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1. Supporting Methods

1.1. *Pristionchus pacificus* metabolite naming. All newly identified compounds are named with four letter "SMID"s (Small Molecule IDentifiers), e.g. "icas#3" or "ascr#10" or "npar#1". The SMID database (www.smid-db.org) is an electronic resource maintained by Frank C. Schroeder and Lukas Mueller at the Boyce Thompson Institute in collaboration with Paul Sternberg and WormBase (www.wormbase.org). This database catalogues newly identified nematode small molecules, assigns a unique four-letter SMID (a searchable, gene-style Small Molecule IDentifier), and for each compound includes a list of other names and abbreviations used in the literature. In this work, we introduce the following new four-letter SMIDs: pasc (**p**henylethanolamide **asc**aroside), ubas (3-**u**reido iso**b**utyrate **as**caroside), dasc (**d**imeric **asc**aroside), part (**par**a**t**oside), and npar (**n**ucleoside-based **par**atoside).

1.2. Analytical instrumentation. NMR spectra were recorded on a Varian INOVA-600 (600 MHz for ^{1}H, 151 MHz for ^{13}C), INOVA-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C), and INOVA-400 (400 MHz for ^{1}H, 100 MHz for ^{13}C) instruments. HPLC-MS, MS/MS, and single-ion monitoring (SIM-LCMS) was performed using an Agilent 1100 Series HPLC system equipped with a diode array detector and connected to a Quattro II spectrometer (Micromass/Waters). High resolution mass spectra were acquired using a Xevo G2 QTOF mass spectrometer. Flash chromatography was performed using a Teledyne ISCO CombiFlash system. HPLC fractionation was performed using an Agilent 1100 Series HPLC system equipped with an Agilent Eclipse XDB-C18 column (9.4 x 250 mm, 5 µm particle diameter) coupled to a Teledyne ISCO Foxy 200 fraction collector.

1.3. *P. pacificus* strains and culture conditions. The following *P. pacificus* strains were used for this study: RS2333 (exo-metabolome preparation), RS5134 (dauer formation assay), RSB020 (mouth-form dimorphism assay). Plates and liquid cultures of worms were prepared as described previously.[1] For axenic cultures, *P. pacificus* (RS2333) gravid adults from ten 10 cm plates were washed with M9 buffer and treated with alkaline hypochlorite solution to isolate eggs.[2] Isolated eggs were washed thoroughly with M9 buffer and allowed to hatch in fresh sterile M9 for 24 h. The resulting synchronized *J2* larvae were transferred to the modified chemically defined growth medium described earlier[3] and allowed to grow for 26 days at 20 °C and 80 rpm. After 26 days the population consisted of mostly of gravid adults and large numbers of *J2* larvae.

1.4. Preparation of exo-metabolome extracts and preliminary fractionation. 3 L culture supernatant of *P. pacificus* strain RS2333 was filtered and centrifuged at 10,000 rpm for 10 min. The culture supernatant was applied to a C18 column (Chromabond, Macherey Nagel), which was followed by elution with 50% MeOH in H_2O. This step removed strongly lipophilic components (e.g. triglycerides, long-chain fatty acids) but did not reduce bioactivity. The eluate was evaporated and resuspended with mixture of chloroform and methanol (2:1). The sample was applied to a SiOH column (Chromabond, Macherey Nagel) equilibrated with chloroform/methanol (2:1). The column was washed with chloroform/methanol (2:1, fraction I), chloroform/methanol (1:5, fraction II), and chloroform/methanol/water (6:10:1, fraction III). Fraction II showed the most activity in subsequent dauer formation assays and was used for 2D NMR spectroscopic analysis. Several additional 1 L-batches of culture supernatant were processed analogously to obtain larger quantities of the compounds detected by 2D NMR.

For high-resolution HPLC-MS analysis, 100 mL sample of unfractionated culture supernatant were lyophilized to a fine powder, which was subsequently extracted with 50 mL of a 95:5 mixture of ethanol and water for 16 h. The extract was concentrated *in vacuo*, resuspended in 150 µL of methanol, filtered, and used for HPLC-MS. For bacterial control experiments. 1 L of *E. coli* OP50 bacteria culture grown overnight was lyophilized and extracted as described above.

For the analysis of *P. pacificus* axenic cultures, the culture was centrifuged at the end of the 26-day incubation period, and the supernatant was lyophilized and extracted with 50 mL of methanol. To remove the large amounts of glucose contained in the axenic medium, the extract was loaded onto 8 g of ethyl acetate-washed Celite® and filtered over a RediSep Rf GOLD 30 g HP C18 reverse-phase column using a water-methanol solvent gradient, starting with 15 min of 98% water, followed by a linear increase of methanol content up to 100% at 60 min. The first 300 mL of eluate contained mostly glucose and were discarded. The remainder of the eluate was concentrated *in vacuo*. The resulting extract was resuspended in 100 µL methanol, filtered, and analyzed by selective ion monitoring (SIM)-LCMS.

1.5. 2D NMR spectroscopic metabolome analyses. Non-gradient phase-cycled dqfCOSY spectra were acquired using the following parameters: 0.8 s acquisition time, 400-600 complex increments, 8-32 scans per increment. dqfCOSY spectra were zero-filled to 8k × 4k and a cosine bell-shaped window function was applied in both dimensions before Fourier transformation. Gradient and non-gradient HSQCAD and HMBC spectra were acquired using 0.25 s acquisition time and 256-500 complex increments. NMR spectra were processed using Varian VNMR, MestreLabs' MestReC, and MNova software packages.

1.6. HPLC protocol, LC-MS/MS, and SIM-LCMS analyses. HPLC-MS was performed using an Agilent 1100 Series HPLC system equipped with an Agilent Eclipse XDB-C18 column (9.4 x 250 mm, 5 µm particle diameter) connected to a Quattro II spectrometer (Micromass/Waters) using a 10:1 split. A 0.1% acetic acid-acetonitrile solvent gradient was used at a flow rate of 3.6 mL/min, starting with an acetonitrile content of 5% for 5 min which was increased to 100% over a period of 40 min. Exo-metabolome fractions were analyzed by HPLC-ESI-MS in negative and positive ion modes using a capillary voltage of 4.0 kV and a cone voltage of -40 V and +20 V respectively. LC-MS/MS screening for precursor ions of m/z = 73.0 (negative mode) performed using argon as collision gas at 2.1 mtorr and 40 eV. The HPLC protocol mentioned in this section is also used for synthetic sample purification as well as enrichment of minor components of the *P. pacificus* exo-metabolome. For the analysis of exo-metabolome samples from *P. pacificus* axenic cultures, the spectrometer was operated in selective ion monitoring (SIM) mode, and the following ions were selectively observed: *m/z* = 247 (ascr#9, part#9), 466 (pasc#9), 533 (dasc#1), 605 (ubas#1), and 641 (npar#1).

1.7. General methods for chemical synthesis. Thin-layer chromatography (TLC) was used to monitor progress of reactions unless stated otherwise using J. T. Baker Silica Gel IB2-F. Unless stated otherwise, reagents were purchased from Sigma-Aldrich and used without further purification. *N,N*-dimethylformamide (DMF), dichloromethane (DCM) were dried over 4 Å molecular sieves prior to use. Tetrahydrofuran (THF) and 1,4-dioxane were distilled prior to use. Optical rotations were measured on a Perkin Elmer 241 polarimeter. Solvent used for taking optical rotations (methanol) was not further purified prior to use.

1.8. Dauer formation assay. Dauer formation assay was performed as described previously[1] using heat- or kanamycin-killed *E. coli* OP50. Synthetic compounds were dissolved in ethanol (0.5 mM, stock solution) and combined with water to make a 100 µL solution and subsequently added to 3 mL NGM-agar without peptone (3, 1, 0.3, 0.1 µM final concentrations). The dauer formation assay was conducted in triplicate for each compound and concentration. 60-100 worms were screened for each condition.

1.9. Mouth-form dimorphism assay. Mouth-form dimorphism assays were performed using *P. pacificus* strain RSB020. The synthetic compounds dissolved in ethanol (0.5 mM) were diluted with water to make 100 µL solution and subsequently added to 3 mL NGM-agar (1 µM final concentration). The assay plates were seeded with 50 µL OP50 culture in LB medium and incubated overnight at 20 °C to allow bacterial growth. Each replicate included the progeny of two mothers, which were picked as adult hermaphrodites of a consistent age (carrying 4-6 eggs) and which were all from the same *P. pacificus* culture plate. Following placement of mothers on assay plates, plates were kept at 20 °C for six days, such that the entire broods were adults at the time of screening. A random sample of 50 hermaphrodite progeny was screened per plate. All animals were screened by differential interference contrast (DIC) microscopy on a Zeiss Axioskop. The following discrete characters were used to discriminate eurystomatous from stenostomatous individuals, respectively: (1) claw-shaped vs. flint-shaped (i.e. dorsoventrally symmetrical) dorsal tooth; (2) presence vs. absence of a subventral tooth; (3) strongly vs. weakly sclerotized stomatal walls. No intermediate mouth-forms were observed. Experiments were conducted in triplicate for each treatment.

In assays of responses to compounds of several concentrations (1, 0.3, 0.1, 0.03, 0.01 µM final concentrations), experiments were performed as described above, with the following modifications. To allow greater resolution of responses to lower concentrations, 60 randomly screened individuals in each of five replicates per concentration per compound were assayed. All concentration-curve experiments were performed in parallel using mothers picked randomly from the same two source populations. To prepare large numbers of individual mothers for these experiments, source populations were established from virgin hermaphrodites to constrain the presence of males and were conditioned to well-fed and ambient conditions for at least one generation before mothers were picked for the assays.

1.10. Statistical analysis. Error bars represent a 95% confidence interval in Figure 3a-d calculated using a binomial test on the total count data. All experiments were conducted in triplicate (or in five replicates for mouth-form concentration-curve assays) for each treatment. Significant differences (*P<0.01 and **P<0.001) between each chemical treatment and the control (EtOH) treatment in Figure 3a, b were determined using Fisher's exact test in the program R.

2. Supporting Figures

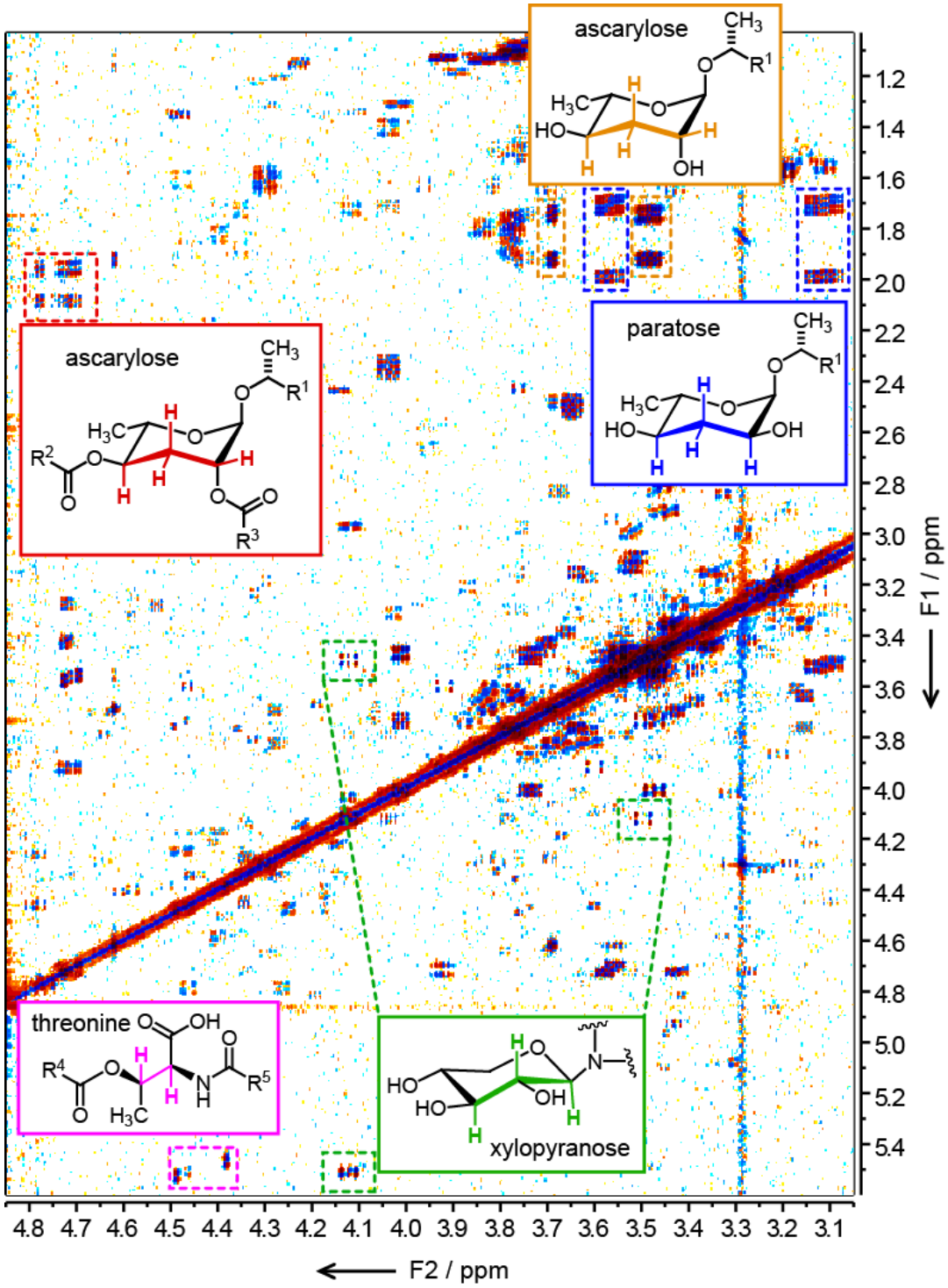


Figure S1. Example section of 2D NMR (dqfCOSY) spectrum of *P. pacificus* exo-metabolome fraction (see **Supporting Information, Section 1.4**), revealing a complex metabolite mixture, including known primary metabolites as well as unknown components. Detailed analysis of crosspeak fine structure and additional HMBC spectra led to detection of a series of unusual chemical structures based on combinations of ascarylose, paratose, threonine, xylose, and other building blocks.

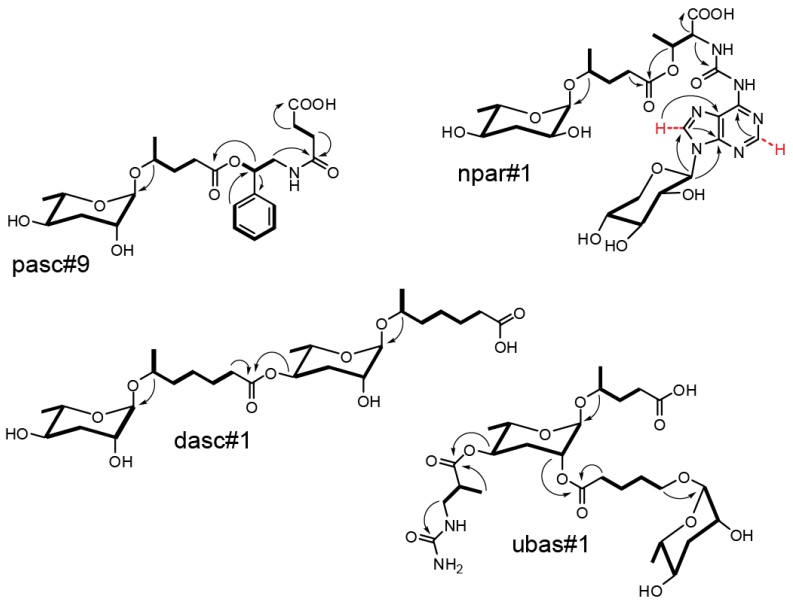


Figure S2. NMR spectroscopic structure elucidation of major *P. pacificus* small molecules: pasc#9, npar#1, dasc#1, and ubas#1. The **bold** lines indicate spin systems in dqfCOSY spectra. Curved arrows indicate key HMBC correlations used to assign the structures. Marked protons (---H) in **npar#1** are characteristic of N^6-carbamoyl adenosine and observed in ^{1}H, HSQCAD, and HMBC spectra.

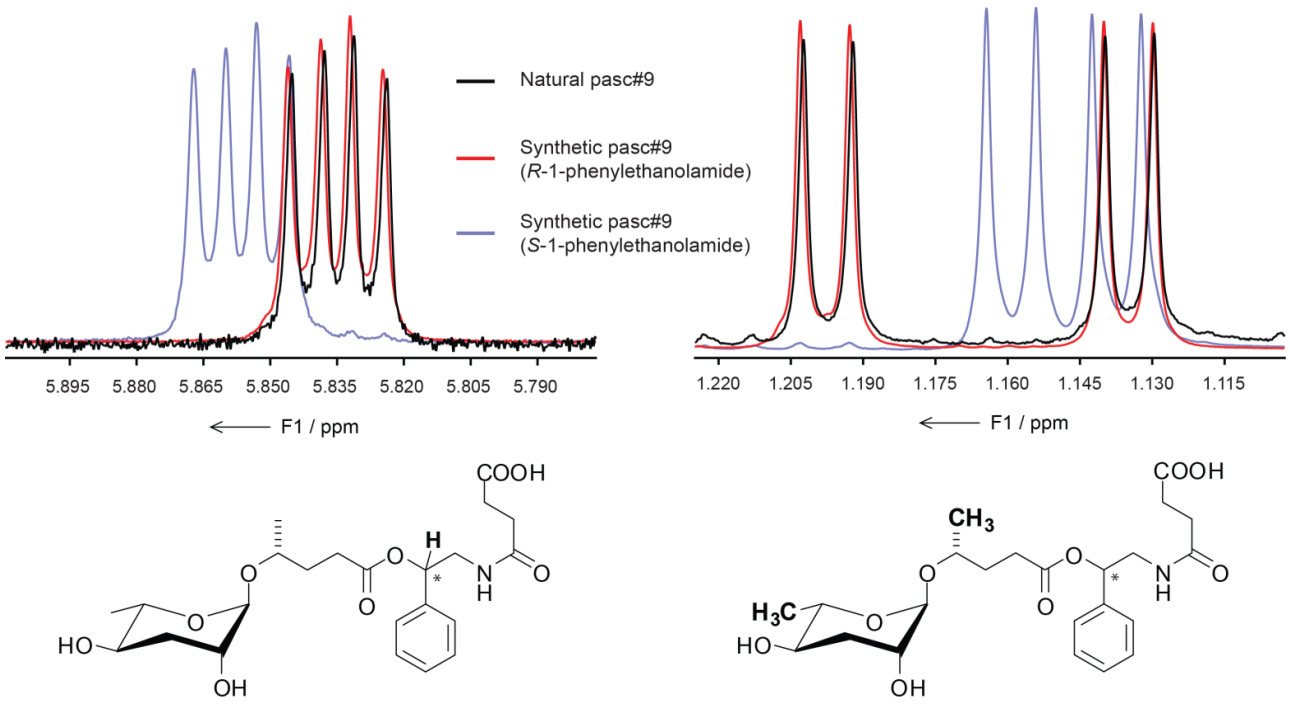


Figure S3. Determination of stereochemistry of *N*-succinyl-1-phenylethanolamide moiety in pasc#9. Comparison of sections of ^{1}H-NMR spectra of natural pasc#9 (black), synthetic pasc#9 including a (*R*)-*N*-succinyl-1-phenylethanolamide moiety (red), and synthetic pasc#9 including a (*S*)-*N*-succinyl-1-phenylethanolamide moiety (blue) shows that the ^{1}H NMR for the natural sample matches that of the (*R*)-*N*-succinyl-1-phenylethanolamide diastereomer, indicating that natural pasc#9 contains (*R*)-*N*-succinyl-1-phenylethanolamide.

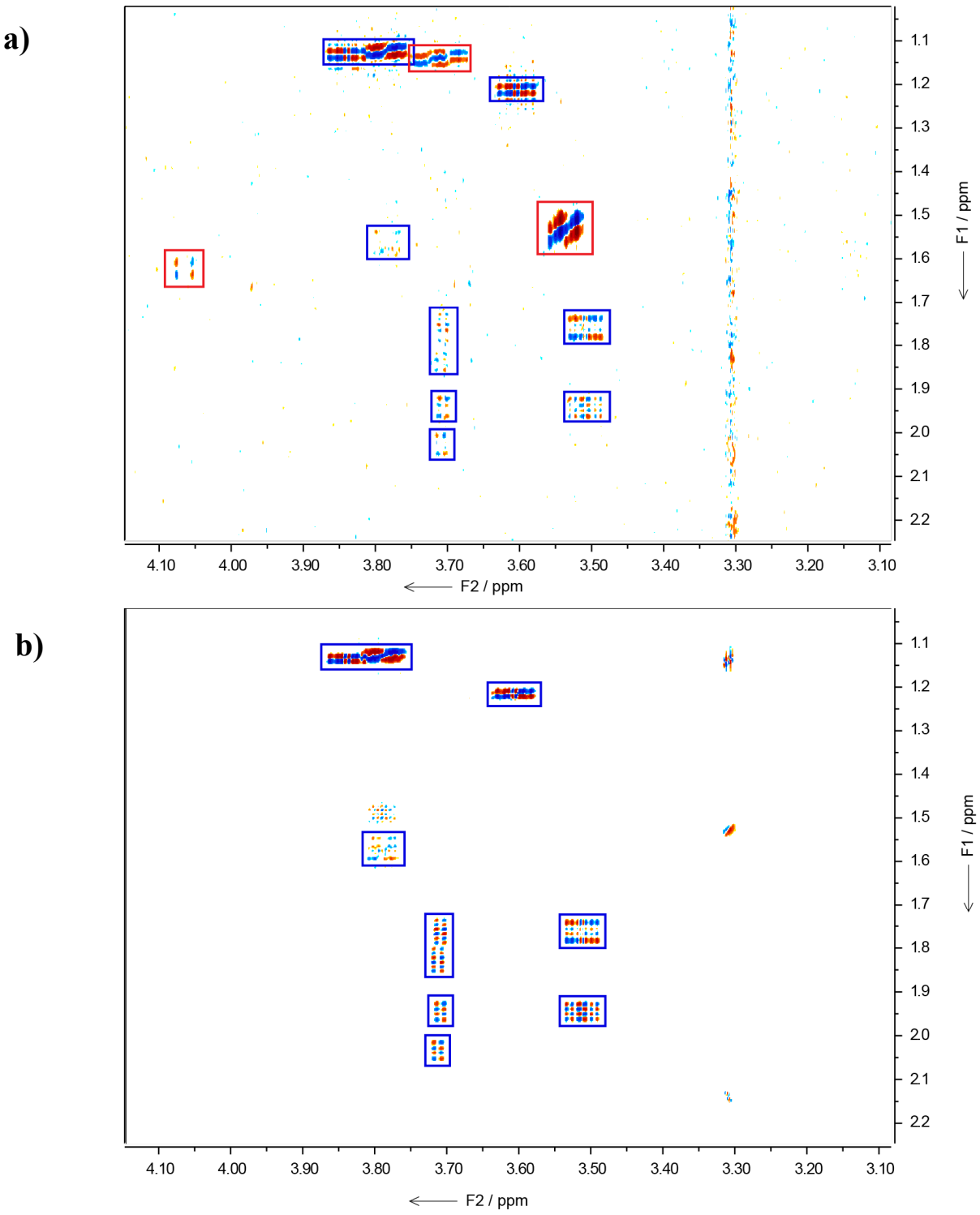


Figure S4. Sections of dqfCOSY spectra (600 MHz, methanol-d_4) confirming presence of dasc#1 in *P. pacificus* exo-metabolome. a) HPLC-enriched *P. pacificus* exo-metabolome extract fraction containing dasc#1. **b)** Synthetic sample of dasc#1. Characteristic crosspeaks for dasc#1 are boxed blue whereas unrelated crosspeaks from other metabolites present in the natural sample are boxed red. The precise match of crosspeaks between the natural and synthetic sample proves dasc#1 structural and stereochemical assignments.

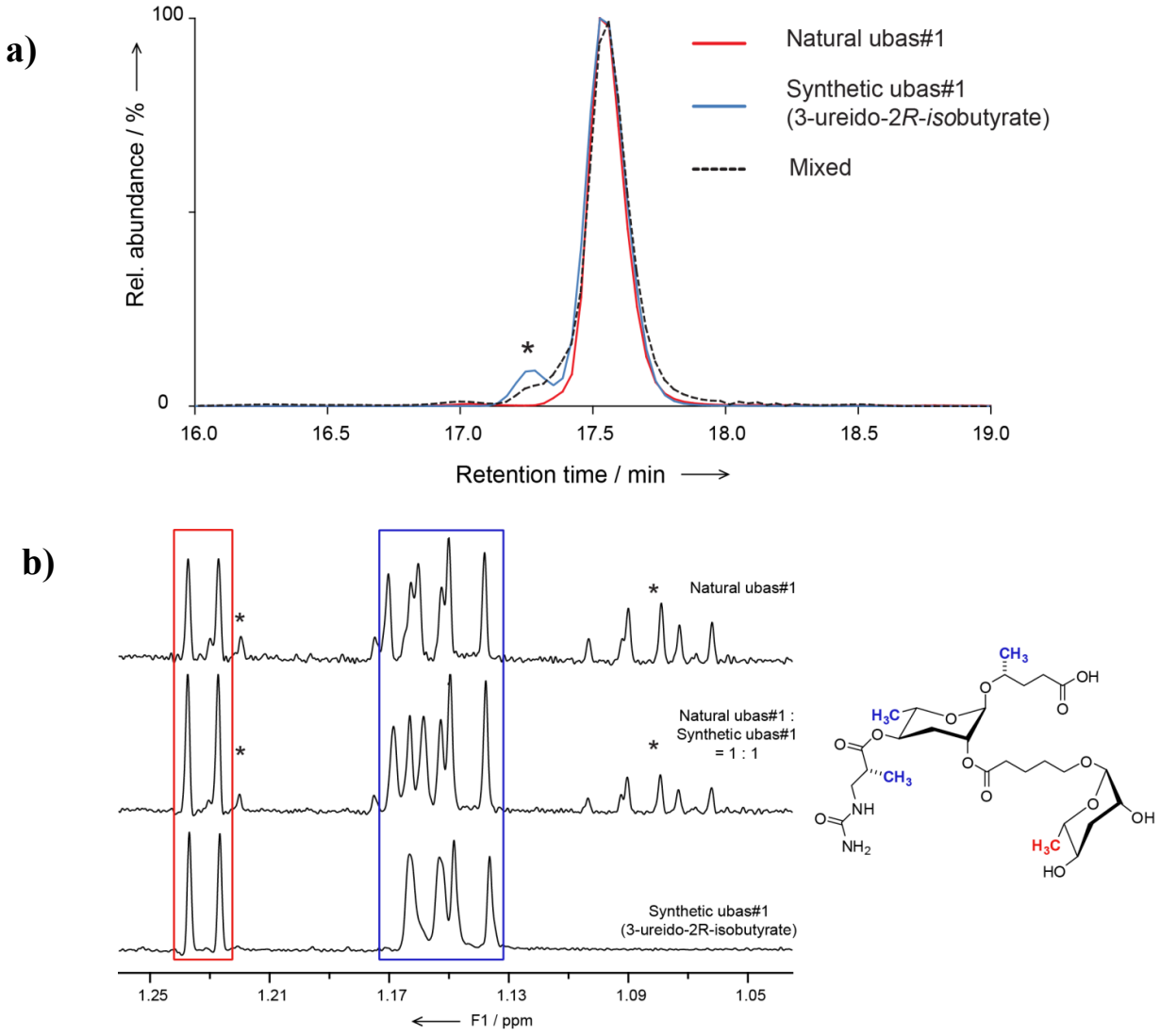


Figure S5. Determination of stereochemistry of ubas#1. a) Comparison of HPLC-MS retention times (ESI^-, ion chromatogram for *m/z* = 605) of natural ubas#1 (red), a synthetic mixture of ubas#1 diastereomers containing the 3-ureido-2*R*-*iso*butyrate and 3-ureido-2*S*-*iso*butyrate in a ~95:5 ratio (blue), and a mixture of the natural and synthetic samples (dotted black). The HPLC-retention time of synthetic (3-ureido-2*R*-*iso*butyrate)-derived ubas#1 matches that of natural ubas#1 and is distinctly different from the (3-ureido-2*S*-*iso*butyrate)-derived ubas#1 diastereomer (marked *) indicating that natural ubas#1 includes a 3-ureido-2*R*-*iso*butyrate moiety. **b)** Comparison of sections of ^{1}H-NMR spectra of synthetic (3-ureido-2*R*-*iso*butyrate)-derived ubas#1 (bottom), a natural sample containing ubas#1 (top), and a 1:1 mixture of these two samples (middle) shows that the relative intensity of the four characteristic methyl doublets (indicated by the red and blue boxes in the accompanying structure) increases upon adding synthetic ubas#1 to the natural sample (unrelated peaks in the natural sample are marked *). This confirms that natural ubas#1 contains 3-ureido-2*R*-*iso*butyrate, and not 3-ureido-2*S*-*iso*butyrate. Differences in pH and concentrations between the natural and synthetic samples slightly affect chemical shifts of the methyl doublets, resulting in small changes of chemical shift values upon mixing of natural and synthetic sample.

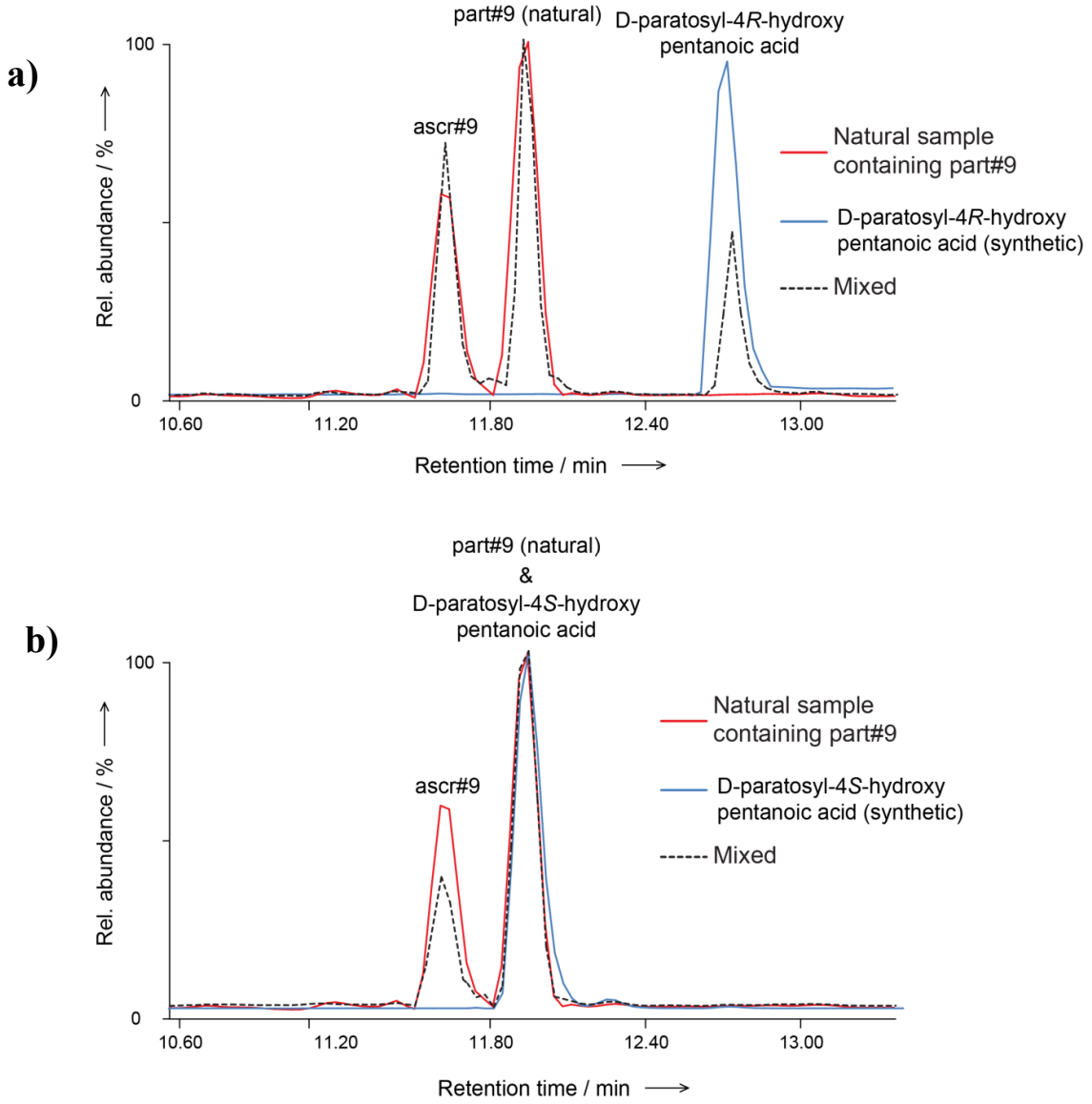


Figure S6. Determination of stereochemistry of part#9. Comparison of HPLC-MS retention times (ESI^-, ion chromatogram for m/z = 247) of natural mixture of ascr#9 and part#9 (red), synthetic samples of part#9 (blue), and a 1:1 mixture of the natural and synthetic sample (dotted black). **a)** Synthetic D-paratosyl-4*R*-hydroxypentanoic acid. HPLC-retention times do not match natural part#9, indicating that neither D-paratosyl-4*R*-hydroxypentanoic acid nor its enantiomer could be natural part#9. **b)** Synthetic D-paratosyl-4*S*-hydroxypentanoic acid. HPLC-retention times of D-paratosyl-4*S*-hydroxypentanoic acid match that of natural part#9. This indicates that natural part#9 is either D-paratosyl-4*S*-hydroxypentanoic acid or its enantiomer L-paratosyl-4*R*-hydroxypentanoic acid. Comparison of NMR spectra and HPLC-retention times of natural npar#1 with the two synthetic npar#1 diastereomers derived from either D-paratosyl-4*S*-hydroxypentanoic acid or L-paratosyl-4*R*-hydroxypentanoic acid (Supporting Information, Figure S7) and chiral derivatization experiments with Mosher's acid chlorides (Figure S8) reveal that natural part#9 and npar#1 are based on L-paratosyl-4*R*-hydroxypentanoic acid.

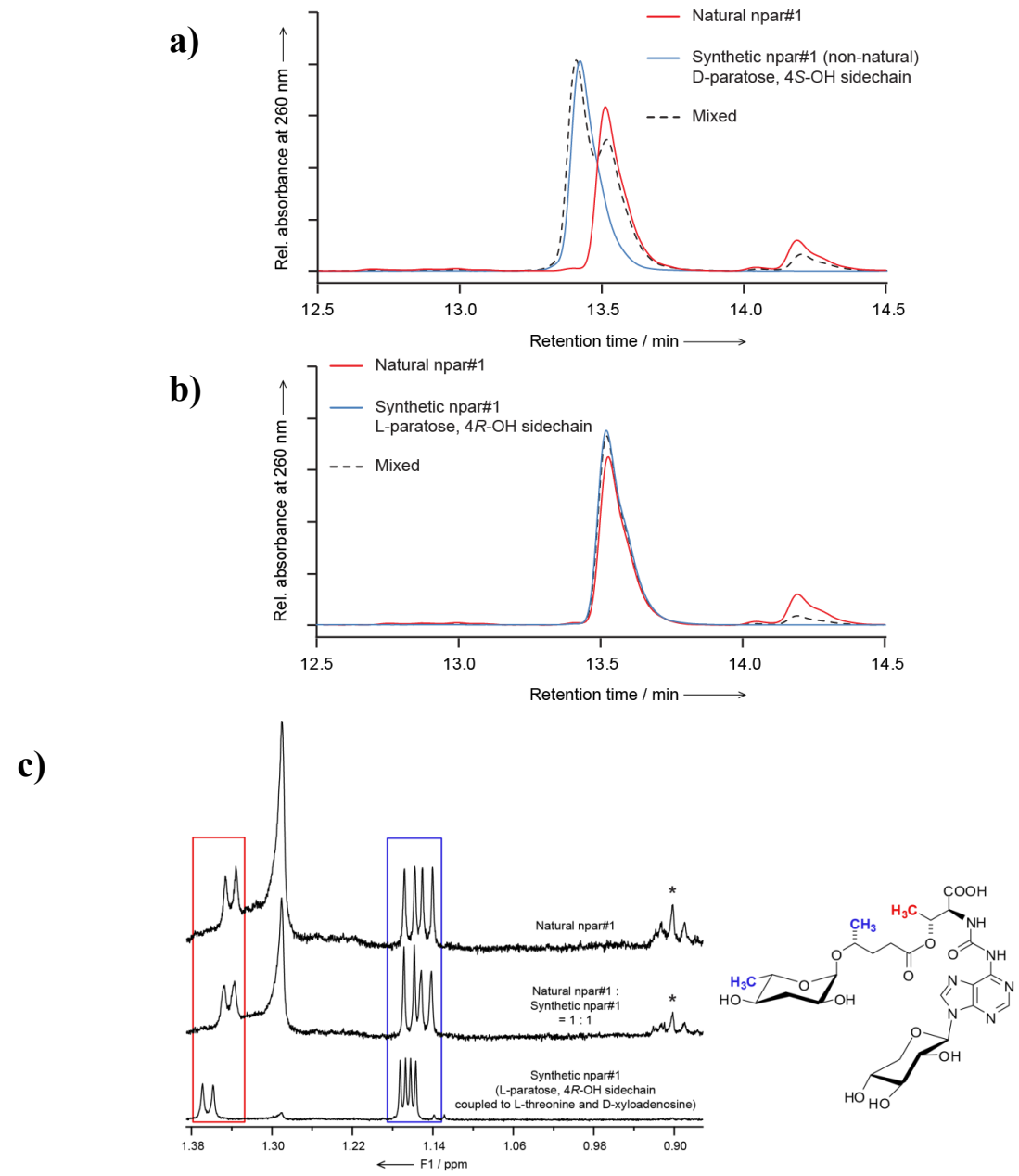
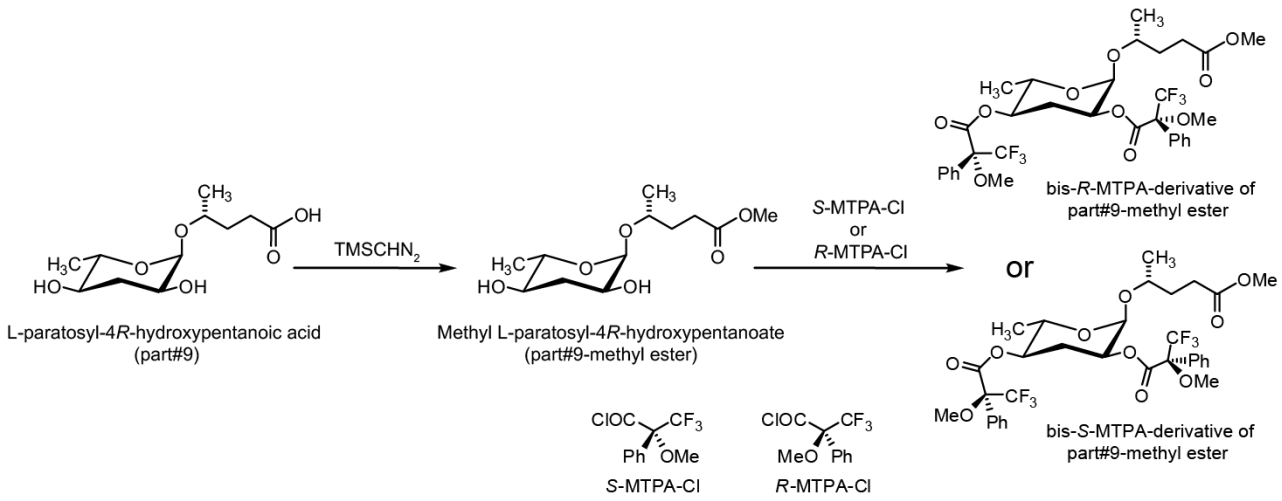


Figure S7. Determination of stereochemistry of npar#1. Comparison of HPLC-UV retention times (260 nm) of natural sample containing npar#1 (red), synthetic samples of npar#1 (blue), and mixtures of the natural and synthetic samples (dotted black). **a)** Synthetic npar#1 diastereomer derived from D-paratosyl-4*S*-hydroxypentanoic acid coupled to L-threonine and D-xyloadenosine. HPLC-retention times do not match that of natural npar#1. **b)** Synthetic npar#1 diastereomer derived from L-paratosyl-4*R*-hydroxypentanoic acid coupled to L-threonine and D-xyloadenosine. HPLC-retention times match that of natural npar#1. **c)** Comparison of sections of ^{1}H-NMR spectra of synthetic npar#1 derived from L-paratosyl-4*R*-hydroxypentanoic acid coupled to L-threonine and D-xyloadenosine (bottom), natural npar#1 (top), and a 1:1 mixture of the two (middle) shows that changes in pH and concentrations affect the shifts of the three characteristic methyl doublets (indicated by the red and blue boxes in the accompanying structure). In the mixed sample however, no new peaks show up and the relative intensity of the methyl doublets increases in comparison to unrelated peaks in the natural sample (marked with *). In combination with the HPLC-UV results from a) and b), these findings show that natural npar#1 consists of L-paratosyl-4*R*-hydroxypentanoic acid coupled to L-threonine and D-xyloadenosine.

a)



b)

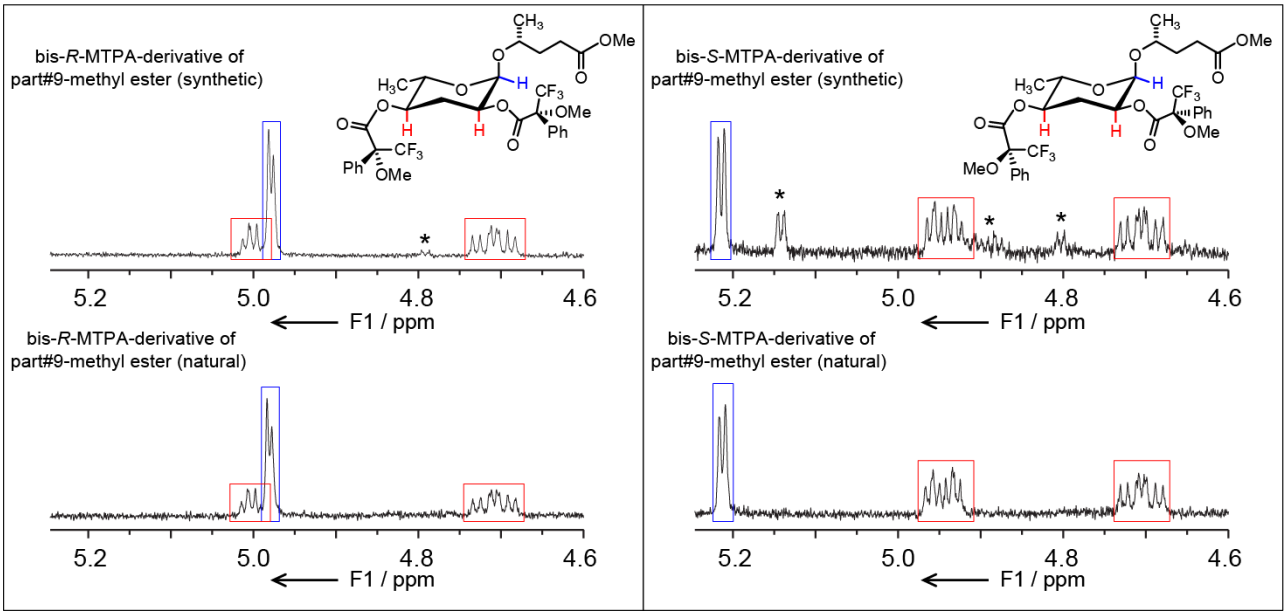


Figure S8. Determination of absolute configuration of part#9. a) Conversion of synthetic L-paratosyl-4*R*-hydroxypentanoic acid and isolated natural part#9 into the corresponding methyl esters, which were reacted with *S*- and *R*-α-methoxy-α-trifluoromethylphenylacetyl chlorides (Mosher's acid chlorides, *S*- and *R*-MTPA-Cl) to form the diasteromeric di-esters following previously published reaction protocols[4] (see Supporting Information, Section 4.3 for reaction conditions). **b)** Comparison of ^{1}H-NMR spectra ($CDCl_3$, 600 MHz) of the derivatization products of natural and syntehtic part#9 etablish natural part#9 as L-paratosyl-4*R*-hydroxypentanoic acid. (*)s indicate peaks due to side products resulting from incomplete reaction of starting matrerials.

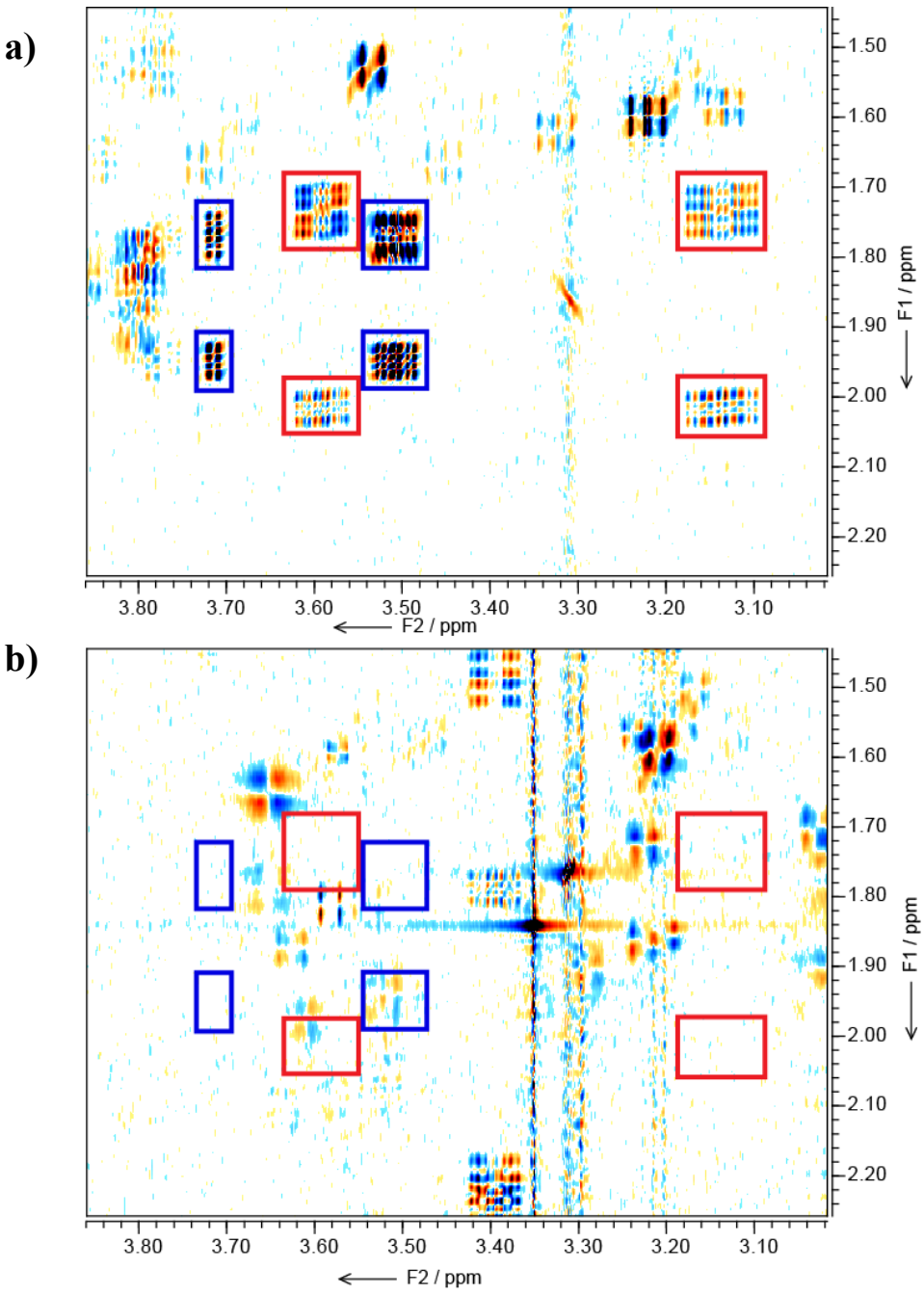


Figure S9. Small molecule architectures identified from *P. pacificus* exo-metabolome are not of bacterial origin. Sections of dqfCOSY spectra (600 MHz, methanol-d_4) of **a)** *P. pacificus* exo-metabolome extract and **b)** *E. coli* OP50 metabolome extract. Characteristic crosspeaks for ascarosides are boxed blue and that of paratosides are boxed red. Comparison of the two spectra indicates that the complex small molecules identified from *P. pacificus* exo-metabolome are not of bacterial origin. Correspondingly, HPLC-MS analyses of bacterial extracts did not show any of the peaks detected in *P. pacificus* exo-metabolome samples.

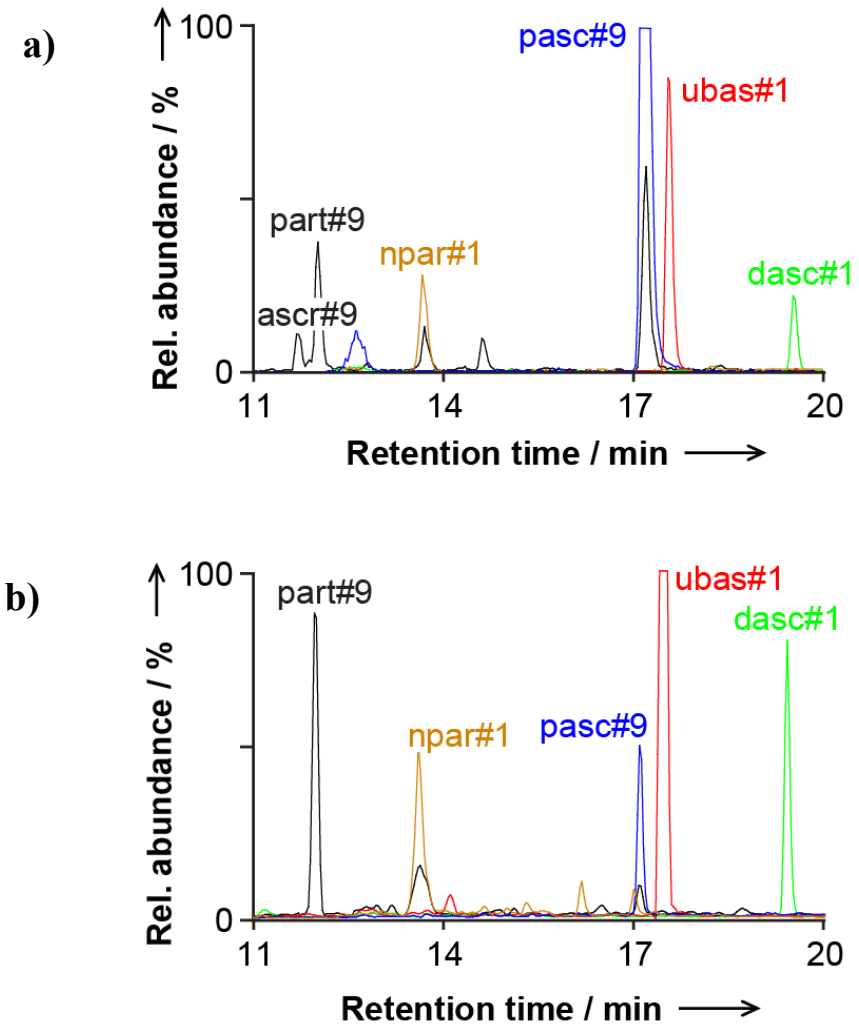


Figure S10. a) LCMS analysis of exo-metabolome extract from *P. pacificus* cultures fed with *Pseudomonas sp.* and **b)** SIM-LCMS analysis of exo-metabolome extract from *P. pacificus* axenic cultures.

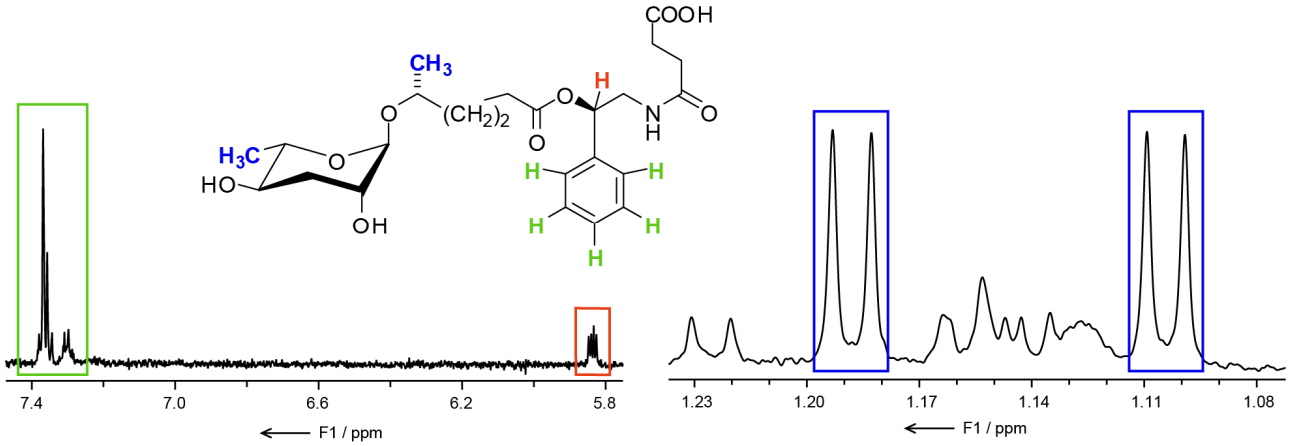


Figure S11. Characteristic ^{1}H NMR signals for pasc#12 in HPLC-enriched *P. pacificus* exo-metabolome extract fraction.

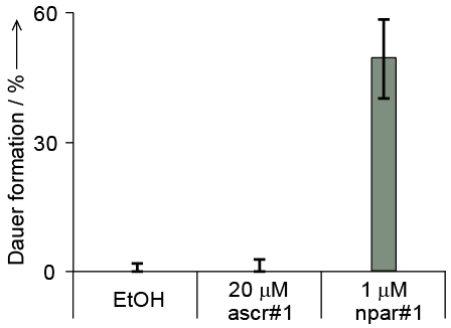


Figure S12. ascr#1 is not active in dauer formation assays. ascr#1 does not induce dauer formation in *P. pacifus*, even at very high concentrations (20 μM). npar#1 (1 μM) was used as a positive control for *P. pacificus* dauer formation.

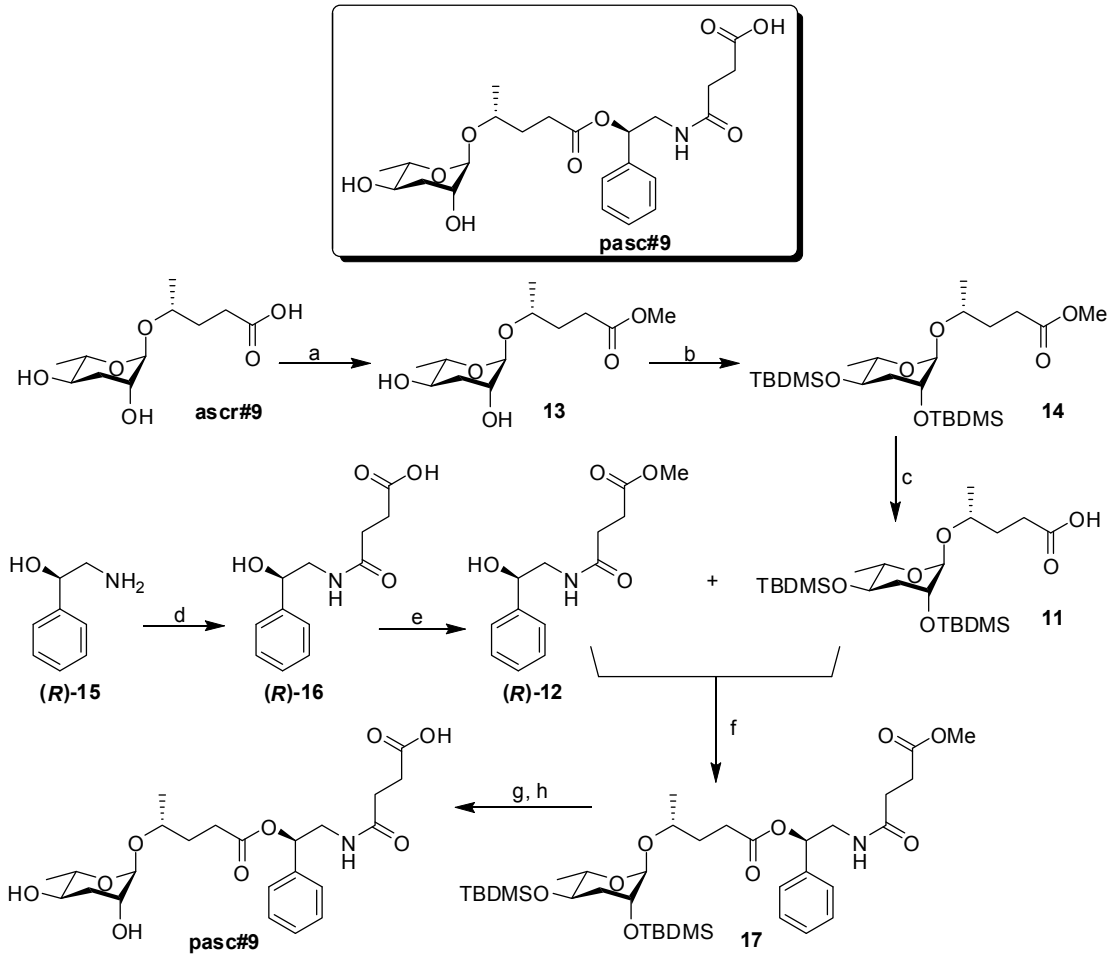
3. Supporting Table S1

SMID	Molecular formula	LC retention time [Min] ±SD	*m/z* [M-H]$^-$ calculated	*m/z* [M-H]$^-$ observed**	Estimated concentrations in culture supernatant (μM)***
ascr#9*	$C_{11}H_{20}O_6$	11.68 ± 0.02	247.1187	247.1185	0.3-0.6
ascr#12*	$C_{12}H_{22}O_6$	13.10 ± 0.01	261.1344	261.1305	0.1-0.3
ascr#1*	$C_{13}H_{24}O_6$	14.51 ± 0.02	275.1500	275.1494	0.4-0.8
pasc#9*	$C_{23}H_{33}NO_9$	17.10 ± 0.04	466.2083	466.2089	1.0-2.0
pasc#12	$C_{24}H_{35}NO_9$	17.81 ± 0.03	480.2239	480.2231	0.2-0.5
pasc#1	$C_{25}H_{37}NO_9$	18.59 ± 0.05	494.2396	494.2390	0.05-0.10
ubas#1*	$C_{27}H_{46}N_2O_{13}$	17.51 ± 0.06	605.2927	605.2928	0.2-0.4
ubas#2	$C_{28}H_{48}N_2O_{13}$	18.11 ± 0.05	619.3084	619.3067	0.1-0.2
dasc#1*	$C_{26}H_{46}O_{11}$	19.50 ± 0.01	533.2967	533.2951	0.2-0.5
part#9*	$C_{11}H_{20}O_6$	11.99 ± 0.02	247.1187	247.1181	0.5-1.0
npar#1*	$C_{26}H_{38}N_6O_{13}$	13.64 ± 0.05	641.2424	641.2443	0.5-1.0
npar#2	$C_{21}H_{30}N_6O_9$	14.34 ± 0.07	509.2002	509.1999	0.05-0.10

*Confirmed using synthetic standards.
**HRMS data was obtained from *P. pacificus* exo-metabolome extract analysis.
***Quantifications were based on intetegration of HPLC-MS signals from the corresponding ion-traces. Concentrations were calculated using response factors determined for synthetic standards. Concentrations for minor compounds that were not synthesized were based on extrapolation of available standards of closely related structures. A range of concentrations are reported as observed for multiple biological repeats.

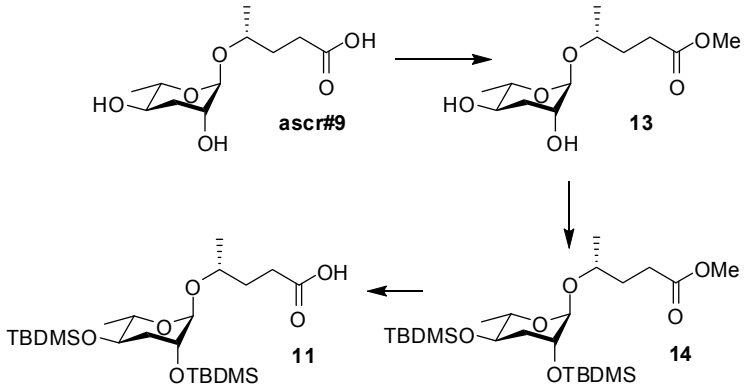
4. Chemical Synthesis and Spectroscopic Data

4.1. Synthesis of pasc#9



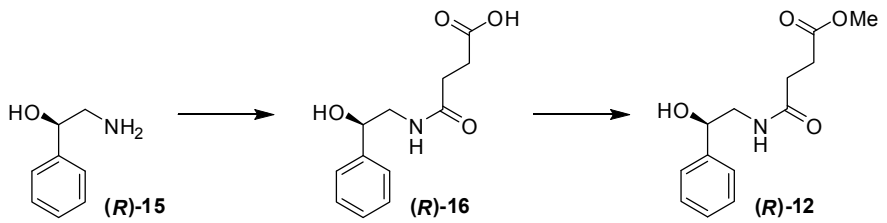
Synthetic Scheme 1. Overview of synthesis of pasc#9. Reagents and conditions: **(a)** $TMSCHN_2$, toluene/MeOH; **(b)** TBDMSCl, imidazole, DMF; **(c)** LiOH, THF/dioxane/H_2O, 67 °C; **(d)** succinic anhydride, DCM; **(e)** $TMSCHN_2$, toluene/MeOH; **(f)** EDC, DMAP, DCM; **(g)** 40% HF, MeCN; **(h)** LiOH, THF/dioxane/H_2O, 60 °C.

Synthesis of (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (11)



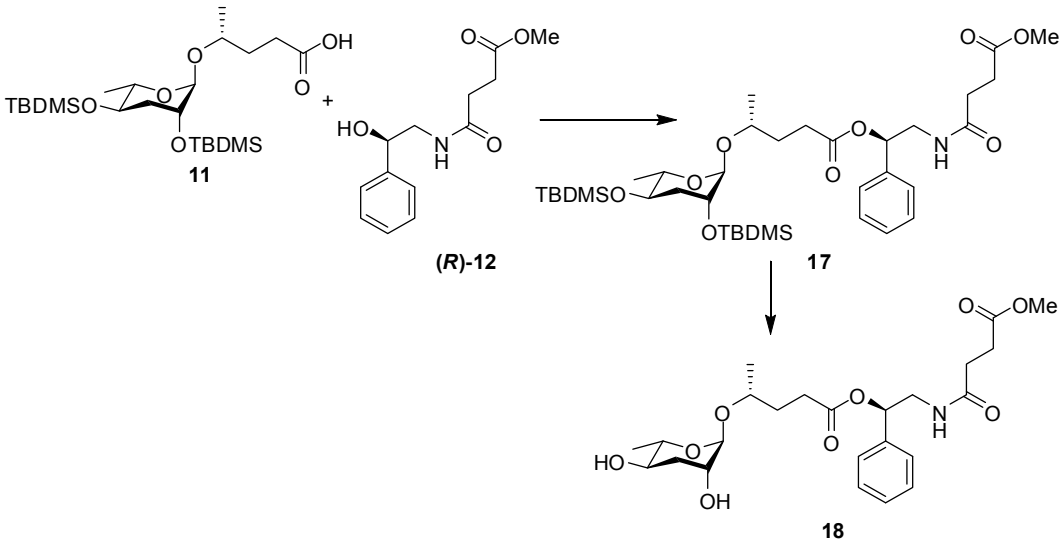
A solution of **ascr#9**[3b] (30 mg, 121 µmol) in a 3:2 mixture (*v/v*) of methanol and toluene (2 mL) was treated with 2.0 M (trimethylsilyl)diazomethane solution (120 µl) in diethyl ether. After stirring for 30 minutes, excess reagent was destroyed by addition of acetic acid and the solution was concentratred *in vacuo*. The crude residue was used in the next step without further purification. The residue **13** was dissolved in dry DMF (1.5 mL), cooled to 0 °C, and treated with imidazole (91 mg, 1.34 mmol) and stirred for 5 minutes. This mixture was treated with *tert*-butylchlorodimethylsilane (182 mg, 1.21 mmol) and left to stir overnight. The reaction was quenched with brine (5 mL), extracted with diethyl ether, dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-25% ethyl acetate in hexanes afforded **14** (55 mg, 112 µmol, 93% over two steps) as a colorless oil. A solution of **14** (55 mg, 112 µmol) in dry tetrahydrofuran (1 mL) was added to a mixture of LiOH (11 mg, 457 µmol) and water (0.4 mL) in 1,4-dioxane (2 mL). After stirring at 67 °C for 3 h the solution was acidified with glacial acetic acid and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-30% ethyl acetate with 0.1% acetic acid in hexanes afforded **11** (50 mg, 105 µmol, 94%) as a colorless oil. ^{1}H NMR (600 MHz, chloroform-*d*): δ (ppm) 4.55 (s, 1H), 3.87-3.80 (m, 1H), 3.78-3.75 (m, 1H), 3.68-3.61 (m, 1H), 3.58-3.52 (m, 1H), 2.56-2.42 (m, 2H), 1.89-1.71 (m, 4H), 1.18 (d, *J* = 6.3 Hz, 3H), 1.13 (d, *J* = 6.2 Hz, 3H), 0.91-0.87 (m, 18H), 0.07-0.03 (m, 12H).

Synthesis of (*R*)-methyl 4-((2-hydroxy-2-phenylethyl)amino)-4-oxobutanoate ((*R*)-12)



A solution of (*R*)-(-)-2-amino-1-phenylethanol **((*R*)-15)** (281 mg, 2.05 mmol) and succinic anhydride (220 mg, 2.2 mmol) in dry dichloromethane (7 mL) was stirred overnight. The reaction was then concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-30% methanol in dichloromethane containing 0.25% acetic acid afforded **(*R*)-16** (470 mg, 1.98 µmol, 97%) as a white powder. A solution of **(*R*)-16** (288 mg, 1.22 mmol) in a 3:2 mixture (*v/v*) of methanol and toluene (10 mL) was treated with 2.0 M (trimethylsilyl)diazomethane solution (900 µl) in diethyl ether. After stirring for 30 minutes, excess reagent was destroyed by addition of acetic acid and the solution was concentrated *in vacuo*. Crude **(*R*)-12** was used in the next step without further purification. (300 mg, 1.20 mmol, 98%). ^{1}H NMR (400 MHz, acetone-d_6): δ (ppm) 7.41-7.20 (m, 5H), 4.76 (dd, *J* = 7.7 Hz, *J* = 3.8 Hz, 1H), 3.62 (s, 3H), 3.50 (ddd, *J* = 13.6 Hz, *J* = 6.4 Hz, *J* = 4.0 Hz, 1H), 3.26 (ddd, *J* = 13.6 Hz, *J* = 8.0 Hz, *J* = 5.2 Hz, 1H), 2.60-2.54 (m, 2H), 2.52-2.46 (m, 2H). ^{13}C NMR (100 MHz, acetone-d_6): δ (ppm) 173.7, 172.7, 144.3, 128.9, 127.9, 126.8, 73.6, 51.7, 48.5, 31.0, 29.7.

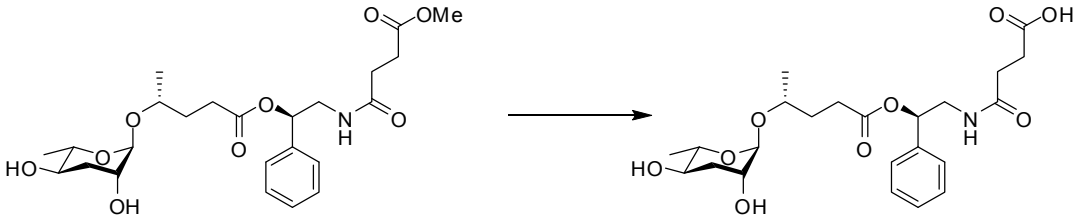
Synthesis of (*R*)-(*R*)-2-(4-methoxy-4-oxobutanamido)-1-phenylethyl 4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (18)



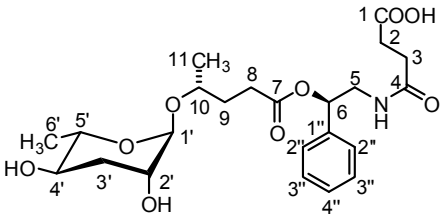
A solution of **11** (17 mg, 36 µmol) in 3 mL dry dichloromethane was treated with 4-dimethylaminopyridine (1 mg, 8.2 µmol) and EDC hydrochloride (11 mg, 57 µmol). After stirring for 30

minutes, **(*R*)-12** (18 mg, 71 µmol) in 1 mL dry dichloromethane was added to the mixture. After stirring for 2 h, the reaction was concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 10-70% ethyl acetate in hexanes afforded **17** (17 mg, 24 µmol, 67%) as a colorless oil. A solution of **17** (17 mg, 24 µmol) in acetonitrile (750 µL) was cooled to 0 °C and was treated with 1 drop of 40% HF while stirring. The reaction was allowed to warm to r.t. and stirred for 1.5 h. The reaction was re-cooled to 0 °C and quenched with saturated aq. $NaHCO_3$ solution (4 drops) and immediately acidified with glacial acetic acid. The reaction was concentrated *in vacuo* and flash column chromatography on silica using a gradient of 0-30% methanol in dichloromethane afforded **18** (6.6 mg, 13.7 µmol, 57%) as a colorless oil. ^{1}H NMR (500 MHz, methanol-d_4): δ (ppm) 7.41-7.27 (m, 5H), 5.84 (dd, J = 8.4 Hz, J = 4.4 Hz, 1H), 4.64 (s, 1H), 3.84-3.76 (m, 1H), 3.73-3.68 (m, 1H), 3.66 (s, 3H), 3.61-3.45 (m, 4H), 2.6-2.44 (m, 6H), 1.98-1.91 (m, 1H), 1.88-1.71 (m, 3H), 1.20 (d, J = 6.1 Hz, 3H), 1.14 (d, J = 6.1 Hz, 3H). ^{13}C NMR (125 MHz, methanol-d_4): δ (ppm) 174.7, 174.6, 174.3, 139.7, 129.6, 129.3, 127.5, 97.4, 75.7, 71.6, 71.4, 69.9, 68.3, 52.2, 45.4, 36.0, 33.3, 31.6, 31.3, 30.1, 19.1, 18.1.

Synthesis of 4-(((*R*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (pasc#9)



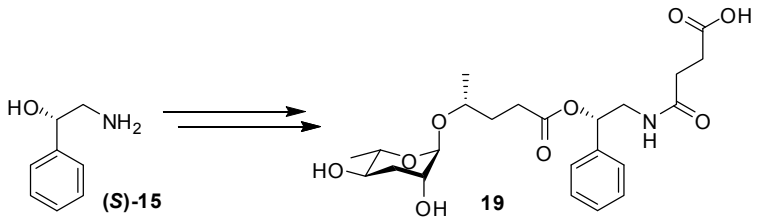
A solution of **18** (6.6 mg, 14 µmol) in dry tetrahydrofuran (200 µl) was treated with a solution of LiOH (0.3 mg, 12 µmol) in water (80 µl) and 1,4-dioxane (400 µl). After stirring at 60 °C for 5 minutes, the solution was acidified with glacial acetic acid and concentrated *in vacuo*. HPLC purification (see Methods) of the crude reaction mixture afforded **pasc#9** (1.8 mg, 4 µmol, 29%) as a colorless oil. α_D^{20} = -110.0 (*c.* 0.18, methanol). For NMR spectroscopic data, see next page.



NMR Spectroscopic data for **pasc#9**. ^{1}H (600 MHz), ^{13}C (151 MHz), and HMBC NMR spectroscopic data for **pasc#9** in methanol-d_4. Chemical shifts were referenced to ($CD_2\underline{H}OD$) = 3.31 ppm and ($\underline{C}D_3OD$) = 49.00 ppm.

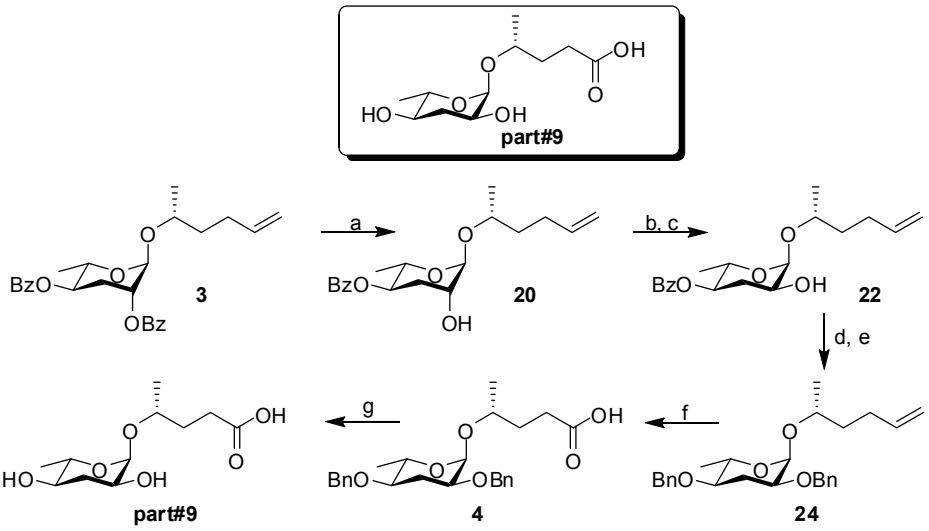
Position	δ ^{13}C [ppm]	δ ^{1}H [ppm]	^{1}H-^{1}H-coupling constants (Hz)	Key HMBC correlations
1	175.8	---		
2	31.3	2.44	$J_{2,3}$ = 7.2	C-1
3	30.1	2.56		C-4
4	174.4	---		
5	45.1	5a = 3.51 5b = 3.58	$J_{5a,5b}$ = 13.7, $J_{5a,6}$ = 8.5 $J_{5b,6}$ = 4.4	C-4
6	75.4	5.84		C-7, C-1″
7	173.8	---		
8	31.3	2.54		C-7
9	33.0	1.81		
10	71.3	3.80	$J_{10,11}$ = 6.6	C-1′
11	18.8	1.14		
1′	97.0	4.64	$J_{1',2'}$ = 2.3	C-2′, C-3′, C-5′
2′	69.4	3.72	$J_{2',3'(ax)}$ = 6.6, $J_{2',3'(eq)}$ = 6.6	
3′	35.6	1.70 (ax) 1.95 (eq)	$J_{3'(ax),3'(eq)}$ = 13.0, $J_{3'(ax),4'}$ = 11.8 $J_{3'(eq),4'}$ = 4.9	
4′	67.8	3.51	$J_{4',5'}$ = 11.8	
5′	71.0	3.58	$J_{5',6'(eq)}$ = 6.4	
6′	17.8	1.20		
1″	139.4	---		
2″	127.3	7.29 – 7.37		C-1″, C-6
3″	129.1	7.29 – 7.37		
4″	128.9	7.29 – 7.37		

Synthesis of 4-(((*S*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (19, non-natural isomer of pasc#9)



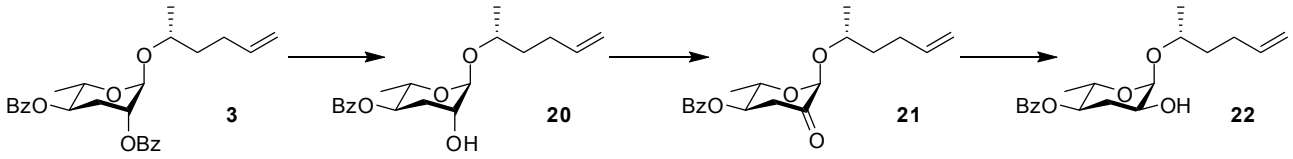
19 (pasc#9 with (*S*)-*N*-succinyl-1-phenylethanolamide) was prepared using an analogous reaction sequence starting from (*S*)-(+)-2-amino-1-phenylethanol **(*S*)-15.** ^{1}H NMR (600 MHz, methanol-d_4): δ (ppm) 7.40-7.34 (m, 4H), 7.32-7.28 (m, 1H), 5.86 (dd, J = 8.5 Hz, J = 4.3 Hz, 1H), 4.63 (s, 1H), 3.84-3.78 (m, 1H), 3.67-3.64 (m, 1H), 3.60-3.53 (m, 2H), 3.52-3.47 (m, 2H), 2.62-2.43 (m, 6H), 1.95-1.89 (m, 1H), 1.88-1.77 (m, 2H), 1.77-1.71 (m, 1H), 1.16 (d, J = 6.2 Hz, 3H), 1.14 (d, J = 6.1 Hz, 3H). ^{13}C NMR (151 MHz, methanol-d_4): δ (ppm) 176.1, 174.6, 174.1, 139.4, 129.4, 129.0, 127.3, 97.0, 75.4, 71.3, 71.1, 69.6, 68.0, 45.3, 35.6, 33.0, 31.29, 31.25, 30.2, 18.8, 17.9.

4.2. Synthesis of part#9



Synthetic Scheme 2. Overview of synthesis of part#9. Reagents and conditions: **(a)** LiOH, THF/dioxane/H_2O, 67 °C; **(b)** Dess-Martin periodinane, DCM; **(c)** $NaBH_4$, DCM/MeOH; **(d)** LiOH, THF/dioxane/H_2O, 67 °C; **(e)** BnBr, NaH, DMF; **(f)** $RuCl_3 \cdot H_2O$, $NaIO_4$, DCM/MeCN/H_2O; **(g)** 10% Pd/C, H_2 (*g*), 10% formic acid in MeOH.

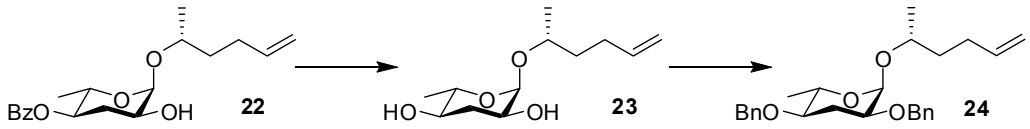
Synthesis of (2*S*,3*R*,5*S*,6*R*)-6-((*R*)-hex-5-en-2-yloxy)-5-hydroxy-2-methyltetrahydro-2*H*-pyran-3-yl benzoate (22)



A solution of **3**[3b] (181.5, 413 µmol) in dry tetrahydrofuran (0.5 mL) was added to a mixture of LiOH (8.9 mg, 371 µmol) and water (0.2 mL) in 1,4-dioxane (1 mL). After stirring at 67 °C for 40 minutes the solution was acidified with few drops of glacial acetic acid and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 10-40% ethyl acetate in hexanes afforded **20** (48.5 mg, 145 µmol, 35%) as a colorless oil. A solution of **20** (48.5 mg, 145 µmol) in dry dichloromethane (2 mL) was treated with Dess-Martin periodinane (88 mg, 208 µmol). After 5 h the solution was diluted with 10 mL dichloromethane and washed three times with a solution of 5% $Na_2S_2O_3$ in H_2O. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-30% ethyl acetate in hexanes afforded **21** (26.8 mg, 81 µmol, 56%) as a colorless oil. A solution of **21** (24.5 mg, 74 µmol) in 1:1 dichloromethane: methanol (0.7 mL) was treated with $NaBH_4$ (12 mg, 317 µmol). After 10 minutes the solution was acidified with glacial acetic acid and diluted with

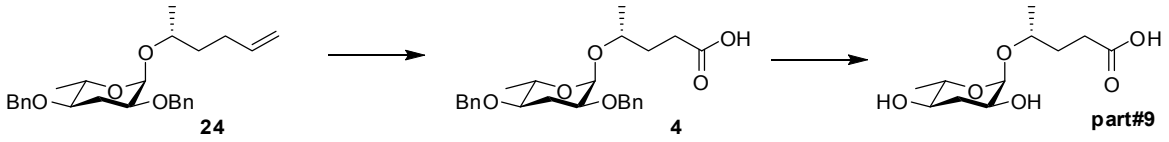
dichloromethane and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-40% ethyl acetate in hexanes afforded **22** (18.2 mg, 54 µmol, 74%) as a colorless oil.[1]H NMR (600 MHz, acetone-d_6): δ (ppm) 8.04-8.01 (m, 2H), 7.67-7.63 (m, 1H), 7.55-7.50 (m, 2H), 5.89 (ddt, *J* = 17.1 Hz, *J* = 10.3 Hz, *J* = 6.6 Hz, 1H), 5.09-5.04 (m, 1H), 4.99-4.95 (m, 1H), 4.84 (d, *J* = 3.7, 1H), 4.69 (ddd, *J* = 11.4 Hz, *J* = 9.8 Hz, *J* = 4.6 Hz, 1H), 4.04-3.98 (m, 1H), 3.89-3.82 (m, 1H), 3.78-3.71 (m, 1H), 2.29-2.16 (m, 3H), 1.93-1.86 (m, 1H), 1.79-1.72 (m, 1H), 1.65-1.58 (m, 1H), 1.19 (d, *J* = 6.1 Hz, 3H), 1.16 (d, *J* = 6.3 Hz, 3H).[13]C NMR (151 MHz, acetone-d_6): δ (ppm) 165.9, 139.6, 134.1, 131.1, 130.2, 129.5, 114.9, 96.4, 73.7, 72.9, 67.8, 66.8, 37.3, 34.3, 30.7, 19.5, 17.9.

Synthesis of (2*R*,3*S*,5*R*,6*S*)-3,5-bis(benzyloxy)-2-((*R*)-hex-5-en-2-yloxy)-6-methyltetrahydro-2*H*-pyran (24)

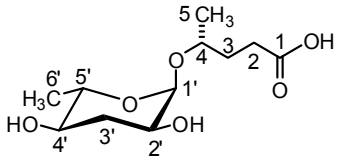


A solution of **22** (18.2 mg, 54 µmol) in dry tetrahydrofuran (0.5 mL) was added to a mixture of LiOH (13.5 mg, 563 µmol) and water (0.2 mL) in 1,4-dioxane (1 mL). After stirring at 67 °C for 3 h the solution was acidified with glacial acetic acid and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-30% methanol in dichloromethane afforded **23** (8.5 mg, 37 µmol, 67%) as a colorless oil. A solution of **23** (8.5 mg, 37 µmol) in DMF (700 µl), cooled to 0 °C, was treated with sodium hydride (10 mg, 60% suspension in mineral oil, 250 µmol). After stirring for 20 minutes, benzylbromide (15 µl) was added and the mixture stirred overnight. Excess reagent was destroyed by addition of methanol (300 µl), the residue diluted with ethyl acetate (2 mL), and the organic phase washed with water (3 × 0.5 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-25% ethyl acetate in hexanes afforded **24** (13 mg, 32 µmol, 80%) as a colorless oil.[1]H NMR (400 MHz, chloroform-*d*): δ (ppm) 7.38-7.25 (m, 10H), 5.82 (ddt, *J* = 17.1 Hz, *J* = 10.4 Hz, *J* = 6.5 Hz, 1H), 5.06-4.99 (m, 1H), 4.98-4.93 (m, 1H), 4.89 (d, *J* = 3.4 Hz, 1H), 4.65 (d, *J* = 11.6 Hz, 1H), 4.59 (s, 2H), 4.46 (d, *J* = 11.6 Hz, 1H), 3.86-3.74 (m, 2H), 3.51-3.43 (m, 1H), 3.07 (ddd, *J* = 11.1 Hz, *J* = 9.4 Hz, *J* = 4.3 Hz, 1H), 2.33-2.06 (m, 3H), 1.93-1.82 (m, 1H), 1.83-1.73 (m, 1H), 1.63-1.52 (m, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.19 (d, *J* = 6.1 Hz, 3H). 34 H total. [13]C NMR (100 MHz, chloroform-*d*): δ (ppm) 138.6, 138.41, 138.38, 128.55 (2C), 127.92, 127.89, 127.85 (2C), 114.7, 93.2, 78.2, 74.1, 71.6, 70.90, 70.86, 67.6, 52.4, 36.5, 30.3, 19.7, 17.9.

Synthesis of (*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (part#9)



A solution of **24** (5.4 mg, 13 μmol) in a 1:1:1 mixture (*v/v/v*) of dichloromethane : acetonitrile : H_2O (300 μL) was first treated with $NaIO_4$ (13 mg, 61 μmol) and then with a solution of $RuCl_3 \cdot H_2O$ (145 μg, 0.7 μmol) in H_2O (50 μL). After 1.75 h, the mixture was diluted with H_2O (1 mL), extracted with dichloromethane (3 × 1 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-20% methanol in dichloromethane containing 0.25% glacial acetic acid afforded **4** (4.6 mg, 11 μmol, 81%) as a colorless oil. A suspension of Pd/C (11 mg, 10%, *w/w*) in 500 μL of methanol containing 10% formic acid was first flushed with argon for 5 minutes and subsequently with a moderate flow of H_2 gas. To this stirring mixture was added a solution of **4** (4.1 mg, 9.3 μmol) in 500 μL methanol. After 4.5 h, the reaction was filtered over a pad of silica and concentrated *in vacuo*. HPLC purification (see Methods) afforded **part#9** (1.5 mg, 6.0 μmol, 65%) as a colorless oil. α_D^{20} = -128.6 (*c.* 0.15, methanol). For NMR spectroscopic data, see next page.

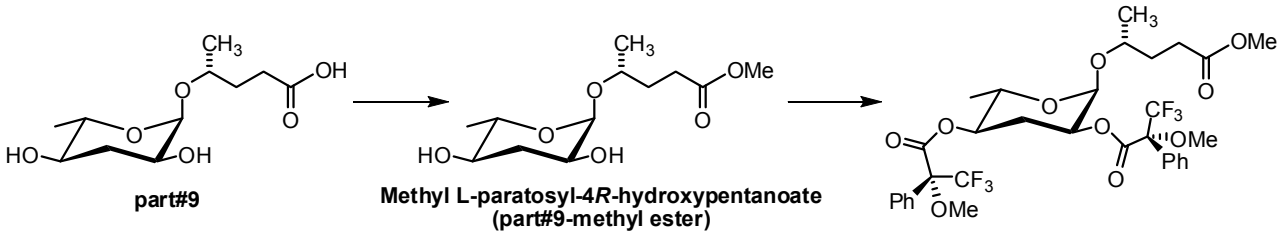


NMR Spectroscopic data for **part#9**. ^{1}H (600 MHz), ^{13}C (151 MHz), and HMBC NMR spectroscopic data for **part#9** in methanol-d_4. Chemical shifts were referenced to ($CD_2\underline{H}OD$) = 3.31 ppm and ($\underline{C}D_3OD$) = 49.00 ppm.

Position	δ ^{13}C [ppm]	δ ^{1}H [ppm]	^{1}H-^{1}H-coupling constants (Hz)	Key HMBC correlations
1	178.3	---		
2	31.8	2.43	$J_{2,3}$ = 7.1	C-1, C-3
3	33.5	1.85		
4	72.4	3.83	$J_{4,5}$ = 6.3	C-1′
5	19.0	1.179		
1′	95.9	4.74	$J_{1',2'}$ = 3.9	C-2′, C-3′, C-5′
2′	68.4	3.60	$J_{2',3'\ (ax)}$ = 12.1; $J_{2',3'\ (eq)}$ = 5.5	
3′	36.8	1.74 (ax) 2.02 (eq)	$J_{3'\ (eq),3'\ (ax)}$ = 12.3; $J_{3'\ (eq),4'}$ = 4.7 $J_{3'\ (ax),4'}$ = 10.9	
4′	71.6	3.15	$J_{4',5'}$ = 9.4	
5′	69.9	3.58	$J_{5',6'\ (eq)}$ = 6.1	
6′	17.5	1.18		C-4, C-5

4.3 Synthesis of bis-*R*- and bis-*S*-MTPA derivatives of part#9-methyl ester

Synthesis of bis-*R*-MTPA-derivative of part#9 methyl ester

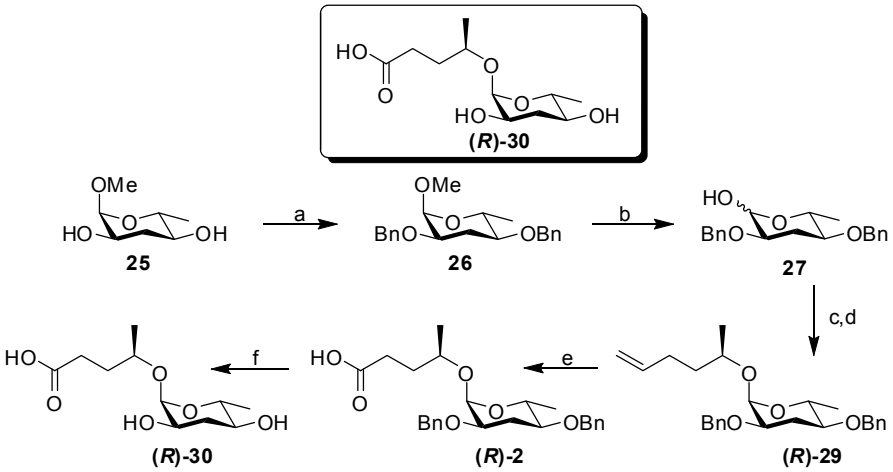


part#9 | **Methyl L-paratosyl-4*R*-hydroxypentanoate (part#9-methyl ester)** | **bis-*R*-MTPA-derivative of part#9-methyl ester**

A solution of **part#9** (240 µg, 0.97 µmol) in a 1:1 mixture (*v/v*) of methanol and toluene (200 µL) was treated with 2.0 M (trimethylsilyl)diazomethane solution (70 µL) in diethyl ether. After stirring for 30 minutes excess reagent was destroyed by addition of acetic acid and the solution concentrated *in vacuo* to yield **part#9-methyl ester,** which was used without further purification. A solution of **part#9-methyl ester** (110 µg, 0.42 µmol) in $CDCl_3$ (300 µL) and dry pyridine (3 µL,, 37.5 µmol) was stirred with 4-dimethylaminopyridine (1.4 mg, 11.5 µmol) for 5 min under argon atmosphere and then treated with (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride[4] (*S*-MTPA-Cl) (7 µL, 36.4 µmol) and allowed to stir at r.t. After 8 h, the crude reaction mixture was diluted with $CDCl_3$ (300 µL) and was directly placed in an NMR tube for ^{1}H-NMR analysis.

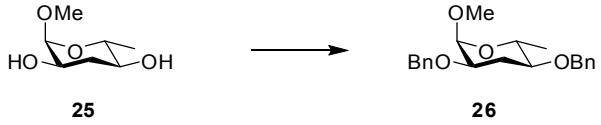
Synthesis of bis-*S*-MTPA-derivative of part#9-methyl ester. bis-*S*-MTPA-derivative of part#9-methyl ester was prepared following analogous reaction conditions from part#9-methyl ester and using *R*-(-)-α-methoxy-α-trifluoromethylphenylacetyl chloride[4] (*R*-MTPA-Cl).

4.4. Synthesis of D-paratosyl-4*R*-hydroxypentanoic acid (non-natural diastereomer of part#9)



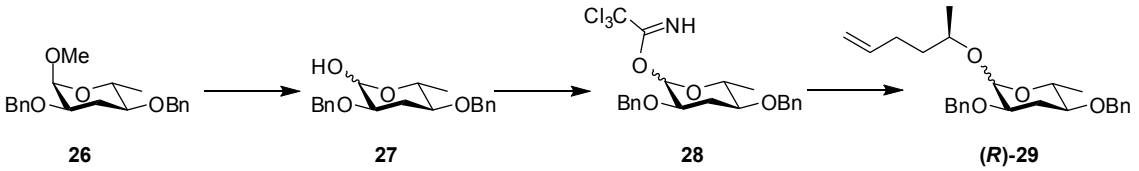
Synthetic Scheme 3. Overview of synthesis of D-paratosyl-4*R*-hydroxypentanoic acid (non-natural diastereomer of part#9). Reagents and conditions: **(a)** BnBr, NaH, DMF; **(b)** H_2SO_4, AcOH; **(c)** CCl_3CN, DBU, DCM; **(d)** (*R*)-5-hexen-2-ol, TMSOTf, DCM, 0 °C; **(e)** $RuCl_3 \cdot H_2O$, $NaIO_4$, DCM/MeCN/H_2O; **(f)** 10% Pd/C, H_2 (*g*), 10% formic acid in MeOH.

Synthesis of (2*S*,3*R*,5*S*,6*R*)-3,5-bis(benzyloxy)-2-methoxy-6-methyltetrahydro-2*H*-pyran (26)



A solution of **25**[5] (137 mg, 845 μmol) in DMF (2 mL) was cooled to 0 °C, and treated with sodium hydride (203 mg, 60% suspension in mineral oil, 5.1 mmol). After 30 minutes benzyl bromide (630 μL) was added and the mixture stirred overnight. After cooling the reaction mixture to 0 °C, excess reagent was destroyed by addition of methanol (3 mL), the residue diluted with diethyl ether (5 mL), and the organic phase washed with water (3 × 2 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-25% ethyl acetate in hexanes afforded **26** (217 mg, 634 μmol, 75%) as a colorless oil. ^{1}H NMR (400 MHz, chloroform-*d*): δ (ppm) 7.41-7.27 (m, 10H), 4.68-4.56 (m, 4H), 4.46 (d, *J* = 11.6 Hz, 1H), 3.75-3.66 (m, 1H), 3.53-3.45 (m, 1H), 3.43 (s, 3H), 3.12-3.03 (m, 1H), 2.36-2.29 (m, 1H), 1.92-1.81 (m, 1H), 1.26 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, chloroform-*d*): δ (ppm) 138.3, 138.2, 128.49, 128.46, 127.90, 127.86, 127.78, 127.75, 97.1, 77.9, 74.1, 71.1, 70.7, 67.0, 54.8, 30.0, 17.8.

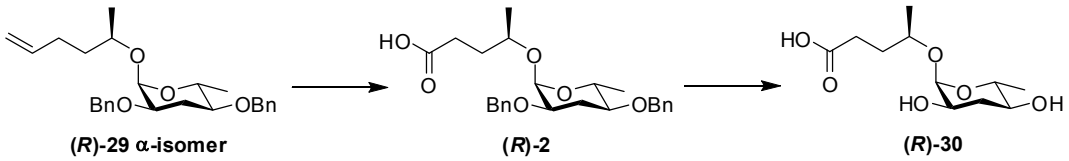
Synthesis of (3*R*,5*S*,6*R*)-3,5-bis(benzyloxy)-2-((*R*)-hex-5-en-2-yloxy)-6-methyltetrahydro-2*H*-pyran ((*R*)-29)



26 **27** **28** **(*R*)-29**

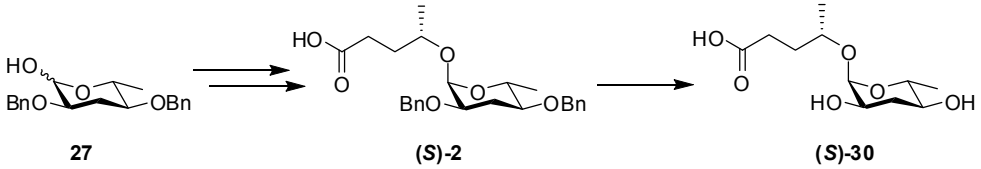
A solution of **26** (217 mg, 634 μmol) in a mixture of 3 M H_2SO_4 (0.5 mL) and acetic acid (2 mL) was heated at 100 °C for 2 h. After cooling, the reaction mixture was dried *in vacuo*. To the residue saturated aq. $NaHCO_3$ (5 mL) was added and the resulting mixture was stirred for 10 minutes and then extracted with dichloromethane (3 × 2 mL). Flash column chromatography on silica using a gradient of 0-30% ethyl acetate in hexanes afforded **27** (177 mg, 539 μmol, 85%) as a colorless oil. A solution of **27** (177 mg, 539 μmol) in dry dichloromethane (4 mL) was treated with trichloroacetonitrile (115 μL, 1.15 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (9 μL, 60.3 μmol). After 30 minutes, the reaction was concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 10-20% ethyl acetate in hexanes afforded **28** (110 mg, 233 μmol, 43%) as a colorless oil. A solution of **28** (110 mg, 233 μmol) in dry dichloromethane (2 mL) was cooled to -20 °C and treated with (*R*)-2-hexenol (60 μL, 500 μmol) and trimethylsilyl trifluoromethanesulfonate (5 μL, 28 μmol). After stirring at 0 °C for 3 h, the reaction was quenched with saturated aq. $NaHCO_3$, dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexanes afforded **(*R*)-29** α-anomer (40.5 mg, 99 μmol, 43%) and **(*R*)-29** β-anomer (35 mg, 85 μmol, 37 %) as colorless oils. For **(*R*)-29** α-anomer, ^{1}H NMR (500 MHz, chloroform-*d*): δ (ppm) 7.38-7.26 (m, 10H), 5.82 (ddt, *J* = 17.0 Hz, 10.3 Hz, 6.6 Hz, 1H), 5.04-4.98 (m, 1H), 4.97-4.93 (m, 1H), 4.87 (d, *J* = 3.4 Hz, 1H), 4.65 (d, *J* = 11.5 Hz, 1H), 4.59 (s, 2H), 4.46 (d, *J* = 11.5 Hz, 1H), 3.86-3.78 (m, 1H), 3.78-3.72 (m, 1H), 3.49-3.43 (m, 1H), 3.80 (ddd, *J* = 11.1 Hz, 9.4 Hz, 4.4 Hz, 1H), 2.34-2.28 (m, 1H), 2.25-2.11 (m, 2H), 1.94-1.85 (m, 1H), 1.75-1.66 (m, 1H), 1.58-1.49 (m, 1H), 1.25 (d, *J* = 6.3 Hz, 3H), 1.22 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (125 MHz, chloroform-*d*): δ (ppm) 138.7, 138.39, 138.37, 128.54, 128.52, 127.91, 127.86, 127.84, 127.80, 114.6, 95.7, 78.2, 74.5, 74.4, 71.0, 70.9, 67.4, 35.9, 30.2, 29.7, 21.5, 17.9.

Synthesis of (*R*)-4-(((2*S*,3*R*,5*S*,6*R*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid ((*R*)-30)



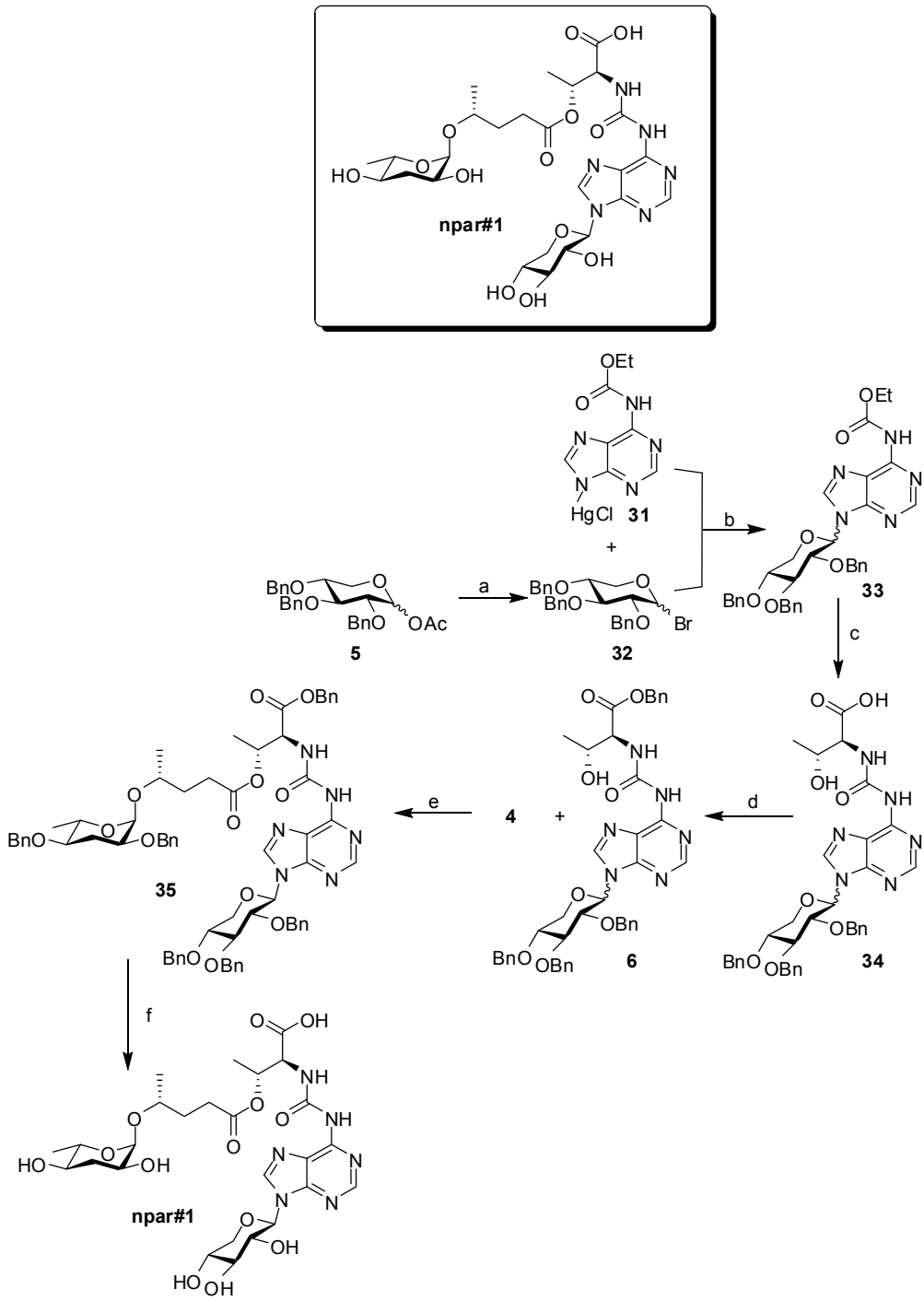
A solution of **(*R*)-29** α-anomer (20.3 mg, 49 μmol) in a 1:1:1 mixture (*v/v/v*) of dichloromethane : acetonitrile : H_2O (360 μL) was first treated with $NaIO_4$ (43 mg, 203 μmol) and then with a solution of $RuCl_3 \cdot H_2O$ (547 μg, 2.6 μmol) in H_2O (80 μL). After 2.75 h, the mixture was diluted with H_2O (1.2 mL), extracted with dichloromethane (3 × 1 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-20% methanol in dichloromethane containing 0.25% glacial acetic acid afforded **(*R*)-2** (16 mg, 37 μmol, 76%) as a colorless oil. A suspension of Pd/C (20 mg, 10%, *w/w*) in 500 μL of methanol containing 10% formic acid was first flushed with argon for 5 minutes and subsequently with a moderate flow of H_2 gas. To this stirred mixture was added a solution of **(*R*)-2** (7.0 mg, 16.3 μmol) in 500 μL methanol. After 1 h, the reaction was filtered over a pad of silica and concentrated *in vacuo*, affording **(*R*)-30** (4.0 mg, 16.1 μmol, 98%) as a colorless oil.^{1}H NMR (500 MHz, methanol-d_4): δ (ppm) 4.70 (d, J = 3.6 Hz, 1H), 3.81-3.72 (m, 1H), 3.63-3.54 (m, 2H), 3.16 (ddd, J = 11.4 Hz, 9.4 Hz, 4.6 Hz, 1H), 2.45 (t, J = 7.6 Hz, 2H), 2.04-1.97 (m, 1H), 1.85-1.77 (m, 2H), 1.77-1.69 (m, 1H), 1.26 (d, J = 6.2 Hz, 3H), 1.17 (d, J = 6.3 Hz, 3H). ^{13}C NMR (125 MHz, methanol-d_4): δ (ppm) 178.0, 99.6, 76.1, 71.9, 69.9, 69.0, 37.0, 33.1, 31.0, 21.8, 17.7.

Synthesis of (*S*)-4-(((2*S*,3*R*,5*S*,6*R*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid ((*S*)-30)



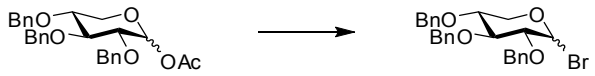
(*S*)-30 (enantiomer of part#9) was prepared following analogous reaction steps using (*S*)-2-hexenol. NMR spectroscopic characterization of **(*S*)-30** was identical to that of **part#9**.

4.5. Synthesis of npar#1



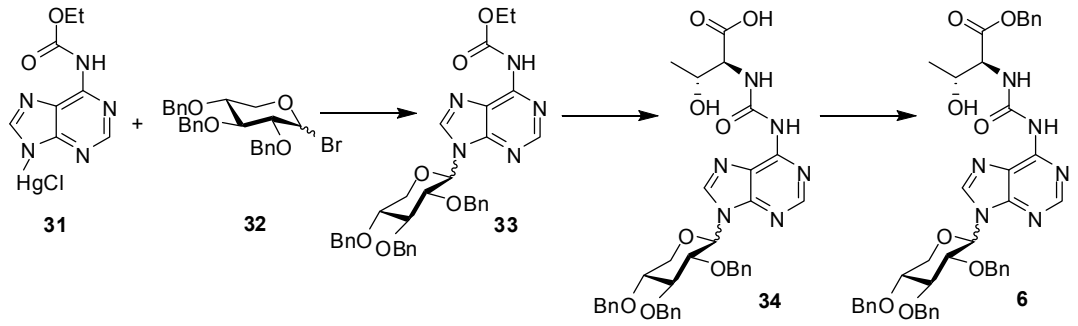
Synthetic Scheme 4. Overview of synthesis of npar#1. Reagents and conditions: **(a)** TMSBr, DCM, -40 °C to r.t.; **(b)** toluene, reflux; **(c)** L-threonine, pyridine, 107 °C; **(d)** 2-benzyloxy-1-methylpyridinium triflate[6], Et_3N, $PhCF_3$, 83 °C; **(e)** EDC, DMAP, DCM; **(f)** 10% Pd/C, H_2 (*g*) 10% formic acid in MeOH.

Synthesis of (3*R*,4*S*,5*R*)-3,4,5-tris(benzyloxy)-2-bromotetrahydro-2*H*-pyran (32)



To a solution of **5**[7] (550 mg, 1.19 mmol) in dry dichloromethane (1.5 mL) cooled to -40 °C was added trimethylsilyl bromide (3.2 mL, 24.2 mmol) dropwise with constant stirring. The reaction mixture was then allowed to warm up to r.t. and stirred for 45 minutes. The excess reagent and solvent was removed *in vacuo*. The product decomposed in contact to moisture and hence was not characterized further and used for the next step directly.

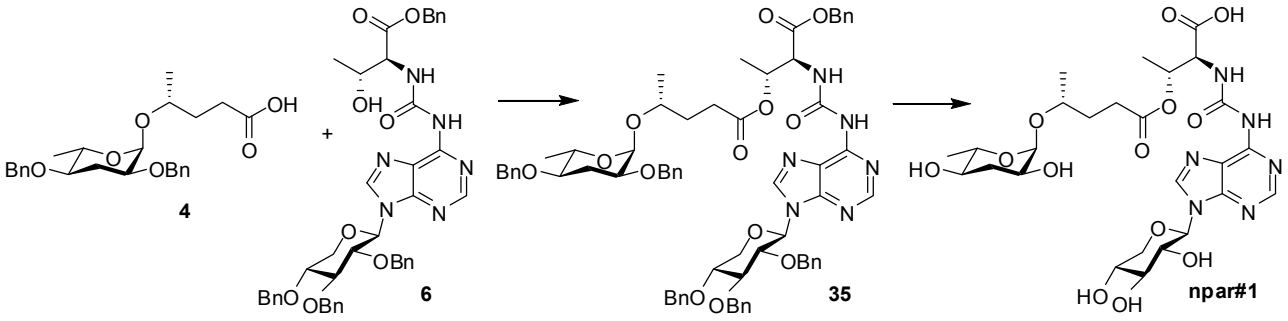
Synthesis of (2*S*,3*R*)-benzyl 3-hydroxy-2-(3-(9-((3*R*,4*S*,5*R*)-3,4,5-tris(benzyloxy)tetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoate (6)



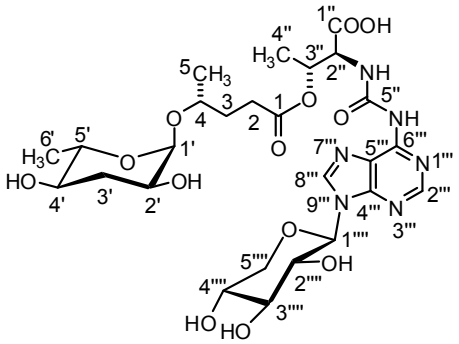
31[8] (500 mg, 1.12 mmol) was dried thorougly *in vacuo* and added to a solution of **32** in 12 mL dry toluene. The reaction mixture was refluxed for 2.5 h. Toluene was evaporated to reduce the volume to ~3 mL *in vacuo* and 3 mL of petroleum ether was added to it. The resulting brown suspension was filtered and the precipitate washed with warm chloroform (3 x 10 mL). The filtrate and the washings were combined and washed with 10 mL 30% aq. KI solution, 10 mL water, dried over Na_2SO_4, and concentrated *in vacuo.* Flash column chromatography on silica using a gradient of 0-20% methanol in dichloromethane afforded **33** (160 mg, 262 µmol, 22% over two steps, mixture of α and β anomers in a ratio of ~2:3) as a pale yellow oil. This mixture of anomers of **33** was reacted with L-threonine and worked up following a procedure reported for the corresponding 2,3,5-tri-*O*-acetylribofuranoside-derivative.[8] Flash column chromatography on silica using a gradient of 0-30% methanol in dichloromethane containing 0.25% acetic acid afforded **34** (117 mg, 172 µmol, 66%, mixture of α and β-anomers in ratio ~ 2:3) as a yellow solid. A mixture of **34** (72 mg, 106 µmol) and 15 µl triethylamine (210 µmol) in 300 µl trifluoromethylbenzene was then treated with 2-benzyloxy-1-methylpyridinium triflate[6] (71 mg, 210 µmol) and stirred at 83 °C for 15 h. The reaction was partitioned between 2 mL

ethyl acetate and 2 mL water, and the organic phase was washed with 1 mL water, 1 mL brine, dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-20% isopropanol in dichloromethane afforded **6** (8.1 mg, 10 µmol, 10%, β-anomer) as a yellow solid. ^{1}H NMR (500 MHz, methanol-d_4): δ (ppm) 8.39 (s, 1H), 8.27 (s, 1H), 7.43-7.25 (m, 15H), 6.99-6.95 (m, 1H), 6.91-6.86 (m, 2H), 6.67-6.62 (m, 2H), 5.53 (d, J = 8.9 Hz, 1H), 5.25 (d, J = 12.7 Hz, 1H), 5.23 (d, J = 12.7 Hz, 1H), 5.01 (d, J = 11.2 Hz, 1H), 4.88 (d, J = 11.2 Hz, 1H), 4.74 (s, 2H), 4.62-4.56 (m, 2H), 4.48 (dq, J = 6.4 Hz, 2.5 Hz, 1H), 4.26-4.15 (m, 3H), 3.94-3.88 (m, 1H), 3.84-3.79 (m, 1H), 3.53-3.46 (m, 1H), 1.31 (d, J = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, methanol-d_4): δ (ppm) 172.2, 156.6, 152.1, 151.5, 151.4, 143.7, 139.9, 139.7, 138.4, 137.2, 129.65, 129.53, 129.46, 129.37, 129.24, 129.13, 129.08, 129.06, 128.90, 128.88, 128.74, 128.71, 121.5, 86.5, 85.6, 79.6, 78.8, 76.5, 75.7, 74.1, 68.5, 68.1, 67.7, 60.6, 20.7.

Synthesis of (2*S*,3*R*)-3-(((*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (npar#1)



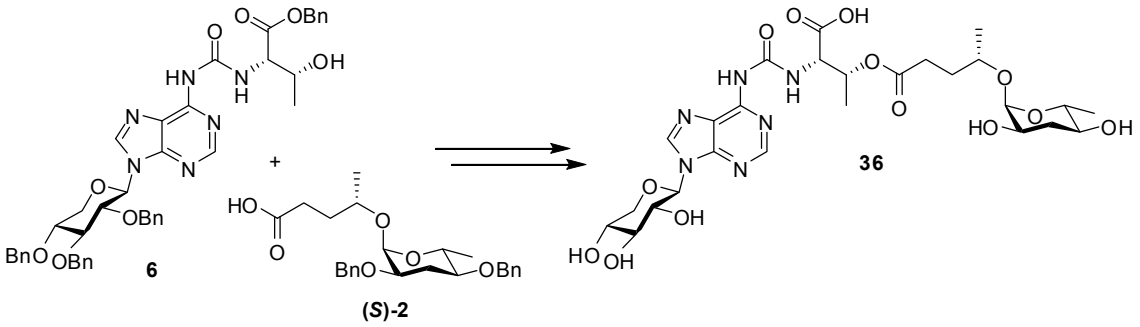
A solution of **4** (4 mg, 9 µmol) in 450 µL dry dichloromethane was treated with 4-dimethylaminopyridine (2.5 mg, 20 µmol) and EDC hydrochloride (4 mg, 21 µmol). After stirring for 15 minutes, **6** (7.3 mg, 9 µmol) in 300 µL dry dichloromethane was added to the mixture. After stirring for 12 h, the reaction was concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-15% isopropanol in dichloromethane afforded **35** (5.5 mg, 4.6 µmol, 51%). A solution of Pd/C (7 mg, 10%, *w/w*) in 500 µL of methanol containing 10% formic acid was first flushed with argon for 5 minutes and subsequently with a moderate flow of H_2 gas. To this stirring solution was added a solution **35** (5.5 mg, 4.6 µmol) in 500 µL methanol. After 4 h, the reaction was filtered over a pad of silica and concentrated *in vacuo*. HPLC purification (see Methods) afforded **npar#1** (1.1 mg, 1.7 µmol, 37%) as a colorless oil. α_D^{20} = -14.5 (*c.* 0.11, methanol). For NMR spectroscopic data, see next page.



NMR Spectroscopic data for **npar#1**. ^{1}H (600 MHz), ^{13}C (151 MHz), and HMBC NMR spectroscopic data for **npar#1** in methanol-d_4. Chemical shifts were referenced to ($CD_2\underline{H}OD$) = 3.31 ppm and ($\underline{C}D_3OD$) = 49.00 ppm.

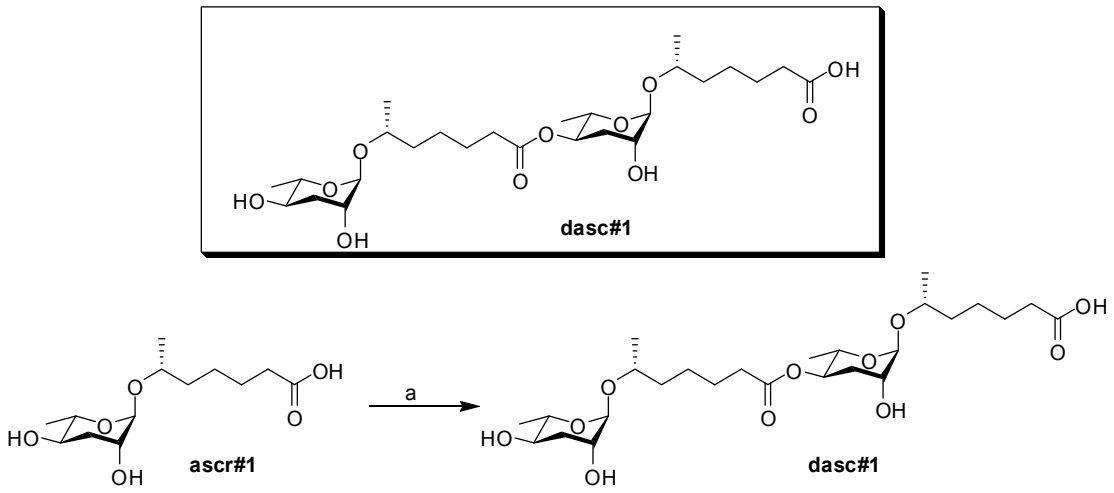
Position	δ ^{13}C [ppm]	δ ^{1}H [ppm]	^{1}H-^{1}H-coupling constants (Hz)	Key HMBC correlations
1	173.6	---		
2	31.5	2.59, 2.49		C-1
3	33.1	1.84-1.97		
4	72.6	3.82	$J_{4,5}$ = 6.2	C-1′
5	19.0	1.17		
1′	96.1	4.73	$J_{1',2'}$ = 3.9	C-2′, C-3′, C-5′
2′	68.3	3.61	$J_{2',3'\ (ax)}$ = 12.1; $J_{2',3'\ (eq)}$ = 5.8	
3′	36.7	1.73 (ax) 2.02 (eq)	$J_{3'\ (eq),3'\ (ax)}$ = 12.4; $J_{3'\ (eq),4'}$ = 4.6 $J_{3'\ (ax),4'}$ = 11.7	
4′	71.5	3.15	$J_{4',5'}$ = 9.7	
5′	69.9	3.53	$J_{5',6'\ (eq)}$ =6.3	
6′	17.6	1.173		C-5′
1″	174.7	---		
2″	58.4	4.69	$J_{2'',3''}$ = 6.3	C-1″, C-3″, C-5″
3″	71.7	5.58	$J_{3'',4''}$ = 6.8	
4″	17.4	1.38		
5″	154.7	---		
2‴	152.1	8.66		C-6‴
4‴	151.9	---		
5‴	121.2	---		
6‴	151.6	---		
8‴	143.3	8.47		C-4‴, C-5‴
1⁗	85.7	5.56	$J_{1'''',2''''}$ = 9	C-4‴, C-8‴, C-2⁗, C-3⁗
2⁗	72.8	4.15	$J_{2'''',3''''}$ = 9.2	
3⁗	78.6	3.53	$J_{3'''',4''''}$ = 9.2	
4⁗	70.4	3.76	$J_{4'''',5''''\ (ax)}$ = 10.4, $J_{4'''',5''''\ (eq)}$ = 5.5	
5⁗	69.7	3.50 (ax) 4.04 (eq)	$J_{5''''\ (ax),5''''\ (eq)}$ = 11.5	

Synthesis of (2*S*,3*R*)-3-(((*S*)-4-(((2*S*,3*R*,5*S*,6*R*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (36)



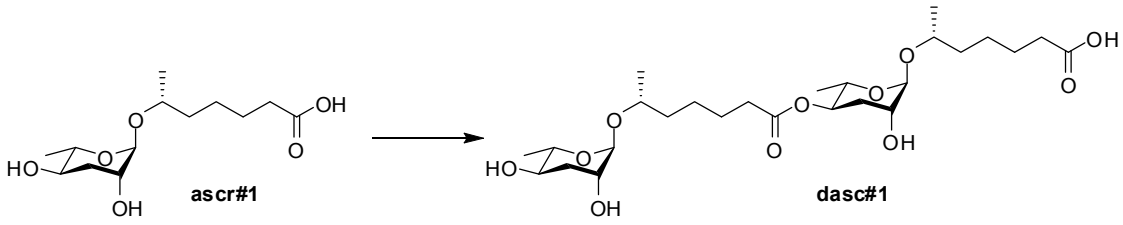
36 was prepared following analogous reaction steps as for **npar#1** using **(*S*)-2**. ^{1}H NMR (600 MHz, methanol-d_4): δ (ppm) 8.65 (s, 1H), 8.46 (s, 1H), 5.59-5.54 (m, 1H), 5.55 (d, J = 9.4 Hz, 1H), 4.71 (d, J = 3.8 Hz, 1H), 4.67-4.63 (m, 1H), 4.14 (t, J = 9.1 Hz, 1H), 4.04 (dd, J = 11.3 Hz, 5.5 Hz, 1H), 3.84-3.73 (m, 2H), 3.62-3.56 (m, 1H), 3.55-3.47 (m, 3H), 3.13 (ddd, J = 11.3 Hz, 9.3 Hz, 4.4 Hz, 1H), 2.60-2.47 (m, 2H), 2.04-1.98 (m, 1H), 1.94-1.84 (m, 2H), 1.75-1.68 (m, 1H), 1.37 (d, J = 6.3 Hz, 3H), 1.16 (d, J = 6.1 Hz, 3H), 1.15 (d, J = 6.3 Hz, 3H). ^{13}C NMR (151 MHz, methanol-d_4): δ (ppm) 173.7, 173.5, 153.5, 152.3, 151.8, 151.5, 143.3, 121.1, 96.0, 85.7, 78.6, 72.8, 72.4, 71.9, 71.6, 70.5, 70.1, 69.7, 68.4, 58.5, 36.8, 33.2, 31.5, 19.1, 17.61, 17.57.

4.6. Synthesis of dasc#1

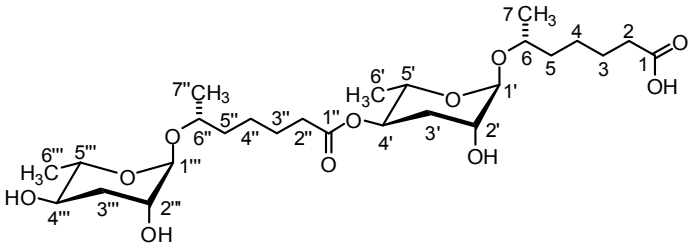


Synthetic Scheme 5. Overview of synthesis of dasc#1. Reagents and conditions: **(a)** EDC, DMAP, DMF.

Synthesis of (*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoyl)oxy)-3-hydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoic acid (dasc#1)



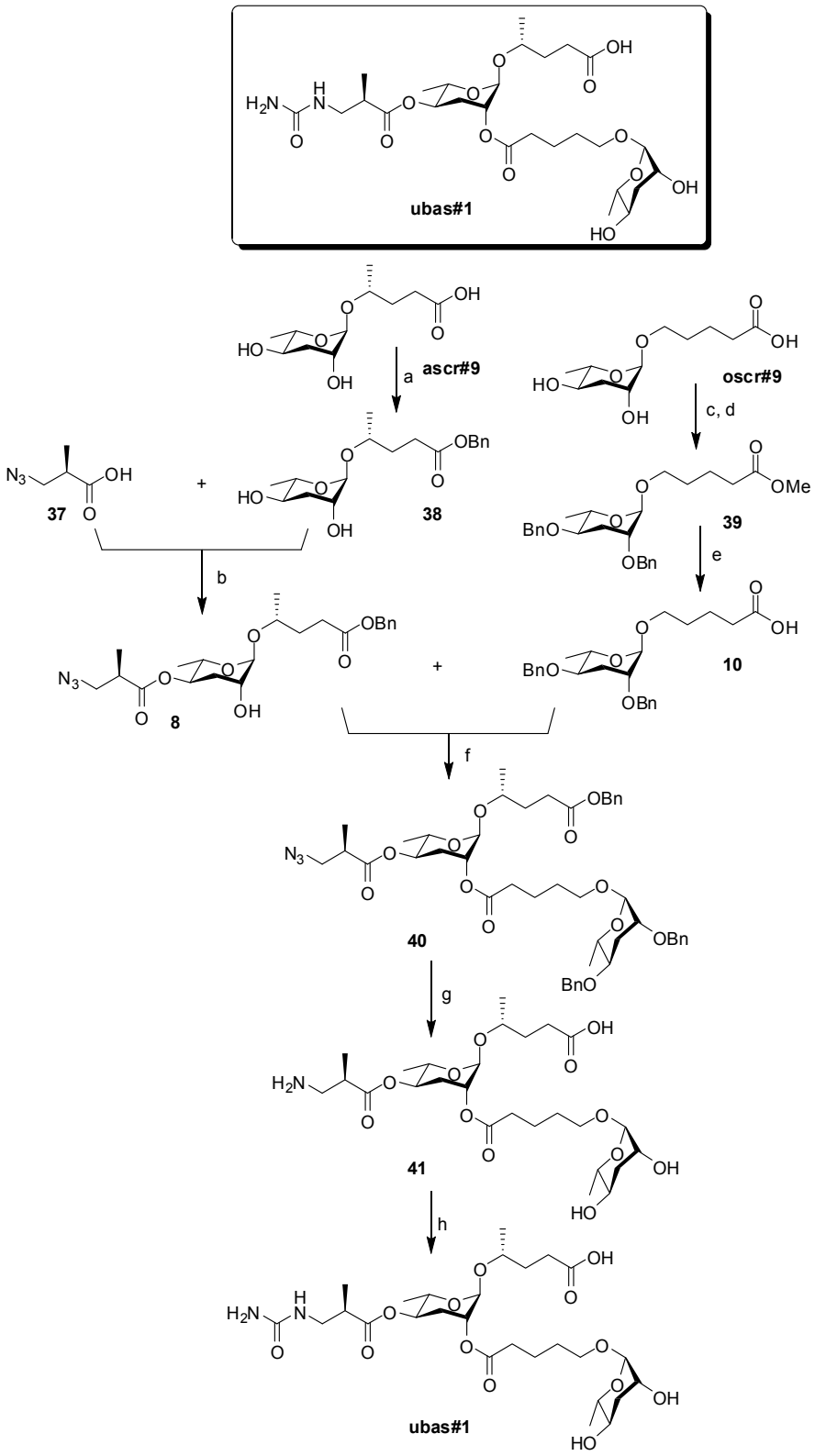
A solution of **ascr#1** (15 mg, 54 µmol) in 15 mL dry DMF was added to a solution of 4-dimethylaminopyridine (13.5 mg, 110.7 µmol) and EDC hydrochloride (11 mg, 57.3 µmol) in 7 mL dry DMF. The reaction was monitored by ESI$^-$ MS and was quenched with few drops of glacial acetic acid and concentrated *in vacuo* when polymer peaks (*m/z* = 791 etc.) were observed in significant quantities. Flash column chromatography on silica using a gradient of 0-30% methanol in dichloromethane containing 0.25% and further HPLC purification (see Methods) of crude product mixture afforded **dasc#1** (1.1 mg, 2.1 µmol, 7.8 %) as a colorless oil. α_D^{20} = -115.0 (*c.* 0.11, methanol). For NMR spectroscopic data, see next page.



NMR Spectroscopic data for **dasc#1**. ^{1}H (600 MHz), ^{13}C (151 MHz), and HMBC NMR spectroscopic data for **dasc#1** in methanol-d_4. Chemical shifts were referenced to ($CD_2\underline{H}OD$) = 3.31 ppm and ($\underline{C}D_3OD$) = 49.00 ppm.

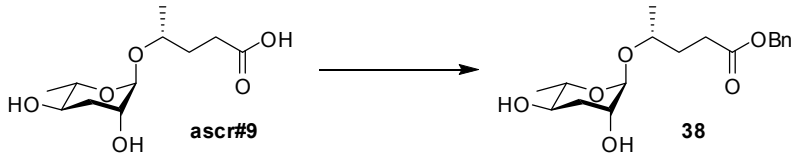
Position	δ ^{13}C [ppm]	δ ^{1}H [ppm]	^{1}H-^{1}H-coupling constants (Hz)	Key HMBC correlations
1	177.0	---		
2	37.8	2.25	$J_{2,3}$ = 7.7	C-1
3	25.9 or 26.2	1.64		
4	26.4 or 27.1	1.36-1.68		
5	37.9	1.45-1.62		
6	71.9 or 72.7	3.79	$J_{6,7}$ = 6.3	C-1′
7	19.0	1.13		
1′	97.4	4.68	$J_{1',2'}$ = 2.0	C-2′, C-3′, C-5′
2′	69.4	3.72	$J_{2',3'\ (ax)}$ = 6.3; $J_{2',3'\ (eq)}$ = 5.9	
3′	32.8	1.83 (ax) 2.04 (eq)	$J_{3'\ (eq),3'\ (ax)}$ = 13.5; $J_{3'\ (eq),4'}$ = 5.0 $J_{3'\ (ax),4'}$ = 11.7	
4′	71.1	4.86	$J_{4',5'}$ = 10.1	C-1″
5′	68.0	3.84	$J_{5',6'\ (eq)}$ = 6.4	
6′	17.9	1.14		C-4′, C-5′
1″	174.4	---		
2″	34.9	2.35	$J_{2'',3''}$ = 7.5	C-1″
3″	25.9 or 26.2	1.64		
4″	26.4 or 27.1	1.36-1.68		
5″	37.9	1.45-1.62		
6″	71.9 or 72.7	3.79	$J_{6'',7''}$ = 6.3	C-1‴
7″	19.0	1.13		
1‴	97.2	4.64	$J_{1''',2'''}$ = 2.4	C-2‴, C-3‴, C-5‴
2‴	69.4	3.71	$J_{2''',3'''\ (ax)}$ = 6.2; $J_{2''',3'''\ (eq)}$ = 6.0	
3‴	35.7	1.76 (ax) 1.95 (eq)	$J_{3'''\ (eq),3'''\ (ax)}$ = 13.4; $J_{3'''\ (eq),4'''}$ = 4.7 $J_{3'''\ (ax),4'''}$ = 11.8	
4‴	68.1	3.51	$J_{4''',5'''}$ = 9.4	
5‴	70.9	3.61	$J_{5''',6'''\ (eq)}$=6.4	
6‴	17.9	1.22		C-4‴, C-5‴

4.7. Synthesis of ubas#1



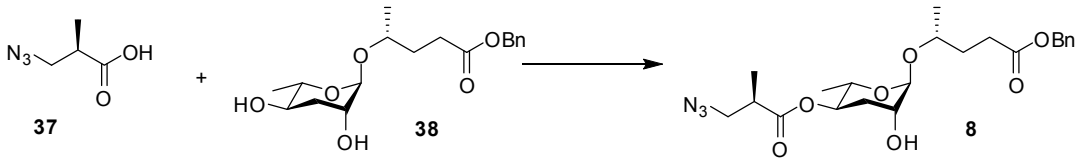
Synthetic Scheme 6. Overview of synthesis of ubas#1. Reagents and conditions: **(a)** 2-benzyloxy-1-methylpyridinium triflate[6], Et_3N, $PhCF_3$, 83 °C; **(b)** EDC, DMAP, DCM; **(c)** $TMSCHN_2$, toluene/MeOH; **(d)** BnBr, NaH, DMF; **(e)** LiOH, THF/dioxane/H_2O, 67 °C; **(f)** EDC, DMAP, DCM; **(g)** 10% Pd/C, H_2 (*g*), 5% HCl in MeOH; **(h)** KCNO, HCl, H_2O, 75 °C.

Synthesis of (*R*)-benzyl 4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (38)



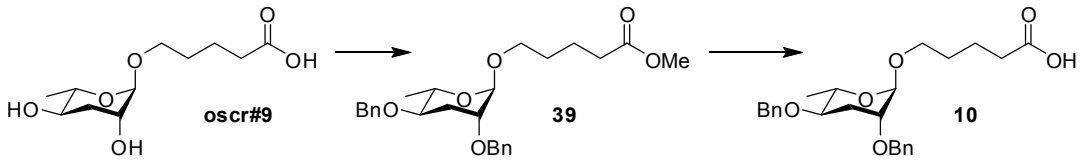
A mixture of **ascr#9**[3b] (24.0 mg, 97 µmol) and 28 µl triethylamine (200 µmol) in 300 µl trifluoromethyl benzene was treated with 70 mg 2-benzyloxy-1-methylpyridinium triflate[6] (200 µmol) and stirred at 83 °C for 18 h. The products were partitioned between 2 mL ethylacetate and 2 mL water, the organic phase washed with 1 mL water, 1 mL saturated aq. NaCl solution, dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-10% methanol in dichloromethane afforded **38** (22.6 mg, 66.8 µmol, 69%) as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ (ppm) 7.39-7.30 (m, 5H), 5.12 (s, 2H), 4.68 (s, 1H), 3.88-3.80 (m, 1H), 3.80-3.74 (m, 1H), 3.63-3.52 (m, 2H), 2.54-2.41 (m, 2H), 2.06-2.01 (m, 1H), 1.90-1.84 (m, 2H), 1.82-1.75 (m, 1H), 1.24 (d, *J* = 6.1 Hz, 3H), 1.14 (d, *J* = 6.2 Hz, 3H).^{13}C NMR (125 MHz, chloroform-*d*): δ (ppm) 173.6, 136.0, 128.7, 128.39, 128.37, 95.8, 70.3, 70.1, 69.3, 68.1, 66.5, 35.3, 32.2, 30.8, 18.8, 17.8.

Synthesis of (*R*)-benzyl 4-(((2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-3-azido-2-methylpropanoyl)oxy)-3-hydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (8)



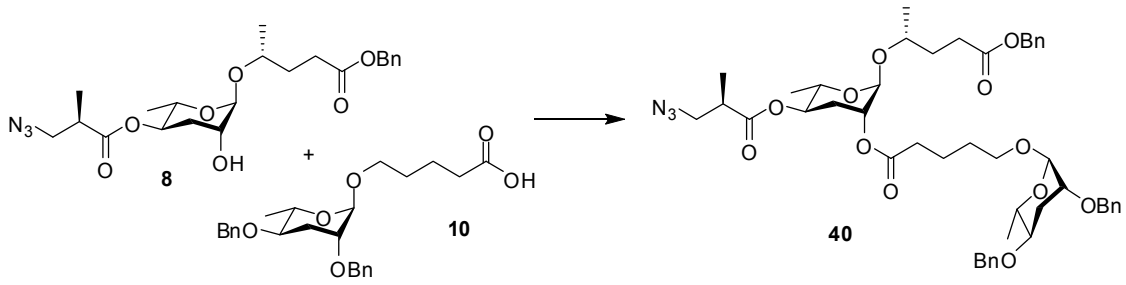
A solution of **38** (22.6 mg, 66.8 µmol) and 3-azido-(2*R*)-methylpropanoic acid[9] (**37**, 8.6 mg, 66.8 µmol) in 2 mL dichloromethane was treated with 4-dimethylaminopyridine (16.3 mg, 133.6 µmol) and EDC hydrochloride (25.7 mg, 133.6 µmol). After stirring at r.t. for 12 h the reaction was quenched by addition of 5% aq. acetic acid (100 µl), dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-10% isopropanol in dichloromethane afforded **8** (5.2 mg, 11.6 µmol, 17%) as a colorless oil. ^{1}H NMR (400 MHz, chloroform-*d*): δ (ppm) 7.40-7.31 (m, 5H), 5.15 (d, *J* = 13.6 Hz, 1H), 5.11 (d, *J* = 13.6 Hz, 1H), 4.86 (ddd, *J* = 10.9 Hz, 9.4 Hz, 4.6 Hz, 1H), 4.73-4.70 (m, 1H), 3.90-3.76 (m, 3H), 3.52 (dd, *J* = 12.2 Hz, 7.5 Hz, 1H), 3.38 (dd, *J* = 12.2 Hz, 5.6 Hz, 1H), 2.71-2.60 (m, 1H), 2.57-2.42 (m, 2H), 2.13-2.05 (m, 2H), 1.93-1.83 (m, 3H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.17 (d, *J* = 6.3 Hz, 3H), 1.16 (d, *J* = 6.2 Hz, 3H).

Synthesis of 5-(((2*R*,3*R*,5*R*,6*S*)-3,5-bis(benzyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (10)



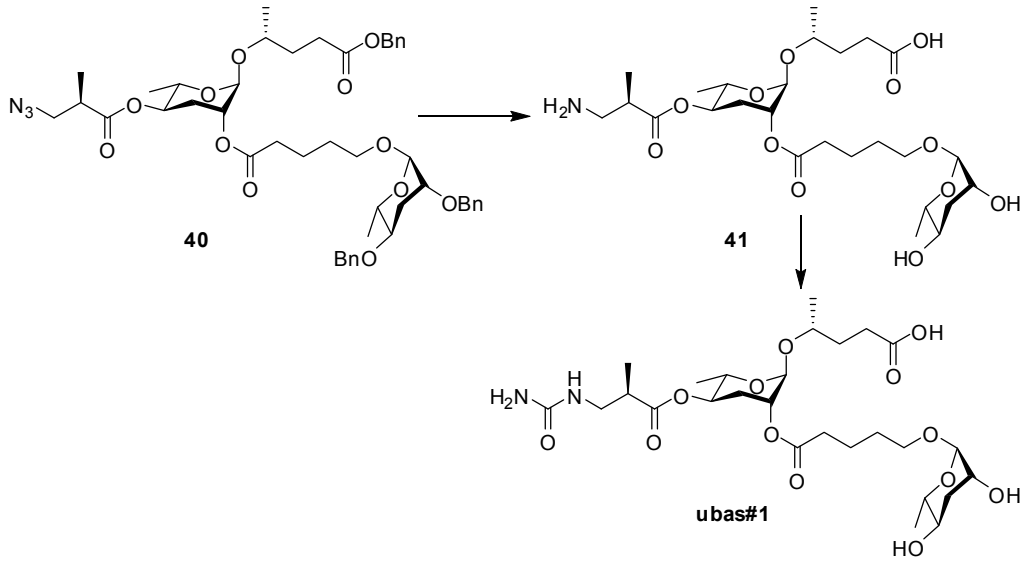
A solution of **oscr#9**[10] (17.6 mg, 71 µmol) in a 1:1 mixture (*v/v*) of methanol and toluene (2 mL) was treated with 2.0 M (trimethylsilyl)diazomethane solution (200 µl) in diethyl ether. After stirring for 30 minutes excess reagent was destroyed by addition of acetic acid and the solution concentrated *in vacuo*. The residue was dissolved in DMF (500 µl), cooled to 0 °C, and treated with sodium hydride (17 mg, 60% suspension in mineral oil, 425 µmol). After 10 minutes benzyl bromide (51 µl) was added and the mixture stirred overnight. Excess reagent was destroyed by addition of methanol (300 µl), the residue diluted with ethyl acetate (2 mL), and the organic phase washed with water (3 × 1 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-40% ethyl acetate in hexanes afforded **39** (14.4 mg, 33 µmol, 46% over two steps) as a colorless oil. A solution of **39** (14.4 mg, 33 µmol) in THF (1 mL) was treated with 3.3 M aq. lithium hydroxide solution (100 µl, 330 µmol) in dioxane (2 mL) at 67 °C. After 3 h the reaction was quenched by addition of acetic acid, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-20% methanol in dichloromethane afforded **10** (11.8 mg, 28 µmol, 85%) as a colorless oil. ^{1}H NMR (500 MHz, acetone-d_6): δ (ppm) 7.32-7.38 (m, 8H), 7.30-7.25 (m, 2H), 4.69 (s, 1H), 4.62 (d, J = 11.8 Hz, 1H), 4.58 (s, 2H), 4.48 (d, J = 11.8 Hz, 1H), 3.73-3.64 (m, 2H), 3.64-3.60 (m, 1H), 3.46-3.38 (m, 2H), 2.37-2.30 (m, 3H), 1.73-1.57 (m, 5H), 1.21 (d, J = 6.2 Hz, 3H). ^{13}C NMR (125 MHz, acetone-d_6): δ (ppm) 174.6, 140.0, 139.9, 129.1, 129.0, 128.6, 128.4, 128.19, 128.21, 97.7, 76.4, 76.0, 71.4, 71.2, 68.9, 67.3, 33.9, 30.2, 29.8, 22.6, 18.6.

Synthesis of (2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-3-azido-2-methylpropanoyl)oxy)-2-(((*R*)-5-(benzyloxy)-5-oxopentan-2-yl)oxy)-6-methyltetrahydro-2*H*-pyran-3-yl 5-(((2*R*,3*R*,5*R*,6*S*)-3,5-bis(benzyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (40)

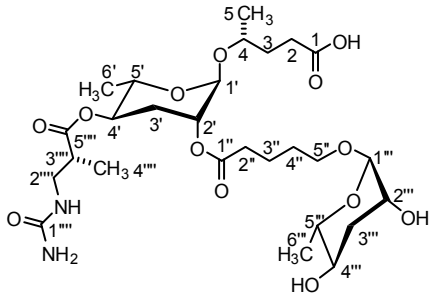


A solution of **8** (5.2 mg, 11.6 µmol) and **10** (6.4 mg, 14.9 µmol) in 1 mL dichloromethane was treated with 4-dimethylaminopyridine (3.7 mg, 30 µmol) and EDC hydrochloride (5.8 mg, 30 µmol). After stirring at r.t for 12 h the reaction was quenched by addition of 5% aq. acetic acid (50 µl), dried over Na_2SO_4, and concentrated *in vacuo*. Flash column chromatography on silica using a gradient of 0-50% ethyl acetate in hexane afforded **40** (9.6 mg, 11.2 µmol, 97%) as a colorless oil. ^{1}H NMR (500 MHz, acetone-d_6): δ (ppm) 7.40-7.25 (m, 15H), 5.15 (d, *J* = 12.3 Hz, 1H), 5.12 (d, *J* = 12.3 Hz, 1H), 4.84-4.78 (m, 2H), 4.66 (s, 1H), 4.74 (s, 1H), 4.58 (d, *J* = 12.3 Hz, 1H), 4.57 (d, *J* = 11.4 Hz, 1H), 4.53 (d, *J* = 12.3 Hz, 1H), 4.46 (d, *J* = 11.4 Hz, 1H), 3.87-3.80 (m, 2H), 3.75-3.67 (m, 2H), 3.60-3.56 (m, 1H), 3.51 (dd, *J* = 12.2 Hz, 7.6 Hz, 1H), 3.47-3.34 (m, 3H), 2.68-2.60 (m, 1H), 2.55-2.41 (m, 2H), 2.38 (t, *J* = 7.4 Hz, 2H), 2.24-2.18 (m, 1H), 2.12-2.06 (m, 1H), 1.96-1.85 (m, 3H), 1.77-1.65 (m, 3H), 1.64-1.55 (m, 2H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.19 (d, *J* = 7.1 Hz, 3H), 1.16 (d, *J* = 6.2 Hz, 3H), 1.15 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (125 MHz, acetone-d_6): δ (ppm) 173.4, 173.2, 172.9, 138.6, 138.5, 136.0, 128.7, 128.52, 128.51, 128.45, 128.38, 128.0, 127.79, 127.77, 97.2, 93.5, 75.6, 75.4, 71.4, 71.24, 71.22, 70.5, 70.4, 68.3, 67.0, 66.8, 66.5, 55.8, 40.1, 34.1, 32.1, 30.6, 29.9, 29.7, 29.5, 29.1, 21.8, 18.9, 18.3, 17.7, 14.9. ESI$^+$ MS: *m/z* = 882.5 [M+Na$^+$] and 898.5 [M+K$^+$].

Synthesis of (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3-((5-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-6-methyl-5-(((*R*)-2-methyl-3-ureidopropanoyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (ubas#1)

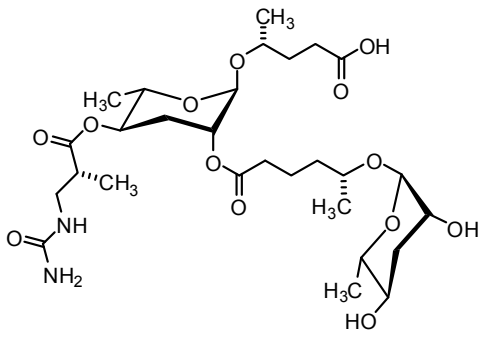


A solution of Pd/C (5.4 mg, 10%, *w/w*) in 0.7 mL of methanol containing 5% 1 M aq. HCl was flushed with argon gas for 5 minutes and subsequently with a moderate flow of H_2 gas for 5 minutes. To this stirring solution was added a solution of **40** (4.3 mg, 5.0 µmol) in 1.3 mL methanol via syringe and the H_2 gas was continuously flowed through the reaction. The reaction was monitored by direct injection ESI^- MS. After 20 minutes, the reaction was filtered over a pad of silica with additional methanol. The product was concentrated *in vacuo* and the crude mixture of **40** and **41** (3.7 mg) was used in the next step without further purification. A solution of aq. HCl (200 µL, 50 µmol), aq. KCNO (200 µL, 50 µmol) and H_2O (100 µL) was prepared. This aq. HCl/KCNO solution was added to the crude mixture of **40** and **41** (3.7 mg) and was placed in a 75 °C oil bath for 5 minutes. Additional aq. HCl solution (50 µL, 12.5 µmol) was added to the reaction and this was allowed to stir for an additional 2.5 minutes. The pH of the reaction mixture was periodically checked to ensure the pH was not basic. The reaction was monitored by direct injection ESI^- MS. The mixture was concentrated *in vacuo* and HPLC purification (see Methods) afforded **ubas#1** (200 µg, 0.3 µmol, 7% over two steps) as a colorless oil. For NMR spectroscopic data, see next page.



NMR spectroscopic data for **ubas#1**. ^{1}H (600 MHz), ^{13}C (151 MHz), and HMBC NMR spectroscopic data for **ubas#1** in methanol-d_4. Chemical shifts were referenced to ($CD_2\underline{H}OD$) = 3.31 ppm and ($\underline{C}D_3OD$) = 49.00 ppm.

Position	δ ^{13}C [ppm]	δ ^{1}H [ppm]	^{1}H-^{1}H-coupling constants (Hz)	Key HMBC correlations
1	174.6	---		
2	35.0	2.31	$J_{2,3}$ = 7.4	C-1
3	34.3	1.83	$J_{3,4}$ = 6.2	
4	72.7	3.84	$J_{4,5}$ = 6.4	C-1′
5	18.9	1.16		
1′	94.2	4.77	$J_{1',2'}$ = 2.4	C-2′, C-3′, C-5′
2′	71.8	4.80	$J_{2',3'\,(ax)}$ = 6.4; $J_{2',3'\,(eq)}$ = 5.8	C-1″
3′	30.7	2.01(ax) 2.10(eq)	$J_{3'\,(eq),3'\,(ax)}$ = 13.7; $J_{3'\,(eq),4'}$ = 4.2 $J_{3'\,(ax),4'}$ = 11.7	
4′	71.1	4.73	$J_{4',5'}$ = 9.2	C-5‴″
5′	67.9	3.99	$J_{5',6'\,(eq)}$ = 6.4	
6′	17.8	1.16		
1″	173.9	---		
2″	34.5	2.43	$J_{2'',3''}$ = 7.0	C-1″
3″	22.7	1.75		
4″	29.6	1.67	$J_{4'',5''}$ = 6.2	
5″	67.6	5a″ = 3.45 5b″ = 3.76		C-1‴
1‴	100.1	4.51	$J_{1''',2'''}$ = 2.6	C-2‴, C-3‴, C-5‴
2‴	69.1	3.79	$J_{2''',3'''\,(ax)}$ = 6.1, $J_{2''',3'''\,(eq)}$ = 5.9	
3‴	35.7	1.78 (ax) 1.95 (eq)	$J_{3''',3'''\,(ax)}$ = 13.1, $J_{3''',4'''}$ = 4.3 $J_{3''',4'''}$ = 11.2	
4‴	68.1	3.51	$J_{4''',5'''}$ = 9.5	
5‴	70.5	3.57	$J_{5''',6'''\,(eq)}$ = 6.4	
6‴	17.9	1.23		
1‴″	161.7	---		
2‴″	43.4	3.26	$J_{2'''',3''''}$ = 6.8	C-1‴″
3‴″	41.5	2.68	$J_{3'''',4''''}$ = 6.9	C-5‴″
4‴″	14.7	1.14		C-5‴″
5‴″	175.6			

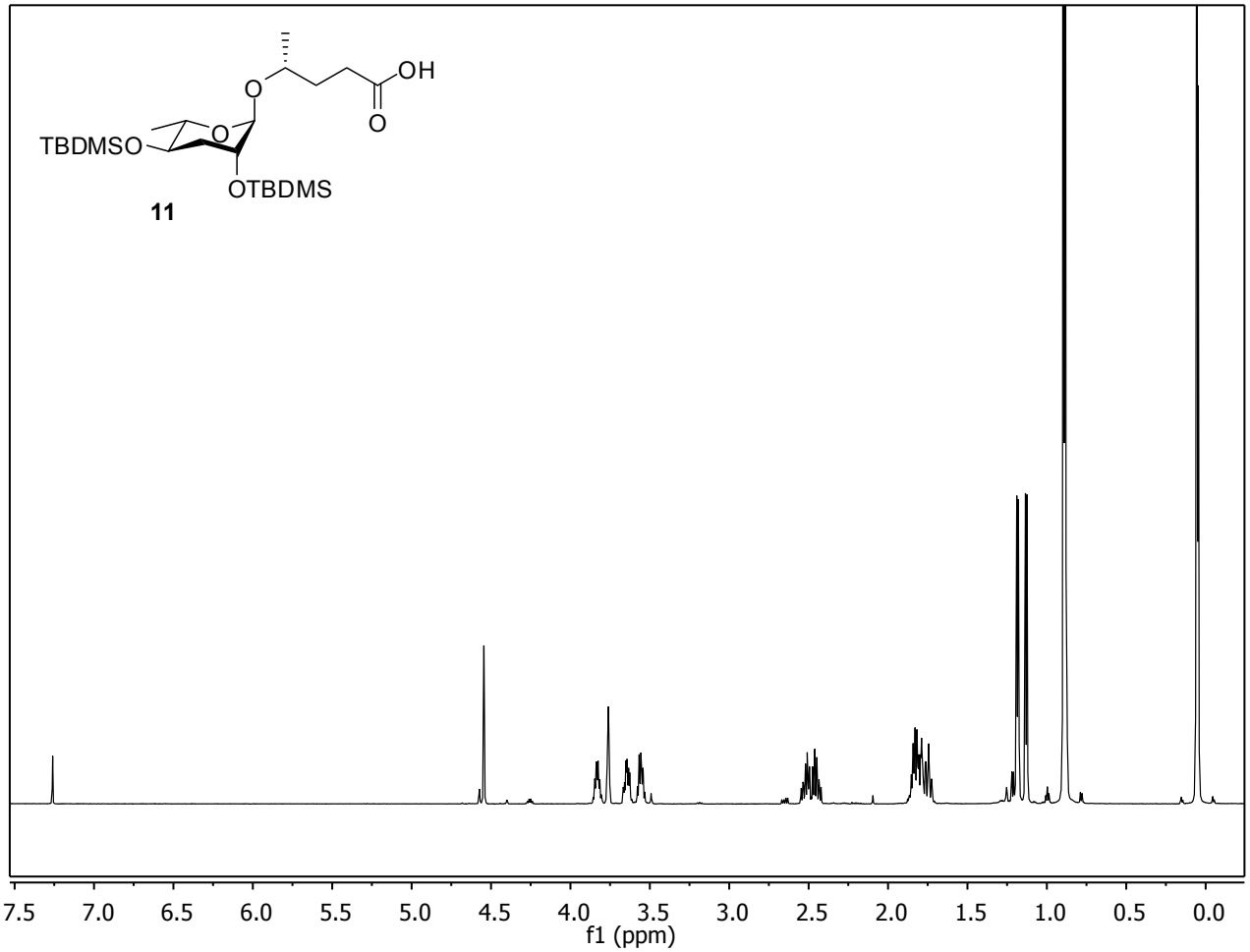


NMR Spectroscopic data for (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3-(((*R*)-5-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)hexanoyl)oxy)-6-methyl-5-(((*R*)-2-methyl-3-ureidopropanoyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (ubas#2)

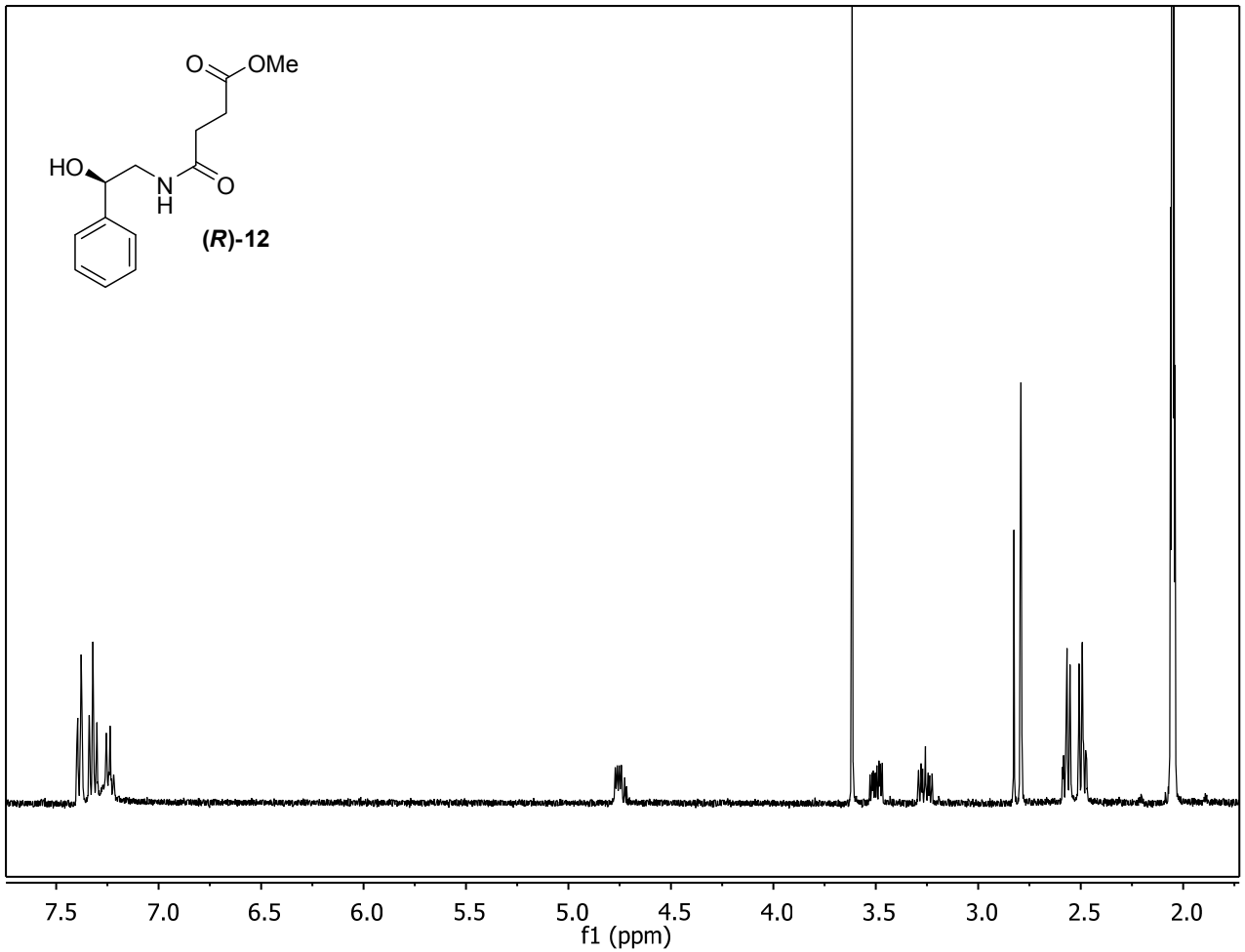
An enriched **ubas#2** sample was obtained following HPLC enrichment of crude *P. pacificus* exo-metabolome extract. ^{1}H NMR (600 MHz, methanol-d_4): δ (ppm) 4.80 (m, 1H), 4.79 (s, 1H), 4.74 (m, 1H), 4.65 (s, 1H), 3.99 (m, 1H), 3.84 (m, 1H), 3.82 (m, 1H), 3.72 (m, 1H), 3.62 (m, 1H), 3.51 (m, 1H), 3.26 (m, 2H), 2.68 (m, 1H), 2.42 (m, 2H), 2.34 (m, 2H), 2.10 (m, 1H), 2.01 (m, 1H), 1.95 (m, 1H), 1.83 (m, 2H), 1.78 (m, 1H), 1.64-1.57 (m, 4H), 1.23 (d, J = 6.3 Hz, 3H), 1.157 (d, J = 6.2 Hz, 3H), 1.156 (d, J = 6.3 Hz, 3H), 1.147 (d, J = 6.2 Hz, 3H), 1.142 (d, J = 7.0 Hz, 3H).

5. NMR Spectra of Synthetic Compounds

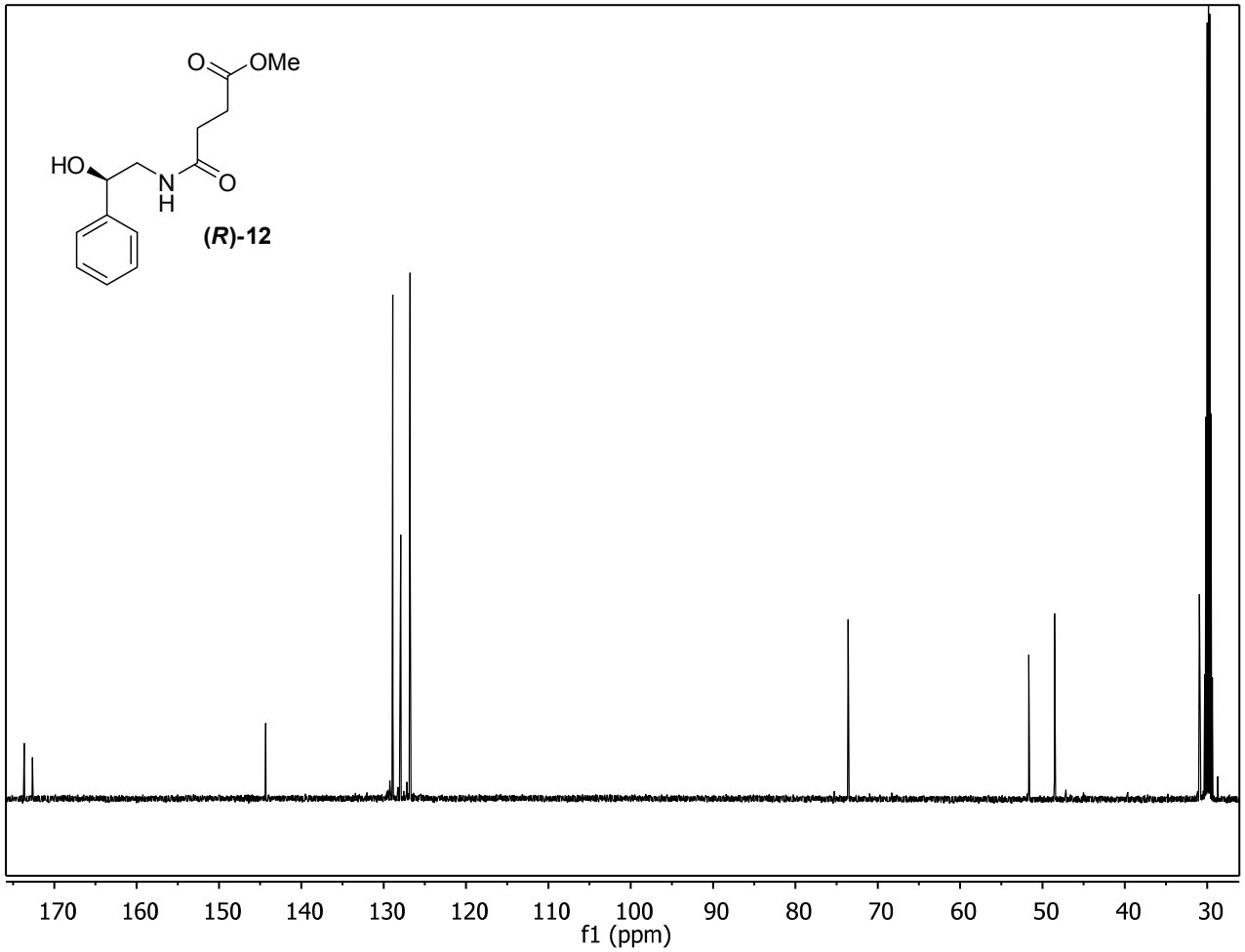
^{1}H NMR spectrum (600 MHz, chloroform-*d*) of (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-bis((*tert*-butyldimethylsilyl)oxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (11)



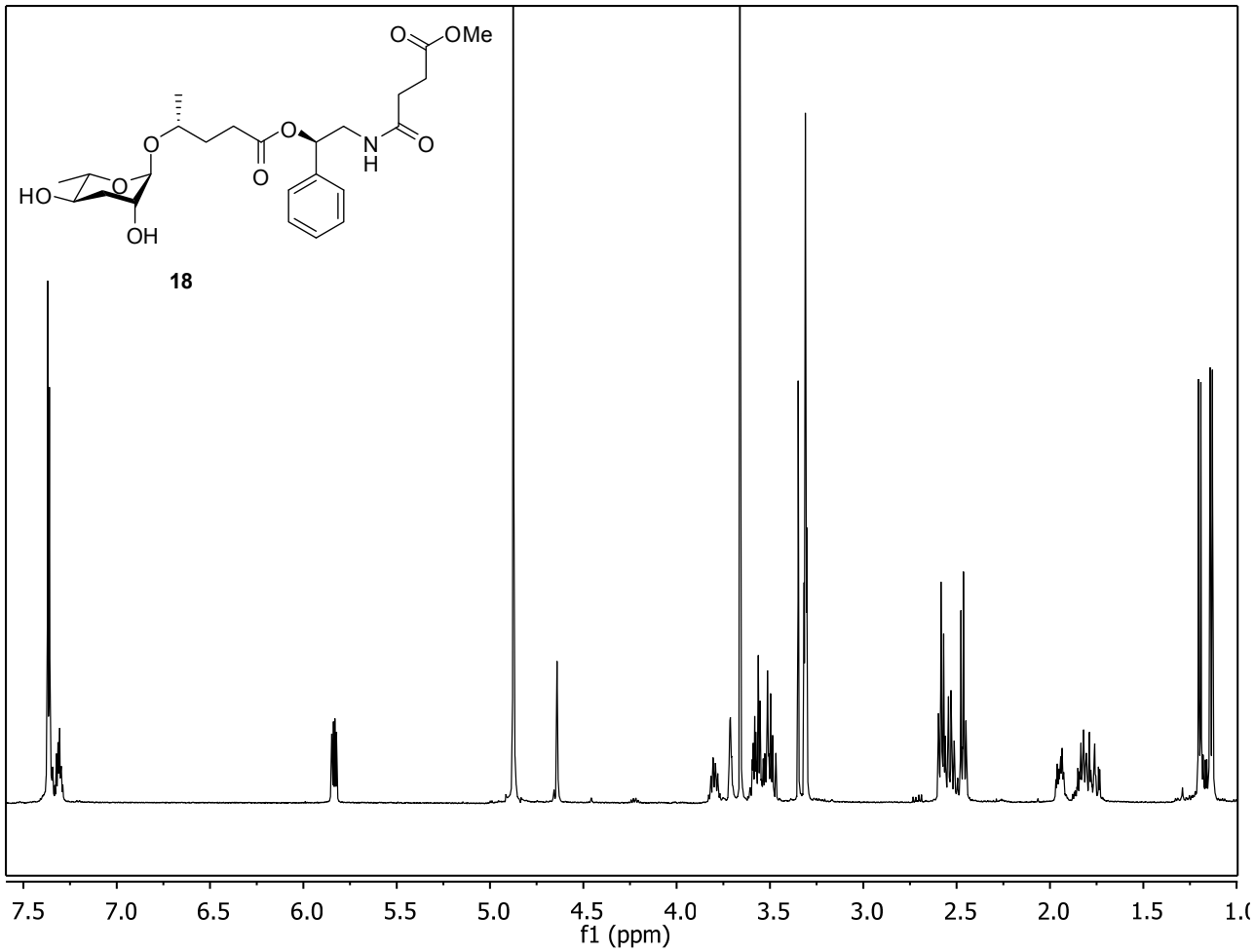
^{1}H NMR spectrum (400 MHz, acetone-d_6) of (*R*)-methyl 4-((2-hydroxy-2-phenylethyl)amino)-4-oxobutanoate ((*R*)-12)



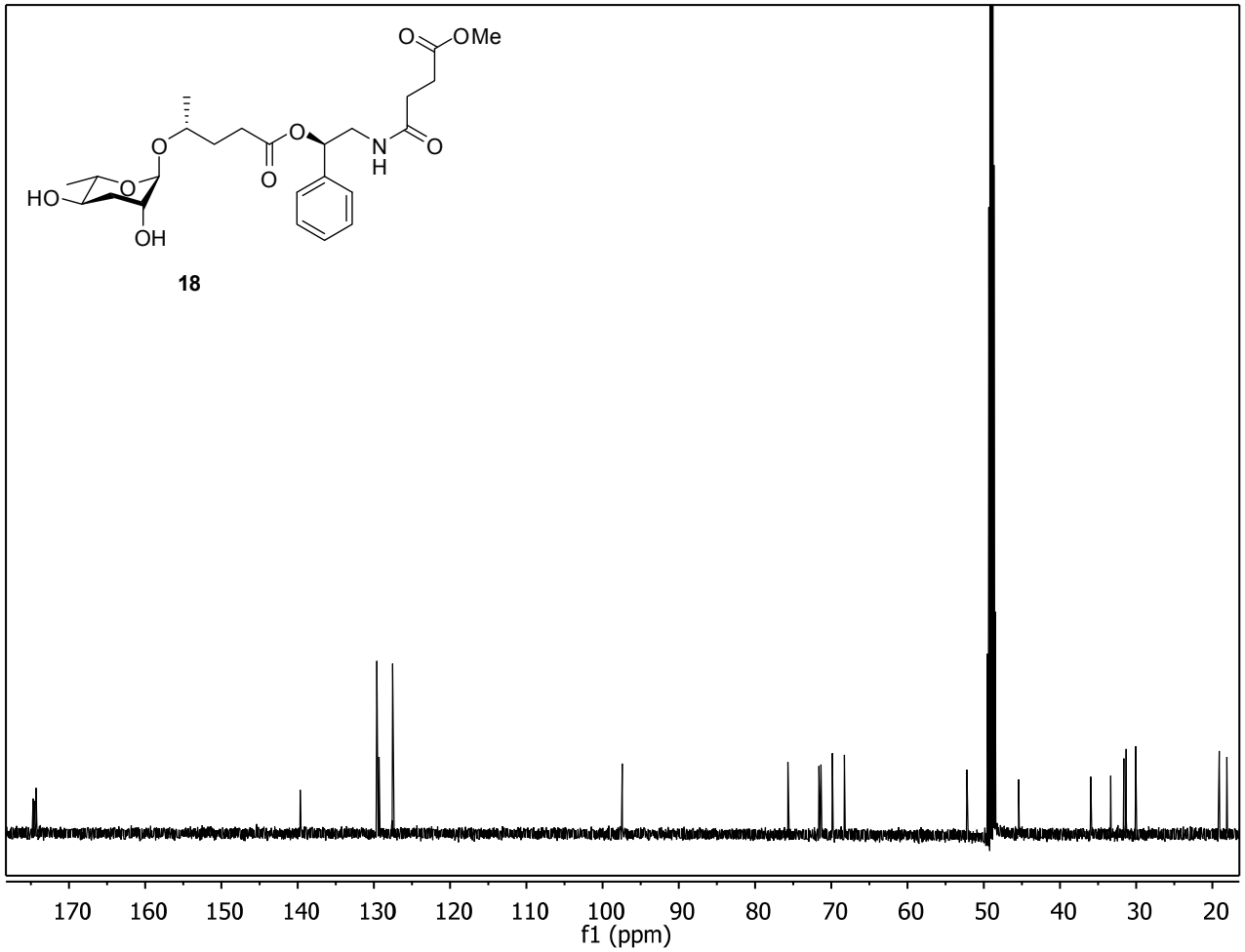
^{13}C NMR spectrum (100 MHz, acetone-d_6) of (*R*)-methyl 4-((2-hydroxy-2-phenylethyl)amino)-4-oxobutanoate ((*R*)-12)



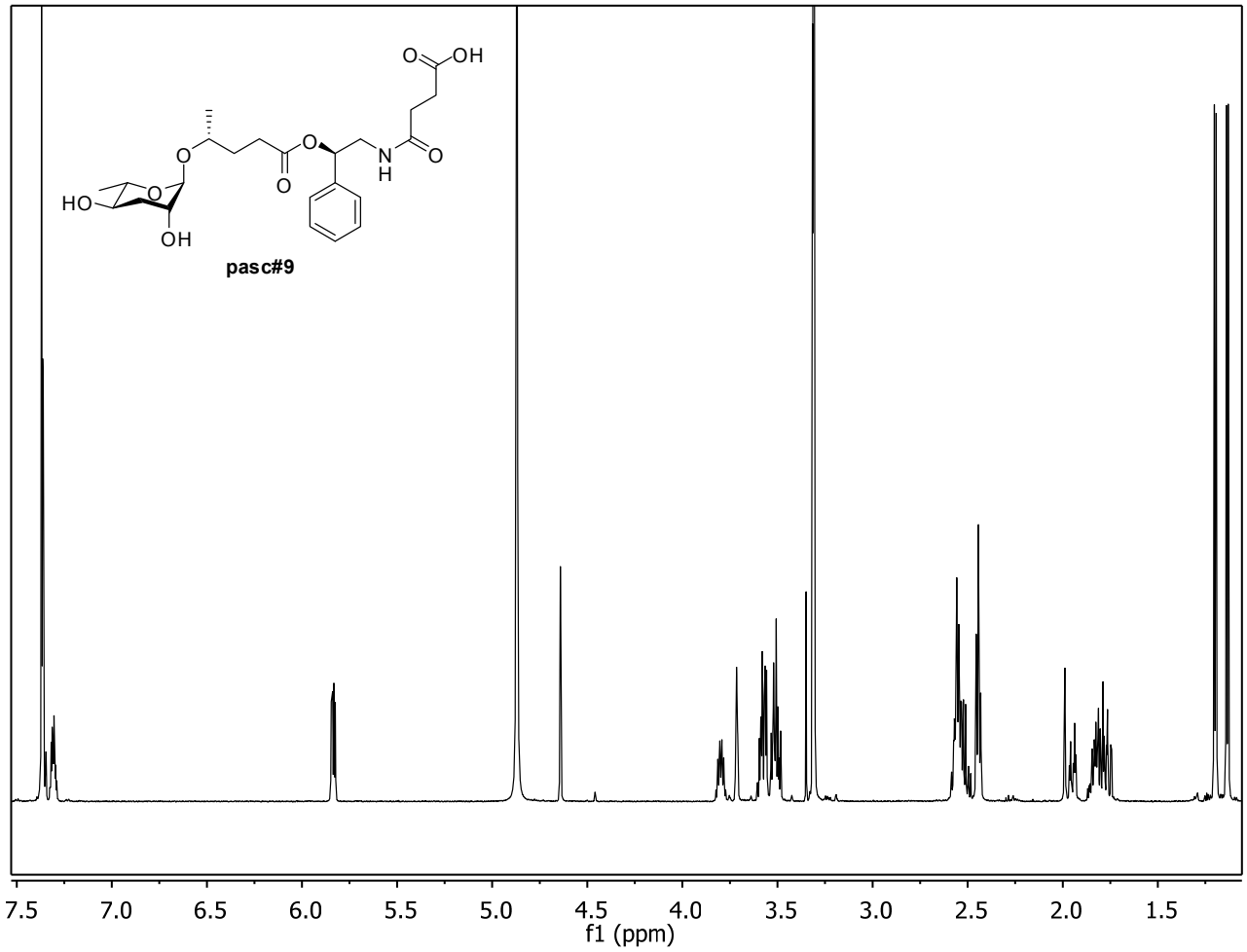
^{1}H NMR spectrum (500 MHz, methanol-d_4) of (*R*)-(*R*)-2-(4-methoxy-4-oxobutanamido)-1-phenylethyl 4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (18)



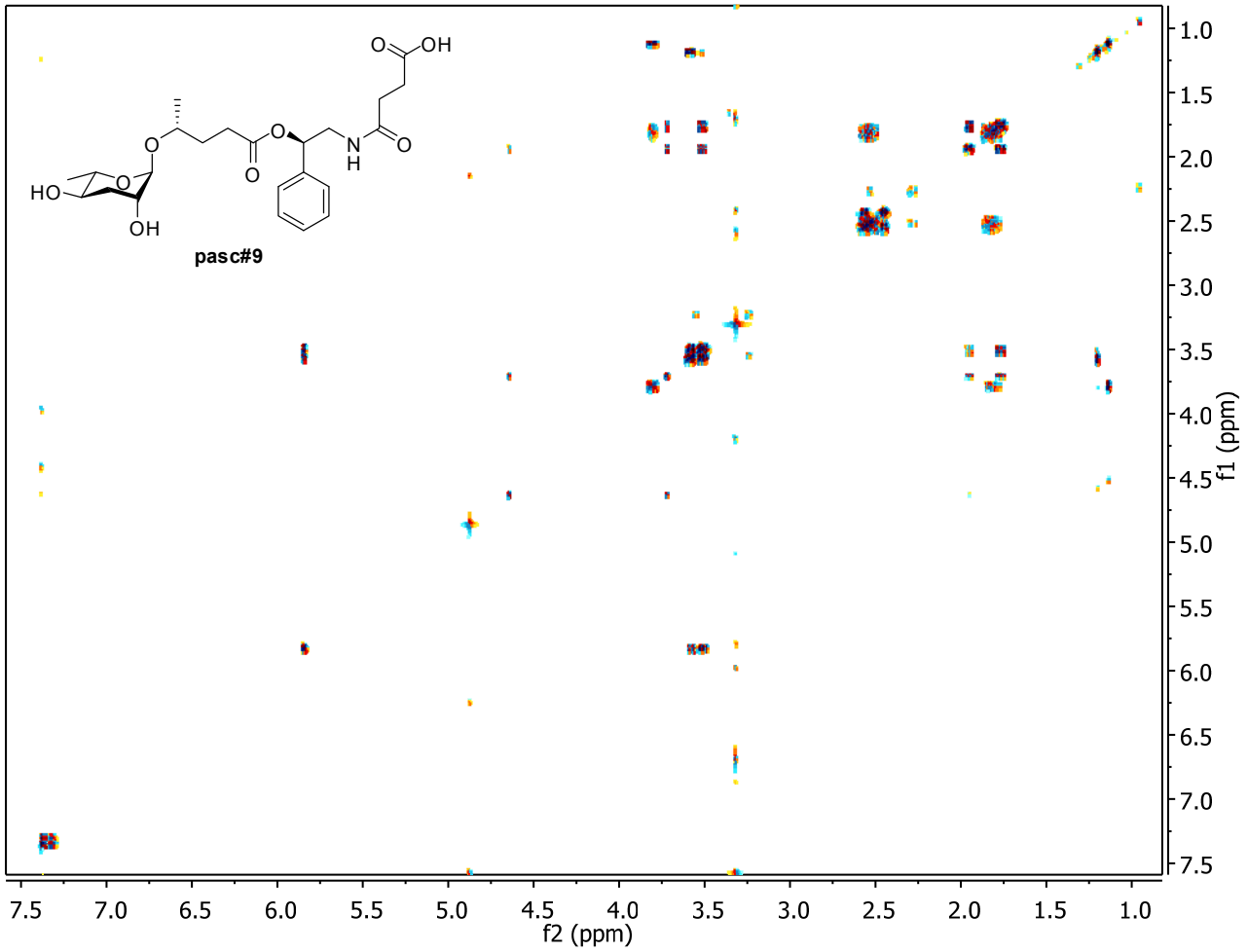
^{13}C NMR spectrum (125 MHz, methanol-d_4) of (*R*)-(*R*)-2-(4-methoxy-4-oxobutanamido)-1-phenylethyl 4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (18)



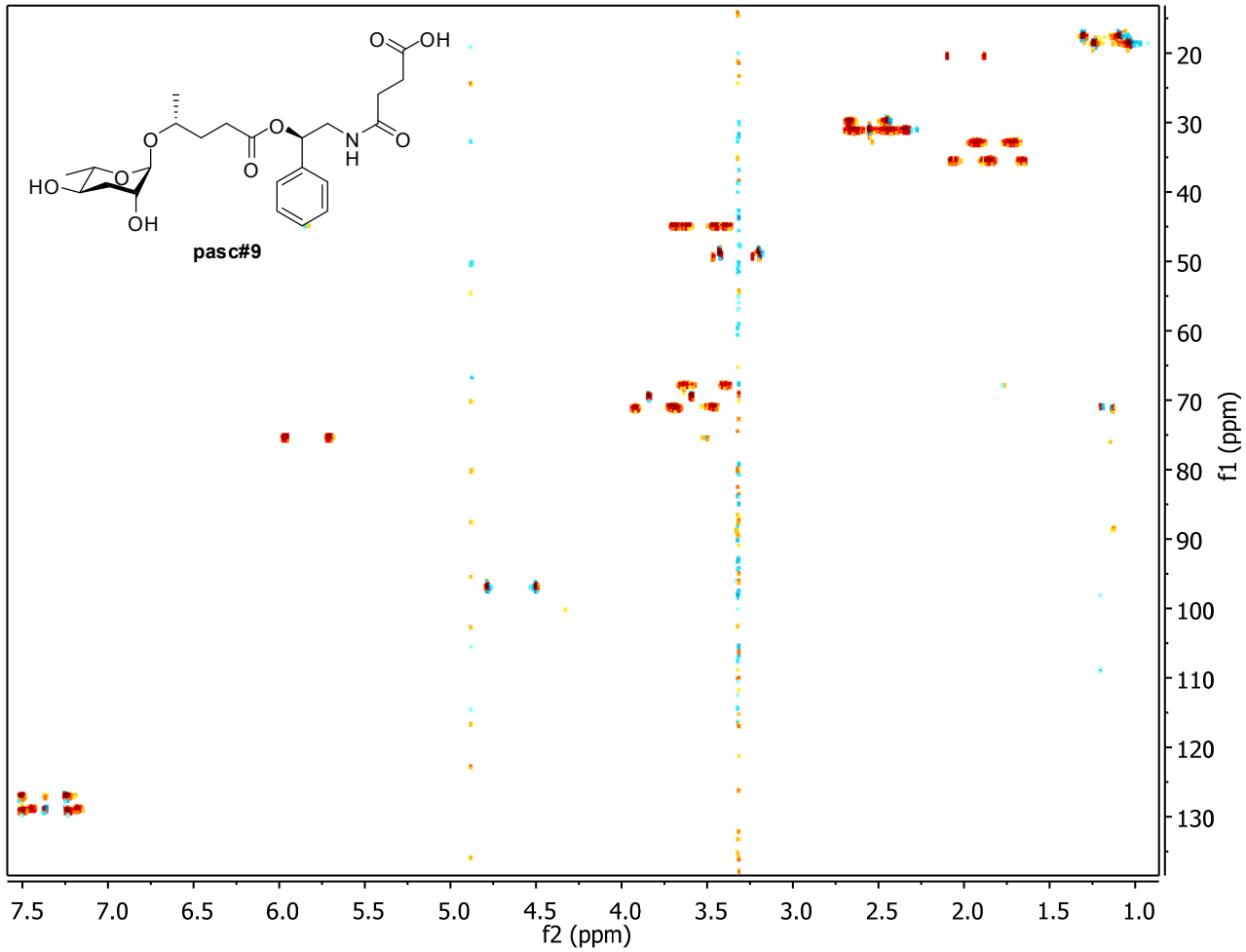
^{1}H NMR spectrum (600 MHz, methanol-d_4) of 4-(((*R*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (pasc#9)



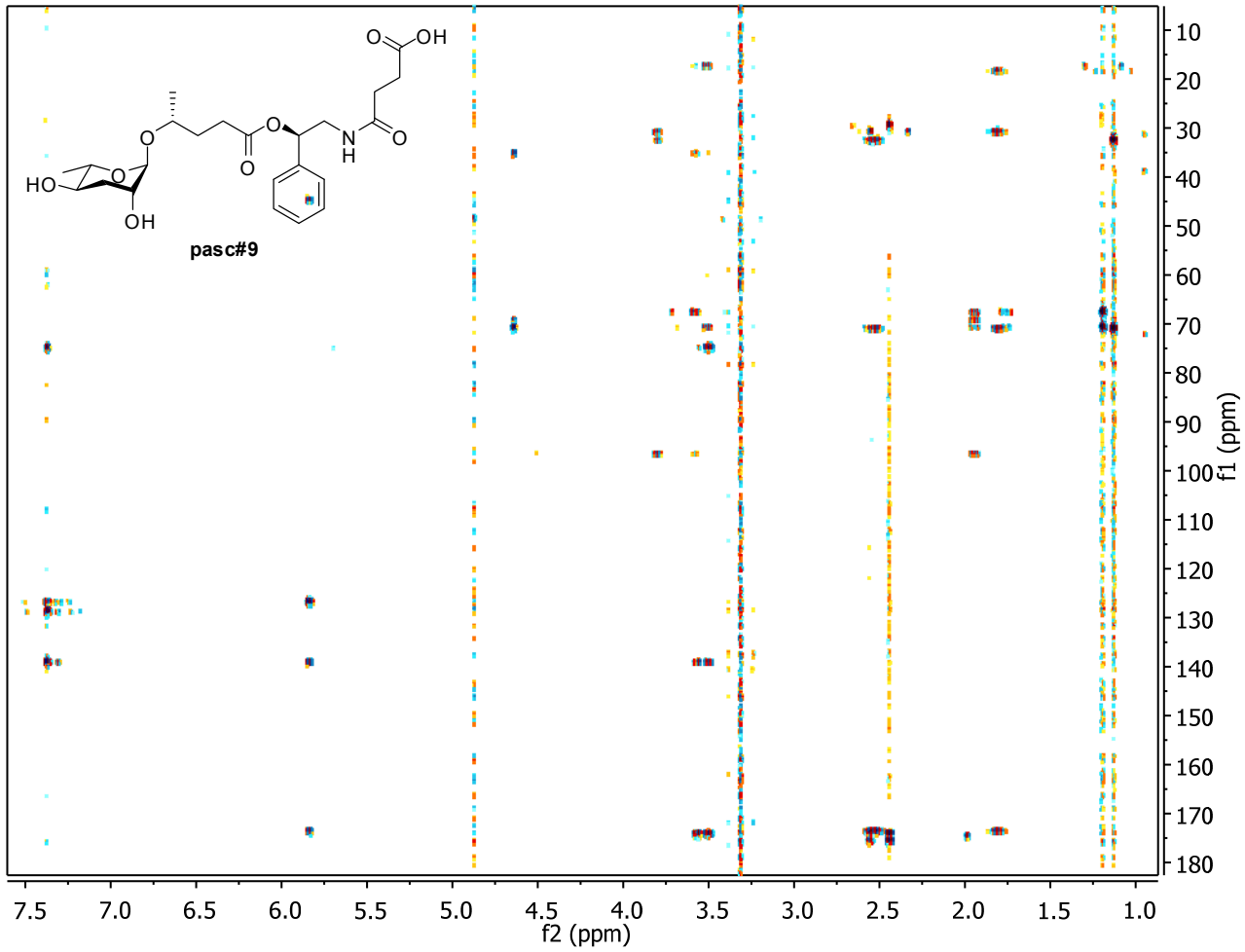
dqfCOSY spectrum (600 MHz, methanol-d_4) of 4-(((*R*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (pasc#9)



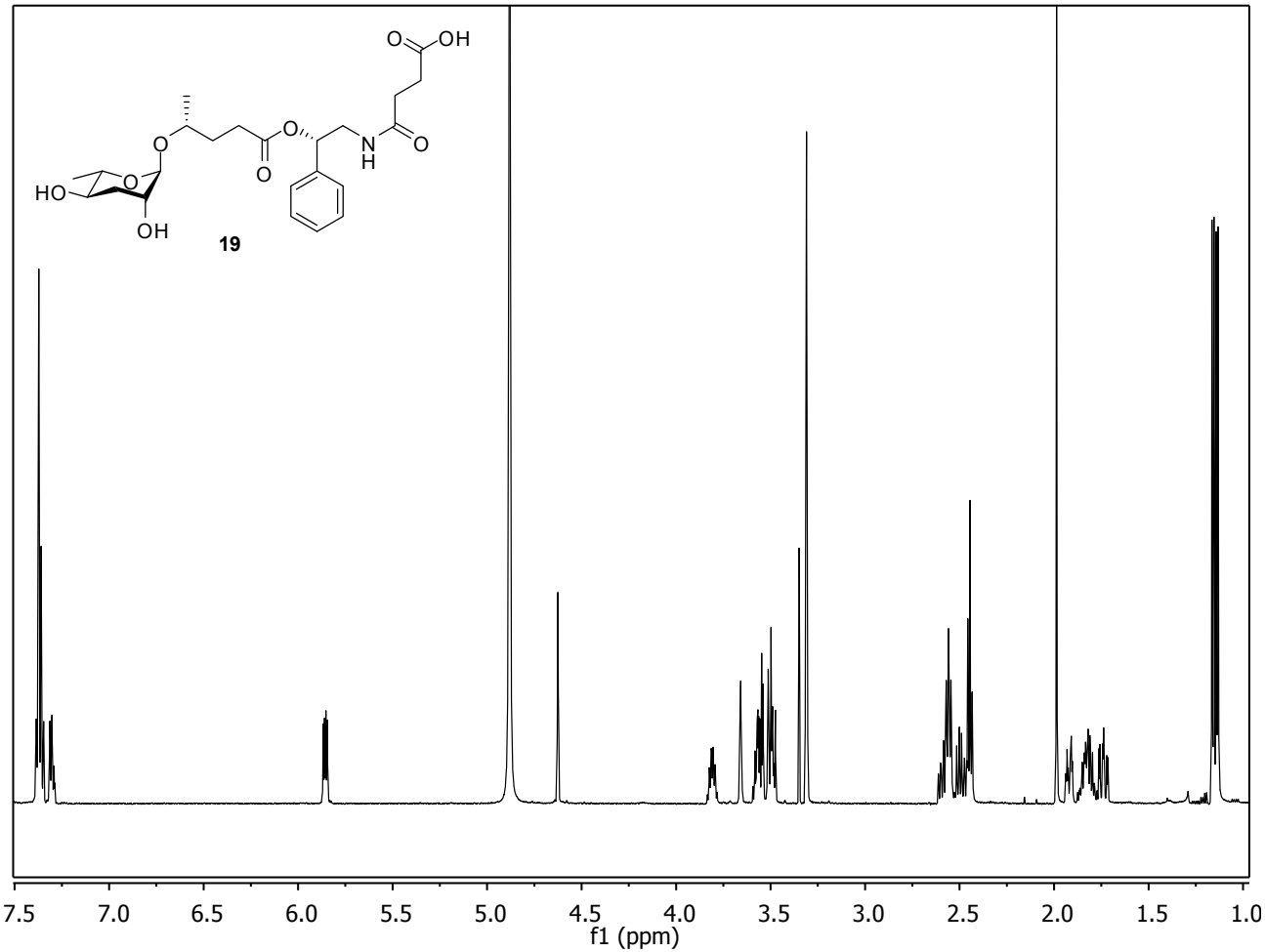
HMQC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of 4-(((*R*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (pasc#9)



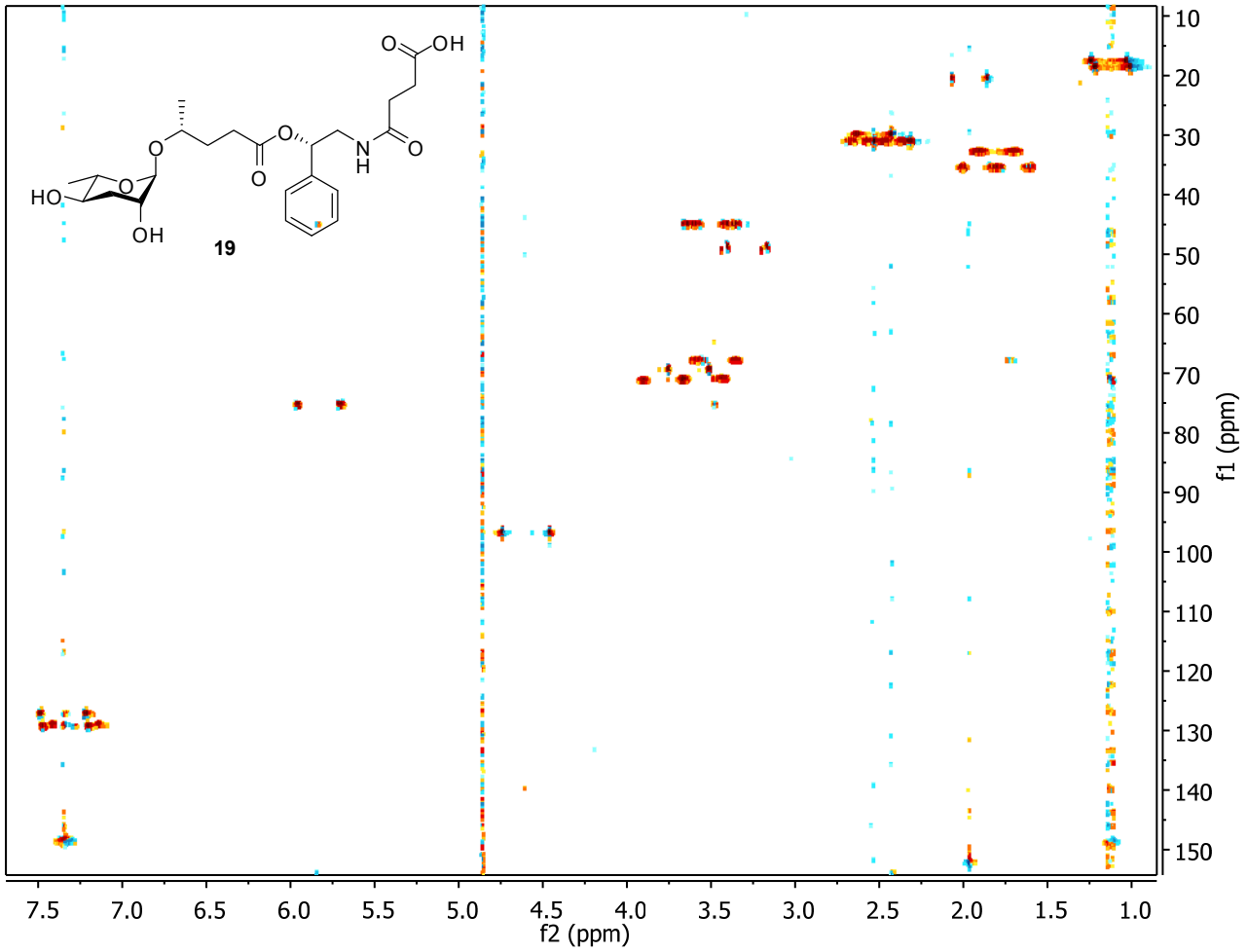
HMBC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of 4-(((*R*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (pasc#9)



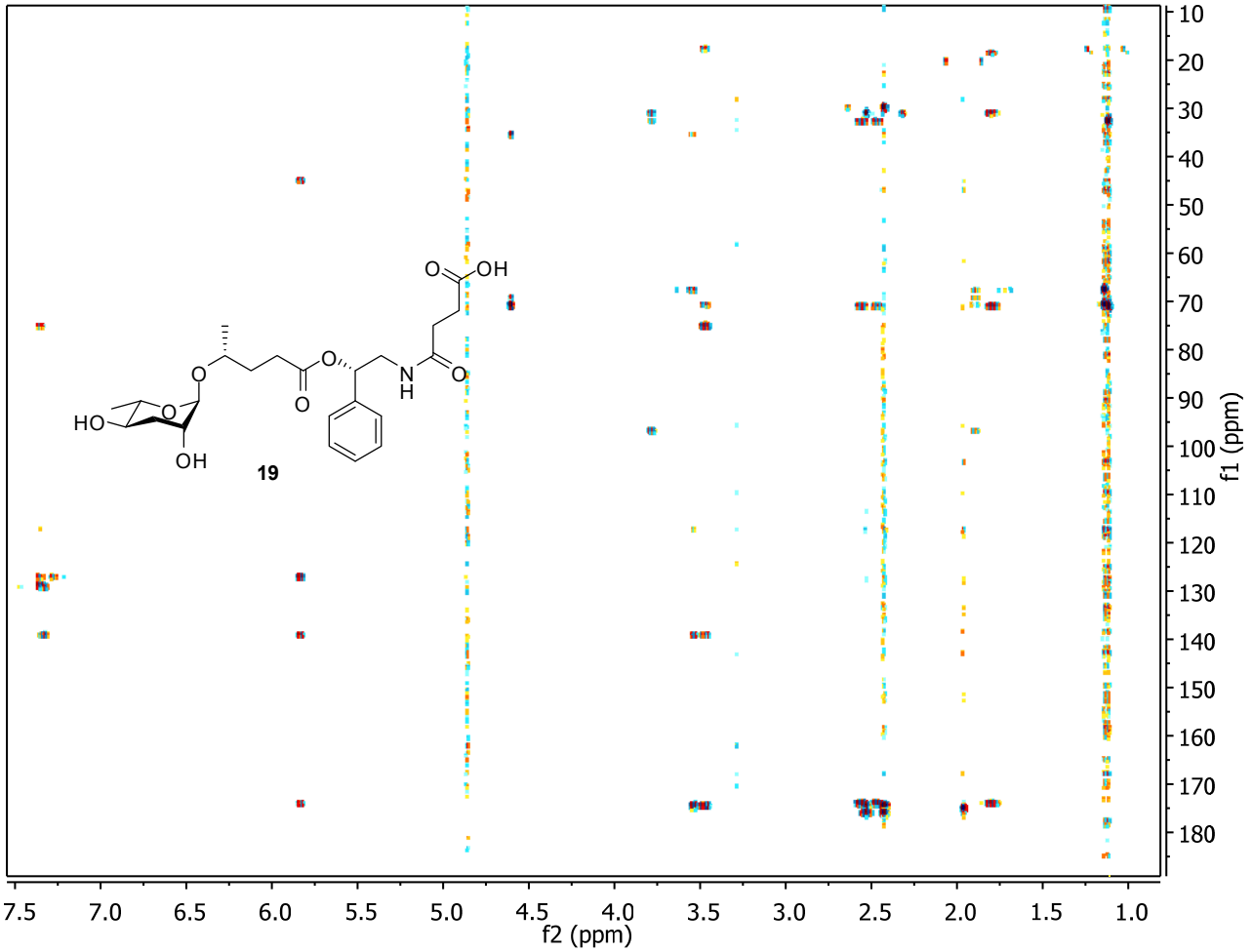
^{1}H NMR spectrum (600 MHz, methanol-d_4) of 4-(((*S*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (19)



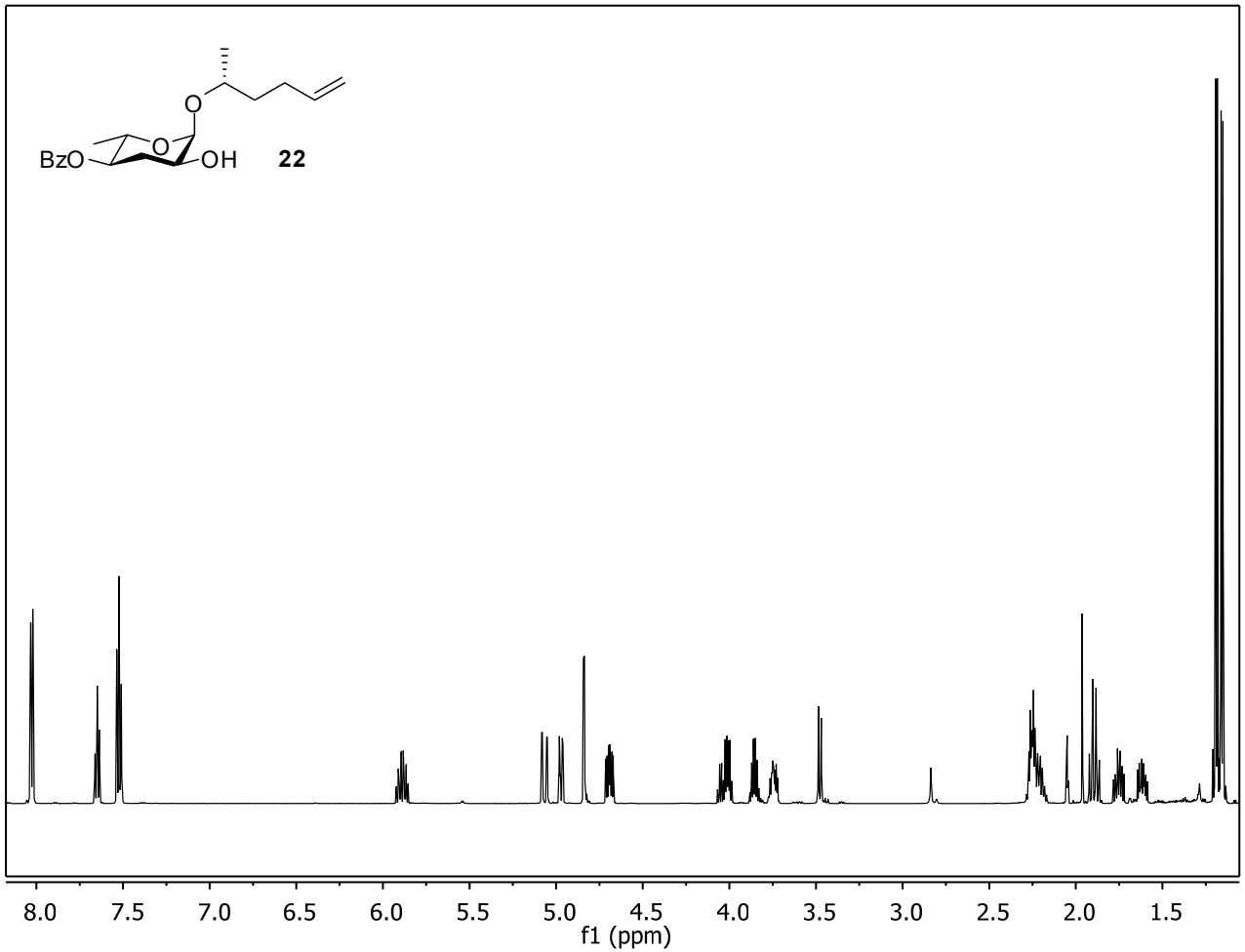
HMQC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of 4-(((*S*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (19)



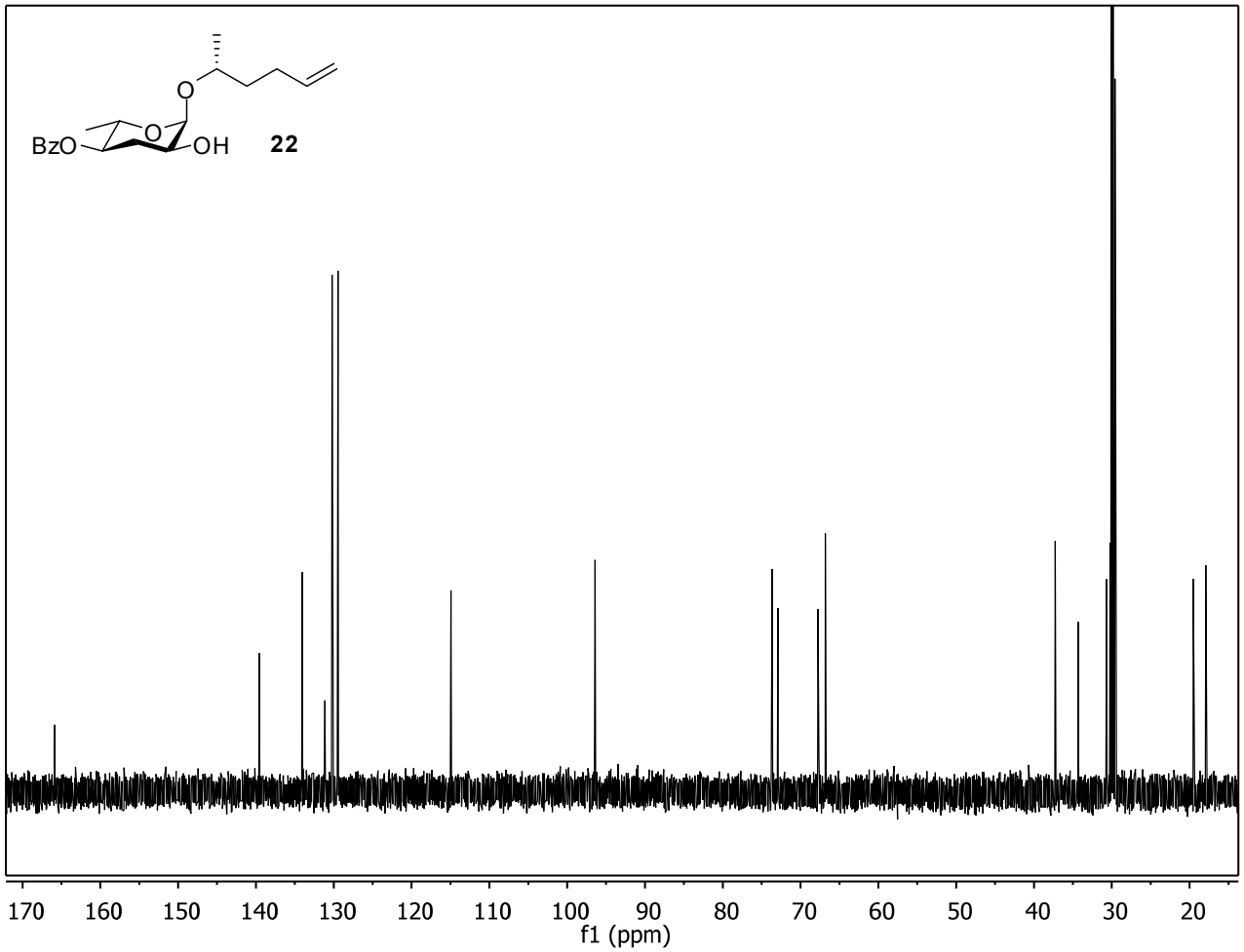
HMBC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of 4-(((*S*)-2-(((*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-phenylethyl)amino)-4-oxobutanoic acid (19)



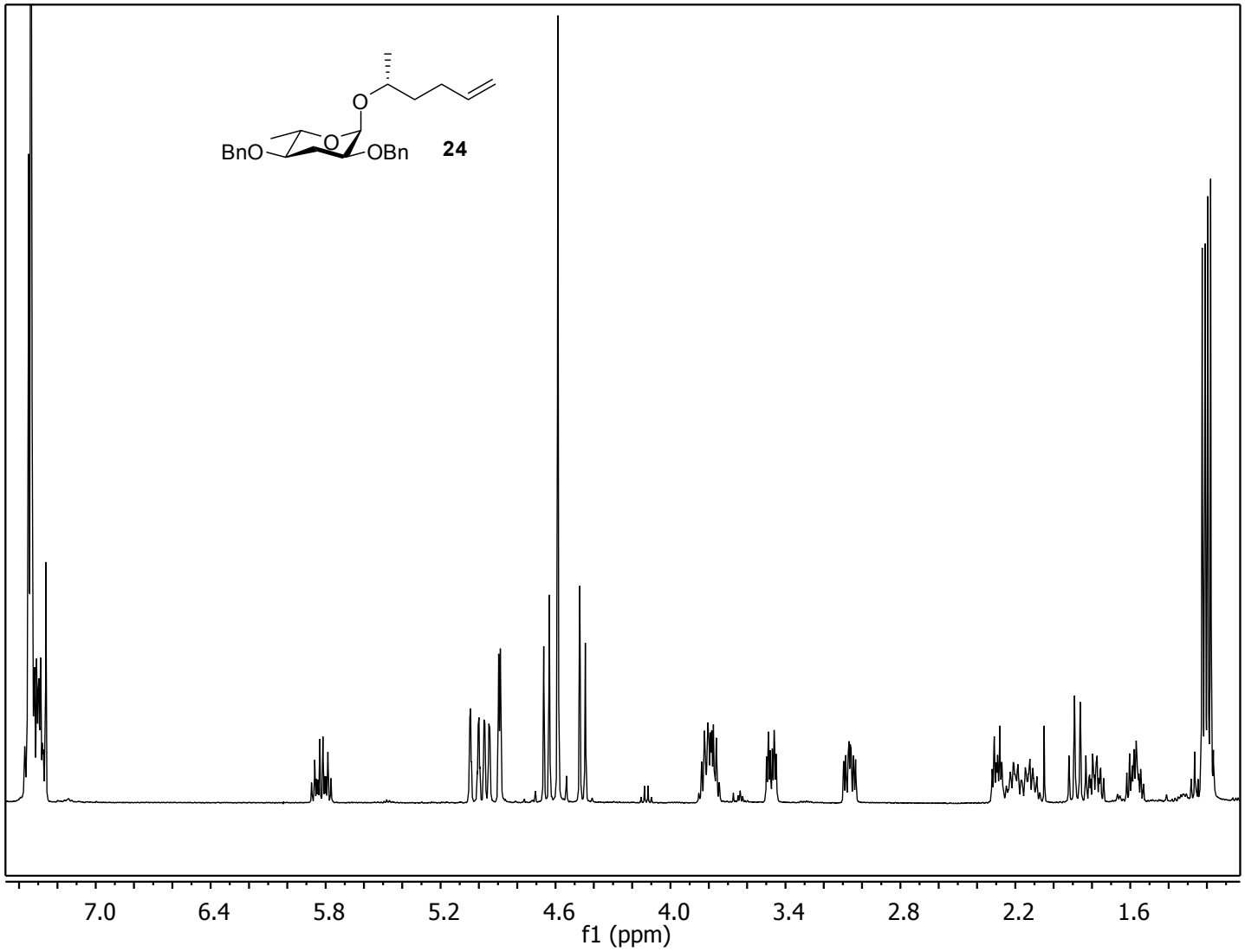
^{1}H NMR spectrum (600 MHz, acetone-d_6) of (2*S*,3*R*,5*S*,6*R*)-6-((*R*)-hex-5-en-2-yloxy)-5-hydroxy-2-methyltetrahydro-2*H*-pyran-3-yl benzoate (22)



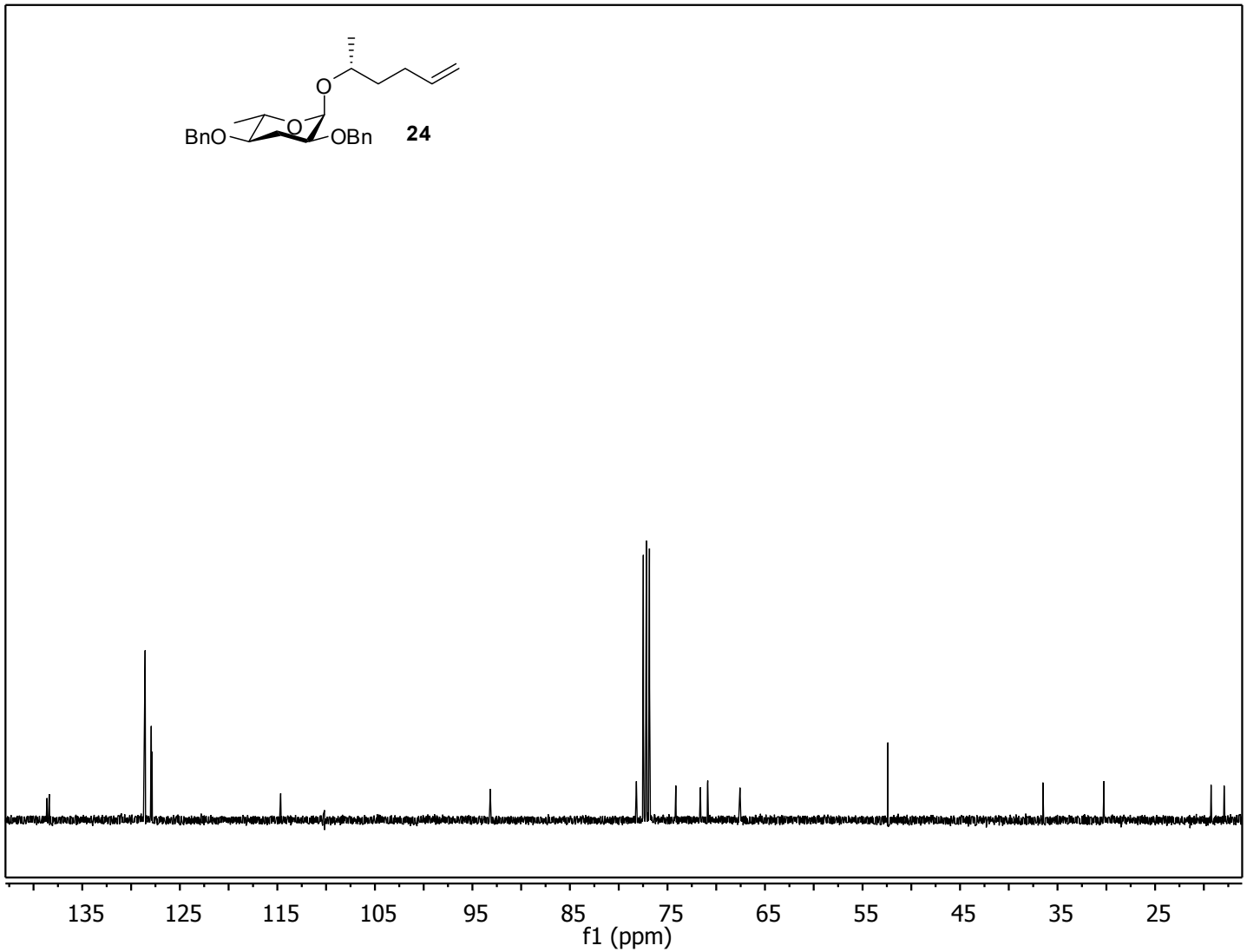
^{13}C NMR spectrum (151 MHz, acetone-d_6) of (2*S*,3*R*,5*S*,6*R*)-6-((*R*)-hex-5-en-2-yloxy)-5-hydroxy-2-methyltetrahydro-2*H*-pyran-3-yl benzoate (22)



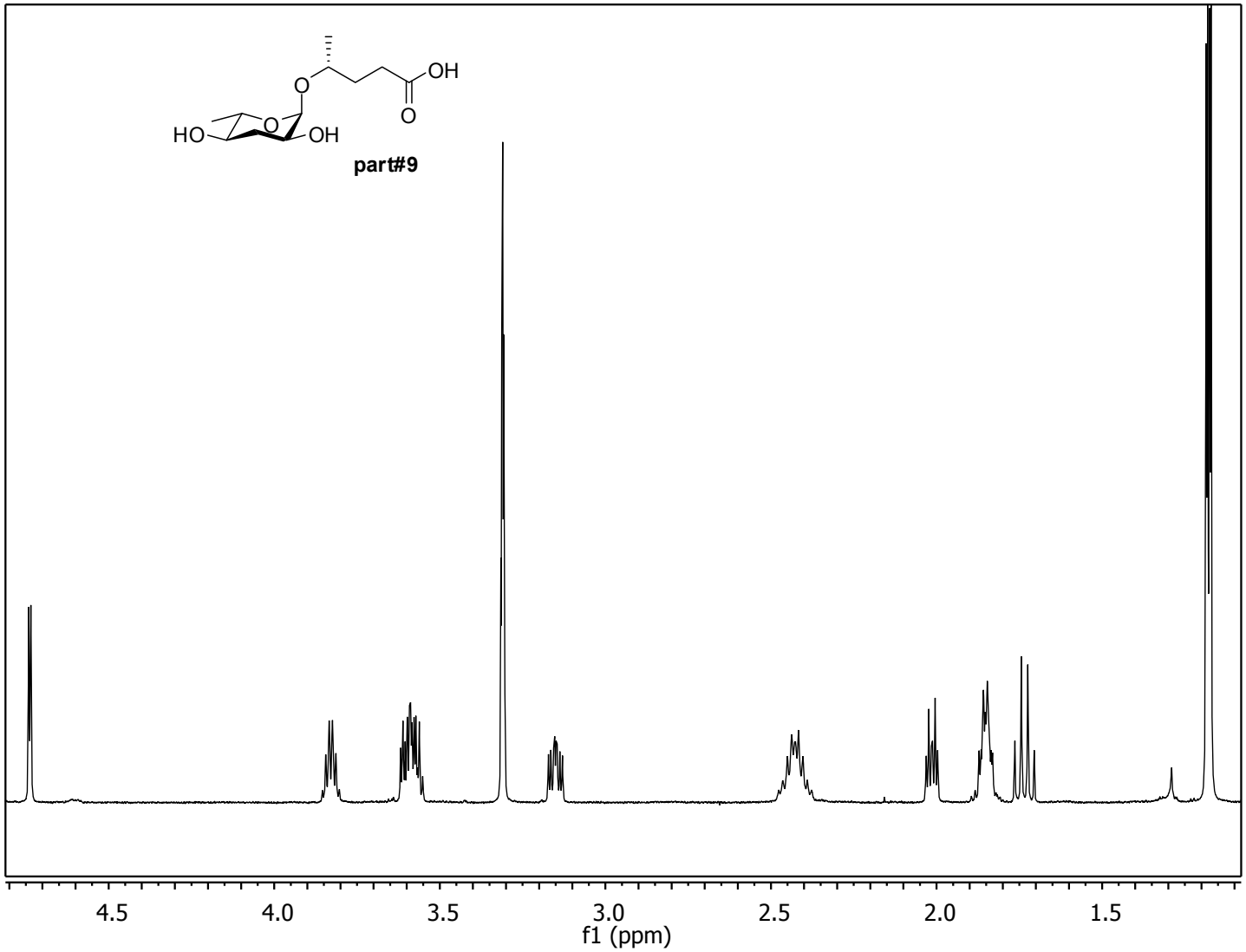
^{1}H NMR spectrum (400 MHz, chloroform-*d*) of (2*R*,3*S*,5*R*,6*S*)-3,5-bis(benzyloxy)-2-((*R*)-hex-5-en-2-yloxy)-6-methyltetrahydro-2*H*-pyran (24)



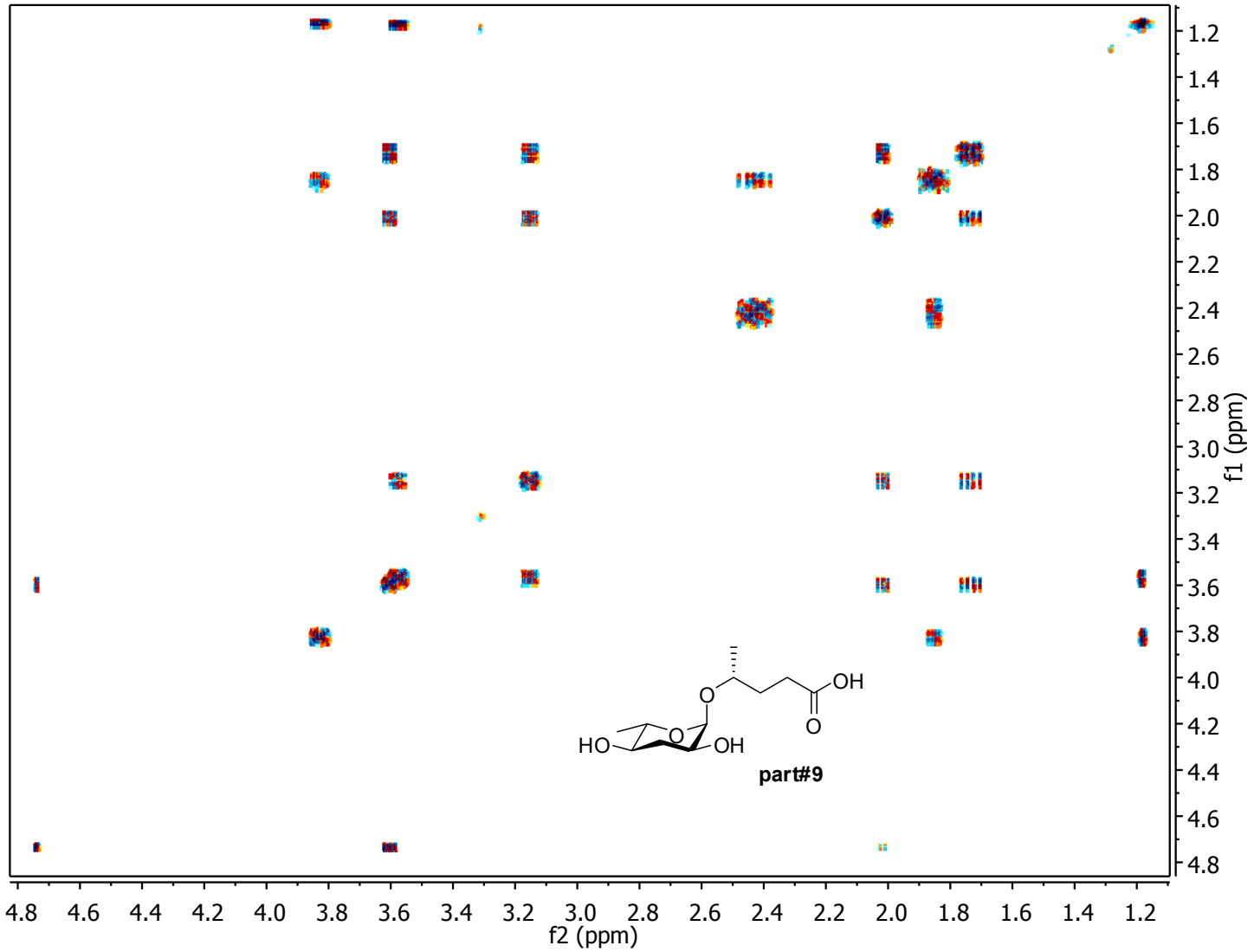
^{13}C NMR spectrum (100 MHz, chloroform-*d*) of (2*R*,3*S*,5*R*,6*S*)-3,5-bis(benzyloxy)-2-((*R*)-hex-5-en-2-yloxy)-6-methyltetrahydro-2*H*-pyran (24)



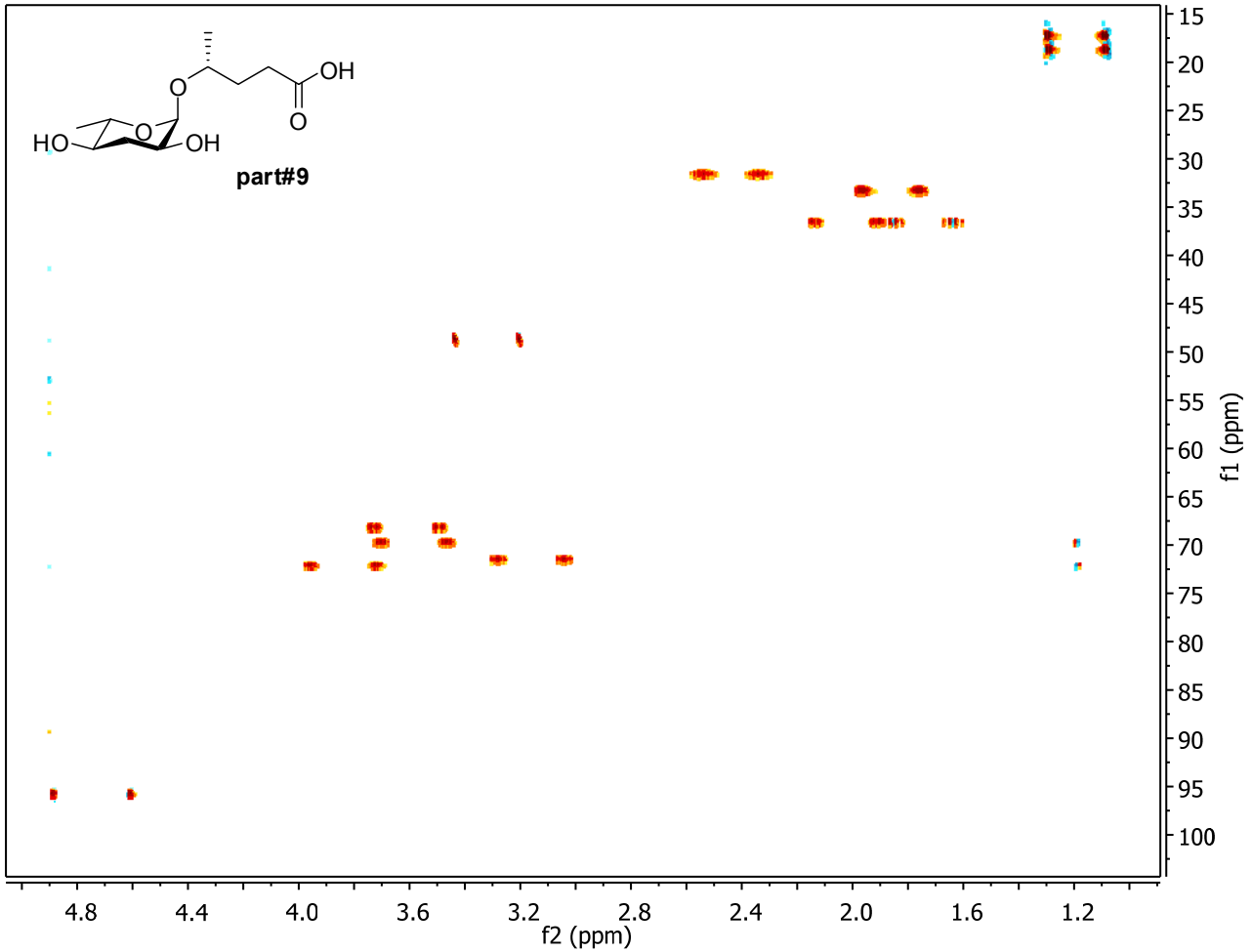
^{1}H NMR spectrum (600 MHz, methanol-d_4) of (*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (part#9)



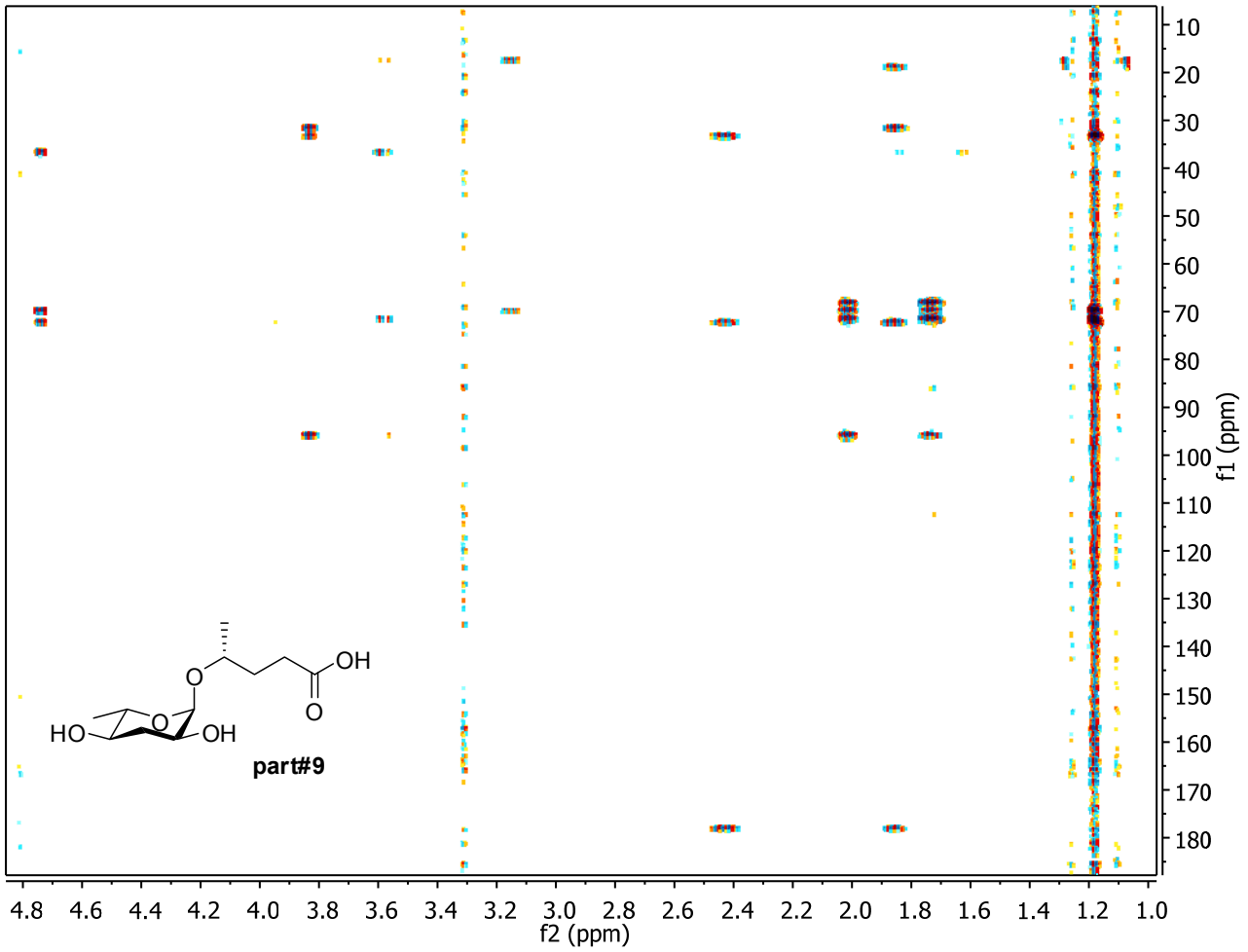
dqfCOSY spectrum (600 MHz, methanol-d_4) of (*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (part#9)



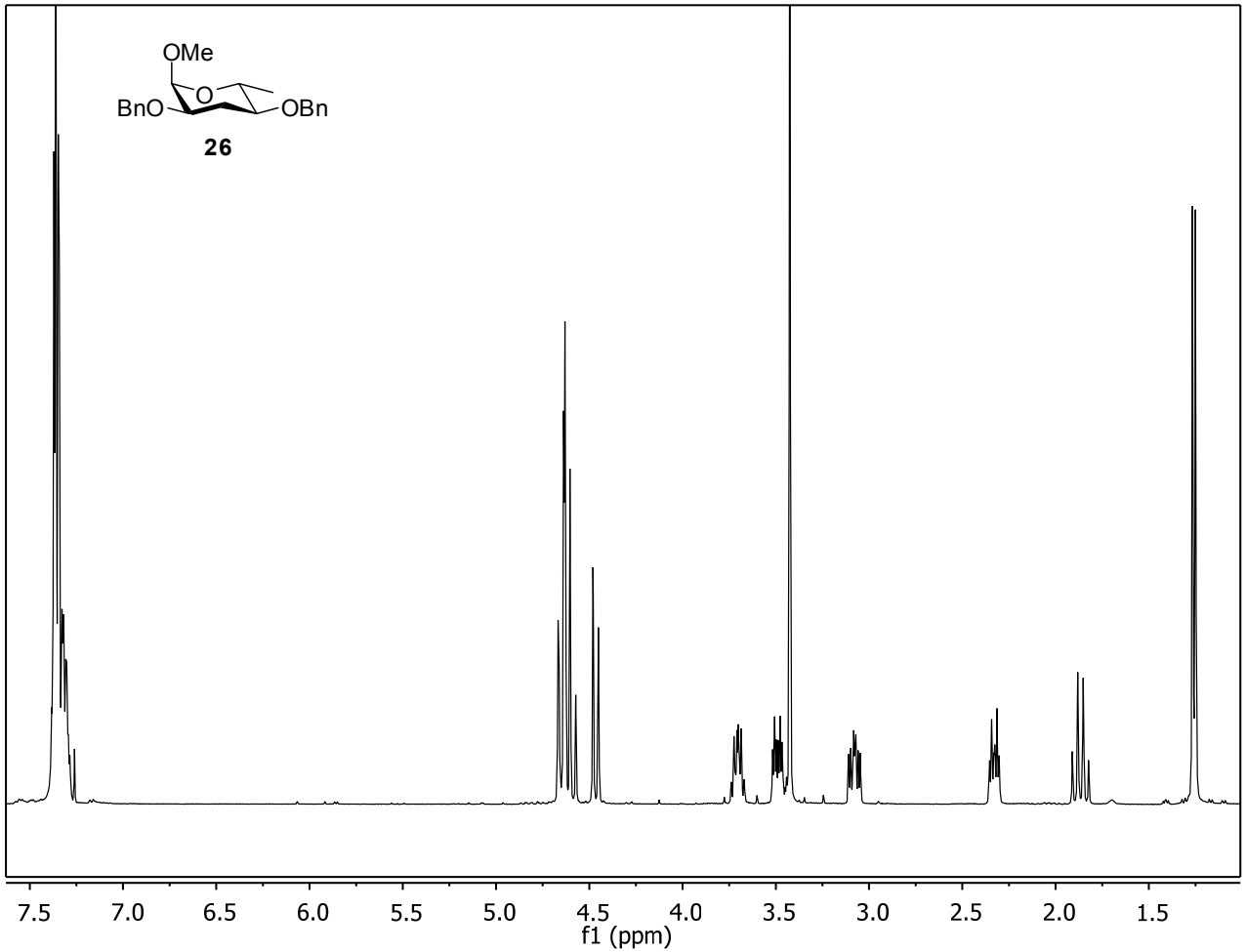
HMQC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (part#9)



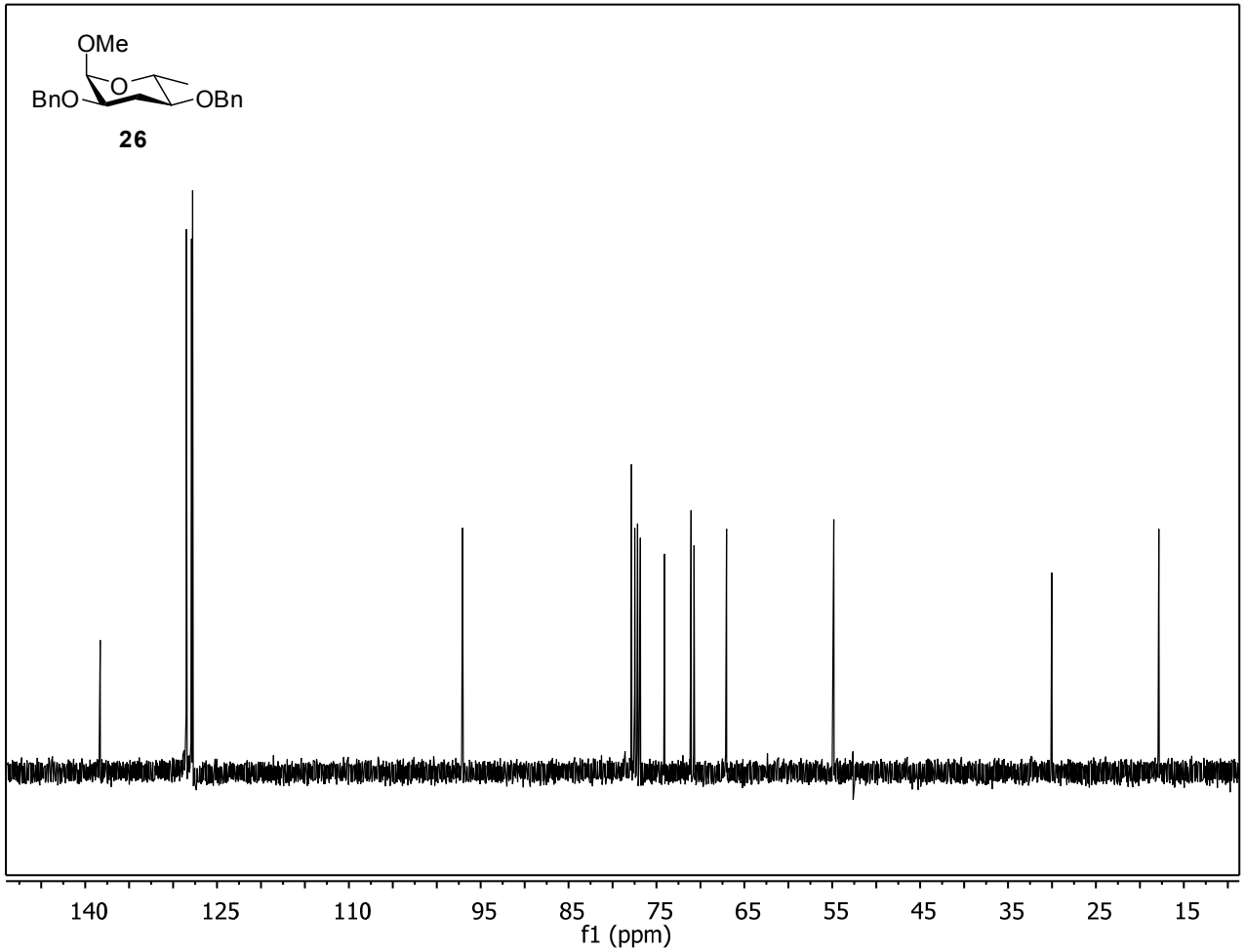
HMBC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (part#9)



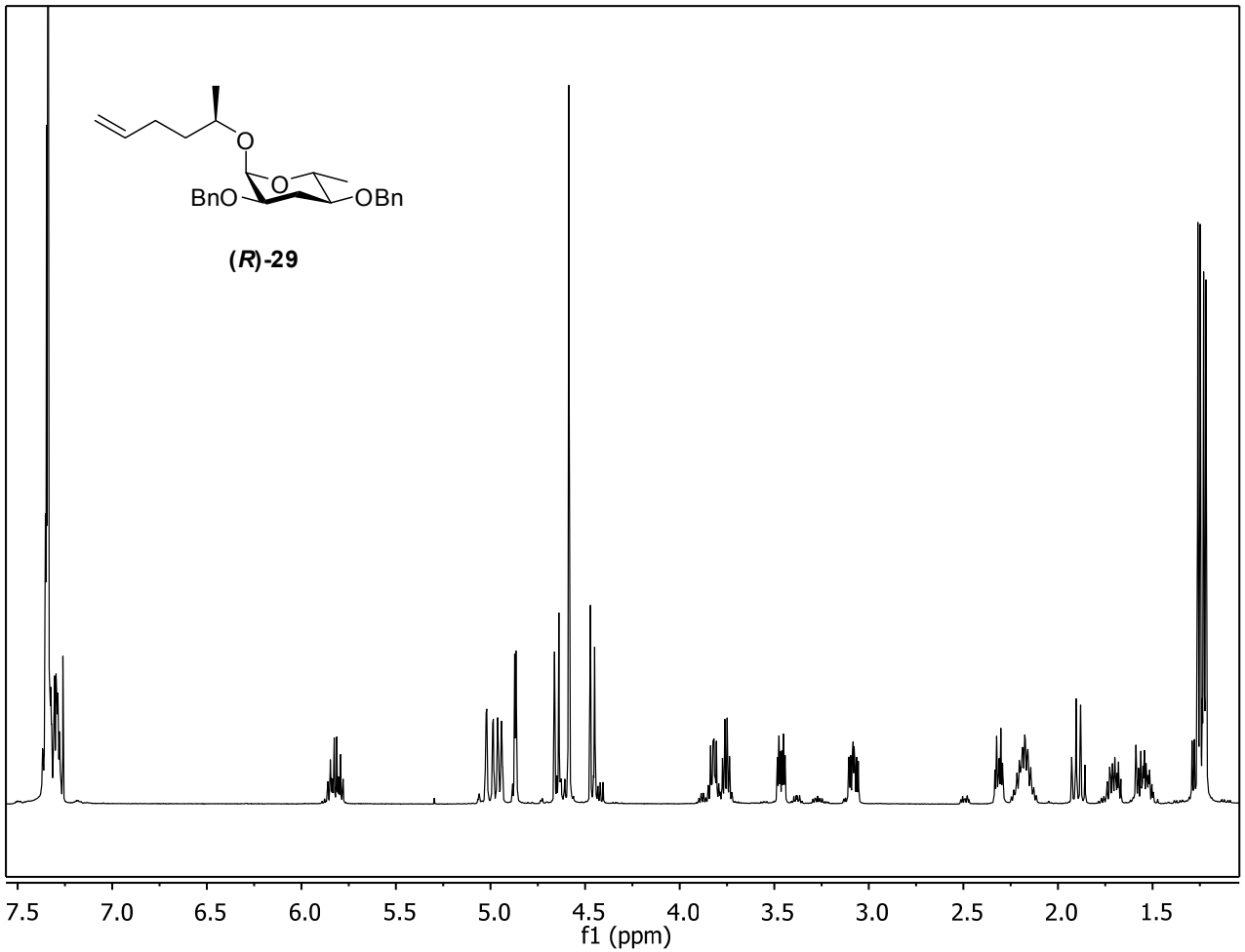
^{1}H NMR spectrum (400 MHz, chloroform-*d*) of (2*S*,3*R*,5*S*,6*R*)-3,5-bis(benzyloxy)-2-methoxy-6-methyltetrahydro-2*H*-pyran (26)



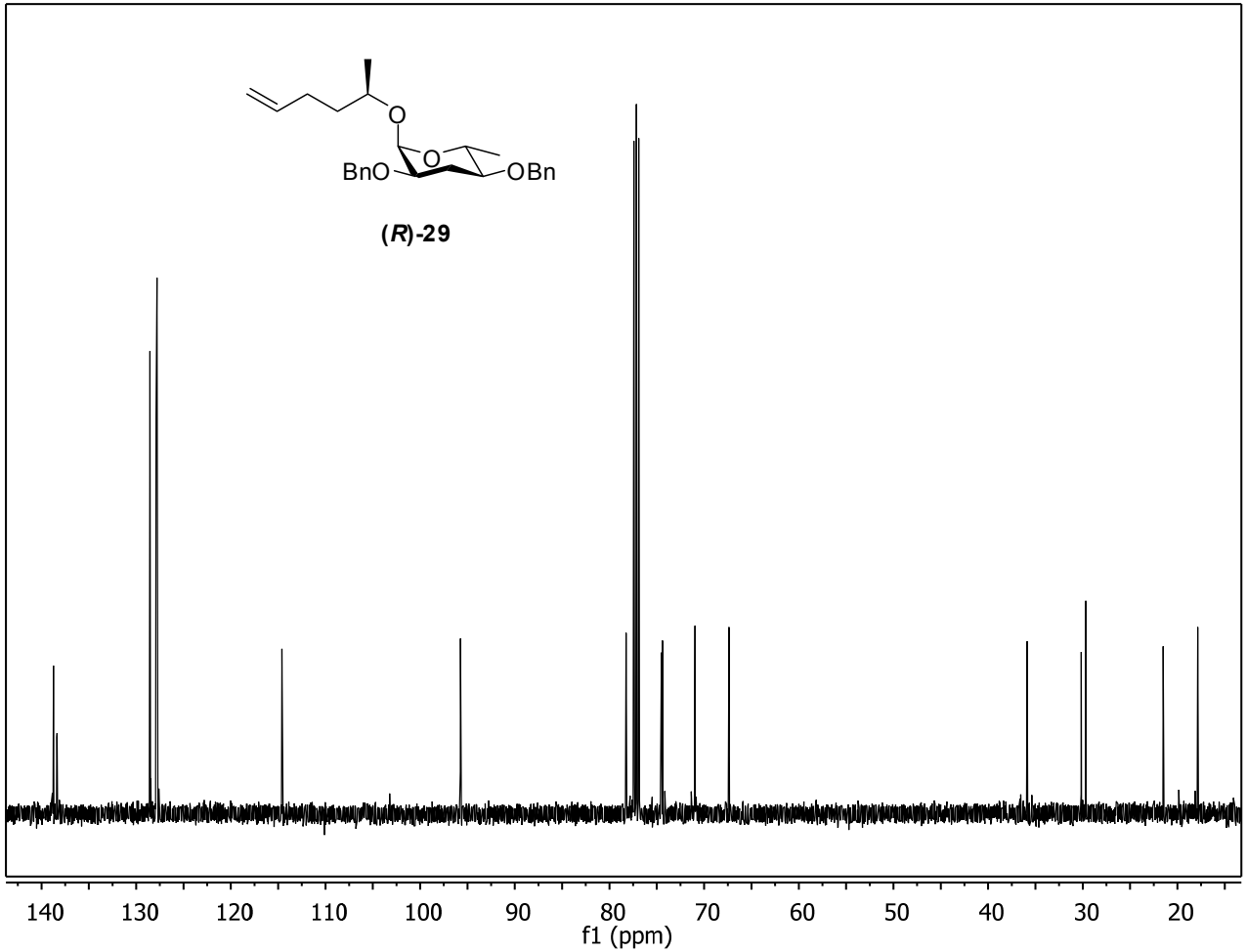
^{13}C NMR spectrum (100 MHz, chloroform-*d*) of (2*S*,3*R*,5*S*,6*R*)-3,5-bis(benzyloxy)-2-methoxy-6-methyltetrahydro-2*H*-pyran (26)



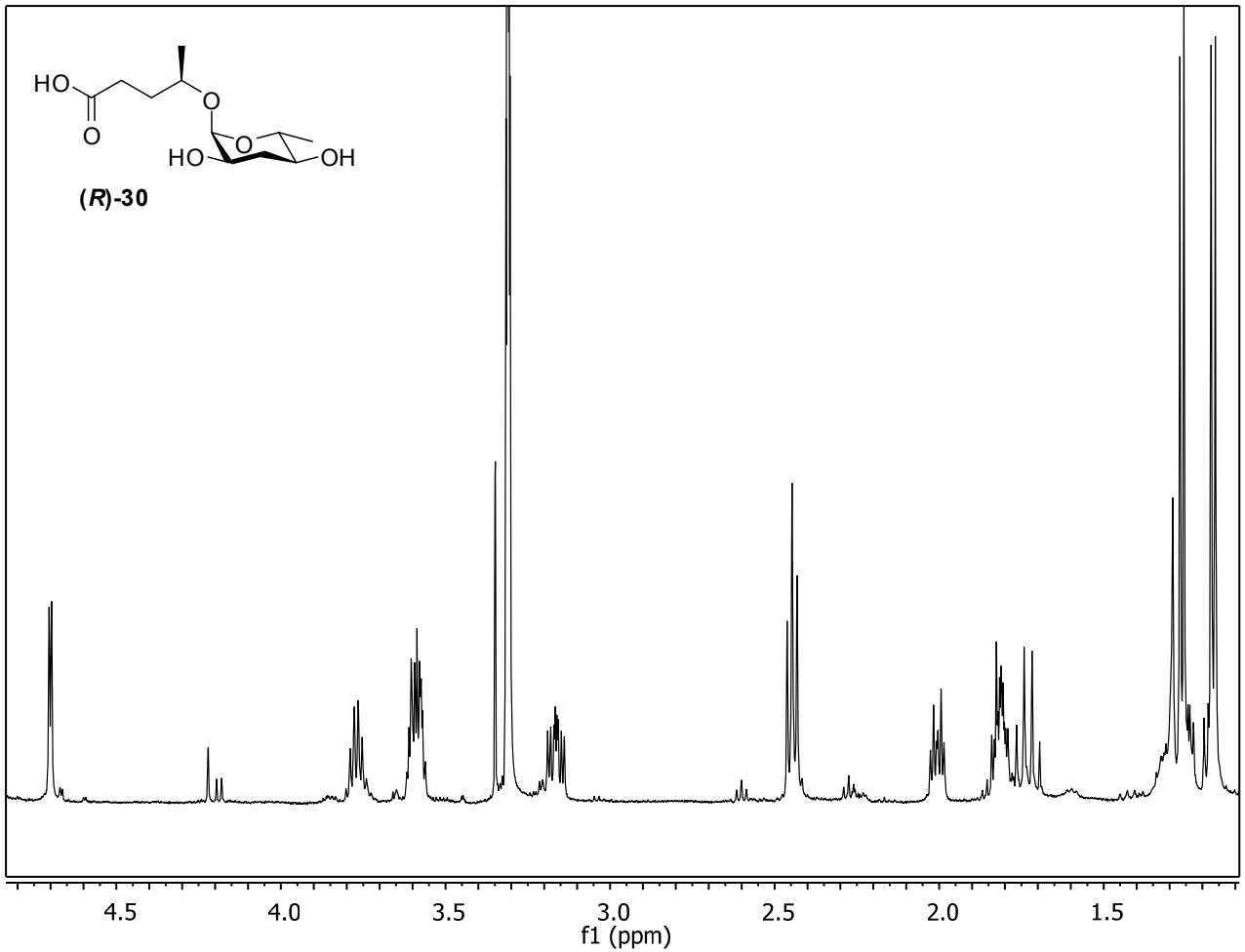
^{1}H NMR spectrum (500 MHz, chloroform-*d*) of (3*R*,5*S*,6*R*)-3,5-bis(benzyloxy)-2-((*R*)-hex-5-en-2-yloxy)-6-methyltetrahydro-2*H*-pyran ((*R*)-29, α-anomer)



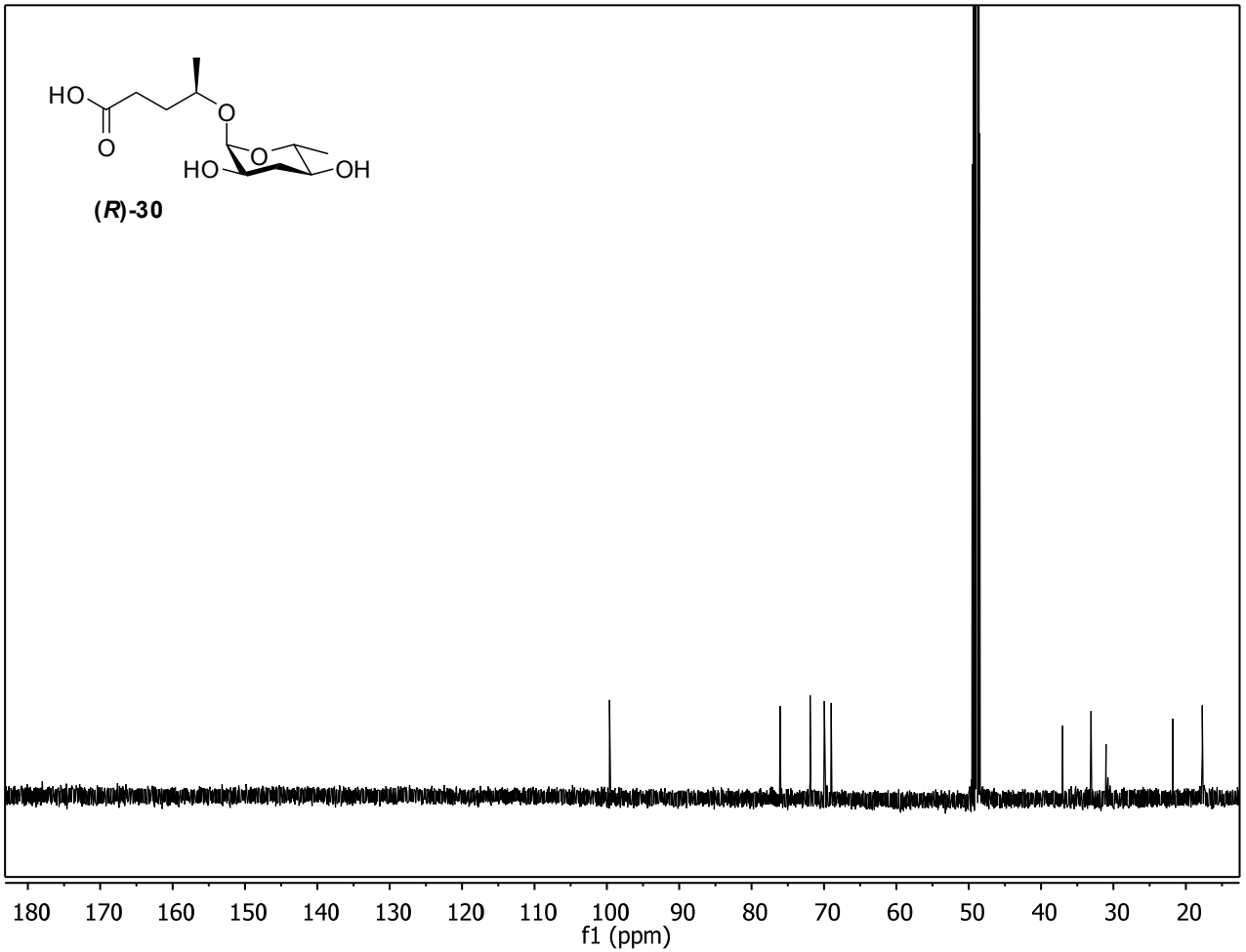
^{13}C NMR spectrum (125 MHz, chloroform-*d*) of (3*R*,5*S*,6*R*)-3,5-bis(benzyloxy)-2-((*R*)-hex-5-en-2-yloxy)-6-methyltetrahydro-2*H*-pyran ((*R*)-29 α-anomer)



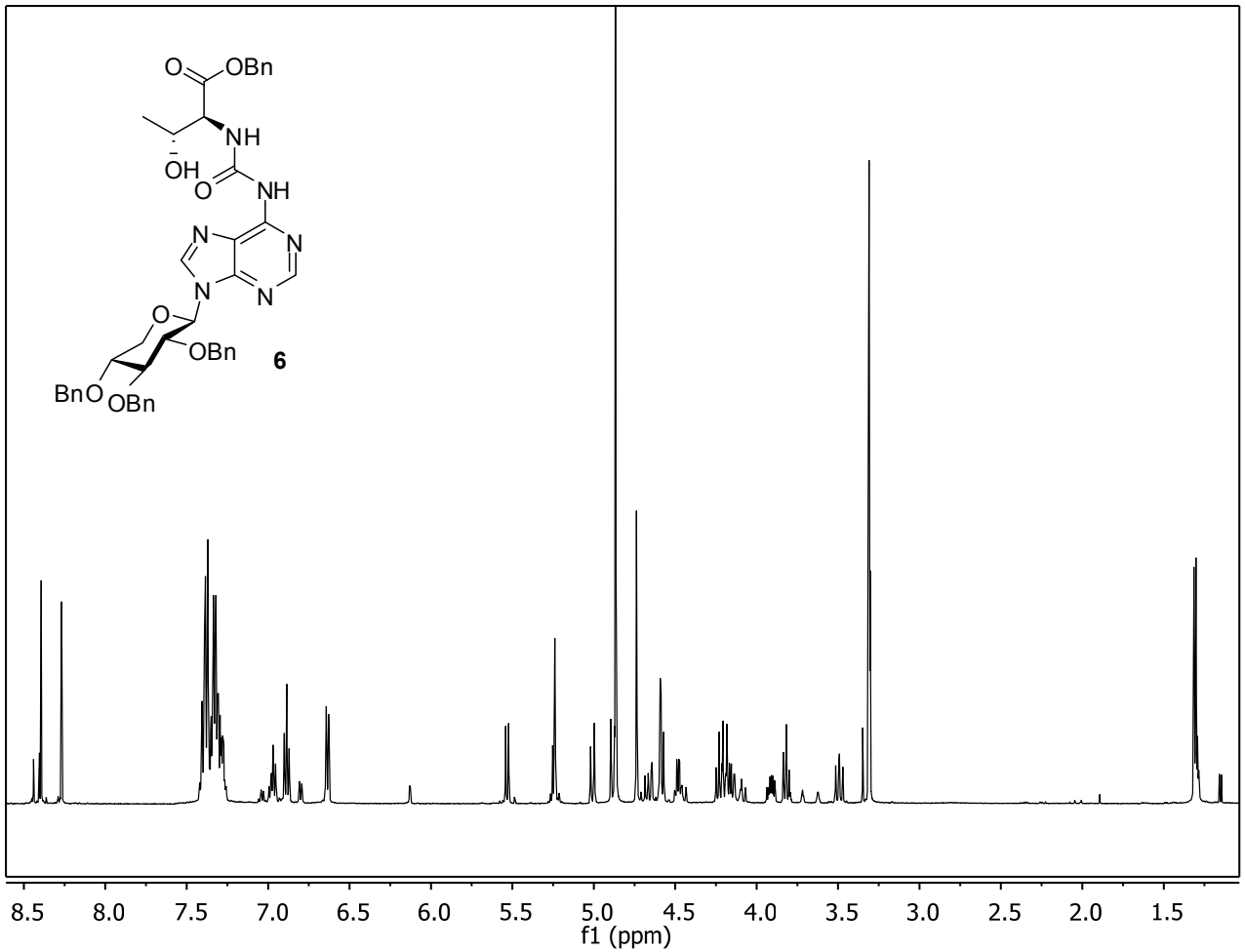
^{1}H NMR spectrum (500 MHz, methanol-d_4) of (*R*)-4-(((2*S*,3*R*,5*S*,6*R*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid ((*R*)-30)



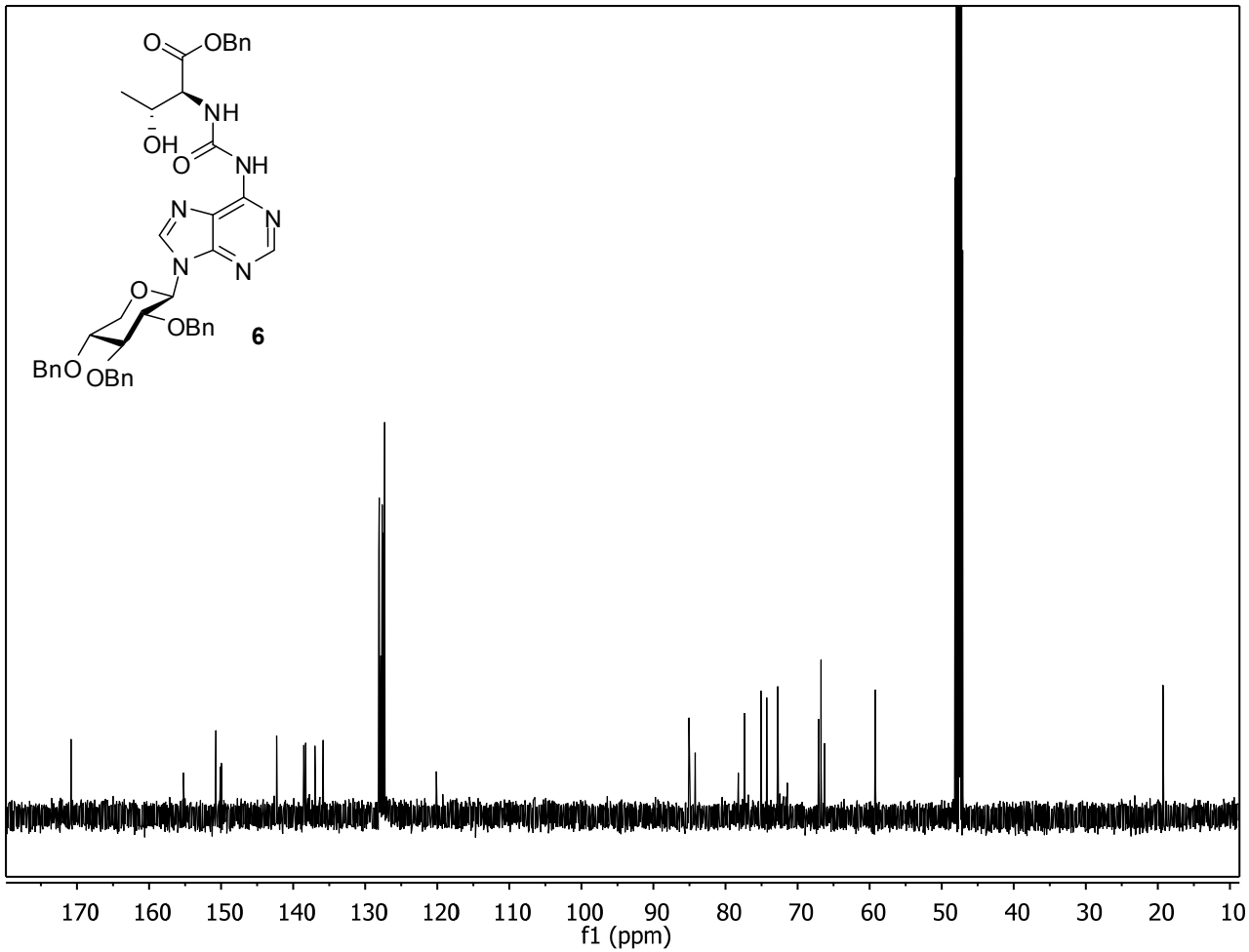
^{13}C NMR spectrum (125 MHz, methanol-d_4) of (*R*)-4-(((2*S*,3*R*,5*S*,6*R*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid ((*R*)-30)



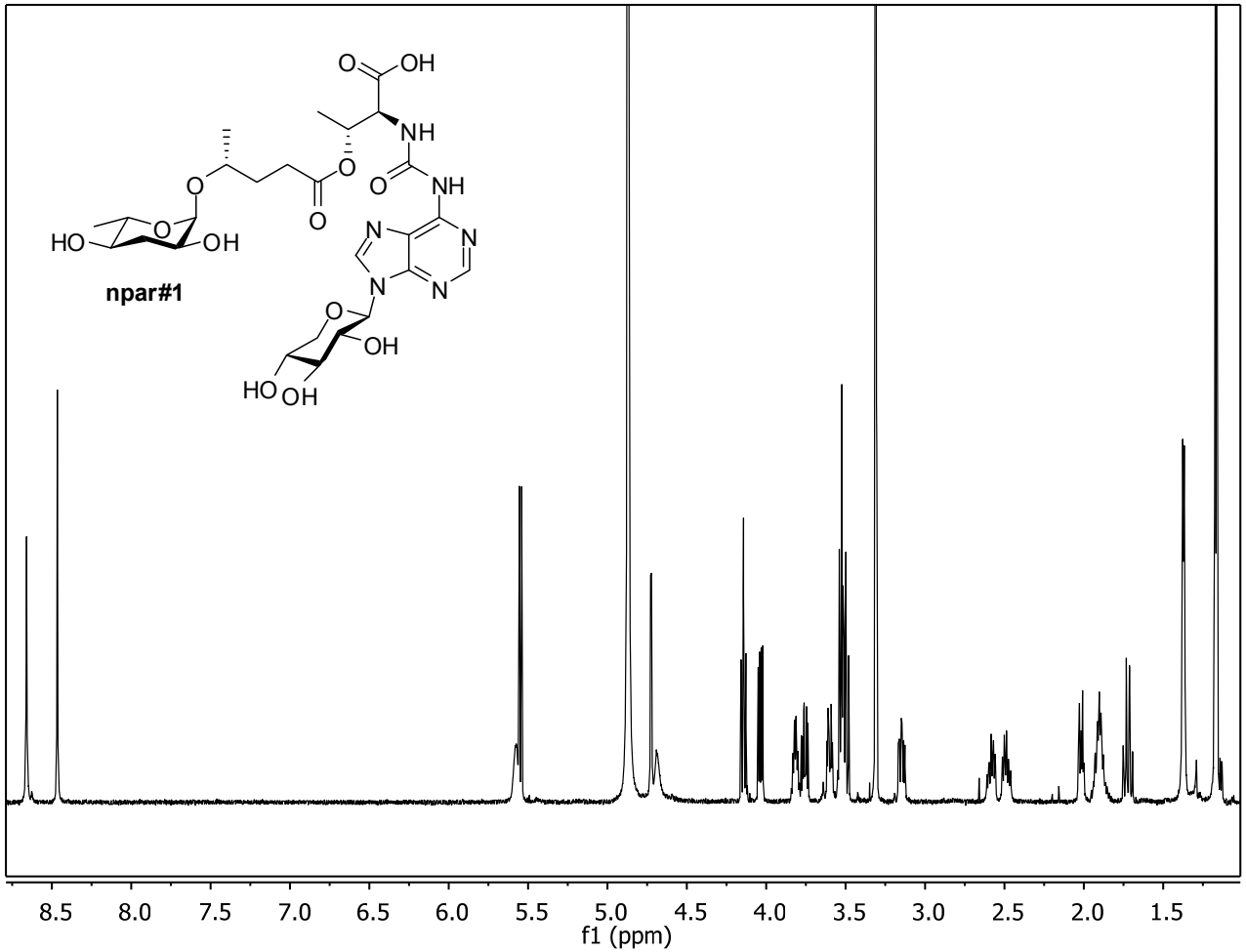
^{1}H NMR spectrum (500 MHz, methanol-*d*$_4$) of (2*S*,3*R*)-benzyl 3-hydroxy-2-(3-(9-((3*R*,4*S*,5*R*)-3,4,5-tris(benzyloxy)tetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoate (6)



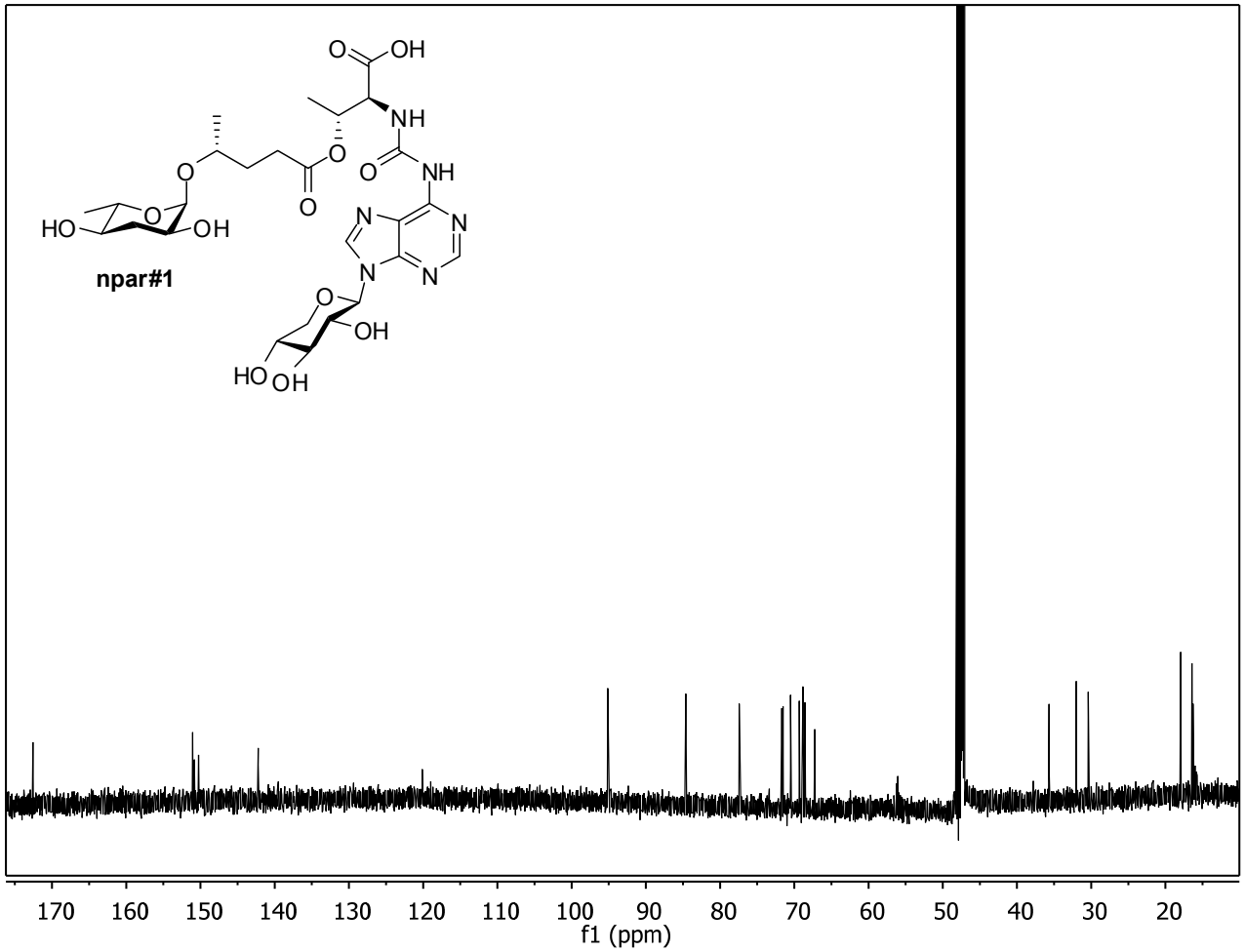
^{13}C NMR spectrum (125 MHz, methanol-d_4) of (2*S*,3*R*)-benzyl 3-hydroxy-2-(3-(9-((3*R*,4*S*,5*R*)-3,4,5-tris(benzyloxy)tetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoate (6)



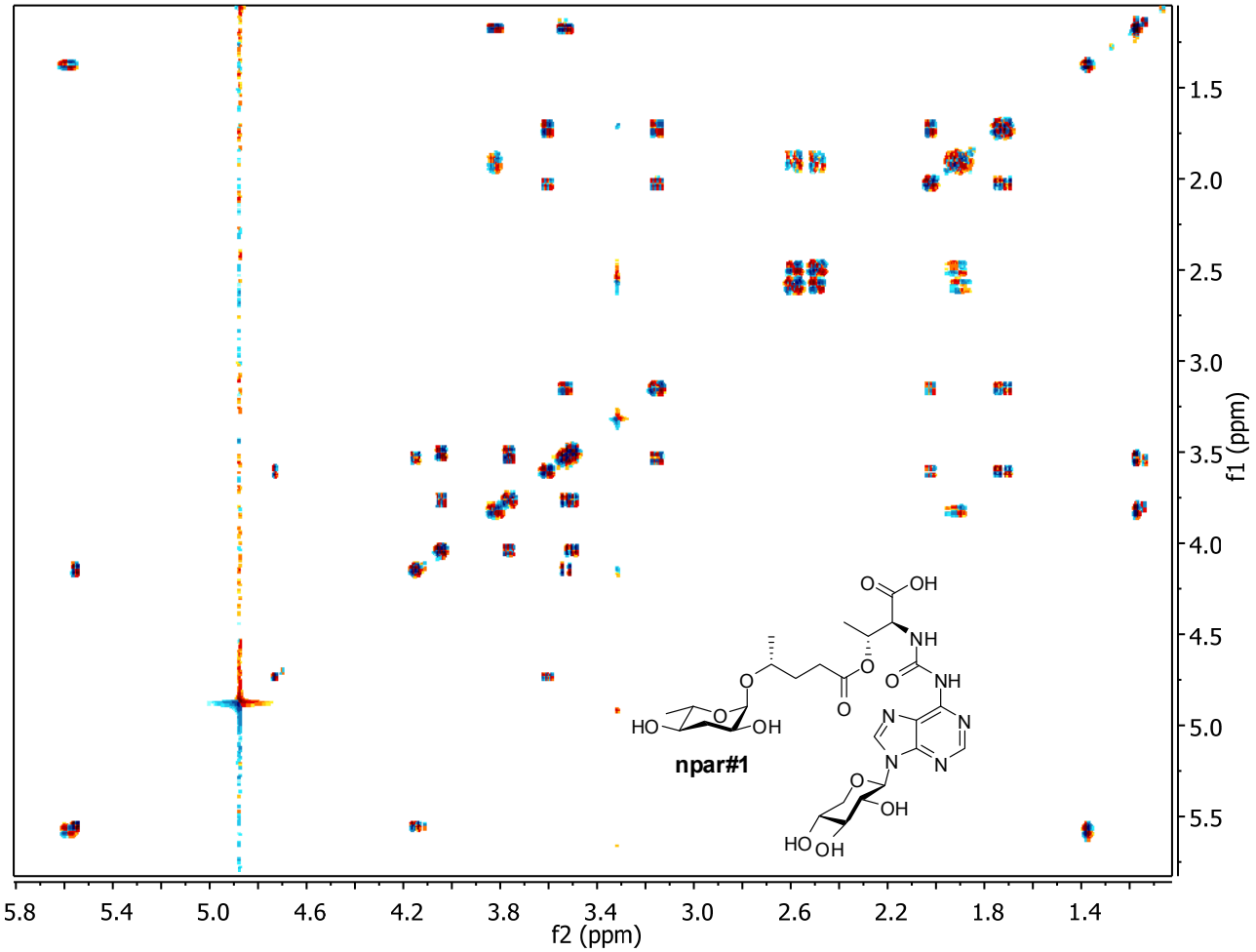
^{1}H NMR spectrum (600 MHz, methanol-d_4) of (2*S*,3*R*)-3-(((*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (npar#1)



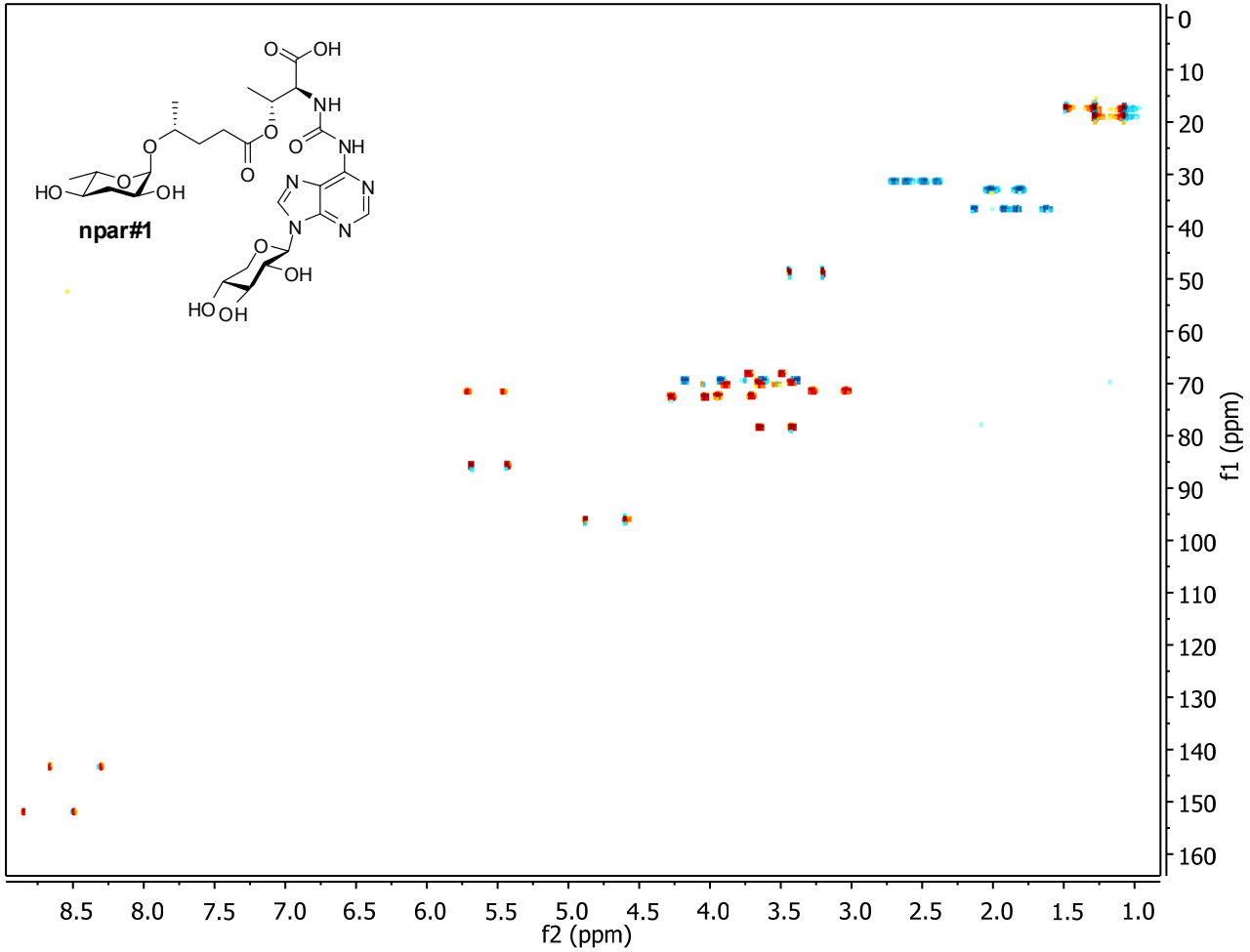
^{13}C NMR spectrum (600 MHz, methanol-d_4) of (2*S*,3*R*)-3-(((*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (npar#1)



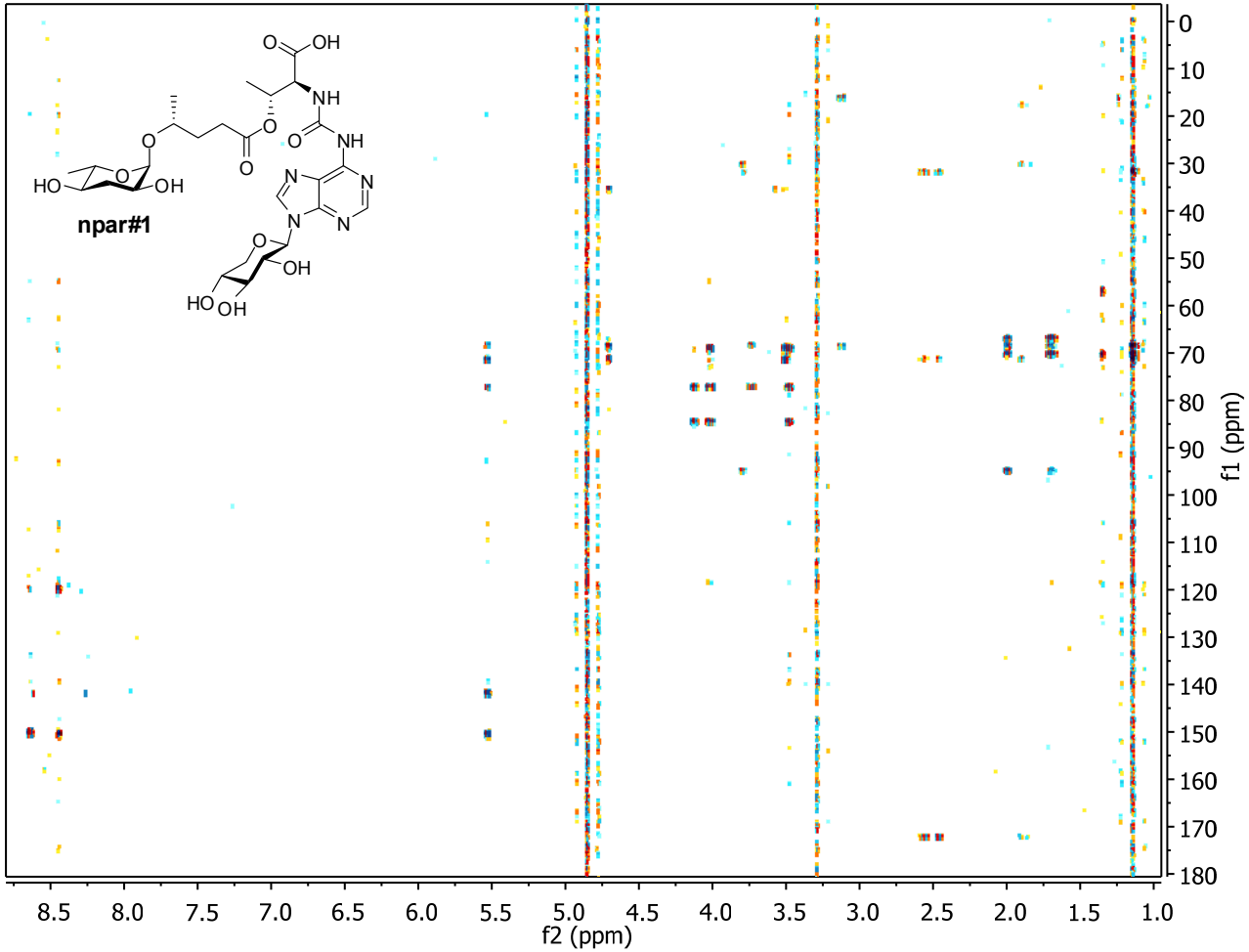
dqfCOSY spectrum (600 MHz, methanol-d_4) of (2*S*,3*R*)-3-(((*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (npar#1)



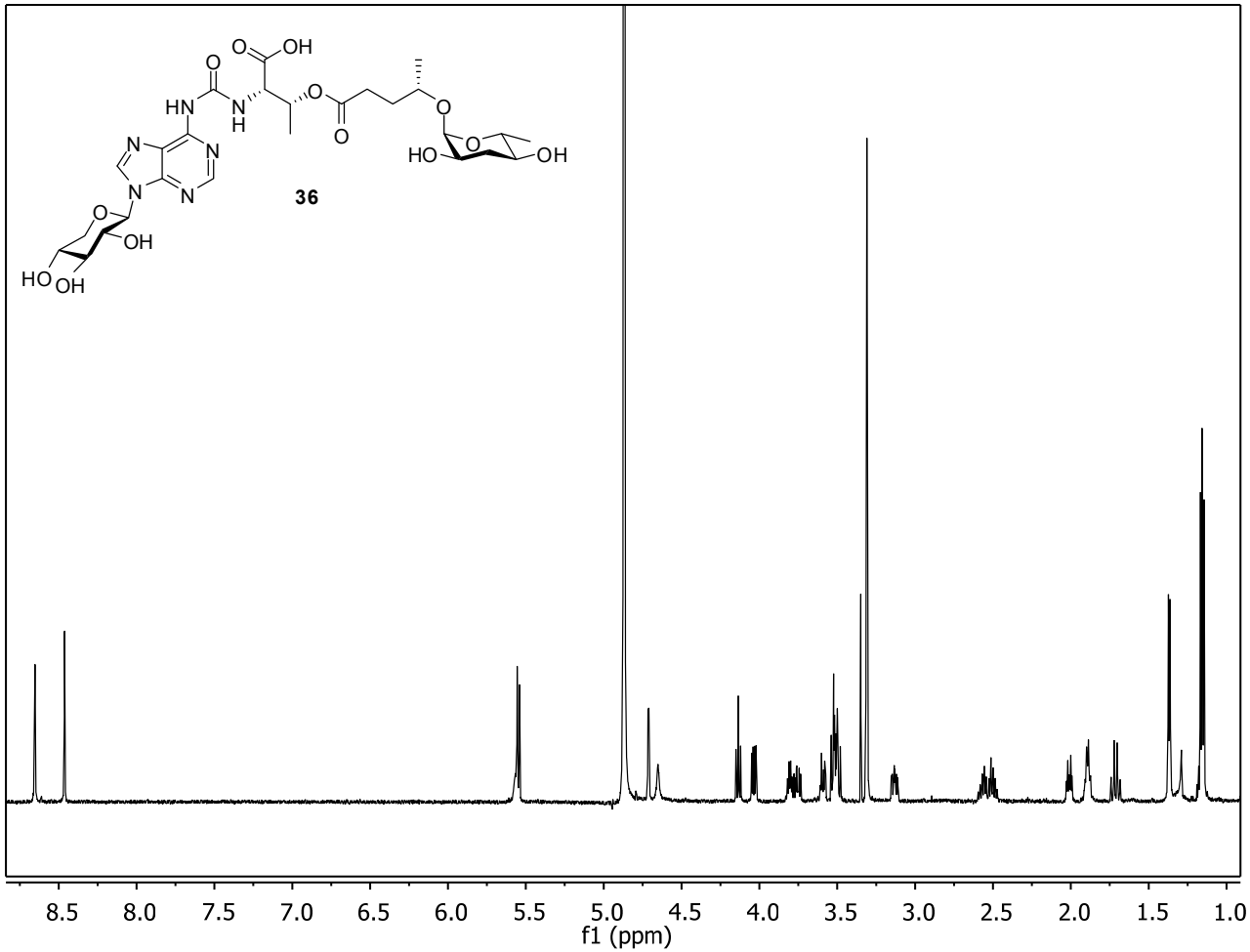
HSQCAD spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (2*S*,3*R*)-3-(((*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (npar#1)



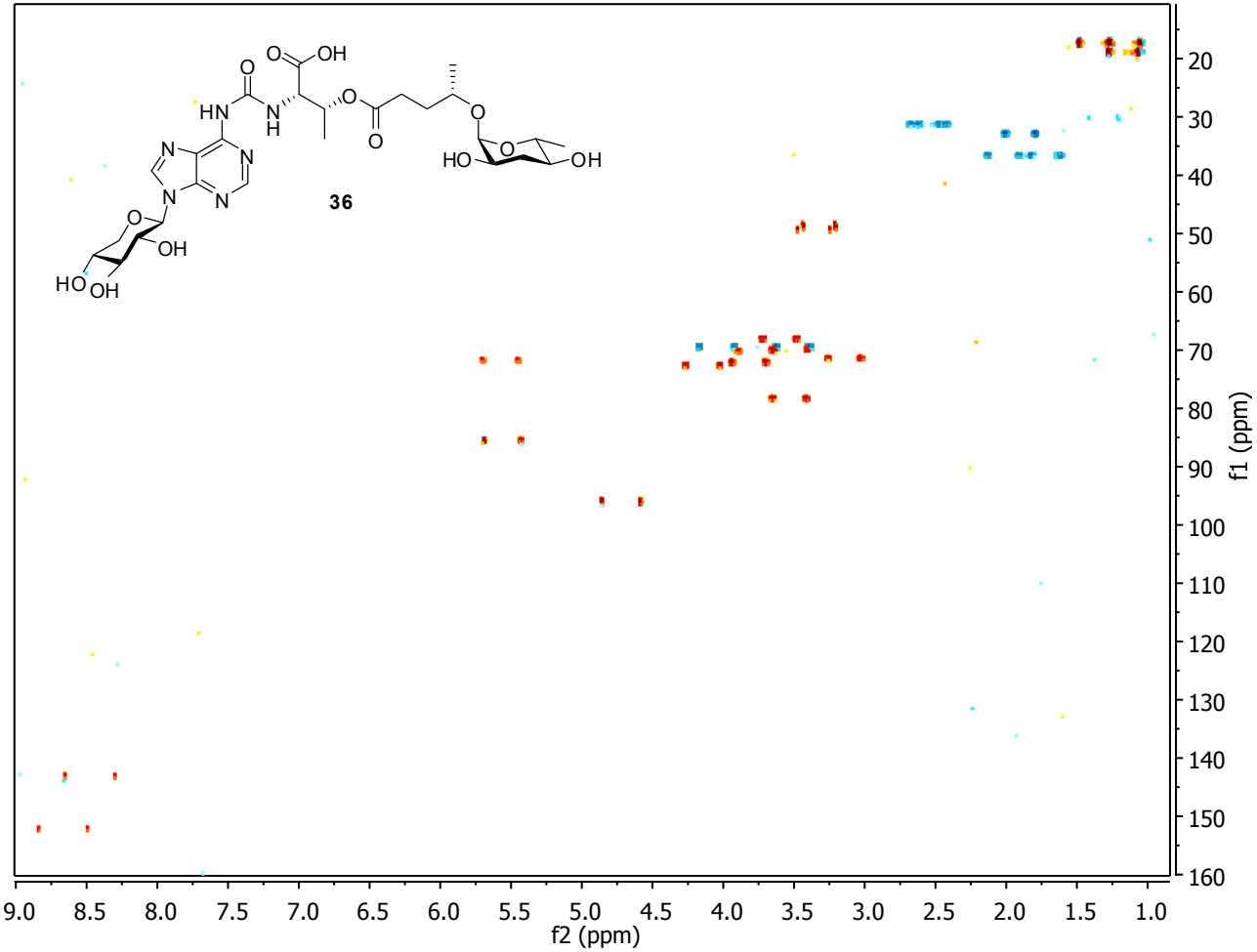
HMBC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (2*S*,3*R*)-3-(((*R*)-4-(((2*R*,3*S*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (npar#1)



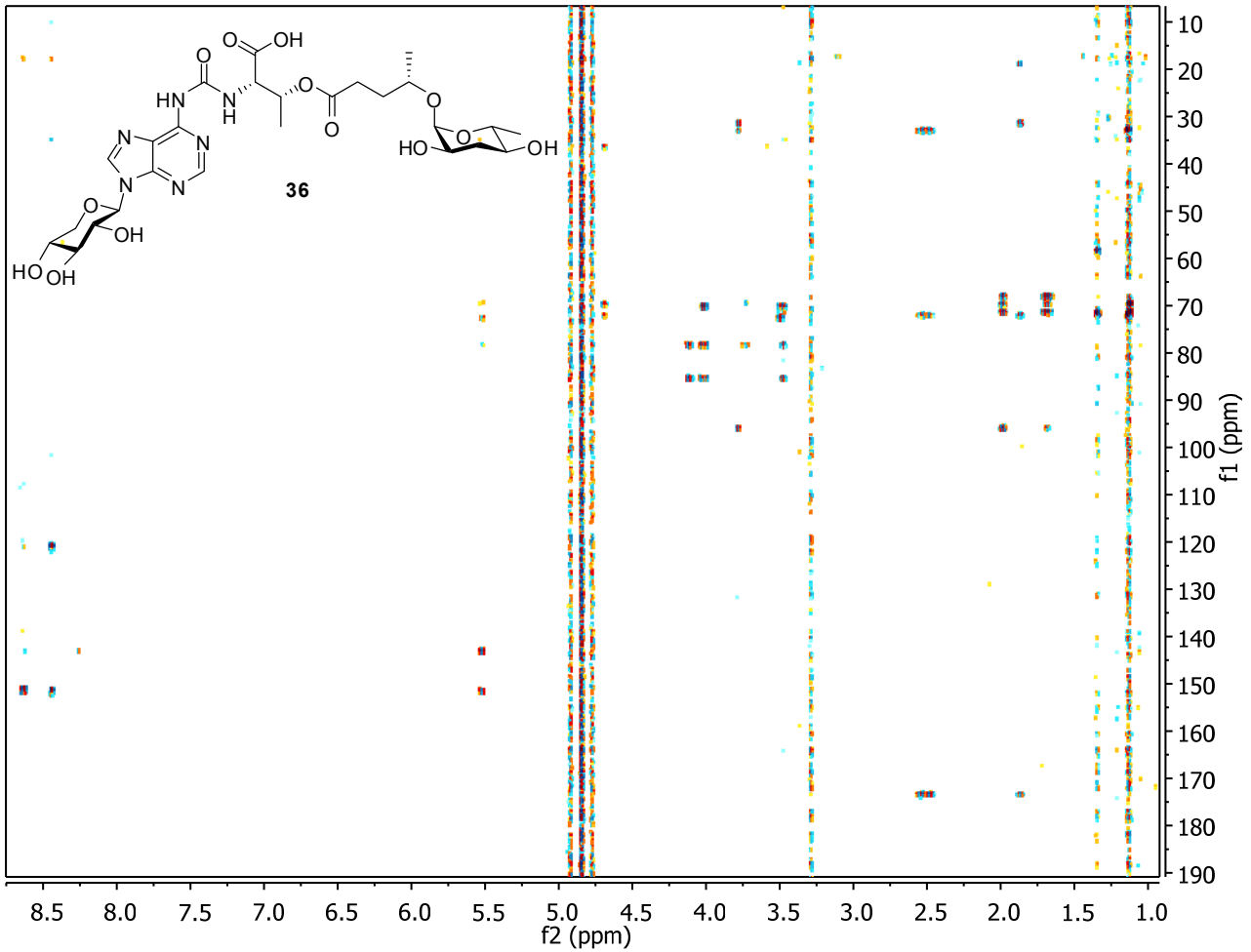
^{1}H NMR spectrum (600 MHz, methanol-d_4) of (2*S*,3*R*)-3-(((*S*)-4-(((2*S*,3*R*,5*S*,6*R*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (36)



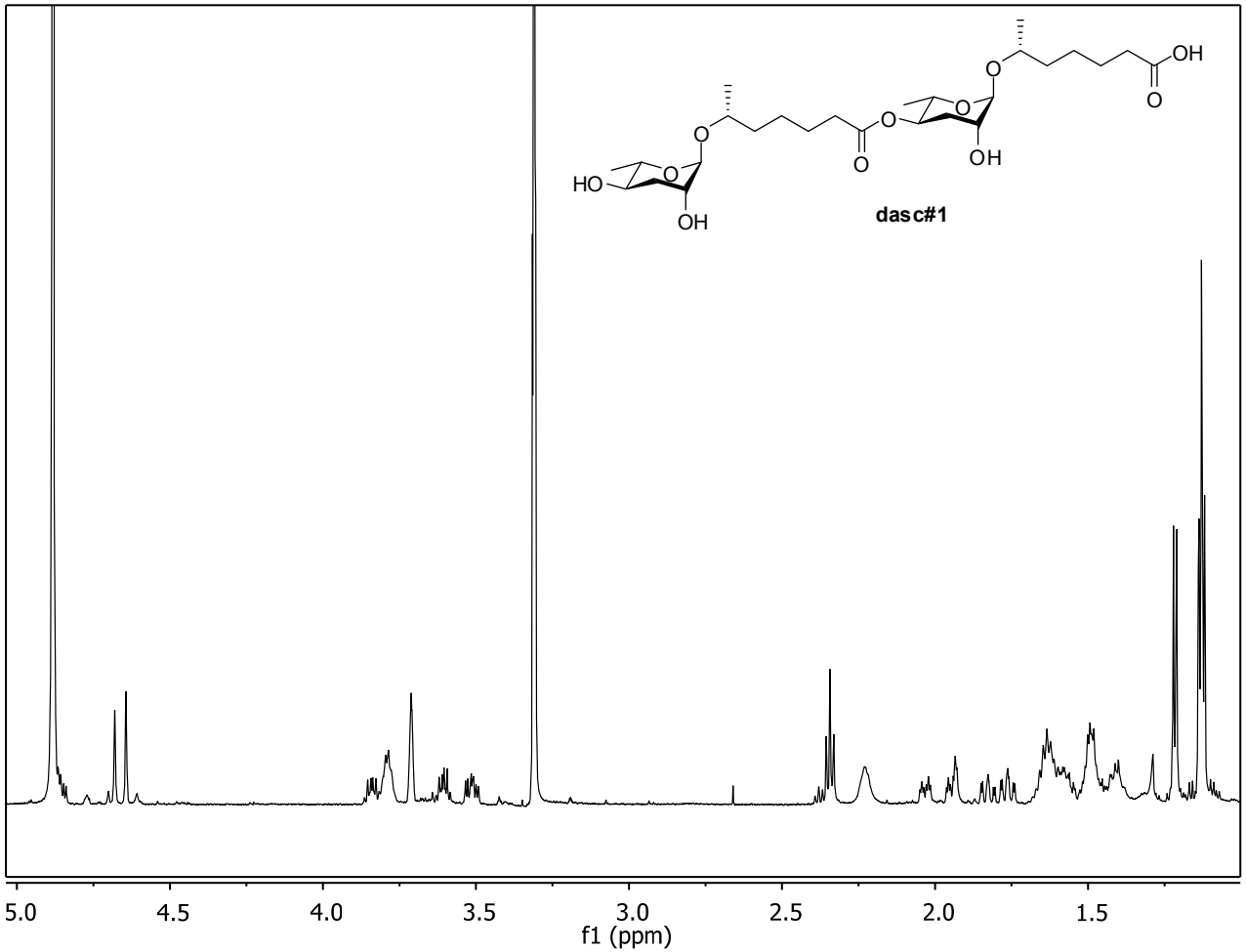
HSQCAD spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (2*S*,3*R*)-3-(((*S*)-4-(((2*S*,3*R*,5*S*,6*R*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (36)



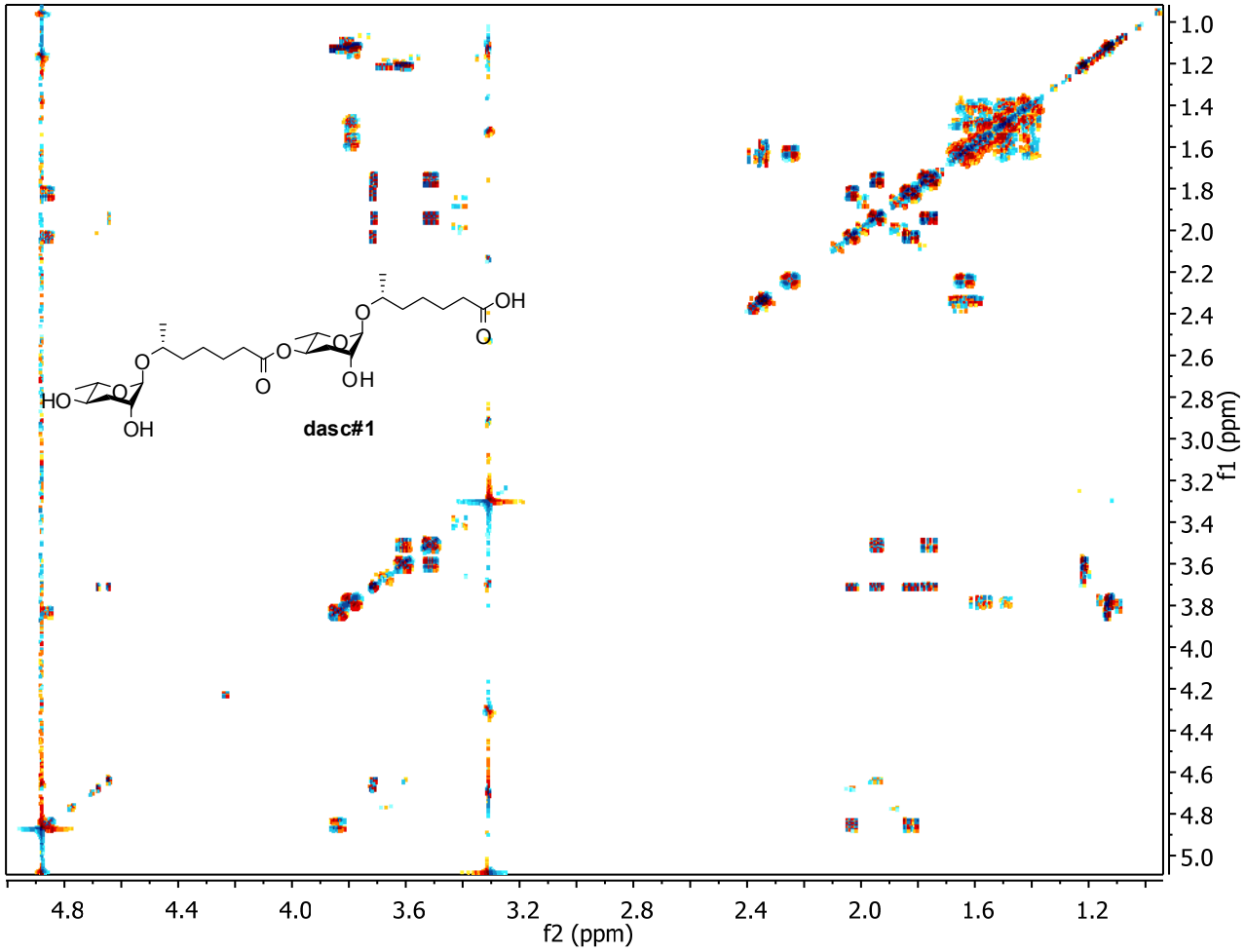
HMBC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (2*S*,3*R*)-3-(((*S*)-4-(((2*S*,3*R*,5*S*,6*R*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-2-(3-(9-((2*R*,3*R*,4*S*,5*R*)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)-9*H*-purin-6-yl)ureido)butanoic acid (36)



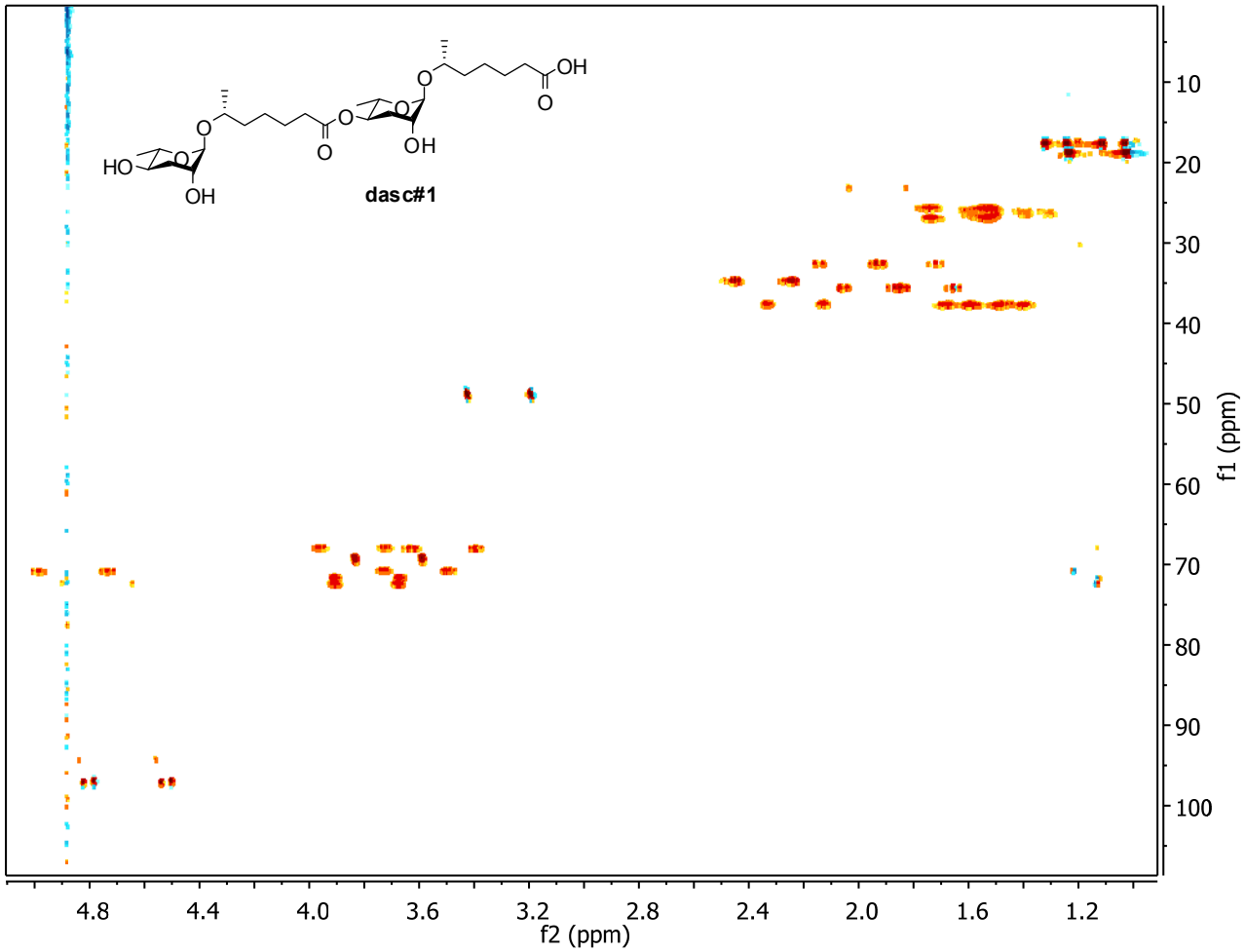
^{1}H NMR spectrum (600 MHz, methanol-d_4) of (*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoyl)oxy)-3-hydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoic acid (dasc#1)



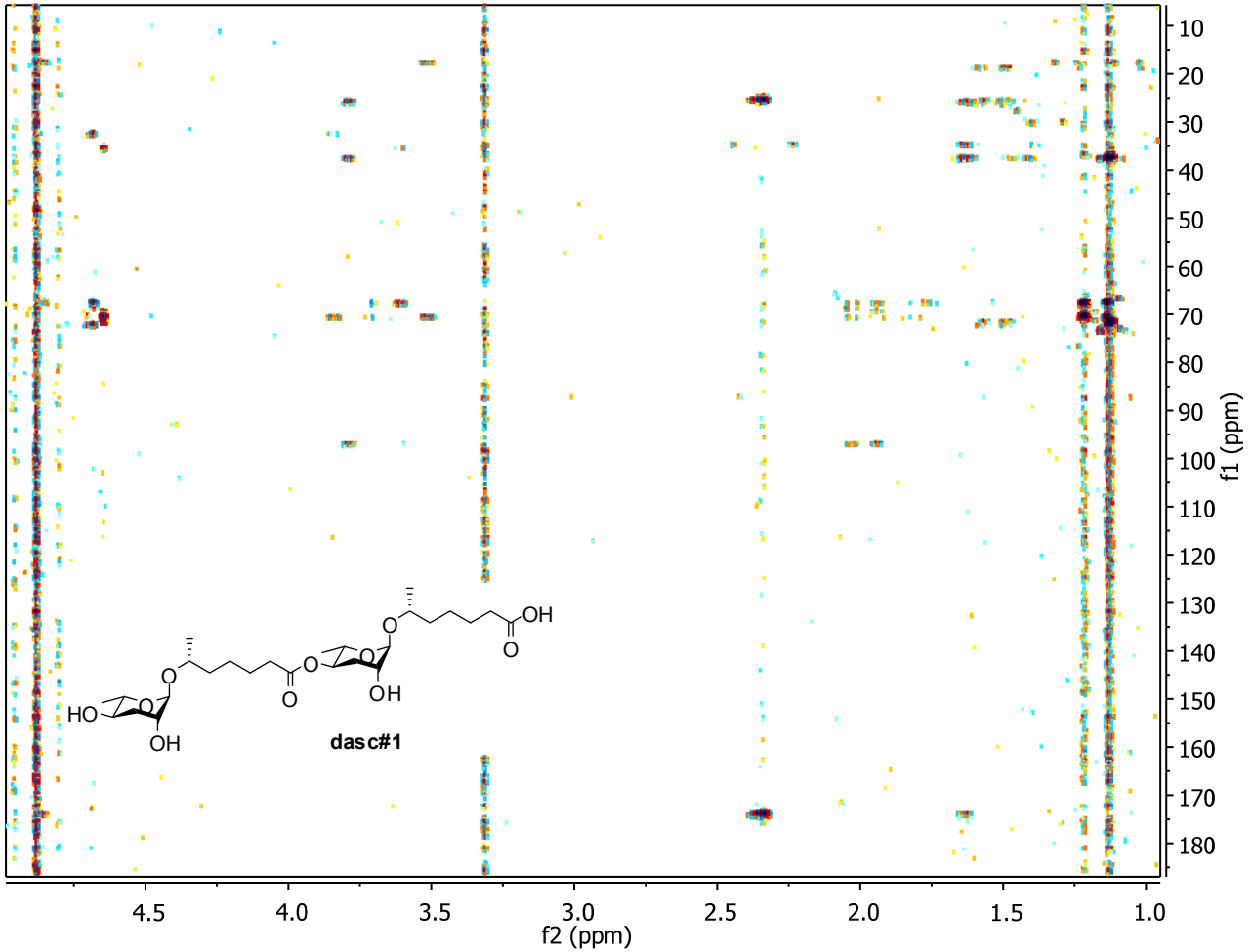
dqfCOSY spectrum (600 MHz, methanol-d_4) of (*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoyl)oxy)-3-hydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoic acid (dasc#1)



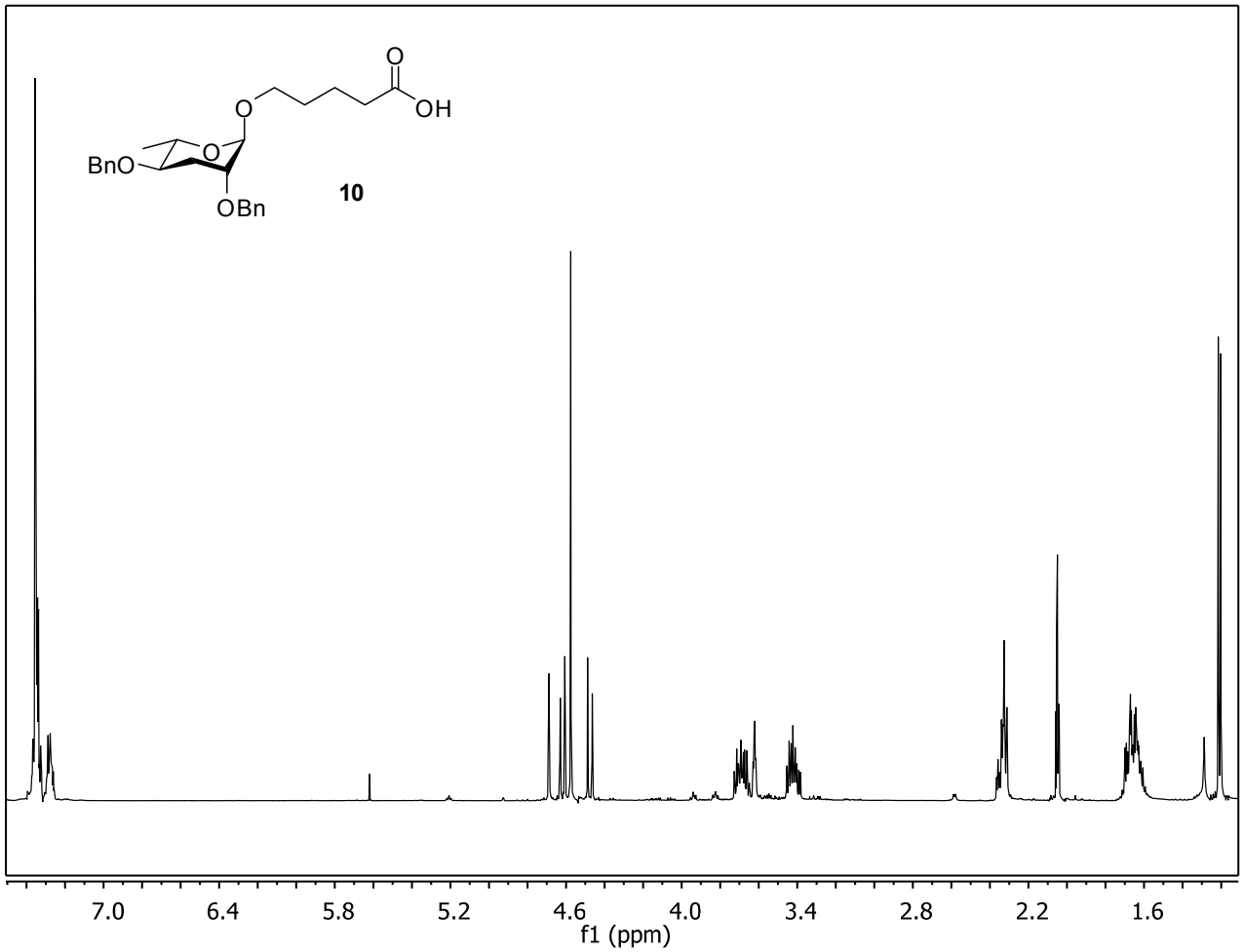
HMQC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoyl)oxy)-3-hydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoic acid (dasc#1)



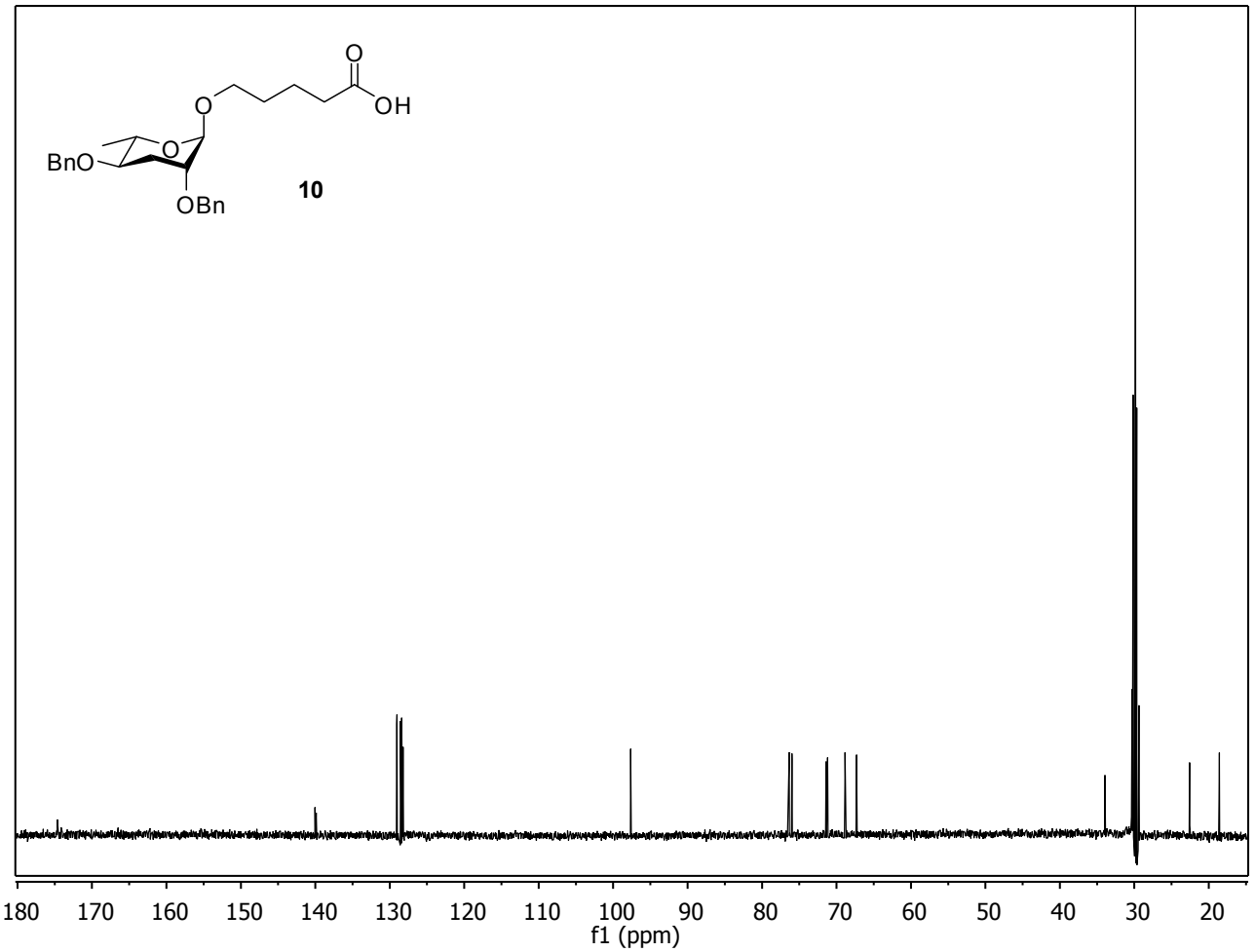
HMBC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-6-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoyl)oxy)-3-hydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)heptanoic acid (dasc#1)



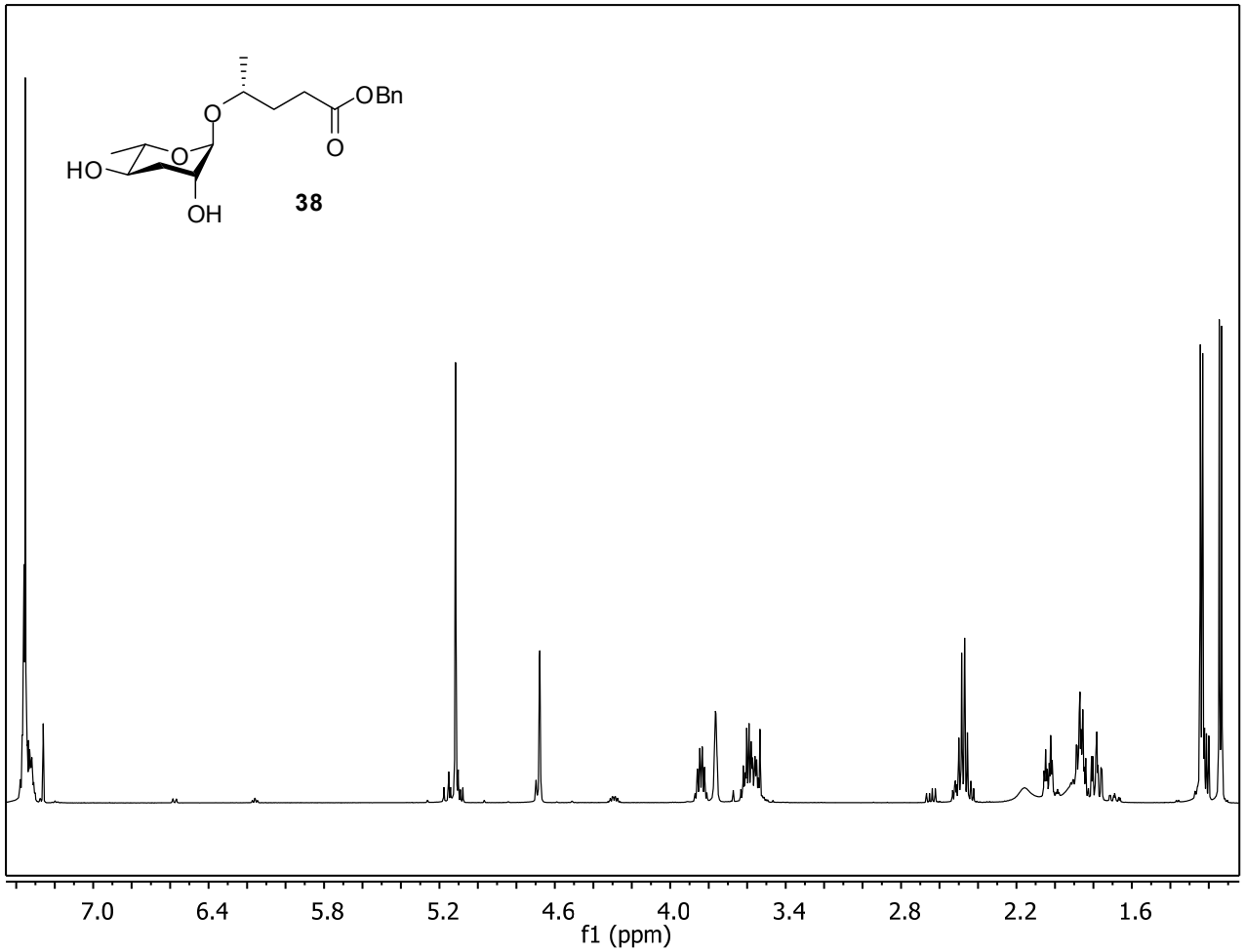
^{1}H NMR spectrum (500 MHz, acetone-d_6) of 5-(((2*R*,3*R*,5*R*,6*S*)-3,5-bis(benzyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (10)



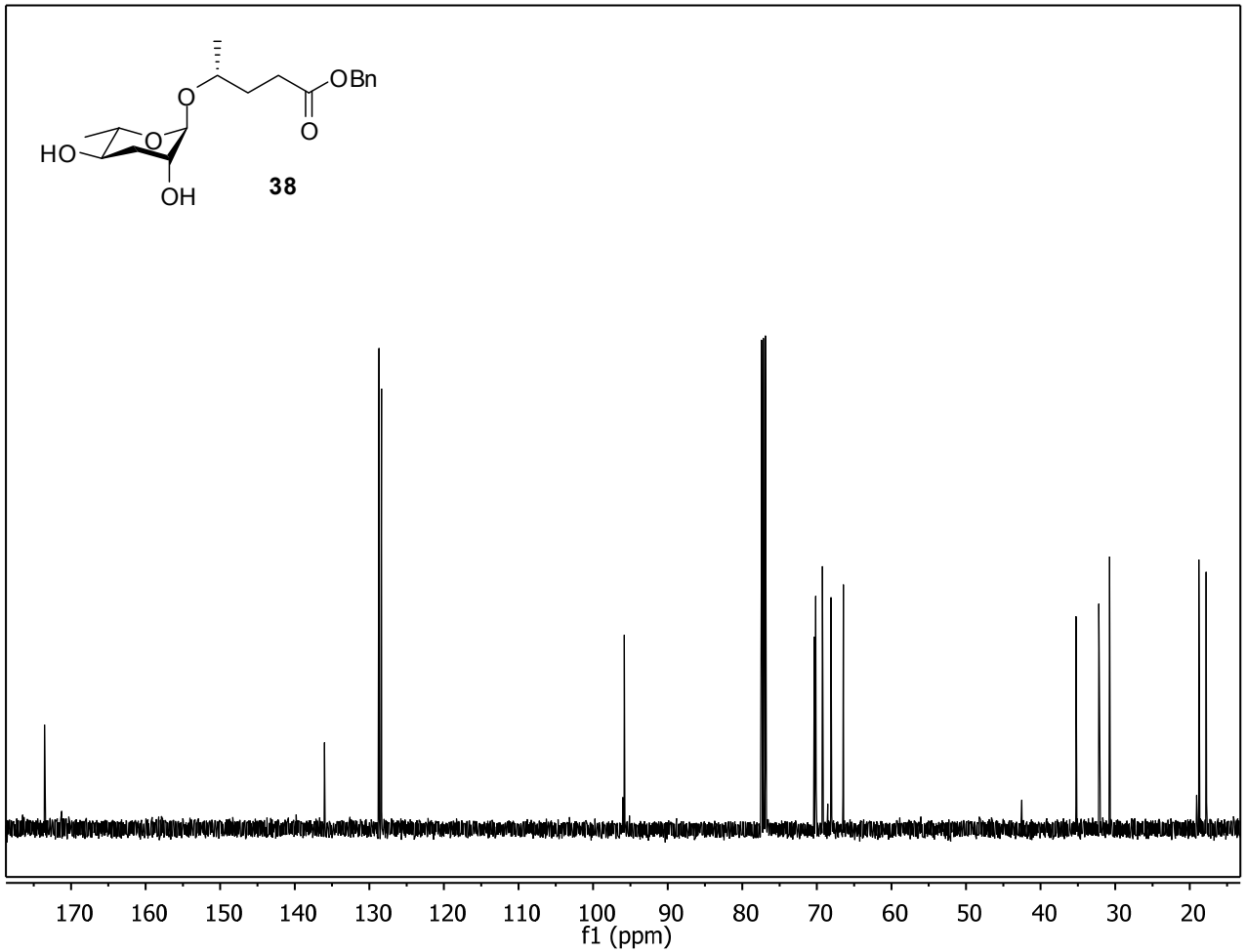
^{13}C NMR spectrum (125 MHz, acetone-d_6) of 5-(((2*R*,3*R*,5*R*,6*S*)-3,5-bis(benzyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (10)



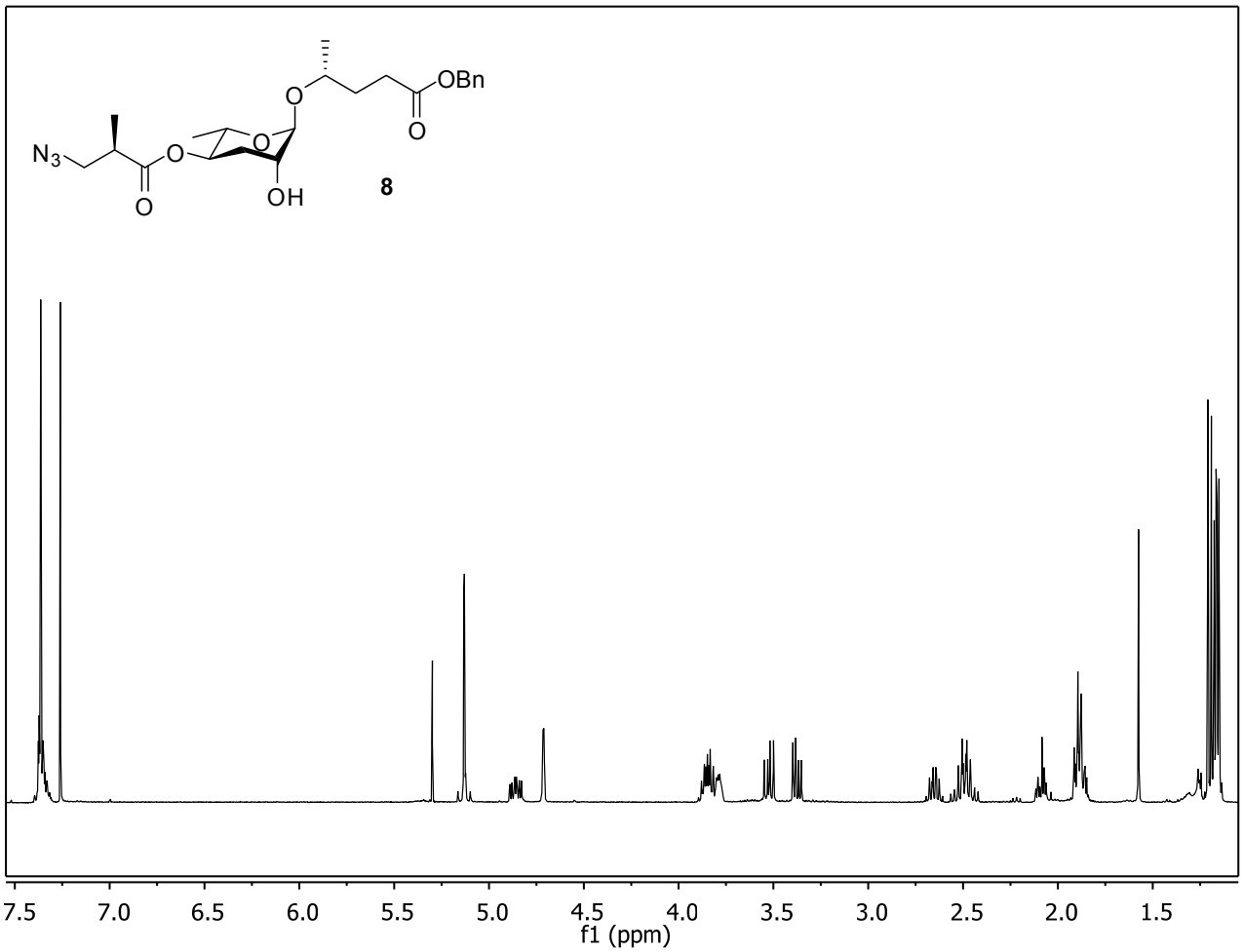
^{1}H NMR spectrum (500 MHz, chloroform-*d*) of (*R*)-benzyl 4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (38)



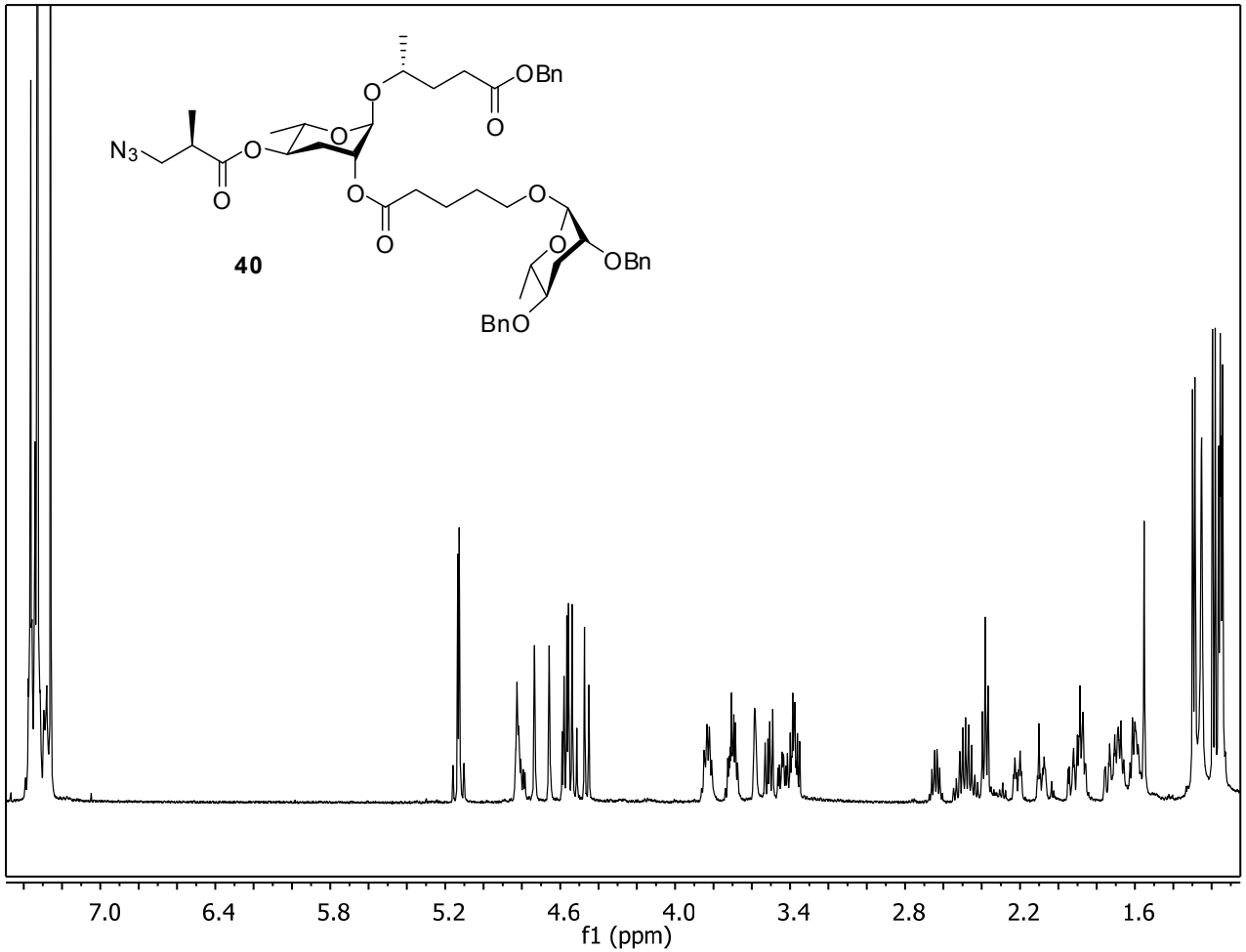
^{13}C NMR spectrum (125 MHz, chloroform-*d*) of (*R*)-benzyl 4-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (38)



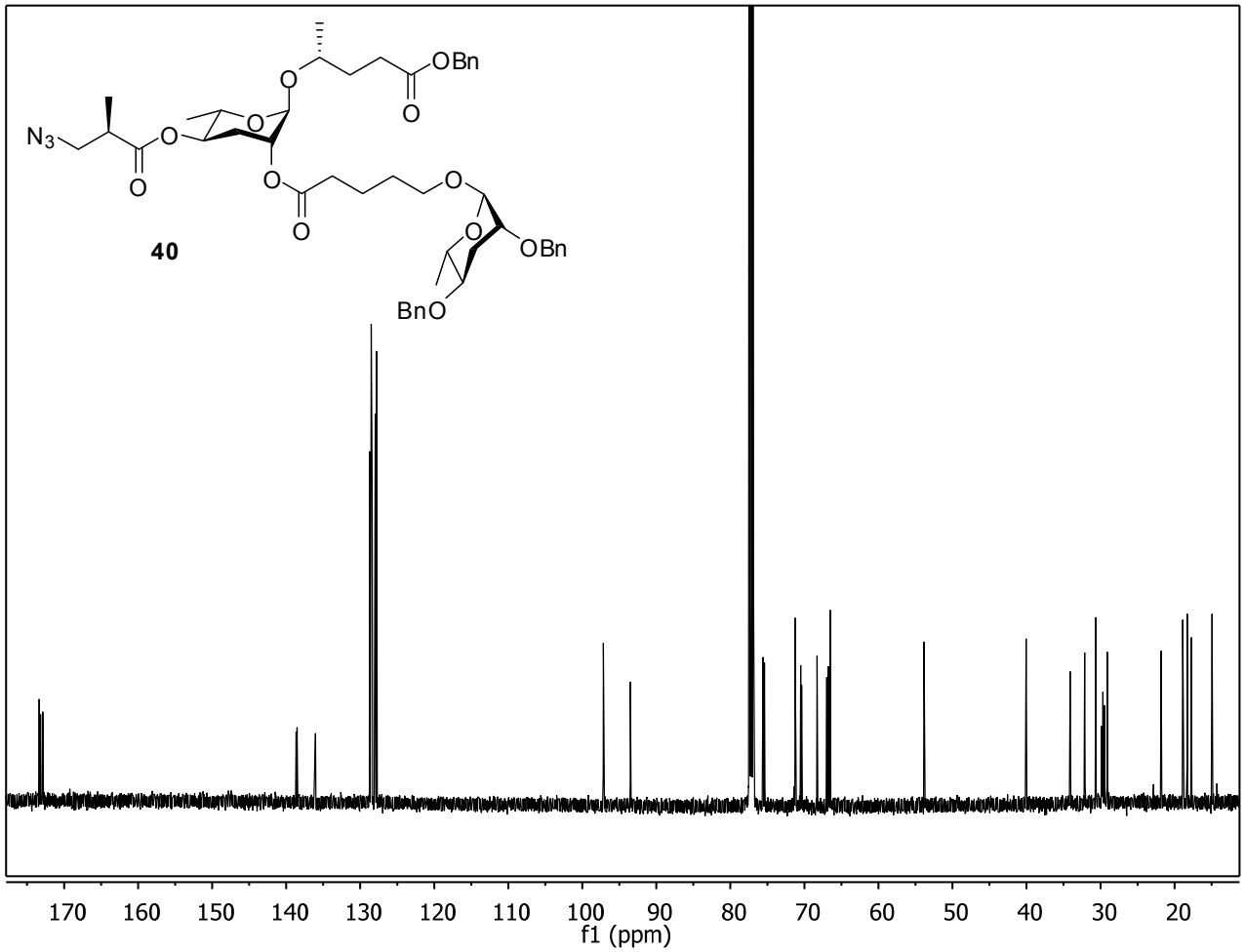
^{1}H NMR spectrum (400 MHz, chloroform-*d*) of (*R*)-benzyl 4-(((2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-3-azido-2-methylpropanoyl)oxy)-3-hydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (8)



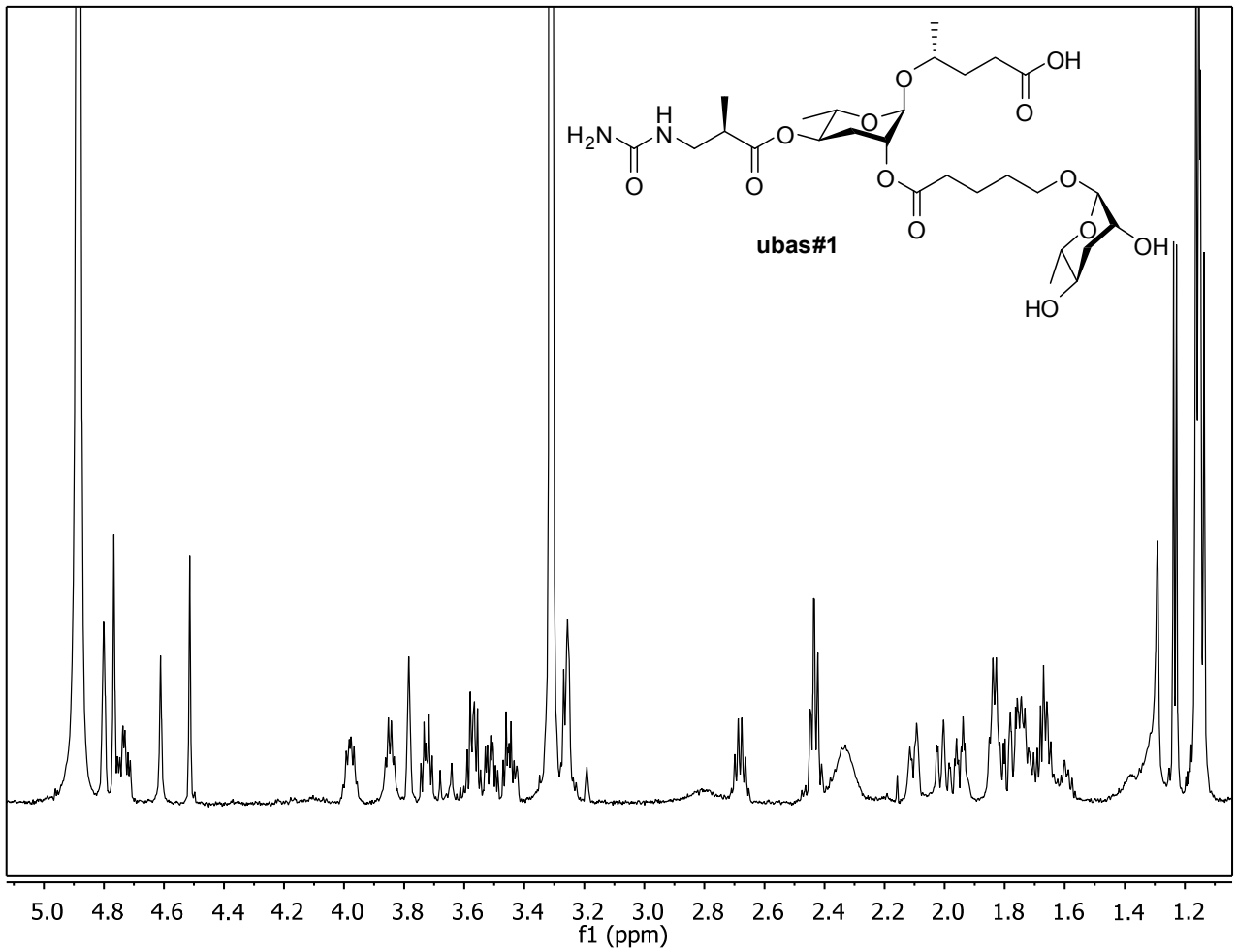
^{1}H NMR spectrum (500 MHz, acetone-d_6) of (2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-3-azido-2-methylpropanoyl)oxy)-2-(((*R*)-5-(benzyloxy)-5-oxopentan-2-yl)oxy)-6-methyltetrahydro-2*H*-pyran-3-yl 5-(((2*R*,3*R*,5*R*,6*S*)-3,5-bis(benzyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (40)



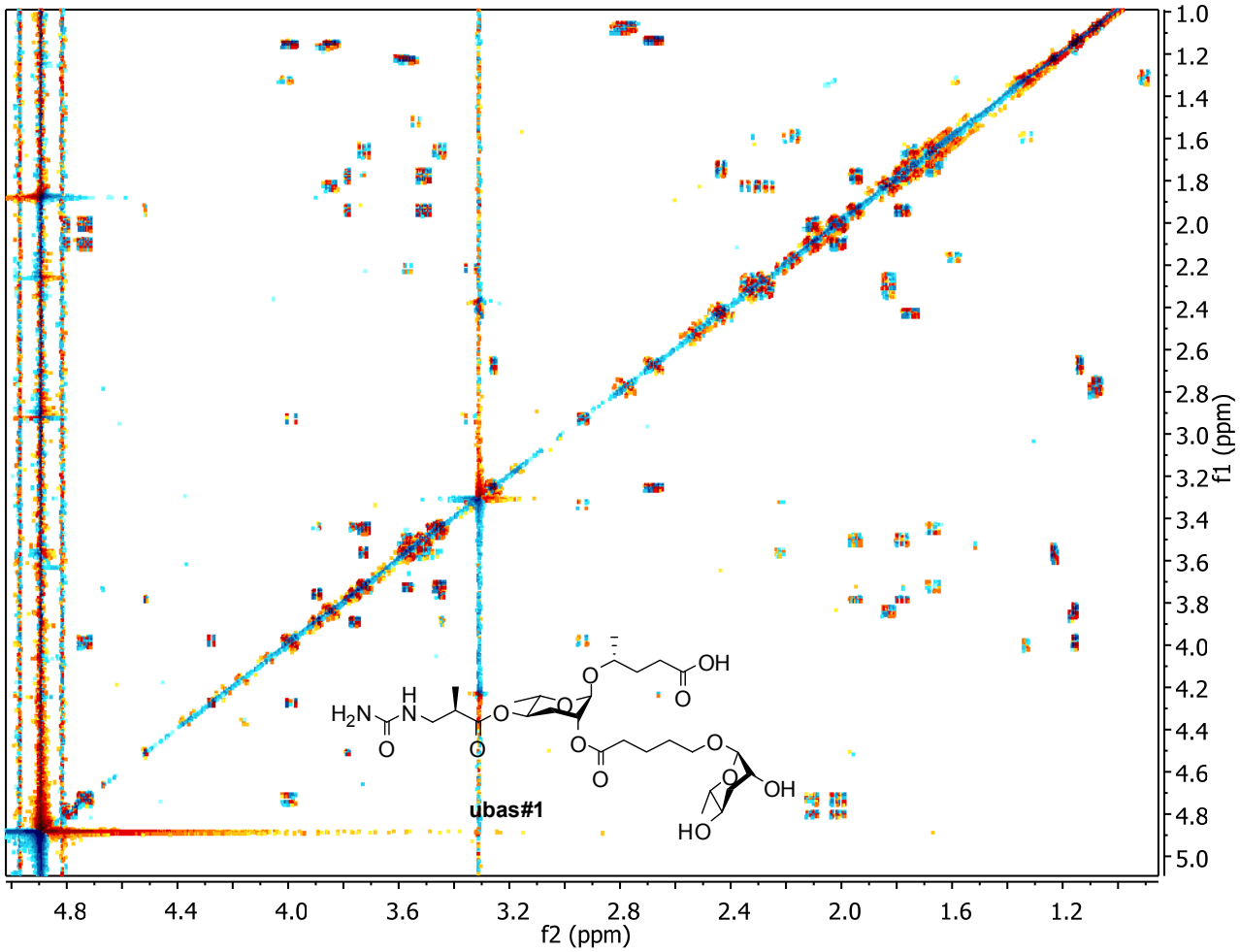
^{13}C NMR spectrum (125 MHz, acetone-d_6) of (2*R*,3*R*,5*R*,6*S*)-5-(((*R*)-3-azido-2-methylpropanoyl)oxy)-2-(((*R*)-5-(benzyloxy)-5-oxopentan-2-yl)oxy)-6-methyltetrahydro-2*H*-pyran-3-yl 5-(((2*R*,3*R*,5*R*,6*S*)-3,5-bis(benzyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoate (40)



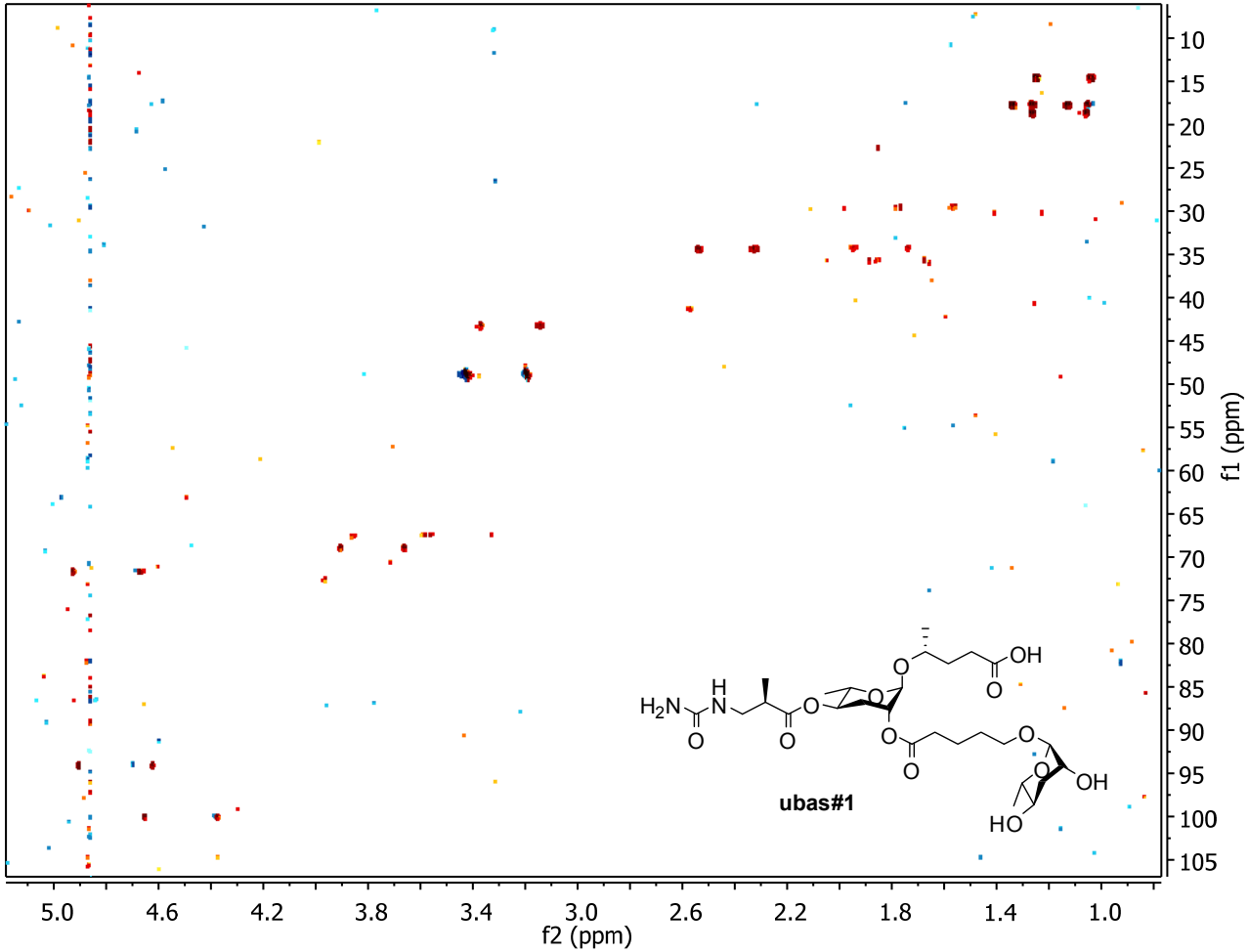
^{1}H NMR spectrum (600 MHz, methanol-d_4) of (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3-((5-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-6-methyl-5-(((*R*)-2-methyl-3-ureidopropanoyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (ubas#1)



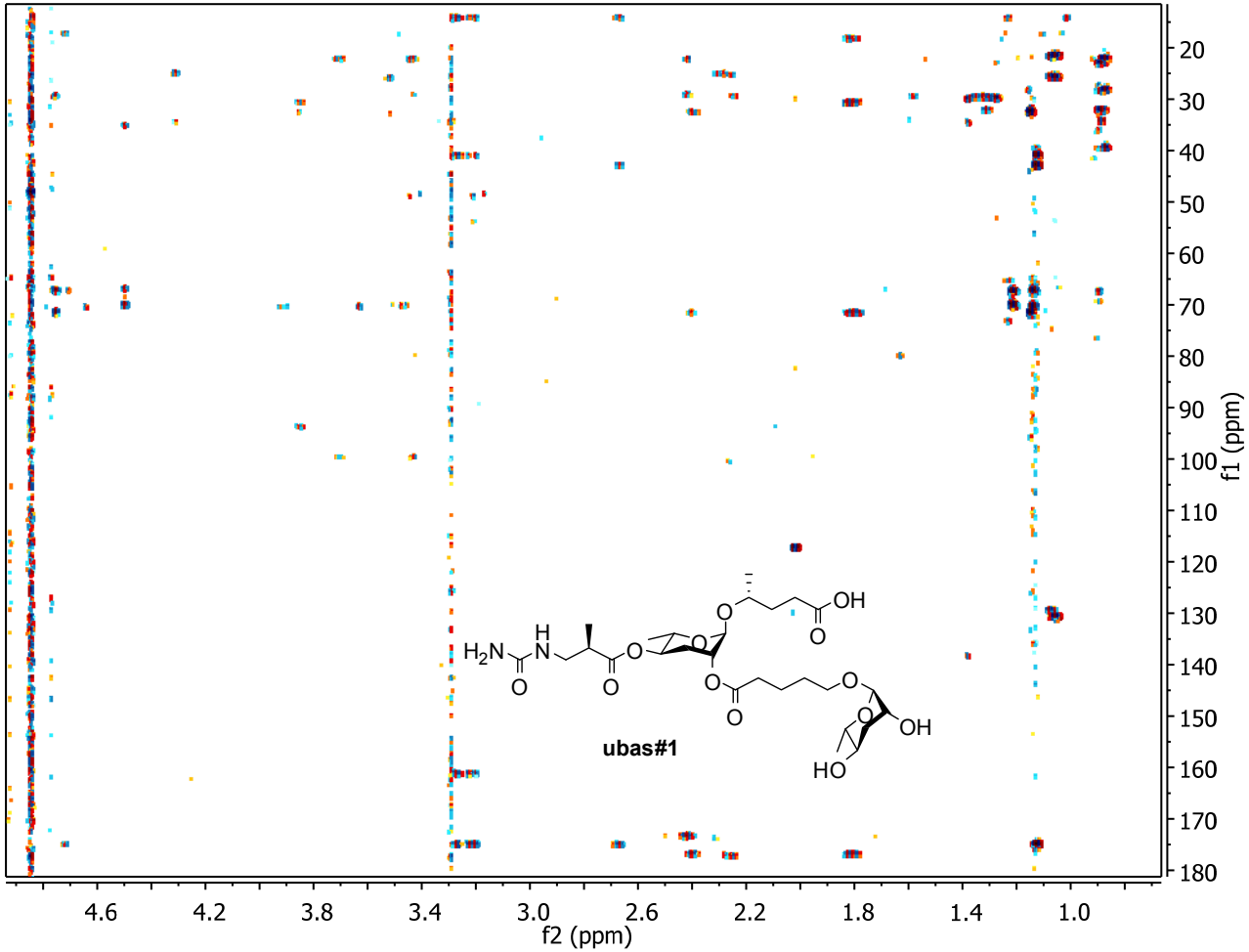
dqfCOSY spectrum (600 MHz, methanol-d_4) of (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3-((5-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-6-methyl-5-(((*R*)-2-methyl-3-ureidopropanoyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (ubas#1)



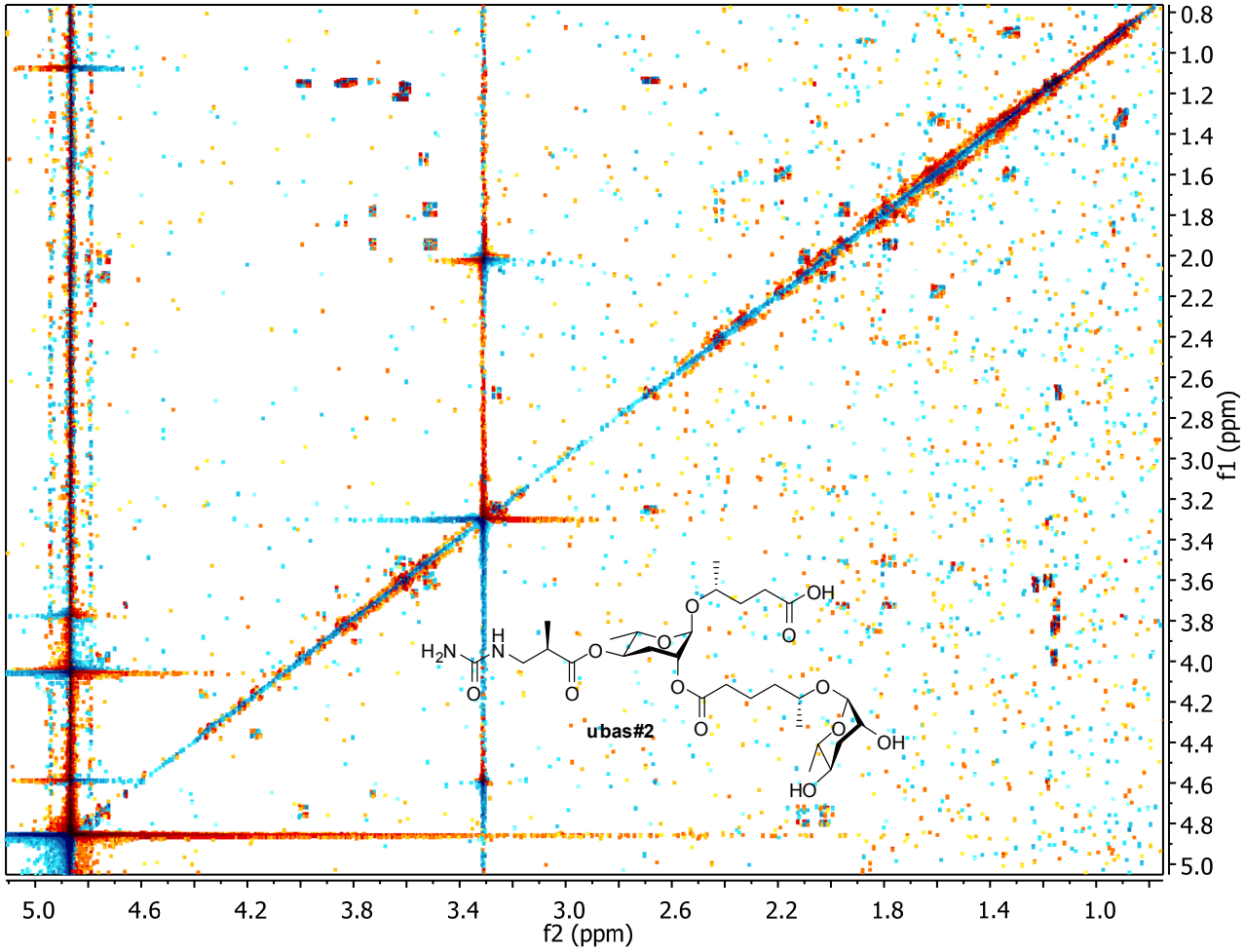
HMQC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3-((5-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-6-methyl-5-(((*R*)-2-methyl-3-ureidopropanoyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (ubas#1)



HMBC spectrum (600 MHz for ^{1}H, 151 MHz for ^{13}C, methanol-d_4) of natural sample containing (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3-((5-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)pentanoyl)oxy)-6-methyl-5-(((*R*)-2-methyl-3-ureidopropanoyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (ubas#1)



dqfCOSY spectrum (600 MHz, methanol-d_4) of natural sample containing (*R*)-4-(((2*R*,3*R*,5*R*,6*S*)-3-(((*R*)-5-(((2*R*,3*R*,5*R*,6*S*)-3,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)hexanoyl)oxy)-6-methyl-5-(((*R*)-2-methyl-3-ureidopropanoyl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)pentanoic acid (ubas#2)



6. Supporting References

[1] A. Ogawa, A. Streit, A. Antebi, R. J. Sommer, *Curr. Biol.* **2009**, *19*, 67-71.
[2] T. Stiernagle, Maintenance of *C. elegans*, *WormBook*, ed. The *C. elegans* Research Community **2006**, 1-11.
[3] a) N. C. Lu, K. M. Goetsch, *Nematologica* **1993**, *39*, 303-311; b) J. Srinivasan, S. H. von Reuss, N. Bose, A. Zaslaver, P. Mahanti, M. C. Ho, O. G. O'Doherty, A. S. Edison, P. W. Sternberg, F. C. Schroeder, *PLoS Biol.* **2012**, *10*, e1001237.
[4] T. R. Hoye, C. S. Jeffrey, F. Shao, *Nat. Protoc.* **2007**, *2*, 2451-2458.
[5] Z. B. Zhao, H. W. Liu, *J. Org. Chem.* **2001**, *66*, 6810-6815.
[6] J. Tummatorn, P. A. Albiniak, G. B. Dudley, *J. Org. Chem.* **2007**, *72*, 8962-8964.
[7] C. G. Lucero, K. A. Woerpel, *J. Org. Chem.* **2006**, *71*, 2641-2647.
[8] G. B. Chheda, C. I. Hong, *J. Med. Chem.* **1971**, *14*, 748-753.
[9] R. Rej, D. Nguyen, B. Go, S. Fortin, J. F. Lavallee, *J. Org. Chem.* **1996**, *61*, 6289-6295.
[10] S. H. von Reuss, N. Bose, J. Srinivasan, J. J. Yim, J. C. Judkins, P. W. Sternberg, F. C. Schroeder, *J. Am. Chem. Soc.* **2012**, *134*, 1817-1824.