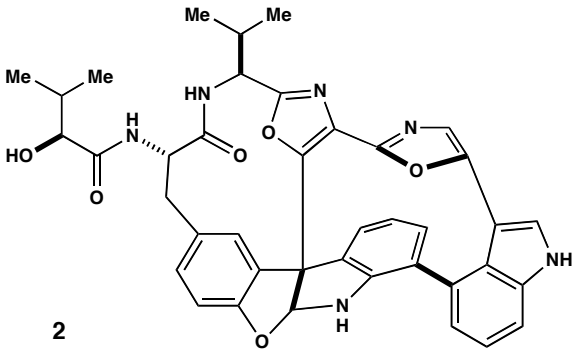
Supporting Text

Synthetic diazonamides: Spectroscopic data for AB-5 and probe reagent syntheses

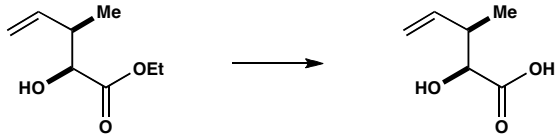
Preparation of the core diazonamide ring system from which the molecules below derive is described in Burgett AW, Li Q, Wei Q, Harran PG (2003) *Angew Chem Intl Ed Engl* 42:4961-4966.



2

(aka AB-5)

$[\alpha]^{25}_{D}$ = -230.9° (c = 0.01, 30% $CH_3OH/CHCl_3$). IR (film): 3396, 2360, 1651, 1493, 668 cm^{-1}. ^1H NMR (400 MHz, 90% $CD_3OD/CHCl_3$): δ 7.52 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.46 (s, 1H), 7.40 (d, *J* = 1.6 Hz, 1H), 7.34 (m, 1H), 7.21–7.17 (m, 2H), 7.00 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.89 (s, 1H), 6.82 (dd, *J* = 7.6, 0.8, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.61 (t, *J* = 7.6 Hz, 1H), 6.36 (s, 1H), 4.60 (dd, *J* = 11.6, 3.6 Hz, 1H), 3.89 (d, *J* = 3.6, 1H), 3.43–3.34 (m, 1H), 2.80 (dd, *J* = 11.6, 3.2 Hz, 1H), 2.27–2.22 (m, 1H), 2.14–2.00 (m, 1H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (300 MHz, 30% $CD_3OD/CHCl_3$): δ 174.3, 173.0, 160.7, 158.0, 154.1, 151.9, 149.2, 148.2, 137.1, 130.8, 130.2, 130.1, 129.7, 128.3, 128.1, 127.6, 127.5, 126.3, 124.8, 123.7, 122.9, 122.8, 122.6, 121.3, 120.4, 111.8, 110.3, 104.5, 102.4, 75.6, 61.3, 55.8, 54.9, 37.9, 31.7, 30.1, 18.9, 18.6, 17.6, 15.4. ES-MS: calculated. for $C_{40}H_{36}N_6O_6$ $[M+H]^+$ 697.27, found:697.20; calculated. for $C_{43}H_{40}Cl_2N_6O_7$ $[M-H]^-$ 695.28, found:695.25.



(2S,3R)-**3**

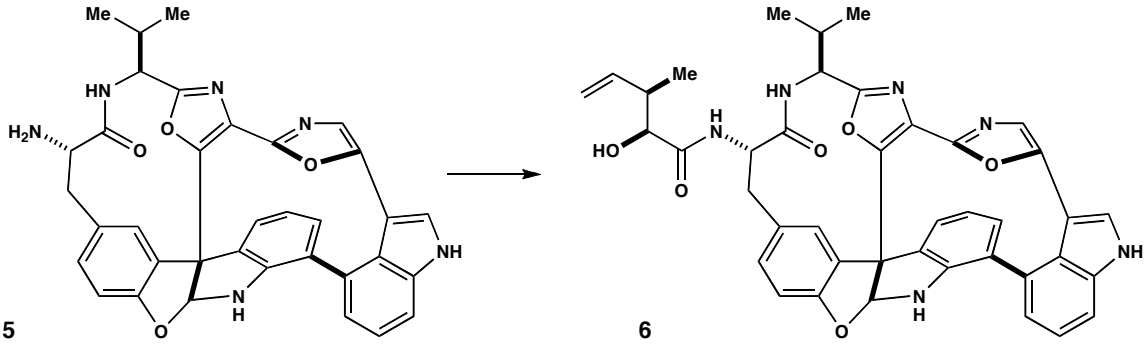
4

Evans et al
J. Am. Chem. Soc.
(**2000**) 122, 7936-7943.

(2*S*,3*R*)-Ethyl 3-methyl-2-hydroxy-4-pentenoate (**3**) (20.0 mg, 0.127 mmol, prep HPLC purified) was dissolved in 0.7 mL MeOH and treated with 0.7 mL 10% aq KOH. The solution was stirred at room temperature for 2 h, diluted with saturated

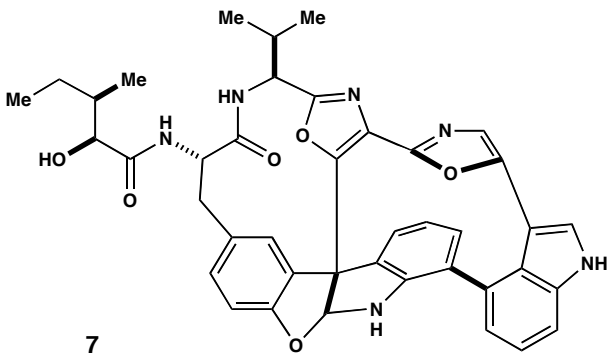
NH_4Cl, and extracted with EtOAc (3x). The organic layers were combined, washed with brine, dried (Na_2SO_4) and concentrated in vacuo. Crude **4** thus obtained (10.0 mg) was used without further purification.

4: ^{1}H-NMR (400 MHz, CD_3OD): δ 5.87–5.78 (m, 1H), 5.06 (d, *J* = 16.8 Hz, 1H), 5.01 (d, *J* = 10.0 Hz, 1H), 4.05 (d, *J* = 3.6 Hz, 1H), 2.65 (br s, 1H), 1.12 (d, *J* = 7.2 Hz, 3H).



Amine **5** (3.0 mg, 5 μmol) was dissolved in 0.2 mL THF and cooled to 0°C under N_2. Carboxylic acid **4** was added as a stock solution (0.08M in dry THF, 90 μL, 7 μmol). $(EtO)_2P(O)CN$ (4.3 mg, 0.026 mmol) was then added, followed by 4-methylmorpholine (3.7 mg, 0.026 mmol). The solution was warmed to room temperature and stirred for 1.5 h. The reaction was diluted in 10 mL EtOAc, washed with $NaHCO_3$, H_2O, sat aq NH_4Cl, brine, and dried over Na_2SO_4. Preparative TLC (10% $MeOH/CH_2Cl_2$) afforded acyl derivative **6** (2 mg, 60% yield) as a white film.

6: ^{1}H-NMR (400 MHz, CD3OD):δ 7.52 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.46 (s, 1H), 7.39 (d, *J* = 1.6 Hz, 1H), 7.34 (m, 1H), 7.19 - 7.16 (m, 2H), 7.00 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.89 (s, 1H), 6.83 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.78 (d, *J* = 8.4, 1H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.35(s, 1H), 5.89–5.80 (m, 1H), 5.11 – 5.05 (m, 2H), 4.57 (dd, *J* = 12.0, 3.2 Hz, 1H), 3.98 (d, *J* = 3.6 Hz, 1H), 3.35 (app t, *J* = 12.0 Hz, 1H), 2.76 (dd, *J* = 12.8, 3.2 Hz, 1H), 2.68 (m, 1H), 2.24 (m, 1H), 1.15 (d, *J* = 10.8 Hz, 3H), 1.06 (d, *J* = 10.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz).

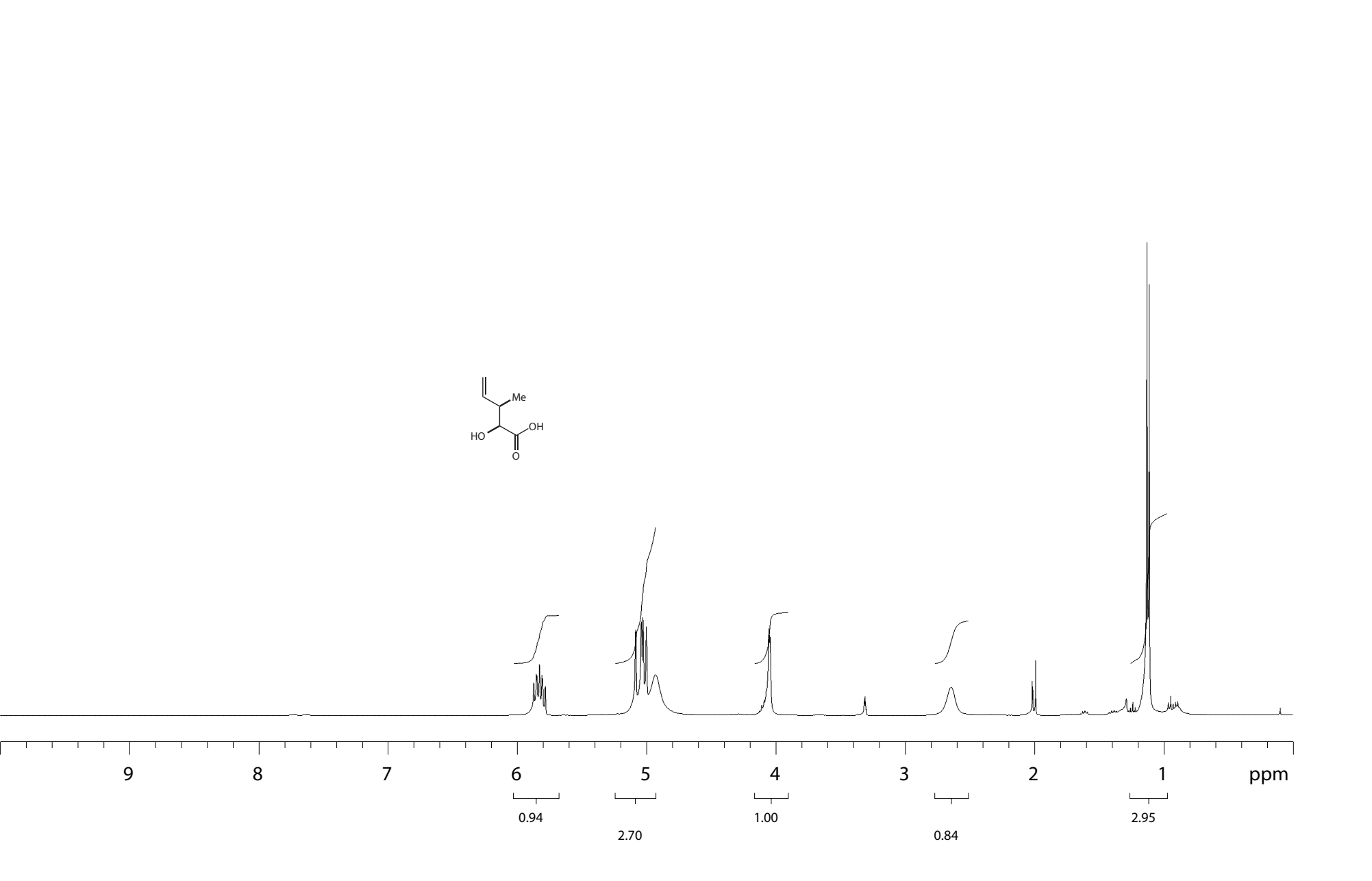


7

(aka AB-9)

Olefin **6** (2.0 mg, 3 μmol) and 10% Pd/C (~ 1 mg) were suspended in 0.3 mL anhydrous MeOH under an atmosphere of H_2 (balloon). The reaction was stirred vigorously for 30 min, filtered through a plug of celite and concentrated. Preparative HPLC [Higgins C18, 60→100% CH_3OH/H_2O gradient] provided hydrogenation product **7** (~ 2.0 mg) as a white film.

7 (AB-9): ^{1}H-NMR (400 MHz, CD3OD): δ7.52 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.45 (s, 1H), 7.40 (d, *J* = 1.6 Hz, 1H), 7.34 (m, 1H), 7.21–7.17 (m, 2H), 7.00 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.89 (s, 1H), 6.83(d, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.36 (s, 1H), 4.59 (dd, *J* = 12.0, 3.2 Hz, 1H), 3.93 (d, *J* = 4.4 Hz, 1H), 3.43- 3.34 (m, 1H), 2.79 (dd, *J* = 12.8, 3.6 Hz, 1H), 2.30–2.21 (m, 1H), 1.88–1.84 (m, 1H), 1.54–1.48 (m, 1H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.943 (t, *J* = 7.6 Hz, 3H).
ES-MS: calculated. for $C_{41}H_{38}N_6O_6$ $[M+H]^+$ 711.28, found: 711.25; calculated. for $C_{43}H_{40}Cl_2N_6O_7$ $[M-H]^-$ 709.28, found: 709.35.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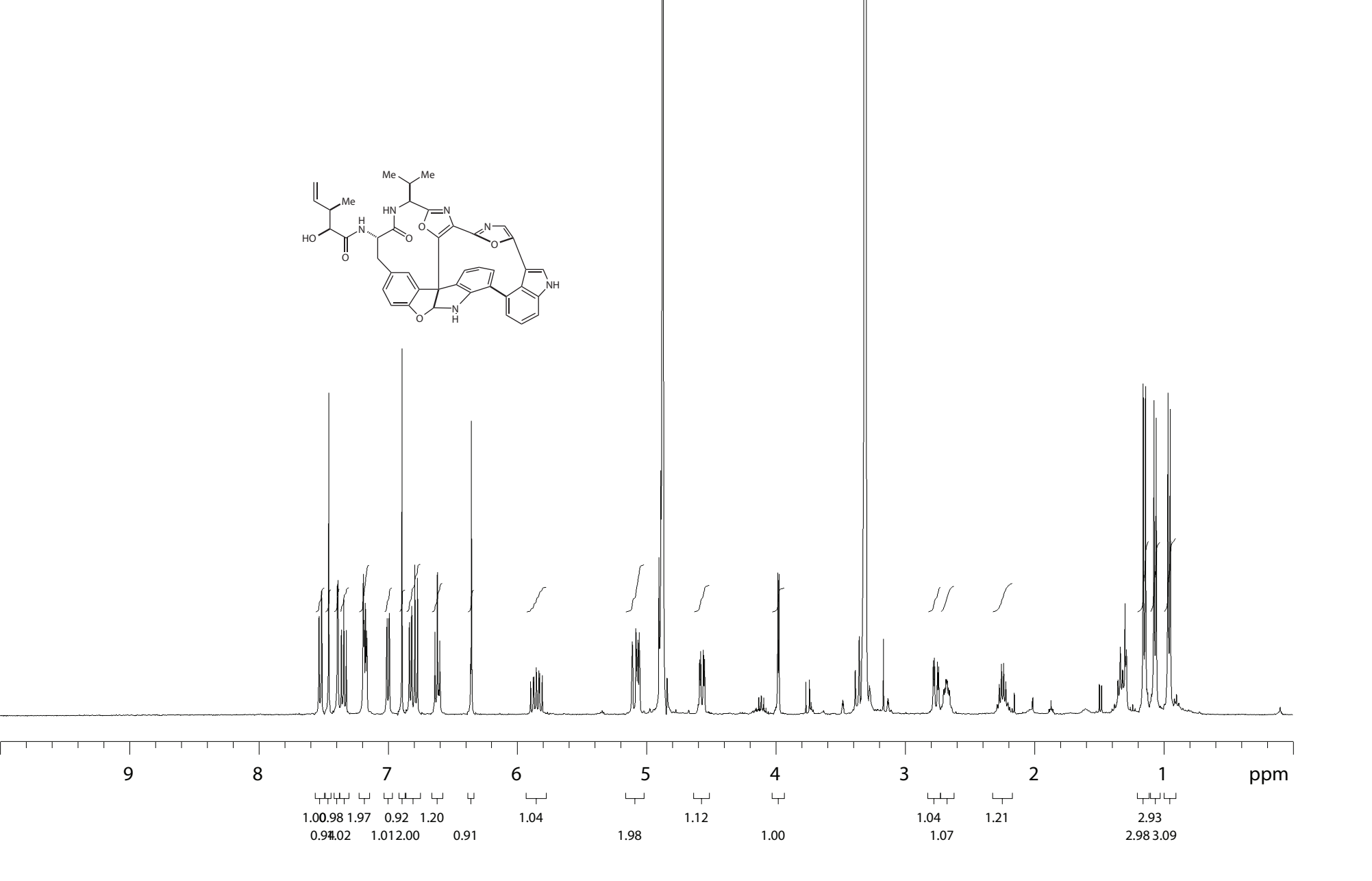
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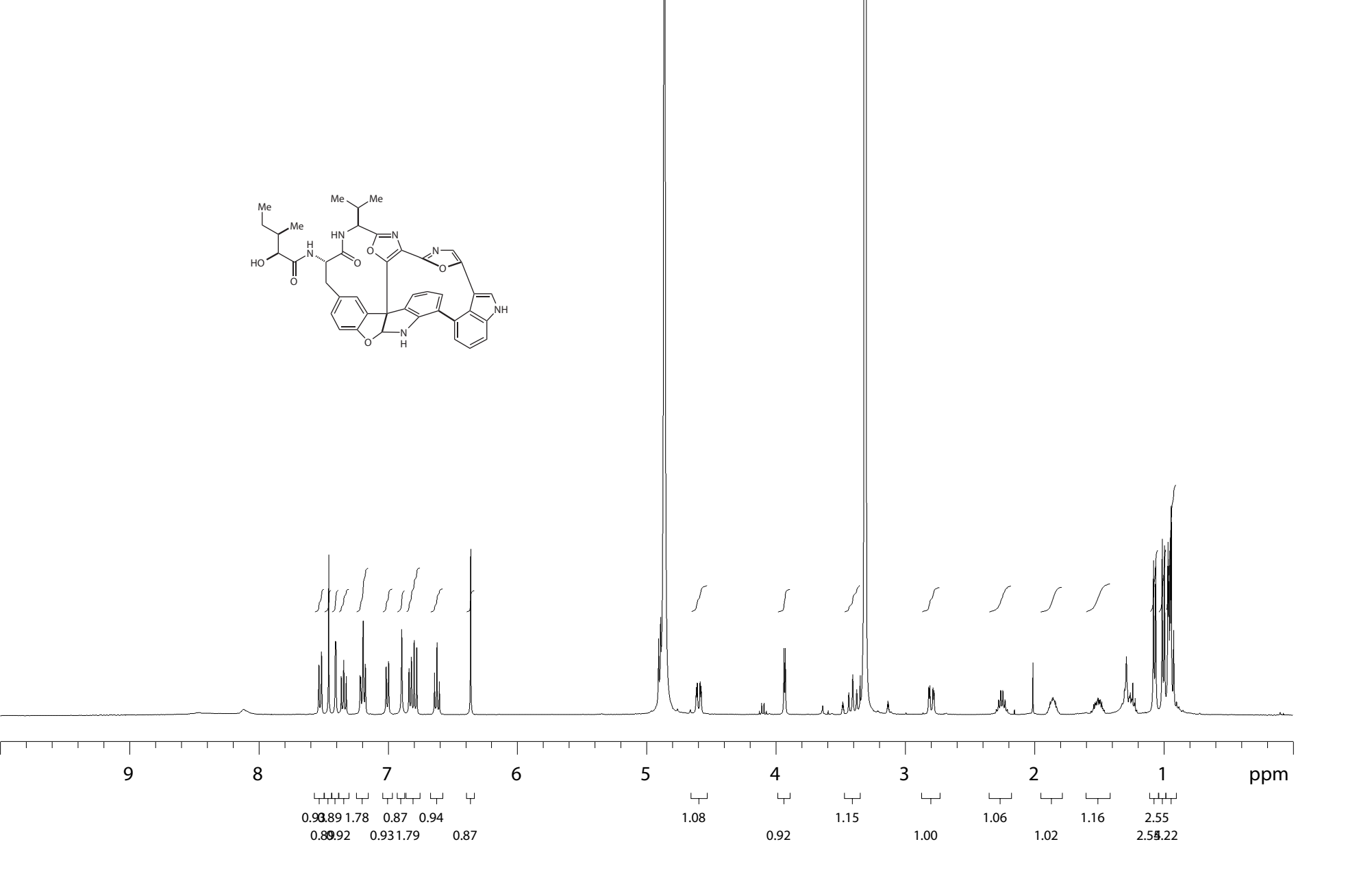
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#273B (ABVII237"AB-5

exp1 std1h

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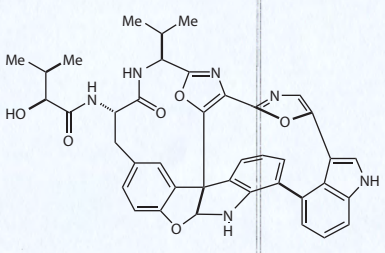
nm cdc ph



1CH3

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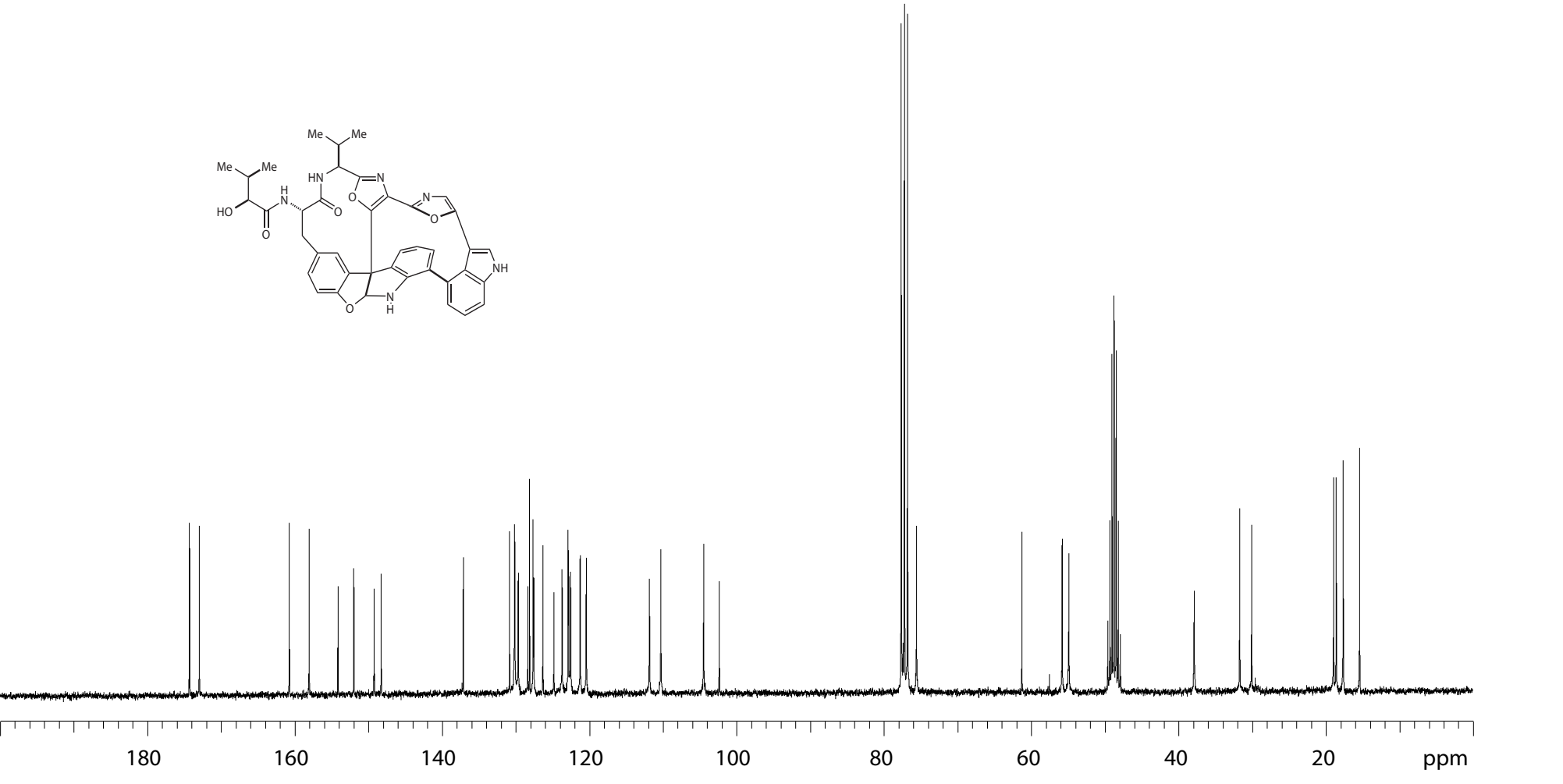
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