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Supporting Information

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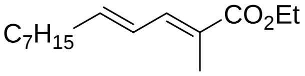
Synthesis and Stereochemical Assignment of FR252921, A Promising Immunosuppressive

J. R. Falck,* Anyu He, Hiroki Fukui, Hideyuki Tsutsui, and Akella Radha

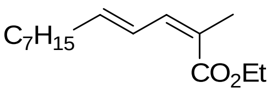
Departments of Biochemistry and Pharmacology
University of Texas Southwestern Medical Center
Dallas, Texas, 75390 U. S. A.

Experimental procedures, characterization of new compounds, scanned ^{1}H spectra of compounds **24-27** and natural FR252921, and ORTEP illustration from the X-ray diffraction study of compound **17** are included.

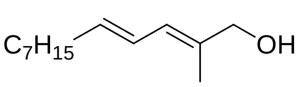
General Procedures. ^{1}H and ^{13}C spectra were recorded in $CDCl_3$ using tetramethylsilane as internal reference unless otherwise stated. The Michigan State University Mass Spectroscopy Facility provided high-resolution mass spectral analyses. All reactions were maintained under an argon atmosphere. Anhydrous solvents were freshly distilled from sodium benzophenone ketyl, except for CH_2Cl_2, which was distilled from CaH_2. Extracts were dried over anhydrous Na_2SO_4 and then filtered prior to removal of all volatiles under reduced pressure.



Ethyl 2-methyldodeca-2(*E*),4(*E*)-dienoate (2). Commercial ethyl 2-(diethoxyphosphoryl)propionate (15.7 mL, 71.9 mmol) was added to a suspension of NaH (60% suspension in oil, 3.14 g, 78.4 mmol) in dry THF (200 mL) at 0 ºC. After 1 h, the generation of H_2 gas ceased and a solution of dec-2(*E*)-enal (**1**) (12.0 mL, 65.3 mmol) in THF (10 mL) was added dropwise to the colorless reaction solution at 0ºC. After 2 h, the reaction was quenched with water and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried with Na_2SO_4, concentrated *in vacuo*, and the residue was purified via SiO_2 column chromatography eluting with hexane/EtOAc (10:1) to give **2** and its (2*Z*,4*E*)-isomer as a colorless oil in 92% combined yield (~12:1 2*E*,4*E*/2*Z*/4*E*). They were separated chromatographically. **2:** TLC (SiO_2) hexane/EtOAc (10:1), $R_f \approx 0.53$; IR (neat, NaCl) 1706 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (1H, d, *J* = 12 Hz), 6.33 (1H, ddt, *J* = 15, 12, 2 Hz), 6.08 (1H, dt, *J* = 15, 7 Hz), 4.20 (2H, q, *J* = 7 Hz), 2.18 (2H, dt, *J* = 7, 7 Hz), 1.93 (3H, s), 1.47–1.39 (2H, m), 1.38–1.28 (8H, m), 0.88 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 143.4, 138.8, 126.1, 125.2, 60.6, 33.5, 32.0, 29.4, 29.3, 29.2, 22.8, 14.5, 14.3, 12.7. HRMS (FAB, NBA) Calcd. for $C_{15}H_{27}O_2$ [MH$^+$] *m/z* 239.2011, found 239.2012.

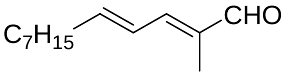


Ethyl 2-methyldodeca-2(*Z*),4(*E*)-dienoate (2*Z*,4*E*-2). TLC (SiO_2) hexane/EtOAc (10:1), $R_f \approx 0.61$; IR (neat, NaCl) 1706 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (1H, ddt, *J* = 15, 12, 2 Hz), 6.40 (1H, d, *J* = 12 Hz), 5.91 (1H, dt, *J* = 15, 7 Hz), 4.22 (2H, q, *J* = 7 Hz), 2.15 (2H, dt, *J* = 7, 7 Hz), 1.94 (3H, s), 1.47–1.39 (2H, m), 1.38–1.27 (8H, m), 0.88 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 142.3, 141.0, 127.8, 124.1, 60.3, 33.2, 32.0, 29.6, 29.41, 29.36, 29.2, 22.9, 20.9, 14.5, 14.3. HRMS (FAB, NBA) Calcd. for $C_{15}H_{27}O_2$ [MH$^+$] *m/z* 239.2011, found 239.2010.

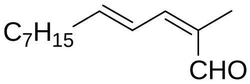


2-Methyldodeca-2(*E*),4(*E*)-dien-1-ol (3). DIBAL (80.5 mL, 80.5 mmol, 1 M toluene soln) was added to a solution of ethyl 2-methyldodeca-2(*E*),4(*E*)-dienoate (**2**) (8.0 g, 33.6 mmol) in CH_2Cl_2 (150 mL) at 0°C. After 25 min, the reaction was quenched with MeOH (20 mL), poured into 1N aq. HCl (50 mL) with stirring, and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried and concentrated in vacuo to give crude 2-methyldodeca-2(*E*),4(*E*)-dien-1-ol (**3**) in nearly quantitative yield which was used without further purification in the next step. TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.50$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.24 (1H, ddt, *J* = 15, 11, 1 Hz), 6.01 (1H, d, *J* = 11 Hz), 5.69 (1H, dt, *J* = 15, 7 Hz), 4.04 (2H, s), 2.11 (2H, dt, *J* = 7, 7 Hz), 1.77 (3H, s), 1.42–1.36 (2H, m), 1.36–1.24

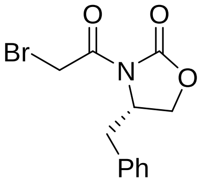
(8 H, m), 0.88 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.4, 134.8, 126.0, 125.5, 68.8, 33.2, 32.0, 29.6, 29.4, 22.8, 14.3, 14.2; HRMS (FAB, NBA) Calcd. for $C_{13}H_{24}O$ [M^+] *m/z* 196.1827, found 196.1826.



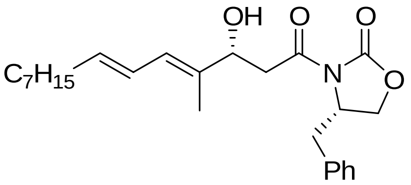
2-Methyldodeca-2(*E*),4(*E*)-dienal (4). MnO_2 (20.6 g, Aldrich, 85% active, 237.4 mmol) was added to a mixture of 2-methyldodeca-2(*E*),4(*E*)-dien-1-ol (**3**) and $MgSO_4$ (20 g) in CH_2Cl_2 (150 mL) and shaked at room temperature. After 2 d, the reaction mixture was filtrated over Celite® and the filter cake was flushed with fresh CH_2Cl_2. The combined filtrate was concentrated and the residue was purified via silica gel column chromatography (hexane/EtOAc, 10:1) to give 2-methyldodeca-2(*E*),4(*E*)-dienal (**4**) (6.1 g, 93% yield over two steps) as a pale yellow oil. TLC: SiO_2, hexane/EtOAc (2:1), $R_f \approx 0.69$; IR (neat, NaCl) 1693.9 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.42 (1H, s), 6.83 (1H, br d, *J* = 11 Hz), 6.52 (1H, ddt, *J* = 15, 11, 1 Hz), 6.25 (1H, dt, *J* = 15, 7 Hz), 2.24 (2H, dt, *J* = 7, 7 Hz), 1.83 (3H, s), 1.51–1.42 (2H, m), 1.38–1.22 (8H, m), 0.89 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 149.6, 146.3, 136.1, 126.0, 33.7, 32.0, 29.4, 29.3, 29.0, 22.8, 14.3, 9.6; HRMS (FAB, NBA) Calcd. for $C_{13}H_{21}O$ [$(M-1)^+$] *m/z* 193.1592 found 193.1592.



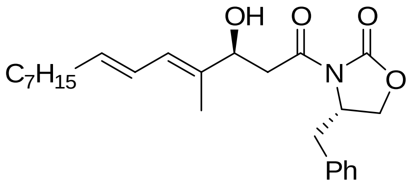
2-Methyldodeca-2(*Z*),4(*E*)-dienal. TLC: SiO_2, hexane/EtOAc (2:1), $R_f \approx 0.72$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.3 (1H, s), 6.98 (1H, br dt, *J* = 13, 12 Hz), 6.90 (1H, dd, *J* = 12, 1 Hz), 6.03 (1H, dt, *J* = 14, 7 Hz), 2.21 (2H, dt, *J* = 7, 7 Hz), 1.83 (3H, s), 1.48–1.40 (2H, m), 1.38–1.24 (8H, m), 0.89 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.6, 146.5, 144.2, 133.1, 123.3, 33.2, 31.9, 29.34, 29.28, 29.0, 22.8, 16.4, 14.2.



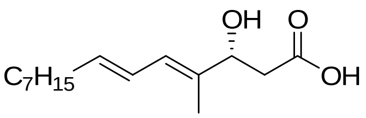
4(*S*)-Benzyl-3-(2-bromoacetyl)oxazolidin-2-one (9). *n*BuLi (48.8 mL, 122.0 mmol. 2.5 M in THF) was added dropwise to a solution of 4(*S*)-benzyloxazolidin-2-one (19.65 g, 110.9 mmol) in THF (500 mL) at −78°C. After stirring for 1 h at the temperature, 2-bromoacetyl bromide (11.6 mL, 133.1 mmol) was added to the reaction mixture and the whole was warmed room temperature. After 3 h, the reaction was quenched with sat. aq. NH_4Cl and extracted with EtOAc. The combined organic extracts were washed with brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was purified via SiO_2 column chromatography (hexane/EtOAc, 3:2) to give (4*S*)-3-bromoacetyloxazolidin-2-one (26.8 g, 81%) as a pale yellow solid. TLC: SiO_2, hexane/EtOAc (2:1), $R_f \approx 0.35$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.20 (5H, m), 4.73–4.65 (1H, m), 4.52 (2H, dt, *J* = 2, 1 Hz), 4.29–4.19 (2H, m), 3.30 (1H, dd, *J* = 13, 2 Hz), 2.81 (1H, dd, *J* = 13, 10 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 153.0, 134.8, 129.5, 129.1, 127.5, 66.7, 55.4, 37.4, 28.5.



4(*S*)-Benzyl-3-(3(*R*)-hydroxy-4-methyltetradeca-4(*E*),6(*E*)-dienoyl)-oxazolidin-2-one (5). A solution of (*S*)-4-benzyl-3-(2-bromoacetyl)oxazolidin-2-one (**9**) (1.49 g, 5.00 mmol) and 2-methyldodeca-2(*E*),4(*E*)-dienal (777 mg, 4.00 mmol) in THF (15 mL) was added to a 0.1 M solution of SmI_2 (8.8 mL, 0.88 mmol) in THF at –86°C. After 17 h, the reaction was quenched with sat. aq. $Na_2S_2O_3$ and then extracted with EtOAc. The combined organic extracts were washed with sat. aq. $NaHCO_3$, brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was purified via SiO_2 column chromatography (hexane/EtOAc, 4:1) to give 4(*S*)-benzyl-3-(3(*R*)-hydroxy-4-methyltetradeca-4(*E*),6(*E*)-dienoyl)-oxazolidin-2-one (**5**) (1.33 g, 81%) and 4(*S*)-benzyl-3-(3(*S*)-hydroxy-4-methyltetradeca-4(*E*),6(*E*)-dienoyl)-oxazolidin-2-one (**6**) (157 mg, 10%) as colorless oils. **Compound 5**. TLC: SiO_2, hexane/EtOAc (2:1), $R_f \approx 0.18$; IR (neat, NaCl) 3492, 1784, 1694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.25 (3H, m), 7.21 (2H, br d, *J* = 7 Hz), 6.24 (1H, br dd, *J* = 15, 11 Hz), 6.11 (1H, br d, *J* = 11 Hz), 5.71 (1H, dt, *J* = 15, 7 Hz), 4.71–4.67 (1H, m), 4.64–4.60 (1H, m), 4.22–4.15 (2H, m), 3.29 (1H, dd, *J* = 13, 3 Hz), 3.22–3.18 (2H, m), 2.91 (1H, br s), 2.78 (1H, dd, *J* = 13, 10 Hz), 2.10 (2H, dt, *J* = 7, 7 Hz), 1.80 (3H, br s) 1.40–1.24 (10H, m), 0.88 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 153.4, 135.6, 135.3, 135.2, 129.3, .2, 125.7, 125.5, 72.6, 66.2, 55.0, 41.2, 37.7, 32.9, 31.7, 29.3, 29.1, 22.6, 14.0, 12.6; HRMS (FAB, NBA) Calcd. for $C_{25}H_{35}NO_4$ [M^+] *m/z* 413.2566, found 413.2568.

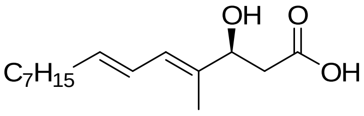


Compound 6. TLC: SiO_2, hexane/EtOAc (2:1), $R_f \approx 0.24$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.25 (3H, m), 7.22–7.19 (2H, m), 6.24 (1H, br dd, *J* = 15, 11 Hz), 6.10 (1H, br d, *J* = 11 Hz), 5.70 (1H, dt, *J* = 15, 7 Hz), 4.72–4.65 (1H, m), 4.58 (1H, dd, *J* = 9, 3 Hz), 4.22–4.13 (2H, m), 3.34–3.25 (2H, m), 3.12 (1H, br s), 3.09 (2H, dd, *J* = 17, 3 Hz), 2.78 (2H, dd, *J* = 14, 9 Hz), 2.09 (2H, dt, *J* = 7, 7 Hz), 1.79 (3H, br s) 1.38–1.18 (10H, m), 0.88 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 153.6, 136.0, 135.2, 129.5, 129.0, 127.4, 125.9, 125.8, 73.1, 66.4, 55.2, 41.4, 37.8, 33.1, 31.9, 29.5, 29.3, 22.7, 14.2, 12.7; HRMS (FAB, NPOE) Calcd. for $C_{25}H_{35}NO_4$ [M^+] *m/z* 413.25661, found 413.2568.

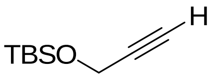


3(R)-Hydroxy-4-methyltetradeca-4(*E*),6(*E*)-dienoic acid (7). $LiOH{\cdot}H_2O$ (105 mg, 2.49 mmol) was added to a solution of 4(*S*)-benzyl-3-(3(*R*)-hydroxy-4-methyltetradeca-4(*E*),6(*E*)-dienoyl)-oxazolidin-2-one (**5**) (859 mg, 2.08 mmol) and H_2O_2 (0.94 mL of 30% soln, 8.31 mmol) in THF/water (16 mL/4 mL) at 0ºC. After 3h, the reaction was quenched with aq. $NaHSO_3$ (pH = 5-6) and then 20% aq. citric acid was added to adjust the pH of the mixture to 3-4.

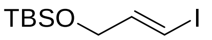
The reaction mixture was extracted with EtOAc and then the combined extracts were washed with brine, dried with Na_2SO_4, and concentration in vacuo. The residue was purified via SiO_2 column chromatography (hexanes/EtOAc/AcOH, 1:1:0.01) to give 3(*R*)-hydroxy-4-methyltetradeca-4(*E*),6(*E*)-dienoic acid (**7**) (0.50 g, 97%) as colorless oil. TLC: SiO_2, hexane/EtOAc/AcOH (50:50:1), $R_f \approx 0.26$; IR (neat, NaCl) 3406 (br), 1715 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) d 6.22 (1H, br dd, *J* = 15, 11 Hz), 6.07 (1H, br d, *J* = 11 Hz), 5.73 (1H, dt, *J* = 15, 7 Hz), 4.50 (1H, dd, *J* = 8, 4 Hz), 2.68-2.53 (2H, m), 2.10 (2H, dt, *J* = 7, 7 Hz), 1.75 (3H, br s), 1.42–1.22 (10 H), 0.88 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) d177.2, 136.4, 134.6, 126.3, 125.7, 73.3, 40.1, 33.2, 32.0, 29.5, 29.4, 22.8, 14.2, 12.5;HRMS (FAB, NBA) Calcd. for $C_{15}H_{26}O_3$ [M^+] *m/z* 254.1882 found, 254.1881.



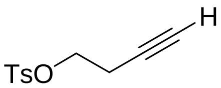
3(*S*)-Hydroxy-4-methyltetradeca-4(*E*),6(*E*)-dienoic acid (8). HRMS (FAB, NBA) Calcd. for $C_{15}H_{26}O_3$ [M^+] *m/z* 254.18820, found 254.1881.



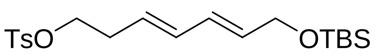
***tert*-Butyldimethyl(prop-2-ynyloxy)silane.** To a solution of 2-propynol (44.1 mL, 0.758 mol) in CH_2Cl_2 (300 mL) was added *tert*-butyldimethylsilyl chloride (120 g, 0.796 mol) and imidazole (103.2g, 1.516 mol) at 0ºC. After 1h, the reaction mixture was washed with water, dried over Na_2SO_4, and was concentrated in vacuo. Distillation of the residue gave *tert*-butyldimethyl(prop-2-ynyloxy)silane as colorless oil (95ºC/155 mmHg, quantitative yield). TLC: SiO_2, hexane/EtOAc (10:1), $R_f \approx 0.55$; ^1H NMR (300 MHz, $CDCl_3$) δ 4.31 (2H, d, *J* = 2 Hz), 2.39 (1H, t, *J* = 2 Hz), 0.91 (9H, s), 0.131 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 82.5, 73.1, 51.6, 25.9, 18.4, –5.0.



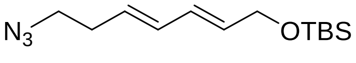
1(*E*)-iodo-3-*tert*-butyldimethylsilyloxy)propene. A solution of *tert*-butyldimethyl(prop-2-ynyloxy)silane (11.1 g, 65.2 mmol) in THF (30 mL) was added to a suspension of bis(cyclopentadienyl)zirconium(IV) chloride hydride (18.5 g, 71.7 mmol) in THF (250 mL) at room temperature. After 1 h, the now yellow reaction mixture was cooled to 0ºC and I_2 (24.8 g, 97.8 mmol) was added. Following another 1 h, the reaction was quenched with aq. $Na_2S_2O_3$, diluted with toluene, filtered through Celite, and the filtrate was extracted with toluene. The combined organic extracts were washed with brine, dried with Na_2SO_4, and concentration in vacuo. The residue was purified via SiO_2 column chromatography (hexanes/EtOAc, 10:1) to afford 1(*E*)-iodo-3-*tert*-butyldimethylsilyloxy)propene as a pale yellow oil (13.1 g, 67%). TLC: SiO_2, hexane/EtOAc (20:1), $R_f \approx 0.63$; ^1H NMR (300 MHz, $CDCl_3$) δ 6.61 (1H, dt, *J* = 14, 5 Hz), 6.29 (1H, dt, *J* = 14, 2 Hz), 4.11 (2H, dd, *J* = 5, 2 Hz), 0.91 (9H, s), 0.07 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 76.1, 65.5, 26.1, 18.5, –5.2.



But-3-ynyl 4-methylbenzenesulfonate (10). *p*-Toluenesulfonyl chloride (136 g, 0.713 mol) was added to a solution of 3-butynol (50 g, 0.713 mol), triethylamine (109 mL, 0.784 mol), and 4-dimethylaminopyridine (87 mg, 0.713 mmol) in CH_2Cl_2 (500 mL) at 0ºC. After 3 h, the reaction was quenched with H_2O, extracted with CH_2Cl_2, and the combined organic extracts were dried with Na_2SO_4 and concentrated in vacuo. Purification of the residue via SiO_2 column chromatography (hexanes/EtOAc, 1:1) gave but-3-ynyl 4-methylbenzenesulfonate (**10**) as a pale yellow oil (nearly quantitatively). TLC: SiO_2, hexane/EtOAc (2:1), $R_f \approx 0.38$; IR (neat, NaCl) 3292.5 cm^{-1}; ^{1}H NMR (300 MHz,$CDCl_3$) δ 7.81 (2H, dt, *J* = 8, 2 Hz), 7.34 (2H, br d, *J* = 8 Hz), 4.11 (2H, t, *J* = 7 Hz), 2.56 (2H, dt *J* = 7, 3 Hz), 2.46 (3H, s), 1.98 (1H, t, *J* = 3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 132.9, 130.1, 128.2, 78.6, 71.0, 67.6, 21.8, 19.6.

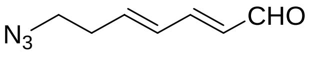


7-(*tert*-Butyldimethylsilyloxy)hepta-3(*E*),5(*E*)-dienyl 4-methylbenzenesulfonate (11). A solution of but-3-ynyl 4-methylbenzenesulfonate (**10**) (10.5 g, 46.6 mmol) in THF (10 mL) was added to a suspension of bis(cyclopentadienyl)zirconium(IV) chloride hydride (12.9 g, 50.0 mmol) in THF (110 mL) at room temperature. After 1.5 h, $Pd(OAc)_2$ (190 mg, 0.848 mmol), 2-dicyclohexylphosphino-2'-(*N*,*N*-dimethylamino)biphenyl (467 mg, 1.188 mmol), and 1(*E*)-iodo-3-*tert*-butyldimethylsilyloxy)propene (12.9 g, 42.4 mmol) in THF (10 mL) were added to the yellow mixture at room temperature. After 10 h, the reaction was quenched with H_2O and extracted with EtOAc. The combined organic extracts were dried with Na_2SO_4, concentrated in vacuo, and the residue was purified via SiO_2 column chromatography (hexane/EtOAc, 5:1) to give 7-(*tert*-butyldimethylsilyloxy)hepta-3(*E*),5(*E*)-dienyl 4-methylbenzenesulfonate (**11**) as a pale yellow oil (16.5 g, 98%). TLC: SiO_2, hexane/EtOAc (4:1), $R_f \approx 0.46$; IR (neat, NaCl) 1599 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (2H, d, *J* = 8 Hz), 7.34 (2H, d, *J* = 8 Hz), 6.01–6.13 (2H), 5.67 (1H, dt, *J* = 15, 5 Hz), 5.46 (1H, dt, *J* = 15, 5 Hz), 4.19 (2H, br d, *J* = 5 Hz), 4.04 (2H, t, *J* = 7 Hz), 2.45 (3H, s), 2.42 (2H, dt, *J* = 7, 7 Hz), 0.91 (9H, s), 0.07 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.8, 133.1, 132.2, 129.9, 129.2, 128.0, 126.8, 118.3, 69.7, 63.4, 32.1, 26.0, 21.7, 18.5, –5.1; HRMS (FAB, NBA) Calcd. for $C_{20}H_{33}O_4SiS$ [MH^+] *m/z* 397.1869, found 397.1868.

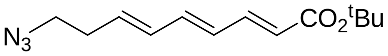


1-(*tert*-Butyldimethylsilyloxy)-7-azidohepta-3(*E*),5(*E*)-diene. NaN_3 (1.74 g, 26.7 mmol) was added to a solution of 7-(*tert*-butyldimethylsilyloxy)hepta-3(*E*),5(*E*)-dienyl 4-methylbenzenesulfonate (**11**) (5.3 g, 13.4 mmol) in DMF (40 mL) at room temperature. After 14 h, the reaction was quenched with H_2O and extracted with toluene. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified via SiO_2 column chromatography (hexane/EtOAc, 4:1) to give 1-(*tert*-butyldimethylsilyloxy)-7-azidohepta-3(*E*),5(*E*)-diene as a pale yellow oil (3.22 g, 90%). TLC: SiO_2, hexane/EtOAc (4:1), $R_f \approx 0.59$; IR (neat, NaCl) 2099 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.26–6.11 (2H, m), 5.76–5.57 (2H, m), 4.21 (2H, d, *J* = 5 Hz), 3.32 (2H, t, *J* = 7 Hz), 2.38 (2H, dt, *J* = 7, 7 Hz), 0.92 (9H, s), 0.08 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.7, 132.2, 129.5, 129.0, 63.6, 51.1, 32.4, 26.2, 18.6, –5.0; HRMS (FAB, NBA) Calcd. for $C_{13}H_{24}N_3OSi$ [$(M-1)^+$] *m/z* 266.1689, found 266.1687.

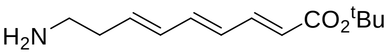
7-Azidohepta-2(*E*),4(*E*)-dien-1-ol. 1*M* solution of *tetra-n*-butylammonium fluoride in THF (43.4 mL, 43.4 mmol) was added to a solution of 1-(*tert*-butyldimethylsilyloxy)-7-azidohepta-3(*E*),5(*E*)-diene (8.3 g, 31.0 mmol) in THF (150 mL) at 0 ºC. After 1 h, the reaction was quenched with water and extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo to give 7-azidohepta-2(*E*),4(*E*)-dien-1-ol which was used without further purification in the next step. TLC: SiO_2, hexane/EtOAc (4:1), $R_f \approx 0.11$; IR (neat, NaCl) 3342, 2099 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.12–6.28 (2H, m), 5.79 (1H, dt, *J* = 14, 6 Hz), 5.66 (1H, dt, *J* = 14, 7 Hz), 4.18 (2H, br d, *J* = 6 Hz), 3.32 (2H, t, *J* = 7 Hz), 2.39 (2H, dt, *J* = 7, 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.5, 131.4, 131.2, 130.1, 63.5, 51.0, 32.4.



7-Azidohepta-2(*E*),4(*E*)-dienal (12). MnO_2 (15.3 g, 88% active, 155 mmol) was added to a mixture of 7-azidohepta-2(*E*),4(*E*)-dien-1-ol and $MgSO_4$ (25 g) in CH_2Cl_2 (400 mL) at room temperature. After 14 h on a mechanical shaker, the reaction mixture was filtered over Celite, and concentrated in vacuo. The residue was purified via SiO_2 column chromatography (hexanes/EtOAc, 5:1) to give 7-azidohepta-2(*E*),4(*E*)-dienal (**12**) as a pale yellow oil (4.3 g, 92% over two steps). TLC: SiO_2, hexane/EtOAc (4:1), $R_f \approx 0.22$; IR (neat, NaCl) 2099.1, 1681.8, 1643.1 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.31 (1H, d, *J* = 8 Hz), 6.90 (1H, dd, *J* = 15, 11 Hz), 6.25–6.15 (1H, m), 6.02 (1H, dt, *J* = 15, 7 Hz), 5.86 (1H, ddd, *J* = 15, 8, 1 Hz), 3.19 (2H, t, *J* = 7 Hz), 2.39 (2H, ddt, *J* = 7, 7, 1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.1, 151.2, 141.1, 130.43, 130.38, 49.4, 32.0; HRMS (FAB, NBA) Calcd. for $C_7H_{10}N_3O$ [MH^+] *m/z* 152.0824, found 152.0825.

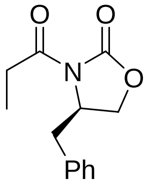


***tert*-Butyl 9-azido-nona-2(*E*),4(*E*),6(*E*)-trienoate.** *tert*-Butyl *P*,*P*-dimethylphosphonoacetate (3.5 mL, 17.7 mmol) was added to a suspension of NaH (739 mg of 60% oil suspension, 18.5 mmol) in THF (250 mL) at 0 ºC with gas evolution. After 1 h, a solution of 7-azidohepta-2(*E*),4(*E*)-dienal (**12**) (2.43 g, 16.1 mmol) in THF (20 mL) was added at 0 ºC. The reaction was stirred for 1h and then quenched with water. The mixture was extracted with EtOAc and the combined organic extracts were dried over Na_2SO_4, concentrated, and the residue was purified via SiO_2 column chromatography (hexane/EtOAc, 4:1) to give *tert*-butyl 9-azido-nona-2(*E*),4(*E*),6(*E*)-trienoate as a pale yellow oil (3.79g, 95%). TLC: SiO_2, hexane/EtOAc (4:1), $R_f \approx 0.43$; IR (neat, NaCl) 2099, 1704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.19 (1H, dd, *J* = 15, 11 Hz), 6.50 (1H, dd, *J* = 15, 11 Hz), 6.29–6.19 (2H, m), 5.85 (1H, dt, *J* = 16, 7 Hz), 5.81 (1H, d, *J* = 16 Hz), 3.36 (2H, t, *J* = 7Hz), 2.44 (2H, dt, *J* = 7, 7Hz), 1.49 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 143.5, 139.6, 134.1, 132.7, 129.6, 123.2, 80.4, 50.8, 32.6, 28.4; HRMS (FAB, NBA) Calcd. for $C_{13}H_{19}N_3O_2$ [M^+] *m/z* 249.1477, found 249.1478.

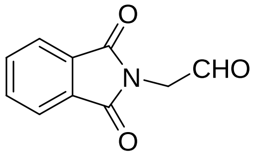


***tert*-butyl-9-amino-nona-2(*E*),4(*E*),6(*E*)-trienoate (13).** Triphenylphosphine (4.23 g, 16.12 mmol) was added to a solution of *tert*-butyl 9-azidonona-2(*E*),4(*E*),6(*E*)-trienoate (3.35 g, 13.44 mmol) in THF/H_2O (4:1; 100 mL) at rt.

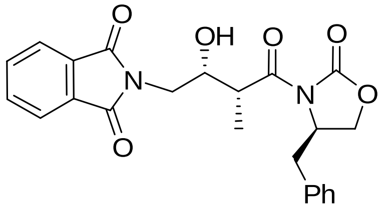
After 20 h, the reaction was quenched with 1N HCl (pH~1-2), washed with toluene, basified with 10% NaOH (pH~11) and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4 and then concentrated to give *tert*-butyl 9-amino-nona-2(*E*),4(*E*),6(*E*)-trienoate (**13**) (2.78 g, 93%). TLC: SiO_2, CH_2Cl_2/MeOH (20:1), $R_f \approx 0.03$; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (1H, dd, *J* = 15, 12 Hz), 6.50 (1H, dd, *J* = 15, 11 Hz), 6.21 (1H, dd, *J* = 15, 11 Hz) 6.18 (1H, dd, *J* = 15, 10 Hz), 5.86 (1H, dt, *J* = 15, 7 Hz), 5.78 (1H, d, *J* = 15 Hz), 2.77 (2H, t, *J* = 7 Hz), 2.27 (2H, dt, *J* = 7, 7 Hz), 1.48 (9H, s), 1.15 (2H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 143.2, 139.7, 136.5, 131.4, 128.1, 122.1, 79.6, 41.1, 36.9, 27.8; HRMS (FAB, NBA) Calcd. for $C_{13}H_{22}NO_2$ [MH^+] *m/z* 224.16505, found 224.1650.



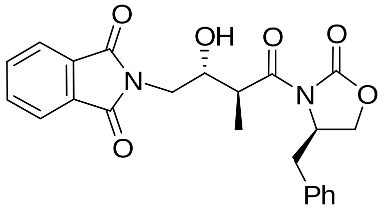
4(*R*)-Benzyl-3-propionyloxazolidin-2-one (21). *n*-BuLi (62.1 mL of 2.5 M THF soln, 155.2 mmol) was added to a solution of 4(*R*)-benzyl-3-propionyloxazolidin-2-one (25 g, 141.1 mmol) in THF (400 mL) at −78 ºC. After 1 h, propanoyl chloride (14.8 mL, 169.3 mmol) was added to the reaction mixture at the same temperature. Then, the reaction was warmed to 0 ºC and stirred for an additional 1 h. The reaction was quenched with saturated aq. NH_4Cl and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified via SiO_2 column chromatography (hexanes/EtOAc, 4:1) to give 4(*R*)-benzyl-3-propionyloxazolidin-2-one (**21**) (32 g, 97%) as a white needle. TLC: SiO_2, hexane/EtOAc (4:1), $R_f \approx 0.29$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.20 (5H, m), 4.71–4.64 (1H, m), 4.24–4.14 (2H, m), 3.31 (1H, dd, *J* = 14, 3 Hz), 3.07–2.85 (2H, m), 2.77 (1H, dd, *J* = 13, 10 Hz), 1.21 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 153.5, 135.4, 129.4, 128.9, 127.2, 66.2, 55.0, 37.8, 29.1, 8.3.



2-(1,3-Dioxoisoindolin-2-yl)acetaldehyde (15). A suspension of 2-(1,3-dioxoisoindolin-2-yl)-ethanol (16.9 g, 88.6 mmol) and IBX (62 g, 221 mmol) in EtOAc (200 mL) was refluxed. After 12 h, the mixture was filtrated with Celite and then concentrated. The residue was dissolved in CH_2Cl_2 and filtered to remove IBX. The filtrate was concentrated to give 2-(1,3-dioxoisoindolin-2-yl)acetaldehyde (**15**) (16 g, 96%) as a white solid. TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.35$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.67 (1H, s), 7.90 (2H, dd, *J* = 5, 3 Hz), 7.77 (2H, dd, *J* = 5, 3 Hz), 4.57 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 167.7, 134.5, 132.1, 123.8, 47.5.



2-((2*R*,3*R*)-4-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (16). 1 M solution of dibutylboran trifluoromethansulfonate (5.5 mL, 5.5 mmol) in CH_2Cl_2 was added to a solution of (*S*)-4-benzyl-3-propionyloxazolidin-2-one (1.16 g, 5.0 mmol) in CH_2Cl_2 (15 mL) at 0˚C followed by *i*-Pr_2NEt (1.05 mL, 6.0 mmol). After stirred for 45min, the reaction mixture was cooled to −78˚C for 10 min. Then, a solution of 2-(1,3-dioxoisoindolin-2-yl)-ethanal (1.04 g, 5.5 mmol) in CH_2Cl_2 (5 mL) was added to the reaction mixture at -78˚C. The reaction was stirred for 1 h at −78˚C, then warmed up to 0˚C and stirred for another 1 h. After quenched with pH = 7 buffer solution, the reaction mixture was extracted with CH_2Cl_2 and the combined organic layer was dried with Na_2SO_4 and concentrated. The residue was purified with silica-gel column chromatography (hexenes/EtOAc 2:1) to give 2-((2*R*,3*R*)-4-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (**16**) (1.9 g, 90%) as a pale yellow foam. TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.35$; $[\alpha]_{20} = +79.6$ (c = 1, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, dd, *J* = 5, 3 Hz), 7.72 (2H, dd, *J* = 5, 3 Hz), 7.35–7.28 (3H, m), 7.21 (2H, br d, *J* = 7 Hz), 4.79–4.73 (1H, m), 4.33–4.27 (2H, m), 4.18 (1H, dd, *J* = 9, 3 Hz), 4.01 (1H, dd, *J* = 14, 6 Hz), 3.84–3.74 (2H), 3.24 (2H, dd, *J* = 14, 3 Hz), 3.05 (2H, d, *J*= 4 Hz), 2.80 (2H, dd, *J* = 14, 9 Hz), 1.40 (3H, d, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 169.2, 153.2, 135.3, 134.4, 132.0, 129.6, 129.1, 127.6, 123.7, 70.8, 66.5, 55.3, 41.7, 40.8, 38.1, 12.9.



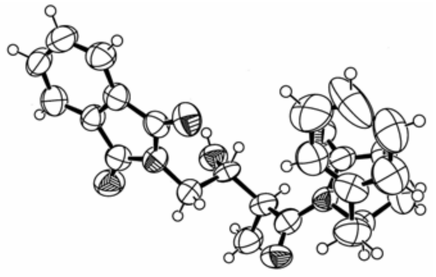
2-((2*R*,3*S*)-4-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (17). 1 M solution of dibutylborane trifluoromethansulfonate (42.9 mL, Aldrich, 1M in CH_2Cl_2, 42.9 mmol) was added to a solution of (*R*)-4-benzyl-3-propionyloxazolidin-2-one (5 g, 21.4 mmol) in CH_2Cl_2 (100 mL) at 0˚C followed by *i*-Pr_2NEt (3.73 mL, 21.4 mmol). After stirred for 40 min, the reaction mixture was cooled to −78˚C for 10 min. Then, a solution of 2-(1,3-dioxoisoindolin-2-yl)acetaldehyde (3.86 g, 20.4 mmol) in CH_2Cl_2 (10 mL) was added to the reaction mixture at −78˚C. The reaction was stirred for 0.5 h at −78ºC, then warmed up to 0˚C and stirred for another 1 h. After quenched with pH = 7 buffer solution, the reaction mixture was extracted with CH_2Cl_2 and the combined organic layer was dried with Na_2SO_4 and concentrated. The residue was purified with silica-gel column chromatography (Hex/EtOAc 2:1) to give 2-((2*R*,3*S*)-4-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (**17**) (3.8 g, 44%) as white solid and 2-((2*S*,3*S*)-4-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (**18**) (4.0 g, 46%) [*non*-Evans syn] as pale yellow foam.

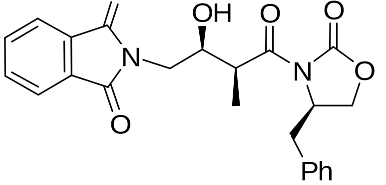
Column purified mixture of the two isomers can also be separated by carefully recrystallization.

Most of the mixture was first dissolved in small amount of warm ethanol (40-50˚C), CH_2Cl_2 was added at same temperature to dissolve all the solid. Most CH_2Cl_2 was then evaporated slowly at 50˚C. The solution was cooled to rt, then left in freezer (–30˚C). 2-((2*R*,3*S*)-4-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (**17**) was recrystallized out and left the other isomer (**18**) in the mother liquor.

2-((2*R*,3*S*)-4-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (17). White solid, mp 179.5-181.6°C; TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.40$; $[\alpha]_{20} = -11.2$ (c = 1, $CHCl_3$); IR (neat, NaCl) 3432.0, 1773.7, 1708.3, 1638.1 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (2H, dd, *J* = 5, 3 Hz), 7.73 (2H, dd, *J* = 5, 3 Hz), 7.36–7.26 (5H, m), 4.70–4.65 (1H, m), 4.18–4.17 (2H, m), 4.07–3.87 (4H, m), 3.51 (1H, d, *J*= 8 Hz), 3.50 (1H, dd, *J* = 14, 3 Hz), 2.83 (1H, dd, *J* = 14, 10 Hz), 1.35 (3H, d, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 168.8, 153.4, 135.7, 134.3, 132.1, 129.6, 129.1, 127.4, 123.6, 73.1, 66.2, 55.9, 42.0, 40.3, 37.7, 14.6. HRMS (FAB, NBA) Calcd. for $C_{23}H_{23}N_2O_6$ $[MH^+]$ *m/z* 423.1556, found 423.1553.

Absolute structure of compound **1**7 was confirmed by X-Ray:





2-((2*S*,3*S*)-4-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (18). TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.38$; $[\alpha]_{20} = +1.2$ (c = 1, $CHCl_3$);^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (2H, dd, *J* = 6, 3 Hz), 7.72 (2H, dd, *J* = 6, 3 Hz), 7.36–7.24 (5H, m), 4.69–4.64 (1H, m), 4.37–4.33 (1H, m), 4.18–4.17 (2H, m), 3.97 (1H, dd, *J*= 14, 7 Hz), 3.91 (1H, dd, *J*= 7, 5 Hz), 3.85 (1H, dd, *J*= 14, 5 Hz), 3.43 (1H, dd, *J*= 13, 4 Hz), 3.10 (1H, d, *J* = 5 Hz), 2.79 (1H, dd, *J* = 14, 10 Hz), 1.35 (3H, d, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 169.0, 153.2, 135.6, 134.3, 132.1, 129.6, 129.1, 127.5, 123.6, 70.3, 66.4, 55.7, 41.5, 40.7, 38.0, 11.6.

The stereochemistry of the syn isomers were confirmed by comparison of $J_{2\text{-}3}$ values of ^1H NMR of corresponding methyl ester, obtained by treatment with NaOMe, with reported values[1]:

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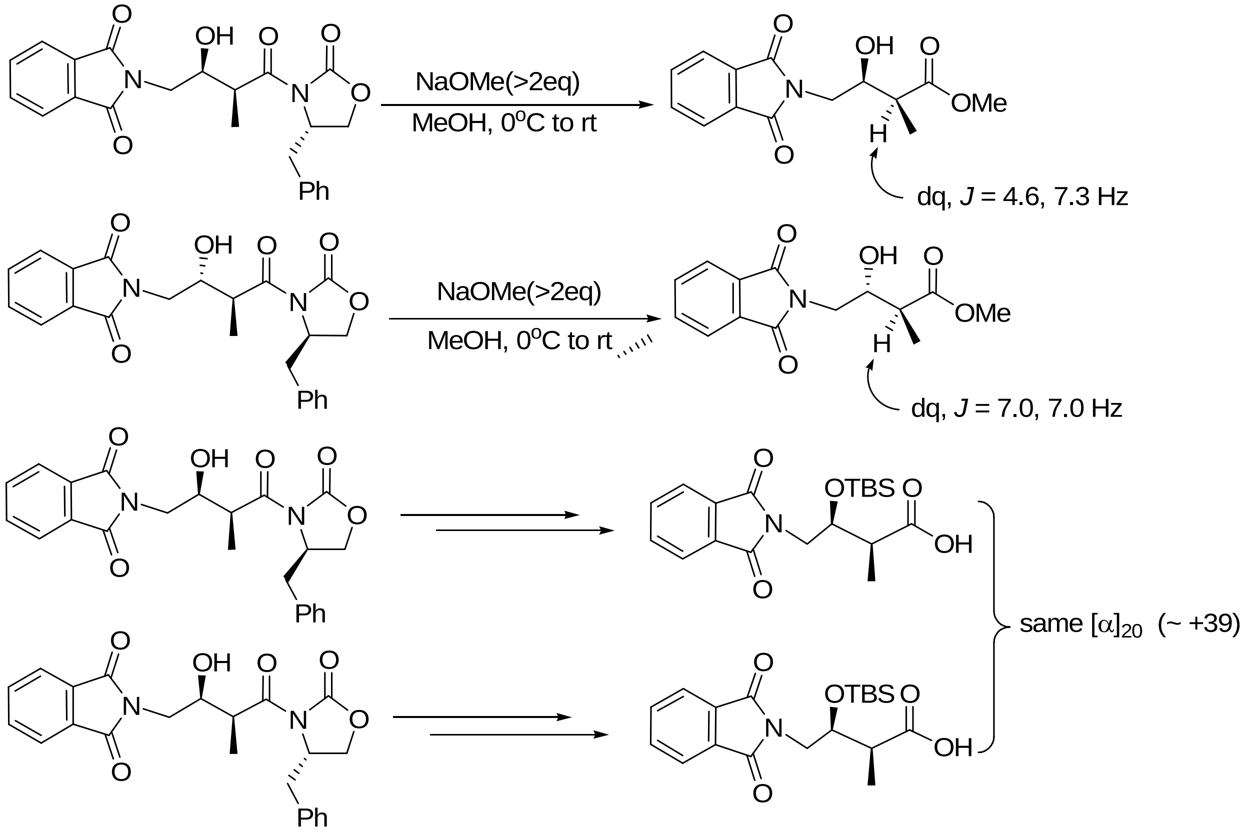
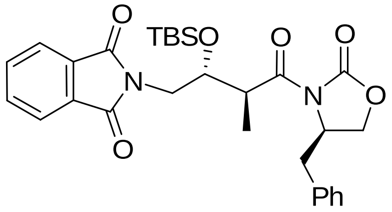
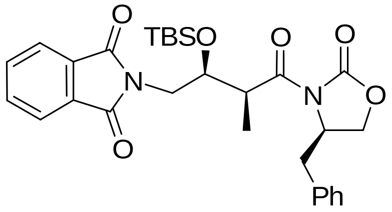
[1] P. O.Gallagher, C. S. P.McErlean, M. F.Jacobs, D. J.Watters, W. Kitching, *Tetrahedron. Lett.* **2002**, *43*, 531-535.

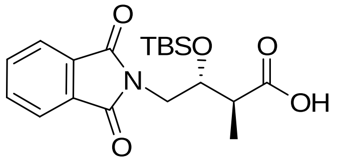




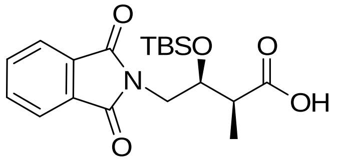
2-((2*R*,3*S*)-4-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-2-(tert-butyldimethylsilyloxy)-3-methyl-4-oxobutyl)isoindoline-1,3-dione. TBSOTf (2.409 mL, 9.114 mmol) was added to a solution of 2-((2*R*,3*S*)-4-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-2-hydroxy-3-methyl-4-oxobutyl)isoindoline-1,3-dione (3.5 g, 8.285 mmol) in CH_2Cl_2 (80 mL) at 4˚C. After stirred for 9 h at 4˚C, the reaction was quenched with pH 7 buffer and extracted with CH_2Cl_2. The combined organic extracts were washed with 20% aq. citric acid and brine. Then, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified via SiO_2 column chromatography (hexanes/EtOAc 2:1) to give 2-((2*R*,3*S*)-4-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-2-(tert-butyldimethylsilyloxy)-3-methyl-4-oxobutyl)isoindoline-1,3-dione (4.42 g, 99%) as white foam. TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.63$; $[\alpha]_{20} = +13.2$ (c = 1, $CHCl_3$); IR (neat, NaCl) 1779, 1716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.84 (2H, dd, *J* = 5, 3 Hz), 7.70 (2H, dd, *J* = 5, 3 Hz), 7.36–7.26 (5H, m), 4.75–4.70 (1H, m), 4.62 (1H, ddd, *J* = 9, 4, 3 Hz), 4.24–4.20 (2H, m), 4.10 (1H, dd, *J*= 7, 4 Hz), 3.99 (1H, dd, *J* = 14, 10 Hz), 3.54 (1H, dd, *J*= 14, 3 Hz), 3.44 (1H, dd, *J*= 14, 3 Hz), 2.86 (1H, dd, *J* = 14, 11 Hz), 1.34 (3H, d, *J* = 7 Hz), 0.79 (9H, s), 0.11 (3H, s), –0.22 (3H, s); ^{13}C NMR (75Hz, $CDCl_3$) δ 173.6, 168.2, 153.0, 135.6, 134.0, 132.0, 129.4, 128.9, 127.2, 123.1, 68.2, 66.3, 55.5, 43.4, 40.5, 38.0, 25.6, 17.7, 9.2, –4.8, –5.4; HRMS (FAB, NBA) Calcd. for $C_{29}H_{37}N_2O_6Si$ [MH^+] *m/z* 537.2421, found 537.2425.



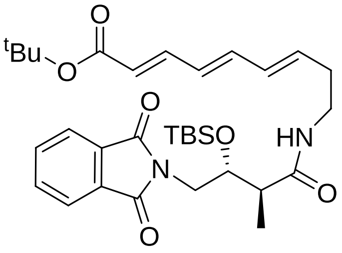
2-((2*S*,3*S*)-4-((*R*)-4-Bbenzyl-2-oxooxazolidin-3-yl)-2-(tert-butyldimethylsilyloxy)-3-methyl-4-oxobutyl)isoindoline-1,3-dione. TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.60$; $[\alpha]_{20} = +18.0$ (c = 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.84 (2H, dd, *J* = 5, 3 Hz), 7.70 (2H, dd, *J* = 5, 3 Hz), 7.36–7.26 (5H, m), 4.75–4.70 (1H, m), 4.62 (1H, ddd, *J* = 9, 4, 3 Hz), 4.24–4.20 (2H, m), 4.10 (1H, dd, *J*= 7, 4 Hz), 3.99 (1H, dd, *J* = 14, 10 Hz), 3.54 (1H, dd, *J*= 14, 3 Hz), 3.44 (1H, dd, *J*= 14, 3 Hz), 2.86 (1H, dd, *J* = 14, 11 Hz), 1.34 (3H, d, *J* = 7 Hz), 0.79 (9H, s), 0.11 (3H, s), –0.22 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 168.2, 153.0, 135.6, 134.0, 132.0, 129.4, 128.9, 127.2, 123.1, 68.2, 66.3, 55.5, 43.4, 40.5, 38.0, 25.6, 17.7, 9.2, –4.8, –5.4.



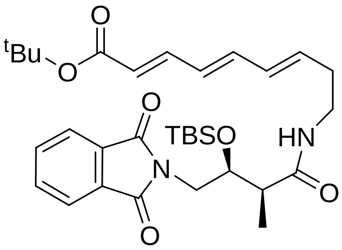
(2*S*,3*R*)-3-(tert-Butyldimethylsilyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbutanoic acid (19). LiOH·H_2O (340 mg. 8.105 mmol) was added to a solution of 2-((2*R*,3*S*)-4-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-2-(tert-butyldimethylsilyloxy)-3-methyl-4-oxobutyl)isoindoline-1,3-dione (4.35 g, 8.105 mmol) and H_2O_2 (2.76 mL, 30% w/v, 24.32 mmol) in THF at 4ºC. After 17h, the reaction was quenched with aq. $NaHSO_3$ solution (to pH~3) then extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified with SiO_2 column chromatography (hexanes/EtOAc 1:1) to give (2S,3R)-3-(tert-butyldimethylsilyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbutanoic acid (**19**) (1.9 g, 89%) as white solid. mp 161-165°C; TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.29$; $[\alpha]_{20} = -9.4$ (c = 1, $CHCl_3$); IR (neat, NaCl) 3500-2400 (br), 1776, 1716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (2H, dd, *J* = 5, 3 Hz), 7.70 (2H, dd, *J* = 5, 3 Hz), 4.40 (1H, ddd, *J* = 10, 5, 4 Hz), 3.79 (2H, dd, *J*= 7, 6 Hz), 2.69 (1H, dd, *J*= 7, 5 Hz), 1.26 (3H, d, *J* = 7 Hz), 0.81 (9H, s), 0.05 (3H, s), –0.11 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.9, 168.4, 134.2, 132.2, 123.5, 70.3, 44.6, 41.1, 25.8, 17.9, 11.3, –4.6, –4.9; HRMS (FAB, NBA) Calcd. for $C_{19}H_{28}NO_5Si$ $[MH^+]$ *m/z* 378.1737, found 378.1734.



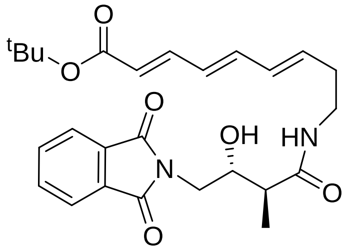
(2*S*,3*S*)-3-(tert-Butyldimethylsilyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbutanoic acid (20). White solid, mp 184-185°C; TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.31$; $[\alpha]_{20} = +39.3$ (c = 0.56, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, dd, *J* = 5, 3 Hz), 7.73 (2H, dd, *J* = 5, 3 Hz), 4.40 (1H, ddd, *J* = 7, 7, 3 Hz), 3.76 (2H, dd, *J*= 7, 7 Hz), 2.55-2.49 (1H, m), 1.28 (3H, d, *J* = 7 Hz), 0.84 (9H, s), 0.04 (3H, s), –0.02 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.3, 168.4, 134.3, 132.1, 123.6, 70.2, 43.2, 41.5, 25.8, 18.0, 9.7,



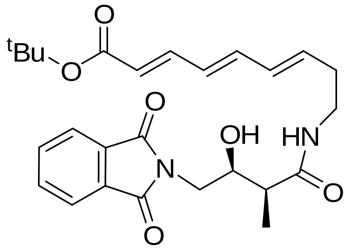
(2*E*, 4*E*, 6*E*)-*tert*-Butyl 9-((2*S*,3*R*)-3-(*tert*-butyldimethylsilyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbutanamido)nona-2,4,6-trienoate. 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide (657 mg, Alfa Aesar, 4.23 mmol) and 1-hydroxybenzotriazote (484 mg, Aldrich, 3.58 mmol) were added to a solution of (2*S*,3*R*)-3-(tert-butyldimethylsilyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbutanoic acid (1.229 g, 3.26 mmol) and (2*E*,4*E*,6*E*)-tert-butyl 9-aminonona-2,4,6-trienoate (0.80 g, 3.58 mol) in CH_2Cl_2 (25 mL) at rt. After 2h, the reaction was quenched with aq. 20% citric acid solution and extracted with CH_2Cl_2. The combined organic extracts were washed with sat. Na_2CO_3 and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified with SiO_2 column chromatography (hexanes/EtOAc 1:1) to give (2*E*, 4*E*, 6*E*)-*tert*-butyl 9-((2*S*,3*R*)-3-(*tert*-butyldimethylsilyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbutanamido)nona-2,4,6-trienoate as a pale yellow foam (1.85 g, 97%). TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.34$; $[\alpha]_{20} = -23.0$ (c = 1, $CHCl_3$); IR (neat, NaCl) 3356, 1775, 1715.9 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, dd, *J* = 6, 3 Hz), 7.73 (2H, dd, *J* = 6, 3 Hz), 7.17 (1H, dd, *J* = 15, 11 Hz), 6.83 (1H, br t, *J* = 6Hz), 6.51 (1H, dd, *J* = 15, 11 Hz), 6.24 (1H, dd, *J* = 15, 11 Hz), 6.20 (1H, dd, *J* = 15, 11 Hz), 5.92 (1H, dt, *J* = 15, 7 Hz), 5.77 (1H, d, *J* = 15 Hz), 4.16 (1H, td, *J* = 7, 3 Hz), 3.79 (1H, dd, *J* = 6, 6 Hz), 3.50-3.42 (1H, m), 3.36-3.30 (1H, m), 2.45-2.36 (3H, m), 1.48 (9H, s), 1.24 (3H, d, *J* = 7 Hz), 0.88 (9H, s), 0.09 (3H, s), –0.04 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 168.5, 166.7, 143.7, 140.1, 136.0, 134.4, 132.3, 132.1, 129.0, 123.6, 122.8, 80.3, 71.6, 44.8, 42.0, 38.6, 33.3, 28.4, 26.0, 18.1, 16.0, –4.3, –4.6; HRMS (FAB, NBA) Calcd. for $C_{32}H_{47}N_2O_6Si$ [MH^+] *m/z* 583.32035, found 583.3201.



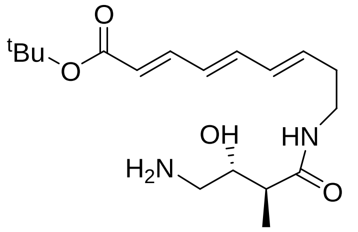
(2*E*,4*E*,6*E*)-tert-Butyl 9-((2*S*,3*S*)-3-(tert-butyldimethylsilyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbutanamido)nona-2,4,6-trienoate. TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.35$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (2H, dd, *J* = 5, 3 Hz), 7.72 (2H, dd, *J* = 5, 3 Hz), 7.16 (1H, dd, *J* = 15, 11 Hz), 6.61 (1H, br t, *J* = 6 Hz), 6.51 (1H, dd, *J* = 15, 11 Hz), 6.21 (1H, dd, *J* = 15, 11 Hz), 6.19 (1H, dd, *J* = 15, 11 Hz), 5.91 (1H, dt, *J* = 15, 7 Hz), 5.75 (1H, d, *J* = 15 Hz), 4.20 (1H, td, *J* = 7, 5 Hz), 3.74 (2H, dd, *J* = 8, 6 Hz), 3.51-3.40 (1H, m), 3.31-3.20 (1H, m), 2.48 (1H, dd, *J* = 7, 5 Hz), 2.40 (2H, dd, *J* = 7, 7 Hz), 1.48 (9H, s)1.22 (3H, d, *J* = 8 Hz), 0.80 (9H, s), –0.02 (3H, s), –0.12 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 168.1, 166.3, 143.4, 139.9, 135.7, 134.0, 131.91, 131.89, 128.6, 123.0, 122.4, 79.9, 71.3, 44.8, 40.4, 38.5, 33.0, 28.1, 25.6, 17.6, 12.9, –4.9, –5.0.



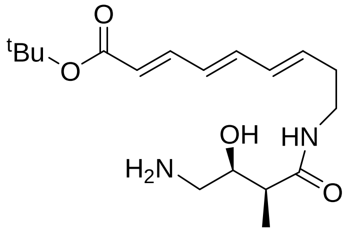
(2*E*, 4*E*, 6*E*)-tert-Butyl 9-((2*S*,3*R*)-4-(1,3-dioxoisoindolin-2-yl)-3-hydroxy-2-methylbutanamido)nona-2,4,6-trienoate. 1.0M TBAF in THF (2.2 mL, 2.24 mmol) was added to a solution of (2*E*, 4*E*, 6*E*)-*tert*-butyl 9-((2*S*,3*R*)-3-(*tert*-butyldimethylsilyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbutanamido)nona-2,4,6-trienoate (0.87 g, 1.49 mmol) and AcOH (172 μL, 2.99 mmol) in THF (30 mL) at rt. After stirred for 15h (followed by TLC), the reaction was quenched with water and extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified with SiO_2 column chromatography (EtOAc) to give (2*E*, 4*E*, 6*E*)-tert-butyl 9-((2*S*,3*R*)-4-(1,3-dioxoisoindolin-2-yl)-3-hydroxy-2-methylbutanamido)nona-2,4,6-trienoate as white foam (0.64 g, 91%). TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.07$; $[\alpha]_{20} = +6.2$ (c = 1, $CHCl_3$); IR (neat, NaCl) 3348, 1773, 1714 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (2H, br d, *J* = 3 Hz), 7.62 (1H, br d, *J* = 3 Hz), 7.04 (1H, dd, *J* = 15, 11 Hz), 6.72 (1H, b s), 6.40 (1H, dd, *J* = 15, 11 Hz), 6.16–6.04 (2H, m), 5.79 (1H, dt, *J* = 15, 7 Hz), 5.63 (1H, d, *J* = 15 Hz), 4.36(1H, br s), 3.84–3.710 (2H, m), 3.61 (2H, dd, *J* = 13, 4 Hz), 3.32–3.24 (2H, m), 2.34-2.26 (3H, m), 1.38 (9H, s) 1.20 (3H, d, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3, 168.9, 166.6, 143.5, 139.9, 135.4, 134.4, 132.5, 132.0, 129.1, 123.6, 122.9, 80.4, 72.5, 43.1, 42.8, 38.7, 33.2, 28.3, 16.1; HRMS (FAB, NBA) Calcd. for $C_{26}H_{33}N_2O_6$ $[MH^+]$ *m/z* 469.2339, found 469.2337.



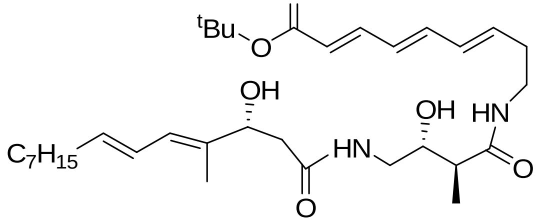
(2*E*,4*E*,6*E*)-tert-Butyl 9-((2*S*,3*S*)-4-(1,3-dioxoisoindolin-2-yl)-3-hydroxy-2-methylbutanamido)nona-2,4,6-trienoate. TLC: SiO_2, hexane/EtOAc (1:1), $R_f \approx 0.08$; $[\alpha]_{20} = -4.4$ (c = 0.36, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.80-7.76 (2H, m), 7.72-7.68 (2H, m), 7.11 (1H, dd, *J* = 15, 11 Hz), 6.73 (1H, t, *J* = 5 Hz), 6.47 (1H, dd, *J* = 15, 11 Hz), 6.22–6.12 (2H, m), 5.85 (1H, dt, *J* = 15, 7 Hz), 5.71 (1H, d, *J* = 15 Hz), 4.19-4.14 (2H, m), 3.81-3.70 (2H, m), 3.41–3.25 (2H, m), 3.45 (1H, dd, *J* = 7, 4 Hz), 2.41-2.34 (2H, m), 1.47(9H, s) 1.26 (3H, d, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2, 168.7, 166.5, 143.5, 139.8, 135.5, 134.2, 132.2, 131.9, 128.9, 123.3, 122.6, 80.2, 70.4, 43.5, 41.3, 38.5, 33.0, 28.2, 12.2.



(2*E*,4*E*,6*E*)-tert-Butyl 9-((2*S*,3*R*)-4-amino-3-hydroxy-2-methylbutanamido)nona-2,4,6-trienoate (22). The reaction mixture of (2*E*, 4*E*, 6*E*)-tert-butyl 9-((2*S*,3*R*)-4-(1,3-dioxoisoindolin-2-yl)-3-hydroxy-2-methylbutanamido)nona-2,4,6-trienoate (365 mg, 0.779 mol) and $NH_2NH_2 \cdot H_2O$ (1.89 mL, 38.9 mmol) in EtOH (20 mL) was stirred for 5 min (followed by TLC) at 45°C. After diluted with CH_2Cl_2, the reaction was quenched with sat. Na_2CO_3 aq. The mixture was extracted with CH_2Cl_2 and the combined organic extracts were dried over K_2CO_3 and then concentrated in vacuo to give (2*E*,4*E*,6*E*)-tert-butyl 9-((2*S*,3*R*)-4-amino-3-hydroxy-2-methylbutanamido)nona-2,4,6-trienoate (**22**) as pale yellow oil (quantitative yield). TLC: SiO_2, CH_2Cl_2/MeOH (10:1), $R_f \approx 0.01$; $[\alpha]_{20} = +22.3$ (c = 0.36, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (1H, dd, *J* = 15, 11 Hz), 6.81 (1H, b s), 6.41 (1H, dd, *J* = 15, 11 Hz), 6.18–6.06 (2H, m), 5.76 (1H, dt, *J* = 15, 7 Hz), 5.71 (1H, d, *J* = 15 Hz), 3.52–3.44 (1H, m), 3.30–3.15 (2H, m), 3.03 (3H, br s), 2.71 (1H, br d, *J* = 11 Hz), 2.58–2.50 (1H, m), 2.30-2.22 (3H, m), 1.41 (9H, s), 1.09 (3H, d, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8, 166.6, 143.5, 139.8, 135.6, 132.1, 128.9, 122.8, 80.3, 73.9, 45.5, 44.3, 38.5, 33.1, 28.2, 15.3; HRMS (FAB, NBA) Calcd. for $C_{18}H_{31}N_2O_4$ [MH^+] *m/z* 339.2284, found 339.2289.

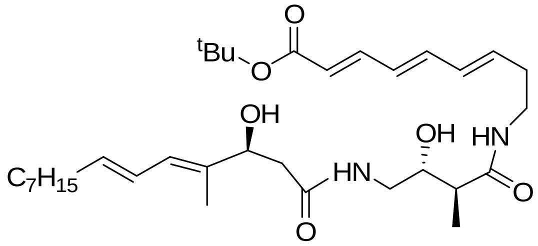


(2*E*,4*E*,6*E*)-tert-Butyl 9-((2*S*, 3*S*)-4-amino-3-hydroxy-2-methylbutanamido)nona-2,4,6-trienoate. TLC: SiO_2, CH_2Cl_2/MeOH (10:1), $R_f \approx 0.01$; $[\alpha]_{20} = +15$ (c=0.2, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (1H, dd, *J* = 15, 11 Hz), 6.81 (1H, b s), 6.41 (1H, dd, *J* = 15, 11 Hz), 6.18–6.06 (2H, m), 5.76 (1H, dt, *J* = 15, 7 Hz), 5.71 (1H, d, *J* = 15 Hz), 3.52–3.44 (1H, m), 3.30–3.15 (2H, m), 3.03 (3H, br s), 2.71 (1H, br d, *J* = 11 Hz), 2.58–2.50 (1H, m), 2.30-2.22 (3H, m), 1419Hs 1.09 (3H, d, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 166.6, 143.5, 139.8, 135.6, 132.2, 129.0, 122.9, 80.4, 72.9, 44.3, 43.9, 38.5, 33.2, 28.3, 12.7.

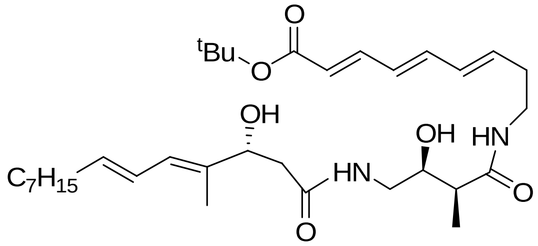


(2*E*,4*E*,6*E*)-*tert*-Butyl 9-((2*S*,3*R*)-3-hydroxy-4-((*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoate (23). EDC (164 mL, 0.925 mmol) was added to a solution of (2*E*,4*E*,6*E*)-

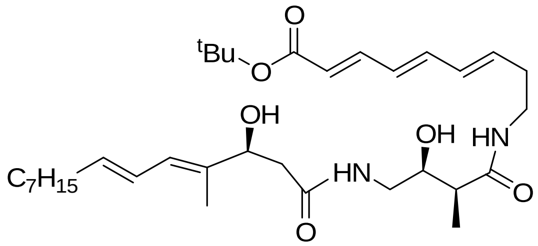
tert-butyl 9-((2*S*,3*R*)-4-amino-3-hydroxy-2-methylbutanamido)nona-2,4,6-trienoate (265 mg, 0.783 mmol), (*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienoic acid (181 mg, 0.712 mmol) and 1-hydroxybenzotriazote (106 mg, 0.783 mmol) in CH_2Cl_2 (20 mL) at room temperature. After 2.5 h, the reaction was quenched with aq. 20% citric acid solution and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified via SiO_2 column chromatography (CH_2Cl_2 to CH_2Cl_2/MeOH 20;1) to give (2*E*,4*E*,6*E*)-*tert*-butyl 9-((2*S*,3*R*)-3-hydroxy-4-((*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoate (**23**) as a pale yellow oil (376 mg, 92%). TLC: SiO_2, CH_2Cl_2/MeOH (10:1), $R_f \approx 0.40$; $[\alpha]_{20} = -10.4$ (c=1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.23 (1H, br s), 7.17 (1H, dd, *J* = 15, 11 Hz), 6.90 (1H, br s), 6.48 (1H, dd, *J* = 15, 11 Hz), 6.23-6.14 (3H, m), 6.05 (1H, d, *J* = 11 Hz), 5.83 (1H, dt, *J* = 15, 7 Hz), 5.79 (1H, d, *J* = 16 Hz), 5.69 (1H, dt, *J* = 16, 7 Hz), 4.87 (1H, br d, *J* = 5 Hz), 4.44 (1H, d, *J* = 9 Hz), 4.40 (1H, br s), 3.74 (1H, br s), 3.63 (1H, br s), 3.38-3.30 (1H, m), 3.28-3.22 (1H, m), 2.98-2.92 (1H, m), 2.49-2.30 (5H, m), 2.09 (1H, dt, *J* = 7, 7 Hz), 1.72 (3H, s), 1.48 (9H, s), 1.40-1.20 (10H, m), 1.19 (3H, d, *J* = 7 Hz), 0.88 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 173.0, 166.7, 143.6, 139.9, 136.0, 135.7, 135.4, 132.2, 129.1, 125.8, 125.5, 122.9, 80.4, 73.8, 72.8, 44.1, 44.0, 41.9, 38.7, 33.2, 33.1, 32.0, 29.6, 29.4, 29.3, 28.3, 22.8, 15.5, 14.2, 12.8; HRMS (FAB, NBA) Calcd. for $C_{33}H_{54}N_2O_6$ [M^+] *m/z* 574.3982, found 574.3979.



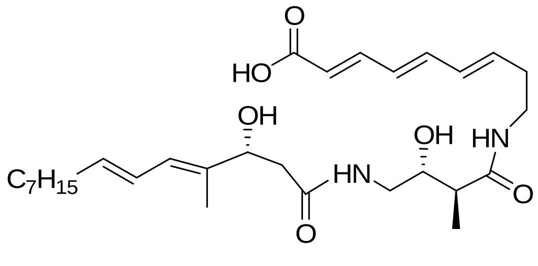
(2*E*,4*E*,6*E*)-tert-Butyl 9-((2*S*,3*R*)-3-hydroxy-4-((*S*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoate. TLC: SiO_2, CH_2Cl_2/MeOH (10:1), $R_f \approx 0.37$; $[\alpha]_{20} = 0.6$ (c=1.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (1H, dd, *J* = 15, 11 Hz), 6.91 (1H, br s), 6.73 (1H, br t, *J* = 5 Hz), 6.62 (1H, dd, *J* = 15, 11 Hz), 6.24-6.15 (3H, m), 6.05 (1H, d, *J* = 11 Hz), 5.82 (1H, dt, *J* = 15, 7 Hz), 5.79 (1H, d, *J* = 16 Hz), 5.68 (1H, dt, *J* = 15, 7 Hz), 4.69 (1H, br s), 4.42 (1H, br d, *J* = 8 Hz), 3.99 (1H, br s), 3.69-3.64 (1H, m), 3.46-3.42 (1H, m), 3.35-3.28 (2H, m), 3.25-3.20 (1H, m), 2.45-2.30 (5H, m), 2.08 (1H, dd, *J* = 14, 7 Hz), 1.72 (3H, s), 1.48 (9H, s), 1.40-1.24 (10H, m), 1.20 (3H, d, *J* = 7 Hz), 0.87 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 173.2, 166.7, 143.6, 139.9, 136.1, 135.6, 135.4, 132.3, 129.2, 125.8, 125.7, 123.0, 80.5, 73.8, 73.2, 44.0, 43.6, 42.0, 38.7, 33.20, 33.16, 32.0, 29.6, 29.41, 29.35, 28.3, 22.8, 15.7, 14.3, 12.8; HRMS (FAB, NBA) Calcd. for $C_{33}H_{54}N_2O_6$ [M^+] *m/z* 574.3982, found 574.3977.



(2*E*,4*E*,6*E*)-tert-Butyl 9-((2*S*,3*S*)-3-hydroxy-4-((*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoate. TLC: SiO$_2$, CH$_2$Cl$_2$/MeOH (10:1), R$_f$ ≈ 0.40; $[\alpha]_{20}$ = +15.5 (c=0.85, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.17 (1H, dd, *J* = 15, 11 Hz), 6.92 (1H, br s), 6.65 (1H, br s), 6.48 (1H, dd, *J* = 15, 11 Hz), 6.25-6.15 (3H, m), 6.05 (1H, d, *J* = 11 Hz), 5.83 (1H, dt, *J* = 15, 7 Hz), 5.79 (1H, d, *J* = 15 Hz), 5.69 (1H, dt, *J* = 15, 7 Hz), 4.67 (1H, br s), 4.42 (1H, br d, *J* = 6 Hz), 3.96 (1H, br s), 3.86-3.80 (1H, m), 3.38-3.26 (4H, m), 2.98-2.92 (1H, m), 2.47-2.28 (5H, m), 2.09 (1H, dd, *J* = 14, 7 Hz), 1.72 (3H, s), 1.48 (9H, s), 1.40-1.24 (10H, m), 1.16 (3H, d, *J* = 7 Hz), 0.88 (3H, t, *J* = 6 Hz); ^{13}C NMR (75 MHz, CDCl$_3$) δ 175.6, 173.5, 166.7, 143.6, 139.9, 136.0, 135.7, 135.5, 132.2, 129.1, 125.8, 125.6, 122.8, 80.4, 73.8, 72.1, 44.1, 43.4, 42.2, 38.8, 33.2, 33.1, 32.0, 29.6, 29.4, 29.3, 28.3, 22.8, 14.2, 13.1, 12.8.

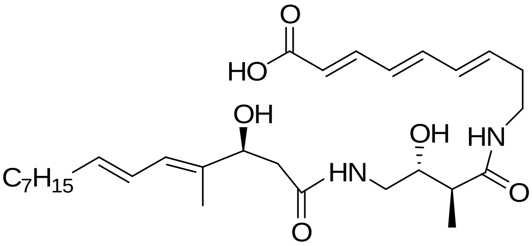


(2*E*,4*E*,6*E*)-tert-Butyl 9-((2*S*,3*S*)-3-hydroxy-4-((*S*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoate. TLC: SiO$_2$, CH$_2$Cl$_2$/MeOH (10:1), R$_f$ ≈ 0.40; $[\alpha]_{20}$ = −53.3 (c=0.08, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.18 (1H, dd, *J* = 15, 11 Hz), 6.88 (1H, br t, *J* = 6 Hz), 6.59 (1H, br t, *J* = 6 Hz), 6.48 (1H, dd, *J* = 15, 11 Hz), 6.25-6.15 (3H, m), 6.06 (1H, d, *J* = 11 Hz), 5.83 (1H, dt, *J* = 15, 7 Hz), 5.79 (1H, d, *J* = 15 Hz), 5.70 (1H, dt, *J* = 15, 7 Hz), 4.65 (1H, br s), 4.42 (1H, br d, *J* = 6 Hz), 3.88-3.84 (2H, m), 3.48-3.43 (1H, m), 3.32 (2H, dd, *J* = 12, 6 Hz), 3.19-3.13 (1H, m), 2.46-2.33 (5H, m), 2.09 (1H, dd, *J* = 14, 7 Hz), 1.73 (3H, s), 1.48 (9H, s), 1.40-1.24 (10H, m), 1.16 (3H, d, *J* = 7 Hz), 0.88 (3H, t, *J* = 76 Hz); ^{13}C NMR (75 MHz, CDCl$_3$) δ 175.6, 173.5, 166.7, 143.6, 139.9, 136.1, 135.6, 135.5, 132.2, 129.1, 125.8, 125.6, 122.9, 80.4, 73.8, 72.0, 44.1, 43.6, 42.1, 38.7, 33.2, 33.1, 32.0, 29.6, 29.4, 29.3, 28.3, 22.8, 14.3, 12.9, 12.8.

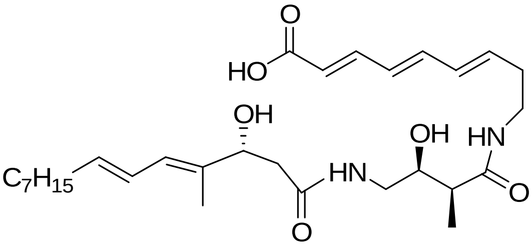


(2*E*,4*E*,6*E*)-9-((2*S*,3*R*)-3-Hydroxy-4-((*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoic acid. TMSOTf (218 mL, 1.13 mmol) was added to a solution of (2*E*,4*E*,6*E*)-*tert*-butyl 9-((2*S*,3*R*)-3-hydroxy-4-((*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoate (95 mg, 0.165 mmol) and 2,6-lutidine (262 mL, 2.26 mmol) in CH$_2$Cl$_2$ (8 mL) at 0^{o}C. After 2h (followed by TLC), 15 mL of MeOH was added to the reaction solution, and then citric acid (620 mg, 3.226 mmol) was added, the reaction was moved to cold room (4 ^{o}C). After 14h, the reaction was quenched with water and extracted with CH$_2$Cl$_2$. The combined organic extracts were washed with brine, dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified with PTLC (CH$_2$Cl$_2$/MeOH 10:1) to give (2*E*,4*E*,6*E*)-9-((2*S*,3*R*)-3-

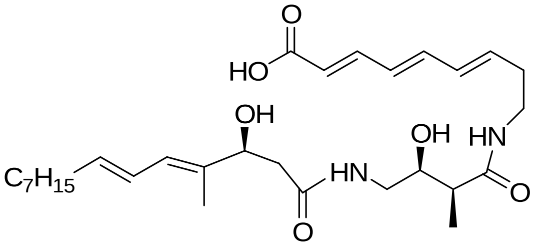
hydroxy-4-((*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoic acid as a pale yellow foam (78 mg, 91%). TLC: SiO_2, CH_2Cl_2/MeOH (10:1), $R_f \approx 0.18$; $[\alpha]_{20} = +7.7$ (c=1.2, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ (1H, dd, *J* = 15, 11 Hz), 6.37 (1H, dd, *J* = 14, 11 Hz), 6.19-6.08 (3H, m), 5.92 (1H, d, *J* = 11 Hz), 5.77 (1H, d, *J* = 15 Hz), 5.74 (1H, dt, *J* = 15, 7 Hz), 5.56 (1H, dt, *J* = 15, 7 Hz), 4.31 (1H, dd, *J* = 8, 5 Hz), 3.61-3.56 (1H, m), 3.30 (1H, dd, *J* = 14, 4 Hz), 3.15 (2H, dd, *J* = 7, 7 Hz), 3.03 (1H, dd, *J* = 14, 7 Hz), 2.36-2.20 (5H, m), 1.99 (2H, dd, *J* = 14, 7 Hz), 1.63 (3H, s), 1.30-1.14 (10H, m), 1.00 (3H, d, *J* = 7 Hz), 0.78 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 177.6, 174.9 (br), 174.4, 142.5, 139.5, 137.4, 136.3, 135.6, 133.5, 131.0, 128.0, 127.4, 126.9, 75.2, 73.4, 45.5, 44.6, 43.3, 39.9, 34.1, 34.0, 33.1, 30.7, 30.43, 30.41, 23.8, 15.3, 14.6, 12.5; HRMS (FAB, Gly) Calcd. for $C_{29}H_{47}N_2O_6$ [MH$^+$] *m/z* 519.3434, found 519.3437.



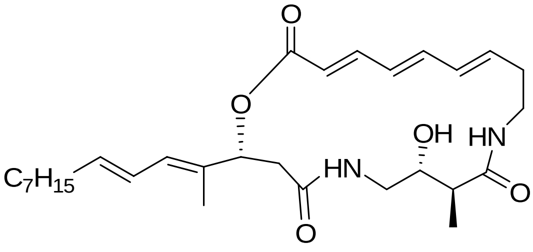
(2*E*,4*E*,6*E*)-9-((2*S*,3*R*)-3-Hydroxy-4-((*S*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoic acid. TLC: SiO_2, CH_2Cl_2/MeOH (10:1), $R_f \approx 0.18$; $[\alpha]_{20} = +12.8$ (c=1.65, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 7.03 (1H, dd, *J* = 15, 11 Hz), 6.44 (1H, dd, *J* = 15, 10 Hz), 6.28-6.18 (3H, m), 6.05 (1H, d, *J* = 11 Hz), 5.91 (1H, d, *J* = 15 Hz), 5.83 (1H, dt, *J* = 15, 7 Hz), 5.67 (1H, dt, *J* = 15, 7 Hz), 4.42 (1H, dd, *J* = 8, 5 Hz), 3.71-3.67 (1H, m), 3.38 (1H, dd, *J* = 14, 4 Hz), 3.32-3.19 (3H, m), 2.49-2.32 (5H, m), 2.11 (2H, dd, *J* = 14, 7 Hz), 1.75 (3H, s), 1.42-1.25 (10H, m), 1.12 (3H, d, *J* = 7 Hz), 0.90 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 177.5, 175.8, 174.4, 141.5, 138.8, 137.4, 136.3, 135.1, 133.6, 131.2, 129.4, 127.4, 126.9, 75.2, 73.5, 45.4, 44.5, 43.3, 39.9, 34.1, 34.0, 33.1, 30.7, 30.42, 30.40, 23.8, 15.3, 14.6, 12.5; HRMS (FAB, NBA) Calcd. for $C_{29}H_{46}N_2O_6Na$ [MNa$^+$] *m/z* 541.3254, found 541.3258.



(2*E*,4*E*,6*E*)-9-((2*S*,3*S*)-3-Hydroxy-4-((*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoic acid. TLC: SiO_2, CH_2Cl_2/MeOH (10:1), $R_f \approx 0.18$; $[\alpha]_{20} = +14.5$ (c=0.55, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 7.96 (1H, t, *J* = 6 Hz), 7.86 (1H, t, *J* = 6 Hz), 7.29 (1H, dd, *J* = 15, 11 Hz), 6.61 (1H, dd, *J* = 15, 11 Hz), 6.32 (1H, dd, *J* = 15, 11 Hz), 6.27 (1H, dd, *J* = 15, 11 Hz), 6.26 (1H, dd, *J* = 15, 11 Hz), 6.05 (1H, d, *J* = 11 Hz), 5.96 (1H, dt, *J* = 15, 7 Hz), 5.85 (1H, d, *J* = 15 Hz), 5.68 (1H, dt, *J* = 15, 7 Hz), 4.42 (1H, dd, *J* = 9, 4 Hz), 3.72-3.68 (1H, m), 3.27-3.20 (4H, m), 2.48-2.32 (5H, m), 2.11 (2H, dd, *J* = 14, 7 Hz), 1.75 (3H, s), 1.41-1.26 (10H, m), 1.17 (3H, d, *J* = 7 Hz), 0.90 (3H, t, *J* = 7 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 177.4, 174.3, 170.7, 146.7, 142.3, 137.7, 137.4, 136.4, 133.3, 130.0, 127.4, 126.9, 121.8, 75.2, 72.8, 46.0, 44.7, 43.4, 39.8, 34.14, 34.08, 33.2, 30.8, 30.5, 30.4, 23.9, 14.6, 14.3, 12.5.

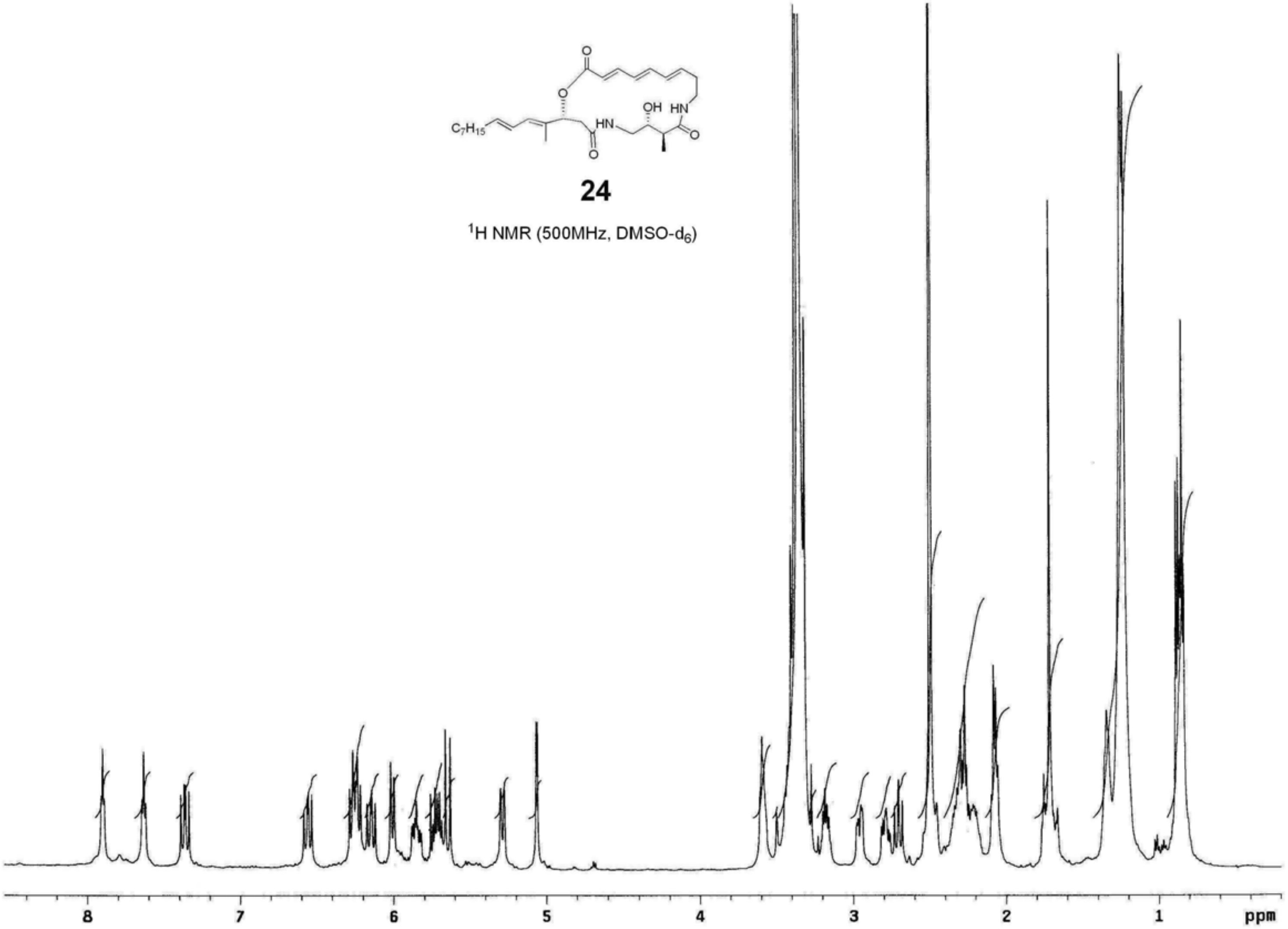


(2*E*,4*E*,6*E*)-9-((2*S*,3*S*)-3-Hydroxy-4-((*S*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoic acid. TLC: SiO$_2$, CH$_2$Cl$_2$/MeOH (10:1), R$_f$ ≈ 0.18; [α]$_{20}$ = +38 (c=0.1, MeOH);^{1}H NMR (400 MHz, CD$_3$OD) δ 7.02 (1H, dd, *J* = 15, 11 Hz), 6.44 (1H, dd, *J* = 15, 11 Hz), 6.28-6.18 (3H, m), 6.05 (1H, d, *J* = 11 Hz), 5.91 (1H, d, *J* = 15 Hz), 5.81 (1H, dt, *J* = 15, 7 Hz), 5.67 (1H, dt, *J* = 15, 7 Hz), 4.42 (1H, dd, *J* = 8, 4 Hz), 3.74-3.70 (1H, m), 3.38-3.24 (3H, m), 3.10 (1H, dd, *J* = 14, 8 Hz), 2.47-2.31 (5H, m), 2.11 (2H, dd, *J* = 14, 7 Hz), 1.75 (3H, s), 1.44-1.26 (10H, m), 1.16 (3H, d, *J* = 7 Hz), 0.90 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, CD$_3$OD) δ 177.4, 176.1, 174.4, 141.2, 138.6, 137.5, 136.3, 134.9, 133.7, 131.3, 129.8, 127.4, 126.9, 75.2, 72.8, 46.0, 44.8, 43.3, 39.9, 34.1, 34.0, 33.2, 30.7, 30.43, 30.41, 23.9, 14.6, 14.3, 12.5.



(2*R*,7*R*,8*S*,13*E*,15*E*,17*E*)-2-((2*E*,4*E*)-Dodeca-2,4-dien-2-yl)-7-hydroxy-8-methyl-1-oxa-5,10-diazacyclononadeca-13,15,17-triene-4,9,19-trione (24). A solution of (2*E*,4*E*,6*E*)-9-((2*S*,3*R*)-3-hydroxy-4-((*R*,4*E*,6*E*)-3-hydroxy-4-methyltetradeca-4,6-dienamido)-2-methylbutanamido)nona-2,4,6-trienoic acid (50 mg, 96 μmol) in THF (10 mL) was added to a solution of and 2-methyl-6-nitrobenzoic anhydride (100 mg, 289 μmol) and DMAP (42 mg, 347 μmol) in THF (150 mL) at rt over 20 h through syringe drive. After 5 days (followed by reverse phase HPLC, Waters μBondapak C18 250mm × 4.6mm, CH$_3$CN/MeOH/H$_2$O 3:2:2, 1 mL/min), the reaction was quenched with water and extracted with EtOAc, and then the organic layer was washed with brine. It was dried with Na$_2$SO$_4$ and then concentrated. The residue was purified with PTLC (CH$_2$Cl$_2$/MeOH 20:1) first then continue purified with reverse phase TLC (RP-18 F$_{254}$) to give to (2*R*,7*R*,8*S*,13*E*,15*E*,17*E*)-2-((2*E*,4*E*)-dodeca-2,4-dien-2-yl)-7-hydroxy-8-methyl-1-oxa-5,10-diazacyclononadeca-13,15,17-triene-4,9,19-trione (**24**) as white solid. (~30% yield by HPLC, isolated yield ~10-15%). mp 138-142°C; HPLC retention time: 14.6 min (Waters μBondapak C18 250mm×4.6mm, CH$_3$CN/MeOH/H$_2$O 3:2:2 1 mL/min); TLC: SiO$_2$, CH$_2$Cl$_2$/MeOH (10:1), R$_f$ ≈ 0.50; [α]$_{20}$ = −240 (c=0.2, DMSO); ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 7.90 (1H, t, *J* = 5 Hz), 7.63 (1H,t, *J* = 6 Hz), 7.35 (1H, dd, *J* = 16, 12 Hz), 6.56 (1H, dd, *J* = 15, 11 Hz), 6.26 (1H, dd, *J* = 15, 11 Hz), 6.24 (1H, dd, *J* = 15, 11 Hz), 6.15 (1H, dd, *J* = 15, 11 Hz), 6.01 (1H, d, *J* = 11 Hz), 5.85 (1H, ddd, *J* = 15, 11, 5 Hz), 5.71 (1H, dt, *J* = 15, 7 Hz), 5.65 (1H, d, *J* = 16 Hz), 5.29 (1H, d, *J* = 10 Hz), 5.06 (1H, d, *J* = 4 Hz), 3.61-3.56 (1H, m), 3.45-3.42 (1H, m), 3.21-3.15 (1H, m), 2.98-2.94 (1H, m), 2.82-2.76

(1H, m), 2.70 (1H, dd, J = 14, 12 Hz), 2.36-2.17 (4H, m), 2.10-2.05 (2H, m), 1.72 (3H, s), 1.36-1.18 (10H, m), 0.88 (3H, d, J = 8 Hz), 0.85 (3H, t, J = 8 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.7, 169.4, 165.4, 147.4, 143.8, 139.1, 135.6, 133.0, 131.4, 126.5, 125.8, 125.4, 118.2, 76.2, 70.7, 44.4, 42.4, 40.7, 37.1, 32.3, 32.1, 31.3, 28.9, 28.59, 28.55, 22.1, 14.0, 12.9, 10.5; HRMS (FAB, NBA) Calcd. for $C_{29}H_{45}N_2O_5$ [MH$^+$] *m/z* 501.3329, found 501.3331.



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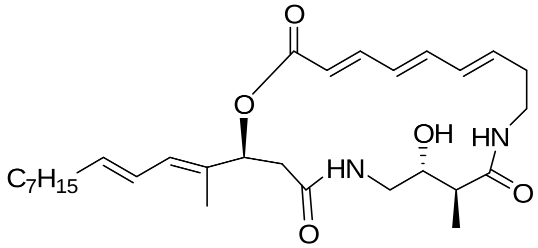
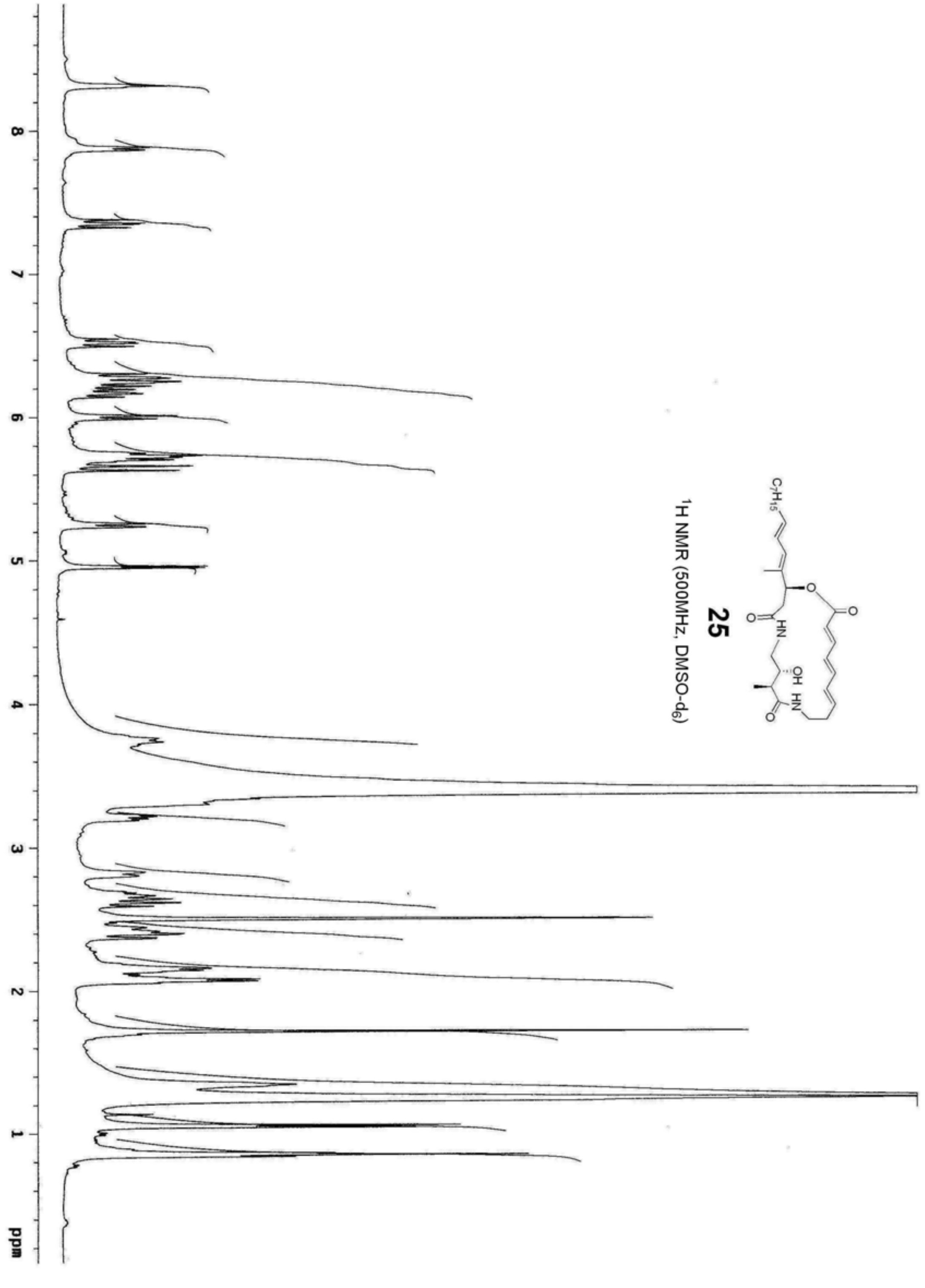
^{1}H NMR (500MHz, DMSO-d$_6$)

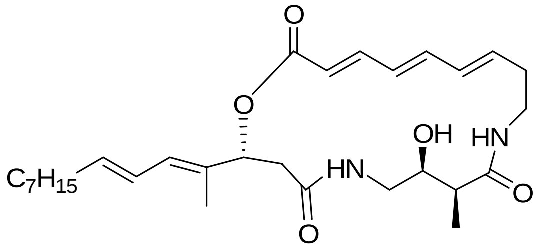


(2*S*,7*R*,8*S*,13*E*,15*E*,17*E*)-2-((2*E*,4*E*)-Dodeca-2,4-dien-2-yl)-7-hydroxy-8-methyl-1-oxa-5,10-diazacyclononadeca-13,15,17-triene-4,9,19-trione(25). HPLC retention time: 14.7 min (Waters μBondapak C18 250mm×4.6mm, $CH_3CN/MeOH/H_2O$ 3:2:2 1mL/min); TLC: SiO_2, $CH_2Cl_2/MeOH$ (10:1), $R_f \approx 0.50$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.31 (1H, t, *J* = 5 Hz), 7.88 (1H, d, *J* = 8 Hz), 7.35 (1H, dd, *J* = 15, 11 Hz), 6.52 (1H, dd, *J* = 15, 11 Hz), 6.28 (1H, dd, *J* = 16, 12 Hz), 6.24 (1H, dd, *J* = 16, 12 Hz), 6.17 (1H, dd, *J* = 15, 12 Hz), 6.00 (1H, d, *J* = 11 Hz), 5.74-5.69 (2H, m), 5.64 (1H, d, *J* = 16), 5.25 (1H, d, *J* = 10 Hz), 4.95 (1H, d, *J* = 6 Hz), 3.78-3.71 (1H, m), 3.60-3.30 (1H, m), 3.21 (1H, dd, *J* = 14, 6 Hz), 2.82 (1H, br d, *J* = 13 Hz), 2.69-2.59 (3H, m), 2.44-2.37 (2H, m), 2.19-2.06 (4H, m), 1.71 (3H, s), 1.35-1.24 (10H, m), 1.05 (3H, d, *J* = 7 Hz), 0.85 (3H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.6, 170.6, 165.6, 147.4, 143.7, 138.8, 135.6, 132.9, 131.9, 126.8, 125.7, 125.3, 118.3, 76.4, 72.3, 44.9, 42.2, 40.6, 36.0, 33.3, 32.4, 31.3, 28.9, 28.62, 28.58, 22.1, 14.6, 14.0, 13.0; HRMS (FAB, NBA) Calcd. for $C_{29}H_{45}N_2O_5$ [MH^+] *m/z* 501.3329, found 501.3331.

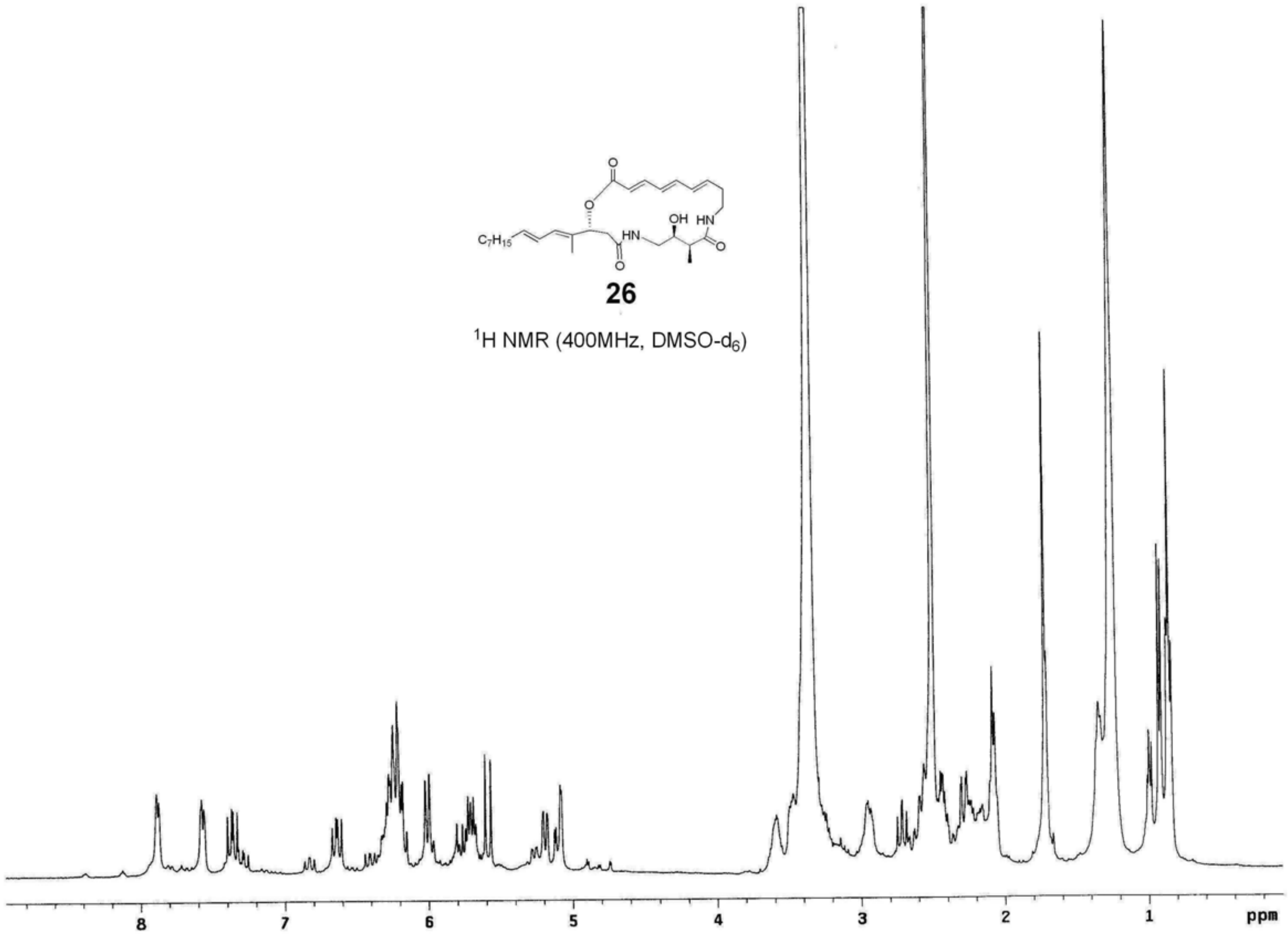


25

^1H NMR (500MHz, DMSO-d_6)

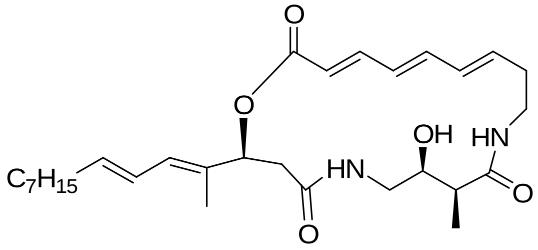


(2*R*,7*S*,8*S*,13*E*,15*E*,17*E*)-2-((2*E*,4*E*)-Dodeca-2,4-dien-2-yl)-7-hydroxy-8-methyl-1-oxa-5,10-diazacyclononadeca-13,15,17-triene-4,9,19-trione (26). HPLC retention time: 12.6 min (Waters μBondapak C18 250mm×4.6mm, $CH_3CN/MeOH/H_2O$ 3:2:2 1mL/min); TLC: SiO_2, $CH_2Cl_2/MeOH$ (10:1), $R_f \approx 0.48$; ^1H NMR (400 MHz, DMSO-d_6) δ 7.88 (1H, br d, J = 6 Hz), 7.57 (1H, d, J = 9, 3 Hz), 7.37 (1H, dd, J = 15, 11 Hz), 6.64 (1H, dd, J = 15, 11 Hz), 6.29-6.21 (2H, m), 6.18 (1H, dd, J = 15, 11 Hz), 6.01 (1H, d, J = 11 Hz), 5.72 (1H, dd, J = 14, 7 Hz), 5.70 (1H, dt, J = 14, 7 Hz), 5.59 (1H, d, J = 16 Hz), 5.19 (1H, br d, J = 10 Hz), 5.08 (1H, d, J = 3 Hz), 3.62-3.54 (1H, m), 3.52-3.45 (1H, m), 3.30-3.20 (1H, m), 3.00-2.90 (1H, m), 2.71 (1H, dd, J = 14, 12 Hz), 2.62-2.55 (1H, m), 2.46-2.40 (1H, m), 2.32-2.08 (5H, m), 1.72 (3H, s), 1.38-1.20 (10H, m), 0.92 (3H, d, J = 7 Hz), 0.85 (3H, t, J = 7 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.5, 169.8, 166.3, 149.5, 146.9, 142.4, 136.1, 133.8, 130.4, 126.5, 126.0, 125.6, 117.6, 77.2, 73.4, 45.5, 42.3, 41.4, 38.8, 33.0, 31.9, 31.2, 29.5, 29.3, 29.2, 22.8, 14.8, 14.6, 13.5; HRMS (FAB, NBA) Calcd. for $C_{29}H_{45}N_2O_5$ $[MH^+]$ *m/z* 501.3329, found 501.3331.

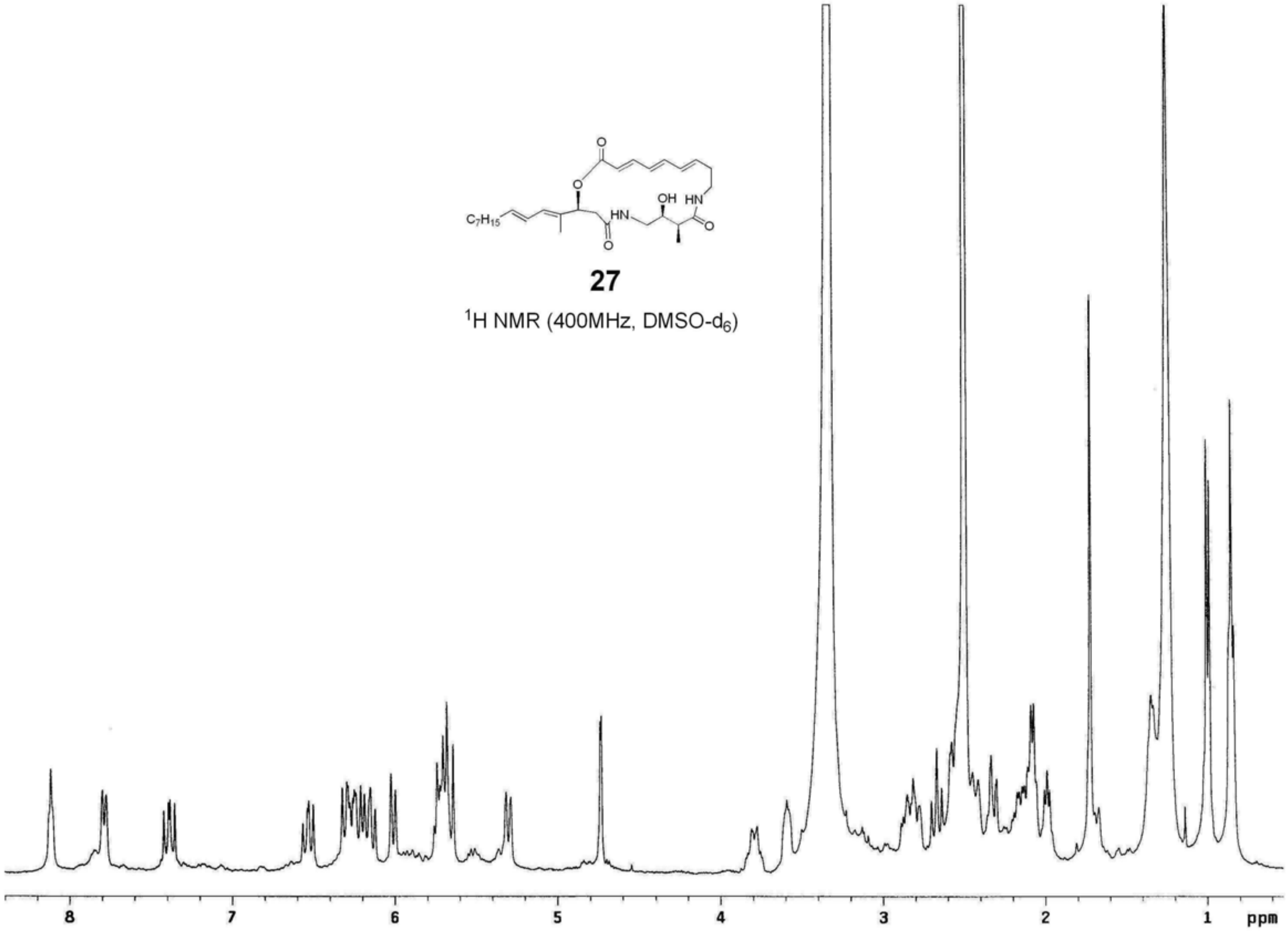


26

^1H NMR (400MHz, DMSO-d_6)

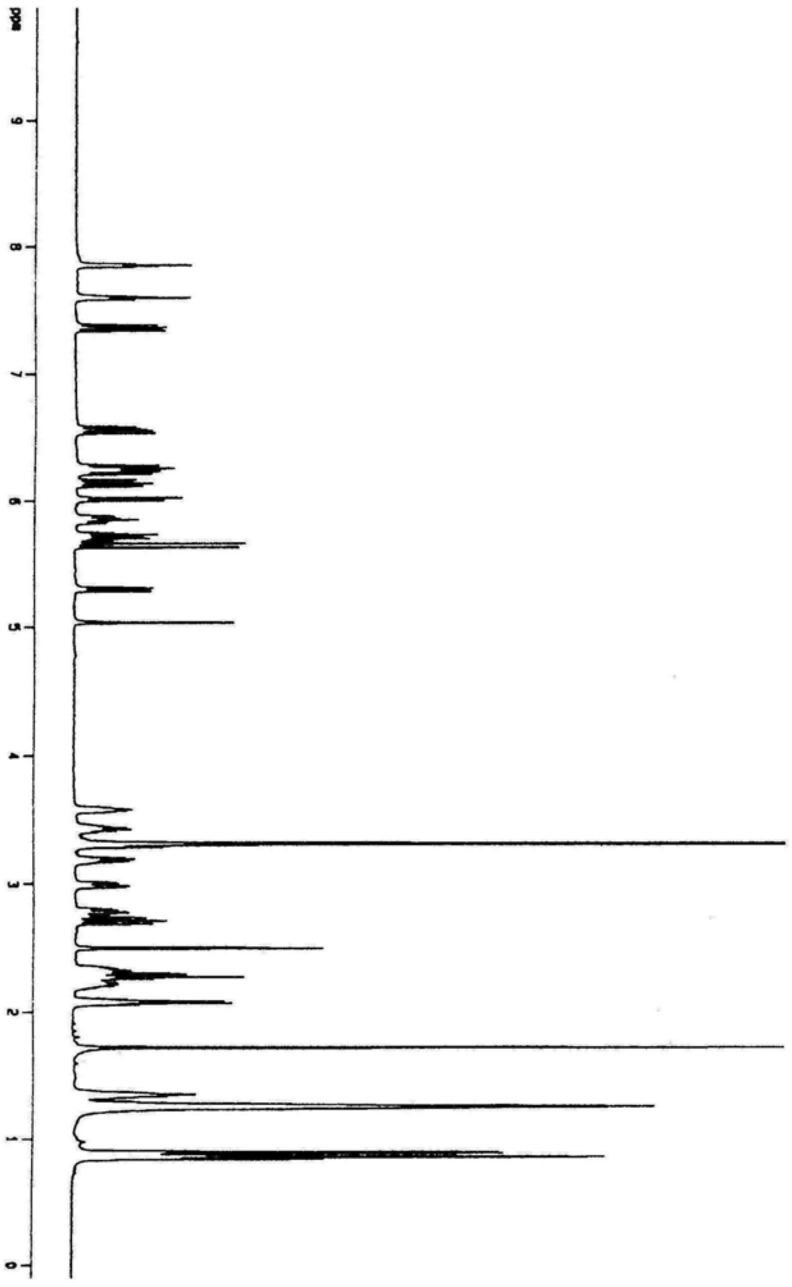


(2*S*,7*S*,8*S*,13*E*,15*E*,17*E*)-2-((2*E*,4*E*)-Ddodeca-2,4-dien-2-yl)-7-hydroxy-8-methyl-1-oxa-5,10-diazacyclononadeca-13,15,17-triene-4,9,19-trione (27). HPLC retention time: 14.7 min (Waters μBondapak C18 250mm×4.6mm, $CH_3CN/MeOH/H_2O$ 3:2:2 1mL/min); TLC: SiO_2, $CH_2Cl_2/MeOH$ (10:1), $R_f \approx 0.50$; ^1H NMR (400 MHz, DMSO-d_6) δ 8.12(1H, t, $J = 5$ Hz), 7.79 (1H, d, $J = 9$ Hz), 7.39 (1H, dd, $J = 15, 11$ Hz), 6.53 (1H, dd, $J = 15, 11$ Hz), 6.29 (1H, dd, $J = 15, 11$ Hz), 6.25 (1H, dd, $J = 15, 11$ Hz), 6.16 (1H, dd, $J = 14, 12$ Hz), 6.01 (1H, d, $J = 11$ Hz), 5.76-5.67 (2H, m), 5.66 (1H, d, $J = 15$), 5.30 (1H, d, $J = 11$ Hz), 4.74 (1H, d, $J = 3$ Hz), 3.85-3.75 (1H, m), 3.62-3.56 (1H, m), 2.89-2.78 (2H, m), 2.67 (1H, dd, $J = 13, 12$ Hz), 2.60-2.40 (2H, m), 2.34-2.28 (1H, m), 2.15 (1H, dd, $J = 12, 5$ Hz), 2.11-2.07 (2H, m), 1.99 (1H, t, $J = 6$ Hz), 1.72 (3H, s), 1.37-1.22 (10H, m), 1.00 (3H, d, $J = 7$ Hz), 0.86 (3H, t, $J = 7$ Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 176.8, 170.8, 166.1, 147.5, 143.4, 138.8, 136.3, 133.6, 133.0, 128.1, 126.4, 126.1, 119.5, 77.0, 71.7, 45.2, 43.6, 42.6, 36.6, 34.3, 33.0, 31.9, 29.5, 29.3, 29.2, 22.9, 14.6, 14.2, 13.6; HRMS (FAB, NBA) Calcd. for $C_{29}H_{45}N_2O_5$ [MH^+] *m/z* 501.3329, found 501.3331.



27

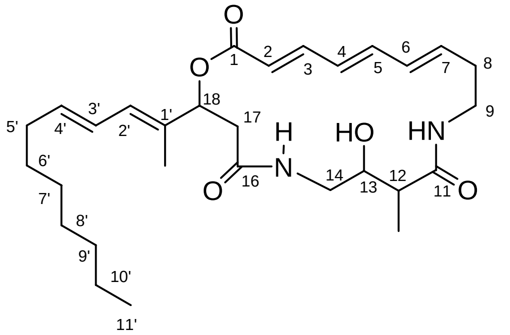
^{1}H NMR (400MHz, DMSO-d_6)



Natural FR252921

^{1}H NMR (500 MHz, DMSO-d_6)

Comparison of δ_H value of natural FR252921 and compounds **24-27**



Position	Natural FR252921*	**24**	**25**	**26**	**27**
2	5.65 (d, 1H)	5.65 (d, 1H)	5.64 (d, 1H)	5.59 (d, 1H)	5.66 (d, 1H)
3	7.37 (dd, 1H)	7.35 (dd, 1H)	7.35 (dd, 1H)	7.37 (dd, 1H)	7.39 (dd, 1H)
4	6.26 (dd, 1H)	6.26 (dd, 1H)	6.28 (dd, 1H)	6.29-6.21 (m, 1H)	6.29 (dd, 1H)
5	6.56 (dd, 1H)	6.56 (dd, 1H)	6.52 (dd, 1H)	6.64 (dd, 1H)	6.53 (dd, 1H)
6	6.14 (dd, 1H)	6.15 (dd, 1H)	6.17 (dd, 1H)	6.18 (dd, 1H)	6.16 (dd, 1H)
7	5.86 (ddd, 1H)	5.85 (ddd, 1H)	5.74-5.69 (m, 1H)	5.72 (dd, 1H)	5.76-5.67 (m, 1H)
8	2.33 (m, 1H) 2.22 (m, 1H)	2.36-2.17 (m, 2H)	2.44-2.37 (m, 2H)	2.46-2.40 (m, 1H) 2.32-2.08 (m, 1H)	2.60-2.40 (m, 1H) 2.34-2.28 (m, 2H)
9	3.42 (m, 1H) 3.18 (m, 1H)	3.45-3.42 (m, 1H) 3.21-3.15 (m, 1H)	3.60-3.30 (m, 1H) 3.21 (dd, 1H)	3.52-3.45 (m, 1H) 3.30-3.20 (m, 1H)	3.62-3.56 (m, 1H) 2.89-2.78 (m, 1H)
10	7.60 (t, 1H)	7.63 (t, 1H)	7.88 (d, 1H)	7.57 (dd, 1H)	7.79 (d, 1H)
12	2.27 (m, 1H)	2.36-2.17 (m, 1H)	2.19-2.06 (m, 1H)	2.32-2.08 (m, 1H)	2.34-2.28 (m, 1H)
13	3.57 (m, 1H)	3.61-3.56 (m, 1H)	3.78-3.71 (m, 1H)	3.62-3.54 (m, 1H)	3.85-3.75 (m, 1H)
14	2.97 (m, 1H) 2.78 (m, 1H)	2.98-2.94 (m, 1H) 2.82-2.76 (m, 1H)	2.82 (d, 1H) 2.69-2.59 (m, 1H)	3.00-2.90 (m, 1H) 2.71 (dd, 1H)	2.89-2.78 (m, 1H) 2.60-2.40 (m, 1H)
15	7.85 (t, 1H)	7.90 (t, 1H)	8.31 (t, 1H)	7.88 (d, 1H)	8.12 (t, 1H)
17	2.71 (dd, 1H) 2.29 (dd, 1H)	2.70 (dd, 1H) 2.36-2.17 (m, 1H)	2.69-2.59 (m, 1H) 2.19-2.06 (m, 1H)	2.62-2.55 (m, 1H) 2.32-2.08 (m, 1H)	2.15 (dd, 1H) 1.99 (t, 1H)
18	5.30 (d, 1H)	5.29 (d, 1H)	5.25 (d, 1H)	5.19 (d, 1H)	5.30 (d, 1H)
12-CH_3	0.88 (d, 3H)	0.88 (d, 3H)	1.05 (d, 3H)	0.92 (d, 3H)	1.00 (d, 3H)
13-OH	5.04 (d, 1H)	5.06 (d, 1H)	4.95 (d, 1H)	5.08 (d, 1H)	4.74 (d, 1H)
2´	6.02 (d, 1H)	6.01 (d, 1H)	6.00 (d, 1H)	6.01 (d, 1H)	6.01 (d, 1H)
3´	6.24 (dd, 1H)	6.24 (dd, 1H)	6.24 (dd, 1H)	6.29-6.21 (m, 1H)	6.25 (dd, 1H)
4´	5.71 (dt, 1H)	5.71 (dt1H)	5.74-5.69 (m, 1H)	5.70 (dt, 1H)	5.76-5.67 (m, 1H)
5´	2.08 (m, 2H)	2.10-2.05 (m, 2H)	2.19-2.06 (m, 2H)	2.32-2.08 (m, 2H)	2.11-2.075 (m, 2H)
6´	1.35 (m, 2H)	1.36-1.18 (m, 2H)	1.35-1.24 (m, 2H)	1.38-1.20 (m, 2H)	1.37-1.22 (m, 8H)
7´-10´	1.30-1.20 (m, 8H)	1.36-1.18 (m, 8H)	1.35-1.24 (m, 8H)	1.38-1.20 (m, 8H)	1.37-1.22 (m, 8H)
11´	0.86 (t, 3H)	0.85 (t, 3H)	0.85 (t, 3H)	0.85 (t, 3H)	0.86 (t, 3H)
1´-CH_3	1.72 (s, 3H)	1.72 (s, 3H)	1.71 (s, 3H)	1.72 (s, 3H)	1.72 (s, 3H)
R_t (HPLC)**	14.68 min	14.60 min	14.68 min	12.59 min	14.70 min

* δ_H data kindly provided by Astellas Pharma, Inc.

** Column: μBondapak C18 250mm×4.6mm, 305nm, Acetonitrile/MeOH/H_2O 3:2:2, 1mL/min.