Chemical Synthesis of (+)-Ryanodine and (+)-20-Deoxyspiganthine

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Supporting Information:

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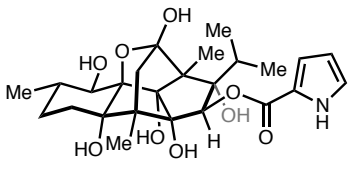
1. General Procedures

Unless otherwise stated, reactions were performed under an inert atmosphere (dry N_2 or Ar) with freshly dried solvents utilizing standard Schlenk techniques. Glassware was oven-dried at 120 °C for a minimum of four hours, or flame-dried utilizing a Bunsen burner under high vacuum. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), *N,N*-dimethylformamide (DMF), benzene (PhH), and toluene (PhMe) were dried by passing through activated alumina columns. 2-Methyltetrahydrofuran (anhydrous, >99%, inhibitor-free) was purchased from Sigma-Aldrich and stored under argon. Methanol (HPLC grade) was purchased from Fisher Scientific. Pyridine (Pyr) was distilled from calcium hydride immediately prior to use. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV (254 nm), *p*-anisaldehyde, CAM, and/or $KMnO_4$ staining. Flash column chromatography was performed using silica gel (SiliaFlash® P60, particle size 40-63 microns [230 to 400 mesh]) purchased from Silicycle. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III HD with Prodigy Cryoprobe (at 400 MHz and 101 MHz, respectively), Varian Inova 500 (at 500 MHz and 126 MHz, respectively), or Varian Inova 600 (at 600 MHz and 150 MHz, respectively), and are reported relative to internal $CHCl_3$ (^1H, δ = 7.26), C_6H_6 (^1H, δ = 7.16), or CD_2HOD (^1H, δ = 3.31), and $CDCl_3$ (^{13}C, δ = 77.0), C_6D_6 (^{13}C, δ = 128.0), or CD_3OD (^{13}C, δ = 49.0). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm.

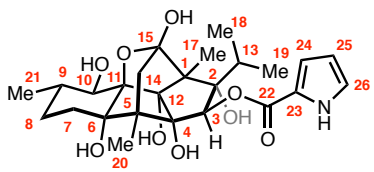
Reagents were purchased from commercial vendors as follows: *trans*-Dichlorobis(triphenylphosphine) palladium was purchased from Strem Chemicals and stored in a nitrogen-filled glovebox. Sodium hydride (dry, 95%), 2-(trichloroacetyl)pyrrole, solid potassium bis(trimethylsilyl)amide (KHMDS, 95%), and tris(dimethylamino)sulfonium difluorotrimethylsilicate (TAS-F) were purchased from Sigma-Aldrich and stored in a nitrogen-filled glovebox. Platinum oxide (Adam's catalyst) and vanadyl acetylacetonate were purchased from Strem Chemicals. *Tert*-butyl hydroperoxide (TBHP, 5.5 M in decane over 4 Å MS), solid $LiBH_4$ (>95%), lithium (wire stored in mineral oil, 99.9% trace metal basis), and 4,4'-di-*tert*-butylbiphenyl were purchased from Sigma-Aldrich.

2. Positional numbering system

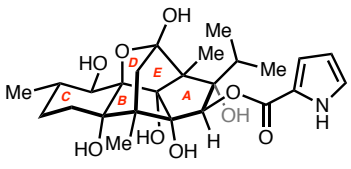
The carbon numbering system and ring assignment as outlined by Deslongchamps[1-5] and used by Inoue[6-9] are utilized throughout this Supplementary Materials file for ^1H and ^{13}C NMR assignments of all intermediates. Assignments were made with the aid of 2D ^1H-^1H (NOESY and COSY) and ^1H-^{13}C coupling experiments (HSQC and HMBC).



***ryanodine* (1)**



numbering system

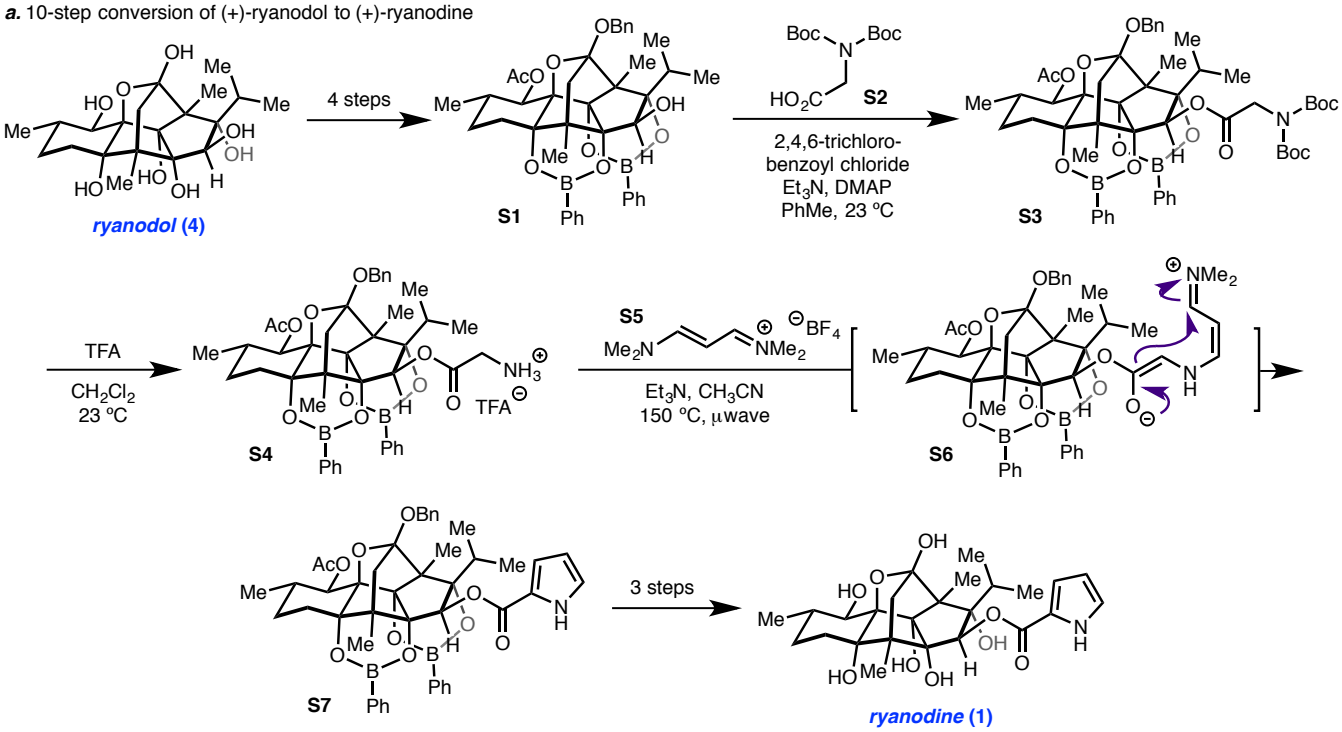


ring assignment

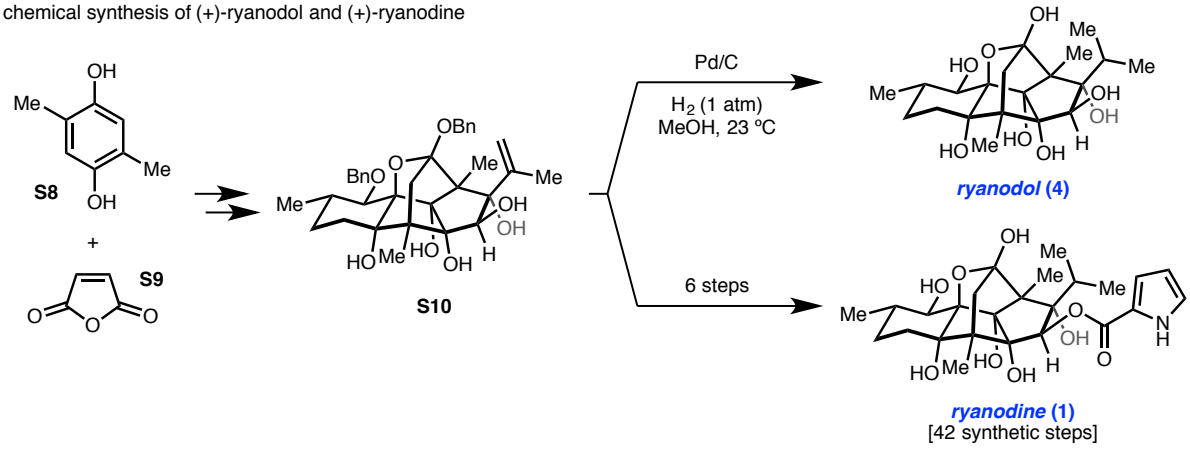
3. Synthetic Scheme of Inoue's Synthesis of Ryanodine and Conversion of Ryanodol to Ryanodine

Scheme S1. Inoue's Total Synthesis of Ryanodine and Conversion of Ryanodol to Ryanodine

a. 10-step conversion of (+)-ryanodol to (+)-ryanodine

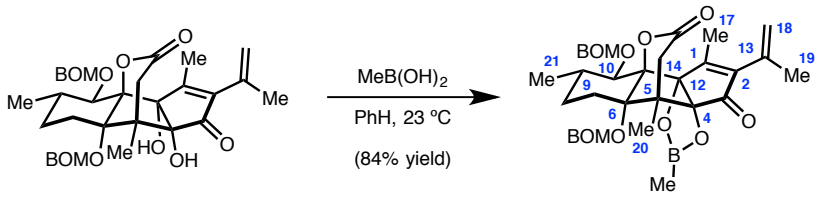


b. Total chemical synthesis of (+)-ryanodol and (+)-ryanodine



4. Synthetic Procedures

Preparation of boronate ester 13:

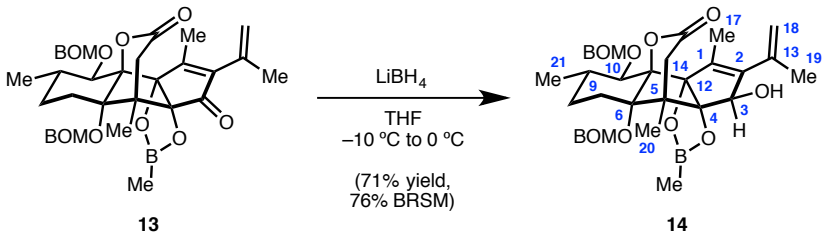


12 **13**

In slight modification of a procedure[9] detailed by Inoue and coworkers, PhH (66 mL) was added to a mixture of **12** (1.06 g, 1.71 mmol, 1.0 equiv) and $MeB(OH)_2$ (1.02 g, 17.1 mmol, 10 equiv) in an oven-dried, 200 mL round-bottomed flask. The resultant mixture was concentrated *in vacuo*. This azeotropic procedure of adding PhH (66 mL) and concentrating was repeated 10 times to complete the conversion of **12** to boronate ester **13**. Purification of the crude mixture by SiO_2 flash chromatography (25% EtOAc/hexanes) afforded the desired product **13** as a white foam (920 mg, 1.43 mmol, 84% yield).

TLC (25% EtOAc/hexanes): R_f 0.40 (UV, $KMnO_4$).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.30 (m, 10H, ***Ph***CH_2OCH_2O), 5.30 (p, *J* = 1.6 Hz, 1H, C_{18}), 5.25 (d, *J* = 6.5 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.09 (d, *J* = 7.0 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.05 (d, *J* = 6.6 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.90 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.86 (dt, *J* = 1.9, 1.0 Hz, 1H, C_{18}), 4.82 (d, *J* = 7.0 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.68 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.78 (d, *J* = 11.3 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.46 (d, *J* = 11.3 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.16 (d, *J* = 10.6 Hz, 1H, C_{10}), 2.53 (d, *J* = 19.8 Hz, 1H, C_{14}), 2.41 (d, *J* = 19.9 Hz, 1H, C_{14}), 2.32 (s, 3H, C_{17}), 2.21 – 2.09 (m, 1H, C_9), 1.99 (ddd, *J* = 14.6, 4.4, 1.9 Hz, 1H, C_7), 1.90 (q, *J* = 11.3 Hz, 1.5 Hz, 3H, C_{19}), 1.94 – 1.79 (m, 1H, C_8), 1.66 (dtd, *J* = 13.5, 4.6, 1.7 Hz, 1H, C_8), 1.61-1.52 (m, 1H, C_7), 1.31 (s, 3H, C_{20}), 1.18 (d, *J* = 6.5 Hz, 3H, C_{21}), 0.37 (s, 3H, $BC\boldsymbol{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$): δ 199.5 (C_3=O), 168.3 (C_1), 166.6 (C_{15}=O), 145.8 (C_2), 137.8 (C_{Ph}), 136.8 (C_{Ph}), 135.3 (C_{13}), 128.6 (C_{Ph}), 128.5 (C_{Ph}), 128.1 (C_{Ph}), 127.9 (C_{Ph}), 127.8 (C_{Ph}), 118.7 (C_{18}), 97.1 (C_{11}), 97.1 (C_{12}), 94.3 (C_4), 93.5 ($PhCH_2O\boldsymbol{C}H_2O$), 91.0 ($C_6$), 90.6 ($PhCH_2O\boldsymbol{C}H_2O$), 79.6 ($C_{10}$), 71.0 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.8 ($Ph\boldsymbol{C}H_2OCH_2O$), 46.7 ($C_5$), 40.6 ($C_{14}$), 32.5 ($C_9$), 27.7 ($C_8$), 21.5 ($C_{19}$), 21.3 ($C_7$), 18.9 ($C_{21}$), 15.3 ($C_{15}$), 15.1 ($C_{17}$), –5.1 ($B\boldsymbol{C}H_3$).
FTIR (NaCl, thin film): 2956, 2872, 1755, 1716, 1361, 1268, 1022, 1020 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M+H]^+$ 643.3078, found 643.3072.
$[\alpha]_D^{25}$: +175° (*c* = 0.505, $CHCl_3$).

Preparation of alcohol 14:



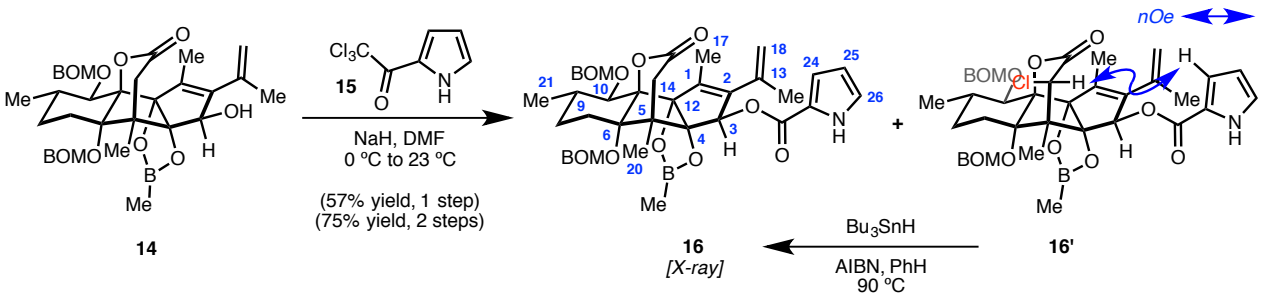
13 **14**

To an oven-dried, 200 mL round-bottomed flask was added enone **13** (920 mg, 1.43 mmol, 1.0 equiv) and anhydrous THF (57 mL). The solution was cooled to –10 °C in an ice/acetone bath and solid $LiBH_4$ (156 mg, 7.16 mmol, 5.0 equiv) was added. After 1 h, a second portion of solid $LiBH_4$ (156 mg, 7.16 mmol, 5.0 equiv) was

added before warming the reaction mixture to 0 ºC with an ice/water bath. Stirring was continued at 0 ºC for another 1 h before a third portion of solid $LiBH_4$ (156 mg, 7.16 mmol, 5.0 equiv) was added. The reaction was allowed to stir at 0 ºC an additional 1 h before sat. aq. NH_4Cl (40 mL) was slowly added to the reaction at 0 ºC [Caution! Vigorous evolution of H_2 gas occurs, particularly in the initial stages of addition. Careful, controlled dropwise addition is advised in order to avoid a violent reaction]. The mixture was diluted with EtOAc (40 mL), the two layers separated, and the organic layer washed with sat. aq. NH_4Cl (40 mL). The combined aqueous layers were extracted with EtOAc (2 x 20 mL), and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (30 to 40 to 50% EtOAc/hexanes) to afford recovered starting material enone **13** (61 mg, 0.095 mmol, 7% yield) and the desired alcohol **14** as a white foam (650 mg, 1.01 mmol, 71% yield, 76% BRSM).

TLC (40% EtOAc/hexanes): R_f 0.30 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.30 (m, 10H, ***Ph***CH_2OCH_2O), 5.25 (d, *J* = 6.8 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.23 (t, *J* = 1.7 Hz, 1H, C_{18}), 5.09 (d, *J* = 6.9 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.98 (d, *J* = 6.8 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.93 – 4.90 (m, 1H, C_3), 4.90 – 4.87 (m, 1H, C_{18}), 4.89 (d, *J* = 8.0 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.80 (d, *J* = 7.0 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.77 (d, *J* = 11.6 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.62 (d, *J* = 12.0 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.42 (d, *J* = 11.4 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.10 (d, *J* = 10.4 Hz, 1H, C_{10}), 3.79 (d, *J* = 19.9 Hz, 1H, C_{14}), 2.33 (d, *J* = 19.8 Hz, 1H, C_{14}), 2.21 – 2.10 (m, 1H, C_9), 2.08 (d, *J* = 4.4 Hz, 1H, O***H***), 1.92 (d, *J* = 2.4 Hz, 3H, C_{17}), 1.88 – 1.83 (m, 3H, C_{19}), 1.98-1.89 (m, 1H, C_7), 1.93-1.82 (m, 1H, C_8), 1.69-1.61 (m, 1H, C_8), 1.64-1.53 (m, 1H, C_7), 1.31 (s, 3H, C_{20}), 1.18 (d, *J* = 6.5 Hz, 3H, C_{21}), 0.33 (s, 3H, $BC\boldsymbol{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$): δ 168.6 (C_{15}=O), 145.8 (C_2), 138.2 (C_{13}), 138.0 (C_{Ph}), 137.1 (C_{Ph}), 135.0 (C_1), 128.5 (C_{Ph}), 128.4 (C_{Ph}), 128.0 (C_{Ph}), 127.8 (C_{Ph}), 127.8 (C_{Ph}), 127.6 (C_{Ph}), 117.7 (C_{18}), 102.3 (C_{12}), 98.7 (C_4), 97.2 ($PhCH_2O\boldsymbol{C}H_2O$), 92.1 ($C_6$), 91.0 ($C_{11}$), 90.5 ($PhCH_2O\boldsymbol{C}H_2O$), 84.6 ($C_3$), 80.3 ($C_{10}$), 70.8 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.6 ($Ph\boldsymbol{C}H_2OCH_2O$), 49.3 ($C_5$), 39.0 ($C_{14}$), 32.6 ($C_9$), 27.9 ($C_8$), 21.5 ($C_{19}$), 21.0 ($C_7$), 19.1 ($C_{21}$), 16.5 ($C_{20}$), 13.3 ($C_{17}$), –5.1 ($B\boldsymbol{C}H_3$).
FTIR (NaCl, thin film): 3453, 2924, 1747, 1362, 1037 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M+NH_4]^+$ 662.3500, found 662.3509.
$[\alpha]_D^{25}$: +67° (*c* = 0.385, $CHCl_3$).

Preparation of pyrrole ester 16:



An oven-dried, 50 mL round-bottomed flask was charged with NaH (95%, 51 mg, 2.0 mmol, 4.0 equiv) in a nitrogen-filled glovebox. The flask was capped with a rubber septum, removed from the glovebox and cooled to 0 ºC. Alcohol **14** (322 mg, 0.5 mmol, 1.0 equiv) in anhydrous DMF (5.0 mL) was next *rapidly* added and another portion of DMF (5.0 mL) was then used to render the transfer quantitative. The resulting reaction mixture was stirred for 30 min at 0 ºC before 2-(trichloroacetyl)pyrrole (425 mg, 2.0 mmol, 4.0 equiv) in anhydrous DMF (5.0 mL) was added dropwise via syringe. After continued stirring for 30 min at 0 ºC, the resulting dark-brown mixture was warmed to ambient temperature and stirring was continued for 48 h. The reaction was diluted with Et_2O (15 mL) and then carefully quenched with the addition of sat. aq. NH_4Cl (15 mL). The layers were separated

and the organic layer was washed with H_2O (2 x 20 mL). The combined aqueous layers were extracted with Et_2O (3 x 20 mL) and the combined organic layers were then washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (15 to 20 to 25 to 30% EtOAc/hexanes) to afford pyrrole ester **16** (212 mg, 0.287 mmol, 57% yield) and chloride **16′** (69.7 mg, 0.089 mmol, 18% yield). The stereochemistry of the chloride substituted C_{14}–H was determined by nOe analysis.

An oven-dried, 50 mL Schlenk tube was charged with chloride **16′** (69.7 mg, 0.089 mmol, 1.0 equiv) and benzene (8.9 mL) under N_2. The Schlenk tube was then placed in a preheated oil bath (90 ºC) before a solution of AIBN (14.6 mg, 0.089 mmol, 1.0 equiv) and Bu_3SnH (0.178 mL, 0.178 mmol, 2.0 equiv) in benzene (8.9 mL) was added dropwise via syringe at 90 ºC. Upon complete addition, the reaction mixture was stirred for 1 h at 90 ºC at which point TLC analysis indicated the complete consumption of starting material. The reaction mixture was cooled to ambient temperature, transferred to a 50 mL round-bottomed flask and concentrated in *vacuo*. The crude residue was purified by SiO_2 flash chromatography (25% EtOAc/hexanes) to afford pyrrole ester **16**, which was combined with the pure material obtained in the previous step to give a combined 277 mg of pyrrole ester **16** (0.376 mmol, 75% combined yield).

Pyrrole ester 16:

TLC (25% EtOAc/hexanes): R_f 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.32 (s, 1H, N***H***), 7.44 – 7.29 (m, 10H, ***Ph***CH_2OCH_2O), 7.05 (td, *J* = 2.7, 1.4 Hz, 1H, C_{26}), 6.94 (ddd, *J* = 3.8, 2.4, 1.4 Hz, 1H, C_{24}), 6.32 (dt, *J* = 3.9, 2.5 Hz, 1H, C_{25}), 6.25 (q, *J* = 2.3 Hz, 1H, C_3), 5.26 (d, *J* = 6.8 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.14 (p, *J* = 1.6 Hz, 1H, C_{18}), 5.04 (d, *J* = 6.9 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.01 (d, *J* = 6.8 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.91 (d, *J* = 11.8 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.91-4.88 (m, 1H, C_{18}), 4.77 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.77 (d, *J* = 6.9 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.64 (d, *J* = 6.9 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.40 (d, *J* = 11.3 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.12 (d, *J* = 10.5 Hz, 1H, C_{10}), 3.57 (d, *J* = 19.8 Hz, 1H, C_{14}), 2.46 (d, *J* = 19.7 Hz, 1H, C_{14}), 2.16 (dddd, *J* = 11.6, 8.9, 6.6, 5.1 Hz, 1H, C_9), 1.98 (d, *J* = 2.5 Hz, 3H, C_{17}), 1.97-1.90 (m, 1H, C_7), 1.93-1.85 (m, 1H, C_8), 1.69-1.60 (m, 1H, C_8), 1.64-1.56 (m, 1H, C_7), 1.75 (d, *J* = 1.2 Hz, 3H, C_{19}), 1.19 (d, *J* = 6.5 Hz, 3H, C_{21}), 1.11 (s, 3H, C_{20}), 0.38 (s, 3H, $BC\boldsymbol{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ 168.1 (C_{15}=O), 159.8 (C_{22}=O), 143.3 (C_2), 138.0 (C_{13}), 137.3 (C_{Ph}), 137.0 (C_{Ph}), 137.0 (C_1), 128.5 (C_{Ph}), 128.4 (C_{Ph}), 128.0 (C_{Ph}), 127.8 (C_{Ph}), 127.6 (C_{Ph}), 124.2 (C_{26}), 121.6 (C_{23}), 117.9 (C_{18}), 116.1 (C_{24}), 110.9 (C_{25}), 102.5 (C_{12}), 98.7 (C_4), 97.2 ($PhCH_2O\boldsymbol{C}H_2O$), 92.1 ($C_6$), 91.1 ($C_{11}$), 90.5 ($PhCH_2O\boldsymbol{C}H_2O$), 83.4 ($C_3$), 80.2 ($C_{10}$), 70.9 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.6 ($Ph\boldsymbol{C}H_2OCH_2O$), 49.3 ($C_5$), 39.3 ($C_{14}$), 32.6 ($C_9$), 27.9 ($C_8$), 21.1 ($C_{19}$), 21.1 ($C_7$), 19.0 ($C_{21}$), 16.2 ($C_{20}$), 13.4 ($C_{17}$), –4.9 ($B\boldsymbol{C}H_3$).

FTIR (NaCl, thin film): 3307, 2928, 1750, 1707, 1042, 1016 cm^{-1}.

HRMS (MM:ESI–APCI): calc'd for $[M+H]^+$ 738.3450, found 738.3456.

$[\alpha]_D^{25}$: +2° (*c* = 0.630, $CHCl_3$).

Chloride 16′:

TLC (25% EtOAc/hexanes): R_f 0.45 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.28 (s, 1H, N***H***), 7.43 – 7.29 (m, 10H, ***Ph***CH_2OCH_2O), 7.07 (td, *J* = 2.7, 1.4 Hz, 1H, C_{26}), 7.00 (ddd, *J* = 3.9, 2.5, 1.4 Hz, 1H, C_{24}), 6.34 (dt, *J* = 3.8, 2.5 Hz, 1H, C_{25}), 6.30 (q, *J* = 2.4 Hz, 1H, C_3), 5.64 (s, 1H, C_{14}), 5.24 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.19 – 5.10 (m, 1H, C_{18}), 5.05 (d, *J* = 6.9 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.01 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.90 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.88 – 4.84 (m, 1H, C_{18}), 4.76 (d, *J* = 6.9 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.74 (d, 11.3 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.65 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.40 (d, *J* = 11.3 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.10 (d, *J* = 10.5 Hz, 1H, C_{10}), 2.22 – 2.10 (m, 1H, C_9), 2.09 – 2.00 (m, 2H, C_7), 1.98 (d, *J* = 2.5 Hz, 3H, C_{17}), 1.92 – 1.79 (m, 1H, C_8), 1.75 (d, *J* = 1.2 Hz, 3H, C_{19}), 1.68 (d, *J* = 1.4 Hz, 1H, C_8), 1.35 (s, 3H, C_{20}), 1.19 (d, *J* = 6.4 Hz, 3H, C_{21}), 0.39 (s, 3H, $BC\boldsymbol{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.8 (C_{15}=O), 159.3 (C_{22}=O), 143.5 (C_2), 137.9 (C_{13}), 136.9 (C_{Ph}), 136.8 (C_{Ph}), 136.8 (C_1), 128.6 (C_{Ph}), 128.4 (C_{Ph}), 128.0 (C_{Ph}), 127.8 (C_{Ph}), 127.7 (C_{Ph}), 127.7 (C_{Ph}), 124.5 (C_{26}), 121.1 (C_{23}),

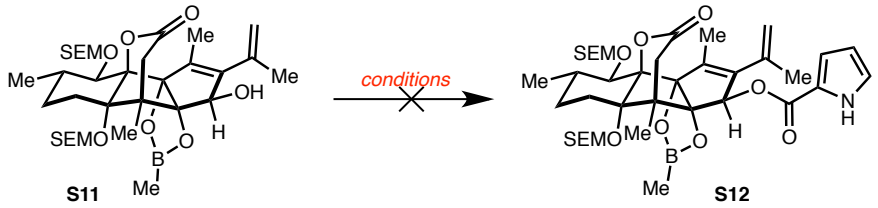
118.4 (C_{18}), 116.5 (C_{24}), 111.2 (C_{25}), 101.9 (C_{12}), 98.9 (C_4), 97.2 (PhCH$_2$O***C***H$_2$O), 92.1 (C_6), 91.2 (C_{11}), 90.6 (PhCH$_2$O***C***H$_2$O), 82.9 (C_3), 80.2 (C_{10}), 70.9 (Ph***C***H$_2$OCH$_2$O), 70.7 (Ph***C***H$_2$OCH$_2$O), 57.2 (C_{14}), 54.7 (C_5), 32.8 (C_9), 27.9 (C_8), 23.3 (C_7), 21.1 (C_{19}), 19.0 (C_{21}), 15.2 (C_{20}), 13.5 (C_{17}), –5.0 (B***C***H$_3$).

FTIR (NaCl, thin film): 3326, 2947, 1758, 1710, 1361, 1154, 1044, 1015, 747 cm^{-1}.

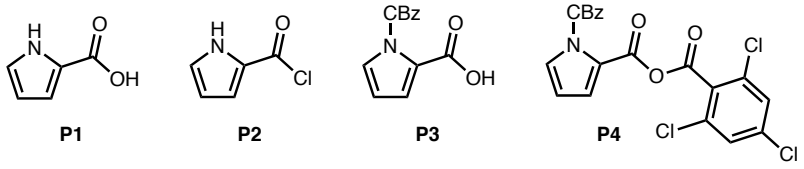
HRMS (MM:ESI–APCI): calc'd for [M+H]$^+$ 772.3060, found 772.3066.

$[\alpha]_D^{25}$**:** –52° (*c* = 0.595, CHCl$_3$).

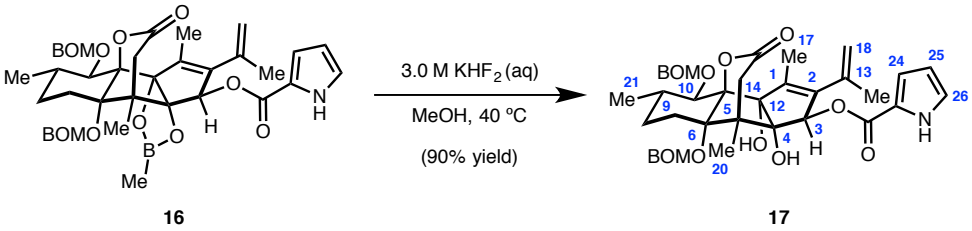
Table S1. Representative examples of unsuccessful pyrrole coupling attempts



entry	coupling partner	conditions	results
1	**P1**	DMAP, DCC, THF/DCM, 24 h	no reaction
2	**P2**	NaH, DMF, rt, 24 h	no reaction
3	**P3**	2,4,6-trichlorobenzoyl chloride, Et_3N, DMAP, PhMe, 24 h	no reaction
4	**P3**	2-methyl-6-nitrobenzoic anhydride, Et_3N, DMAP, CH_2Cl_2, 80 °C	no reaction
5	**P4**	NaH, DMAP, DMF, rt, 24h	no reaction
6	**P4**	Et_3N, DMAP, CH_2Cl_2, rt, 24h	no reaction
7	**P4**	NaH, DMAP, DMF, 50 °C, 8 h	translactonization



Preparation of diol 17:

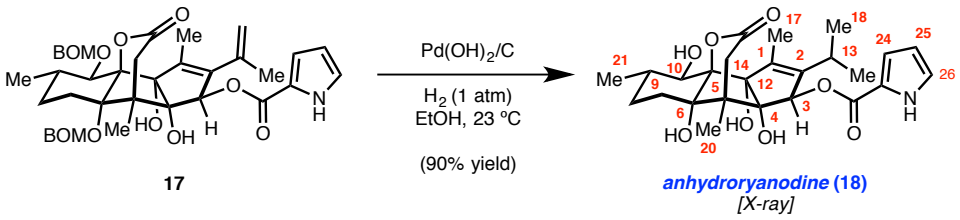


In slight modification of a procedure[9] detailed by Inoue and coworkers, pyrrole ester **16** (332 mg, 0.450 mmol, 1.0 equiv) was dissolved in MeOH (45 mL) and KHF_2 (3.0 M in H_2O, 3 mL, 20 equiv) was then added. The resulting solution was warmed to 40 ºC and stirring continued for 4 h at which point LCMS showed full consumption of the starting material. The reaction mixture was then cooled to ambient temperature and filtered through a plug of Na_2SO_4 (18 g) and silica gel (18 g) to remove H_2O and HF generated from KHF_2 (Note: If the reaction mixture was directly concentrated without filtration, the acidity of the reaction mixture resulted in the removal of the C_{10} BOM group), washing with EtOAc to ensure complete elution of the desired product. The filtrate was concentrated *in vacuo* and the crude residue was purified by SiO_2 flash chromatography (40% EtOAc/hexanes) to afford free diol **17** as a white foam (288 mg, 0.403 mmol, 90% yield).

TLC (40% EtOAc/hexanes): R_f 0.40 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.31 (s, 1H, N***H***), 7.45 – 7.29 (m, 10H, ***Ph***CH_2OCH_2O), 7.04 (td, *J* = 2.7, 1.4 Hz, 1H, C_{26}), 6.90 (ddd, *J* = 3.8, 2.4, 1.5 Hz, 1H, C_{24}), 6.30 (dt, *J* = 3.9, 2.5 Hz, 1H, C_{25}), 6.26 (q, *J* = 2.3 Hz, 1H, C_3), 5.19 (d, *J* = 6.3 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.10 (p, *J* = 1.6 Hz, 1H, C_{18}), 4.94 (s, 2H, $PhCH_2OC\boldsymbol{H}_2O$), 4.91 (d, *J* = 6.3 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.91 – 4.87 (m, 1H, C_{18}), 4.83 (d, *J* = 12.2 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.71(d, *J* = 8.0 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.69 (d, *J* = 8.0 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.65 (d, *J* = 12.2 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.43 (s, 1H, OH, $C_4O\boldsymbol{H}$), 4.05 (s, 1H, $C_{12}O\boldsymbol{H}$), 3.94 (d, *J* = 10.3 Hz, 1H, C_{10}), 3.42 (d, *J* = 19.8 Hz, 1H, C_{14}), 2.42 (d, *J* = 19.7 Hz, 1H, C_{14}), 2.17 – 2.03 (m, 1H, C_9), 1.94 (d, *J* = 2.4 Hz, 3H, C_{17}), 1.83 (ddd, *J* = 14.4, 4.1, 1.9 Hz, 1H, C_8), 1.75 (d, *J* = 1.2 Hz, 3H, C_{19}), 1.67 (ddt, *J* = 10.3, 4.1, 1.5 Hz, 1H, C_7), 1.62 – 1.52 (m, 1H, C_8), 1.46 (td, *J* = 12.7, 4.1 Hz, 1H, C_7), 1.13 (s, 3H, C_{20}), 1.12 (d, *J* = 5.8 Hz, 3H, C_{21}).
^{13}C NMR (101 MHz, $CDCl_3$): δ 168.2 (C_{15}=O), 160.4 (C_{22}=O), 140.9 (C_2), 138.9 (C_{13}), 137.7 (C_{Ph}), 137.4 (C_{Ph}), 136.6 (C_1), 128.7 (C_{Ph}), 128.4 (C_{Ph}), 128.4 (C_{Ph}), 128.2 (C_{Ph}), 127.7 (C_{Ph}), 127.7 (C_{Ph}), 123.9 (C_{26}), 121.9 (C_{23}), 117.4 (C_{18}), 115.8 (C_{24}), 110.7 (C_{25}), 97.3 ($PhCH_2O\boldsymbol{C}H_2O$), 91.9 ($C_{12}$), 91.4 ($C_4$), 90.7 ($C_6$), 90.3 ($PhCH_2O\boldsymbol{C}H_2O$), 88.6 ($C_{11}$), 82.9 ($C_3$), 80.6 ($C_{10}$), 71.9 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.5 ($Ph\boldsymbol{C}H_2OCH_2O$), 49.3 ($C_5$), 39.8 ($C_{14}$), 33.2 ($C_9$), 28.1 ($C_7$), 21.1 ($C_{19}$), 21.0 ($C_8$), 18.9 ($C_{21}$), 15.9 ($C_{20}$), 13.2 ($C_{17}$).
FTIR (NaCl, thin film): 3448, 2929, 1744, 1703, 1159, 1115, 1010 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M+Na]^+$ 736.3098, found 772.3099.
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{25}}$**:** –70° (*c* = 0.460, $CHCl_3$).

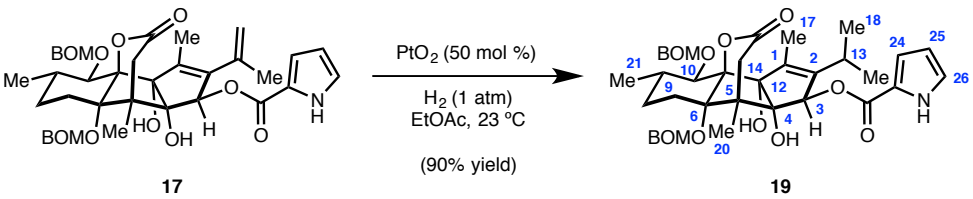
Preparation of anhydroryanodine (18):



An oven-dried, 2 dram vial was charged with **17** (15 mg, 0.021 mmol, 1.0 equiv), $Pd(OH)_2/C$ (20 wt %, 23 mg), followed by absolute EtOH (2.1 mL). The suspension was sparged with N_2 for 3 min, then H_2 for 3 min via a three-walled balloon. The suspension was subsequently stirred for 1 h at ambient temperature under H_2, then sparged with N_2 to remove excess H_2, diluted with EtOAc (5 mL), filtered through a short pad of Celite, and concentrated *in vacuo*. Purification of the crude residue by SiO_2 flash chromatography (5% MeOH/$CHCl_3$) afforded (+)-anhydroryanodine (**18**) as a white powder (9 mg, 0.019 mmol, 90% yield).

TLC (5% MeOH/$CHCl_3$): R_f 0.35 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, CD_3OD): δ 7.09 (dd, *J* = 2.6, 1.5 Hz, 1H, C_{26}), 6.90 (dd, *J* = 3.8, 1.5 Hz, 1H, C_{24}), 6.28 (dd, *J* = 3.8, 2.5 Hz, 1H, C_{25}), 6.20 (q, *J* = 2.3 Hz, 1H, C_3), 4.03 (d, *J* = 10.3 Hz, 1H, C_{10}), 3.45 (d, *J* = 19.8 Hz, 1H, C_{14}), 2.80 (p, *J* = 7.1 Hz, 1H, C_{13}), 2.56 (d, *J* = 19.7 Hz, C_{14}, 1H), 1.89 (d, *J* = 2.3 Hz, 3H, C_{17}), 1.83 (td, *J* = 10.5, 5.8 Hz, 1H, C_9), 1.66-1.58 (m, 2H, C_7), 1.57-1.49 (m, 2H, C_8), 1.12 (d, *J* = 7.0 Hz, 3H, C_{19}), 1.11 (d, *J* = 7.0 Hz, 3H, C_{18}), 1.01 (d, *J* = 7.0 Hz, 3H, C_{21}), 0.99 (s, 3H, C_{20}).
^{13}C NMR (101 MHz, $CDCl_3$): δ 172.3 (C_{15}=O), 161.8 (C_{22}=O), 144.6 (C_2), 138.3 (C_1), 125.8 (C_{26}), 123.2 (C_{23}), 117.0 (C_{24}), 111.1 (C_{25}), 94.0 (C_{12}), 92.7 (C_4), 90.2 (C_6), 84.7 (C_3), 84.2 (C_{11}), 72.6 (C_{10}), 40.5 (C_{14}), 35.2 (C_9), 28.7 (C_7), 28.2 (C_{13}), 26.3 (C_8), 21.5 (C_{18}/ C_{19}), 19.5 (C_{21}), 18.8 (C_{18}/C_{19}), 14.3 (C_{20}), 12.4 (C_{17}).
FTIR (NaCl, thin film): 3408, 2963, 1740, 1690, 1409, 1315, 1165 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M–H]^-$ 474.2128, found 474.2112.
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{25}}$**:** +18° (*c* = 0.345, MeOH).

Preparation of 19:

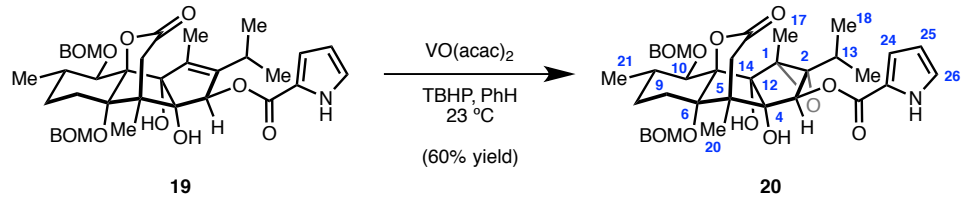


17 19

A 20 mL scintillation vial was charged with diene **17** (94 mg, 0.132 mmol, 1.0 equiv), PtO_2 (15 mg, 0.066 mmol, 0.5 equiv), followed by EtOAc (6 mL). The suspension was sparged with N_2 for 3 min, then H_2 for 3 min via a three-walled balloon. The suspension was subsequently stirred for 25 min at ambient temperature under H_2, then sparged with N_2 to remove excess H_2, diluted with EtOAc (5 mL), filtered through a short pad of Celite, and concentrated *in vacuo*. Purification of the crude residue by SiO_2 flash chromatography (40% EtOAc/hexane) afforded **19** (85 mg, 0.119 mmol, 90% yield) as a white foam.

TLC (40% EtOAc/hexanes): R_f 0.40 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.29 (s, 1H, N***H***), 7.43 – 7.29 (m, 10H, ***Ph***CH_2OCH_2O), 7.07 (td, *J* = 2.7, 1.4 Hz, 1H, C_{26}), 6.92 (ddd, *J* = 3.8, 2.4, 1.4 Hz, 1H, C_{24}), 6.33 (dt, *J* = 3.8, 2.6 Hz, 1H, C_{25}), 6.23 (q, *J* = 2.3 Hz, 1H, C_3), 5.18 (d, *J* = 6.4 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.92 (d, *J* = 6.4 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.92 (s, 2H, $PhCH_2OC\boldsymbol{H}_2O$), 4.83 (d, *J* = 12.2 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.71 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.67 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.65 (d, *J* = 12.2 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.39 (s, 1H, O***H***), 3.95 (s, 1H, O***H***), 3.92 (d, *J* = 10.4 Hz, 1H, C_{10}), 3.41 (d, *J* = 19.7 Hz, 1H, C_{14}), 2.80 (p, *J* = 7.0 Hz, 1H, C_{13}), 2.39 (d, *J* = 19.7 Hz, 1H, C_{14}), 2.18 – 2.03 (m, 1H, C_9), 1.91 (d, *J* = 2.4 Hz, 3H, C_{17}), 1.82 (dt, *J* = 13.2, 3.2 Hz, 1H, C_8), 1.70-1.63 (m, 1H, C_7), 1.60 – 1.51 (m, 1H, C_7), 1.46 (td, *J* = 12.3, 3.6 Hz, 1H, C_8), 1.13 (d, *J* = 7.0 Hz, 3H, C_{19}), 1.12 (d, 1.08 *J* = 7.0 Hz, 3H, C_{21}), 1.08 (s, 3H, C_{20}), 1.00 (d, *J* = 7.0 Hz, 3H, C_{18}).
^{13}C NMR (101 MHz, $CDCl_3$): δ 168.1 (C_{15}=O), 160.4 (C_{22}=O), 143.0 (C_2), 137.7 (C_{Ph}), 137.1 (C_{Ph}), 136.6 (C_1), 128.7 (C_{Ph}), 128.4 (C_{Ph}), 128.3 (C_{Ph}), 128.2 (C_{Ph}), 127.7 (C_{Ph}), 127.7 (C_{Ph}), 124.0 (C_{26}), 122.1 (C_{23}), 115.7 (C_{24}), 110.9 (C_{25}), 97.4 ($PhCH_2O\boldsymbol{C}H_2O$), 92.0 ($C_{12}$), 91.0 ($C_4$), 90.8 ($PhCH_2O\boldsymbol{C}H_2O$), 90.2 ($C_6$), 88.5 ($C_{11}$), 84.0 ($C_3$), 80.7 ($C_{10}$), 71.8 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.5 ($Ph\boldsymbol{C}H_2OCH_2O$), 49.3 ($C_5$), 39.9 ($C_{14}$), 33.2 ($C_9$), 28.0 ($C_7$), 26.8 ($C_{13}$), 21.2 ($C_{18}$), 21.0 ($C_8$), 19.0 ($C_{19}$), 18.9 ($C_{21}$), 15.9 ($C_{20}$), 11.8 ($C_{17}$).
FTIR (NaCl, thin film): 3455, 2927, 1744, 1708, 1159, 1026 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M+Na]^+$ 738.3254, found 738.3262.
$[\alpha]_D^{25}$: +36° (*c* = 0.380, $CHCl_3$).

Preparation of epoxide 20:



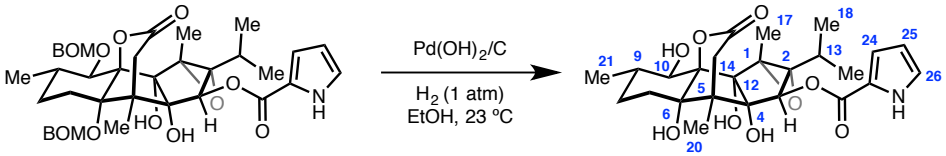
19 20

A 50 mL, oven-dried, round-bottomed flask was charged with **19** (144 mg, 0.201 mmol, 1.0 equiv), $VO(acac)_2$ (80 mg, 0.302 mmol, 1.5 equiv) and PhH (10.1 mL). The resulting green solution was stirred at ambient temperature for 5 min prior to the dropwise addition of TBHP (5.0-5.5 M in decane, 0.2 mL, 1.01 mmol, 5.0 equiv). The resulting dark-brown solution was stirred for 2 h at ambient temperature before additional TBHP (5.0-5.5 M in decane, 0.2 mL, 1.005 mmol, 5.0 equiv) was added to the reaction mixture. Stirring was continued

for 1 h until TLC analysis indicated complete consumption of starting material. The mixture was diluted with EtOAc (12 mL) and sat. aq. $Na_2S_2O_3$ (12 mL) was next slowly added. The two layers were separated, and the organic layer washed with sat. aq. $Na_2S_2O_3$ (2 x 12 mL) and sat. aq. $NaHCO_3$ (2 x 12 mL). The combined aqueous layers were extracted with EtOAc (2 x 6 mL), and the combined organic layers were washed with brine (6 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (30 to 40% EtOAc/hexanes) to afford epoxide **20** (88 mg, 0.120 mmol, 60% yield).

TLC (40% EtOAc/hexanes): R_f 0.40 (UV, *p*-anisaldehyde).
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.40 (s, 1H, N***H***), 7.42 – 7.29 (m, 10H, ***Ph***CH_2OCH_2O), 7.09 (td, *J* = 2.8, 1.4 Hz, 1H, C_{26}), 6.93 (ddd, *J* = 3.8, 2.5, 1.4 Hz, 1H, C_{24}), 6.35 (dt, *J* = 3.7, 2.6 Hz, 1H, C_{25}), 5.76 (s, 1H, C_3), 5.19 (d, *J* = 6.6 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.03 (d, *J* = 6.6 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.90 (d, *J* = 6.2 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.86 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.82 (d, *J* = 6.1 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.69 (d, *J* = 11.8 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.65 (d, *J* = 11.8 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.65 (d, *J* = 12.0 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.00 (d, *J* = 10.5 Hz, 1H, C_{10}), 3.98 (d, *J* = 0.7 Hz, 1H, O***H***), 3.87 (d, *J* = 20.4 Hz, 1H, C_{14}), 3.19 (s, 1H, O***H***), 2.56 (d, *J* = 20.3 Hz, 1H, C_{14}), 2.18 – 2.07 (m, 1H, C_9), 1.86 – 1.80 (m, 1H, C_8), 1.77 (dd, *J* = 13.8, 6.6 Hz, 1H, C_{13}), 1.71 (s, 3H, C_{17}), 1.71-1.64 (m, 1H, C_7), 1.62-1.53 (m, 1H, C_8), 1.57 – 1.47 (m, 1H, C_7), 1.22 (d, *J* = 7.4 Hz, 3H, C_{19}), 1.16 (d, *J* = 6.5 Hz, 3H, C_{21}), 1.02 (d, *J* = 7.0 Hz, 3H, C_{18}), 1.00 (s, 3H, C_{20}).
^{13}C NMR (126 MHz, $CDCl_3$): δ 168.1 (C_{15}=O), 159.3 (C_{22}=O), 137.9 (C_{Ph}), 136.3 (C_{Ph}), 128.6 (C_{Ph}), 128.4 (C_{Ph}), 128.3 (C_{Ph}), 128.2 (C_{Ph}), 127.7 (C_{Ph}), 127.6 (C_{Ph}), 124.6 (C_{26}), 121.5 (C_{23}), 115.8 (C_{24}), 111.0 (C_{25}), 97.6 ($PhCH_2O\boldsymbol{C}H_2O$), 93.2 ($C_4$), 91.2 ($C_6$), 91.1 ($C_{11}$), 90.6 ($C_{12}$), 89.6 ($PhCH_2O\boldsymbol{C}H_2O$), 81.3 ($C_{10}$), 81.0 ($C_3$), 76.2 ($C_1$), 74.8 ($C_2$), 71.3 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.6 ($Ph\boldsymbol{C}H_2OCH_2O$), 50.3 ($C_5$), 38.6 ($C_{14}$), 32.6 ($C_9$), 29.4 ($C_{13}$), 27.9 ($C_7$), 20.6 ($C_8$), 18.9 ($C_{21}$), 17.6 ($C_{18}$), 17.2 ($C_{19}$), 16.3 ($C_{20}$), 14.5 ($C_{17}$).
FTIR (NaCl, thin film): 3282, 2933, 1748, 1715, 1020 cm^{-1}.
HRMS (MM:ESI–APCI) : calc'd for $[M+Na]^+$ 754.3203, found 738.3215.
$[\alpha]_D^{25}$: +40° (*c* = 0.450, $CHCl_3$).

Preparation of anhydroryanodine epoxide (21):



20 **21**

A 25 mL round-bottomed flask was charged with epoxide **20** (50 mg, 0.068 mmol, 1.0 equiv), $Pd(OH)_2/C$ (20 wt %, 75 mg), followed by absolute EtOH (6.8 mL). The suspension was sparged with N_2 for 3 min, then H_2 for 3 min via a three-walled balloon. The suspension was subsequently stirred for 3 h at ambient temperature under H_2, then sparged with N_2 to remove excess H_2, diluted with EtOAc (5 mL), filtered through a short pad of Celite, and concentrated *in vacuo*. The resulting white powder was used in the next step without further purification.

A sample of anhydroryanodine epoxide (**21**) was purified by preparative thin-layer chromatography (5% $MeOH/CHCl_3$) for characterization purposes.

TLC (10% $MeOH/CHCl_3$): R_f 0.50 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, CD_3OD): δ 7.12 (dd, *J* = 2.5, 1.4 Hz, 1H, C_{26}), 6.93 (dd, *J* = 3.8, 1.5 Hz, 1H, C_{24}), 6.31 (dd, *J* = 3.8, 2.5 Hz, 1H, C_{25}), 5.66 (s, 1H, C_3), 4.09 (d, *J* = 10.5 Hz, 1H, C_{10}), 3.90 (d, *J* = 20.4 Hz, 1H, C_{14}), 2.75 (d, *J*

= 20.4 Hz, 1H, C_{14}), 1.91 – 1.81 (m, 1H, C_9), 1.77 (p, J = 7.2 Hz, 1H, C_{13}), 1.68 (s, 3H, C_{17}), 1.64 – 1.50 (m, 2H, C_8), 1.62-1.49 (m, 2H, C_7), 1.20 (d, J = 7.3 Hz, 3H, C_{19}), 1.11 (d, J = 6.4 Hz, 3H, C_{21}), 1.00 (d, J = 7.0 Hz, 3H, C_{18}), 0.93 (s, 3H, C_{20}).

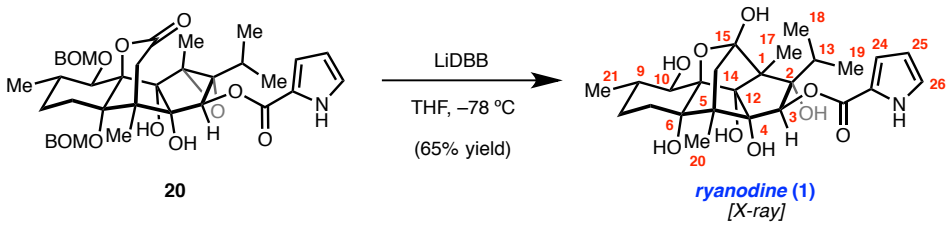
^{13}C NMR (101 MHz, CD_3OD): δ 171.5 (C_{15}=O), 160.8 (C_{22}=O), 126.3 (C_{26}), 122.6 (C_{23}), 117.1 (C_{24}), 111.3 (C_{25}), 95.0 (C_{12}), 92.6 (C_4), 91.9 (C_{11}), 85.2 (C_6), 82.1 (C_3), 77.3 (C_1), 75.3 (C_2), 72.9 (C_{10}), 50.2 (C_5), 39.4 (C_{14}), 34.7 (C_9), 30.6 (C_{13}), 28.6 (C_8), 25.9 (C_7), 18.7 (C_{21}), 18.2 (C_{19}), 17.6 (C_{18}), 15.5 (C_{17}), 14.7 (C_{20}).

FTIR (NaCl, thin film): 3419, 2967, 1749, 1707, 1402, 1324, 1128, 1085 cm^{-1}.

HRMS (MM:ESI–APCI): calc'd for $[M–H]^-$ 490.2083, found 490.2103.

$[\alpha]_D^{25}$: +18° (c = 0.705, MeOH).

Preparation of ryanodine (1):



Fresh LiDBB[10] was prepared according to the following procedure: An oven-dried, 25 mL Schlenk tube containing a borosilicate glass-coated magnetic stirbar was charged with 4,4′-di-*tert*-butylbiphenyl (550 mg, 2.0 mmol) and freshly cut lithium wire (14.0 mg, 2.0 mmol) (Note: Immediately prior to use, lithium wire was washed with hexanes, hammered out into a foil, and cut into several small strips). The Schlenk tube was evacuated and refilled with Ar three times before anhydrous THF (12.5 mL) was added and the resulting reaction mixture was then cooled to 0 ºC via an ice/water bath. After vigorously stirring (900-1000 rpm) at 0 ºC for 10 min, the solution became a deep-green, characteristic of the DBB radical-anion. After the reaction mixture was stirred at 0 ºC for approximately 4 h, the LiDBB solution (~0.16 M) was immediately used.

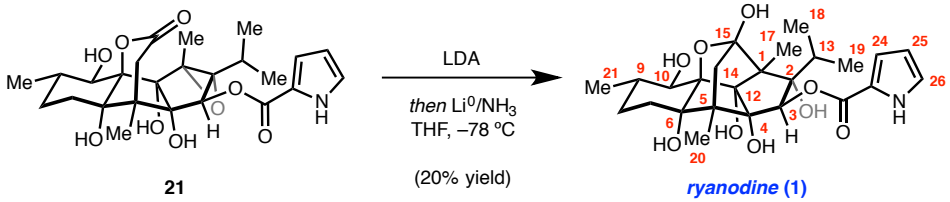
An oven-dried, 50 mL round-bottomed flask containing a borosilicate glass-coated magnetic stirbar was charged with epoxide **20** (64 mg, 0.087 mmol, 1.0 equiv) and anhydrous THF (4.3 mL) under Ar. The resulting solution was cooled to –78 ºC via a dry ice/acetone bath. Freshly prepared LiDBB (0.16 M, 5.4 mL, 0.87 mmol, 10 equiv) was added dropwise via syringe along the side of the flask until the dark green color persisted. The deep green mixture was stirred for 0.5 h at –78 ºC and then sat. aq. NH_4Cl (10 mL) was added before the reaction mixture was warmed to ambient temperature. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (0 to 5 to 10% MeOH/$CHCl_3$) to afford ryanodine (**1**) as a white solid (28 mg, 0.057 mmol, 65% yield) (Note: The purification was made easier by first flushing with $CHCl_3$ (100 mL) until all of the excess 4,4′-di-*tert*-butylbiphenyl was removed).

TLC (10% MeOH/$CHCl_3$): R_f 0.33 (UV, *p*-anisaldehyde).

^{1}H NMR (600 MHz, CD_3OD): δ 7.04 (dd, J = 2.5, 1.5 Hz, 1H, C_{26}), 6.88 (dd, J = 3.7, 1.5 Hz, 1H, C_{24}), 6.24 (dd, J = 3.8, 2.5 Hz, 1H, C_{25}), 5.64 (s, 1H, C_3), 3.80 (d, J = 10.2 Hz, 1H, C_{10}), 2.57 (d, J = 13.6Hz, 1H, C_{14}), 2.27 (h, J = 6.8 Hz, C_{13}), 2.10 (td, J = 12.9, 5.2 Hz, 1H, C_7), 1.94 (d, J = 13.6 Hz, 1H, C_{14}), 1.85 (tdd, J = 10.2, 8.5, 5.6 Hz, 1H, C_9), 1.54 (dtd, J = 12.4, 5.2, 1.8 Hz, 1H, C_8), 1.48 (td, J = 13.0, 4.7 Hz, 1H, C_8), 1.40 (s, 3H, C_{17}), 1.26 (ddd, J = 12.7, 4.6, 2.0 Hz, 1H, C_7), 1.12 (d, J = 6.7 Hz, 3H, C_{19}), 1.02 (d, J = 6.5 Hz, 3H, C_{21}), 0.90 (s, 3H, C_{20}), 0.76 (d, J = 6.5 Hz, 3H, C_{18}).

^{13}C NMR (101 MHz, CD_3OD): δ 161.8 (C_{22}=O), 125.6 (C_{26}), 123.3 (C_{23}), 117.0 (C_{24}), 110.9 (C_{25}), 102.9 (C_{15}), 96.7 (C_{12}), 92.3 (C_4), 90.8 (C_3), 87.4 (C_{11}), 86.5 (C_6), 84.3 (C_2), 72.8 (C_{10}), 65.9 (C_1), 49.6 (C_5), 41.8 (C_{14}), 35.4 (C_9), 30.9 (C_{13}), 29.3 (C_8), 26.8 (C_7), 19.5 (C_{19}), 19.0 (C_{21}), 18.9 (C_{18}), 12.6 (C_{20}), 10.2 (C_{17}).
FTIR (NaCl, thin film): 3335, 2969, 1691, 1410, 1324, 1164, 988, 750 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M–H]^-$ 492.2239, found 492.2250.
$[\alpha]_D^{25}$**:** +15° (*c* = 0.705, MeOH).

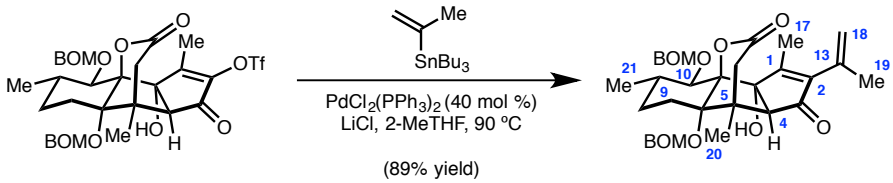
Table 1, entry 2:



21 ***ryanodine* (1)**

An oven-dried, 1 dram vial was charged with anhydroryanodine epoxide **21** (5 mg, 0.010 mmol, 1.0 equiv) and THF (1 mL). The solution was cooled to –78 ºC via a dry ice/acetone bath before a freshly prepared solution of LDA (1.0 M in THF, 60 µL, 0.060 mmol, 5.9 equiv) was added. After 1 h of stirring at –78 ºC, the pale-yellow solution was transferred to a pre-cooled dark-blue solution of lithium (1.7 mg) in freshly distilled ammonia (3 mL) via syringe at –78 ºC and the resulting reaction mixture was stirred for 15 min. After the addition of solid ammonium chloride (50 mg), stirring was halted and the colorless reaction mixture was removed from the dry ice/acetone bath and warmed to ambient temperature over 45 min, resulting in the slow evaporation of ammonia. The residue was dissolved in water (1 mL) and extracted with $CHCl_3$ (3 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude mixture was purified by preparative thin-layer chromatography (10% MeOH/$CHCl_3$) to afford ryanodine (**1**) (1 mg, 0.002 mmol, 20% yield).

Preparation of enone 22:

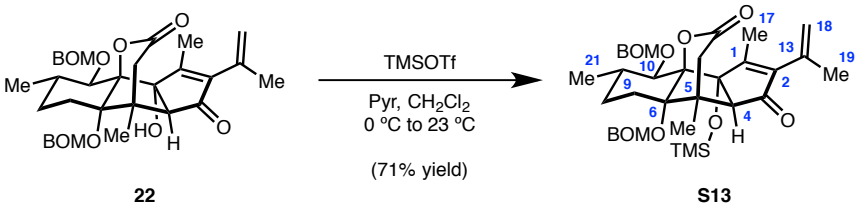


8 **22**

In a nitrogen-filled glovebox, an oven-dried, 20 mL scintillation vial was charged with vinyl triflate **8** (302 mg, 0.425 mmol, 1.0 equiv), $PdCl_2(PPh)_3$ (119 mg, 0.170 mmol, 40 mol %), anhydrous LiCl (108 mg, 2.55 mmol, 6.0 equiv), tributyl(2-propenyl)stannane (422 mg, 1.27 mmol, 3.0 equiv), and anhydrous 2-methyltetrahydrofuran (6.4 mL). The vial was sealed with a Teflon-lined cap, and placed in a preheated heating block at 90 ºC. After 14 h, the vial was removed from the heating block and allowed to cool to ambient temperature, then sat. aq. KF (10 mL) was added. The biphasic mixture was vigorously stirred for 45 min, then diluted with EtOAc (30 mL). The two layers were separated and the organic layer washed with additional sat. aq. KF (10 mL). The combined aqueous layers were extracted with EtOAc (2 x 30 mL), and the combined organic layers next washed with brine (20 mL), dried over Na_2SO_4, filtered over Celite, and concentrated *in vacuo* to afford an orange oil. Purification by SiO_2 flash chromatography (30 to 40 to 50% EtOAc/hexanes) afforded the desired product **22** as a pale yellow foam (228 mg, 0.378 mmol, 89% yield).

TLC (40% EtOAc/hexanes): R_f 0.45 (UV, CAM).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.27 (m, 10H, ***Ph***CH_2OCH_2O), 5.22 (p, *J* = 1.7 Hz, 1H, C_{18}), 5.07 (d, *J* = 5.4 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.02 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.97 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.84 (d, *J* = 5.4 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.79 (dd, *J* = 1.9, 1.0 Hz, 1H, C_{18}), 4.77 (d, *J* = 12.1 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.71 (d, *J* = 12.1 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.71 (d, *J* = 12.3 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.65 (d, *J* = 12.3 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.55 (s, 1H, OH), 4.00 (d, *J* = 10.5 Hz, 1H, C_{10}), 2.90 (d, *J* = 1.4 Hz, 1H, C_4), 2.36 (d, *J* = 19.6 Hz, 1H, C_{14}), 2.27 (dd, *J* = 19.6, 1.6 Hz, 1H, C_{14}), 2.20 (s, 3H, C_{17}), 2.12 – 2.04 (m, 1H, C_9), 1.96 – 1.89 (m, 1H, C_7), 1.87 (t, *J* = 1.3 Hz, 3H, C_{19}), 1.62 (td, *J* = 7.7, 7.1, 3.1 Hz, 2H, C_8), 1.58 – 1.49 (m, 1H, C_7), 1.28 (s, 3H, C_{20}), 1.05 (d, *J* = 6.6 Hz, 3H, C_{21}).
^{13}C NMR (101 MHz, $CDCl_3$): δ 204.9 (C_3=O), 169.6 (C_1), 167.1 (C_{15}=O), 145.9 (C_2), 137.0 (C_{Ph}), 136.8 (C_{Ph}), 136.3 (C_{13}), 128.7 (C_{Ph}), 128.6 (C_{Ph}), 128.6 (C_{Ph}), 128.1 (C_{Ph}), 128.1 (C_{Ph}), 128.0 (C_{Ph}), 127.7 (C_{Ph}), 117.6 (C_{18}), 97.0 ($PhCH_2O\boldsymbol{C}H_2O$), 91.5 ($C_6$), 91.1 ($C_{11}$), 89.7 ($PhCH_2O\boldsymbol{C}H_2O$), 89.3 ($C_{12}$), 79.9 ($C_{10}$), 71.0 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.3 ($Ph\boldsymbol{C}H_2OCH_2O$), 66.0 ($C_4$), 45.4 ($C_5$), 39.2 ($C_{14}$), 33.2 ($C_9$), 27.9 ($C_8$), 21.7 ($C_{19}$), 21.1 ($C_7$), 19.9 ($C_{20}$), 18.5 ($C_{21}$), 14.6 ($C_{17}$).
FTIR (NaCl, thin film): 3387, 2928, 1748, 1698, 1027 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M+H]^+$ 603.2952, found 603.2959.
$[\alpha]_D^{25}$: +100° (*c* = 0.200, $CHCl_3$).

Preparation of TMS ether S13:

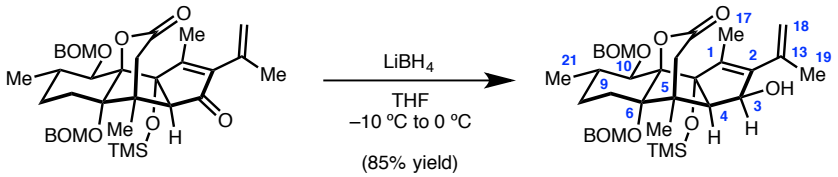


To an oven-dried, 100 mL round-bottomed flask was added enone **22** (944 mg, 1.57 mmol, 1.0 equiv), anhydrous CH_2Cl_2 (31 mL), and freshly distilled pyridine (1.27 mL, 15.7 mmol, 10 equiv). The solution was cooled to 0 ºC in an ice/water bath and TMSOTf (0.85 mL, 4.70 mmol, 3.0 equiv) was added via syringe. The ice/water bath was then removed and stirring was continued at ambient temperature. Additional portions of TMSOTf (0.85 mL, 4.70 mmol, 3.0 equiv) and pyridine (1.27 mL, 15.7 mmol, 10.0 equiv) were added every 12 h until TLC analysis indicated complete consumption of the starting material (*ca.* 36 h). The reaction mixture was next diluted with CH_2Cl_2 (15 mL) and carefully quenched with the addition of sat. aq. $NaHCO_3$ (30 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with brine (15 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (20 to 30 to 35% EtOAc/hexanes) to afford TMS ether **S13** (750 mg, 1.11 mmol, 71% yield) as a colorless foam.

TLC (30% EtOAc/hexanes): R_f 0.34 (UV, CAM).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.28 (m, 10H, ***Ph***CH_2OCH_2O), 5.24 (p, *J* = 1.6 Hz, 1H, C_{18}), 5.08 (d, *J* = 7.0 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 5.01 (s, 2H, $PhCH_2OC\boldsymbol{H}_2O$), 4.92 (d, *J* = 7.0 Hz, $PhCH_2OC\boldsymbol{H}_2O$), 4.84 (d, *J* = 11.9 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.81 (d, *J* = 10.9 Hz, $Ph\boldsymbol{C}H_2OCH_2O$), 4.79 (s, 1H, C_{18}), 4.60 (d, *J* = 11.9 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.57 (d, *J* = 10.9 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.02 (d, *J* = 10.5 Hz, 1H, C_{10}), 3.00 (s, 1H, C_4), 2.33 (d, *J* = 19.5 Hz, 1H, C_{14}), 2.27 (d, *J* = 19.5 Hz, 1H, C_{14}), 2.20 (s, 3H, C_{17}), 2.14 – 2.00 (m, 1H, C_9), 1.99 – 1.90 (m, 1H, C_7), 1.88 (t, *J* = 1.2 Hz, 3H, C_{19}), 1.78 (qd, *J* = 13.0, 4.2 Hz, 1H, C_8), 1.71- 1.58 (m, 1H, C_8), 1.56 – 1.44 (m, 1H, C_7), 1.22 (s, 3H, C_{20}), 1.15 (d, *J* = 6.5 Hz, 3H, C_{21}), 0.11 (s, 9H, TMS).

^{13}C NMR (101 MHz, $CDCl_3$): δ 205.0 (C_3=O), 170.8 (C_1), 167.3 (C_{15}=O), 145.6 (C_2), 137.9 (C_{Ph}), 137.0 (C_{Ph}), 136.1 (C_{13}), 128.6 (C_{Ph}), 128.4 (C_{Ph}), 128.0 (C_{Ph}), 127.7 (C_{Ph}), 127.7 (C_{Ph}), 127.6 (C_{Ph}), 117.5 (C_{18}), 98.1 ($PhCH_2O\boldsymbol{C}H_2O$), 92.9 ($C_{11}$), 91.7 ($C_{12}$), 91.0 ($C_6$), 89.9 ($PhCH_2O\boldsymbol{C}H_2O$), 81.7 ($C_{10}$), 70.5 ($Ph\boldsymbol{C}H_2OCH_2O$), 65.1 ($C_4$), 46.6 ($C_5$), 39.2 ($C_{14}$), 32.9 ($C_9$), 27.9 ($C_8$), 21.5 ($C_{19}$), 21.1 ($C_7$), 20.4 ($C_{20}$), 19.0 ($C_{21}$), 14.7 ($C_{17}$), 1.9 (Si(*Me*)$_3$).
FTIR (NaCl, thin film): 2954, 1751, 1699, 1025 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M+H]^+$ 675.3348, found 675.3349.
$[\alpha]_D^{25}$: +124° (*c* = 0.245, $CHCl_3$).

Preparation of alcohol 23:

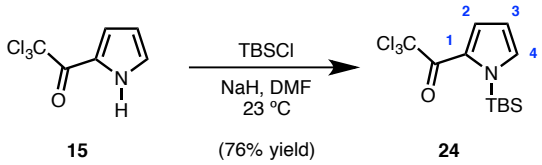


S13 **23**

To an oven-dried, 100 mL round-bottomed flask was added enone **S13** (749 mg, 1.11 mmol, 1.0 equiv) and anhydrous THF (22 mL). The solution was cooled to –10 ºC in an ice/acetone bath and solid $LiBH_4$ (121 mg, 5.55 mmol, 5.0 equiv) was added. After 1 h, a second portion of solid $LiBH_4$ (121 mg, 5.55 mmol, 5.0 equiv) was added before warming the reaction mixture to 0 ºC with an ice/water bath. Stirring was continued at 0 ºC for 1 h after which a third portion of solid $LiBH_4$ (121 mg, 5.55 mmol, 5.0 equiv) was added at 0 ºC. The reaction was allowed to stir at 0 ºC an additional 1 h before sat. aq. NH_4Cl (35 mL) was *slowly* added to the reaction. The mixture was diluted with EtOAc (15 mL), the two layers separated, and the organic layer washed with an additional portion of sat. aq. NH_4Cl (35 mL). The combined aqueous layers were extracted with EtOAc (3 x 40 mL), and the combined organic layers next dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (30 to 40 to 50% EtOAc/hexanes) to afford the desired product **23** as a colorless foam (635 mg, 0.94 mmol, 85% yield).

TLC (40% EtOAc/hexanes): R_f 0.37 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.27 (m, 10H, $\boldsymbol{Ph}CH_2OCH_2O$), 5.21 (p, *J* = 1.7 Hz, 1H, C_{18}), 5.22 – 5.19 (m, 1H, C_3), 5.02 (d, *J* = 6.6 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.97 (d, *J* = 7.9 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.95 (d, *J* = 7.9 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.92 (d, *J* = 6.6 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.90 (dd, *J* = 2.0, 1.0 Hz, 1H, C_{18}), 4.84 (d, *J* = 11.9 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.78 (d, *J* = 11.6 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.61 (d, *J* = 11.6 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 4.55 (d, *J* = 11.9 Hz, 1H, $Ph\boldsymbol{C}H_2OCH_2O$), 3.95 (d, *J* = 10.4 Hz, 1H, C_{10}), 3.33 (d, *J* = 19.6 Hz, 1H, C_{14}), 3.06 (dd, *J* = 8.0, 1.4 Hz, 1H, C_4), 2.17 (dd, *J* = 19.6, 1.4 Hz, 1H, C_{14}), 2.11 – 1.98 (m, 1H, C_9), 1.88 (t, *J* = 1.2 Hz, 3H, C_{19}), 1.89 – 1.86 (m, 1H, C_7), 1.81 (d, *J* = 2.2 Hz, 3H, C_{17}), 1.73 (d, *J* = 3.2 Hz, 1H, OH), 1.70 – 1.59 (m, 2H, C_8), 1.56 – 1.45 (m, 1H, C_7), 1.20 (s, 3H, C_{20}), 1.14 (d, *J* = 6.5 Hz, 3H, C_{21}), 0.10 (s, 9H, TMS).
^{13}C NMR (101 MHz, $CDCl_3$): δ 169.4 (C_{15}=O), 146.3 (C_1), 139.0 (C_2), 138.2 (C_{Ph}), 138.0 (C_{13}), 137.3 (C_{Ph}), 128.5 (C_{Ph}), 128.3 (C_{Ph}), 127.9 (C_{Ph}), 127.8 (C_{Ph}), 127.7 (C_{Ph}), 127.4 (C_{Ph}), 116.7 (C_{18}), 98.2 ($PhCH_2O\boldsymbol{C}H_2O$), 97.2 ($C_{12}$), 93.0 ($C_{11}$), 89.5 ($C_6$), 89.3 ($PhCH_2O\boldsymbol{C}H_2O$), 82.3 ($C_{10}$), 74.5 ($C_3$), 70.3 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.1 ($Ph\boldsymbol{C}H_2OCH_2O$), 58.0 ($C_4$), 47.1 ($C_5$), 39.2 ($C_{14}$), 33.3 ($C_9$), 28.0 ($C_8$), 21.4 ($C_{19}$), 21.2 ($C_{20}$), 20.3 ($C_7$), 19.1 ($C_{21}$), 12.7 ($C_{17}$), 1.8 (Si(*Me*)$_3$).
FTIR (NaCl, thin film): 3459, 2954, 1716, 1026 cm^{-1}.
HRMS (MM:ESI–APCI): calc'd for $[M+Na]^+$ 699.3324, found 699.3325.
$[\alpha]_D^{25}$: –17° (*c* = 0.275, $CHCl_3$).

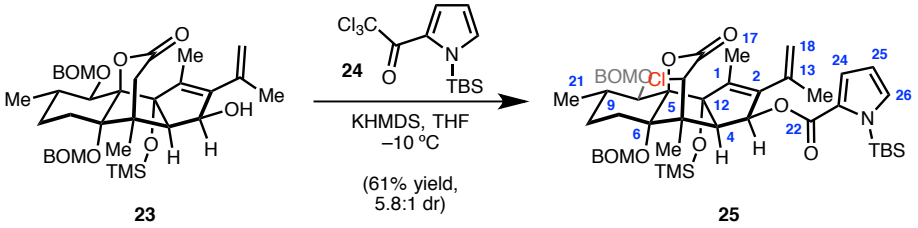
Preparation of TBS-protected pyrrole 24:



To a 100 mL, oven-dried flask was added NaH (dry, 339 mg, 14.1 mmol, 1.0 equiv) in a nitrogen-filled glovebox. The flask was capped with a rubber septum, removed from the glovebox, and anhydrous DMF (12 mL) was then added. The resulting slurry was cooled to 0 ºC in an ice/water bath and after 15 min, 2-(trichloroacetyl)pyrrole (3.0 g, 14.1 mmol, 1.0 equiv) in anhydrous DMF (12 mL) was added dropwise by cannula transfer over 10 min. [Caution! Rapid generation of H_2 gas. A vent needle was routinely used to prevent over-pressurization.] Upon complete addition, the reaction mixture was warmed to ambient temperature and stirring was continued for another 30 min before TBSCl (2.55 g, 16.9 mmol, 1.2 equiv) in anhydrous DMF (12 mL) was added dropwise by cannula transfer over 10 min, during which time the yellow-brown solution fades to a pale pink slurry. The reaction was continued for 30 min then diluted with Et_2O (50 mL) and carefully quenched with the addition of sat. aq. NH_4Cl (50 mL). The layers were separated and the aqueous layer next extracted with Et_2O (2 x 50 mL). The combined organic layers were washed with H_2O (30 mL), brine (30 mL), then dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford an orange oil. Purification by SiO_2 flash chromatography (1 to 2 to 3% Et_2O/hexanes) afforded TBS-protected pyrrole **24** as a thick, slightly yellow oil (3.52 g, 10.8 mmol, 76% yield) that solidifies to a colorless solid upon cooling to –20 ºC.

TLC (2% Et_2O/hexanes): R_f 0.44 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, J = 4.0, 1.3 Hz, 1H, C_2), 7.27 (dd, J = 2.5, 1.3 Hz, 1H, C_4), 6.40 (dd, J = 3.9, 2.5 Hz, 1H, C_3), 0.95 (s, 9H, Si(***t-Bu***)Me_2), 0.54 (s, 6H, Si(*t*-Bu)***Me***$_2$).
^{13}C NMR (125 MHz, $CDCl_3$): δ 172.8 (*C*=O), 136.7 (C_4), 127.9 (C_1), 126.8 (C_2), 112.1 (C_3), 96.1 (***C***Cl_3), 27.3 (Si–C(***C***$H_3)_3$), 19.6 (Si–***C***$(CH_3)_3$), –1.4 (Si(***C***$H_3)_2$).
FTIR (NaCl, thin film): 2954, 2932, 2896, 2860, 1677 cm^{-1}.
HRMS: calc'd for $[M-H]^-$ 324.0150, found 324.0153.

Preparation of chloride 25:



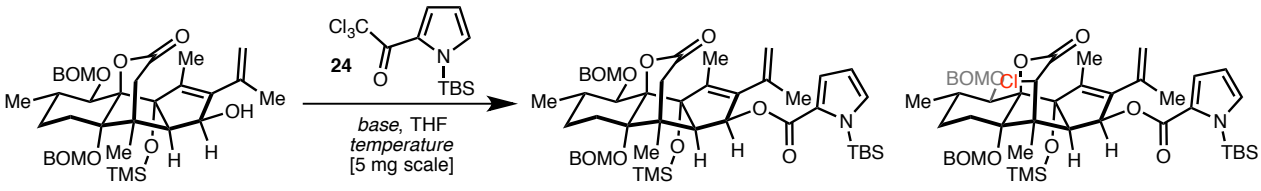
In a nitrogen-filled glovebox, an oven-dried, 50 mL round-bottomed flask was charged with solid KHMDS (95%, 388 mg, 1.85 mmol, 2.0 equiv). The flask was capped with a rubber septum, removed from the glovebox, and anhydrous THF (3.7 mL) was added. The resulting mixture was stirred at ambient temperature for 10-15 min to ensure complete dissolution of the solid, then cooled to –10 ºC in an ice/acetone bath and stirring continued for 15 min before adding alcohol **23** (625 mg, 0.92 mmol, 1.0 equiv) in anhydrous THF (7.0 mL) (Note: alcohol **23** was azeotroped with PhH three times immediately prior to use) dropwise via syringe before another portion of THF (1.2 mL) was used to render the transfer quantitative. The pale-yellow reaction mixture was stirred an additional 10 min at –10 ºC before TBS-protected pyrrole **24** (754 mg, 2.31 mmol, 2.5 equiv) in

anhydrous THF (4.1 mL) was added dropwise via syringe (Note: pyrrole **24** was azeotroped with PhH three times immediately prior to use). The resulting dark pink-orange reaction mixture was allowed 20 min at –10 ºC then quenched with the addition of sat. aq. NH_4Cl (5 mL), warmed to ambient temperature, and diluted with EtOAc (5 mL). The two layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by SiO_2 flash chromatography (5 to 10 to 15% EtOAc/hexanes) afforded a 5.8:1 inseparable diastereomeric mixture of chloride **25** as a yellow-orange foam (515 mg, 0.56 mmol, 61% yield).

An analytical sample of the major diastereomer of chloride **25** was obtained by a second round of purification via SiO_2 flash chromatography (1.5% EtOAc/CH_2Cl_2). The stereochemistry of the major diastereomer of the chloride substituted C_{14}–H was determined by nOe analysis.

TLC (10% EtOAc/hexanes): R_f 0.32 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.33 (m, 10H, ***Ph***CH_2OCH_2O), 7.11 (s, 1H, C_{26}), 7.10 (s, 1H, C_{24}), 6.38 (dd, *J* = 7.8, 2.4 Hz, 1H, C_3), 6.30 (t, *J* = 3.1 Hz, 1H, C_{25}), 5.26 (s, 1H, C_{14}), 5.10 (s, 1H, C_{18}), 5.00 (d, *J* = 6.5 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.99 (d, *J* = 6.3 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.96 (d, J = 6.4 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.89 (d, *J* = 6.6 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.87 (dd, *J* = 1.9, 1.0 Hz, 1H, C_{18}), 4.84 (d, *J* = 11.9 Hz, 1H, $Ph\boldsymbol{CH}_2OCH_2O$), 4.76 (d, *J* = 11.5 Hz, 1H, $Ph\boldsymbol{CH}_2OCH_2O$), 4.62 (d, *J* = 11.5 Hz, 1H, $Ph\boldsymbol{CH}_2OCH_2O$), 4.58 (d, *J* = 11.9 Hz, 1H, $Ph\boldsymbol{CH}_2OCH_2O$), 3.96 (d, *J* = 10.4 Hz, 1H, C_{10}), 3.43 (d, *J* = 7.9 Hz, 1H, C_4), 2.04 (m, 1H, C_9), 2.00 – 1.96 (m, 2H, C_7), 1.86 (d, *J* = 2.3 Hz, 3H, C_{17}), 1.73 (s, 3H, C_{19}), 1.66 – 1.59 (m, 2H, C_8), 1.21 (s, 3H, C_{20}), 1.15 (d, *J* = 6.5 Hz, 3H, C_{21}), 0.93 (s, 9H, Si(***t-Bu***)Me_2), 0.53 (s, 3H, Si(*t*-Bu)$\boldsymbol{Me}_2$), 0.52 (s, 3H, Si(*t*-Bu)$\boldsymbol{Me}_2$), 0.17 (s, 9H, TMS).
^{13}C NMR (101 MHz, $CDCl_3$): δ 166.3 (C_{15}=O), 160.0 (C_{22}=O), 145.0 (C_2), 139.4 (C_1), 138.0 (C_{Ph}), 137.4 (C_{13}), 137.1 (C_{Ph}), 133.4 (C_{24}), 128.6 (C_{Ph}), 128.4 (C_{Ph}), 128.0 (C_{Ph}), 127.8 (C_{Ph}), 127.8 (C_{Ph}), 127.5 (C_{Ph}), 127.2 (C_{23}), 121.9 (C_{26}), 117.5 (C_{18}), 111.3 (C_{25}), 98.3 ($PhCH_2O\boldsymbol{C}H_2O$), 96.6 ($C_{12}$), 94.1 ($C_{11}$), 89.5 ($PhCH_2O\boldsymbol{C}H_2O$), 88.7 ($C_6$), 82.1 ($C_{10}$), 73.4 ($C_3$), 70.4 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.3 ($Ph\boldsymbol{C}H_2OCH_2O$), 58.5 ($C_4$), 58.2 ($C_{14}$), 51.7 ($C_5$), 33.6 ($C_9$), 28.1 ($C_8$), 27.1 (Si(***t-Bu***)$Me_2$), 22.5 ($C_7$), 20.6 ($C_{19}$), 20.0 ($C_{20}$), 19.3 (Si–$\boldsymbol{C}(CH_3)_3$), 19.1 ($C_{21}$), 12.9 ($C_{17}$), 1.8 (TMS), –1.9 (Si(*t*-Bu)$\boldsymbol{Me}_2$), –1.9 (Si(*t*-Bu)$\boldsymbol{Me}_2$).
FTIR (NaCl, thin film): 2953, 2930, 1754, 1715, 1262, 1150 cm^{-1}.
HRMS: calc'd for $[M+NH_4]^+$ 935.4458, found 935.4459.
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{25}}$: –69º (*c* = 0.840, $CHCl_3$).

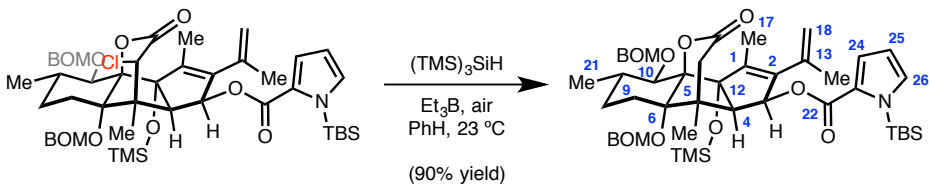
Table S2. Optimization of acylation of C3-alcohol 23



23 **26** **25**

entry	base	equiv	temperature	major product	isolated yield	
1	NaHMDS	1.1 equiv	–78 ºC	translactonization	28% (desired **26**)	*lower temperatures avoid chlorination, but suffer from poor conversion and large amounts of translactonization*
2	LHMDS	1.1 equiv	–78 ºC	SM **23**	0%	
3	KHMDS	1.1 equiv	–78 ºC	SM **23**	trace	
4	NaHMDS	1.5 equiv	–60 ºC	translactonization	25% (desired **26**)	
5	NaHMDS	1.5 equiv	–40 ºC	translactonization	28% (desired **26**)	
6	NaHMDS	1.2 equiv	–10 ºC	translactonization	20% (chloride **25**)	*higher temperatures favor chlorination, very short reaction times (10-15 min), lowering equiv avoids chlorination to a degree, but allowing reaction to run even 5-10 additional mins leads to clean conversion to chloride **25***
7	NaHMDS	2.0 equiv	–10 ºC	translactonization	18% (chloride **25**)	
8	KHMDS	2.0 equiv	–10 ºC	chloride **25**	69% (chloride **25**)	
9	KHMDS	1.2 equiv	–10 ºC	chloride **25**	20% (**26**) + 45% (**25**)	
10	LHMDS	2.0 equiv	–10 ºC	SM **23**	0%	
11	NaH	2.0 equiv	0 ºC to 23 ºC	TMS deprotect.	10% (desired–TMS)	
12	NaH	4.0 equiv	0 ºC to 23 ºC	TMS deprotect.	12% (desired–TMS)	

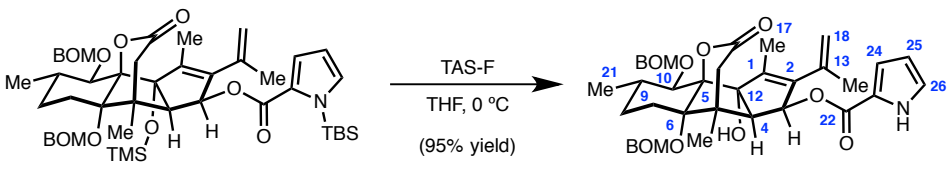
Preparation of pyrrole ester 26:



To an oven-dried, 25 mL round-bottomed flask was added chloride **25** (395 mg, 0.43 mmol, 1.0 equiv) and anhydrous PhH (8.6 mL). The solution was treated with $(TMS)_3SiH$ (0.27 mL, 0.86 mmol, 2.0 equiv) and Et_3B (1.0 M in hexanes, 0.43 mL, 0.43 mmol, 1.0 equiv) before air (4.0 mL) was slowly sparged through the reaction mixture via syringe. Stirring was continued at ambient temperature for 1 h before additional portions of $(TMS)_3SiH$ (0.27 mL, 0.86 mmol, 2.0 equiv), Et_3B (1.0 M in hexanes, 0.43 mL, 0.43 mmol, 1.0 equiv) and air (4.0 mL) were added via syringe. Stirring was then continued until TLC analysis indicated complete consumption of the starting material (*ca.* 1.5 h), during which time the reaction mixture turns dark red-orange. The reaction mixture was next concentrated *in vacuo* and the crude residue was directly purified via SiO_2 flash chromatography (15 to 20 to 25% EtOAc/hexanes) to afford pyrrole ester **26** as a yellow foam (342 mg, 0.39 mmol, 90% yield).

TLC (20% EtOAc/hexanes): R_f 0.36 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.27 (m, 10H, ***Ph***CH_2OCH_2O), 7.08 (dd, *J* = 9.5, 3.0 Hz, 1H, C_{26}), 7.06 (dd, *J* = 6.5, 3.1 Hz, 1H, C_{24}), 6.34 (dq, *J* = 7.9, 2.2 Hz, 1H, C_3), 6.27 (dd, *J* = 3.6, 2.6 Hz, 1H, C_{25}), 5.10 (p, *J* = 1.6 Hz, 1H, C_{18}), 4.98 (s, 2H, $PhCH_2OC\boldsymbol{H_2}O$), 4.98 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H_2}O$), 4.89 (s, 1H, C_{18}), 4.88 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H_2}O$), 4.85 (d, *J* = 11.9 Hz, 1H, $PhC\boldsymbol{H_2}OCH_2O$), 4.77 (d, *J* = 11.6 Hz, 1H, $PhC\boldsymbol{H_2}OCH_2O$), 4.63 (d, *J* = 11.5 Hz, 1H, $PhC\boldsymbol{H_2}OCH_2O$), 4.57 (d, *J* = 11.9 Hz, 1H, $PhC\boldsymbol{H_2}OCH_2O$), 3.97 (d, *J* = 10.3 Hz, 1H, C_{10}), 3.23 (dd, *J* = 3.6, 1.5 Hz, 1H, C_4), 3.21 (d, *J* = 19.5 Hz, 1H, C_{14}), 2.24 (dd, *J* = 19.5, 1.5 Hz, 1H, C_{14}), 2.10 – 2.01 (m, 1H, C_9), 1.87 (d, *J* = 2.3 Hz, 3H, C_{17}), 1.85 – 1.80 (m, 1H, C_7), 1.73 (s, 3H, C_{19}), 1.69 – 1.62 (m, 2H, C_8), 1.58 – 1.45 (m, 1H, C_7), 1.15 (d, *J* = 6.4 Hz, 3H, C_{21}), 0.96 (s, 3H, C_{20}), 0.93 (s, 9H, Si(***t-Bu***)Me_2), 0.52 (s, 3H, Si(*t*-Bu)$\boldsymbol{Me_2}$), 0.52 (s, 3H, Si(*t*-Bu)$\boldsymbol{Me_2}$), 0.17 (s, 9H, TMS).
^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0 (C_{15}=O), 160.4 (C_{22}=O), 144.2 (C_2), 139.0 (C_1), 138.2 (C_{Ph}), 138.0 (C_{13}), 137.2 (C_{Ph}), 133.1 (C_{26}), 128.5 (C_{Ph}), 128.3 (C_{Ph}), 127.9 (C_{23}), 127.9 (C_{Ph}), 127.8 (C_{Ph}), 127.5 (C_{Ph}), 121.6 (C_{24}), 116.9 (C_{18}), 110.9 (C_{25}), 98.2 ($PhCH_2O\boldsymbol{C}H_2O$), 97.2 ($C_{12}$), 93.0 ($C_{11}$), 89.5 ($C_6$), 89.3 ($PhCH_2O\boldsymbol{C}H_2O$), 82.3 ($C_{10}$), 74.4 ($C_3$), 70.3 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.3 ($Ph\boldsymbol{C}H_2OCH_2O$), 57.4 ($C_4$), 46.9 ($C_5$), 39.0 ($C_{14}$), 33.4 ($C_9$), 28.0 ($C_8$), 27.1 (Si(***t-Bu***)$Me_2$), 20.8 ($C_{20}$), 20.7 ($C_{19}$), 20.3 ($C_7$), 19.2 (Si–$\boldsymbol{C}(CH_3)_3$), 19.1 ($C_{21}$), 12.8 ($C_{17}$), 1.8 (TMS), –1.8 (Si(*t*-Bu)$\boldsymbol{Me_2}$), –1.9 (Si(*t*-Bu)$\boldsymbol{Me_2}$).
FTIR (NaCl, thin film): 2929, 1948, 1712, 1262, 1150, 1094, 1042, 1026 cm^{-1}.
HRMS: calc'd for $[M+NH_4]^+$ 901.4849, found 901.4846.
$[\alpha]_D^{25}$: –53° (*c* = 0.335, $CHCl_3$).

Preparation of alcohol S14:



26 **S14**

To an oven-dried, 25 mL round-bottomed flask was added silyl ether **26** (271 mg, 0.31 mmol, 1.0 equiv) and anhydrous THF (6.1 mL). The resulting solution was cooled to 0 ºC in an ice/water bath and stirring was continued for 15 min prior to the dropwise addition of TAS-F (253 mg, 0.92 mmol, 3.0 equiv) in a minimal amount of anhydrous DMF (1 mL) via syringe, producing a golden yellow solution (Note: TAS-F was stored and handled in a nitrogen-filled glovebox to maintain the integrity of the reagent). After 30 min at 0 ºC, an additional portion of TAS-F (169 mg, 0.61 mmol, 2.0 equiv) in a minimal amount of anhydrous DMF (0.5 mL) was added (Note: On smaller scales (<50 mg scale), a small excess of TAS-F was routinely used without issue; however, on scale-up, the reaction consistently stalled at about 50-60% conversion with the TMS group intact and required additional portions of TAS-F). Stirring at 0 ºC was continued for another 30 min at which point TLC and LCMS analysis indicated complete consumption of the starting material. The reaction mixture was diluted with Et_2O (6 mL) and filtered through a short pad of SiO_2, washing with 65% EtOAc/hexanes until TLC analysis indicated complete elution of the desired product. The filtrate was concentrated *in vacuo* and the crude residue was purified by SiO_2 flash chromatography (30 to 40 to 50% EtOAc/hexanes) to afford alcohol **S14** as a clear oil that solidifies into a white solid upon standing (203 mg, 0.259 mmol, 95% yield).

TLC (45% EtOAc/hexanes): R_f 0.43 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, C_6D_6): δ 8.77 (s, 1H, N***H***), 7.42 – 7.34 (m, 2H, ***Ph***CH_2OCH_2O), 7.30 – 7.19 (m, 4H, ***Ph***CH_2OCH_2O), 7.14 – 7.09 (m, 2H, ***Ph***CH_2OCH_2O), 7.05 – 7.00 (m, 1H, ***Ph***CH_2OCH_2O), 6.98 (td, *J* = 2.5, 1.3 Hz, 1H, C_{25}), 6.87 – 6.81 (m, 1H, C_3), 6.28 (td, *J* = 2.7, 1.4 Hz, 1H, C_{26}), 6.05 (dt, *J* = 3.7, 2.5 Hz, 1H, C_{24}), 5.29 (dd, *J* = 2.2, 1.1 Hz, 1H, C_{18}), 5.09 (t, *J* = 1.9 Hz, 1H, C_{18}), 4.93 (d, *J* = 5.4 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.70 (d, *J* = 5.5 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.63 (d, *J* = 11.8 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.54 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.52 (d, *J* = 11.8 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.45 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.35 (d, *J* = 12.4 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.35 (s, 1H, O***H***), 4.30 (d, *J* = 12.4 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.08 (d, *J* = 10.3 Hz, 1H, C_{10}), 3.51 (dd, *J* = 7.9, 1.4 Hz, 1H, C_4), 3.38 (d, *J* = 19.2 Hz, 1H, C_{14}), 2.32 (d, *J* = 2.3 Hz, 3H, C_{17}), 2.21 – 2.14 (m, 1H, C_9), 2.09 (dd, *J* = 19.2, 1.6 Hz, 1H, C_{14}), 1.71 (s, 3H, C_{18}), 1.42 (qd, *J* = 13.1, 12.7, 4.5, 1H, C_8), 1.22 – 1.15 (m, 2H, C_8/C_7), 1.13 – 1.03 (m, 1H, C_7), 0.98 (d, *J* = 6.5 Hz, 3H, C_{21}), 0.82 (s, 3H, C_{20}).

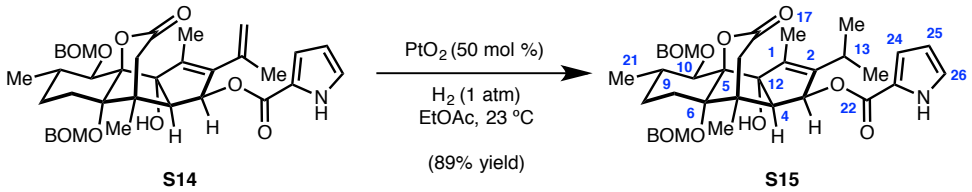
^{13}C NMR (101 MHz, C_6D_6): δ 167.8 (C_{15}=O), 160.8 (C_{22}=O), 144.2 (C_2), 139.5 (C_1), 139.0 (C_{13}), 138.3 (C_{Ph}), 137.8 (C_{Ph}), 128.8 (C_{Ph}), 128.7 (C_{Ph}), 128.4 (C_{Ph}), 128.1 (C_{Ph}), 123.8 (C_{26}), 122.6 (C_{23}), 117.1 (C_{18}), 116.0 (C_{25}), 110.7 (C_{24}), 97.8 ($PhCH_2O\boldsymbol{C}H_2O$), 95.3 ($C_{12}$), 91.4 ($C_{11}$), 90.4 ($C_6$), 89.6 ($PhCH_2O\boldsymbol{C}H_2O$), 81.8 ($C_{10}$), 76.0 ($C_3$), 70.9 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.2 ($Ph\boldsymbol{C}H_2OCH_2O$), 59.4 ($C_4$), 46.5 ($C_5$), 39.8 ($C_{14}$), 33.8 ($C_9$), 28.3 ($C_8$), 21.0 ($C_{18}$), 20.2 ($C_{20}$), 20.1 ($C_7$), 18.9 ($C_{21}$), 13.2 ($C_{17}$).

FTIR (NaCl, thin film): 3408, 3307, 2929, 1742, 1699, 1313, 1158, 1034 cm^{-1}.

HRMS: calc'd for $[M+NH_4]^+$ 715.3589, found 715.3589.

$[\alpha]_D^{25}$: –37º (*c* = 0.685, $CHCl_3$).

Reduction of alkene S14:

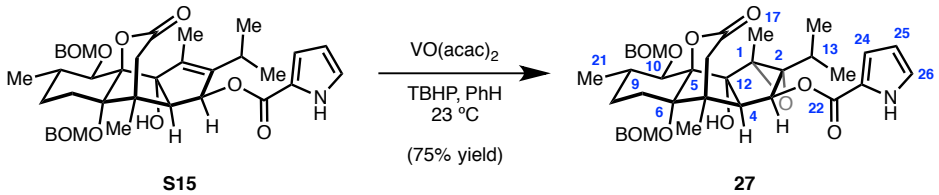


S14 **S15**

An oven-dried, 50 mL round-bottomed flask was charged with diene **S14** (225 mg, 0.32 mmol, 1.0 equiv), PtO_2 (80% w/w, 36.6 mg, 0.16 mmol, 50 mol %), and EtOAc (13 mL). The vial was capped with a rubber septum and the reaction mixture was vigorously stirred while flushing the headspace with H_2 for 5 minutes via a double-walled balloon, during which time the brown suspension turns black. The suspension was vigorously stirred under H_2 until LCMS indicated complete consumption of the starting material (*ca.* 25 min), flushed with Ar to remove excess H_2, then diluted with EtOAc (13 mL), filtered through a short pad of Celite, and concentrated *in vacuo*. Purification of the crude residue by SiO_2 flash chromatography (40 to 50% EtOAc/hexanes) afforded **S15** as a clear oil that solidifies into a white solid upon standing (201 mg, 0.29 mmol, 89% yield).

TLC (45% EtOAc/hexanes): R_f 0.42 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, C_6D_6): δ 8.87 (s, 1H, N***H***), 7.42 – 7.34 (m, 2H, ***Ph***CH_2OCH_2O), 7.31 – 7.20 (m, 4H, ***Ph***CH_2OCH_2O), 7.17 – 7.08 (m, 3H, ***Ph***CH_2OCH_2O), 7.08 – 6.99 (m, 1H, ***Ph***CH_2OCH_2O), 6.98 (ddd, *J* = 3.9, 2.5, 1.5 Hz, 1H, C_{25}), 6.81 (dq, *J* = 7.9, 2.2 Hz, 1H, C_3), 6.33 (td, *J* = 2.7, 1.4 Hz, 1H, C_{26}), 6.09 (dt, *J* = 3.8, 2.5 Hz, 1H, C_{24}), 4.97 (d, *J* = 5.6 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.74 (d, J = 5.6 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.61 (d, *J* = 11.8 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.53 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.50 (d, *J* = 11.8 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.43 (d, *J* = 6.7 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.41 (d, *J* = 12.4 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.36 (d, *J* = 12.4 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.12 (s, 1H, O***H***), 4.07 (d, *J* = 10.3 Hz, 1H, C_{10}), 3.45 (dd, *J* = 8.0, 1.4 Hz, 1H, C_4), 3.38 (d, *J* = 19.2 Hz, 1H, C_{14}), 2.77 (p, *J* = 7.0 Hz, 1H, C_{13}), 2.23 – 2.13 (m, 1H, C_9), 2.18 (d, *J* = 2.3 Hz, 1H, C_{17}), 2.09 (dd, *J* = 19.1, 1.6 Hz, 1H, C_{14}), 1.42 (qd, *J* = 13.1, 4.5 Hz, 1H, C_8), 1.35 (d, *J* = 7.1 Hz, 3H, C_{18}), 1.21 – 1.15 (m, 2H, C_8/C_7), 1.13 – 1.02 (m, 1H, C_7), 1.00 (d, *J* = 6.5 Hz, 3H, C_{21}), 0.96 (d, *J* = 6.9 Hz, 3H, C_{19}), 0.82 (s, 3H, C_{20}).
^{13}C NMR (101 MHz, C_6D_6): δ 167.5 (C_{15}=O), 160.7 (C_{22}=O), 146.0 (C_2), 138.3 (C_{Ph}), 137.9 (C_{Ph}), 137.4 (C_1), 128.8 (C_{Ph}), 128.7 (C_{Ph}), 128.4 (C_{Ph}), 123.7 (C_{26}), 122.9 (C_{23}), 115.6 (C_{25}), 110.8 (C_{24}), 97.9 ($PhCH_2O\boldsymbol{C}H_2O$), 95.3 ($C_{12}$), 90.9 ($C_6$), 90.5 ($C_{11}$), 89.6 ($PhCH_2O\boldsymbol{C}H_2O$), 82.0 ($C_{10}$), 77.0 ($C_3$), 71.0 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.3 ($Ph\boldsymbol{C}H_2OCH_2O$), 59.3 ($C_4$), 46.4 ($C_5$), 39.7 ($C_{14}$), 33.8 ($C_9$), 28.3 ($C_8$), 27.6 ($C_{13}$), 22.0 ($C_{18}$), 20.2 ($C_{20}$), 20.1 ($C_7$), 19.0 ($C_{19}$), 18.9 ($C_{21}$), 11.8 ($C_{17}$).
FTIR (NaCl, thin film): 3417, 3306, 2962, 1934, 1743, 1699, 1158, 1026 cm^{-1}.
HRMS: calc'd for $[M+Na]^+$ 722.3300, found 722.3299.
$[\alpha]_D^{25}$: +7° (*c* = 0.675, $CHCl_3$).

Preparation of epoxide 27:



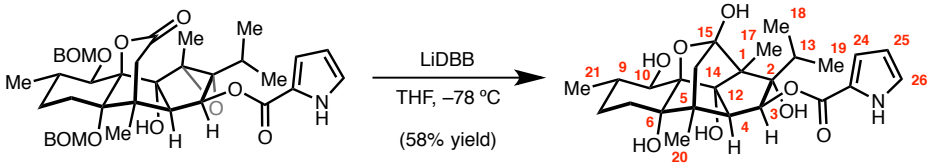
S15 **27**

To an oven-dried, 25 mL round-bottomed flask was added alcohol **S15** (175 mg, 0.25 mmol, 1.0 equiv) and anhydrous PhH (5.0 mL). The solution was treated with $VO(acac)_2$ (33.2 mg, 0.13 mmol, 0.5 equiv) and then TBHP (5.5 M in decanes, 0.14 mL, 0.75 mmol, 3.0 equiv) was added via syringe along the side of the flask,

during which time the green solution turns a deep red. After 30 min, additional portions of $VO(acac)_2$ (16.6 mg, 62.5 μmol, 0.25 equiv) and then TBHP (5.5 M in decanes, 0.14 mL, 0.75 mmol, 3.0 equiv) were added and stirring was continued at ambient temperature until LCMS indicated complete consumption of the starting material (*ca*. 30-45 min), at which point the reaction mixture fades to a bright orange. The reaction mixture was diluted with EtOAc (5 mL) and quenched with the addition of sat. aq. $Na_2S_2O_3$ (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by SiO_2 flash chromatography (35 to 45% EtOAc/hexanes) afforded epoxide **27** as an off-white foam (135 mg, 0.19 mmol, 75% yield).

TLC (45% EtOAc/hexanes): R_f 0.48 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, C_6D_6): δ 8.89 (s, 1H, N***H***), 7.38 – 7.35 (m, 4H, ***Ph***CH_2OCH_2O), 7.27 – 7.23 (m, 2H, ***Ph***CH_2OCH_2O), 7.21 – 7.16 (m, 2H, ***Ph***CH_2OCH_2O), 7.15 – 7.05 (m, 2H, ***Ph***CH_2OCH_2O), 6.96 (ddd, J = 3.9, 2.5, 1.4 Hz, 1H, C_{25}), 6.34 (td, J = 2.7, 1.4 Hz, 1H, C_{26}), 6.29 (d, J = 8.9 Hz, 1H, C_3), 6.09 (dt, J = 3.8, 2.5 Hz, C_{24}), 5.20 (d, J = 6.4 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.98 (d, J = 6.4 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.77 (d, J = 12.2 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.61 (d, J = 11.7 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.54 (d, J = 12.1 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.51 (d, J = 11.7 Hz, 1H, $PhC\boldsymbol{H}_2OCH_2O$), 4.47 (d, J = 6.8 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.38 (d, J = 6.8 Hz, 1H, $PhCH_2OC\boldsymbol{H}_2O$), 4.16 (d, J = 10.5 Hz, 1H, C_{10}), 3.70 (d, J = 19.8 Hz, 1H, C_{14}), 3.20 (s, 1H, O***H***), 3.12 (dd, J = 8.9, 1.6 Hz, 1H, C_4), 2.24 – 2.13 (m, 1H, C_9), 2.16 (dd, J = 19.8, 1.7 Hz, 1H, C_{14}), 1.97 (s, 3H, C_{17}), 1.74 (p, J = 7.2 Hz, 1H, C_{13}), 1.40 (d, J = 7.2 Hz, 3H, C_{18}), 1.39 – 1.30 (m, 1H, C_8), 1.24 – 1.21 (m, 1H, C_8), 1.18 (d, J = 6.5 Hz, 3H, C_{21}), 1.15 – 1.09 (m, 2H, C_7), 1.07 (d, J = 7.2 Hz, 3H, C_{19}), 0.74 (s, 3H, C_{20}).
^{13}C NMR (101 MHz, C_6D_6): δ 167.8 (C_{15}=O), 160.1 (C_{22}=O), 138.8 (C_{Ph}), 138.1 (C_{Ph}), 128.7 (C_{Ph}), 128.6 (C_{Ph}), 128.5 (C_{Ph}), 127.6 (C_{Ph}), 124.6 (C_{26}), 122.1 (C_{23}), 116.0 (C_{25}), 111.0 (C_{24}), 98.0 ($PhCH_2OC\boldsymbol{H}_2O$), 91.8 ($C_{12}$), 91.7 ($C_{11}$), 90.3 ($C_6$), 88.9 ($PhCH_2OC\boldsymbol{H}_2O$), 81.8 ($C_{10}$), 80.2 ($C_2$), 76.2 ($C_1$), 73.4 ($C_3$), 70.6 ($Ph\boldsymbol{C}H_2OCH_2O$), 70.5 ($Ph\boldsymbol{C}H_2OCH_2O$), 64.2 ($C_4$), 47.7 ($C_5$), 38.9 ($C_{14}$), 33.1 ($C_9$), 30.7 ($C_{13}$), 28.4 ($C_8$), 20.5 ($C_{20}$), 19.9 ($C_7$), 19.2 ($C_{21}$), 18.0 ($C_{18}$), 17.4 ($C_{19}$), 14.6 ($C_{17}$).
FTIR (NaCl, thin film): 3305, 2964, 1747, 1705, 1026 cm^{-1}.
HRMS: calc'd for $[M+Na]^+$ 738.3249, found 738.3250.
$[\alpha]_D^{25}$: +37° (c = 0.900, $CHCl_3$).

Preparation of 20-deoxyspiganthine (3):



An oven-dried, 100 mL round-bottomed flask equipped with a borosilicate glass-coated magnetic stirbar was charged with epoxide **27** (135 mg, 0.19 mmol, 1.0 equiv) and anhydrous THF (18 mL) under Ar (Note: epoxide **27** was azeotroped with PhH three times immediately prior to use). The solution was cooled to –78 ºC via a dry ice/acetone bath and stirring continued for 15 min before a freshly prepared solution of LiDBB (0.16 M, 11.8 mL, 1.89 mmol, 10 equiv) was carefully added dropwise via syringe along the side of the flask. The resulting deep green mixture was stirred for 0.5 h at –78 ºC, at which point LCMS analysis indicated complete conversion to the desired product. Sat. aq. NH_4Cl (10 mL) was carefully added before the reaction mixture was warmed to ambient temperature. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 x 20

mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (0 to 5 to 10% MeOH/$CHCl_3$) to afford 20-deoxyspiganthine (**3**) (51.8 mg, 0.11 mmol, 58% yield) as a white powder (Note: The purification was made easier by first flushing with $CHCl_3$ (100 mL) until all of the excess 4,4′-di-*tert*-butylbiphenyl was removed).

TLC (10% MeOH/CH_2Cl_2): R_f 0.29 (UV, *p*-anisaldehyde).
^{1}H NMR (400 MHz, CD_3OD): δ 7.01 (dd, *J* = 2.5, 1.5 Hz, 1H, C_{26}), 6.86 (dd, *J* = 3.8, 1.5 Hz, 1H, C_{24}), 6.22 (dd, *J* = 3.8, 2.5 Hz, 1H, C_{25}), 5.65 (d, *J* = 8.5, Hz, 1H, C_3), 3.75 (d, *J* = 10.3 Hz, 1H, C_{10}), 3.23 (dd, *J* = 8.5, 1.8 Hz, 1H, C_4), 2.41 (h, *J* = 6.6 Hz, C_{13}), 2.35 (d, *J* = 13.5, 1H, C_{14}), 2.04 (td, *J* = 12.5, 5.9 Hz, 1H, C_7), 1.77 – 1.87 (m, 1H, C_9), 1.77 (dd, *J* = 13.5, 2.0 Hz, 1H, C_{14}), 1.45 – 1.58 (m, 2H, C_8), 1.37 (s, 3H, C_{17}), 1.22 (ddd, *J* =13.0, 4.3, 2.4, 1H, C_7), 1.17 (d, *J* = 6.5 Hz, 3H, C_{18}), 1.02 (d, *J* = 6.5 Hz, 3H, C_{21}), 0.84 (d, *J* = 6.4 Hz, 3H, C_{19}), 0.77 (s, 3H, C_{20}).
^{13}C NMR (101 MHz, CD_3OD): δ 161.9 (C_{22}), 125.3 (C_{26}), 123.6 (C_{23}), 116.8 (C_{24}), 110.9 (C_{25}), 103.6 (C_{15}), 97.7 (C_{12}), 86.8 (C_{11}), 86.8 (C_2), 85.2 (C_3), 84.3 (C_6), 72.8 (C_{10}), 64.7 (C_1), 57.7 (C_4), 48.2 (C_5), 41.4 (C_{14}), 35.4 (C_9), 31.1 (C_{13}), 29.9 (C_8), 26.4 (C_7), 19.5 (C_{18}), 19.1 (C_{19}), 19.0 (C_{21}), 16.7 (C_{20}), 9.7 (C_{17}).
FTIR (NaCl, thin film): 3436, 2929, 1682, 1411, 1319 cm^{-1}.
HRMS: calc'd for $[M-H]^-$ 476.2290, found 476.2290.
$[\alpha]_D^{25}$: +6° (*c* = 0.160, MeOH).

5. ^{1}H and ^{13}C NMR Comparison Tables for (+)-Ryanodine and (+)-20-Deoxyspiganthine

Table S3. Comparison of ^{1}H NMR data for (+)-Ryanodine

Proton No.	Inoue et al. Report, Synthetic (+)-Ryanodine[8] ^{1}H NMR, 400 MHz, CD_3OD ^{1}H [δ, multi., *J* (Hz)]	This Work, Synthetic (+)-Ryanodine ^{1}H NMR, 600 MHz, CD_3OD ^{1}H [δ, multi., *J* (Hz)]
1		
2		
3	5.64 (s)	5.64 (s)
4		
5		
6		
7a	1.26 (ddd, *J* = 12.7, 4.5, 2.3)	1.26 (ddd, *J* = 12.7, 4.6, 2.0)
7b	2.10 (ddd, *J* =12.7, 12.7, 5.4)	2.10 (td, *J* = 12.9, 5.2)
8a	1.46 (dddd, *J* = 13.1, 5.4, 5.4, 2.3)	1.48 (td, *J* = 13.0, 4.7)
8b	1.53 (dddd, *J* = 13.1, 5.2, 1.6)	1.54 (dtd, *J* = 12.4, 5.2, 1.8)
9	1.85 (ddqd, *J* = 13.1, 10.4, 6.8, 5.4)	1.85 (tdd, *J* = 10.2, 8.5, 5.6)
10	3.80 (d, *J* = 10.4)	3.80 (d, *J* = 10.2)
11		
12		
13	2.27 (qq, *J* = 6.8, 6.3)	2.27 (h, *J* = 6.8)
14a	1.93 (d, *J* = 13.6)	1.94 (d, *J* = 13.6)
14b	2.57 (d, *J* = 13.6)	2.57 (d, *J* = 13.6)
15		
17	1.39 (s)	1.40 (s)
18	0.76 (d, *J* = 6.3)	0.76 (d, *J* = 6.5)
19	1.12 (d, *J* = 6.8)	1.12 (d, *J* = 6.7)
20	0.90 (s)	0.90 (s)
21	1.02 (d, *J* = 6.8)	1.02 (d, *J* = 6.5)
22		
23		
24	6.88 (dd, *J* = 3.6, 1.4)	6.88 (dd, *J* = 3.7, 1.5)
25	6.24 (dd, *J* = 3.6, 2.7)	6.24 (dd, *J* = 3.8, 2.5)
26	7.04 (dd, *J* =2.7, 1.4)	7.04 (dd, *J* = 2.5, 1.5)

Table S4. Comparison of ^{13}C NMR data for (+)-Ryanodine

Carbon No.	Inoue et al. Report, Synthetic (+)-Ryanodine[8] ^{13}C NMR, 100 MHz, CD_3OD ^{13}C (δ) ppm	This Work, Synthetic (+)-Ryanodine ^{13}C NMR, 101 MHz, CD_3OD ^{13}C (δ) ppm	Chemical Shift Difference, Δδ
1	65.9	65.9	0
2	84.4	84.3	0.1
3	90.9	90.8	0.1
4	92.4	92.3	0.1
5	49.7	49.6	0.1
6	86.6	86.5	0.1
7	26.8	26.8	0
8	29.3	29.3	0
9	35.4	35.4	0
10	72.8	72.8	0
11	87.4	87.4	0
12	96.7	96.7	0
13	30.9	30.9	0
14	41.8	41.8	0
15	102.9	102.9	0
17	10.2	10.2	0
18	18.9	18.9	0
19	19.5	19.5	0
20	12.5	12.6	0.1
21	19.0	19.0	0
22	161.8	161.8	0
23	123.4	123.3	0.1
24	117.0	117.0	0
25	110.9	110.9	0
26	125.6	125.6	0

Note: The carbon assignment of C_5 by Inoue and coworkers was deduced from HMBC correlation.

Table S5. Comparison of ^{1}H NMR data for (+)-20-Deoxyspiganthine

Proton No.	Hübner et al. Report, Natural (+)-20-Deoxyspiganthine[11] ^{1}H NMR, 360 MHz, CD_3OD ^{1}H [δ, multi., *J* (Hz)]	This Work, Synthetic (+)-20-Deoxyspiganthine ^{1}H NMR, 400 MHz, CD_3OD ^{1}H [δ, multi., *J* (Hz)]
1		
2		
3	5.65 (d, *J* = 8.5)	5.65 (d, *J* = 8.5)
4	3.23 (dd, *J* = 8.5, 2)	3.23 (dd, *J* = 8.5, 1.8)
5		
6		
7a	2.04 (ddd, *J* = 13.5, 12, 6)	2.04 (td, *J* = 12.5, 5.9)
7b	1.22 (ddd, *J* = 13.5, 4.5, 4)	1.22 (ddd, *J* = 13.0, 4.3, 2.4)
8a	1.45–1.58 (m)	1.45–1.58 (m)
8b	1.45–1.58 (m)	1.45–1.58 (m)
9	1.77–1.87 (m)	1.77–1.87 (m)
10	3.75 (d, *J* = 10)	3.75 (d, *J* = 10.3)
11		
12		
13	2.41 (qq, *J* = 6.5, 6.5)	2.41 (h, *J* = 6.6)
14a	2.35 (d, *J* = 13.5)	2.35 (d, *J* = 13.5)
14b	1.77 (dd, 13.5, 2)	1.77 (dd, *J* = 13.5, 2.0)
15		
17	1.36 (s)	1.37 (s)
18	1.16 (d, *J* = 6.5)	1.17 (d, *J* = 6.4)
19	0.84 (d, *J* = 6.5)	0.84 (d, *J* = 6.5)
20	0.77 (s)	0.77 (s)
21	1.01 (d, *J* = 6.5)	1.02 (d, *J* = 6.5)
22		
23		
24	6.85 (dd, *J* = 4, 1.5)	6.86 (dd, *J* = 3.8, 1.5)
25	4.22 (dd, *J* = 4, 2.5)	6.22 (dd, *J* = 3.8, 2.5)
26	7.01 (dd, *J* = 2.5, 1.5)	7.01 (dd, *J* = 2.5, 1.5)

Note: In the isolation report, Hübner and coworkers report that $C_{25}\boldsymbol{H}$ has a ^{1}H NMR chemical shift of 4.22 ppm; however, all related ryanodines and spiganthines reported in the same paper share a $C_{25}\boldsymbol{H}$ ^{1}H NMR chemical shift between 6.22 and 6.25 ppm, as observed in our synthetic sample. This is assumed to be a typographical error made by the isolation team.

Table S6. Comparison of ^{13}C NMR data for (+)-20-Deoxyspiganthine

Carbon No.	Hübner et al. Report, Natural (+)-20-Deoxyspiganthine[11] ^{13}C NMR, 90 MHz, CD_3OD ^{13}C (δ) ppm	This Work, Synthetic (+)-20-Deoxyspiganthine ^{13}C NMR, 101 MHz, CD_3OD ^{13}C (δ) ppm	Chemical Shift Difference, Δδ
1	64.7	64.7	0
2	86.6	86.8	0.2
3	85.2	85.2	0
4	57.7	57.7	0
5	48.3	48.2	0.1
6	84.3	84.3	0
7	26.4	26.4	0
8	29.9	29.9	0
9	35.4	35.4	0
10	72.9	72.8	0.1
11	86.8	86.8	0
12	97.8	97.7	0.1
13	31.1	31.1	0
14	41.5	41.4	0.1
15	103.6	103.6	0
17	9.6	9.7	0.1
18	19.5	19.5	0
19	19.1	19.1	0
20	16.7	16.7	0
21	18.9	19.0	0.1
22	162.0	161.9	0.1
23	123.6	123.6	0
24	116.8	116.8	0
25	110.9	110.9	0
26	125.3	125.3	0

6. Single Crystal X-ray Diffraction Data

Low-temperature diffraction data (φ- and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON 100 CMOS detector with Cu-K_α radiation (λ = 1.54178 Å) from a $I_\mu S$ HB micro-focus sealed X-ray tube. All diffractometer manipulations, including data collection, integration, and scaling were carried out using the Bruker APEXII software.[12] Absorption corrections were applied using SADABS.[13] The structure was solved by intrinsic phasing using SHELXT[14] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[14] using established refinement techniques.[15] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups and hydroxyl groups). Absolute configuration was determined by anomalous dispersion.[16] Crystallographic data for **16**, **18**, **1**, and **3** can be obtained free of charge from The Cambridge Crystallographic Data Centre (CCDC) via www.ccdc.cam.ac.uk/data_request/cif under CCDC deposition numbers 1508482–1508485. Graphical representation of the structures with 50% probability thermal ellipsoids was generated using Mercury visualization software.

Table S7. Crystal and refinement data for compounds 16, 18, 1, and 3.

	CX-10-028	**CX-10-036**	**CX-10-076**	**6-AH-235**
CCDC Number	1508483	1508482	1508484	1508485
Empirical formula	$C_{42}H_{48}BNO_{10}$	$C_{25}H_{33}NO_8$	$C_{33}H_{57}NO_{12}$	$C_{58}H_{90.76}N_2O_{18.38}$
Formula weight	737.62	475.52	659.79	1110.22
T (K)	100	100	200	100
Crystal system	Monoclinic	Orthorhombic	Orthorhombic	Trigonal
Space group	$P2_1$	$P2_12_12$	$P2_12_12_1$	$P3_2$
a, Å	8.7826(4)	18.9642(8)	10.9374(3)	20.8804(7)
b, Å	22.1496(10)	11.2161(4)	11.9604(3)	20.8804(7)
c, Å	10.3099(5)	13.5628(5)	27.4814(7)	11.5639(5)
α, °	90	90	90	90
β, °	109.928(2)	90	90	90
γ, °	90	90	90	120
Volume, $Å^3$	1885.50(15)	2884.87(19)	3595.00(16)	4366.3(3)
Z	2	4	4	3
d_{calc}, g/cm^3	1.299	1.095	1.219	1.267
Abs. coeff. (mm^{-1})	0.749	0.676	0.759	0.770
θ range, °	3.991 to 79.080	3.258 to 66.577	3.216 to 79.361	4.234 to 79.349
Abs. correction	Semi-empirical	Semi-empirical	Semi-empirical	Semi-empirical
GOF	1.047	1.055	1.045	1.023
R_1,[a] wR_2,[b] [I>2σ(I)]	0.0311, 0.0732	0.0563, 0.1375	0.0389, 0.1064	0.0448, 0.1071
Flack parameter	0.12(5)	0.23(12)	0.05(3)	0.07(6)
Extinction coefficient	0.00071(18)	n/a	n/a	n/a

[a] $R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$. [b] $wR_2 = [\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$.

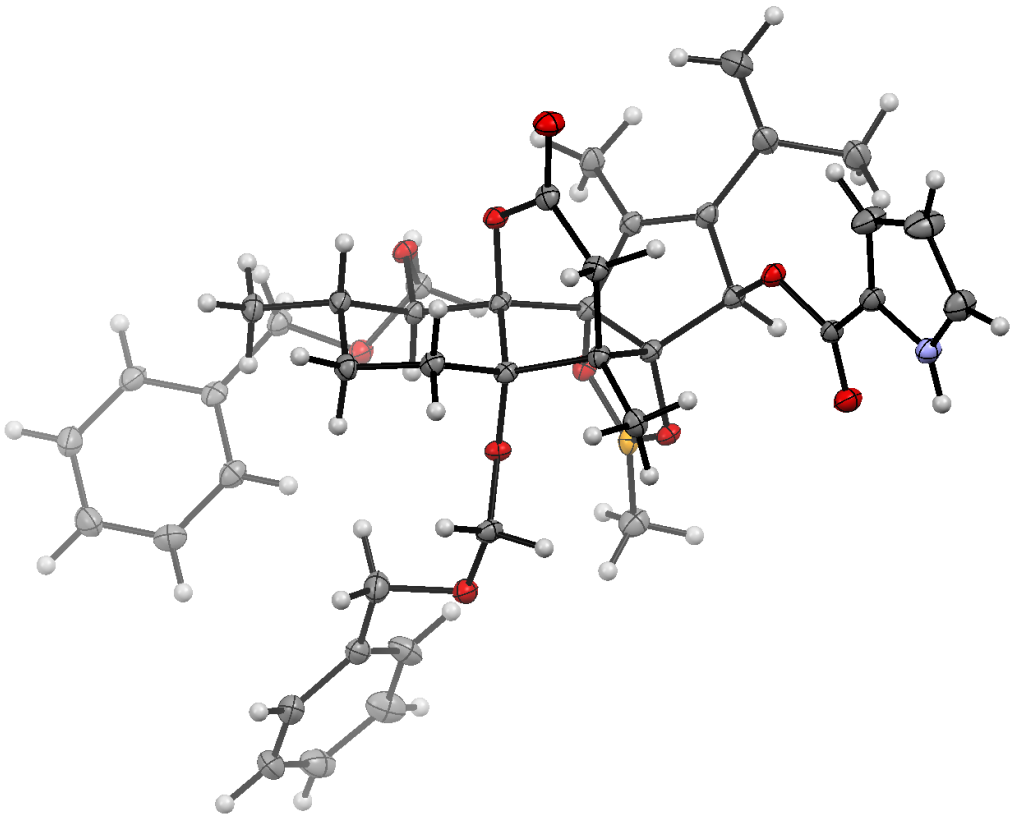


Figure S1. Structure of **16** with 50% probability anisotropic displacement ellipsoids.

Special Refinement Details for 16

Compound **16** crystallizes in the monoclinic space group $P2_1$ with one molecule in the asymmetric unit. Absolute configuration was determined by anomalous dispersion (Flack = 0.12(5)).[16]

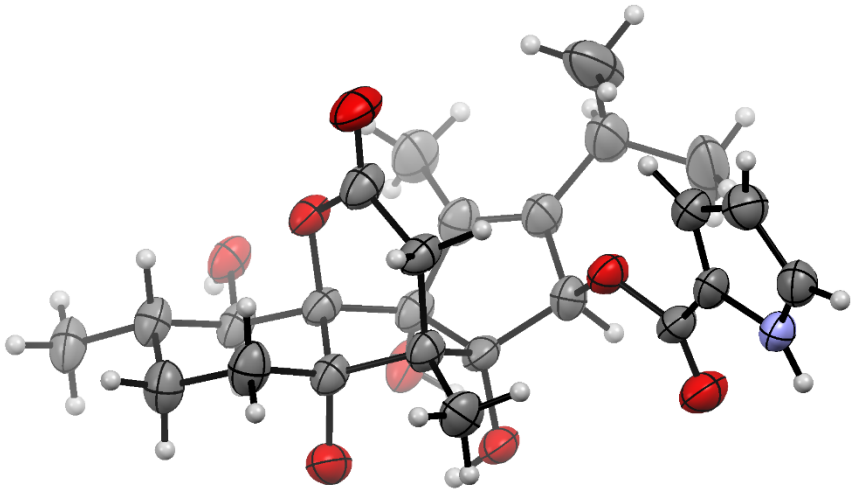


Figure S2. Structure of **18** with 50% probability anisotropic displacement ellipsoids.

Special Refinement Details for 18

Compound **6** crystallizes in the orthorhombic space group $P2_12_12$ with one molecule in the asymmetric unit. The coordinates for the hydrogen atoms bound to N1, O5, O6, O7, and O8 were located in the difference Fourier synthesis, however, refinement was unstable and they were included into the model at geometrically calculated positions and refined using a riding model. A void analysis with the program PLATON[17] revealed the presence of two large voids and the program SQUEEZE[18] was used to remove the contribution of the disordered electron density inside this void from the structure factors. Absolute configuration was determined by anomalous dispersion (Flack = 0.23(12)).[16] Bayesian statistics further confirm the absolute stereochemistry: P2(true) = 1.000, P3(true) = 0.977, P3(rac-twin) = 0.023, and P3(false) = 0.2×10^{-13}.[17]

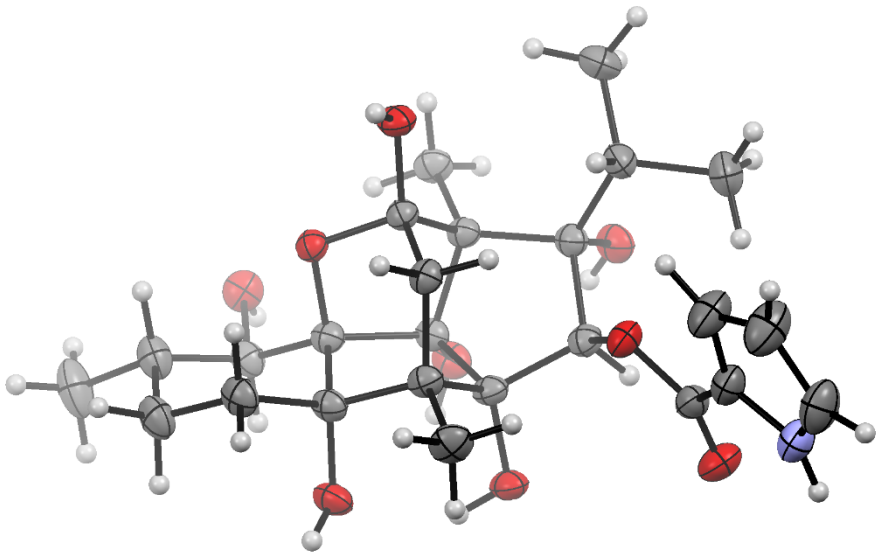


Figure S3. Structure of **1** with 50% probability anisotropic displacement ellipsoids. Co-crystallized diethyl ether and water molecules are omitted for clarity.

Special Refinement Details for 1

Compound **1** crystallizes in the orthorhombic space group $P2_12_12_1$ with one molecule in the asymmetric unit, along with two molecules of diethyl ether and one molecule of water. One ether molecule was disordered over multiple positions, however refinement was unstable and the disorder was not included in the model. The bond distances of all hydrogen atoms bound to O and N atoms were refined with bond restraints. Absolute configuration was determined by anomalous dispersion (Flack = 0.05(3)).[16]

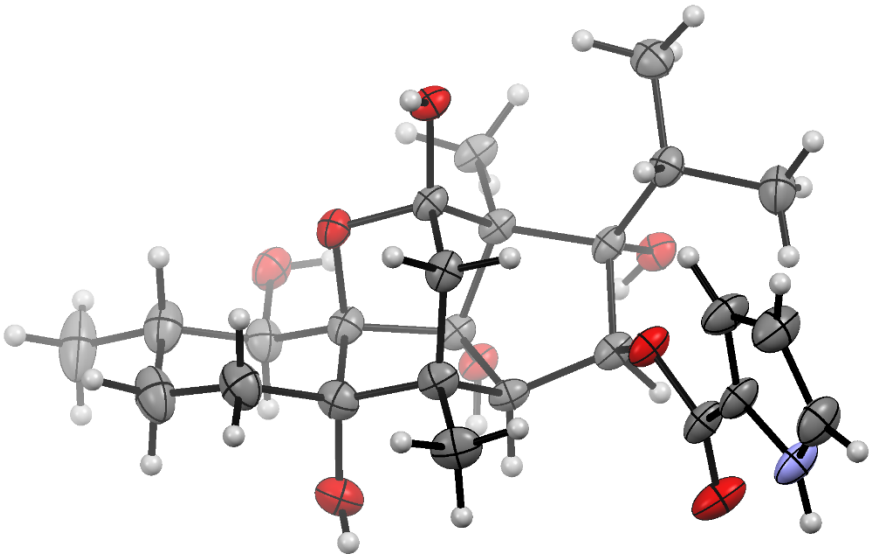


Figure S4. Structure of **3** with 50% probability anisotropic displacement ellipsoids. Co-crystallized diethyl ether, water, and the second molecule of **3** are omitted for clarity.

Special Refinement Details for 3

Compound **3** crystallizes in the trigonal space group $P3_2$ with two molecules in the asymmetric unit, along with two molecules of diethyl ether and 0.38 molecules of water. One ether molecule was disordered over multiple positions, however refinement was unstable and the disorder was not included in the model. The highest electron density maxima was modeled as a partially occupied water (0.38). The hydrogen atoms for this water molecule were not located in the difference Fourier synthesis, and were included into the model at geometrically calculated positions that fulfilled H-bonding interactions and refined using a riding model. The bond distances of all hydrogen atoms bound to O and N atoms were refined with bond restraints. No hydrogen bond acceptor was found for H7A. Absolute configuration was determined by anomalous dispersion (Flack = 0.07(6)).[16]

6. References

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7. ^{1}H and ^{13}C NMR Spectral Data

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Nucleus	1H
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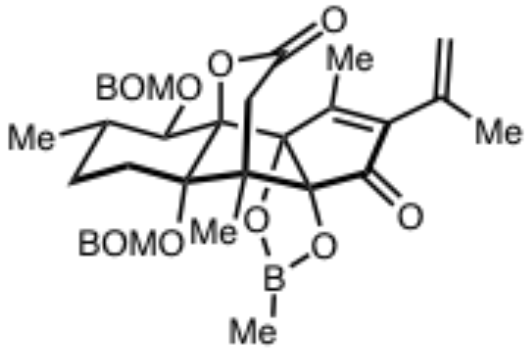

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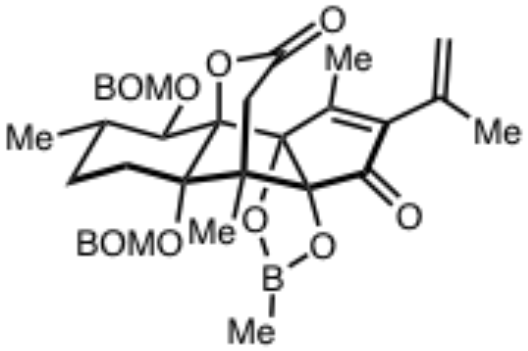

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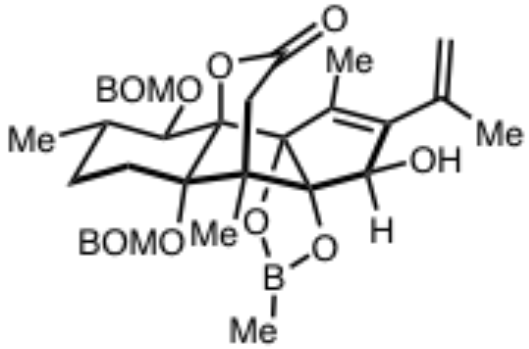

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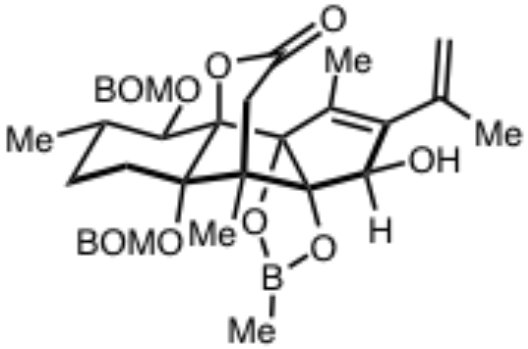

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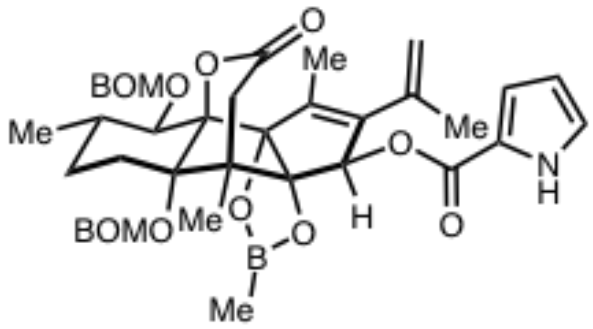
Spectral Size	65536



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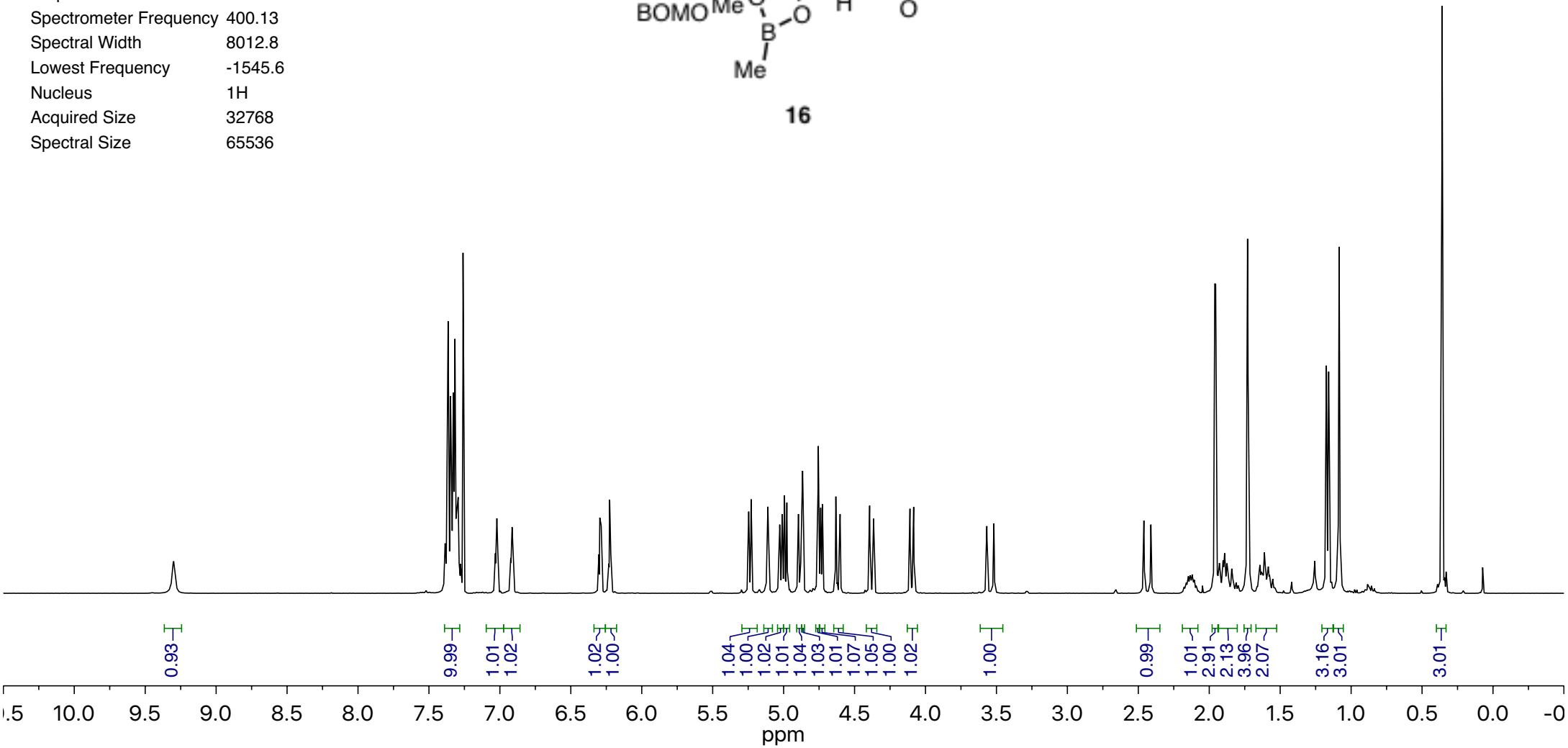

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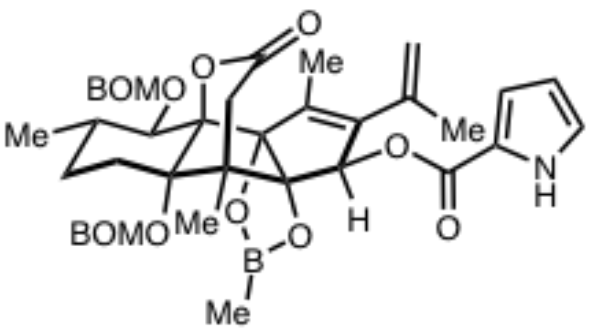

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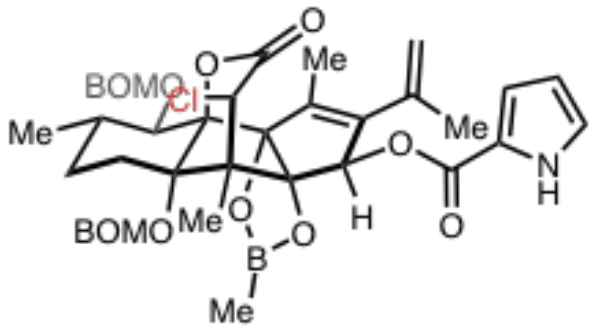
Spectral Size	65536



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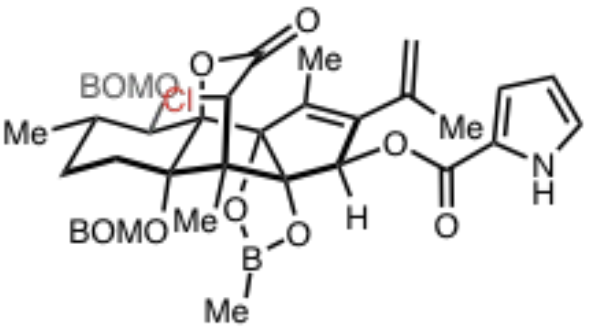

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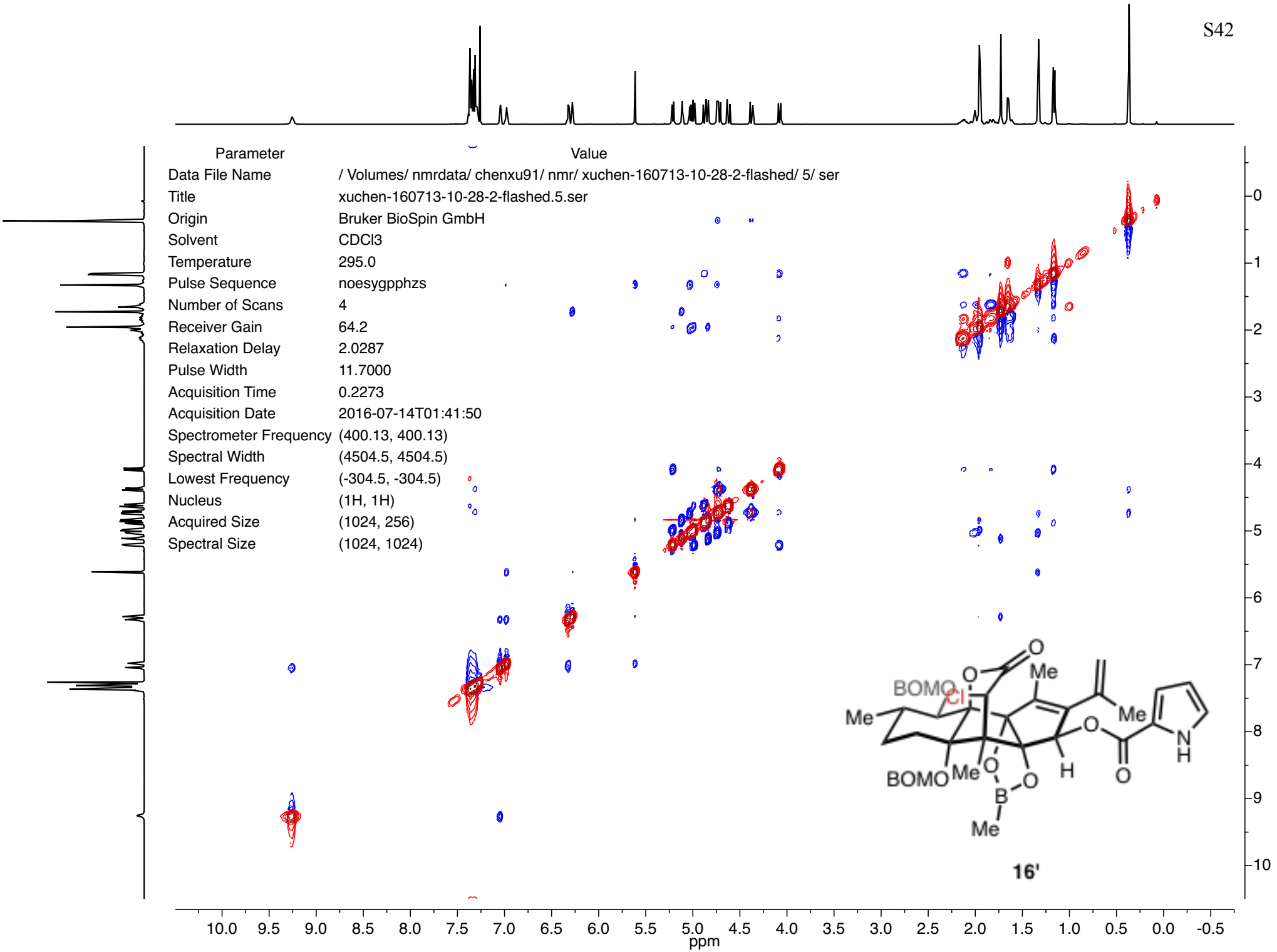
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H
N
H
16'
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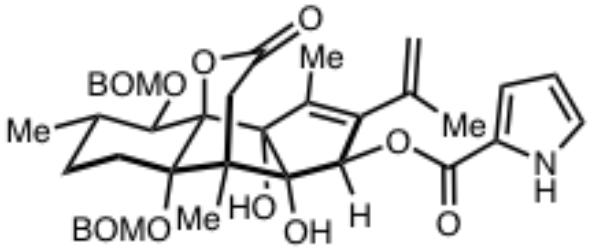

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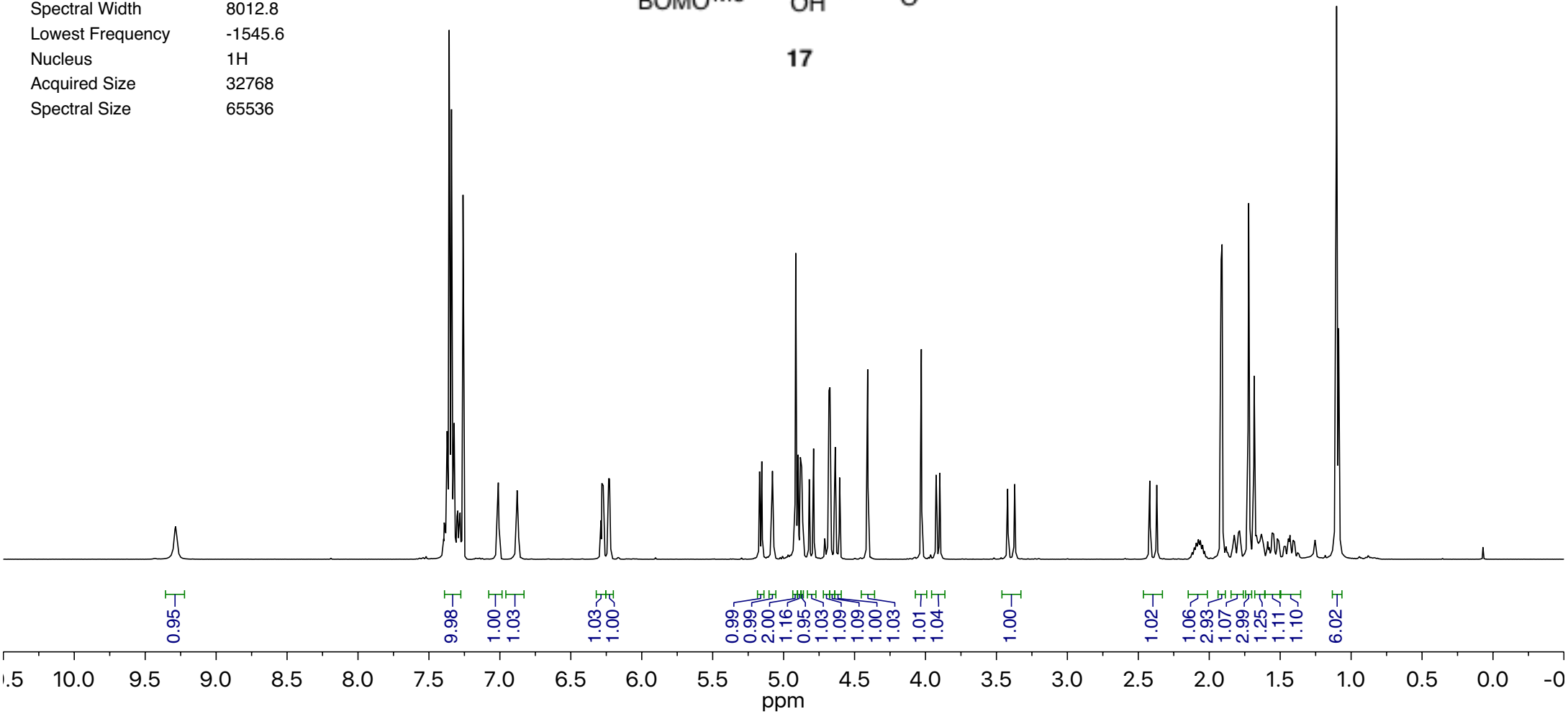

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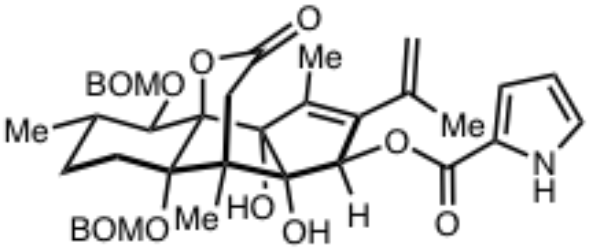

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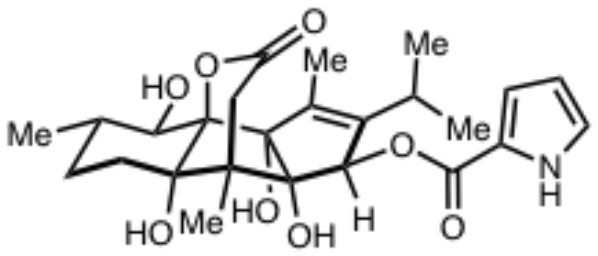

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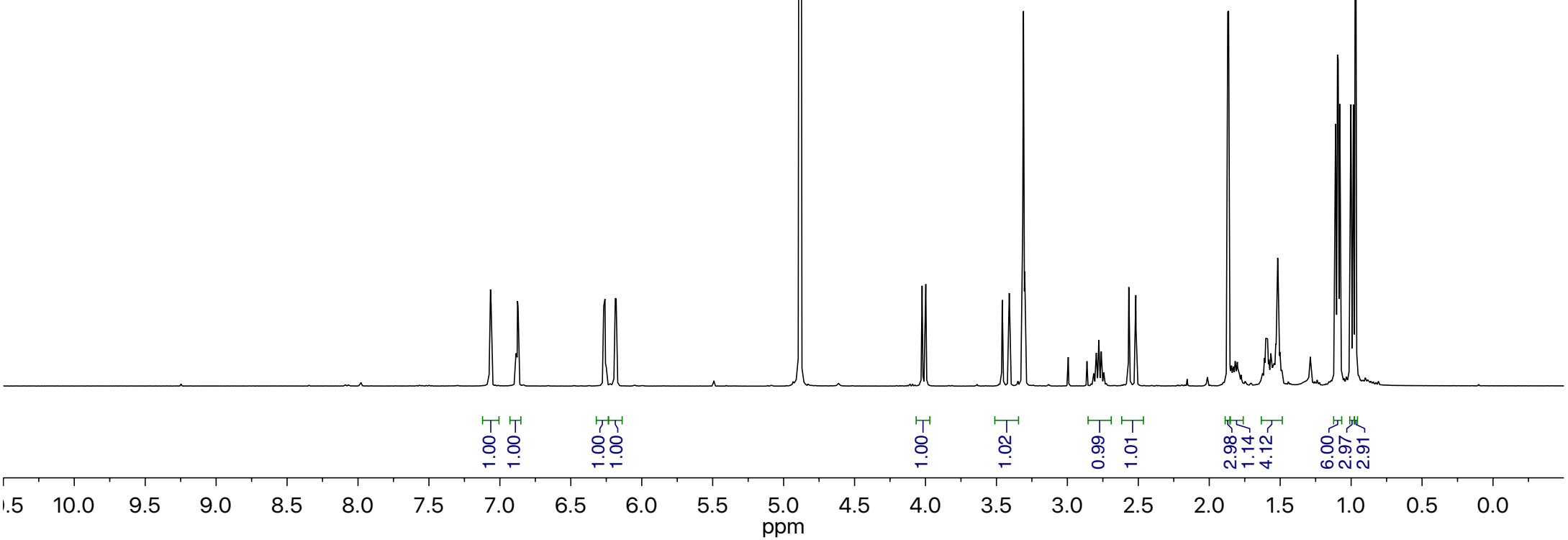

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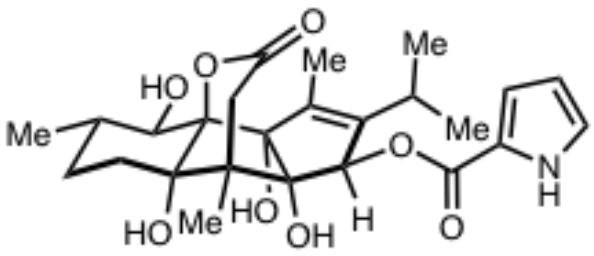

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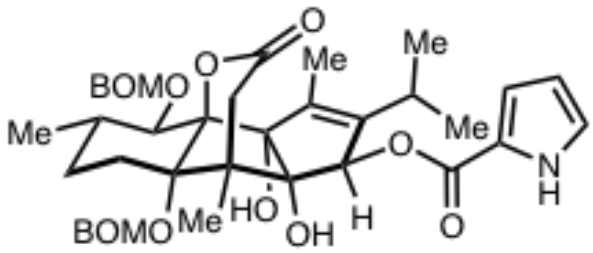

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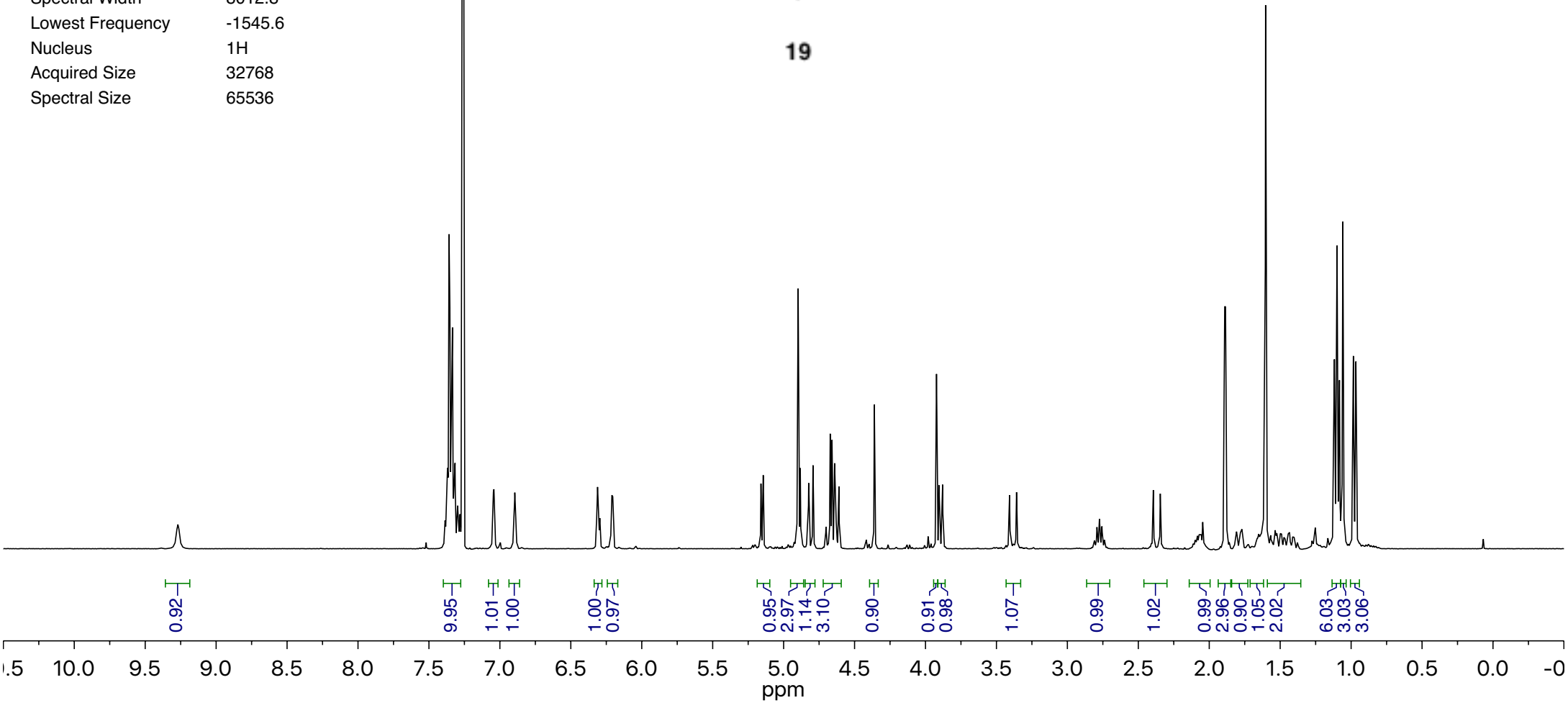

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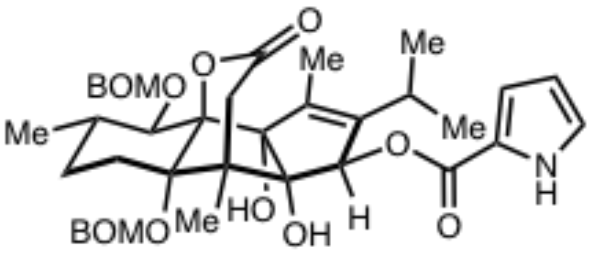

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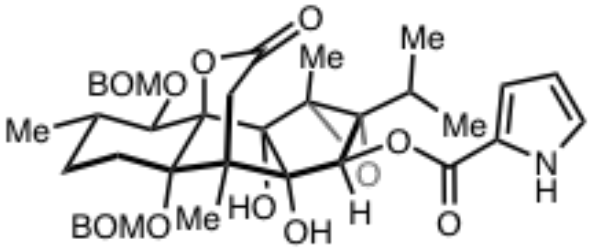

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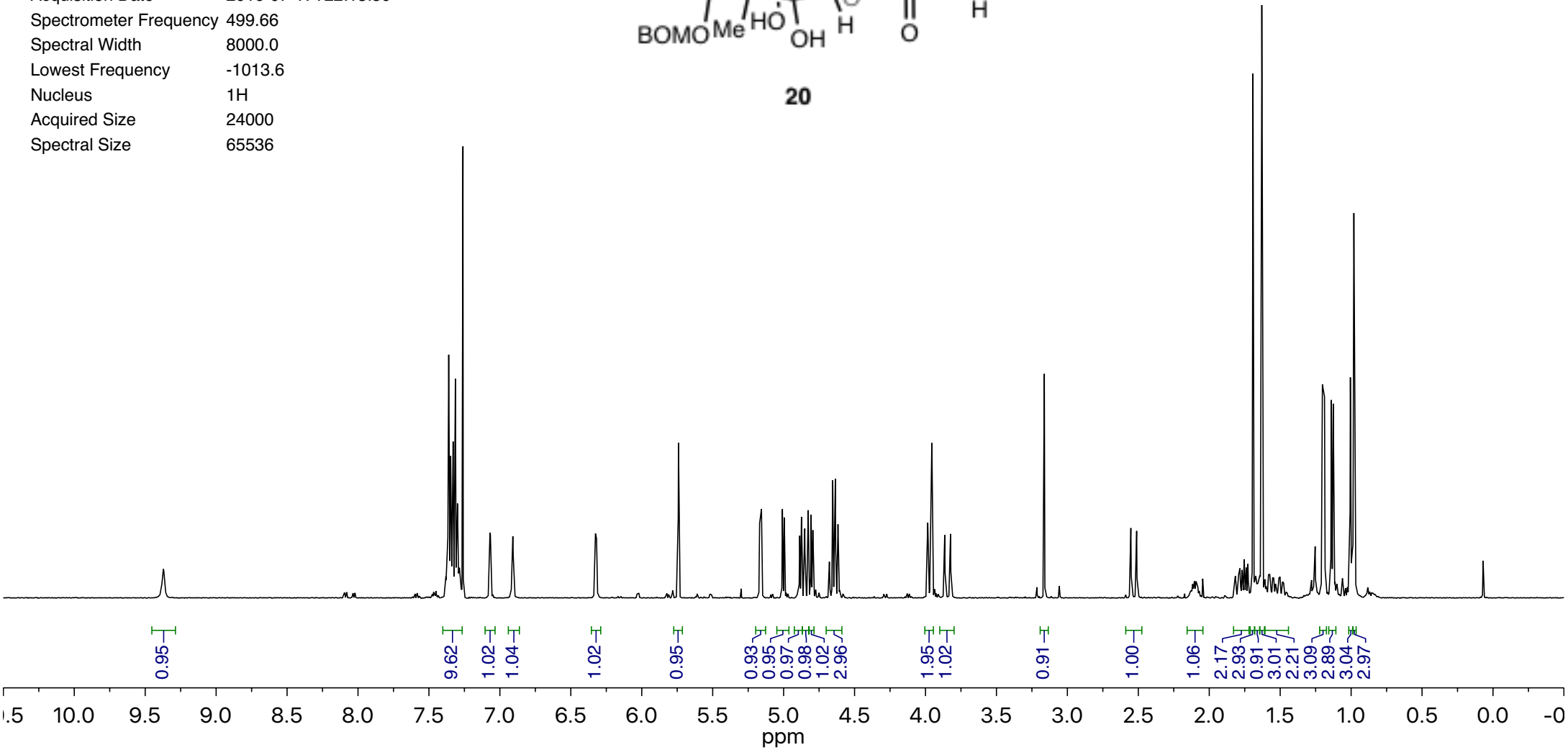

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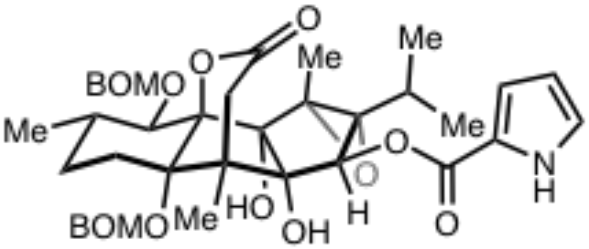
Data File Name	/ Volumes/ nmrdata-1/ chenxu91/ vnmrsys/ data/ xuchen-160717-10-42-1/ CARBON02.fid/ fid
Title	CARBON02
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	3000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.5000
Acquisition Time	1.0420
Acquisition Date	2016-07-18T00:45:43
Spectrometer Frequency	125.65
Spectral Width	31446.5
Lowest Frequency	-1906.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



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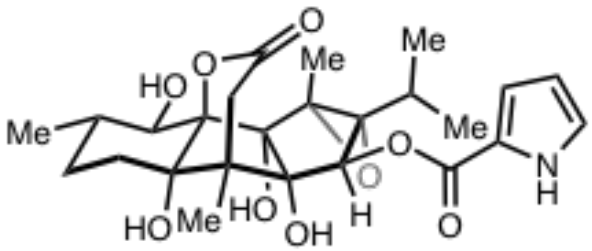
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ chenxu91/ nmr/ xuchen-160813-10-75-preptlc/ 1/ fid
Title	xuchen-160813-10-75-preptlc.1.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	294.9
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	156.2
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-08-13T20:46:42
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1543.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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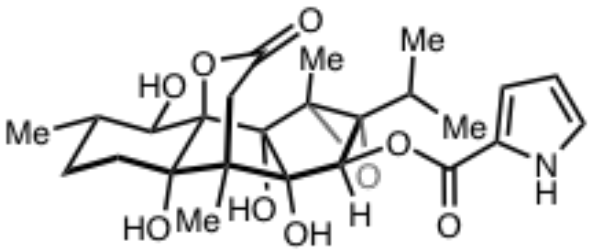
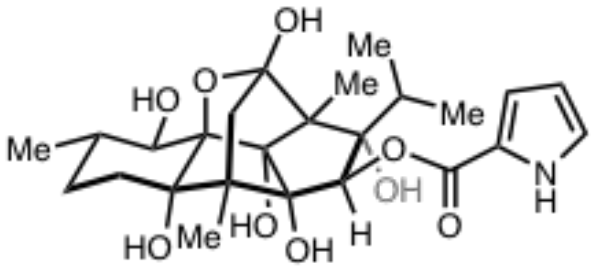
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ chenxu91/ nmr/ xuchen-160813-10-75-preptlc/ 3/ fid
Title	xuchen-160813-10-75-preptlc.3.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	1024
Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-14T00:07:31
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1817.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



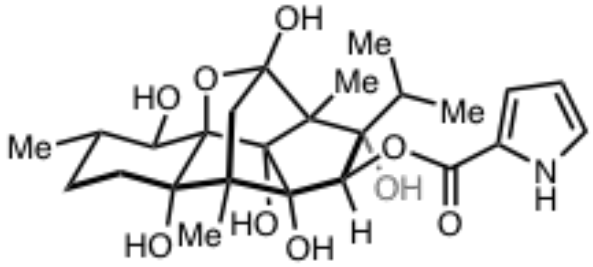
21

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ chenxu91/ vnmrsys/ data/ xuchen-160805-10-67-flashed/ PROTON_01.fid/ fid
Title	PROTON_01
Origin	Varian
Solvent	MeOD
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	8
Receiver Gain	58
Relaxation Delay	1.0000
Pulse Width	3.2000
Acquisition Time	1.7046
Acquisition Date	2016-08-05T20:22:35
Spectrometer Frequency	599.62
Spectral Width	9611.9
Lowest Frequency	-1207.1
Nucleus	1H
Acquired Size	16384
Spectral Size	65536



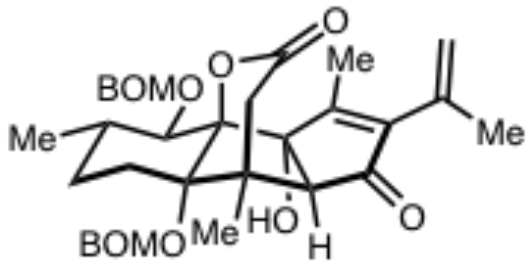
***ryanodine* (1)**

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ chenxu91/ nmr/ xuchen-160805-10-67-flashed/ 2/ fid
Title	xuchen-160805-10-67-flashed.2.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	1024
Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-06T01:33:49
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1818.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

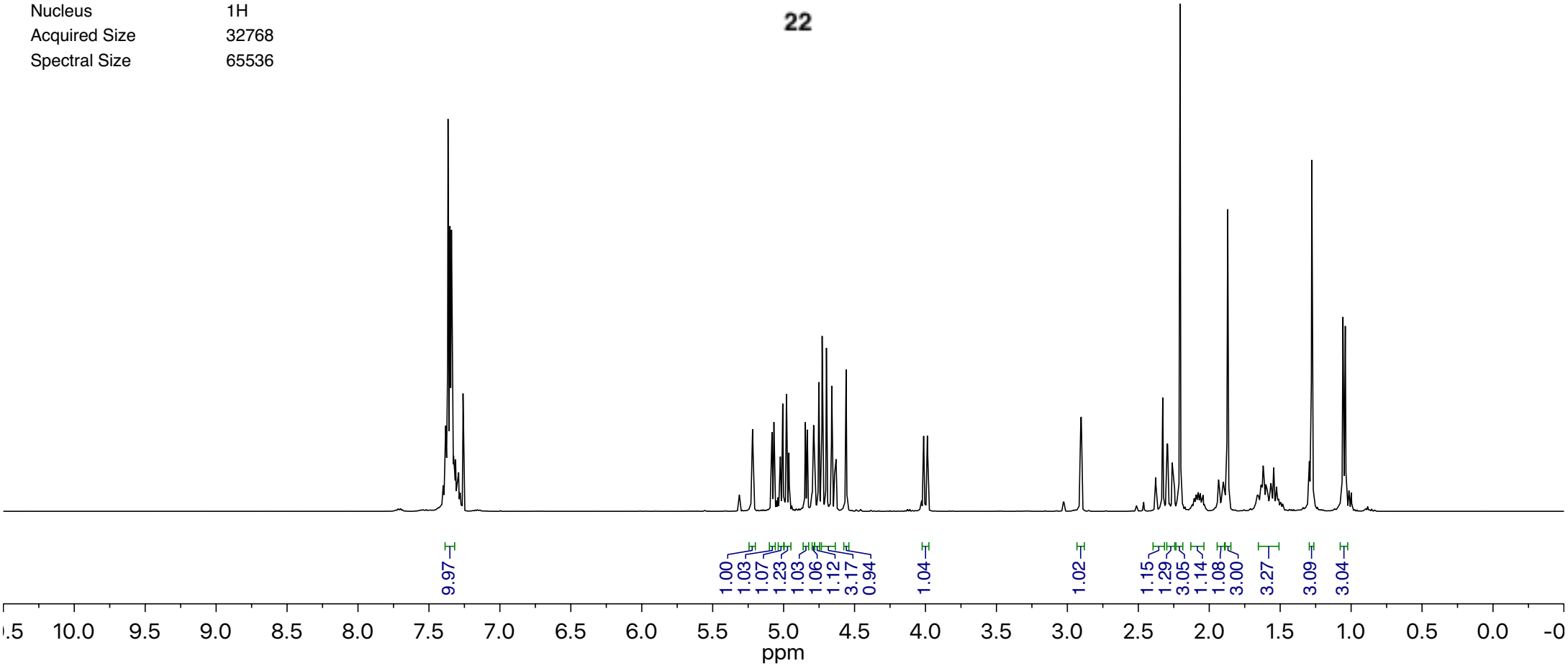


***ryanodine* (1)**

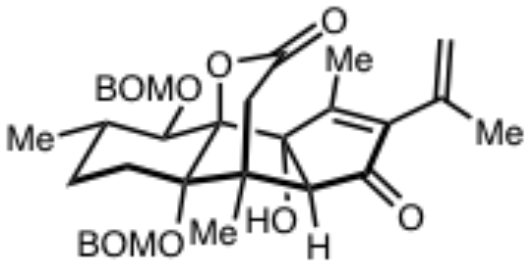
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-217-2-CH/ 1/ fid
Title	6-AH-217-2-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-08-31T13:44:13
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



22

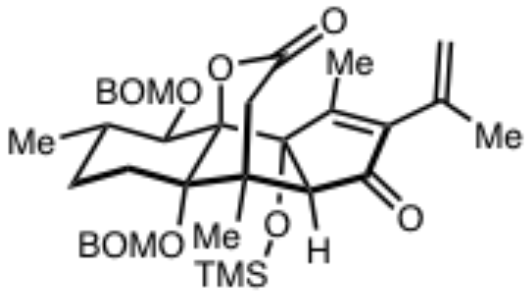


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-217-2-CH/ 2/ fid
Title	6-AH-217-2-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	101
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-31T13:48:49
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1965.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

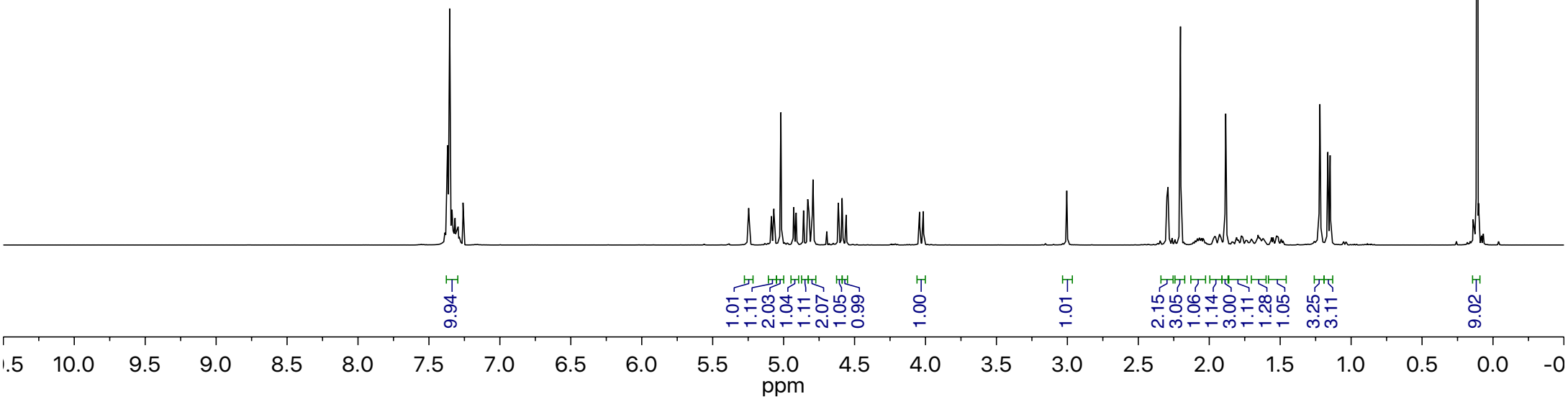


22

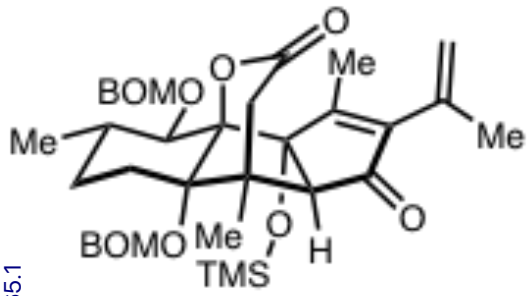
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-265-CH/ 1/ fid
Title	6-AH-265-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-09-02T09:14:07
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



S13

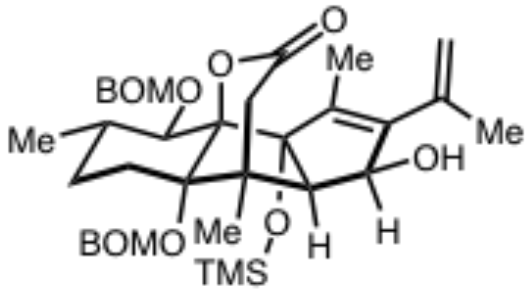


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-265-CH/ 2/ fid
Title	6-AH-265-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	105
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-09-02T09:18:53
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1965.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

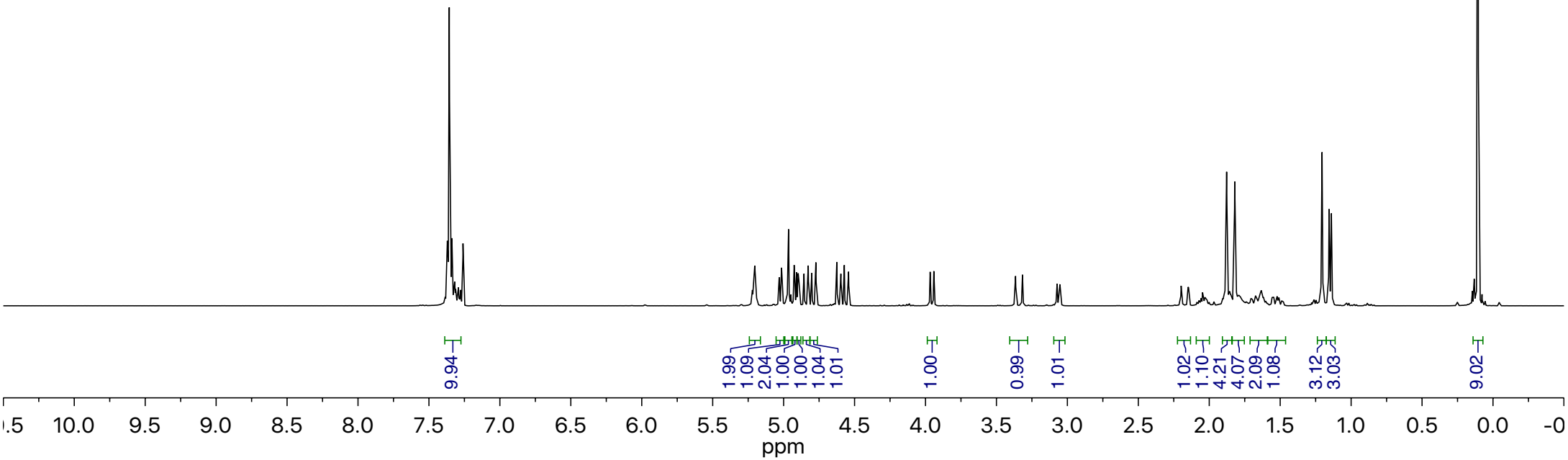


S13

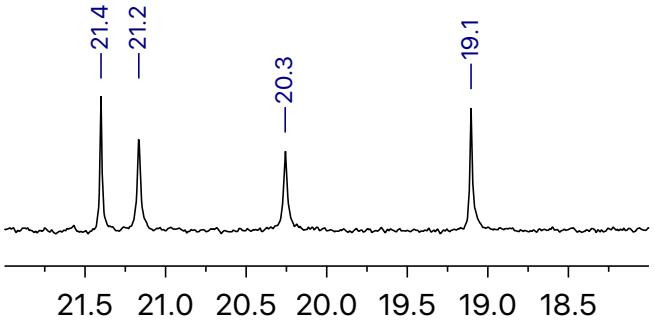
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-225-CH/ 1/ fid
Title	6-AH-225-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zg30
Number of Scans	6
Receiver Gain	30.3
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-09-06T11:57:21
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.5
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

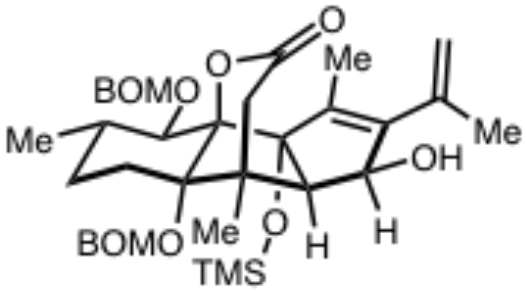


23

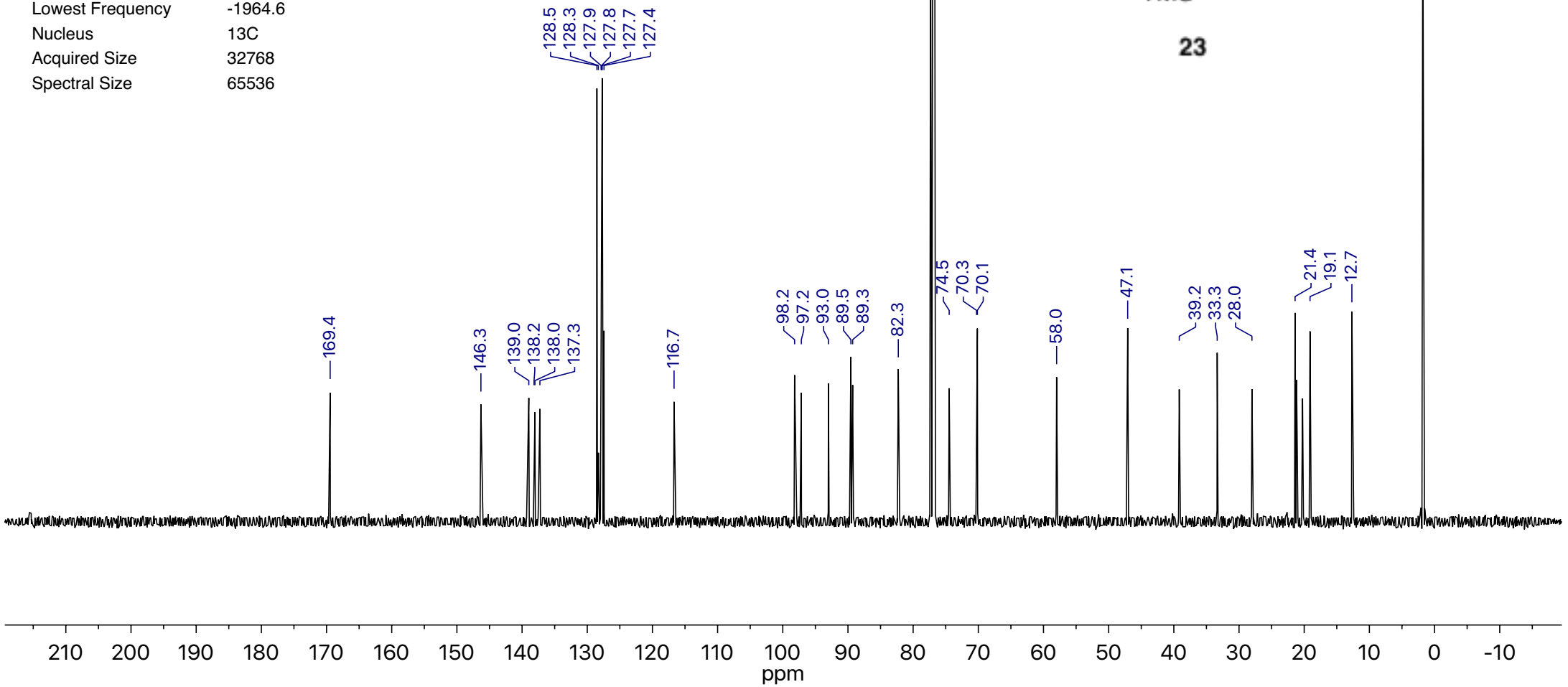


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-225-CH/ 2/ fid
Title	6-AH-225-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	101
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-09-06T12:01:57
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1964.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

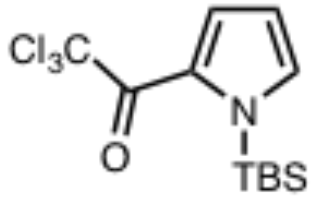




23

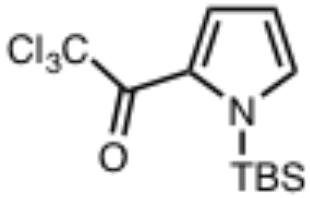


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-211-CH/ 1/ fid
Title	6-AH-211-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-07-20T20:19:29
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.7
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



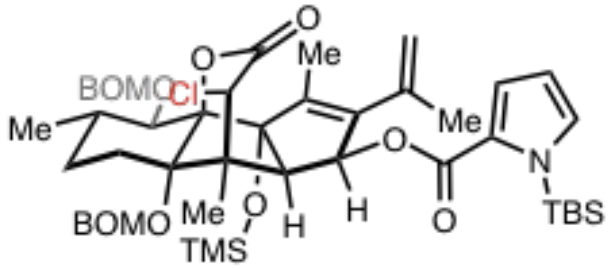
24

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-211-CH/ 5/ fid
Title	6-AH-211-CH.5.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	78.7
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-07-20T21:16:39
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1960.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



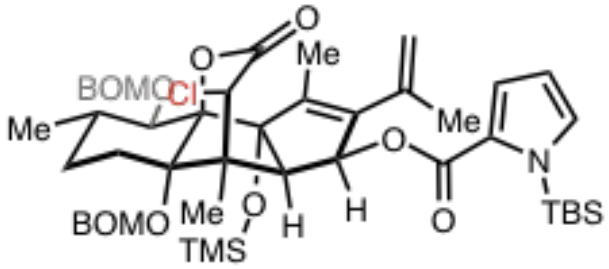
24

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-273-CH/ 1/ fid
Title	6-AH-273-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	127.1
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-09-07T19:17:41
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

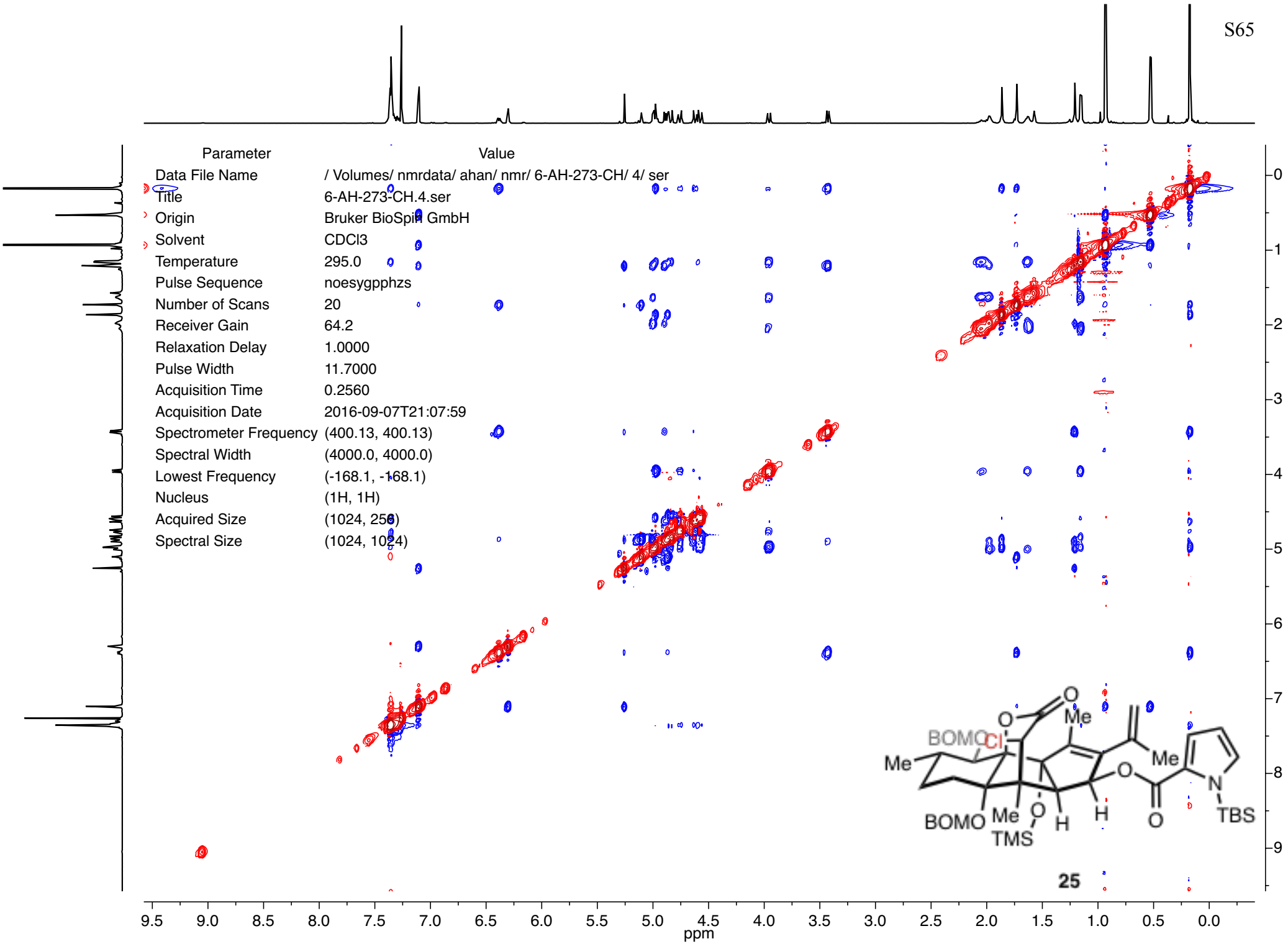


25

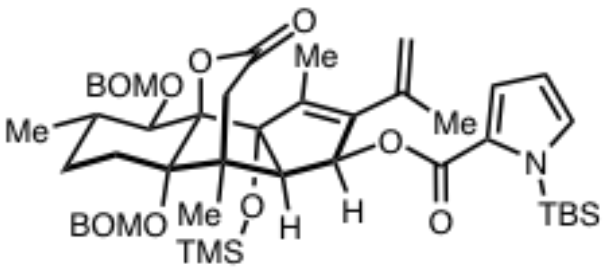
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-273-CH/ 7/ fid
Title	6-AH-273-CH.7.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	3000
Receiver Gain	55.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-09-08T03:12:22
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



25


Parameter Value
Data File Name / Volumes/ nmrdata/ ahan/ nmr/ 6-AH-273-CH/ 4/ ser
Title 6-AH-273-CH.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.0
Pulse Sequence noesygpphzs
Number of Scans 20
Receiver Gain 64.2
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2016-09-07T21:07:59
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Lowest Frequency (-168.1, -168.1)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
BOMO
Cl
Me
Me
Me
O
O
O
O
N
TBS
BOMO
Me
TMS
O
H
H
25
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
ppm
0 1 2 3 4 5 6 7 8 9

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-250-CH/ 1/ fid
Title	6-AH-250-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.0
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	127.1
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-08-21T11:46:16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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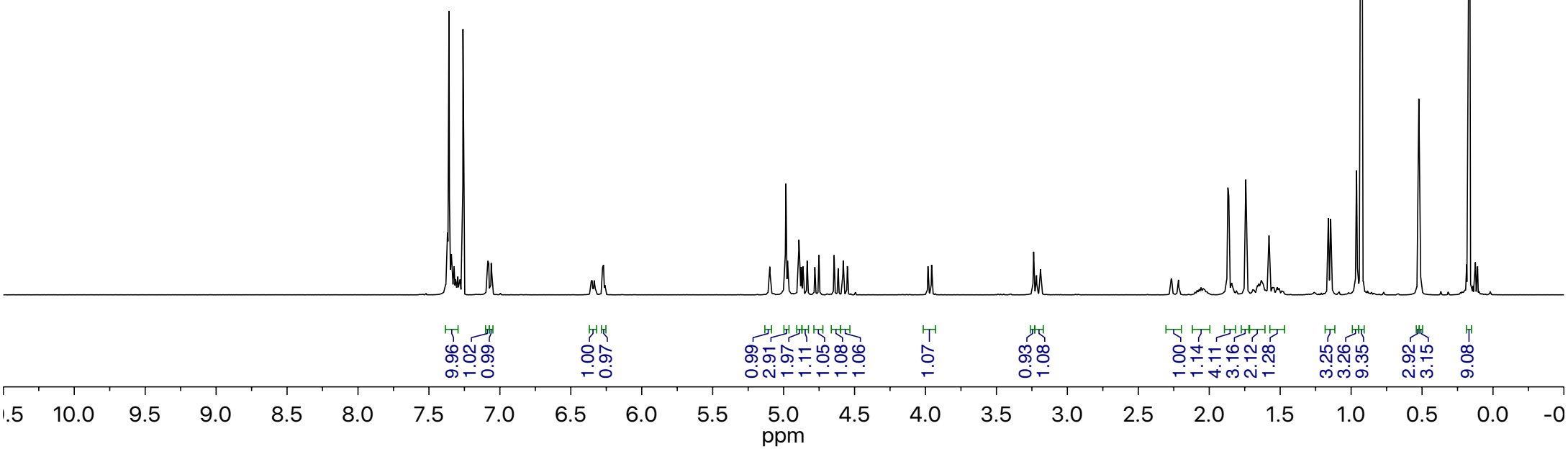
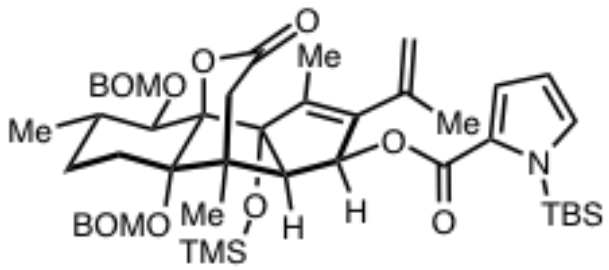
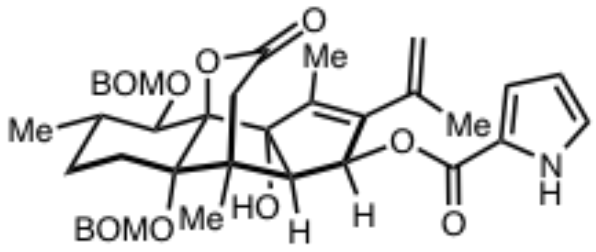


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-250-CH/ 4/ fid
Title	6-AH-250-CH.4.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	1470
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-21T13:55:55
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

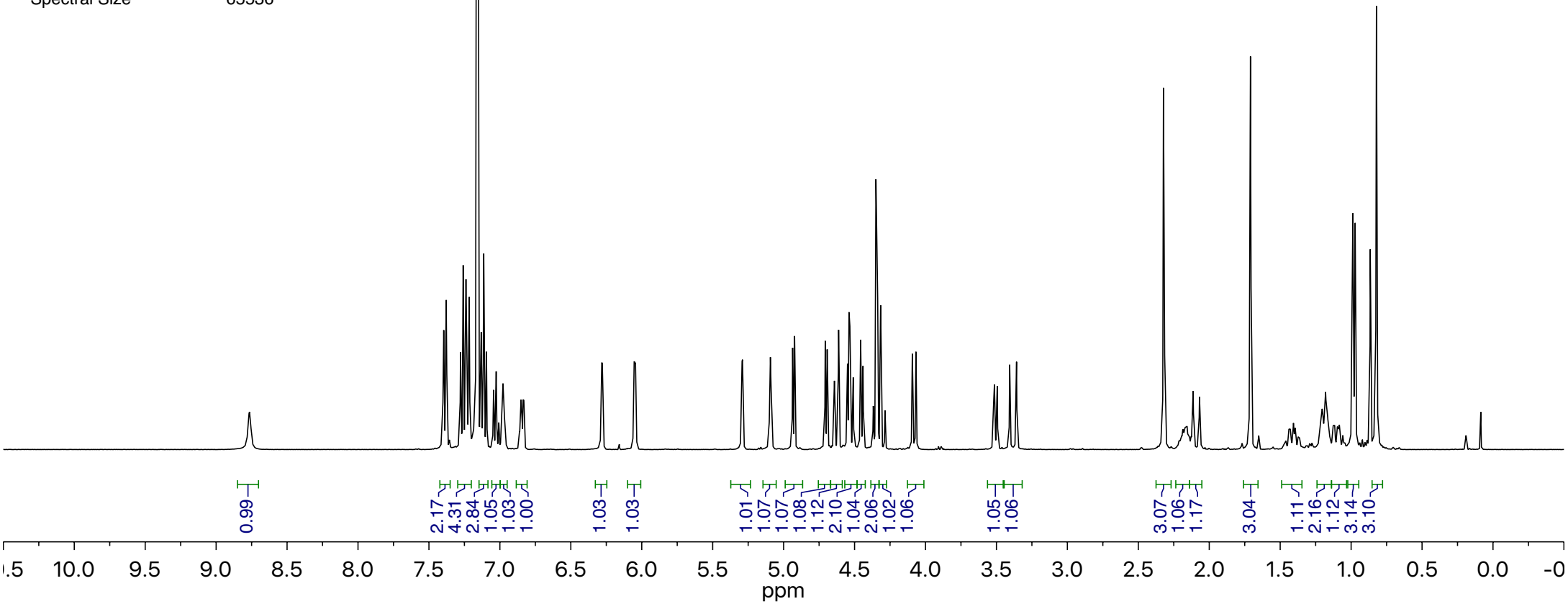


26

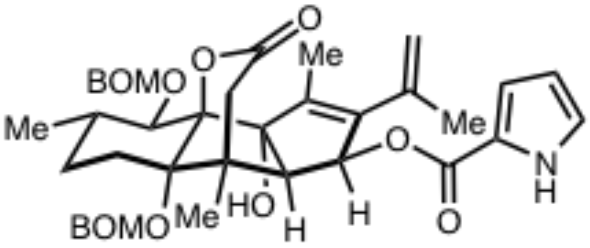
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ chenxu91/ nmr/ 6-AH-251-CH/ 1/ fid
Title	6-AH-251-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.0
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-08-21T17:40:27
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1532.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



S14

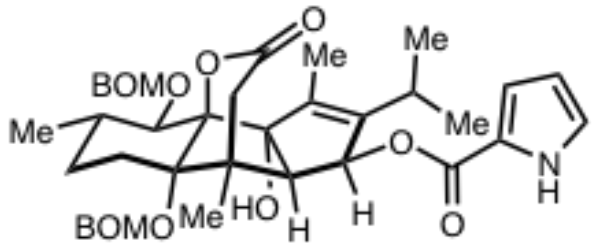


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ chenxu91/ nmr/ 6-AH-251-CH/ 4/ fid
Title	6-AH-251-CH.4.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	1470
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-21T19:43:05
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1927.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

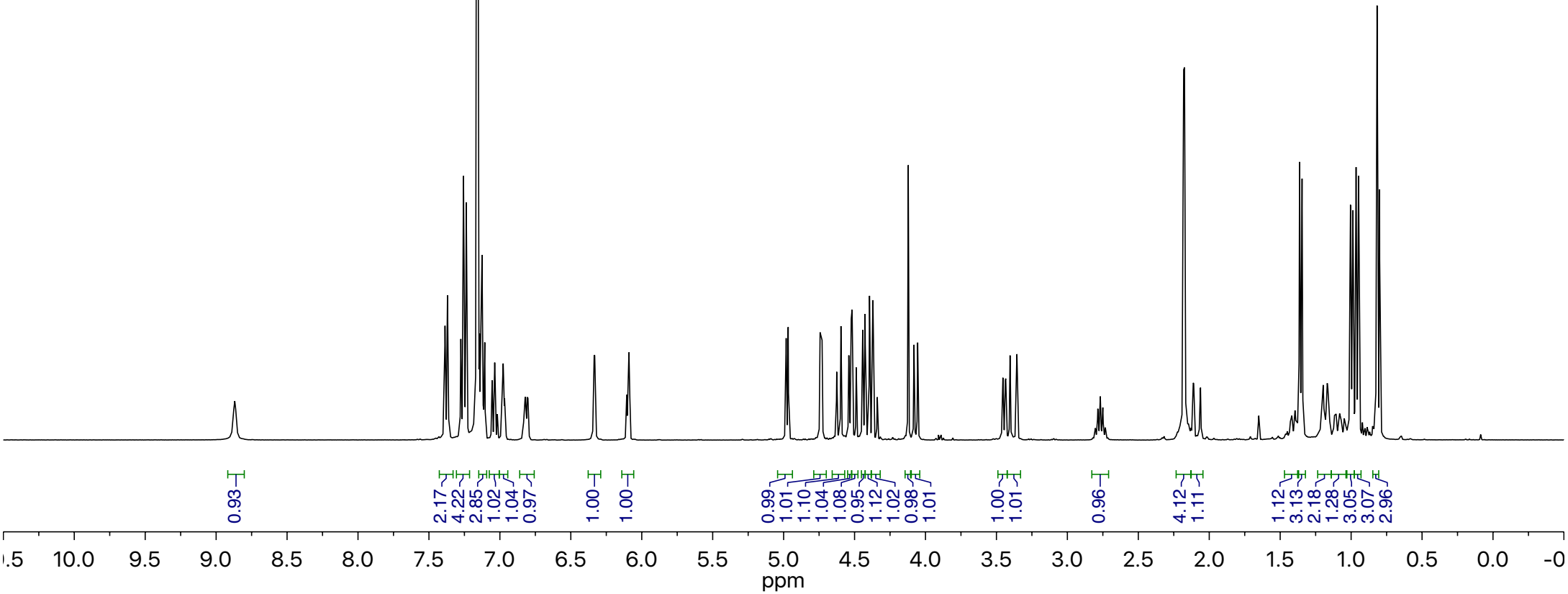


S14

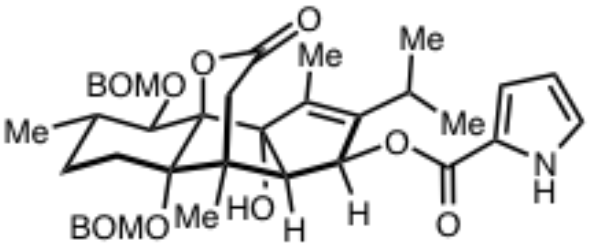
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-252-CH/ 1/ fid
Title	6-AH-252-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	294.9
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-08-22T08:05:18
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1532.5
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



S15

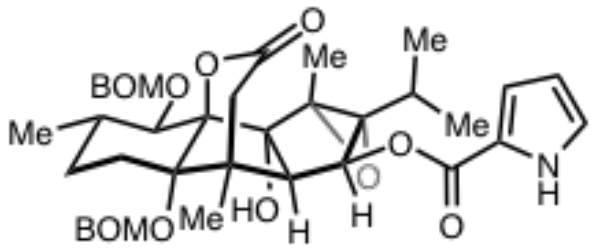


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-252-CH/ 4/ fid
Title	6-AH-252-CH.4.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	1475
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-22T10:08:05
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1927.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



S15

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ chenxu91/ nmr/ 6-AH-253-CH/ 1/ fid
Title	6-AH-253-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.0
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-08-22T15:50:51
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1532.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



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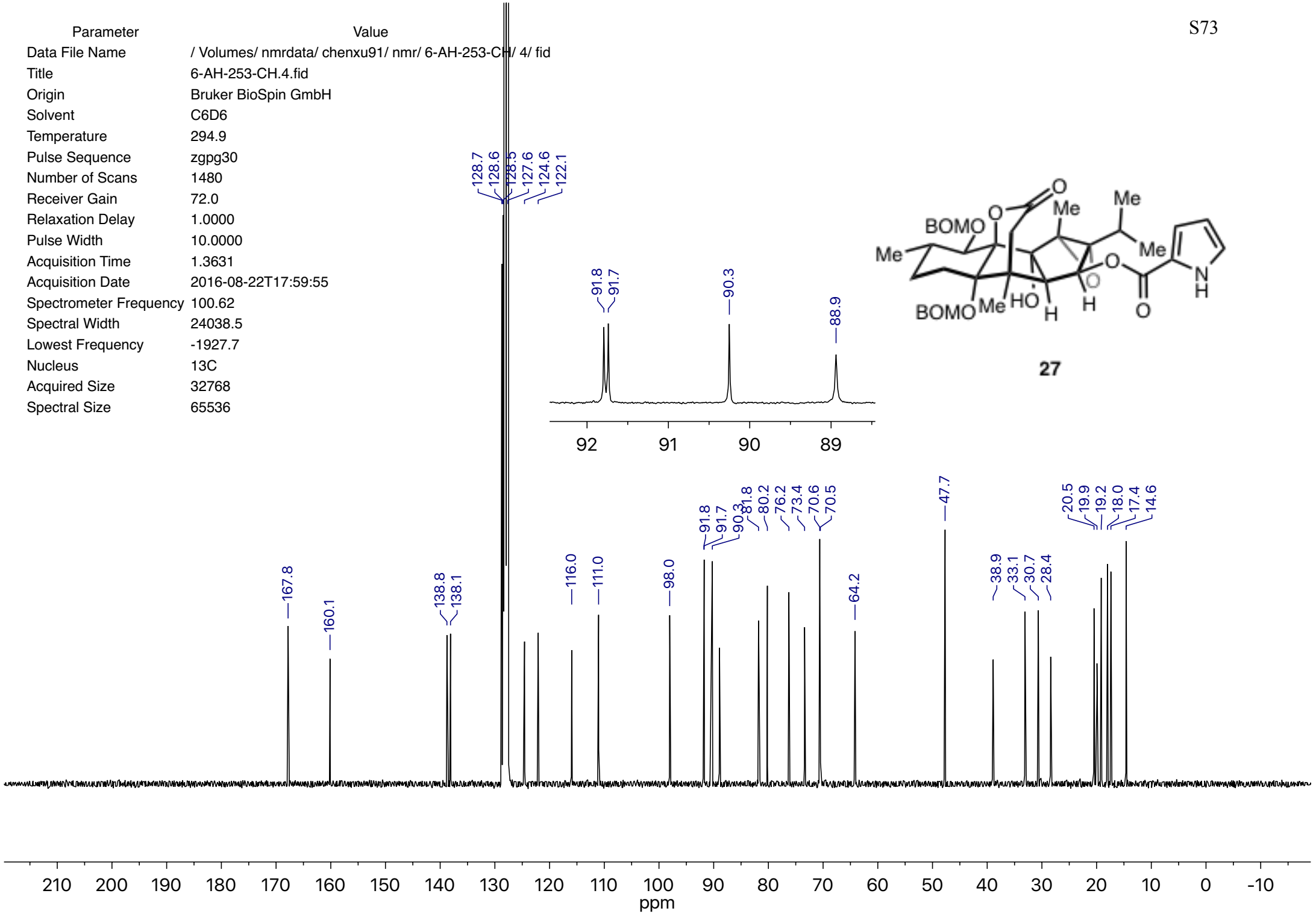
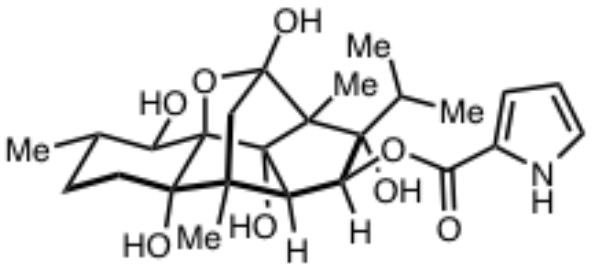
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ chenxu91/ nmr/ 6-AH-253-CH/ 4/ fid
Title	6-AH-253-CH.4.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	294.9
Pulse Sequence	zgpg30
Number of Scans	1480
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-22T17:59:55
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1927.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



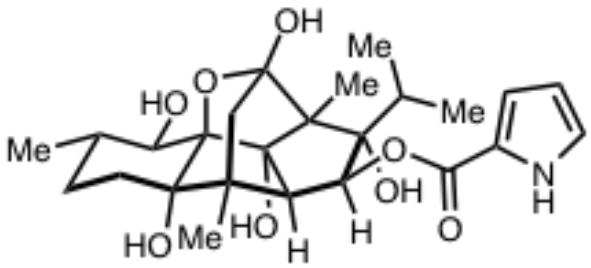
27

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-254-CH/ 1/ fid
Title	6-AH-254-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	294.9
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	176.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2016-08-23T22:24:54
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1543.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



20-deoxyspiganthine (3)

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 6-AH-254-CH/ 2/ fid
Title	6-AH-254-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	295.0
Pulse Sequence	zgpg30
Number of Scans	3500
Receiver Gain	87.8
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2016-08-24T01:45:58
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1817.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



***20-deoxyspiganthine* (3)**