mmol scale. After chromatography (Hexanes/Ethyl Acetate = 8:1), the epoxide **19** was obtained as a white solid (20 mg, 59%), m.p. 90−92 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.35 (m, 2H), 7.32−7.28 (m, 2H), 7.25−7.21 (m, 1H), 3.33 (dd, *J* = 12.4, 1.9 Hz, 1H), 3.03 (d, *J* = 12.4 Hz, 1H), 2.42−2.33 (m, 1H), 2.29−2.20 (m, 1H), 2.14 (dd, *J* = 15.9, 2.0 Hz, 1H), 2.08 (d, *J* = 15.9 Hz, 1H), 2.00−1.95 (m, 3H), 1.83−1.78 (m, 2H), 1.73−1.42 (m, 6H), 1.40−1.28 (m, 2H), 1.25−1.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.6, 136.3, 130.9, 129.1, 126.9, 60.9, 60.5, 50.7, 39.1, 38.9, 36.1, 34.9, 34.6, 32.2, 29.5, 27.0, 26.2, 20.8, 19.7; IR (NaCl, cm^{-1}): 2931, 2859, 1708, 1438, 741, 691; HRMS (FAB+) calcd for $C_{21}H_{27}O_2S$ (M+H): 343.1732, found 343.1741.

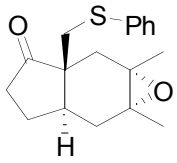


21

The epoxide **21** was synthesized by **procedure A** in 0.1 mmol scale. After chromatography (Hexanes/Ethyl Acetate = 8:1), the epoxide **21** was obtained as a white solid (30 mg, 86%), m.p. 103−105°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.34 (m, 2H), 7.32−7.28 (m, 2H), 7.25−7.21 (m, 1H), 3.26 (dd, *J* = 12.0, 1.6 Hz, 1H), 2.92 (d, *J* = 12.0 Hz, 1H), 2.31 (d, *J* = 13.2 Hz, 1H), 2.16−2.10 (dd, *J* = 16.0, 1.6 Hz, 1H), 2.10−2.06 (d, J = 16.0 Hz, 1H), 2.05−1.93 (m, 2H),

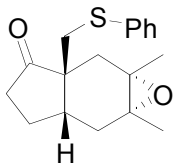
1.90 (dd, J = 14.9, 4.6 Hz, 1H), 1.67 (dd, J = 14.8, 12.1 Hz, 1H), 1.58 (t, J = 13.4 Hz, 1H), 1.31 (s, 3H), 1.30−1.23 (m, 1H), 1.21 (s, 3H), 1.01 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.0, 136.2, 130.6, 129.1, 126.9, 61.2, 60.7, 51.5, 49.5, 40.3, 35.8, 35.6, 35.0, 34.6, 34.5, 32.1, 25.8, 21.9, 19.2; IR (NaCl, cm^{-1}): 2955, 2924, 1708, 1437, 739, 691; HRMS (FAB+) calcd for $C_{21}H_{29}O_2S$ (M+H): 345.1888, found 345.1891.



23

The epoxide **23** was synthesized by **procedure A** in 0.1 mmol scale. After chromatography (Hexanes/Ethyl Acetate = 8:1), the epoxide **23** was obtained as a colorless oil (28 mg, 93%).

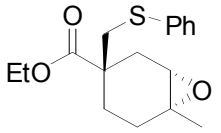
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.34 (m, 2H), 7.31−7.27 (m, 2H), 7.23−7.20 (m, 1H), 3.04 (dd, J = 12.6, 1.6 Hz, 1H), 2.88 (d, J = 12.6 Hz, 1H), 2.33−2.23 (m, 2H), 2.17−2.02 (m, 3H), 1.95−1.90 (m, 1H), 1.89−1.78 (m, 2H), 1.78−1.70 (m, 1H), 1.34 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.1, 136.6, 130.4, 129.1, 126.8, 63.1, 61.0, 49.5, 37.9, 36.1, 35.2, 34.6, 32.9, 23.0, 22.1, 19.7; IR (NaCl, cm^{-1}): 2954, 2919, 1738, 1438, 741, 690; HRMS (FAB+) calcd for $C_{18}H_{22}O_2S$ (M+): 302.1341, found 302.1351.



25

The epoxide **25** was synthesized by **procedure B** in 0.1 mmol scale. After chromatography on preparative TLC (Hexanes/Ethyl Acetate = 2:1), the epoxide **25** was obtained as a colorless oil (12 mg, 40%).

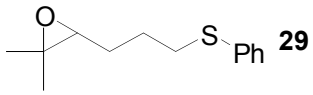
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.31 (m, 2H), 7.30−7.23 (m, 2H), 7.20−7.18 (m, 1H), 2.88 (d, *J* = 12.2 Hz, 1H), 2.84 (d, *J* = 12.2 Hz, 1H), 2.60−2.45 (m, 2H), 2.31 (d, *J* = 14.6 Hz, 1H), 2.26 (m, 1H), 2.21 (t, *J* = 12.9 Hz, 1H), 2.12−2.02 (m, 2H), 1.84 (dd, *J* = 15.3, 1.2 Hz, 1H), 1.75−1.67 (m, 1H), 1.29 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 219.5, 136.5, 129.4, 129.0, 126.3, 60.5, 60.2, 50.3, 42.6, 36.9, 35.8, 35.5, 35.5, 26.8, 19.1, 18.7; IR (NaCl, cm^{-1}): 2956, 2916, 1736, 1438, 739, 690; HRMS (FAB+) calcd for $C_{18}H_{22}O_2S$ (M+): 302.1341, found 302.1343.



27

The epoxide **27** was synthesized by **procedure A** in 0.1 mmol scale. After chromatography (Hexanes/Ethyl Acetate = 8:1), the epoxide **27** was obtained as a colorless oil (24mg, 77%).

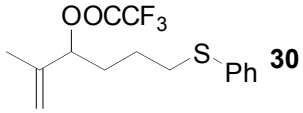
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.35 (m, 2H), 7.31−7.23 (m, 2H), 7.20−7.17 (m, 1H), 4.05−3.93 (m, 2H), 3.19 (d, *J* = 12.8 Hz, 1H), 3.05 (d, *J* = 12.8 Hz, 1H), 2.94 (d, *J* = 3.3 Hz, 1H), 2.43 (d, *J* = 15.4 Hz, 1H), 2.08−1.98 (m, 2H), 1.95−1.81 (m, 1H), 1.80−1.69 (m, 1H), 1.62−1.51 (m, 1H), 1.30 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 136.4, 130.1, 128.8, 126.4, 60.6, 57.9, 56.6, 43.6, 42.0, 32.8, 25.5, 25.4, 23.3, 14.0; IR (NaCl, cm^{-1}): 2978, 2925, 1727, 1439, 1201, 1177, 1047, 741, 691; HRMS (FAB+) calcd for $C_{17}H_{23}O_3S$ (M+H): 307.1368, found 307.1356.



29

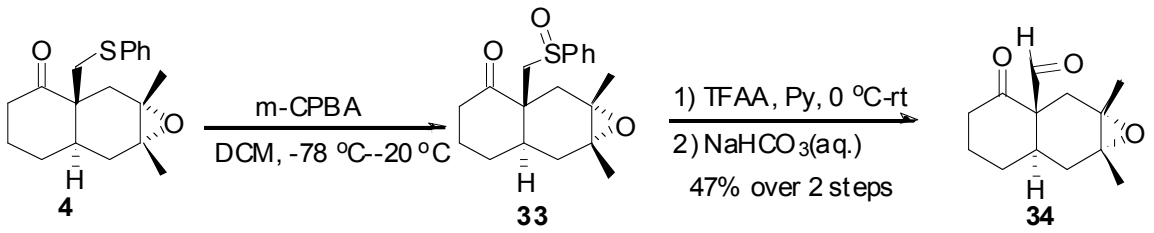
The epoxide **29** was synthesized by **procedure A** in 0.15 mmol scale. After chromatography (Hexanes/Ethyl Acetate = 8:1), the epoxide **29** was obtained as a colorless oil (8 mg, 22%) together with byproduct compound **30** as a colorless oil (24 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.31 (m, 2H), 7.29−7.25 (m, 2H), 7.21−7.13 (m, 1H), 3.07−2.88 (m, 2H), 2.71 (dd, *J* = 6.8, 5.3 Hz, 1H), 1.92−1.55 (m, 4H), 1.30 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 129.2, 128.8, 125.9, 63.7, 58.1, 33.4, 27.9, 26.2, 24.8, 18.7; IR (NaCl, cm^{-1}): 2958, 2924, 2851, 1480, 1438, 1377, 738, 690; HRMS (FAB+) calcd for $C_{13}H_{19}OS$ (M+H): 223.1157, found 223.1156.



30

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.27 (m, 4H), 7.22−7.16 (m, 1H), 5.32 (t, *J* = 6.7 Hz, 1H), 5.02 (s, 1H), 4.99 (s, 1H), 2.94 (t, *J* = 7.1 Hz, 2H), 1.94−1.87 (m, 2H), 1.73 (s, 3H), 1.72−1.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8 (O=C-CF3), 156.4 (O=C-CF3), 140.4, 135.8, 129.5, 128.9, 126.2, 115.9 (O=C-CF3), 115.2, 113.0 (O=C-CF3), 81.5, 33.3, 30.9, 24.4, 17.4; IR (NaCl, cm^{-1}): 2925, 2860, 1783, 1439, 1221, 1165, 908, 738, 690; HRMS (FAB+) calcd for $C_{15}H_{17}O_2F_3S$ (M+): 318.0901, found 318.0912.



4 **33** **34**

To a solution of sulfide **4** (0.030 g, 0.095 mmol) in DCM (2 mL) at −78 °C was added *m*-CPBA (0.026 g, 77% purity) in one portion. The resulting mixture was warmed to −20 °C over 2 hours, and then quenched with saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$. The mixture was extracted with DCM, washed with aqueous saturated $NaHCO_3$, dried over anhydrous $MgSO_4$, filtered and concentrated at reduced pressure. The crude sulfoxide **33** was directly used in the next step without further purification.

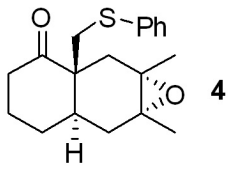
To the crude sulfoxide **33** in DCM (1.5 mL) at 0 °C was added pyridine (0.022 g, 0.285 mmol) and TFAA (0.060 g, 0.285 mmol). The resulting mixture was stirred at 0 °C for 0.5 h and rt for another 0.5 h. Then to the mixture was added 1 mL aqueous saturated $NaHCO_3$. The biphasic mixture was stirred at rt for 4 h, then extracted with DCM and organic extract was concentrated at reduced pressure. Chromatography of the residue gave compound **34** (10 mg, 47% over 2 steps) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 2.58−2.54 (m, 2H), 2.26 (q, J = 16.2 Hz, 2H), 2.19−2.13 (m, 1H), 2.09−1.95 (m, 2H), 1.98−1.86 (m, 1H), 1.84−1.65 (m, 3H), 1.42 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 199.9, 65.3, 61.6, 60.8, 41.2, 39.7, 35.9, 32.6, 27.4, 25.6, 21.6, 18.9; IR (NaCl, cm^{-1}): 2929, 2866, 1722, 1698, 1453, 1169; HRMS (FAB+) calcd for $C_{13}H_{19}O_3$ (M+H): 223.1334, found 223.1339.

References:

1) Lee, J. H.; Zhang, Y.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2010**, *132*, 14330-14333.
2) Singleton, D. A.; Merrigan, S. R.; Beno, B. R.; Houk, K. N. *Tetrahedron Lett*. **1999**, *40*, 5817-5821.
3) Eng, H. M.; Myles, D. C. *Tetrahedron Lett*. **1999**, *40*, 2275-2278.

zyd-9-190

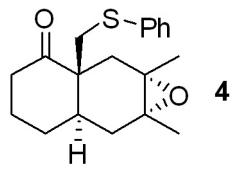


4

8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

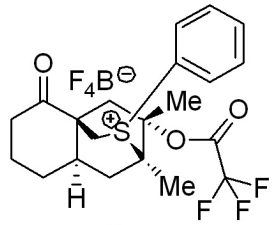
f1 (ppm)

zyd-9-190
carbon 13



4

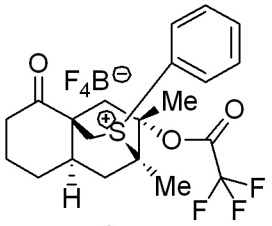
zyd-10-50/1
proton



9

f1 (ppm)

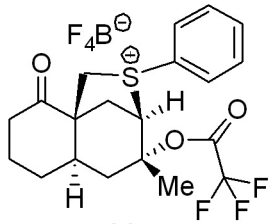
zyd-10-50


O
F4B⊖
Me
O
⊕S
O
Me
F
F
F
H

9

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

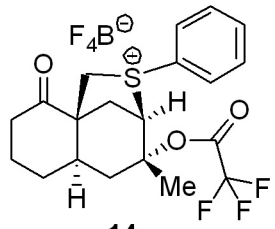
zyd-10-94


F4B
O
S
H
O
O
Me
F
F
F
H

14

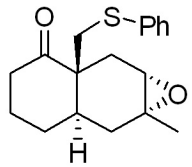
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

zyd-10-94
carbon 13



14

zyd-9-200

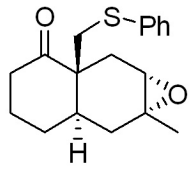


15

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

f1 (ppm)

zyd-9-200
carbon 13

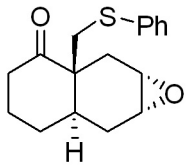


15

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

zyd-9-272

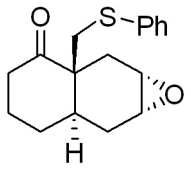


17

8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0

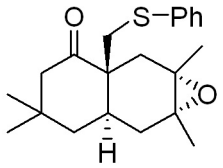
f1 (ppm)

zyd-9-272
carbon 13



17

zyd-10-16
proton

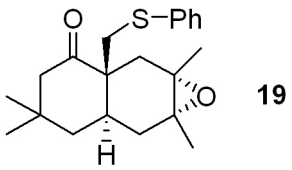


19

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

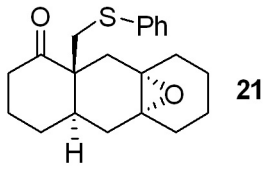
zyd-10-16


O
S–Ph
O
H

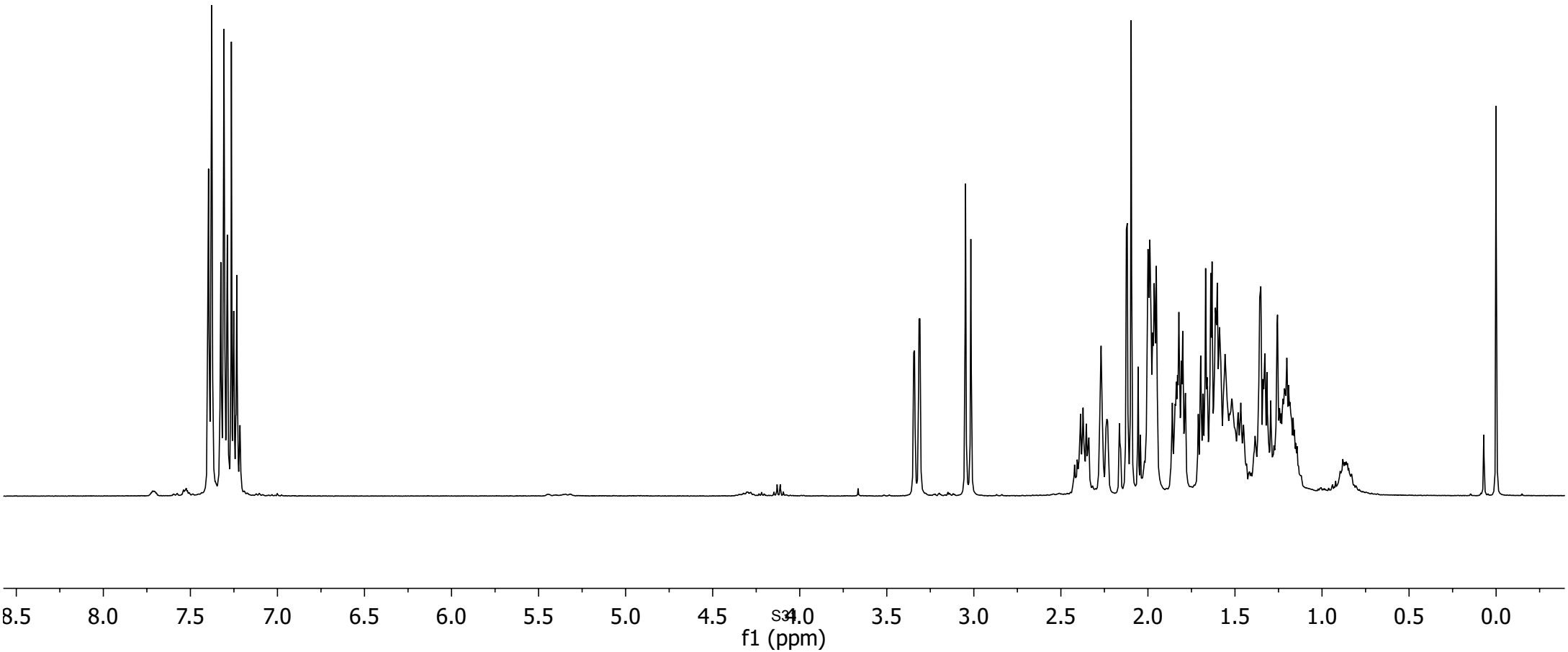
19

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

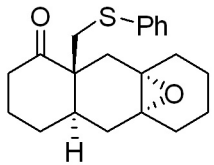
zyd-10-18
proton



21



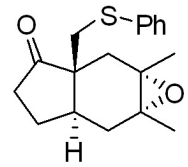
zyd-10-18



21

f1 (ppm)

zyd-9-214

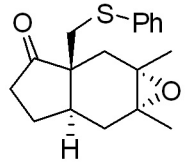


23

8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0

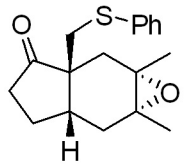
f1 (ppm)

zyd-9-214
carbon 13



23

zyd-9-236

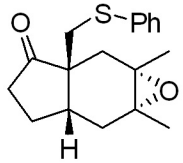


25

8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

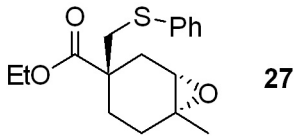
f1 (ppm)

zyd-9-236
carbon 13



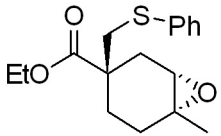
25

zyd-9-276



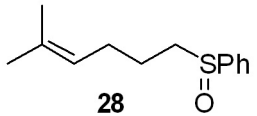
27

zyd-9-276
carbon 13



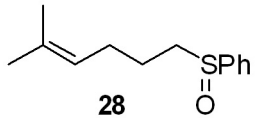
27

zyd-9-232



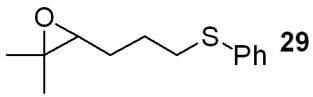
28

zyd-9-232
carbon 13



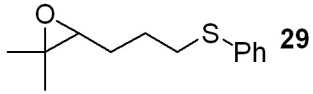
28

zyd-10-100-2
proton



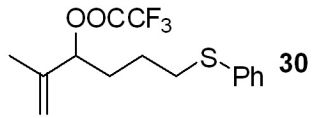
29

zyd-10-100-2



29

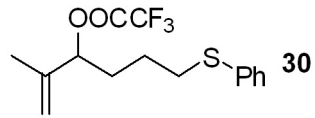
zyd-9-274-1


OOCCF3
S
Ph

30

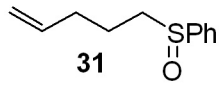
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

zyd-10-100-1
carbon 13



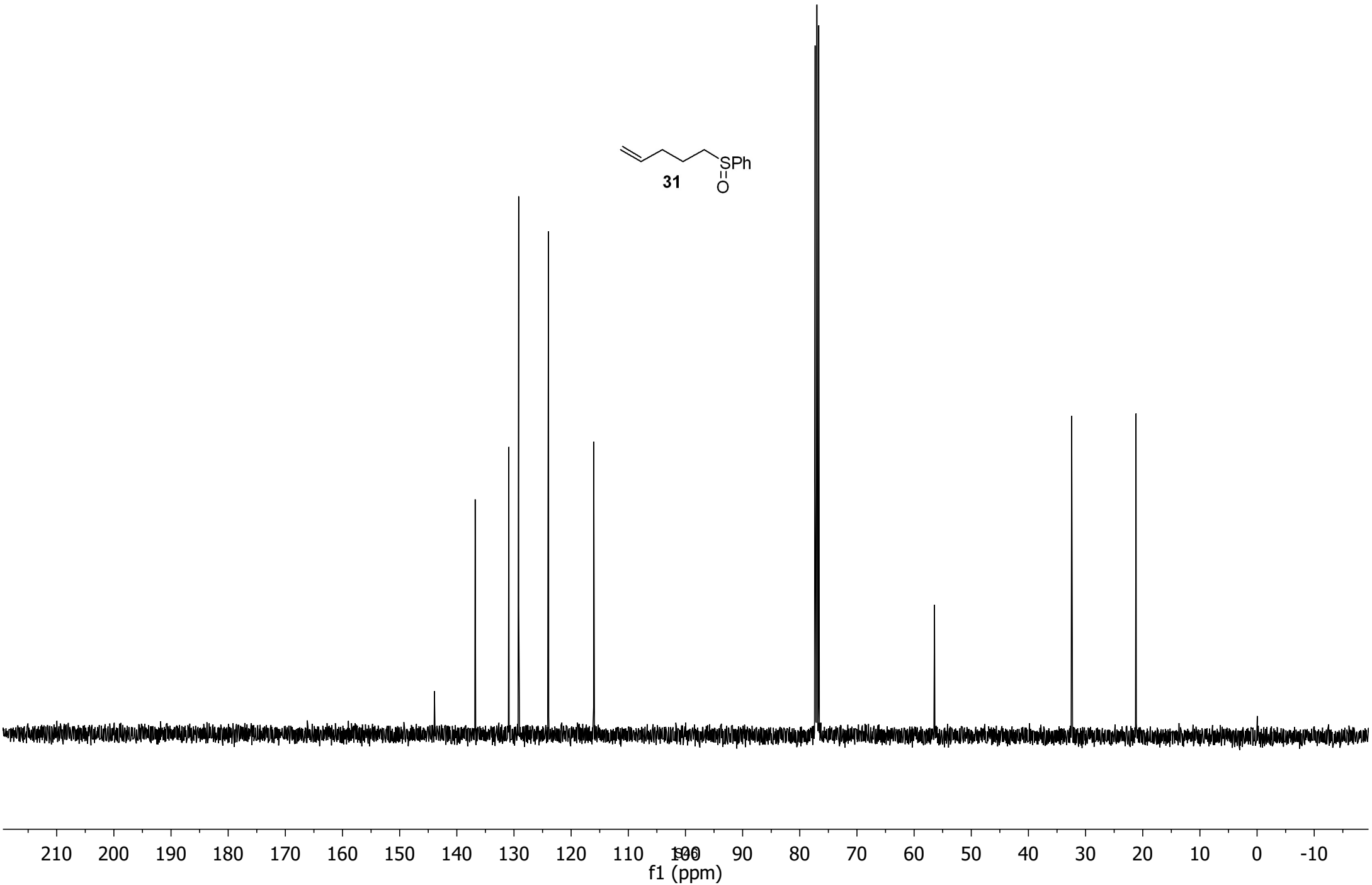
30

zyd-9-286
proton

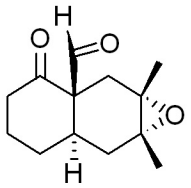


31

zyd-9-286


SPh
O
31
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

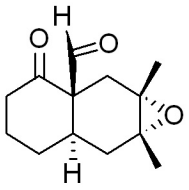
zyd-10-42



34

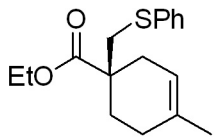
f1 (ppm)

zyd-10-42
carbon 13



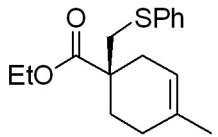
34

zyd-9-208-34



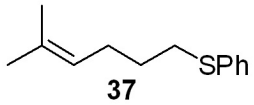
36

zyd-9-208-34
carbon 13



36

zyd-9-230
proton

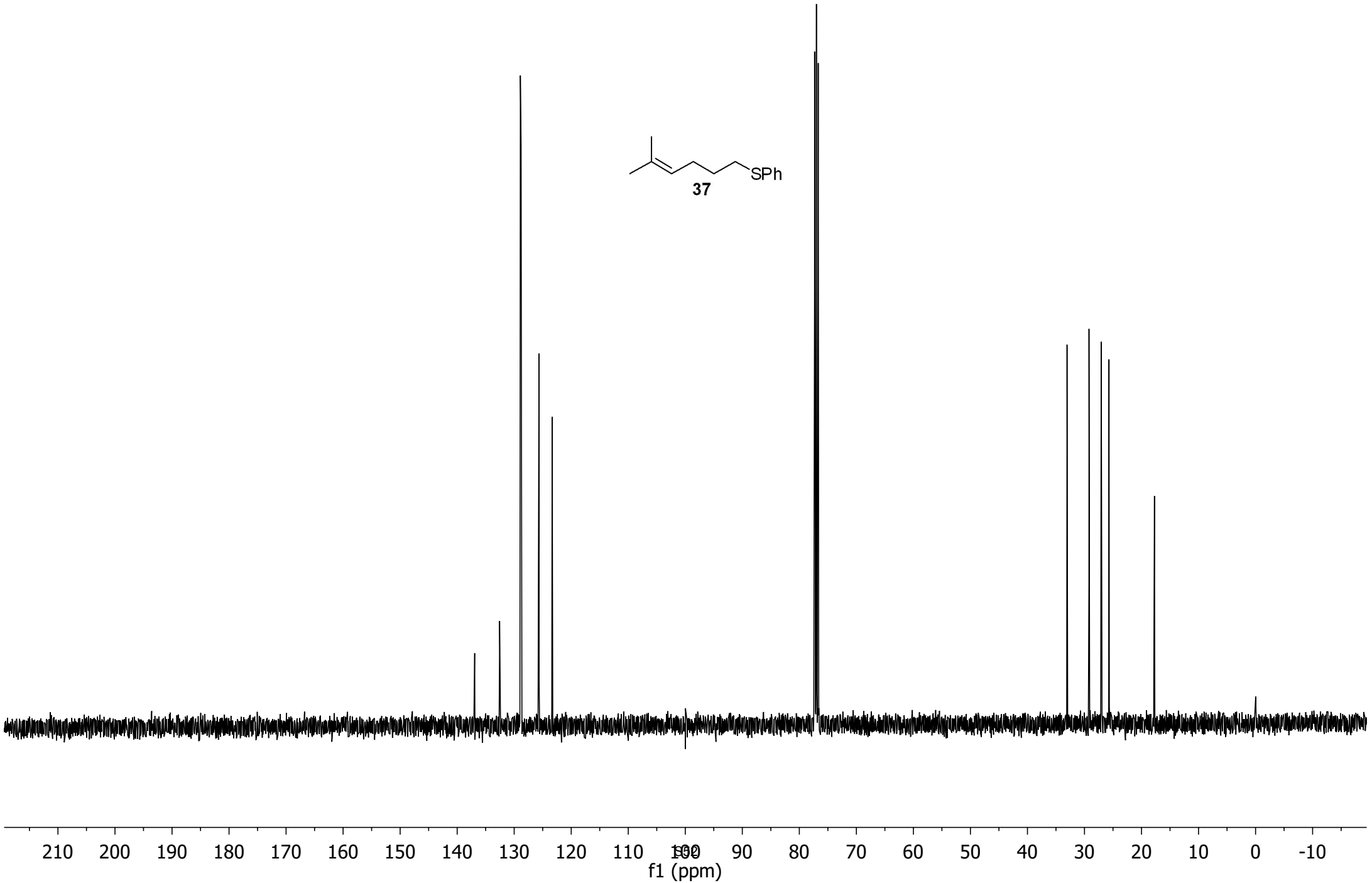


37

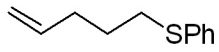
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

zyd-9-230

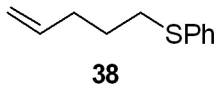

SPh
37
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

zyd-9-280



38

zyd-9-280
carbon 13



38