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Supporting Information

Nucleophile-Directed Stereocontrol Over Glycosylations Using Geminal-Difluorinated Nucleophiles

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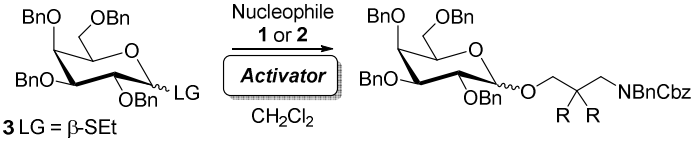
Table of Contents

I Supporting Figures and Tables

I.1 The Scope of Nucleophile-directed Stereocontrol Using Different Activators and Leaving Groups

The influence of *O*-nucleophilicity on stereoselectivity in relationship to the anomeric leaving group and activator was studied (Table S1). First, several well-known thioglycoside activation conditions were used to react thioglycoside **3** with alcohols **1** or **2**. NIS/TfOH (*see* Table 1, entry 2), the mild thiophilic promoter DMTST in the presence of the base TTBPy[1] and the Ph_2SO/Tf_2O[2] activator system, which favors the formation of anomeric triflate intermediates,[3] showed opposing selectivities when **1** (10-11.5:1 α:β) and **2** (1:4-6 α:β) were compared. Similar stereoselectivities were found using glycosyl phosphate **S-4**[4] with nucleophiles **1** (10:1 α:β) and **2** (1:10 α:β). Glycosyl imidates **S-5**[5] and **S-6**[6] exhibited the same trend albeit with a less pronounced effect. Thus, *O*-nucleophilicity impacts stereoselectivity largely independent of the leaving groups and activators.

Table S1. Nucleophiles **1** and **2** Induce Opposing Stereoselectivities Using Different Activators and Leaving Groups.



3 LG = β-SEt
S-4 LG = α/β-OPO(OBu)$_2$
S-5 LG = α/β-C(NH)CCl$_3$
S-6 LG = α/β-C(NPh)CF$_3$

4α/β R = **F**
5α/β R = **H**

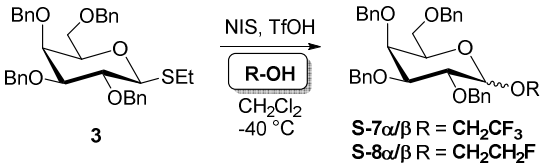
Entry[a]	Substrate, activator	*Selectivity* / α:β (*yield* / %)[b][c]	
		R = **F** (**4α:β**)	R = **H** (**5α:β**)
1	**3**, DMTST/TTBPy[d][e]	10:1 (66)	1:4 (77)
2	**3**, Ph_2SO/Tf_2O/TTBPy[d][e][f]	11.5:1 (58)	1:6 (67)
3	**S-4**, TMSOTf[g][h]	10:1 (81)	1:10 (66)
4	**S-5**, TMSOTf[g][h]	2:1 (62)	1:9.6 (89)
5	**S-6**, TMSOTf[g][h]	1.3:1 (69)	1:3 (93)

[a]1.0 equiv. nucleophile **1** or **2**, 1.5 equiv. glycosylating agent. [b]Selectivities determined by HPLC. [c]Isolated yields. [d]Temperature -40 °C to r.t. [e] 4 Å mol. sieves. [f]Pre-activation. [g]Temperature -40 °C.[h]3 Å-AW mol. Sieves. DMTST = dimethyl(thiomethyl)sulfonium trilfuoromethanesulfonate. TMSOTf = trimethylsilyl trifluoromethanesulfonate. TTBPy = tri-*tert*-butylpyridine.

I.2 Correlation of Nucleophile Reactivity with Stereoselectivity

To determine the influence of alcohol nucleophilicity on stereoselectivity, alcohols with different fluorine substitutions were used in glycosylation reactions with thioglycoside **3** (Table S2). Consistent with the results obtained using nucleophiles **1** and **2** (*see* Table 1), opposing stereoselectivities were observed with the nucleophiles 2,2,2-trifluoroethanol (24:1 α:β) and ethanol (1:5 α:β). Interestingly, monofluorinated 2-fluoroethanol with intermediate nucleophilicity did not induce stereoselectivity (1:1.5 α:β), indicating that nucleophilicity correlates with stereoselectivity.

Table S2. Alcohol Nucleophilicity Correlates with Stereoselectivity.



Entry[a][b][c]	Nucleophile	*Selectivity* / α:β (*yield* / %)[d][e]
1	2,2,2-Trifluoroethanol	24:1 (83)[e]
2	2-Fluoroethanol	1:1.5 (96)[f]
3	Ethanol	1:5 (92)[f]

[a]1.0 equiv. nucleophile, 1.1 equiv. glycosylating agent. [b]3 Å-AW mol. sieves. [c]1.5 equiv. NIS, 0.2 equiv. TfOH. [d]Isolated yields. [e]Selectivity determined by HPLC. [f]Selectivity determined by ^{1}H NMR.

I.3 Molecular Modeling

Ground state conformations of **1** (Fig. S1), **2** (Fig. S3) as well as the corresponding oxyanions (Fig. S2 and S4) were calculated as depicted in the experimental section. Absolute energies and charge densities on the alcohol oxygen atoms were calculated (Table S1). In addition to a general lower charge density on the alcohol oxygen, fluorinated alcohol **1** exhibits a relative stabilization of the corresponding oxyanion over the alcohol by 0.01565612 au (41.1 kJ/mol) with respect to non-fluorinated alcohol **2** (see below).

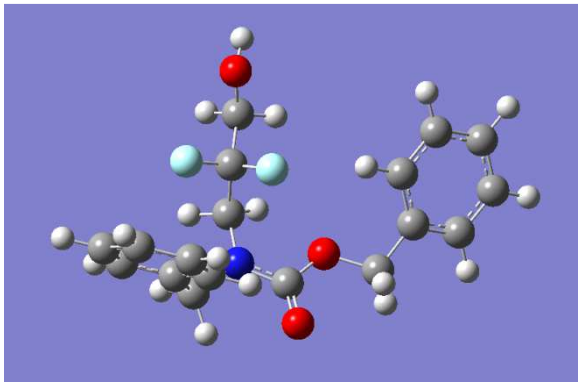


Figure S1. Minimized energy conformation of fluorinated alcohol **1**.

Coordinates for **1***:*

0 1

N	-0.86224700	-0.79581000	-1.23398100
C	-2.24094200	-1.29152600	-1.36252800
C	-3.18979800	-0.91066600	-0.23883200
C	-4.39517800	-0.26274000	-0.52864000
C	-5.29863600	0.05328200	0.48915400
C	-4.99955000	-0.27097600	1.81306700
C	-3.79630900	-0.91764300	2.11156800
C	-2.89951800	-1.23928400	1.09301100
C	-0.53075700	0.55152700	-1.66983000
C	0.08238500	-1.63498200	-0.70848900
O	1.32049700	-1.08476000	-0.74094600
C	2.38061400	-1.86476000	-0.14504400
C	3.52784700	-0.94479100	0.19020900
C	4.84337100	-1.35307500	-0.05643300
C	5.91884200	-0.53644000	0.30207700
C	5.68643100	0.70319100	0.90025800
C	4.37395900	1.12082900	1.14016700
C	3.30015600	0.30131700	0.79132500
O	-0.14895000	-2.75842200	-0.27620800
C	-0.63486600	1.61929600	-0.57062400
C	0.10515700	2.90288800	-0.91751100
O	-0.13996300	3.85060400	0.09960300
F	-1.95818900	1.90923700	-0.33728500
F	-0.14415300	1.11701300	0.61567000

H	-2.63520400	-0.92198100	-2.31512600
H	-2.16996900	-2.37996500	-1.43279600
H	-4.62977300	-0.00129300	-1.55971600
H	-6.23183900	0.55800400	0.24694400
H	-5.69915800	-0.02314200	2.60876900
H	-3.55871200	-1.17780000	3.14126800
H	-1.97297300	-1.75524800	1.32767900
H	0.48510000	0.55928400	-2.06797700
H	-1.21275400	0.83981900	-2.47536000
H	1.98402600	-2.35959200	0.74758700
H	2.69236700	-2.64578100	-0.84681400
H	5.02891100	-2.31534800	-0.53167000
H	6.93681000	-0.86664400	0.10549600
H	6.52247700	1.34307500	1.17488600
H	4.18589200	2.08764200	1.60296800
H	2.28125600	0.62938600	0.97007700
H	1.17240200	2.65597300	-1.01338700
H	-0.25192100	3.24302400	-1.90260700
H	0.37794900	4.65294700	-0.10483900

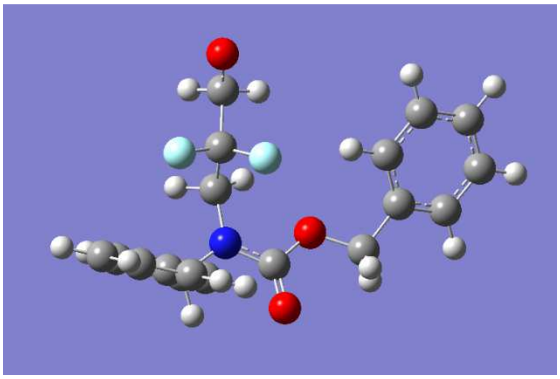


Figure S2. Minimized energy conformation of the anion of fluorinated alcohol **1**.

Coordinates for the oxyanion of ***1****:*

-1 1

N	-0.84913600	-0.64803800	-1.28056100
C	-2.22946000	-1.11895500	-1.44943300
C	-3.17913800	-0.86902600	-0.28875400
C	-4.40001200	-0.22419300	-0.51343000
C	-5.31352500	-0.03840600	0.52683400
C	-5.00942100	-0.48972900	1.81191500
C	-3.79032300	-1.13317000	2.04621400
C	-2.88344700	-1.32522400	1.00379700
C	-0.50860000	0.73619300	-1.61481500
C	0.06928300	-1.52857900	-0.79534100
O	1.32496800	-1.01478800	-0.79922800
C	2.34133700	-1.82693600	-0.18206400
C	3.52070200	-0.95001200	0.15995900
C	4.82099300	-1.45002500	0.02434300
C	5.92228400	-0.67281800	0.39123600
C	5.73158100	0.61875600	0.88602000
C	4.43529400	1.12599100	1.01420700
C	3.33347800	0.34705600	0.65807700
O	-0.18434300	-2.67230800	-0.42098400
C	-0.62319300	1.74121600	-0.46662100
C	0.03666400	3.11967800	-0.73357500
O	-0.16432300	4.02767200	0.20618500
F	-1.96504900	1.90852100	-0.16771300
F	-0.07593300	1.16490800	0.67829600
H	-2.62800500	-0.64031600	-2.34987900
H	-2.17061400	-2.19404900	-1.64288900
H	-4.63788500	0.13899800	-1.51235600
H	-6.25755100	0.46770400	0.33374200
H	-5.71598300	-0.34207500	2.62630900
H	-3.54675600	-1.49030800	3.04517100
H	-1.94362300	-1.83696300	1.18670500
H	0.51343100	0.76793500	-1.99496700
H	-1.17610300	1.06506100	-2.41580100
H	1.91625400	-2.29721700	0.71148700
H	2.63361300	-2.63134200	-0.86655000
H	4.97447800	-2.45292100	-0.37232000
H	6.92790900	-1.07390600	0.28081100
H	6.58781400	1.22965900	1.16499100
H	4.27964900	2.13422600	1.39305700

H	2.32752000	0.74409800	0.75042800
H	1.11714200	2.82319200	-0.94532400
H	-0.34589700	3.36812800	-1.78311600

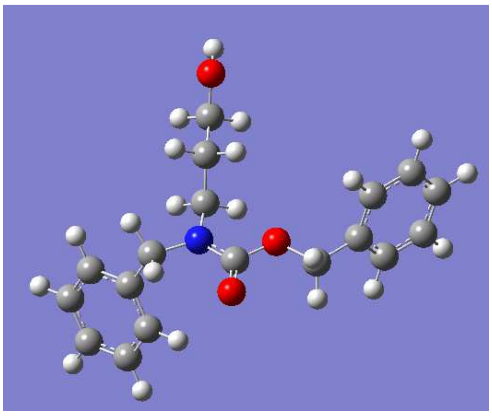


Figure S3. Minimized energy conformation of non-fluorinated alcohol **2**.

Coordinates for ***2****:*

0 1

N	-1.04051100	0.22545100	0.68888300
C	-2.38882800	0.24250400	1.26680000
C	-3.44951100	-0.32704000	0.34160700
C	-4.48052500	0.48079100	-0.15046900
C	-5.45498400	-0.04646600	-1.00392600
C	-5.40501800	-1.39092200	-1.37336100
C	-4.37992400	-2.20719700	-0.88270600
C	-3.40977800	-1.67936100	-0.03189400
C	-0.70168000	1.24858700	-0.30499600
C	-0.14764000	-0.70389800	1.13112400
O	1.07114200	-0.54348500	0.55444600
C	2.07507200	-1.51506400	0.95006400
C	3.34772700	-1.18890200	0.21643500
C	3.68282100	-1.86627100	-0.96216900
C	4.86020000	-1.55901600	-1.64737600
C	5.71358100	-0.56718500	-1.15882900
C	5.38615100	0.11534600	0.01611100
C	4.21010000	-0.19544100	0.69949700
O	-0.39540600	-1.58842300	1.94765300
C	-0.11494800	2.52166400	0.31744600
C	0.15732500	3.60165600	-0.72288500
O	0.71288600	4.72863400	-0.05273400
H	-2.34438600	-0.33214700	2.19418300
H	-2.64051300	1.27694600	1.52709900
H	-4.52518700	1.53046800	0.13861900
H	-6.24994600	0.59487600	-1.37933800
H	-6.16178500	-1.80432600	-2.03702100
H	-4.33996500	-3.25828900	-1.16209200
H	-2.61679700	-2.31639000	0.35405000
H	0.00082300	0.82049500	-1.02298600
H	-1.62286900	1.47792100	-0.85275600
H	2.20715200	-1.45767700	2.03458000
H	1.71427500	-2.51780600	0.70353300
H	3.01922400	-2.64147000	-1.34254200
H	5.11234400	-2.09589100	-2.55960300
H	6.63342100	-0.32899900	-1.68922000
H	6.05015400	0.88596300	0.40247500
H	3.95932200	0.33291400	1.61809400
H	-0.80290000	2.92385000	1.07173400
H	0.82120000	2.27433800	0.82949000
H	0.84824100	3.21430500	-1.48978800
H	-0.78037800	3.86845500	-1.23826600
H	0.89232600	5.41779500	-0.72017400

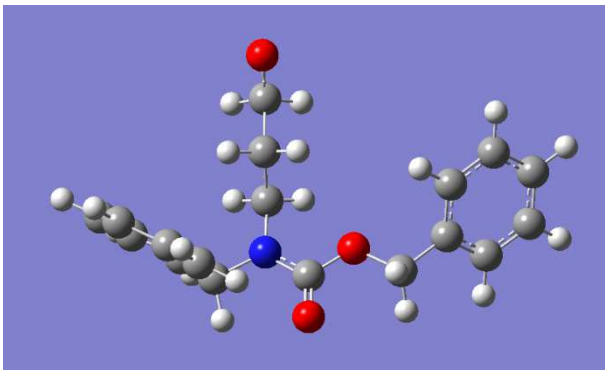


Figure S4. Minimized energy conformation of anion of non-fluorinated alcohol **2**.

Coordinates for the oxyanion of ***2****:*

-1 1

N	-0.88527000	-0.52464700	-1.14345800
C	-2.22560700	-1.05003500	-1.42228700
C	-3.27776400	-0.75134800	-0.36581700
C	-3.15518900	-1.26883700	0.93289700
C	-4.13335800	-1.01210900	1.89297100
C	-5.25343700	-0.23974200	1.56858400
C	-5.38684000	0.27389700	0.27824000
C	-4.40260400	0.01880000	-0.68095700
C	-0.59661100	0.89758800	-1.42727700
C	0.01991000	-1.36400900	-0.57951500
O	1.23566100	-0.77379700	-0.41719100
C	2.24047100	-1.60768100	0.20426300
C	3.51228300	-0.80857500	0.31707800
C	4.64968200	-1.17789900	-0.40940700
C	5.83707300	-0.45036500	-0.29144000
C	5.89305100	0.66050700	0.55159700
C	4.75934300	1.03952200	1.27777200
C	3.57804300	0.30779700	1.16311100
O	-0.19690600	-2.53421500	-0.25645200
C	-0.79359800	1.86914300	-0.26358100
C	-0.50593900	3.36068600	-0.64228100
O	-0.67642600	4.22709200	0.35605600
H	-2.54958900	-0.63505100	-2.38284300
H	-2.12420500	-2.13176500	-1.54098700
H	-2.28996400	-1.87701400	1.18238900
H	-4.02479400	-1.41869500	2.89678200
H	-6.01615300	-0.04036800	2.31874500
H	-6.25340200	0.87820400	0.01678800
H	-4.50860200	0.42482800	-1.68600100
H	0.43146100	0.96183900	-1.79330400
H	-1.25063500	1.18055000	-2.26067000
H	1.87373600	-1.92078400	1.18799500
H	2.39037900	-2.50864300	-0.39774800
H	4.60641100	-2.04223000	-1.07041900
H	6.71483900	-0.75045500	-0.86031300
H	6.81546400	1.23038400	0.64422900
H	4.79714200	1.90590800	1.93499900
H	2.69767800	0.60607500	1.72886800
H	-1.82178100	1.80658700	0.11422500
H	-0.12853600	1.59324200	0.56536100
H	0.54016600	3.33463800	-1.10594900
H	-1.15480800	3.53859200	-1.57094500

Energy and charge density (alcohol. oxygen) of the optimized structures:

Difluorinated alcohol **1**: neutral (-1177.51833947 au, -.572 charge)
Difluorinated alcohol **1**: oxyanion (-1176.97514365 au, -.820 charge)
Difference D_1 = 0.54319582 au

Non-fluorinated alcohol **2**: neutral (-979.04647222 au, -.584 charge)
Non-fluorinated alcohol **2**: oxyanion (-978.48762028 au, -.851 charge)
Difference D_2 = 0.55885194 au

Relative stability difference: $D_{stab} = D_1 - D_2$ = 0.01565612 au = 41.1 kJ/mol.

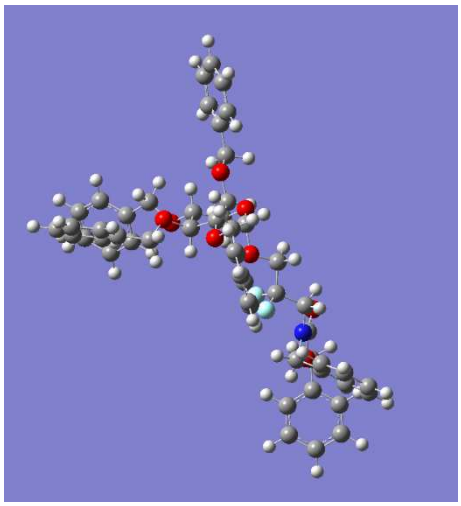


Figure S5. Minimized energy conformation of difluorinated glucoside **15α**.

Coordinates for **15α**:

0 1

O	-1.49223800	-0.07426100	-2.25339700
C	-1.74044600	-0.93055600	-1.12069400
C	-2.19656100	1.93725500	-1.05846300
C	-1.11003600	1.23759300	-1.90712600
O	-1.75909700	3.18799100	-0.55853200
O	-3.75532400	1.56981700	0.79074200
C	-2.01476000	-2.32730300	-1.65018200
C	-0.77733200	5.32548700	-0.98765500
C	-2.89817200	-0.35920500	-0.28980200
C	-2.59088400	1.07557300	0.15123600
C	0.45117700	4.96693100	-0.41524100
C	-0.21087800	7.66712900	-0.69347900
O	-3.08987100	-1.18820500	0.84999000
C	-3.55988900	2.56685100	1.79953700
C	-3.39550900	-2.98222300	2.92286000
C	-3.52546800	-3.78999300	4.05509100
O	-3.26872200	-2.35196500	-2.30797800
C	-1.71785300	4.25796700	-1.49675100
C	1.33590600	5.95472700	0.01486900
C	1.01050500	7.30635800	-0.12502000
C	-4.43109800	-1.63355700	1.02950600
C	-1.10172800	6.67904000	-1.11729700
C	-5.72403800	-4.61305400	-3.73015900
C	-6.90266900	-4.55043900	-4.47518800
C	-3.56151900	-3.60496000	-2.90472700
C	-4.66164100	2.45492500	2.82631300
C	-4.86851100	1.24547100	3.50444300
C	-5.87096800	1.13466900	4.46550400
C	-6.67710000	2.23617000	4.76790800
C	-6.47625700	3.44416800	4.10087400
C	-5.47561200	3.54910400	3.13144800
C	2.32689400	0.56949800	-0.84493900
C	1.22719000	0.82530300	-1.86353100
C	-4.53076400	-2.48810100	2.27258900
C	3.67205100	0.19996900	-1.47690900
F	2.48409800	1.70820700	-0.07053100
C	-4.78847900	-4.11609500	4.54806700
C	-5.92668100	-3.62420300	3.90422100
C	-5.79708800	-2.81383800	2.77764400
O	0.08602000	1.27647700	-1.16139000
C	-4.86201000	-3.51353600	-3.66769000
C	-7.23617600	-3.38025500	-5.15777900
C	-6.38397200	-2.27573300	-5.09226400
C	-5.20196600	-2.34221000	-4.35553500
F	1.92536700	-0.42417900	0.00585000
N	4.62071200	-0.35676100	-0.53294300
C	6.25470500	1.50140500	-0.22960200
C	7.52813200	1.06083700	-0.61633300
C	8.42265300	1.93416500	-1.23216500
C	8.05491800	3.26094600	-1.47282300
C	6.78935500	3.70813000	-1.09435200
C	5.89474400	2.83157100	-0.47556600
C	5.28028500	0.54454400	0.43056900
C	9.74896700	-3.85221000	1.43237900
C	9.56408900	-4.11184600	2.79152800

C	8.27212200	-4.18285700	3.31584000
C	7.16980000	-3.99382700	2.48253600
C	7.34428400	-3.73259300	1.11831200
C	8.64407900	-3.66415000	0.60220400
C	6.15656100	-3.50725700	0.22313700
O	5.84216100	-2.09107300	0.25439900
C	4.88578700	-1.70018800	-0.62899600
O	4.34913800	-2.45985000	-1.42018300
H	-0.83790700	-0.97922200	-0.49683500
H	-3.08607900	2.05613900	-1.69591900
H	-0.96944800	1.74070100	-2.87379700
H	-2.00515800	-3.02997600	-0.80407300
H	-1.20650600	-2.61079300	-2.34225600
H	-3.79636100	-0.35227300	-0.91687000
H	-1.74668800	1.05921900	0.85500800
H	0.69990000	3.91645000	-0.30064400
H	-0.47637400	8.71520800	-0.79839900
H	-2.58087900	2.41292900	2.27628300
H	-3.54341600	3.56758900	1.35289400
H	-2.41538600	-2.72126100	2.54082700
H	-2.63475300	-4.16357700	4.55271700
H	-1.36608600	3.89751800	-2.47556300
H	-2.72644700	4.67050900	-1.65319400
H	2.28303300	5.66896800	0.46413800
H	1.70256200	8.07246600	0.21273300
H	-5.10269200	-0.76955400	1.11567500
H	-4.74694600	-2.21220500	0.14680300
H	-2.05864000	6.96378000	-1.54846000
H	-5.47477400	-5.52333200	-3.18992800
H	-7.56339200	-5.41178800	-4.51368100
H	-2.74073800	-3.88677900	-3.58799000
H	-3.62256000	-4.39598700	-2.13964000
H	-4.24117700	0.39106700	3.26908700
H	-6.02233400	0.18890700	4.97791800
H	-7.45758800	2.15109300	5.51878800
H	-7.10121700	4.30328700	4.32812500
H	-5.32701300	4.48926800	2.60586400
H	1.02361700	-0.10925300	-2.39874100
H	1.56819900	1.57946800	-2.58889900
H	3.50337900	-0.55031700	-2.25074400
H	4.08739800	1.10188600	-1.93981600
H	-4.88754100	-4.74434100	5.42858000
H	-6.91547300	-3.86764700	4.28279100
H	-6.68692300	-2.42746700	2.28574100
H	-8.15610200	-3.32707200	-5.73281300
H	-6.64086200	-1.35976000	-5.61697600
H	-4.53967000	-1.48514000	-4.29314000
H	7.81379300	0.02980700	-0.42511500
H	9.40937900	1.58308500	-1.52057600
H	8.75361800	3.94172600	-1.95034600
H	6.49739000	4.73821000	-1.27767400
H	4.90737900	3.17787000	-0.18058700
H	5.79380600	-0.08191800	1.15708200
H	4.50531600	1.10412600	0.95877500
H	10.75198800	-3.80097300	1.01900000
H	10.42315900	-4.26259000	3.43870700
H	8.12341900	-4.38822300	4.37186500
H	6.16433100	-4.05055400	2.89153000
H	8.78855400	-3.46739600	-0.45717400
H	5.27999200	-4.06728400	0.56211300
H	6.36136500	-3.79857100	-0.80977600

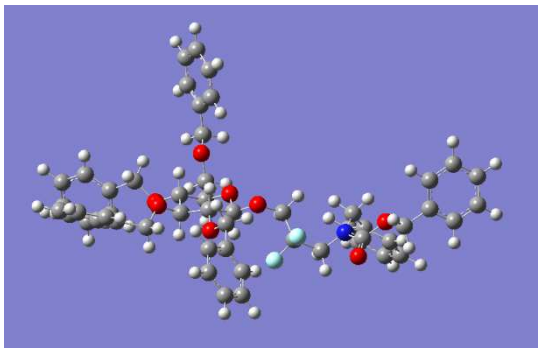


Figure S6. Minimized energy conformation of difluorinated glucoside **15β**.

Coordinates for **15β**:

0 1

O	-0.85939400	-1.09280800	0.22895600
C	-2.05510200	-1.36049000	0.95948500
C	-1.56336100	1.16026500	-0.40941900
C	-0.49124500	0.28130500	0.25152500
O	-1.28284500	2.53686200	-0.21355800
O	-3.99309500	1.47721500	-0.51154400
C	-2.25460700	-2.86658600	1.01981000
C	-0.25968000	4.59895600	-0.82816100
C	-3.22961800	-0.62019400	0.29922400
C	-2.93804400	0.88266800	0.22327000
O	0.69447000	0.40123000	-0.48340700
C	-0.95579700	5.63253400	-1.46270600
C	-0.46895500	3.15978200	-1.22288600
C	0.12596900	7.26589000	-0.04853900
O	-4.40303500	-0.84964300	1.06978700
C	-4.33096100	2.82760800	-0.17341200
C	-6.71481600	-1.50407100	1.21796400
C	-7.96859500	-1.76204200	0.64625800
C	-0.76356500	6.96124700	-1.07881000
O	-2.59543100	-3.35253200	-0.26445500
C	0.82350500	6.23899300	0.59318500
C	0.63327300	4.91408300	0.20522700
C	-5.52094700	-1.30279100	0.31230400
C	-2.98621200	-5.20173300	-1.73547900
C	-5.78953500	3.05963200	-0.48629900
C	-6.77365500	2.29452700	0.15551800
C	-8.12372300	2.50267500	-0.11763900
C	-8.50974400	3.48621500	-1.03321700
C	-7.53830100	4.25471300	-1.67366600
C	-6.18491900	4.03741500	-1.40293300
C	-2.40073600	-4.51990300	-2.80897700
C	-2.72704100	-4.76338900	-0.31326000
C	1.86626800	-0.06081600	0.16578700
C	2.62040900	1.08446000	0.83648400
C	-9.08665200	-1.97604600	1.45017500
C	-8.96885100	-1.92912500	2.84171400
C	-7.72613700	-1.66702200	3.41687300
C	-6.60428200	-1.45675600	2.61108400
C	3.91091300	0.71837400	1.57830700
F	2.88487100	2.04277400	-0.10376300
C	-2.61041000	-4.95494700	-4.11731200
C	-3.39925000	-6.07963300	-4.36820400
C	-3.98465200	-6.76360700	-3.30219400
C	-3.78260500	-6.32227200	-1.99379000
F	1.79159500	1.67582400	1.77546100
N	4.95588300	0.16802900	0.72952400
C	5.62607300	-1.92399600	1.94225100
C	6.94214500	-1.69760700	2.37147500
C	7.40849200	-2.26924900	3.55332500
C	6.56782700	-3.07708300	4.32438000
C	5.25977300	-3.31249700	3.90431000
C	4.79411300	-2.73748300	2.71923100
C	5.11370200	-1.29539800	0.65767100
C	9.87630200	-1.00674000	-3.28477100
C	11.04370700	-1.22772600	-2.55041200
C	11.20171500	-0.62808300	-1.30044700
C	10.19336700	0.18818500	-0.78620900
C	9.02002300	0.41588500	-1.51409500
C	8.87249200	-0.18850100	-2.76918300
C	7.92652100	1.28193800	-0.95152800

O	6.91048000	0.40658200	-0.39295500
C	5.91848300	1.04770100	0.28217400
O	5.89447700	2.25058800	0.46698200
H	-1.95163300	-1.00208100	1.99892600
H	-1.60437500	0.90550000	-1.47834500
H	-0.34398800	0.60948400	1.29318800
H	-3.05271100	-3.08721700	1.74385600
H	-1.32321800	-3.33280300	1.37846500
H	-3.34841300	-1.01456300	-0.71549400
H	-2.92545800	1.28248100	1.25008400
H	-1.64893600	5.39548500	-2.26642000
H	0.49018000	2.63950400	-1.29936100
H	-0.97752500	3.09484000	-2.19629100
H	0.27871100	8.29867000	0.25177800
H	-4.14329500	2.99004400	0.89800000
H	-3.69560400	3.53349800	-0.71957800
H	-8.06888300	-1.79351400	-0.43638700
H	-1.30693400	7.75529100	-1.58320300
H	1.52093300	6.47281200	1.39252900
H	1.17861300	4.11414300	0.69684800
H	-5.76352700	-0.56979800	-0.46810400
H	-5.26509200	-2.24931700	-0.18996200
H	-6.47301800	1.53154300	0.86770700
H	-8.87371000	1.89818700	0.38441500
H	-9.56245700	3.65109400	-1.24485700
H	-7.83096400	5.01909000	-2.38803200
H	-5.42874500	4.63218100	-1.90935900
H	-1.79553800	-3.64225300	-2.60788100
H	-1.80076400	-5.23223500	0.06448700
H	-3.54410400	-5.10154500	0.34488500
H	1.63384200	-0.83840300	0.90163000
H	2.51238000	-0.49082800	-0.60412400
H	-10.05088200	-2.17528900	0.99101800
H	-9.84002400	-2.09211800	3.46958600
H	-7.62588200	-1.62375900	4.49793600
H	-5.63817700	-1.24750100	3.05539900
H	4.26941500	1.64100000	2.03847200
H	3.67188700	0.00483100	2.37252200
H	-2.15683800	-4.41431700	-4.94327200
H	-3.56082200	-6.41714700	-5.38786100
H	-4.60690900	-7.63432900	-3.48818500
H	-4.25149600	-6.85141700	-1.16738500
H	7.59991000	-1.07940500	1.76762300
H	8.43112300	-2.08978900	3.87238500
H	6.93377200	-3.52253600	5.24472600
H	4.60104300	-3.94206200	4.49537300
H	3.77550600	-2.93176600	2.39036800
H	5.78955000	-1.50663300	-0.17019100
H	4.14364800	-1.73459100	0.40312800
H	9.75128300	-1.46791100	-4.26006100
H	11.82834600	-1.86130000	-2.95345300
H	12.10946900	-0.79298700	-0.72751400
H	10.31909100	0.65773200	0.18619800
H	7.96570200	-0.01467300	-3.34267200
H	7.45984200	1.90280100	-1.72223600
H	8.29285200	1.94474000	-0.16449600

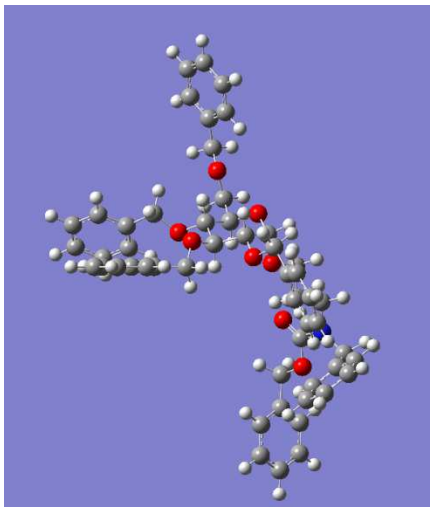


Figure S7. Minimized energy conformation of non-fluorinated glucoside **23α**.

Coordinates for **23α***:*

0 1

O	-1.68720900	-0.00463700	-2.38686400
C	-1.91538200	-0.96009200	-1.33843700
C	-1.78172200	1.89434900	-0.87379100
C	-0.98404000	1.15139400	-1.96684900
O	-1.08002200	3.02152200	-0.37701200
O	-2.98376100	1.54148700	1.23001400
C	-2.58152700	-2.17643000	-1.95895800
C	1.21241400	0.37096100	-2.43198300
C	-2.74735300	-0.32564100	-0.21302700
C	-2.08474900	0.95650100	0.30231900
O	0.29082200	0.86088700	-1.45543000
C	3.55214700	-0.54735000	-2.70357900
C	-0.09310700	5.16086200	-0.79334500
C	1.18443200	4.66646300	-0.50339400
C	-1.21107100	4.20879800	-1.14955000
C	2.23050500	5.54349100	-0.21996900
C	2.01388300	6.92342300	-0.22821000
C	0.74245000	7.42159500	-0.51544500
C	-0.30652200	6.54286000	-0.79137300
C	-3.30144600	2.23659500	3.50037900
C	-3.59091800	0.99550700	4.08505500
C	-4.41179300	0.91517700	5.20765000
C	-4.95022700	2.07798400	5.76686200
C	-4.66510000	3.31705800	5.19435400
C	-3.84771400	3.39287500	4.06368800
O	-2.86561000	-1.27107600	0.84401500
C	-2.40216900	2.30818900	2.28931700
C	-4.21611000	-2.52900300	2.38680700
C	-5.38118900	-2.69671100	3.14782200
C	-5.43928300	-3.65513200	4.15834000
C	-4.32719500	-4.45630500	4.42880800
C	-3.16208400	-4.28924700	3.68085400
C	-3.10580400	-3.33304800	2.66414700
O	-3.90453000	-1.85181400	-2.34736900
C	-4.20274200	-1.50627700	1.27346000
C	-5.91299800	-2.43960600	-3.51154300
C	-6.06881700	-1.13437100	-3.99359600
C	-7.29780100	-0.71245900	-4.49966200
C	-8.38310400	-1.59058300	-4.53764800
C	-8.23400800	-2.89258900	-4.05899400
C	-7.00619000	-3.31144000	-3.54416700
C	-4.57124400	-2.91536400	-3.00599900
N	4.80530300	-0.95657500	-2.06432900
C	5.93928500	1.13597300	-1.24064600
C	5.82185600	2.42279700	-1.77522100
C	5.80251700	3.54460900	-0.94226800
C	5.89834600	3.38704700	0.44003000
C	6.01504700	2.10454400	0.98420800
C	6.03797900	0.98834400	0.15094700
C	5.98017600	-0.08158100	-2.14969000
C	8.30552300	-3.10102600	2.94669300
C	9.52985000	-3.56955900	2.46616800
C	9.61841400	-4.07708100	1.16886600
C	8.48584500	-4.11321900	0.35529500
C	7.25389300	-3.64505600	0.82670800

C	7.17523500	-3.14023500	2.13072100
C	6.03609700	-3.66275600	-0.05666000
O	5.97614000	-2.39504700	-0.75877400
C	4.78910700	-2.14101400	-1.38213300
O	3.82574000	-2.89116700	-1.32835700
C	2.52002900	0.03657500	-1.72830900
H	-0.95344800	-1.28612400	-0.91957300
H	-2.74124800	2.19993900	-1.31666200
H	-0.89805900	1.75954000	-2.87873700
H	-2.58167900	-2.99240700	-1.22127900
H	-1.98965500	-2.49892000	-2.82966200
H	0.79863600	-0.51831300	-2.92598400
H	1.36441700	1.13927600	-3.20818400
H	-3.73436500	-0.07324100	-0.61615300
H	-1.13928100	0.69620100	0.79812400
H	3.80781100	0.18626100	-3.47558900
H	3.12715700	-1.42377300	-3.20250800
H	1.33858400	3.59258200	-0.49014700
H	-1.16316600	3.97307300	-2.22470800
H	-2.19148300	4.67723000	-0.97050900
H	3.21509500	5.14464300	0.00691100
H	2.82905400	7.60634900	-0.00624700
H	0.56329900	8.49304100	-0.51521700
H	-1.29859100	6.93538100	-1.00257100
H	-3.17217800	0.09268900	3.65034300
H	-4.63064300	-0.05452100	5.64551300
H	-5.58861700	2.01631100	6.64372400
H	-5.08247000	4.22446900	5.62180800
H	-3.63377600	4.35918700	3.61354800
H	-1.41066100	1.89815000	2.53145800
H	-2.25143100	3.34725100	1.97494600
H	-6.24757800	-2.07022300	2.94796900
H	-6.35030100	-3.77291400	4.73842400
H	-4.36917200	-5.20066300	5.21874400
H	-2.29052400	-4.90418200	3.88779900
H	-2.19953500	-3.19667200	2.08545200
H	-4.65490600	-0.56831200	1.62129900
H	-4.80336400	-1.86755100	0.42310900
H	-5.22381000	-0.45516000	-3.95324800
H	-7.40902500	0.30444300	-4.86558100
H	-9.33949300	-1.26043500	-4.93276900
H	-9.07482700	-3.58013500	-4.07665100
H	-6.89849700	-4.32361200	-3.16128600
H	-3.95399500	-3.26982000	-3.85070200
H	-4.70150800	-3.77424100	-2.32733300
H	5.75266100	2.55129300	-2.85302200
H	5.71566800	4.53723800	-1.37461600
H	5.88954900	4.25643000	1.09108900
H	6.09586500	1.97682900	2.05985200
H	6.14340600	-0.00665800	0.57352900
H	6.07452500	0.24770400	-3.19122600
H	6.85570900	-0.68883500	-1.91888400
H	8.23035900	-2.71096900	3.95751700
H	10.40999800	-3.54368800	3.10198100
H	10.56768000	-4.44663000	0.79218300
H	8.55580100	-4.50948200	-0.65449700
H	6.22076300	-2.78187900	2.50808300
H	5.11474800	-3.78879500	0.51617200
H	6.08534500	-4.46957600	-0.79473400
H	2.91988700	0.93450100	-1.24675600
H	2.32187700	-0.70227700	-0.94633500

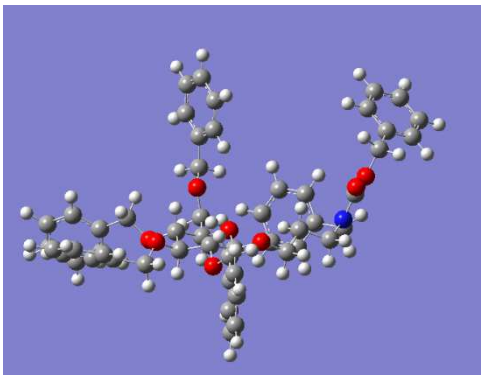


Figure S8. Minimized energy conformation of non-fluorinated glucoside **23β**.

Coordinates for **23β**:

0 1

O	0.22691300	0.43770400	-0.55866300
C	1.00545900	-0.60922800	-1.13496900
C	2.17014800	1.70567200	0.17316300
C	0.85700000	1.71391700	-0.62724200
O	2.88434100	2.92149400	-0.00154600
O	4.19906100	0.37868300	0.54155700
C	0.16699700	-1.87765000	-1.14181500
C	3.46181700	5.15076400	0.67545500
C	3.07992200	0.56461800	-0.30715500
C	-3.55127000	2.93965300	-1.39638900
C	3.82809900	6.01749000	1.71228600
C	4.57118300	6.62375100	-0.90054600
O	3.11920000	-1.75415100	-0.99422000
C	5.36154800	1.16513000	0.25793000
C	4.55074400	7.18040700	1.44626800
C	4.92592100	7.48699400	0.13713000
C	4.33682000	-3.87913500	-2.29163100
C	3.84091300	5.46481000	-0.63464000
C	5.09988300	-4.82596600	-2.97794200
O	-0.00948400	-2.32773700	0.18921700
C	3.58650100	-2.78190600	-0.12395300
C	6.58994400	0.40457600	0.69685900
C	6.86661000	-0.85555700	0.14806800
C	8.00236400	-1.56322800	0.53509200
C	8.88273800	-1.01628900	1.47345600
C	8.61732500	0.23780200	2.02232300
C	7.47315000	0.94138100	1.63737600
C	-1.41741300	-4.98795300	2.21566500
C	-1.73598500	-5.23233500	3.55251600
C	4.42589800	-3.77102600	-0.89975000
C	-0.91250800	-3.41506400	0.30432900
O	0.00794700	2.66504100	-0.08016100
C	5.95714400	-5.67885200	-2.28261100
C	6.05280400	-5.57537500	-0.89303300
C	5.29582300	-4.62517500	-0.20865400
C	-1.19822200	-3.68277800	1.76340300
C	-1.82735200	-4.17111700	4.45371100
C	-1.60040400	-2.86629400	4.01001400
C	-1.29125600	-2.62173000	2.67249600
C	-2.35782900	2.27291200	-0.69670900
C	-1.08631400	3.09803600	-0.89661200
C	2.32117300	-0.76527300	-0.35375500
C	2.63114800	3.92574300	0.97956900
N	-4.81787400	2.21612600	-1.25219400
C	-4.70767300	0.06526900	-2.56493400
C	-3.87400900	-0.19430200	-3.65779800
C	-3.31680200	-1.46117700	-3.84828100
C	-3.59229400	-2.48615600	-2.94315600
C	-4.42226800	-2.23599100	-1.84580800
C	-4.97487700	-0.97049400	-1.65791000
C	-5.34047600	1.43472000	-2.37840800
C	-9.37879500	-1.47995200	1.76504300
C	-10.55320900	-1.17908200	1.07413300
C	-10.68939600	0.05850000	0.44111600
C	-9.65384300	0.98987300	0.50084500
C	-8.47007300	0.69715800	1.18999200
C	-8.34346200	-0.54590600	1.82065500
C	-7.34582100	1.69609300	1.23597300
O	-6.59952300	1.57992200	-0.00182100
C	-5.46155600	2.33257800	-0.05195300

O	-5.07244800	3.02480800	0.87627200
H	1.24723100	-0.36792200	-2.18533300
H	1.92190900	1.54265900	1.23096200
H	1.07764700	1.95263300	-1.68656600
H	0.68356500	-2.63880100	-1.74579400
H	-0.80297800	-1.66093300	-1.61302300
H	3.42086300	0.80414500	-1.32781900
H	-3.69119800	3.94783300	-0.99233900
H	-3.35964300	3.03654700	-2.47086100
H	3.54826800	5.77918300	2.73595700
H	4.86432000	6.85228600	-1.92150400
H	5.40756200	1.36520500	-0.82272800
H	5.30403500	2.13712600	0.76071200
H	4.82851300	7.84156300	2.26226000
H	5.49457500	8.38863400	-0.07123500
H	3.67689400	-3.20821800	-2.82969800
H	3.56983000	4.78779200	-1.43706500
H	5.02451200	-4.89508700	-4.05968600
H	4.18011000	-2.34393800	0.68854900
H	2.72413900	-3.29341800	0.33294500
H	6.18175500	-1.27999500	-0.58004800
H	8.19960700	-2.54056700	0.10394800
H	9.76993600	-1.56639100	1.77425800
H	9.29543900	0.66742200	2.75431400
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H	5.38279000	-4.54220100	0.87217600
H	-2.06809600	-4.35957900	5.49601600
H	-1.66430900	-2.03626800	4.70802900
H	-1.10505400	-1.61206600	2.32172100
H	-2.20835700	1.25663200	-1.06966500
H	-2.56918300	2.20867100	0.37437100
H	-1.26710200	4.13916500	-0.60584600
H	-0.77750600	3.09815300	-1.95313100
H	2.07231500	-1.06923800	0.66830800
H	1.56286400	4.17749300	0.98488600
H	2.88177900	3.54327500	1.98123000
H	-3.66664000	0.59812400	-4.37335700
H	-2.67713400	-1.64744500	-4.70629100
H	-3.17162000	-3.47601400	-3.09489800
H	-4.64845900	-3.03247200	-1.14251600
H	-5.62787600	-0.77945700	-0.81161300
H	-5.19402900	2.02715700	-3.28900100
H	-6.41522200	1.32561400	-2.23034800
H	-9.26946100	-2.43912600	2.26259900
H	-11.36122700	-1.90363300	1.03223200
H	-11.60343500	0.29843300	-0.09423000
H	-9.76179100	1.95397300	0.01052700
H	-7.43031300	-0.78006500	2.36193800
H	-6.67063000	1.51239300	2.07495100
H	-7.71706700	2.72173400	1.32514200

Energies of the optimized molecules:

Difluorinated glucose glycoside **15β**: -2671.24458608 a.u.
Difluorinated glucose glycoside **15α**: -2671.24633568 a.u.
Difference D_3 = 0.0017496 a.u. = 4.59 kJ/mol.

Non-fluorinated glucose glycoside **23β**:-2869.71978654 a.u.
Non-fluorinated glucose glycoside **23α**: -2869.71790545 a.u.
Difference D_4 = 0.00188109 a.u. = 4.94 kJ/mol.

I.4 Glycan Microarray Analysis

Amines **35** and **36** were spotted on *N*-hydroxysuccinimide-activated glass slides using two different spotting buffers (pH 8.5 or pH 7.4) and four different spotting concentrations, as depicted in the experimental section. To exclude pipetting errors, spotting solutions were prepared from two different batches of solid **35** or **36**. Incubation with fluorescently labeled concanavalin A revealed similar binding of **35** and **36** at pH 8.5, and better recognition of fluorinated mannose **36** at pH 7.4 (Fig. S9).

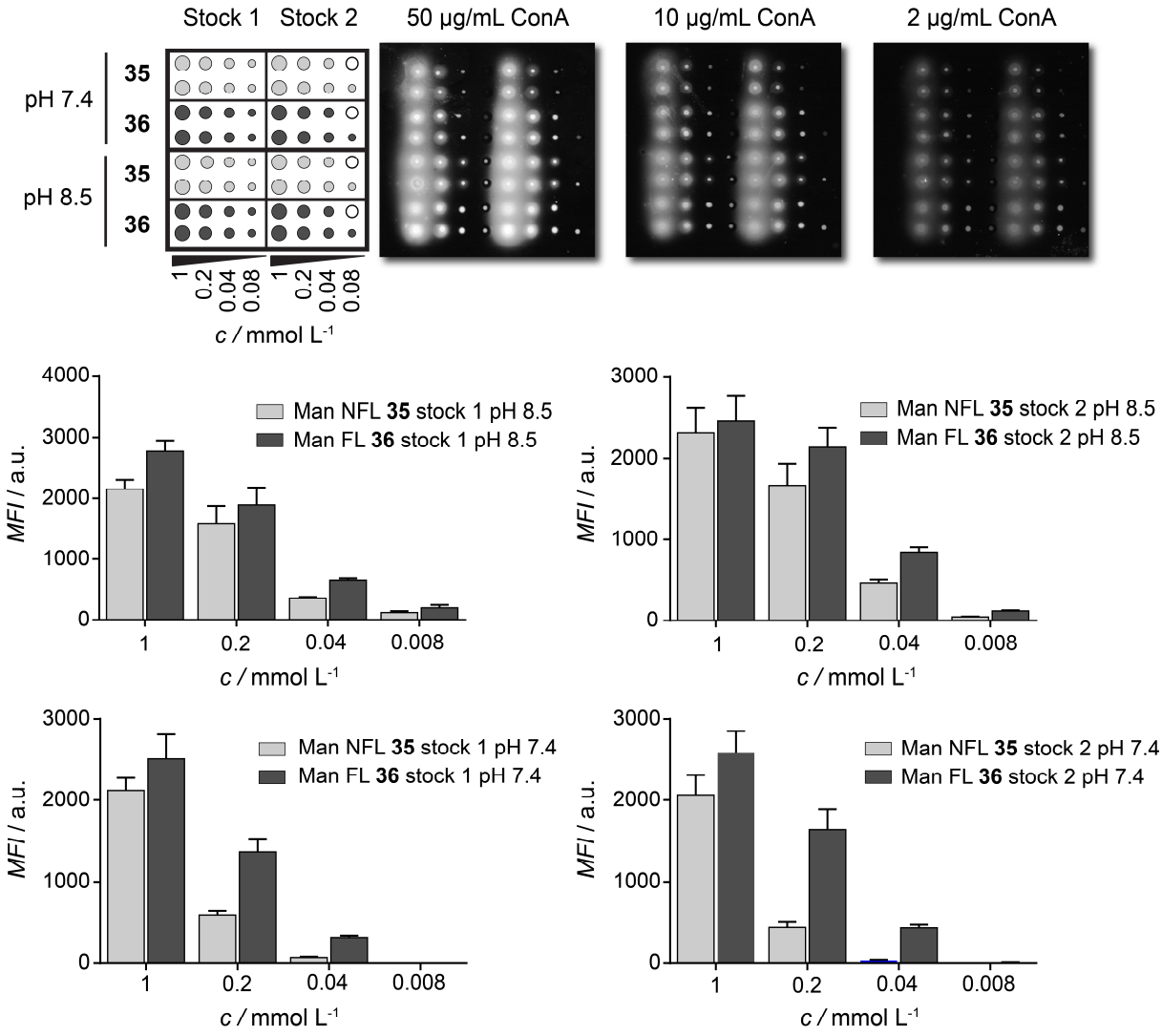


Fig. S9. Glycan Microarray Analysis of Glycans Bearing Difluorinated and Non-fluorinated Linkers. Representative fluorescent images at different concentrations of FITC-ConA (upper panel) and quantification after fluorescence readout using different spotting concentrations (lower panel). Hollow spots indicate buffer. Bars represent mean + SD of at least three spots in duplicate wells. MFI = mean fluorescent intensity.

II Experimentals

II.1 General Experimental Details

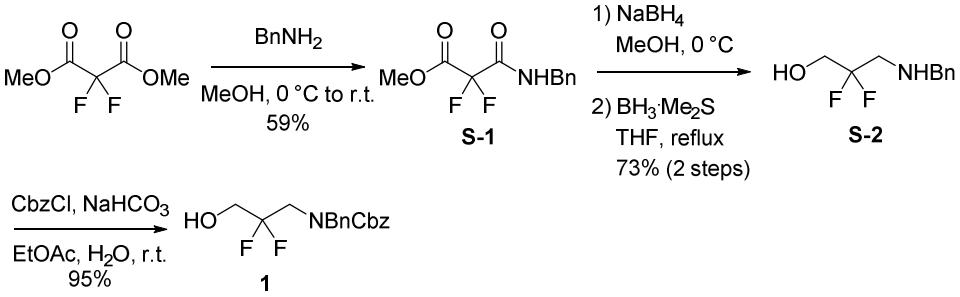
Commercial grade solvents and reagents were used unless stated otherwise. Anhydrous solvents were obtained from a Dry Solvent System (Waters, Milford, USA). Solvents for chromatography were of technical grade and distilled under reduced pressure prior to use. Sensitive reactions were carried out in heat-dried glassware and under an argon atmosphere. Analytical thin layer chromatography (t.l.c.) was performed on Kieselgel 60 F254 glass plates pre-coated with silica gel of 0.25 mm thickness (Macherey-Nagel, Düren, Germany). Spots were visualized with sugar stain (0.1% (v/v) 3-methoxyphenol, 2.5% (v/v) sulfuric acid in EtOH) or CAM stain (5% (w/v) ammonium molybdate, 1% (w/v) cerium(II) sulfate and 10% (v/v) sulfuric acid in water) dipping solutions. Flash chromatography was performed on Kieselgel 60 with 230-400 mesh (Sigma-Aldrich, St. Louis, USA). Solvents were removed under reduced pressure using a rotary evaporator and high vacuum (<1 mbar).

All automated glycosylations were performed on a prototype automated oligosaccharide synthesizer using anhydrous solvents. Activator, deprotection, acidic wash and building block solutions were freshly prepared and kept under argon during the automation run. Modules were adopted from a previous publication.[1] In all reactions, the resin was bubbled with Ar from the bottom of the reaction vessel.

^{1}H, ^{13}C, ^{19}F and two-dimensional NMR spectra were measured with a Varian 400-MR spectrometer or a Varian 600 spectrometer (both Agilent, Santa Clara, USA) at 298 K. Chemical shifts (δ) are reported in parts per million (ppm) relative to the respective residual solvent peaks ($CDCl_3$: δ 7.26 in ^{1}H and 77.16 in ^{13}C NMR; CD_3OD: δ 3.31 in ^{1}H and 49.00 in ^{13}C; DMSO-D_6: δ 2.50 in ^{1}H and 39.25 in ^{13}C; D_2O: δ 4.79 in ^{1}H; 2,2,2-trifluoroethanol (TFE): 77.03 in ^{19}F). Two-dimensional NMR experiments (HH-COSY, CH-HSQC, CH-HMBC) were performed to assign peaks in ^{1}H and ^{13}C spectra. The following abbreviations are used to indicate peak multiplicities: *s* singlet; *d* doublet; *dd* doublet of doublets; *t* triplet; *p* pentet; *m* multiplet. Coupling constants (*J*) are reported in Hertz (Hz). NMR spectra were evaluated using MestreNova 6.2 (MestreLab Research SSL, Santiago de Compostella, Spain). High resolution mass spectrometry by electrospray ionization (ESI-HRMS) was performed at Freie Universität Berlin, Mass Spectrometry Core Facility, with a 6210 ESI-TOF mass spectrometer (Agilent). High performance liquid chromatography (HPLC) and low resolution mass spectrometry by electrospray ionization (ESI-LRMS) was carried out with a 1200 HPLC-MS system equipped with an Evaporating Light Scattering Detector (both Agilent).

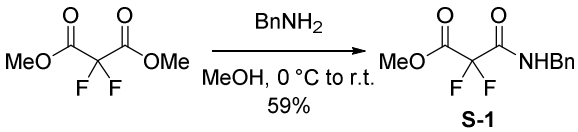
Schemes were prepared using ChemBioDraw Ultra 12.0.2 (Cambridgesoft, Waltham, USA) and Illustrator CS5 (Adobe Systems, San Jose, USA)

II.2 Solution-Phase Reactions and Experimental Procedures



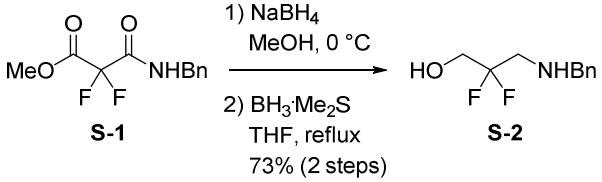
Scheme S1. Synthesis of difluorinated linker **1**.

Methyl *N*-benzyl-2,2-difluoromalonate monoamide (S-1)



To a stirred solution of dimethyl 2,2-difluoromalonate (3.0 g, 17.85 mmol) in MeOH (100 mL) was added dropwise at 0 °C a solution of benzylamine (1.56 mL, 14.28 mmol) in MeOH (10 mL). The mixture was warmed to room temperature, stirred for 18 h at that temperature, filtered and concentrated. The residue was purified by flash chromatography (EtOAc/toluene 1:50 to 1:10) to give monoamide **S-1** (2.06 g, 8.47 mmol, 59%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 5H), 6.71 (s, 1H), 4.54 (d, *J* = 5.8 Hz, 2H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 129.1, 128.3, 128.0, 54.3, 44.0; HRMS (ESI): *m/z* calcd. for $C_{11}H_{11}F_2NNaO_3$ $[M+Na]^+$ 266.0604 found 266.0597.

***N*-Benzyl-2,2-difluoro-3-amino-1-propanol (S-2)**

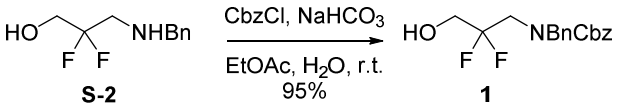


S-1 **S-2**

To a stirred solution of ester **S-1** (2.0 g, 8.22 mmol) in MeOH (50 mL) was added at 0 °C sodium borohydride (1.56 g, 41.1 mmol). The mixture was stirred for 2 h at that temperature, quenched with water (1 mL) and concentrated. The residue was dissolved in EtOAc (25 mL) and water (50 mL). After separation, the aqueous phase was extracted with EtOAc (2x25 mL), the combined organic fractions were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (EtOAc/toluene 1:50 to 1:10) to give the intermediate monoamide (1.4 g) as a white foam.

To a stirred solution of the intermediate monoamide in THF (25 mL) was added dropwise at room temperature borane dimethylsulfide (2 M solution in THF, 16.3 mL, 32.5 mmol). The reaction was refluxed for 3 h, slowly quenched with MeOH (5 mL) and cooled to room temperature. The mixture was stirred for 18 h at that temperature and concentrated. The residue was purified by flash chromatography (EtOAc/hexanes 1:10 to 1:1) to give amine **S-2** (1.2 g, 5.96 mmol, 73% over two steps) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 3.93 – 3.82 (m, 4H), 3.11 (t, *J* = 13.1 Hz, 2H), 2.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 128.8, 128.3, 127.7, 123.5, 121.1, 118.7, 64.7, 64.4, 64.1, 53.8, 51.8, 51.5, 51.2; HRMS (ESI): *m*/*z* calcd. for $C_{10}H_{14}F_2NO$ $[M+H]^+$ 202.1043 found 202.1043.

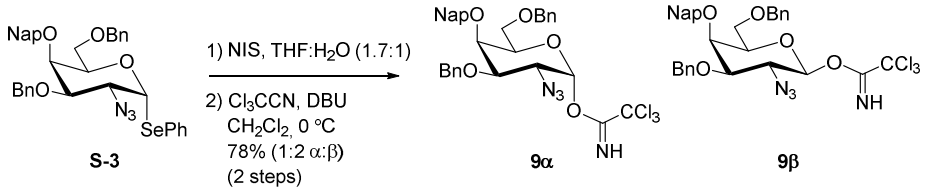
***N*-Benzyl-*N*-benzyloxycarbonyl-2,2-difluoro-3-amino-1-propanol (1)**



S-2 **1**

To a stirred solution of amine **S-2** (1.2 g, 5.96 mmol) in EtOAc (50 mL) and sat. aq. $NaHCO_3$ (50 mL) was added at room temperature benzyl chloroformate (1.02 mL, 7.16 mmol). The mixture was stirred for 2 h at that temperature and the layers were separated. The aqueous layer was extracted with EtOAc (3x20 mL), the combined organic fractions were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (EtOAc/hexanes 1:20 to 1:5) to give carbamate **1** (1.89 g, 5.64 mmol, 95%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.28 (m, 8H), 7.23 – 7.06 (m, 2H), 5.23 (s, 2H), 4.60 (s, 2H), 4.23 (t, *J* = 7.9 Hz, 1H), 3.77 – 3.54 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 136.2, 135.7, 129.0, 128.8, 128.6, 128.2, 128.0, 127.7, 127.1, 124.9, 122.4 (t, $J^1_{C\text{-}F}$ = 246 Hz), 120.0, 77.4, 68.7, 61.4 (t, $J^2_{C\text{-}F}$ = 33 Hz), 51.8, 47.0 (t, $J^2_{C\text{-}F}$ = 32 Hz); ^{19}F NMR (564 MHz, $CDCl_3$, TFE) δ 109.8 (p, *J* = 11.7 Hz), -110.6 (p, *J* = 12.2 Hz); HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{20}F_2NNaO_3$ $[M+Na]^+$ 358.1230 found 358.1221.

2-Azido-2-deoxy-3,6-di-*O*-benzyl-4-*O*-(2-naphthylmethyl)-αβ-D-galactopyranosyl trichloroacetimidate (9α and 9β)

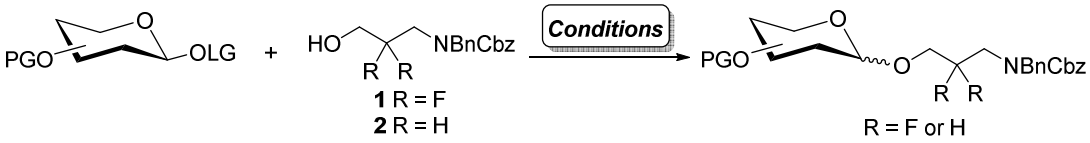


S-3 **9α** **9β**

To a stirred solution of glycosyl selenide **S-3**[2] (250 mg, 0.376 mmol) in THF:water (1.7:1 (v/v), 11 mL) was added NIS (169 mg, 0.752 mmol). The reaction was stirred at room temperature for 2 h and quenched with 10% aq. $Na_2S_2O_3$ (10 mL). The mixture was diluted with CH_2Cl_2 (30 mL) and washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (EtOAc/hexanes 1:2) to give the intermediate lactol mixture.

The intermediate lactol mixture was in CH_2Cl_2 (4 mL) was treated at 0 °C with trichloroacetonitrile (0.5 mL, 3.81 mmol) and DBU (0.038 mmol, 4 µL). The reaction was stirred at that temperature for 2 h and concentrated. The residue purified by flash chromatography (EtOAc/hexanes 1:4) to give trichloroacetimidate **9** (200 mg, 0.299 mmol, 78% over two steps) as a 1:2 α:β mixture. Analytical data for **9β**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.84 – 7.81 (m, 1H), 7.80 – 7.76 (m, 2H), 7.71 (s, 1H), 7.52 – 7.46 (m, 3H)7.42 – 7.37 (m, 4H), 7.34 – 7.28 (m, 4H), 7.25 – 7.19 (m, 2H), 5.59 (d, *J* = 8.5 Hz, 1H), 5.06 (d, *J* = 11.5 Hz, 1H), 4.80 (d, *J* = 11.5 Hz, 1H), 4.75 – 4.67 (m, 2H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.39 (d, *J* = 11.7 Hz, 1H), 4.13 (dd, *J* = 10.2, 8.5 Hz, 1H), 4.04 (d, *J* = 2.7 Hz, 1H), 3.75 – 3.68 (m, 2H), 3.68 – 3.61 (m, 1H), 3.48 (dd, *J* = 10.3, 2.8 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.5, 137.7, 137.5, 135.6, 133.3, 133.2, 128.7, 128.68, 128.6, 128.3, 128.2, 128.15, 128.11, 128.1, 128.09, 128.07, 128.05, 128.04, 128.02, 128.0, 127.99, 127.9, 127.8, 127.2, 126.6, 126.2, 126.1, 97.3, 80.8, 75.0, 74.7, 73.6, 72.8, 71.9, 68.0, 62.9; HRMS (ESI): *m*/*z* calcd. for $C_{33}H_{31}Cl_3N_4NaO_8$ $[M+Na]^+$ 693.1228 found 693.1241.

General Glycosylation Procedures Using Alcohols 1 and 2 as Nucleophiles



Thioglycoside activation using NIS/TfOH

Typically, aminoalcohol linker **1** or **2** (0.075 mmol) and thioglycoside (0.112 mmol) were co-evaporated twice with anhydrous toluene and kept for 30 min under high vacuum. The mixture was dissolved in the indicated solvent (2 mL), and activated molecular sieves (3 Å-AW) were added. The solution was stirred for 15 min at room temperature and cooled to the indicated temperature. The mixture was treated with NIS (25 mg, 0.112 mmol) and TfOH (1.3 µL, 0.015 mmol) and stirred until t.l.c. indicated consumption of the thioglycoside (at least 1.5 h). The reaction was then quenched with Et_3N (1 mL) and stirred for another 10 min. The mixture was filtered, then diluted with CH_2Cl_2 (9 mL) and sat. aq. $NaHCO_3$ solution (3 mL), separated the layers. The organic layer was dried over Na_2SO_4, filtered and concentrated. An analytical sample was taken for HPLC analysis and the residue was purified by flash chromatography using the indicated solvent combinations.

Thioglycoside Activation Using DMTST

Aminoalcohol linker **1** or **2** (0.075 mmol) and thioglycoside **3**[3] (0.112 mmol) were co-evaporated twice with anhydrous toluene and kept for 30 min under high vacuum. The mixture was dissolved in CH_2Cl_2 (2 mL), and TTBPy (41 mg, 0.164 mmol) and activated molecular sieves (4 Å) were added. The solution was stirred for 15 min at room temperature and cooled to -40 °C. The mixture was treated with a solution of DMTST (38.5 mg, 0.149 mmol) in CH_2Cl_2 (1 mL) and kept at that temperature for 15 min. The reaction was slowly warmed to room temperature over 1.5 h, quenched with sat. aq. $NaHCO_3$ (1 mL) and stirred for another 10 min. The mixture was diluted with CH_2Cl_2 (9 mL), and the layers were separated. The organic layer was dried over Na_2SO_4, filtered and concentrated. An analytical sample was taken for HPLC analysis and the residue was purified by flash chromatography using the indicated solvent combinations.

Thioglycoside Activation Using Ph_2SO/Tf_2O

Thioglycoside **3** (0.112 mmol) was co-evaporated twice with anhydrous toluene and kept for 30 min under high vacuum. Ph_2SO (45 mg, 0.224 mmol) and TTBPy (37 mg, 0.15 mmol) were added, the mixture was dissolved in CH_2Cl_2 (2 mL) and activated molecular sieves (4 Å) were added. The solution was stirred for 15 min at room temperature and cooled to -40 °C. The mixture was treated with Tf_2O (25 µL, 0.15 mmol) and kept at that temperature for 10 min. Aminoalcohol linker **1** or **2** (0.075 mmol) was added in CH_2Cl_2 (1 mL), the reaction was kept at that temperature for 15 min and slowly warmed to room temperature over 1.5 h. The reaction was then quenched with sat. aq. $NaHCO_3$ (3 mL) and stirred for another 10 min. The mixture was filtered, then diluted with CH_2Cl_2 (9 mL), and the layers separated. The organic layer was dried over Na_2SO_4, filtered and concentrated. An analytical sample was taken for HPLC analysis and the residue was purified by flash chromatography using the indicated solvent combinations.

Glycosyl Phosphate Activation

Aminoalcohol linker **1** or **2** (0.075 mmol) and glycosyl phosphate **S-4**[4] (0.112 mmol) were co-evaporated twice with anhydrous toluene and kept for 30 min under high vacuum. The mixture was dissolved in the indicated solvent (2 mL), and activated molecular sieves (3 Å-AW) were added. The solution was stirred for 15 min at room temperature and cooled to -40 °C. The mixture was treated with TMSOTf (20 µL, 0.112 mmol) and stirred until t.l.c. indicated consumption of the glycosylating agent (at least 1.5 h). The reaction was then quenched with sat. aq. $NaHCO_3$ (5 mL) and stirred for another 10 min. The mixture was filtered, then diluted with CH_2Cl_2 (9 mL), and the layers separated. The organic layer was dried over Na_2SO_4, filtered and concentrated. An analytical sample was taken for HPLC analysis and the residue was purified by flash chromatography using the indicated solvent combinations.

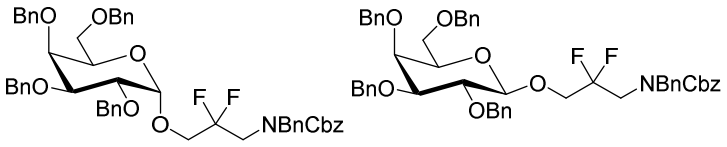
Glycosyl Imidate Activation

Aminoalcohol linker **1** or **2** (0.075 mmol) and glycosyl imidate **S-5**[5] or **S-6**[6] (0.112 mmol) were co-evaporated twice with anhydrous toluene and kept for 30 min under high vacuum. The mixture was dissolved in the indicated solvent (2 mL), and activated molecular sieves (3 Å-AW) were added. The solution was stirred for 15 min at room temperature and cooled to -40 °C. The mixture was treated with TMSOTf (2.7 µL, 0.015 mmol) and stirred until t.l.c. indicated consumption of the glycosylating agent (at least 1.5 h). The reaction was then quenched with Et_3N (1 mL) and stirred for another 10 min. The mixture was diluted with CH_2Cl_2 (9 mL), filtered and concentrated. An analytical sample was taken for HPLC analysis and the residue was purified by flash chromatography using the indicated solvent combinations.

HPLC Conditions

For analytical HPLC, a YMC-Pack-Silica column (150 x 4.6 mm, particle size 5 µm, YMC, Kyoto, Japan) was used with hexanes as mobile phase A and ethyl acetate as mobile phase B. Methods used for analysis was Gradient 1) (A:B) = T0-T5 (100:0), T5-T30 (100:0-80:20), T30-T35 (80:20), T35-T40 (80:20-100:0); 2) (A:B) = T0-T5 (100:0), T5-T30 (100:0-80:20), T30-T35 (80:20), T35-T45 (80:20-50:50), T45-T50 (50:50-100:0), T50-T60 (100:0), at 1 mL/min flow rate, 25 °C.

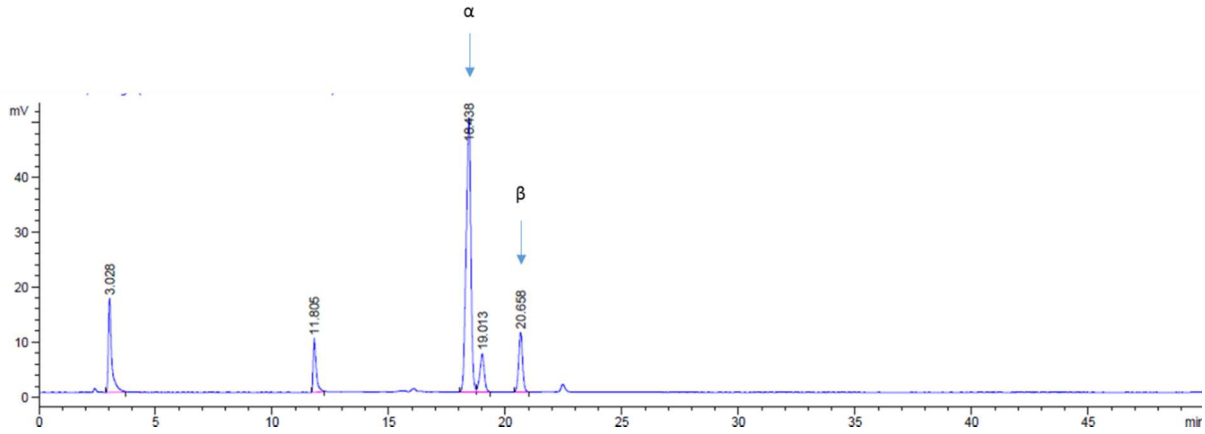
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl (2,3,4,6-tetra-*O*-benzyl)-αβ-D-galactopyranoside (4α and 4β)



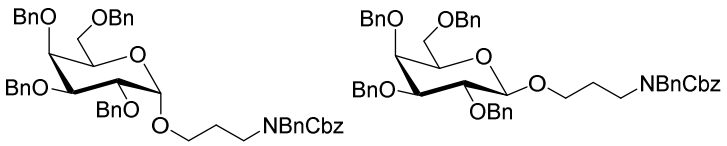
4α **4β**

Thioglycoside **3**[3] (65.4 mg, 0.112 mmol) was glycosylated with aminoalcohol **1** (25 mg, 0.075 mmol) using Thioglycoside Activation at -40 °C to give the crude product as a 5.5:1 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give glycosides **4α** and **4β** (53 mg, 0.062 mmol, 83%). Analytical data for **4α**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.07 (m, 30H), 5.15 (s, 2H), 4.92 – 4.32 (m, 11H), 4.12 – 3.40 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.7, 138.1, 128.7, 128.6, 128.54, 128.5, 128.44, 128.4, 128.2, 128.0, 127.9, 127.7, 127.6, 127.5, 98.4 ($^{1}J_{C\text{-}H}$ = 173.3 Hz, α), 78.8, 76.4, 74.9, 73.6, 73.3, 69.8, 68.8, 68.0, 51.3, 48.1. Analytical data for **4β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.09 (m, 30H), 5.16 (d, *J* = 14.1 Hz, 2H), 4.94 (d, *J* = 11.5 Hz, 1H), 4.87 – 4.31 (m, 10H), 4.22 – 3.39 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.8, 138.6, 138.5, 137.9, 137.02, 137.0, 136.5, 128.8, 128.6, 128.5, 128.48, 128.45, 128.4, 128.3, 128.2, 128.1, 128.03, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 104.2, 104.0 ($^{1}J_{C\text{-}H}$ = 163.1 Hz, β), 82.0, 79.2, 75.3, 74.8, 74.8, 73.7, 73.6, 73.5, 73.2, 68.7, 68.0, 51.2, 51.1, 47.9, 46.8; HRMS (ESI): *m/z* calcd. for $C_{52}H_{53}F_2NNaO_8$ [mixture of anomers, M+Na]$^{+}$ 880.3637 found 880.3641.

HPLC data for **4** *(Gradient 1)*



(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl (2,3,4,6-tetra-*O*-benzyl)-αβ-D-galactopyranoside (5α and 5β)

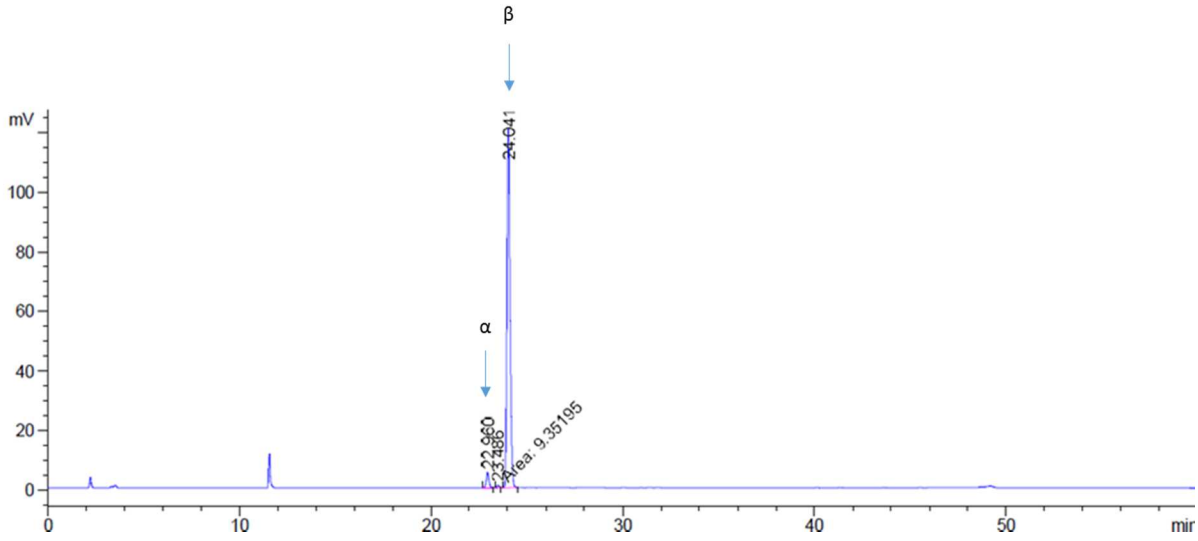


5α **5β**

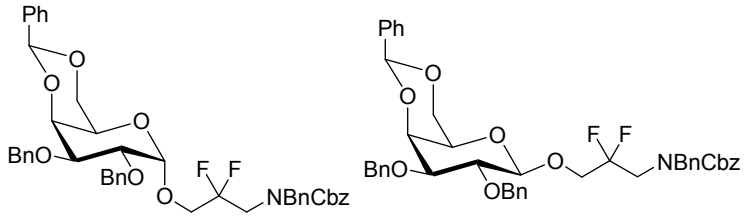
Thioglycoside **3** (54 mg, 0.092 mmol) was glycosylated with aminoalcohol **2** (25 mg, 0.084 mmol) using Thioglycoside Activation at -40 °C to give the crude product as a 1:26 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give an inseparable mixture of glycosides **5α** and **5β** (50 mg, 0.061 mmol, 73%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 – 6.99 (m, 30H), 5.17 (s, 2H), 4.95 (d, *J* = 11.6 Hz, 1H), 4.86 – 4.22 (m, 10H), 4.06 – 3.77 (m, 3H), 3.66 – 3.23 (m, 7H), 2.16 – 1.71 (m, 2H); ^{13}C NMR (150 MHz,

$CDCl_3$) δ 156.9, 156.2, 138.81, 138.8, 138.6, 138.0, 136.9, 128.62, 128.6, 128.55, 128.5, 128.47, 128.42, 128.41, 128.35, 128.33, 128.3, 128.2, 128.1, 128.01, 128.0, 127.94, 127.91, 127.9, 127.81, 127.8, 127.7, 127.64, 127.6, 127.5, 127.4, 103.9 ($^1J_{C\text{-}H}$ = 166.6 Hz, β), 97.8 ($^1J_{C\text{-}H}$ = 173.0 Hz, α), 82.3, 79.6, 79.1, 76.7, 75.3, 74.9, 74.7, 73.7, 73.64, 73.6, 73.5, 73.3, 73.1, 68.9, 67.3, 50.9, 50.8, 44.9, 43.9, 28.8, 28.3; HRMS (ESI): *m/z* calcd. for $C_{52}H_{55}NNaO_8$ $[M+Na]^+$ 844.3825 found 844.3799.

HPLC data for **5** *(Gradient 2)*



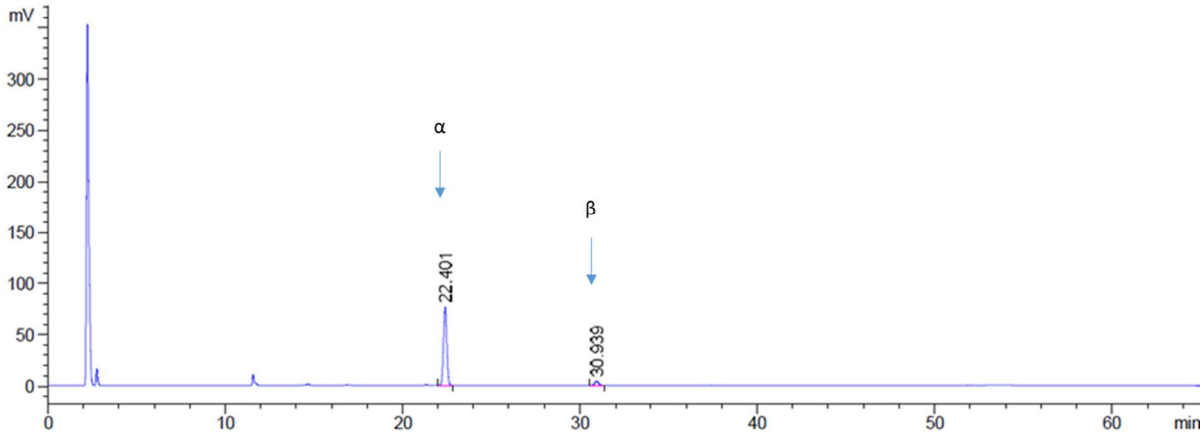
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl (2,3-di-*O*-benzyl-4,6-*O*-benzylidene)-αβ-D-galactopyranoside (14α and 14β)



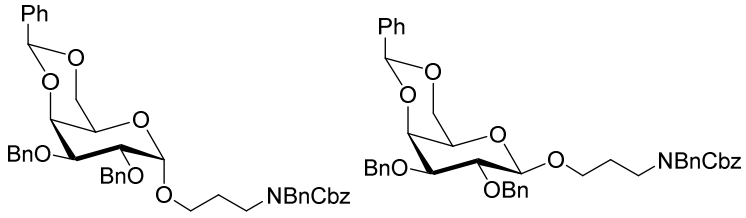
14α **14β**

Thioglycoside **6**[7] (55.1 mg, 0.112 mmol) was glycosylated with aminoalcohol **1** (25 mg, 0.075 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 13.8:1 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give glycosides **14α** and **14β** (40 mg, 0.052 mmol, 70%). Analytical data for **14α**: clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.03 (m, 25H), 5.47 (s, 1H), 5.37 – 5.09 (m, 2H), 4.95 – 4.92 (m, 1H), 4.85 – 4.50 (m, 6H), 4.25 – 3.41 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 138.9, 137.9, 137.1, 129.0, 128.8, 128.7, 128.53, 128.5, 128.4, 128.3, 128.27, 128.1, 128.0, 127.7, 126.4, 101.2, 99.2 ($^1J_{C\text{-}H}$ = 172.4 Hz, α), 75.9, 75.5, 74.7, 73.6, 72.3, 69.4, 68.0, 63.2, 51.4, 48.2. Analytical data for **14β**: clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 6.93 (m, 25H), 5.50 (s, 1H), 5.17 (s, 2H), 4.96 – 4.53 (m, 6H), 4.52 – 4.35 (m, 1H), 4.31 – 3.21 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 138.5, 137.9, 137.0, 129.1, 128.8, 128.6, 128.5, 128.48, 128.4, 128.35, 128.3, 128.2, 128.1, 127.9, 127.86, 127.7, 127.6, 126.5, 103.9 ($^1J_{C\text{-}H}$ = 165.2 Hz, β), 101.4, 79.1, 78.2, 75.4, 73.9, 72.2, 69.2, 68.0, 66.7, 51.3, 48.1; HRMS (ESI): *m/z* calcd. for $C_{45}H_{45}F_2NaO_8$ [mixture of anomers, $M+Na]^+$ 788.3011 found 788.3012.

HPLC data for **14** *(Gradient 2)*



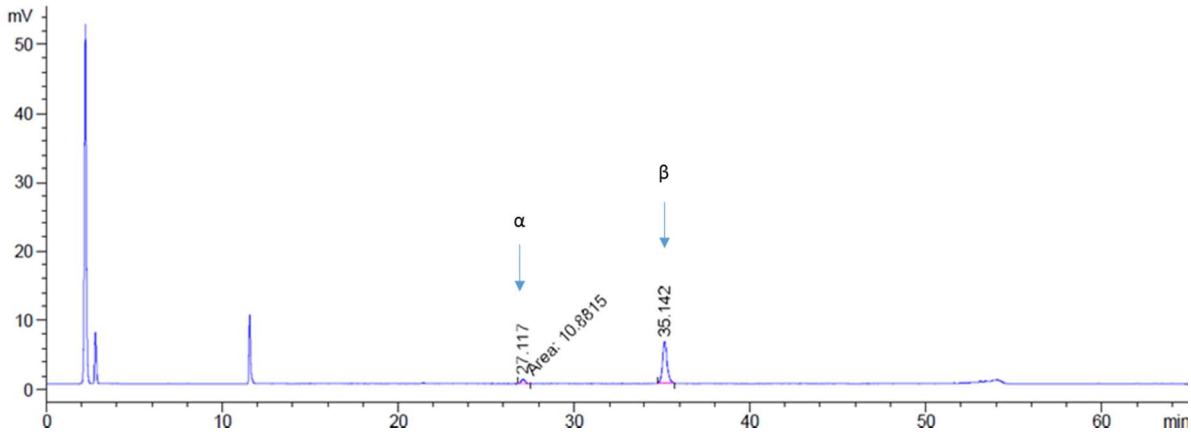
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl (2,3-di-*O*-benzyl-4,6-*O*-benzylidene)-αβ-D-galactopyranoside (22α and 22β)



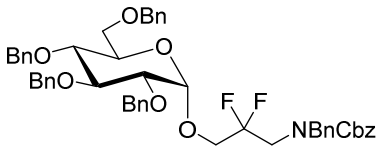
22α **22β**

Thioglycoside **6** (62 mg, 0.125 mmol) was glycosylated with aminoalcohol **2** (25 mg, 0.084 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 1:10 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:2) to give glycosides **22α** and **22β** (49 mg, 0.067 mmol, 80%). Analytical data for **22α**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 – 7.05 (m, 25H), 5.46 (s, 1H), 5.21-5.12 (m, 2H), 4.89 – 4.39 (m, 7H), 4.20 – 3.87 (m, 5H), 3.74 – 3.18 (m, 5H), 1.95 – 1.70 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.8, 156.3, 139.0, 138.9, 138.0, 136.9, 129.0, 128.7, 128.4, 128.2, 128.1, 128.04, 127.97, 127.8, 127.71, 127.66, 127.4, 126.5, 101.2, 98.5, 98.45 ($^{1}J_{C\text{-}H}$ = 172.1 Hz, α), 76.2, 75.7, 74.8, 73.7, 72.2, 69.6, 69.5, 67.4, 67.3, 66.1, 62.8, 50.9, 50.6, 44.7, 43.8, 28.5, 28.1.; HRMS (ESI): *m/z* calcd. for $C_{45}H_{47}NNaO_8$ $[M+Na]^+$ 752.3199 found 752.3255. Analytical data for **22β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 2H), 7.44 – 7.07 (m, 23H), 5.49 (s, 1H), 5.22 - 5.10 (m, 2H), 4.87 – 4.66 (m, 4H), 4.65 - 4.55 (m, 1H), 4.51 - 4.41 (m, 1H), 4.40 – 4.21 (m, 2H), 4.11 (d, *J* = 3.7 Hz, 1H), 4.05 – 3.88 (m, 2H), 3.84 - 3.75 (m, 1H), 3.61 – 3.18 (m, 5H), 1.89 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.9, 156.3, 138.9, 138.5, 138.1, 138.0, 129.0, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.94, 127.86, 127.8, 127.40, 127.35, 127.3, 126.6, 103.6, 101.4 ($^{1}J_{C\text{-}H}$ = 160.7 Hz, β), 79.3, 78.6, 75.4, 74.1, 72.1, 69.4, 67.3, 67.1, 66.5, 51.0, 50.9, 44.8, 43.8, 28.8, 28.3; HRMS (ESI): *m/z* calcd. for $C_{45}H_{47}NNaO_8$ $[M+Na]^+$ 752.3199 found 752.3263.

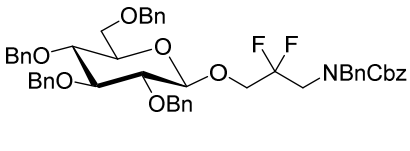
HPLC data for **22** *(Gradient 2)*



(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl (2,3,4,6-tetra-*O*-benzyl)-αβ-D-glucopyranosyl (15α and 15β)



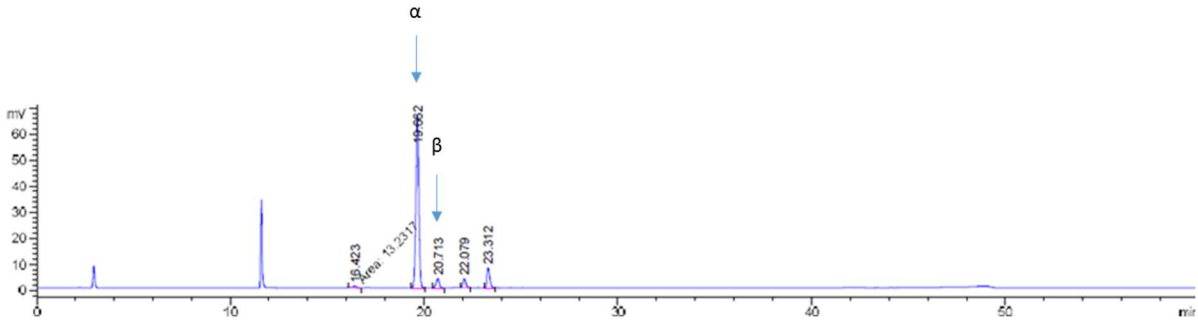
15α



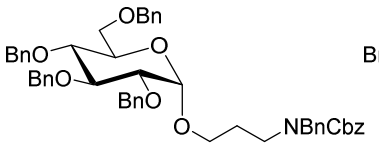
15β

Thioglycoside **7**[8] (65 mg, 0.112 mmol) was glycosylated with aminoalcohol **1** (25 mg, 0.075 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 19:1 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give an inseparable mixture of glycosides **15α** and **15β** (49 mg, 0.057 mmol, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 – 7.02 (m, 30H), 5.25 – 5.12 (m, 2H), 4.97 – 4.79 (m, 3H), 4.78 – 4.53 (m, 6H), 4.47 (t, *J* = 10.8 Hz, 2H), 4.00 – 3.34 (m, 10H).; ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.9, 138.3, 138.0, 137.1, 128.8, 128.7, 128.61, 128.56, 128.52, 128.5, 128.3, 128.2, 128.13, 128.10, 128.07, 128.02, 127.97, 127.9, 127.7, 127.6, 103.9 ($^{1}J_{C\text{-}H}$ = 164.4 Hz, β), 98.0 ($^{1}J_{C\text{-}H}$ = 173.6 Hz, α), 84.6, 82.0, 81.9, 79.9, 77.5, 75.8, 75.3, 74.9, 73.6, 73.3, 73.1, 70.9, 68.8, 68.4, 68.0, 51.3, 48.2, 47.1; HRMS (ESI): *m/z* calcd. for $C_{52}H_{53}F_2NNaO_8$ $[M+Na]^+$ 880.3637 found 880.3680.

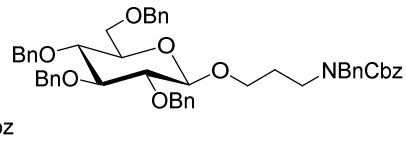
HPLC data for **15** *(Gradient 2)*



(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl (2,3,4,6-tetra-*O*-benzyl)-αβ-D-glucopyranoside (23α and 23β)



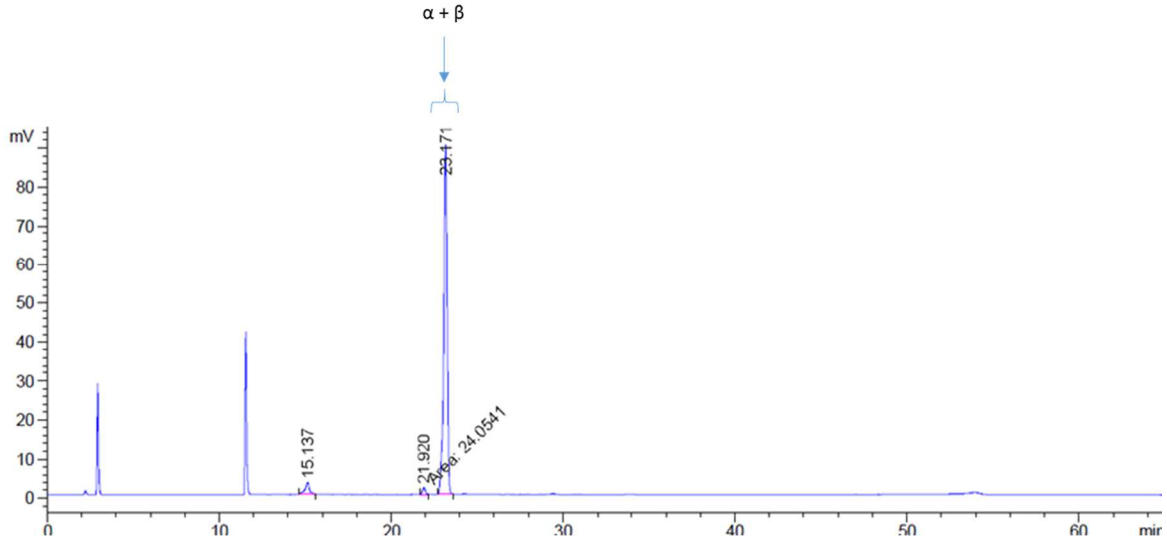
23α



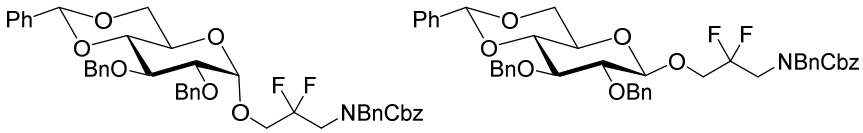
23β

Thioglycoside **7** (73 mg, 0.125 mmol) was glycosylated with aminoalcohol **2** (25 mg, 0.084 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as an inseparable α:β mixture (HPLC and NMR, major β). The mixture was purified by flash chromatography (EtOAc/hexanes 1:3) to give an inseparable mixture of glycosides **23α** and **23β** (49 mg, 0.059 mmol, 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 – 7.68 (m, 2H), 7.60 – 6.95 (m, 28H), 5.16 (bs, 2H), 4.98 – 4.26 (m, 11H), 3.94 (m, 1H), 3.77 – 3.23 (m, 9H), 1.99 – 1.74 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.3, 138.7, 138.6, 138.4, 138.2, 138.0, 129.9, 128.7, 128.54, 128.52, 128.49, 128.48, 128.11, 128.09, 128.04, 128.0, 127.9, 127.7, 127.5, 127.4, 103.7 ($^{1}J_{C\text{-}H}$ = 162.9 Hz, β), 97.2 ($^{1}J_{C\text{-}H}$ = 171.3 Hz, α), 84.8, 82.2, 80.2, 78.0, 77.8, 75.8, 75.1, 74.9, 73.6, 70.5, 69.0, 68.6, 67.3, 65.7, 50.9, 45.0, 43.9, 28.9, 28.4; HRMS (ESI): *m/z* calcd. for $C_{52}H_{55}NNaO_8$ $[M+Na]^+$ 844.3825 found 844.3863.

HPLC data for **23** *(Gradient 2)*



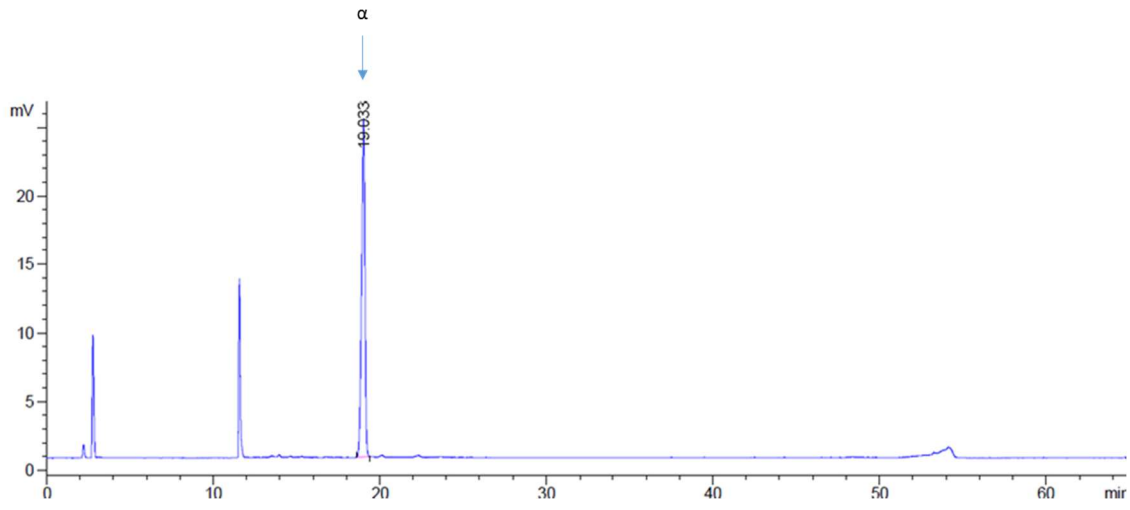
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl (2,3-di-*O*-benzyl-4,6-*O*-benzylidene)-αβ-D-glucopyranoside (16α and 16β)



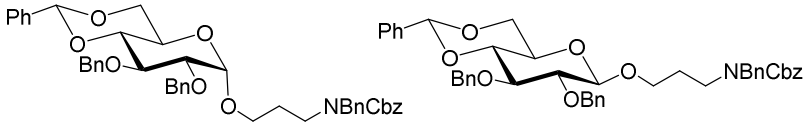
16α **16β**

Thioglycoside **8**[9] (55.3 mg, 0.112 mmol) was glycosylated with aminoalcohol **1** (25 mg, 0.075 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 1:0 α:β mixture (HPLC and NMR). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give **16α** (51.5 mg, 0.067 mmol, 90%) without detectable **16β**, but with inseparable traces of hydrolyzed **8**. Analytical data for **16α**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 – 7.03 (m, 25H), 5.58 (s, 1H), 5.29 – 5.05 (m, 2H), 5.01 – 4.46 (m, 7H), 4.33 – 4.12 (m, 1H), 4.09 – 3.49 (m, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.9, 138.9, 138.8, 138.3, 138.2, 137.7, 137.5, 137.0, 136.3, 129.0, 128.8, 128.64, 128.62, 128.59, 128.53, 128.50, 128.42, 128.40, 128.37, 128.33, 128.29, 128.22, 128.15, 128.12, 128.09, 128.05, 128.04, 128.02, 127.98, 127.96, 127.9, 127.71, 127.68, 127.65, 127.6, 126.3, 126.2, 126.1, 101.4, 98.9 ($^{1}J_{C\text{-}H}$ = 172.9 Hz, α), 82.0, 79.3, 78.4, 75.4, 75.1, 73.4, 73.0, 73.5, 69.0, 68.0, 63.1, 63.0, 51.3, 48.2, 47.1; HRMS (ESI): *m/z* calcd. for $C_{45}H_{45}F_2NNaO_8$ $[M+Na]^+$ 788.3011 found 788.3016.

HPLC data for **16** *(Gradient 2)*



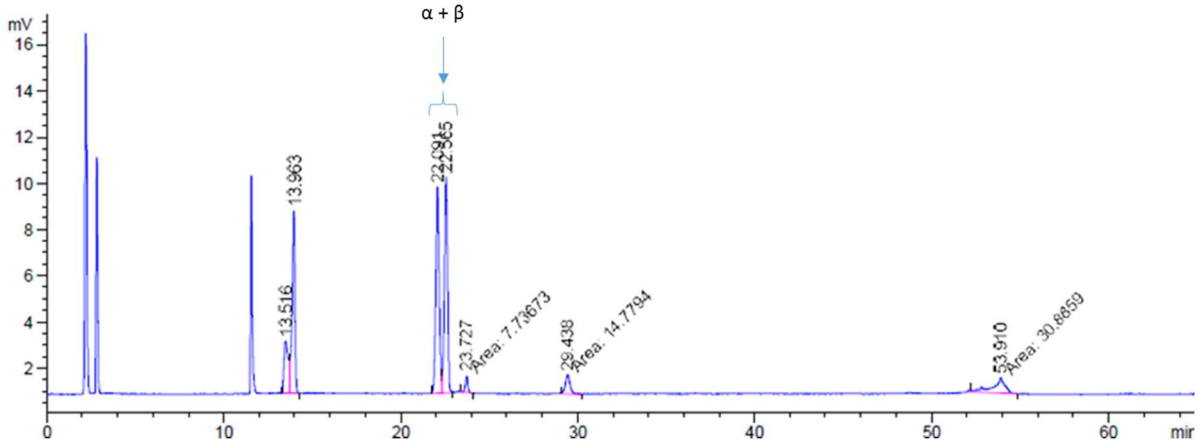
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl (2,3-di-*O*-benzyl-4,6-*O*-benzylidene)-αβ-D-glucopyranoside (24α and 24β)



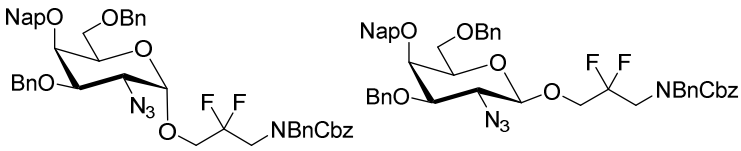
24α **24β**

Thioglycoside **8** (62 mg, 0.125 mmol) was glycosylated with aminoalcohol **2** (25 mg, 0.084 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 1:1 α:β mixture (HPLC and NMR). The mixture was purified by flash chromatography (EtOAc/hexanes 1:2) to give an inseparable mixture of glycosides **24α** and **24β** (35 mg, 0.048 mmol, 57%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 – 7.46 (m, 2H), 7.44 – 7.09 (m, 23H), 5.56 (s, 1H), 5.24 – 5.13 (m, 2H), 4.91 (d, *J* = 11.3 Hz, 1H), 4.86 – 4.19 (m, 7H), 4.06 – 3.30 (m, 9H), 1.98 – 1.76 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.8, 156.3, 138.9, 138.6, 138.42, 138.37, 138.0, 137.5, 137.4, 136.9, 129.1, 129.0, 128.7, 128.6, 128.52, 128.51, 128.43, 128.41, 128.36, 128.3, 128.14, 128.06, 128.0, 128.0, 127.8, 127.74, 127.68, 127.4, 127.3, 126.25, 126.15, 126.1, 104.1 ($^{1}J_{C\text{-}H}$ = 163.8 Hz, β), 101.3, 101.2, 98.2 ($^{1}J_{C\text{-}H}$ = 171.1 Hz, α), 82.3, 82.2, 81.6, 81.0, 80.9, 79.5, 78.6, 75.42, 75.39, 75.2, 73.7, 73.6, 69.2, 68.9, 68.0, 67.8, 67.4, 67.3, 66.1, 66.0, 62.7, 51.0, 50.9, 50.8, 44.82, 44.81, 44.7, 43.8, 28.8, 28.5, 28.4, 28.1; HRMS (ESI): *m/z* calcd. for $C_{45}H_{47}NNaO_8$ $[M+Na]^+$ 752.3199 found 752.3240.

HPLC data for **24** *(Gradient 2)*



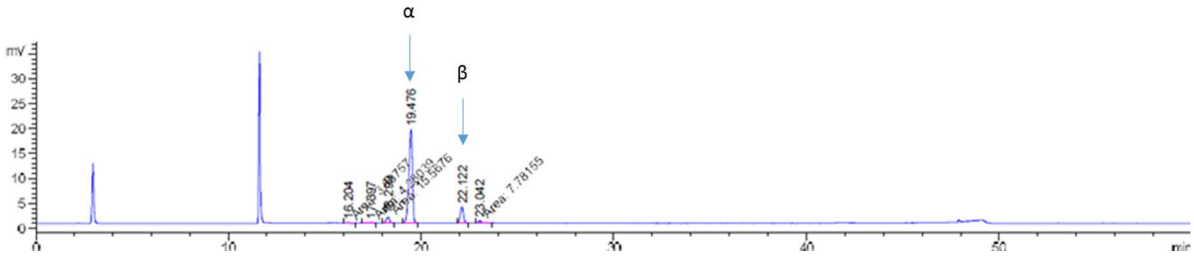
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl [2-azido-2-deoxy-3,6-di-*O*-benzyl-4-*O*-(2-naphthylmethyl)]-αβ-D-galactopyranoside (17α and 17β)



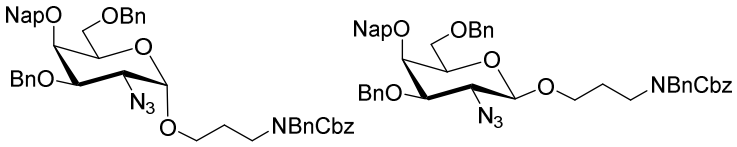
17α **17β**

Imidate **9** (55 mg, 0.082 mmol) was glycosylated with aminoalcohol **1** (25 mg, 0.075 mmol) using Imidate Activation at -40 °C to 0 °C to give the crude product as a 6.5:1 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give glycosides **17α** and **17β** (34 mg, 0.040 mmol, 54%). Analytical data for **17α**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 – 6.98 (m, 27H), 5.24 – 5.10 (m, 2H), 5.05 – 4.80 (m, 2H), 4.77 – 4.54 (m, 5H), 4.53 – 4.33 (m, 2H), 4.23 – 3.44 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.9, 156.7, 137.0, 133.3, 133.2, 128.81, 128.77, 128.7, 128.64, 128.61, 128.58, 128.4, 128.33, 128.29, 128.26, 128.12, 128.09, 128.04, 127.97, 127.95, 127.9, 127.8, 127.6, 127.5, 127.0, 126.6, 126.4, 126.3, 126.2, 126.1, 99.0 ($^{1}J_{C\text{-}H}$ = 175.0 Hz, α), 77.3, 75.0, 73.7, 72.5, 70.2, 68.6, 68.0, 59.8, 51.4, 48.0; analytical data for **17β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 – 7.00 (m, 27H), 5.27 – 5.13 (m, 2H), 5.01 – 4.98 (m, 1H), 4.79 – 4.53 (m, 5H), 4.49 – 4.16 (m, 3H), 4.11 – 3.26 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 137.7, 137.1, 136.3, 135.3, 133.3, 133.2, 129.0, 128.8, 128.7, 128.61, 128.58, 128.3, 128.1, 128.2, 127.9, 127.8, 127.7, 127.2, 127.0, 126.6, 126.4, 126.2, 126.1, 102.3 ($^{1}J_{C\text{-}H}$ = 163.2 Hz, β), 80.7, 74.9, 73.9, 73.7, 72.9, 72.5, 72.0, 70.2, 68.7, 68.6, 68.4, 68.0, 63.3, 61.4, 59.8, 51.8, 51.4, 47.1; HRMS (ESI): *m/z* calcd. for $C_{49}H_{48}F_2N_4NaO_7$ [mixture of anomers, $M+Na]^+$ 865.3389 found 865.3417.

HPLC data for **17** *(Gradient 2)*



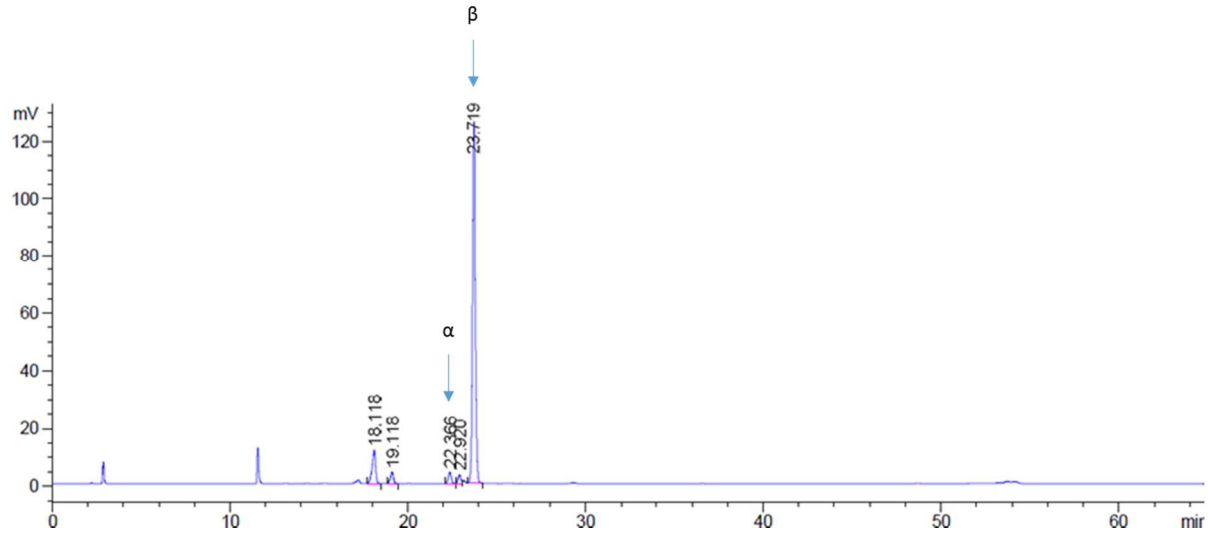
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl [2-azido-2-deoxy-3,6-di-*O*-benzyl-4-*O*-(2-naphthylmethyl)]-αβ-D-galactopyranoside (25α and 25β)



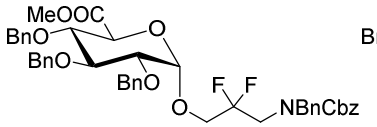
25α **25β**

Thioglycoside **9** (84 mg, 0.125 mmol) was glycosylated with aminoalcohol **2** (25 mg, 0.084 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 1:34 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:4) to give glycosides **25α** and **25β** (53 mg, 0.067 mmol, 80%). Analytical data for **25β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 – 7.78 (m, 1H), 7.77 – 7.73 (m, 2H), 7.68 (bs, 1H), 7.50 – 7.13 (m, 23H), 5.26 – 5.09 (m, 2H), 5.03 (d, *J* = 11.7 Hz, 1H), 4.76 (d, *J* = 11.8 Hz, 1H), 4.68 (s, 2H), 4.59 – 4.45 (m, 2H), 4.40 (d, *J* = 11.8 Hz, 1H), 4.34 (d, *J* = 11.7 Hz, 1H), 4.22 – 3.78 (m, 4H), 3.65 – 3.24 (m, 7H), 1.96 – 1.78 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 156.9, 156.3, 138.1, 137.8, 137.7, 135.8, 133.3, 133.1, 128.68, 128.67, 128.62, 128.58, 128.55, 128.54, 128.53, 128.2, 128.04, 128.02, 128.01, 127.99, 127.97, 127.94, 127.89, 127.8, 127.5, 127.4, 127.2, 126.6, 126.2, 126.0, 102.4, 102.3 ($^{1}J_{C\text{-}H}$ = 163.2 Hz, β), 80.8, 80.7, 74.8, 73.7, 73.6, 72.7, 72.1, 68.6, 67.5, 67.3, 67.2, 63.5, 51.0, 50.9, 44.8, 43.7, 28.6, 28.1; HRMS (ESI): *m/z* calcd. for $C_{49}H_{50}N_4NaO_7$ $[M+Na]^+$ 829.3577 found 829.3628.

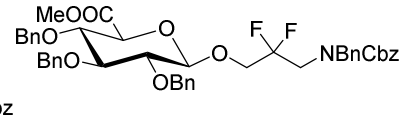
HPLC data for **25** *(Gradient 2)*



(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl methyl(2,3,4-tri-*O*-benzyl-αβ-D-glucopyranosyl)uronate (18α and 18β)



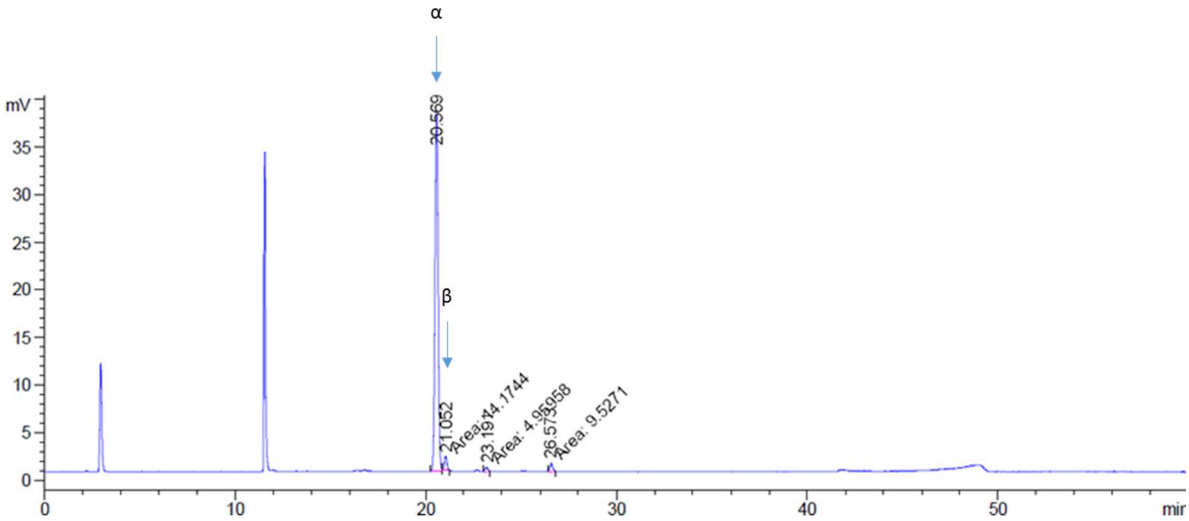
18α



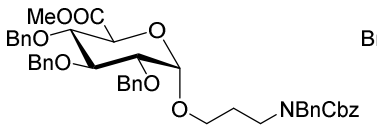
18β

Thioglycoside **10**[10] (58.4 mg, 0.112 mmol) was glycosylated with aminoalcohol **1** (25 mg, 0.075 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 28.6:1 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give an inseparable mixture of glycosides **18α** and **18β** (44.0 mg, 0.055 mmol, 74%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 – 6.79 (m, 25H), 5.27 – 5.12 (m, 2H), 4.96 – 4.52 (m, 9H), 4.23 (dd, *J* = 44.0, 9.5 Hz, 1H), 4.14 – 3.37 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 156.9, 138.7, 138.0, 137.0, 136.3, 128.9, 128.82, 128.78, 128.7, 128.61, 128.55, 128.53, 128.51, 128.4, 128.3, 128.2, 128.14, 128.12, 128.08, 128.05, 128.01, 128.96, 127.8, 127.6, 98.4 ($^{1}J_{C\text{-}H}$ = 173.7 Hz, α), 81.5, 81.1, 79.5, 79.4, 76.0, 75.8, 75.3, 75.2, 75.0, 74.6, 73.5, 73.3, 70.8, 68.1, 68.0, 67.5, 52.7, 51.3, 48.1, 47.1; HRMS (ESI): *m/z* calcd. for $C_{46}H_{47}F_2NNaO_9$ [mixture of anomers, M+Na]$^+$ 818.3117 found 818.3118.

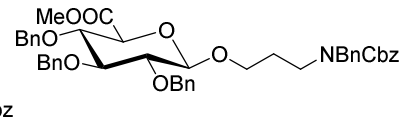
HPLC data for **18** *(Gradient 2)*



(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl methyl(2,3,4-tri-*O*-benzyl-αβ-D-glucopyranosyl)uronate (26α and 26β)



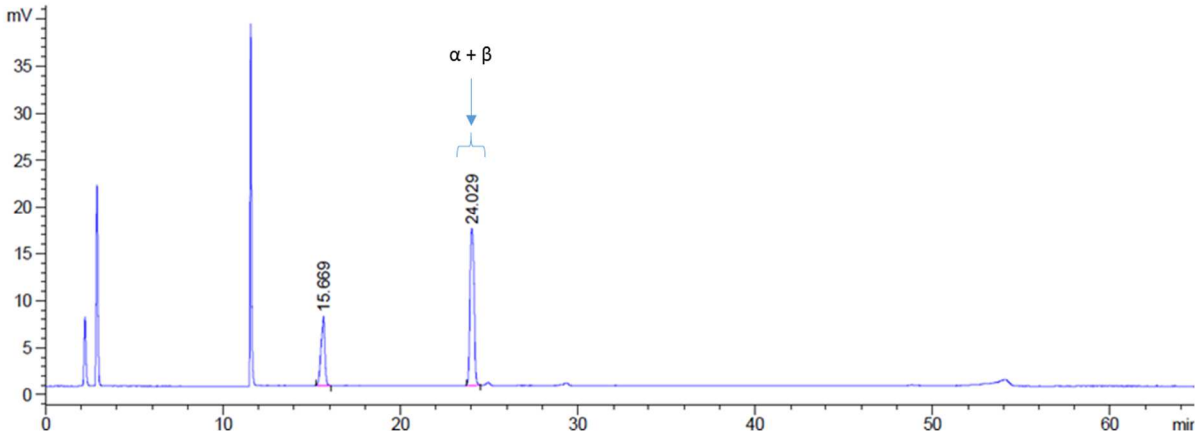
26α



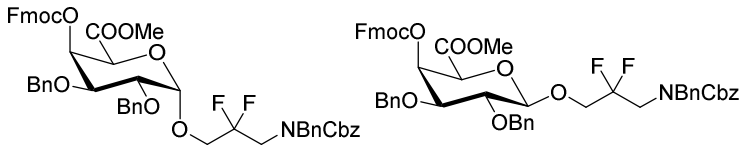
26β

Thioglycoside **10** (65.5 mg, 0.125 mmol) was glycosylated with aminoalcohol **2** (25 mg, 0.084 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 1:1.1 α:β mixture (HPLC and NMR). The mixture was purified by flash chromatography (EtOAc/hexanes 1:3) to give an inseparable mixture of glycosides **26α** and **26β** (50 mg, 0.065 mmol, 78%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 – 7.05 (m, 25H), 5.17 (bs, 2H), 4.97 – 4.31 (m, 9H), 4.23 – 3.25 (m, 11H), 1.97 – 1.75 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$); δ 170.2, 169.1, 156.8, 156.3, 138.7, 138.4, 138.3, 138.1, 138.0, 137.94, 137.90, 136.88, 128.7, 128.58, 128.55, 128.53, 128.50, 128.48, 128.47, 128.2, 128.13, 128.10, 128.07, 128.04, 128.00, 127.98, 127.96, 127.9, 127.82, 127.79, 127.77, 127.5, 127.4, 127.3, 103.9 ($^{1}J_{C\text{-}H}$ = 163.2 Hz, β), 97.7 ($^{1}J_{C\text{-}H}$ = 172.1 Hz, α), 83.9, 81.8, 81.4, 79.7, 79.6, 79.4, 75.9, 75.8, 75.3, 75.2, 74.9, 74.5, 73.5, 73.4, 70.5, 67.9, 67.7, 67.3, 66.2, 66.1, 52.6, 50.9, 50.8, 50.6, 44.8, 44.6, 43.8, 43.6, 28.7, 28.5, 28.3, 27.9; HRMS (ESI): *m/z* calcd. for $C_{46}H_{49}NNaO_9$ [mixture of anomers, M+Na]$^+$ 782.3305 found 782.3353.

HPLC data for **26** *(Gradient 2)*



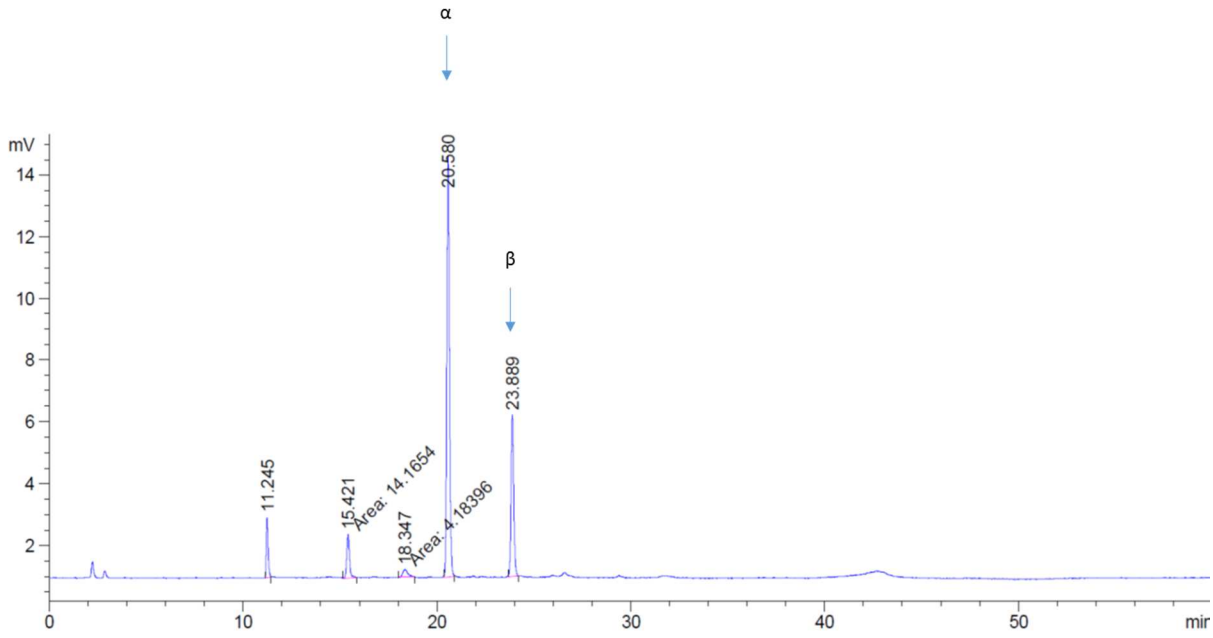
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl methyl(2,3-di-*O*-benzyl-αβ-D-galactopyranosyl)uronate (19α and 19β)



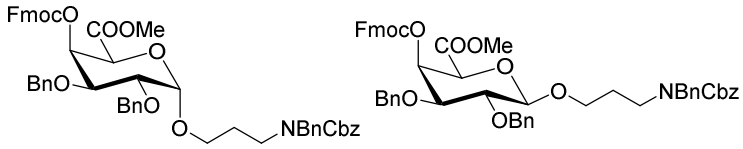
19α **19β**

Glycosyl phosphate **11**[11] (62 mg, 0.077 mmol) was glycosylated with aminoalcohol **1** (20 mg, 0.06 mmol) using Glycosyl Phosphate Activation at -40 °C to room temperature to give the crude product as a 2.6:1 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:5 to 2:7 to 1:3) to give glycosides **19α** and **19β** (33 mg, 0.036 mmol, 60%). Analytical data for **19α**: clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 8.0 Hz, 2H), 7.40 (dd, *J* = 14.4, 6.9 Hz, 2H), 7.37 – 7.24 (m, 18H), 7.23 – 7.08 (m, 4H), 5.70 (d, *J* = 29.3 Hz, 1H), 5.27 – 5.12 (m, 2H), 5.01 (d, *J* = 38.2 Hz, 1H), 4.88 – 4.45 (m, 7H), 4.43 – 4.26 (m, 2H), 4.25 – 4.05 (m, 2H), 4.00 – 3.57 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 154.7, 143.6, 143.3, 141.4, 141.3, 138.4, 137.9, 136.9, 136.2, 128.8, 128.7, 128.6, 128.4, 128.12, 128.06, 128.0, 127.93, 127.87, 127.7, 127.6, 127.3, 125.5, 125.3, 120.12, 120.08, 99.0 ($^{1}J_{C\text{-}H}$ = 175.8 Hz, α), 75.4, 74.9, 74.1, 73.9, 73.1, 72.9, 72.6, 70.4, 69.3, 68.1, 52.9, 51.4, 46.6; analytical data for **19β**: clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.43 – 7.06 (m, 24H), 5.65 (d, *J* = 2.2 Hz, 1H), 5.33 – 5.11 (m, 2H), 5.01 – 4.48 (m, 7H), 4.48 – 4.10 (m, 5H), 3.96 – 3.55 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 156.8, 156.7, 154.7, 143.4, 143.2, 141.3, 141.2, 138.1, 137.4, 136.9, 136.4, 128.7, 128.5, 128.32, 128.31, 128.1, 128.0, 127.92, 127.88, 127.8, 127.6, 127.4, 127.2, 125.4, 125.2, 120.00, 119.97, 103.6, 103.4 ($^{1}J_{C\text{-}H}$ = 163.8 Hz, β), 78.3, 77.8, 75.50, 72.46, 71.7, 70.4, 67.9, 52.8, 51.1, 46.5; HRMS (ESI): *m*/*z* calcd. for $C_{54}H_{51}F_2NNaO_{11}$ [mixture of anomers, M+Na]$^{+}$ 950.3328 found 950.3275.

HPLC data for **19** *(Gradient 2)*



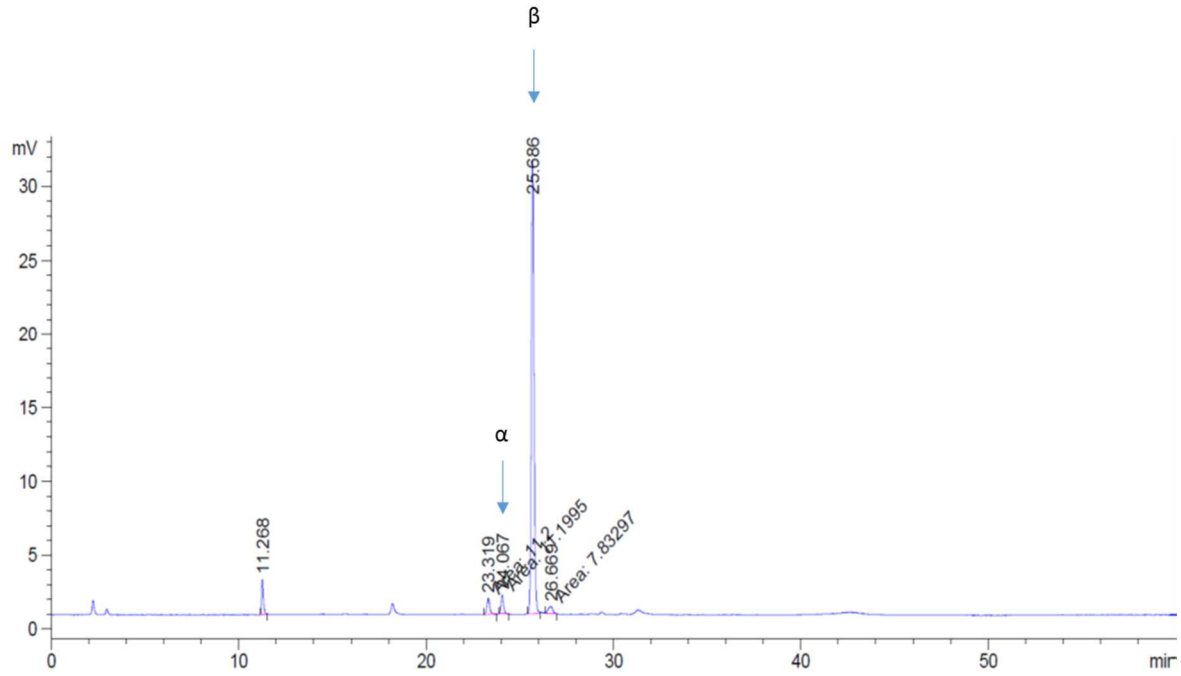
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl methyl(2,3-di-*O*-benzyl-αβ-D-galactopyranosyl)uronate (27α and 27β)



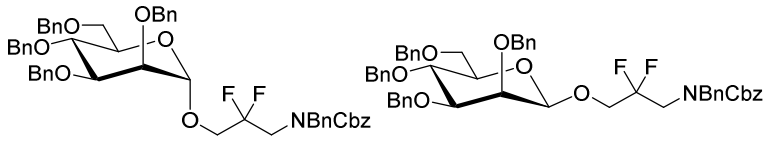
27α **27β**

Glycosyl phosphate **11** (70 mg, 0.077 mmol) was glycosylated with aminoalcohol **2** (20 mg, 0.067 mmol) using Glycosyl Phosphate Activation at -40 °C to room temperature to give the crude product as a 1:27 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:4 to 1:3 to 2:5) to give glycosides **27α** and **27β** (35 mg, 0.039 mmol, 58%). Analytical data for **27α**: clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 8.2 Hz, 2H), 7.44 – 7.31 (m, 18H), 7.19 (dd, *J* = 17.7, 10.6 Hz, 6H), 5.69 (d, *J* = 28.5 Hz, 1H), 5.16 (d, *J* = 12.8 Hz, 2H), 4.95 – 4.72 (m, 3H), 4.68 – 4.14 (m, 8H), 4.09 – 3.85 (m, 2H), 3.79 – 3.60 (m, 4H), 3.54 – 3.23 (m, 3H), 1.92 – 1.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 143.7, 143.3, 141.4, 141.3, 138.5, 137.9, 128.7, 128.6, 128.4, 128.1, 127.99, 127.93, 127.7, 127.3, 127.2, 125.5, 125.3, 120.12, 120.08, 98.4 ($^{1}J_{C\text{-}H}$ = 171.0 Hz, α), 75.7, 75.1, 74.1, 72.5, 70.4, 69.0, 67.4, 66.7, 52.8, 50.9, 50.5, 46.6, 44.4, 43.6, 29.9; analytical data for **27β**: clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 2H), 7.44 – 7.11 (m, 24H), 5.66 (s, 1H), 5.19 (d, *J* = 9.3 Hz, 2H), 4.94 – 4.55 (m, 4H), 4.54 – 4.27 (m, 4H), 4.24 – 3.96 (m, 3H), 3.76 (s, 3H), 3.72 – 3.29 (m, 6H), 2.08 – 1.81 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 154.9, 143.6, 143.4, 141.4, 141.3, 138.4, 138.0, 137.6, 128.8, 128.7, 128.6, 128.4, 128.3, 128.1, 128.03, 127.96, 127.92, 127.85, 127.8, 127.6, 127.5, 127.3, 125.54, 125.4, 120.09, 120.06, 103.4 ($^{1}J_{C\text{-}H}$ = 161.4 Hz, β), 78.7, 78.3, 75.6, 72.5, 72.4, 72.0, 70.5, 67.8, 67.4, 58.6, 52.9, 51.0, 50.4, 46.7, 44.7, 43.7, 43.1, 28.7, 28.3; HRMS (ESI): *m/z* calcd. for $C_{54}H_{53}NNaO_{11}$ [mixture of anomers, M+Na]$^{+}$ 914.3516 found 914.3530.

HPLC data for **27** *(Gradient 2)*



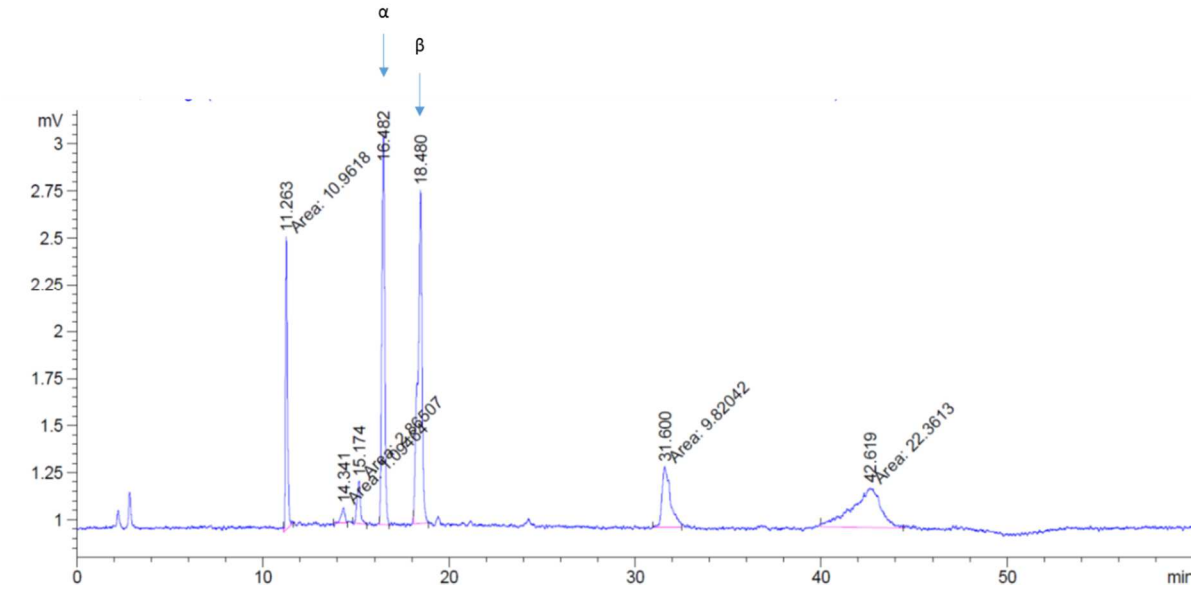
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl (2,3,4,6-tetra-*O*-benzyl)-αβ-D-mannopyranoside (20α and 20β)



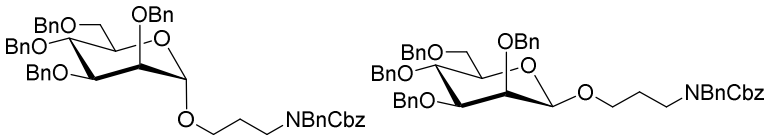
20α **20β**

Thioglycoside **12**[12] (65 mg, 0.112 mmol) was glycosylated with aminoalcohol **1** (25 mg, 0.075 mmol) using Thioglycoside Activation at -40 °C to -20 °C to give the crude product as a 1:1.2 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:5 to 2:9) to give glycosides **20α** and **20β** (45 mg, 0.052 mmol, 70%). Analytical data for **20α**: clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.05 (m, 30H), 5.15 (s, 2H), 5.01 – 4.82 (m, 2H), 4.79 – 4.44 (m, 9H), 4.06 – 3.51 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 138.5, 138.4, 136.9, 136.2, 128.8, 128.6, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 98.9 ($^{1}J_{C\text{-}H}$ = 173.4 Hz, α), 98.7, 80.0, 75.3, 74.7, 74.6, 73.5, 72.9, 72.7, 72.4, 72.3, 69.1, 68.0, 66.6, 66.3, 51.1, 47.7; HRMS (ESI): *m*/*z* calcd. for $C_{52}H_{53}F_2NNaO_8$ $[M+Na]^+$ 880.3637 found 880.3671; analytical data for **20β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 – 7.08 (m, 30H), 5.25 – 5.09 (m, 2H), 4.92 – 4.77 (m, 2H), 4.75 – 4.27 (m, 9H), 4.21 – 3.31 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.9, 138.5, 138.2, 137.0, 136.3, 128.8, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 102.0, 101.6 ($^{1}J_{C\text{-}H}$ = 157.2 Hz, β), 82.2, 76.1, 75.3, 74.8, 74.2, 73.6, 71.6, 69.6, 68.6, 68.4, 68.2, 68.0, 51.3; HRMS (ESI): *m*/*z* calcd. for $C_{52}H_{53}F_2NNaO_8$ $[M+Na]^+$ 880.3637 found 880.3655.

HPLC data for **20** *(Gradient 2)*



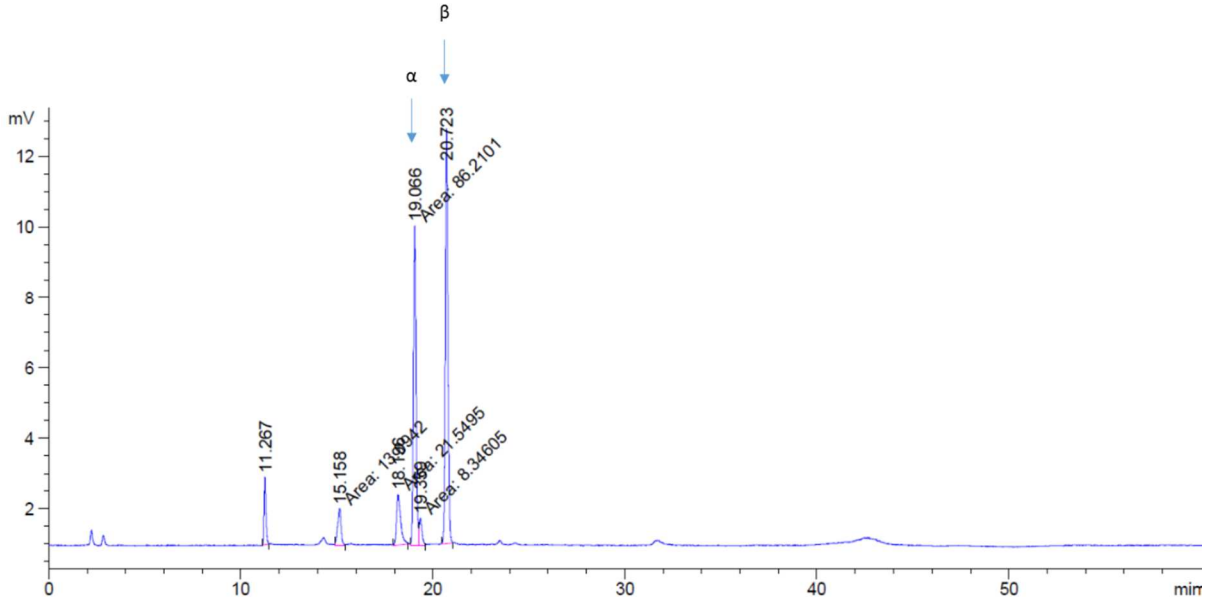
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl (2,3,4,6-tetra-*O*-benzyl)-αβ-D-mannopyranoside (28α and 28β)



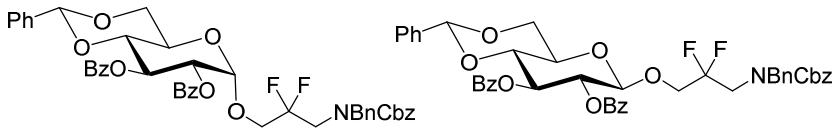
28α **28β**

Thioglycoside **12** (73 mg, 0.125 mmol) was glycosylated with aminoalcohol **2** (25 mg, 0.084 mmol) using Thioglycoside Activation at -40 °C to -20 °C to give the crude product as a 1:1.3 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:5 to 2:9 to 1:4) to give glycosides **28α** and **28β** (51 mg, 0.062 mmol, 74%). Analytical data for **28α**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.00 (m, 30H), 5.14 (d, *J* = 7.3 Hz, 2H), 4.92 – 4.37 (m, 11H), 3.96 (s, 1H), 3.82 (s, 1H), 3.78 – 3.58 (m, 5H), 3.42 – 3.15 (m, 3H), 1.81 – 1.67 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.8, 156.3, 138.7, 138.5, 137.9, 136.93, 136.85, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 127.3, 98.1 ($^{1}J_{C\text{-}H}$ = 172.8 Hz, α), 80.3, 75.3, 75.1, 74.9, 73.5, 72.7, 72.3, 72.1, 69.4, 67.3, 65.3, 50.9, 50.6, 44.7, 43.8, 28.4, 27.9; analytical data for **28β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 – 7.01 (m, 30H), 5.17 (d, *J* = 6.9 Hz, 2H), 4.89 (d, *J* = 10.6 Hz, 2H), 4.81 – 4.70 (m, 1H), 4.68 – 4.35 (m, 7H), 4.28 (d, *J* = 49.4 Hz, 1H), 3.96 (d, *J* = 24.0 Hz, 1H), 3.89 – 3.65 (m, 4H), 3.61 – 3.25 (m, 5H), 2.00 – 1.75 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.9, 156.3, 138.9, 138.5, 138.3, 138.0, 137.0, 136.9, 128.7, 128.6, 128.5, 128.43, 128.40, 128.21, 128.20, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 101.8 ($^{1}J_{C\text{-}H}$ = 154.8 Hz, β), 82.4, 76.0, 75.3, 75.0, 74.04, 73.99, 73.6, 71.5, 69.8, 67.3, 51.0, 50.8, 44.7, 43.9, 28.7, 28.2; HRMS (ESI): *m/z* calcd. for $C_{52}H_{55}NNaO_8$ [mixture of anomers, M+Na]$^{+}$ 844.3825 found 844.3849

HPLC data for **28** *(Gradient 2)*



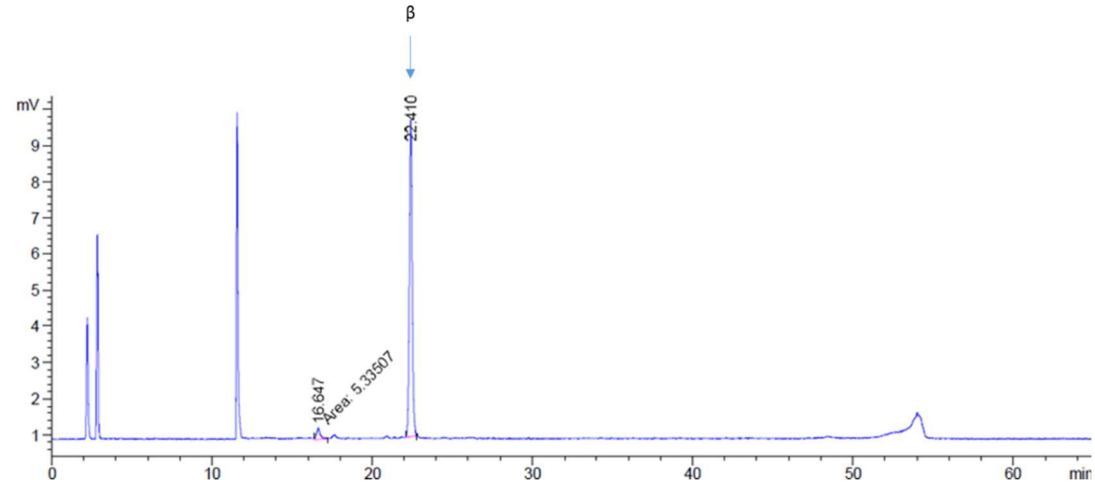
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-2,2-difluoro-1-propyl (2,3-di-*O*-benzoyl-4,6-*O*-benzylidene)-αβ-D-glucopyranoside (21α and 21β)



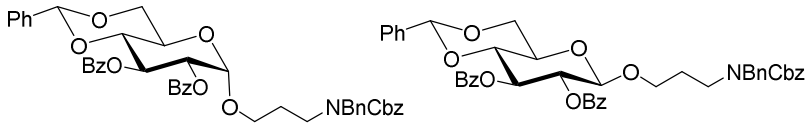
21α **21β**

Thioglycoside **13**[13] (58.4 mg, 0.112 mmol) was glycosylated with aminoalcohol **1** (25 mg, 0.075 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 0:1 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give **24β** (44 mg, 0.055 mmol, 74%) without detectable **21α**. Analytical data for **21β**: clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 6.86 (m, 25H), 5.90 – 5.64 (m, 1H), 5.60 – 5.41 (m, 2H), 5.38 – 5.12 (m, 2H), 4.99 – 4.67 (m, 1H), 4.68 – 4.28 (m, 3H), 4.18 – 3.35 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 165.3, 156.7, 136.9, 136.8, 133.3, 130.04, 129.98, 129.93, 129.89, 129.8, 129.4, 129.2, 128.7, 128.62, 128.59, 128.5, 128.43, 128.40, 128.33, 128.29, 128.2, 128.1, 127.7, 127.6, 127.4, 126.29, 126.27, 126.2, 101.8 ($^{1}J_{C\text{-}H}$ = 165.8 Hz, β), 101.6, 78.7, 72.3, 72.0, 68.6, 67.9, 66.8, 51.4, 48.1, 47.0; HRMS (ESI): *m/z* calcd. for $C_{45}H_{41}F_2NNaO_{10}$ $[M+Na]^+$ 816.2596 found 816.2610.

HPLC data for **21** *(Gradient 2)*



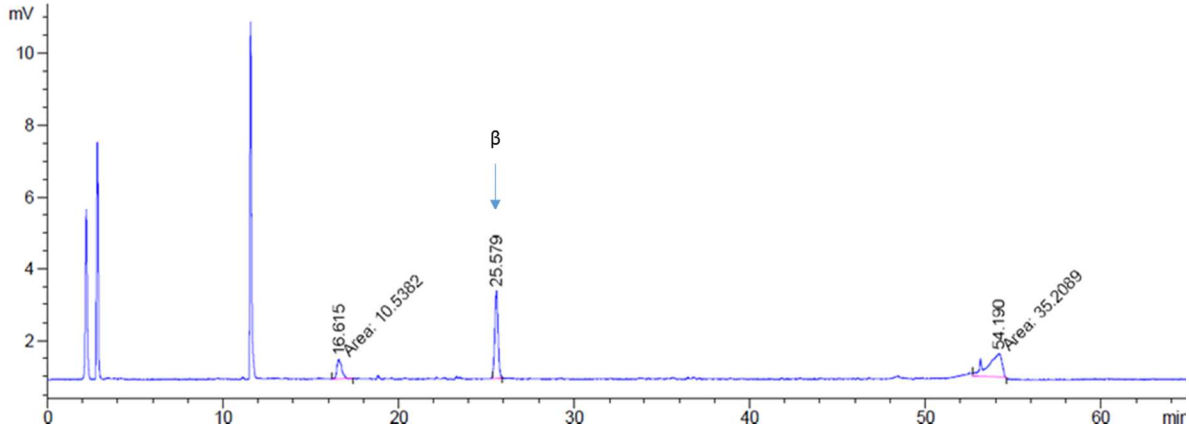
(3-*N*-Benzyl-*N*-benzyloxycarbonylamino)-1-propyl (2,3-di-*O*-benzoyl-4,6-*O*-benzylidene)-αβ-D-glucopyranoside (29α and 29β)



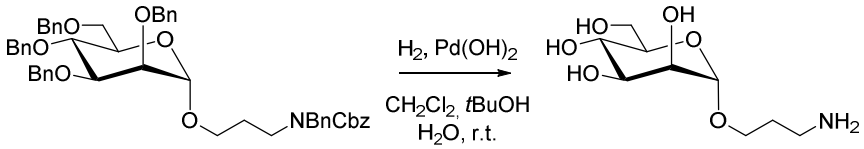
29α **29β**

Thioglycoside **13** (65 mg, 0.125 mmol) was glycosylated with alcohol **2** (25 mg, 0.084 mmol) using Thioglycoside Activation at -40 °C to 0 °C to give the crude product as a 0:1 α:β mixture (HPLC). The mixture was purified by flash chromatography (EtOAc/hexanes 1:2) to give glycoside **29β** (44 mg, 0.059 mmol, 70%) without detectable **29**α. Analytical data for **29β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 7.5 Hz, 2H), 7.57 – 6.91 (m, 21H), 5.71 - 5.62 (m, 1H), 5.44 (bs, 1H), 5.39 - 5.31 (m, 1H), 5.12 - 5.00 (m, 2H), 4.71 - 4.50 (m, 1H), 4.38 – 4.19 (m, 3H), 3.88 - 3.67 (m, 3H), 3.64 – 3.32 (m, 2H), 3.23 – 3.02 (m, 2H), 1.66 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.7, 165.3, 156.7, 156.2, 137.98, 137.96, 136.9, 133.3, 133.2, 130.2, 130.1, 129.9, 129.8, 129.5, 129.4, 129.1, 128.6, 128.5, 128.4, 128.3, 128.0, 127.41, 127.39, 127.3, 126.2, 101.7, 101.66 ($^{1}J_{C\text{-}H}$ = 164.8 Hz, β), 101.6, 78.9, 73.4, 72.6, 72.1, 71.4, 68.7, 67.9, 67.7, 67.3, 66.7, 65.3, 51.1, 51.0, 44.8, 43.7, 28.6, 28.2. HRMS (ESI): *m/z* calcd. for $C_{45}H_{43}NNaO_{10}$ $[M+Na]^+$ 780.2785 found 780.2820.

HPLC data for **29** *(Gradient 2)*



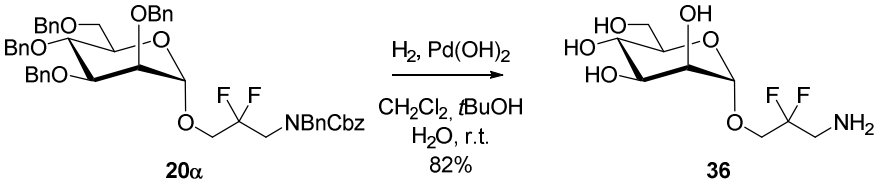
3-Aminopropyl α-D-mannopyranoside (35)



28α **35**

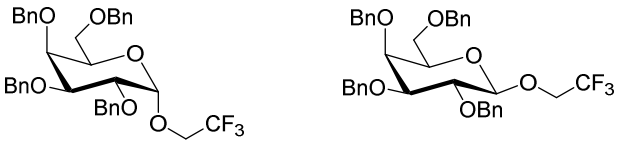
Benzyl ether **28α** (6 mg, 7.3 µmol) in CH_2Cl_2/*t*BuOH/water (1:5:1, 1 mL) was purged with nitrogen and treated with a suspension of $Pd(OH)_2$ on carbon (20% (w/w) loading, 30 mg) in the same solvent mixture (1 mL). The suspension was purged with hydrogen, stirred under hydrogen atmosphere for 2.5 h, filtered and concentrated. The residue was passed through a solid phase extraction cartridge (Chromabond C18, Macherey-Nagel) using water as the solvent and lyophilized to give mannose derivative **35** (1.5 mg, 6.4 µmol, 88%) as a white solid. ^{1}H NMR (400 MHz, D_2O) δ 4.83 (d, *J* = 1.4 Hz, 1H), 3.92 (dd, *J* = 3.3, 1.7 Hz, 1H), 3.89 – 3.79 (m, 2H), 3.79 – 3.66 (m, 2H), 3.65 – 3.48 (m, 3H), 3.14 – 3.02 (m, 2H), 2.04 – 1.87 (m, 2H); ^{13}C NMR (150 MHz, D_2O) δ 102.4, 75.4, 73.2, 72.6, 69.4, 67.5, 63.6, 40.1, 29.2; HRMS (ESI): *m/z* calcd. for $C_9H_{20}NO_6$ $[M+H]^+$ 238.1290 found 238.1058.

3-Amino-2,2-difluoro-1-propyl α-D-mannopyranoside (36)



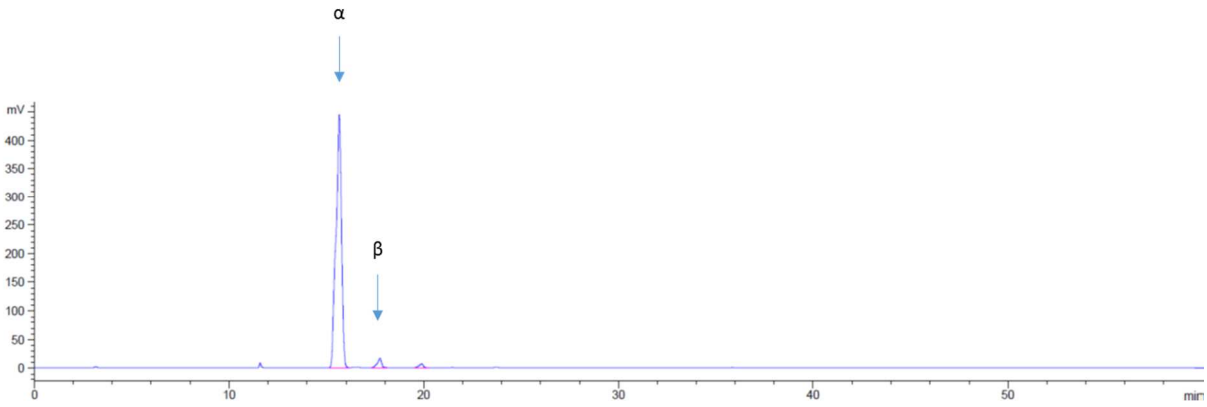
Benzyl ether **20α** (11 mg, 12.8 µmol) in CH_2Cl_2/*t*BuOH/water (1:5:1, 1.5 mL) was purged with nitrogen and treated with a suspension of $Pd(OH)_2$ on carbon (20% (w/w) loading, 30 mg) in the same solvent mixture (1 mL). The suspension was purged with hydrogen, stirred under hydrogen atmosphere for 16 h, filtered and concentrated. The residue was passed through a solid phase extraction cartridge (Chromabond C18, Macherey-Nagel) using water as the solvent and lyophilized to give mannose derivative **36** (2.9 mg, 10.5 µmol, 82%) as a white solid. ^{1}H NMR (400 MHz, D_2O) δ 4.91 (d, *J* = 1.1 Hz, 1H), 4.05 (dd, *J* = 25.4, 12.4 Hz, 1H), 3.98 (dd, *J* = 3.2, 1.7 Hz, 1H), 3.95 – 3.82 (m, 2H), 3.82 – 3.69 (m, 2H), 3.68 – 3.51 (m, 4H); ^{13}C NMR (150 MHz, D_2O) δ 121.5, 102.6, 75.7, 72.7, 72.0, 69.0, 68.6, 68.4, 68.2, 63.3, 43.9, 43.7, 43.5; HRMS (ESI): *m/z* calcd. for $C_9H_{18}F_2NO_6$ $[M+H]^+$ 274.1102 found 274.0880.

2,2,2-Trifluoroethyl (2,3,4,6-tetra-*O*-benzyl)-αβ-D-galactopyranoside (S-7α and S-7β)

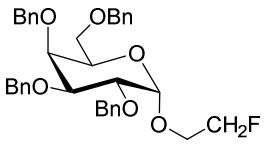


Thioglycoside **3** (100 mg, 0.171 mmol) was glycosylated with 2,2,2-trifluoroethanol (11 µL, 0.155 mmol) using Thioglycoside Activation at -40 °C to give the crude product as a 24:1 α:β mixture (HPLC and NMR). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give glycosides **S-7α** and **S-7β** (80 mg, 0.128 mmol, 83%). Analytical data for **S-7α**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.22 (m, 20H), 4.96 (d, *J* = 11.4 Hz, 1H), 4.91 (d, *J* = 3.7 Hz, 1H), 4.86 (dd, *J* = 20.3, 11.8 Hz, 2H), 4.77 – 4.74 (m, 1H), 4.68 (d, *J* = 11.9 Hz, 1H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.49 (d, *J* = 11.9 Hz, 1H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.09 (dd, *J* = 10.0, 3.7 Hz, 1H), 4.03 – 3.85 (m, 5H), 3.53 (d, *J* = 6.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 138.6, 138.5, 138.0, 128.6, 128.5, 128.4, 128.1, 127.89, 127.86, 127.8, 127.7, 127.6, 123.99 (q, $J^1_{C\text{-}F}$ = 279 Hz), 98.3, 82.0, 79.1, 78.7, 76.3, 75.5, 75.0, 74.9, 74.7, 73.9, 73.7, 73.60, 73.59, 73.52, 73.45, 73.4, 70.2, 68.9, 64.6 (q, $J^2_{C\text{-}F}$ = 35 Hz); LRMS (ESI): *m/z* calcd. for $C_{36}H_{37}F_3NaO_6$ $[M+Na]^+$ 645.2 found 645.2.

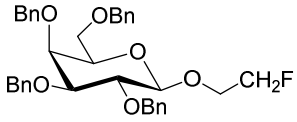
HPLC data for **S-7** *(Gradient 2)*



2-Fluoroethyl (2,3,4,6-tetra-*O*-benzyl)-αβ-D-galactopyranoside (S-8α and S-8β)



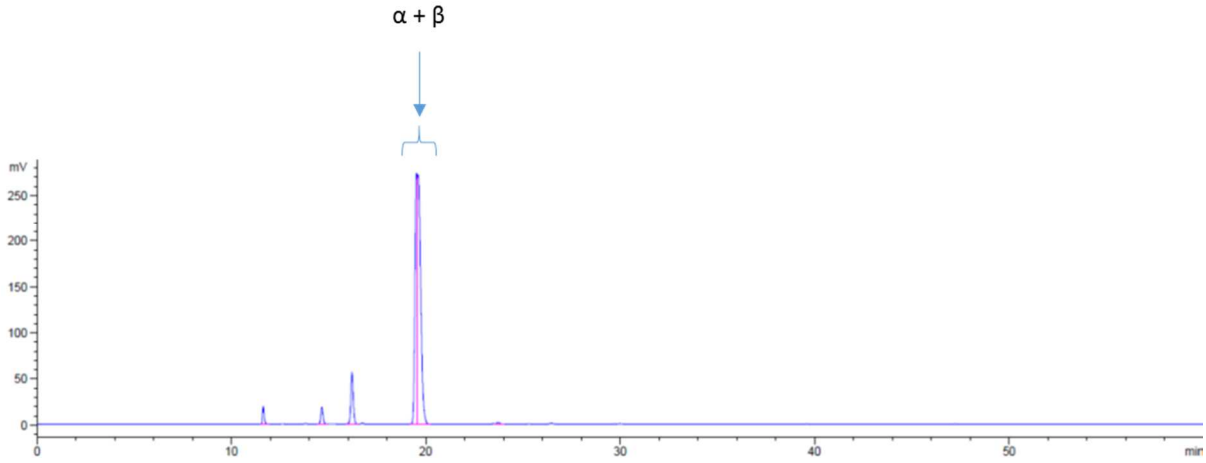
S-8α



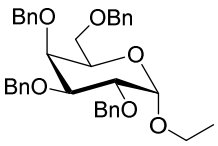
S-8β

Thioglycoside **3** (100 mg, 0.171 mmol) was glycosylated with 2-fluoroethanol (9 µL, 0.155 mmol) using Thioglycoside Activation at -40 °C to give the crude product as a 1:1.5 α:β mixture (HPLC and NMR). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give an inseparable mixture of glycosides **S-8α** and **S-β** (87 mg, 0.148 mmol, 96%). Analytical data for **S-8α and S-8β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 – 7.22 (m, 20H), 4.98-4.94 (m, 1.5H), 4.89 – 4.82 (m, 1H), 4.80 – 4.51 (m, 6H), 4.50 – 4.45 (m, 0.5H), 4.45 – 4.38 (m, 2H), 4.14 – 3.96 (m, 2H), 3.91 – 3.70 (m, 3H), 3.61 – 3.49 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.0, 138.74, 138.72, 138.68, 138.65, 138.60, 138.1, 138.0, 128.6, 128.53, 128.52, 128.49, 128.48, 128.46, 128.40, 128.37, 128.36, 128.34, 128.30, 128.28, 128.2, 128.0, 127.9, 127.84, 127.83, 127.80, 127.71, 127.70, 127.65, 127.59, 127.56, 104.2, 98.1, 82.8 (d, $J^{1}_{C\text{-}F}$ = 169.8 Hz), 82.1, 79.5, 79.1, 76.6, 75.4, 75.2, 74.9, 74.6, 73.7, 73.6, 73.53, 73.51, 73.48, 73.4, 73.2, 69.4, 69.0 (d, $J^{2}_{C\text{-}F}$ = 17 Hz), 68.8 (d, $J^{2}_{C\text{-}F}$ = 20 Hz), 67.1 (d, $J^{2}_{C\text{-}F}$ = 20 Hz); LRMS(ESI): *m/z* calcd. for $C_{36}H_{39}FNaO_6$ [M+Na]$^+$ 609.2 found 609.2.

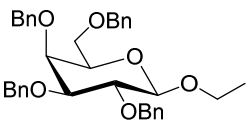
HPLC data for **S-8** *(Gradient 2)*



Ethyl 2,3,4,6-tetra-*O*-benzyl-αβ-D-galactopyranoside (S-9α and S-9β)



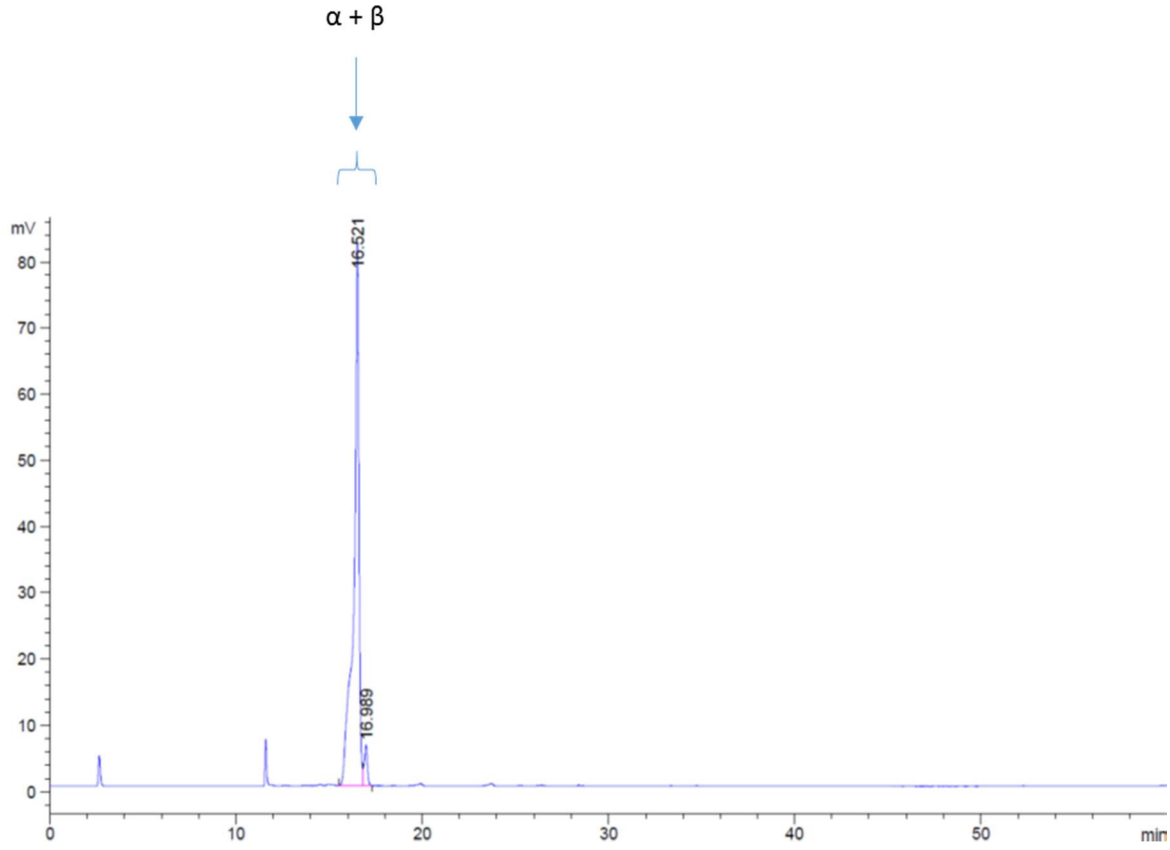
S-9α



S-9β

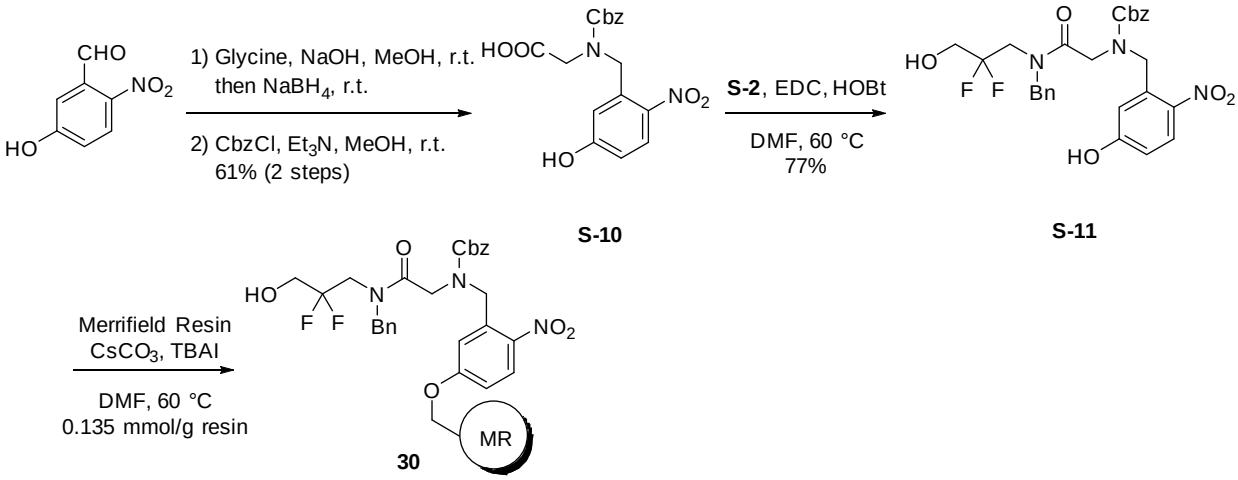
Thioglycoside **3**[3] (100 mg, 0.171 mmol) was glycosylated with ethanol (9 µL, 0.155 mmol) using Thioglycoside Activation at -40 °C to give the crude product as a 1:5 α:β mixture (HPLC and NMR). The mixture was purified by flash chromatography (EtOAc/hexanes 1:6 to 1:2) to give an inseparable mixture of glycosides **S-9α** and **S-9β** (81 mg, 0.142 mmol, 92%). Analytical data for mixture of **S-9α** and **S-9β**: clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.21 (m, 20H), 4.99-4.82 (m, 2H), 4.80 – 4.67 (m, 3H), 4.65 – 4.57 (m, 1H), 4.50 – 4.39 (m, 2H), 4.38 (d, *J* = 7.7 Hz, 1H), 4.11 – 3.95 (m, 2H), 3.90 (dd, *J* = 3.0, 1.0 Hz, 1H), 3.83 (dd, *J* = 9.8, 7.7 Hz, 1H), 3.62 – 3.57 (m, 2H), 3.56 – 3.51 (m, 2H), 1.26 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 128.53, 128.46, 128.4, 128.3, 128.2, 128.0, 127.9, 127.64, 127.61, 103.9, 82.3, 79.8, 75.3, 74.6, 73.7, 73.6, 73.5, 73.1, 69.0, 65.6, 15.4; LRMS (ESI): *m/z* calcd. for $C_{36}H_{40}NaO_6$ [M+Na]$^+$ 591.3 found 591.2.

HPLC data for **S-9** *(Gradient 2)*



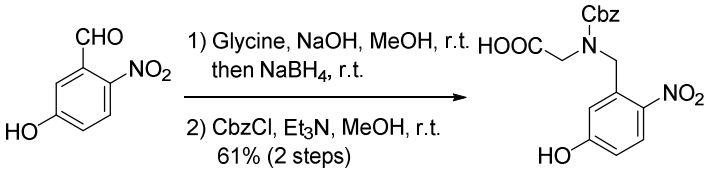
II.3 Automated Glycan Assembly and Experimental Procedures

II.3.1 Resin Preparation



Scheme S2. Synthesis of functionalized resin **30.**

***N*-(3-Hydroxy-6-nitrobenzyl)-*N*-benzyloxycarbonylglycine (S-10)**

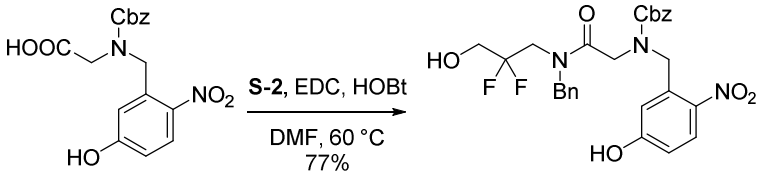


S-10

To a stirred solution of glycine (0.75 g, 10 mmol) and NaOH (0.8 g, 20 mmol) in water (10 mL) was added 3-hydroxy-6-nitrobenzaldehyde (1.67 g, 10 mmol) in MeOH (10 mL). The mixture was stirred for 1 h at room temperature, cooled to 0 °C and treated with $NaBH_4$ (1.5 g, 40.5 mmol). The reaction was warmed to room temperature, stirred for 2 h and neutralized with 2 M aq. HCl. The solution was concentrated under reduced pressure and diluted with CH_2Cl_2 (200 mL) and water (100 mL). After separation, the organic layer was washed with water (2x100 mL), dried over Na_2SO_4 and concentrated to give the crude intermediate amine.

To a stirred solution of the crude intermediate amine in MeOH (20 mL) were added at 0 °C Et_3N (2 mL) and benzyl chloroformate (1.8 g, 10.6 mmol). The mixture was warmed to room temperature, stirred for 3 h and concentrated. The residue was purified by flash chromatography (EtOAc/MeOH 4:1) to give carbamate **S-10** (2.2 g, 6.1 mmol, 61% over two steps) as a clear oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.04 (t, *J* = 8.2 Hz, 1H), 7.45 – 7.09 (m, 5H), 6.84-6.79 (m, 2H), 5.15-4.93 (m, 4H), 3.99-3.97 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 175.1, 164.41, 164.39, 158.5, 158.4, 141.1, 140.9, 138.5, 138.2, 137.7, 137.6, 129.5, 129.44, 129.39, 129.01, 128.95, 128.6, 128.5, 115.3, 115.19, 115.16, 68.8, 68.6, 51.6, 51.3, 51.1, 49.8; LRMS (ESI): *m/z* calcd. For $C_{17}H_{16}N_2NaO_7$ $[M+Na]^+$ 383.1, found 383.0.

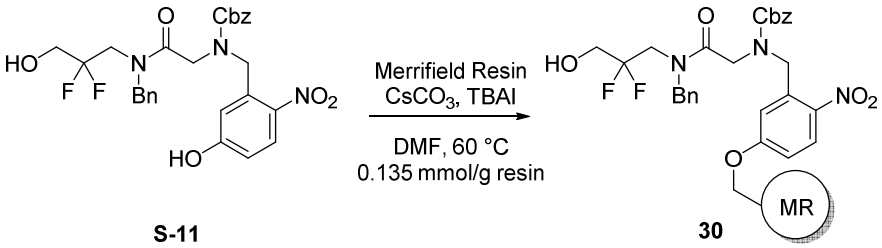
3-[*N*-Benzyl-*N*-[*N*-(3-hydroxy-6-nitrobenzyl)-*N*-benzyloxycarbonyl]-glycinamido]-2,2-difluoro-1-propanol (S-11)



S-10 **S-11**

To a stirred solution of amine **S-2** (93 mg, 0.463 mmol), carboxylic acid **S-10** (333 mg, 0.923 mmol) and benzotriazol-1-ol (142 mg, 0.927 mmol) in DMF (5 mL) were added at room temperature EDC (177 mg, 0.923 mmol) and DIPEA (0.32 mL, 1.837 mmol). The reaction was warmed to 60 °C and stirred for 24 h at that temperature. The mixture was concentrated and the residue was purified by flash chromatography (EtOAc/hexanes 1:10 to 1:1) to give amide **S-11** (192 mg, 0.355 mmol, 77%). NMR characterization was complicated by the presence of four rotamers. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 7.89 (m, 1H), 7.56 – 6.58 (m, 12H), 5.18 – 4.85 (m, 4H), 4.70 – 3.53 (m, 9H), 3.22 – 2.84 (m, 1H); 13C NMR (100 MHz, $CDCl_3$) δ 171.5, 171.3, 169.8, 169.6, 168.2, 168.1, 162.2, 161.8, 157.0, 156.9, 156.6, 140.4, 139.9, 138.5, 138.5, 136.5, 136.4, 136.0, 135.8, 135.5, 134.0, 129.4, 129.3, 129.2, 128.9, 128.72, 128.69, 128.63, 128.62, 128.60, 128.56, 128.4, 128.31, 128.27, 128.25, 128.1, 128.0, 127.9, 127.73, 127.67, 127.65, 127.6, 127.5, 126.3, 126.2, 125.9, 120.6, 115.3, 115.2, 115.1, 115.0, 114.0, 68.3, 68.2, 67.3, 64.3, 63.2, 63.0, 62.8, 62.7, 62.5, 61.3, 60.6, 53.6, 53.4, 52.5, 52.4, 51.7, 51.2, 51.0, 50.8, 50.7, 50.2, 49.8, 49.6, 49.3, 42.7; HRMS (ESI): *m/z* calcd. for $C_{27}H_{27}F_2N_3NaO_7$ $[M+Na]^+$ 566.1715 found 566.1723.

Functionalization of Resin **30**:



S-11 **30**

Merrifield resin (~0.50 mmol/g, 1.0 g, 0.5 mmol) and alcohol **S-11** (1.1 g, 2.02 mmol) were taken up in a minimal amount of anhydrous DMF (4 mL DMF/g resin) to completely swell the resin and solubilize alcohol **S-5**. The suspension was then degassed by placing the flask under HV for 5 min, followed by refilling the evacuated flask with Argon. After repeating this degassing procedure two more times, Cs_2CO_3 (650 mg, 2.00 mmol) and TBAI (184 mg, 0.50 mmol) were added to the flask and the suspension was rotated for 16 h at 60 °C for in the water bath of a rotational evaporator under atmospheric pressure. The suspension was treated with water to dissolve all solids and the resin was subsequently washed six times in a sequence of 1:1 (v/v) THF:water, THF, DMF, MeOH, CH_2Cl_2, MeOH, and finally CH_2Cl_2 (six times each). The resin was then swollen in a minimal amount of DMF (4 mL DMF/g resin) and the flask was degassed as described above.

The suspension was treated with cesium acetate (0.38 g, 1.98 mmol) and rotated for 16 h at 60 °C in the water bath of a rotational evaporator under atmospheric pressure. The resin was washed as described above, dried under high vacuum and stored in the dark.

Loading Determination: An aliquot of the resin (20-30 mg) was swollen in CH_2Cl_2 (1 mL) for 1 hour. To this suspension were subsequently added FmocCl (100 mg 0.387 mmol) and pyridine (100 µL) and the mixture was shaken overnight at room temperature. The resin was drained and washed with MeOH and CH_2Cl_2 (six alternating washes). The resin was then treated with a solution of 20% (v/v) piperidine in DMF (2 mL) and the suspension was shaken at for 4 h at room temperature. A 100 µL aliquot of the solution was taken and diluted to 10 mL using 20% (v/v) piperidine in DMF and the absorbance at 301 nm (ε = 7800 $Lmol^{-1}cm^{-1}$) was measured. The loading was measured to be 0.135 mmol per gram resin.

II.3.2 Stock Solutions

Building Block Solution: 39 mg (0.075 mmol) glycosylating agent **32**[14] was dissolved in 1 mL of CH_2Cl_2.

Activator Solution: 675 mg (5.06 mmol) NIS was dissolved in 40 mL of a 2:1 (v/v) mixture of CH_2Cl_2 and 1,4-dioxane. This solution was treated with 28 µL (0.317 mmol) TfOH. The solution was kept at 0 °C for the duration of the automation run, and could be used for 5 days without loss of activity.

Acidic Wash Solution: 0.9 mL (4.97 mmol) TMSOTf was diluted with 40 mL CH_2Cl_2. The solution was kept at room temperature for the duration of the automation run.

II.3.3 Modules for Automated Glycan Assembly

Module A: Resin Preparation

Automated synthesis was performed on a 0.0125 mmol scale (based on Fmoc loading). Resin **30** or **31**[1] was placed in the reaction vessel and swollen in CH_2Cl_2 (approx. 4 mL) for 30 min at room temperature prior to synthesis. Before the first glycosylation, the resin was washed with DMF, THF, and CH_2Cl_2 (3x2 mL each for 25 s).

Module B: Acidic Wash

Acidic wash of the resin was performed at -20 °C. 350 µL of Acidic Wash Solution was added dropwise to the reaction vessel. After incubating for 1 min, the Acidic Wash Solution was drained and the resin was washed with 2 mL CH_2Cl_2 for 25 s.

Module C: Glycosylation Procedure

The glycosylation was performed immediately after acidic wash. Building Block Solution (1 mL) was delivered to the reaction vessel and the temperature was adjusted to -40 °C. After the set temperature was reached, the reaction was started by the addition of Activator Solution (1 mL). The reaction was warmed to -30 °C and kept for 40 min at that temperature. The solution was drained and the resin was washed three times with CH_2Cl_2.

II.3.4 Post-automation Steps

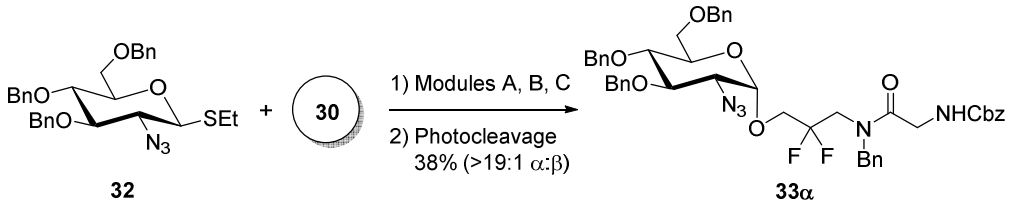
Cleavage from Solid Support

After automated synthesis, oligosaccharides were cleaved from solid support using a continuous-flow photoreactor as described previously.[1]

Analysis and Purification

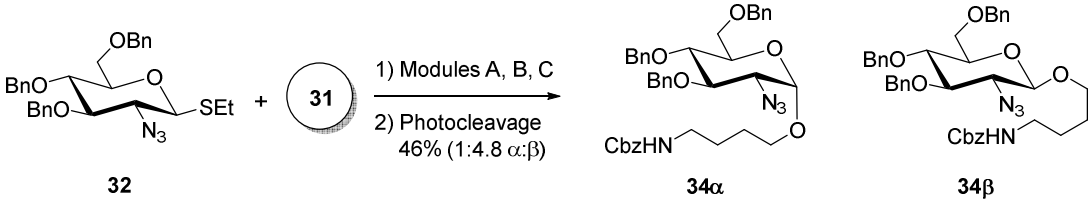
After photocleavage, solvents were evaporated and the residue was purified by preparative HPLC using a preparative Luna silica column (Phenonemex, Torrance, CA), 250x10 mm, flow 5 mL/min using a linear gradient between hexanes as mobile phase A and EtOAc as mobile phase B: (A:B) = T0-T5 (90:10), T5-T45 (90:10-40:60), T45-T50 (40:60-0:100).

3-[*N*-Benzyl-*N*-(*N*-benzyloxycarbonylamino)-glycinamido]-2,2-difluoro-1-propyl (2-azido-2-deoxy-3,4,6-tri-*O*-benzyl)-α-D-glucopyranoside (33α and 33β)



Glycoside **33α**: Foamy solid. 4.0 mg (4.7 µmol, 38% based on resin loading, >19:1 α:β (NMR)); ^{1}H NMR (600 MHz, DMSO-D_6) 1H NMR (600 MHz, DMSO-D_6) δ 7.45 – 7.15 (m, 25H), 5.14 – 4.91 (m, 3H), 4.84 – 4.36 (m, 8H), 4.19 (d, *J* = 16.8 Hz, 1H), 4.10 – 3.67 (m, 9H), 3.60 – 3.48 (m, 3H); ^{13}C NMR (150 MHz, DMSO-D_6) δ 170.4, 170.1, 170.0, 156.4, 138.2, 137.8, 137.6, 136.8, 136.7, 136.2, 128.5, 128.12, 128.1, 128.0, 127.9, 127.6, 127.5, 127.5, 127.41, 127.36, 127.33, 127.27, 127.2, 127.1, 126.9, 126.1, 121.1, 97.6, 97.5, 76.0, 75.8, 73.9, 73.0, 72.1, 70.6, 70.6, 69.3, 68.2, 65.3, 65.1, 58.9, 58.8, 51.5, 50.4, 49.6, 42.0, 41.8, 41.6; HRMS (ESI): *m/z* calcd. for $C_{47}H_{49}N_5NaO_8F_2$ $[M+Na]^+$ 872.3446 found 872.3419.

5-(*N*-Benzyloxycarbonylamino)-1-pentyl (2-azido-2-deoxy-3,4,6-tri-*O*-benzyl)-α-D-glucopyranoside (34α)



Glycosides **34α** and **34β** (inseparable mixture): Foamy solid. 4.2 mg (5.8 µmol, 46% based on resin loading, 1:4.8 α:β (NMR)) ^{1}H NMR (600 MHz, DMSO-D_6) δ 7.45 – 7.07 (m, 20H), 5.11 – 4.66 (m, 6H), 4.58 – 4.41 (m, 4H), 3.88 – 3.36 (m, 8H), 2.99 (q, *J* = 6.6 Hz, 2H), 1.56 (p, *J* = 6.8 Hz, 2H), 1.42 (q, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-D_6) δ 156.1, 138.2, 138.13, 138.08, 138.00, 137.97, 137.3, 128.3, 128.24, 128.22, 128.19, 128.1, 127.72, 127.69, 127.67, 127.66, 127.63, 127.60, 127.58, 127.56, 127.5, 127.4, 100.7, 96.9, 82.1, 79.6, 78.0, 77.7, 74.14, 74.06, 74.0, 73.9, 72.32, 72.26, 70.3, 68.9, 68.5, 68.4, 67.2, 65.6, 65.1, 62.3, 40.2, 40.1, 29.1, 28.7, 22.7; HRMS (ESI): *m/z* calcd. for $C_{40}H_{46}N_4NaO_7$ $[M+Na]^+$ 717.3264 found 717.3245.

II.4 Glycan Microarray Analysis

Microarray slides were fabricated as described recently.[15] Spotting solutions were independently prepared from two different stock solutions of both amine-linked mannose derivatives **30** and **31**, respectively. Serial dilutions of synthetic oligosaccharides in buffered solutions (100 mM sodium phosphate buffer (NaPi) pH 7.4 or 50 mM NaPi pH 8.5) were spotted onto CodeLink *N*-hydroxysuccinimide-activated glass slides (SurModics Inc., Eden Prairie, USA) using an automated piezoelectric arraying robot (Scienion, Berlin, Germany) at 0.4 nL per spot, and incubated for 24 h at room temperature in a humified chamber. Slides were quenched for 1 h at room temperature using 1% (v/v) bovine serum albumin (BSA) in phosphate buffered saline (PBS, 10 mM Na_2HPO_4, 1.8 mM K_2HPO_4, 137 mM NaCl, 2.7 mM KCl), washed with water and stored in an anhydrous chamber until use.

Slides were treated with dilutions of fluorescein isothiocyanate (FITC)-labeled Concanavalin A (Vector Laboratories, Peterborough, United Kingdom) in lectin binding buffer (LBB, 10 mM HEPES pH 7.4, 150 mM NaCl, 1% (v/v) BSA, 2 mM $CaCl_2$, 2 mM $MnCl_2$, 2 mM $MgCl_2$) using a 64-well gasket (FlexWell 64, Grace Bio-Labs, Bend, US). The slides were incubated for 1 h at 37 °C in a humified chamber, washed three times with LBB, washed with water and dried. Fluorescence read-out was performed using an Axon GenePix 4300A microarray scanner and GenePix Pro 7 software (both MDS, Sunnyvale, US). Negative fluorescence intensities were arbitrarily set to zero. All statistical analyses were perfomed using Prism 6 (Graphpad Software Inc., La Jolla, USA). Brightness and contrast of images were adjusted equally using Photoshop CS5 (Adobe Systems).

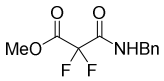
II.5 Molecular Modeling

Molecules **1** and **2** were drawn in ChemBioDraw Ultra 12.0.2 and converted into three-dimensional structures by using Chem3D (Cambridgesoft). The three-dimensional structures were minimized with MM2 level calculations implemented in Chem3D and the termination condition was RMS gradient of 0.01 kcal mol^{-1}. The optimized structure was used as starting point for the semi-empirical quantum mechanical calculations in Maestro 9.9 (Schrödinger, LLC, New York, USA).[16] The calculations were performed using the RM1 method. The optimized structures from semi-empirical quantum mechanical calculations were subsequently used for density functional

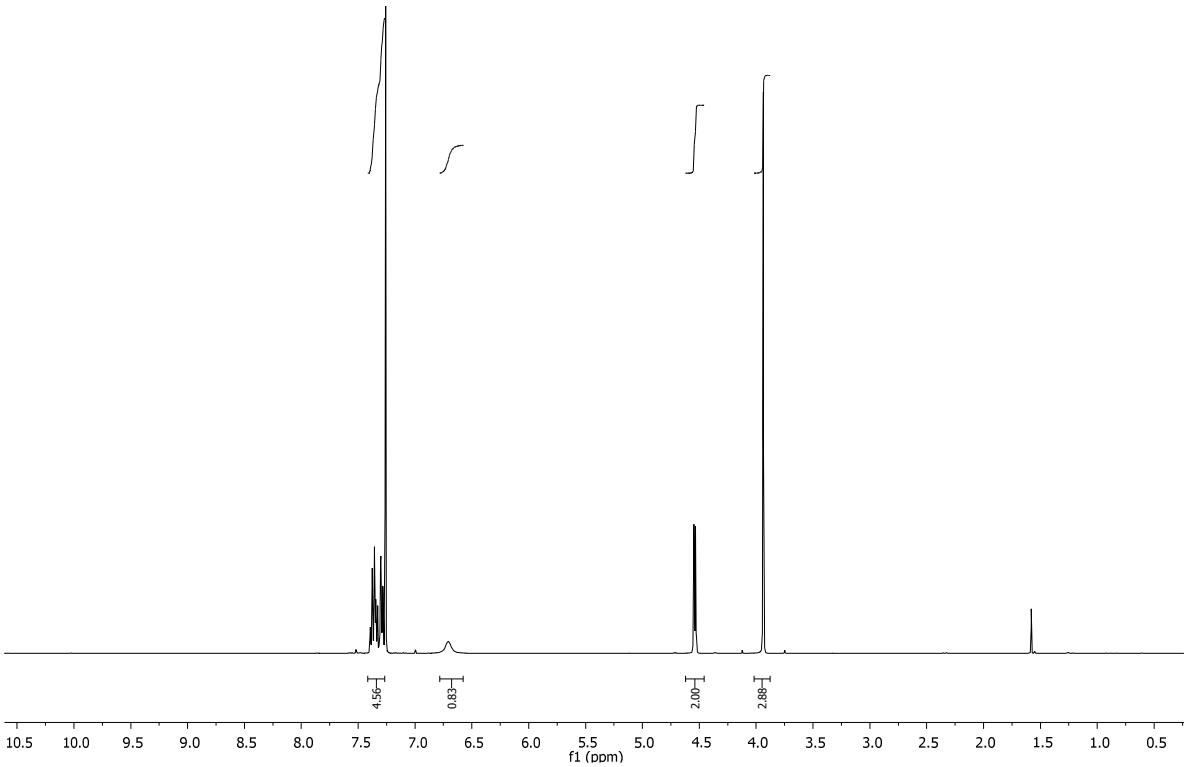
theorem (DFT) calculations using Gaussian 03 (Wallingford, USA).[17] The molecules were optimized with B3LYP/6-31G(d,p) level calculations. A vibration frequency analysis was performed on each optimized conformer to confirm true minima on the potential energy surface. The calculations for molecules **1** and **2** were performed with the solvent *chloroform,* using the *CPCM* approach, and final energies were calculated for pairs of alcohols and alcoholates. Final energies for molecules **15α**/**β** and **23α**/**β** were calculated for optimized structures.

III Spectral Characterization

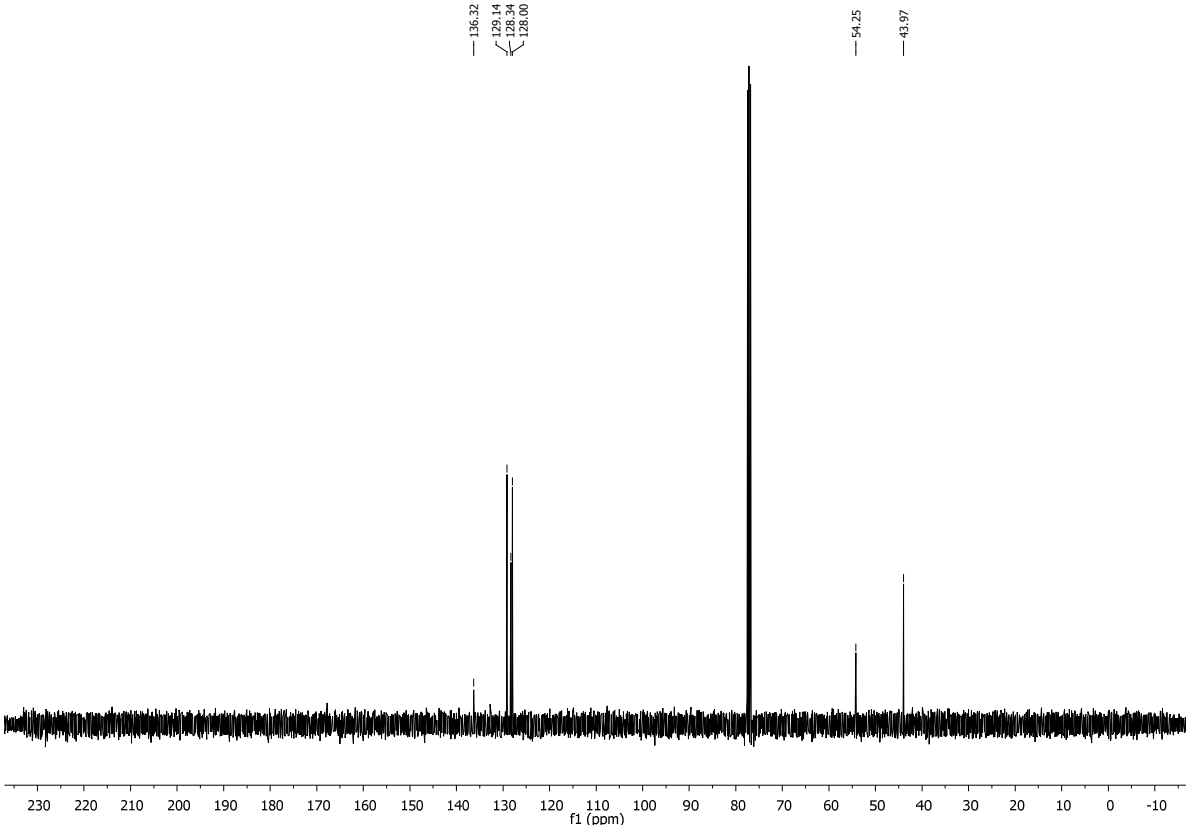
^{1}H NMR, 400 MHz, $CDCl_3$



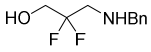
S-1



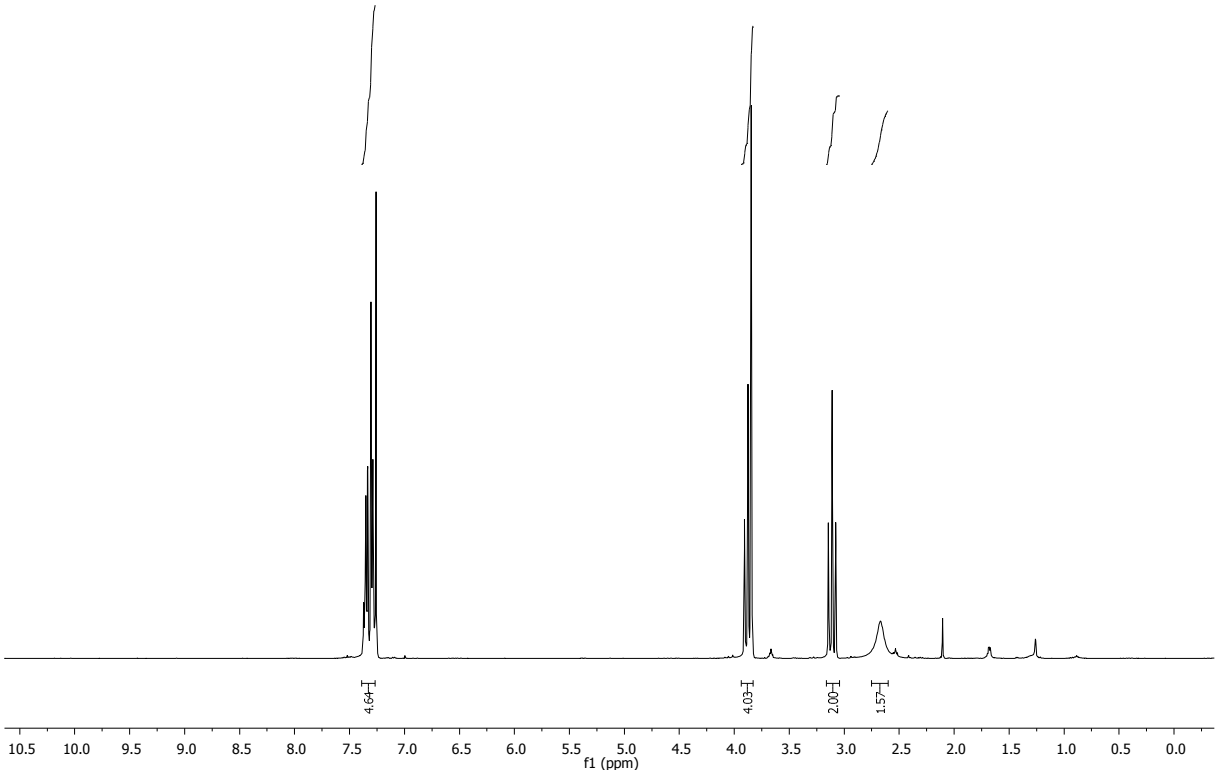
^{13}C NMR, 100 MHz, $CDCl_3$



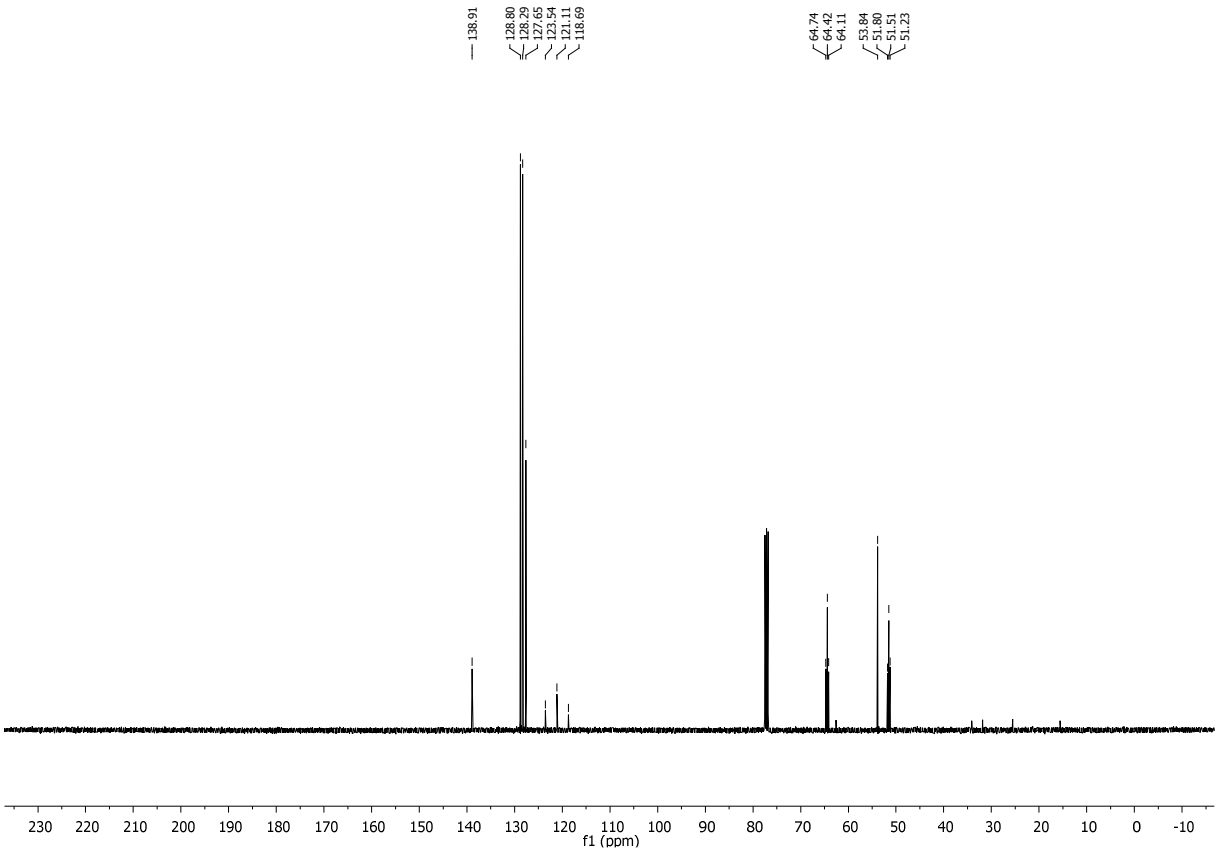
^{1}H NMR, 400 MHz, $CDCl_3$



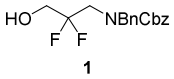
S-2



^{13}C NMR, 100 MHz, $CDCl_3$



^{1}H NMR, 400 MHz, $CDCl_3$



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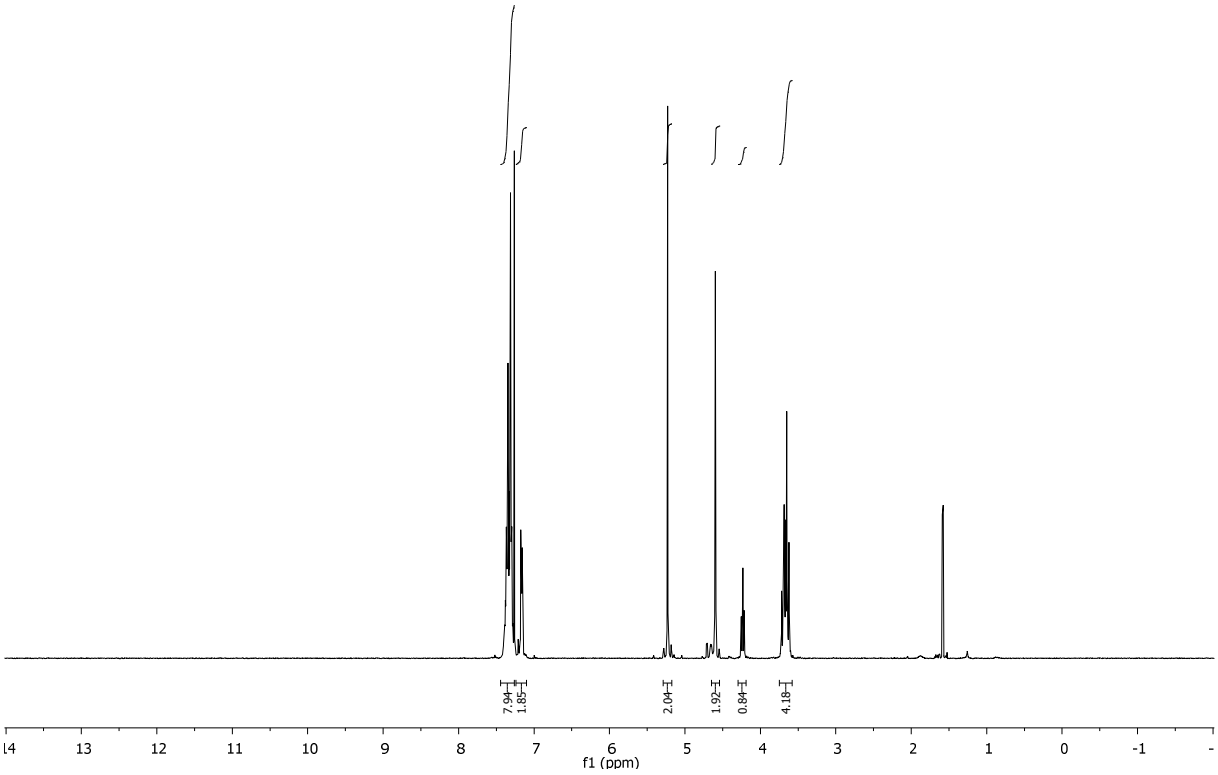
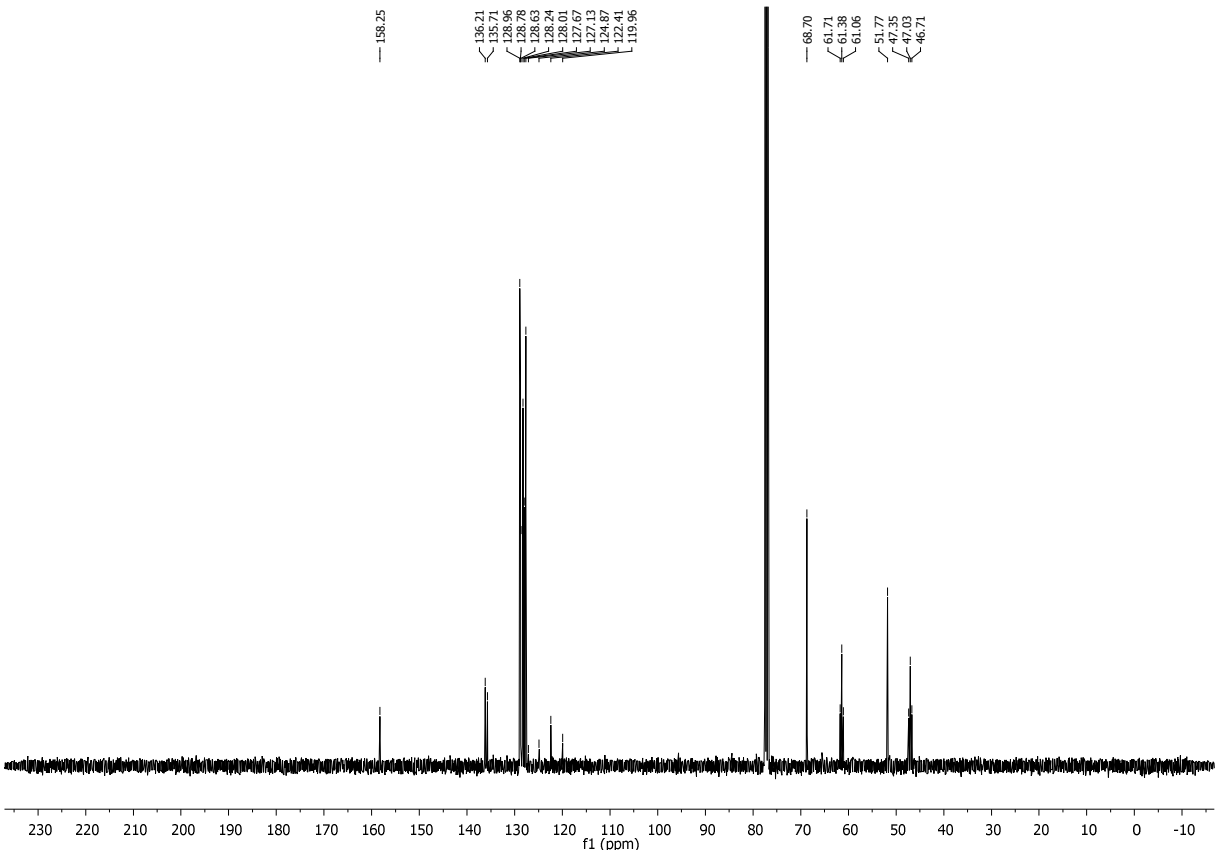
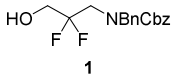


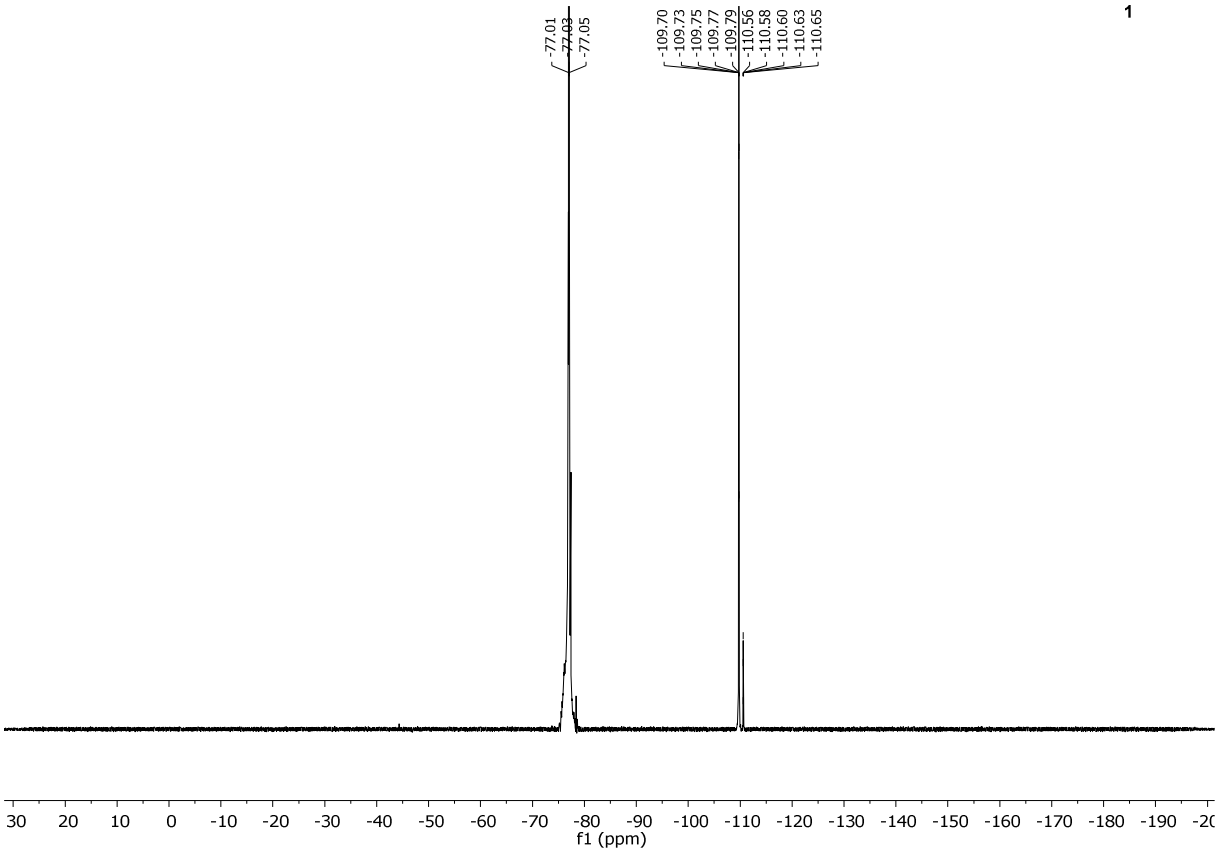
^{13}C NMR, 100 MHz, $CDCl_3$



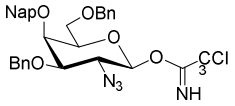
^{19}F NMR, 564 MHz,$CDCl_3$, 2,2,2-trifluoroethanol



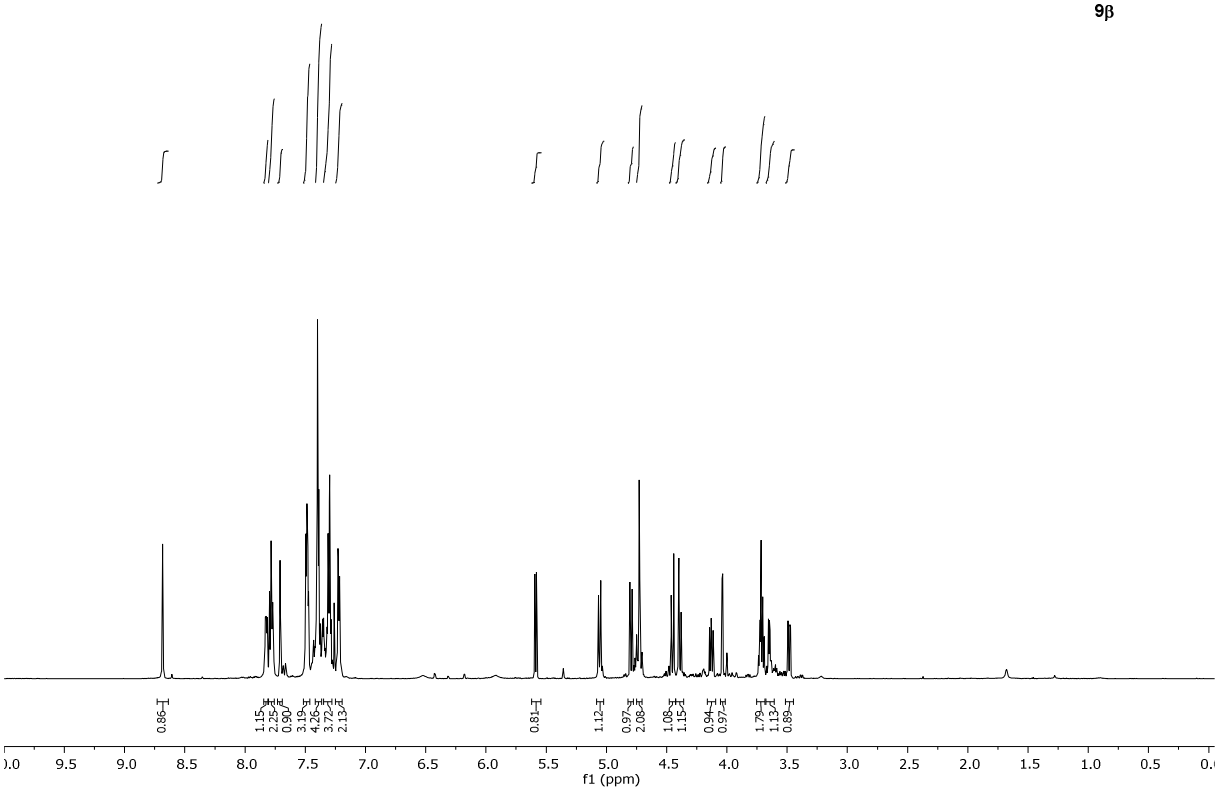
1



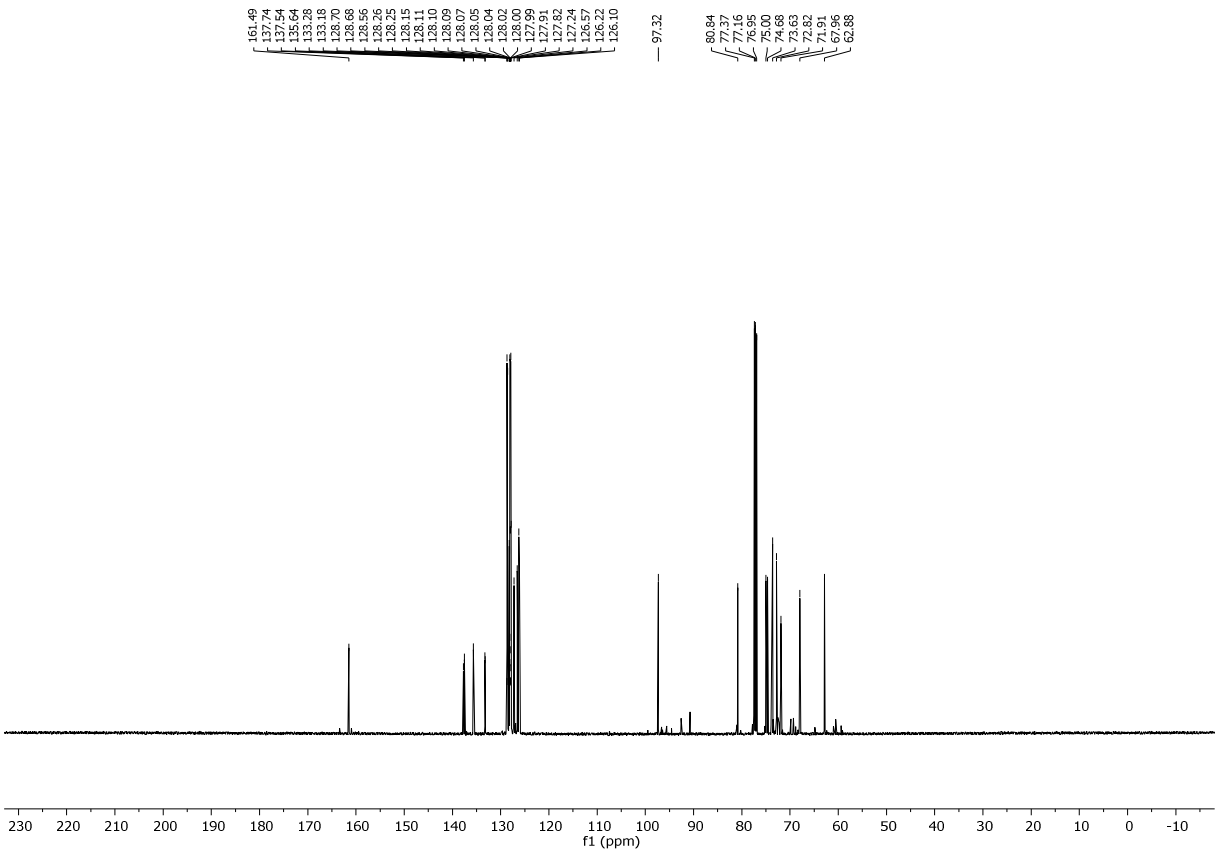
^{1}H NMR, 600 MHz, $CDCl_3$



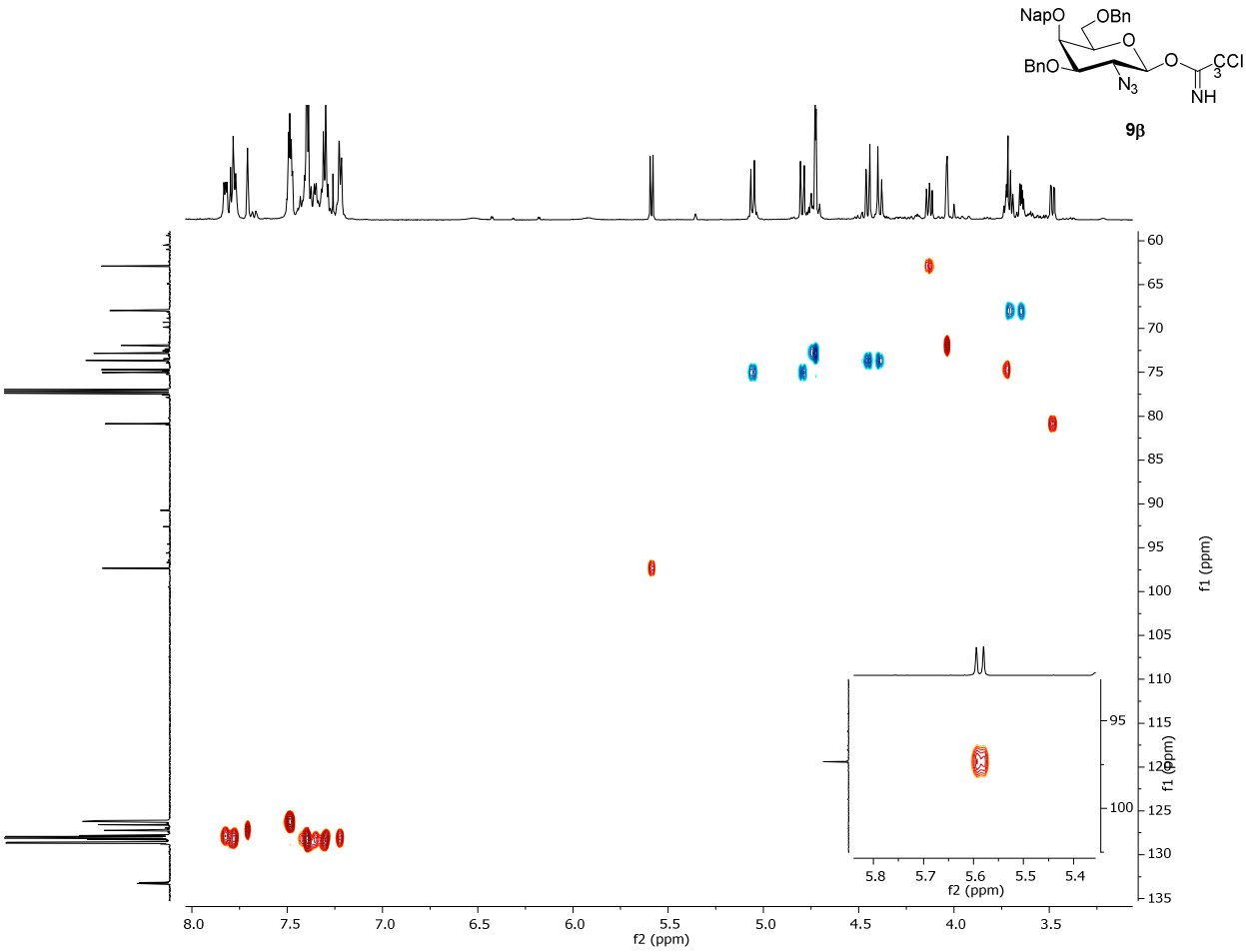
9β



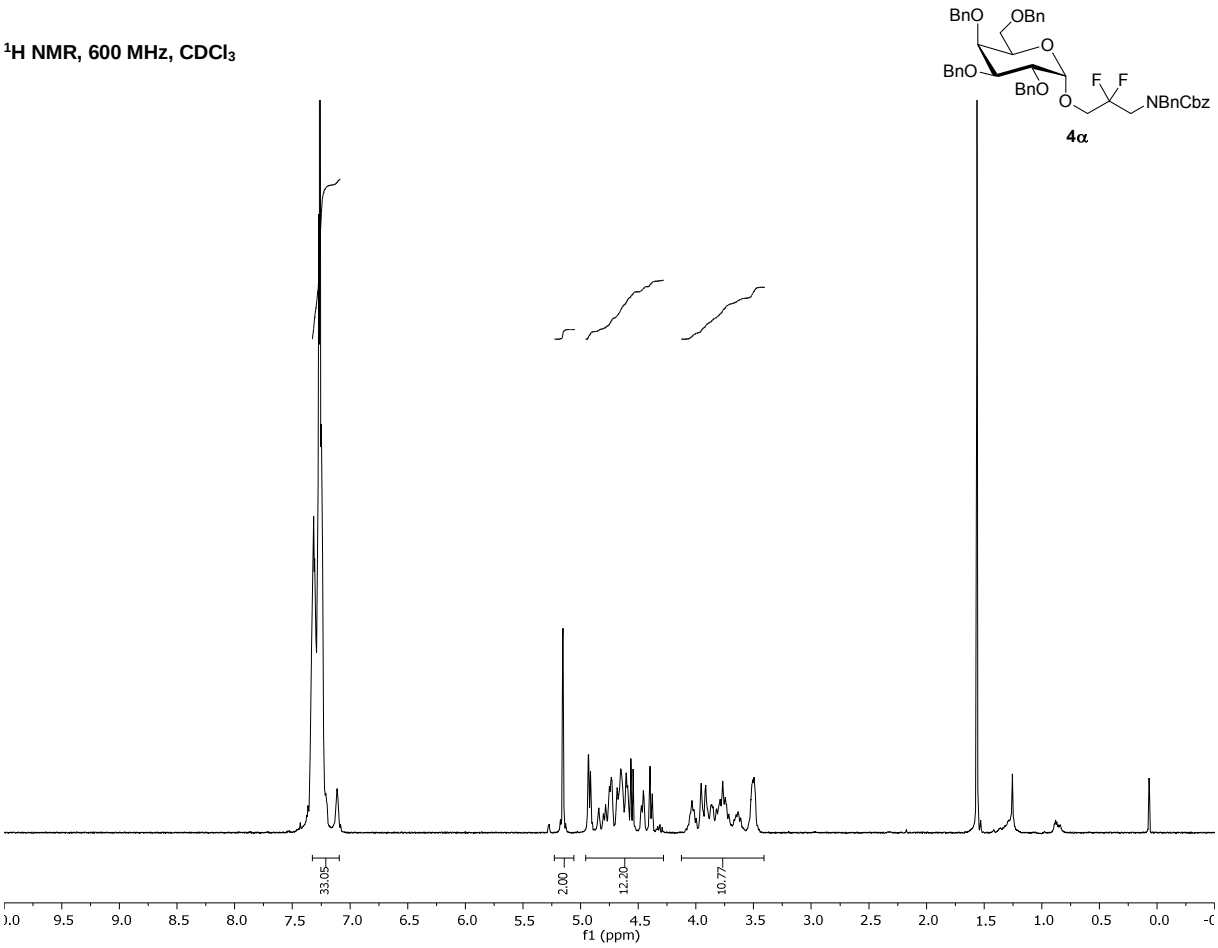
^{13}C NMR, 150 MHz, $CDCl_3$



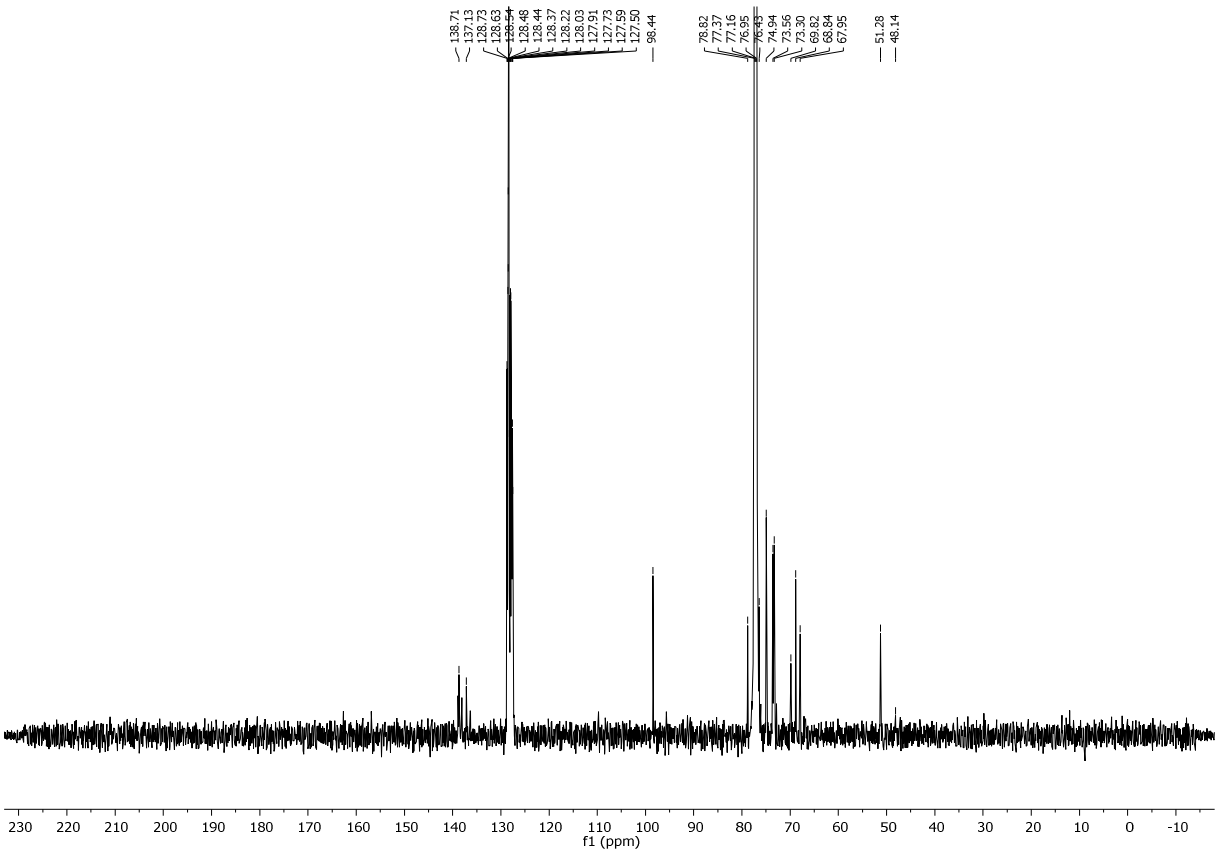
CH-HSQC NMR, 600 MHz, $CDCl_3$



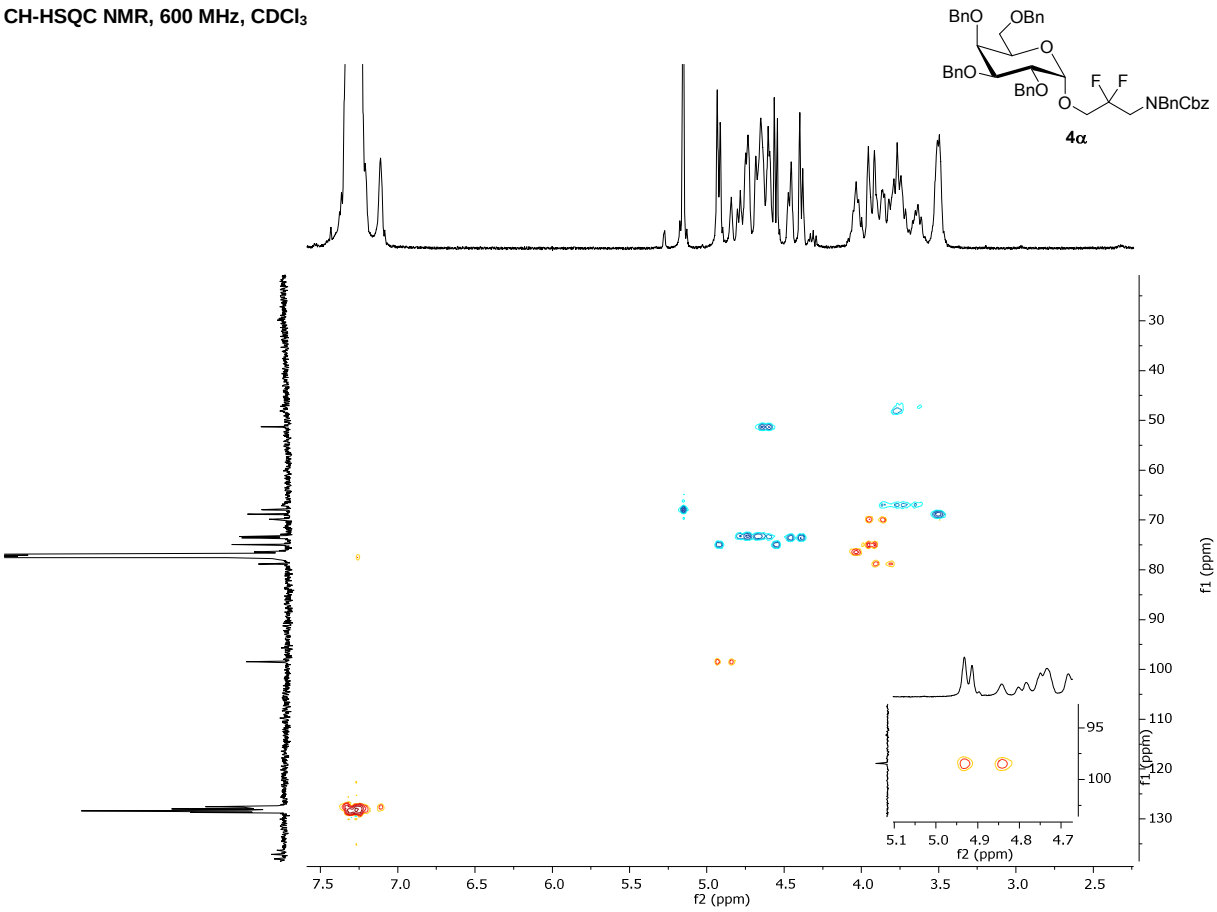
^{1}H NMR, 600 MHz, $CDCl_3$



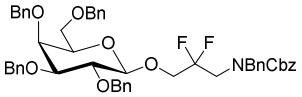
^{13}C NMR, 150 MHz, $CDCl_3$



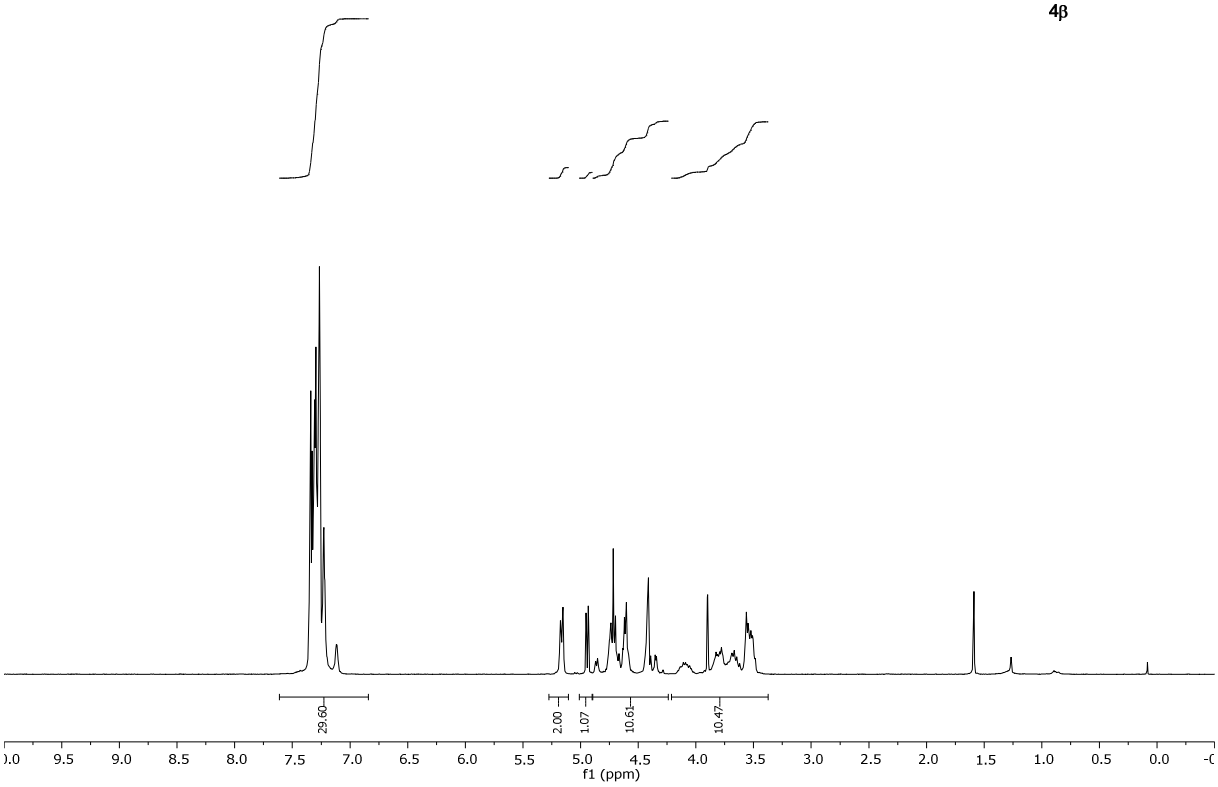
CH-HSQC NMR, 600 MHz, $CDCl_3$



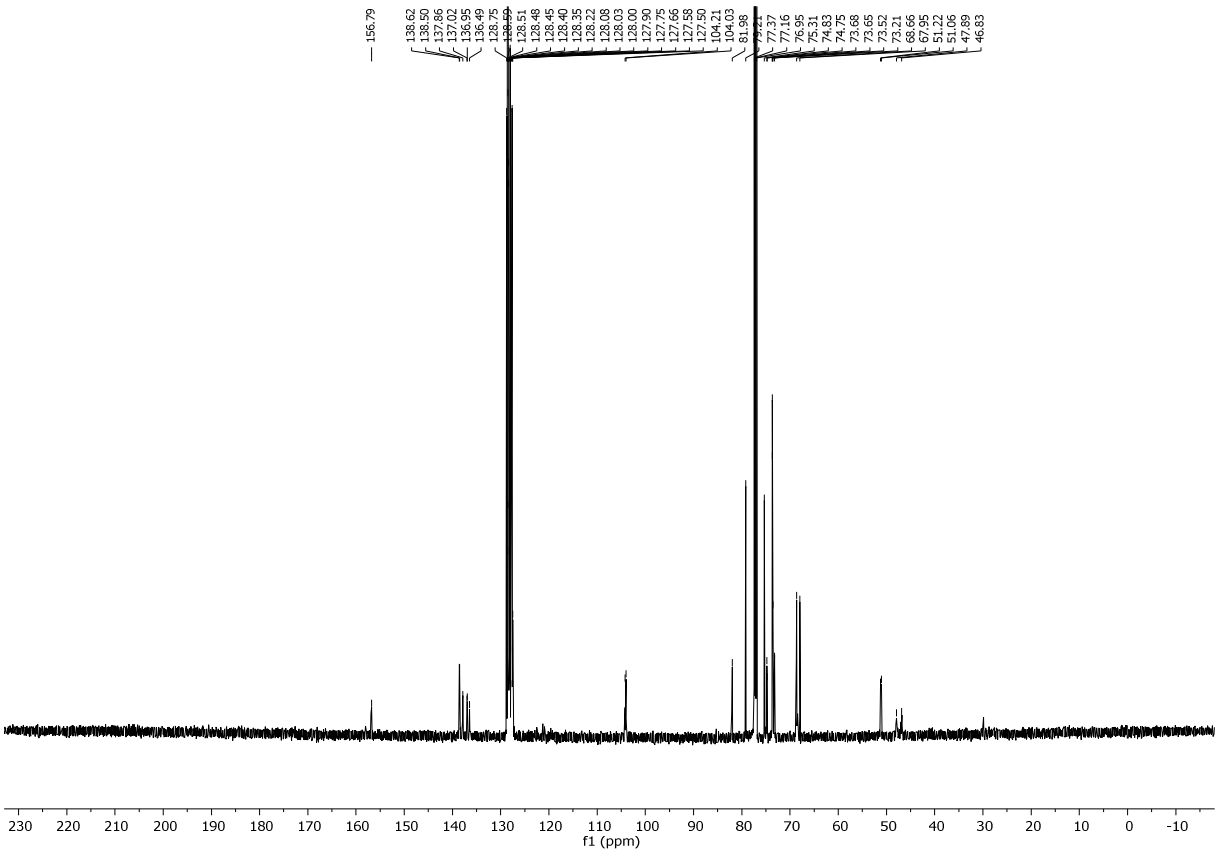
^{1}H NMR, 600 MHz, $CDCl_3$



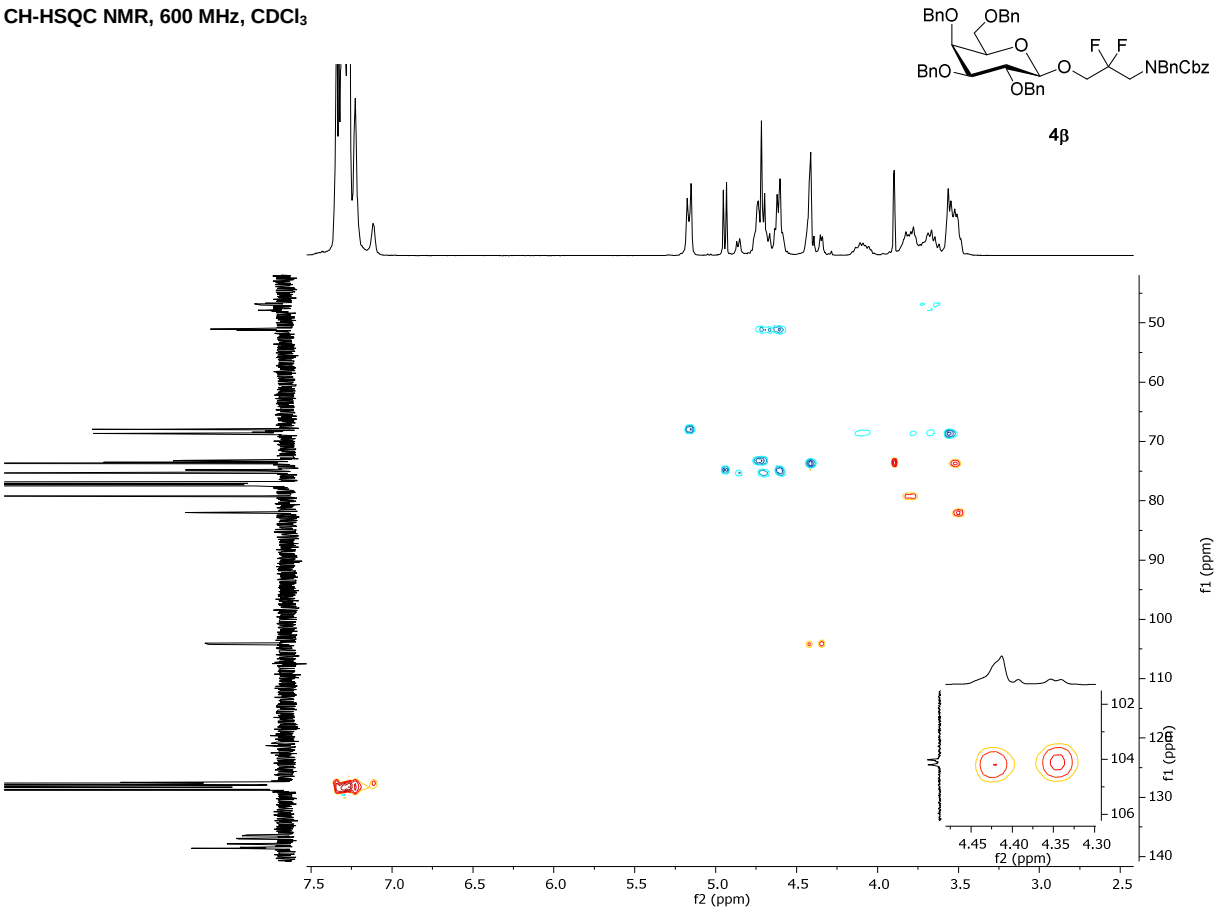
4β



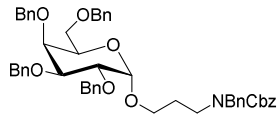
^{13}C NMR, 150 MHz, $CDCl_3$



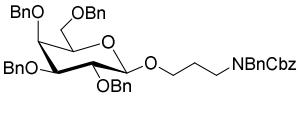
CH-HSQC NMR, 600 MHz, $CDCl_3$



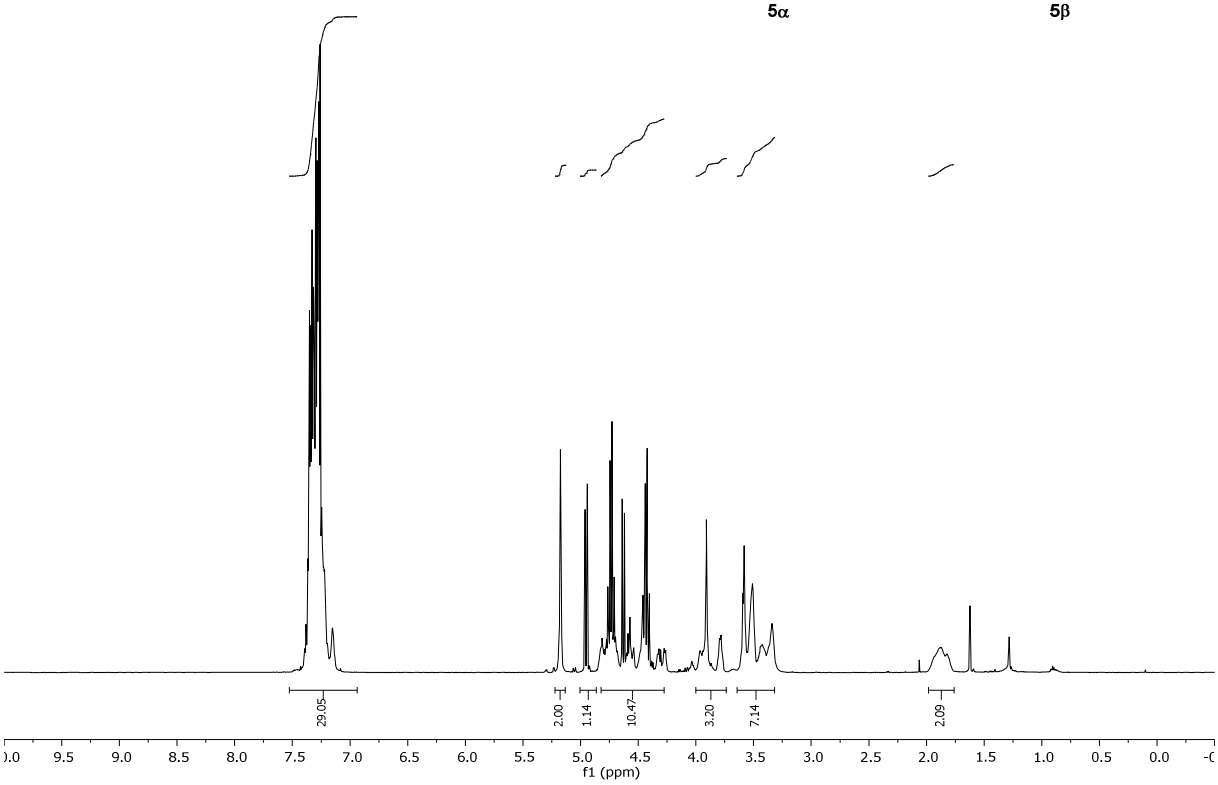
^{1}H NMR, 600 MHz, $CDCl_3$



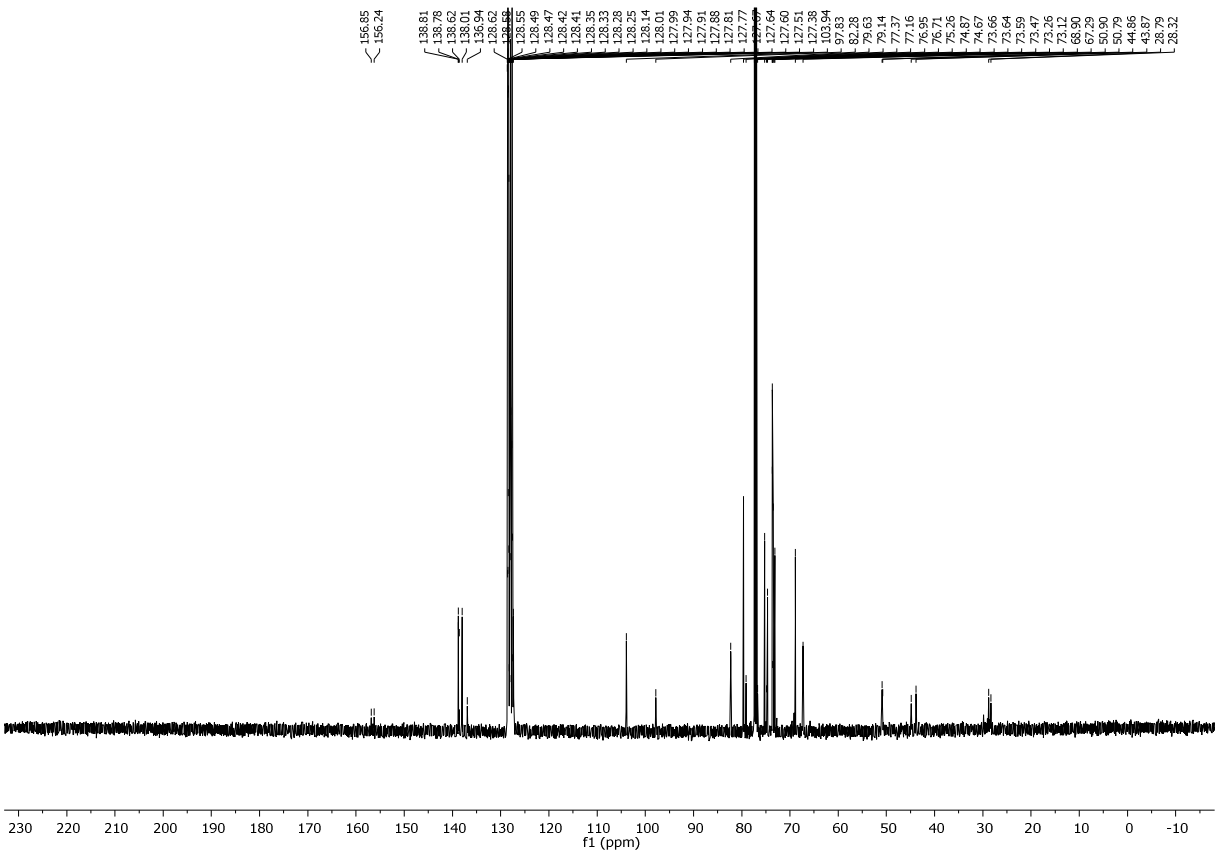
5α



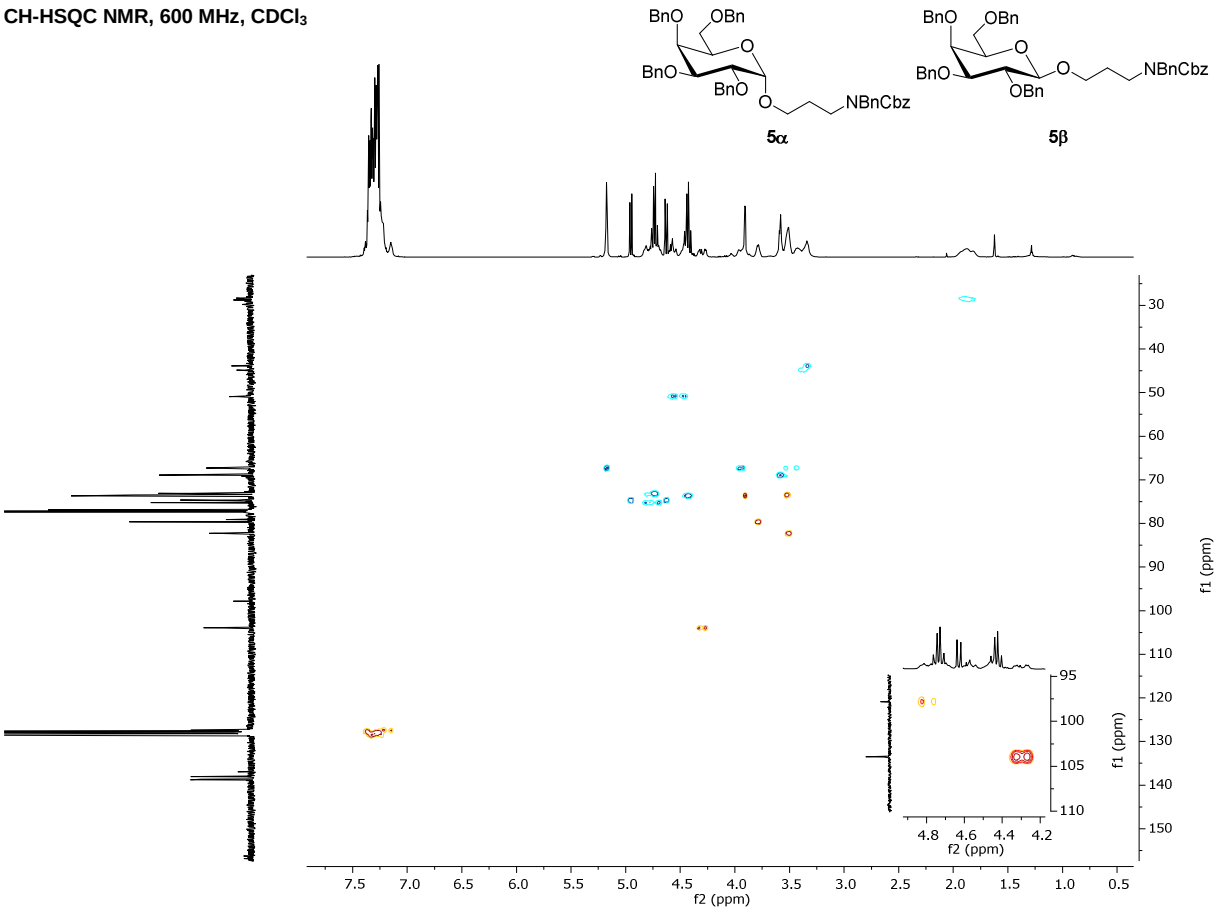
5β



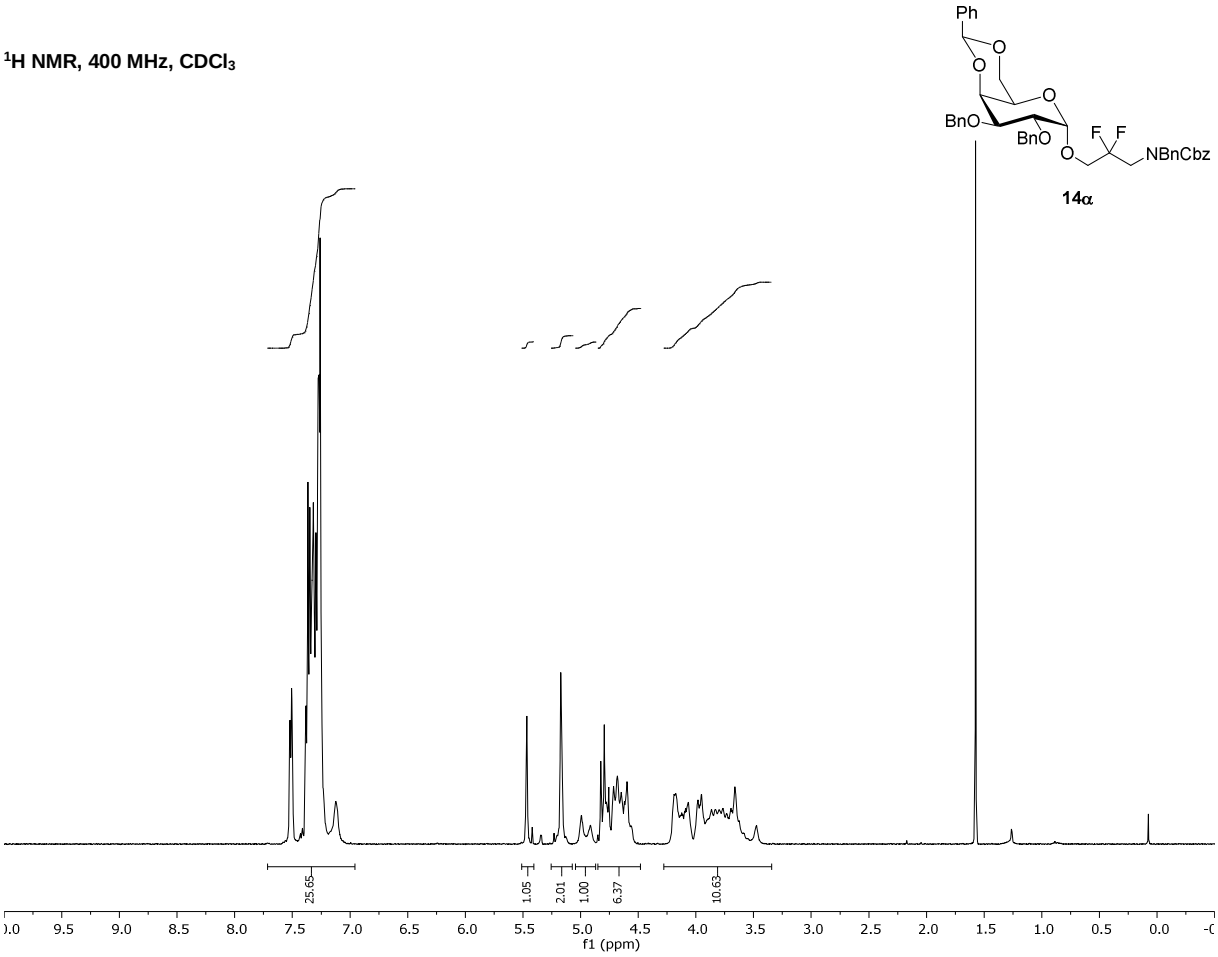
^{13}C NMR, 150 MHz, $CDCl_3$



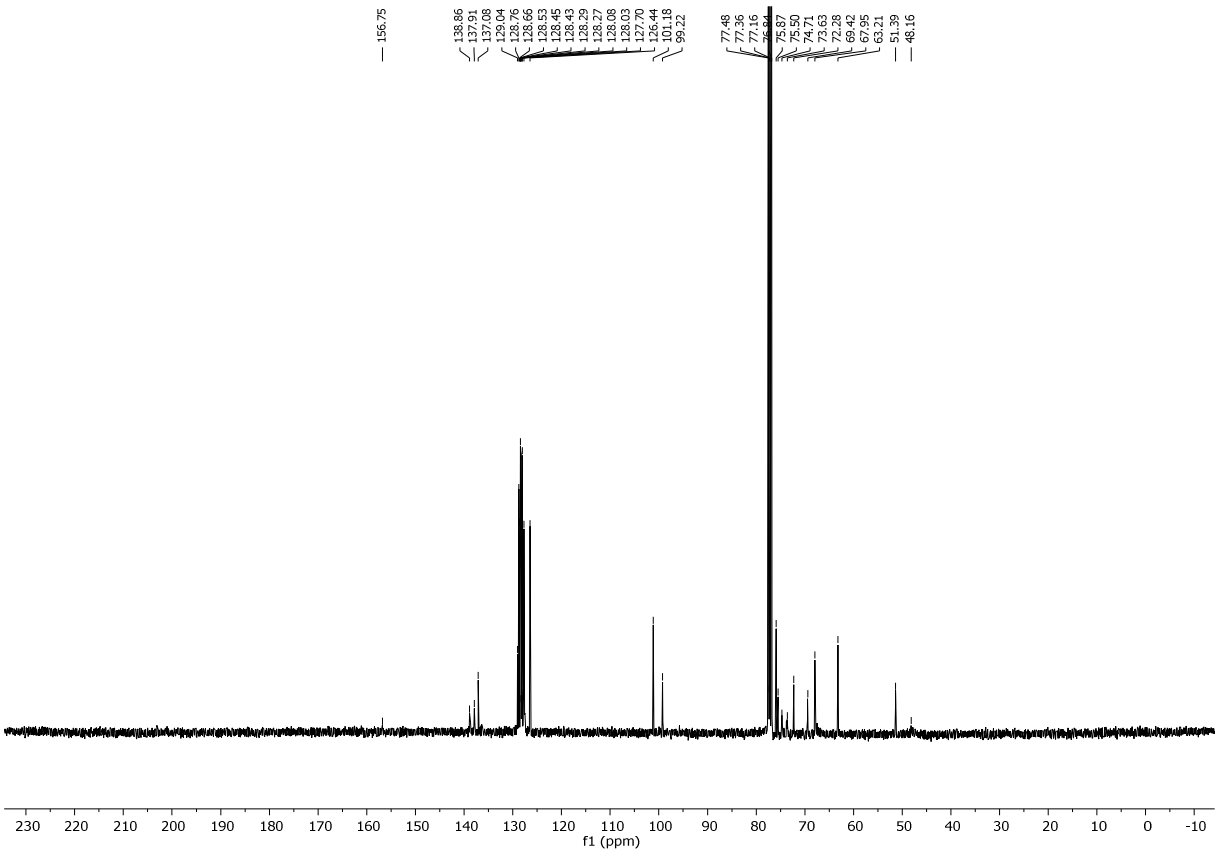
CH-HSQC NMR, 600 MHz, $CDCl_3$



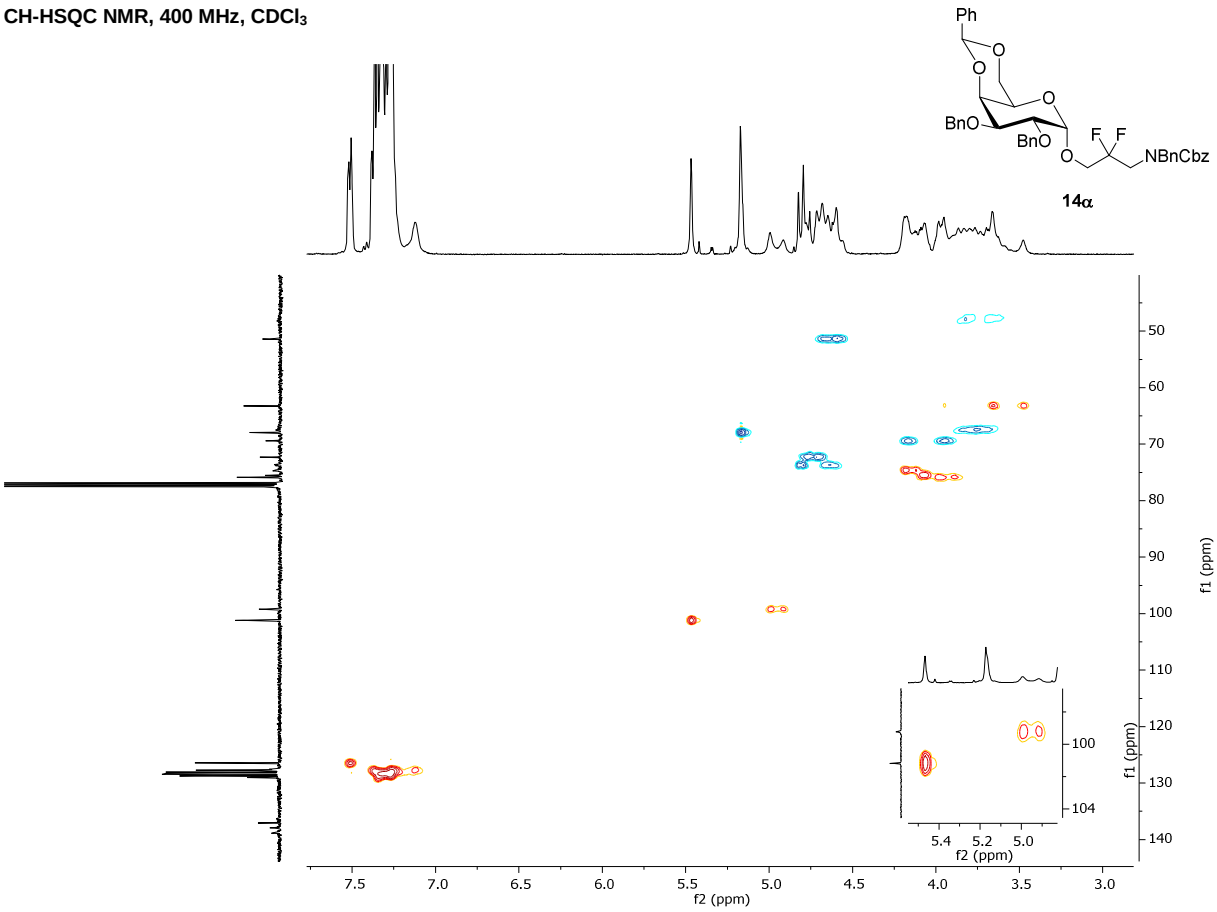
^{1}H NMR, 400 MHz, $CDCl_3$



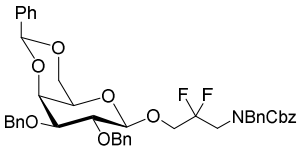
^{13}C NMR, 100 MHz, $CDCl_3$



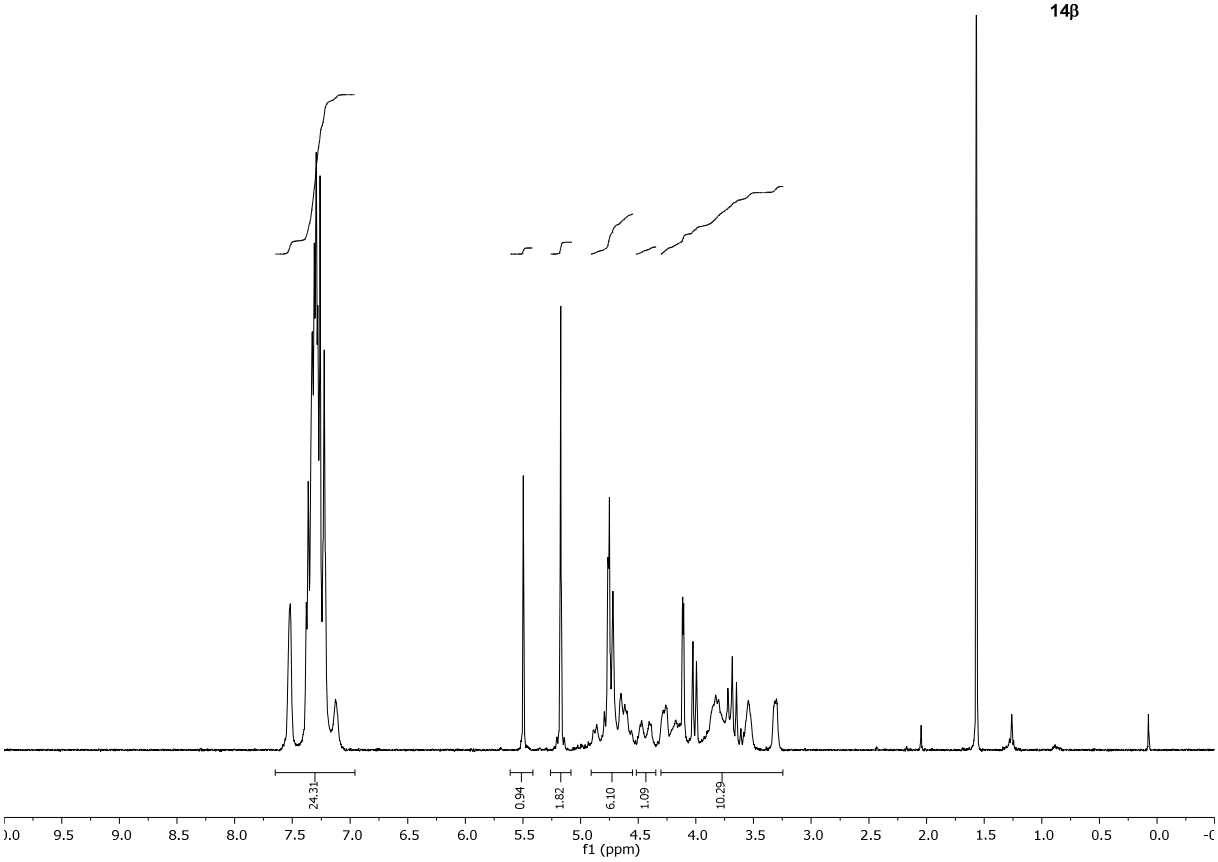
CH-HSQC NMR, 400 MHz, $CDCl_3$



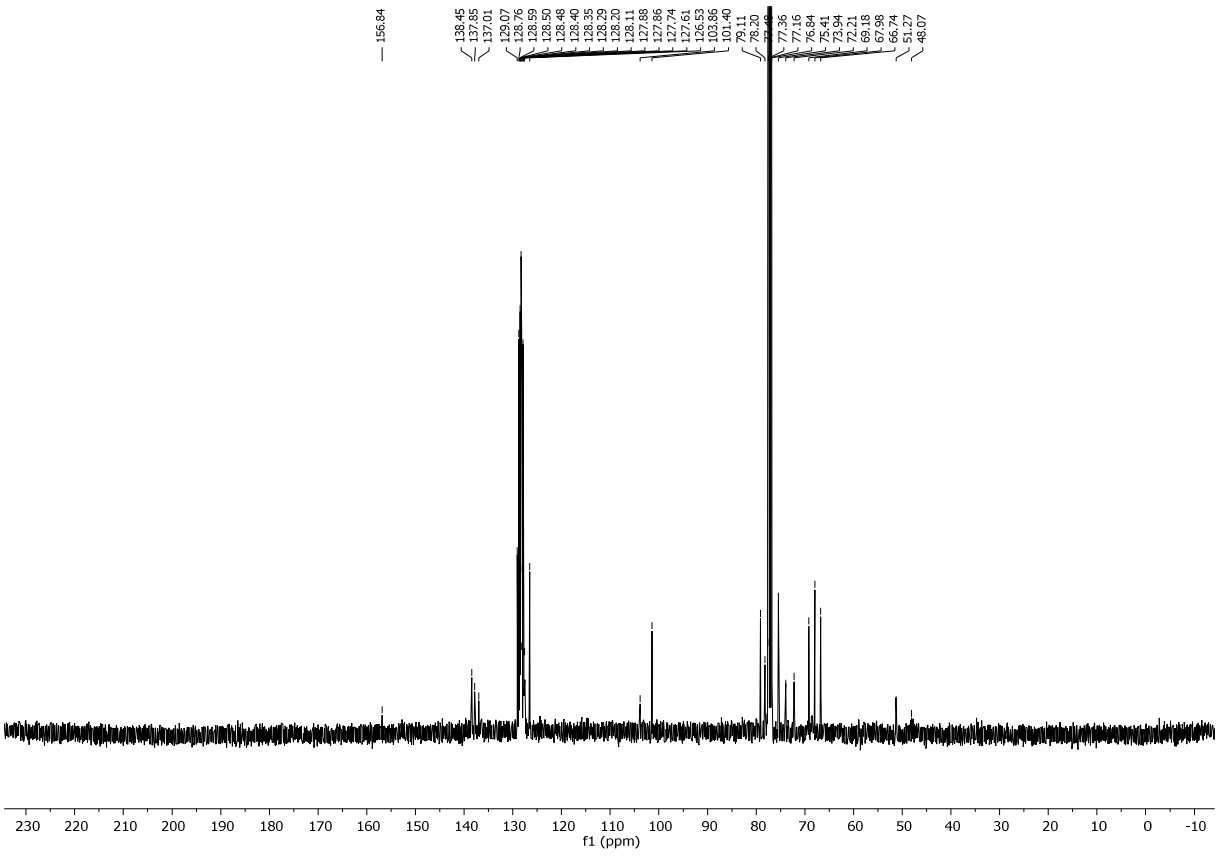
^{1}H NMR, 400 MHz, $CDCl_3$



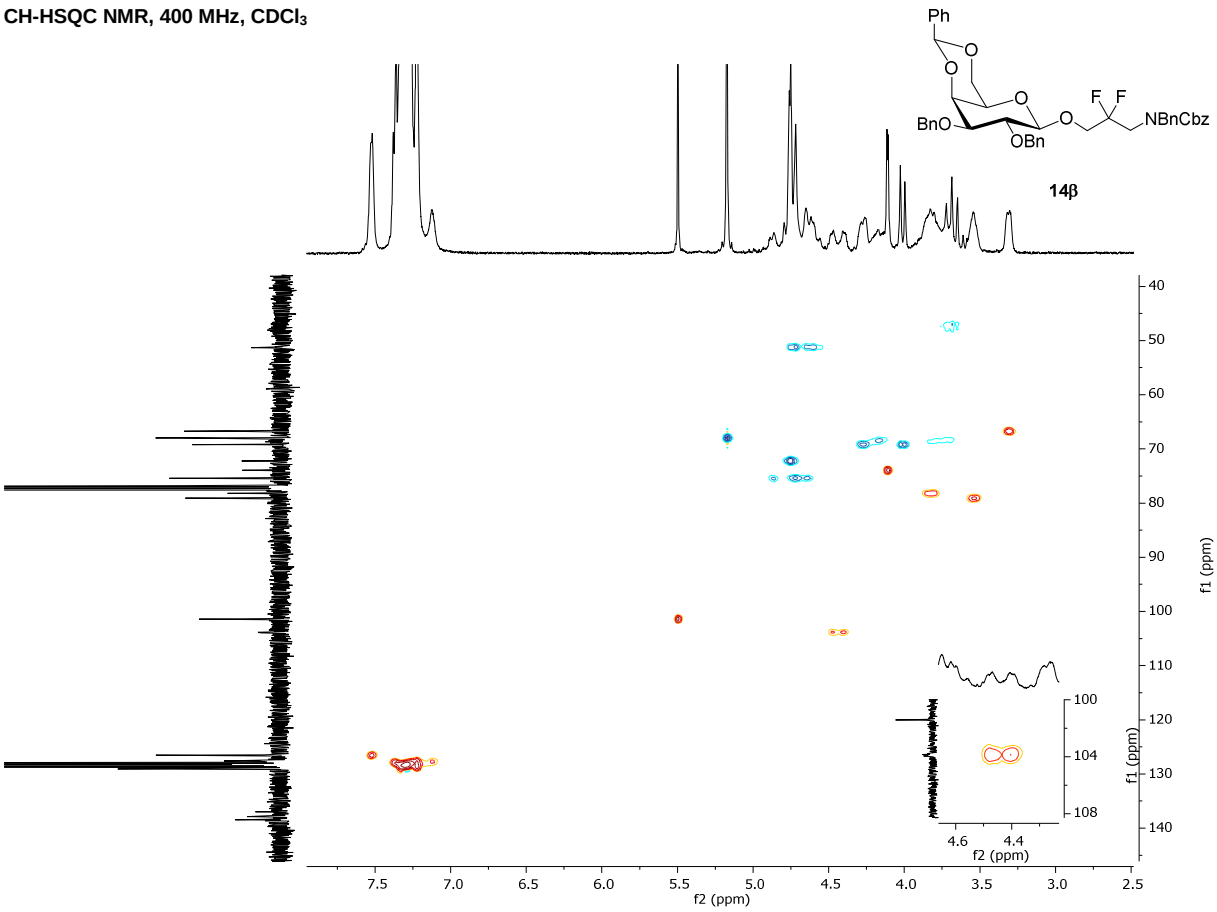
14β



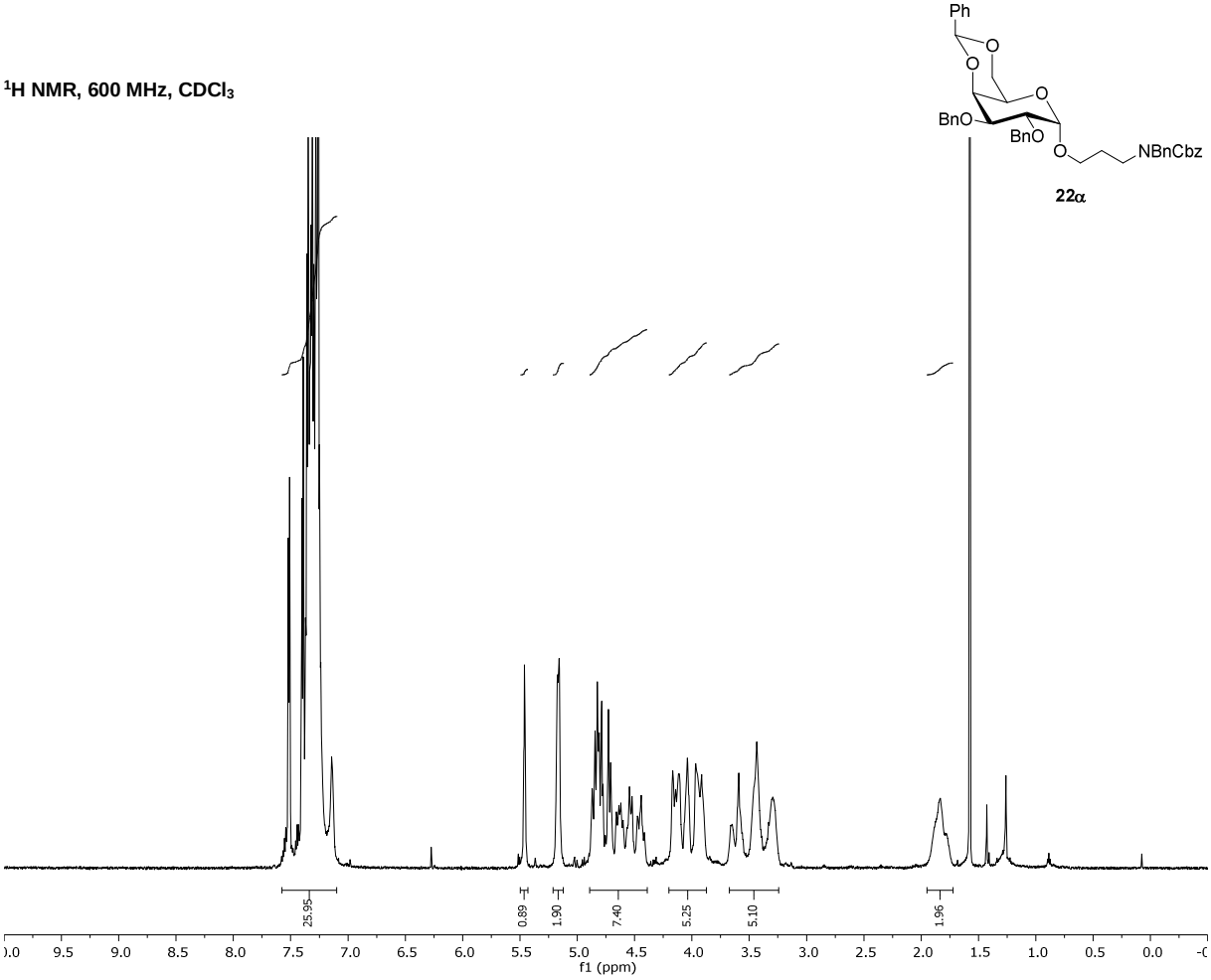
^{13}C NMR, 100 MHz, $CDCl_3$



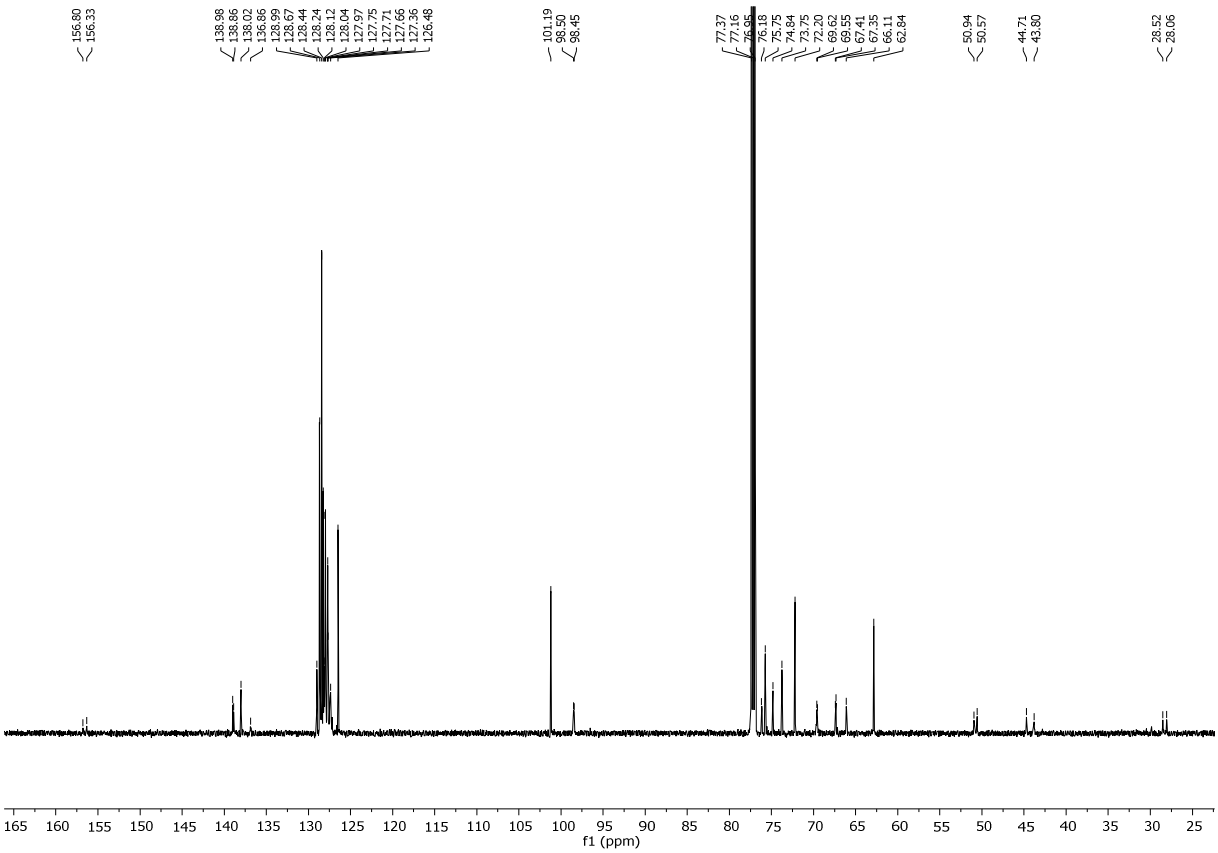
CH-HSQC NMR, 400 MHz, $CDCl_3$



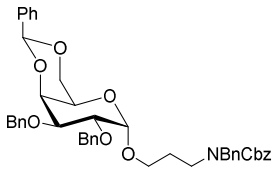
^{1}H NMR, 600 MHz, $CDCl_3$



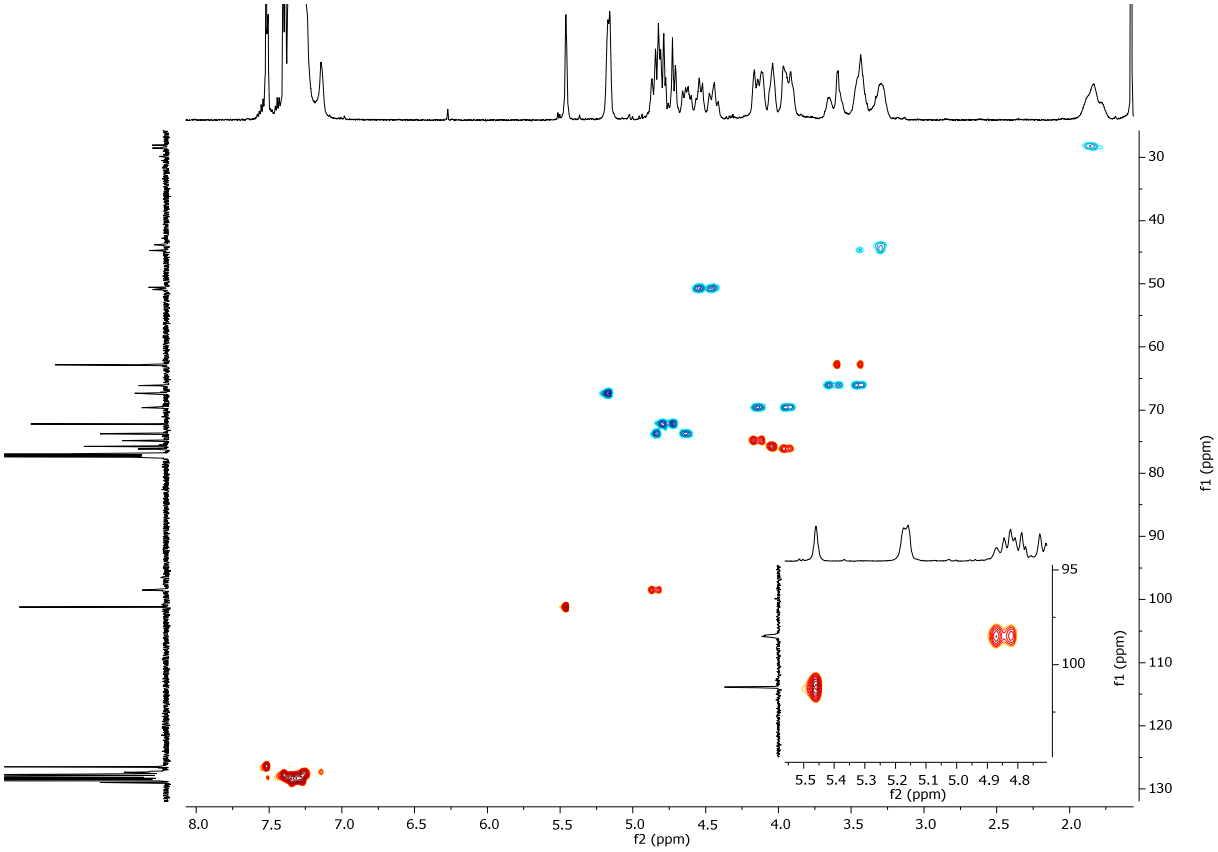
^{13}C NMR, 150 MHz, $CDCl_3$



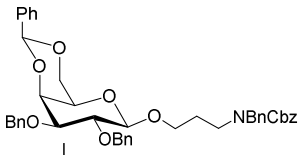
CH-HSQC NMR, 600 MHz, $CDCl_3$



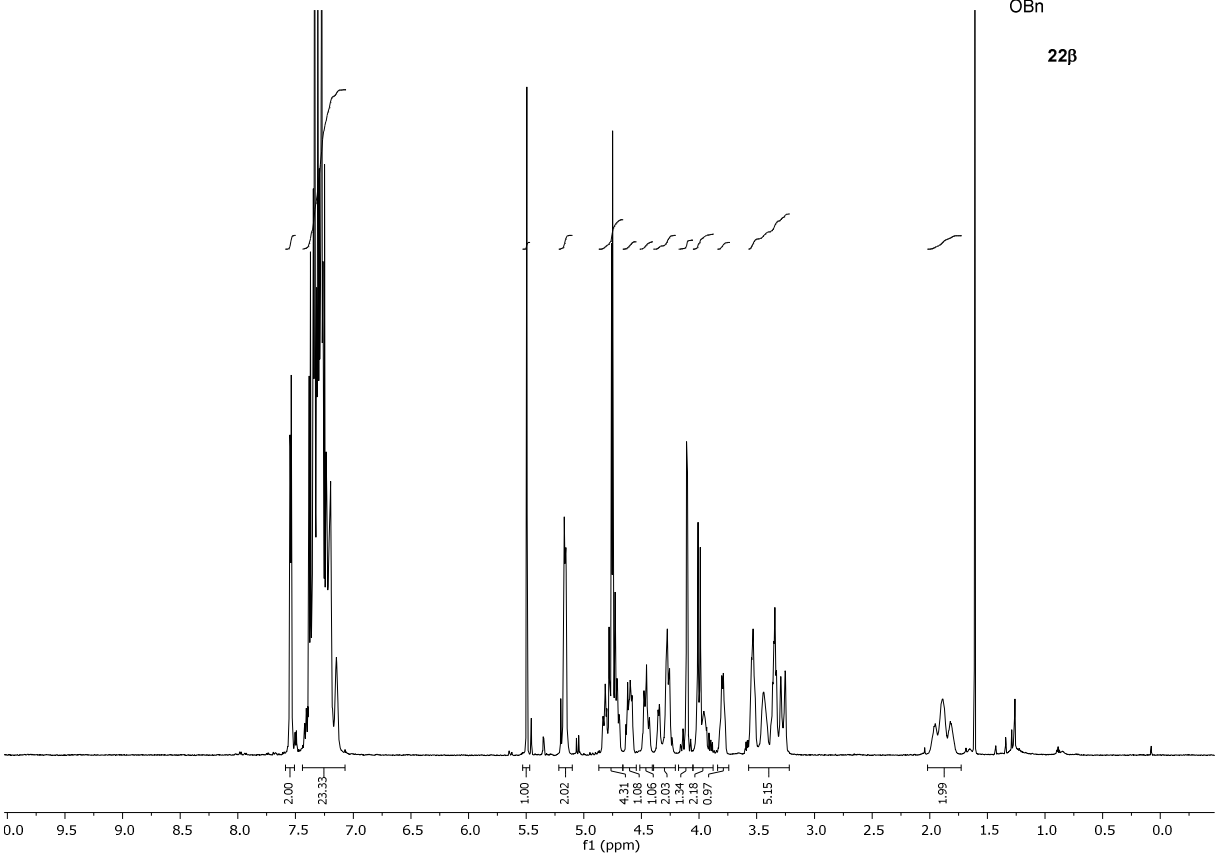
22α



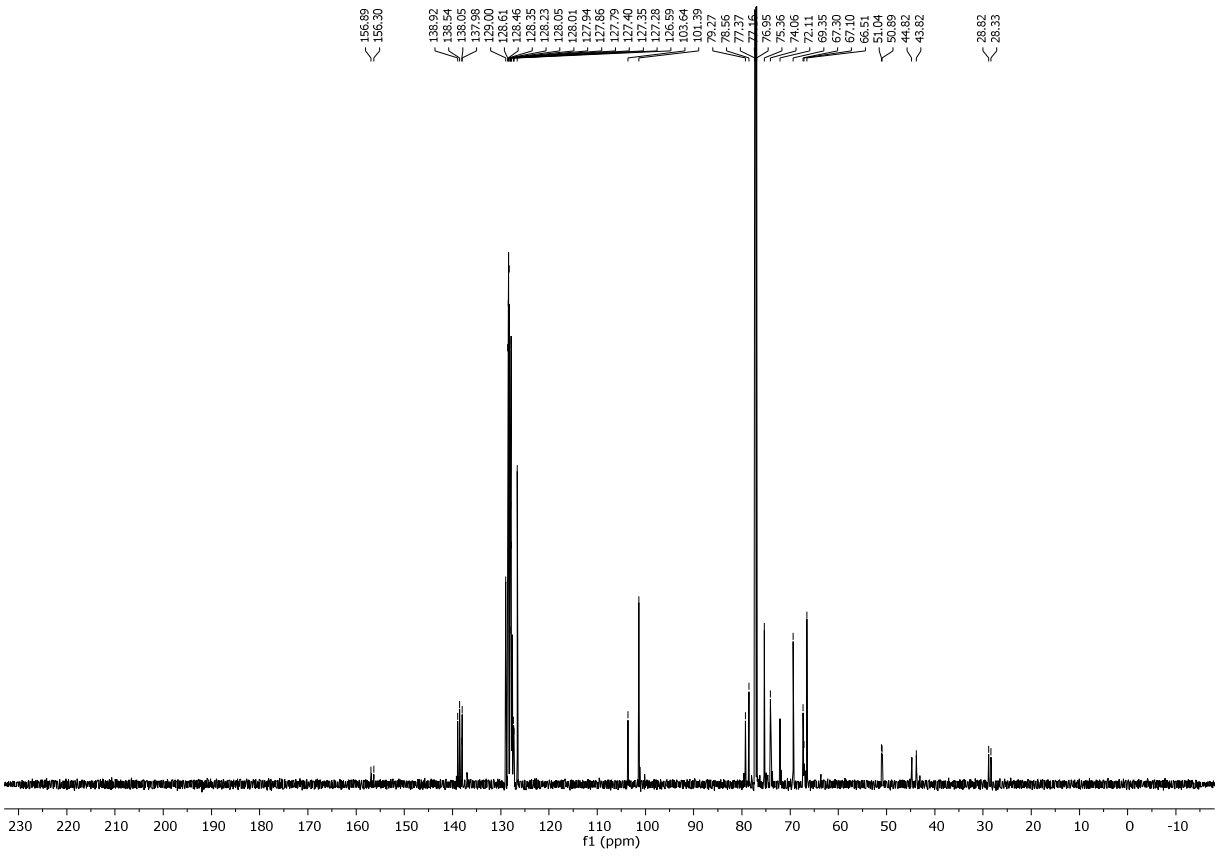
^{1}H NMR, 600 MHz, $CDCl_3$



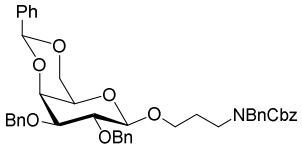
22β



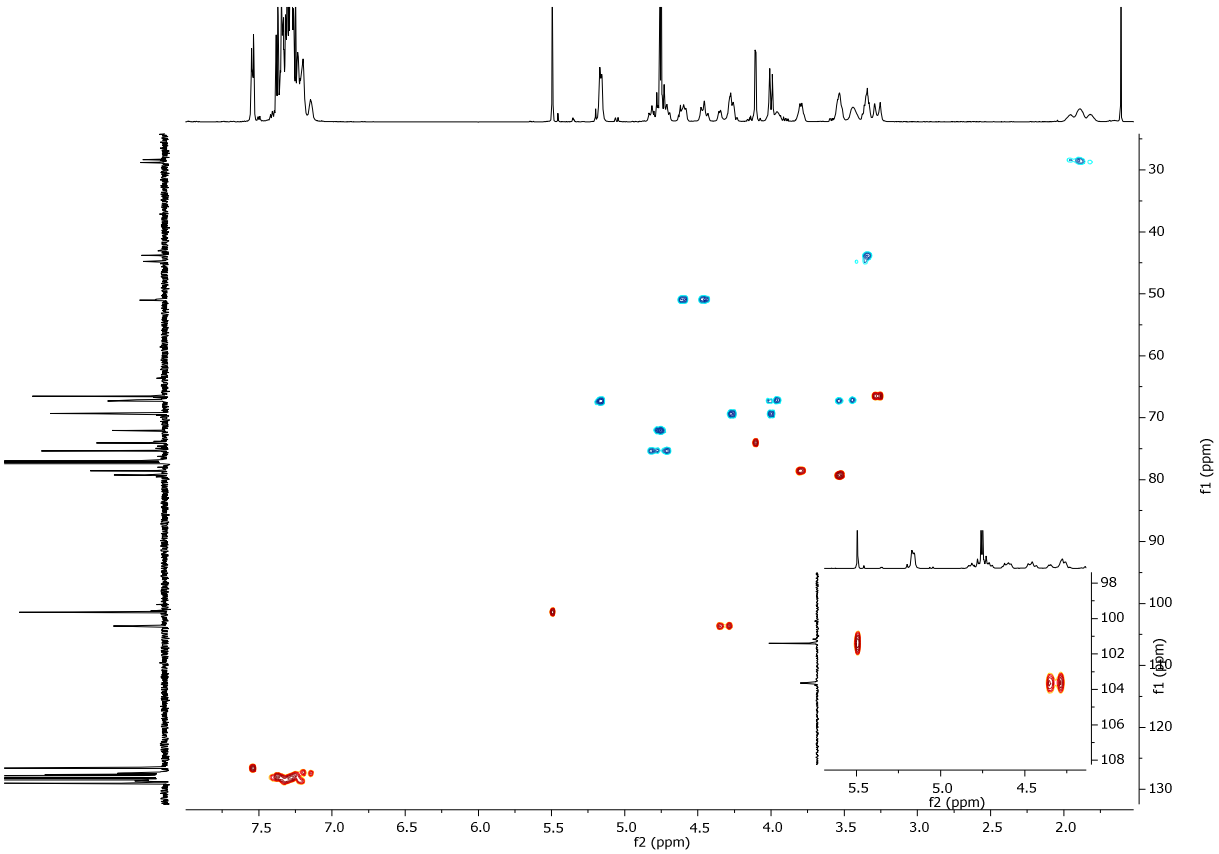
^{13}C NMR, 150 MHz, $CDCl_3$



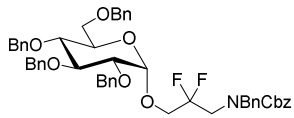
CH-HSQC NMR, 600 MHz, $CDCl_3$



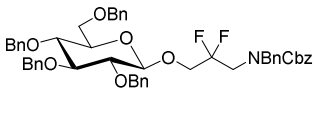
22β



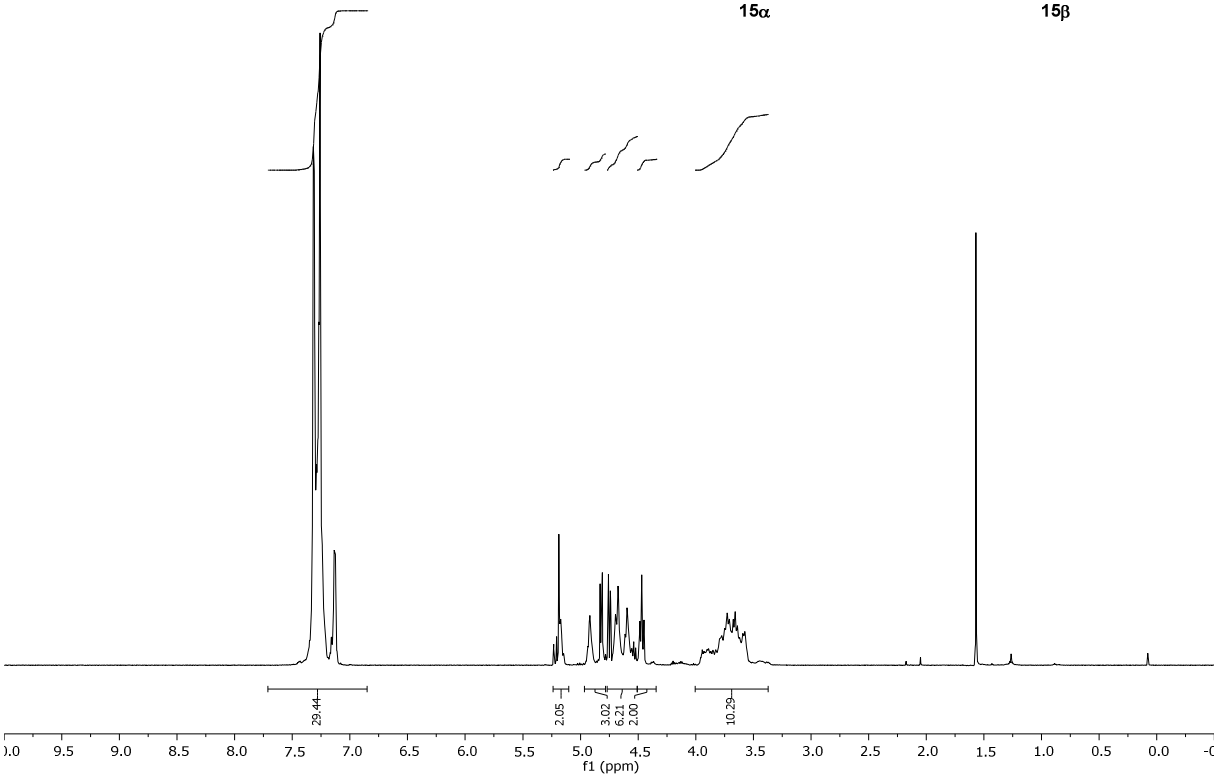
^{1}H NMR, 600 MHz, $CDCl_3$



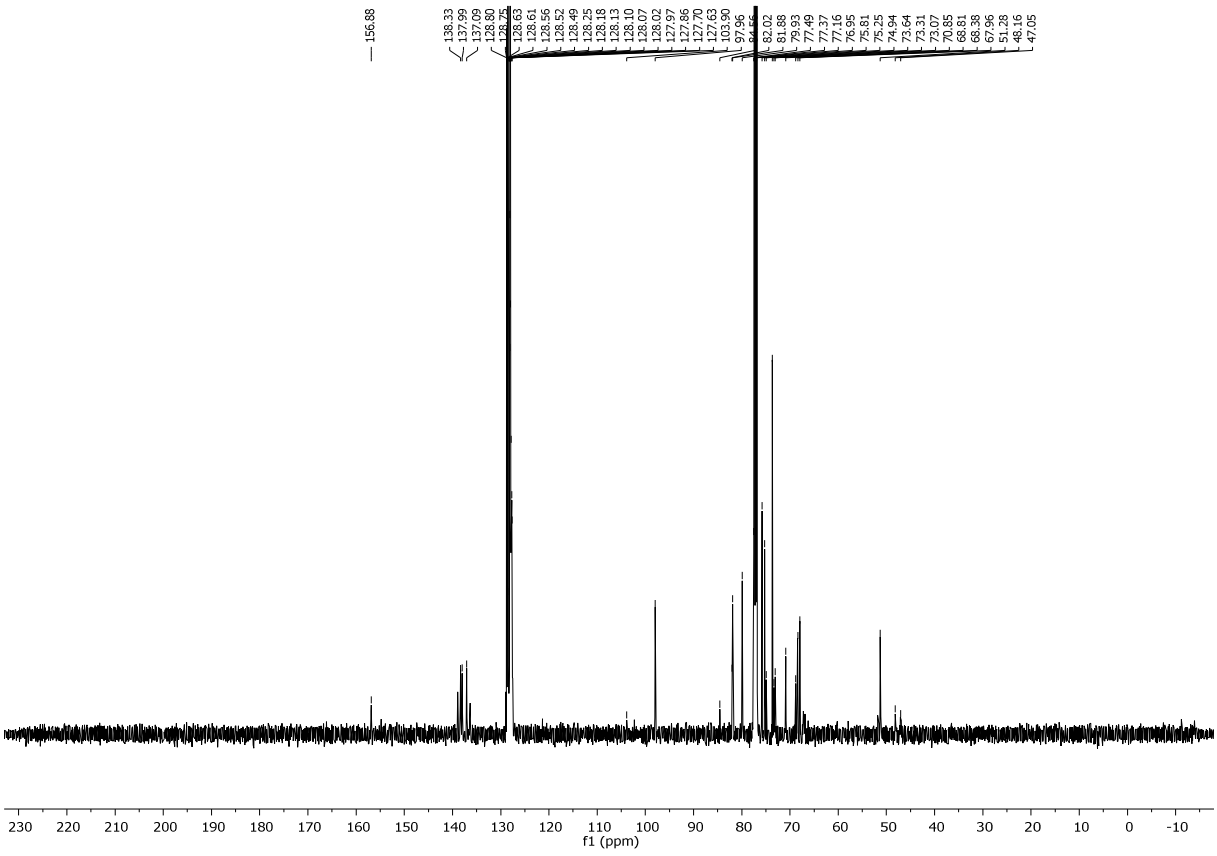
15α



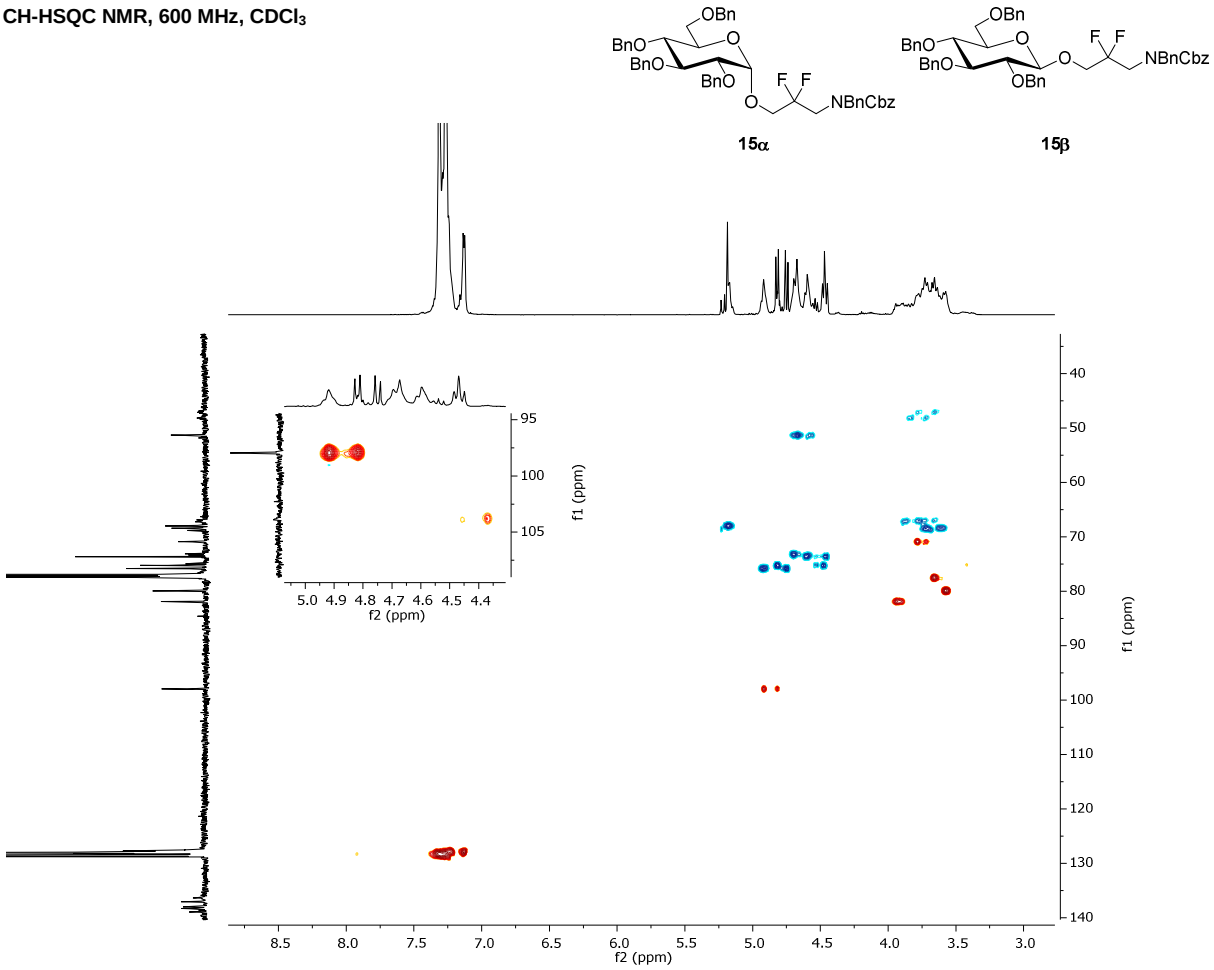
15β



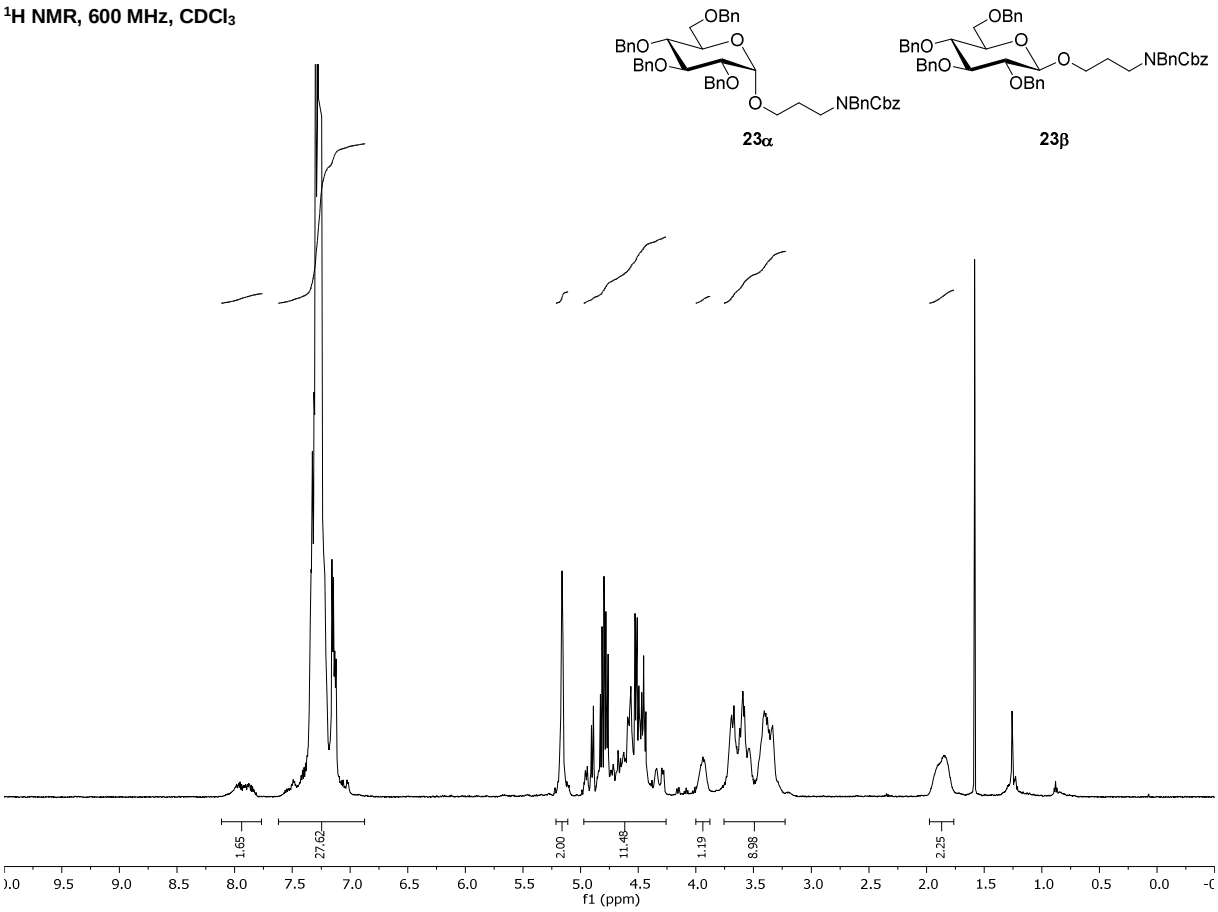
^{13}C NMR, 150 MHz, $CDCl_3$



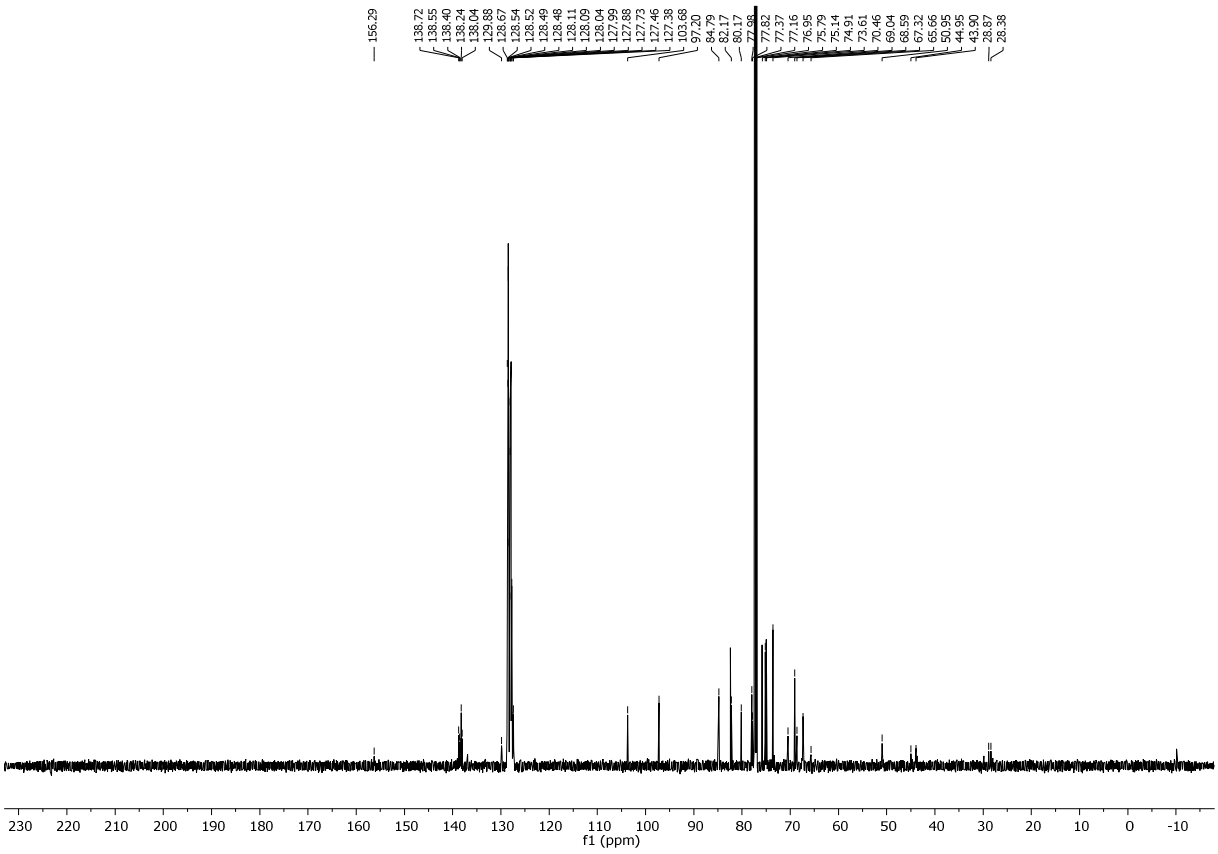
CH-HSQC NMR, 600 MHz, $CDCl_3$



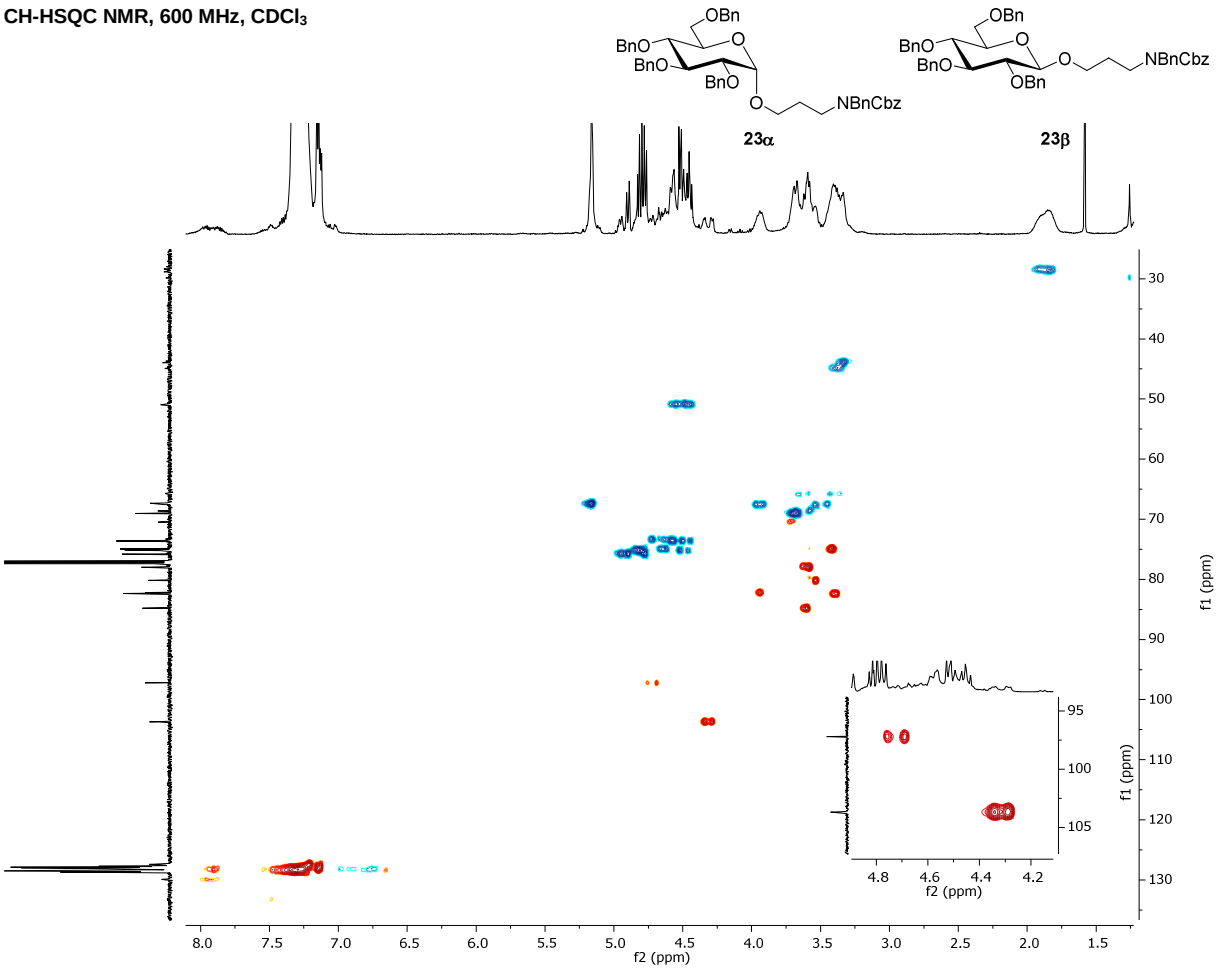
^{1}H NMR, 600 MHz, $CDCl_3$



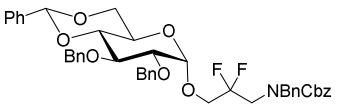
^{13}C NMR, 150 MHz, $CDCl_3$



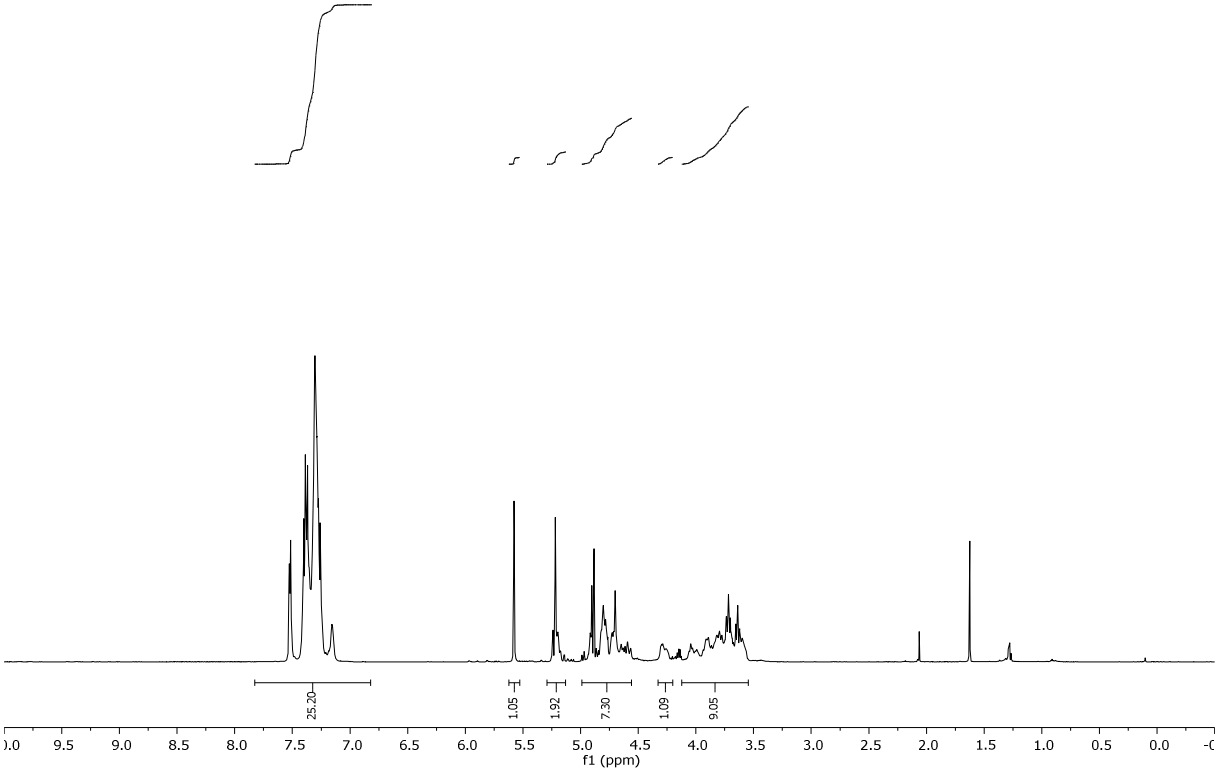
CH-HSQC NMR, 600 MHz, $CDCl_3$



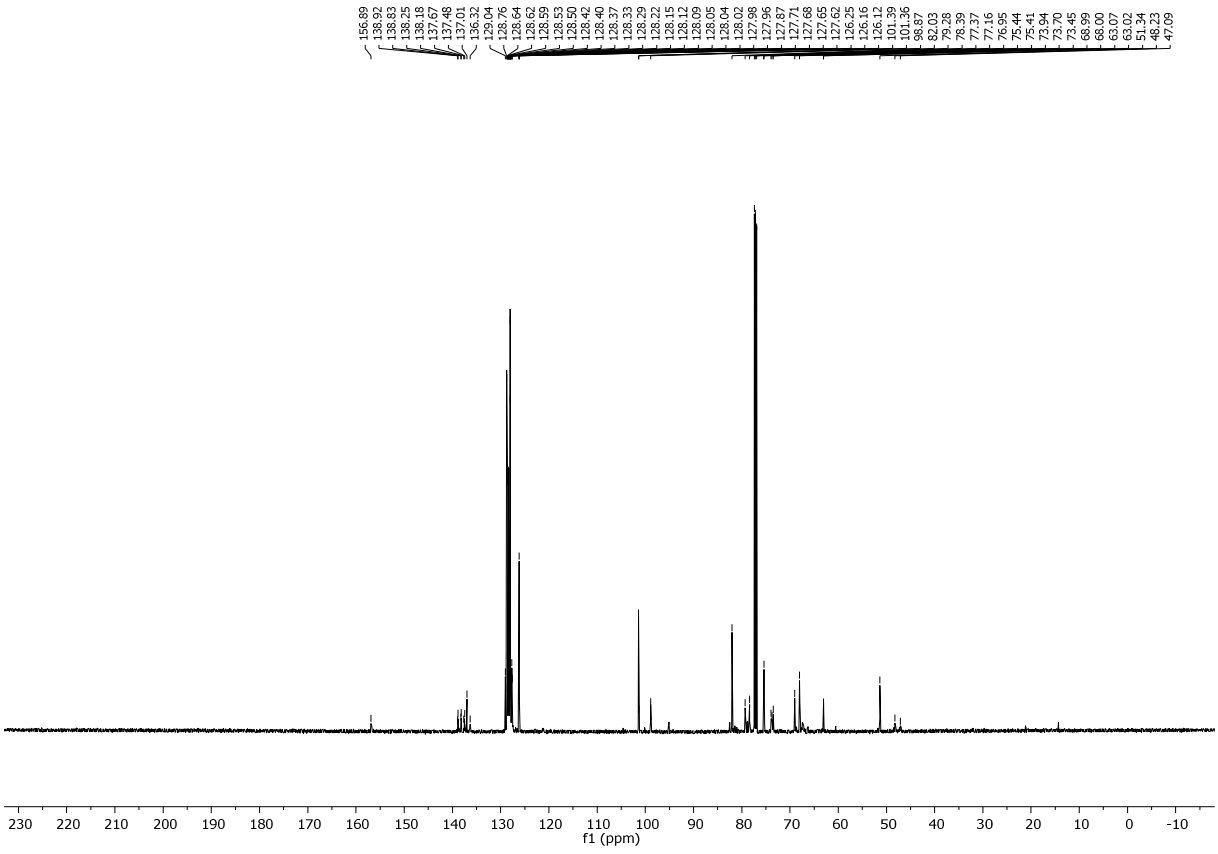
^{1}H NMR, 600 MHz, $CDCl_3$



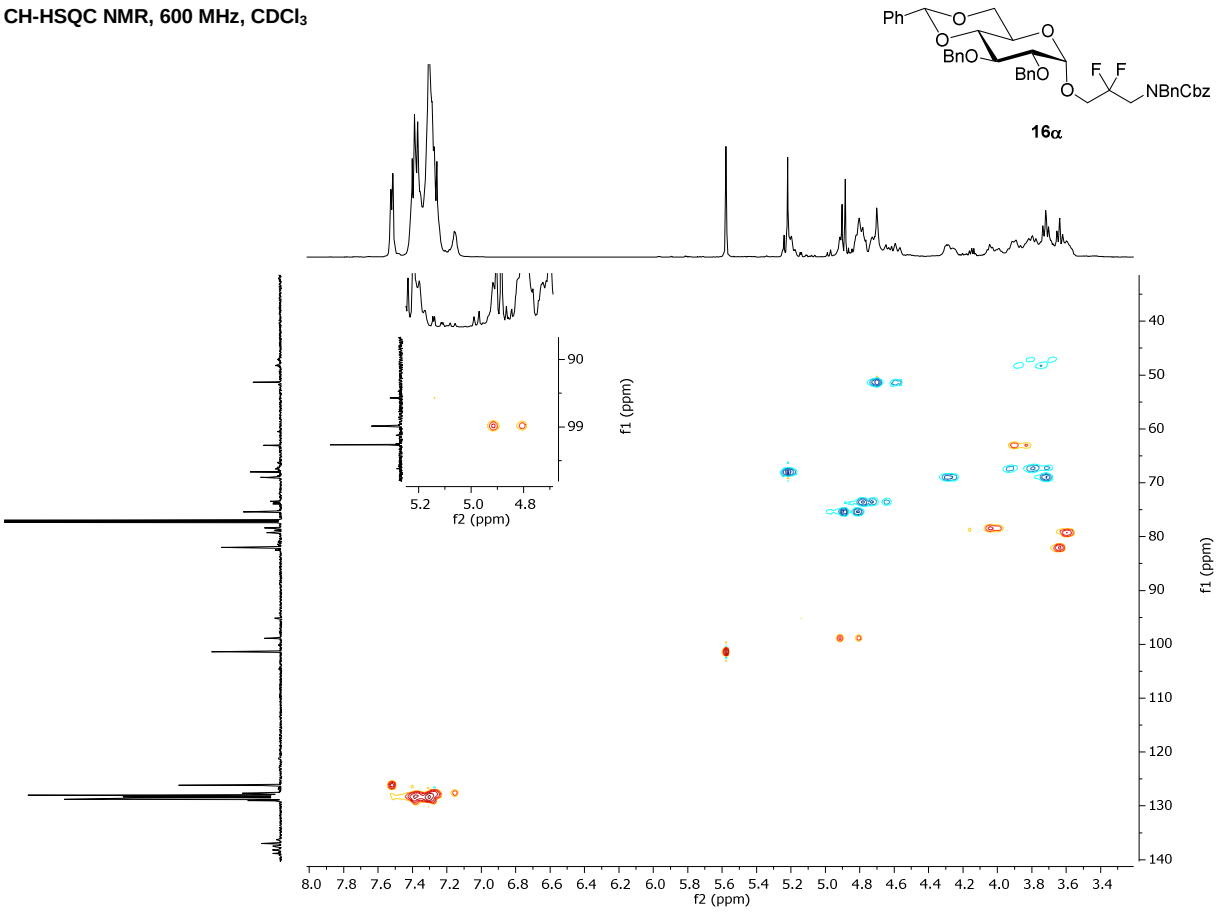
16α



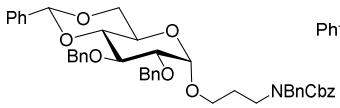
^{13}C NMR, 150 MHz, $CDCl_3$



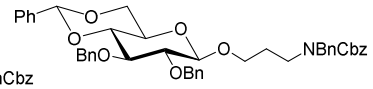
CH-HSQC NMR, 600 MHz, $CDCl_3$



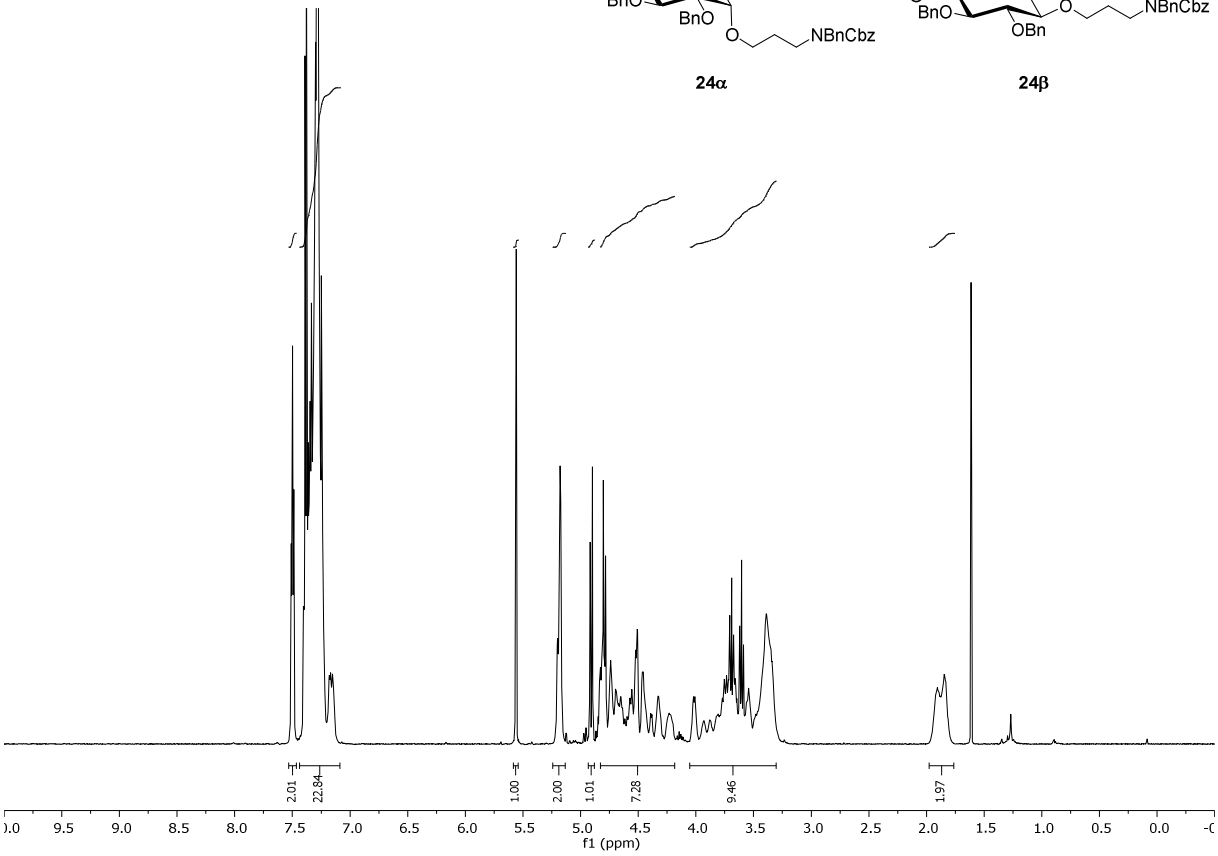
^{1}H NMR, 600 MHz, $CDCl_3$



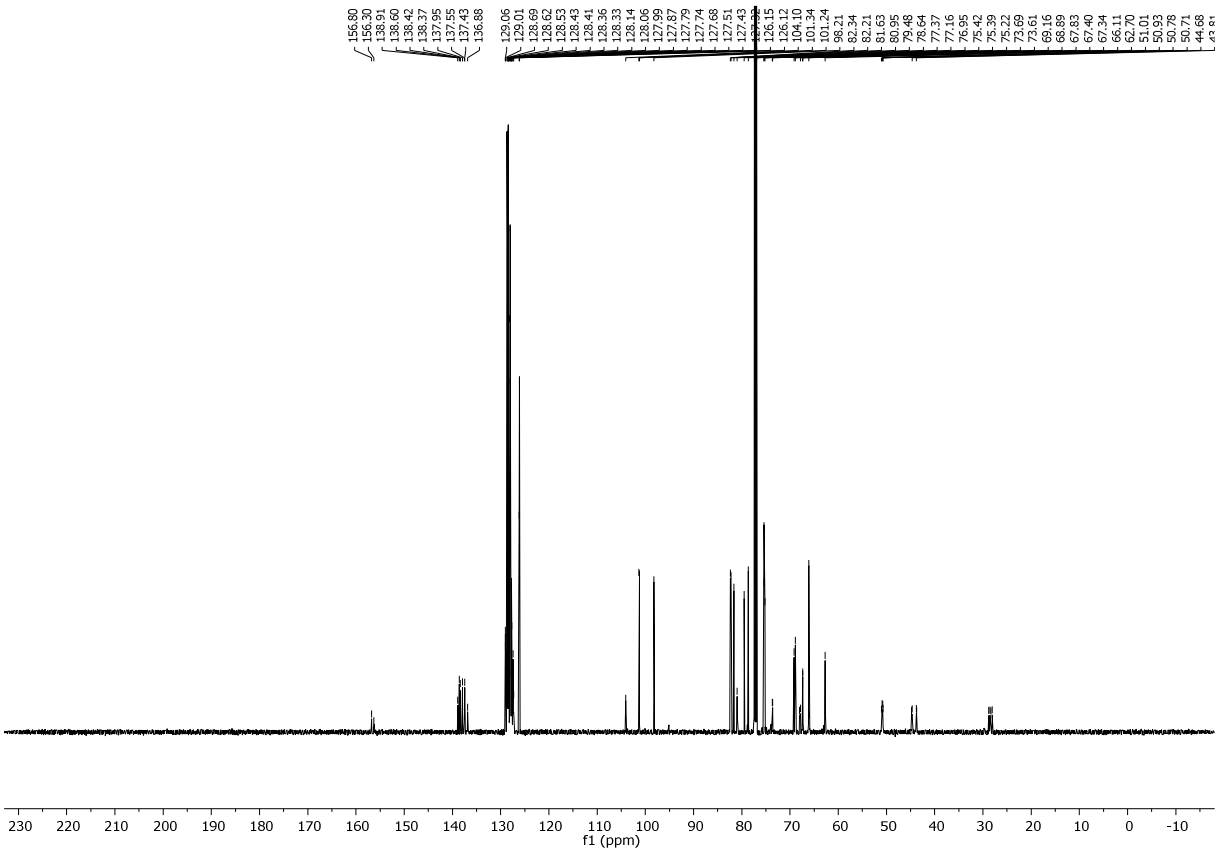
24α



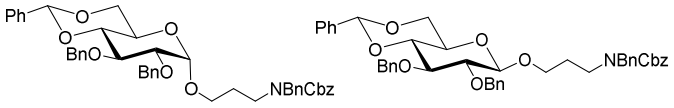
24β



^{13}C NMR, 150 MHz, $CDCl_3$

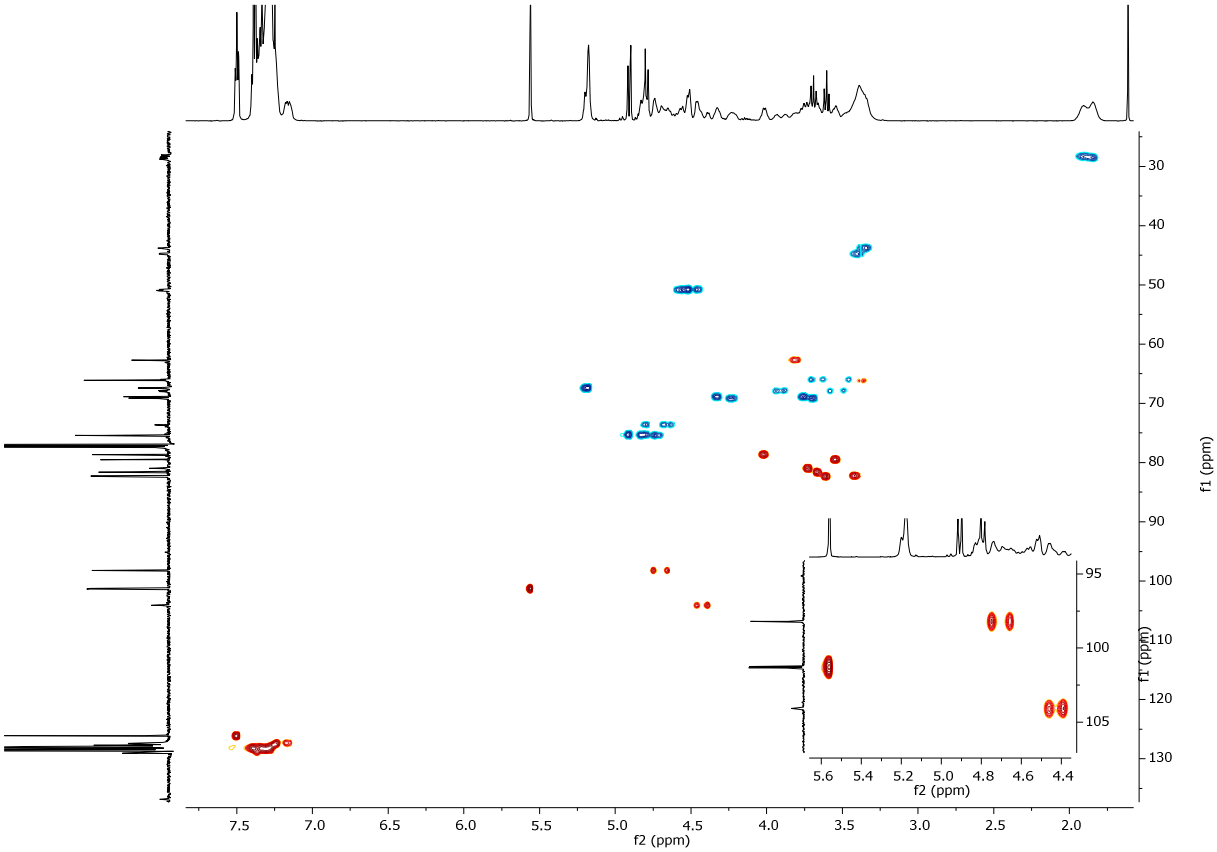


CH-HSQC NMR, 600 MHz, $CDCl_3$

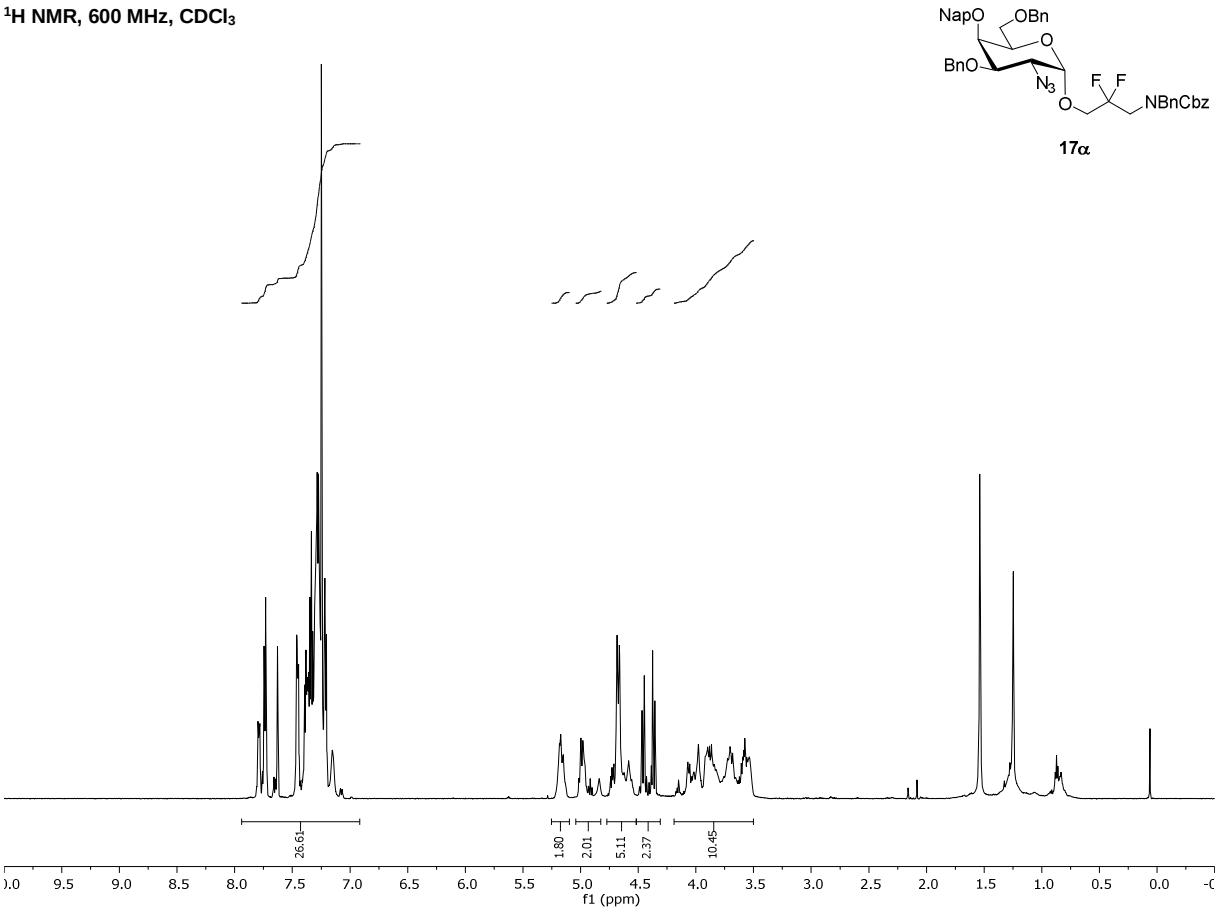


24α

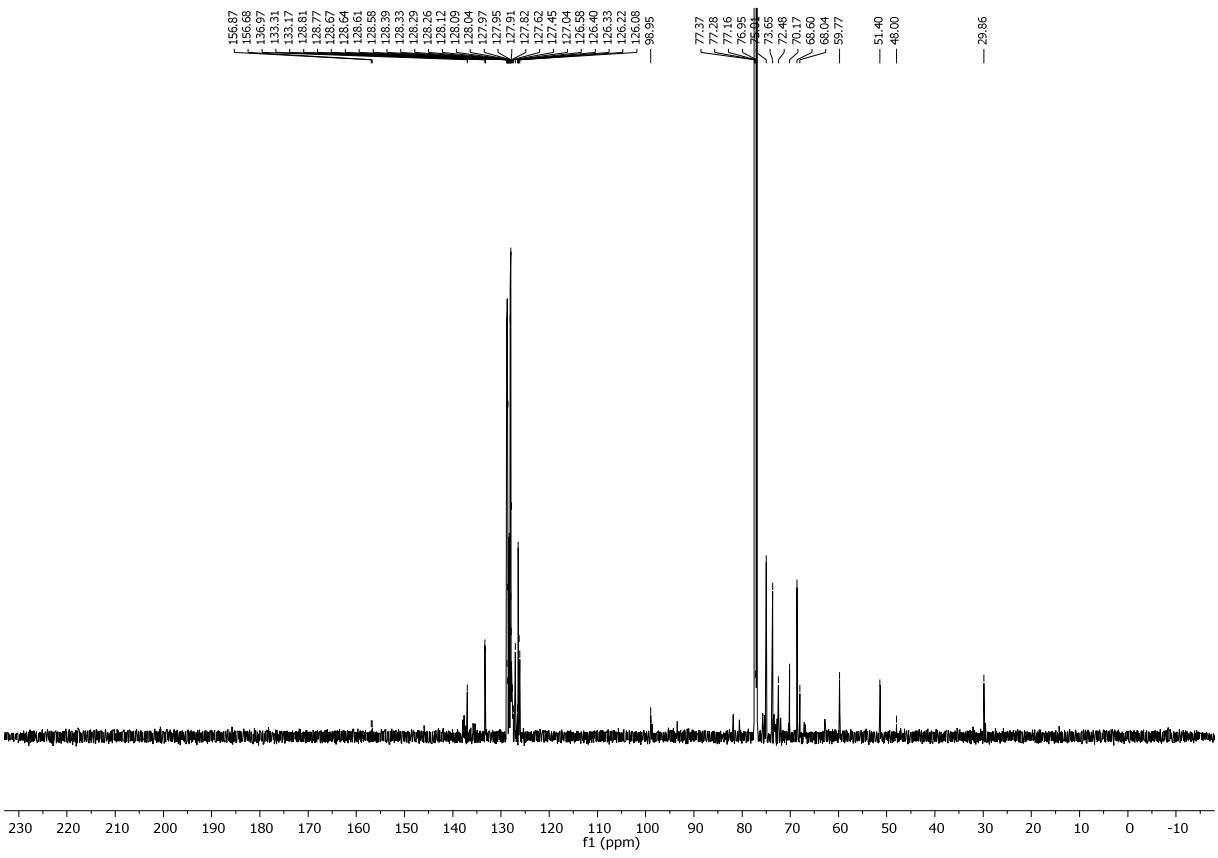
24β



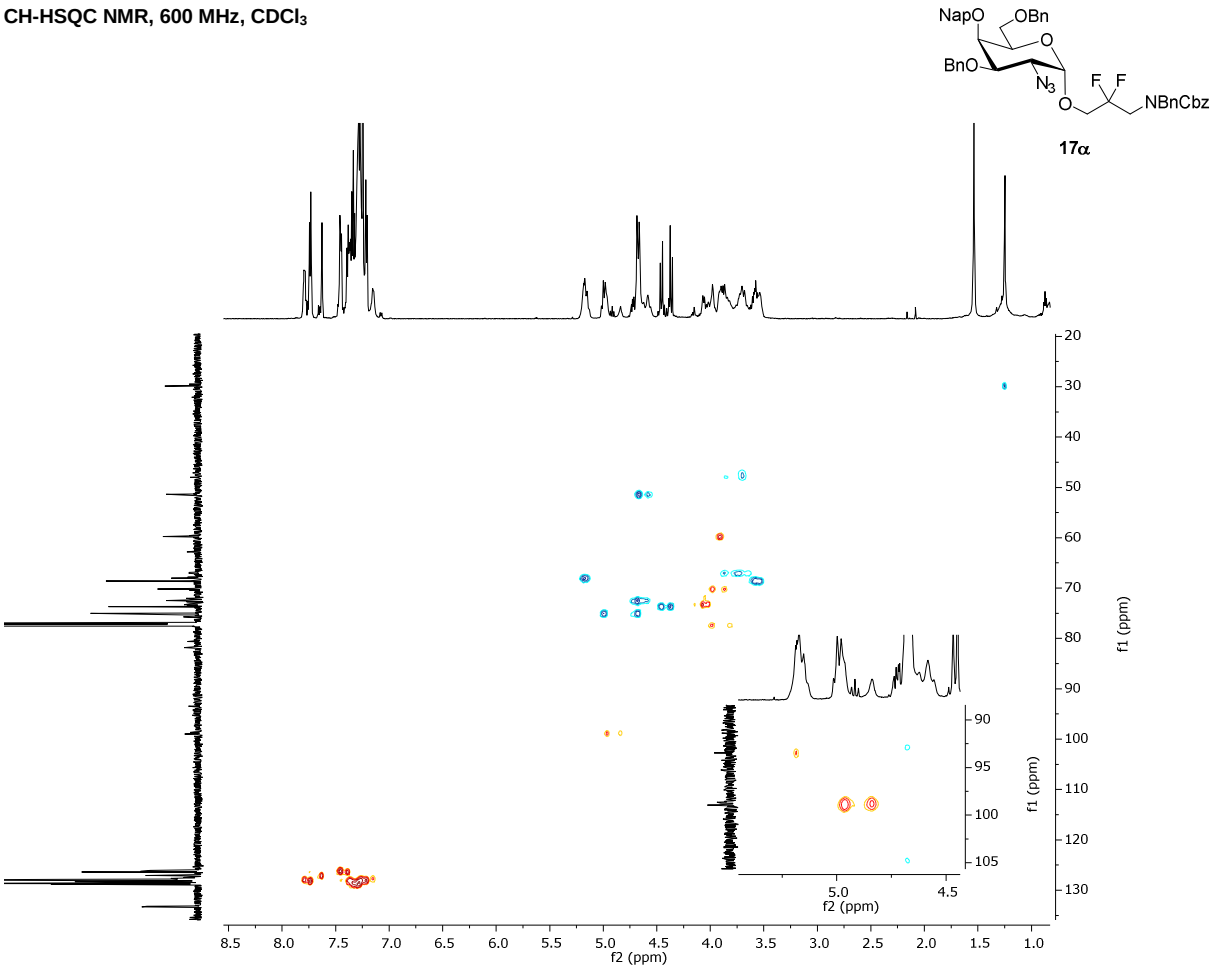
^{1}H NMR, 600 MHz, $CDCl_3$



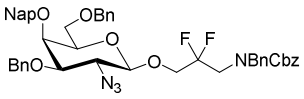
^{13}C NMR, 150 MHz, $CDCl_3$



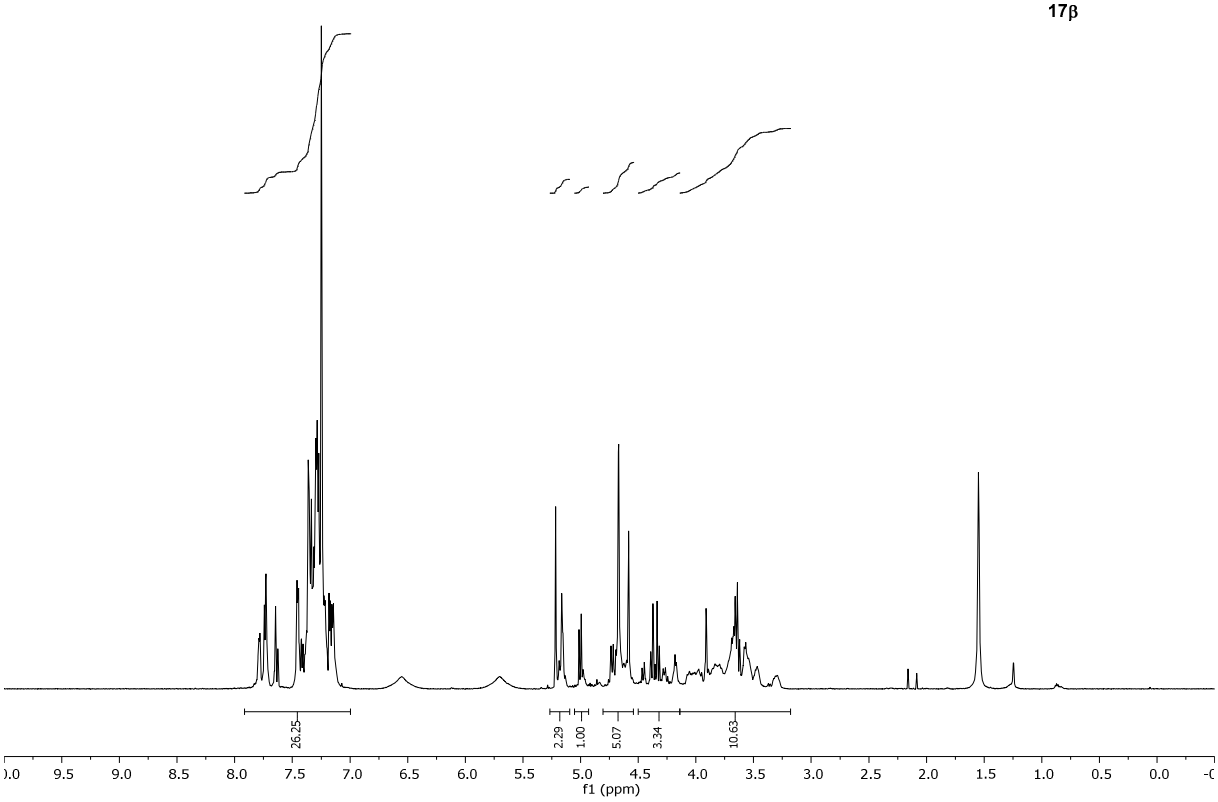
CH-HSQC NMR, 600 MHz, $CDCl_3$



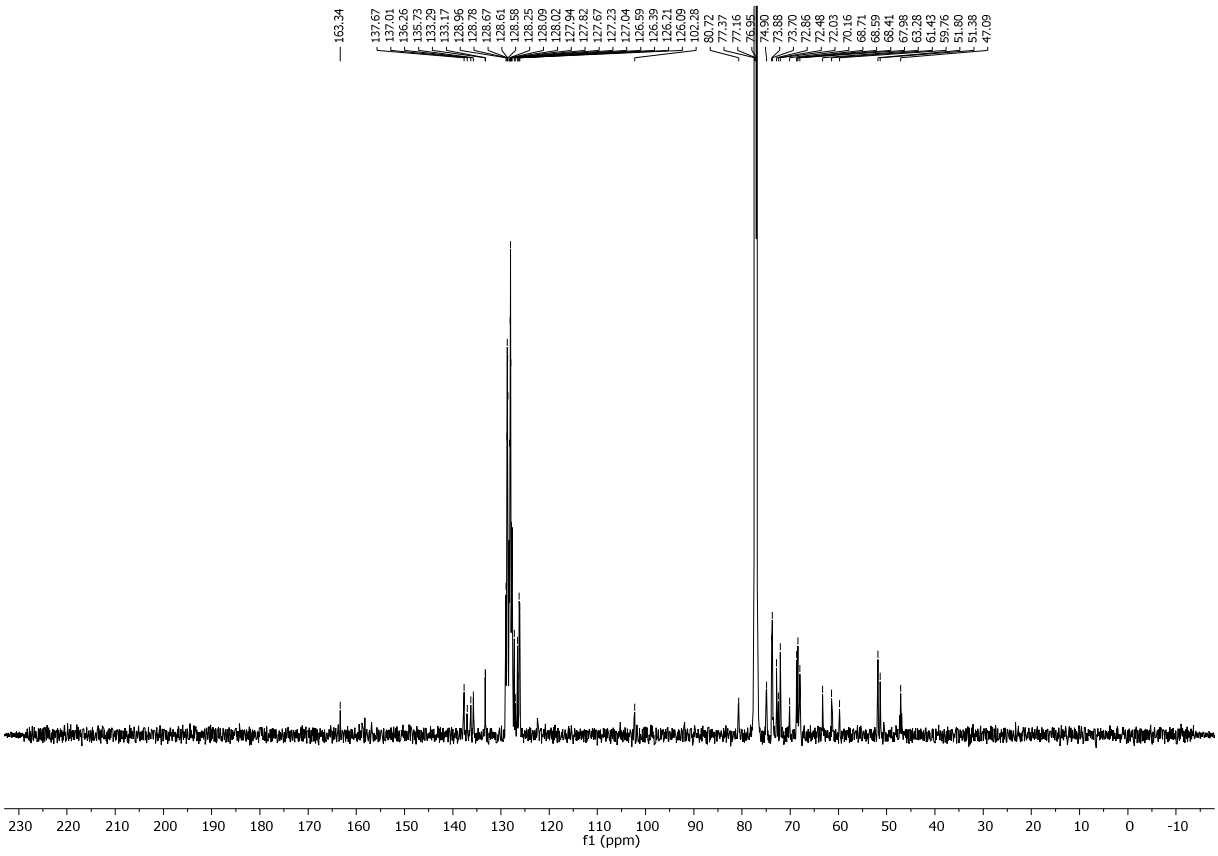
^{1}H NMR, 600 MHz, $CDCl_3$



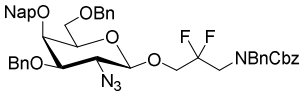
17β



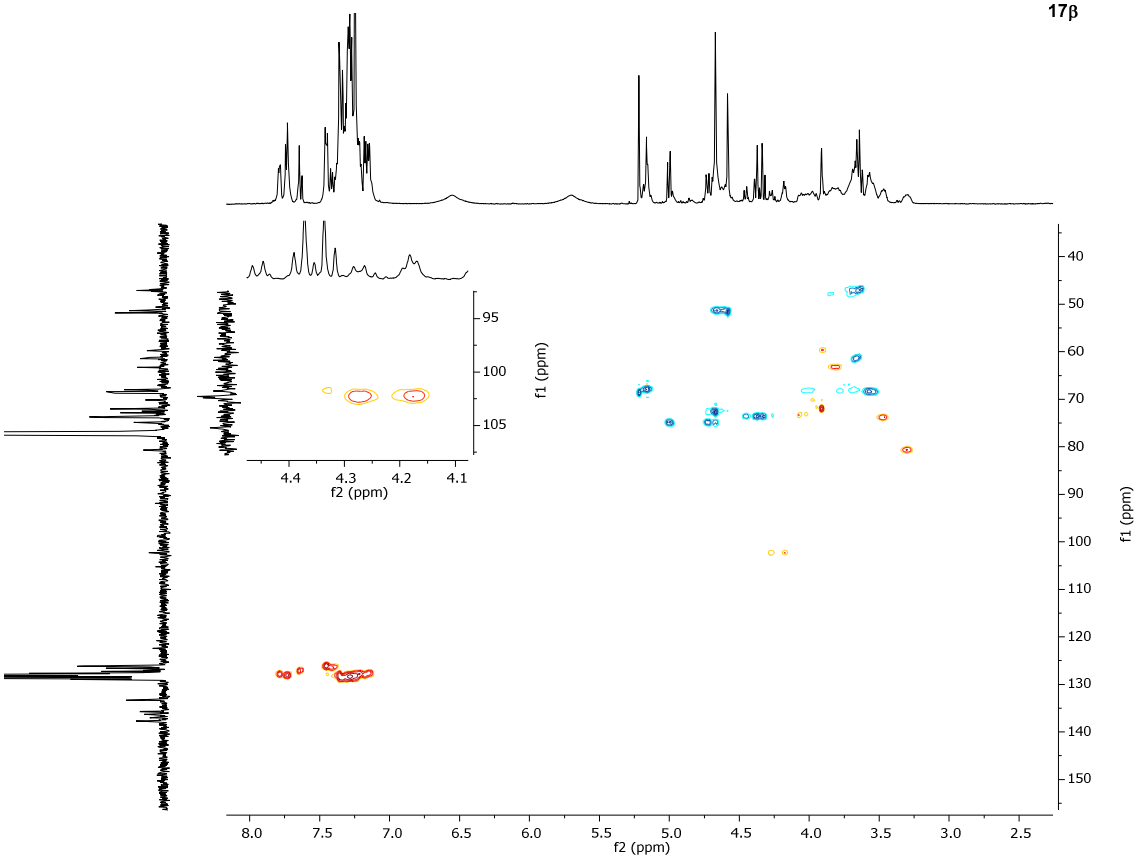
^{13}C NMR, 150 MHz, $CDCl_3$



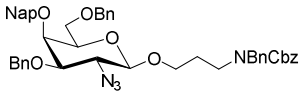
CH-HSQC, 600 MHz, $CDCl_3$



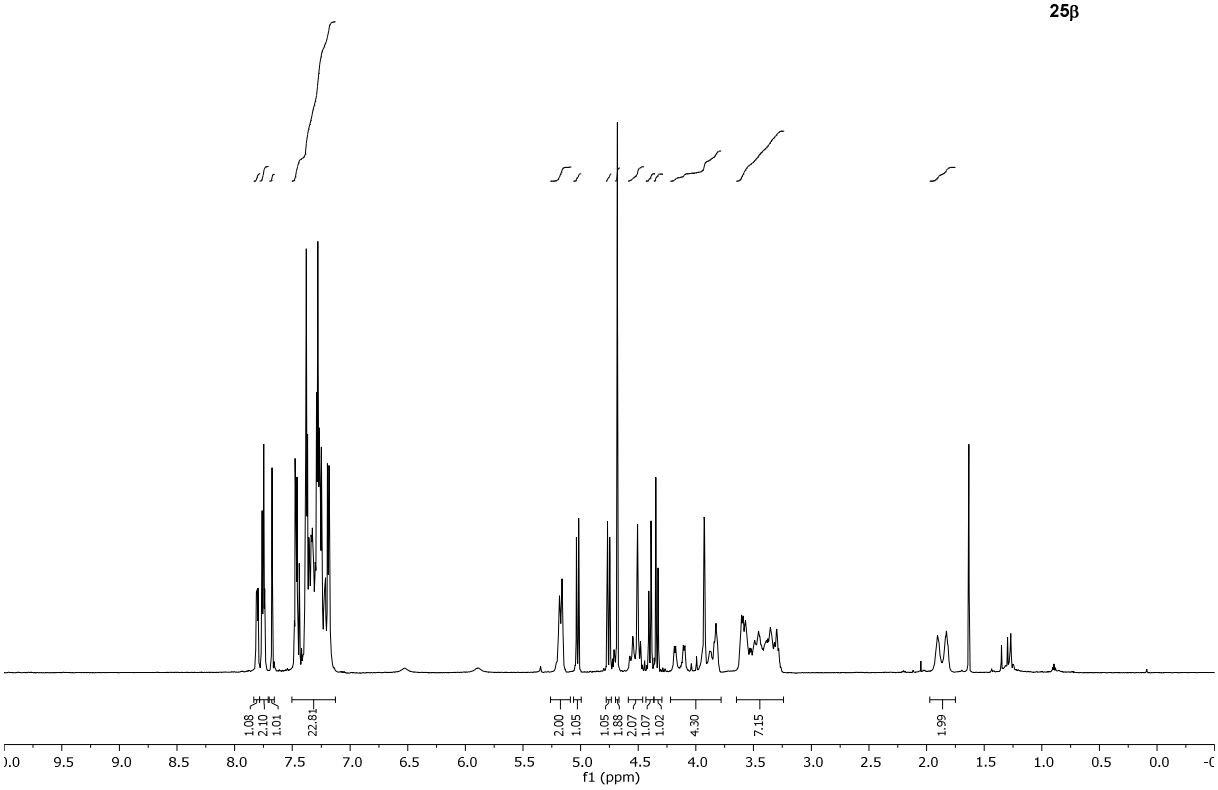
17β



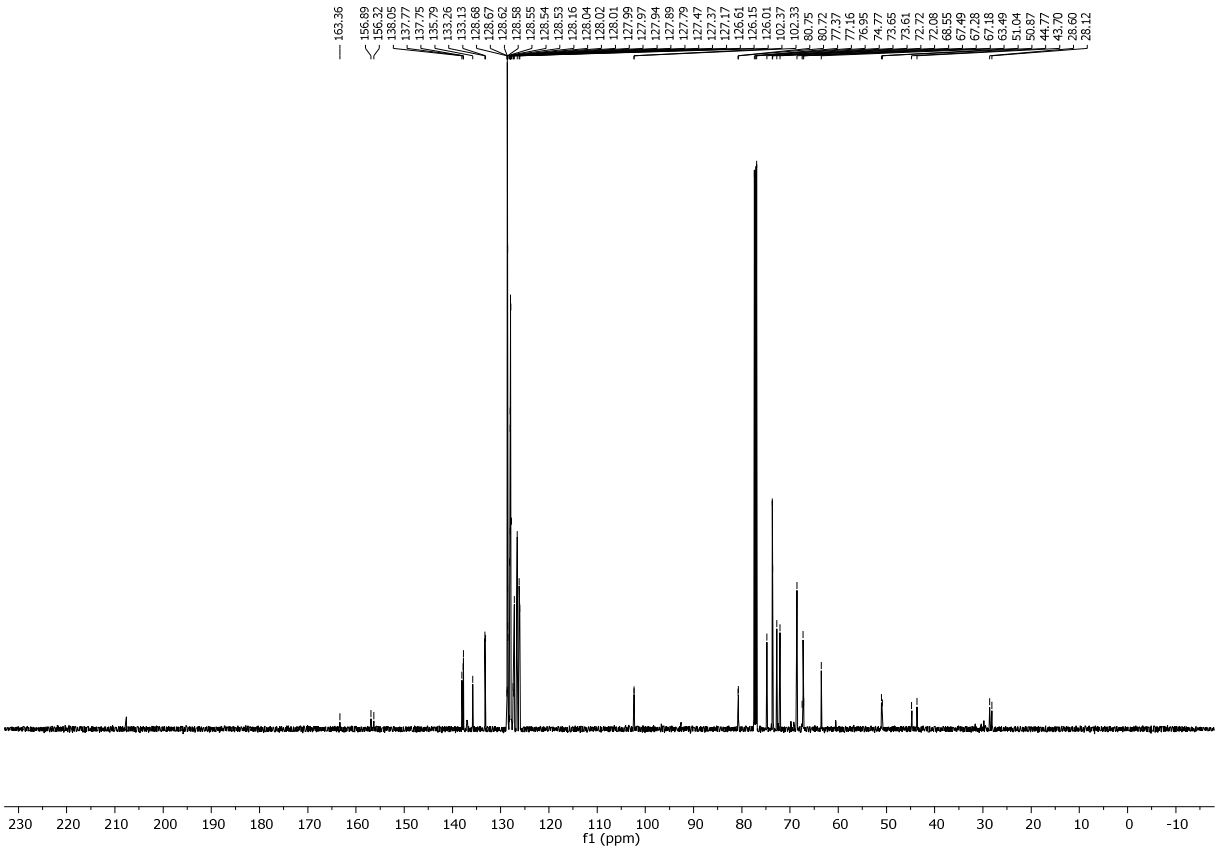
^{1}H NMR, 600 MHz, $CDCl_3$



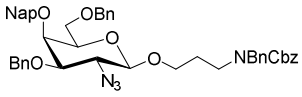
25β

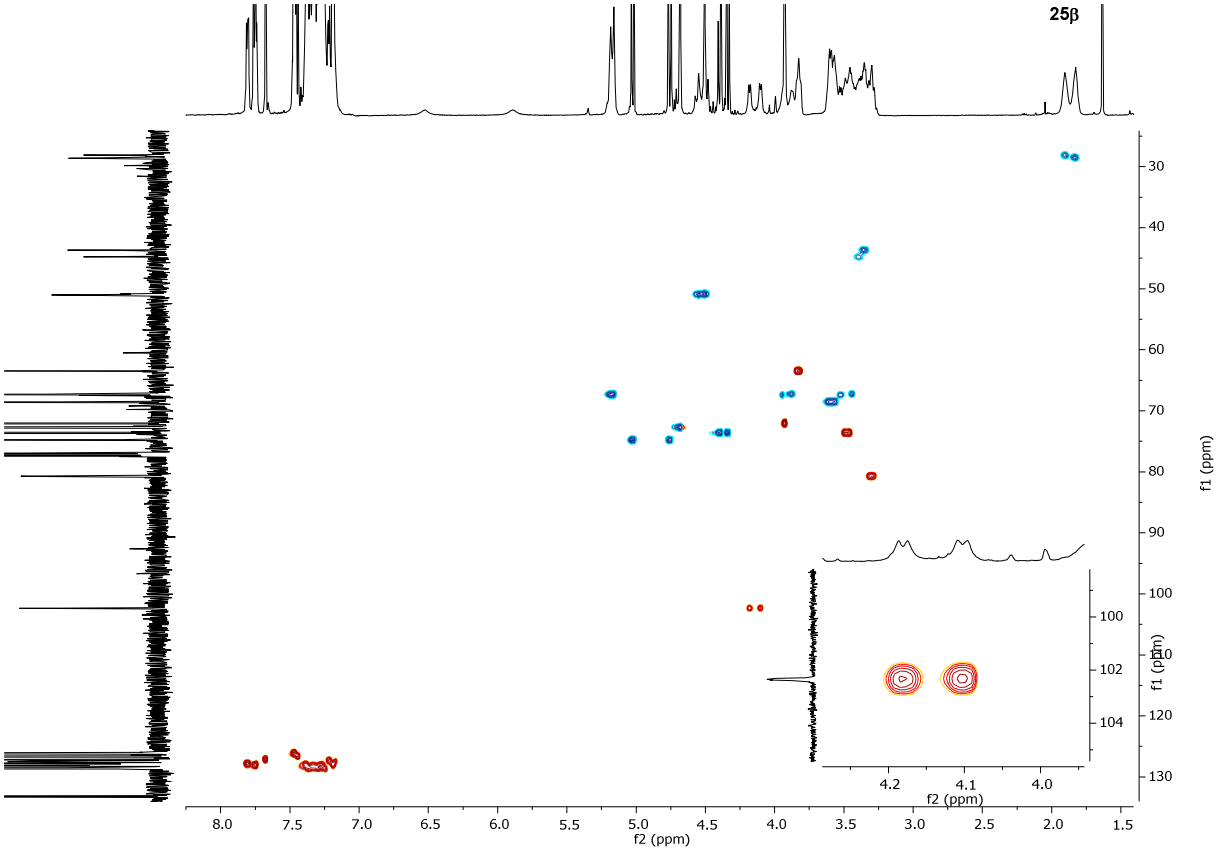


^{13}C NMR, 150 MHz, $CDCl_3$

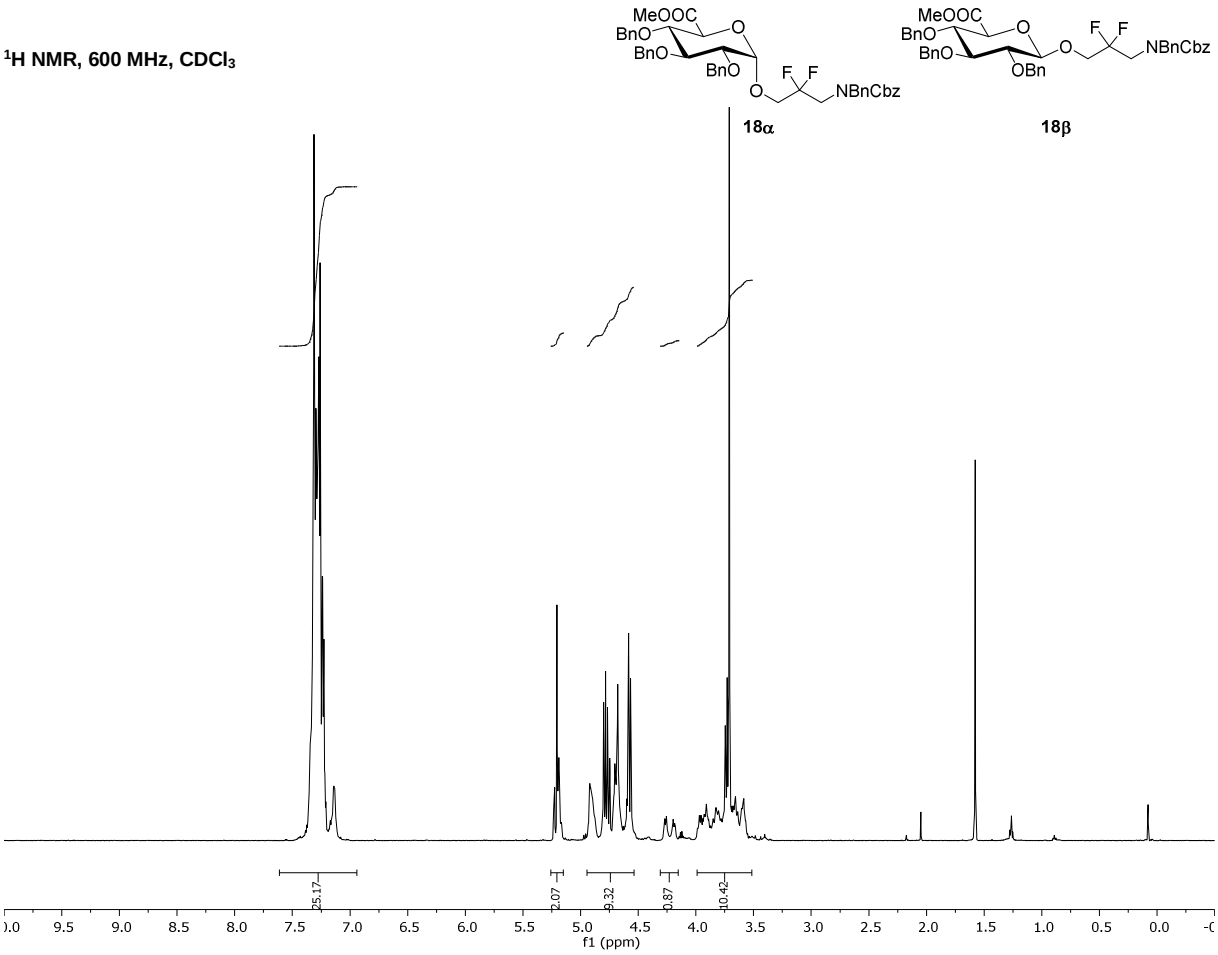


CH-HSQC NMR, 600 MHz, $CDCl_3$

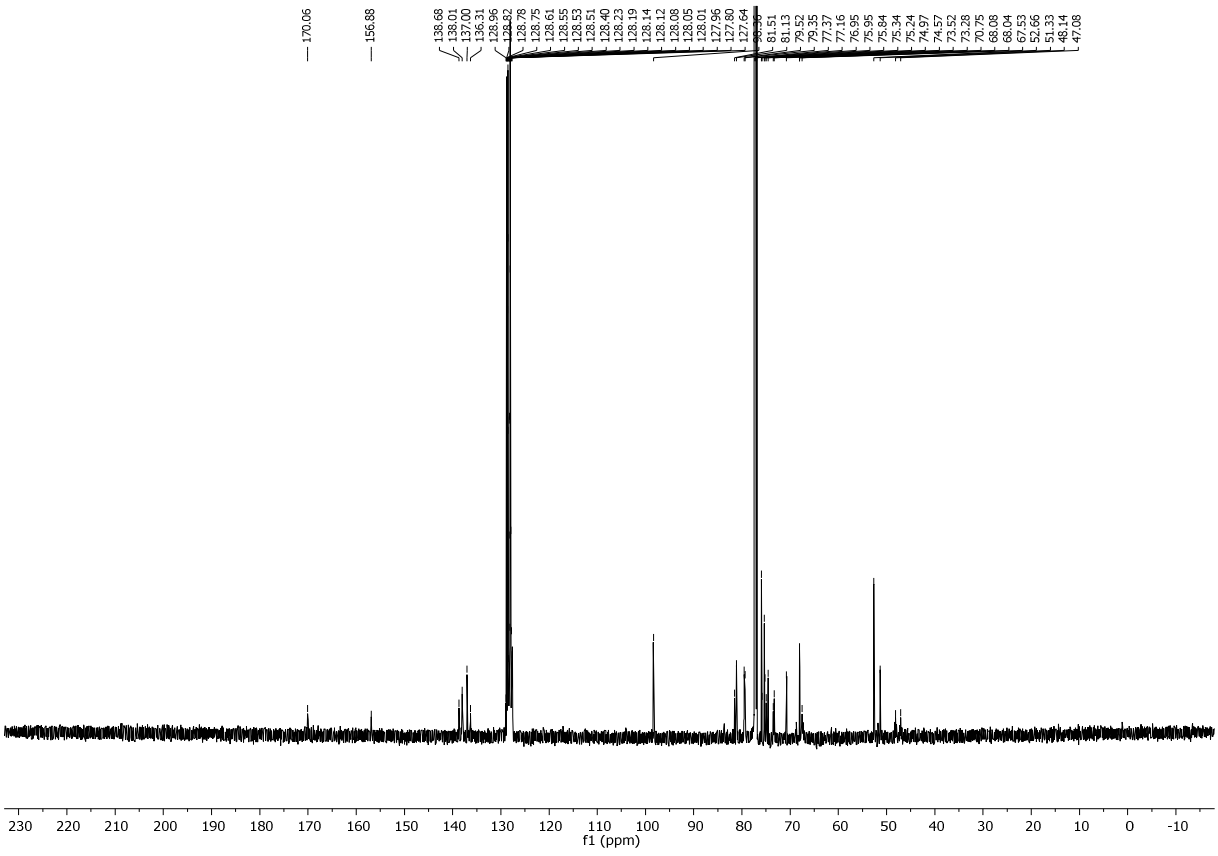




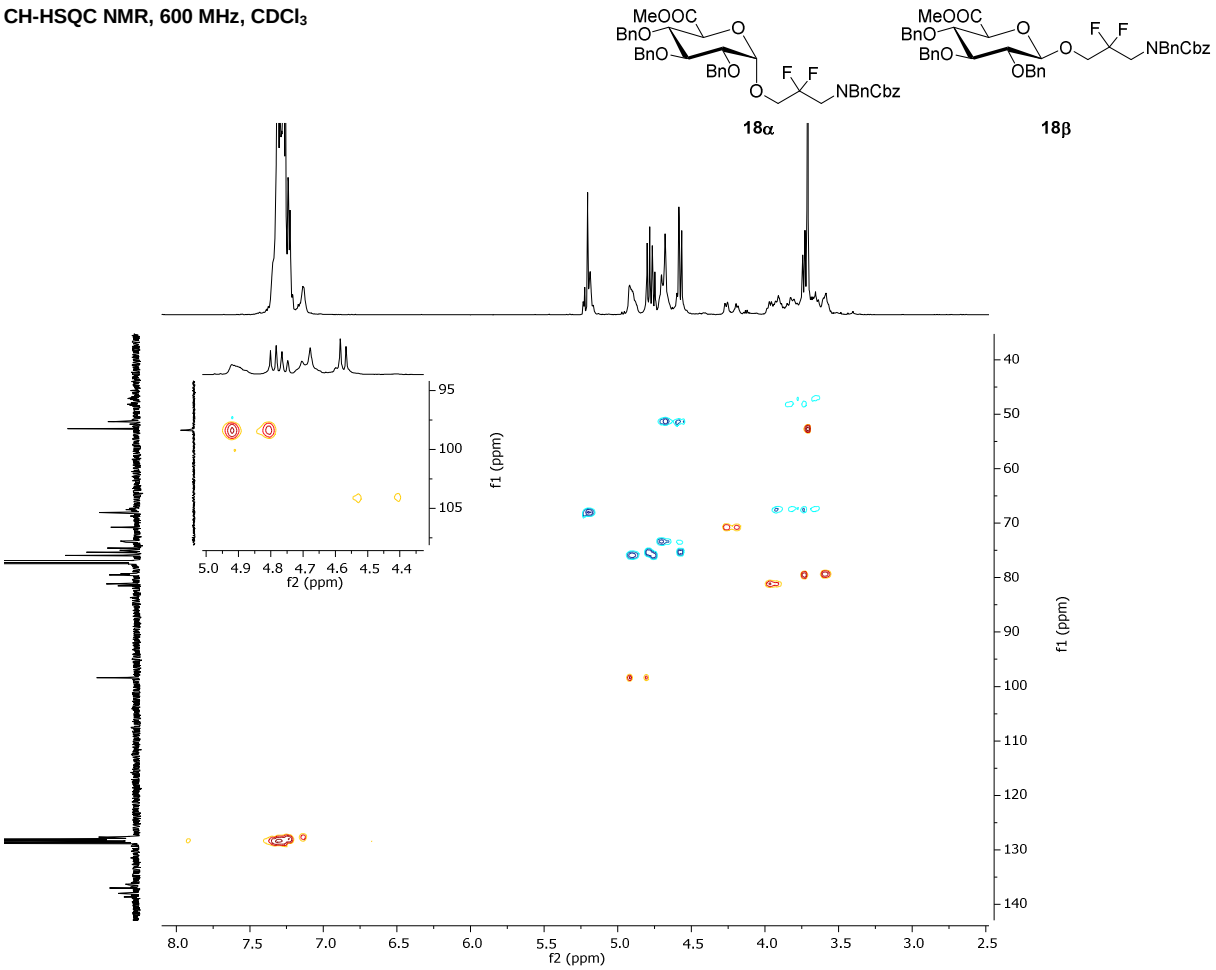
^{1}H NMR, 600 MHz, $CDCl_3$



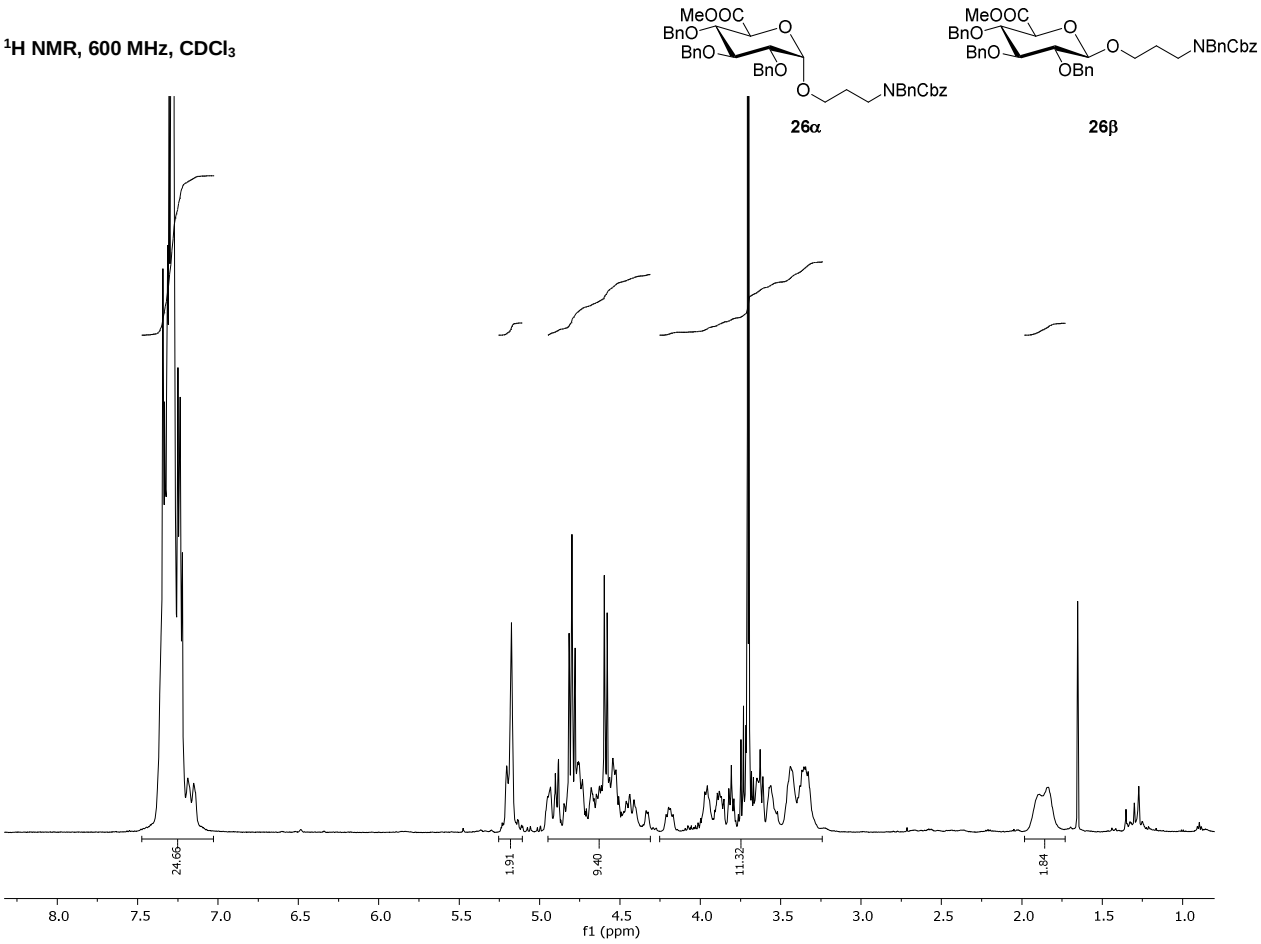
^{13}C NMR, 150 MHz, $CDCl_3$



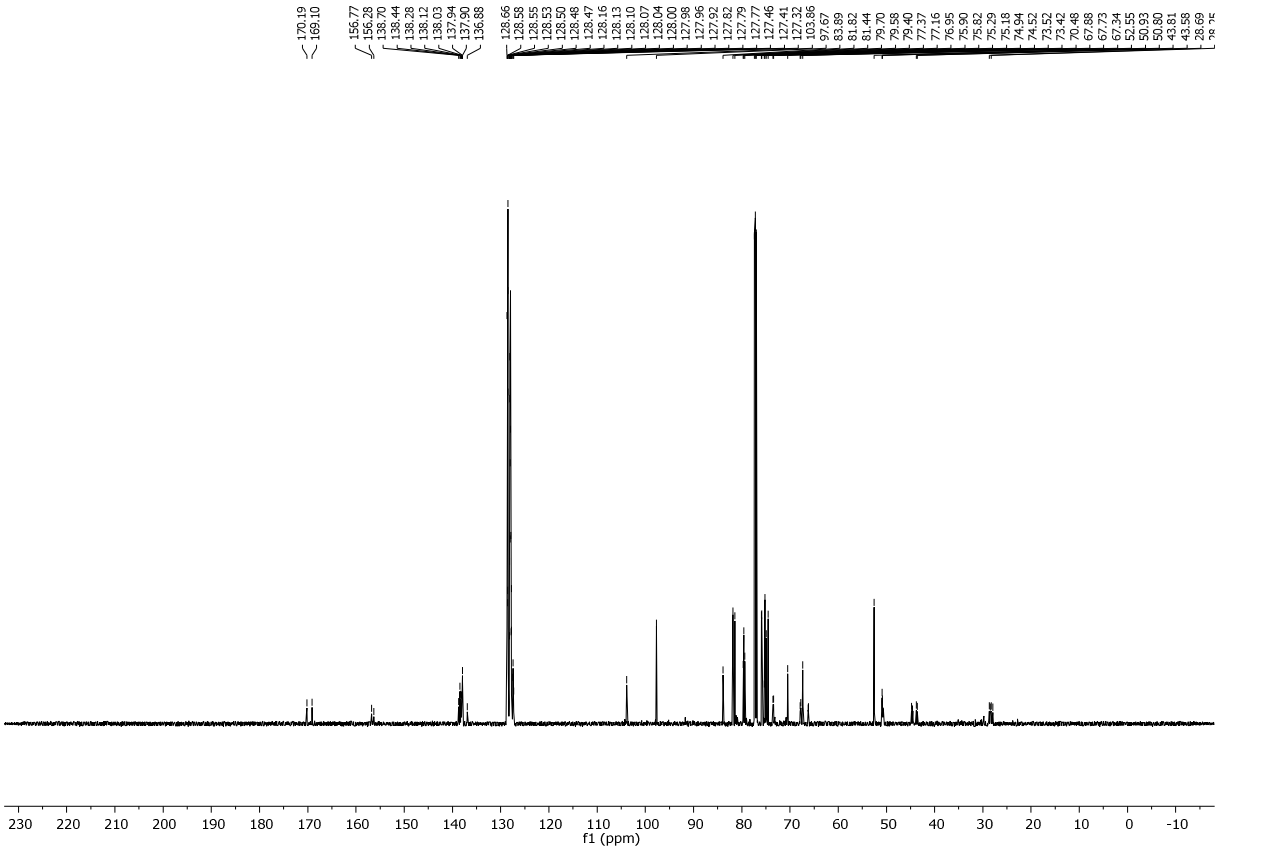
CH-HSQC NMR, 600 MHz, $CDCl_3$



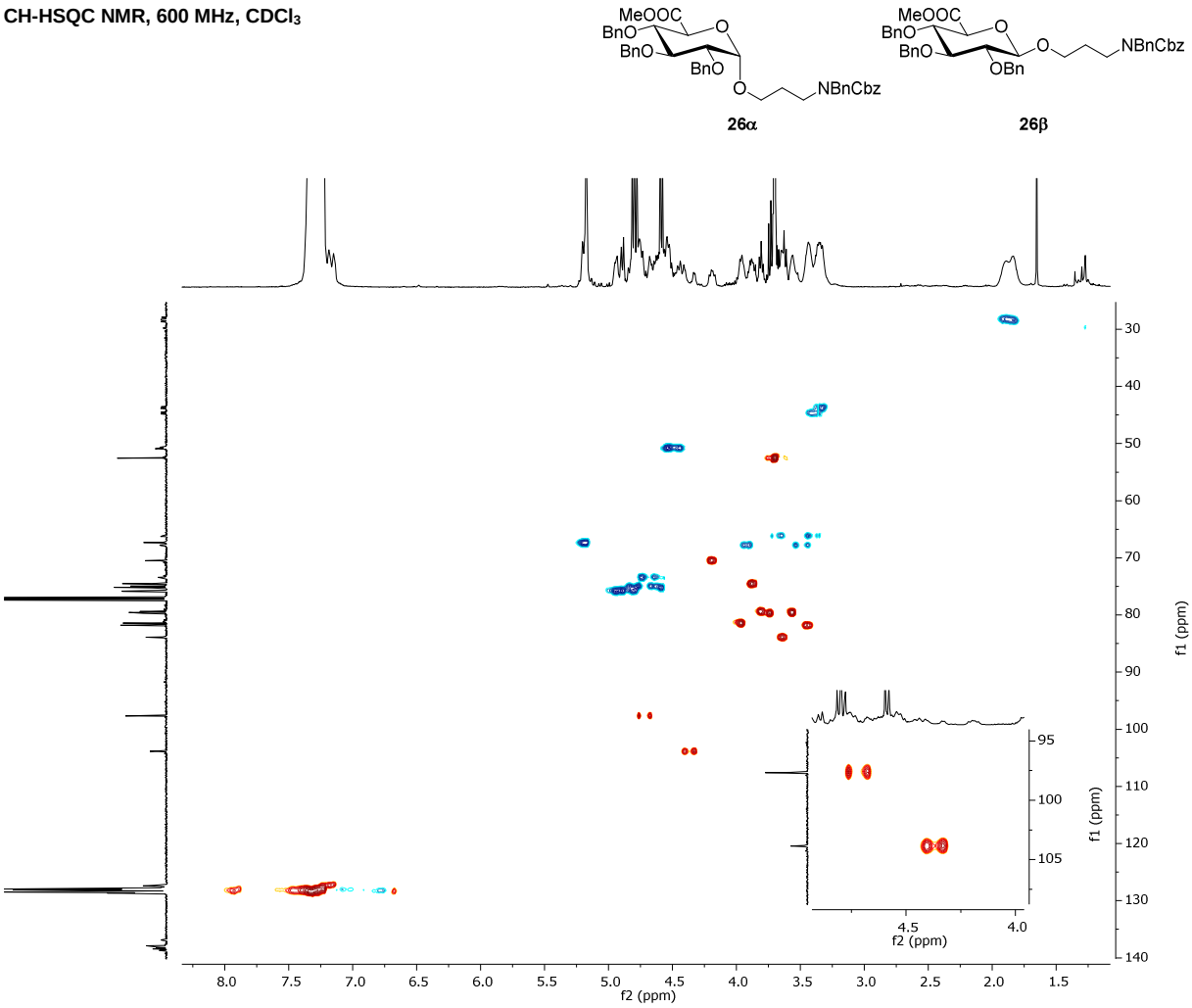
^{1}H NMR, 600 MHz, $CDCl_3$



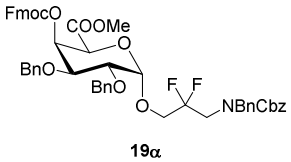
^{13}C NMR, 150 MHz, $CDCl_3$



CH-HSQC NMR, 600 MHz, $CDCl_3$

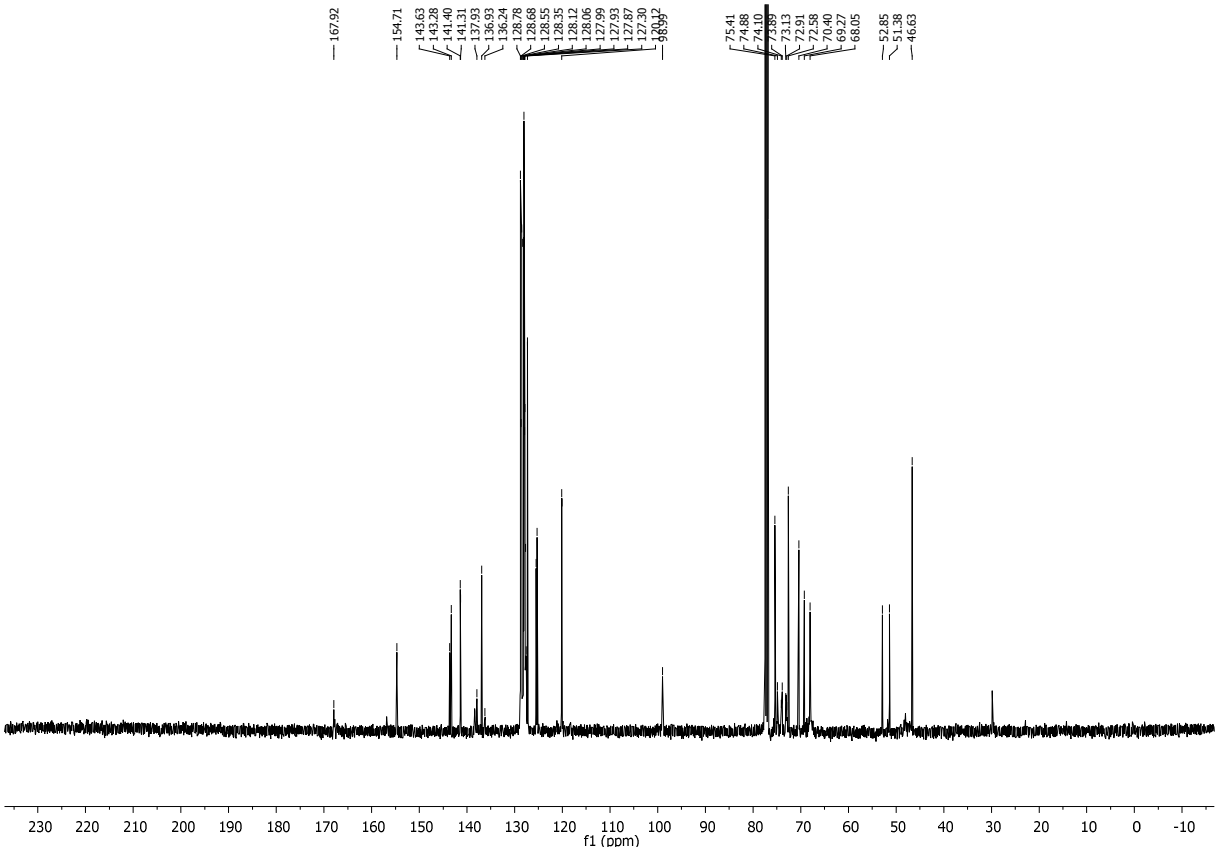


^{1}H NMR, 400 MHz, $CDCl_3$

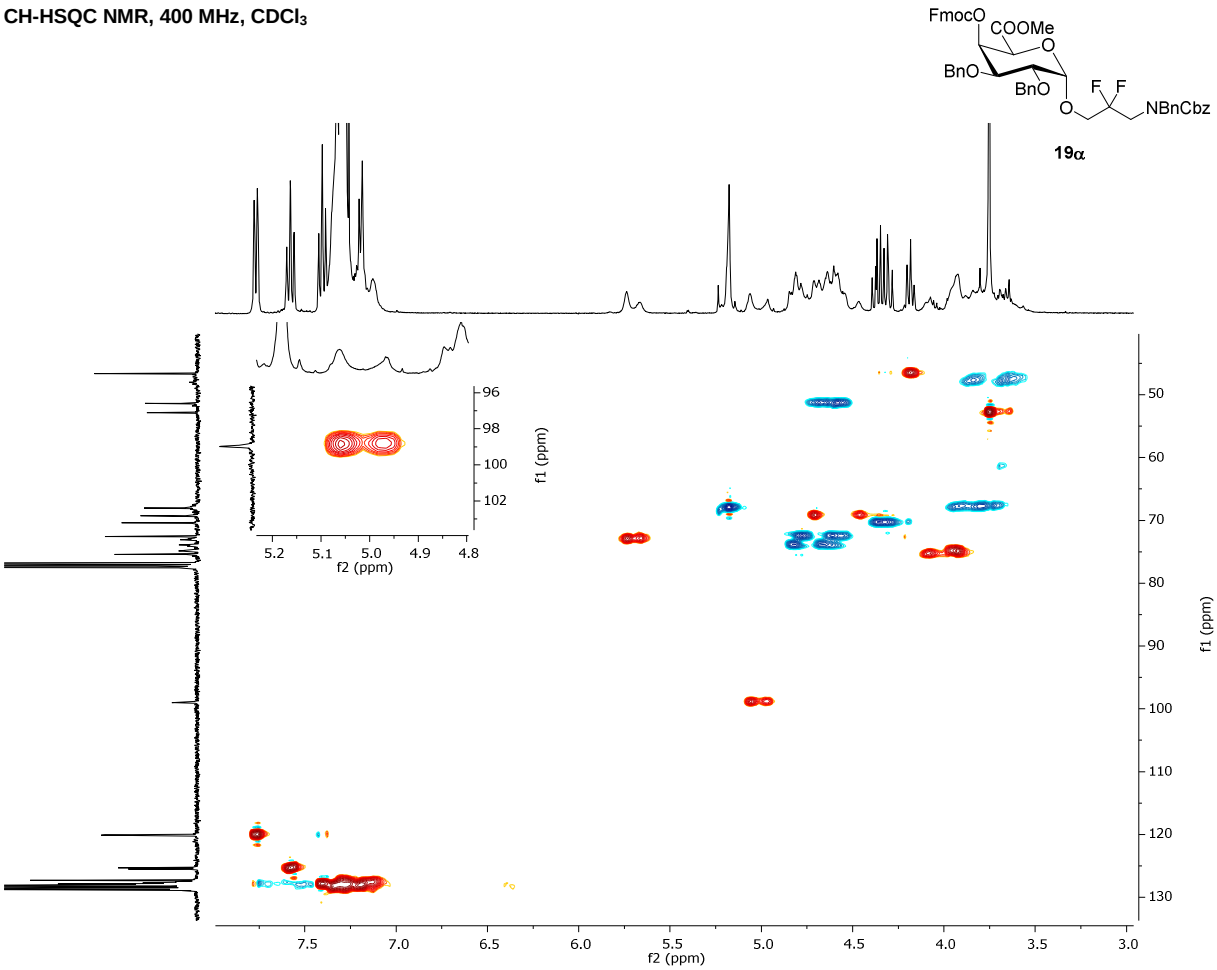


19α

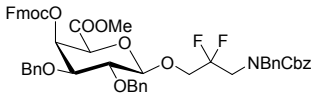
^{13}C NMR, 100 MHz, $CDCl_3$



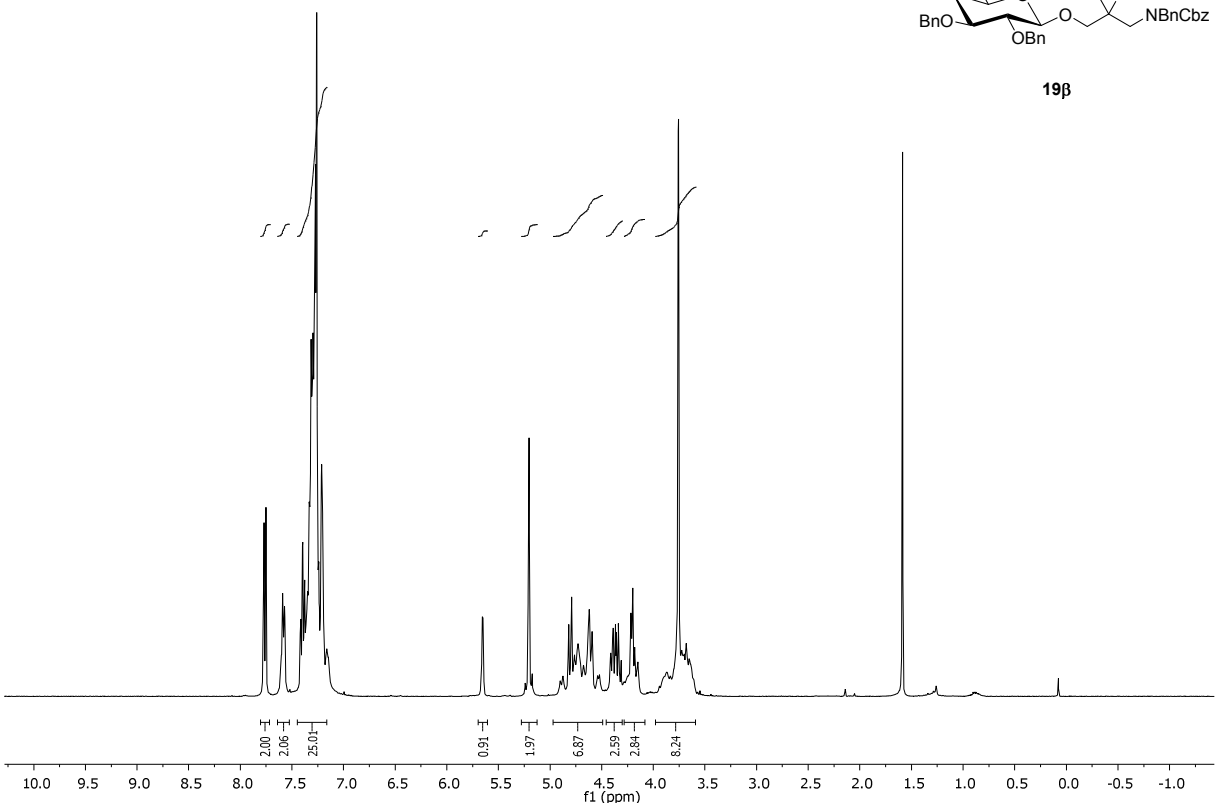
CH-HSQC NMR, 400 MHz, $CDCl_3$



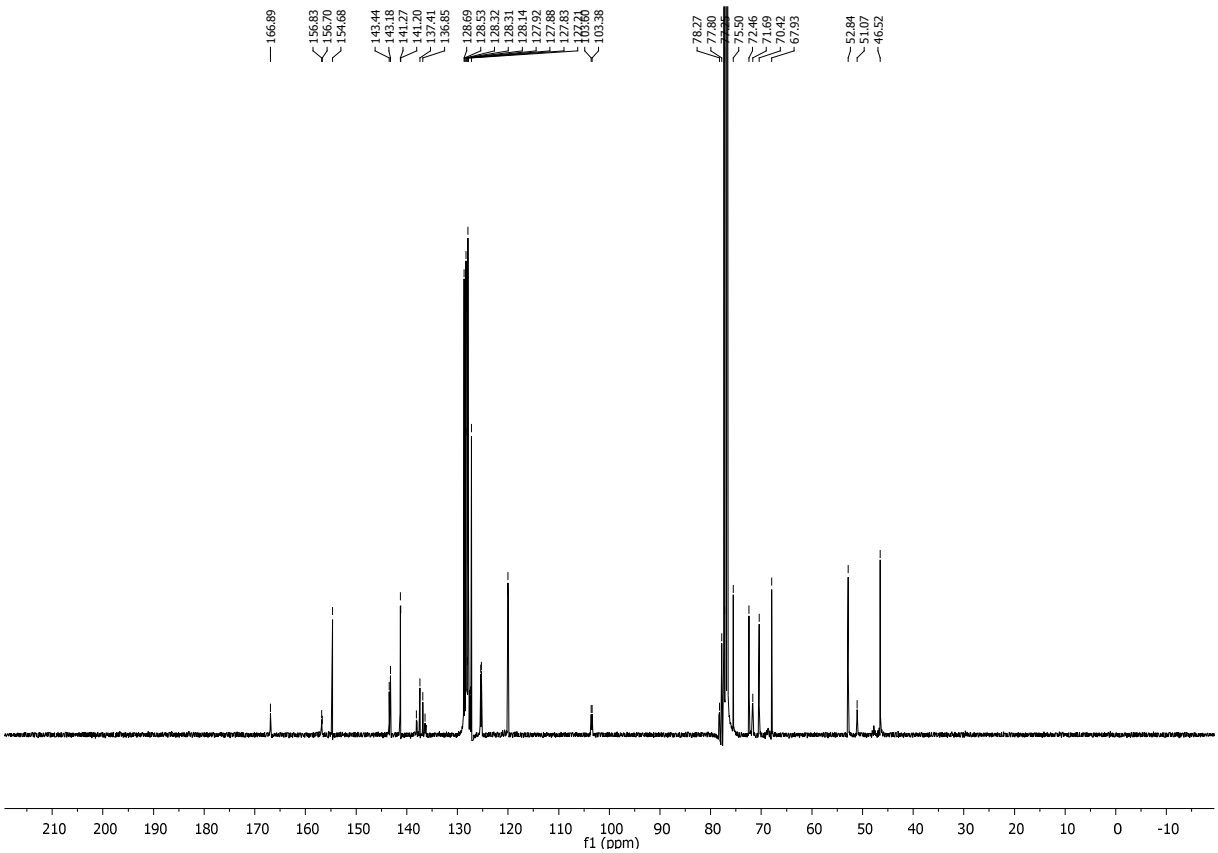
^{1}H NMR, 400 MHz, $CDCl_3$



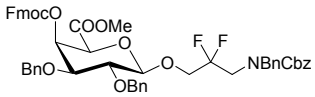
19β



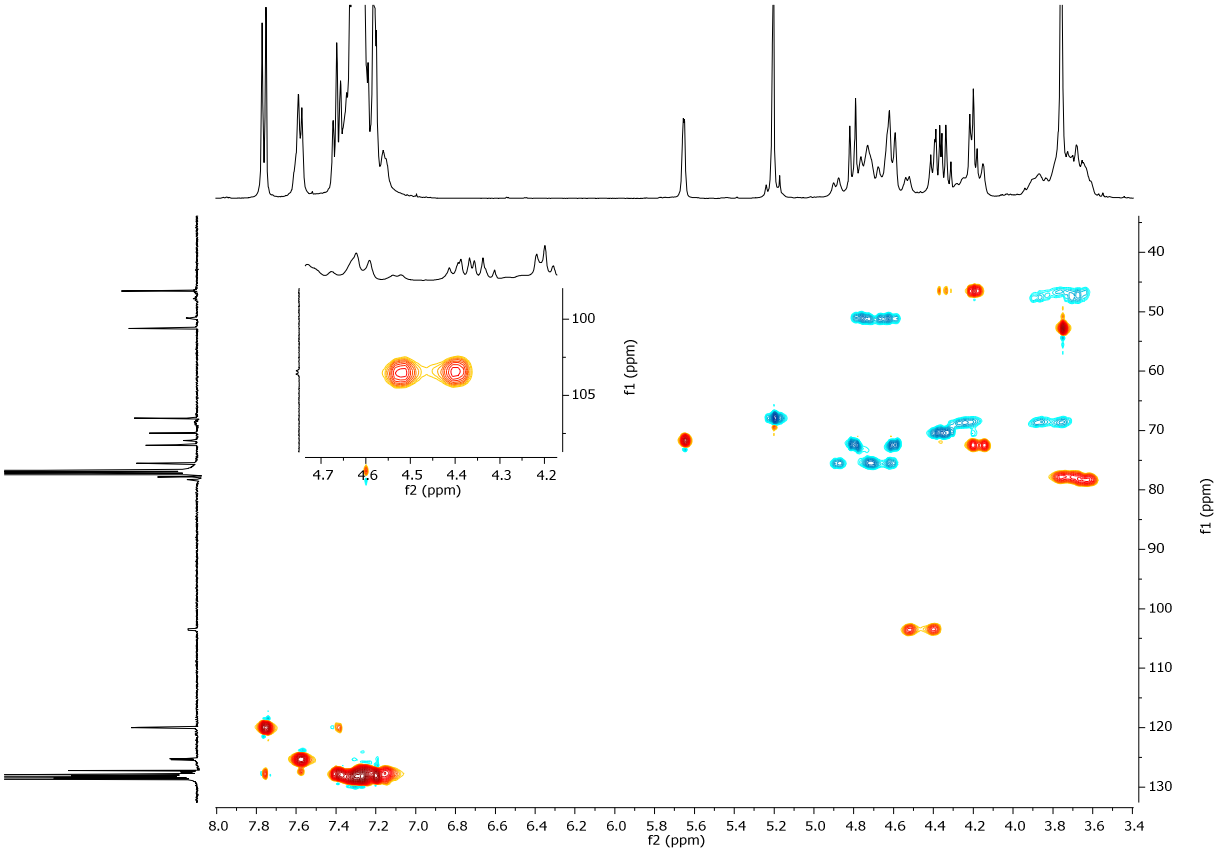
^{13}C NMR, 100 MHz, $CDCl_3$



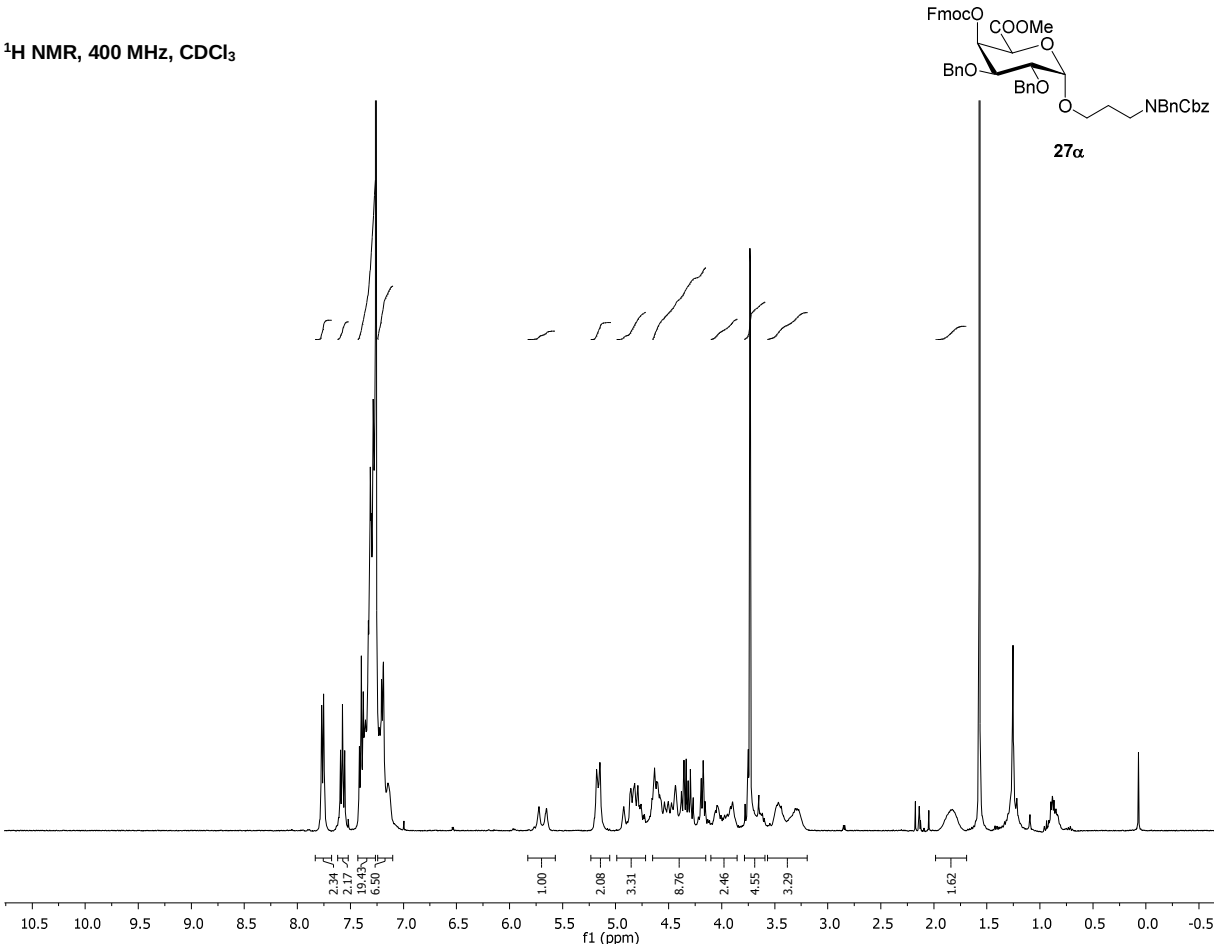
CH-HSQC NMR, 400 MHz, $CDCl_3$



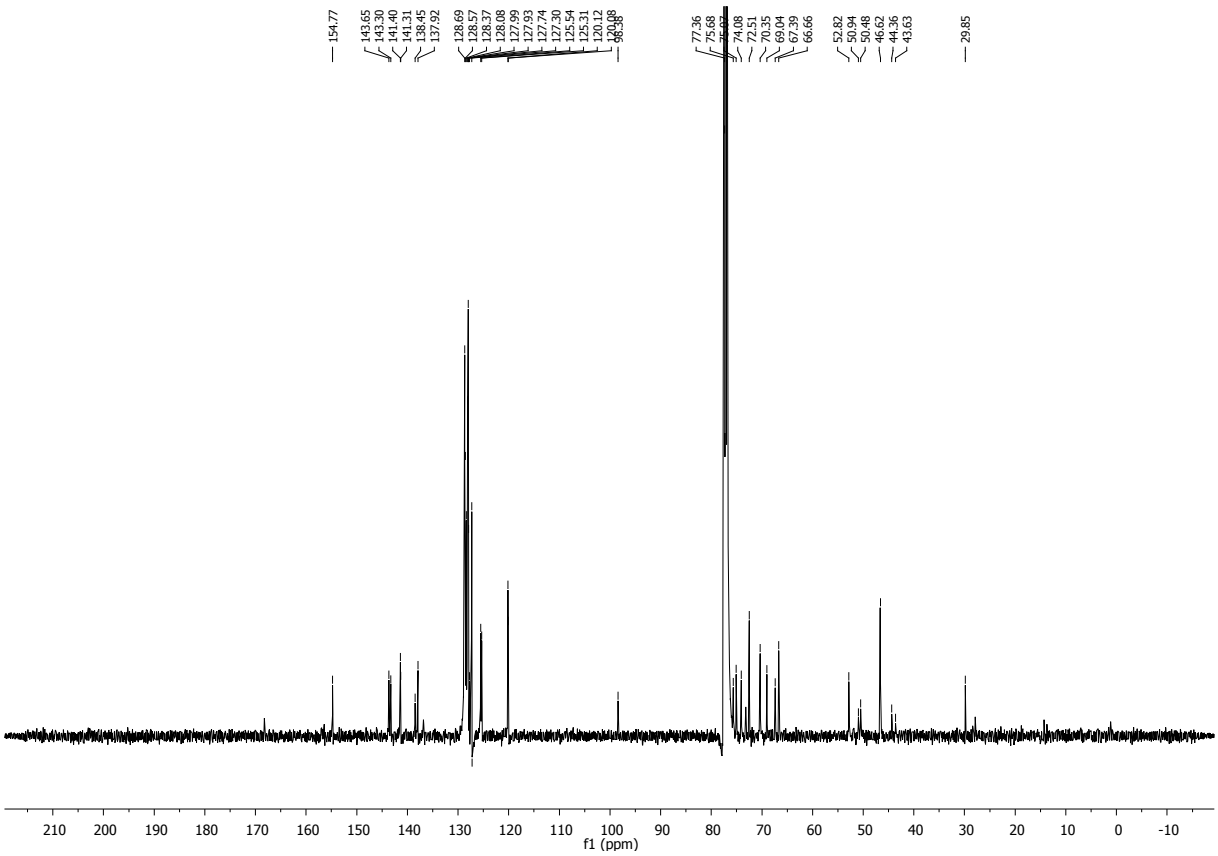
19β



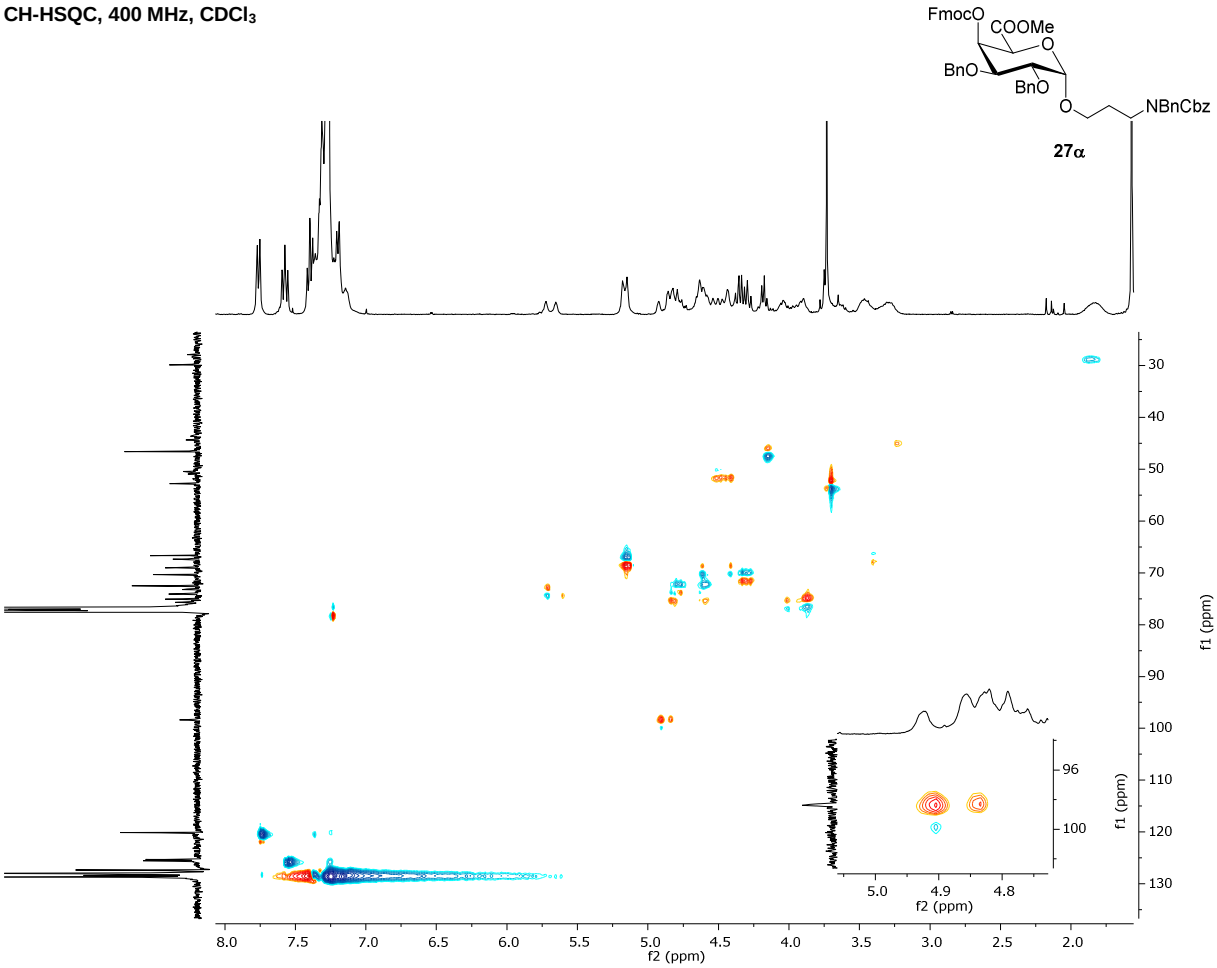
^{1}H NMR, 400 MHz, $CDCl_3$



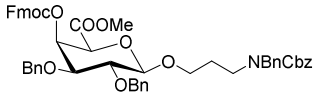
^{13}C NMR, 100 MHz, $CDCl_3$



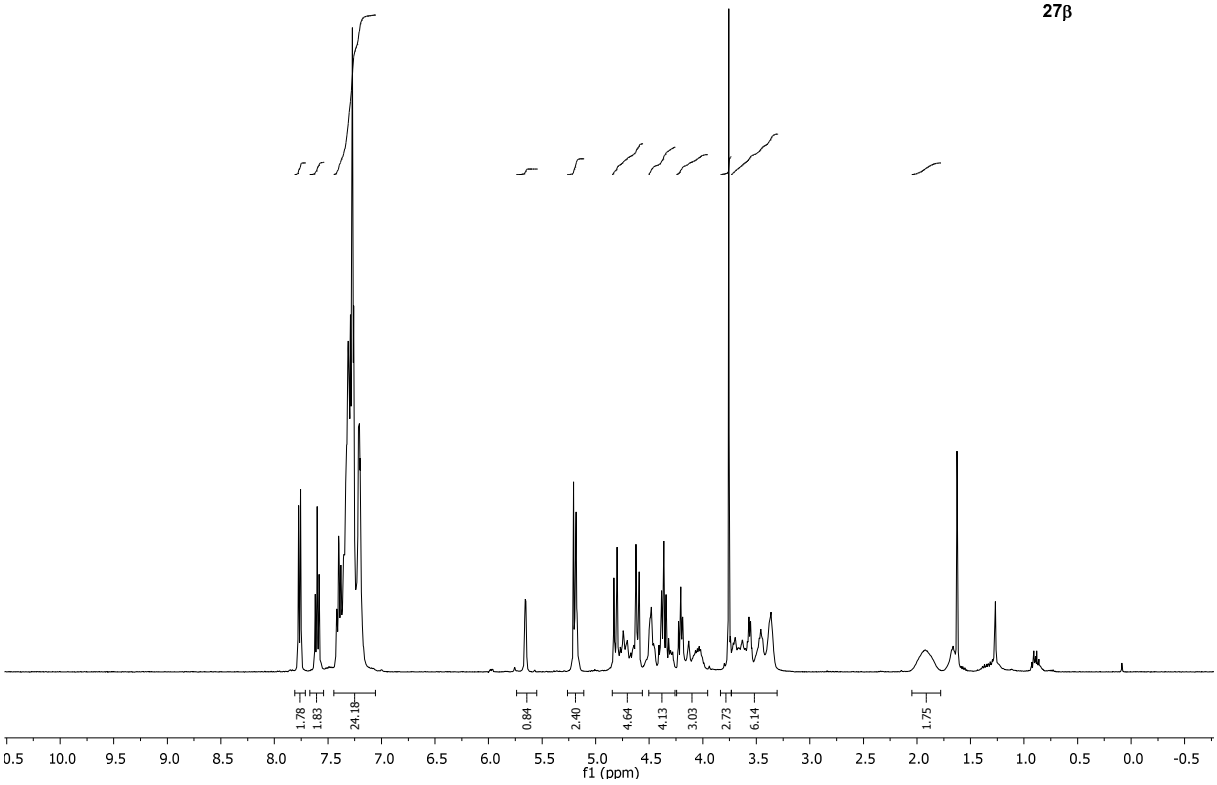
CH-HSQC, 400 MHz, $CDCl_3$



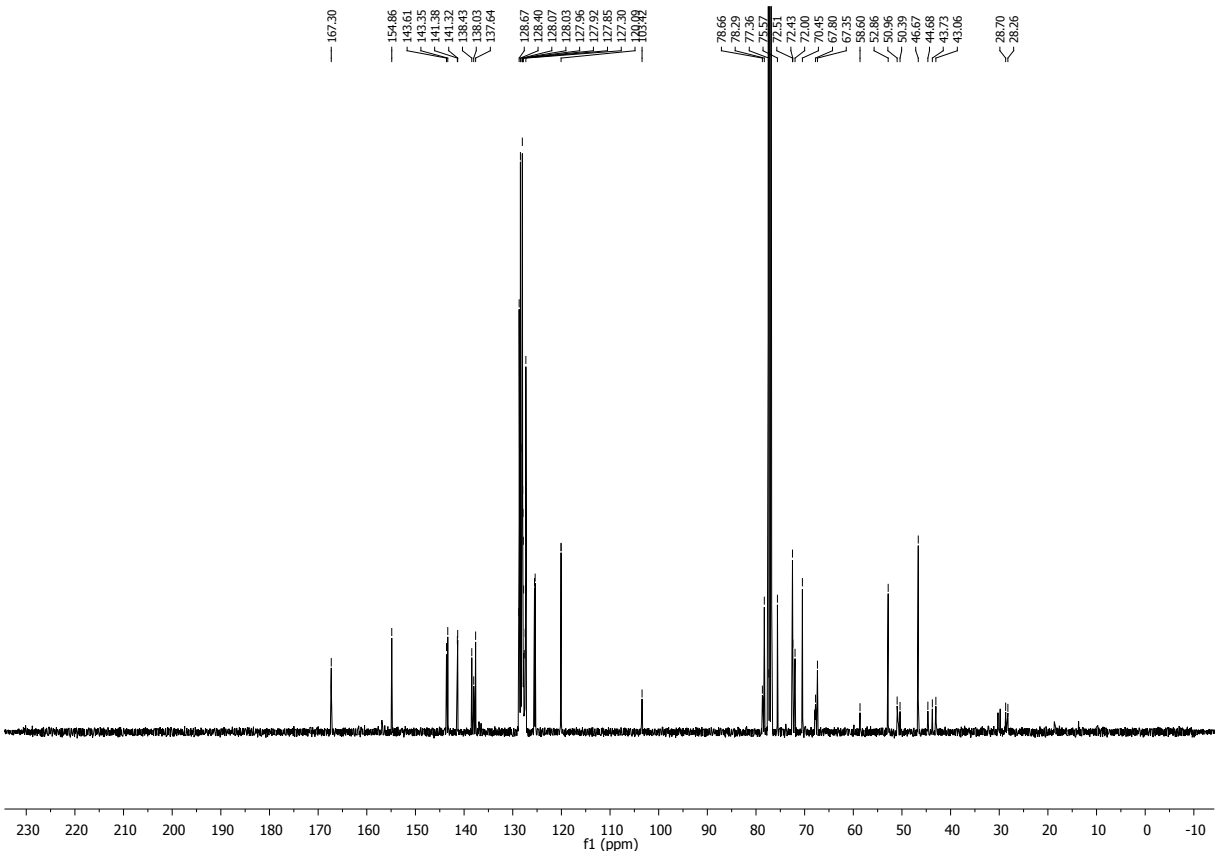
^{1}H NMR, 400 MHz, $CDCl_3$



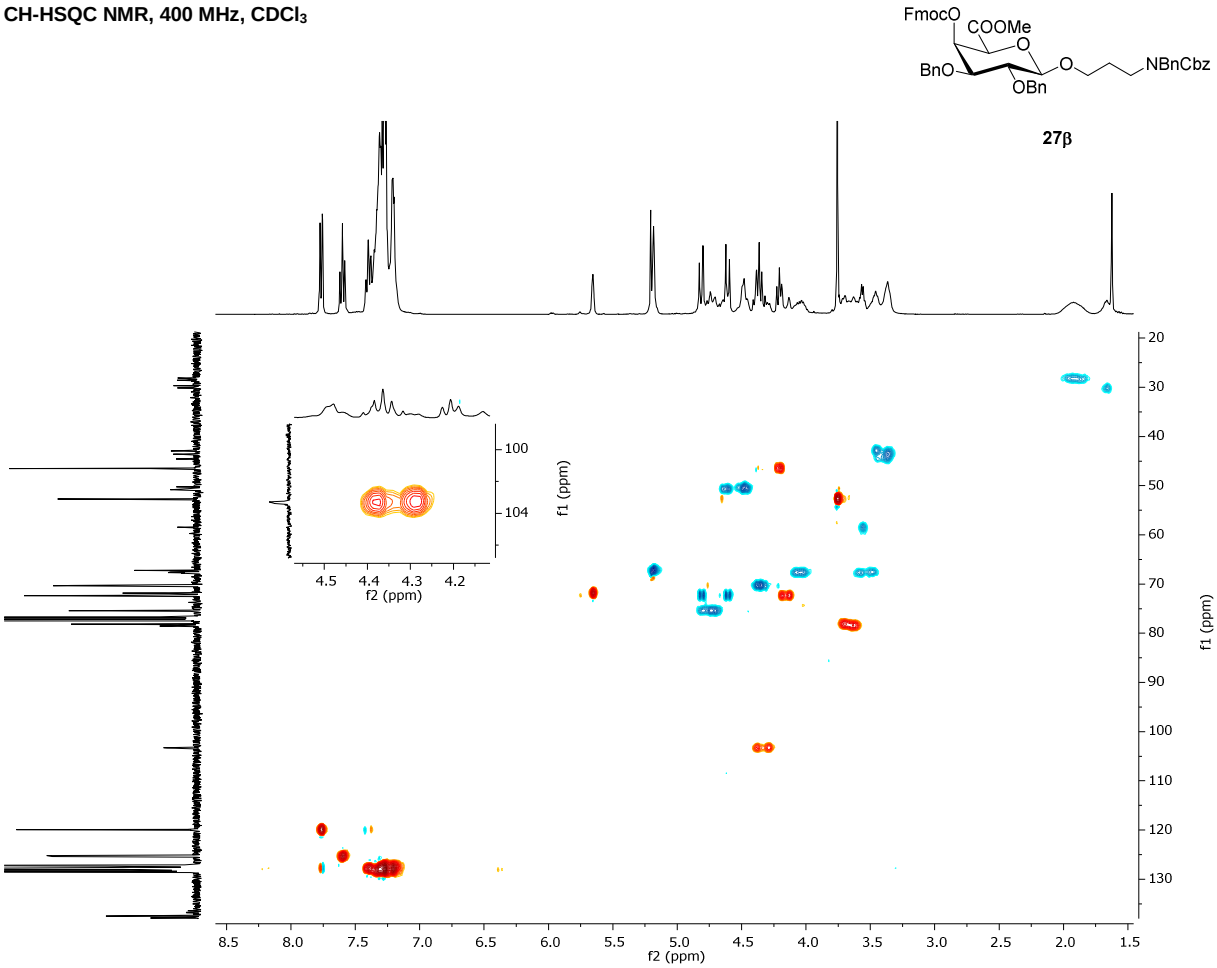
27β



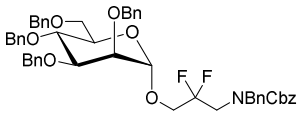
^{13}C NMR, 100 MHz, $CDCl_3$



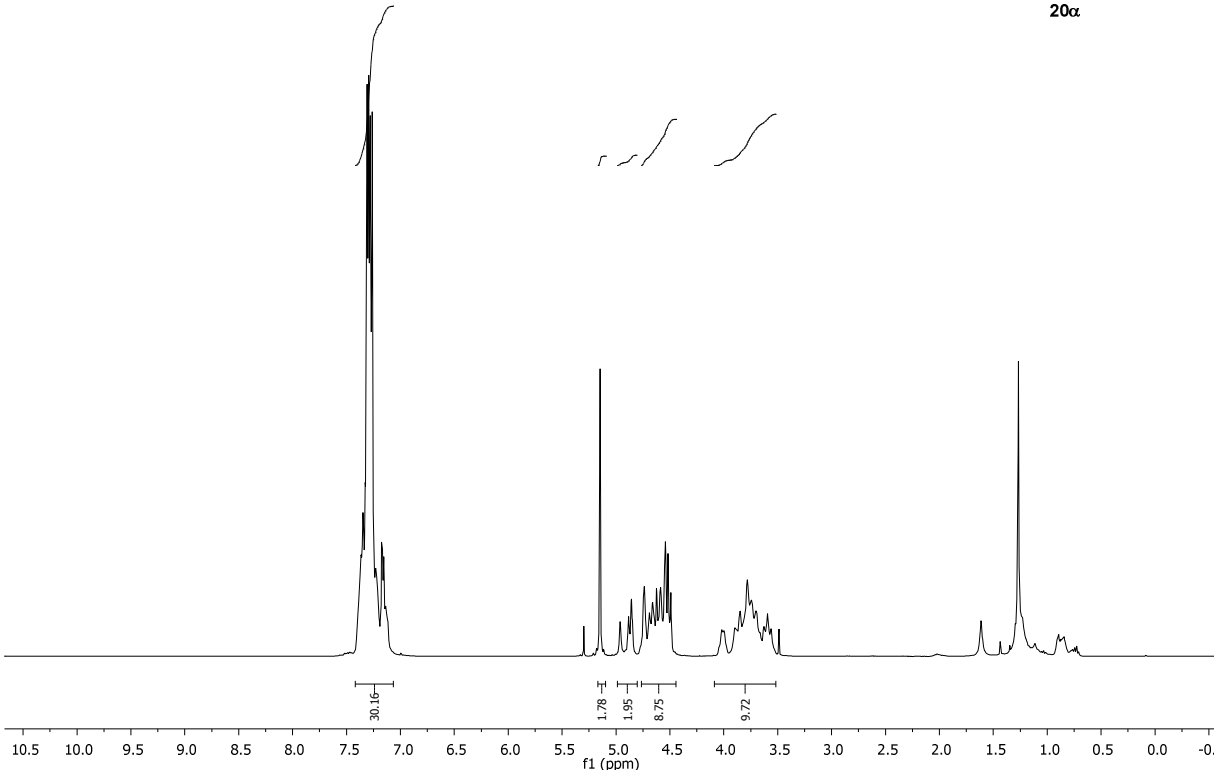
CH-HSQC NMR, 400 MHz, $CDCl_3$



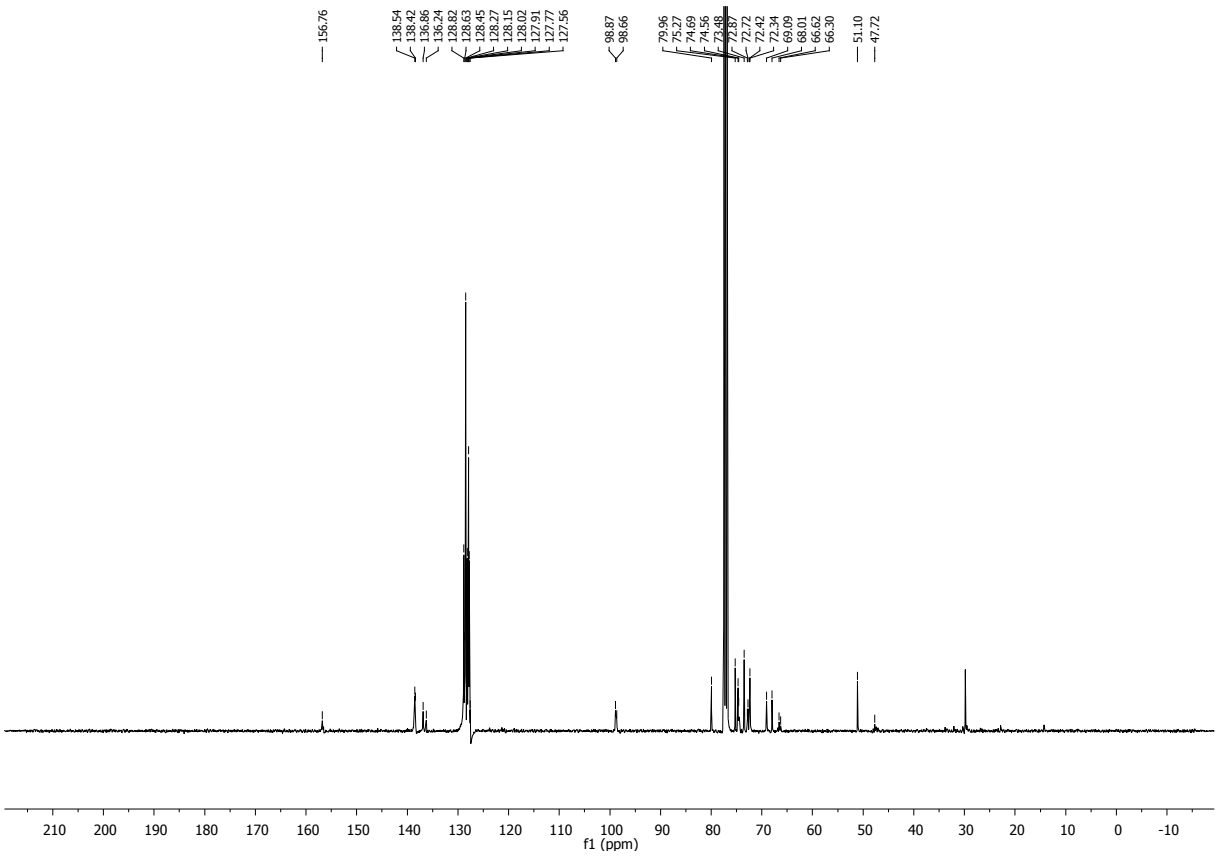
^{1}H NMR, 400 MHz, $CDCl_3$



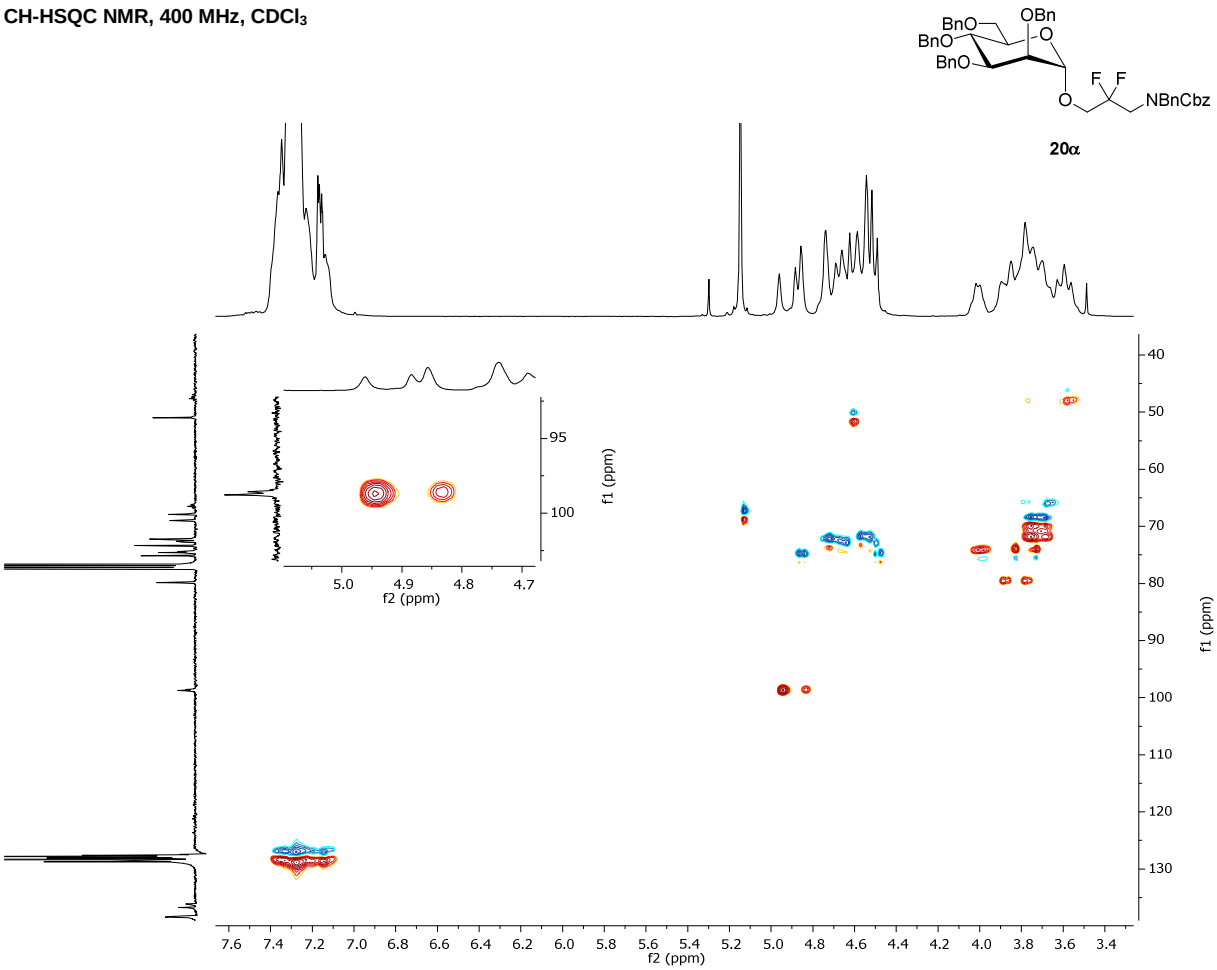
20α



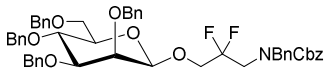
^{13}C NMR, 100 MHz, $CDCl_3$



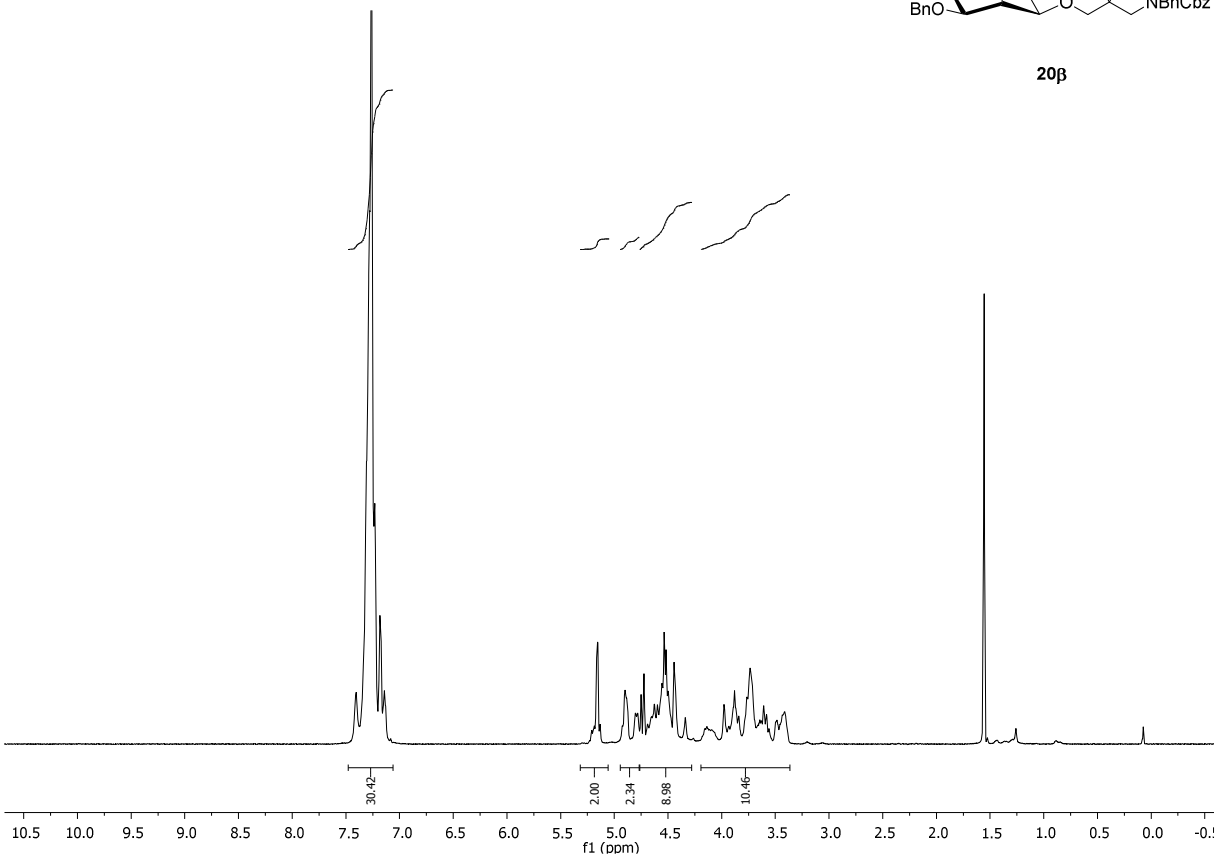
CH-HSQC NMR, 400 MHz, $CDCl_3$



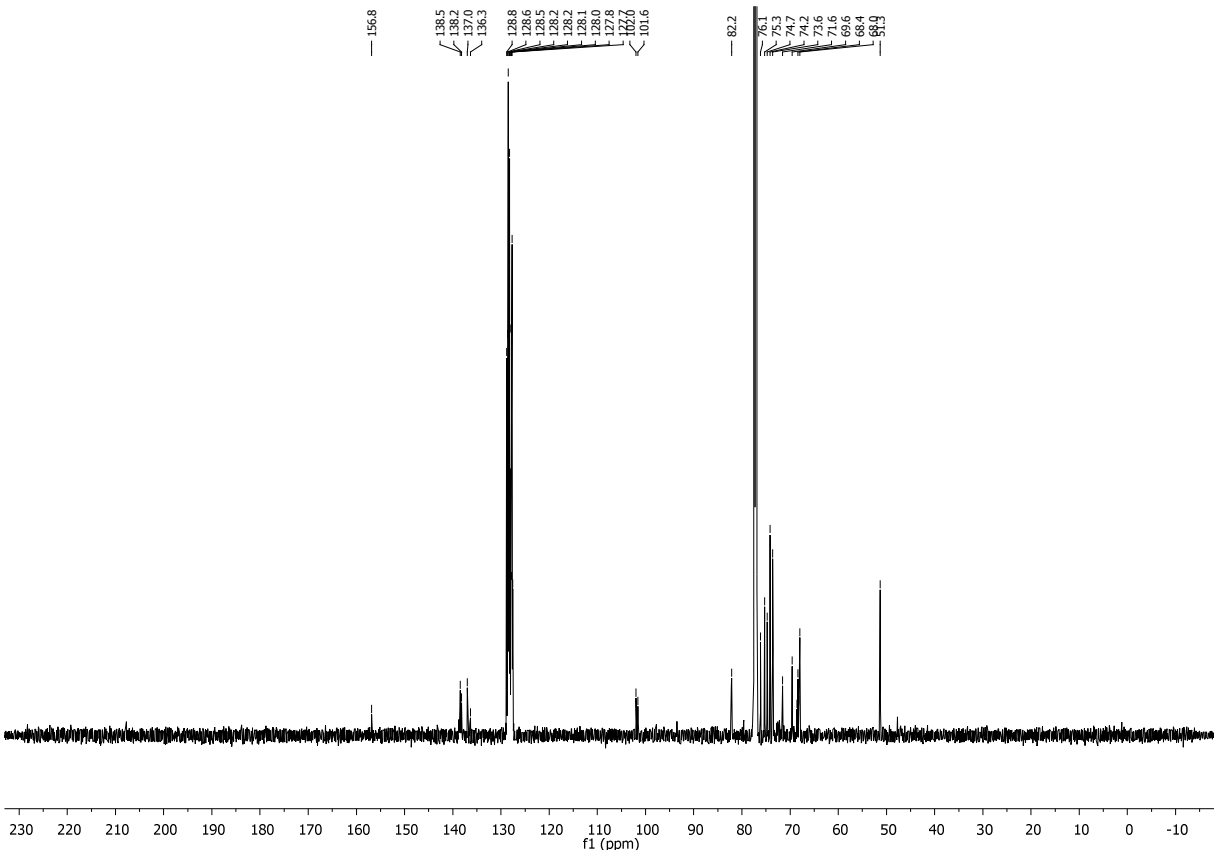
^{1}H NMR, 600 MHz, $CDCl_3$



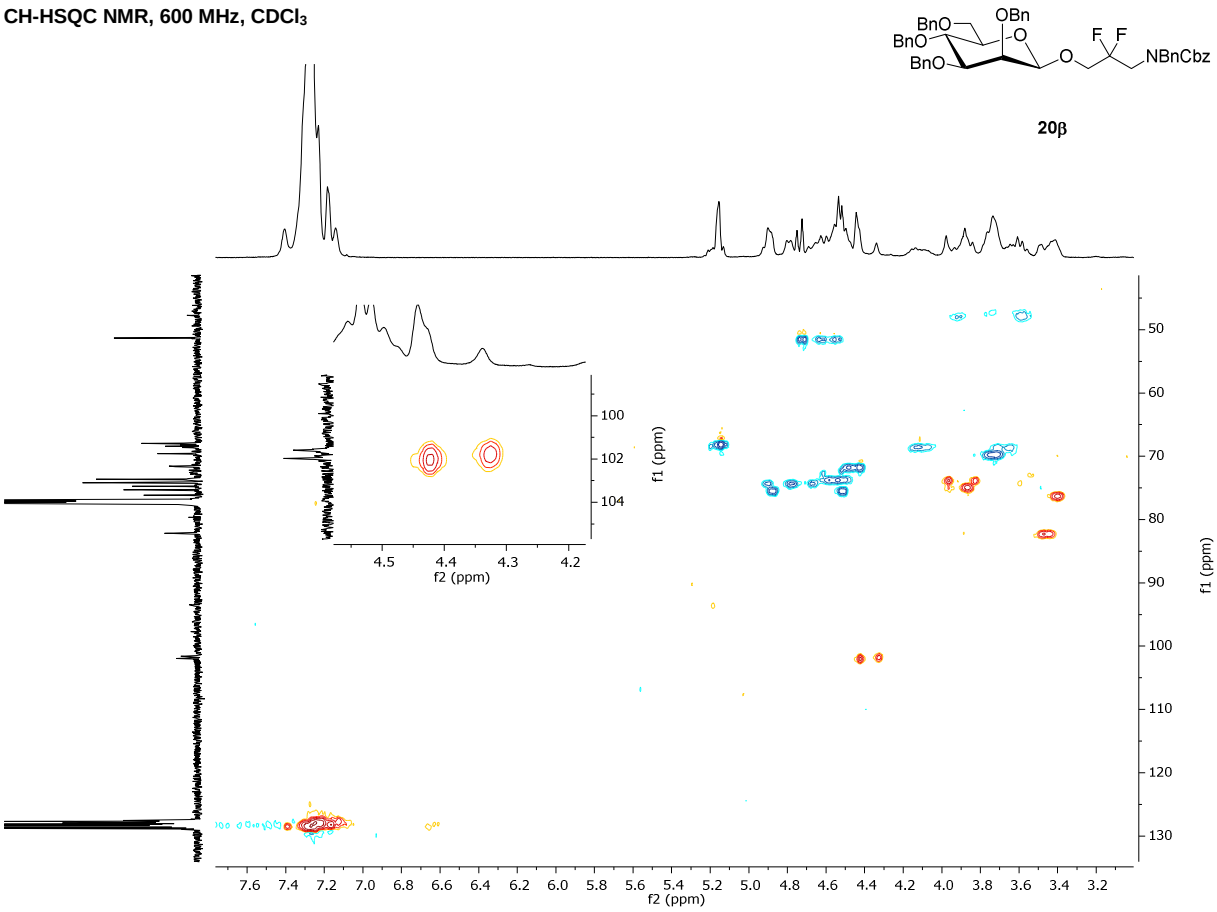
20β



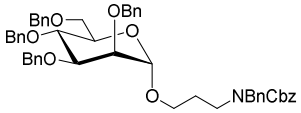
^{13}C NMR, 150 MHz, $CDCl_3$



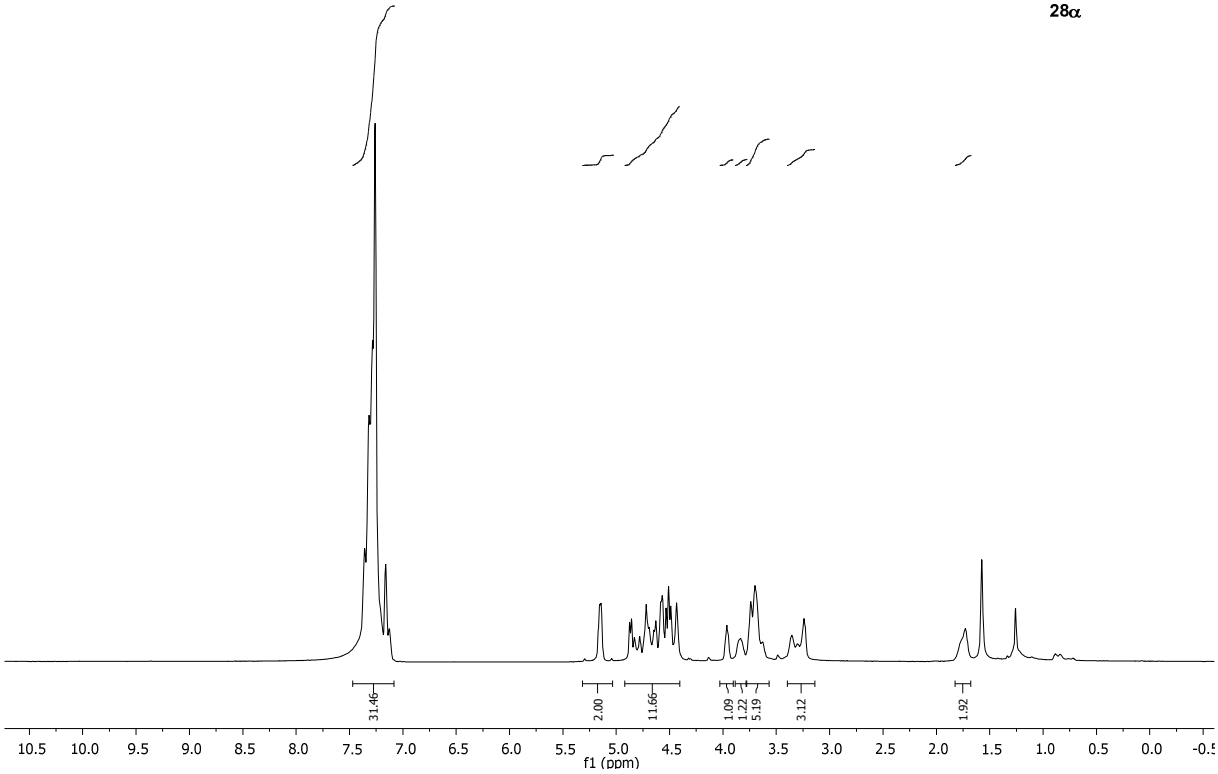
CH-HSQC NMR, 600 MHz, $CDCl_3$



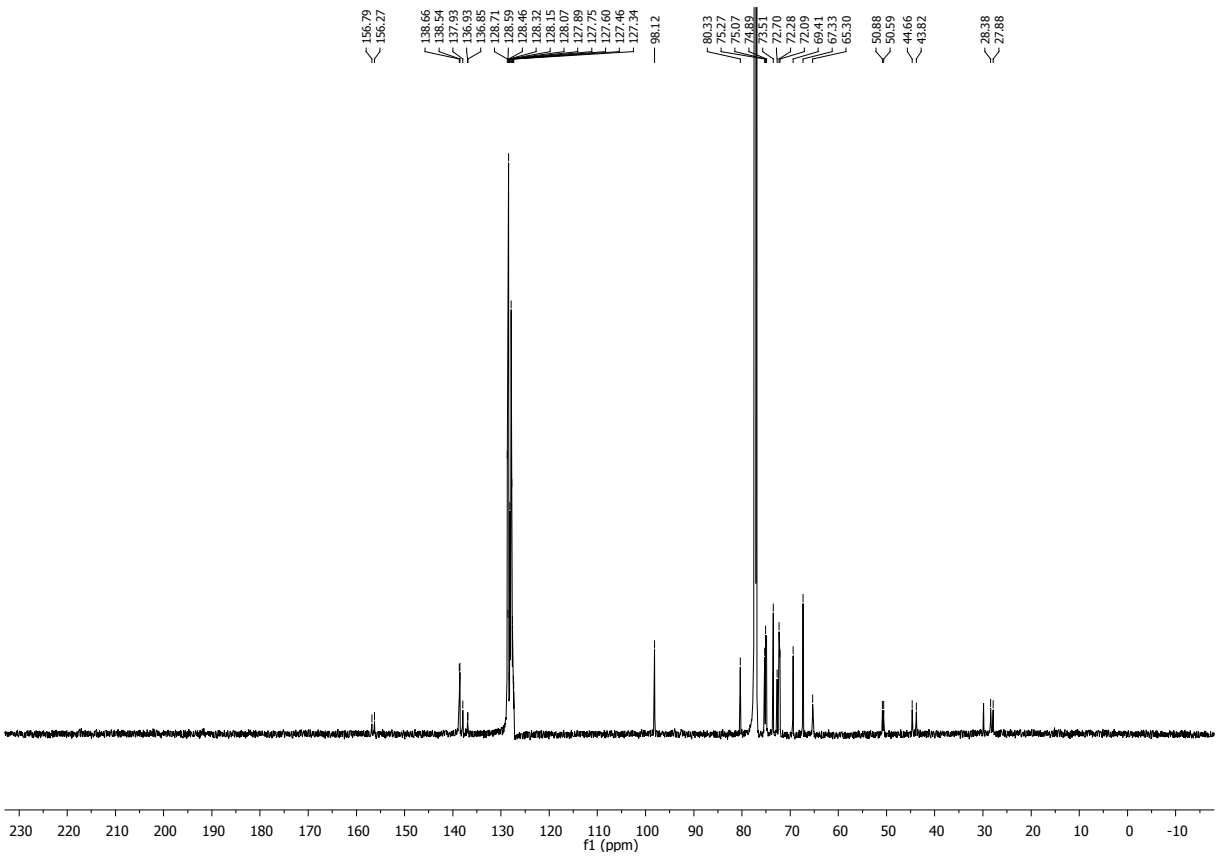
^{1}H NMR, 600 MHz, $CHCl_3$



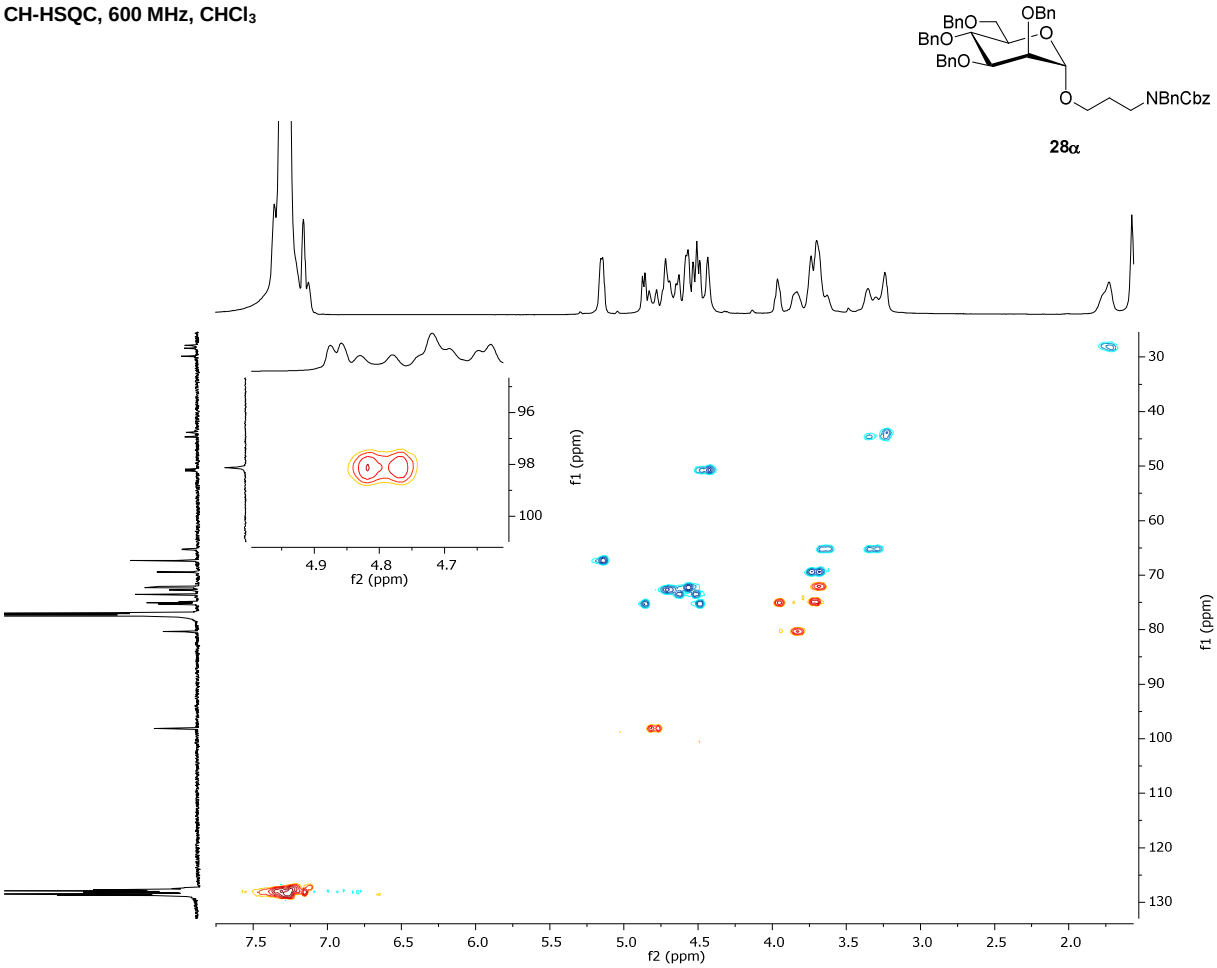
28α



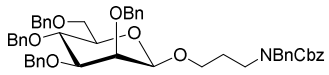
^{13}C NMR, 150 MHz, $CHCl_3$



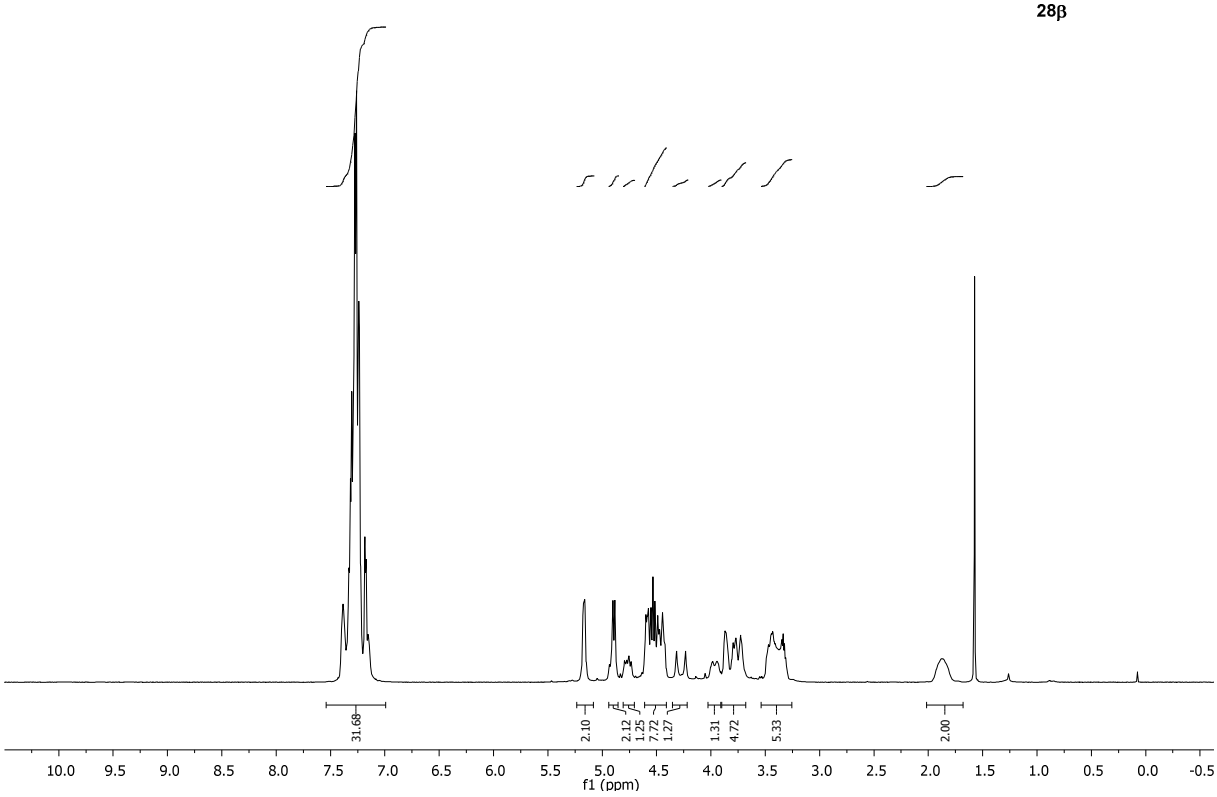
CH-HSQC, 600 MHz, $CHCl_3$



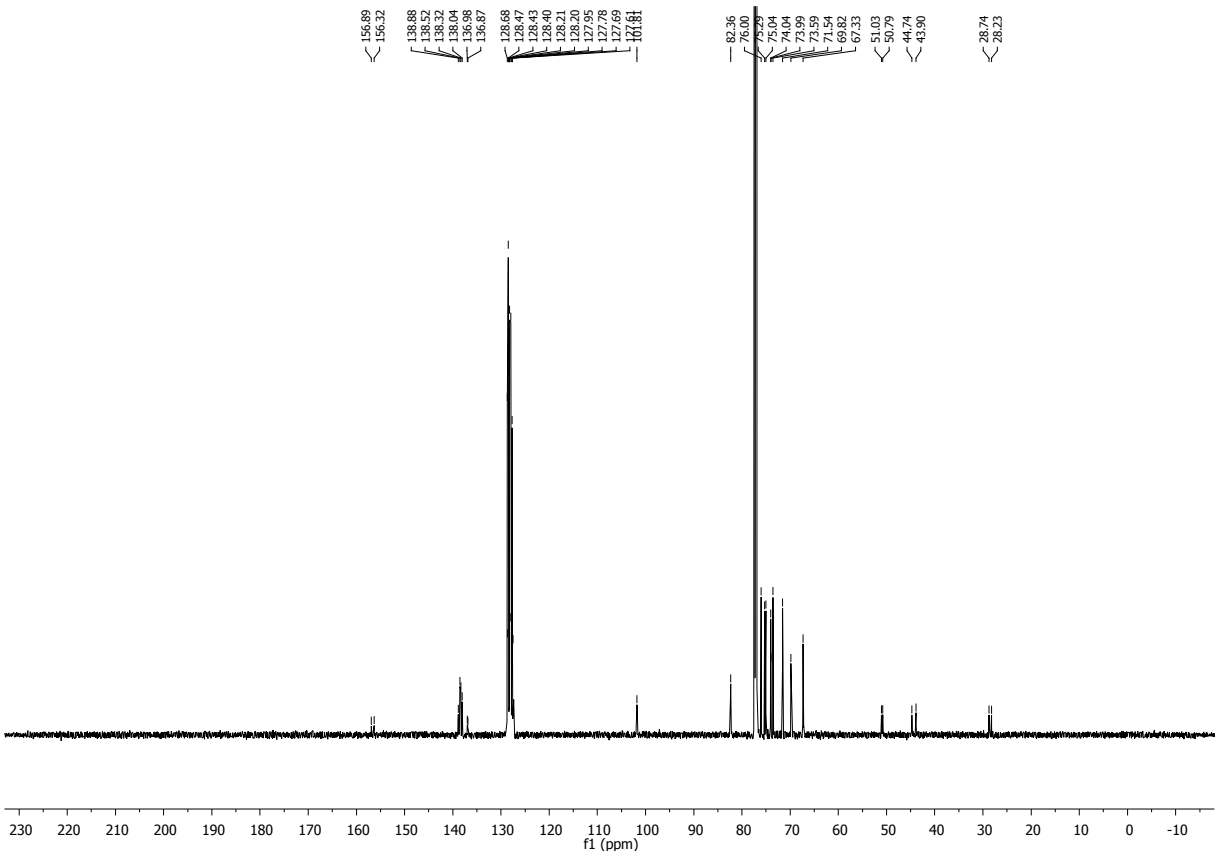
^{1}H NMR, 600 MHz, $CHCl_3$



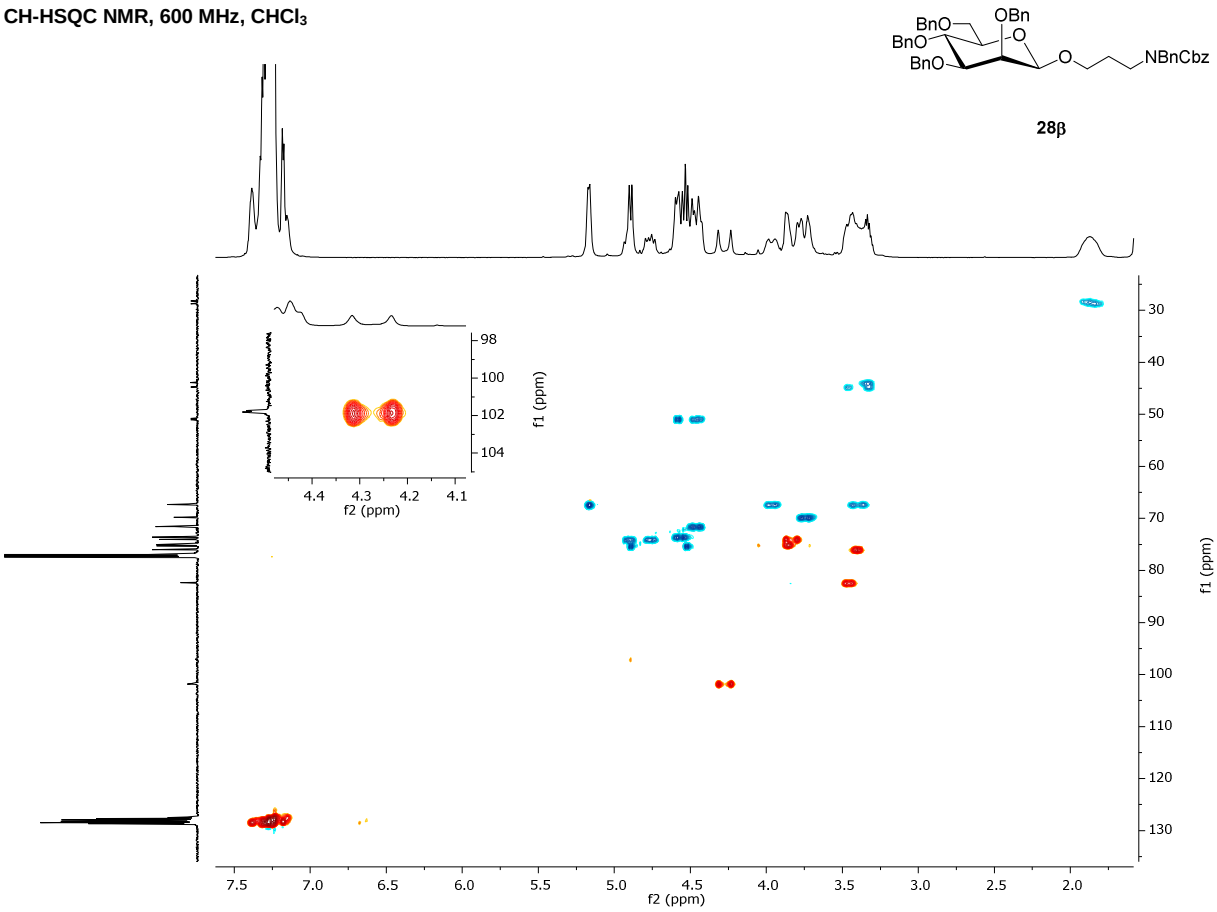
28β



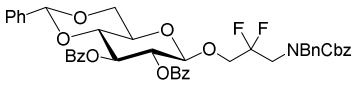
^{13}C NMR, 150 MHz, $CHCl_3$



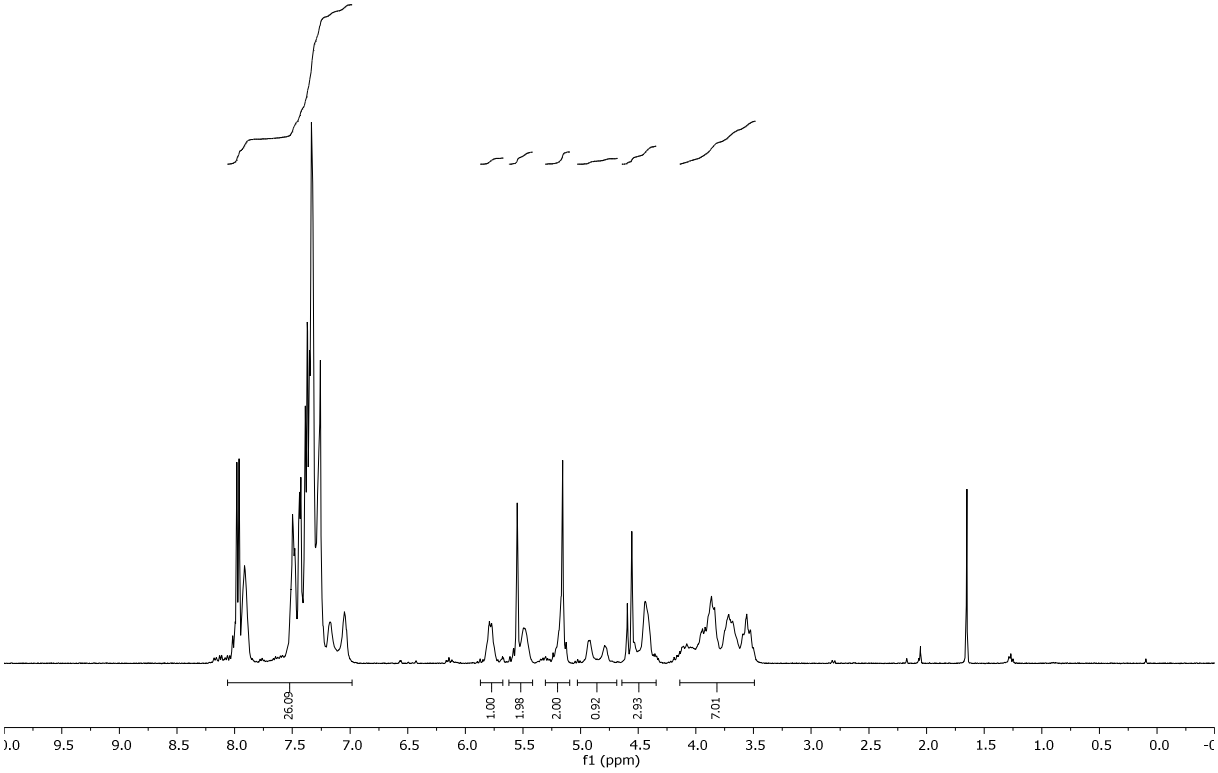
CH-HSQC NMR, 600 MHz, $CHCl_3$



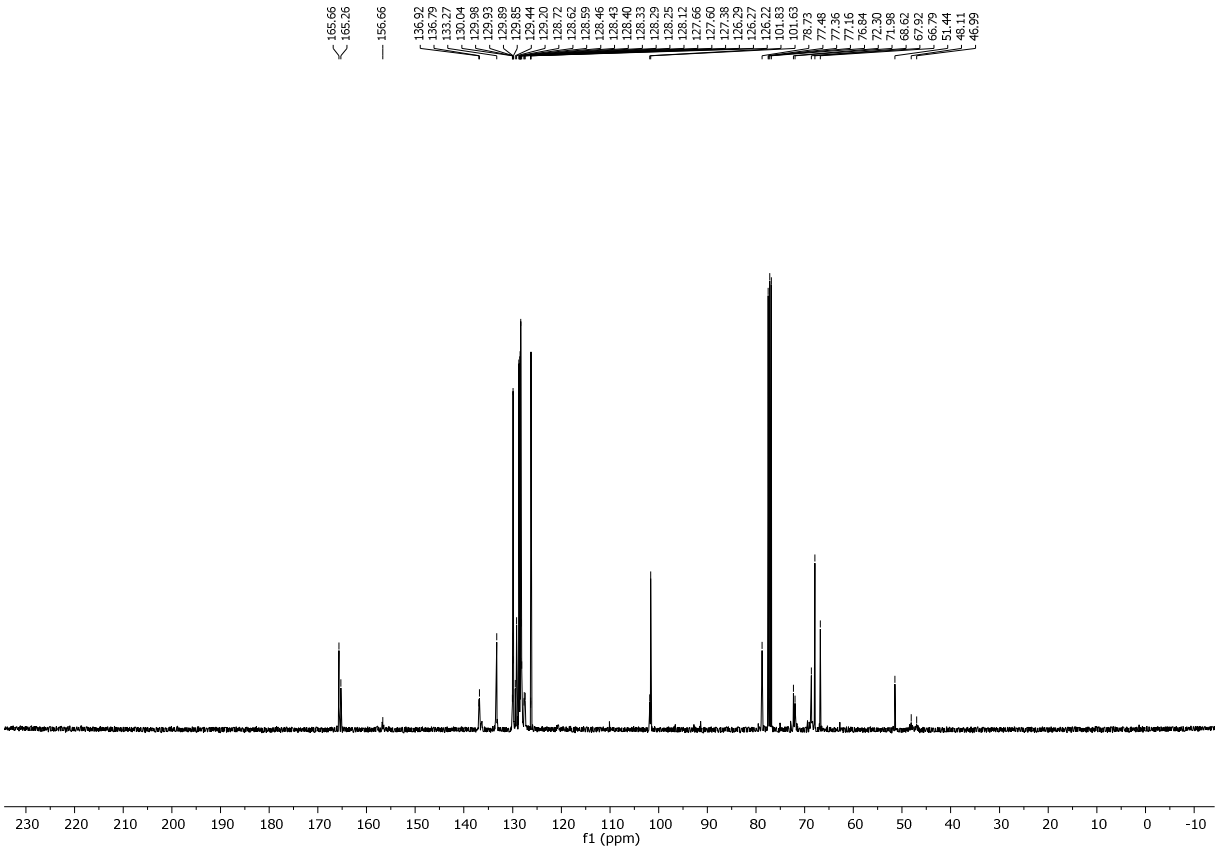
^{1}H NMR, 400 MHz, $CDCl_3$



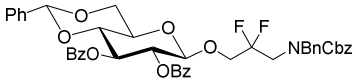
21β



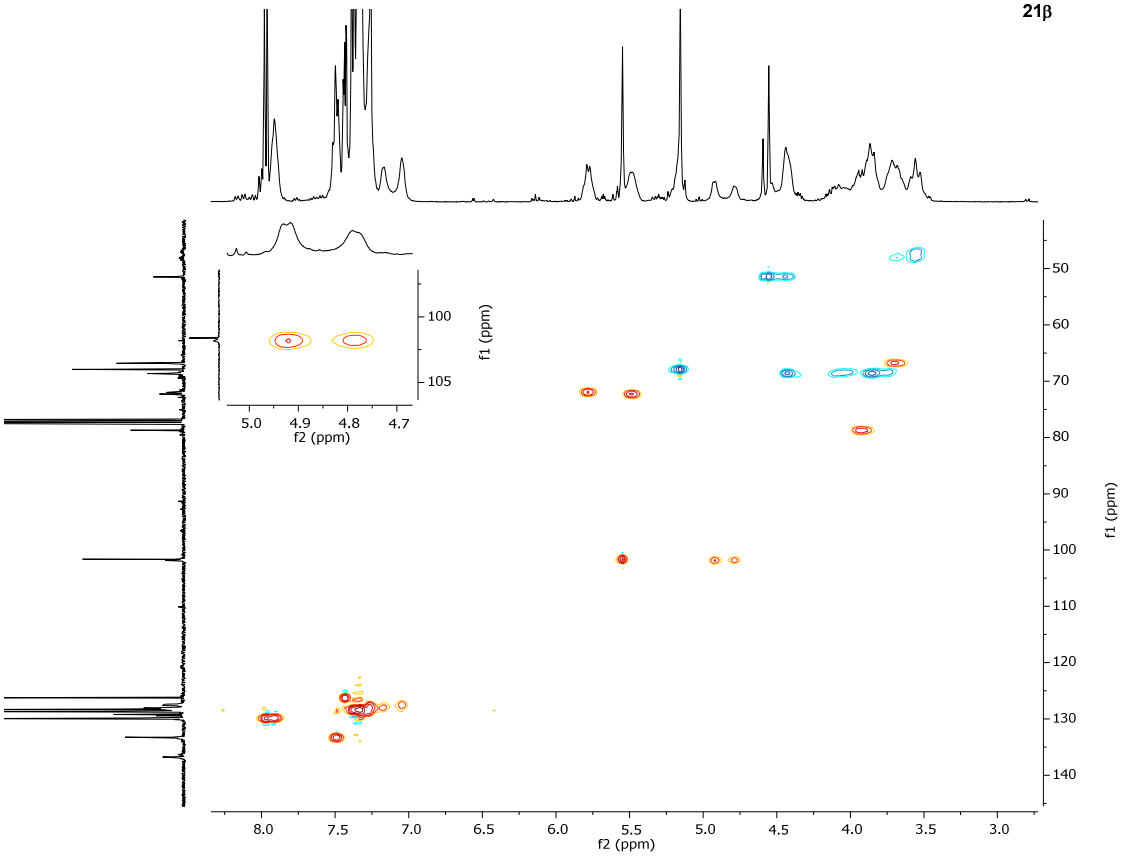
^{13}C NMR, 100 MHz, $CDCl_3$



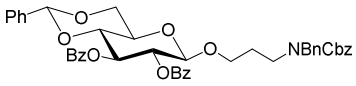
CH-HSQC NMR, 400 MHz, $CDCl_3$



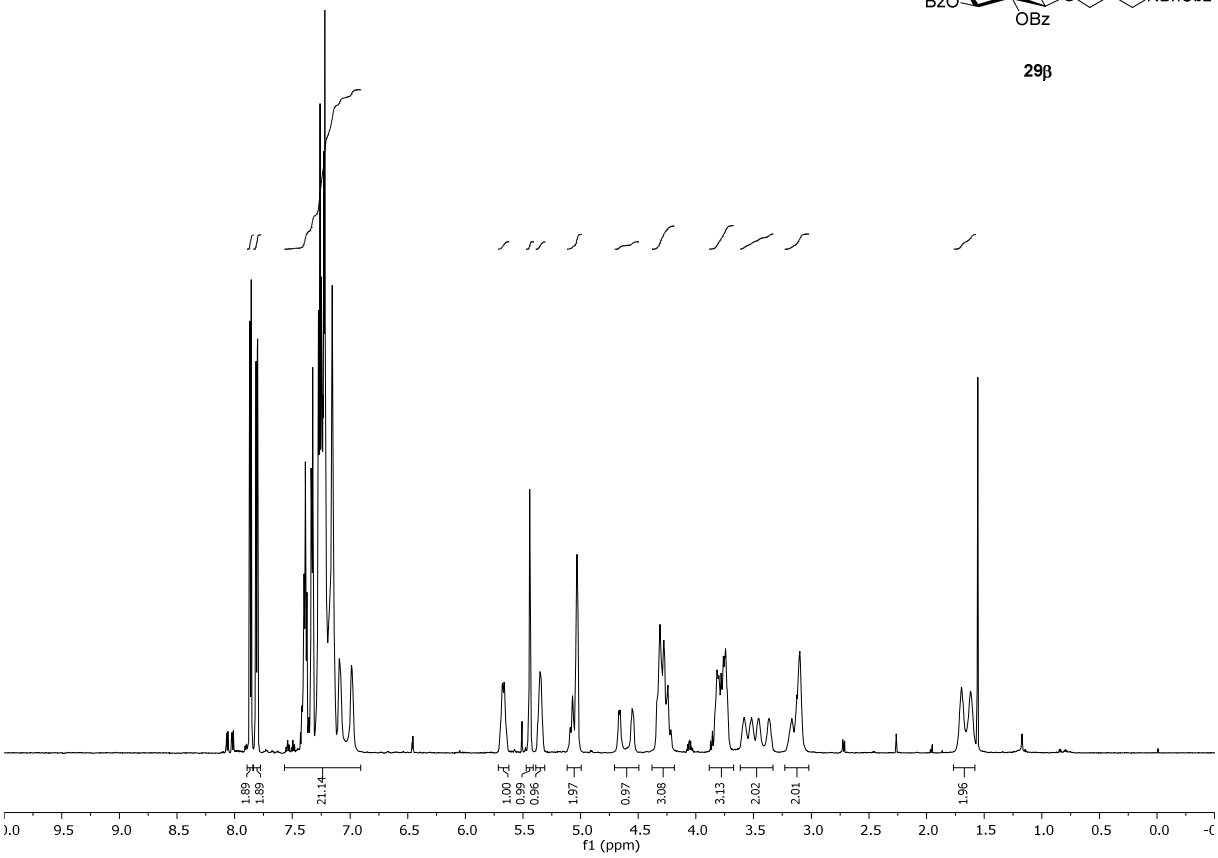
21β



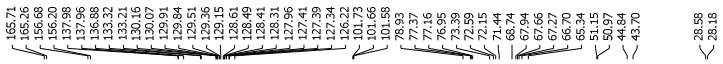
^{1}H NMR, 600 MHz, $CDCl_3$

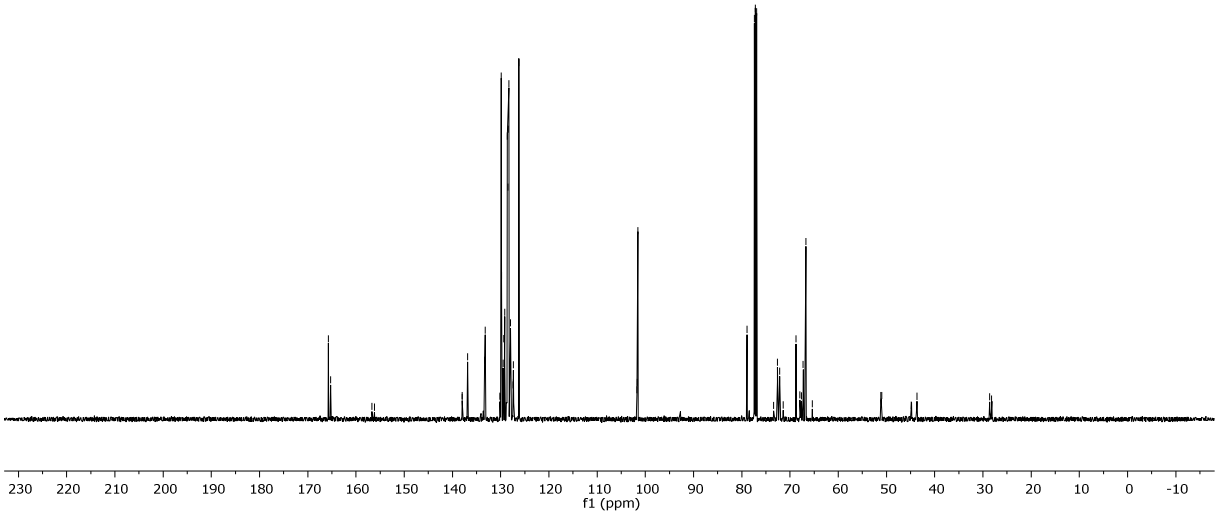


29β

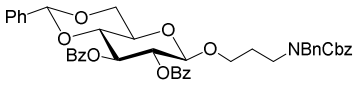


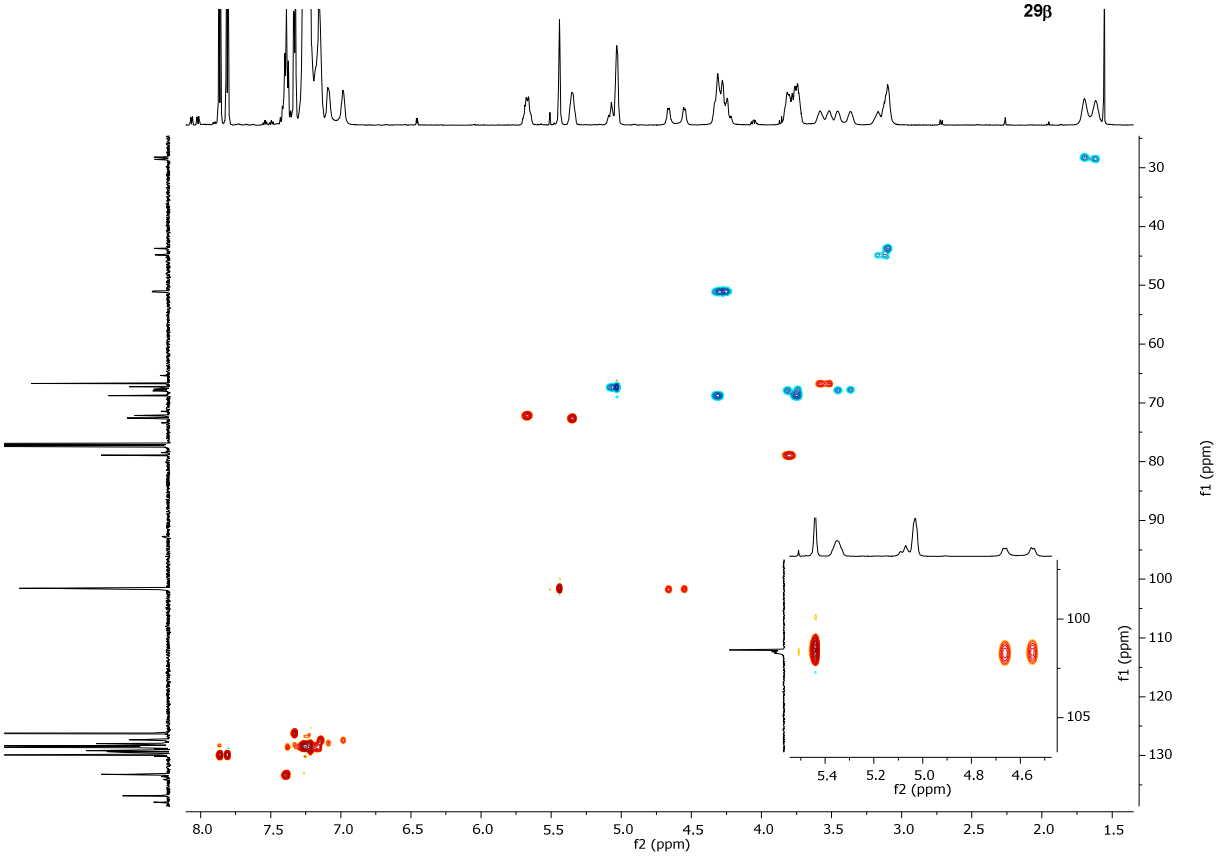
^{13}C NMR, 150 MHz, $CDCl_3$



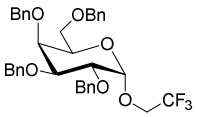


CH-HSQC NMR, 600 MHz, $CDCl_3$

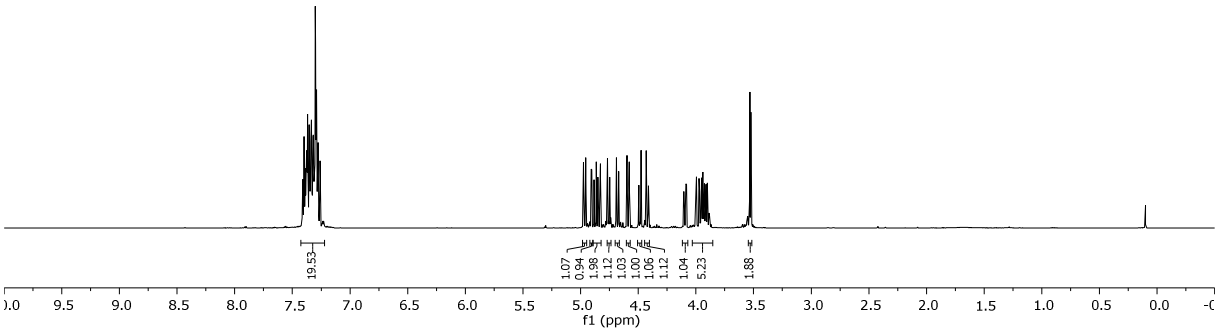




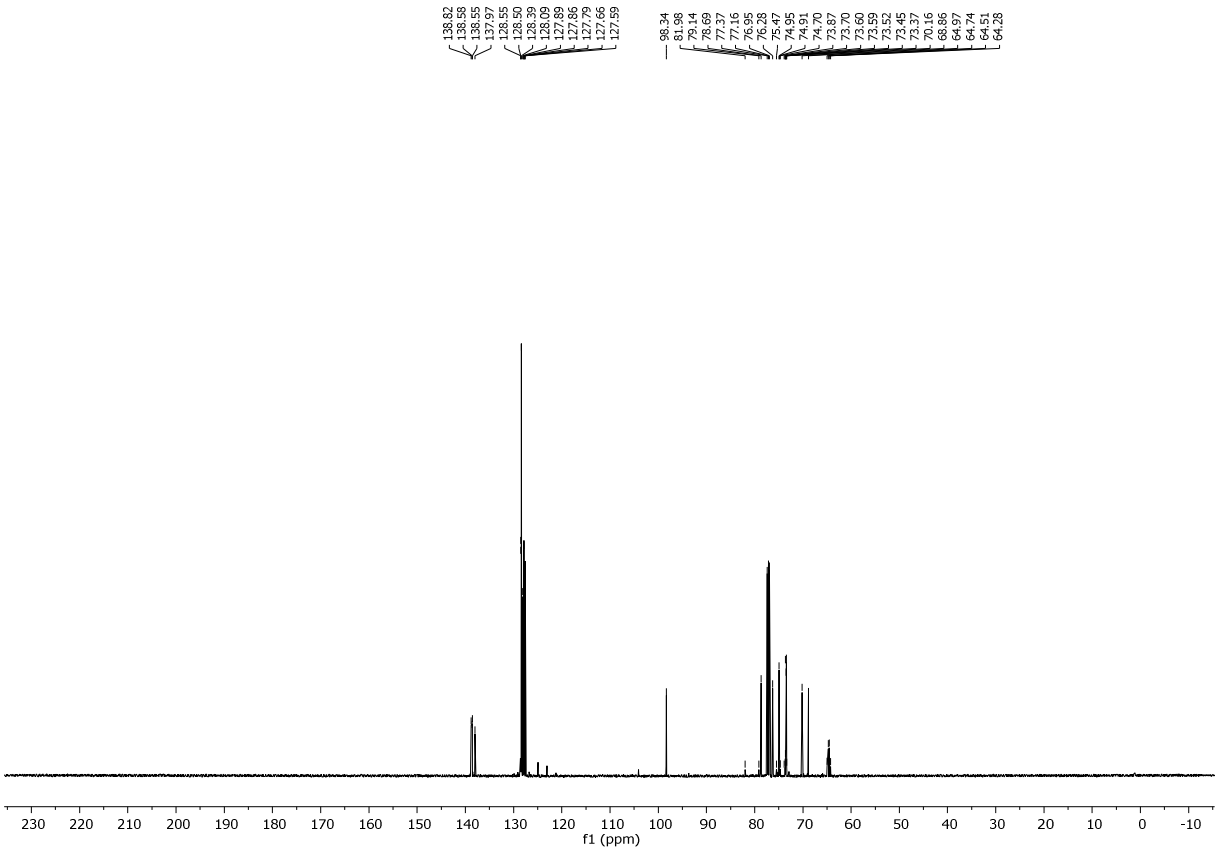
^{1}H NMR, 600 MHz, $CDCl_3$



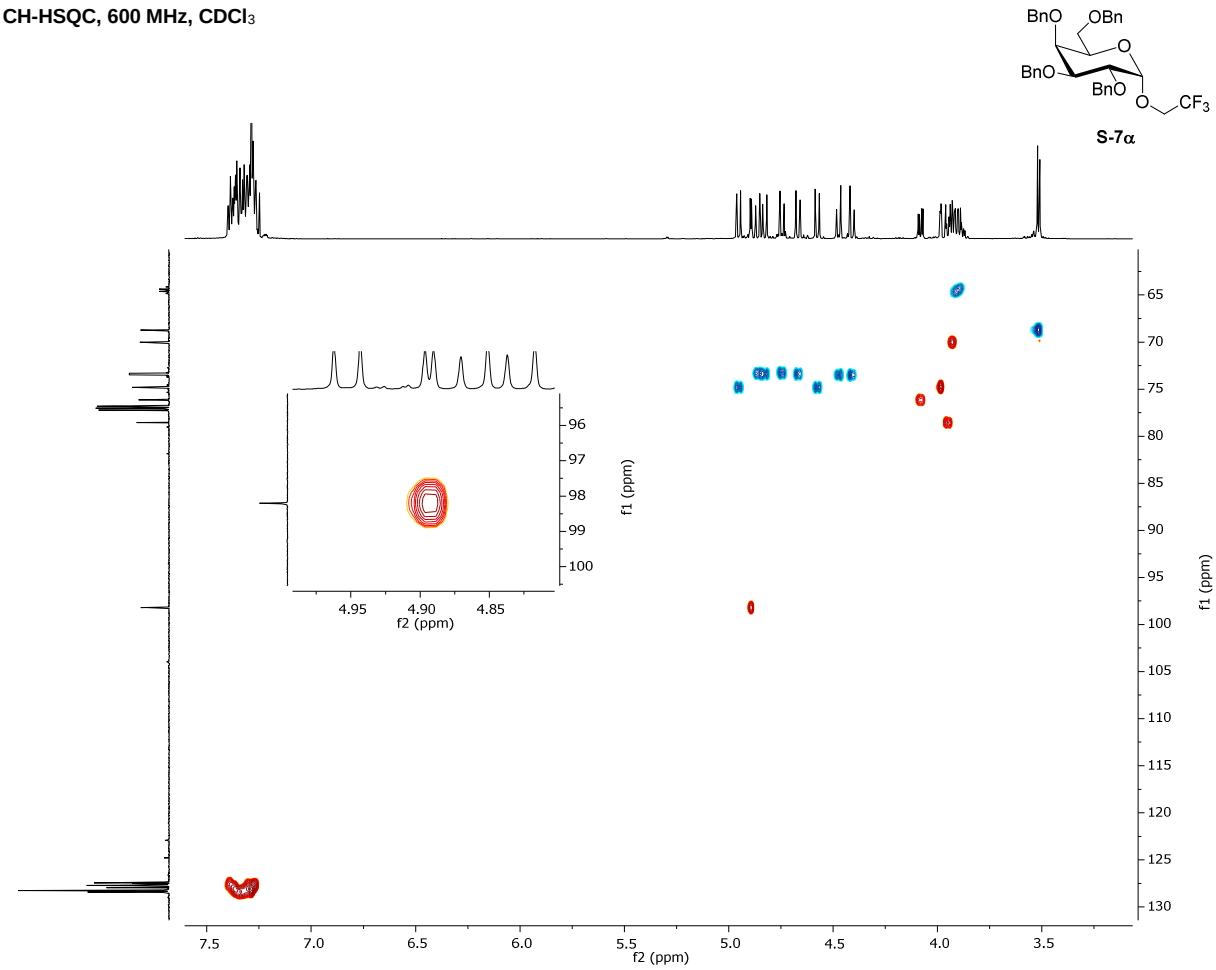
S-7α



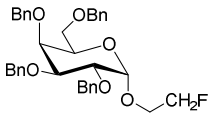
^{13}C NMR, 150 MHz, $CDCl_3$



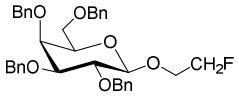
CH-HSQC, 600 MHz, $CDCl_3$



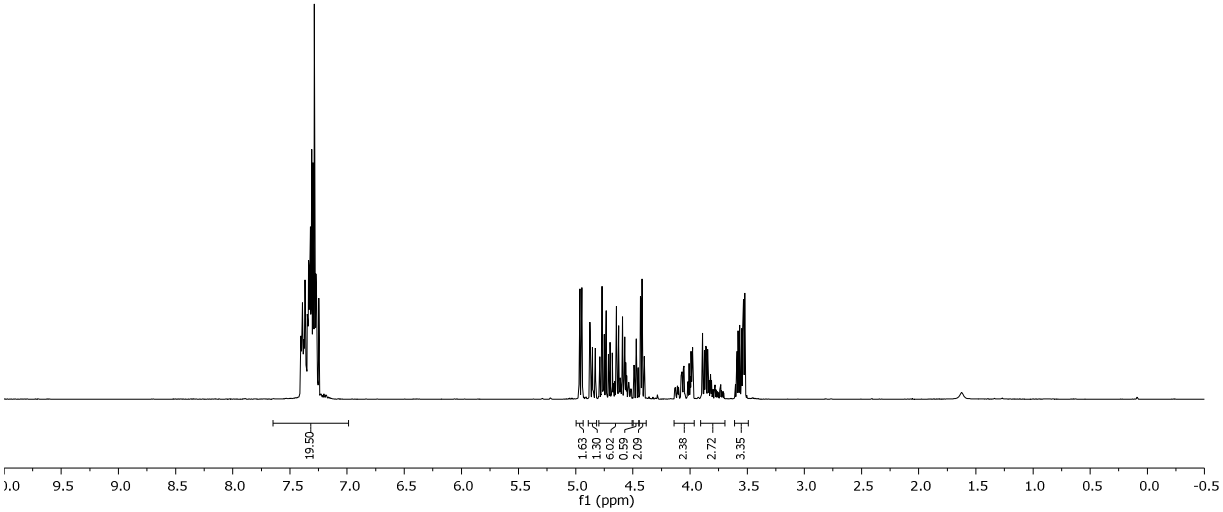
^{1}H NMR, 600 MHz, $CDCl_3$



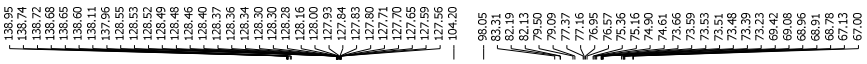
S-8α

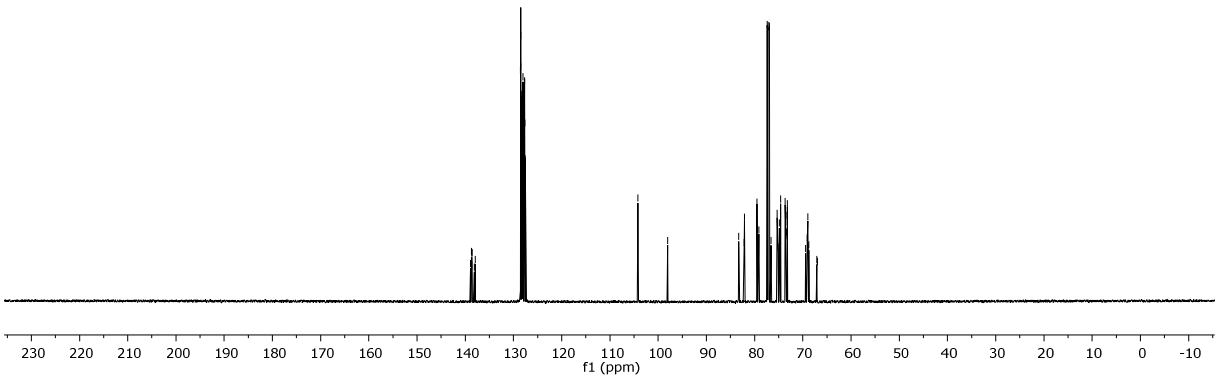


S-8β

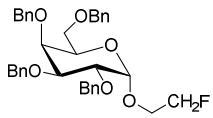


^{13}C NMR, 150 MHz, $CDCl_3$

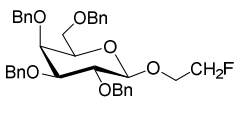




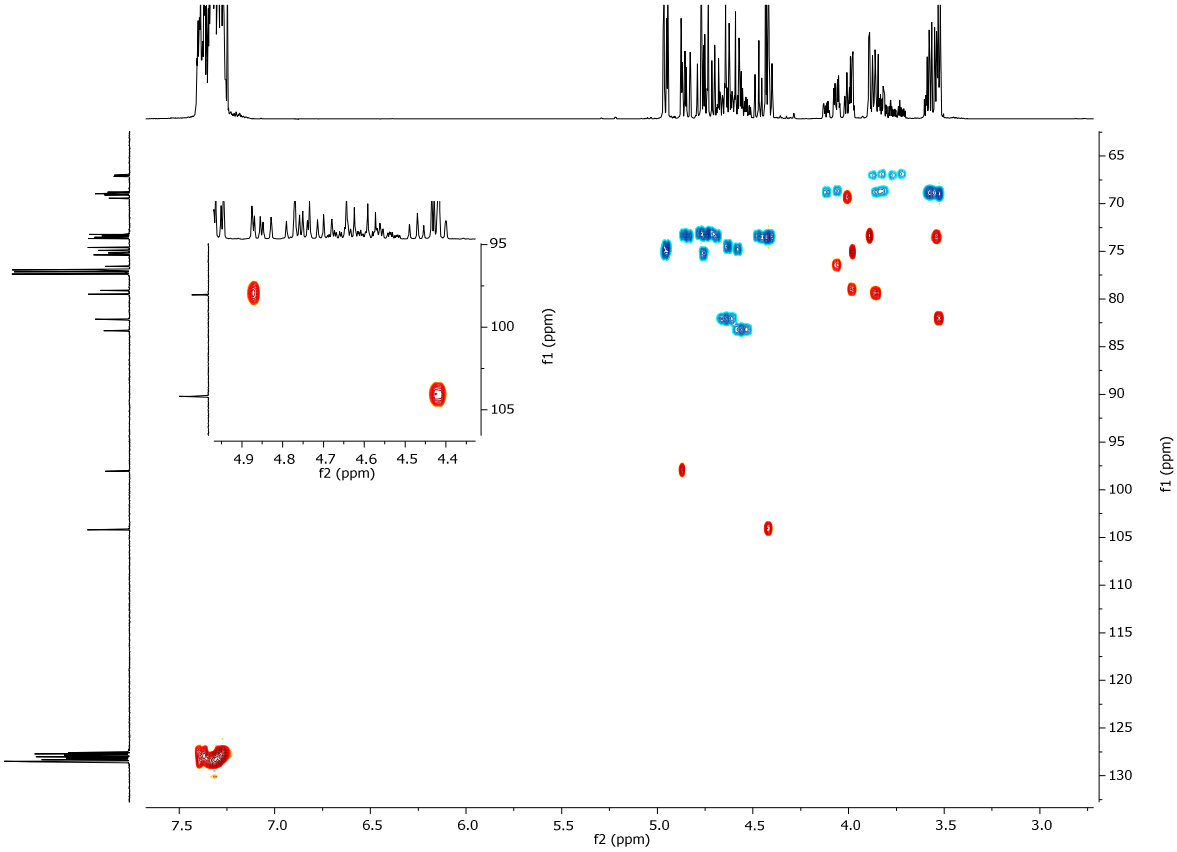
CH-HSQC, 600 MHz, $CDCl_3$



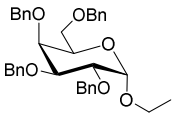
S-8α



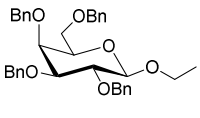
S-8β



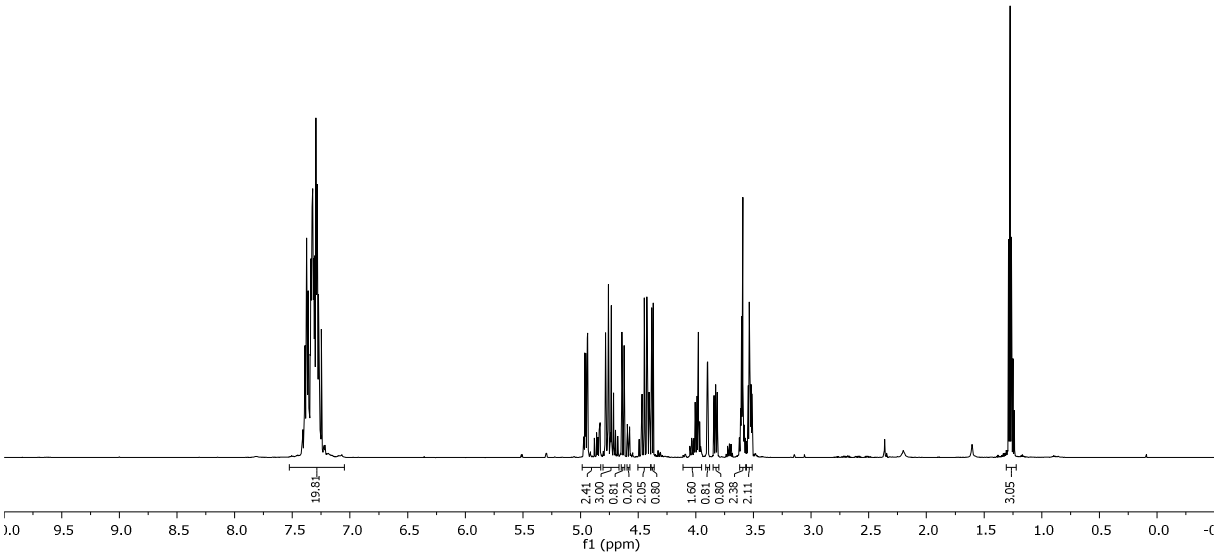
^{1}H NMR, 600 MHz, $CDCl_3$



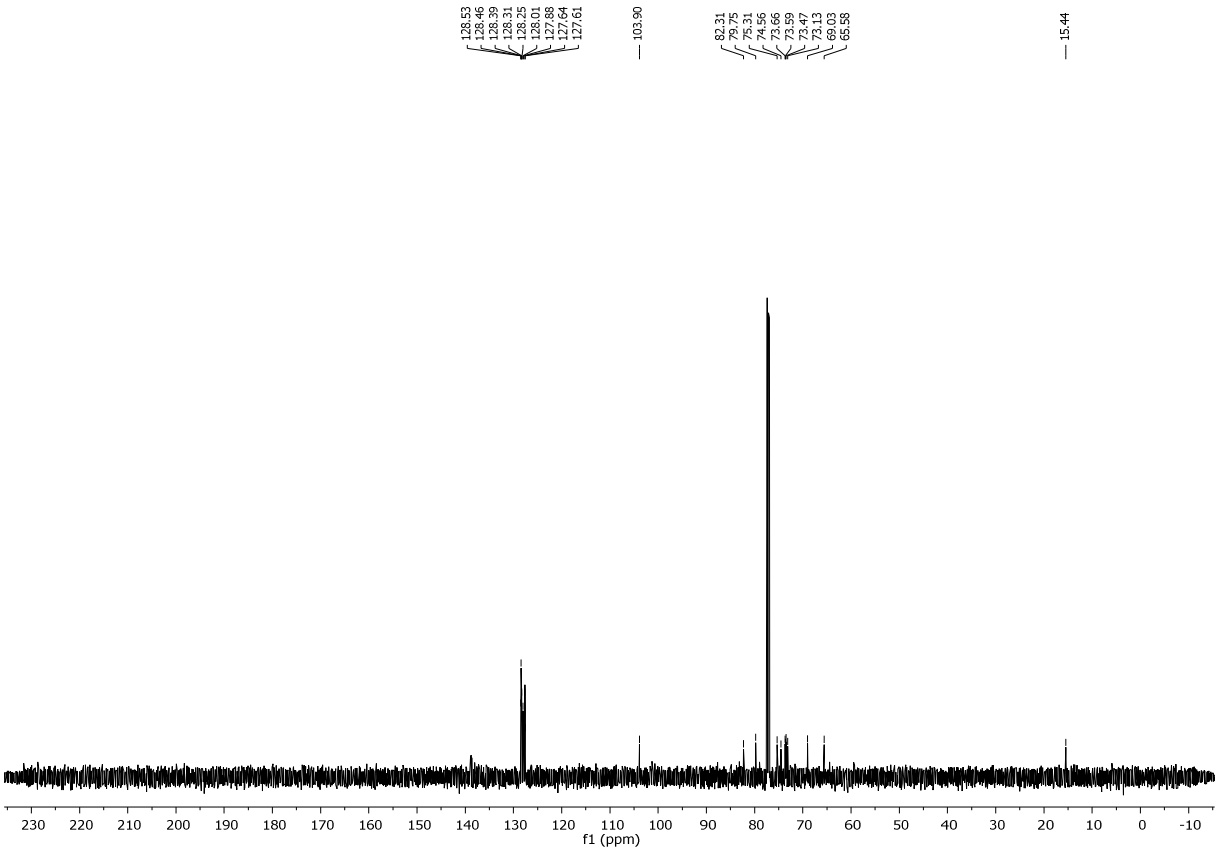
S-9α



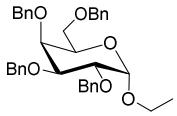
S-9β



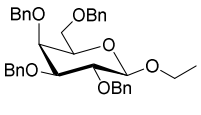
^{13}C NMR, 150 MHz, $CDCl_3$



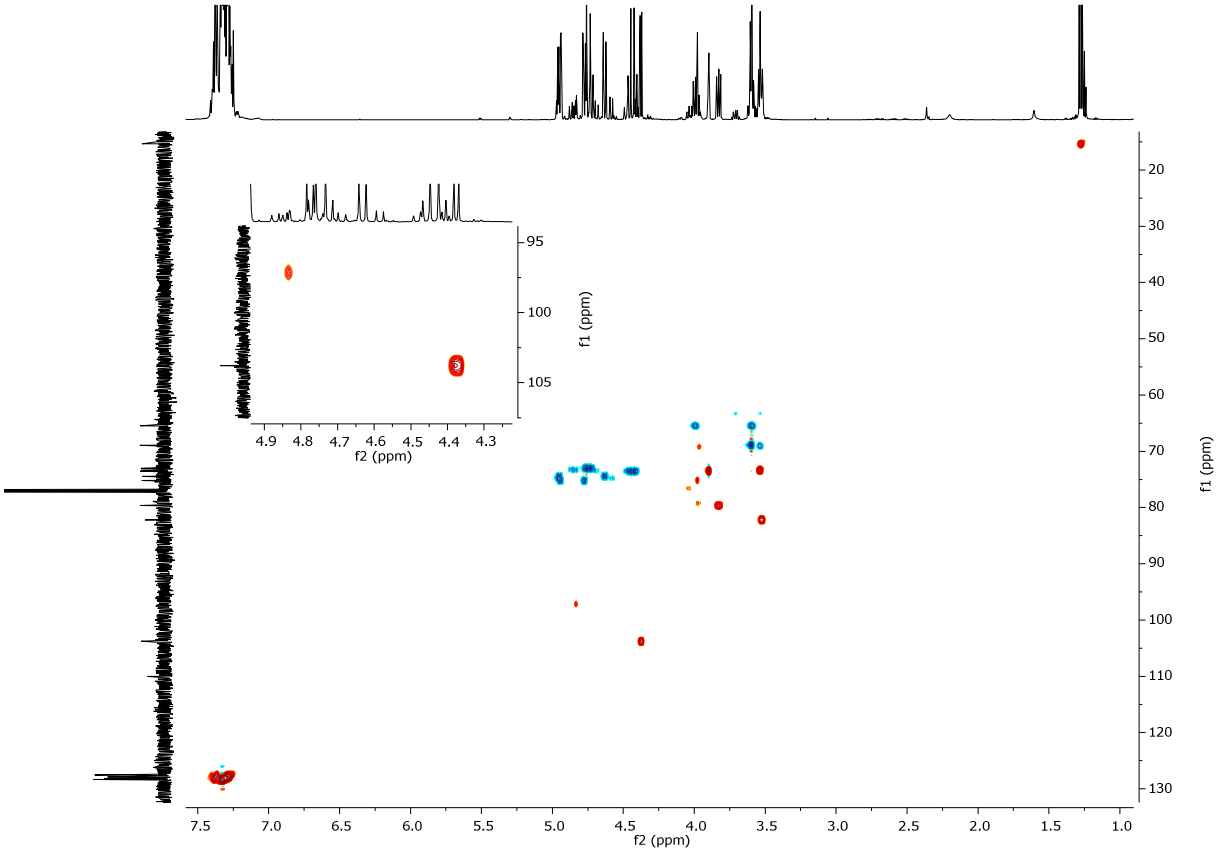
CH-HSQC, 600 MHz, $CDCl_3$



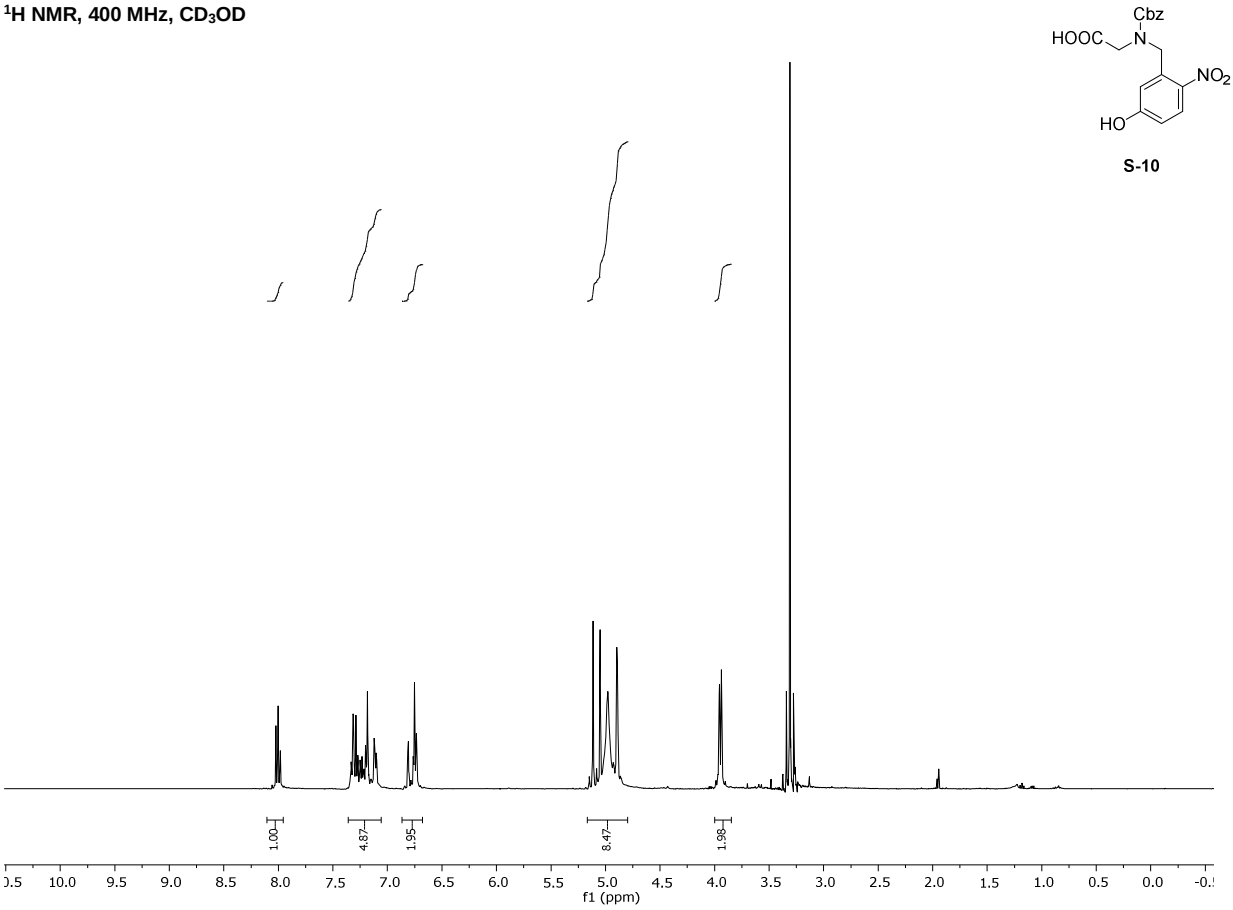
S-9α



S-9β

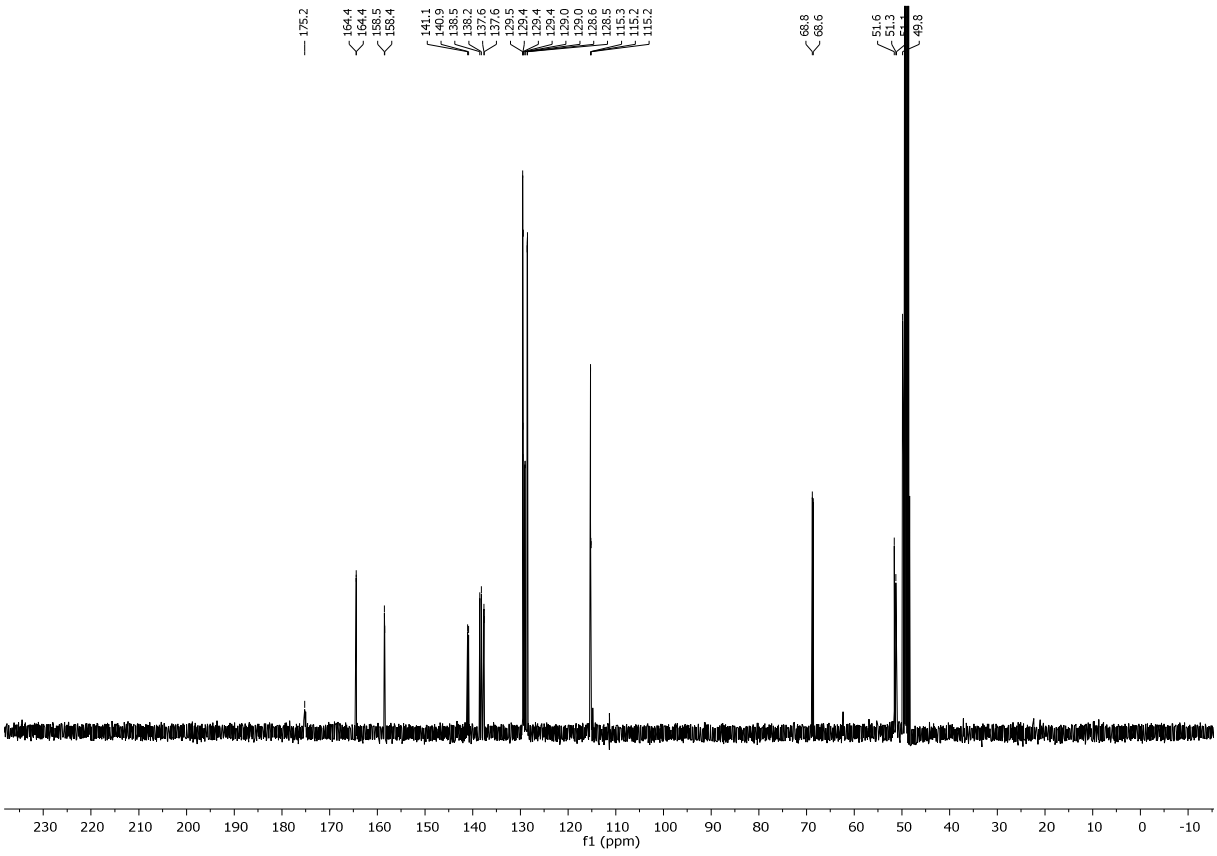


^{1}H NMR, 400 MHz, CD_3OD

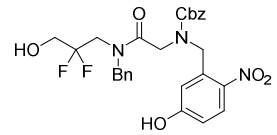


S-10

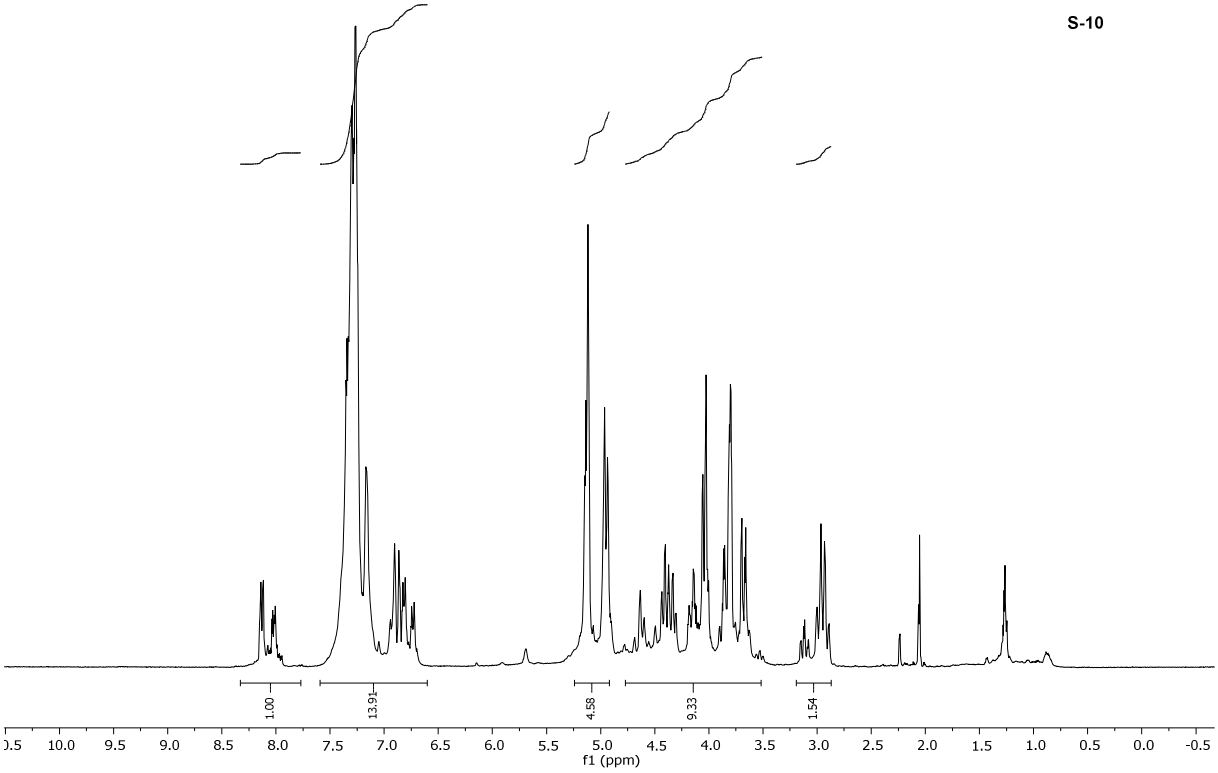
^{13}C NMR, 100 MHz, CD_3OD



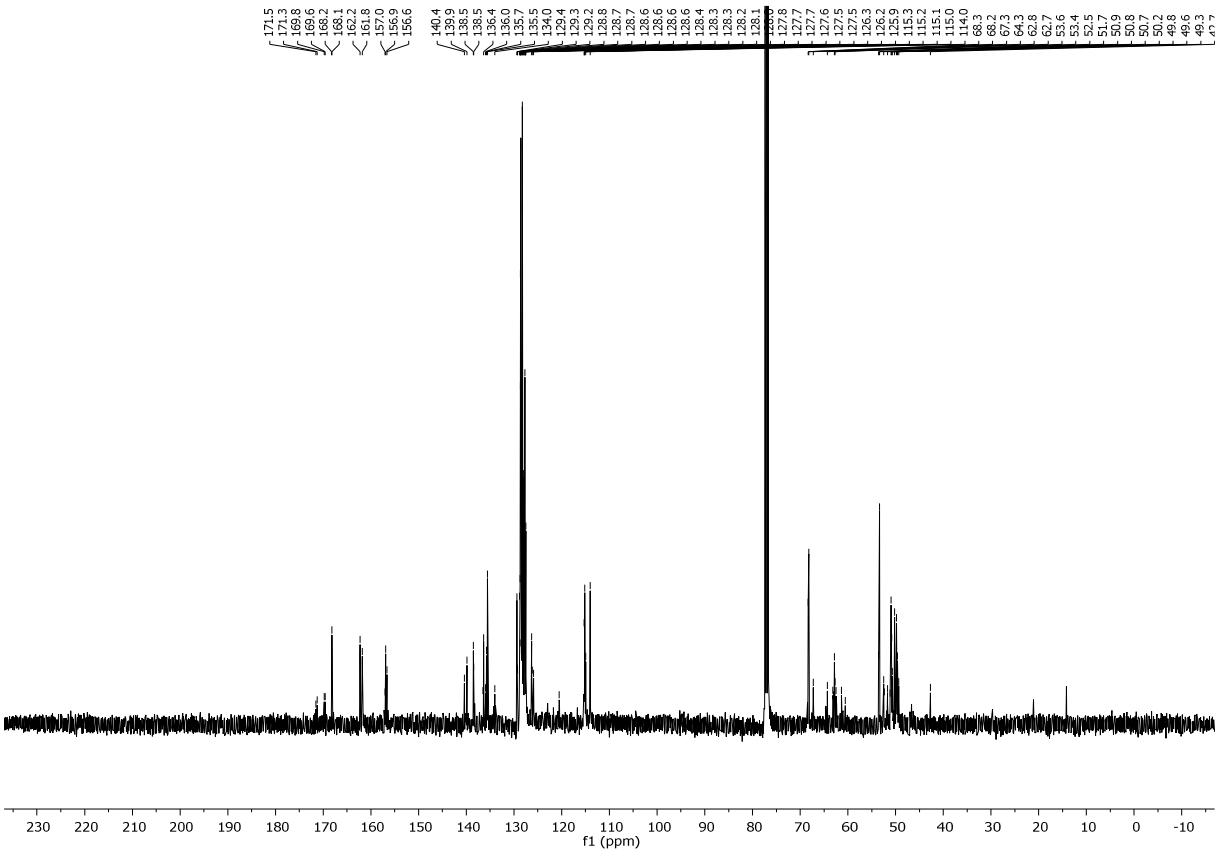
^{1}H NMR, 400 MHz, $CDCl_3$ (mixture of four rotamers)



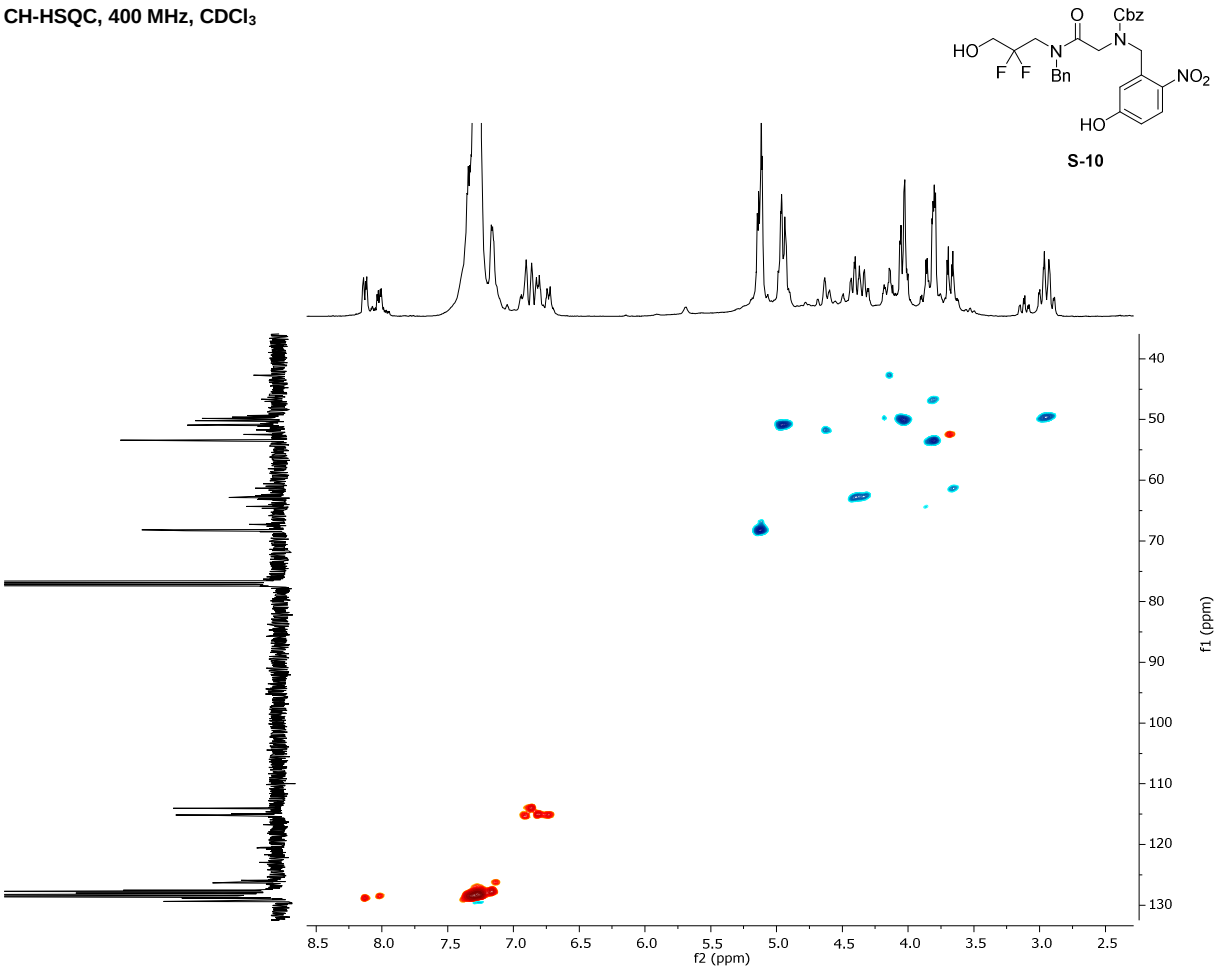
S-10



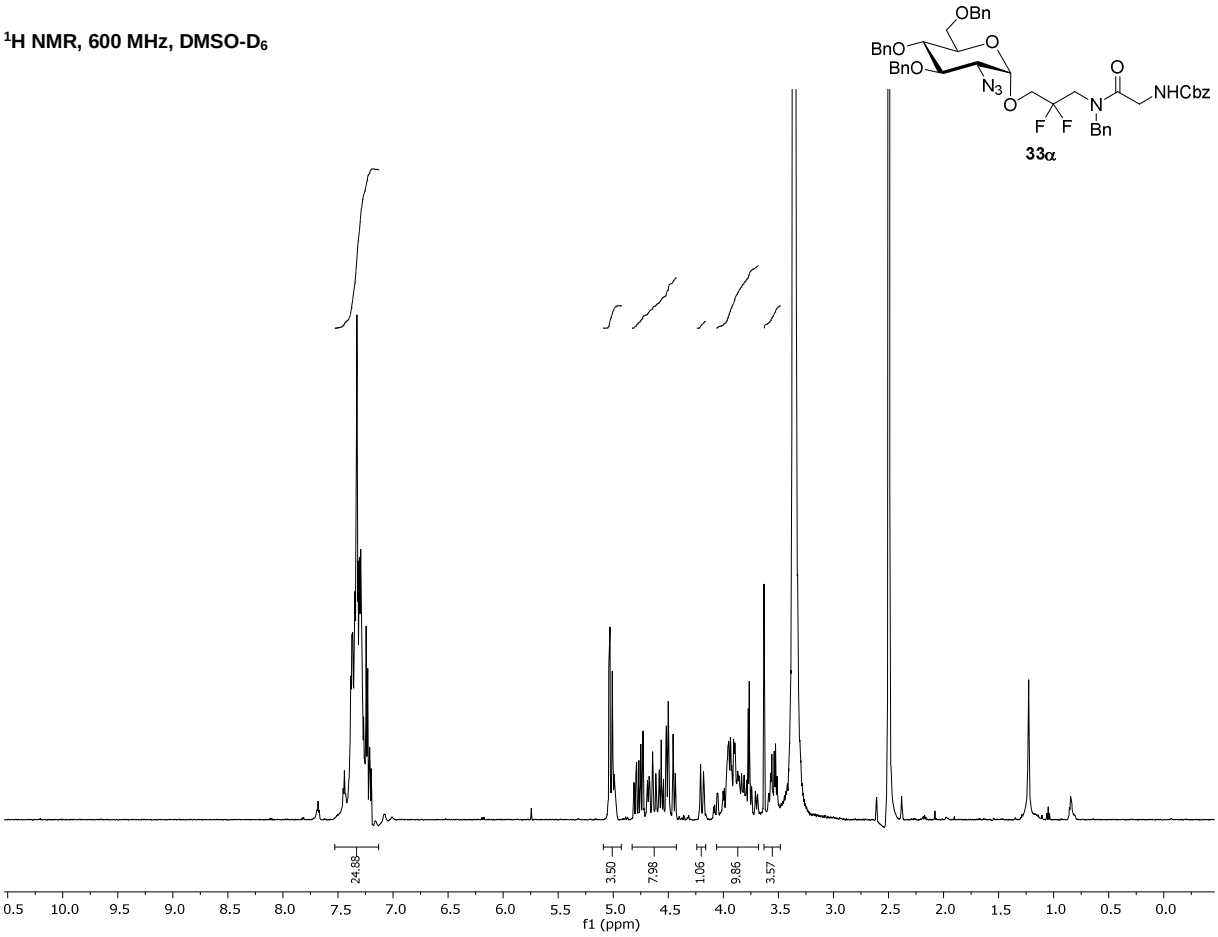
^{13}C NMR, 100 MHz, $CDCl_3$



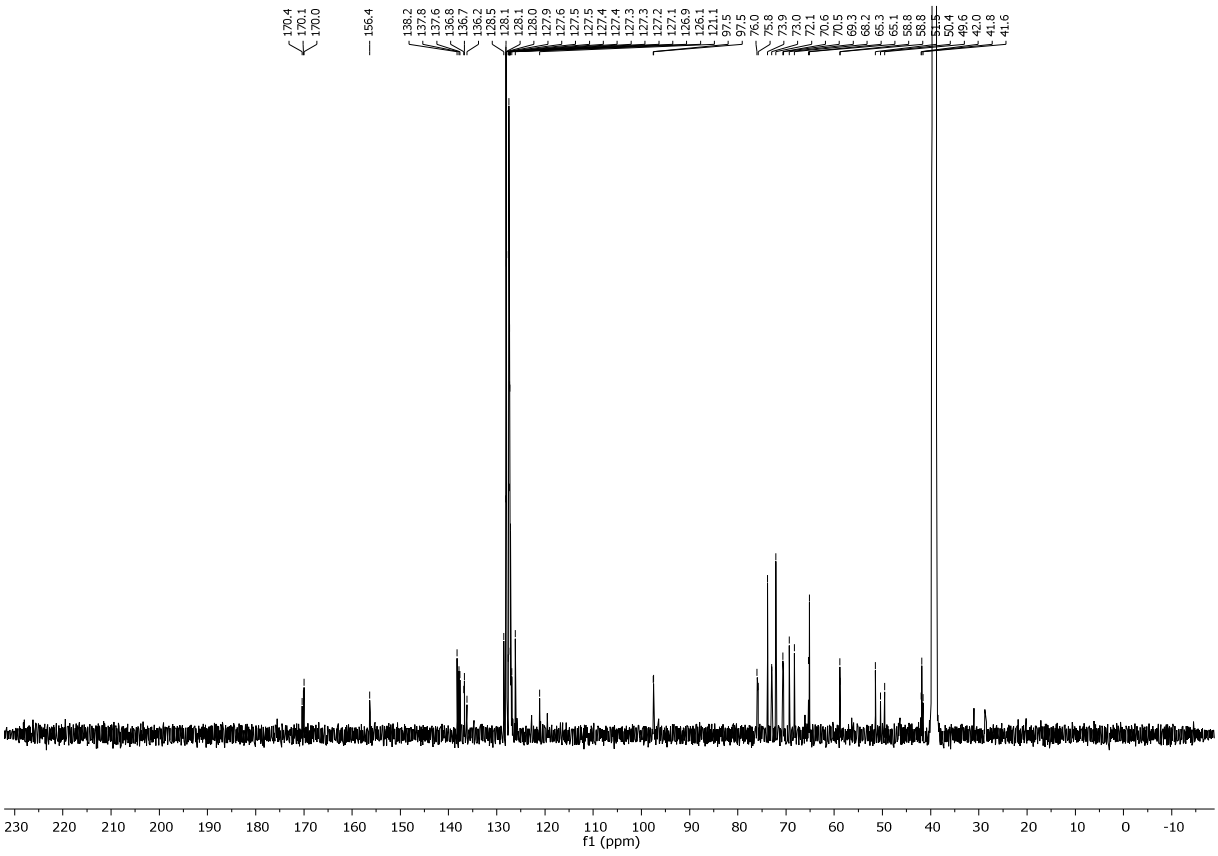
CH-HSQC, 400 MHz, $CDCl_3$



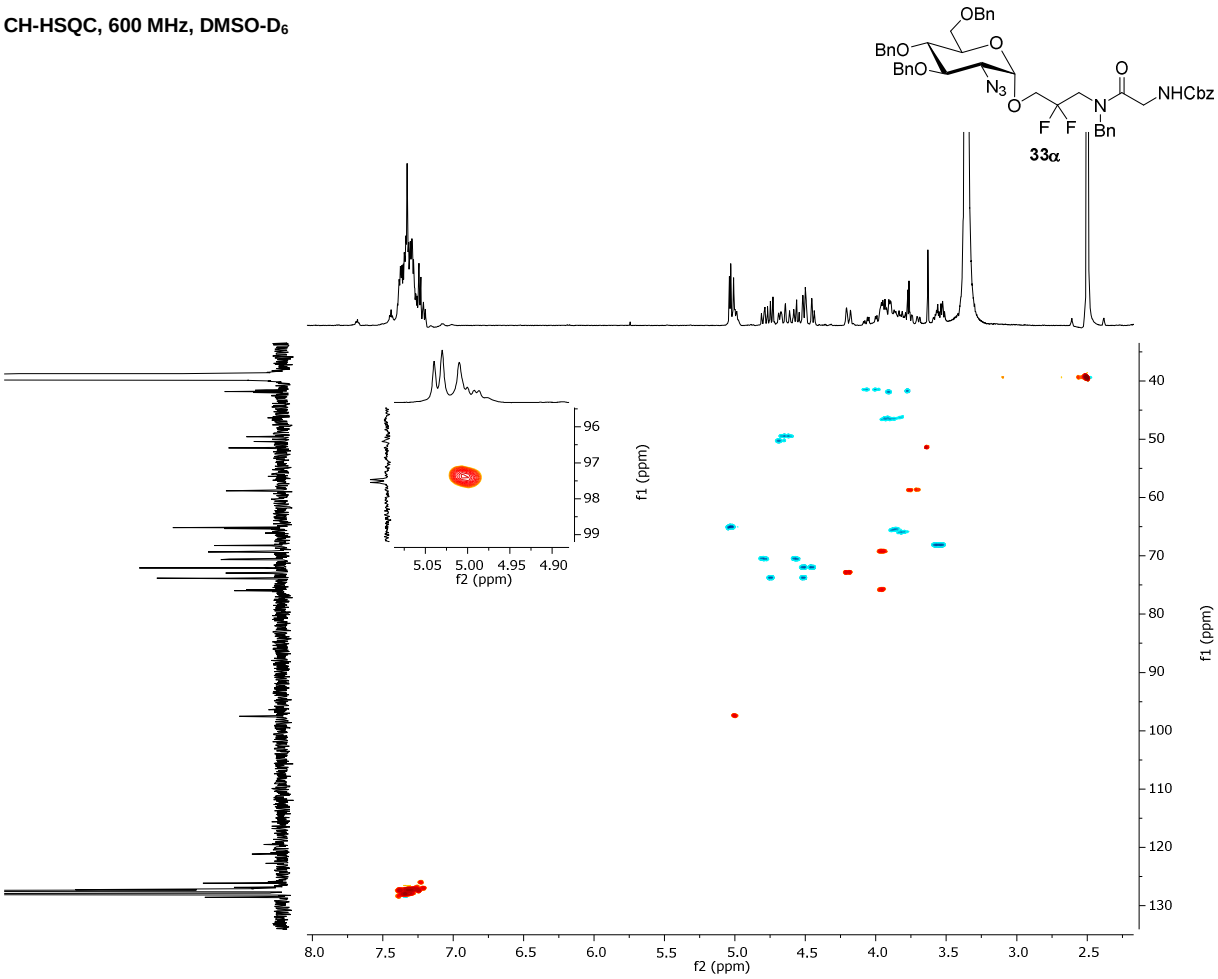
^{1}H NMR, 600 MHz, DMSO-D$_6$



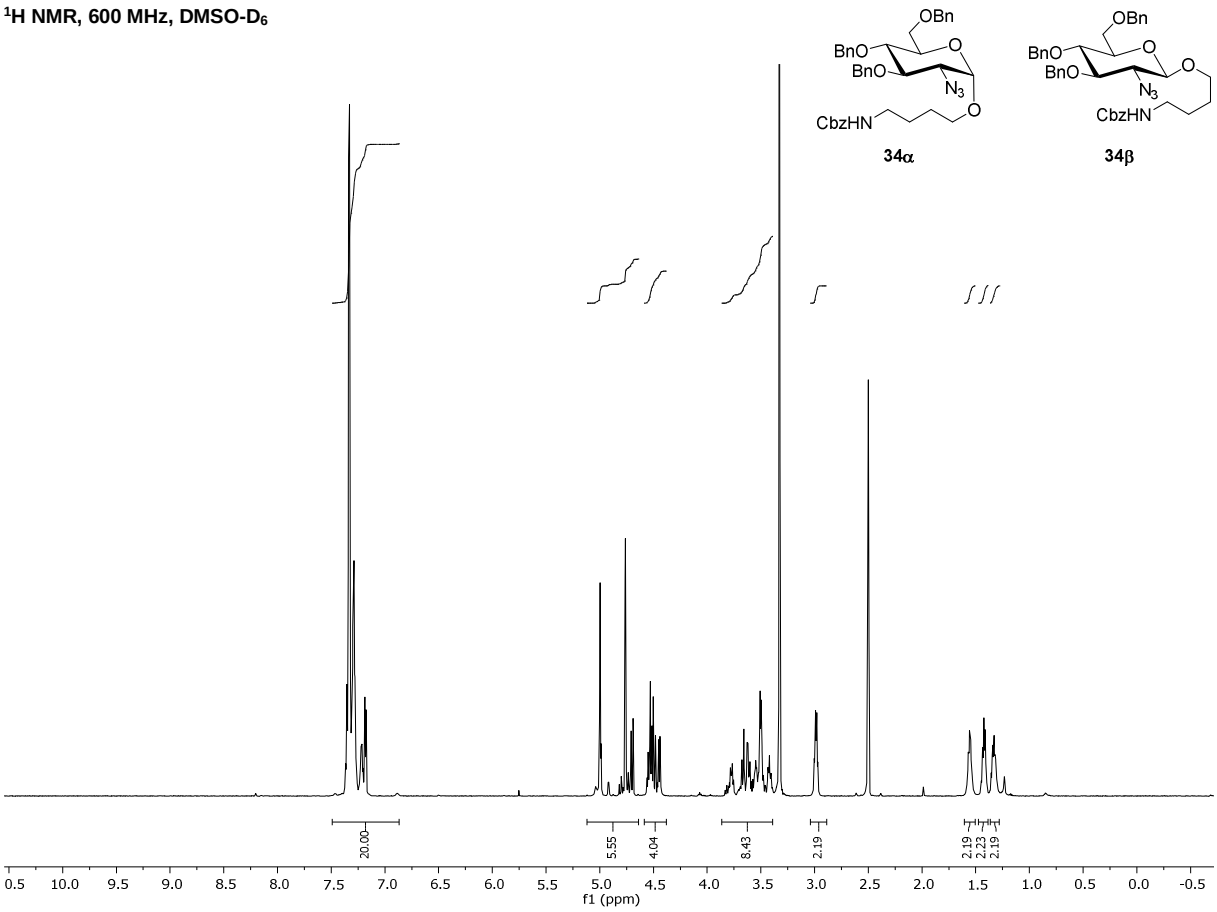
^{13}C NMR, 150 MHz, DMSO-D$_6$



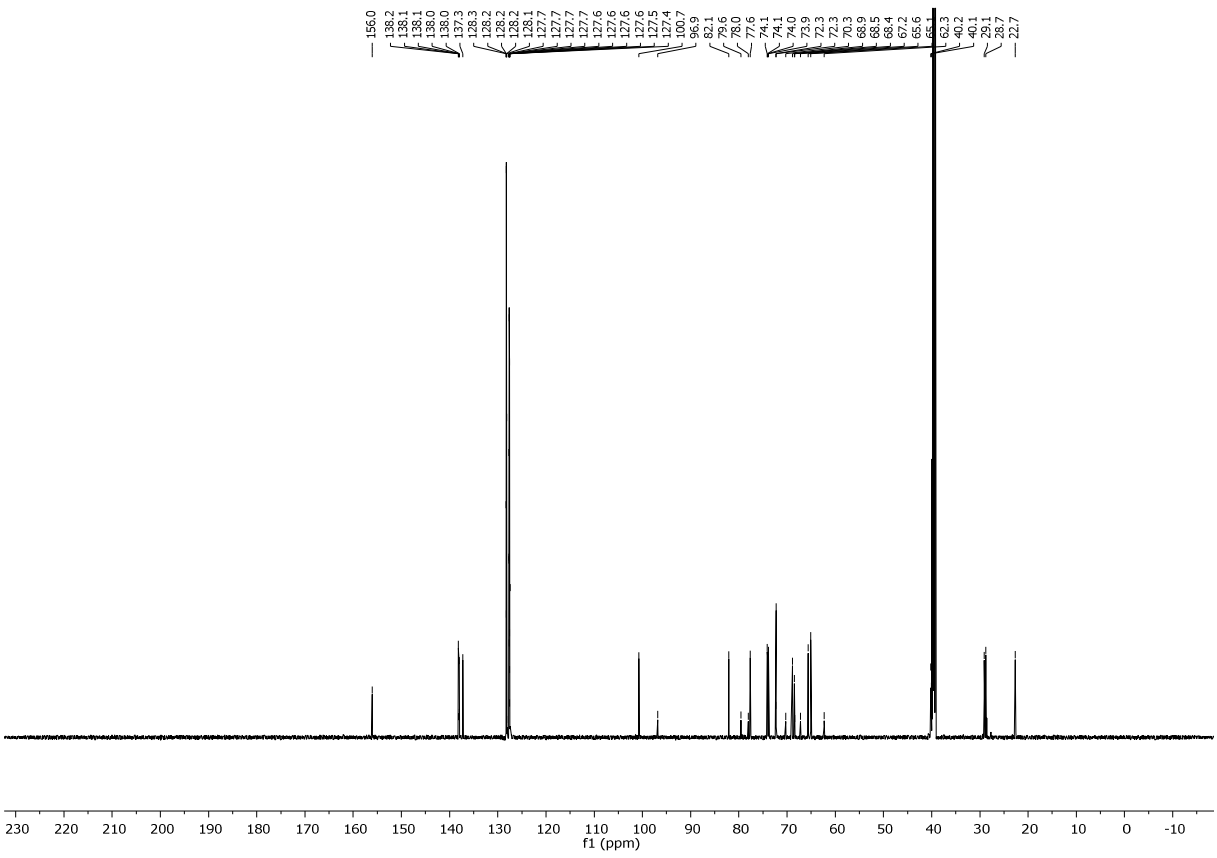
CH-HSQC, 600 MHz, DMSO-D_6



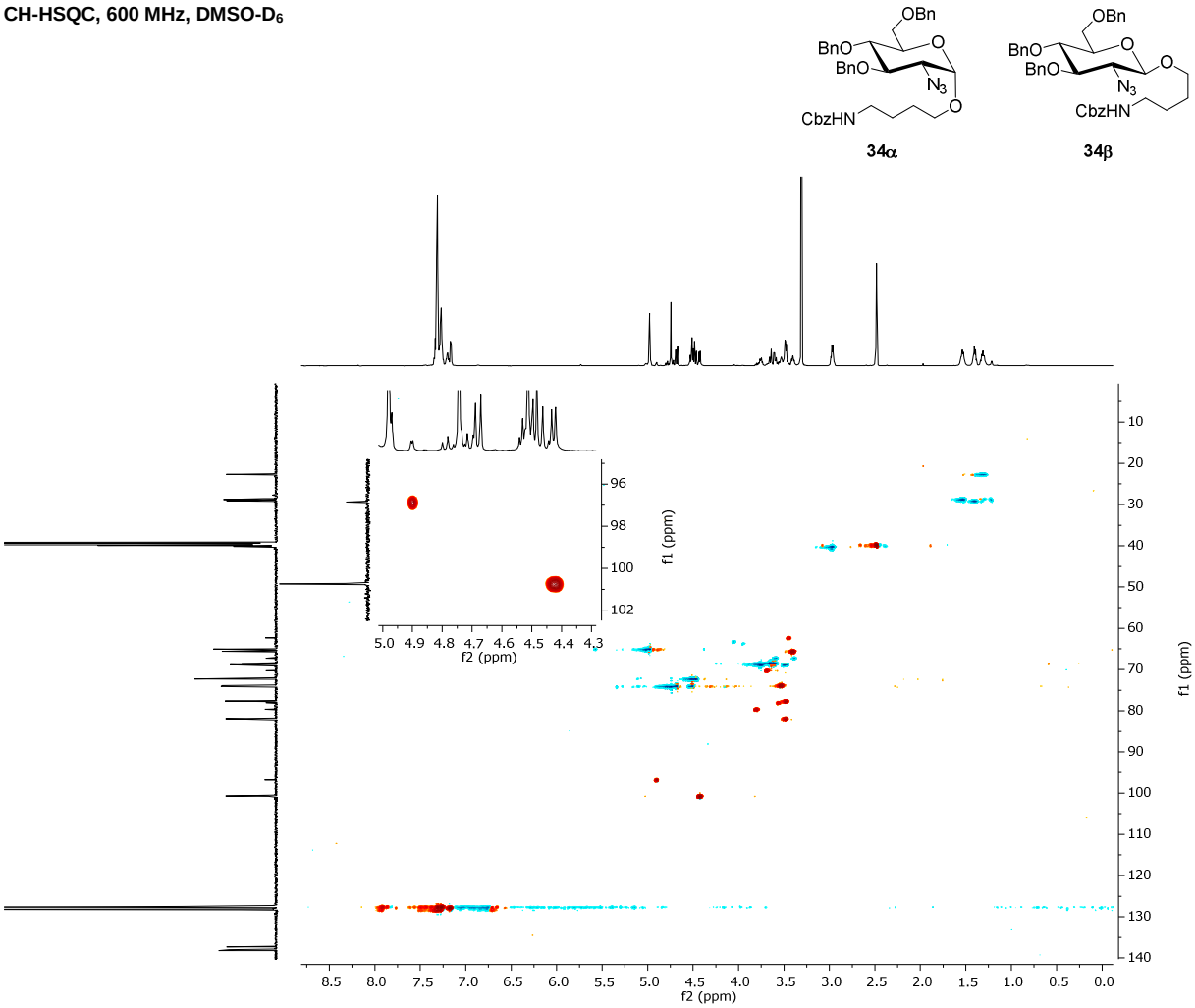
^{1}H NMR, 600 MHz, DMSO-D$_6$



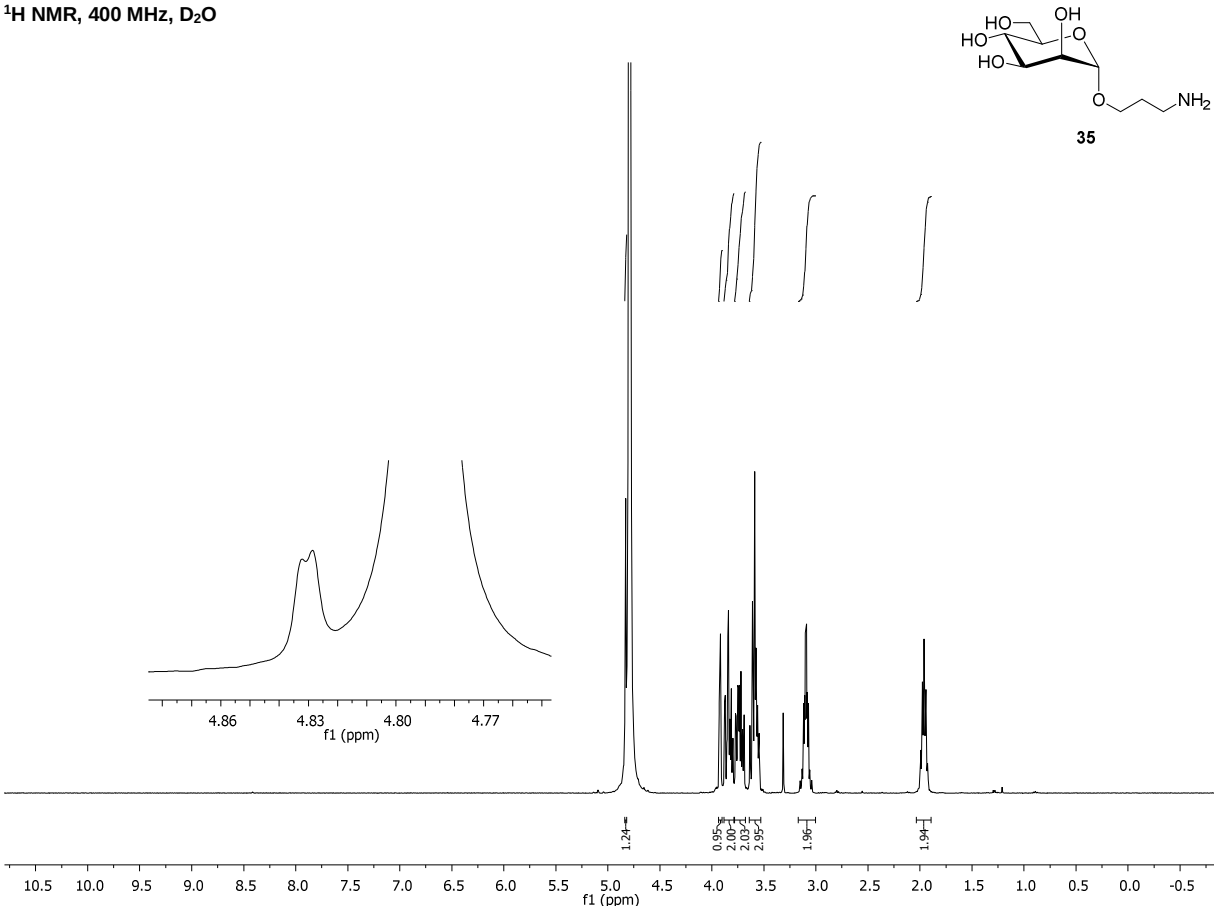
^{13}C NMR, 150 MHz, DMSO-D$_6$



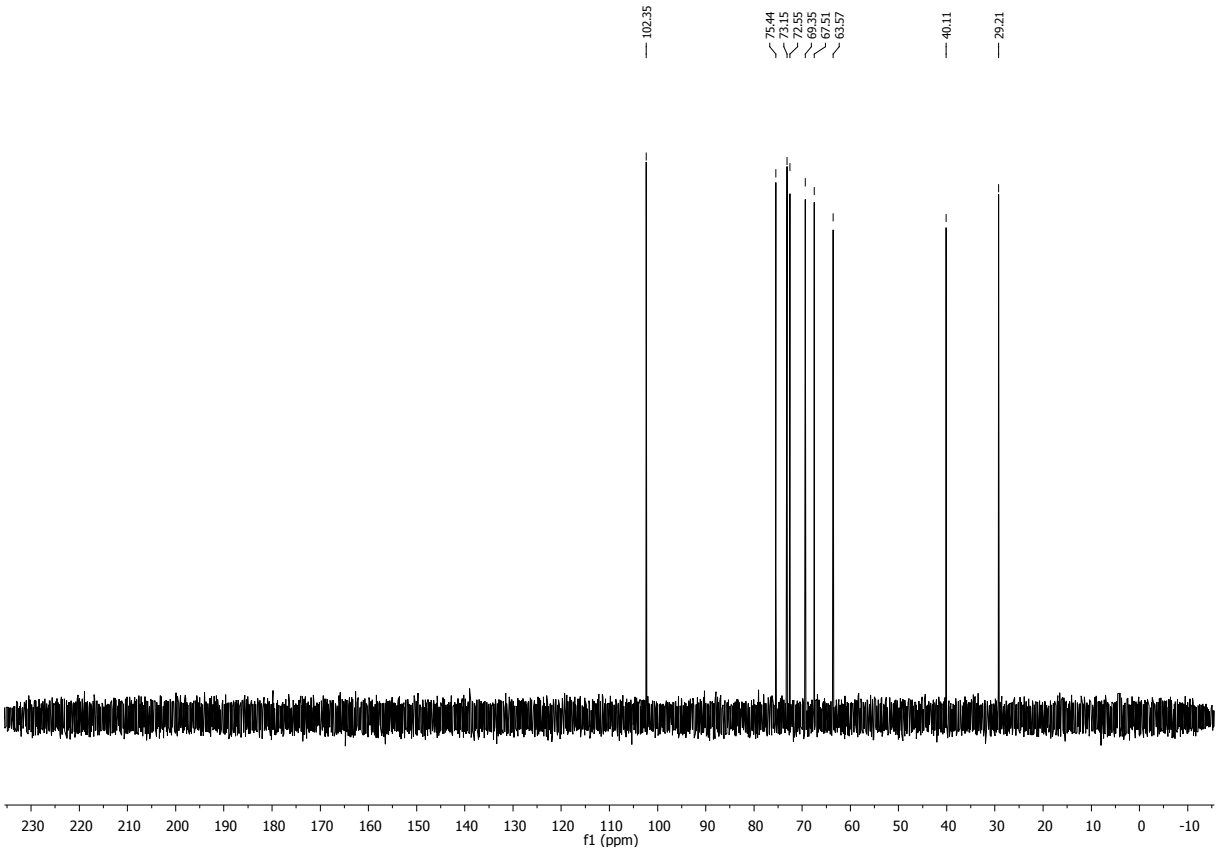
CH-HSQC, 600 MHz, DMSO-D_6



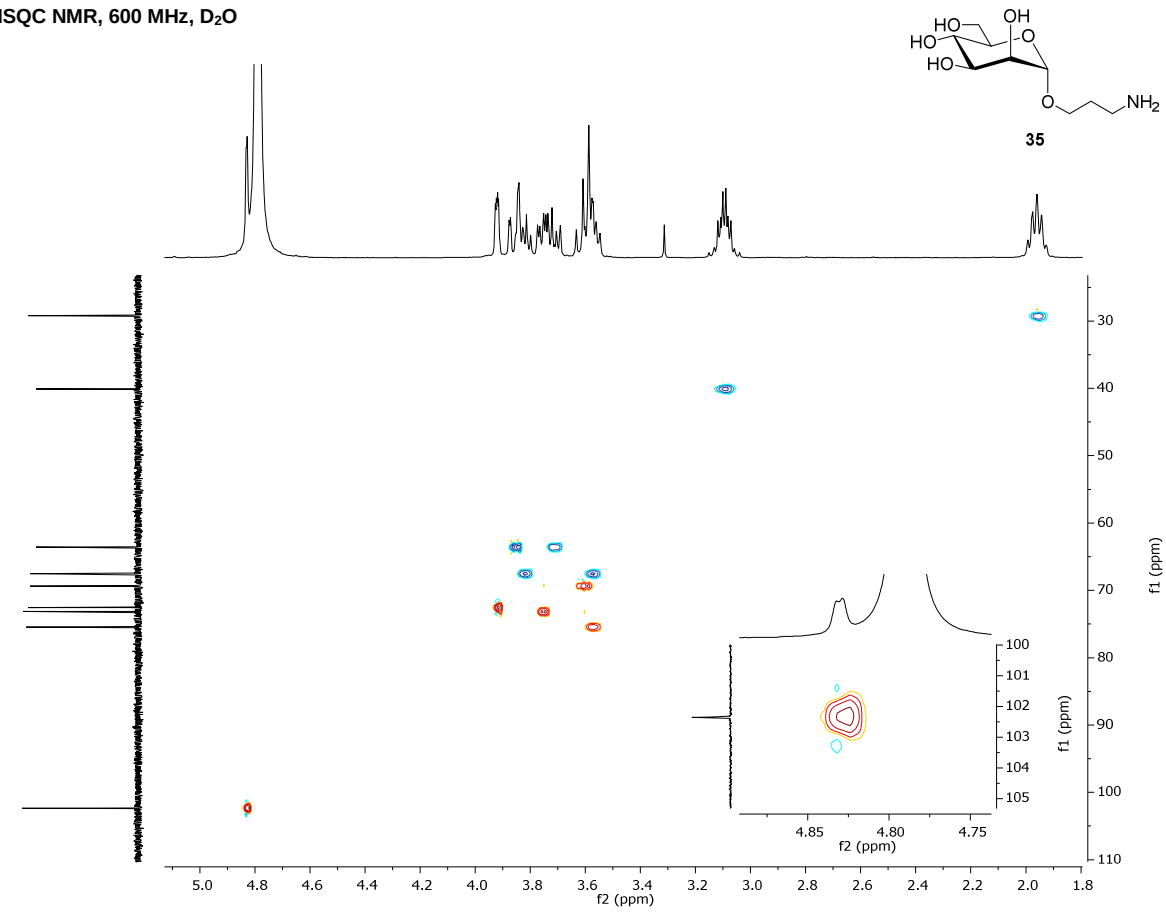
^{1}H NMR, 400 MHz, D_2O



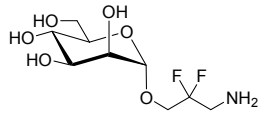
^{13}C NMR, 600 MHz, D_2O



CH-HSQC NMR, 600 MHz, D_2O

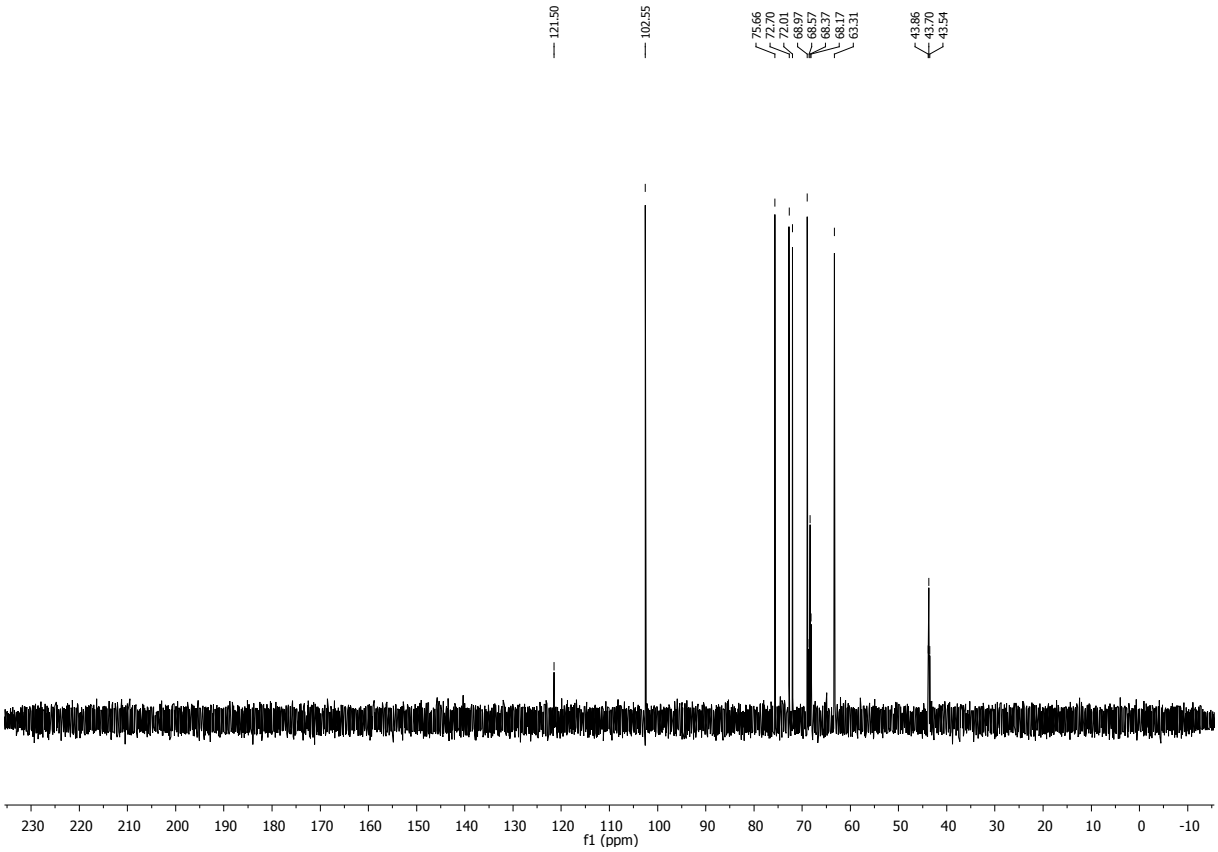


^{1}H NMR, 400 MHz, D_2O

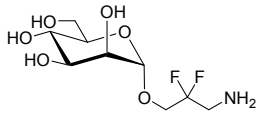


36

^{13}C NMR, 600 MHz, D_2O



CH-HSQC NMR, 600 MHz, D_2O



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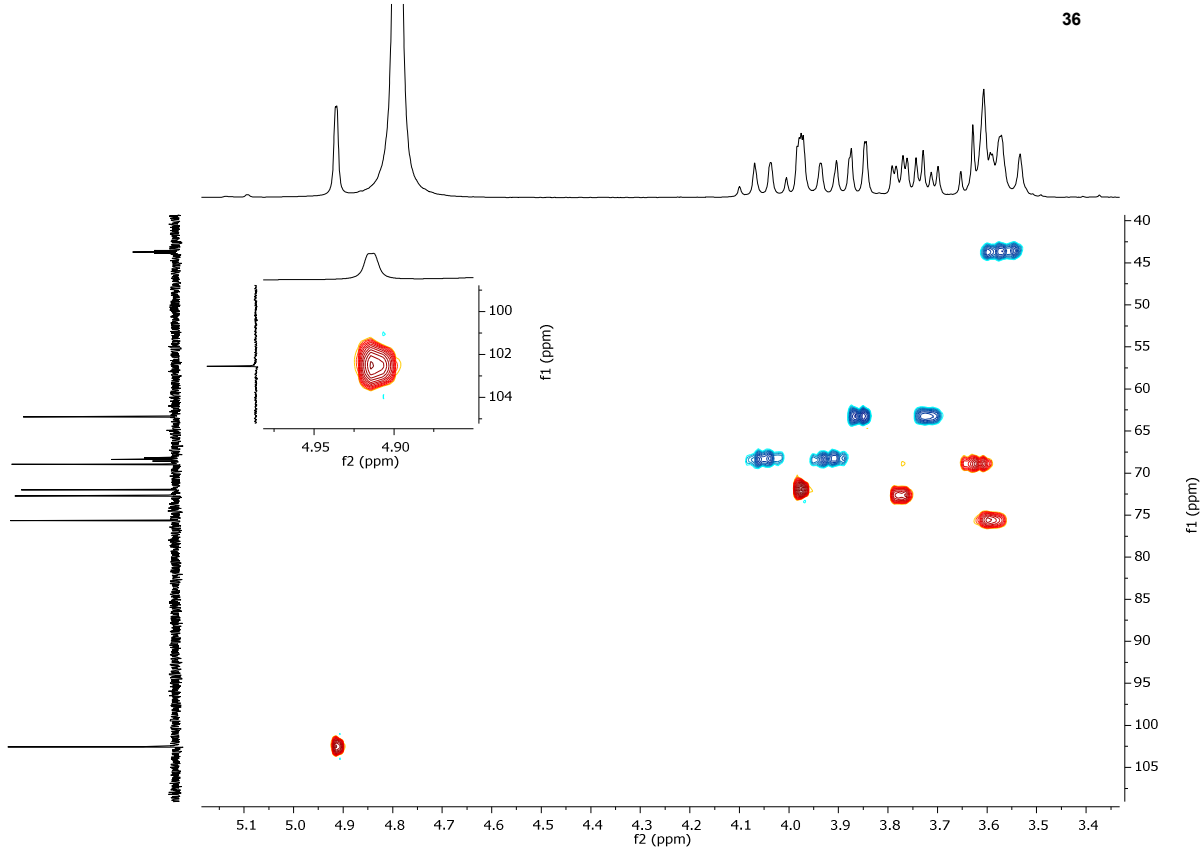

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