Supporting Information

A Photoisomerization-coupled Asymmetric Stetter Reaction: Application to the Total Synthesis of Three Diastereomers of (–)-Cephalimysin A

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Materials and Methods

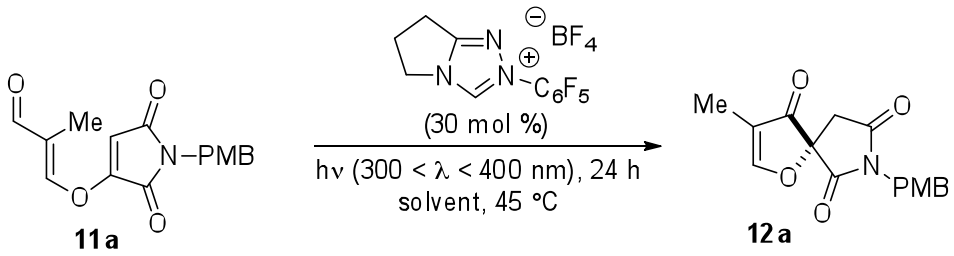
All reactions were carried out under an atmosphere of argon in flame-dried glassware with magnetic stirring unless otherwise stated. Reaction solvents including dichloromethane (CH_2Cl_2), diethyl ether (Et_2O), tetrahydrofuran (THF), toluene (PhMe), benzene, (PhH), Acetonitrile (MeCN), and Methanol (MeOH) were degassed with argon and passed through two columns of neutral alumina. HPLC grade Chloroform preserved with pentane was purchased from Fisher Scientific. ACS grade dimethyl sulfoxide (DMSO) was purchased from EDI chemical Inc. All chemicals were obtained from commercial sources unless otherwise stated. Column chromatography was performed on SiliCycle®Silica*Flash*® P60, 40-63μm 60A. Thin layer chromatography was performed on SiliCycle® 250μm 60A plates. Visualization was accomplished with UV light, cerium ammonium molybdenate, $KMnO_4$, or anisaldehyde stains followed by heating.

^{1}H nmr spectra were recorded on Varian 300 or 400 MHz spectrometers at ambient temperature unless otherwise stated. Data is reported as follows: chemical shift in parts per million (δ, ppm) from $CDCl_3$ (7.26 ppm), toluene-d_8 (7.09, 7.0, 6.98, 2.09 ppm) or benzene-d_6 (7.16 ppm) multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constants (Hz). ^{13}C NMR was recorded on Varian 300 or 400 MHz spectrometers (at 75 or 100 MHz) at ambient temperature. Chemical shifts are reported in ppm from $CDCl_3$ (77.2 ppm) or toluene-d_8 (137.86 (1), 129.4 (3), 128.33 (3), 125.49 (3), 20.4 (5) ppm). Infrared spectra were obtained on a Nicolet Avatar 320 FT-IR spectrometer or Bruker Tensor 27 FT-IR spectrometer. Mass spectra were obtained on a Fisions VG Autospec. HPLC

spectra were obtained on an Agilent 1100 series system. Optical rotation was obtained with an Autopol-III automatic polarimeter.

Reaction Optimization: Solvents and Bases with an Achiral Catalyst.

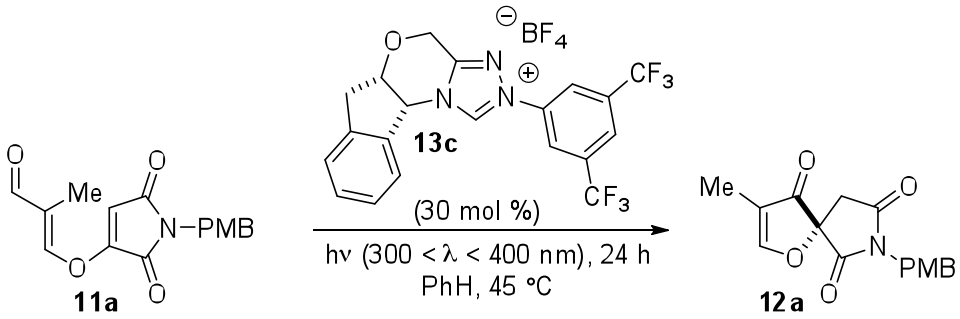
Initial screen of solvents and bases found that sodium acetate in chloroform gave the highest yields. Later screening revealed benzene to be the optimal solvent. See manuscript (Table 1) for further details.



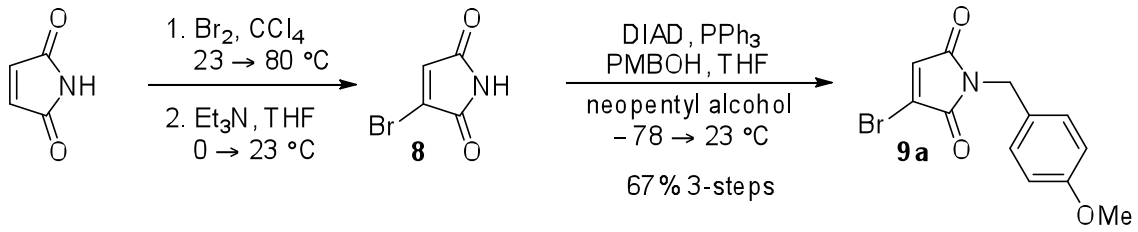
entry	solvent	base (equiv.)	conversion (% yield)
1	PhMe	KHMDS (0.3)	25%
2	PhMe	DIPEA (1.0)	35%
3	$CHCl_3$	DIPEA (1.0)	90% (10)
4	**$CHCl_3$**	**NaOAc (1.0)**	**70% (41)**
5	$CHCl_3$	Cs_2CO_3 (0.3)	decomp.

Reaction Optimization: Bases with Enantioenriched Bis(trifluoromethyl)-phenyl catalyst.

Sodium Acetate (1.0 equivalent) gives the desired product with optimal yield and enantioselectivity.



entry	base (equiv)	yield	ee
1	K_2CO_3 (1.0)	NR	-
2	Cs_2CO_3 (1.0)	27%	84%
3	NaOBz (1.0)	42%	91%
4	NaOAc (0.5)	52%	94%
5	**NaOAc (1.0)**	**58%**	**94%**
6	NaOAc (2.0)	35%	94%



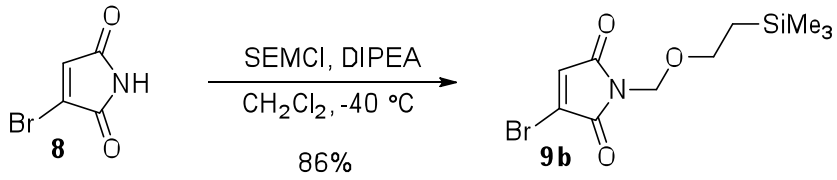
3-bromo-1-(4-methoxybenzyl)-1*H*-pyrrole-2,5-dione (9a). Prepared according to the general procedures.[1] A solution of bromine (12 mL, 232 mmol, 1.1 equiv.) in CCl_4 (200 mL) was added drop wise via addition funnel to maleimide (20.5 g, 212 mmol, 1.0 equiv.) in CCl_4 (300 mL) over 45 min at room temperature. After addition was complete the flask was fitted with a reflux condenser and heated to 80 °C for 1 h. The mixture was then allowed to cool to room temperature and the resulting precipitate was filtered and washed with CCl_4 (2 × 50 mL) to afford dibromosuccinimide as a slightly orange solid (52.8 g).

The crude dibromosuccinimide (52.8 g, 206 mmol, 1.0 equiv.) was dissolved in THF (700 mL and cooled to 0 °C. To the mixture was added triethylamine (31.5 mL, 226 mmol, 1.1 equiv.) as a solution in THF (100 mL) over 30 min via addition funnel. After addition the mixture was allowed to stir at 0 °C for a further 2 h. The reaction was then allowed to warm to room temperature and the organics were concentrated in vacuo. The resulting residue was dissolved in EtOAc (800 mL) and washed with H_2O (2 × 100 mL), brine (50 mL), dried over $MgSO_4$ and concentrated in vacuo to afford 35.4 g of N-H bromomaleimide **8** as a light brown solid which was used in the following step without further purification.

Triphenylphosphine (22.4 g, 85.2 mmol, 1.0 equiv.) was dissolved in THF (580 mL), the resulting solution was cooled to –78 °C. Diisopropyl azodicarboxylate (16.5 mL, 85.2 mmol, 1.0 equiv.) was added over 5 min via syringe and the mixture was allowed to stir for a further 5 min

[1] For N-Ph bromomaleimide, see; M. K. Sahoo, S. B. Mhaske, P. N. Argade, *Synthesis*, 2003, 346; For N-H bromomaleimide, see; L. M. Tedaldi, M. E. B. Smith, R. I. Nathani, J. R. Baker, *Chem. Commun*., 2009, 6583; For benzyl protection of maleimides, see; M. A. Walker, . *J. Org. Chem*. 1995, **60**, 5352.

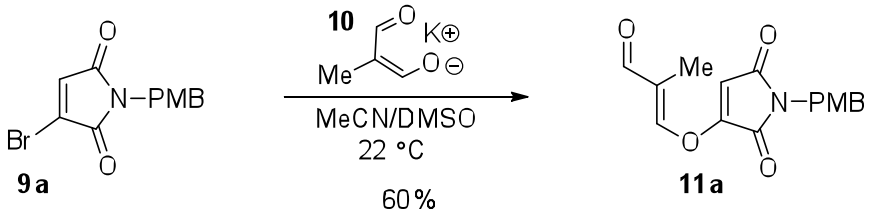
after which *para*-methoxybenzyl alcohol (11.7 mL, 93.8 mmol, 1.1 equiv.) was added in one portion and the mixture was allowed to stir another 5 min. Neopentyl alcohol (4.13 g, 46.9 mmol, 0.55 equiv.) and N-H bromomaleimide **8** (15.0 g, 85.2 mmol,) were added sequentially as solids and the resulting suspension was allowed to stir 5 min at –78 °C before being allowed to warm to room temperature. The reaction was allowed to stir ~12 h at room temperature. After 12 h TLC analysis indicated complete consumption of the maleimide **8**. The mixture was concentrated *in vacuo* and purified via column chromatography 4:1 hexanes/EtOAc to afford 17.0 g (67% yield) of PMB-protected maleimide **9a**. ^{1}H nmr (300 MHz, $CDCl_3$) δ 7.29 (d, 2H, J = 8.6 Hz), 6.85 (s, 1H), 6.83 (d, 2H, J = 8.6 Hz), 4.64 (s, 2H), 3.78 (s, 3H);



3-bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrrole-2,5-dione (9b). Prepared by modification to the known literature procedure.[2] To a solution of N-H bromomaleimide **8** (10.0 g, 56.8 mmol, 1.0 equiv.) in CH_2Cl_2 (500 mL) at –40 °C (MeCN/dry ice) was added diisopropylethylamine (15.8 mL, 90.9 mmol, 1.6 equiv.) followed by 2-(trimethylsilyl)-ethoxyethyl chloride[3] (11.0 mL, 62.5 mmol, 1.1 equiv.). The solution was allowed to stir 1.5 h and then quenched with sat. NH_4Cl (100 mL) and allowed to warm to room temperature. After separation of the organic layer the aqueous layer was extracted once more with CH_2Cl_2 (200 mL). The combined organics were washed with brine (100 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford a dark brown oil. Purification of the crude product by column chromatography

[2] : R. S. Coleman, M. C. Walczak, E. L. Campbell, *J. Am. Chem. Soc.*, 2005, **127**, 16038.
[3] B. H. Lipshutz, J. J. Pegram, *Tetrahedron Lett.*, 1990, **21**, 3343.

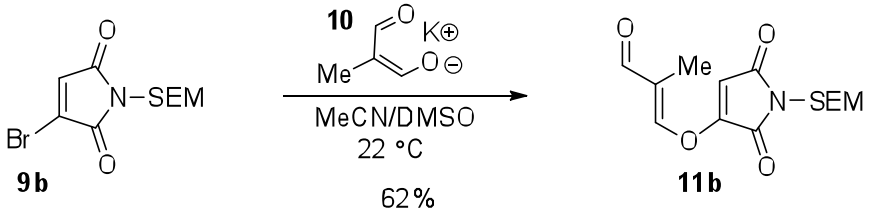
15:1 □ 10:1 hexanes/EtOAc (R_f = 0.4, 6:1 hexanes/EtOAc) affords 14.8 g (86% yield) of **9b** as a yellow oil. ^{1}H nmr (400 MHz, $CDCl_3$) δ 6.93 (s, 1H), 4.93 (s, 2H), 3.56 (t, 2H, *J* = 8.3), 0.90 (t, 2H, *J* = 8.4 Hz), 0.03 (s, 9H) ; ^{13}C nmr (100 MHz, $CDCl_3$) δ 168.2, 165.1, 132.3, 132.0, 67.4, 67.3, 17.9, 1.4; IR (thin film/NaCl) 2954 2896, 1783, 1730, 1589, 1414, 1390, cm^{-1};



(*E*)-3-((1-(4-methoxybenzyl)-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-3-yl)oxy)-2-methyl-acrylaldehyde (11a). To a solution PMB-maleimide **9a** (4.3 g, 14.7 mmol, 1.3 equiv.) in MeCN (30 mL) at room temperature was added **10**[4] (1.4 g, 11.3 mmol, 1.0 equiv.) as a solution in DMSO (60 mL) over 30 min via addition funnel. The reaction was allowed to stir 1 h at ambient temperature and then quenched with sat. NH_4Cl (50 mL) and the mixture was extracted with EtOAc (3 × 150 mL). The combined organics were washed with H_2O (2 × 100 mL), brine (2 × 50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the crude product via column chromatography 12:1 PhMe/EtOAc (R_f = 0.4, 6:1 PhMe/EtOAc) affords 2.04 g (60% yield) of aldehyde **11a** as a light brown oil which solidifies upon standing. The aldehyde was found to decompose if left on the bench top over the course of a couple days. However storage as a solution in CH_2Cl_2 at 0 °C allows for safe keeping for ~ 2 weeks without appreciable decomposition. ^{1}H nmr (300 MHz, $CDCl_3$) δ 9.49 (s, 1H), 7.41 (q, 1H, *J* = 1.3 Hz), 7.30 (d, 2H, *J* = 8.7 Hz), 6.84

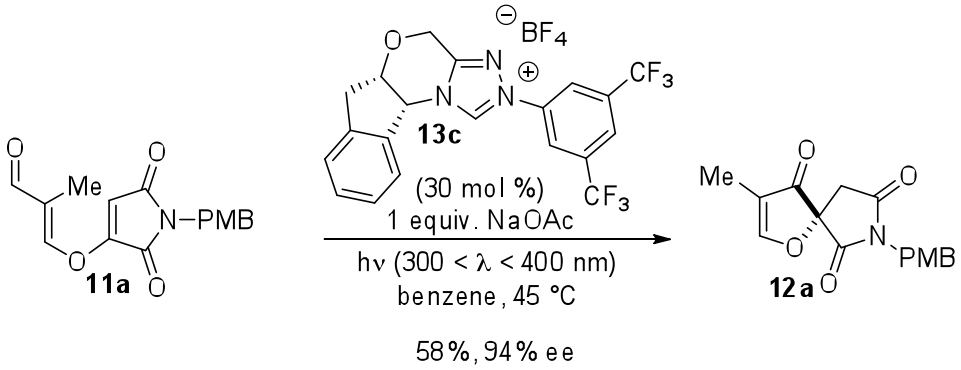
[4] P. T. O'Sullivan, W. Buhr, M. A. M. Fuhry, J. R. Harrison, J. E. Davies, N. Feeder, D. R. Marshall, J. W. Burton, A. B. Holmes, *J. Am. Chem. Soc.*, 2004 **126**, 2194.

(d, 2H, J = 8.7 Hz), 5.83 (s, 1H), 4.63 (s, 2H), 3.78 (s, 3H), 1.87 (d, 3H, J = 1.3 Hz). Full characterization has been carried out for similar aldehyde **11b** (*vide infra)*.



(*E*)-3-((2,5-dioxo-1-((2-(trimethylsilyl)ethoxy)methyl)-2,5-dihydro-1H-pyrrol-3-yl)oxy)-2-methylacrylaldehyde (11b). To a solution SEM-maleimide **9b** (10.0 g, 32.7, mmol, 1.2 equiv.) in MeCN (75 mL) at room temperature was added **10**[5] (3.40 g, 27.2 mmol, 1.0 equiv.) as a solution in DMSO (125 mL) over 30 min via addition funnel. The reaction was allowed to stir 1 h at ambient temperature and then quenched with sat. NH_4Cl (100 mL) and extracted with Et_2O (3 × 150 mL). The combined ethereal extracts were washed with H_2O (2 × 100 mL), brine (2 × 50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the crude product via column chromatography 12:1 to 6:1 PhMe/EtOAc (R_f = 0.4, 6:1 PhMe/EtOAc) affords 5.25 g (62% yield) of aldehyde **11b** as a yellow oil which solidifies upon standing. The aldehyde was found to decompose if left on the bench top over the course of a couple days. However storage as a solution in CH_2Cl_2 at 0 °C allows for safe keeping for ~ 2 weeks without appreciable decomposition. ^{1}H nmr (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.44 (s, 1H), 5.92 (s, 1H), 4.92 (s, 2H), 3.56 (t, 2H, J = 8.2 Hz), 0.90 (t, 2H, J = 8.2 Hz), 0.04 (s, 9H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 190.8, 168.2, 164.3, 156.7, 155.7, 127.8, 102.8, 67.5, 66.8, 18.1, 7.3, 1.3. IR (thin film/NaCl) 2962, 2873, 1792, 1720, 1628, 1515, 1434, cm^{-1}; HRMS $[C_{22}H_{26}NO_5]^+$ calcd 384.1805, found 384.1813.

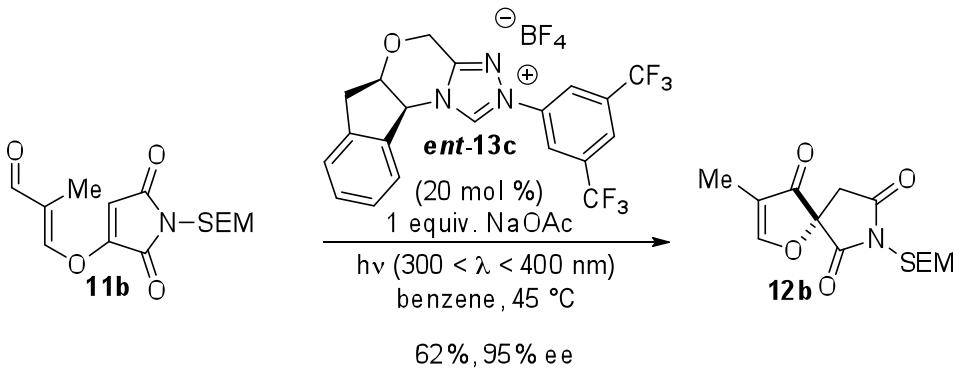
[5]) P. T. O'Sullivan, W. Buhr, M. A. M. Fuhry, J. R. Harrison, J. E. Davies, N. Feeder, D. R. Marshall, J. W. Burton, A. B. Holmes, *J. Am. Chem. Soc.*, 2004 **126**, 2194.



(*S*)-7-(4-methoxybenzyl)-3-methyl-1-oxa-7-azaspiro[4.4]non-2-ene-4,6,8-trione (12a). Triazolium salt **13c**[6] (425 mg, 0.82 mmol, 0.3 equiv.) was added to an oven dried sealed tube under argon (sealed tube typically gives higher yields of the product) followed by benzene (80 mL). Argon was then bubbled through the solution for 5 min. To the homogenous solution was added NaOAc (225 mg, 2.74 mmol, 1.0 equiv.) and the mixture was allowed to stir for 15 min. Aldehyde **11a** (825 mg, 2.74 mmol, 1.0 equiv.) was added to the reaction as a solution in benzene (10 mL, in some cases CH_2Cl_2 was also added to help solubilize the aldehyde) and the reaction was sealed and placed in a Rayonet photochemical reactor equipped with 350 nm UV lamps. The reaction was irradiated for 36-48 h (upon irradiation the internal temperature rose to ~45 °C over the first 1 h). The resulting dark brown mixture was filtered through a plug of silica gel and concentrated *in vacuo*. Purification of the crude product via column chromatography 9:1 PhMe/EtOAc (R_f = 0.4, 6:1 PhMe/EtOAc, the product is slightly less polar than the starting aldehyde) affords 480 mg (58% yield) of spirocylce **11a** as a brown oil. HPLC analysis-Chiracel IA column, 93:7 hexanes/*i*-PrOH, 1.0 mL/min, major enantiomer: 32.9 min, minor enantiomer: 44.3 min, 94% ee; $[\alpha]_D^{21}$ = -103.3 (c = 0.010 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 8.15 (q, 1H, *J* = 1.2 Hz), 7.27 (d, 2H, *J* = 8.8 Hz), 6.82 (d, 2H, *J* = 8.8 Hz), 4.62 (s, 2H), 3.75 (s, 3H),

[6] H. U. Vora, S. P. Lathrop, N. T. Reynolds, M. S. Kerr, J. Read de Alaniz, T. Rovis, *Org. Synth.*, 2010, **87**, 350. (b) H. Takikawa, K. Suzuki, *Org. Lett.*, 2007, **9**, 2713.

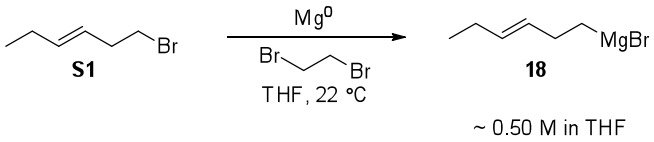
3.07 (d, 1H, J = 18.1 Hz), 2.93 (d, 1H, J = 18.1 Hz), 1.73 (d, 3H, J = 1.2 Hz); ^{13}C nmr (100 MHz, $CDCl_3$) δ 199.5, 175.0, 171.8, 169.2, 159.4, 130.0, 126.8, 115.0, 114.1, 85.2, 55.2, 42.8, 37.0, 5.3; IR (thin film/NaCl) 1791, 1719, 1616, 1514, 1433, cm^{-1}; HRMS $[C_{16}H_{16}NO_5]^+$ calcd 302.1023, found 302.1028.



(*S*)-3-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-1-oxa-7-azaspiro-[4.4]non-2-ene-4,6,8-trione (12b). Triazolium salt ***ent*-13c**[7] (827 mg, 1.60 mmol, 0.2 equiv.) was added to an oven dried sealed tube under argon (sealed tube typically gives higher yields of the product) followed by benzene (150 mL). Argon was then bubbled through the solution for 5 min. To the resulting homogenous solution was added NaOAc (658 mg, 8.02 mmol, 1.0 equiv.) and the mixture was allowed to stir for 15 min. Aldehyde **11b** (2.50 g, 8.02 mmol, 1.0 equiv.) was added to the reaction as a solution in benzene (20 mL, in some cases CH_2Cl_2 was also added to help solubilize the aldehyde) and the reaction was sealed and placed in a Rayonet photochemical reactor equipped with 350 nm UV lamps. The reaction was irradiated for 36-48 h (upon irradiation the internal temperature rose to ~45 °C over the first 1 h). The resulting dark brown mixture was filtered through a plug of silica gel, washed with EtOAc (200 mL) and concentrated *in vacuo*. Purifica-

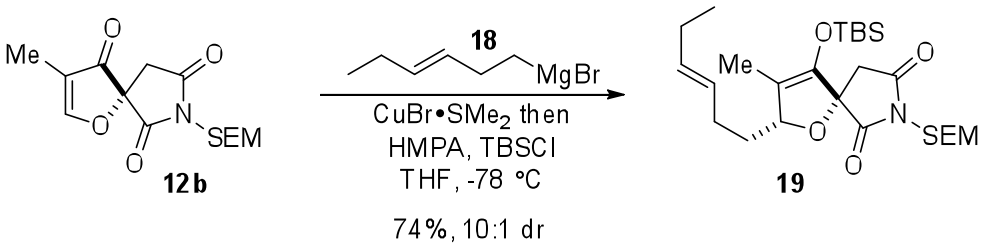
[7] H. U. Vora, S. P. Lathrop, N. T. Reynolds, M. S. Kerr, J. Read de Alaniz, T. Rovis, *Org. Synth.*, 2010, **87**, 350. (b) H. Takikawa, K. Suzuki, *Org. Lett.*, 2007, **9**, 2713.

tion of the crude product via column chromatography 12:1 to 9:1 PhMe/EtOAc (R_f = 0.5, 6:1 PhMe/EtOAc, the product is slightly less polar than the starting aldehyde) affords 1.55 g (62% yield) of spirocylce **12b** as a brown oil. HPLC analysis-Chiracel IA column, 95:5 hexanes/*i*-PrOH, 1.0 mL/min, major enantiomer: 22.8 min, minor enantiomer: 17.2 min, 95% ee; $[\alpha]_D^{21}$ = 85.5 (c = 0.010 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 4.94 (d, 1H, *J* = 10.4 Hz), 4.92 (d, 1H, *J* = 10.4 Hz), 3.56 (t, 2H, *J* = 8.4 Hz), 3.09 (d, 1H, *J* = 18.2 Hz), 2.98 (d, 1H, *J* = 18.2 Hz), 1.73 (s, 3H) 0.89 (t, 2H, *J* = 8.4 Hz), -.0.04 (s, 9H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 199.6, 175.3, 172.0, 169.4, 115.2, 85.4, 68.5, 67.9, 37.1, 18.0, 5.5, 1.3; IR (thin film/NaCl) 3096, 2954, 2896, 1798, 1730, 1619, 1447, 1339, cm^{-1}; HRMS $[C_{14}H_{25}NO_5SiNH_4]^+$ calcd 329.1527, found 329.1540.



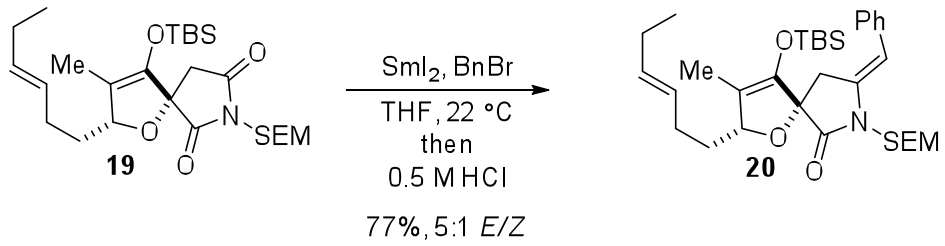
(*E*)-hex-3-en-1-ylmagnesium bromide (18). To a mixture of magnesium turnings (2.68 g, 110.4 mmol, 3.0 equiv.) in THF (20 mL) at room temperature was added the alkyl bromide **S1**[8] (6.0 g, 36.8 mmol, 1.0 equiv) in THF (20 mL) over 1 h via syringe pump. Upon addition of ~ 4 mL of the alkyl bromide solution, dibromoethane (~ 200 μL) was added to the reaction mixture (a rapid exotherm is observed). After full addition of the alkyl bromide solution the mixture is allowed to stir for 30 min and is used in the next step immediately. The reaction typically generates a 0.50 – 0.60 M solution of the Grignard **18** in THF as determined via titration with menthol and 1,10 phenanthroline as the indicator.

[8] G. A. Molander, R. Figueroa, *Org Lett*., 2006, **8**, 75.



(*2R*,*5S*)-4-((tert-butyldimethylsilyl)oxy)-2-((*E*)-hex-3-en-1-yl)-3-methyl-7-((2-(trimethyl-silyl)ethoxy)methyl)-1-oxa-7-azaspiro-[4.4]non-3-ene-6,8-dione (19). To a solution of spiro-cycle **12b** (3.40 g, 10.9 mmol, 1.0 equiv.) and CuBr•SMe_2 (3.37 g, 16.4 mmol, 1.5 equiv.) in THF (80 mL) at –78 °C was added Grignard **18** (30 mL, 16.4 mmol, 0.55 M soln in THF, 1.5 equiv.) over 20 min. The resulting solution was allowed to stir 45 min at –78 °C. Then a solution of TBSCl (3.46 g, 22.9 mmol, 2.1 equiv.) and HMPA (31 mL, 177.0 mmol, 16.2 equiv.) in THF (30 mL) was added drop wise and the reaction was allowed to stir 30 min and then allowed to warm to 0 °C over 1 h. The reaction was quenched with pH 7 phosphate buffer (100 mL) and allowed to warm to room temperature. The resulting mixture was extracted with Et_2O (2 × 250 mL). The combined ethereal extracts were then washed with H_2O (2 × 100 mL), brine (2 × 50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the crude product via column chromatography 30:1 hexanes/EtOAc affords 4.05 g (74% yield) of **19** as a 10:1 mixture of di-astereomers. $[\alpha]_D^{21}$ = –24.7 (c = 0.013 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 5.44 (ddt, 2H, *J* = 5.9, 11.5, 26.8 Hz), 4.93(d, 1H, *J* = 10.3 Hz), 4.92 (m, 1H), 4.88 (d, 1H, *J* = 10.3 Hz), 3.60 (t, 2H, *J* = 8.7 Hz), 3.00 (d, 1H, *J* = 18.5 Hz), 2.70 (d, 1H, *J* = 18.5 Hz), 1.99 (m, 4H), 1.75 (m, 1H), 1.62 (s, 3H), 1.46 (m, 1H), 0.96 (t, 3H, *J* = 7.4 Hz), 0.86 (s, 9H), 0.22 (s, 3H), 0.09 (s, 3H), 0.01 (s, 9H). ^{13}C nmr (100 MHz, $CDCl_3$) δ 180.7, 178.2, 144.8, 136.5, 132.3, 117.6, 90.0, 89.9, 71.7, 71.5, 43.4, 38.2, 31.0, 29.5, 22.0, 21.

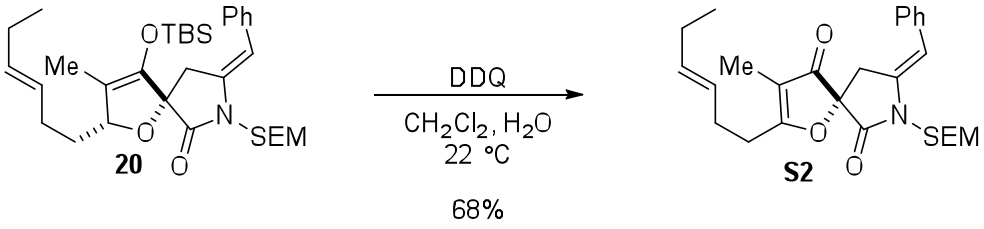
9, 17.8, 13.4, 2.5, 0.06, 0.01; IR (thin film/NaCl) 2956, 2932, 2860, 1793, 1727, 1703, 1389, 1342, 1235, 1088 cm^{-1}; HRMS $[C_{26}H_{47}NO_5Si_2Na]^+$ calcd 532.2885, found 532.2892.



(2*R*,5*S*,*E*)-8-benzylidene-4-((*tert*-butyldimethylsilyl)oxy)-2-((*E*)-hex-3-en-1-yl)-3-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-1-oxa-7-azaspiro[4.4]non-3-en-6-one (20). To a solution of silylenol ether **19** (3.2 g, 6.28 mmol, 1.0 equiv.) and benzyl bromide (1.5 mL, 12.6 mmol, 2.0 equiv.) in THF (60 mL) at room temperature was added a freshly prepared solution of samarium diiodide[9] (250 mL of a 0.1 M in THF, 25.0 mmol, 4.0 equiv.) via filter tip cannula over 30 min. The reaction was allowed to stir for 1 h, then cooled to 0 °C and quenched with 0.05 M HCl (aq) and allowed to warm to room temperature and stir for1 h. The mixture was then extracted with Et_2O (2 × 200 mL). The combined ethereal extracts were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the crude product via column chromatography 30:1 to 15:1 hexanes/EtOAc (R_f = 0.6, 6:1 hexanes/EtOAc) affords 2.8 g (77 % yield) of **20** as a 5:1 mixture of *E*/*Z* olefin isomers. *E* isomer; $[\alpha]_D^{21}$ = –9.0 (c = 0.010 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 7.27 (m, 4H), 7.16 (t, 1H, *J* = 7.2 Hz), 6.16 (t, 1H, *J* = 2.0 Hz), 5.43 (ddt, 2H, *J* = 5.7, 10.9, 26.5 Hz), 5.14 (d, 1H, *J* = 10.8 Hz), 4.98 (d, 1H, *J* = 10.8 Hz), 4.89 (m, 1H), 3.61 (t, 2H, *J* = 7.9 Hz), 3.27 (dd, 1H, *J* = 2.0, 17.1 Hz), 2.97 (dd, 1H, *J* = 2.0, 17.1 Hz), 1.96 (m, 4H), 1.73 (dtd, 1H, *J* = 3.3, 7.7, 19.6 Hz), 1.60 (s, 3H), 1.43 (dq, 1H, *J* = 6.75, 13.8 Hz) 0.92 (t, 3H, *J* = 7.4 Hz), 0.83 (s, 9H), 0.15 (s, 3H), 0.08 (s, 3H), 0.01 (s, 9H). ^{13}C nmr (100 MHz, $CDCl_3$)

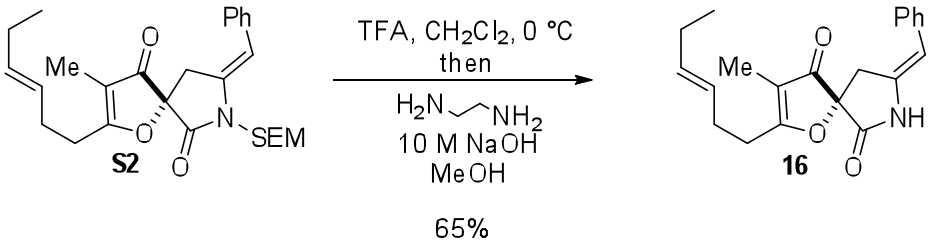
[9] P. Girard, J. L. Namy, H. B. Kagan, *J. Am. Chem. Soc.*, 1980, **102**, 2693.

δ 178.1, 146.2, 141.2, 140.6, 136.2, 132.7, 132.4, 131.9, 129.7, 117.0, 109.4, 90.7, 89.3, 74.2, 70.3, 39.7, 31.1, 29.5, 22.1, 21.8, 17.9, 13.4, 2.6, 0.09, 0.0; IR (thin film/NaCl) 2956, 2931, 2858, 1731, 1702, 1657, 1448, 1332, 1257, 1083 cm^{-1}; HRMS $[C_{33}H_{54}NO_4Si_2]^+$ calcd 584.3586, found 584.3586.



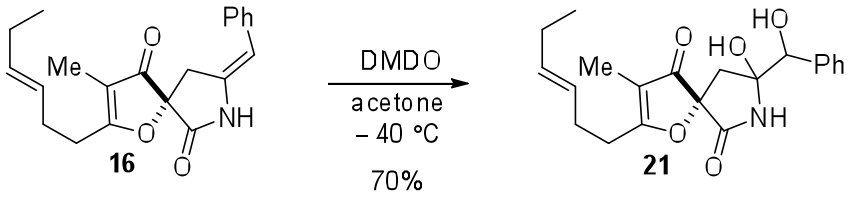
(*S*,*E*)-8-benzylidene-2-((*E*)-hex-3-en-1-yl)-3-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-1-oxa-7-azaspiro[4.4]non-2-ene-4,6-dione (S2). To a solution of silylenol ether **20** (3.6 g, 6.2 mmol, 1.0 equiv.) in CH_2Cl_2 (80 mL) and H_2O (8 mL) was added DDQ (4.2 g, 18.5 mmol, 3.0 equiv.) and the reaction was vigorously stirred for 2–3 h. Excess DDQ was carefully quenched with sat $NaHCO_3$ (50 mL). The mixture was extracted with Et_2O (2 × 200 mL). The combined ethereal extracts were then washed with sat $NaHCO_3$ (50 mL), brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the crude product via column chromatography 15:1 hexanes/EtOAc (R_f = 0.3, 6:1 hexanes/EtOAc) affords 1.96 g (68% yield) of **S2**. $[\alpha]_D^{21}$ = 37.8 (c = 0.0127 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 7.27 (m, 5H), 6.30 (t, 1H, *J* = 1.9 Hz), 5.52 (dtt, 1H, *J* = 1.2, 6.3, 11.2, 16.4 Hz), 5.37 (dtt, 1H, *J* = 1.2, 6.3, 11.2, 16.4), 5.14 (d, 1H, *J* = 11.0 Hz), 5.07 (d, 1H, *J* = 11.0 Hz), 3.56 (m, 2H), 3.42 (dd, 1H, *J* = 1.9, 16.8 Hz), 3.16 (dd, 1H, *J* = 1.9, 16.8 Hz), 2.61 (m, 2H), 2.35 (m, 2H), 1.97 (m, 2H), 1.66 (s, 3H), 0.93 (t, 3H, *J* = 3.7 Hz), 0.01 (s, 9H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 201.9, 190.2, 169.3, 137.2, 136.3, 135.6, 129.9, 129.4, 127.6, 111.7, 108.3, 88.1, 71.8, 67.6, 34.8, 30.6, 30.4, 26.8, 19.1, 15.1, 7.2, 0.00; IR (thin

film/NaCl) 3028, 2958, 2359, 2342, 1738, 1705, 1661, 1633, 1448, 1398, cm^{-1}; HRMS $[C_{27}H_{37}NO_4SiNa]^+$ calcd 490.2384, found 490.2388.



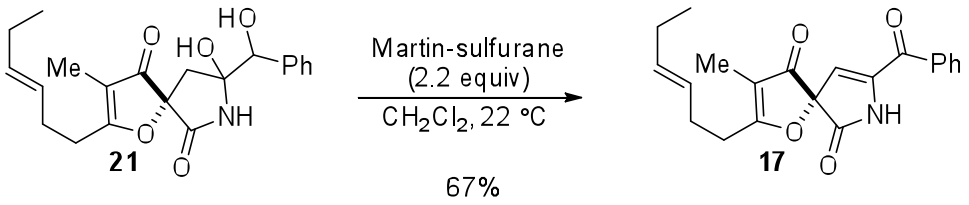
(*S*,*E*)-8-benzylidene-2-((*E*)-hex-3-en-1-yl)-3-methyl-1-oxa-7-azaspiro[4.4]non-2-ene-4,6-dione (16). To a solution of spirocycle **S2** (1.2 g, 2.6 mmol, 1.0 equiv.) in CH_2Cl_2 (125 mL) at 0 °C was added trifluoroacetic acid (14 mL) drop wise over 10 min. The reaction was allowed to warm to room temperature and stirred for 3 h. The reaction was then cooled to 0 °C and carefully quenched with sat $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL). The organics were combined and washed with sat $NaHCO_3$ (50 mL), brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude hemiaminal was dissolved in MeOH (25 mL) and ethylene diamine (186 µl, 2.6 mmol, 1.0 equiv.) and 10 M NaOH (565 µl, 5.7 mmol, 2.2 equiv.) were added and the reaction was allowed to stir 30 min. The majority of the MeOH was removed in vacuo and the resulting residue was dissolved in EtOAc (200 mL) and washed with H_2O (50 mL), brine (50 mL), dried over $MgSO_4$ and concentrated in vacuo. Purification of the crude product via column chromatography 2:1 hexanes/EtOAc affords 564 mg (65% yield) of **16**. $[\alpha]_D^{21}$ = 34.8 (c = 0.010 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.30 (t, 2H, *J* = 7.8 Hz), 7.18 (m, 3H), 6.04 (t, 1H, *J* = 2.0 Hz), 5.55 (dtt, 1H, *J* = 1.2, 6.3, 12.3, 15.0), 5.41 (dtt, 1H, *J* = 1.2, 6.3, 12.3, 15.0), 3.48 (dd, 1H, *J* = 2.0, 17.1), 3.22 (dd, 1H, *J* = 2.0, 17.1 Hz); ^{13}C nmr (100 MHz, $CDCl_3$) δ 200.5, 189.0, 168.4,

135.5, 134.2, 133.2, 128.5, 127.6, 126.2, 110.4, 106.5, 87.0, 34.4, 29.2, 29.0, 25.4, 13.7, 5.8; IR (thin film/NaCl) 2962, 2928, 1735, 1677, 1619, 1496, 1452, 1405 cm^{-1}; HRMS $[C_{21}H_{24}NO_3]^+$ calcd 338.1751, found 338.1755.

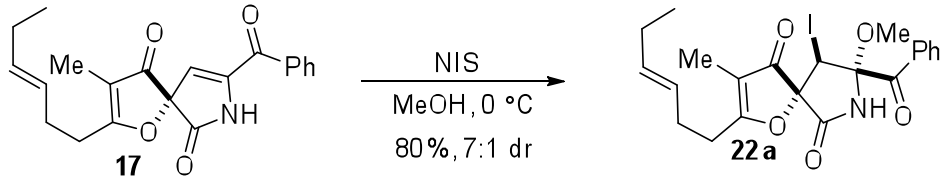


(5*S*)-2-((*E*)-hex-3-en-1-yl)-8-hydroxy-8-(hydroxy(phenyl)methyl)-3-methyl-1-oxa-7-azaspiro[4.4]non-2-ene-4,6-dione (21). To a solution of lactam **16** (207 mg, 0.61 mmol, 1.0 equiv.) in acetone (6 mL) at –78 °C was added DMDO[10] (9 mL of a 0.09 M soln in acetone, 0.80 mmol, 1.3 equiv.). The reaction was then placed in a cold bath at –40 °C and allowed to stir for 10 h. The reaction was then re-cooled to –78 °C and quenched with dimethylsulfide (~200 µl) and allowed to warm to room temperature. The organics were then removed under reduced pressure to afford the crude diol. Purification of the crude product via column chromatography 2:1 hexanes/EtOAc (R_f = 0.4, 1:1 hexanes/EtOAc) affords 160 mg (70% yield) of diol **21** as a 3:1 mixture of diastereomers. Major diastereomer: ^{1}H nmr (400 MHz, $CDCl_3$) δ 7.53 (m, 5H), 7.01 (s, 1H), 6.03 (s, 1H), 5.50 (dtt, 1H, *J* = 1.5, 6.8, 15.2, 15.4 Hz) 5.35 (dtt, 1H, *J* = 1.5, 6.8, 15.2, 15.4 Hz), 4.83 (s, 1H), 3.47 (s, 1H), 2.68 (d, 1H, *J* = 13.3 Hz), 2.65 (m, 2H), 2.34 (m, 2H), 2.13 (d, 1H, *J* = 13.3 Hz), 1.97 (m, 2H), 1.65 (s, 3H), 0.93 (t, 3H, *J* = 7.4 Hz); ^{13}C nmr (100 MHz, $CDCl_3$) δ 202.9, 194.0, 167.5, 138.0, 134.5, 128.6, 128.4, 127.8, 126.2, 110.2, 89.4, 86.8, 86.2, 76.7, 38.4, 29.6, 29.2, 25.6, 13.8, 5.8; IR (thin film/NaCl) 3355 br, 2962, 2928, 1726, 1682 1609, 1453, 1408 cm^{-1}; HRMS $[C_{21}H_{26}NO_5]^+$ calcd 372.1805, found 372.1802.

[10] R. W. Murray, M. Singh, *Org. Synth.* 1997, **74**, 91.

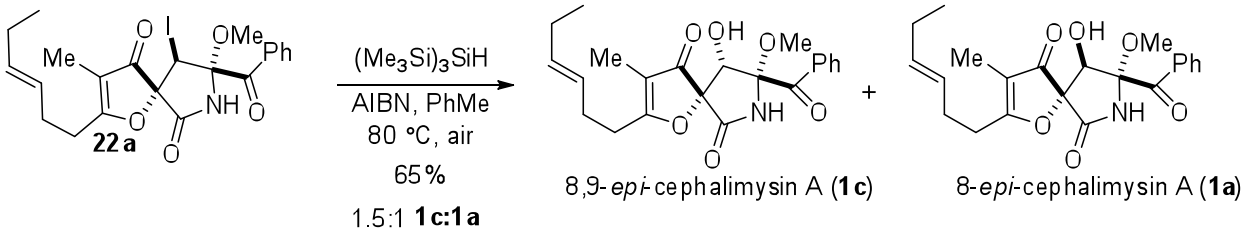


(*S*,*E*)-8-benzoyl-2-(hex-3-en-1-yl)-3-methyl-1-oxa-7-azaspiro[4.4]nona-2,8-diene-4,6-dione (17). To a solution of diol **21** (70 mg, 0.20 mmol, 1.0 equiv.) in CH_2Cl_2 (8 mL) was added a solution of Martin-sulfurane (295 mg, 0.44 mmol, 2.2 equiv.) in CH_2Cl_2 (8 mL) via syringe pump over 30 min at room temperature. After addition the reaction was allowed to stir 10 min and excess Martin-sulfurane was quenched with *i*PrOH (1 mL). The resulting solution was filtered through a plug of silica, eluted with Et_2O (10 mL) and the filtrate was concentrated *in vacuo*. Purification of the crude product via column chromatography 8:1 hexanes/acetone (R_f = 0.4, 2:1 hexanes/EtOAc) affords 47 mg (67% yield) of **17** as a yellow oil. $[\alpha]_D^{21}$ = 90.8 (c = 0.010 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 7.86 (d, 2H, *J* = 8.0 Hz), 7.63 (t, 1H, *J* = 7.5 Hz), 7.57 (bs, 1H), 7.49 (t, 2H, *J* = 8.0 Hz), 5.80 (d, 1H, *J* = 1.8 Hz), 5.56 (dtt, 1H, *J* = 1.4, 6.8, 13.6, 15.0 Hz), 5.41 (dtt, 1H, *J* = 1.4, 6.8, 13.6, 15.0 Hz), 2.68 (m, 2H), 2.40 (m, 2H), 1.99 (m, 2H), 1.73 (s, 3H), 0.94 (t, 3H, *J* = 7.5 Hz) ^{13}C nmr (100 MHz, $CDCl_3$) δ 195.7, 189.6, 185.4, 169.4, 143.5, 135.4, 134.4, 133.6, 129.0, 128.7, 126.0, 124.8, 115.3, 111.3, 90.8, 29.2, 29.0, 25.4, 13.7, 6.2 ; IR (thin film/NaCl) cm^{-1}; HRMS $[C_{21}H_{22}NO_4]^+$ calcd 352.1543, found 352.1544.



(*5S*,*8S*,*9R*)-8-benzoyl-2-((*E*)-hex-3-en-1-yl)-9-iodo-8-methoxy-3-methyl-1-oxa-7-azaspiro[4.4]non-2-ene-4,6-dione (22a). To a solution of spirocycle **17** (5 mg, 0.014 mmol, 1.0

equiv.) in MeOH (0.5 mL) at 0 °C was added a solution of *N*-iodosuccinimide (3.2 mg, 0.014 mmol, 1.0 equiv.) in MeOH (0.3 mL) and the reaction was allowed to stir for 20 min. The crude mixture was filtered through a plug of silica and washed with Et_2O (2 mL). The filtrate was concentrated *in vacuo*. Purification of the crude product via column chromatography 6:1 to 3:1 hexanes/EtOAc (R_f = 0.4, 2:1 hexanes/EtOAc) affords 6 mg (80% yield) of **22a** as a 7:1 mixture of diastereomers. $[\alpha]_D^{21}$ = 42.7 (c = 0.0085 g/mL, CH_2Cl_2) Major diastereomer **22a**: ^{1}H nmr (300 MHz, $CDCl_3$) δ 8.16 (d, 2H, *J* = 7.4 Hz), 7.62 (t, 1H, *J* = 7.5 Hz), 7.48 (t, 2H, *J* =7.9 Hz), 7.24 (bs, 1H), 5.52 (m, 2H), 5.12 (s, 1H), 3.52 (s, 3H), 2.70 (m, 2H), 2.44 (m, 2H), 2.01 (m, 2H), 1.70 (s, 3H), 0.96 (t, 3H, *J* = 7.4 Hz) ^{13}C nmr (100 MHz, $CDCl_3$) δ 197.8, 191.6, 189.0, 163.3, 134.3, 134.1, 133.2, 130.7, 128.6, 126.3, 112.2, 91.7, 85.8, 51.6, 29.4, 29.3, 25.9, 25.5, 13.6, 5.9; IR (thin film/NaCl) 3253 br, 2960, 1735, 1700, 1626, 1447, 1401, 1373 cm^{-1}; HRMS $[C_{22}H_{24}INO_5]^+$ calcd 510.0774, found 510.0771.

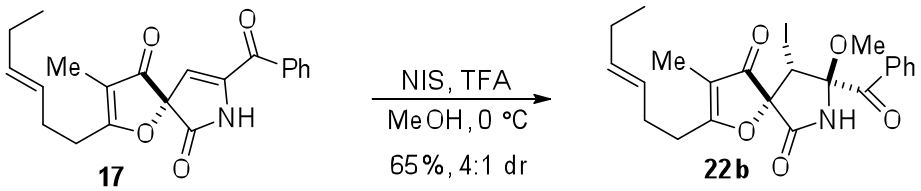


8,9 *epi*-cephalimysin A (1c) and 8-*epi*-cephalimysin A (1a). To a solution of iodide **22a** (5 mg, 0.01 mmol, 1.0 equiv.) in toluene (2 mL) at 80 °C was added a mixture of tristrimehtylsilane (0.03 mmol, 3.0 equiv.) and AIBN (0.015 mmol, 1.5 equiv) in toluene (1 mL) over 2 h via syringe pump. During the addition air was bubbled through the reaction mixture via syringe needle. After addition the reaction was allowed to stir 1 h further at 80 °C. Upon cooling to room temperature the reaction is filtered through a plug of silica and washed with Et_2O (5 mL) and the filtrate is concentrated *in vacuo*. Purification of the crude reaction via column chromatography

3:1 to 2:1 hexanes/EtOAc affords 1.5 mg of **1c** (R_f = 0.2, 2:1 hexanes/EtOAc) and 1.0 mg of **1a** (R_f = 0.3, 2:1 hexanes/EtOAc) (67% combined yield).

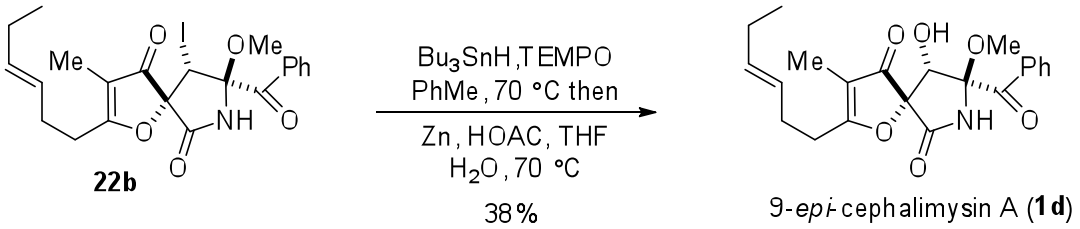
8,9 *epi*-cephalimysin A (1c) $[\alpha]_D^{21}$ = 74.1 (c = 0.0022 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 8.30 (d, 2H, *J* = 8.6 Hz), 7.64 (t, 1H, *J* = 7.4 Hz), 7.48 (t, 2H, *J* = 8.0 Hz), 5.60 (m, 1H), 5.48 (m, 1H), 4.50 (d, 1H, *J* = 12.6 Hz), 3.33 (s, 3H), 3.20 (d, 1H, *J* = 12.6 Hz), 2.72 (m, 2H), 2.43 (m, 2H), 2.05 (m, 2H), 1.69 (s, 3H), 1.00 (t, 3H, *J* = 7.5 Hz) ^{13}C nmr (100 MHz, $CDCl_3$) δ 199.5, 193.8, 188.7, 166.8, 134.5, 134.4, 132.9, 130.6, 128.6, 126.5, 112.5, 92.3, 86.6, 73.1, 51.5, 29.3, 29.0, 25.4, 13.5, 5.7; IR (thin film/NaCl) 3320 br, 2927, 1734, 1685, 1624, 1559, 1507 cm^{-1}; HRMS $[C_{22}H_{25}NO_6]^+$ calcd 400.1755, found 400.1759.

8-*epi*-cephalimysin A (1a) $[\alpha]_D^{21}$ = 87.6 (c = 0.0030 g/mL, CH_2Cl_2) ^{1}H nmr (400 MHz, $CDCl_3$) δ 8.21 (d, 2H, *J* = 8.5 Hz), 7.63 (t, 1H, *J* = 7.4 Hz), 7.50 (t, 2H, *J* = 8.3 Hz), 5.60 (m, 1H), 5.44 (m, 1H), 5.20 (d, 1H *J* = 4.1 Hz), 4.78 (d, 1H, *J* = 4.10), 3.27 (s, 3H), 2.71 (m, 2H), 2.43 (m, 2H), 2.03 (m, 2H), 1.71 (s, 3H), 0.99 (t, 3H, *J* = 7.4 Hz); ^{13}C nmr (100 MHz, $CDCl_3$) δ 201.2, 192.3, 191.3, 167.7, 134.5, 134.0, 133.8, 129.3, 128.7, 125.9, 112.6, 96.5, 85.6, 79.0, 51.4, 29.3, 29.0, 25.4, 13.6, 5.5; HRMS $[C_{22}H_{25}NO_6]^+$ calcd 400.1755, found 400.1757



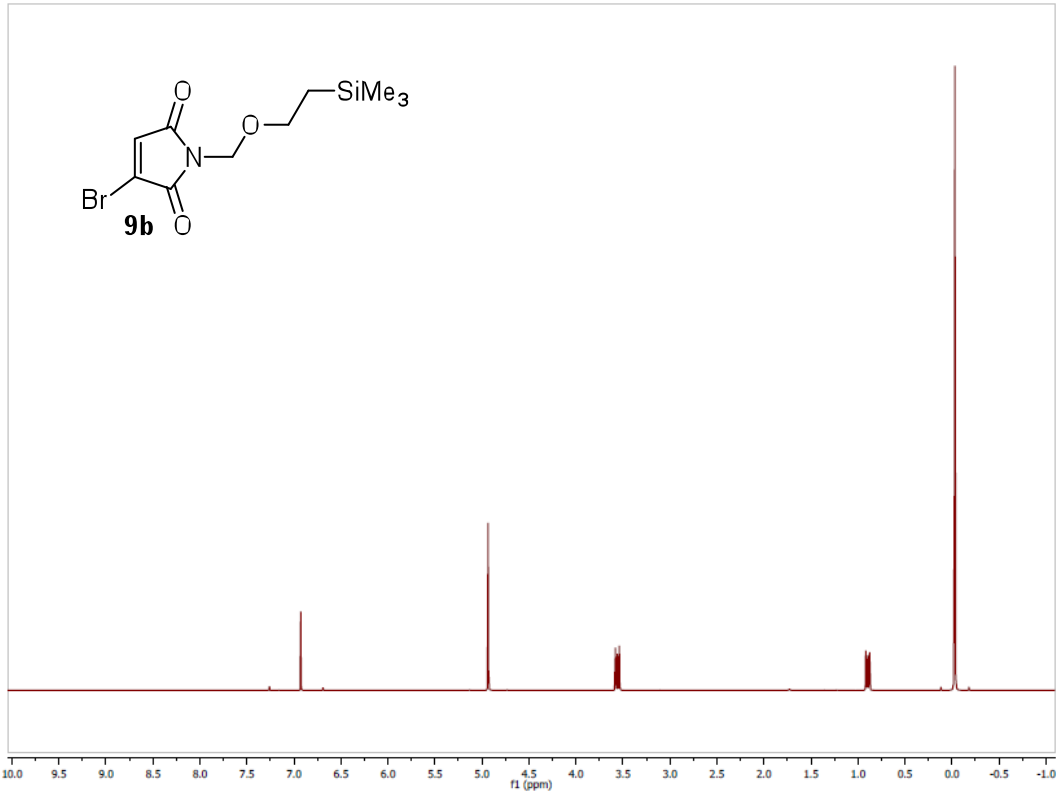
(*5S,8R,9S*)-8-benzoyl-2-((*E*)-hex-3-en-1-yl)-9-iodo-8-methoxy-3-methyl-1-oxa-7-azaspiro[4.4]non-2-ene-4,6-dione (22b). To a solution of spirocycle **17** (10 mg, 0.028, 1.0 equiv.) in MeOH (1.5 mL) at 0 °C was added trifluroacetic acid (5 drops) followed by a solution of *N*-iodosuccinimide (6.4 mg, 0.028 mmol, 1.0 equiv.) in MeOH (0.5 mL). The reaction was

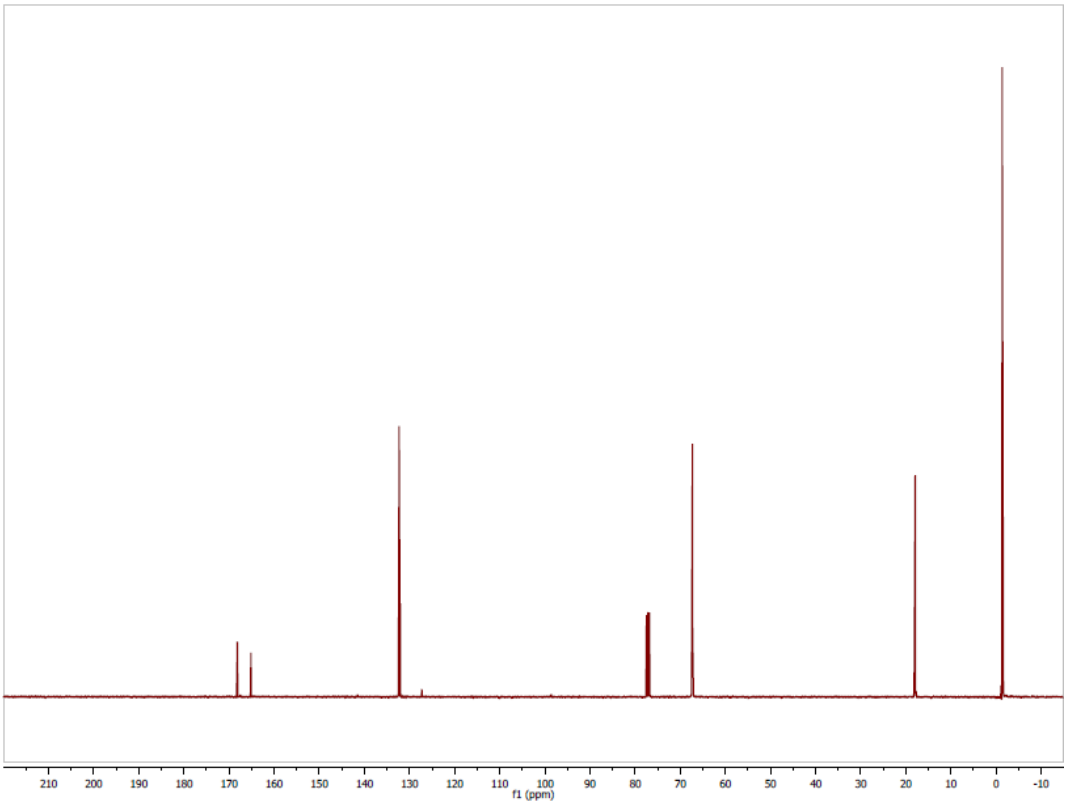
allowed to stir for 15 min and then filtered through a plug of silica gel, eluted with Et_2O (2 mL) and the filtrate was concentrated *in vacuo*. Purification of the crude product via column chromatography 4:1 hexanes/EtOAc (R_f = 0.3, 2:1 hexanes/EtOAc) affords 10 mg (71% yield) of **22b** as a 4:1 mixture of diastereomers. $[\alpha]_D^{21}$ = -65.0 (c = 0.0070 g/mL, CH_2Cl_2) Major diastereomer: ^{1}H nmr (300 MHz, $CDCl_3$) δ 8.21 (d, 2H, *J* = 8.6 Hz), 7.62 (t, 1H, *J* = 7.4 Hz), 7.48 (t, 2H, *J* = 7.5 Hz), 7.27 (bs, 1H), 5.49 (m, 2H), 4.94 (s, 1H), 3.34 (s, 3H), 2.66 (m, 2H), 2.40 (m, 2H), 1.98 (m, 2H), 1.68 (s, 3H), 0.94 (t, 3H, *J* = 7.3); ^{13}C nmr (100 MHz, $CDCl_3$) δ 195.2, 192.1, 188.2, 166.8, 134.2, 133.9, 132.5, 130.1, 128.6, 126.2, 110.8, 94.4, 87.0, 52.1, 29.1, 20.0, 27.6, 13.6, 5.9; IR (thin film/NaCl) 3267 br, 2926, 2359, 1737, 1705, 1629, 1447, 1398, 1069 cm^{-1}; HRMS $[C_{22}H_{24}INO_5Na]^+$ calcd 532.0591, found 532.0578.

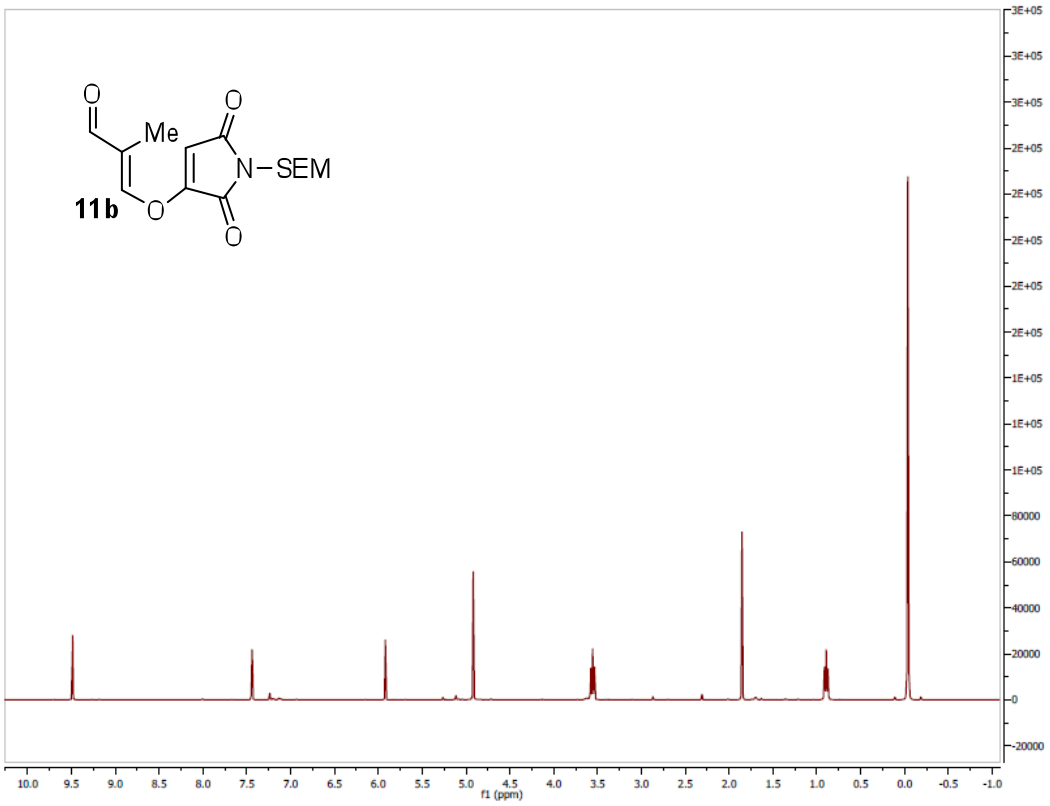


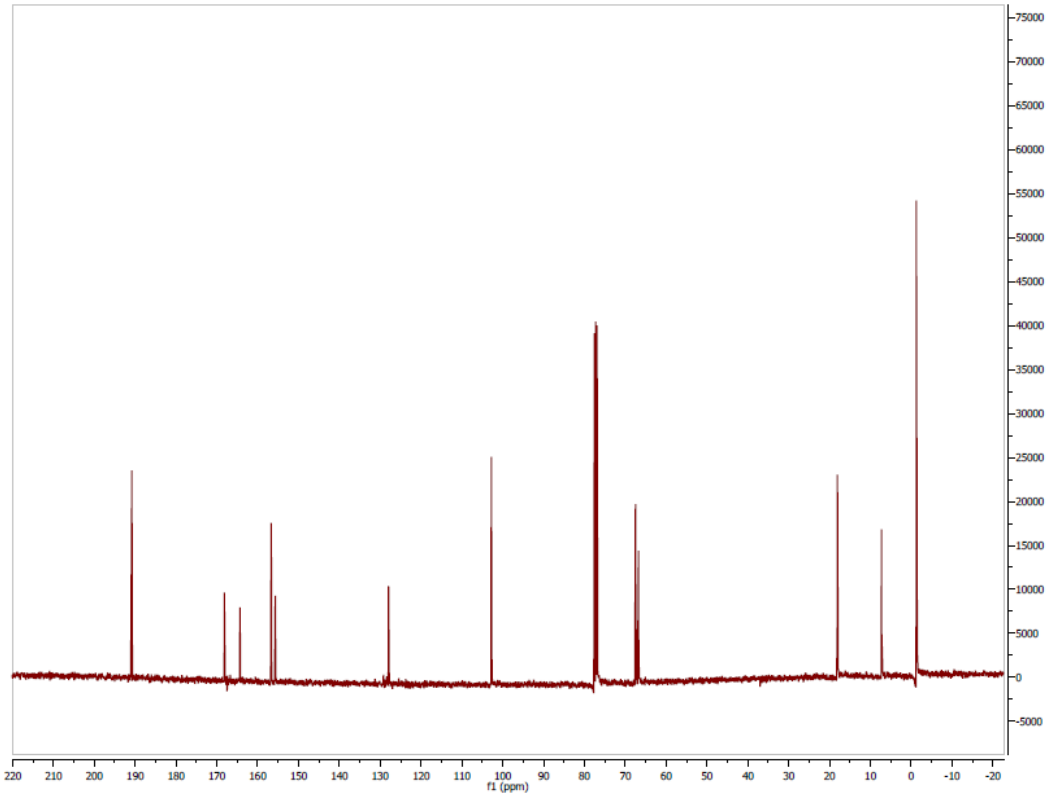
9-*epi*-cephalimysin A (1d). To a solution of iodide **22b** (1 mg, 0.0020 mmol, 1.0 equiv.) in toluene was added TEMPO (1.6 mg, 0.010 mmol, 5.0 equiv.) and tributyltin hydride (20 μL of a 0.1 M soln in PhMe, 0.0020 mmol, 1.0 equiv.). The reaction was heated to 70 °C and during the next 30 min tributyltin hydride (20 μL of a 0.1 M soln in PhMe, 0.0020 mmol, 1.0 equiv.) was added twice more. The reaction was allowed to stir 30 min more and then cooled to room temperature and filtered through a plug of silica, eluted with Et_2O (2 mL) and the filtrate was concentrated *in vacuo*. The crude material was used in the next step without further purification. To a solution of the crude product in acetic acid (0.6 mL), THF (0.2 mL) and H_2O (0.2 mL) was added Zinc dust (1.6 mg, 0.024, 12 equiv.) and the mixture was heated to 70 °C. After 2 h, the

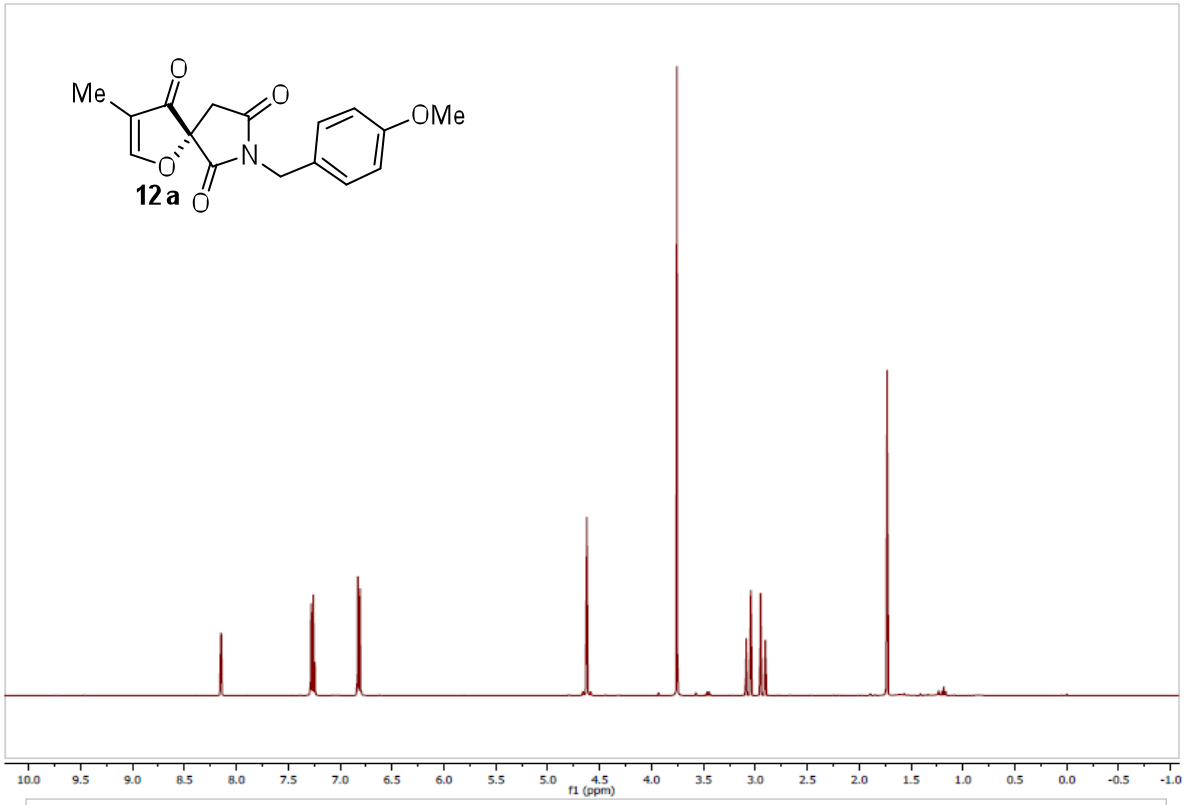
reaction mixture was allowed to cool to room temperature and the zinc was removed via filtration and wash with Et_2O (5 mL). The filtrate was concentrated *in vacuo* and the resulting residue was dissolved in EtOAc and filtered once more. The filtrate was concentrated *in vacuo* to afford the crude product. Purification of crude mixture via column chromatography affords 0.3 mg (38% yield) of **1d**. ^{1}H nmr (400 MHz, $CDCl_3$) δ 8.23 (d, 2H, *J* = 7.2 Hz), 7.62 (t, 1H, *J* = 7.9 Hz), 7.48 (t, 2H, *J* = 7.9 Hz), 5.45 (m, 2H), 4.79 (d, 1H, *J* = 3.6 Hz), 3.32 (s, 3H), 2.55 (d, 1H, *J* = 3.6 Hz), 2.36 (m, 2H), 2.02 (m, 2H), 1.96 (m, 2H), 1.70 (s, 3H), 0.88 (t, 1H, *J* = 7.4 Hz).

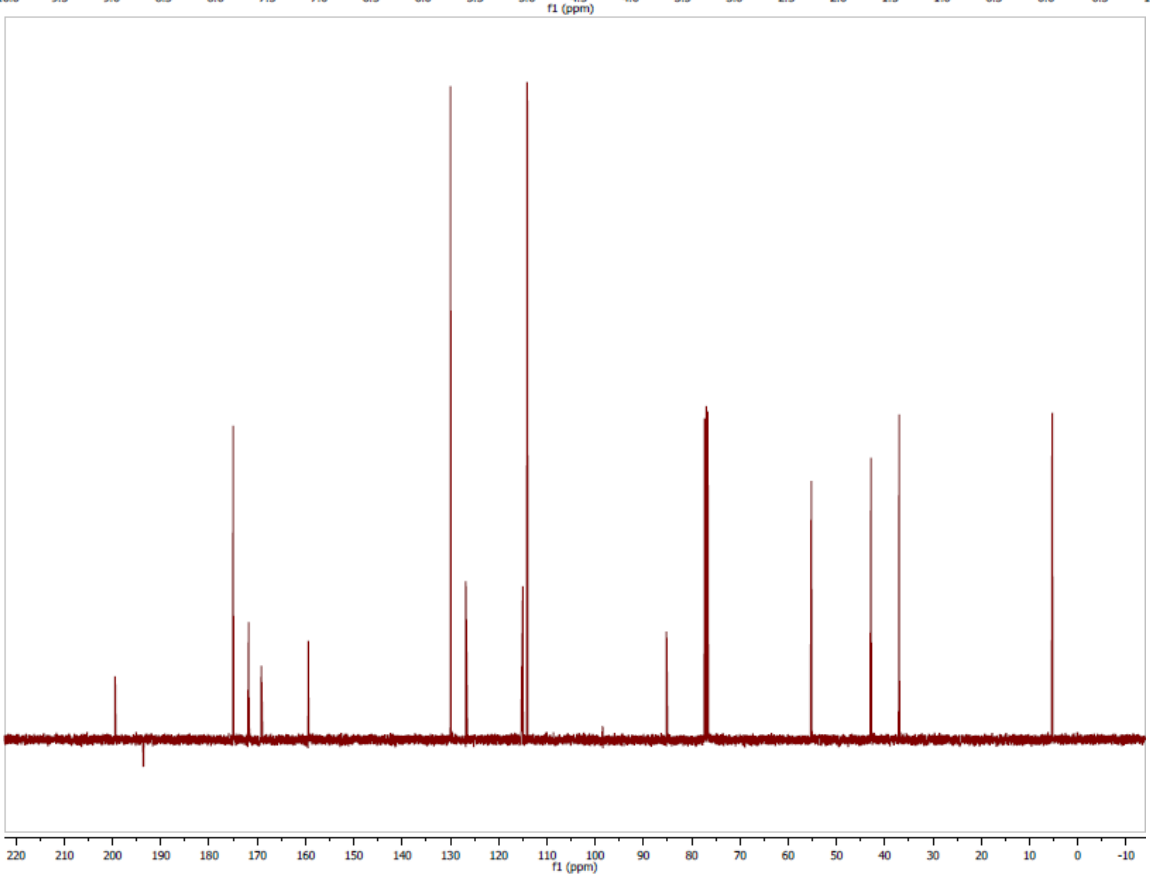


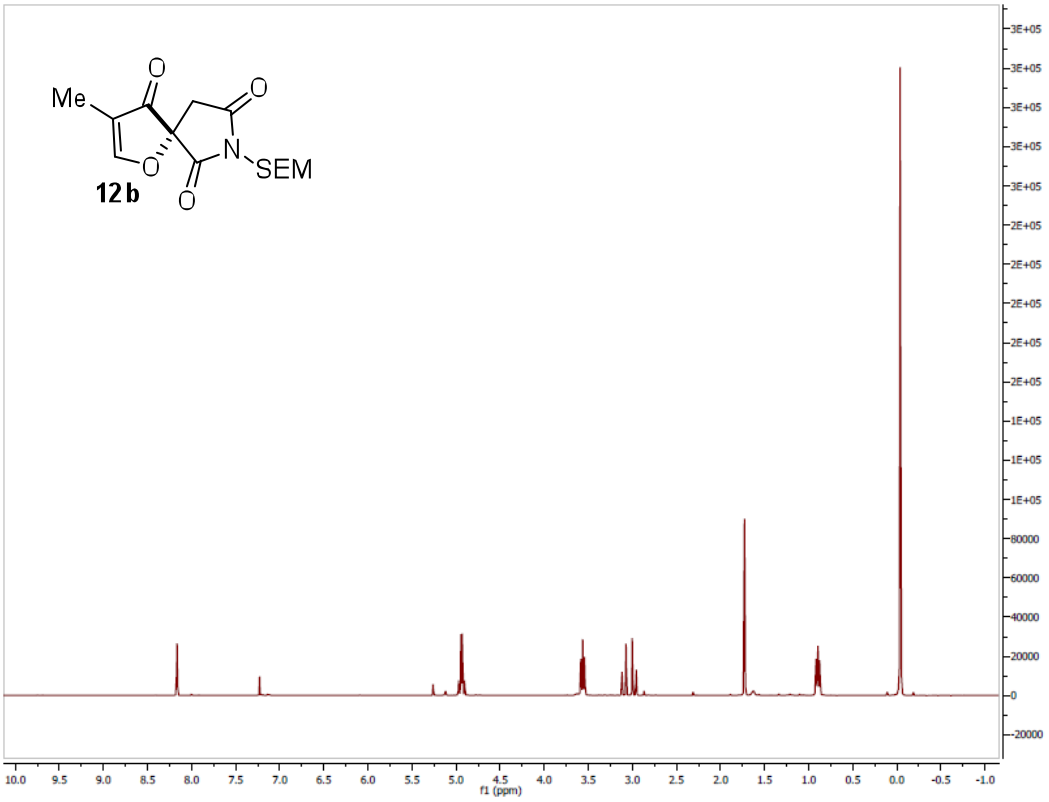


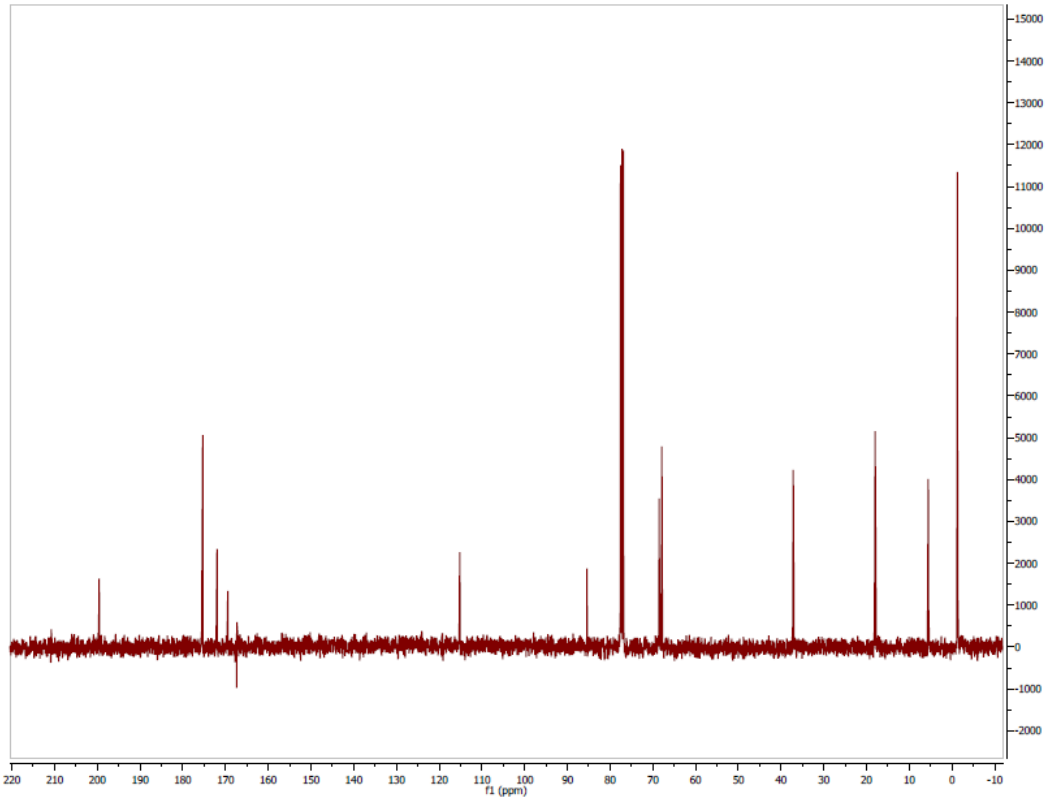


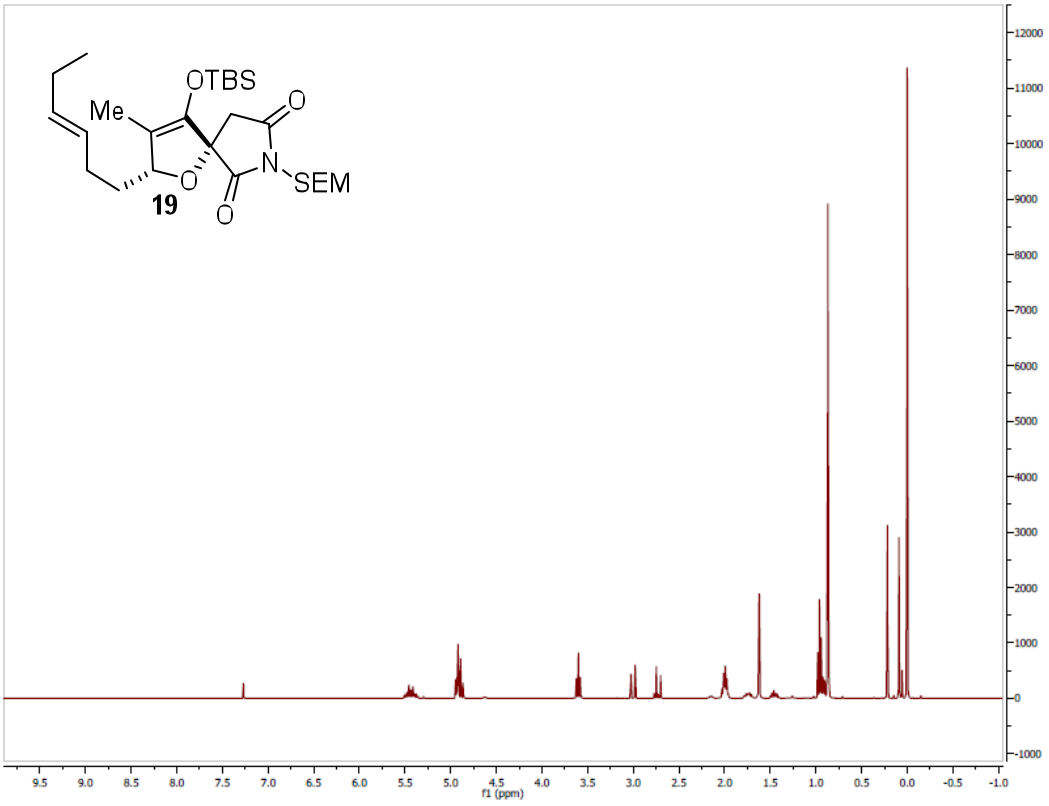


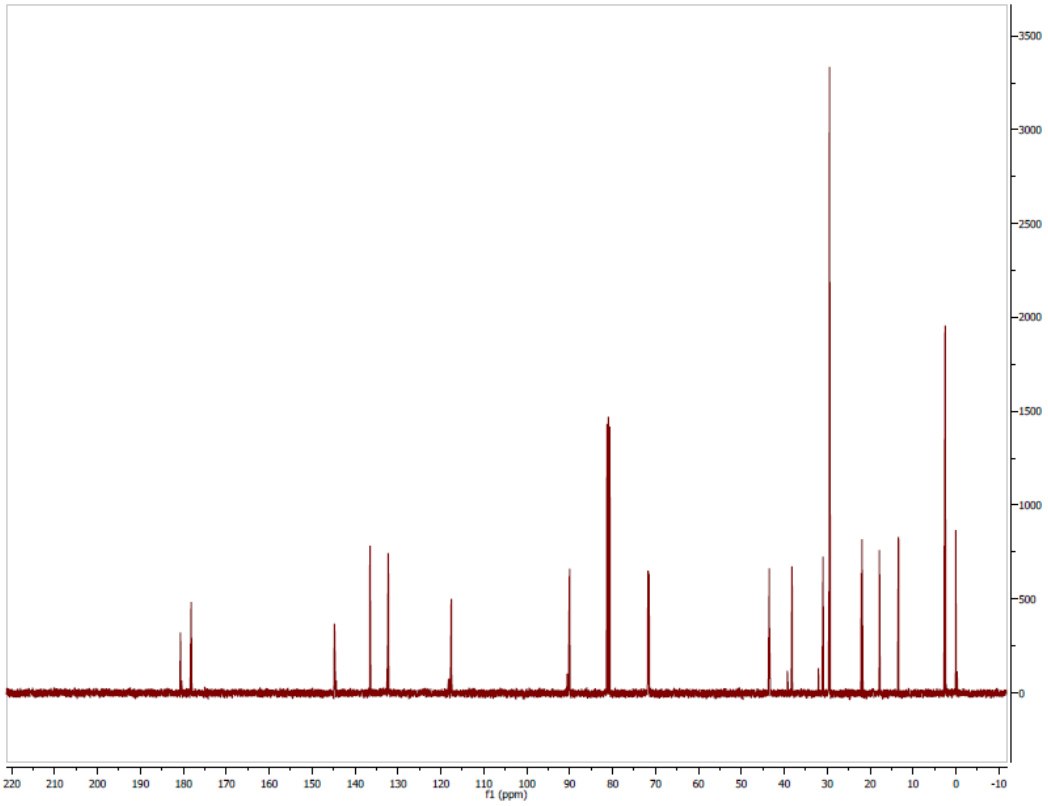


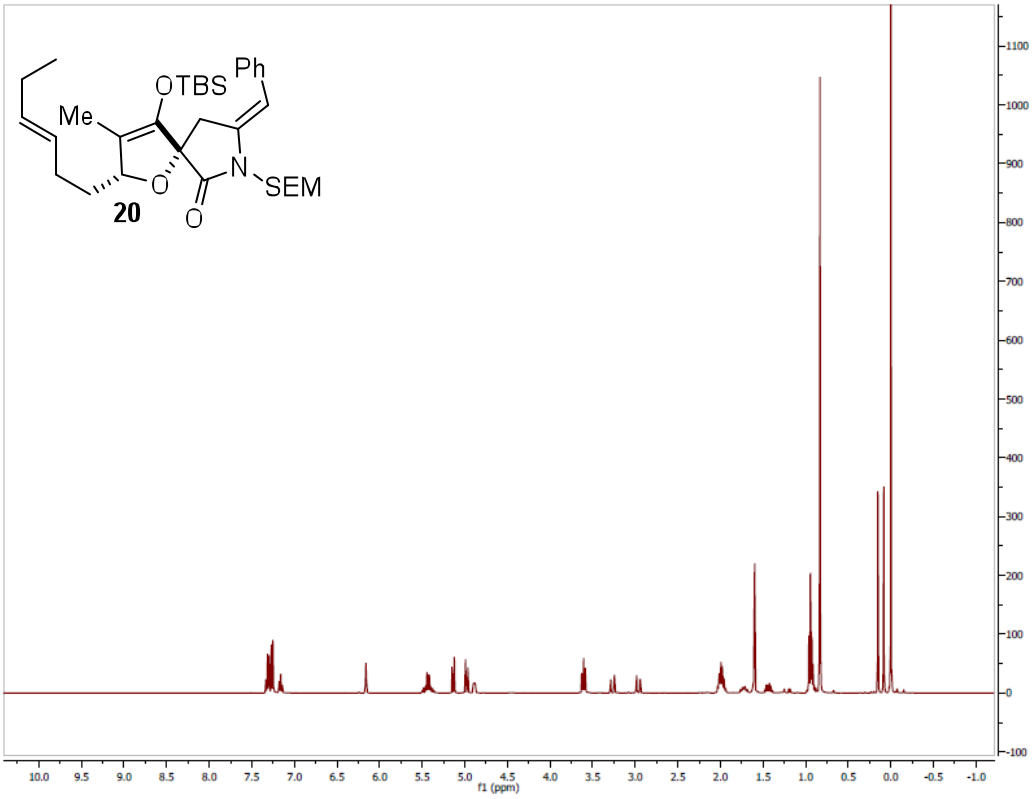


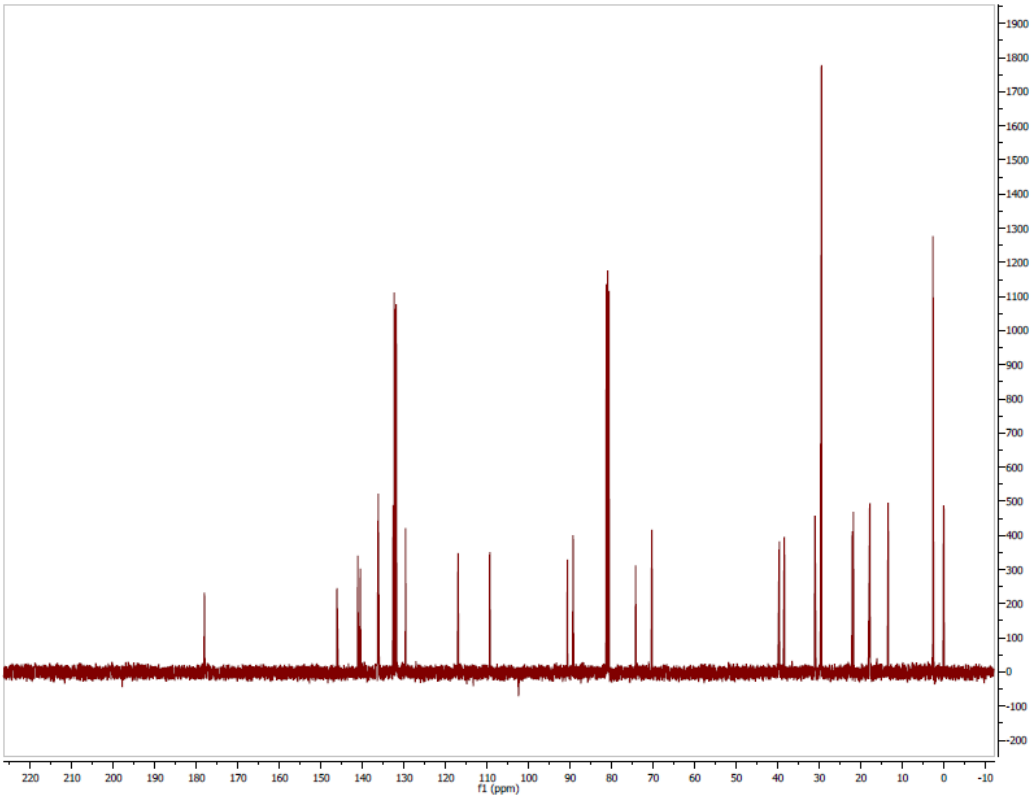


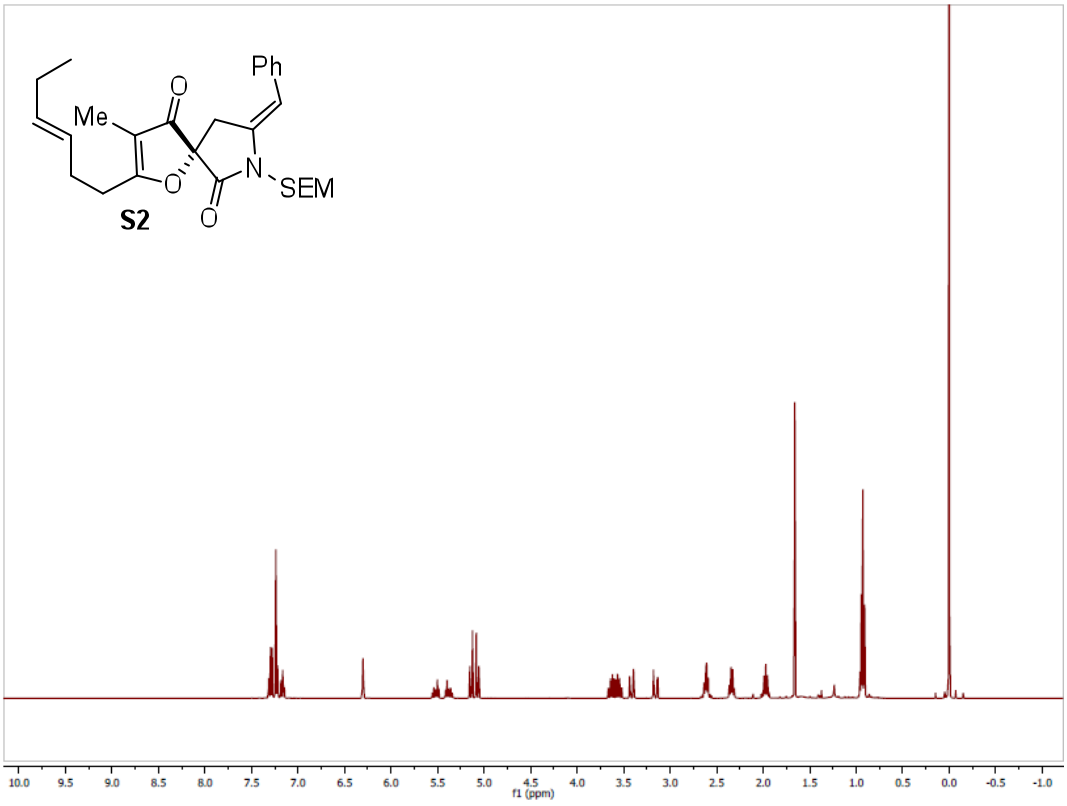


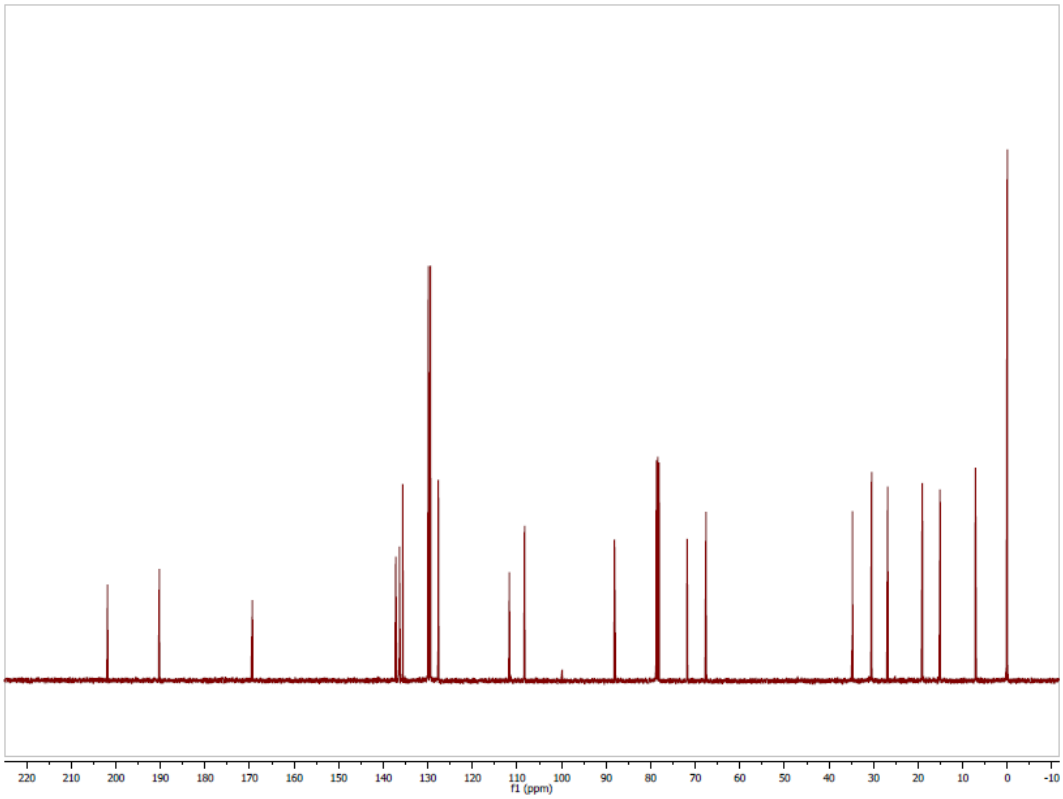

OTBS
Me
O
N
SEM
O
O
19
f1 (ppm)

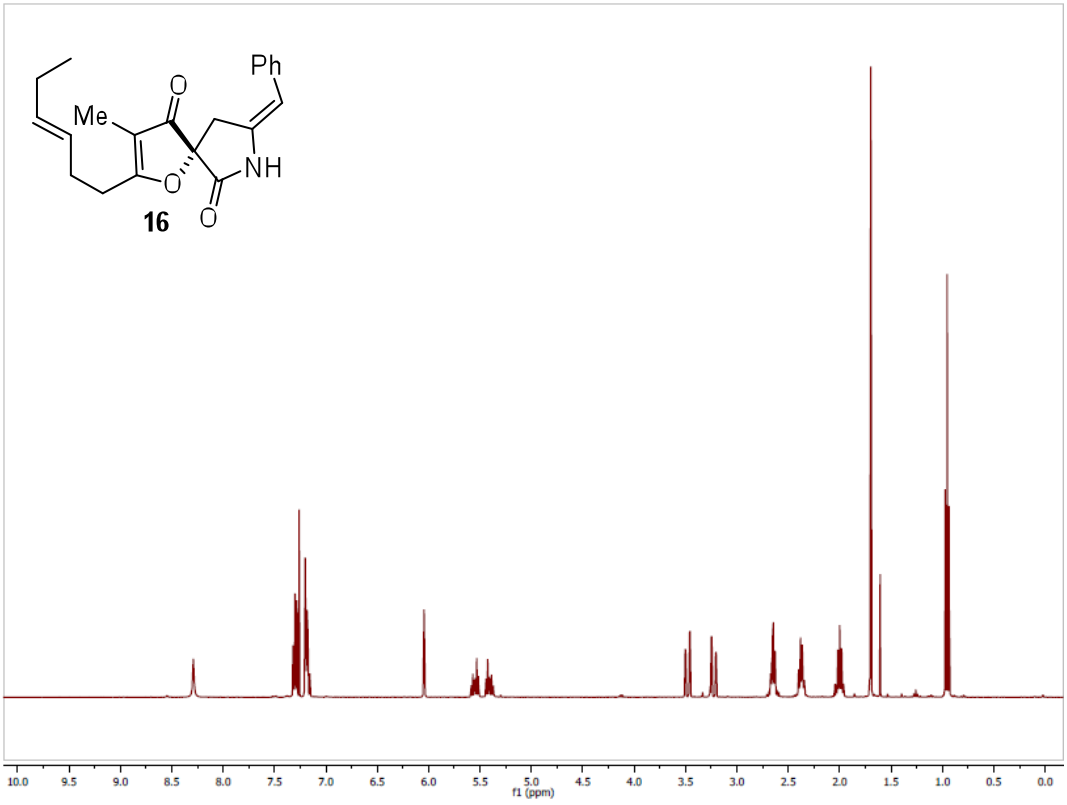

f1 (ppm)

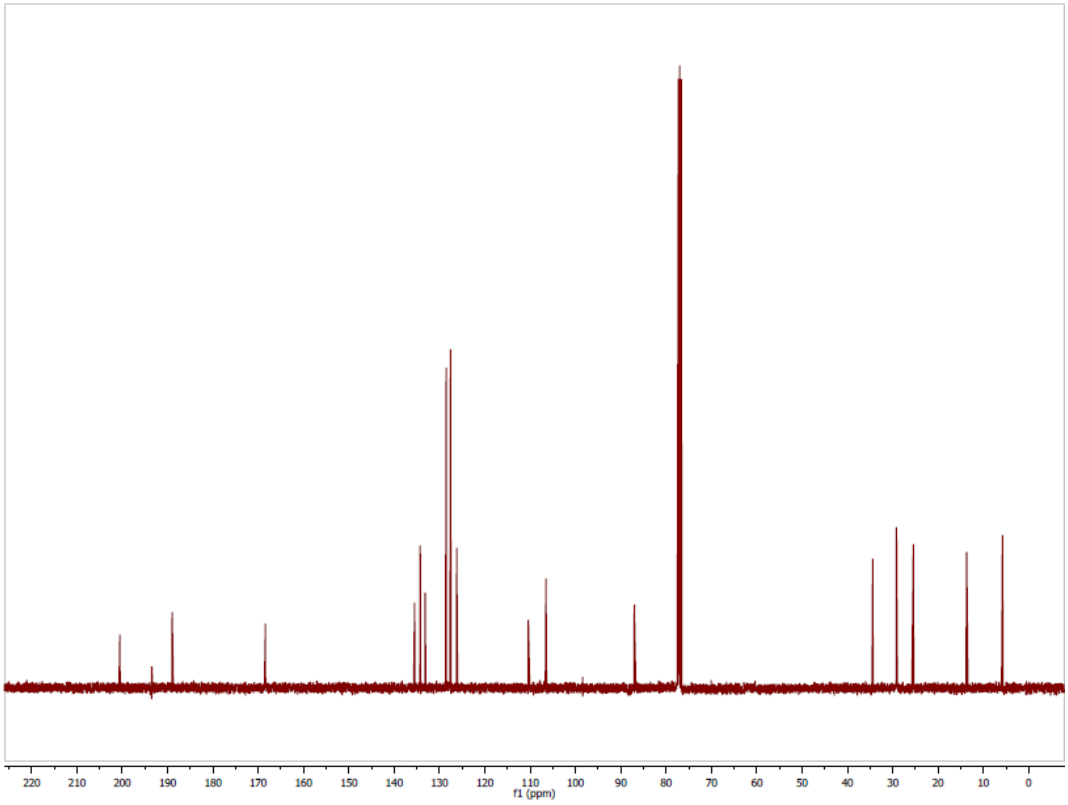


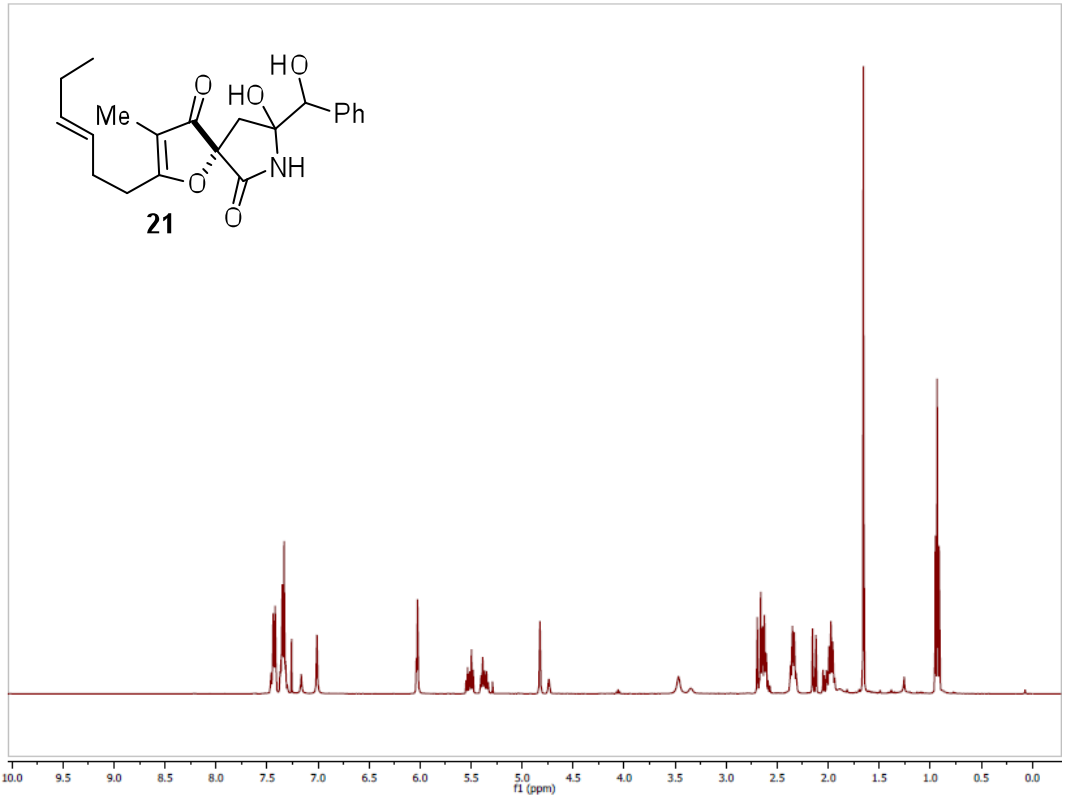


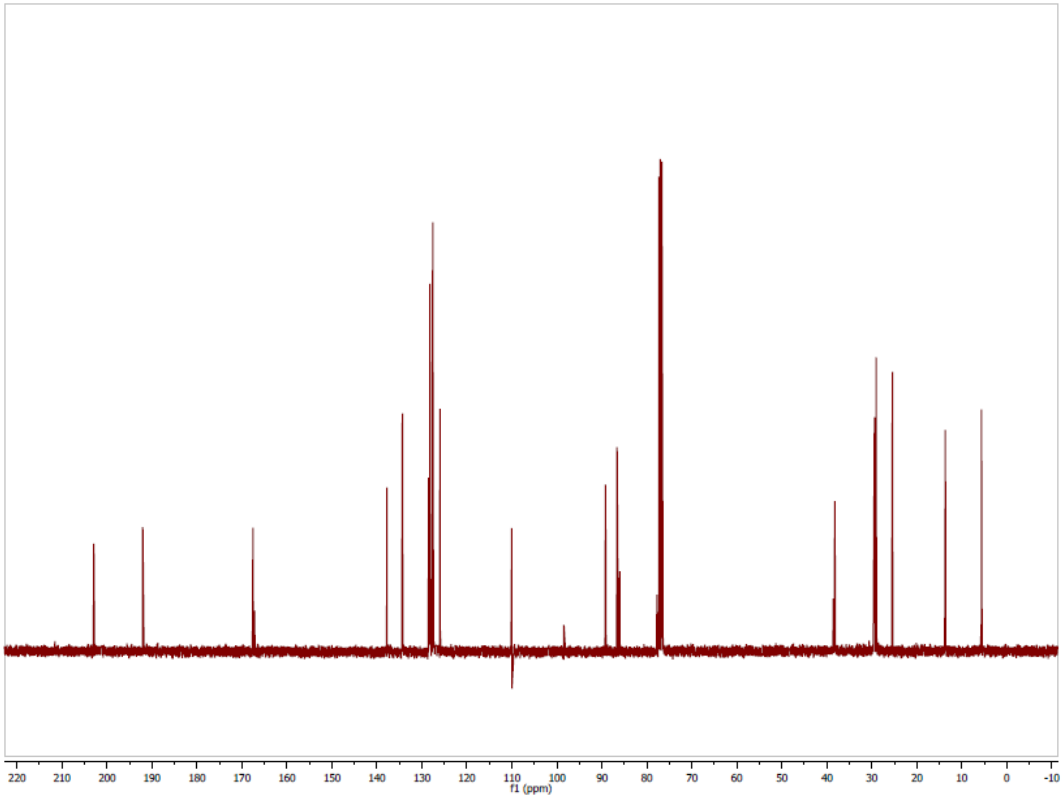


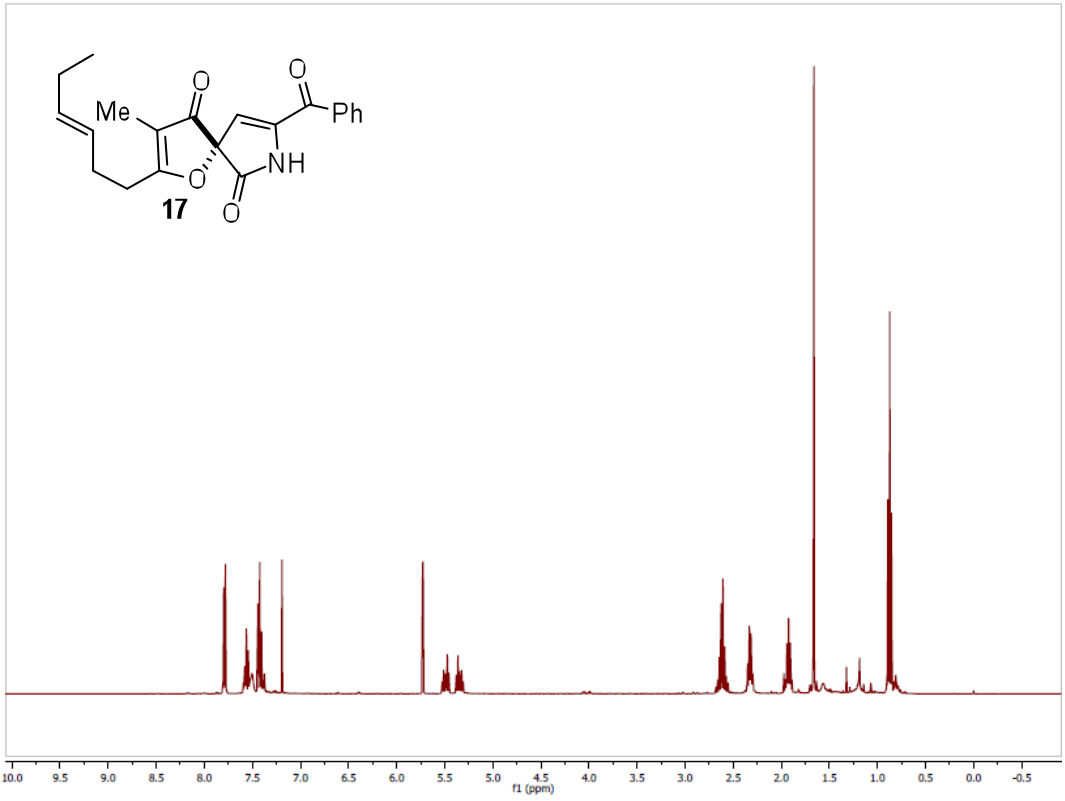


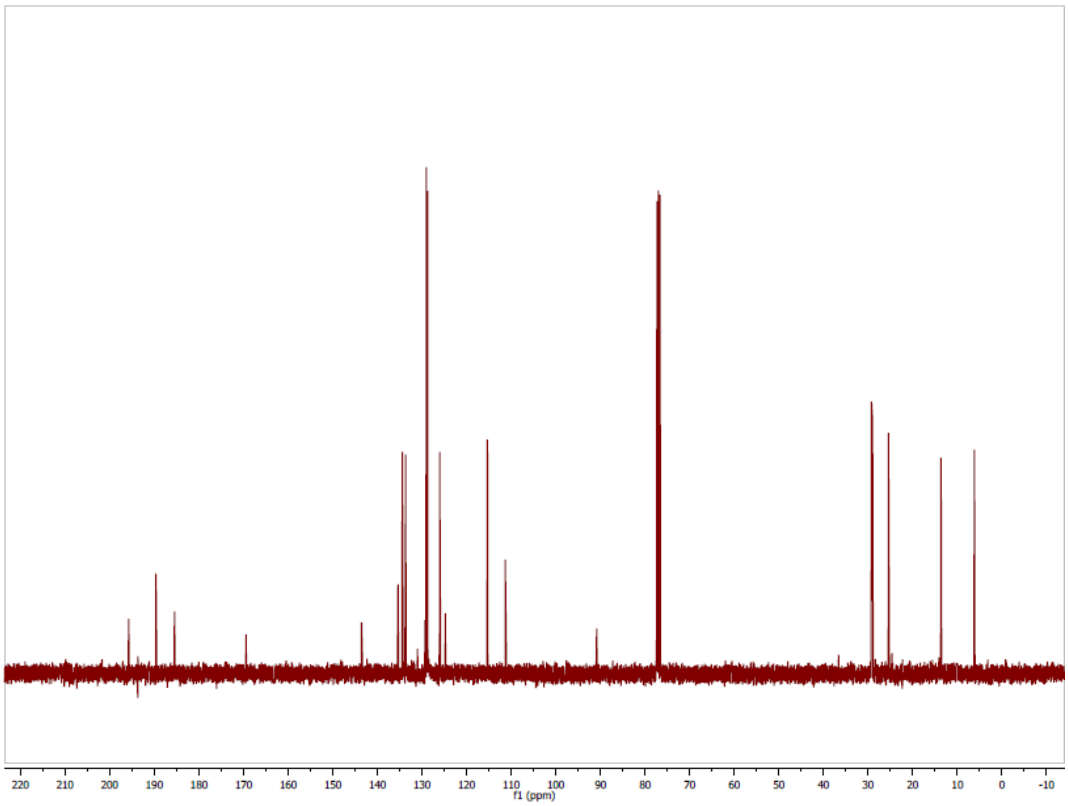


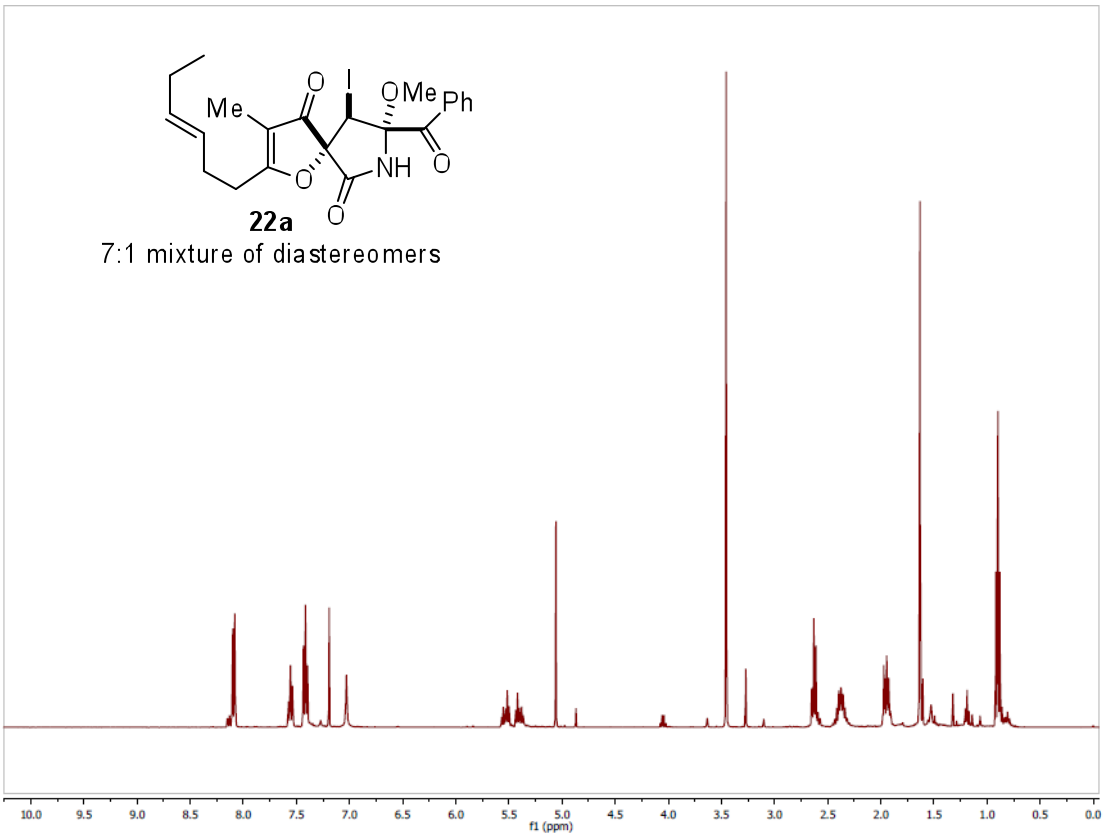


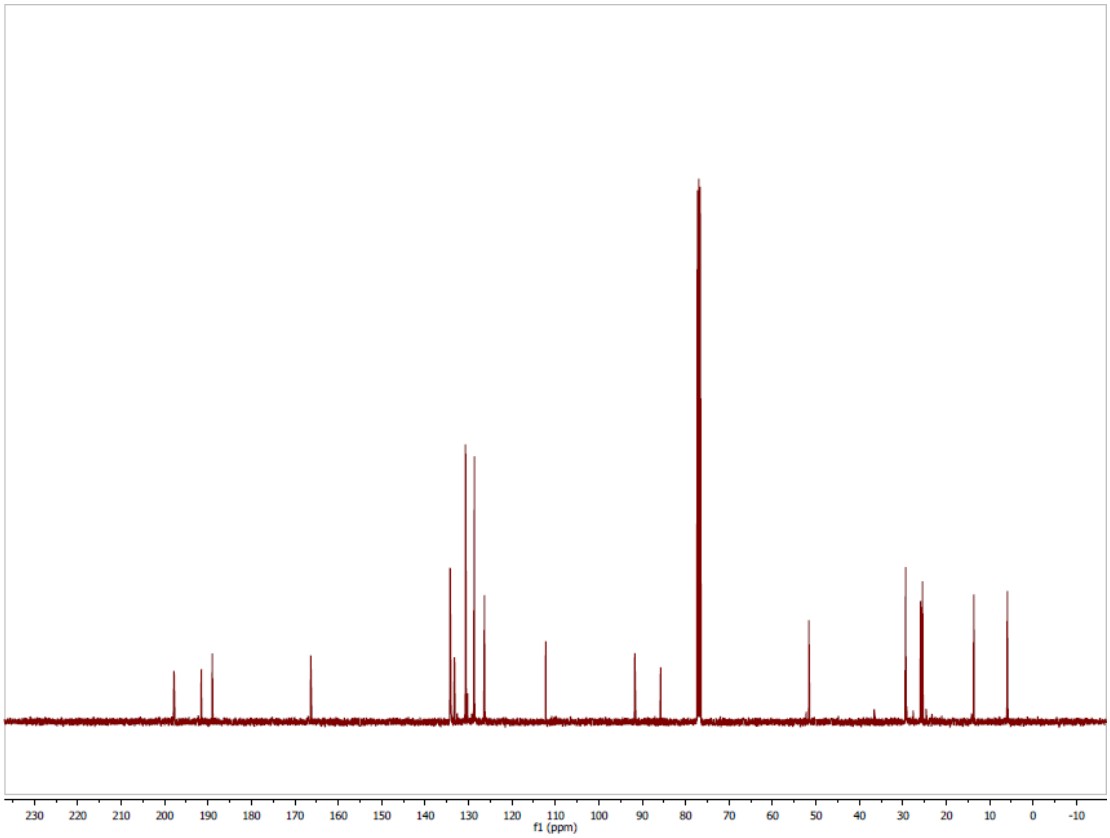


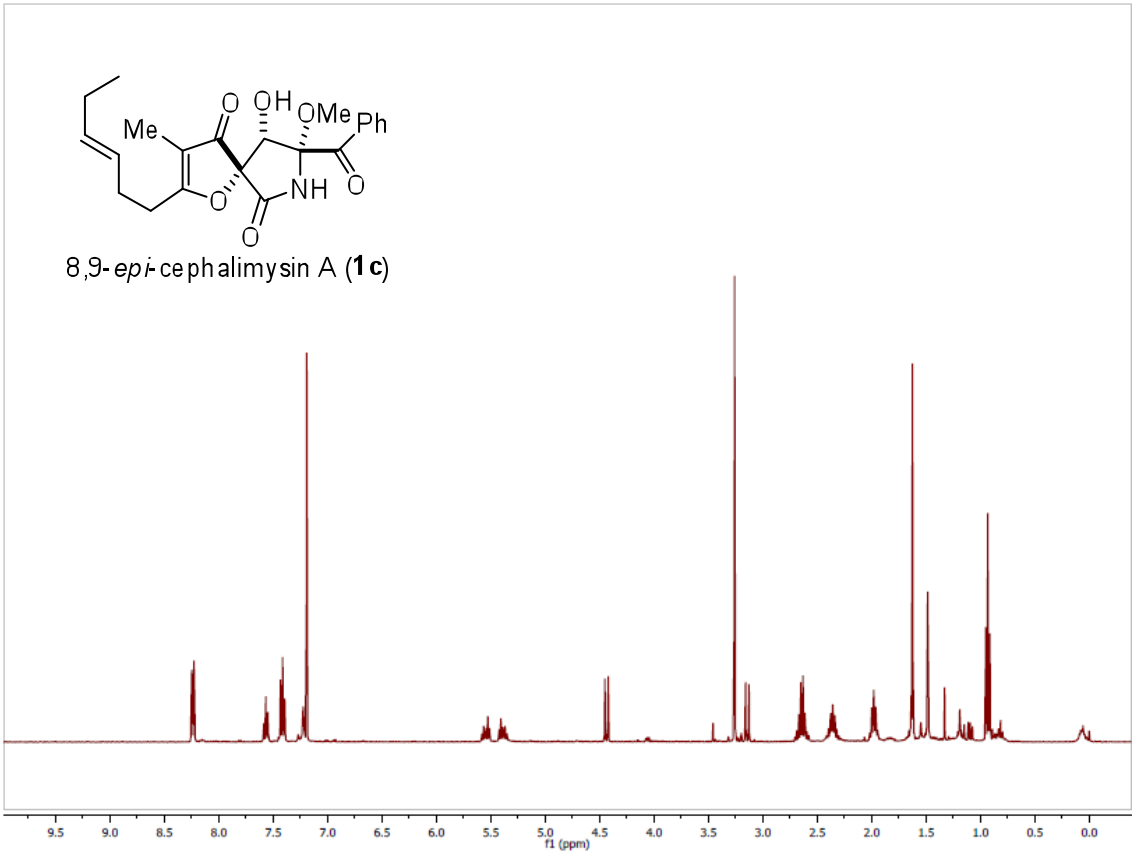




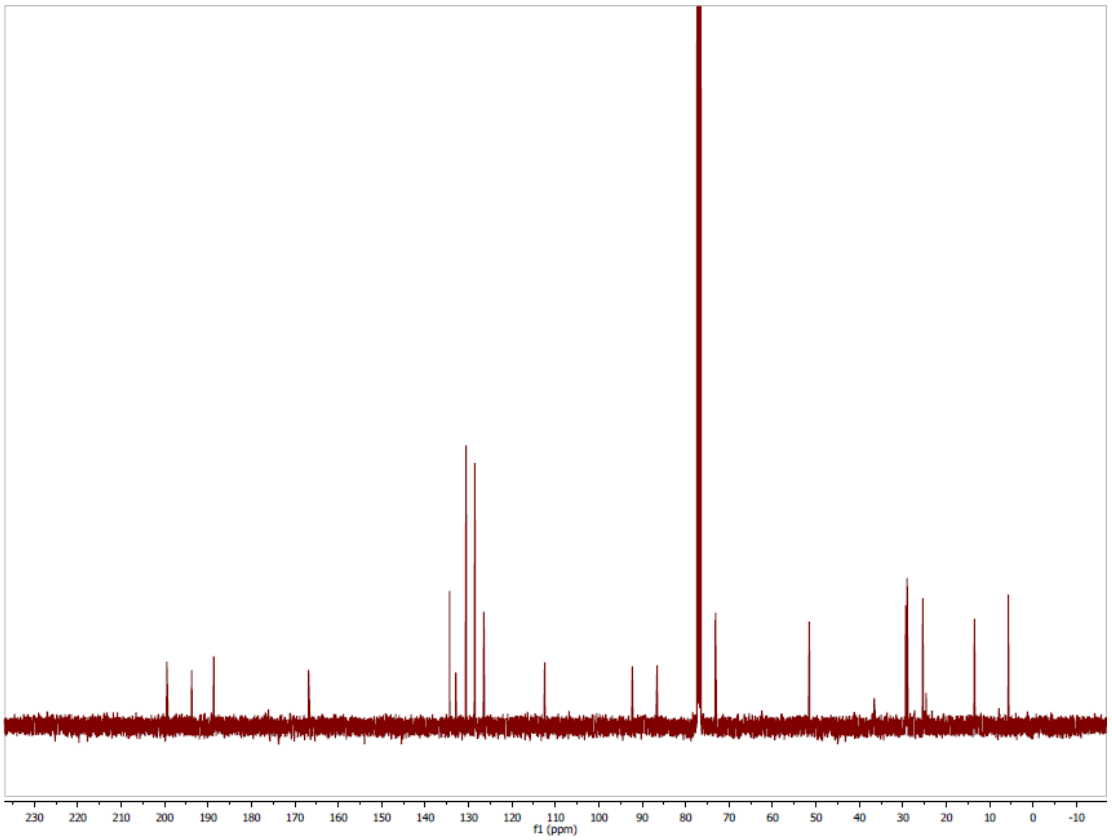


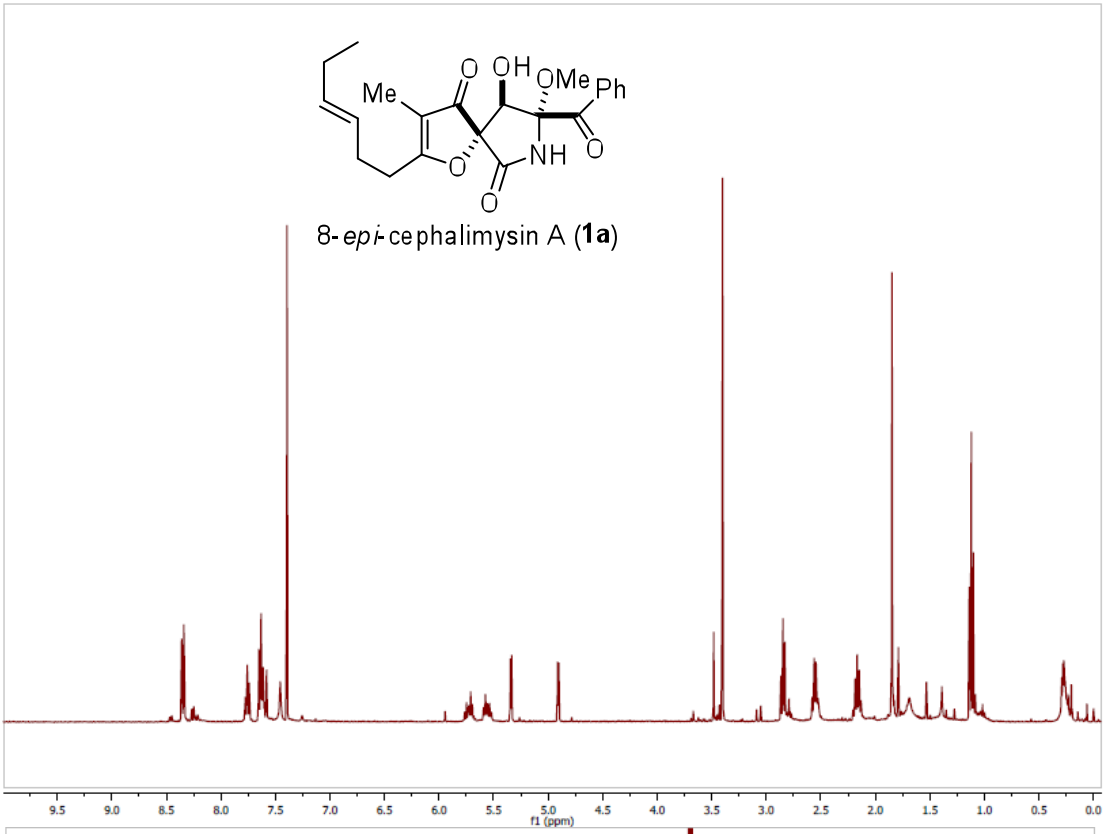

Me
O
I
OMe
Ph
O
NH
O
O
22a
7:1 mixture of diastereomers
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

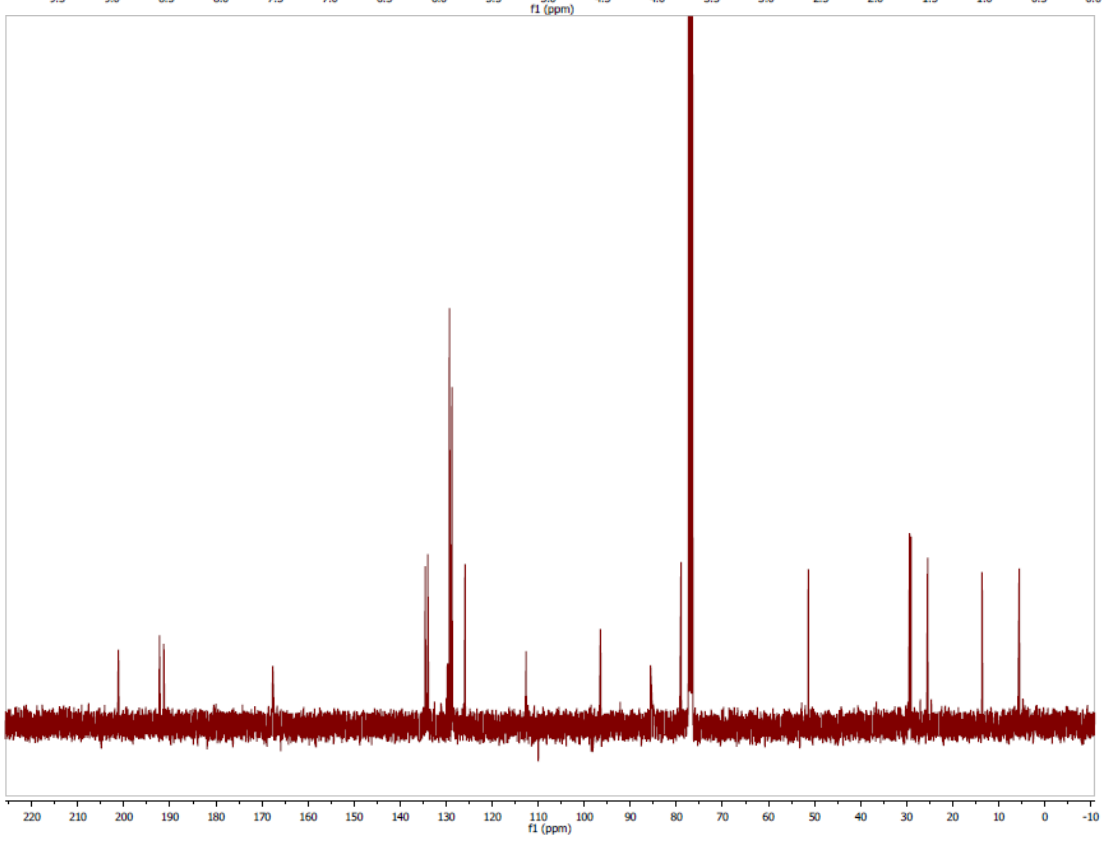


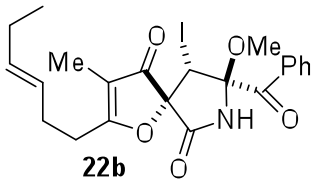
8,9-*epi*-cephalimysin A (**1c**)





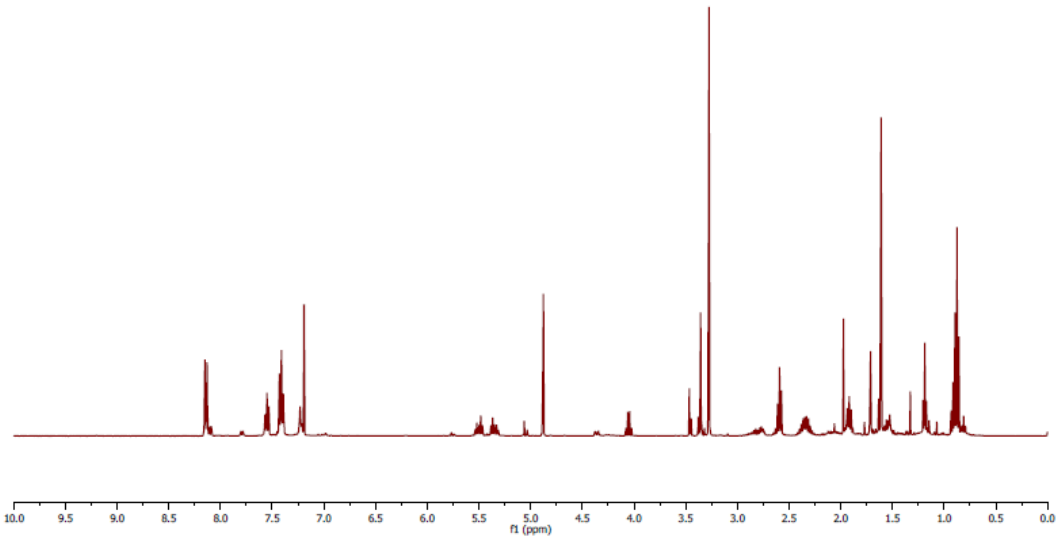
8-*epi*-cephalimysin A (**1a**)

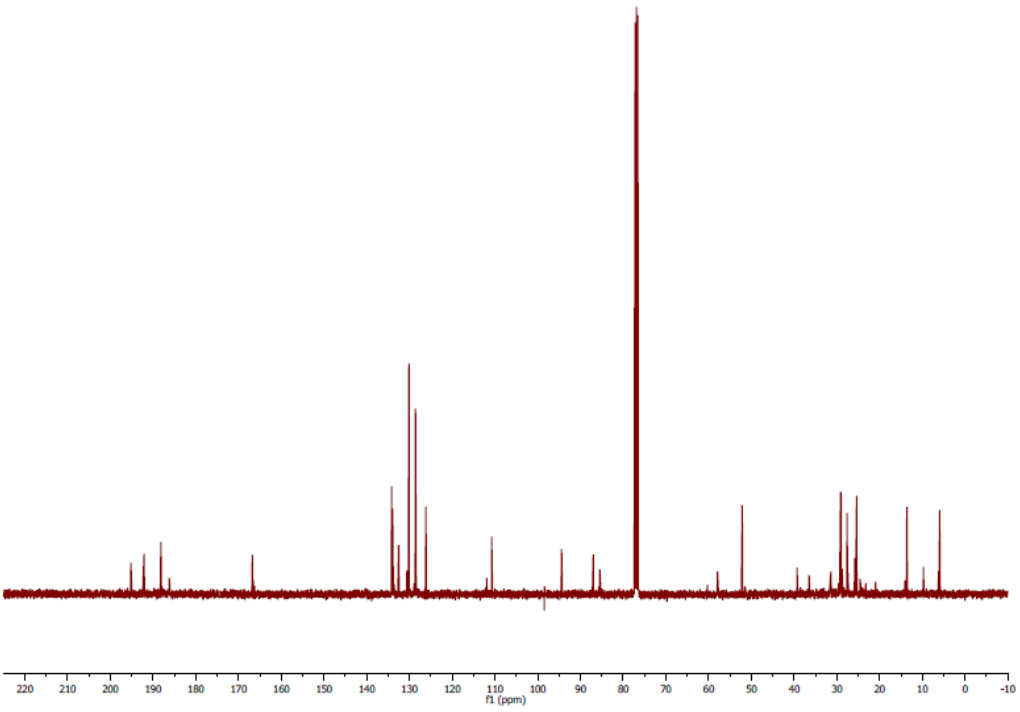


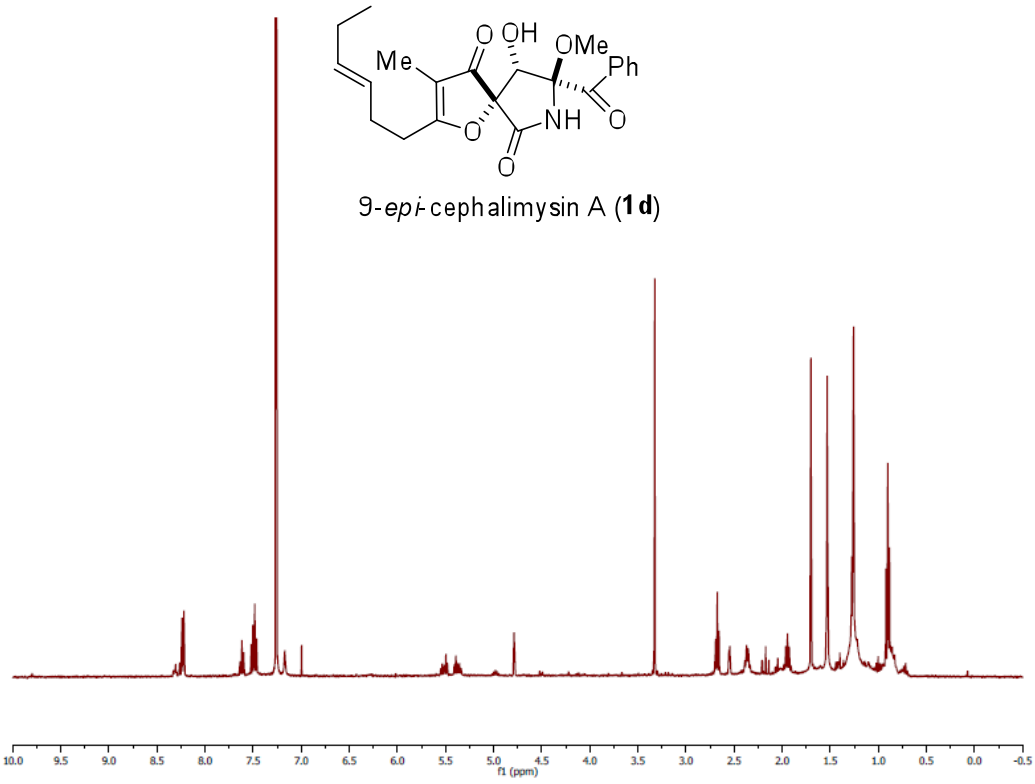


22b

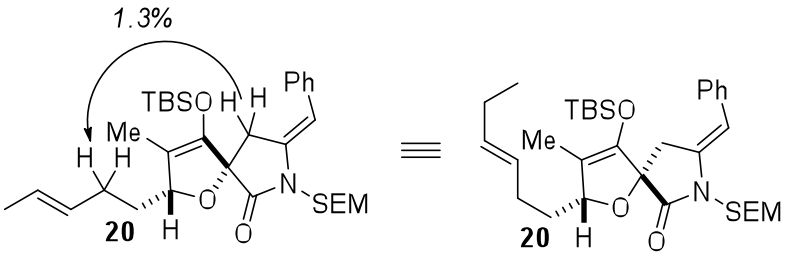
4:1 mixture of diastereomers

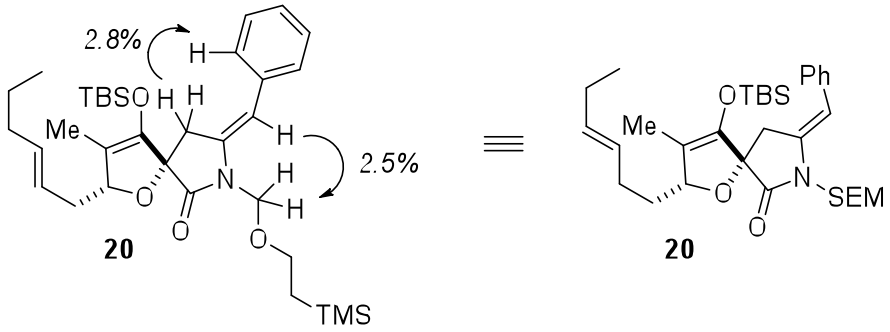





Me
O
OH
OMe
Ph
NH
O
O
O
9-epi-cephalimysin A (1d)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

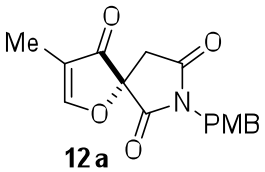
Stereochemical Assignment (nOe Correlations)





HPLC traces of spirocycles 12a and 12b

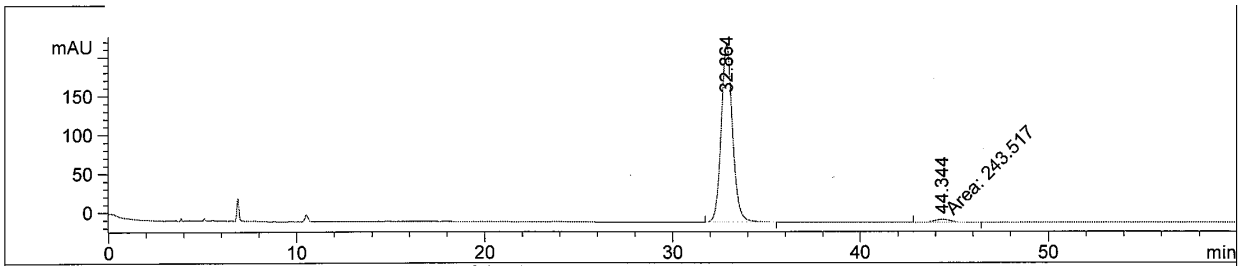
Spirocycle **12a**



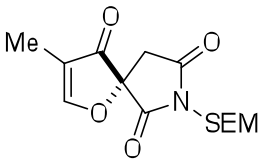
12 a

Analysis Conditions: Chiracel IA column, 93:7 hexanes/*i*-PrOH, 1.0 mL/min.

Enantioenriched

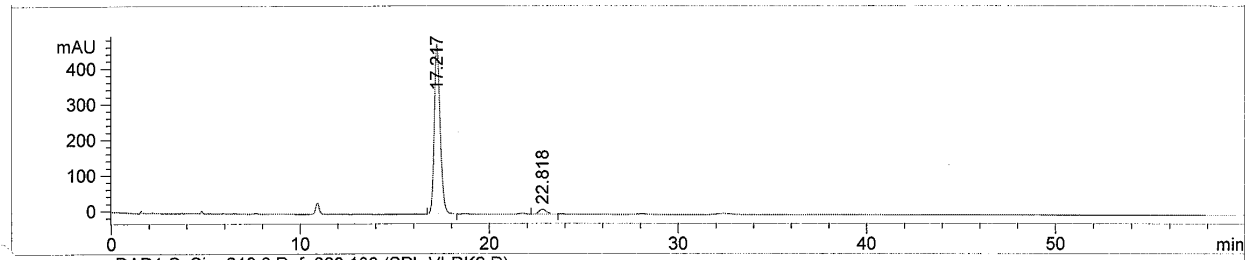


Spirocycle **12b**

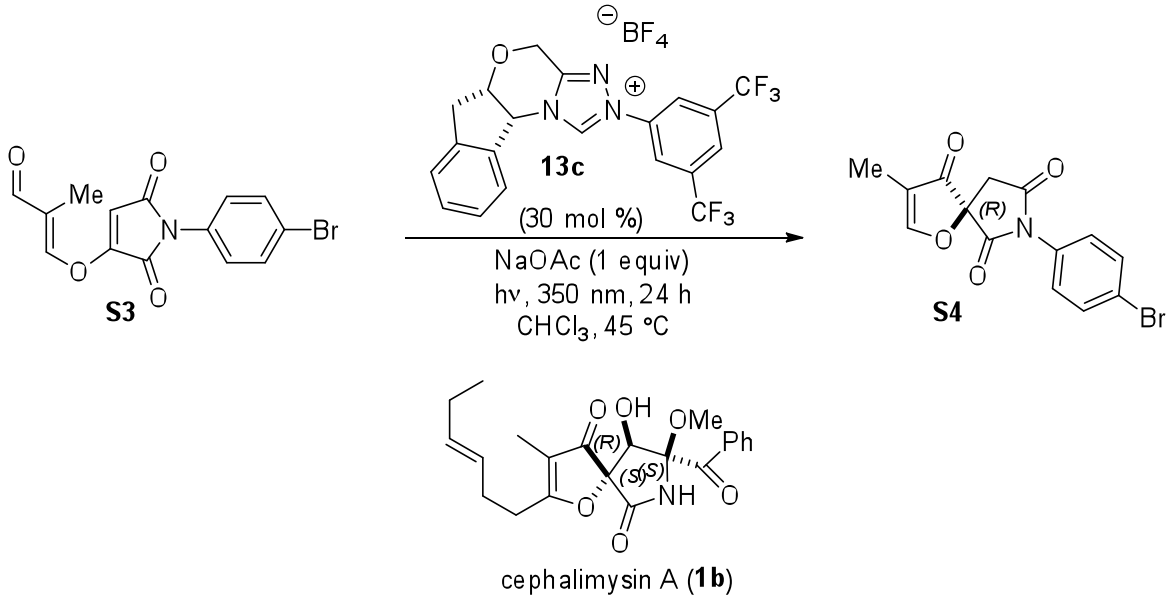


Analysis Conditions: Chiracel IA column, 95:5 hexanes/*i*-PrOH, 1.0 mL/min.

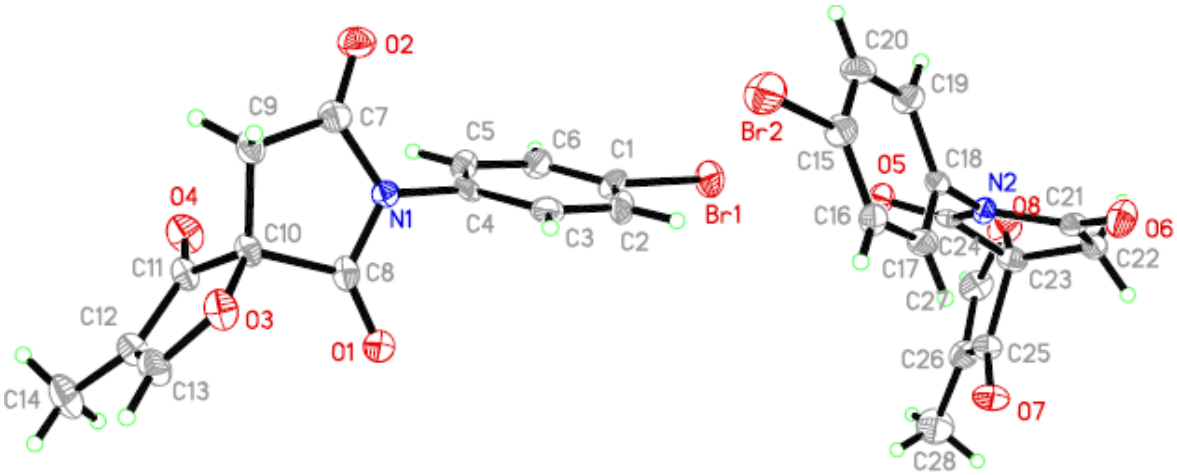
Enantioenriched



Determination of Absolute Configuration of Stetter Product



The absolute configuration was determined by single crystal X-ray analysis of spirocycle **S4**. This revealed that catalyst **13c** yields the (*R*) enantiomer. Therefore ***ent*-13c** catalyst was used to ensure the correct (*S*) absolute stereochemistry of the desired product.



Comments regarding crystal structure: The single crystal was coated in oil, transferred to a goniometer head, and mounted on a Bruker Kappa Apex CCD diffractometer under a stream of dinitrogen. Data collection was performed with Mo Kα radiation and a graphite monochromator. Data sets were taken with complete coverage and fourfold redundancy at 120K. Data was inte-

grated and corrected for absorption effects with the Apex 2 software package.[11] Structures were solved with the SHELXTL software package.[12] The structure contained residual electron density that was treated with SQUEEZE using PLATON.[13]

Table 1. Crystal data and structure refinement for **S4**.

Identification code	**S4**	
Empirical formula	$C_{14}H_{10}BrNO_4$	
Formula weight	336.14	
Temperature	120 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 11.8419(3) Å	α= 90°
	b = 6.55680(10) Å	β= 102.8190(10)°
	c = 20.7441(4) Å	γ = 90°
Volume	1570.53(6) Å^3	
Z	4	
Density (calculated)	1.422 Mg/m^3	
Absorption coefficient	2.628 mm^{-1}	
F(000)	672	
Crystal size	0.21 x 0.16 x 0.09 mm^3	
Theta range for data collection	1.76 to 31.62°.	
Index ranges	-17<=h<=17, -9<=k<=9, -30<=l<=30	
Reflections collected	37895	
Independent reflections	10026 [R(int) = 0.0540]	
Completeness to theta = 31.62°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8017 and 0.6136	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10026 / 1 / 364	
Goodness-of-fit on F^2	0.972	
Final R indices [I>2sigma(I)]	R1 = 0.0497, wR2 = 0.1177	

[11] Bruker AXS Inc., 5465 East Chervl Parkway, Madison, WI 53711-5373 USA
[12] Sheldrick, G. (1997) SHELXL-97 Program for Crystal Structure Refinement, Institüt für Anorganische Chemie der Universität, Göttingen, Germany.
[13] van der Sluis, P.; Spek, A. L. Acta Cryst. 1990, A46, 194-201.

R indices (all data)	R1 = 0.0750, wR2 = 0.1254
Absolute structure parameter	0.051(8)
Largest diff. peak and hole	1.013 and -0.583 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **S4**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	5687(1)	3090(1)	7814(1)	33(1)
Br(2)	8395(1)	9184(1)	7089(1)	37(1)
C(1)	5026(3)	4598(5)	7036(2)	21(1)
C(2)	5347(3)	6630(6)	7000(2)	24(1)
C(3)	4886(3)	7719(6)	6438(2)	24(1)
C(4)	4125(3)	6756(6)	5923(2)	18(1)
C(5)	3823(3)	4729(5)	5957(2)	20(1)
C(6)	4283(3)	3639(5)	6526(2)	23(1)
C(7)	3924(3)	7603(6)	4715(2)	25(1)
C(8)	2792(3)	9400(6)	5319(2)	19(1)
C(9)	3251(3)	9101(6)	4236(2)	23(1)
C(10)	2336(3)	9928(5)	4587(2)	19(1)
C(11)	1146(3)	8904(5)	4354(2)	19(1)
C(12)	330(3)	10537(6)	4246(2)	25(1)
C(13)	935(4)	12266(6)	4347(2)	26(1)
C(14)	-963(4)	10270(8)	4034(2)	39(1)
C(15)	8420(3)	7729(6)	7886(2)	26(1)
C(16)	8025(3)	8725(5)	8392(2)	21(1)
C(17)	8035(3)	7663(6)	8957(2)	23(1)
C(18)	8399(3)	5648(6)	9024(2)	18(1)
C(19)	8812(3)	4692(5)	8525(2)	23(1)
C(20)	8814(3)	5727(6)	7937(2)	26(1)
C(21)	9146(3)	4947(5)	10235(2)	19(1)
C(22)	8869(3)	3439(6)	10735(2)	21(1)
C(23)	7733(3)	2546(5)	10392(2)	21(1)
C(24)	7623(3)	2973(6)	9666(2)	18(1)
C(25)	6667(3)	3494(5)	10592(2)	19(1)
C(26)	5991(4)	1807(6)	10739(2)	25(1)
C(27)	6586(4)	114(6)	10670(2)	26(1)
C(28)	4861(4)	2066(8)	10934(2)	38(1)
N(1)	3607(2)	7875(4)	5337(1)	17(1)

N(2)	8359(3)	4578(4)	9627(1)	16(1)
O(1)	2477(2)	10088(4)	5786(1)	26(1)
O(2)	4595(3)	6320(4)	4624(1)	29(1)
O(3)	2113(2)	12060(4)	4527(1)	24(1)
O(4)	1011(3)	7050(4)	4289(2)	30(1)
O(5)	6986(2)	2131(4)	9203(1)	22(1)
O(6)	9885(3)	6230(5)	10312(1)	29(1)
O(7)	6523(3)	5329(4)	10621(1)	27(1)
O(8)	7598(3)	376(4)	10490(1)	27(1)

Table 3. Bond lengths [Å] and angles [°] for **S4**.

Br(1)-C(1)	1.907(3)
Br(2)-C(15)	1.903(3)
C(1)-C(6)	1.370(5)
C(1)-C(2)	1.392(5)
C(2)-C(3)	1.372(5)
C(3)-C(4)	1.388(5)
C(4)-C(5)	1.382(5)
C(4)-N(1)	1.436(4)
C(5)-C(6)	1.384(5)
C(7)-O(2)	1.200(5)
C(7)-N(1)	1.433(4)
C(7)-C(9)	1.495(5)
C(8)-O(1)	1.200(4)
C(8)-N(1)	1.385(5)
C(8)-C(10)	1.535(5)
C(9)-C(10)	1.532(5)
C(10)-O(3)	1.423(4)
C(10)-C(11)	1.538(5)
C(11)-O(4)	1.230(4)
C(11)-C(12)	1.426(5)
C(12)-C(13)	1.333(6)
C(12)-C(14)	1.506(6)
C(13)-O(3)	1.368(5)
C(15)-C(20)	1.389(6)

C(15)-C(16)	1.403(5)
C(16)-C(17)	1.361(5)
C(17)-C(18)	1.387(5)
C(18)-C(19)	1.388(5)
C(18)-N(2)	1.444(4)
C(19)-C(20)	1.397(5)
C(21)-O(6)	1.199(5)
C(21)-N(2)	1.412(4)
C(21)-C(22)	1.521(5)
C(22)-C(23)	1.496(5)
C(23)-O(8)	1.451(4)
C(23)-C(24)	1.507(5)
C(23)-C(25)	1.545(5)
C(24)-O(5)	1.214(4)
C(24)-N(2)	1.380(5)
C(25)-O(7)	1.218(4)
C(25)-C(26)	1.437(5)
C(26)-C(27)	1.340(6)
C(26)-C(28)	1.491(6)
C(27)-O(8)	1.344(5)

C(6)-C(1)-C(2)	122.3(3)
C(6)-C(1)-Br(1)	119.2(3)
C(2)-C(1)-Br(1)	118.4(3)
C(3)-C(2)-C(1)	118.8(3)
C(2)-C(3)-C(4)	119.0(3)
C(5)-C(4)-C(3)	121.9(3)
C(5)-C(4)-N(1)	118.0(3)
C(3)-C(4)-N(1)	120.1(3)
C(4)-C(5)-C(6)	118.9(3)
C(1)-C(6)-C(5)	119.0(3)
O(2)-C(7)-N(1)	122.9(3)
O(2)-C(7)-C(9)	129.1(3)
N(1)-C(7)-C(9)	108.0(3)
O(1)-C(8)-N(1)	126.1(3)
O(1)-C(8)-C(10)	127.6(3)

N(1)-C(8)-C(10)	106.2(3)
C(7)-C(9)-C(10)	104.3(3)
O(3)-C(10)-C(9)	116.3(3)
O(3)-C(10)-C(8)	109.0(3)
C(9)-C(10)-C(8)	105.1(3)
O(3)-C(10)-C(11)	105.2(3)
C(9)-C(10)-C(11)	113.0(3)
C(8)-C(10)-C(11)	108.0(3)
O(4)-C(11)-C(12)	131.1(4)
O(4)-C(11)-C(10)	123.6(3)
C(12)-C(11)-C(10)	105.3(3)
C(13)-C(12)-C(11)	107.0(3)
C(13)-C(12)-C(14)	128.4(4)
C(11)-C(12)-C(14)	124.6(4)
C(12)-C(13)-O(3)	116.0(3)
C(20)-C(15)-C(16)	123.0(3)
C(20)-C(15)-Br(2)	118.7(3)
C(16)-C(15)-Br(2)	118.3(3)
C(17)-C(16)-C(15)	117.8(3)
C(16)-C(17)-C(18)	121.1(3)
C(17)-C(18)-C(19)	120.6(3)
C(17)-C(18)-N(2)	118.7(3)
C(19)-C(18)-N(2)	120.8(3)
C(18)-C(19)-C(20)	120.1(3)
C(15)-C(20)-C(19)	117.4(3)
O(6)-C(21)-N(2)	123.8(3)
O(6)-C(21)-C(22)	128.8(3)
N(2)-C(21)-C(22)	107.4(3)
C(23)-C(22)-C(21)	103.7(3)
O(8)-C(23)-C(22)	115.6(3)
O(8)-C(23)-C(24)	109.6(3)
C(22)-C(23)-C(24)	105.8(3)
O(8)-C(23)-C(25)	103.6(3)
C(22)-C(23)-C(25)	114.6(3)
C(24)-C(23)-C(25)	107.4(3)
O(5)-C(24)-N(2)	126.1(3)

O(5)-C(24)-C(23)	127.3(3)
N(2)-C(24)-C(23)	106.5(3)
O(7)-C(25)-C(26)	131.2(4)
O(7)-C(25)-C(23)	122.8(3)
C(26)-C(25)-C(23)	105.9(3)
C(27)-C(26)-C(25)	106.5(3)
C(27)-C(26)-C(28)	130.4(4)
C(25)-C(26)-C(28)	123.1(4)
C(26)-C(27)-O(8)	116.5(3)
C(8)-N(1)-C(7)	112.8(3)
C(8)-N(1)-C(4)	123.8(3)
C(7)-N(1)-C(4)	123.4(3)
C(24)-N(2)-C(21)	112.2(3)
C(24)-N(2)-C(18)	124.3(3)
C(21)-N(2)-C(18)	123.2(3)
C(13)-O(3)-C(10)	106.2(3)
C(27)-O(8)-C(23)	107.3(3)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for **S4**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	37(1)	36(1)	23(1)	7(1)	-1(1)	11(1)
Br(2)	46(1)	45(1)	23(1)	12(1)	13(1)	7(1)
C(1)	29(2)	20(2)	13(1)	0(1)	6(1)	-1(1)
C(2)	21(2)	27(2)	22(2)	-6(1)	-4(1)	-2(2)
C(3)	20(2)	24(2)	30(2)	-7(1)	8(1)	2(2)
C(4)	8(2)	24(2)	21(2)	1(1)	3(1)	2(1)
C(5)	18(2)	24(2)	19(1)	-2(1)	4(1)	-7(1)
C(6)	28(2)	18(2)	21(2)	1(1)	4(1)	3(1)
C(7)	20(2)	32(2)	24(2)	5(1)	9(1)	-1(2)
C(8)	17(2)	22(2)	18(1)	6(1)	2(1)	-4(1)
C(9)	20(2)	29(2)	20(1)	9(2)	4(1)	1(2)

C(10)	15(2)	21(2)	21(2)	5(1)	2(1)	-1(1)
C(11)	14(2)	18(2)	23(2)	6(1)	2(1)	-2(1)
C(12)	23(2)	25(2)	26(2)	2(2)	3(2)	4(2)
C(13)	29(2)	17(2)	31(2)	6(2)	2(2)	6(2)
C(14)	22(2)	42(3)	46(3)	4(2)	-5(2)	3(2)
C(15)	25(2)	33(2)	20(2)	4(1)	7(1)	0(2)
C(16)	21(2)	22(2)	20(1)	0(1)	2(1)	0(1)
C(17)	16(2)	29(2)	24(2)	-4(1)	9(1)	-4(1)
C(18)	10(2)	26(2)	18(1)	-3(1)	5(1)	-2(1)
C(19)	30(2)	15(2)	23(2)	-1(1)	5(1)	3(1)
C(20)	23(2)	30(2)	26(2)	0(2)	12(2)	3(2)
C(21)	19(2)	24(2)	17(1)	-1(1)	7(1)	3(1)
C(22)	19(2)	28(2)	17(1)	2(1)	5(1)	2(1)
C(23)	22(2)	15(2)	25(2)	3(1)	7(1)	4(1)
C(24)	15(2)	18(2)	22(1)	-4(1)	5(1)	7(2)
C(25)	23(2)	13(2)	24(2)	2(1)	8(1)	0(1)
C(26)	29(2)	25(2)	21(2)	0(1)	9(2)	-4(2)
C(27)	34(2)	18(2)	28(2)	2(1)	13(2)	-7(2)
C(28)	33(3)	46(3)	40(2)	4(2)	17(2)	-7(2)
N(1)	17(2)	19(1)	17(1)	0(1)	4(1)	0(1)
N(2)	18(2)	15(1)	15(1)	-1(1)	2(1)	0(1)
O(1)	26(2)	28(1)	22(1)	-2(1)	3(1)	4(1)
O(2)	32(2)	32(2)	28(1)	5(1)	14(1)	8(1)
O(3)	26(2)	14(1)	29(1)	5(1)	1(1)	-5(1)
O(4)	29(2)	17(1)	41(2)	-1(1)	2(1)	-4(1)
O(5)	25(2)	22(1)	19(1)	0(1)	4(1)	-4(1)
O(6)	30(2)	36(2)	22(1)	-2(1)	6(1)	-10(1)
O(7)	28(2)	21(1)	35(2)	-1(1)	14(1)	4(1)
O(8)	38(2)	17(1)	28(1)	2(1)	9(1)	4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **S4**.

	x	y	z	U(eq)
H(2)	5863	7239	7350	29
H(3)	5081	9082	6403	29
H(5)	3319	4108	5604	24
H(6)	4090	2275	6562	27
H(9A)	2889	8437	3824	28
H(9B)	3747	10189	4144	28
H(13)	578	13537	4299	32
H(14A)	-1145	9487	3633	58
H(14B)	-1326	11584	3959	58
H(14C)	-1241	9569	4375	58
H(16)	7765	10066	8344	25
H(17)	7793	8299	9304	27
H(19)	9088	3361	8583	28
H(20)	9069	5101	7593	31
H(22A)	9461	2393	10840	25
H(22B)	8805	4125	11140	25
H(27)	6312	-1176	10743	31
H(28A)	4460	784	10894	58
H(28B)	4399	3052	10649	58
H(28C)	4996	2530	11383	58