Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information for

The C29–C34 parts of antitumor macrolide aplyronine A serve as versatile actin-affinity tags

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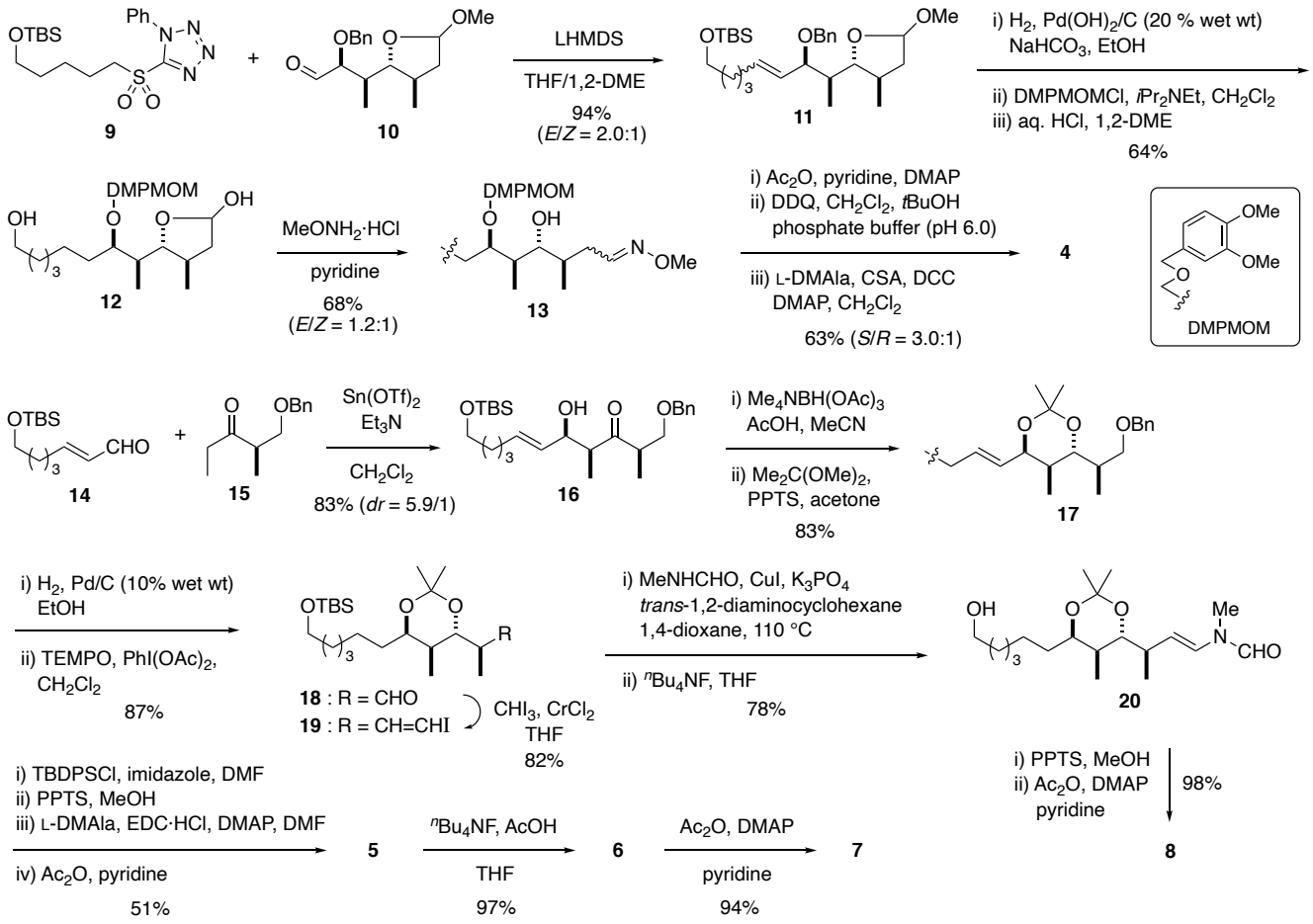
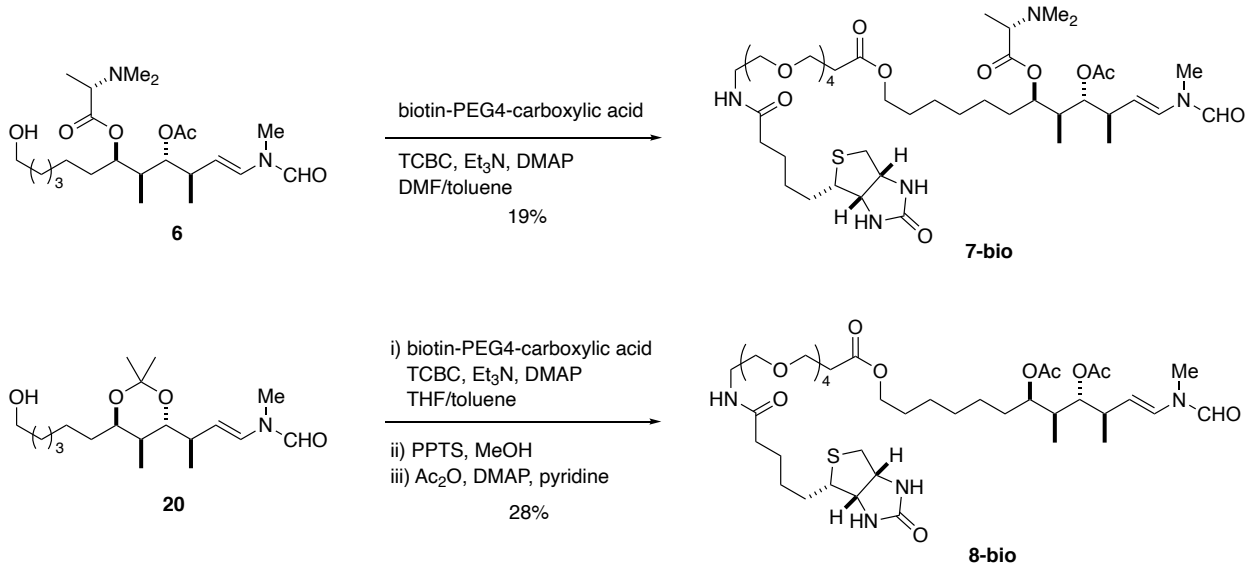
(50 pages)



Scheme S1. Synthesis of analogs **4**–**8**.



Scheme S2. Synthesis of biotin probes **7-bio** and **8-bio**. Primary alcohol **6** was condensed with commercially available biotin-PEG4-COOH using 2,4,6-trichlorobenzoyl chloride (TCBC) and DMAP to directly afford **7-bio**. Similarly, esterification of **20**, removal of an acetonide group, and acetylation provided **8-bio**.

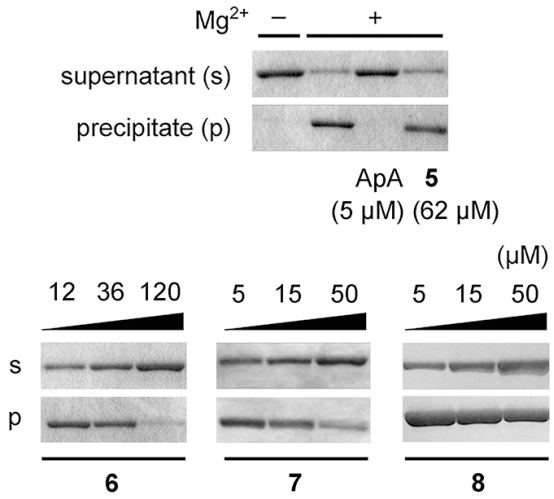
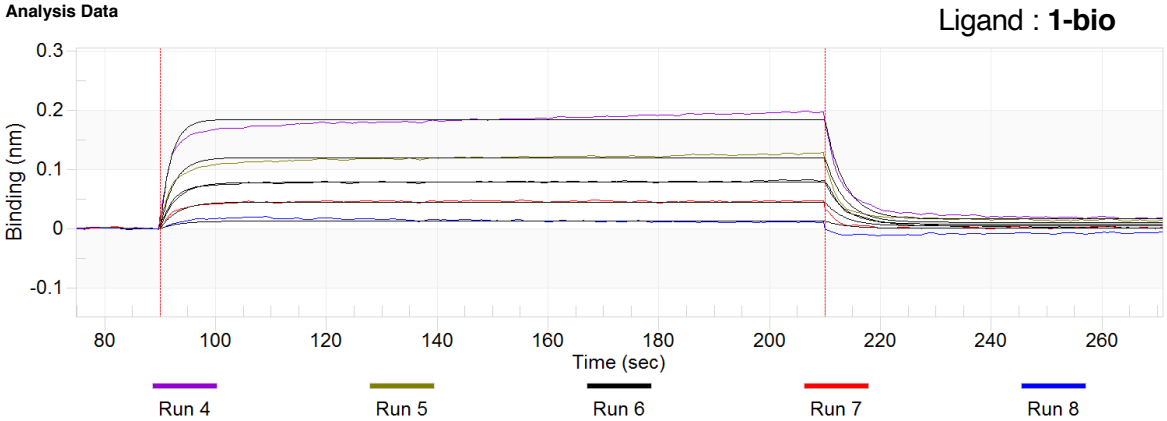


Figure S1. *In vitro* F-actin sedimentation assay. Filamentous (F-) actin (3 μM as a monomer) was precipitated by ultracentrifugation after treatment with ApA or side-chain analogs **5**–**8**. Proteins in the supernatant (S) and the precipitate (P) were analyzed by SDS-PAGE and detected with CBB stain.

Analysis Parameters
Global fitting (1:1)
Step correction: (none)

Analysis Data



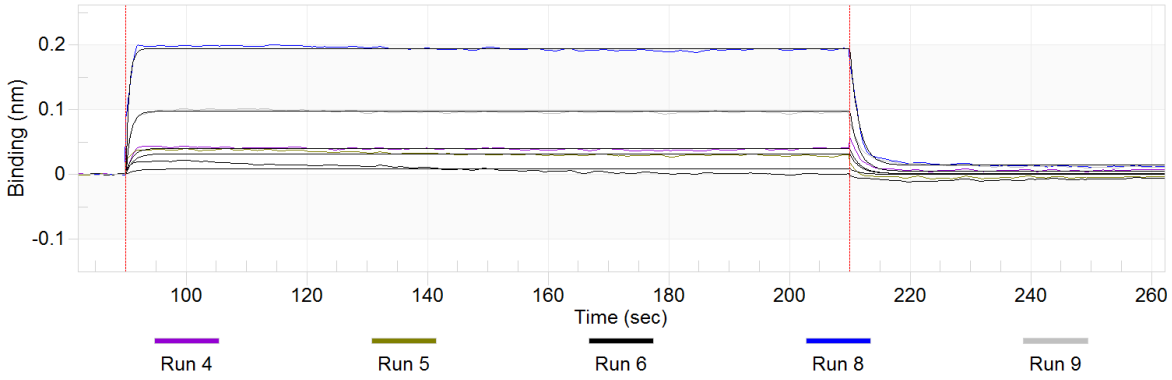
Index	Sample ID	Conc. (uM)	Information	KD (M)	ka (1/Ms)	ka Error	kd (1/s)	kd Error	Rmax	Rmax Error	R equilibrium	X^2	R^2
1	actin 10 uM	10											
2	actin 10 uM bsm	10											
3	actin 0 uM	0											
4	actin 5 uM	5		5.157e-6	5.005e4	7.006e3	2.582e-1	1.09e-2	0.3856	0.0334	0.1898	0.05496	0.992
5	actin 2.5 uM	2.5		5.157e-6	5.005e4	7.006e3	2.582e-1	1.09e-2	0.3858	0.04411	0.126	0.05496	0.992
6	actin 1.25 uM	1.25		5.157e-6	5.005e4	7.006e3	2.582e-1	1.09e-2	0.4307	0.05874	0.08402	0.05496	0.992
7	actin 0.625 uM	0.625		5.157e-6	5.005e4	7.006e3	2.582e-1	1.09e-2	0.4562	0.06898	0.04931	0.05496	0.992
8	actin 0.312 uM	0.312		5.157e-6	5.005e4	7.006e3	2.582e-1	1.09e-2	0.2356	0.03999	0.01344	0.05496	0.992
9	actin 0.156 uM	0.156											
10	actin 10 uM (different ligand)	10											
11	actin 0 uM (different ligand)	0											

Figure S2. (continued)

Analysis Parameters
Global fitting (1:1)
Step correction: (none)

Analysis Data

Ligand : **7-bio**

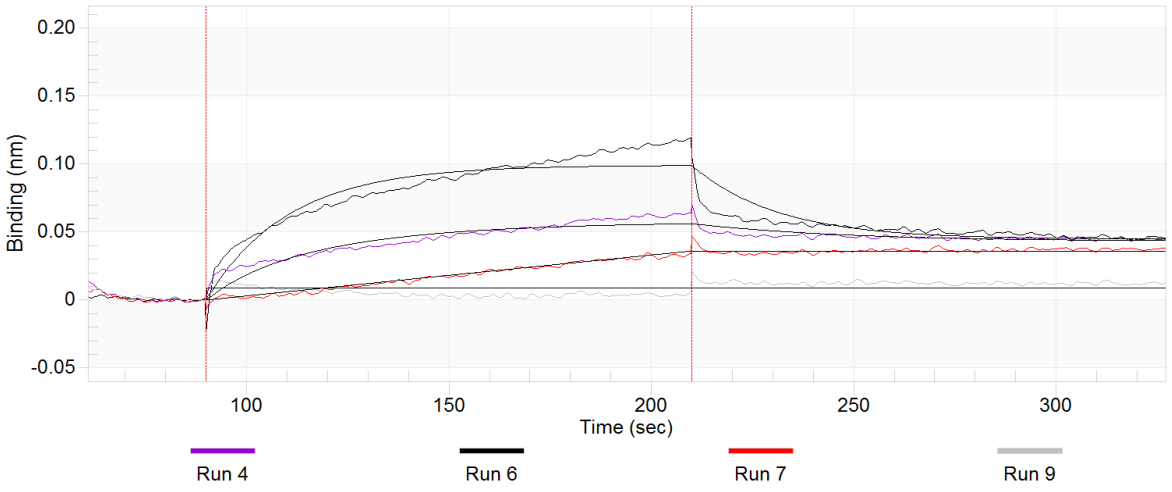


Index	Sample ID	Conc. (nM)	Information	KD (M)	ka (1/Ms)	ka Error	kd (1/s)	kd Error	Rmax	Rmax Error	R equilibrium	X^2	R^2
1	actin 10	10000											
2	actin 10 NSB	10000											
3	actin 0	0											
4	actin 5	5000		1.007e-5	5.974e4	1.14e4	6.016e-1	4.456e-2	0.1233	0.01889	0.04092	0.06178	0.9911
5	actin 2.5	2500		1.007e-5	5.974e4	1.14e4	6.016e-1	4.456e-2	0.1656	0.03063	0.03294	0.06178	0.9911
6	actin 1.25	1250		1.007e-5	5.974e4	1.14e4	6.016e-1	4.456e-2	0.07446	0.017	0.008222	0.06178	0.9911
7	actin 20	20000											
8	actin 20 run2	20000		1.007e-5	5.974e4	1.14e4	6.016e-1	4.456e-2	0.295	0.02289	0.1962	0.06178	0.9911
9	actin 10 run2	10000		1.007e-5	5.974e4	1.14e4	6.016e-1	4.456e-2	0.1986	0.02292	0.09895	0.06178	0.9911
10	actin 10 (186-3)	10000											
11	actin 20 run3	20000											

Analysis Parameters
Local fitting (1:1)
Step correction: (none)

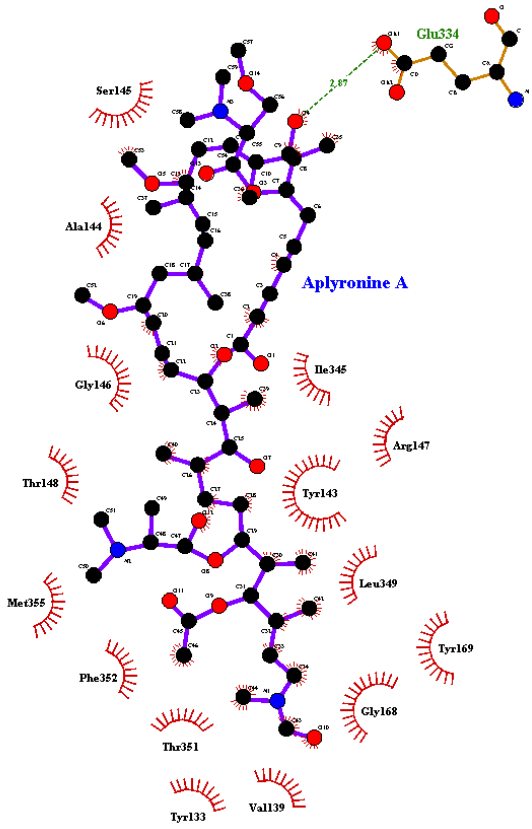
Analysis Data

Ligand : **8-bio**

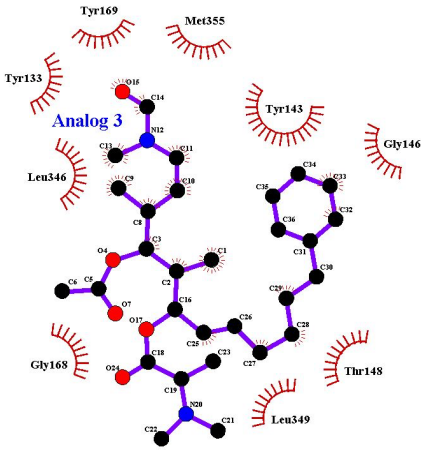


Index	Sample ID	Conc. (uM)	Information	KD (M)	ka (1/Ms)	ka Error	kd (1/s)	kd Error	Rmax	Rmax Error	R equilibrium	X^2	R^2
1	actin 20 (ligand 100)	20											
2	actin 0 (ligand 100)	0											
3	actin 10 (ligand 100)	10											
4	actin 10 (lig 10)	10		2.933e-6	1.985e3	3.531e2	5.823e-3	3.638e-4	0.1203	0.01852	0.09302	0.01759	0.8369
5	actin 0 (lig 10)	0											
6	actin 20 (lig 10)	20		1.241e-4	2.071e2	2.117e2	2.57e-2	1.064e-3	1.2	1.198	0.1665	0.07758	0.8948
7	actin 5 (lig 10)	5		<1e-12	6.224e1	7.956e3	<1e-7		0.9843	125.9	0.9843	0.003446	0.9809
8	actin 2.5 (lig 10)	2.5											
9	actin 2.5 (lig 10) run2	2.5		<1e-12	3.809e6	6.196e7	<1e-7		0.008829	1.581e-4	0.008829	0.02238	0

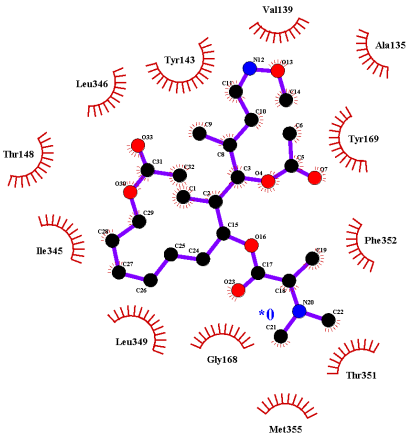
Figure S2. Global and local kinetic fits in Figure 2 (black solid lines) with approximate 1:1 models.



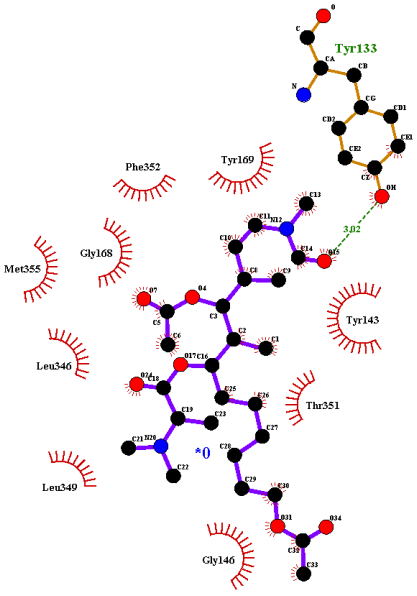
X-ray structure of actin–ApA (1) complex [PDB: 1WUA]



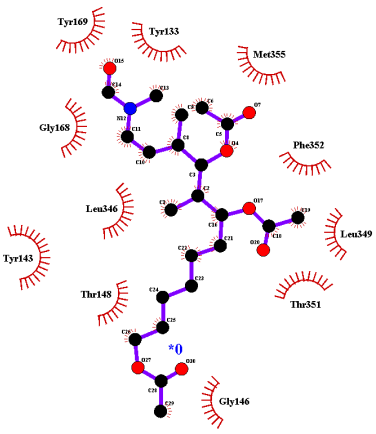
actin–3 complex



actin–4 complex



actin–7 complex



actin–8 complex

Figure S3. LIG-PLOT analysis of the calculated analogs **3**, **4**, **7**, and **8** on the docking models with actin. Hydrogen bonds are shown in dashed lines. Residues that directly interact with each ligand are shown in ball and stick models.

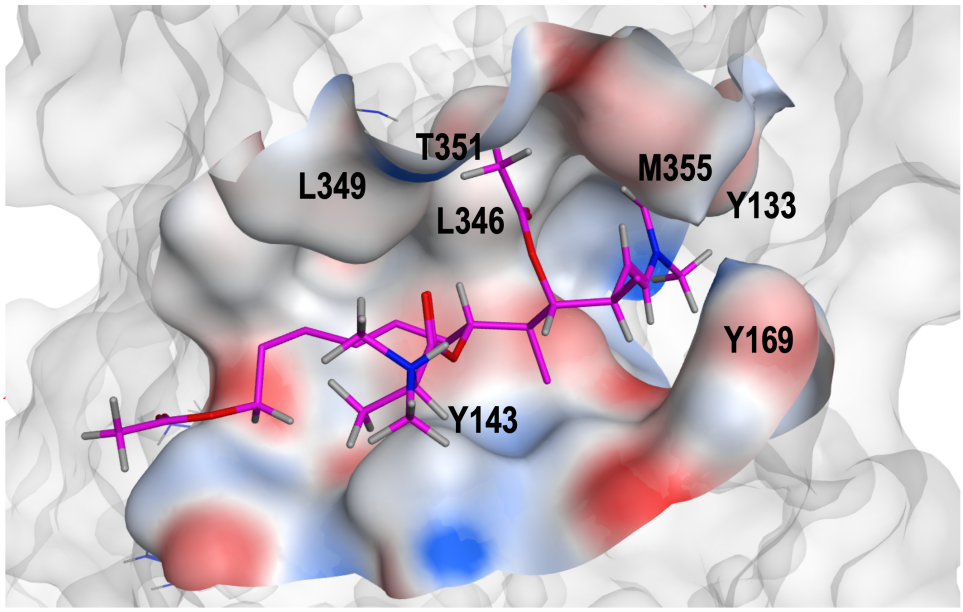


Figure S4. Molecular interactions of **7** with actin on the docking models.

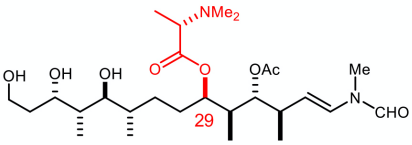
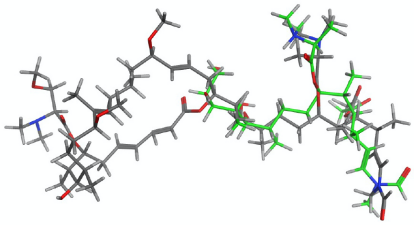
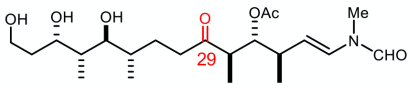
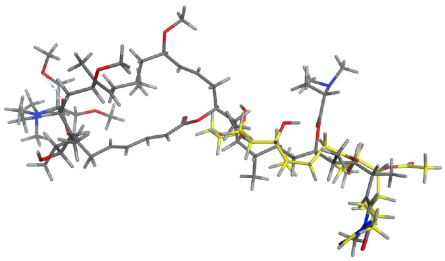
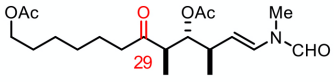
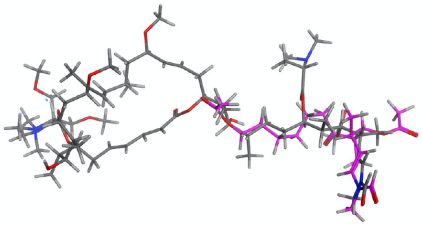
Structure	Binding position on actin	RMSD for **1** (Å)	Free binding energy (kcal/mol)
 **2**		1.98	–8.95
 **2a**		2.73	–7.61
 **7a**		3.17	–7.87

Figure S5. Binding position of the ApA side-chain analogs on actin. ApA (**1**) on the actin–ApA complex (gray, PDB: 1WUA) is superimposed on each model. (*S*)-DMAla ester was used for the modeling study of **2**.

Table S1. Interacted residues of actin on the crystal structure of actin–ApA (**1**) complex and the docked models of the analogs **3**, **4**, **7**, and **8**. s = side-chain, m = macrolide. Common interactions between natural **1** and **7** are highlighted in light yellow.

	Residues	natural ApA (**1**) (X-ray)	Actin-**3**	Actin–**4**	Actin–**7**	Actin–**8**	Residue position
Hydorgen bonds	Tyr133				○		s
	Glu334	○					m
	Total	1	0	0	1	0	
Hydrophobic interactions	Tyr133	○	○			○	s
	Ala135			○			s
	Val139	○		○			s
	Tyr143	○	○	○	○	○	s
	Ala144	○					m
	Ser145	○					m
	Gly146	○	○		○	○	m
	Arg147	○					m
	Thr148	○	○	○		○	s
	Gly168	○	○	○	○	○	s
	Tyr169	○	○	○	○	○	s
	Ile345	○		○			m / s
	Leu346		○	○	○	○	s
	Leu349	○	○	○	○	○	s
	Thr351	○		○	○	○	s
	Phe352	○		○	○	○	s
	Met355	○	○	○	○	○	s
	Total	15	9	12	9	11	

Original gel images

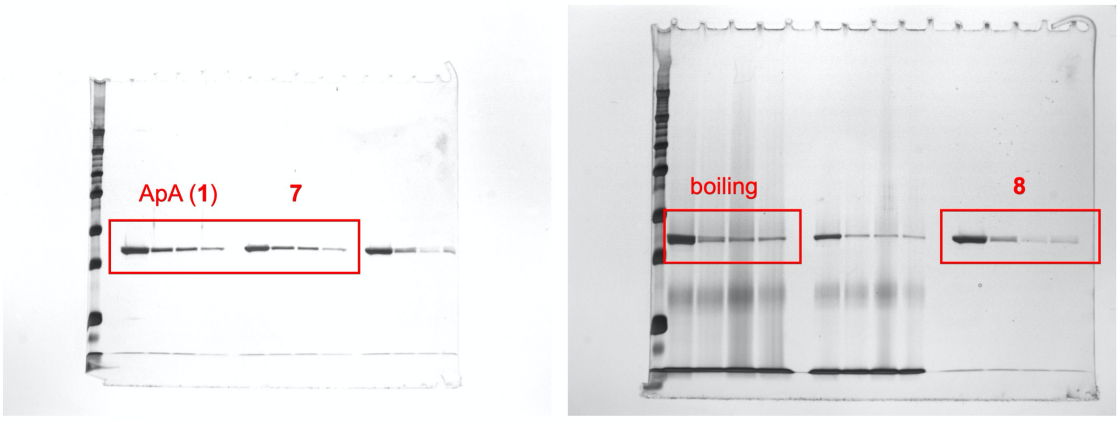


Figure 4 (a)

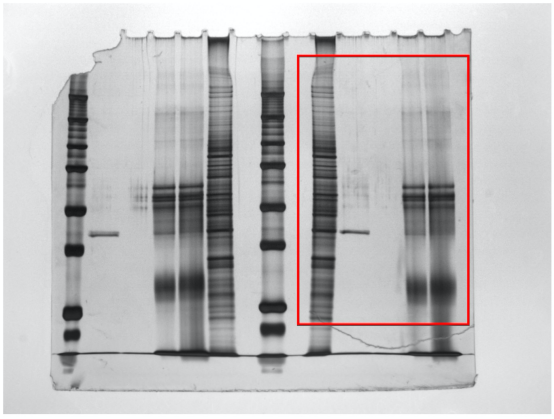


Figure 4 (b)

Figure 4 (c)

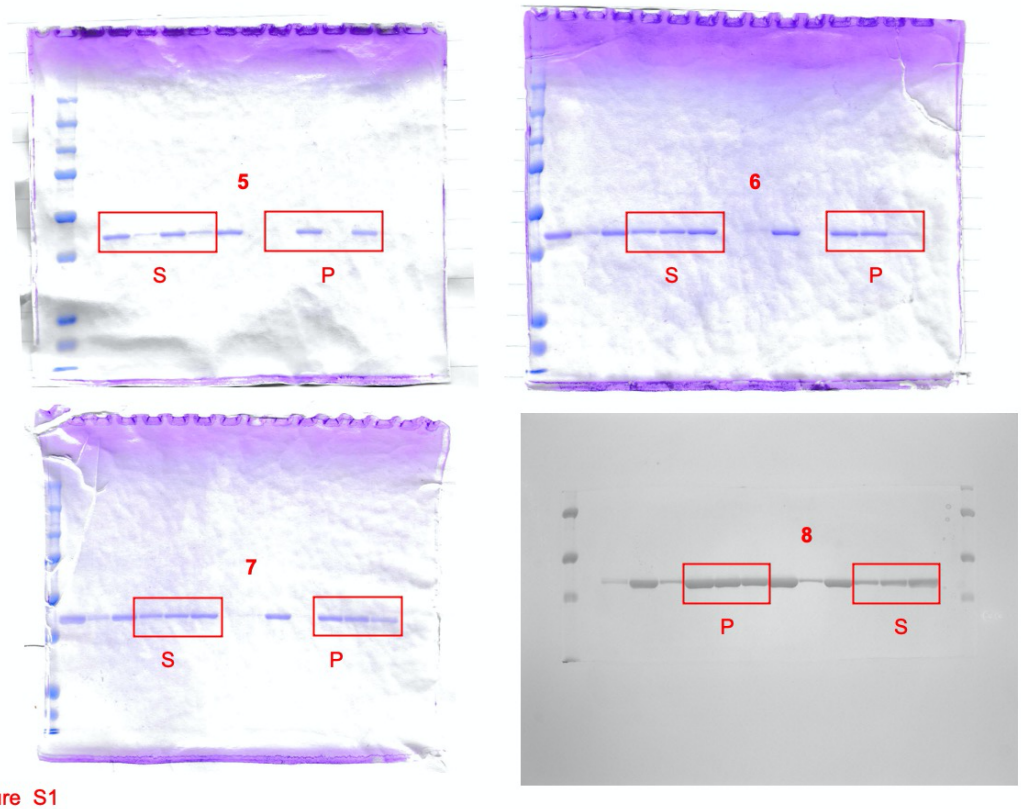


Figure S1

Materials and methods

General Information. All chemicals were obtained commercially unless otherwise noted. Organic solvents and reagents for moisture-sensitive reactions were distilled by the standard procedure. Anhydrous CH_2Cl_2, tetrahydrofuran (THF), 1,2-dimethoxyethane (DME), benzene, pyridine, dimethyl sulfoxide (DMSO), and *N,N*-dimethylformamide (DMF) were obtained commercially. Column chromatography was performed using silica gel BW-820MH or FL60D (75−200 or 45−75 μm, Fuji Silysia Co., Aichi, Japan) or a Yamazen preparative silica gel (40 μm). All moisture-sensitive reactions were performed under an atmosphere of argon or nitrogen, and the starting materials were azeotropically dried with benzene before use. Merck precoated silica gel 60 F254 plates were used for thin layer chromatography.

Spectroscopic analysis. NMR spectra were recorded on Bruker Biospin AVANCE 600 spectrometer (600 MHz for ^{1}H and 150 MHz for ^{13}C) or AVANCE 400 / AVANCE NEO 400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C). Chemical shifts are reported in parts per million (ppm) relative to the solvent peaks at δ_H 7.26 and δ_C 77.0 in $CDCl_3$ or δ_H 3.30 and δ_C 49.0 in CD_3OD respectively. Coupling constants (*J*) are shown in hertz. IR spectra were recorded on a JASCO FT/IR-230 spectrometer. High-resolution mass spectra (HRMS) were measured on an Agilent 6220 TOF spectrometer (for electrospray ionization, ESI).

Cell culture, cytotoxicity, and the preparation of cell lysate.[6c] Human colon carcinoma HCT116 cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum in a humidified atmosphere containing 5% CO_2. The cells (4.0×10^7 cells) in culture were washed twice with cold phosphate buffer saline (PBS), and treated with 0.05% trypsin–EDTA. Suspended cells were collected by centrifugation and washed twice with cold PBS. The cells were lysed in 1.2 mL of lysis buffer (10 mM Tris·HCl [pH 7.4], 0.15 M NaCl, 1% Triton X-100, 10 μg/mL leupeptin) at 4 °C, and the suspensions were centrifuged (15,000 rpm, 4 °C, 30 min) to give the cell lysate with a concentration of 10.0 mg protein/mL. The protein concentration was measured with a Bio-Rad Protein Assay Kit (Bradford's method) with BSA as a standard. The cytotoxicity of the ApA analogs was measured by the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) method.

Actin-depolymerizing activity assay.[11d, 22b] Actin from rabbit skeletal muscle (Cytoskeleton Inc.) was used for the F-actin sedimentation assay. 3 μM of actin in G-buffer [2 mM Tris·HCl (pH 8.0), 0.2 mM $CaCl_2$, 0.2 mM ATP, 0.5 mM 2-mercaptoethanol] (500 μL) was stirred at 25 °C for 1 h to obtain polymerized actin (F-actin). Samples in DMSO (1 μL) were then added and stirred at 25 °C for 30 min. Ultracentrifugation at 150.000 × *g*, at 22 °C was performed for 1 h to separate the actin monomer (supernatant) and the actin filament (precipitate). Both samples were prepared for SDS-PAGE by adding 2 × SDS buffer (Sigma Co.) and boiled at 95 °C for 5 min. A precast 10% polyacrylamide gel (ATTO) was used and CBB staining was performed after running SDS-PAGE. Band quantification was performed using ImageJ software.

Kinetic analysis. Binding kinetics of actin and ApA analogs were measured by a Bio-Layer Interferometry (BLI) method using the BLitz instrument (FortéBio). ApA biotin analog (**1-bio**) and two side-chain analogs **7-bio** and **8-bio** were immobilized in the streptavidin biosensor needle. The analyte actin (Sigma Co.) was dissolved in the Sample Diluent

(FortéBio, part no. 18-1048) with 1 × G-buffer. Data was obtained using the advanced kinetics mode at 25 °C, and the association and dissociation rate constants were determined using BLitz software according to the manufacturer's protocol.

Molecular docking and binding mode analysis. A binding position analysis of ApA and its side-chain analogs on actin was performed through the molecular docking approach using the Molecular Operating Environment (MOE) 2019.01 program package (Chemical Computing Group, Inc.), as described previously.[11d] (*S*)-DMAla ester and (*E*)-oxime stereoisomers were used for the modeling studies of **4**. For docking model studies, all water molecules associated with the actin–ApA complex (PDB: 1WUA) were removed, except for those near the ligand, and all protons on the protein and the ligand were complemented. Docking protocols were performed using the Amber14:EHT force-field with implicit solvent electrostatics (D_{in} = 1, D_{out} = 80). The ligand binding site was specified as the residues within 4.5 Å from the ligand ApA in the X-ray structure of the actin complex. For docking protocols, the Triangle Matcher method with London ΔG scoring was used. Refinements were performed using the Induced-fit approach based on the generalized Born/volume integral implicit solvent model (GBVI/WSA) [S1] with the 10 poses of docking results. The molecular interactions were analyzed using LIGPLOT+ v.1.4.5 software,[S2] and the RMSD calculation was performed using LigRMSD v1.0 software.[S3] FlexibleMatch method was used to select the atoms (C, N, and O) to compare between the side-chain analogs and ApA, which included the C23–C34 aliphatic carbons, the C29 and C31 acetoxy groups, the C30 and C32 methyl groups, and the *N*-methyl enamide group (for **4**, the oxime nitrogen was included).

Affinity purification of actin using biotin probes (pure actin / lysate).[6c] 1 mM solutions of biotinylated ApA and its side-chain analogs **1-bio**, **7-bio**, and **8-bio** (2 μL) were pre-incubated with the NeutrAvidin agarose resin (20 μL, Pierce) equilibrated with G-buffer (250 μL) with a rotator at room temperature for 30 min. After the unbound samples were removed by decantation, actin (50 μg/mL, from rabbit muscle, Cytoskeleton Inc.) in G-buffer (240 μL) was added to the resin and incubated with a rotator at 4 °C for 2 h. The resins were thoroughly washed with PBS (4 × 400 μL). In method A (elution by compounds), the resins were incubated with compounds **1**, **7**, or **8** (50 μM) in 0.1% Triton X-100 (PBS-T, 40 μL) with a rotator at room temperature for 30 min, and the supernatants were collected by filtration. The eluates were mixed with an equal volume of 2× SDS buffer and boiled at 95 °C for 5 min. In method B (elution by boiling), the resins were resuspended in 2× SDS buffer (30 μL) and the bound actins were eluted by boiling at 95 °C for 5 min. SDS-PAGE was performed by using a precast 10% polyacrylamide gel (ATTO Co.), and the gels were stained with a Silver Stain Kit, Protein (GE Healthcare).

For the purification of actin from cell lysate, the HCT116 cell lysate prepared as described above was mixed with Neutravidin agarose (equilibrated with PBS-T) in a rotary tool at 4 °C for 1 hour to remove intrinsic biotin-binding proteins. 1 mM solution of **7-bio** (2 μL) was pre-incubated with NeutrAvidin agarose resin (20 μL) equilibrated with 0.1% Triton PBS (250 μL) with a rotator at room temperature for 30 min. After the supernatant was removed, the cell lysate (330 μL, 3.3 mg protein, from 1.1 × 10^7 cells) prepared as described above was added to the resin and incubated with a rotator at 4 °C for 1 h. The resins were thoroughly washed with PBS-T (2 × 400 μL) followed by PBS (400 μL). Binding proteins were eluted by the method A or B as described above except that 0.1% Triton-PBS was used instead of PBS. SDS-PAGE and silver stain detection were performed as described above. For immunoblot analysis, proteins in the gels after electrophoresis were transferred to PVDF membranes. Proteins were detected incombination with rabbit polyclonal anti-

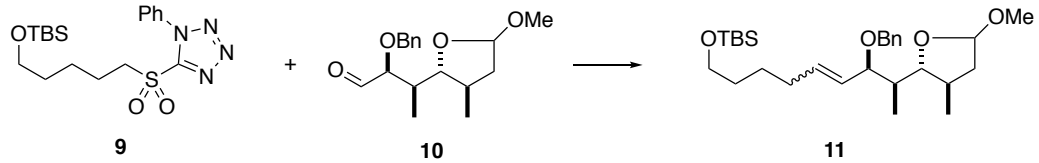
β-actin (1:200, cat. no. A2066, Sigma) and HRP-conjugated anti-rabbit IgG (1:4000, cat. no. NA934, GE Healthcare). The HRP-conjugated bands were visualized with an ImmunoStar LD (Wako), and detected by LAS-1000 imaging scanner.

Synthesis and spectroscopic data of ApA side-chain derivatives.

Summary. Analog **4** was synthesized according to previous SAR studies.[11] Julia–Kochienski olefination [S4] of phenyl tetrazole sulfone **9** [S5] with aldehyde **10** [8a] [prepared from (2*R*)-2-methyl-1-(phenylmethoxy)-3-pentanone (**15**) in 10 steps according to the literature [11a]] and lithium hexamethyldisilazide (LHMDS) as a base afforded an olefin **11** (*E*/*Z* = 2.0:1). Simultaneous catalytic hydrogenation of the olefin and hydrogenolysis of the benzyl group using $Pd(OH)_2$ on carbon, protection of the C29 hydroxy group as a 3,4-dimethoxyphenylmethoxymethyl (DMPMOM) group, and acidic hydrolysis of the C34 methyl acetal gave hemiacetal **12**. Dehydrating condensation with methoxyamine provided *O*-methyloxime **13** (*E*/*Z* = 1.2:1). Subsequent acetylation of the C31 secondary alcohol, deprotection of the DMPMOM group with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), and condensation with L-DMAla using dicyclohexylcarbodiimide (DCC) and camphor-10-sulfonic acid (CSA) provided the oxime analog **4** with a partial epimerization (*S*/*R* = 3.0/1) similar to natural ApA.

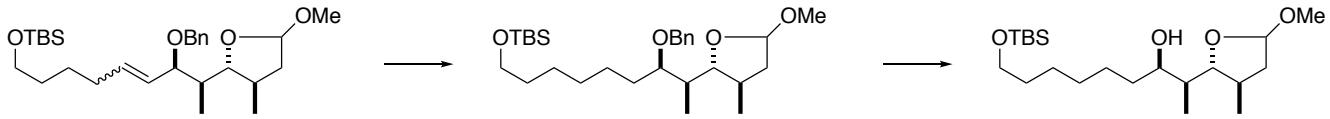
To synthesize analogs **5**–**8** more concisely, we next examined another route using Buchwald amidation [S6] as a key step. Mukaiyama–Paterson aldol condensation using $Sn(OTf)_2$ as a Lewis acid [S7] at –30 °C between enal **14** [S8] and ethyl ketone **15**,[S9] prepared from methyl (*R*)-3-hydroxy-2-methylpropionate in 3 steps, gave desired *syn*-β-hydroxyketone **16** with a *syn*-(*S*,*S*)-isomer (83%, *dr* = 5.9/1). *anti*-Selective reduction of **16** with $Me_4NBH(OAc)_3$ under acidic conditions followed by acetonide protection of the 1,3-diol provided **17**. Simultaneous catalytic hydrogenation of the olefin and removal of the benzyl group using palladium on carbon, and oxidation of the primary alcohol with 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) and $PhI(OAc)_2$ [S10] gave aldehyde **18**. Subsequent Takai olefination [S11] using $CrCl_2$ and CHI_3 yielded iodoolefin **19** (*E*/*Z* = 9/1). Buchwald amidation using *N*-methylformamide [8b, S12] and a copper catalyst to yield the enamide (*E* only), and removal of the TBS group by $^n Bu_4NF$ afforded the common intermediate **20**. Protection of the primary alcohol with a TBDPS group, and removal of an acetonide group under acidic conditions gave the 1,3-diol. Regioselective esterification with L-DMAla at the less-hindered C29 secondary alcohol using EDC·HCl and *N*,*N*-dimethylaminopyridine (DMAP) provided the L-ester without epimerization. Acetylation of the remaining C31 secondary alcohol gave TBDPS ether **5**. Finally, removal of the TBDPS group in **5** with $^n Bu_4NF$ and AcOH yielded primary alcohol **6**, and subsequent acetylation gave diacetate **7**. Similarly, removal of the acetonide group in **20** and acetylation provided triacetate **8**.

In summary, analog **4** was synthesized from aldehyde **10** in 8 steps (25.8% overall yield), and analog **7** was synthesized from ethyl ketone **15** in 14 steps (15.2% overall yield).



Olefin 11. To a stirred solution of PT-sulfone **9** [S5] (1.9 g, 4.6 mmol) in dry 1,2-dimethoxyethane (DME, 37 mL) cooled at –55 °C was added a 1.0 M solution of lithium hexamethyldisilazide in THF (4.6 mL, 4.6 mmol) dropwise under a nitrogen stream. The mixture was stirred at –55 °C for 30 min, then a solution of aldehyde **10** [8a] (0.47 g, 1.6 mmol) in

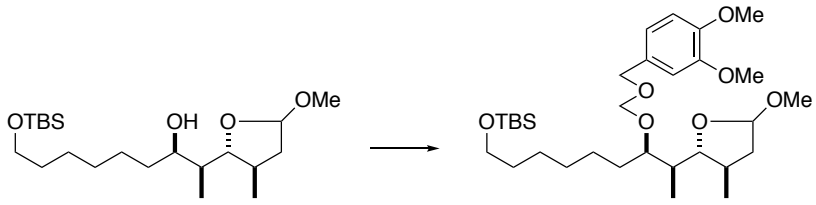
DME (16 mL) was added dropwise, and the resulting mixture was stirred at –55 °C for 2 h and allowed to warm to room temperature for 16 h. The reaction was quenched by addition of brine (15 mL) at 0 °C and extracted with ether (20 mL × 3). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatographies (FL60D 75 g, hexane / acetone = 60/1, 15/1 to 5/2) to give olefin **11** (0.72 g, 94%, *E/Z* = 2.0:1) and recovered sulfone **9** (0.28 g) as light yellow oils. **11**: R_f 0.55 (*n*-hexane / Et_2O = 4:1); $[\alpha]_D^{25}$ +13 (*c* 1.8, $CHCl_3$); IR ($CHCl_3$) 3006, 2955, 2932, 2858, 2364, 2326, 1496, 1470, 1463, 1383, 1319, 1256, 1097, 1029, 991. 909, 837, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.30 (m, 3H), 7.26–7.23 (m, 2H), 5.63 [5.55] (dt, *J* = 15.4, 6.6 Hz, 1H), 5.53 [5.52] (dd, *J* = 15.4, 2.5 Hz, 1H), 4.92 (d, *J* = 4.6 Hz, 1H), 4.57 (d, *J* = 11.9 Hz, 1H), 4.41 (d, *J* = 11.9 Hz, 1H), 4.24 [4.65] (dd, *J* = 7.3, 2.5 Hz, 1H), 3.73 [3.71] (dd, *J* = 9.5, 6.9 Hz, 1H), 3.63 [3.61] (t, *J* = 7.1 Hz, 2H), 3.30 [3.32] (s, 3H), 2.28–2.16 (m, 2H), 2.14–2.04 (m, 2H), 1.70–1.40 (m, 6H), 1.11 [1.09] (d, *J* = 6.6 Hz, 3H), 0.98 [0.95] (d, *J* = 6.6 Hz, 3H), 0.91 (s, 9H), 0.06 [0.05] (s, 6H) Chemical shifts of the *Z*-isomer are within parentheses (square blankets); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 133.1 [132.6], 129.9 [130.3], 128.1 (2C), 127.3 (2C), 127.0, 104.6 [104.7], 87.3, 80.2 [74.6], 70.5 [70.3], 63.0, 54.3 [54.5], 46.4, 42.5, 35.4 [35.5], 32.3 [32.6], 32.1 [27.6], 26.0 (3C), 25.6 [26.0], 19.8, 18.3, 9.5 [9.7], –5.3 (2C); HRMS (ESI) *m/z* 499.3212 (calcd for $C_{28}H_{48}NaO_4Si$ $[M+Na]^+$, Δ –0.8 mmu).



11 **11a** **11b**

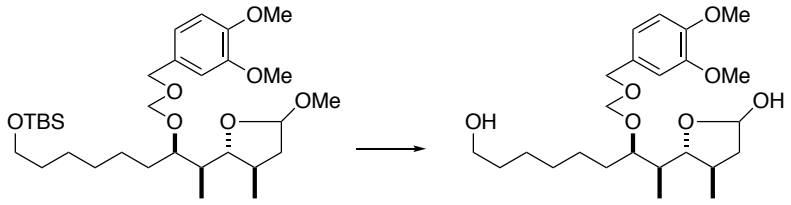
Secondary alcohol 11b. A mixture of olefin **11** (0.50 g, 1.1 mmol, *E/Z* = 2.0:1), $NaHCO_3$ (0.18 g, 2.2 mmol), and palladium hydroxide 20% on carbon (0.15 g) in ethanol (11 mL) was stirred under a hydrogen atmosphere at room temperature for 48 h. The mixture was filtered through a pad of Celite, and the residue was washed with EtOAc. The filtrate and the washings were combined and concentrated. The crude material was purified with a SiO_2 column chromatography (FL60D 10 g, *n*-hexane / EtOAc = 20/1 to 3:1) to give benzyl ether **11a** (0.21 g) and secondary alcohol **11b** (0.24 g, 56%) as light yellow oils.

A mixture of the above compound **11a** (0.21 g, 0.43 mmol), $NaHCO_3$ (73 mg, 0.87 mmol), and palladium hydroxide 20% on carbon (61 mg) in ethanol (4.4 mL) was stirred under a hydrogen atmosphere at room temperature for 17 h. The mixture was filtered through a pad of Celite, and the residue was washed with EtOAc. The filtrate and the washings were combined and concentrated. The crude material was purified with a SiO_2 column chromatography (FL60D 3.5 g, *n*-hexane / EtOAc = 20/1 to 3:1) to give secondary alcohol **11b** (0.13 g, 33%) as a light yellow oil. **11b**: R_f 0.40 (hexane / EtOAc = 3:1); $[\alpha]_D^{25}$ +45 (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3507, 3002, 2929, 2858, 2465, 2038, 1924, 1717, 1463, 1384, 1255, 1213, 1098, 1028, 837 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.90 (d, *J* = 5.0 Hz, 1H), 3.86–3.85 (m, 1H), 3.59 (t, *J* = 7.0 Hz, 2H), 3.56 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.33 (s, 3H), 2.78 (br s, 1H), 2.26 (dddq, *J* = 10.8, 7.6, 2.2, 7.0 Hz, 1H), 2.07 (dd, *J* = 12.8, 7.6 Hz, 1H), 1.69 (ddd, *J* = 13.5, 10.8, 7.0 Hz, 1H), 1.60 (dddd, *J* = 13.5, 7.0, 5.0, 2.2 Hz, 1H), 1.53–1.47 (m, 3H), 1.38–1.24 (m, 7H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 104.9, 89.8, 72.4, 63.3, 55.1, 41.9, 41.7, 35.1, 33.8, 32.8, 29.5, 26.4, 26.0 (3C), 25.8, 18.4, 18.2, 11.5, –5.3 (2C); HRMS (ESI) *m/z* 411.2915 (calcd for $C_{21}H_{44}NaO_4Si$ $[M+Na]^+$, Δ +0.8 mmu).



11b **11c**

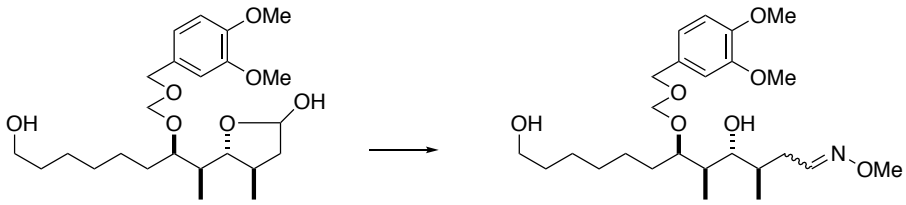
DMPMOM ether 11c. To a stirred solution of secondary alcohol **11b** (0.18 g, 0.46 mmol) in dry CH_2Cl_2 (2.4 mL) were added diisopropylethylamine (3.3 mL, 19 mmol) and a 1.1 M solution of 3,4-dimethoxybenzyloxymethyl (DMPMOM) chloride in dry CH_2Cl_2 (4.2 mL, 4.6 mmol) under a nitrogen atmosphere. After being stirred for 17 h at room temperature, MeOH (10 mL) and sodium bicarbonate (0.15 g) were added. After stirring with 1 h at room temperature, the resulting mixture was diluted with water (20 mL), and extracted with *n*-hexane (20 mL × 3). The combined extracts were washed with water, sat. $NaHCO_3$ aq., and brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (FL60D 40 g, *n*-hexane / EtOAc = 10/1 to 1:1) to give DMPMOM ether **11c** (0.26 g, 97%) as a light yellow oil. **11c**: R_f 0.55 (toluene / Et_2O = 4:1); $[\alpha]_D^{25}$ +35 (*c* 0.32, $CHCl_3$); IR ($CHCl_3$) 3009, 2935, 2858, 1594, 1517, 1465, 1443, 1383, 1260, 1157, 1140, 1097, 1029, 837, 727, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.93 (s, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 4.89 (d, *J* = 4.7 Hz, 1H), 4.82 (AB quart, *J* = 6.9 Hz, 2H), 4.58 (AB quart, *J* = 11.5 Hz, 2H), 4.05 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.58 (t, *J* = 6.3 Hz, 2H), 3.55–3.54 (m, 1H), 3.28 (s, 3H), 2.22 (dddq, *J* = 13.6, 9.8, 2.8, 6.6, 1H), 2.09 (dd, *J* = 12.6, 7.4 Hz, 1H), 1.75–1.59 (m, 2H), 1.49–1.47 (m, 3H), 1.32–1.25 (m, 7H), 1.10 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 148.6, 130.8, 120.5, 111.4, 110.9, 104.7, 94.6, 87.2, 78.4, 69.4, 63.2, 55.9, 55.8, 54.5, 43.8, 42.5, 35.9, 32.8, 32.6, 29.7, 26.1, 26.0 (3C), 25.8, 20.1, 18.4, 8.9, –5.3 (2C); HRMS (ESI) *m/z* 591.3674 (calcd for $C_{31}H_{56}NaO_7Si$ $[M+Na]^+$, Δ –1.9 mmu).



11c **12**

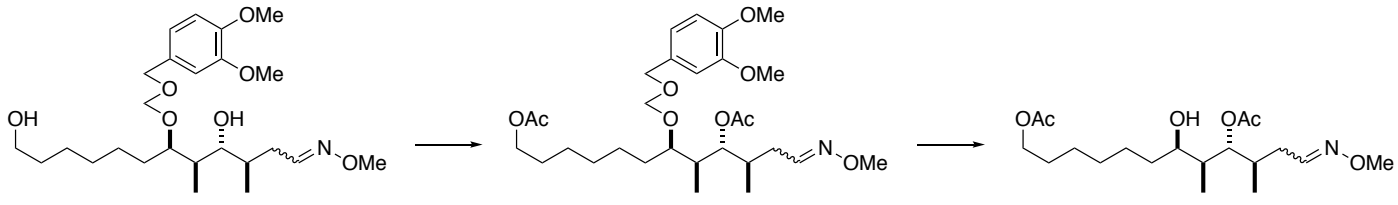
Hemiacetal 12. A mixture of DMPMOM ether **11c** (0.18 g, 0.39 mmol) in 1,2-dimethoxyethane (48 mL) and 1 M HCl aq. (19 mL) was stirred for 4 h at room temperature. The resulting mixture was diluted with EtOAc (30 mL), neutralized with sat. $NaHCO_3$ aq. (5 mL) at 0 °C, and extracted with EtOAc (30 mL × 3). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (FL60D 3.6 g, *n*-hexane / EtOAc = 10/1, 2/1 to 1/1) to give hemiacetal **12** (0.13 g, 74%, a 2.0:1 diastereomer mixture at the hemiacetal carbon) as a colorless oil. **12**: R_f 0.33 (hexane / EtOAc = 1:2); $[\alpha]_D^{25}$ +4.9 (*c* 0.43, $CHCl_3$); IR ($CHCl_3$) 3609, 3008, 2935, 2858, 2364, 2325, 1517, 1465, 1262, 1096, 1029, 909, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.93–6.82 (m, 3H), 5.43 [5.44] (d, *J* = 4.7 Hz, 1H), 4.81 [4.82] (AB quart, *J* = 6.8 Hz, 2H), 4.58 [4.59] (m, 2H), 4.02 [3.93] (ddd, *J* = 7.7, 7.7, 1.5 Hz, 1H), 3.89–3.87 (m, 6H), 3.64–3.61 (m, 2H), 3.53 [3.75] (dd, *J* = 9.0, 7.2 Hz, 1H), 2.89 (br s, 1H), 2.32–2.23 (m, 1H), 2.10 [1.99] (dd, *J* = 12.7, 7.2 Hz, 1H), 1.75–1.49 (m, 7H), 1.38–1.28 (m, 6H), 1.10 [1.19] (d, *J* = 7.1 Hz,

3H), 0.91 [0.91] (d, J = 7.1 Hz, 3H) Chemical shifts of the minor isomers are within parentheses (square brackets); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.9, 148.5, 130.6 [130.5], 120.5 [120.3], 111.3 [111.2], 110.8 [110.9], 98.0 [98.1], 94.2 [94.3], 87.8 [85.9], 77.6 [77.8], 69.4, 62.9 [62.9], 55.9 [55.8], 55.8, 43.0 [43.4], 41.8 [42.0], 35.7 [36.3], 32.5 [32.6], 32.5 [32.3], 29.5 [29.7], 29.2, 25.6 [25.8], 19.7 [21.0], 9.9 [9.6]; HRMS (ESI) *m/z* 463.2673 (calcd for $C_{24}H_{40}NaO_7$ $[M+Na]^+$, Δ +0.1 mmu).



12 **13**

Oxime 13. To a solution of hemiacetal **12** (0.13 g, 0.29 mmol) in dry CH_2Cl_2 (2.9 mL) were added pyridine (46 µL, 0.57 mmol) and *O*-methylhydroxylamine hydrochloride (48 mg, 0.57 mmol) at 0 °C under nitrogen atmosphere. After stirring for 9 h at room temperature, the resulting mixture was diluted with sat. NH_4Cl aq. (5 mL), and extracted with EtOAc (5 mL × 3). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (2 g, *n*-hexane / EtOAc = 5/1, 2/1 to 1/1) to give oxime **13** (91 mg, 68%, *E*/*Z* = 1.2:1 for oxime moiety) as a light yellow oil. **13**: R_f 0.13 (hexane / EtOAc = 1:1); $[\alpha]_D^{25}$ –12 (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) 3627, 3487, 3009, 2938, 2860, 2363, 2325, 2250, 1595, 1517, 1465, 1420, 1383, 1264, 1158, 1028, 909, 668 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 [6.73] (t, J = 6.5 Hz, 1H), 6.87 (m, 2H), 6.83 (d, J = 8.6 Hz, 1H), 4.78 [4.78] (AB quart, J = 6.8 Hz, 2H), 4.61 (d, J = 11.5 Hz, 1H), 4.52 (d, J = 11.5 Hz, 1H), 3.88–3.87 (m, 6H), 3.84 [3.79] (s, 3H), 3.64–3.63 (m, 1H), 3.62 (t, J = 6.6 Hz, 2H), 3.43 (ddd, J = 12.2, 8.3, 4.1 Hz, 1H), 2.36 [2.45] (ddd, J = 16.0, 9.6, 6.2 Hz, 1H), 2.11 [2.26] (ddd, J = 16.0, 9.4, 6.8 Hz, 1H), 1.91–1.84 (m, 2H), 1.66–1.62 (m, 2H), 1.56–1.49 (m, 2H), 1.49–1.45 (m, 2H), 1.41–1.24 (m, 6H), 0.99 [1.01] (d, J = 7.1 Hz, 3H), 0.88 [0.86] (d, J = 7.1 Hz, 3H) Chemical shifts of the *Z*-isomer are within parentheses (square blankets); ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.8 [151.5], 149.0, 148.8, 129.7 [128.3], 120.4, 111.1 [111.0], 110.9, 94.1 [94.0], 80.6 [80.9], 77.4 [77.2], 70.2, 62.9, 61.1 [61.5], 55.9, 55.8, 37.4 [37.6], 33.8 [33.3], 32.6, 30.9 [30.9], 30.0, 29.5, 26.2 [26.2], 25.6, 17.9 [17.4], 11.6 [11.7]; HRMS (ESI) *m/z* 492.2930 (calcd for $C_{25}H_{43}NNaO_7$ $[M+Na]^+$, Δ –0.7 mmu).

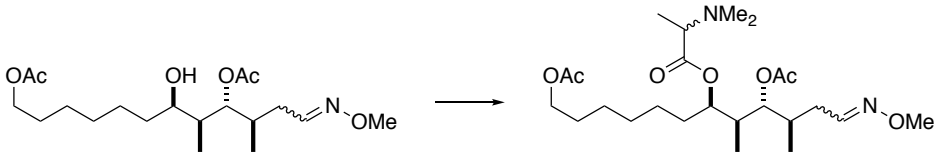


13 **13a** **13b**

Secondary alcohol 13b. A mixture of oxime **13** (21 mg, 45 µmol) and *N*,*N*-dimethyl-4-aminopyridine (DMAP) (5.0 mg, 40 µmol) in dry pyridine (4.3 mL) and acetic anhydride (1.3 mL, 1.3 mmol) was stirred at room temperature for 7 h under a nitrogen atmosphere. The resulting mixture was diluted with EtOAc (8 mL) and sat. $NaHCO_3$ aq. (32 mL) and extracted with EtOAc (5 mL × 3). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude

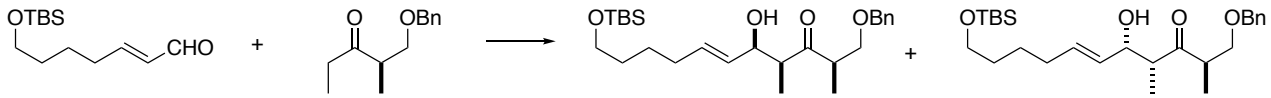
material was purified with a SiO_2 column chromatography (FL60D 1.0 g, *n*-hexane / EtOAc = 20/1, 10/1 to 5/1) to give crude diacetate **13a** (23 mg) as a light yellow oil.

To a stirred solution of the above crude diacetate **13a** (23 mg) in dry CH_2Cl_2 (9.1 mL), *tert*-butyl alcohol (0.45 mL), and 1 M phosphate buffer (pH 6.0, 0.45 mL) was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) (12 mg, 54 μmol) at 0 °C. After being stirred at room temperature for 2 h, DDQ (24 mg, 110 μmol) was further added, and the mixture was stirred at room temperature for 1 h. After being diluted with EtOAc (5 mL) and 1 M phosphate buffer (pH 6.0, 30 mL), the mixture was stirred for 1 h and extracted with EtOAc (5 mL × 3). The combined extracts were washed with 1 M phosphate buffer (pH 6.0), 5% $NaHCO_3$ aq., water, and brine; dried with Na_2SO_4; and concentrated. The crude material was purified with a SiO_2 column chromatography (FL60D 0.4 g, *n*-hexane / EtOAc = 25/1, 10/1 to 1/1) to give secondary alcohol **13b** (13 mg, 76%, *E*/*Z* = 1.1:1 for oxime moiety) as a colorless oil. **13b**: R_f 0.60 (*n*-hexane / EtOAc = 1:1); $[\alpha]_D^{25}$ +1.3 (*c* 0.16, $CHCl_3$); IR ($CHCl_3$) 3631, 3015, 2936, 2856, 1724, 1656, 1524, 1252, 1222, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 [6.70] (t, *J* = 5.5 Hz, 1H), 4.82 [4.84] (dd, *J* = 9.8, 2.6 Hz, 1H), 4.05 (t, *J* = 6.7 Hz, 2H), 3.88 [3.82] (s, 3H), 3.50–3.45 (m, 1H), 2.45–2.27 (m, 2H), 2.15–2.04 (m, 8H), 1.94–1.90 (m, 4H), 1.71–1.51 (m, 3H), 1.44 (m, 1H), 1.40–1.21 (m, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H) Chemical shifts of the *Z*-isomer are within parentheses (square blankets); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4, 171.3, 149.4 [150.0], 79.5 [79.5], 69.5 [69.5], 64.6, 61.3 [61.7], 38.9 [39.1], 34.1, 31.9 [31.6], 29.8 [29.7], 29.3, 28.5, 26.6 [26.0], 25.6, 21.0, 20.8, 17.2 [17.6], 8.7 [8.7] Inseparable DCC-urea was contained in this spectra since the recovered starting material of next step (DMAla condensation) was used; HRMS (ESI) *m/z* 396.2341 (calcd for $C_{19}H_{35}NNaO_6$ $[M+Na]^+$, Δ –2.1 mmu).



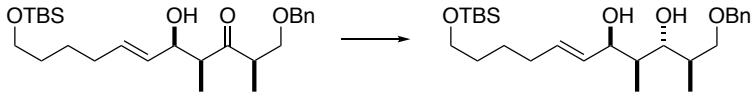
13b **4**

Analog 4. To a mixture of secondary alcohol **13b** (12 mg, 33 μmol), *N*,*N*-dimethyl-L-alanine (13 mg, 110 μmol), (±)-10-camphorsulfonic acid (26 mg, 110 μmol), DMAP (27 mg, 220 μmol), and *N*,*N*'-dicyclohexylcarbodiimide (DCC) (23 mg, 110 μmol) in dry CH_2Cl_2 (0.11 mL) was stirred for 10 h at room temperature under a nitrogen atmosphere. The resulting mixture was diluted with sat. $NaHCO_3$ aq. (7 mL), stirred for 1 h at room temperature, and extracted with EtOAc (5 mL × 3). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (FL60D 0.7 g, *n*-hexane / EtOAc = 20/1, 10/1, 5/1, to 2/1) to give analog **4** (13 mg, 83%, *E*/*Z* = 1.2:1 for oxime moiety and *S*/*R* = 3.0/1 for ester moiety) as a colorless oil. **4**: R_f 0.20 (hexane / EtOAc = 1:1); $[\alpha]_D^{25}$ +7.3 (*c* 0.16, $CHCl_3$); IR ($CHCl_3$) 2959, 2930, 2871, 1731, 1713, 1459, 1365, 1244, 1046, 909 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 [6.78] (t, *J* = 5.6 Hz, 1H), 5.07–5.04 (m, 1H), 4.82–4.78 (m, 1H), 4.09 (t, *J* = 6.6 Hz, 2H), 3.86 [3.79] (s, 3H), 3.20 {3.23} (q, *J* = 7.1 Hz, 1H), 2.36 {2.33} (s, 6H), 2.34–2.10 (m, 4H), 2.08–2.05 (m, 6H), 1.60–1.56 (m, 4H), 1.41–1.30 (m, 6H), 1.32 (d, *J* = 6.6 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H) Chemical shifts of the minor isomers are within parentheses (square brackets for *Z* isomer and curly brackets for *R* isomer, respectively); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.6, 171.2, 170.5, 149.5 [150.1], 71.9, 64.5, 62.9 [62.9], 61.6, 61.3, 41.6, 36.6 [36.7], 32.6, 32.3 [32.1], 30.1, 29.1, 28.5, 25.8, 25.6, 21.0, 20.9, 17.7, 17.4, 15.5, 10.1; HRMS (ESI) *m/z* 495.3020 (calcd for $C_{24}H_{44}N_2NaO_7$ $[M+Na]^+$, Δ –2.6 mmu).



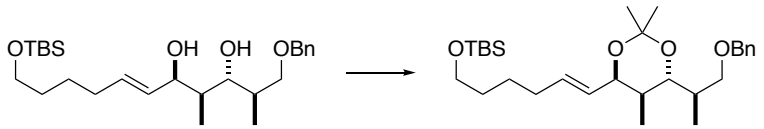
14 **15** **16** **16'**

Hydroxyketone 16. To a mixture of tin(II) trifluoromethanesulfonate (2.6 g, 6.2 mmol) and triethylamine (1.0 mL, 7.2 mmol) in CH_2Cl_2 (55 mL) cooled at –78 °C was added a solution of ethyl ketone **15** [S9] (927 mg, 4.49 mmol) in CH_2Cl_2 (7 mL) dropwise for 10 min under a nitrogen atmosphere. After being stirred for 2.5 h at –78 °C, aldehyde **14** [S8] (2.18 g, 8.99 mmol) in CH_2Cl_2 (7 mL) was added, the reaction mixture was stirred for 2.5 h at –78 °C and –40 °C for 14 h. The mixture was warmed to room temperature and diluted with 0.5 M phosphate buffer (pH 7.0, 65 mL). The organic layer was separated and the water layer was extracted with ether (75 mL × 3). The combined extracts were washed with 0.5 M phosphate buffer and brine, dried with Na_2SO_4, and concentrated. The crude material was purified with two Yamazen preparative silica gel columns (60 g, hexane / EtOAc = 1/0 to 4/1; 90 g, hexane / EtOAc = 1/0 to 82/18) to give hydroxyketone **16** (1.43 g, 71%) and a diastereomer **16'** (250 mg, 12%) as colorless oils. **16**: R_f 0.42 (*n*-hexane / EtOAc = 4:1); $[\alpha]_D^{24}$ +21 (*c* 0.64, MeOH); IR ($CHCl_3$) 3479 (br), 3008, 2932, 2858, 1706, 1456, 1256, 1095, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H), 5.64 (dt, *J* = 15.5, 7.0 Hz, 1H), 5.39 (dd, *J* = 15.5, 6.2 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.44 (m, 1H), 3.63 (t, *J* = 8.6 Hz, 1H), 3.60 (t, *J* = 6.5 Hz, 2H), 3.45 (dd, *J* = 8.6, 5.0 Hz, 1H), 3.16 (m, 1H), 2.94 (br d, *J* = 3.4 Hz, 1H), 2.83 (dq, *J* = 7.1, 3.4 Hz, 1H), 2.02 (dt, *J* = 7.0, 7.0 Hz, 2H), 1.53–1.45 (m, 2H), 1.45–1.34 (m, 2H), 1.07 (d, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 217.8, 137.6, 132.6, 129.3, 128.4 (2C), 127.8, 127.7 (2C), 73.4, 72.9, 72.1, 63.0, 51.3, 45.3, 32.3, 32.1, 26.0 (3C), 25.4, 18.4, 13.5, 9.9, –5.3 (2C); HRMS (ESI) *m/z* 471.2897 (calcd for $C_{26}H_{44}NaO_4Si^+$ $[M+Na]^+$, Δ –0.4 mmu).



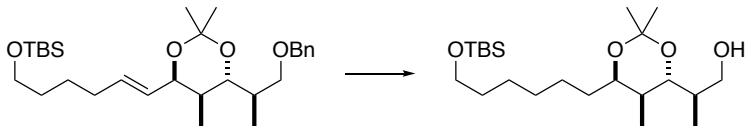
16 **16a**

***anti*-diol 16a.** To a mixture of tetramethylammonium triacetoxyborohydride (611 mg, 2.33 mmol) in acetonitrile (1.2 mL) and acetic acid (1.3 mL) cooled at –25 °C was added a solution of hydroxyketone **16** (100 mg, 233 μmol) in acetonitrile (0.6 mL) dropwise for 10 min under a nitrogen atmosphere. After being stirred for 2 h at –25 °C and for 20 h at –10 °C, the mixture was diluted with 0.5 M aqueous Na/K tartrate (3.3 mL) and vigorously stirred for 1 h at room temperature. The organic layer was separated and the water layer was extracted with ether (4 mL × 4). The combined extracts were washed with water, sat. $NaHCO_3$ aq. and brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a Yamazen preparative silica gel column (40 g, hexane / EtOAc = 10/1 to 0/1) to give diol **16a** (89.6 mg, 88%) as a colorless oil. **16a**: R_f 0.35 (*n*-hexane / EtOAc = 3:1); $[\alpha]_D^{25}$ +47 (*c* 0.14, MeOH); IR ($CHCl_3$) 3442 (br), 3003, 2931, 2858, 1471, 1256, 1092, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5H), 5.66 (dt, *J* = 15.4, 7.0 Hz, 1H), 5.39 (dd, *J* = 15.4, 6.0 Hz, 1H), 4.53 (s, 2H), 4.41 (m, 1H), 4.24 (br d, *J* = 3.4 Hz, 1H), 3.84 (br d, *J* = 3.9 Hz, 1H), 3.70 (dd, *J* = 9.2, 3.9 Hz, 1H), 3.60 (t, *J* = 6.5 Hz, 2H), 3.56 (dd, *J* = 8.3, 4.4 Hz, 1H), 3.50 (t, *J* = 8.3 Hz, 1H), 2.12 (m, 1H), 2.06 (dt, *J* = 7.0, 7.1 Hz, 2H), 1.80 (m, 1H), 1.56–1.48 (m, 2H), 1.48–1.37 (m, 2H), 0.96 (d, *J* = 7.1 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 137.4, 131.4, 130.9, 128.5 (2C), 127.9, 127.7 (2C), 81.4, 75.2, 73.7, 73.2, 63.1, 39.7, 35.5, 32.4, 32.1, 26.0 (3C), 25.5, 18.4, 14.2, 11.7, –5.3 (2C); HRMS (ESI) *m/z* 473.3058 (calcd for $C_{26}H_{46}NaO_4Si^+$ $[M+Na]^+$, Δ ±0.0 mmu).



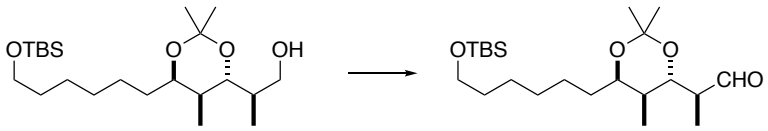
16a **17**

Acetonide 17. To a stirred solution of diol **16a** (125 mg, 277 μmol) in a 1:1 mixture of acetone and 2,2-dimethoxypropane (2.2 mL) was added pyridinium *p*-toluenesulfonate (3.5 mg, 14 μmol) under a nitrogen atmosphere. After being stirred for 17 h at room temperature, the mixture was diluted with sat. $NaHCO_3$ aq. (2.3 mL). The organic layer was separated and the water layer was extracted with ether (4 mL × 4). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (29 g, *n*-hexane / EtOAc = 20/1) to give acetonide **17** (128 mg, 94%) as a colorless oil. **17**: R_f 0.69 (*n*-hexane / EtOAc = 4:1); $[\alpha]_D^{25}$ –4.7 (*c* 0.47, MeOH); IR ($CHCl_3$) 2992, 2932, 2858, 1456, 1380, 1255, 1096, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 5H), 5.64 (dt, *J* = 15.4, 6.8 Hz, 1H), 5.42 (dd, *J* = 15.4, 7.0 Hz, 1H), 4.52 (d *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.29 (dd, *J* = 7.0, 5.5 Hz, 1H), 3.60 (t, *J* = 6.5 Hz, 2H), 3.58 (t, *J* = 9.1 Hz, 1H), 3.36 (dd, *J* = 9.1, 7.0 Hz, 1H), 3.28 (dd, *J* = 7.4, 5.4 Hz, 1H), 2.08 (dt, *J* = 7.2, 6.8 Hz, 2H), 1.96 (m, 1H), 1.87 (m, 1H), 1.51 (m, 2H), 1.42 (m, 2H), 1.32 (s, 6H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 138.8, 132.5, 128.3 (2C), 127.7, 127.5 (2C), 127.4, 100.3, 76.2, 73.1, 72.3, 70.8, 63.1, 38.0, 37.7, 32.4, 32.2, 26.0 (3C), 25.7, 25.3, 23.6, 18.4, 14.3, 13.3, –5.3 (2C); HRMS (ESI) *m/z* 513.3367 (calcd for $C_{29}H_{50}NaO_4Si^+$ $[M+Na]^+$, Δ –0.4 mmu).



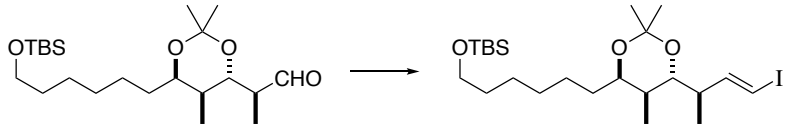
17 **17a**

Primary alcohol 17a. A mixture of acetonide **17** (20 mg, 41 μmol) and palladium 10% on carbon (4.1 mg) in ethanol (0.6 mL) was stirred under a hydrogen atmosphere at room temperature for 4.5 h. The mixture was filtered through a pad of Celite, and the residue was washed with EtOAc. The filtrate and the washings were combined and concentrated. The crude material was purified with a SiO_2 column chromatography (2 g, *n*-hexane / EtOAc = 20/1, 3/1 to 0/1) to give primary alcohol **17a** (16 mg, 94%) as a colorless oil. **17a**: R_f 0.32 (*n*-hexane / EtOAc = 4:1); $[\alpha]_D^{25}$ –46 (*c* 0.69, MeOH); IR ($CHCl_3$) 3509 (br), 2991, 2935, 2858, 1462, 1382, 1255, 1093, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.80 (dt, *J* = 8.7, 4.4 Hz, 1H), 3.75 (ddd, *J* = 11.2, 5.8, 3.0 Hz, 1H), 3.60 (t, *J* = 6.6 Hz, 2H), 3.55 (dd, *J* = 11.2, 6.0 Hz, 1H), 3.27 (br dd, *J* = 7.0, 6.2 Hz, 1H), 2.94 (t, *J* = 5.8 Hz, 1H), 1.83–1.71 (m, 2H), 1.54–1.48 (m, 2H), 1.48–1.38 (m, 2H), 1.35 (s, 3H), 1.33 (s, 3H), 1.35–1.16 (m, 6H), 1.00 (d, *J* = 7.1 Hz, 3H), 0.89 (s, 9H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.05 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 100.6, 80.9, 69.4, 66.8, 63.3, 39.0, 38.2, 32.8, 30.5, 29.5, 26.0, 26.0 (3C), 25.7, 25.4, 23.6, 18.4, 14.1, 12.5, –5.3 (2C); HRMS (ESI) *m/z* 425.3057 (calcd for $C_{22}H_{46}NaO_4Si^+$ $[M+Na]^+$, Δ –0.1 mmu).



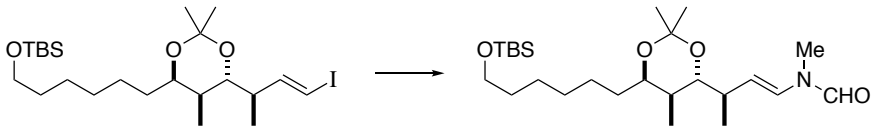
17a **18**

Aldehyde 18. To a stirred solution of primary alcohol **17a** (87.5 mg, 217 μmol) in dry CH_2Cl_2 (0.2 mL) were added 2,2,6,6-tetramethylpiperidine 1-oxyl (3.4 mg, 22 μmol) and iodobenzene diacetate (76 mg, 0.24 mmol) under a nitrogen atmosphere. After being stirred for 2 h at room temperature, CH_2Cl_2 (2 mL) and sat. NaS_2O_3 aq. (0.5 mL) were added. The resulting mixture was extracted with CH_2Cl_2 (4 mL × 4), and the combined extracts were washed with sat. $NaHCO_3$ aq. and brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a Yamazen preparative silica gel column (40 g, *n*-hexane / EtOAc = 1/0 to 87:13) to give aldehyde **18** (81.4 mg, 93%) as a light yellow oil. **18**: R_f 0.64 (*n*-hexane / EtOAc = 4:1); $[\alpha]_D^{25}$ –5.9 (*c* 0.20, MeOH); IR ($CHCl_3$) 2990, 2858, 1724, 1462, 1382, 1214, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.74 (d, *J* = 2.7 Hz, 1H), 3.80 (dt, *J* = 8.8, 4.4 Hz, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.45 (dd, *J* = 7.6, 5.5 Hz, 1H), 2.45 (ddq, *J* = 2.7, 5.5, 7.1 Hz, 1H), 1.87 (m, 1H), 1.54–1.47 (m, 2H), 1.47–1.37 (m, 2H), 1.37–1.16 (m, 6H), 1.33 (s, 3H), 1.23 (s, 3H), 1.15 (d, *J* = 7.1 Hz, 3H), 0.89 (s, 9H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 204.7, 100.7, 76.5, 69.1, 63.2, 49.8, 37.6, 32.8, 30.4, 29.4, 26.0, 26.0 (3C), 25.7, 24.9, 23.5, 18.3, 12.2, 11.2, –5.3 (2C); HRMS (ESI) *m/z* 423.2904 (calcd for $C_{22}H_{44}NaO_4Si^+$ $[M+Na]^+$, Δ +0.3 mmu).



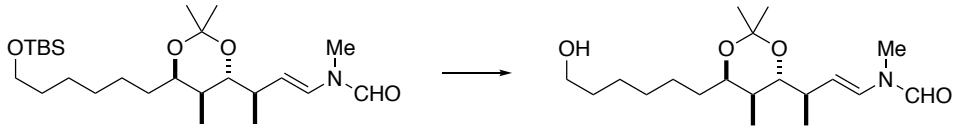
18 **19**

Iodoolefin 19. To a stirred solution of chromium(II) chloride (91.1 mg, 741 μmol) and iodomethane (58.4 mg, 148 μmol) was added a solution of aldehyde **18** (29.7 mg, 74.1 μmol) in dry THF (0.48 mL) dropwise under a nitrogen atmosphere. After being stirred for 3.5 h at room temperature, sat. $NaHCO_3$ aq. (14 mL) was added, and the resulting mixture was extracted with ether (7 mL × 4). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (10 g, *n*-hexane / EtOAc = 50/1, 20/1, 10/1 to 0:1) to give iodoolefin **19** (31.9 mg, 82%, *E*/*Z* = 9/1) as a light yellow oil. **19**: R_f 0.42 (*n*-hexane / EtOAc = 20:1); $[\alpha]_D^{23}$ –3.5 (*c* 0.42, MeOH); IR ($CHCl_3$) 2990, 2934, 2858, 1724, 1602, 1462, 1381, 1255, 1094, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.59 (dd, *J* = 14.6, 8.8 Hz, 1H), 6.01 (d, *J* = 14.6 Hz, 1H), 3.69 (dt, *J* = 8.8, 4.4 Hz, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.13 (dd, *J* = 7.8, 3.6 Hz, 1H), 2.32 (m, 1H), 1.68 (m, 1H), 1.55–1.49 (m, 2H), 1.46–1.16 (m, 8H), 1.30 (s, 6H), 1.07 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.79 (d, *J* = 6.8 Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 148.2, 100.5, 77.6, 75.1, 69.4, 63.3, 43.9, 37.0, 32.8, 30.6, 29.5, 26.1, 26.0 (3C), 25.8, 25.1, 23.5, 18.4, 16.9, 12.0, –5.2 (2C) (*E*-isomer was only shown); HRMS (ESI) *m/z* 547.2073 (calcd for $C_{23}H_{45}INaO_3Si^+$ $[M+Na]^+$, Δ –0.2 mmu).



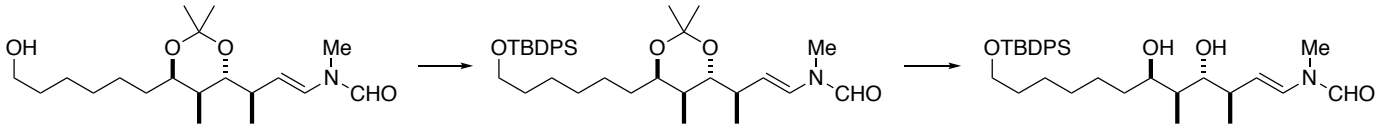
19 **19a**

Enamide 19a. A solution of iodoolefin **19** (27.4 μmol, 52.2 μmol, *E*/*Z* = 9/1), potassium phosphate (64 mg, 300 μmol), copper(I) iodide (9.1 mg, 48 μmol), *N*-methylformamide (85 μL, 1.4 mmol), and *trans*-1,2-diaminocyclohexane (12 μL, 96 μmol) in degassed 1,4-dioxane (0.68 mL) was refluxed for 4 h under a nitrogen atmosphere. The mixture was diluted with water (4 mL), the organic layer was separated, and the water layer was extracted with ether (4 mL × 4). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (4.5 g, *n*-hexane / EtOAc = 20/1, 10/1, 5/1 to 0/1) to give enamide **19a** (18.5 mg, 78%) as a colorless oil. **19a**: R_f 0.35 [0.24] (*n*-hexane / EtOAc = 4:1); $[\alpha]_D^{24}$ –27 (*c* 0.31, MeOH); IR ($CHCl_3$) 2991, 2934, 2858, 1687, 1656, 1462, 1381, 1256, 1080, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 [8.07] (s, 1H), 6.45 [7.11] (d, *J* = 14.1 Hz, 1H), 5.13 [5.16] (dd, *J* = 14.1, 8.8 Hz, 1H), 3.66 (dt, *J* = 8.8, 4.4 Hz, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.18 (dd, *J* = 7.7, 3.5 Hz, 1H), 3.01 [3.06] (s, 3H), 2.31 (m, 1H), 1.69 (m, 1H), 1.51–1.16 (m, 10H), 1.31 (s, 6H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.81 (d, *J* = 6.9 Hz, 3H), 0.04 (s, 6H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (2.0/1) are within parentheses (square blankets); ^{13}C NMR (400 MHz, $CDCl_3$) δ 162.2 [160.9], 128.6 [124.6], 113.1 [114.7], 100.4 [100.3], 78.3 [78.4], 69.5 [69.5], 63.3, 38.3 [38.3], 36.9 [36.9], 32.8 [33.1], 30.6, 29.5, 27.6, 26.1, 26.0 (3C), 25.7, 25.1, 23.6, 18.5 [18.6], 18.4, 12.2 [12.1], –5.3 (2C); HRMS (ESI) *m/z* 478.3321 (calcd for $C_{25}H_{49}NNaO_4Si^+$ $[M+Na]^+$, Δ –0.2 mmu).



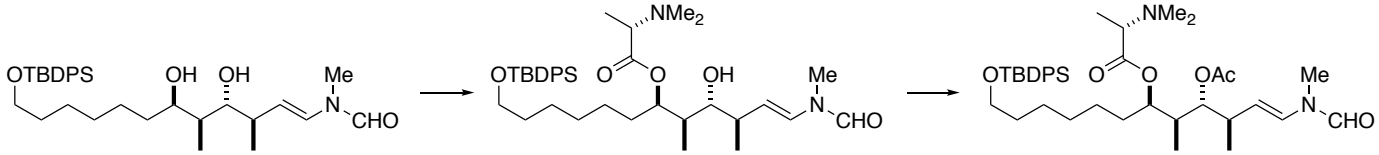
19a **20**

Primary alcohol 20. To a stirred solution of enamide **19a** (3.6 mg, 7.9 μmol) in dry THF (0.1 mL) was added a 1 M solution of tetra-*n*-butylammonium fluoride in THF (16 μL, 16 μmol) under a nitrogen atmosphere. After being stirred for 5 h at room temperature, the reaction mixture was concentrated. The crude material was purified with a SiO_2 column chromatography (1.4 g, *n*-hexane / EtOAc = 3/1, 2/1, 1/1 to 1/2) to give primary alcohol **20** (2.7 mg, 100%) as a colorless oil. **20**: R_f 0.28 [0.17] (*n*-hexane / EtOAc = 1:1); $[\alpha]_D^{24}$ –29 (*c* 0.27, MeOH); IR ($CHCl_3$) 3446 (br), 3018, 2936, 1687, 1656, 1380, 1216, 1078 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 [8.07] (s, 1H), 6.44 [7.11] (d, *J* = 14.1 Hz, 1H), 5.13 [5.16] (dd, *J* = 14.1, 8.9 Hz, 1H), 3.66 (dt, *J* = 8.7, 4.4 Hz, 1H), 3.63 (t, *J* = 6.5 Hz, 2H), 3.18 (dd, *J* = 7.6, 3.5 Hz, 1H), 3.02 [3.05] (s, 3H), 2.29 (m, 1H), 1.69 (m, 1H), 1.59–1.52 (m, 2H), 1.48–1.17 (m, 9H), 1.31 (s, 6H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.9 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (2.0/1) are within parentheses (square blankets); ^{13}C NMR (400 MHz, $CDCl_3$) δ 162.2 [160.9], 128.6 [124.6], 113.1 [114.7], 100.4 [100.3], 78.3 [78.4], 69.4 [69.5], 63.0, 38.3 [38.3], 36.9 [36.8], 32.7 [33.1], 30.5 [30.5], 29.4, 27.6, 26.1, 25.7, 25.1, 23.6, 18.5 [18.6], 12.2 [12.1]; HRMS (ESI) *m/z* 364.2445 (calcd for $C_{19}H_{35}NNaO_4^+$ $[M+Na]^+$, Δ –1.3 mmu).



Silyl ether **20b**. To a stirred solution of primary alcohol **20** (4.9 mg, 14 μmol) in dry DMF (0.3 mL) were added imidazole (5.8 mg, 86 μmol) and *tert*-butyldiphenylchlorosilane (11 μL, 43 μmol) under a nitrogen atmosphere. After being stirred for 2 h at room temperature, the mixture was diluted with sat. $NaHCO_3$ aq. (3 mL). The organic layer was separated, and the water layer was extracted with EtOAc (2 mL × 4). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (0.5 g, *n*-hexane / acetone = 19/1, 9/1 to 3/1) to give crude silyl ether **20a** as an inseparable mixture with silanol (20 mg).

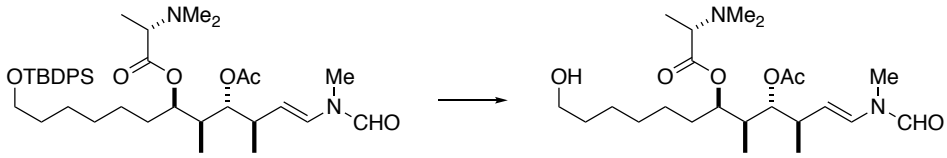
The crude silyl ether **20a** (20 mg) was dissolved in a 1 mg/mL solution of pyridinium *p*-toluenesulfonate in MeOH (1 mL). After being stirred for 2 h at 70 °C, triethylamine (3 drops) was added, and the resulting mixture was concentrated *in vacuo*. The crude material was purified with a SiO_2 column chromatography (0.5 g, $CHCl_3$ / acetone = 19/1, 9/1, 6/1 to 1/1) to give diol **20b** (6.1 mg, 81% in steps) as a colorless oil. **20b**: R_f 0.51 [0.46] ($CHCl_3$ / acetone = 3/1); $[\alpha]_D^{24}$ +22 (*c* 0.26, $CHCl_3$); IR ($CHCl_3$) 3479 (br), 3010, 2933, 2859, 1690, 1656, 1462, 1428, 1390, 1111, 973, 823, 613 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 [8.07] (s, 1H), 7.69–7.64 (m, 4H), 7.45–7.34 (m, 6H), 6.55 [7.20] (d, *J* = 14.1 Hz, 1H), 5.06 [5.12] (dd, *J* = 14.1, 9.0 Hz, 1H), 3.88 (m, 1H), 3.65 (t, *J* = 6.4 Hz, 2H), 3.45 (m, 1H), 3.03 [3.06] (s, 3H), 2.68 (m, 1H), 2.43 (m, 1H), 1.74 (m, 1H), 1.65–1.23 (m, 11H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.04 (s, 9H), 0.95 [0.92] (d, *J* = 7.1 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (2.0/1) are within parentheses (square blankets); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 [160.9], 135.6 (4C), 134.2 (2C), 129.5 (2C), 127.6 (4C), 129.7 [125.4], 111.9 [113.8], 79.1 [79.0], 72.8 [73.2], 63.9, 38.6 [38.8], 38.5, 33.7 [33.5], 32.5 [33.1], 29.4, 27.6, 26.9 (3C), 26.4, 25.8, 19.2, 18.5 [18.6], 11.5 [11.6]; HRMS (ESI) *m/z* 562.3321 (calcd for $C_{32}H_{49}NNaO_4Si^+$ $[M+Na]^+$, Δ –0.2 mmu).



Diester **5**. To a stirred solution of silyl ether **20b** (1.9 mg, 3.5 μmol) and *N*,*N*-dimethyl-L-alanine (2.9 mg, 14 μmol) in dry DMF (0.3 mL) were added *N*,*N*-dimethylaminopyridine (6.3 mg, 35 μmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (7.5 mg, 28 μmol) under a nitrogen atmosphere. After being stirred for 14 h at room temperature and for 6 h at 50 °C, sat. $NaHCO_3$ aq. (3 mL) was added, and the resulting mixture was extracted with (3 mL × 3). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated. The crude material was purified with a SiO_2 column chromatography (0.5 g, $CHCl_3$ / acetone = 9/1, 3/1, to 1/1) to give crude DMAla ester **20c** as an inseparable mixture with DMAP and polar impurities (3 mg) and recovered **20b** (0.4 mg, 21%) as colorless oils.

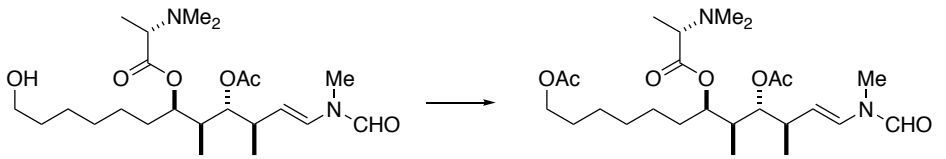
The crude DMAla ester **20c** (3 mg) was dissolved in a 2:1 mixture of pyridine and acetic acid (0.3 mL) at a nitrogen atmosphere. After being stirred for 24 h at room temperature, the resulting mixture was azeotropically concentrated with toluene. The crude material was purified with a SiO_2 column chromatography (0.5 g, $CHCl_3$ / acetone = 9/1, 6/1, to 3/1) to give diester **5** (1.5 mg, 63%) as a colorless oil. **5**: R_f 0.56 ($CHCl_3$ / acetone = 1:1); $[\alpha]_D^{25}$ –24 (*c* 0.74, $CHCl_3$); IR ($CHCl_3$)

3072, 2933, 2858, 1731, 1692, 1656, 1460, 1375, 1241, 1108, 704, 614 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 [8.06] (s, 1H), 7.66–7.64 (m, 4H), 7.43–7.35 (m, 6H), 6.48 [7.15] (d, *J* = 14.0 Hz, 1H), 5.00 (m, 1H), 4.97 (dd, *J* = 14.0, 9.4 Hz, 1H), 4.77 (dd, *J* = 9.8, 3.1 Hz, 1H), 3.64 (t, *J* = 6.4 Hz, 2H), 3.21 (q, *J* = 7.1 Hz, 1H), 3.01 [3.04] (s, 3H), 2.54 (m, 1H), 2.37 (s, 6H), 2.07 (s, 3H), 1.81 (m, 1H), 1.65–1.41 (m, 4H), 1.46–1.42 (m, 6H), 1.29 (d, *J* = 7.1 Hz, 3H), 1.04 (s, 9H), 1.02 [1.01] (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (1.9/1) are within parentheses (square blankets); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 170.5, 162.1 [160.9], 135.5 (4C), 134.1 (2C), 129.5 (2C), 129.3, 127.6 (4C), 110.7, 77.2, 71.9, 63.8, 62.9, 41.5 (2C), 37.5, 37.1, 37.0, 32.5, 32.4, 29.3, 27.6, 26.8 (3C), 25.8, 25.6, 21.0, 19.2, 15.4, 9.9; HRMS (ESI) *m/z* 681.4308 (calcd for $C_{39}H_{61}N_2O_6Si$ $[M+H]^+$, Δ +1.5 mmu).



5 **6**

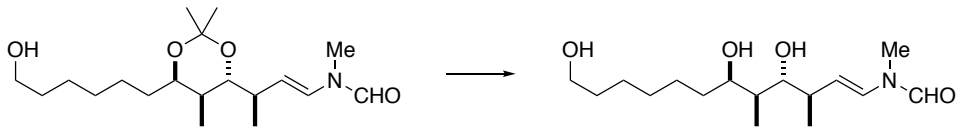
Primary alcohol 6. To a stirred solution of diester **5** (17 mg, 25 μmol) in dry THF (0.5 mL) were added acetic acid (3.8 μL, 63 μmol) and a 1 M solution of tetra-*n*-butylammonium fluoride in THF (0.13 mL, 130 μmol) under a nitrogen atmosphere. After being stirred for 4 h at room temperature and for 10 h at 40 °C, the reaction mixture was concentrated. The crude material was purified with a SiO_2 column chromatography (FL60D 0.5 g, $CHCl_3$ / acetone = 5/1 to 1/1) to give primary alcohol **6** (10.7 mg, 97%) as a colorless oil. **6**: R_f 0.33 ($CHCl_3$ / acetone = 1:1); $[\alpha]_D^{25}$ –40 (*c* 0.40, $CHCl_3$); IR ($CHCl_3$) 3446, 2934, 2858, 1731, 1691, 1655, 1457, 1375, 1241, 1094, 1077 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 [8.08] (s, 1H), 6.48 [7.16] (d, *J* = 14.0 Hz, 1H), 5.00 (m, 1H), 4.97 (dd, *J* = 14.0, 9.5 Hz, 1H), 4.77 (dd, *J* = 9.8, 3.0 Hz, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.23 (q, *J* = 7.1 Hz, 1H), 3.03 [3.07] (s, 3H), 2.54 (m, 1H), 2.38 (s, 6H), 2.08 (s, 3H), 1.80 (m, 1H), 1.60–1.20 (m, 11H), 1.31 (d, *J* = 7.1 Hz, 3H), 1.02 [1.01] (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (1.9/1) are within parentheses (square blankets); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 170.6, 162.2 [160.9], 129.3 [125.4], 110.7 [112.3], 77.2, 71.9, 62.9, 62.8, 41.5 (2C), 37.5 [37.5], 37.0 [37.1], 32.6 [33.1], 32.2 [32.1], 29.1 [29.7], 27.6, 25.7, 25.5, 21.0, 19.3 [19.4], 15.4, 9.9; HRMS (ESI) *m/z* 465.2916 (calcd for $C_{23}H_{42}N_2NaO_6$ $[M+Na]^+$, Δ –1.9 mmu).



6 **7**

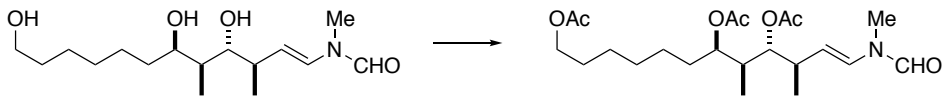
Analog 7. Prepared from primary alcohol **6** (3.5 mg, 7.9 μmol) in 94% yield using the same procedure as that for **13a**. **7**: R_f 0.53 ($CHCl_3$/ acetone = 1:1); $[\alpha]_D^{25}$ –43 (*c* 0.17, $CHCl_3$); IR ($CHCl_3$) 3018, 2933, 2857, 1729, 1692, 1655, 1456, 1243, 1076, 787 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 [8.08] (s, 1H), 6.48 [7.15] (d, *J* = 14.0 Hz, 1H), 5.00 (m, 1H), 4.97 (dd, *J* = 14.0, 9.5 Hz, 1H), 4.77 (dd, *J* = 9.8, 3.0 Hz, 1H), 4.04 (t, *J* = 6.8 Hz, 2H), 3.21 (q, *J* = 7.1 Hz, 1H), 3.02 [3.07] (s, 3H), 2.55 (m, 1H), 2.37 (s, 6H), 2.08 (s, 3H), 2.04 (s, 3H), 1.80 (m, 1H), 1.67–1.57 (m, 2H), 1.43 (m, 1H), 1.35–1.20 (m, 7H), 1.30 (d, *J* = 7.2 Hz, 3H), 1.02 [1.01] (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H) Chemical shifts of the minor

rotamer at the *N*-methylenamide moiety (1.9/1) are within parentheses (square blankets); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.2, 170.5, 162.1 [160.9], 129.3 [125.4], 110.7 [112.3], 77.2, 71.9, 64.4, 62.9, 41.6 (2C), 37.5 [37.6], 37.0 [37.1], 32.4 [33.0], 29.7 [32.3], 29.1, 28.5, 27.6, 25.7 [25.8], 21.0, 19.4, 19.3, 15.5, 10.0 [9.9]; HRMS (ESI) *m/z* 485.3196 (calcd for $C_{25}H_{45}N_2O_7$ $[M+H]^+$, Δ –2.6 mmu).



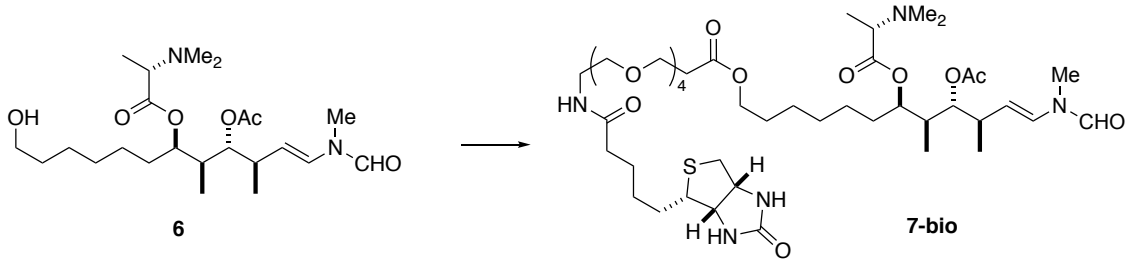
20 **20d**

Triol 20d. A solution of primary alcohol **20** (7.3 mg, 21 μmol) in a 7.4 mM solution of pyridinium *p*-toluenesulfonate in MeOH (100 μL) was refluxed at 70 °C for 2 h under a nitrogen atmosphere. After the addition of triethylamine (100 μL), the resulting mixture was concentrated. The crude material was purified with a SiO_2 column chromatography (1.7 g, *n*-hexane / EtOAc / acetone = 1/9/0, 0/1/0 to 0/4/1) to give triol **20d** (5.3 mg, 82%) as a colorless oil. **20d**: R_f 0.28 [0.20] (EtOAc); $[\alpha]_D^{25}$ +36 (*c* 0.08, $CHCl_3$); IR ($CHCl_3$) 3617, 3462 (br), 3015, 2935, 1690, 1654, 1076 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 [8.06] (s, 1H), 6.55 [7.18] (d, *J* = 14.0 Hz, 1H), 5.06 [5.12] (dd, *J* = 14.0, 9.0 Hz, 1H), 3.86 (m, 1H), 3.63 (t, *J* = 6.4 Hz, 2H), 3.45 (m, 1H), 3.02 [3.06] (s, 3H), 2.89–2.81 (m, 2H), 2.42 (m, 1H), 1.75 (m, 1H), 1.63–1.20 (m, 11H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.93 [0.91] (d, *J* = 7.1 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (2.0/1) are within parentheses (square blankets); ^{13}C NMR (400 MHz, $CDCl_3$) δ 162.2 [160.9], 129.6 [125.4], 112.0 [113.9], 79.1 [79.0], 72.7 [73.0], 62.9, 38.6 [38.8], 38.5 [38.6], 33.6 [33.4], 32.6 [33.1], 29.4, 27.6, 26.3, 25.7, 18.5 [18.6], 11.5 [11.6]; HRMS (ESI) *m/z* 324.2138 (calcd for $C_{16}H_{31}NNaO_4^+$ $[M+Na]^+$, Δ –0.7 mmu).

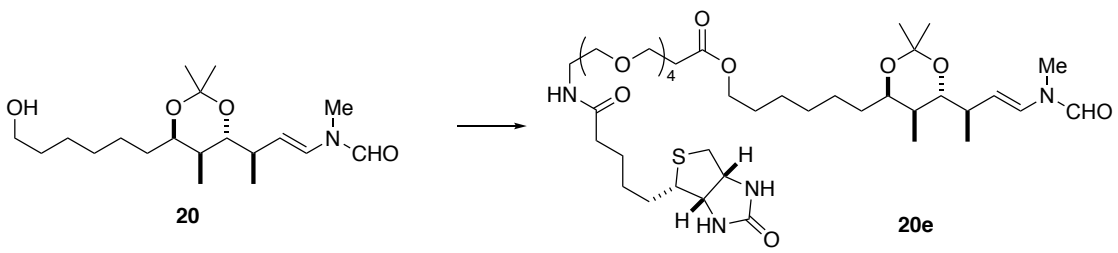


20d **8**

Triacetate 8. Prepared from triol **20d** (5.3 mg, 18 μmol) in 98% yield using the same procedure as that for **13a**. **8**: R_f 0.31 [0.22] (*n*-hexane / EtOAc = 1:1); $[\alpha]_D^{24}$ –52 (*c* 0.25, MeOH); IR ($CHCl_3$) 3019, 2939, 1829, 1726, 1691, 1656, 1371, 1255 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 [8.01] (s, 1H), 6.48 [7.15] (d, *J* = 14.2 Hz, 1H), 4.98 (m, 1H), 4.97 (dd, *J* = 14.2, 9.0 Hz, 1H), 4.81 (dd, *J* = 9.5, 3.4 Hz, 1H), 4.03 (t, *J* = 6.7 Hz, 2H), 3.03 [3.07] (s, 3H), 2.56 (m, 1H), 2.06 (s, 3H), 2.04 (s, 3H), 2.00 (s, 3H), 1.79 (m, 1H), 1.68–1.59 (m, 4H), 1.48–1.15 (m, 6H), 1.01 [1.00] (d, *J* = 6.9 Hz, 3H), 0.93 [0.92] (d, *J* = 6.9 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (1.5/1) are within parentheses (square blankets); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.2, 170.9 [170.9], 170.7, 162.1 [160.9], 129.3 [125.3], 110.8 [112.4], 77.2, 71.7 [71.9], 64.5 [64.5], 37.4 [37.5], 36.9 [37.1], 33.0, 32.3 [32.1], 29.2, 28.5, 27.6, 25.7, 25.7, 21.2, 21.0 [20.9], 19.2 [19.3], 9.8 [9.7]; HRMS (ESI) *m/z* 450.2467 (calcd for $C_{22}H_{37}NNaO_7^+$ $[M+Na]^+$, Δ +0.5 mmu).

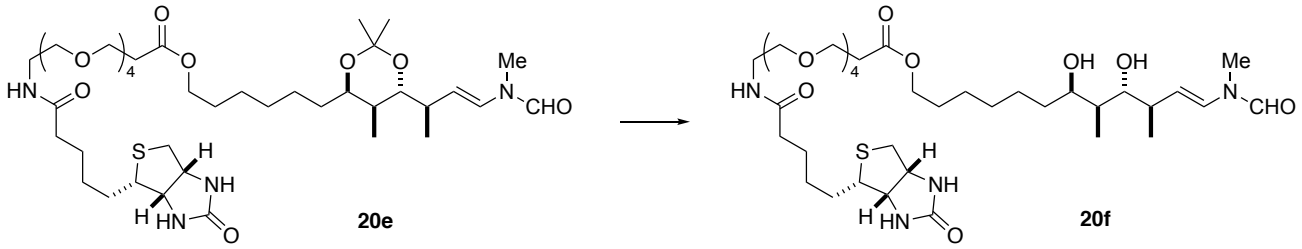


Biotin probe 7-bio. To a solution of Biotin-PEG4-carboxylic acid (7.9 mg, 16 μmol) in a 1:1 mixture of dry THF and DMF (0.24 mL) at 0 °C was added a solution of triethylamine (5.6 μL, 40 μmol), 2,4,6-trichlorobenzoyl chloride (4.6 μL, 30 μmol) in dry THF (0.2 mL) under a nitrogen atmosphere. After stirring for 2.5 h at room temperature, primary alcohol **6** (3.5 mg, 7.9 μmol) and *N*,*N*-dimethylaminopyridine (3.7 mg, 30 μmol) in dry toluene (0.4 mL) were added at 0 °C. After being stirred for 26 h at room temperature, sat. $NaHCO_3$ aq. (3 mL) was added, and the resulting mixture was extracted with $CHCl_3$ (2 mL × 4). The combined extracts were washed with brine, dried with Na_2SO_4, and concentrated *in vacuo*. The crude material was purified with a SiO2 column chromatography (0.4 g, $CHCl_3$ / MeOH = 29/1, 19/1, 9/1 to 4/1) and a Yamazen preparative SiO_2 column (7 g, $CHCl_3$ / MeOH = 1/0, 12/1 to 4/1) to give biotin probe **7-bio** (1.4 mg, 19%) and recovered **5** (1.3 mg, 37%) as colorless oils. **7-bio**: R_f 0.36 ($CHCl_3$ / MeOH = 9:1); $[\alpha]_D^{24}$ +14 (*c* 0.12, $CHCl_3$); IR ($CHCl_3$) 3467, 3309 (br), 3019, 2934, 2871, 1716, 1656, 1457, 1243, 1097, 1019, 937 cm^{-1}; Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (2/1) are within parentheses (square blankets); ^1H NMR (600 MHz, $CDCl_3$) δ 8.29 [8.08] (s, 1H), 6.49 [7.16] (d, *J* = 14.0 Hz, 1H), 6.62 (br s, 1H), 5.62 (m, 1H), 5.01 (m, 1H), 4.97 (dd, *J* = 14.0, 9.5 Hz, 1H), 4.77 (dd, *J* = 9.8, 2.9 Hz, 1H), 4.51 (dd, *J* = 7.0, 5.8 Hz, 1H), 4.33 [4.28] (dd, *J* = 6.5, 5.8 Hz, 1H), 4.06 (t, *J* = 6.8 Hz, 2H), 3.74 (t, *J* = 6.5 Hz, 2H), 4.06 (t, *J* = 6.8 Hz, 2H), 3.65 (s, 6H), 3.64–3.61 (m, 6H), 3.56 (t, *J* = 4.9 Hz, 2H), 3.44 (m, 2H), 3.16 (m, 1H), 3.03 [3.07] (s, 3H), 2.92 (dd, *J* = 12.8, 5.0 Hz, 1H), 2.73 (br d, *J* = 12.8 Hz, 1H), 2.59 (t, *J* = 6.5 Hz, 2H), 2.41–2.35 (m, 4H), 2.22 (m, 2H), 2.08 (s, 3H), 1.80 (m, 1H), 1.76–1.57 (m, 10H), 1.48–1.40 (m, 4H), 1.34–1.19 (m, 5H), 1.31 (d, *J* = 7.3 Hz, 3H), 1.02 [1.00] (d, *J* = 6.7 Hz, 3H), 0.94 [0.94] (d, *J* = 6.9 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (1.5/1) are within parentheses (square blankets); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.0, 173.0, 171.6, 170.6, 162.2, 161.0, 129.3 [125.3], 110.6, 76.5, 70.5, 70.4, 70.4, 70.4, 70.3, 70.1, 69.9, 66.6, 64.6, 61.7 [62.9], 60.0 [60.6], 55.2, 41.6, 40.5, 39.1, 37.5 [37.6], 36.9 [37.1], 35.7, 34.9, 33.1, 32.3, 32.3, 29.1 [29.7], 28.5, 28.0, 28.0, 27.6, 25.7, 25.7, 25.4, 21.0, 19.3 [19.4], 15.4, 9.9, 9.8.HRMS *m/z* 938.5156 (calcd for $C_{44}H_{77}N_5NaO_{13}S^+$ $[M+Na]^+$, Δ +2.5 mmu).

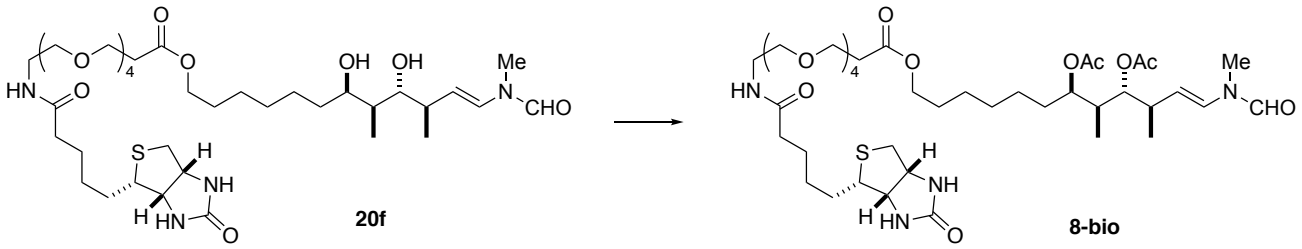


Ester 20e. Prepared from triol **20** (7.7 mg, 22 μmol) in 89% yield using the same procedure as that for **7-bio**. **20e**: R_f 0.37 ($CHCl_3$ / MeOH = 9:1); $[\alpha]_D^{24}$ +7.2 (*c* 0.18, $CHCl_3$); IR ($CHCl_3$) 3466, 3309 (br), 3005, 2935, 2874, 1703, 1656, 1520, 1457, 1380, 1232, 1100, 1020 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 [8.07] (s, 1H), 6.45 [7.11] (d, *J* = 14.4 Hz, 1H), 6.68 (br s, 1H), 5.78 (m, 1H), 5.13 [5.16] (dd, *J* = 14.4, 8.8 Hz, 1H), 4.94 (br s, 1H), 4.50 (m, 1H), 4.32 (m, 1H), 4.06 (t, *J* = 6.8 Hz, 2H), 3.74 (t, *J* = 6.6 Hz, 2H), 3.66–3.61 (m, 8H), 3.56 (t, *J* = 4.9 Hz, 2H), 3.44 (m, 2H), 3.16 (m, 2H), 3.02

[3.06] (s, 3H), 2.91 (dd, *J* = 12.8, 5.0 Hz, 1H), 2.73 (br d, *J* = 12.8 Hz, 1H), 2.59 (t, *J* = 6.5 Hz, 2H), 2.28 (m, 1H), 2.23 (td, *J* = 7.0, 2.2 Hz, 2H), 1.79–1.58 (m, 14H), 1.49–1.21 (m, 10H), 1.32 (s, 3H), 1.31 (s, 3H), 1.11 [1.06] (d, *J* = 6.9 Hz, 3H), 0.81 [0.79] (d, *J* = 6.8 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (2/1) are within parentheses (square blankets); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 171.6, 163.2, 162.2 [160.9], 128.6 [124.6], 113.0, 100.4, 78.3, 70.6, 70.5, 70.4, 70.4, 70.1, 69.9, 69.5, 66.6, 64.7, 61.7, 60.1, 55.3, 40.5, 39.1, 38.3, 37.0, 36.9, 35.8, 35.0, 33.2, 30.6, 29.3, 28.6, 28.0, 27.7, 26.1, 25.9, 25.5, 25.1, 23.6, 18.6, 12.2; HRMS *m/z* 837.4651 (calcd for $C_{40}H_{70}N_4NaO_{11}S^+$ $[M+Na]^+$, Δ –0.3 mmu).



Diol 20f. Prepared from ester **20e** (15.9 mg, 19.5 μmol) in 63% yield using the same procedure as that for **20b**. **20f**: R_f 0.21 ($CHCl_3$ / MeOH = 9:1); $[\alpha]_D^{21}$ +25 (*c* 0.36, $CHCl_3$); IR ($CHCl_3$) 3466, 3309 (br), 3006, 2932, 2873, 1700, 1655, 1603, 1523, 1457, 1380, 1265, 1096, 990, 940 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 [8.06] (s, 1H), 8.22 (br s, 1H), 6.77 (m, 1H) 6.53 [7.18] (d, *J* = 14.1 Hz, 1H), 5.87 (br s, 1H), 5.10 [5.16] (dd, *J* = 14.1, 9.0 Hz, 1H), 5.00 (br s, 1H), 4.50 (m, 1H), 4.32 (m, 1H), 4.08 (t, *J* = 6.6 Hz, 2H), 3.88 (m, 1H), 3.75 (t, *J* = 6.4 Hz, 2H), 3.66–3.61 (m, 10H), 3.56 (t, *J* = 4.9 Hz, 2H), 3.49–3.40 (m, 3H), 3.15 (m, 1H), 3.02 [3.06] (s, 3H), 2.91 (dd, *J* = 12.8, 5.0 Hz, 1H), 2.72 (br d, *J* = 12.8 Hz, 1H), 2.59 (t, *J* = 6.5 Hz, 2H), 2.22 (td, *J* = 7.4, 2.7 Hz, 2H), 1.79–1.58 (m, 9H), 1.57–1.42 (m, 5H), 1.40–1.27 (m, 7H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.91 [0.89] (d, *J* = 7.0 Hz, 3H) Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (2/1) are within parentheses (square blankets); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 171.7, 163.3 [160.9], 162.2, 129.3 [125.1], 112.1 [114.0], 78.5, 72.6 [72.9], 70.5, 70.5, 70.4, 70.4, 70.4, 70.1, 69.9, 66.6, 64.6, 61.8, 60.1, 55.4, 40.5, 39.2 [39.3], 39.1 [39.2], 38.4 [38.5], 35.7, 35.1, 33.6 [33.4], 33.1, 29.2, 28.5, 28.1, 27.6, 26.4, 25.9, 25.5, 18.8 [18.8], 11.5 [11.6]; HRMS *m/z* 797.4321 (calcd for $C_{37}H_{66}N_4NaO_{11}S^+$ $[M+Na]^+$, Δ –2.0 mmu).



Biotin probe 8-bio. Prepared from ester **20f** (5.3 mg, 6.8 μmol) in 50% yield using the same procedure as that for **13a**. **8-bio**: R_f 0.46 ($CHCl_3$ / MeOH = 9:1); $[\alpha]_D^{21}$ +14 (*c* 0.25, $CHCl_3$); IR ($CHCl_3$) 3465, 3308 (br), 3008, 2933, 2873, 1726, 1703, 1656, 1521, 1457, 1373, 1257, 1095, 1020, 955 cm^{-1}; Chemical shifts of the minor rotamer at the *N*-methylenamide moiety (2/1) are within parentheses (square blankets); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 [8.08] (s, 1H), 6.58 (m, 1H) 6.48 [7.15] (d, *J* = 14.0 Hz, 1H), 5.68 (br s, 1H), 5.03–4.95 (m, 2H), 4.93 (br s, 1H), 4.81 (dd, *J* = 9.5, 3.3 Hz, 1H), 5.00 (br s, 1H), 4.50 (m, 1H), 4.33 (m, 1H), 4.06 (t, *J* = 6.8 Hz, 2H), 3.74 (t, *J* = 6.5 Hz, 2H), 3.66–3.61 (m, 12H), 3.56 (t, *J* =

5.0 Hz, 2H), 3.44 (m, 2H), 3.16 (td, *J* = 7.3, 4.5 Hz, 1H), 3.03 [3.06] (s, 3H), 2.92 (dd, *J* = 12.8, 5.0 Hz, 1H), 2.73 (br d, *J* = 12.7 Hz, 1H), 2.58 (t, *J* = 6.6 Hz, 2H), 2.55 (m, 1H), 2.22 (td, *J* = 7.4, 3.3 Hz, 2H), 2.05 (s, 3H), 2.00 [2.00] (s, 3H), 1.82–1.57 (m, 10H), 1.50–1.21 (m, 6H), 1.02 [1.01] (d, *J* = 6.9 Hz, 3H), 0.93 [0.93] (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 171.6, 170.9 [170.9], 170.7, 163.2, 162.2 [161.0], 129.3 [125.3], 110.8 [112.4], 71.7 [71.9], 70.6, 70.5, 70.5, 70.4, 70.4, 70.1, 69.9, 66.6 [64.6], 61.8, 60.1, 55.2, 40.5, 39.2, 37.5 [37.6], 36.9 [37.1], 35.8, 35.0, 33.1, 32.3 [32.2], 29.2, 28.5, 28.1, 28.0, 27.6, 25.7, 25.7, 25.4, 21.2, 21.0, 21.0, 19.2 [19.3], 9.8 [9.8]; HRMS *m/z* 881.4572 (calcd for $C_{41}H_{70}N_4NaO_{13}S^+$ $[M+Na]^+$, Δ +2.0 mmu).

Supporting References

S1 P. Labute, *J. Comput. Chem.,* 2008, **29**, 1693.

S2 R. A. Laskowski, M. B, Swindells, *J. Chem. Inf. Model,* 2011, **51**, 2778.

S3 J. L. Velázquez–Libera, F. Durán–Verdugo, A. Valdés–Jiménez, G. Núñez–Vivanco, J. Caballero, *Bioinformatics,* 2020, **36**, 2912.

S4 (a) P. R. Blakemore, W. J. Cole, P. J. Kocienski, A. Morley, *Synlett,* 1998, 26; (b) P. R. Blakemore, *J. Chem. Soc., Perkin Trans. 1,* 2002, 2563.

S5 T. Huebscher, G. Helmchen, *Synlett,* 2006, 1323.

S6 A. Klapars, J. C. Antilla, X. Huang, S. L. Buchwald, *J. Am. Chem. Soc.,* 2001, **123**, 7727.

S7 I. Paterson, R. D. Tillyer, *Tetrahedron Lett.,* 1992, **33**, 4233.

S8 X. Bantreil, A. Poater, C. A. Urbina–Blanco, Y. D. Bidal, L. Falivene, R. A. M. Randall, L. Cavallo, A. M. Z. Slawin, C. S. J. Cazin, *Organometallics,* 2012, **31**, 7415.

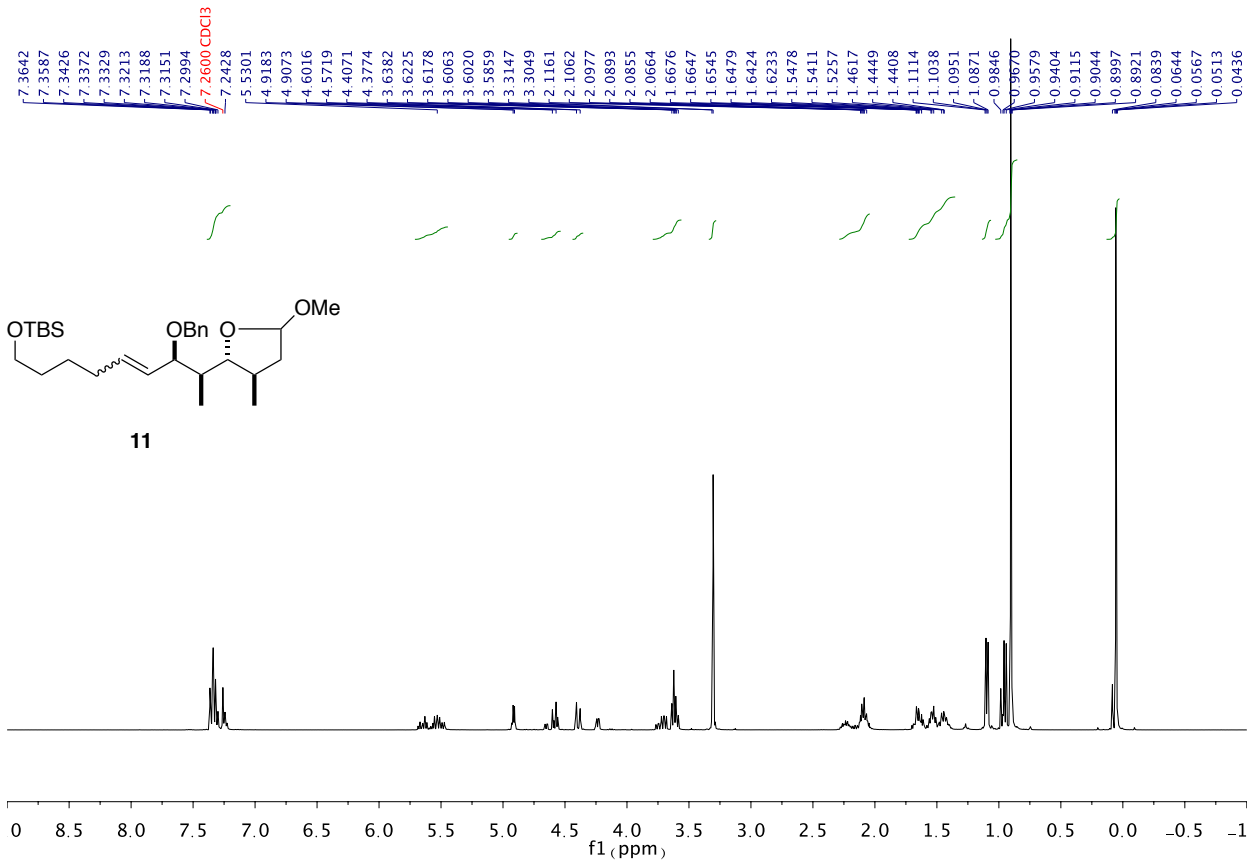
S9 I. Paterson, M. A. Lister, G. R. Ryan, *Tetrahedron Lett.,* 1991, **32**, 1749.

S10 A. De Mico, R. Margarita, L. Parlanti, A. Vescovi, G. Piancatelli, *J. Org. Chem.,* 1997, **62**, 6974.

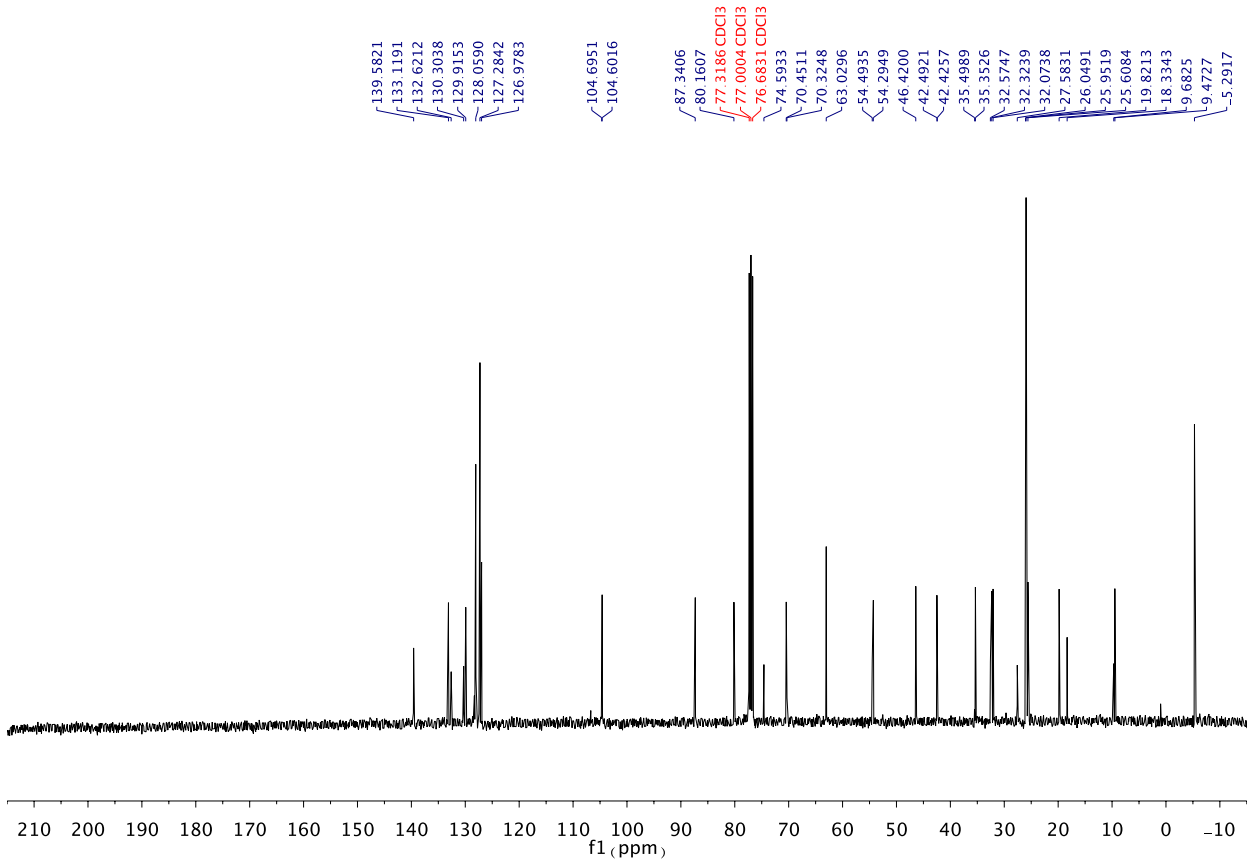
S11 K. Takai, K. Nitta, K. Utimoto, *J. Am. Chem. Soc.,* 1986, **108**, 7408.

S12 (a) R. Nakamura, K. Tanino, M. Miyashita, *Org. Lett.,* 2003, **5**, 3583; (b) D. J. Tetlow, S. J. Winder, C. Aïssa, *Chem. Commun.,* 2016, **52**, 807.

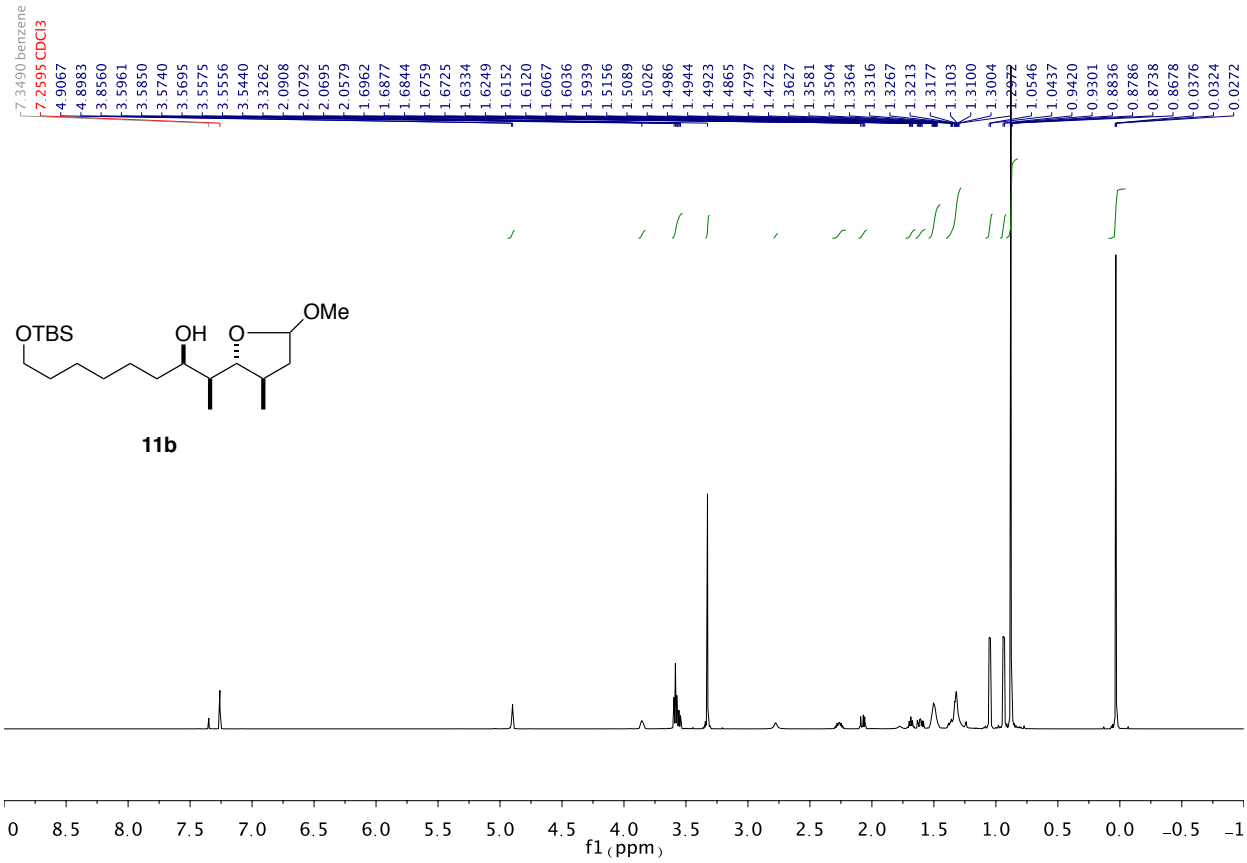
NMR spectra of new compounds



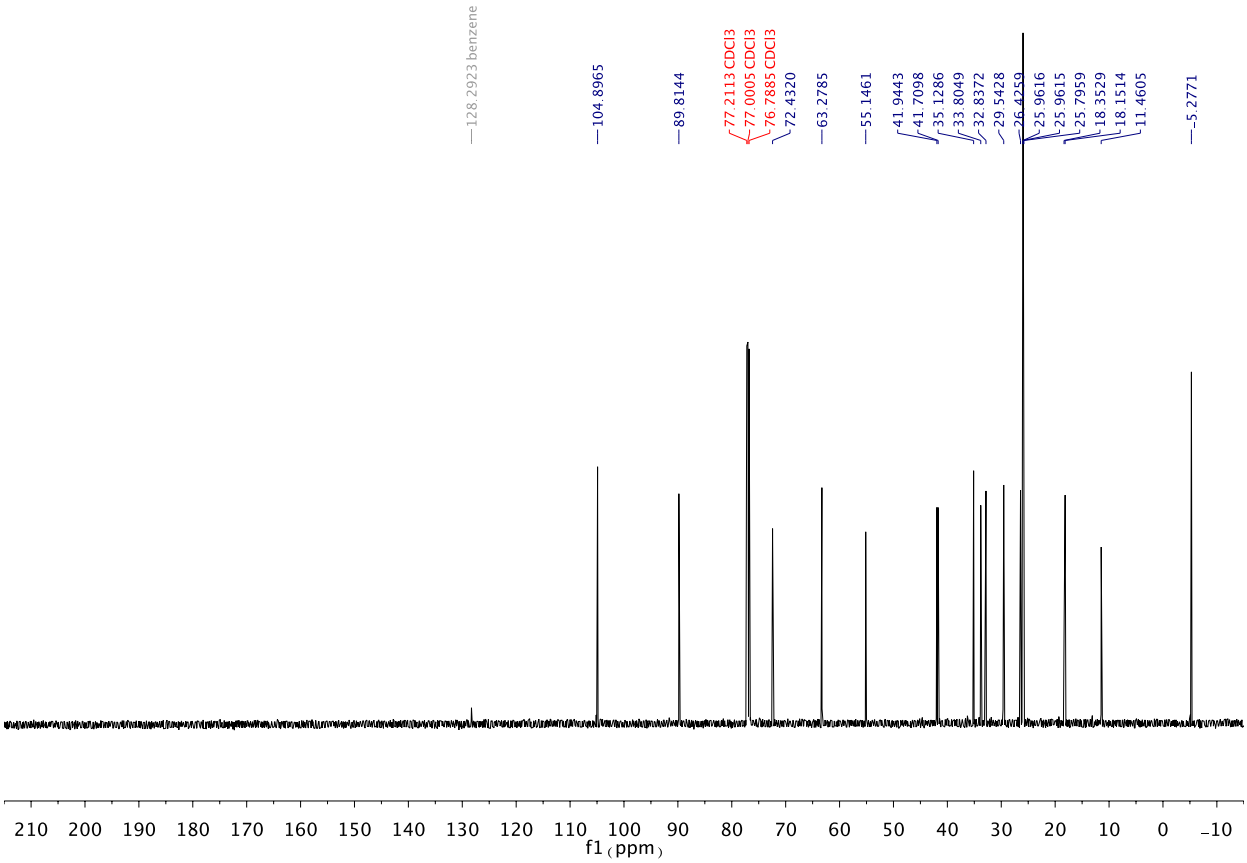
^{1}H NMR spectrum of olefin **11** (400 MHz, $CDCl_3$).



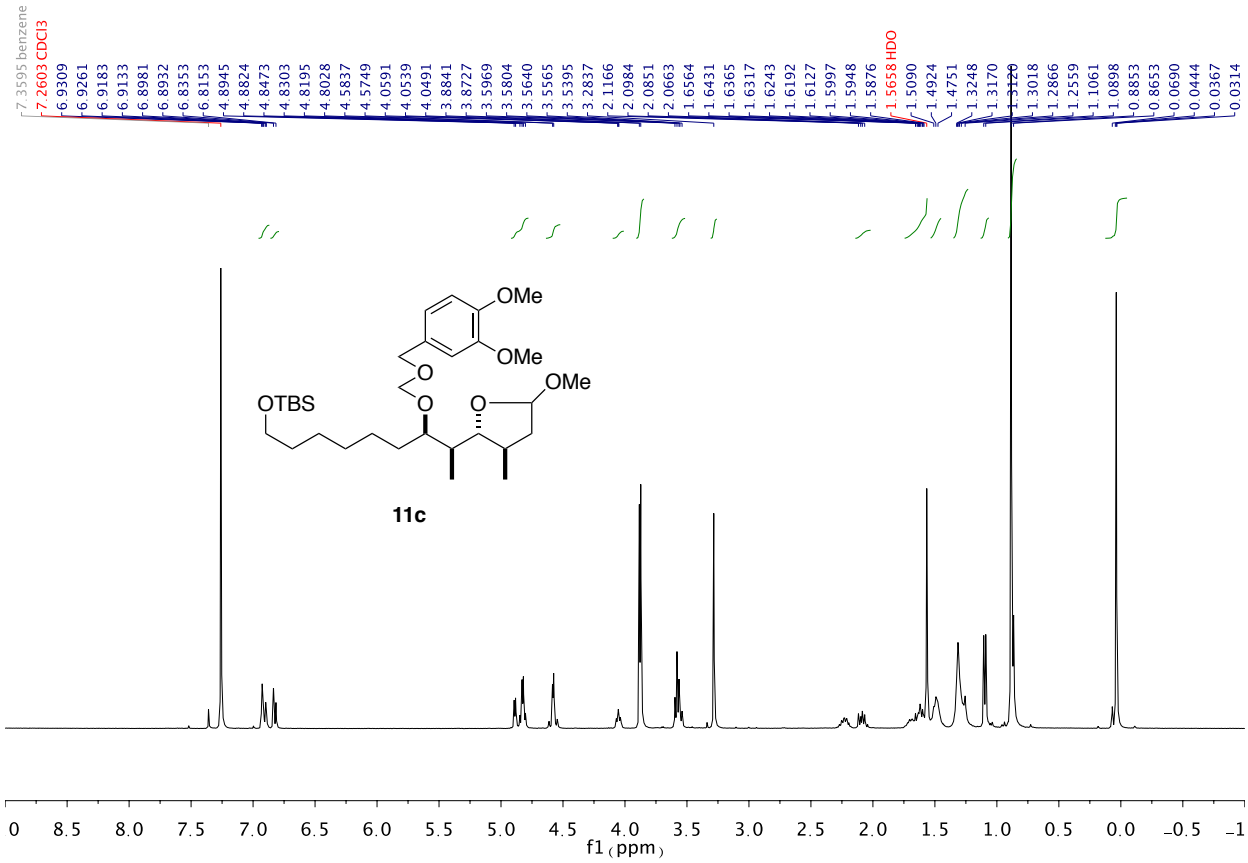
^{13}C NMR spectrum of olefin **11** (100 MHz, $CDCl_3$).



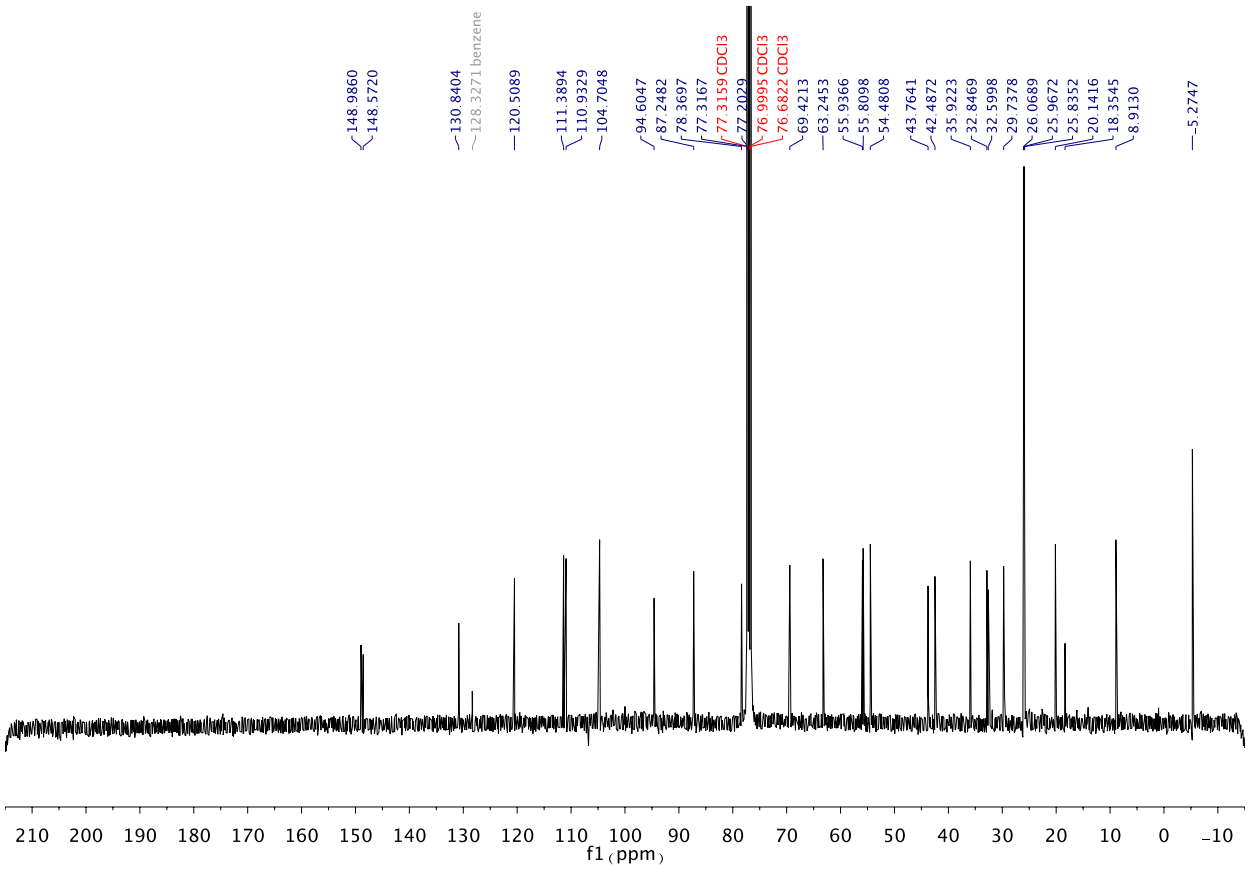
^{1}H NMR spectrum of secondary alcohol **11b** (600 MHz, $CDCl_3$).



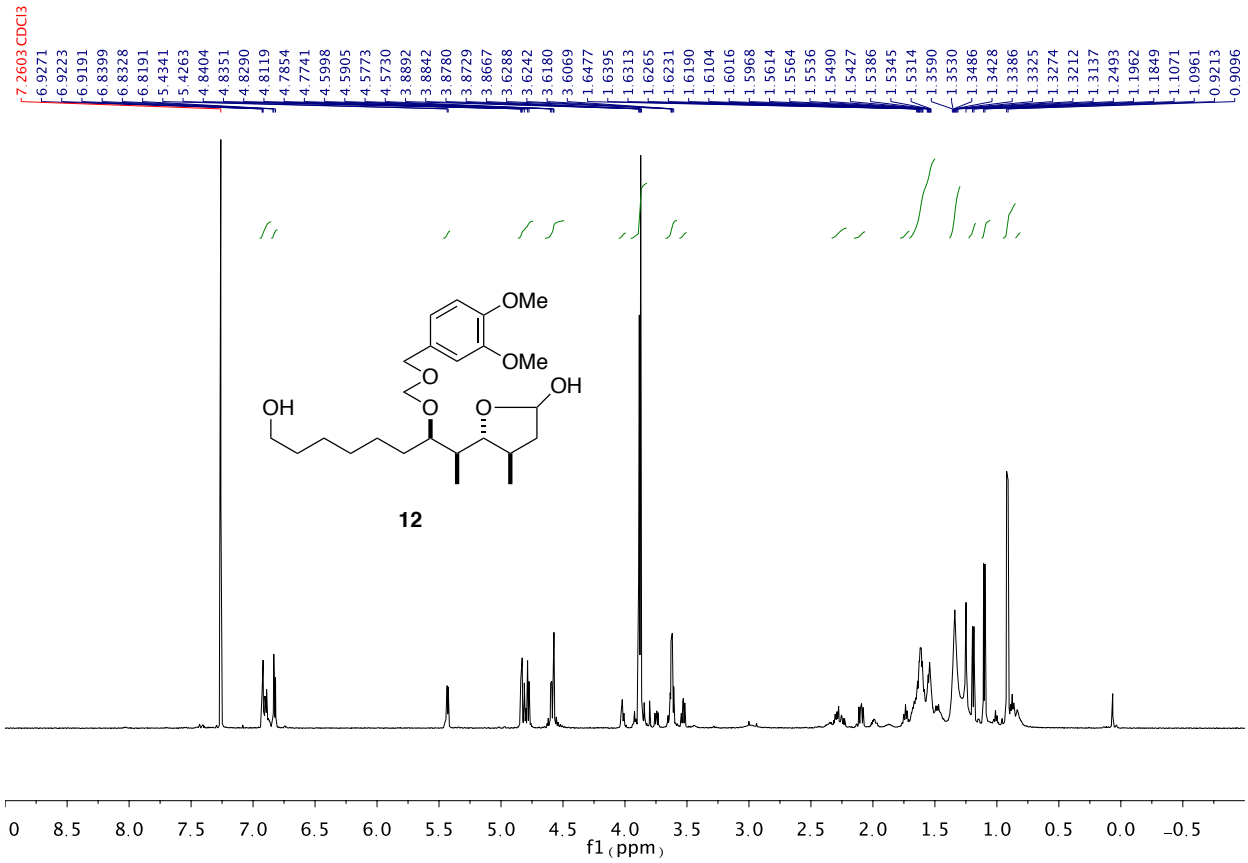
^{13}C NMR spectrum of secondary alcohol **11b** (150 MHz, $CDCl_3$).



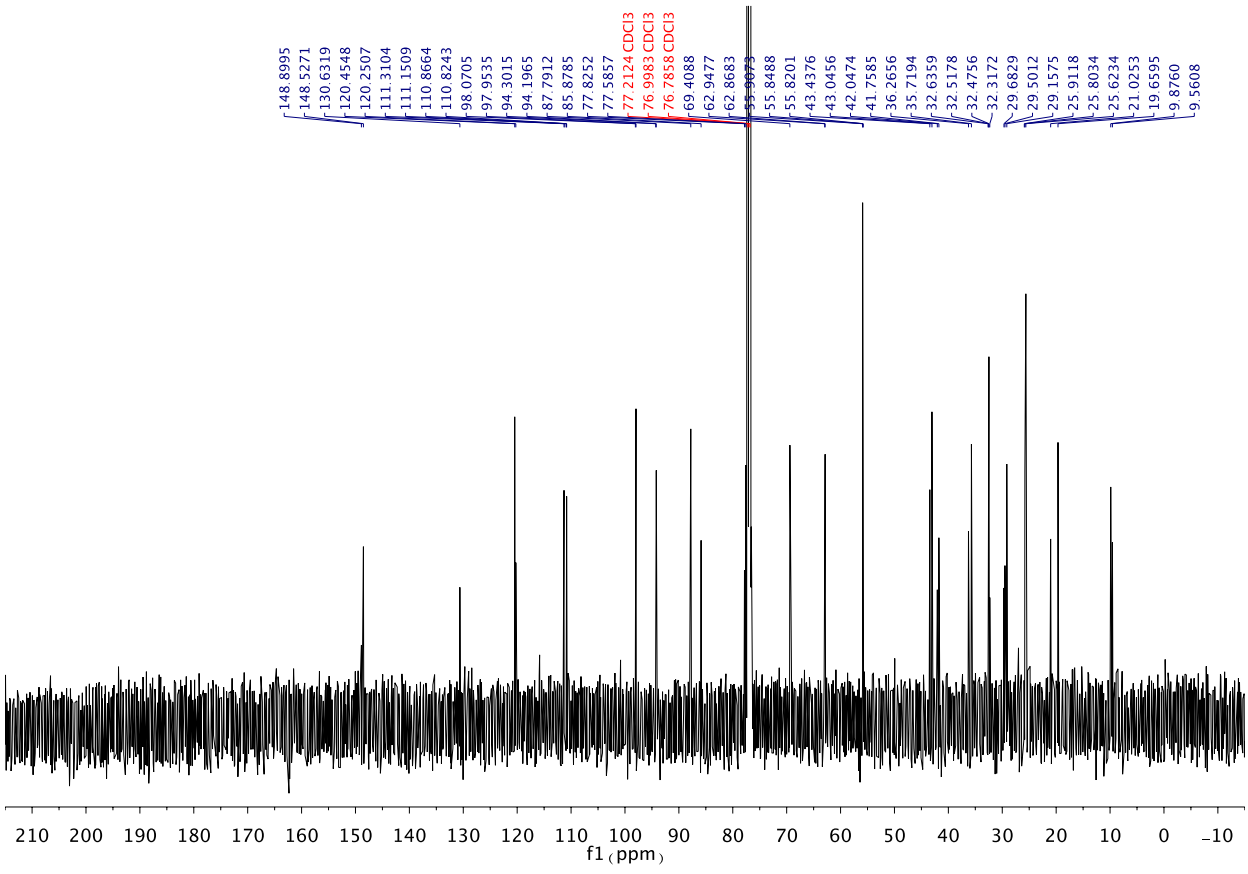
^{1}H NMR spectrum of DMPMOM ether **11c** (400 MHz, $CDCl_3$).



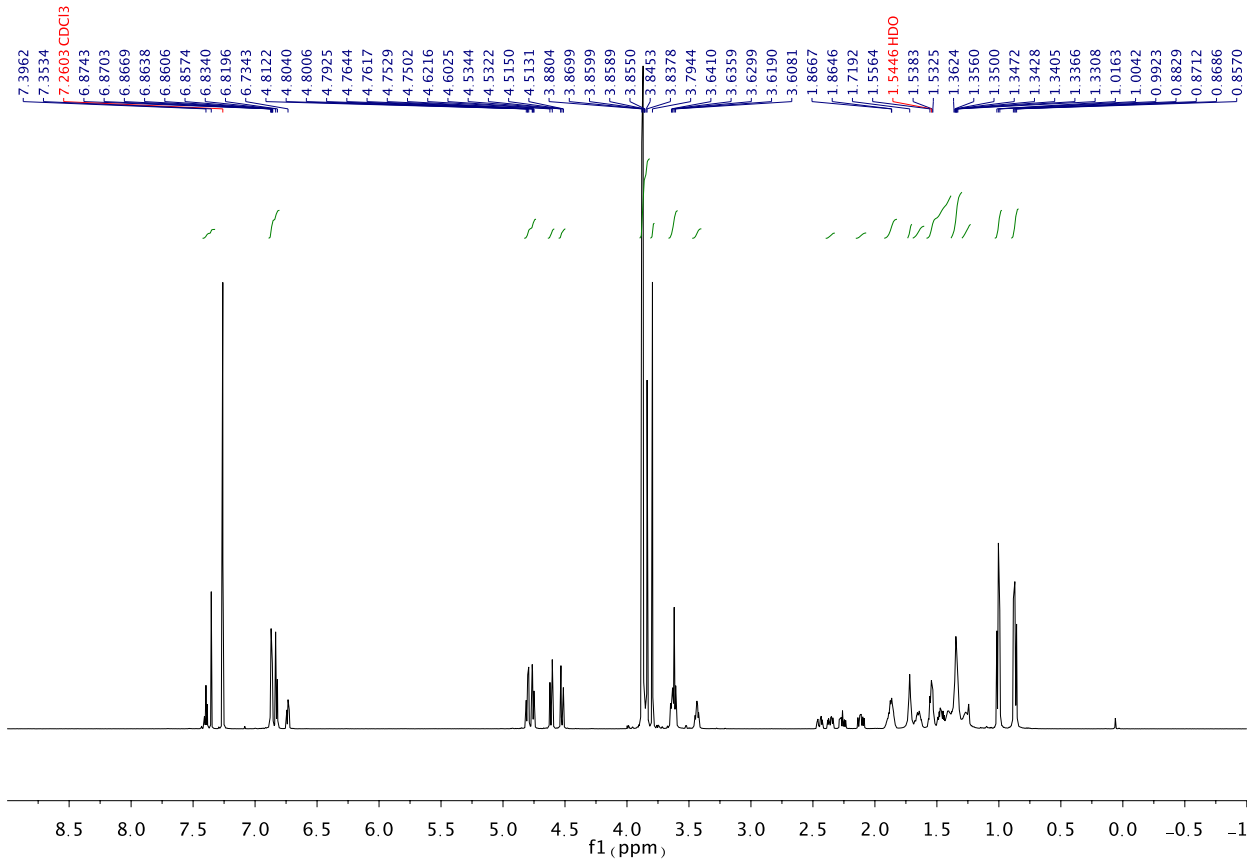
^{13}C NMR spectrum of DMPMOM ether **11c** (100 MHz, $CDCl_3$).



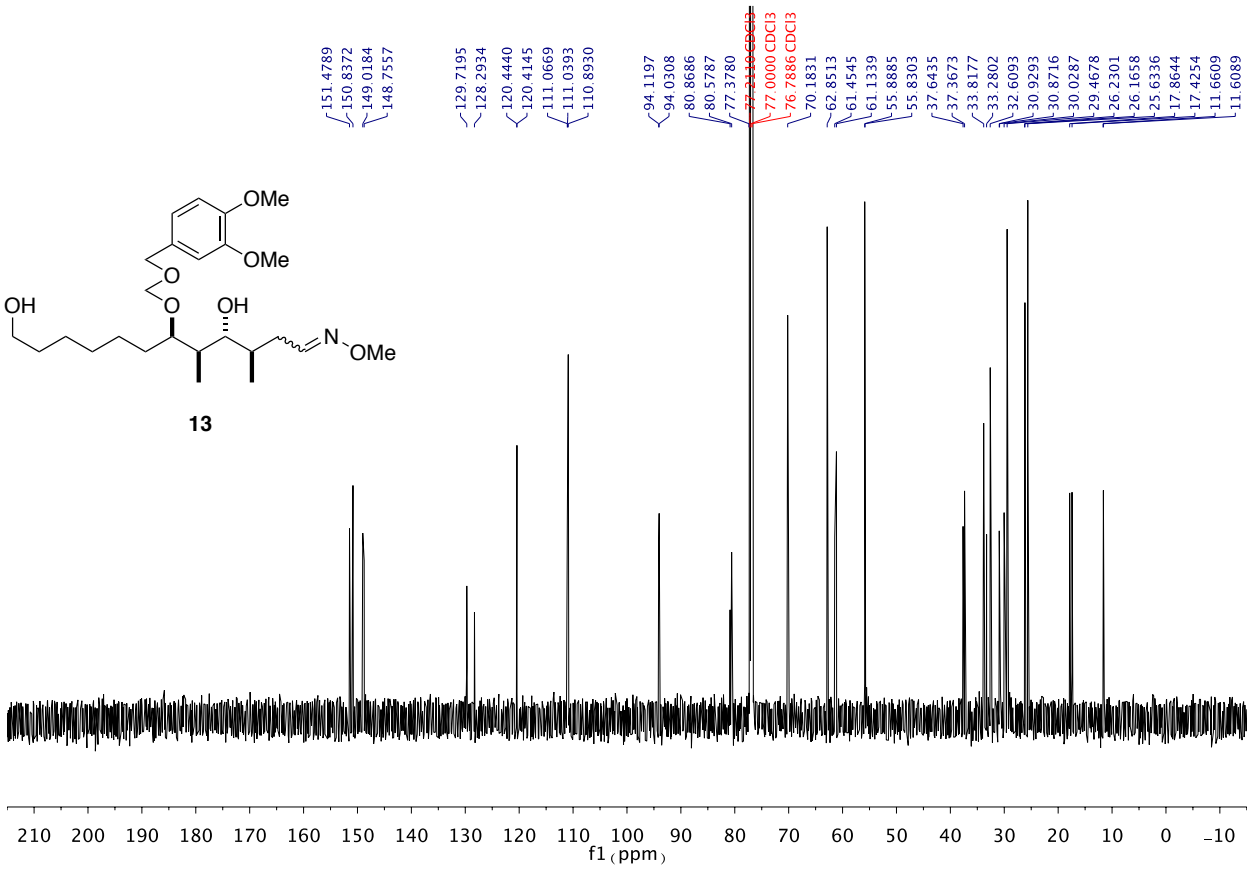
^{1}H NMR spectrum of hemiacetal **12** (600 MHz, $CDCl_3$).



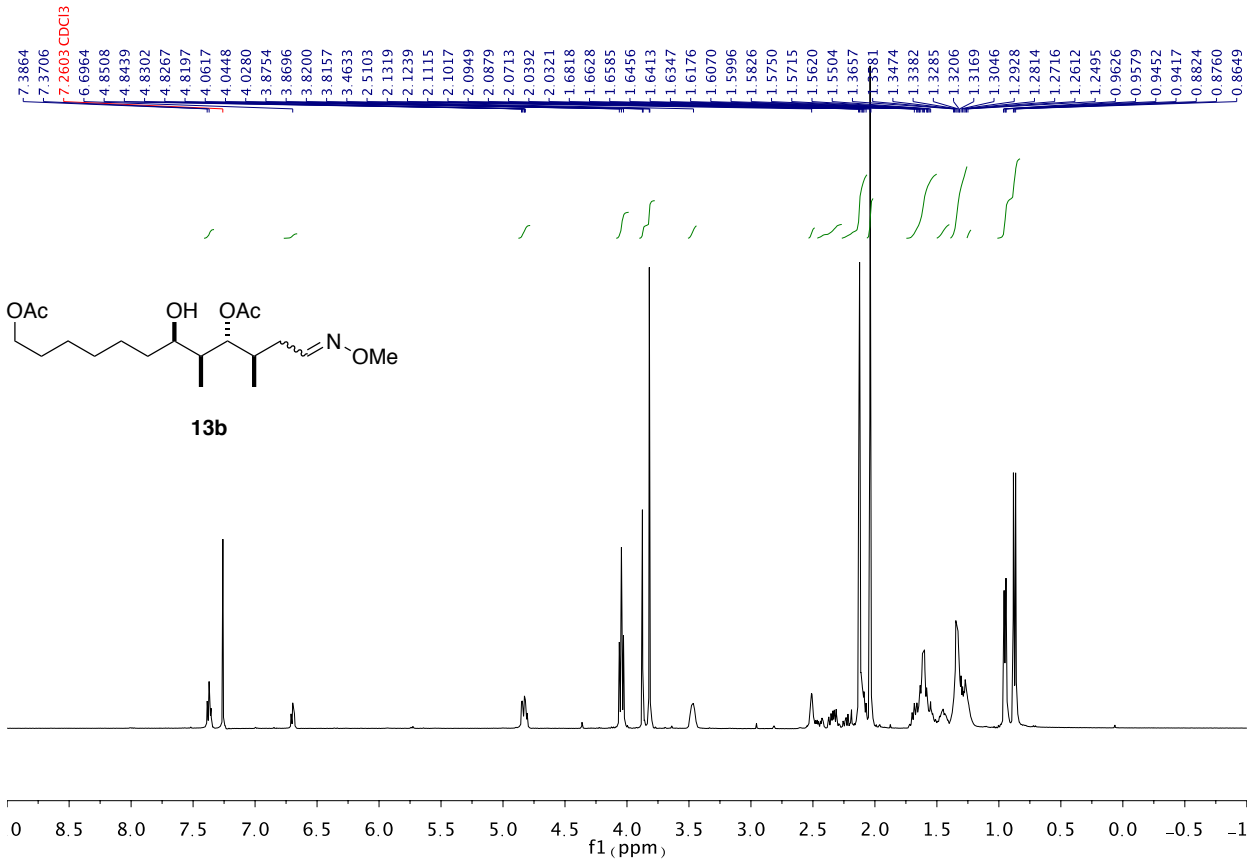
^{13}C NMR spectrum of hemiacetal **12** (150 MHz, $CDCl_3$).



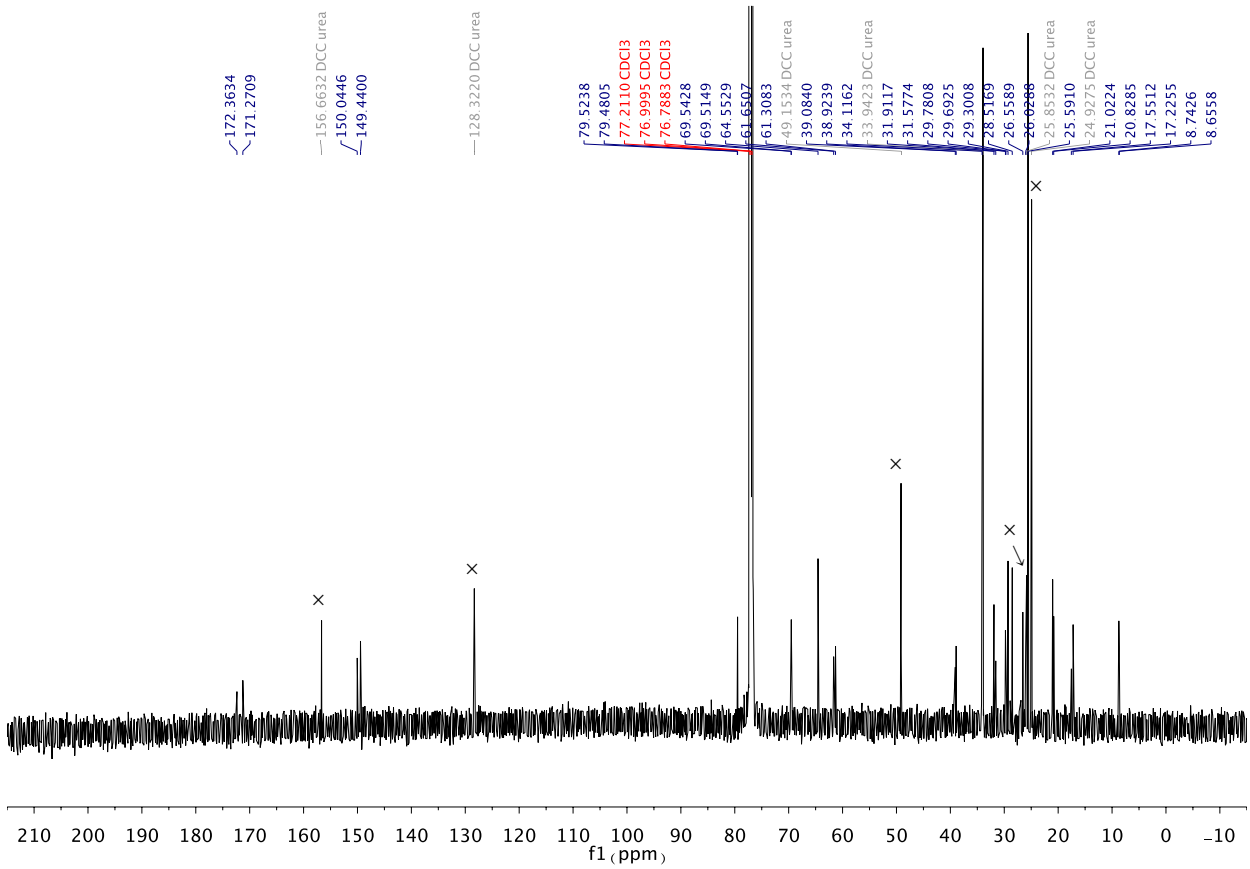
^{1}H NMR spectrum of oxime **13** (600 MHz, $CDCl_3$).



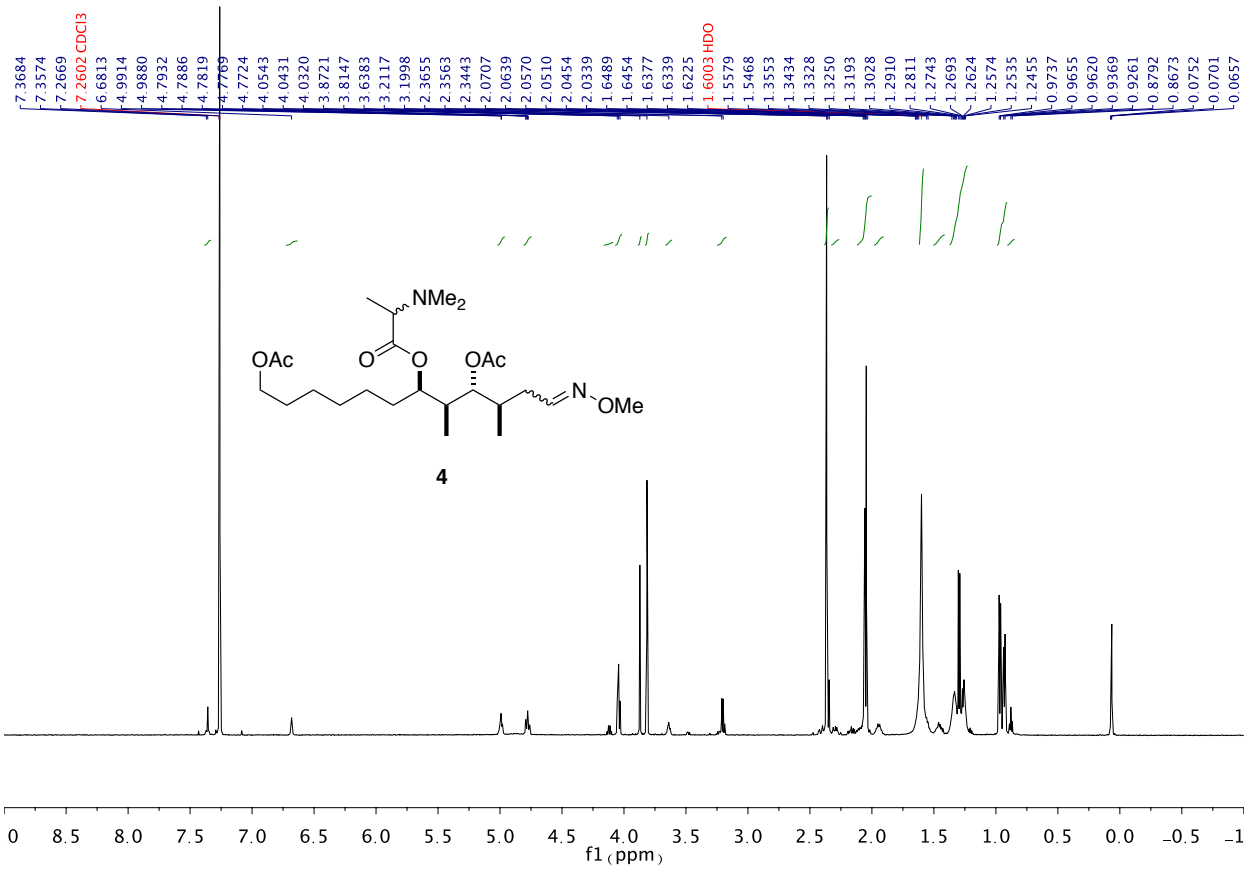
^{13}C NMR spectrum of oxime **13** (150 MHz, $CDCl_3$).



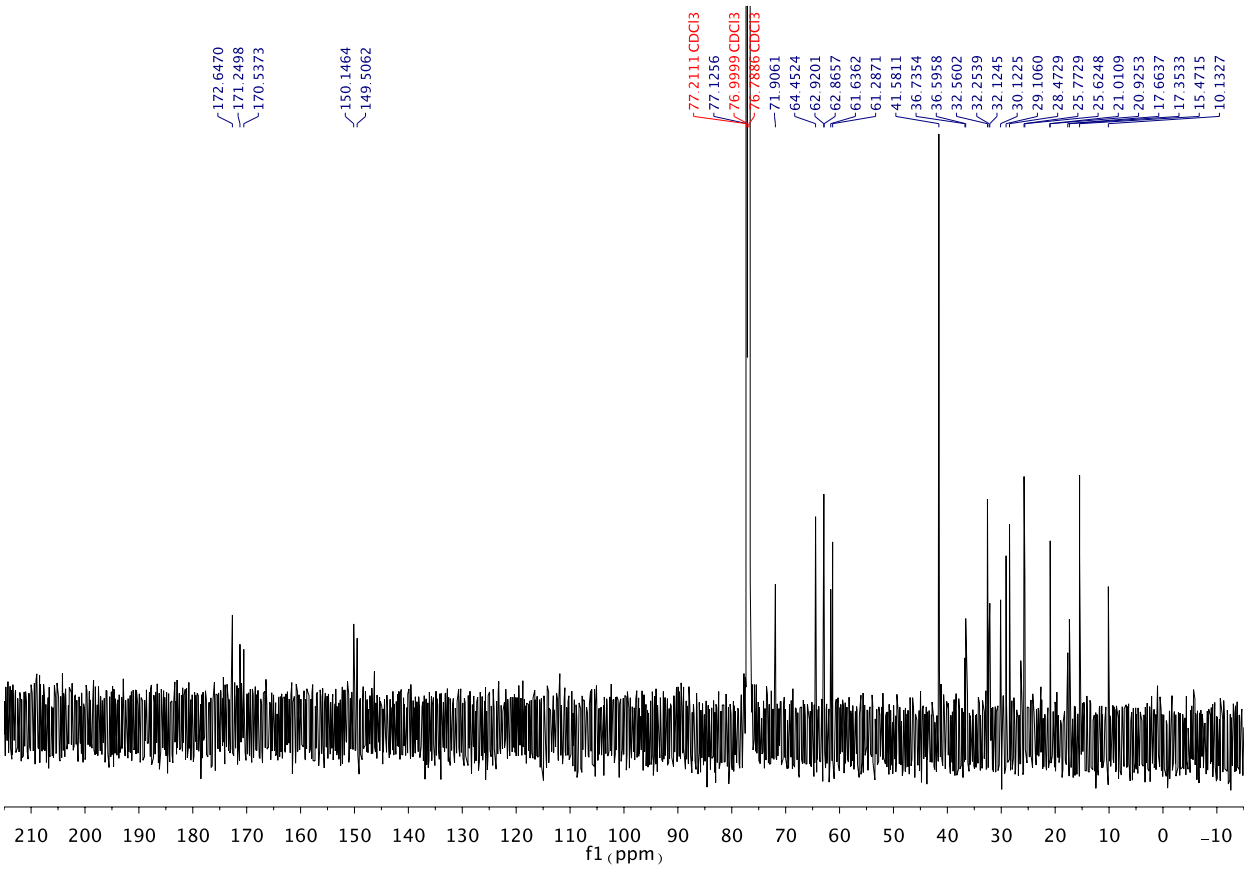
^{1}H NMR spectrum of secondary alcohol **13b** (400 MHz, $CDCl_3$).



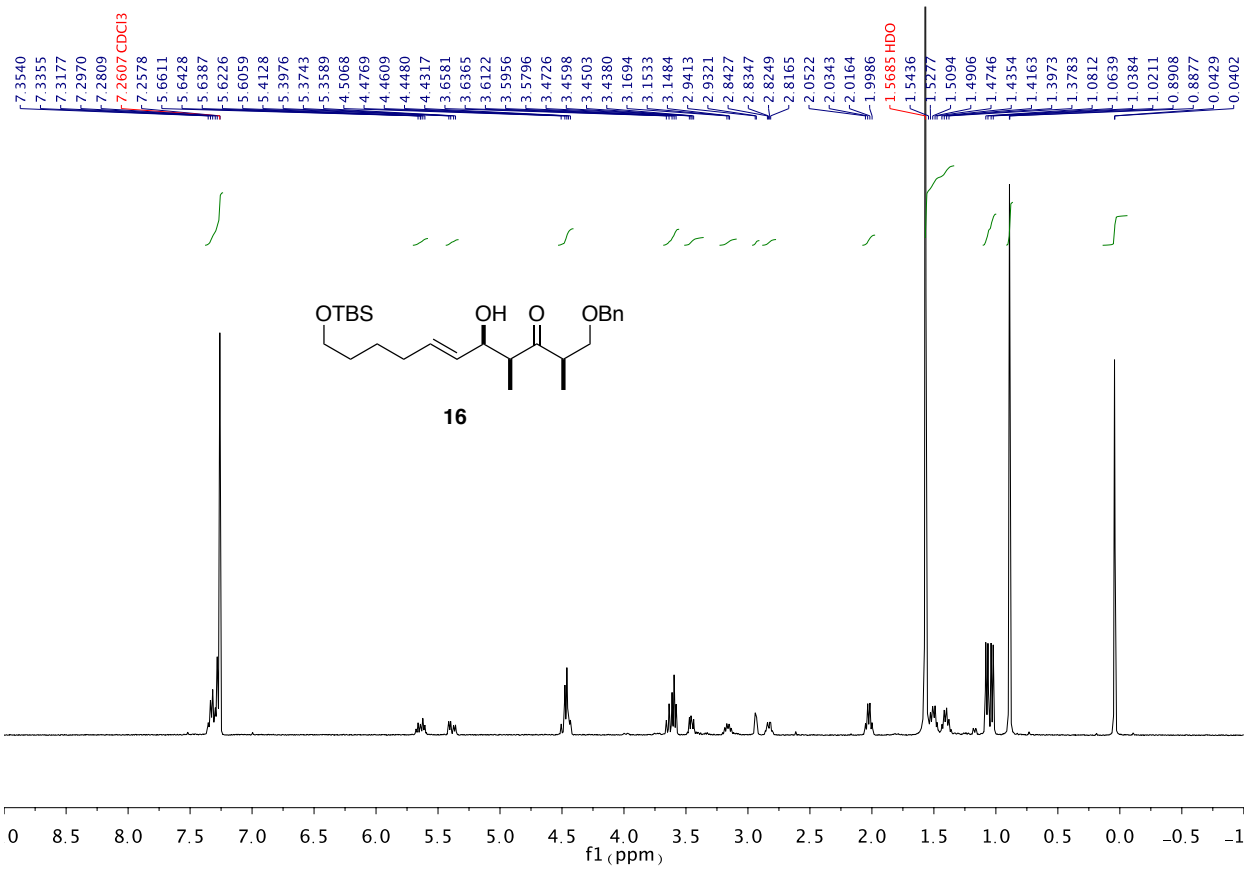
^{13}C NMR spectrum of secondary alcohol **13b** (150 MHz, $CDCl_3$).



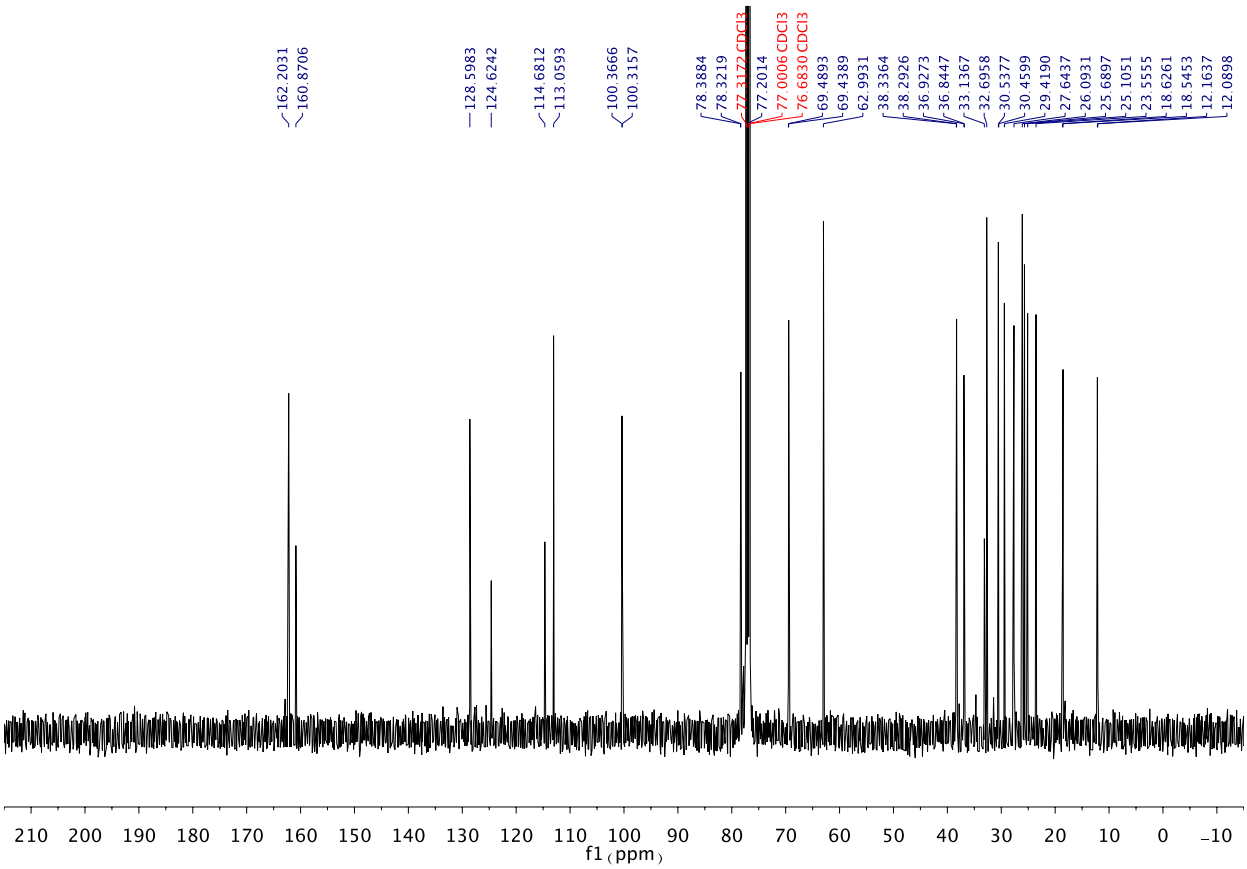
^{1}H NMR spectrum of secondary analog **4** (400 MHz, $CDCl_3$).



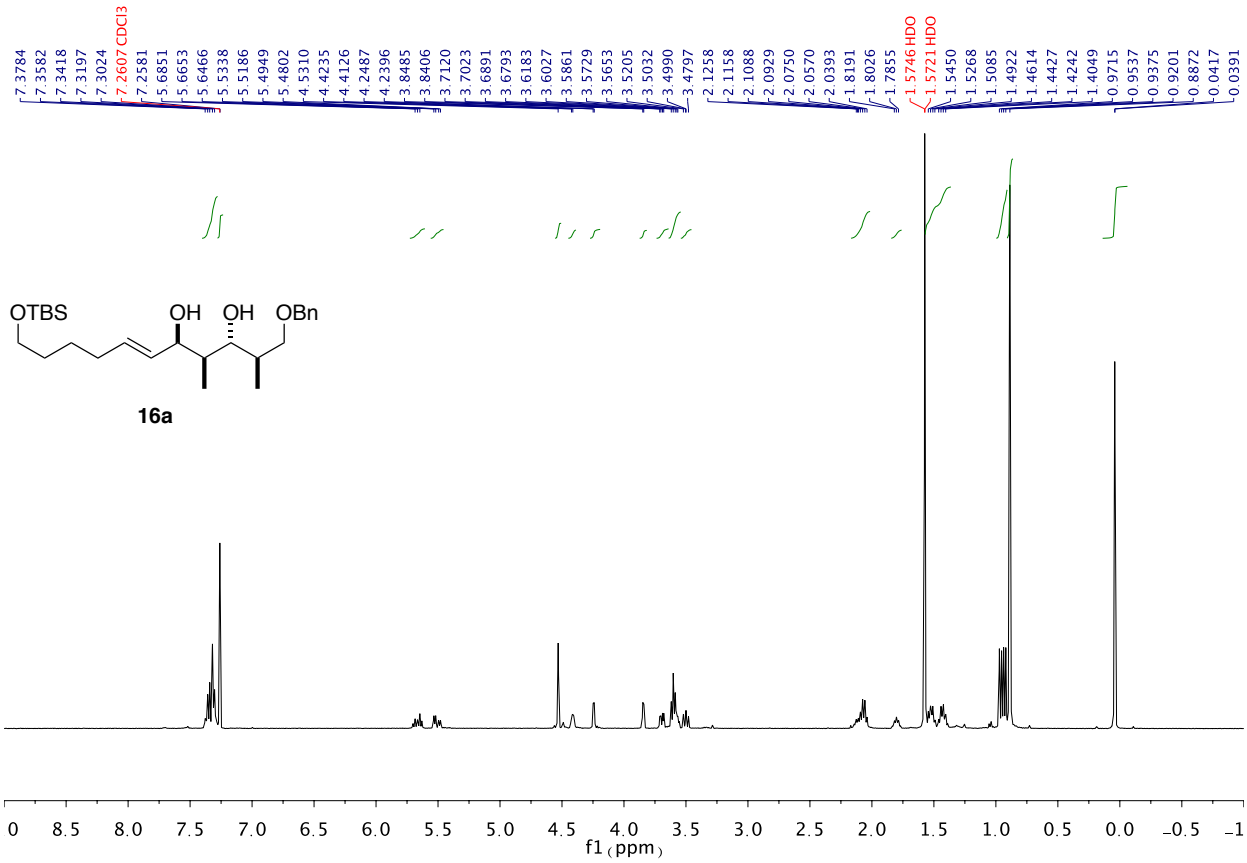
^{13}C NMR spectrum of secondary analog **4** (150 MHz, $CDCl_3$).



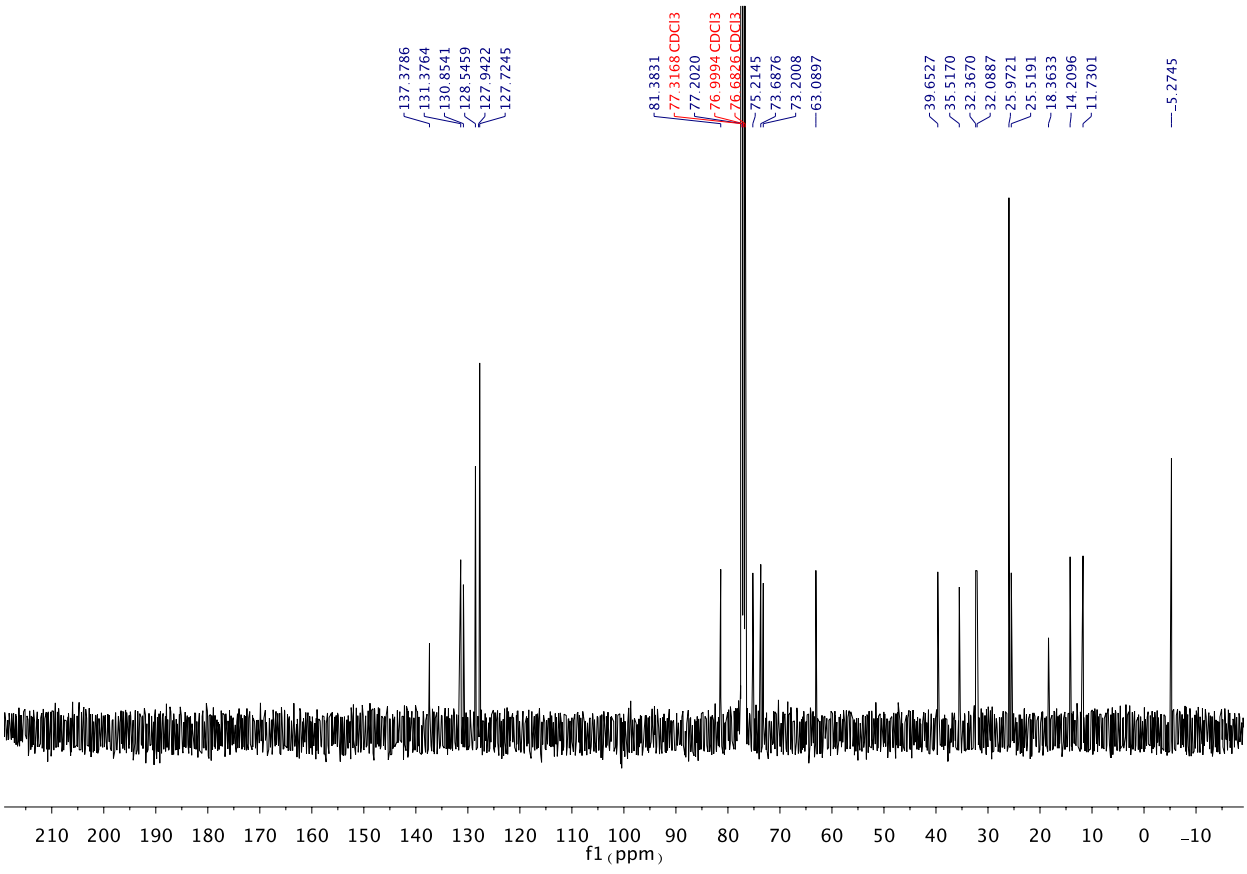
^{1}H NMR spectrum of hydroxyketone **16** (400 MHz, $CDCl_3$).



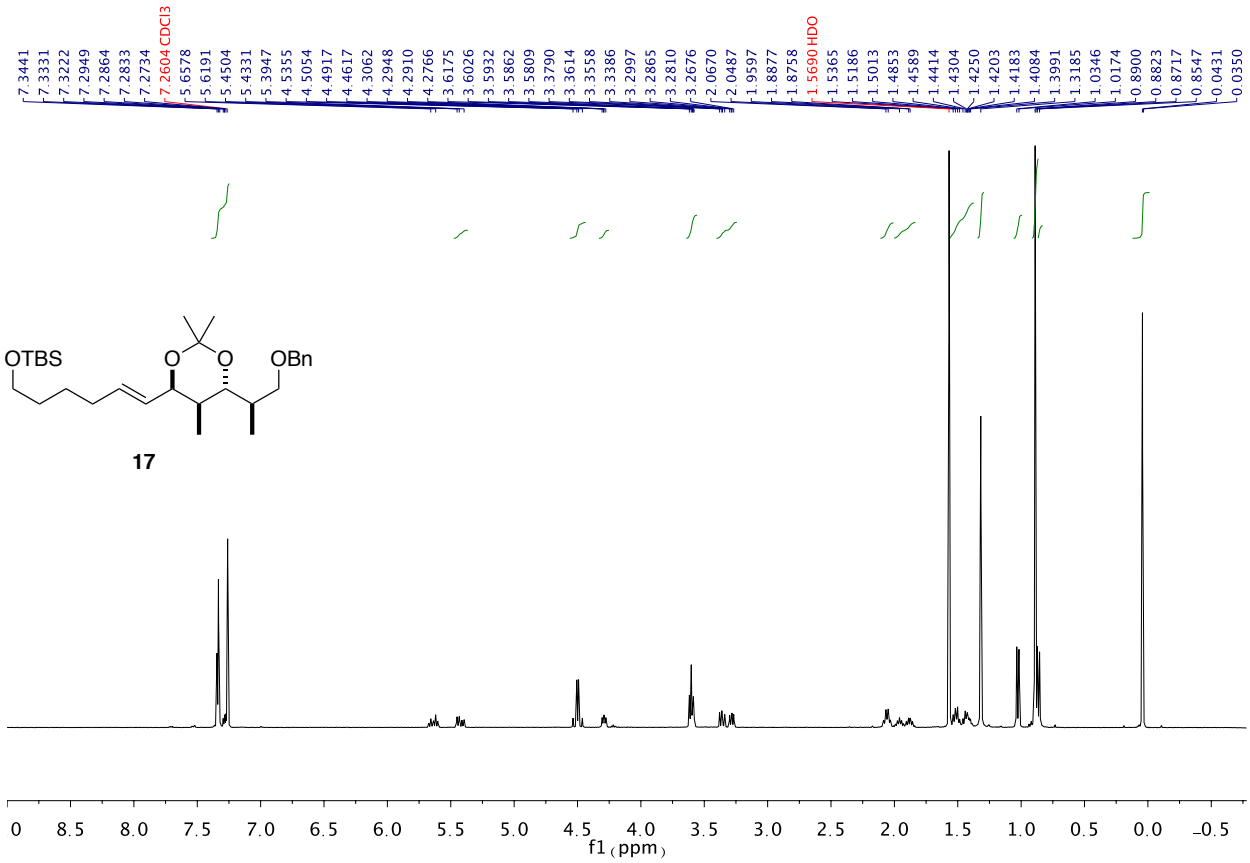
^{13}C NMR spectrum of hydroxyketone **16** (100 MHz, $CDCl_3$).



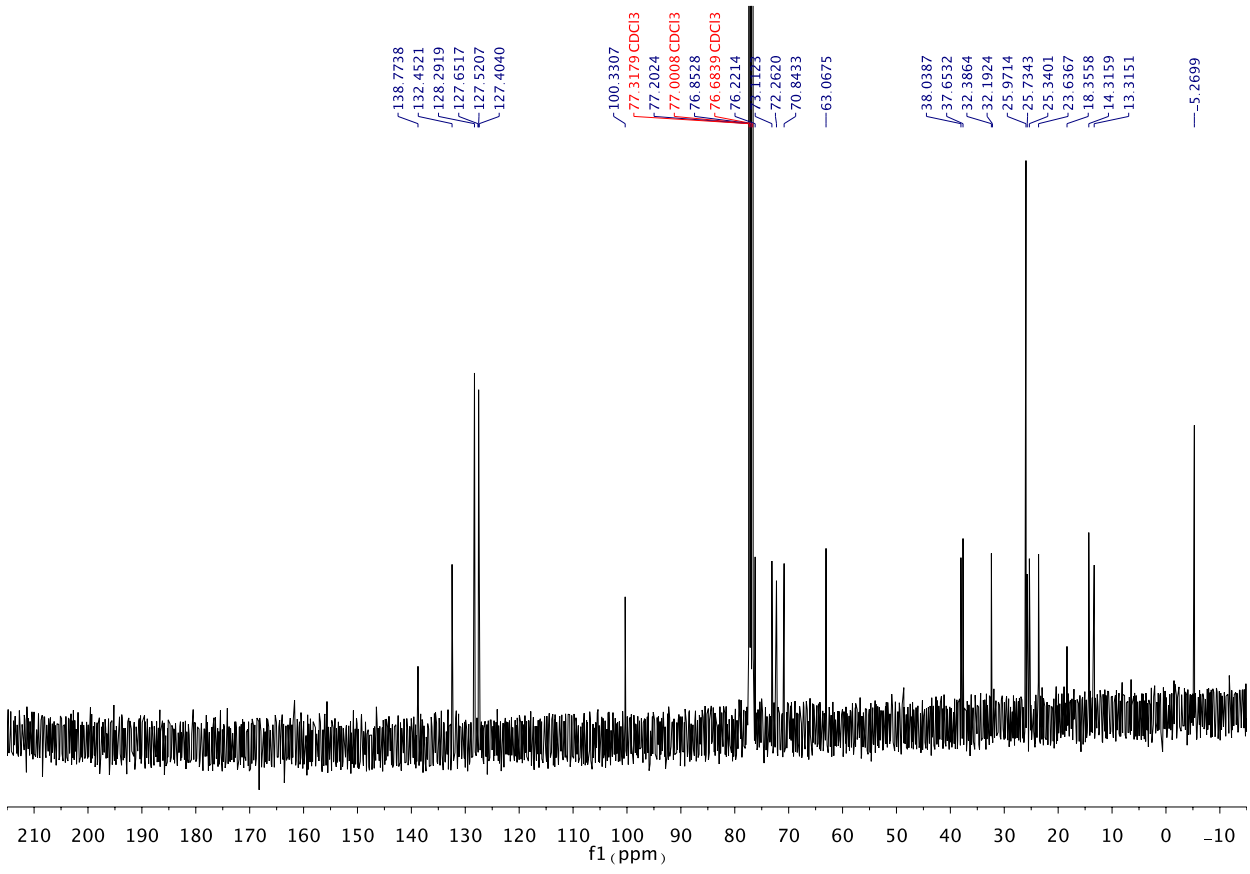
^{1}H NMR spectrum of *anti*-diol **16a** (400 MHz, $CDCl_3$).



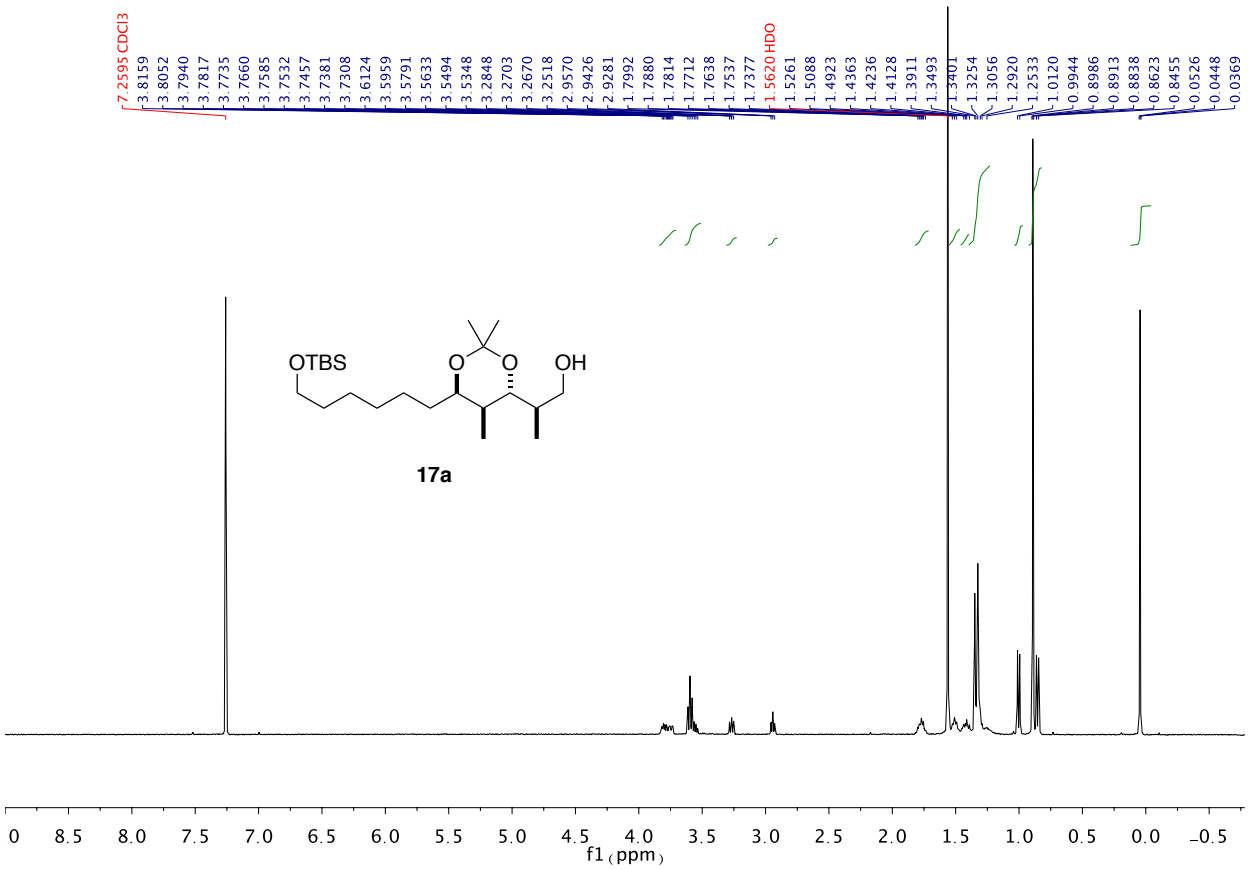
^{13}C NMR spectrum of *anti*-diol **16a** (100 MHz, $CDCl_3$).



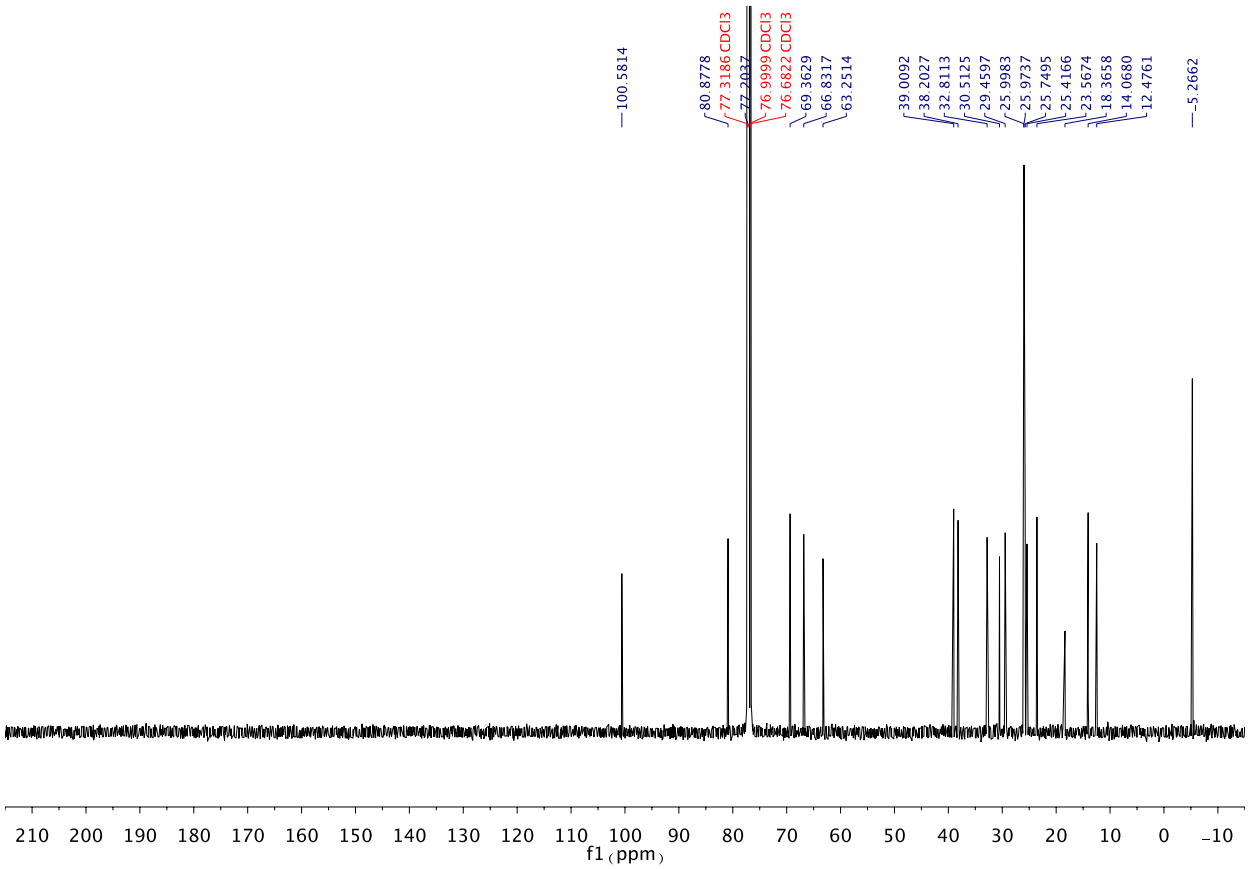
^{1}H NMR spectrum of acetonide **17** (400 MHz, $CDCl_3$).



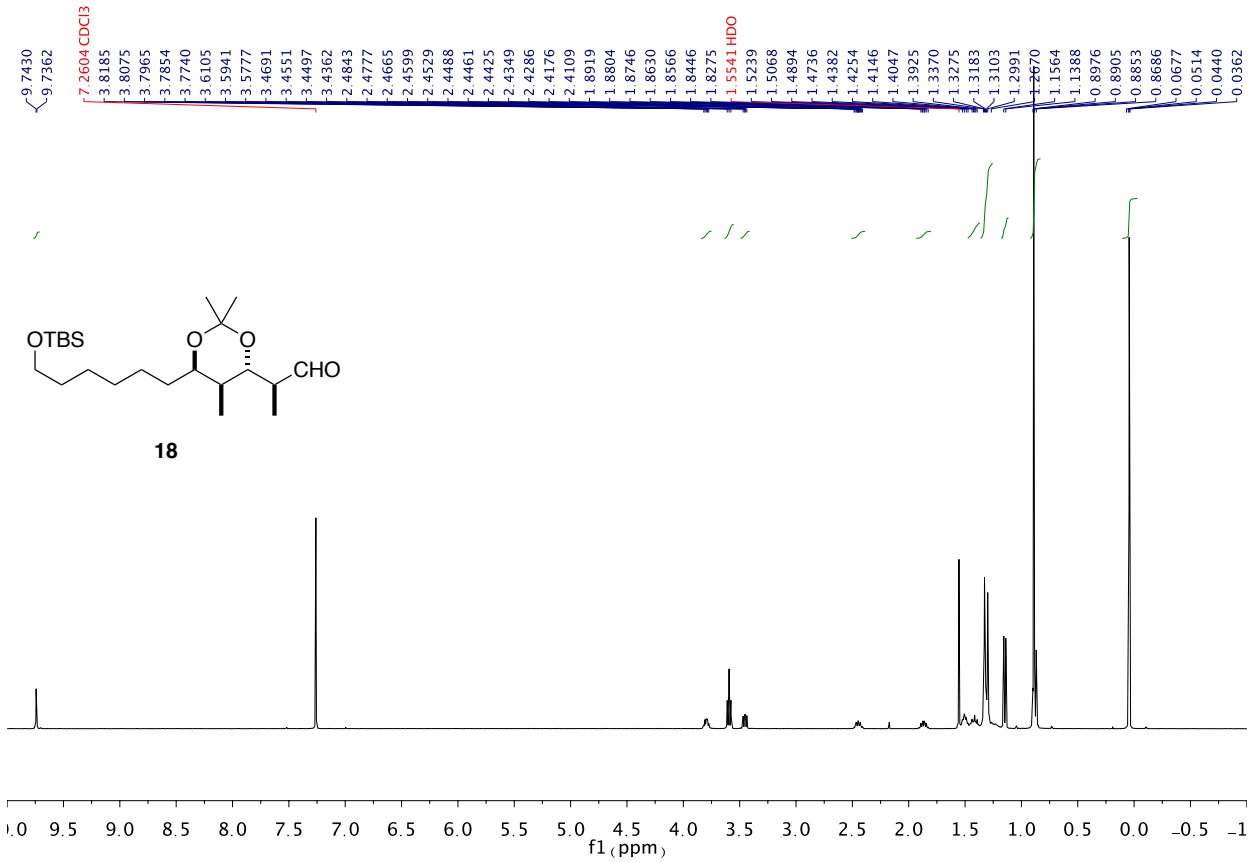
^{13}C NMR spectrum of acetonide **17** (100 MHz, $CDCl_3$).



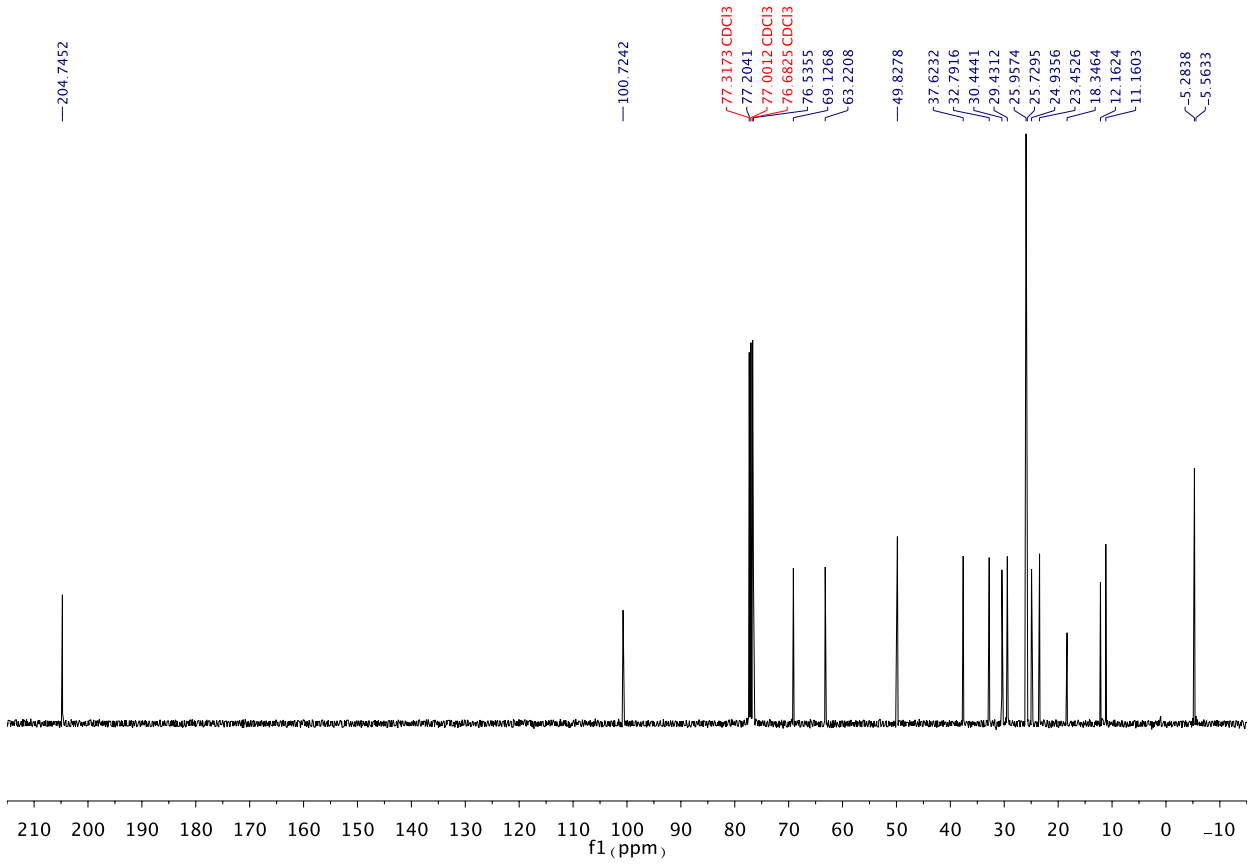
^{1}H NMR spectrum of primary alcohol **17a** (400 MHz, $CDCl_3$).



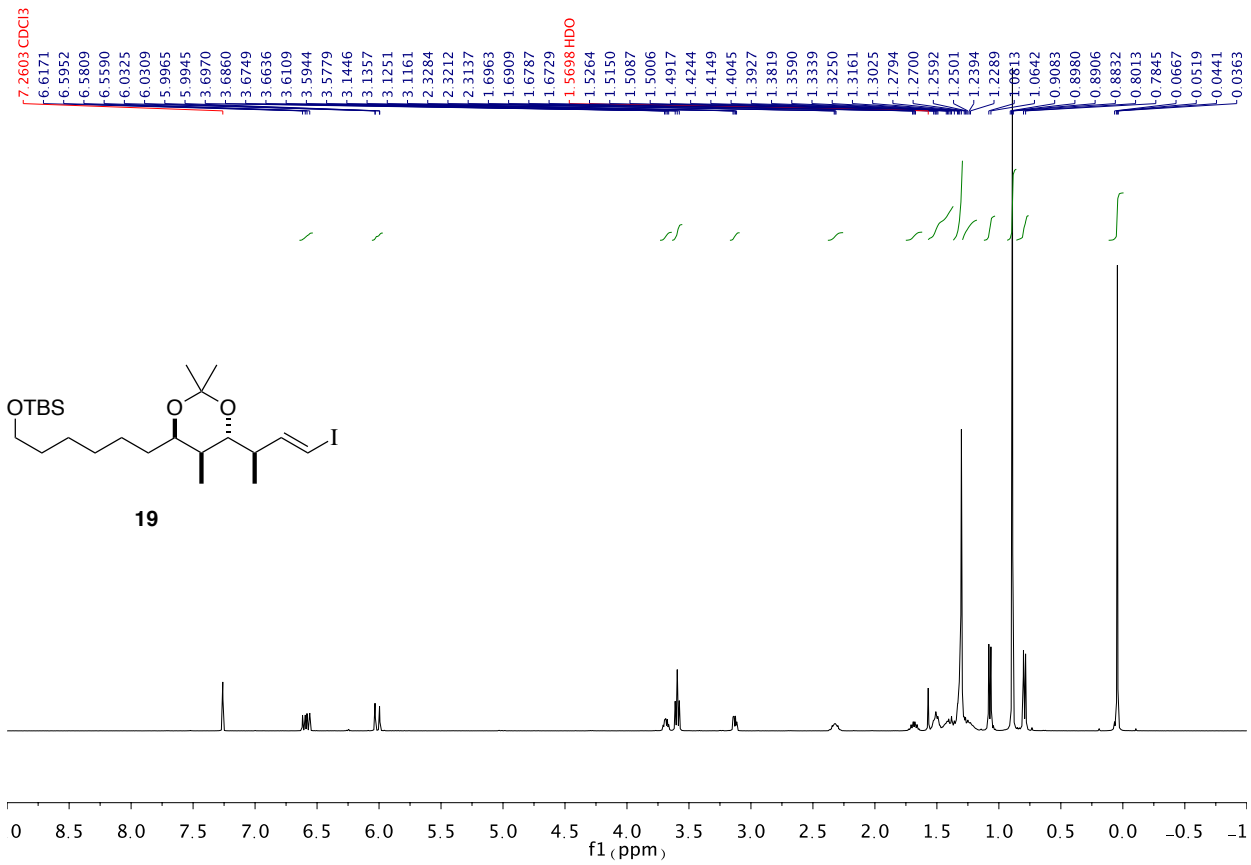
^{13}C NMR spectrum of primary alcohol **17a** (100 MHz, $CDCl_3$).



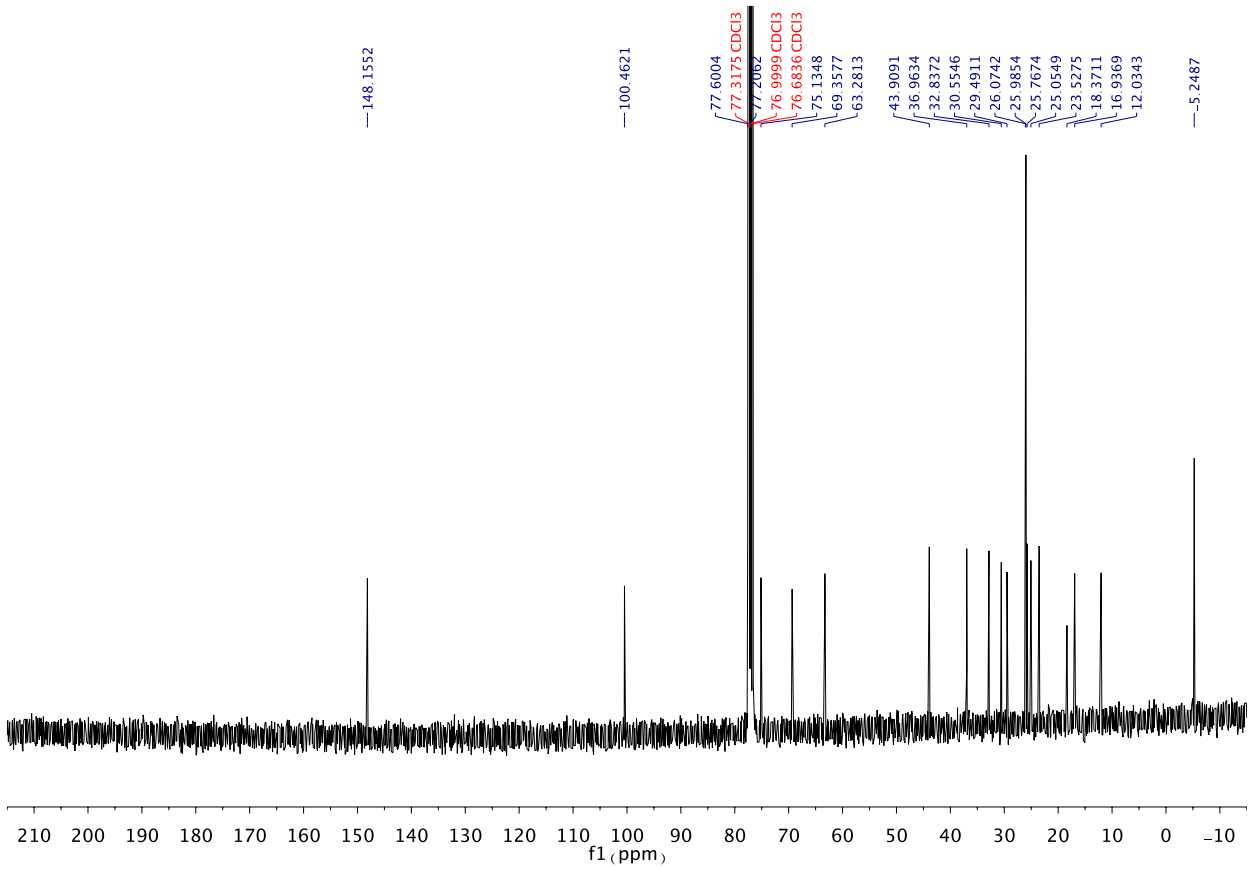
^{1}H NMR spectrum of aldehyde **18** (400 MHz, $CDCl_3$).



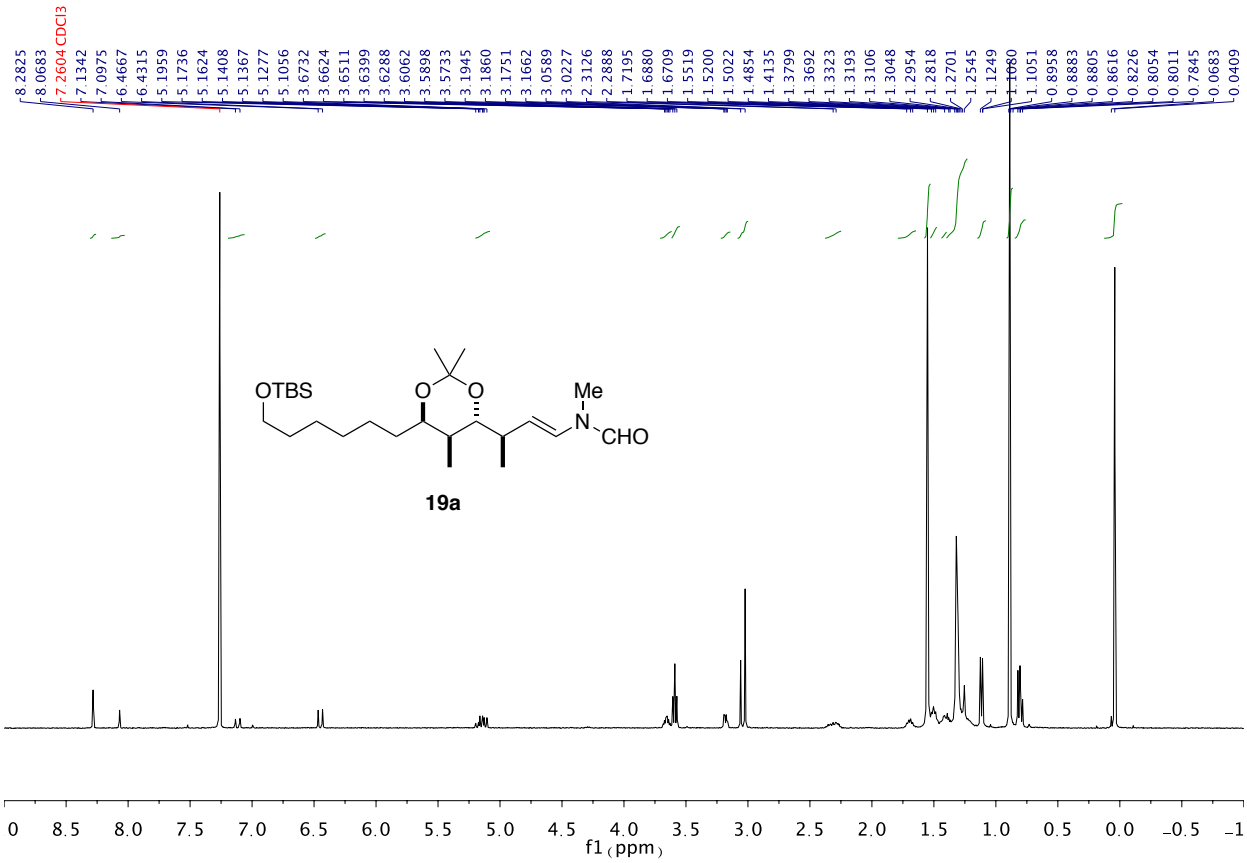
^{13}C NMR spectrum of aldehyde **18** (100 MHz, $CDCl_3$).



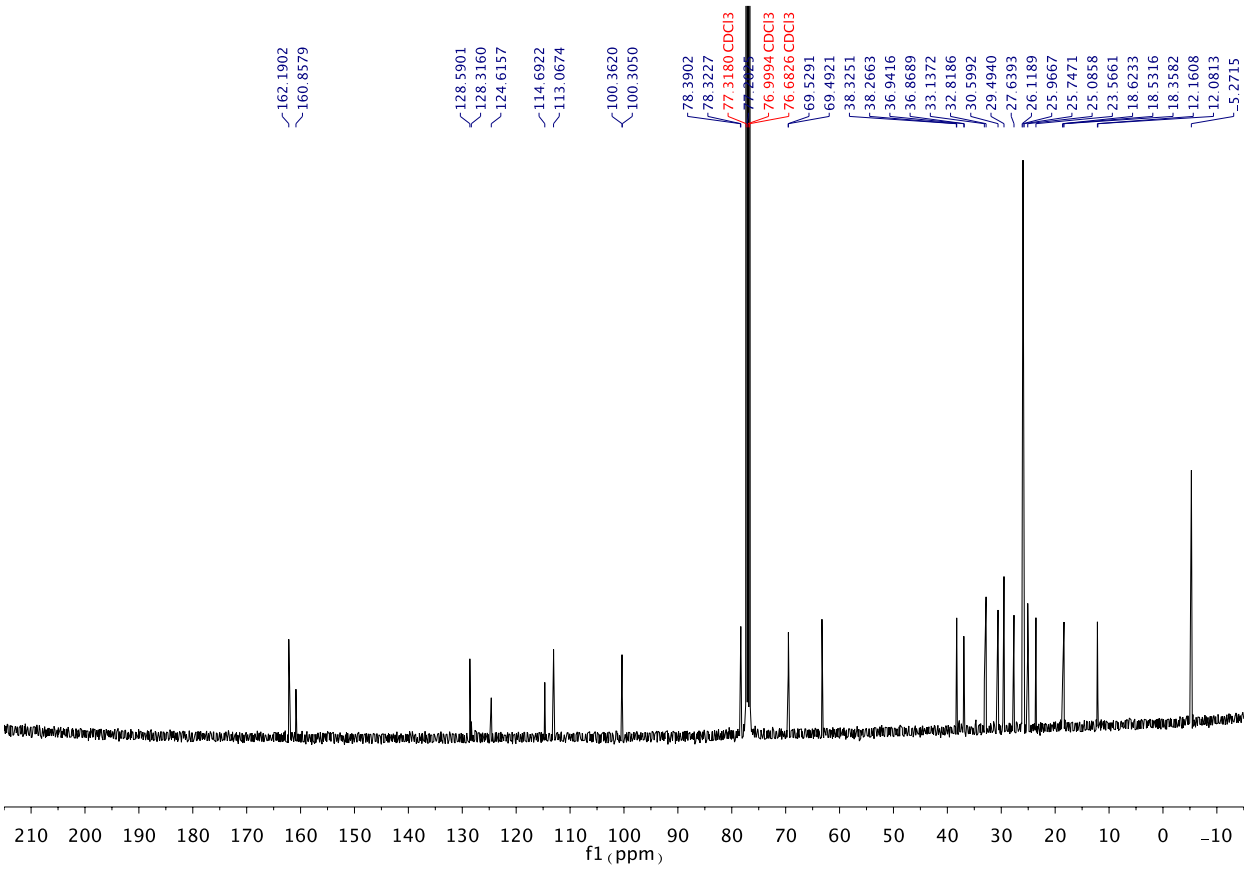
^{1}H NMR spectrum of iodoolefin **19** (400 MHz, $CDCl_3$).



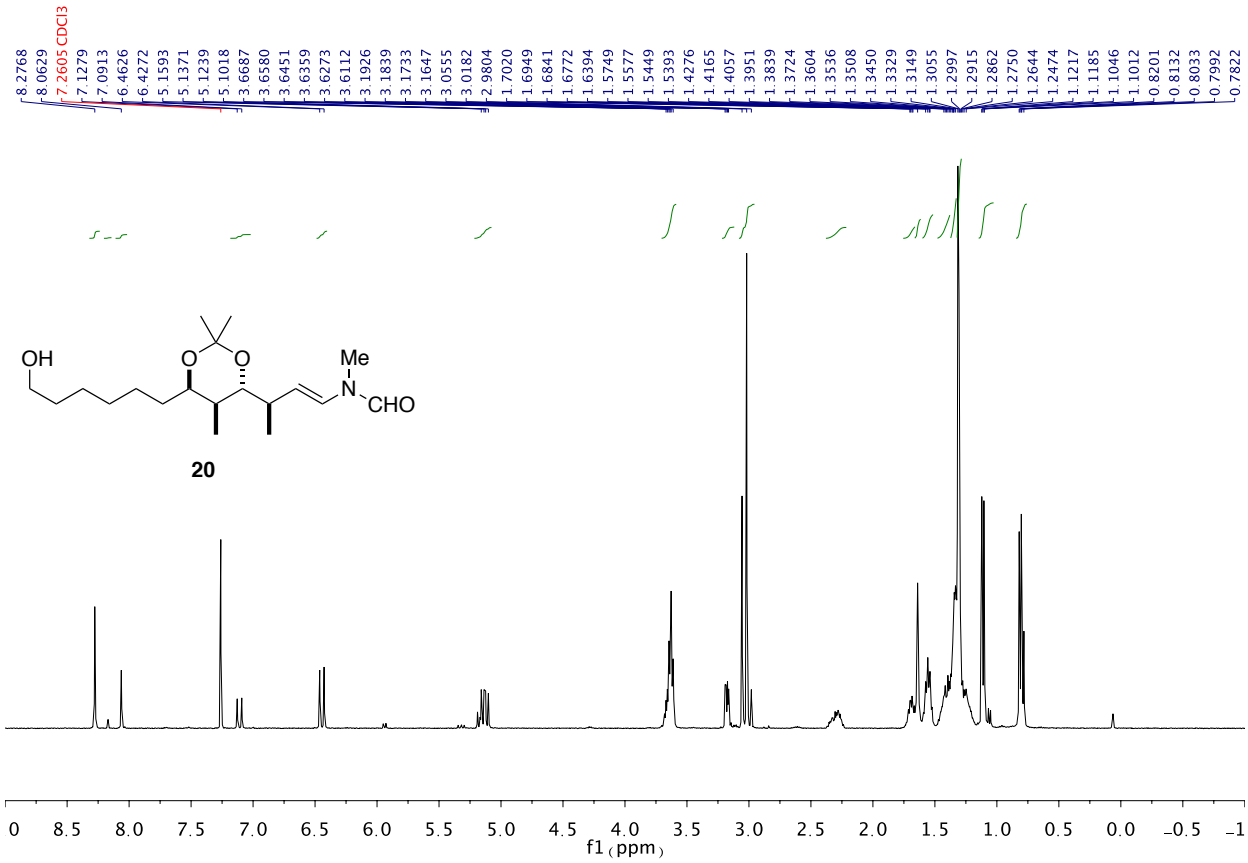
^{13}C NMR spectrum of iodoolefin **19** (100 MHz, $CDCl_3$).



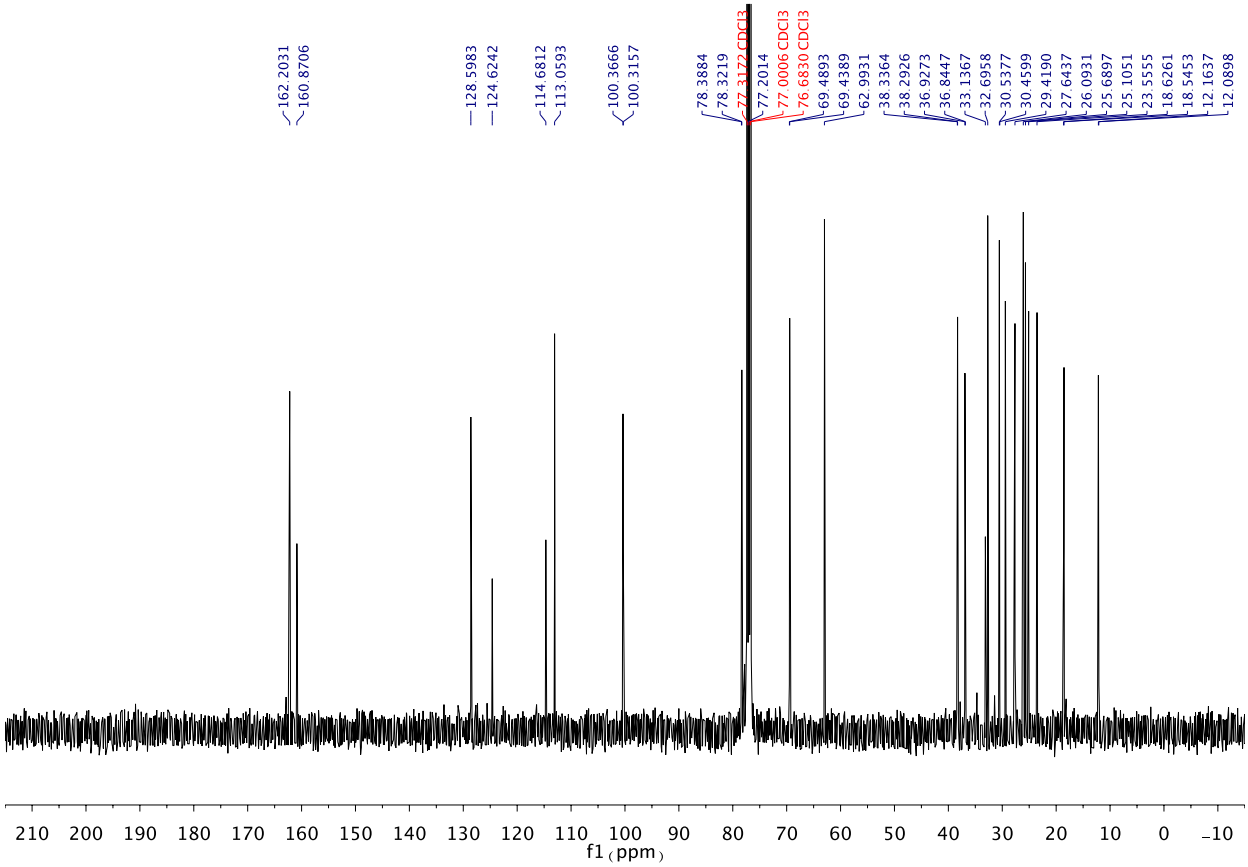
^{1}H NMR spectrum of enamide **19a** (400 MHz, $CDCl_3$).



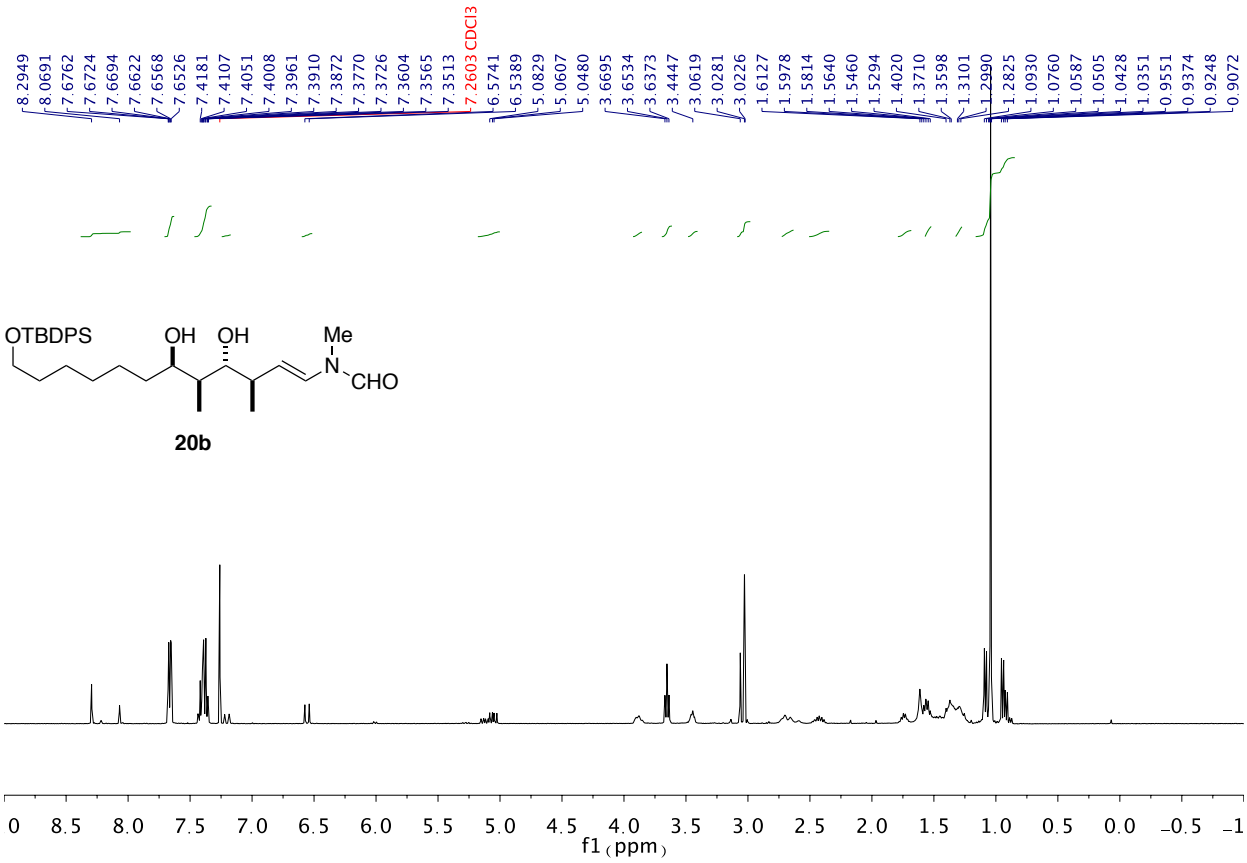
^{13}C NMR spectrum of enamide **19a** (100 MHz, $CDCl_3$).



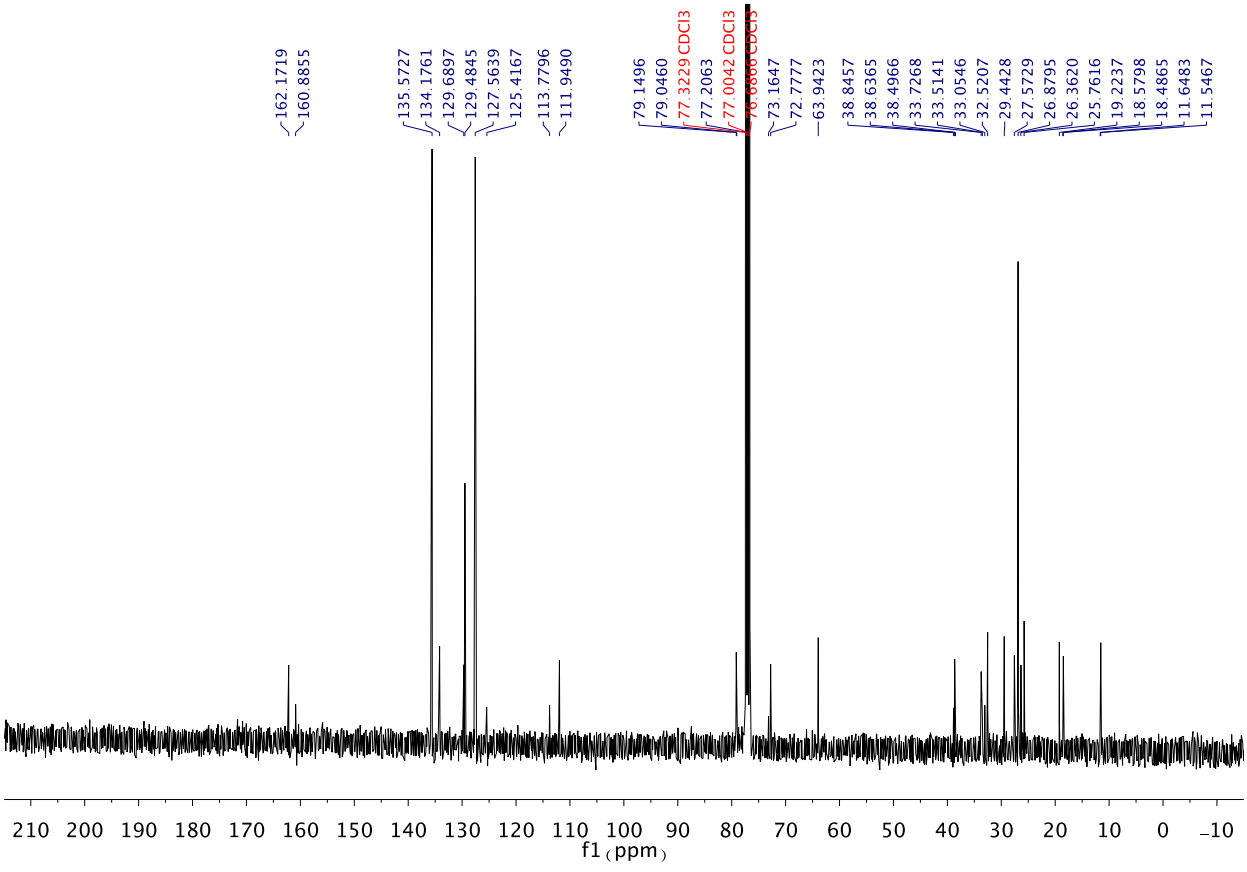
^{1}H NMR spectrum of primary alcohol **20** (400 MHz, $CDCl_3$).



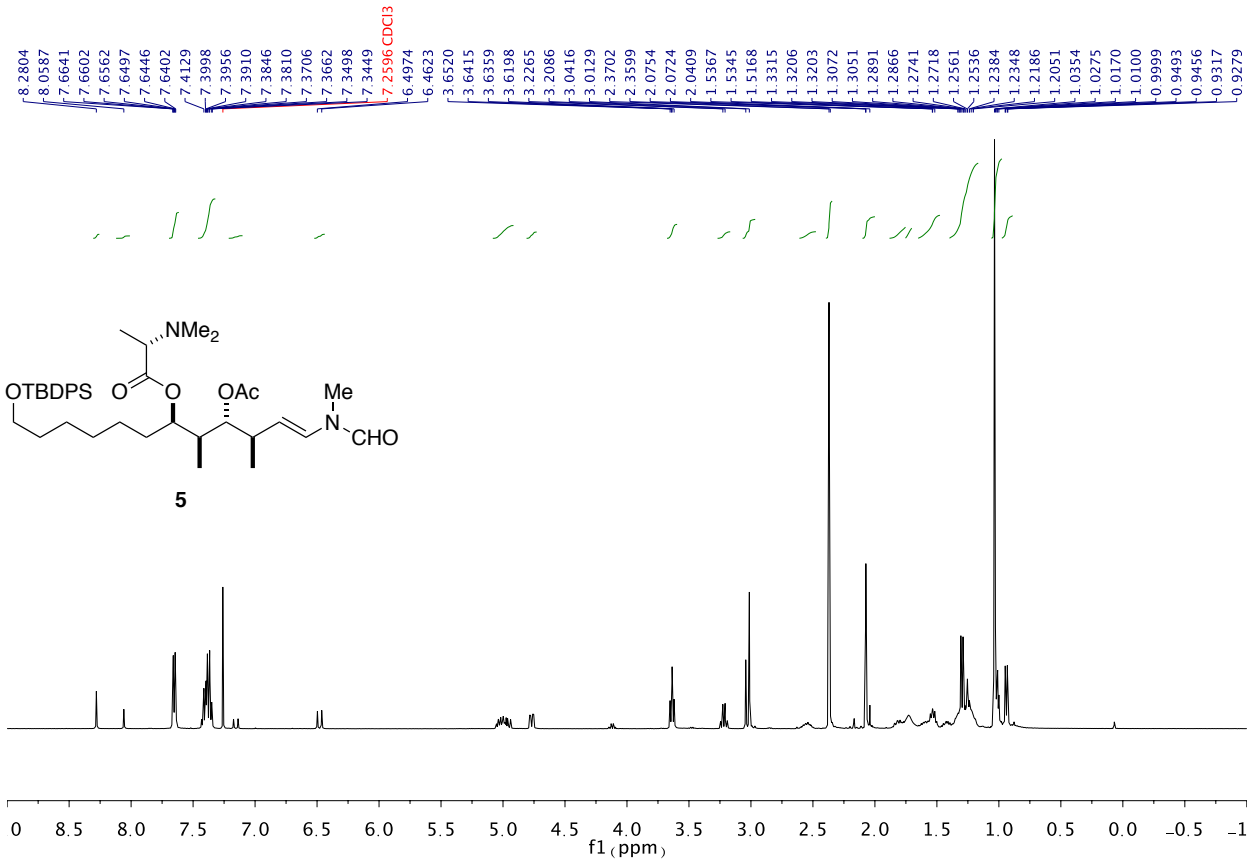
^{13}C NMR spectrum of primary alcohol **20** (100 MHz, $CDCl_3$).



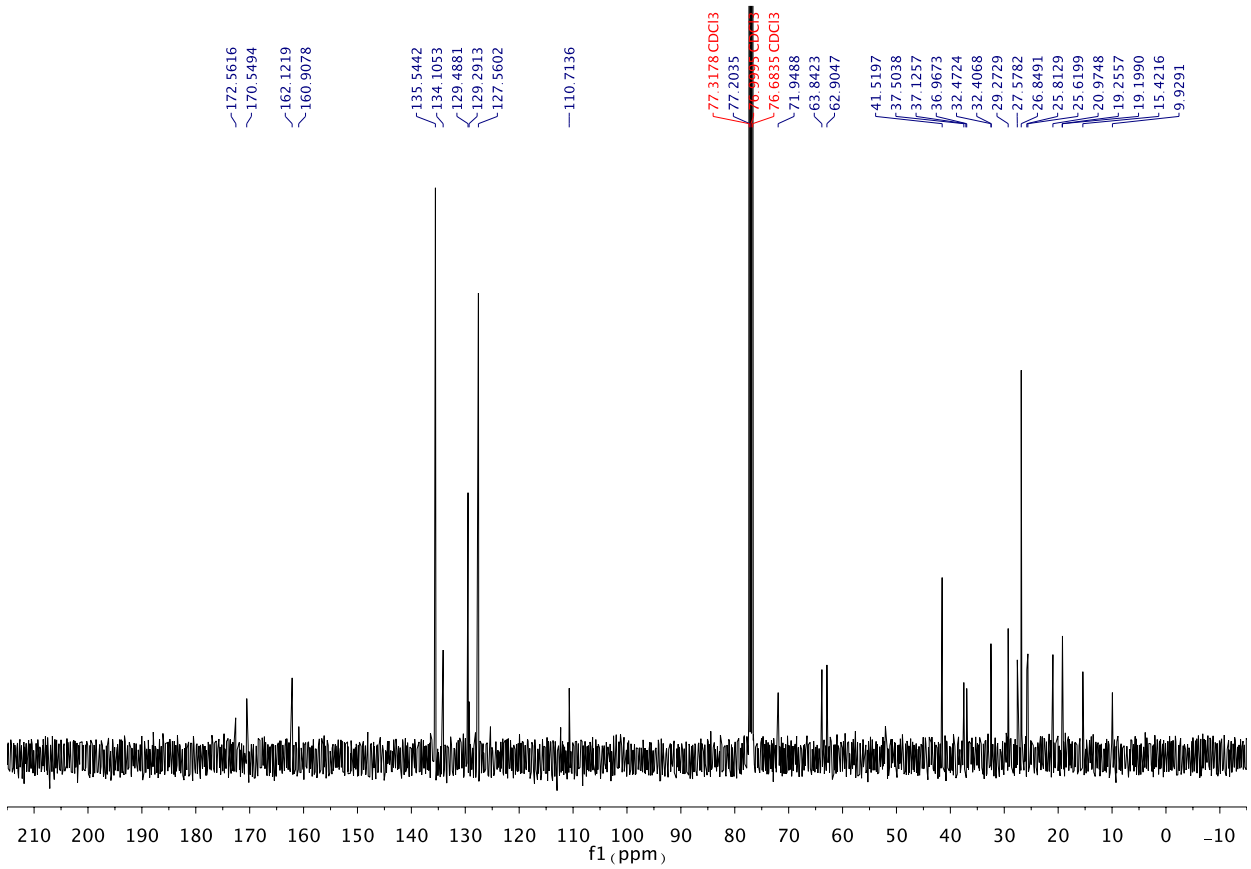
^{1}H NMR spectrum of silyl ether **20b** (400 MHz, $CDCl_3$).



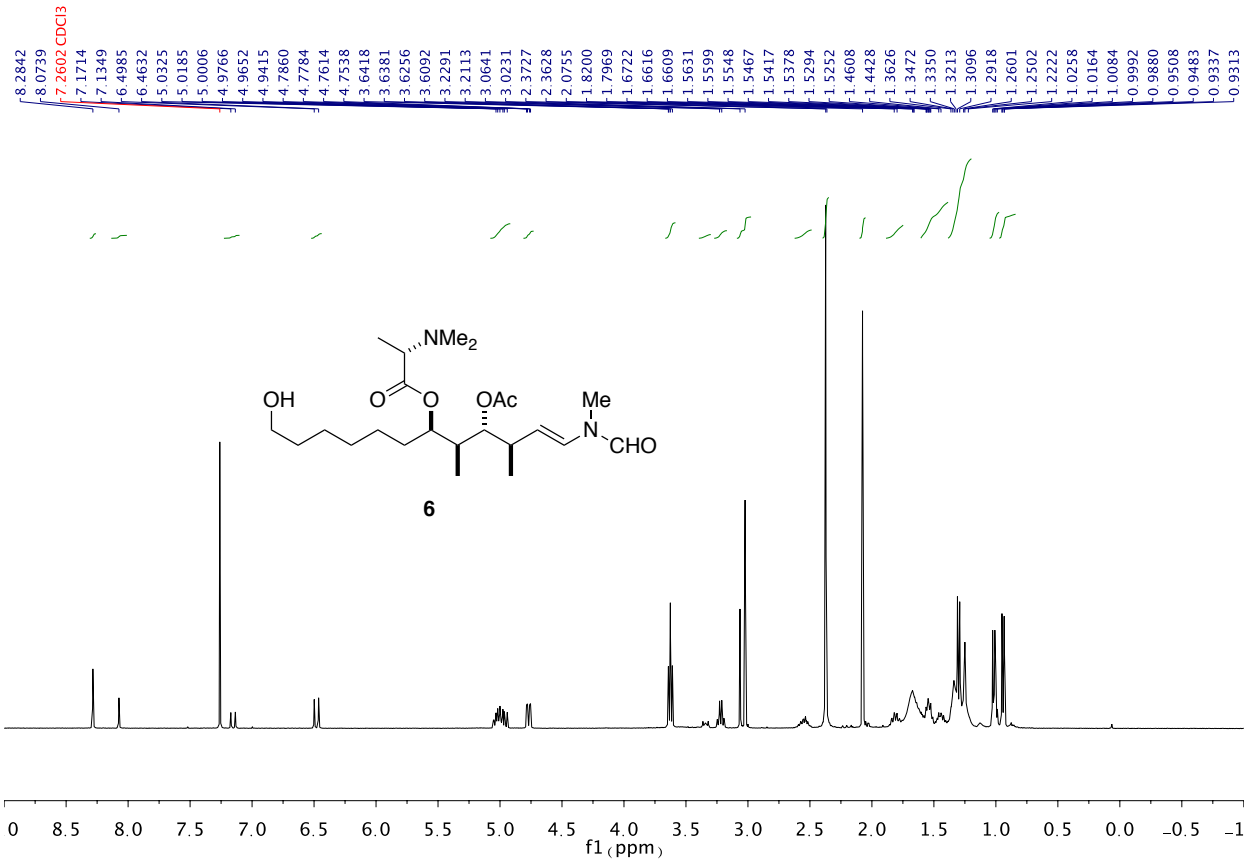
^{13}C NMR spectrum of silyl ether **20b** (100 MHz, $CDCl_3$).



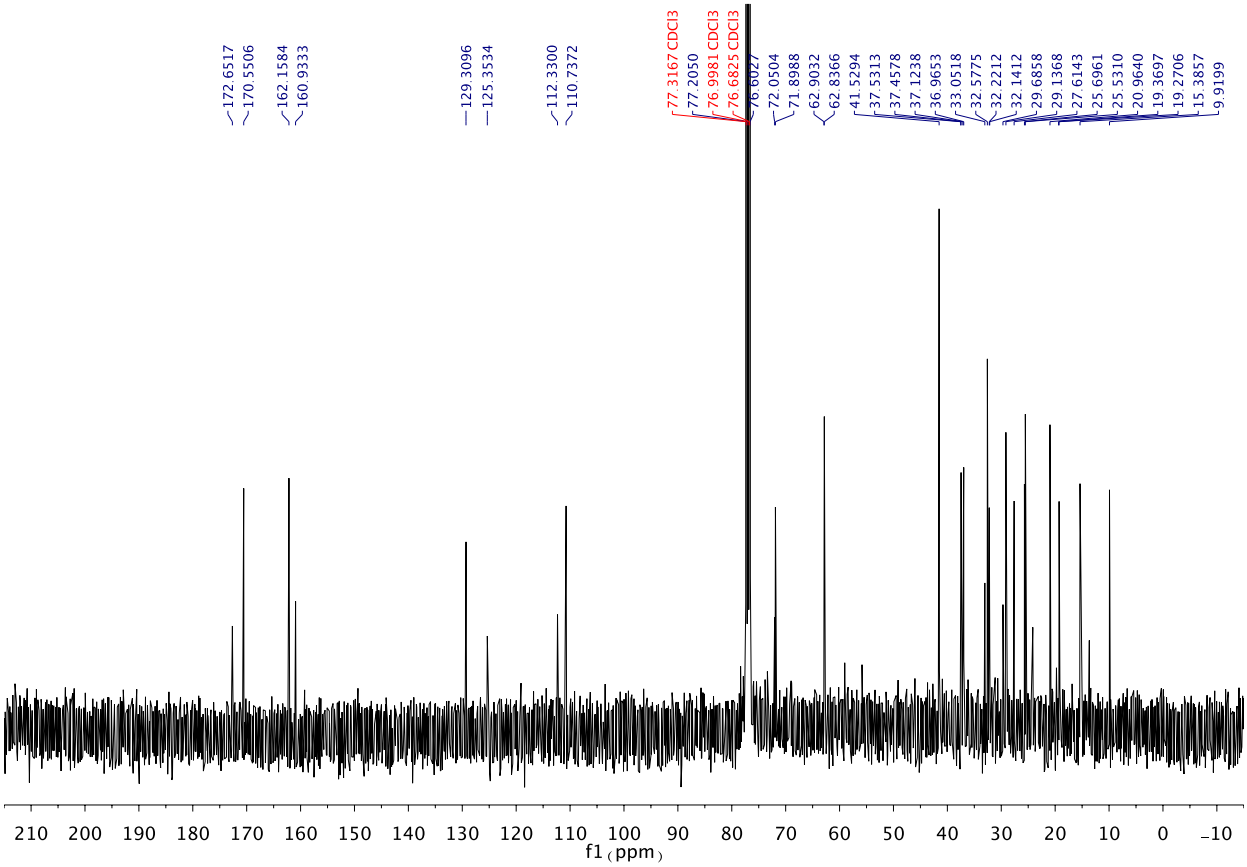
^{1}H NMR spectrum of DMAla ester **5** (400 MHz, $CDCl_3$).



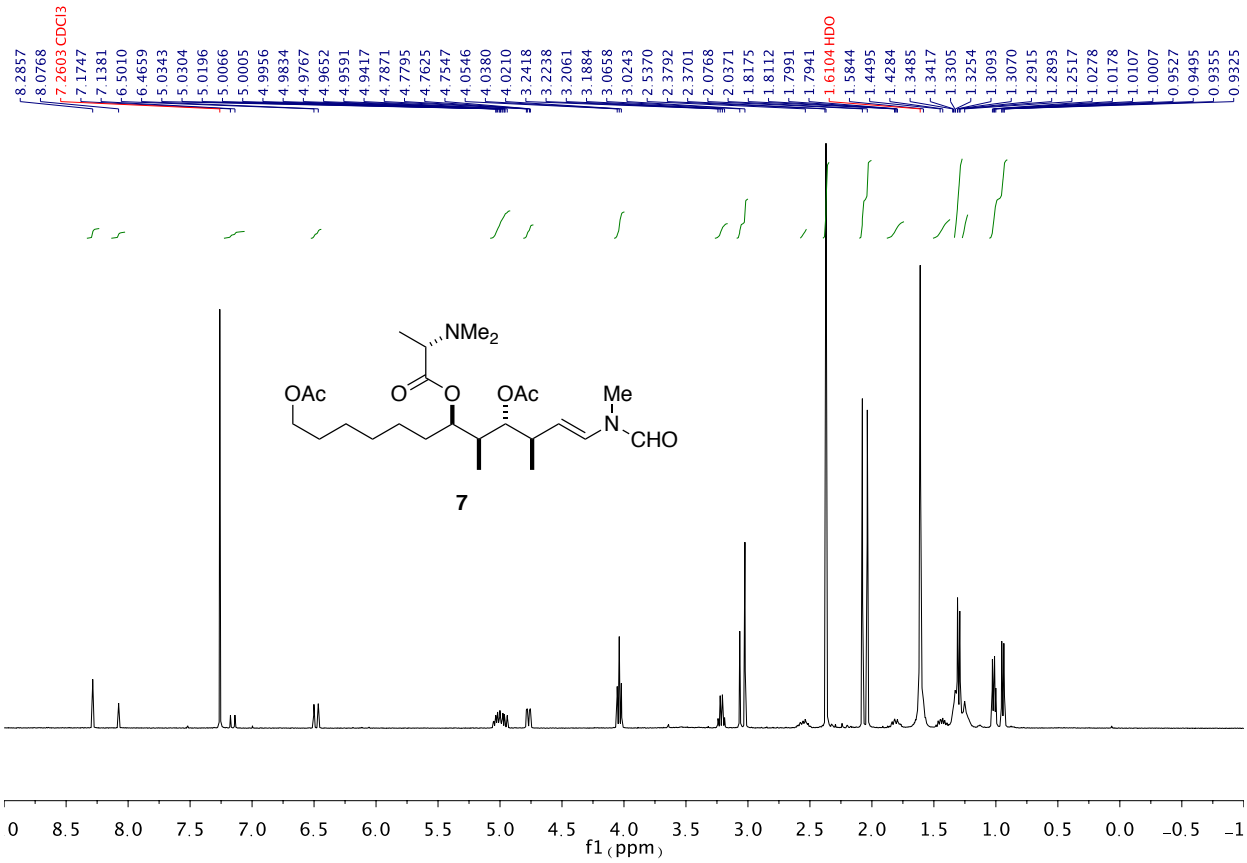
^{13}C NMR spectrum of DMAla ester **5** (100 MHz, $CDCl_3$).



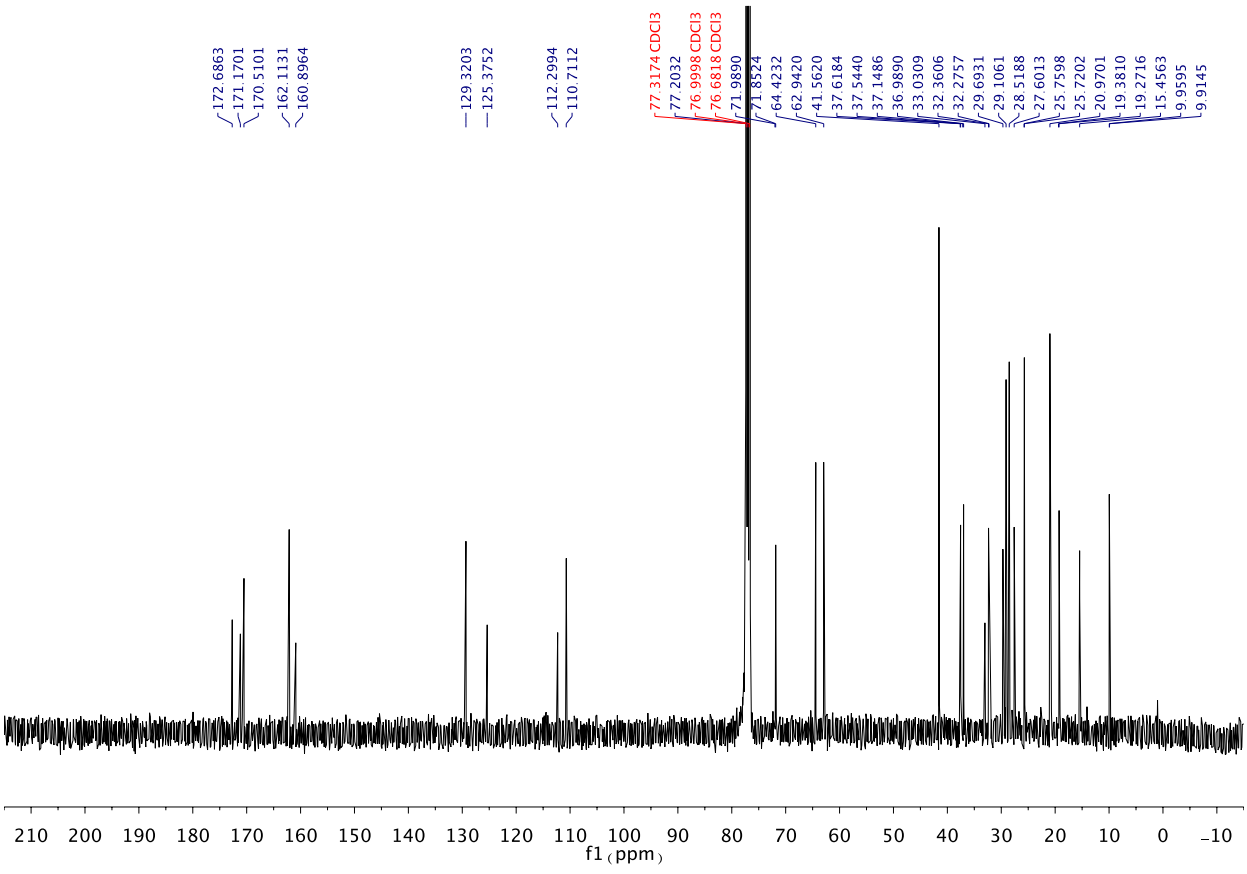
^{1}H NMR spectrum of primary alcohol **6** (400 MHz, $CDCl_3$).



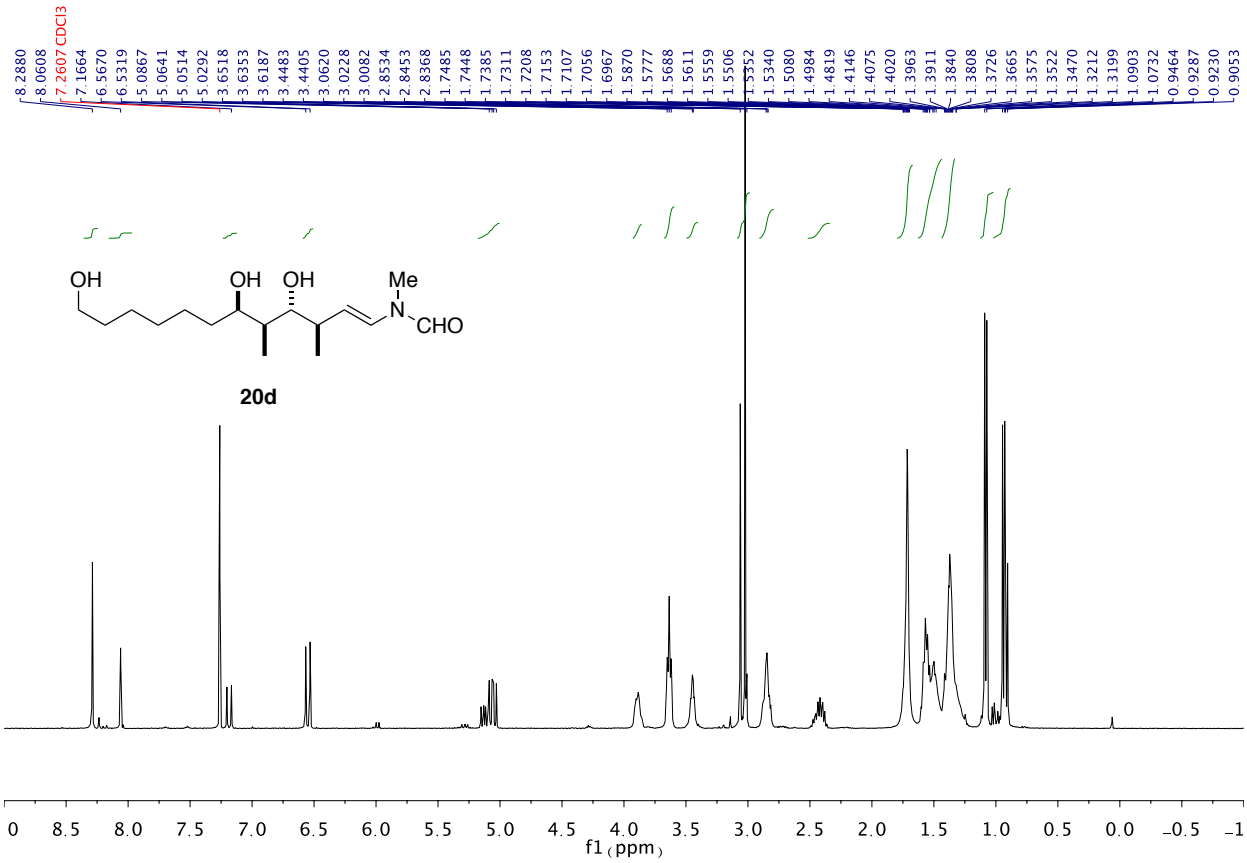
^{13}C NMR spectrum of primary alcohol **6** (100 MHz, $CDCl_3$).



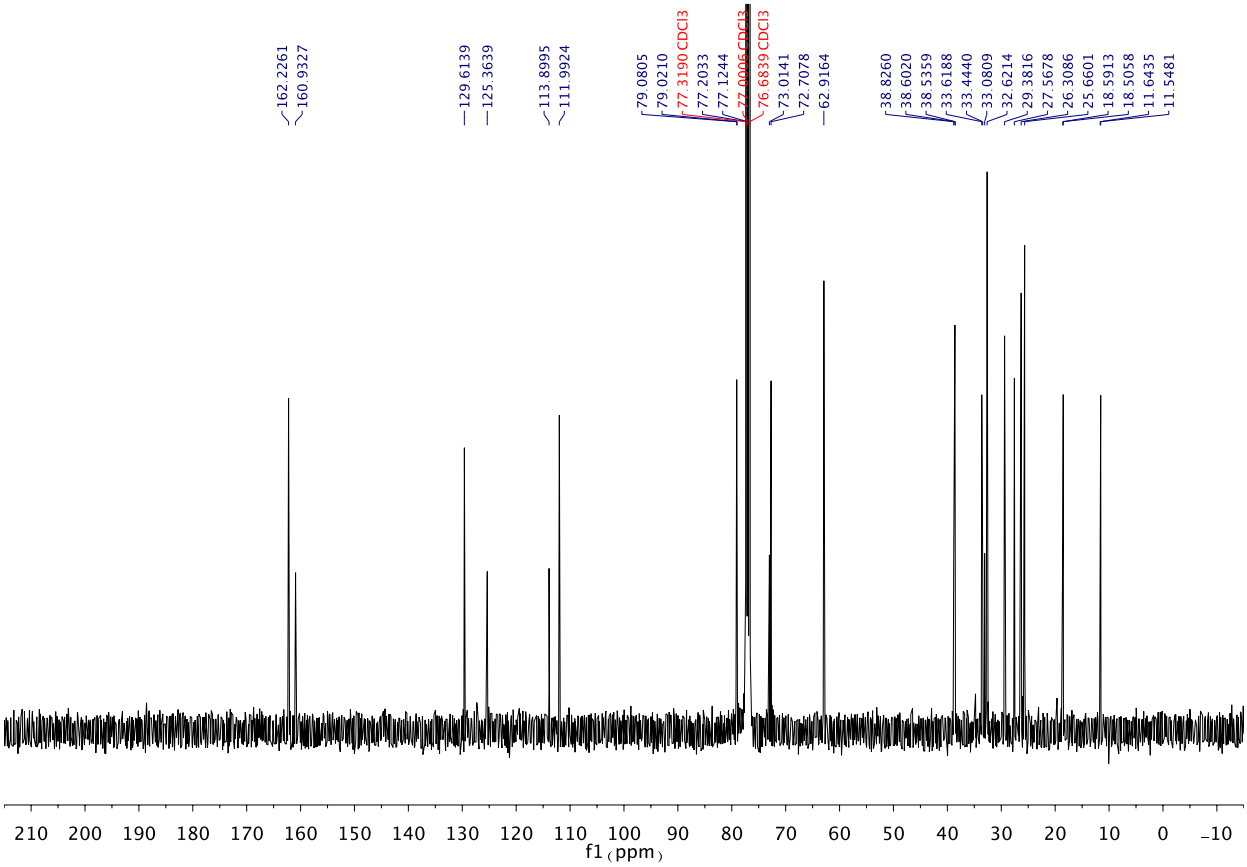
^{1}H NMR spectrum of analog **7** (400 MHz, $CDCl_3$).



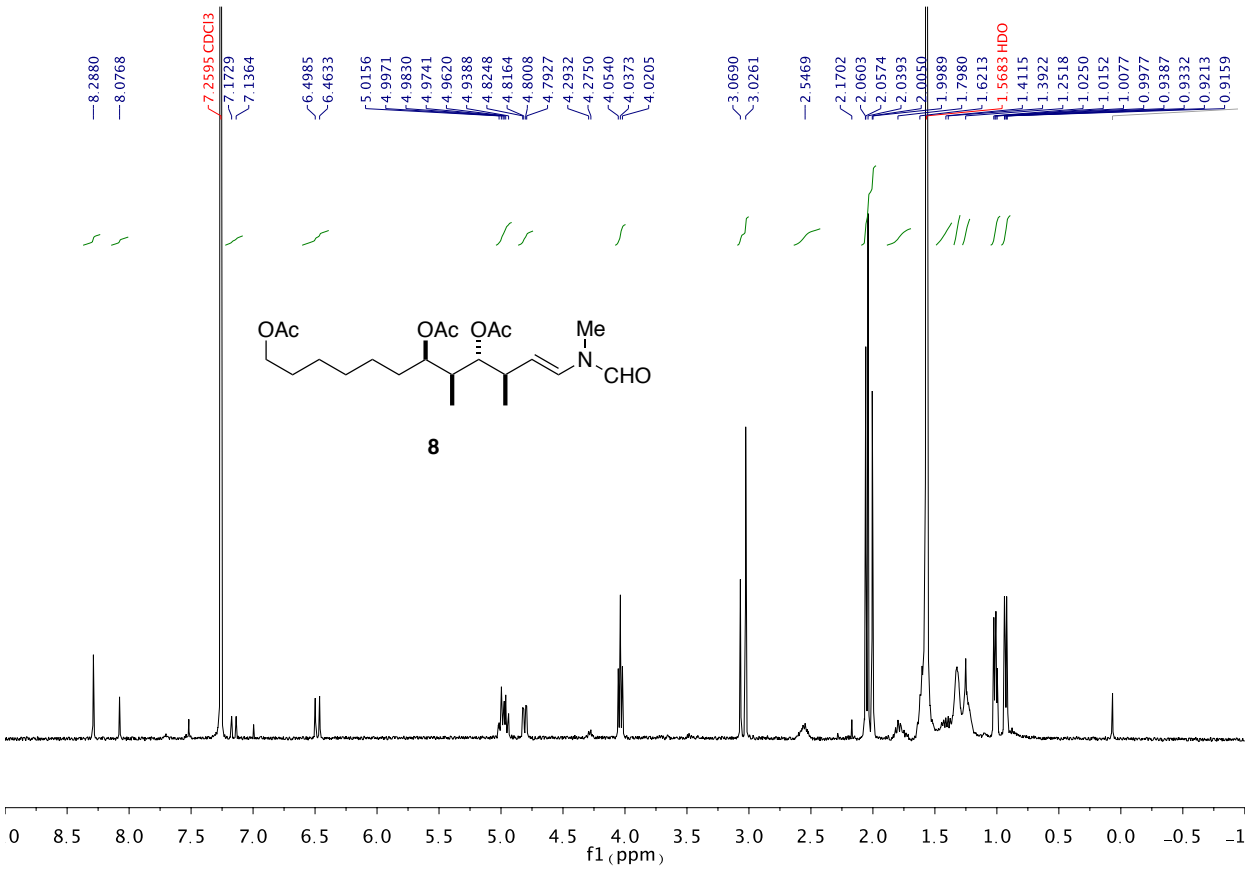
^{13}C NMR spectrum of analog **7** (100 MHz, $CDCl_3$).



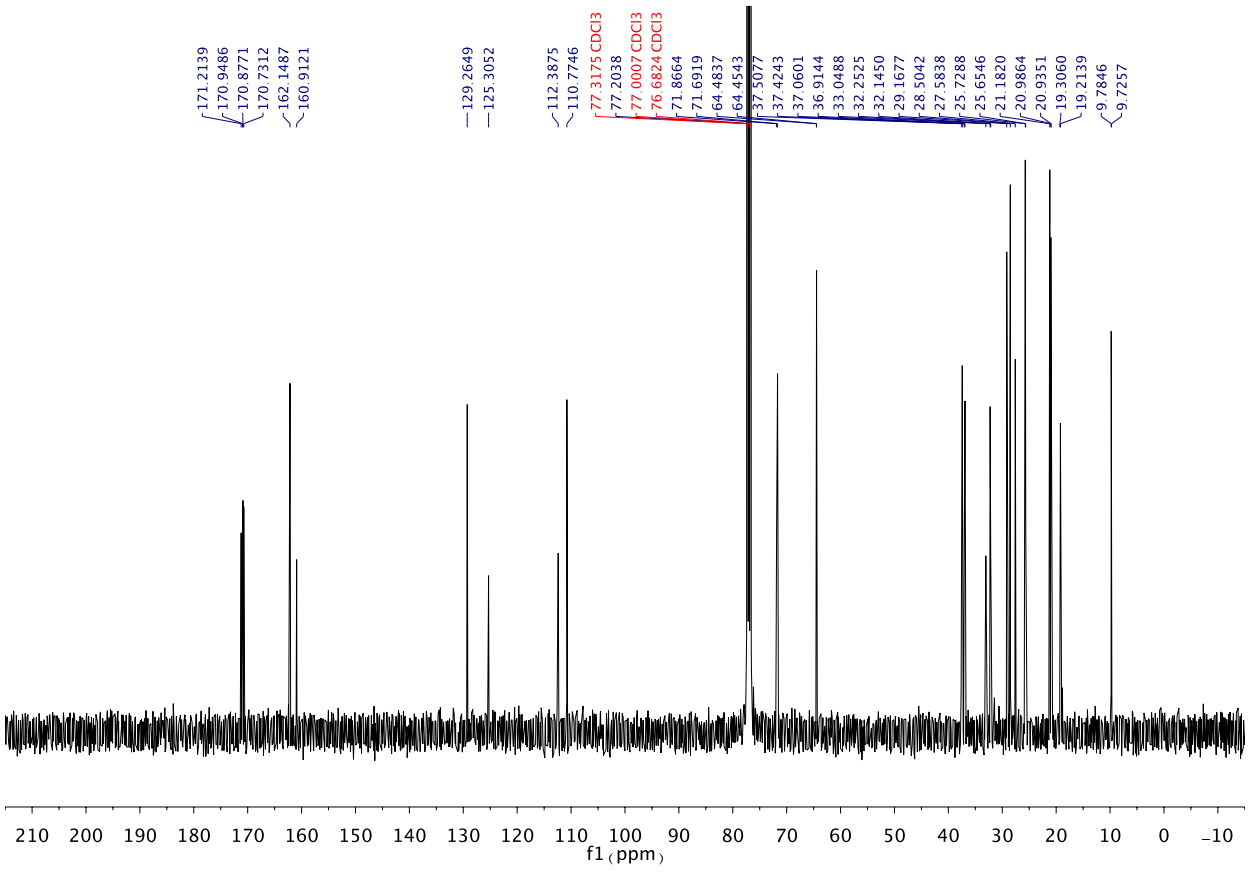
^{1}H NMR spectrum of triol **20d** (400 MHz, $CDCl_3$).



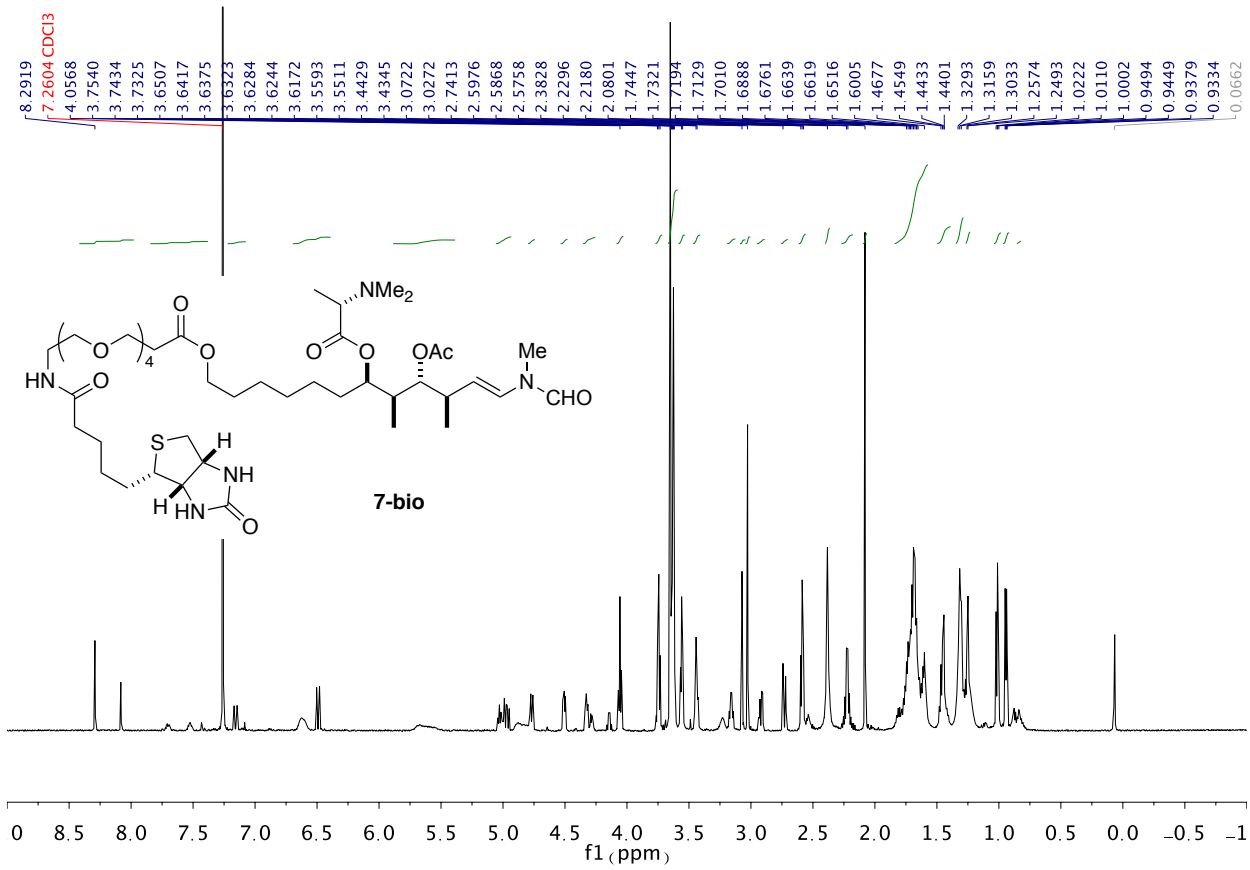
^{13}C NMR spectrum of triol **20d** (100 MHz, $CDCl_3$).



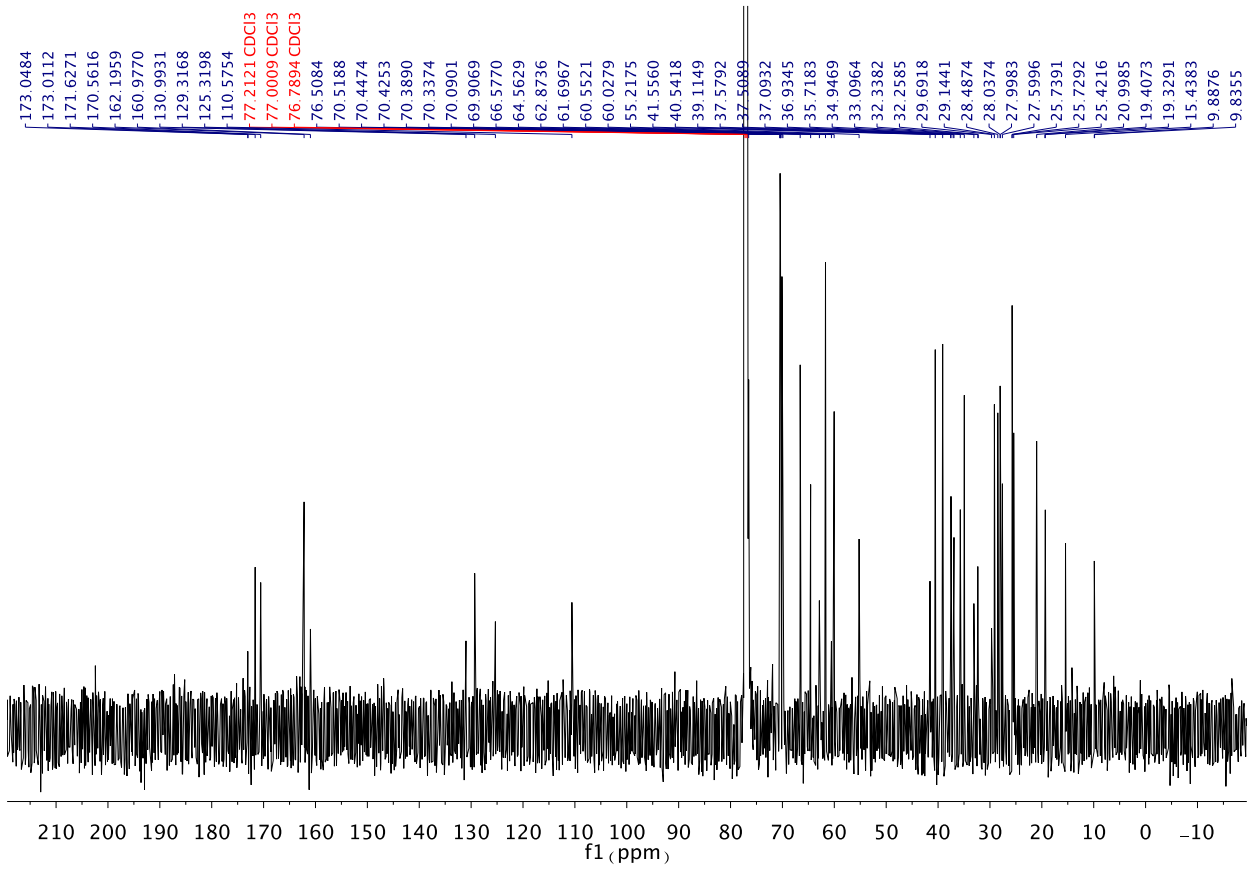
^{1}H NMR spectrum of analogue **8** (400 MHz, $CDCl_3$).



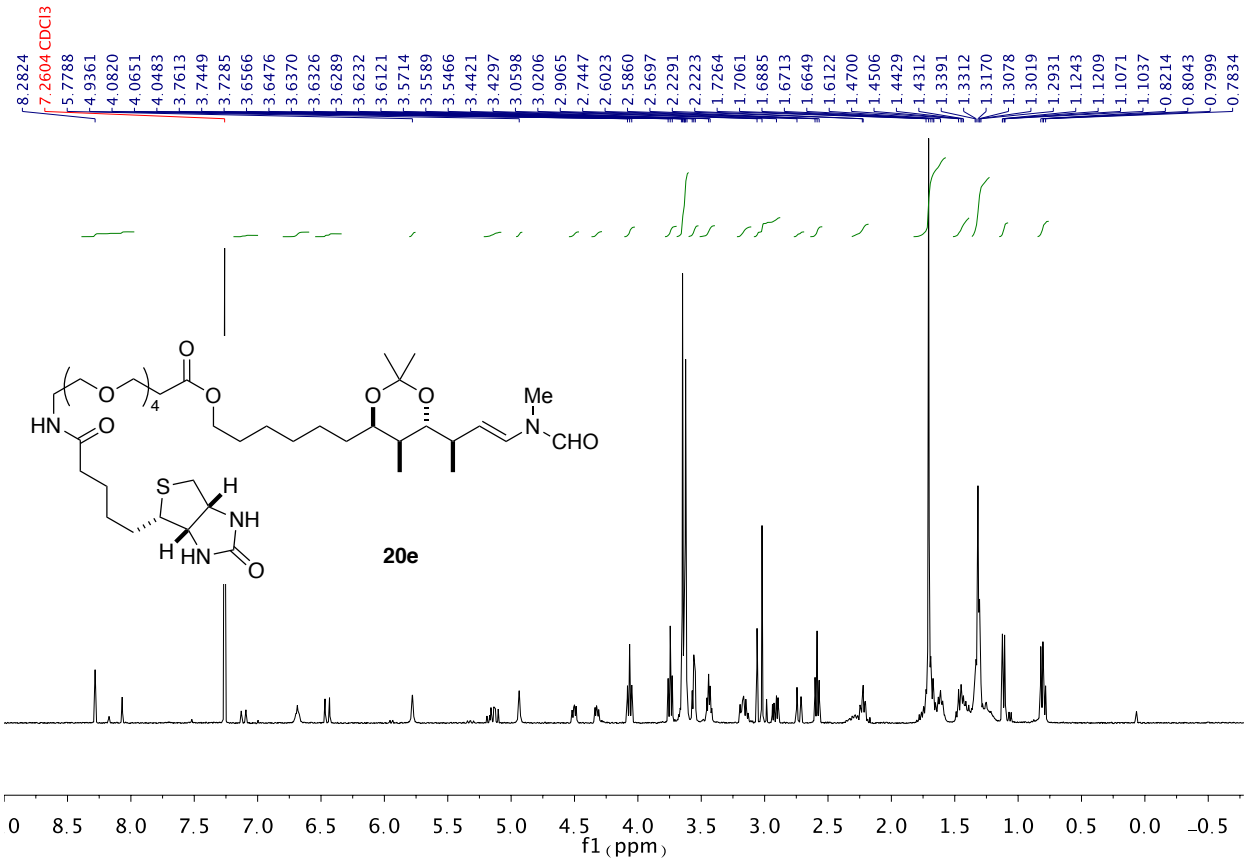
^{13}C NMR spectrum of analogue **8** (100 MHz, $CDCl_3$).



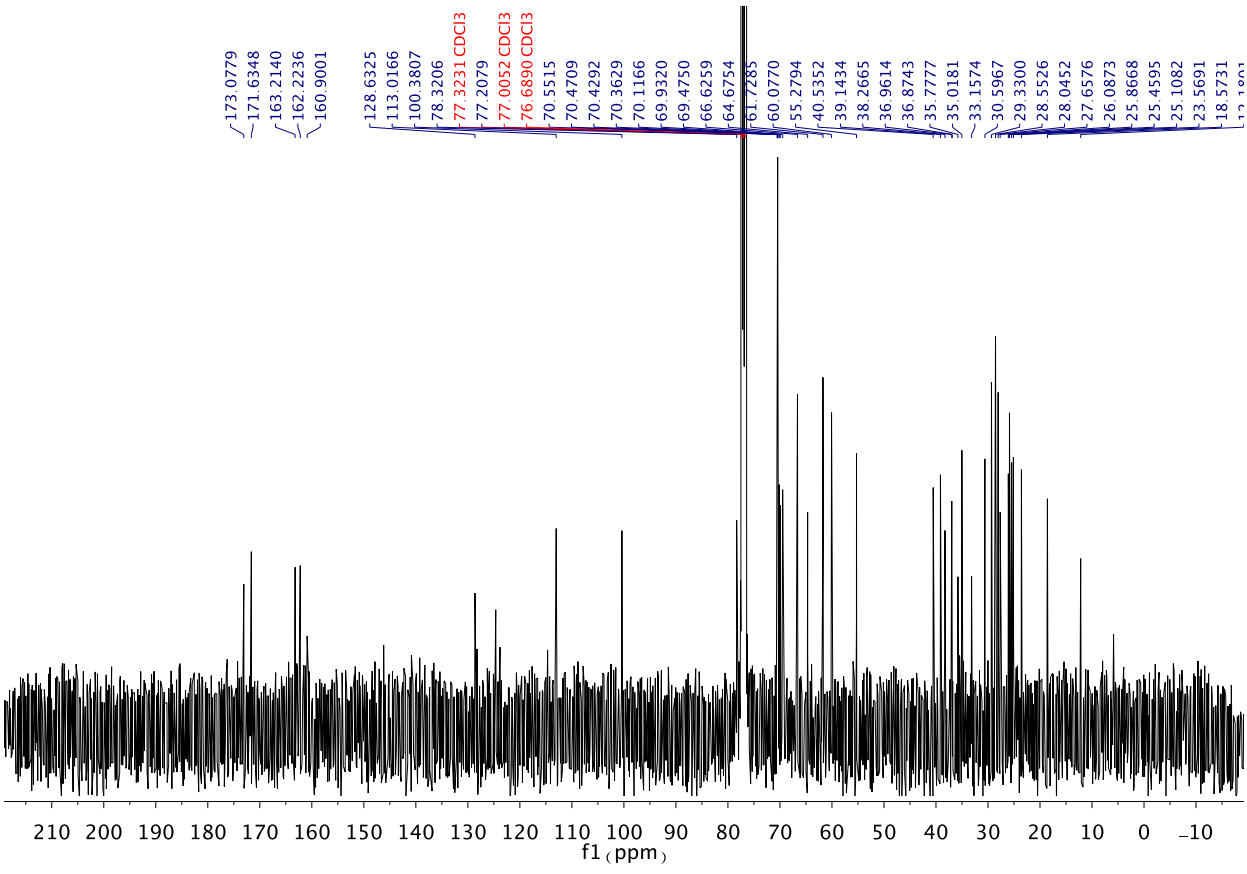
^{1}H NMR spectrum of analogue **7-bio** (600 MHz, $CDCl_3$).



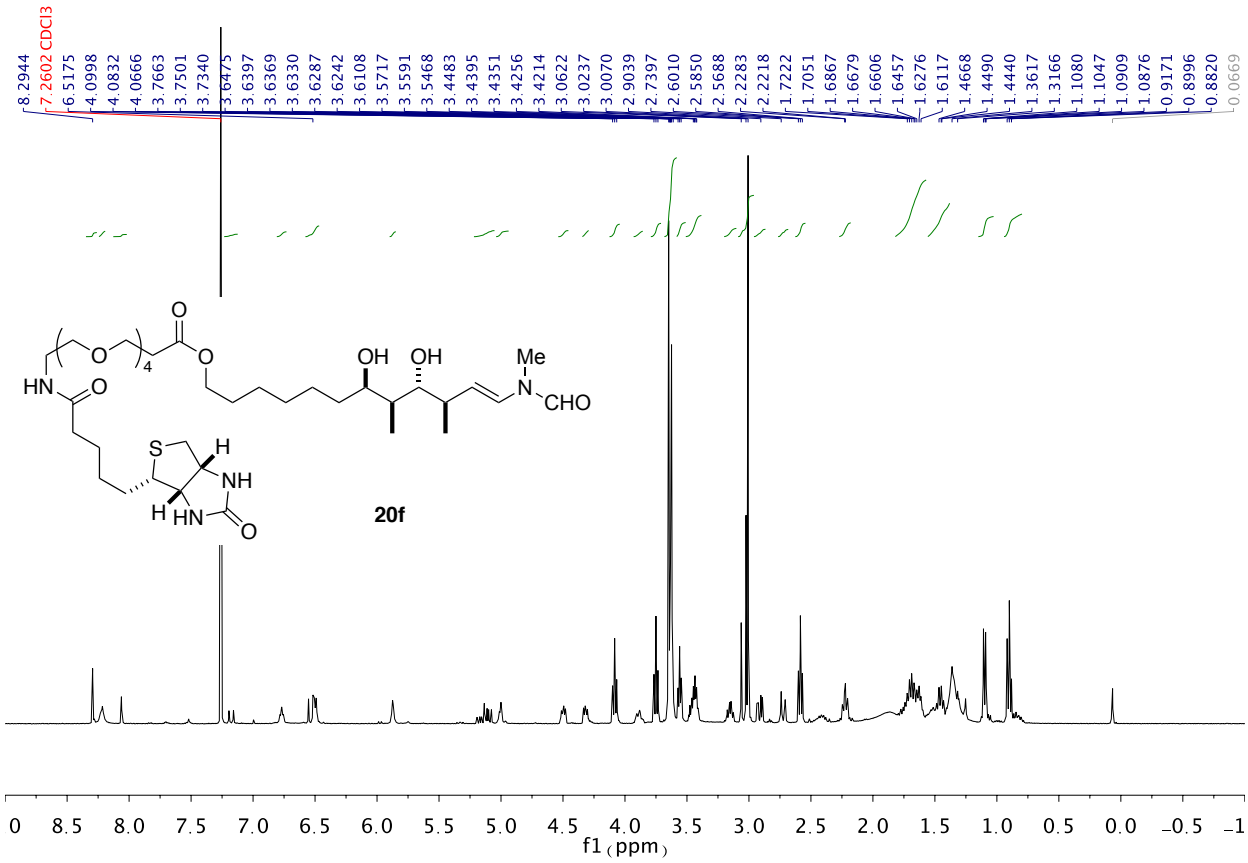
^{13}C NMR spectrum of analogue **7-bio** (150 MHz, $CDCl_3$).



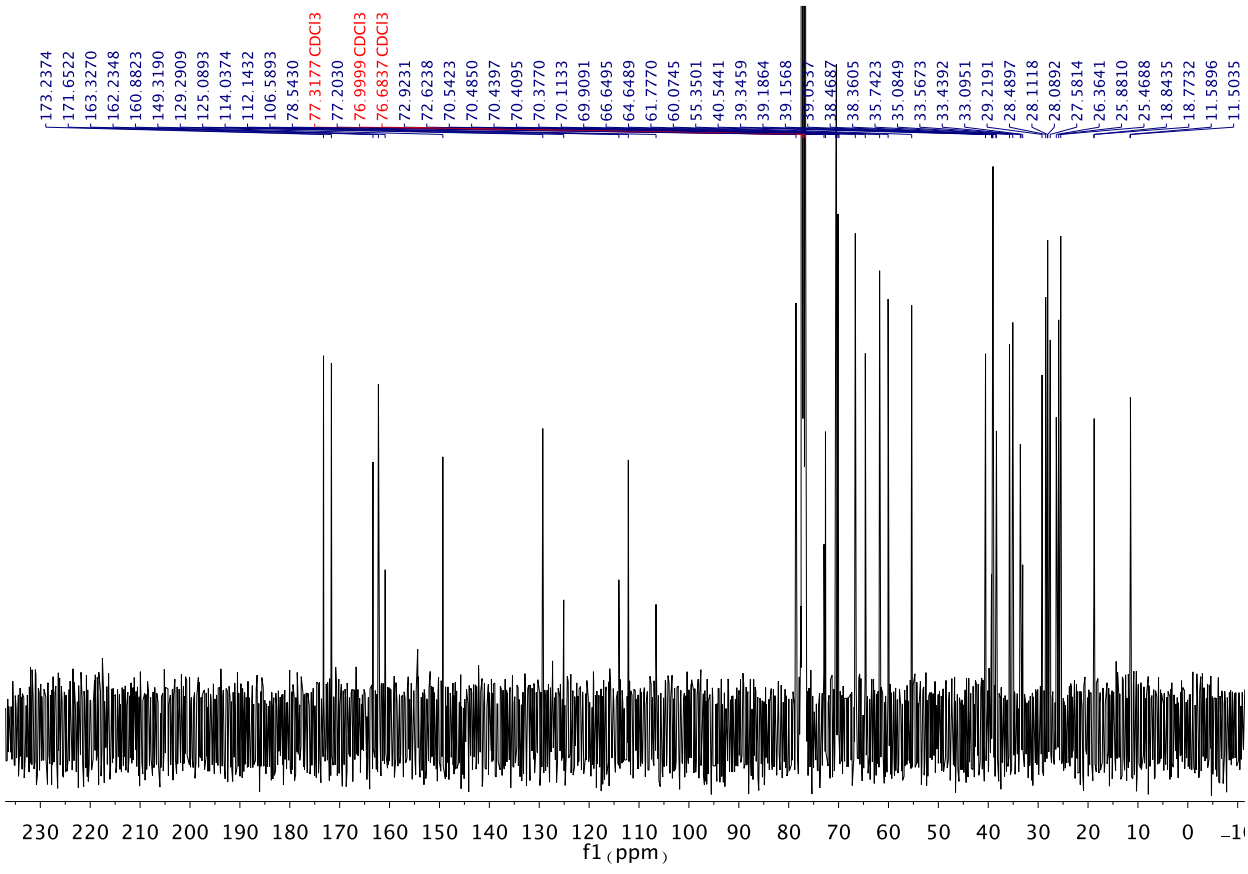
^{1}H NMR spectrum of analogue **20e** (400 MHz, $CDCl_3$).



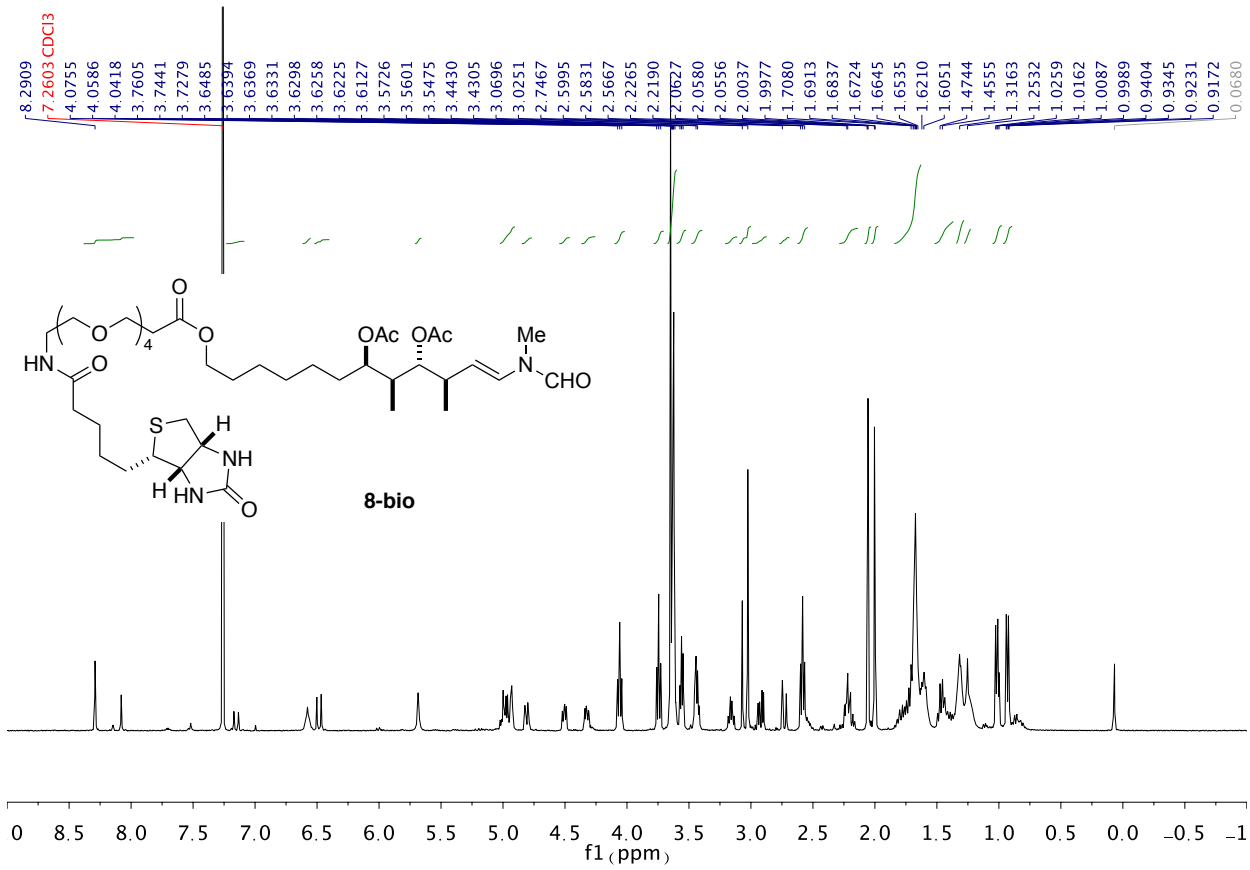
^{13}C NMR spectrum of analogue **20e** (100 MHz, $CDCl_3$).



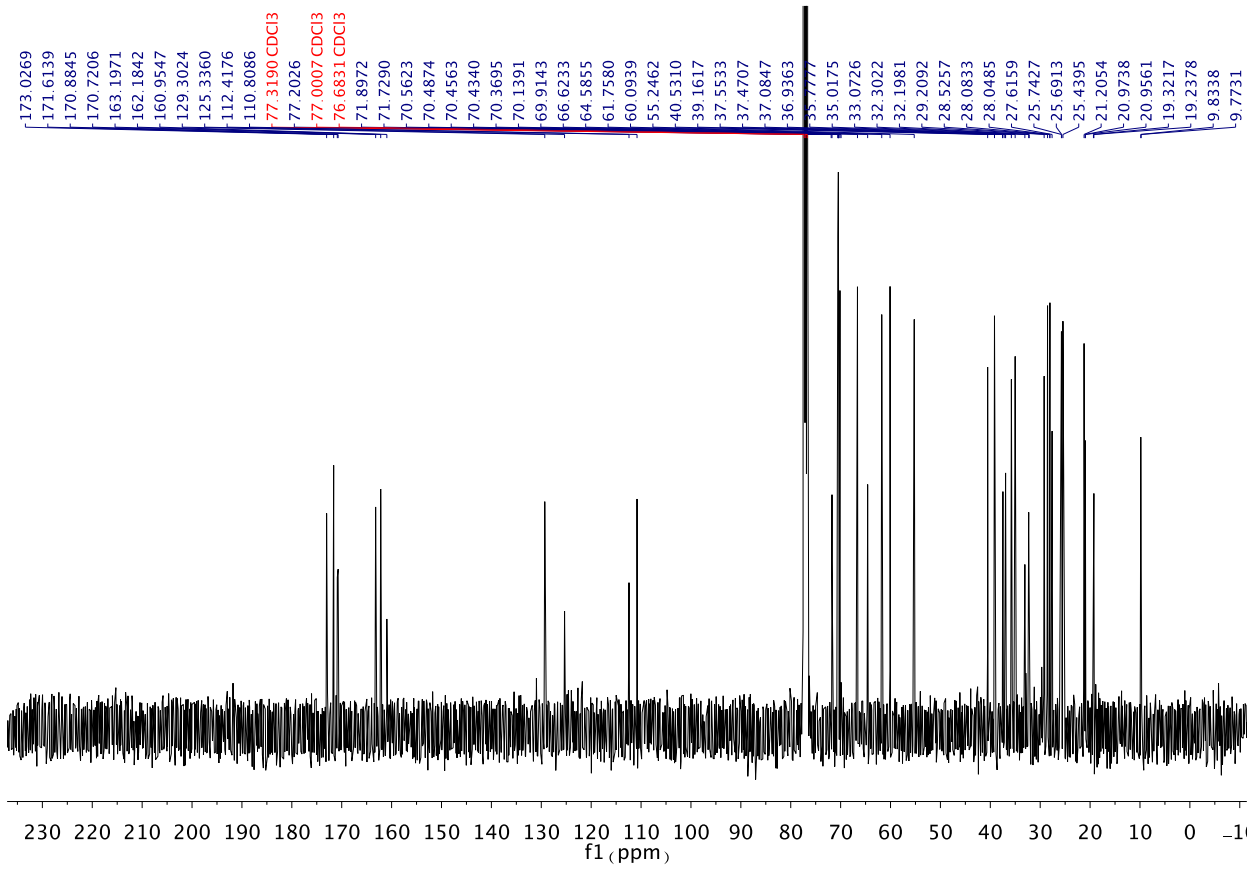
^{1}H NMR spectrum of analogue **20f** (400 MHz, $CDCl_3$).



^{13}C NMR spectrum of analogue **20f** (100 MHz, $CDCl_3$).



^{1}H NMR spectrum of analogue **8-bio** (400 MHz, $CDCl_3$).



^{13}C NMR spectrum of analogue **8-bio** (100 MHz, $CDCl_3$).