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REVISED
Diastereocontrolled Synthesis of Carbon Glycosides of
***N*-Acetylneuraminic Acid *via* Glycosyl Samarium(III)**
Intermediates

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SUPPORTING INFORMATION

General methods. *N*-Acetylneuraminic acid was purchased (Snow Brand Milk Products Company Ltd., Tokyo, Japan). All other reagents and solvents were of reagent grade and were dried using standard procedures. Optical rotations were measured with a Perkin Elmer 141 polarimeter at 22°C. ¹H NMR spectra were recorded at 25°C on a Varian Unity 500 MHz spectrometer and chemical shifts are given in ppm from tetramethylsilane as internal standard. All reactions were monitored by thin layer chromatography on aluminum sheets, silica gel 60 F₂₅₄ (Merck); detection under short wavelength UV light (254 nm) and by dipping the plates into staining solution (1.0 g ceric ammonium sulfate and 24.0 g ammonium molybdate in 31 mL sulfuric acid 470 mL water) then heating. Flash chromatography was performed using 230-400 mesh silica gel 60 (Aldrich).

Synthesis and Analysis of New Compounds 10 and 11:

Methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-2-C-((S)-hydroxy-[3-(methyl 2,4,6-tri-O-benzyl-3-deoxy- α -D-galactopyranosidyl)]-methyl)-D-erythro-L-manno-nononate (10): To a vigorously stirred neat mixture of 120 mg (0.2 mmol) [methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy- α -D-glycero-D-galacto-2-nonulopyranosyl)onate] 2-pyridyl sulfone (**8**) and 165 mg (0.3 mmol) methyl 2,4,6-tri-*O*-benzyl-3-deoxy-3-*C*-(formyl)- α -D-galactopyranoside (**9**) under argon a 0.1M solution of freshly prepared SmI₂ in THF (7 mL, 0.7 mmol) was added dropwise at 20°C. Stirring was continued for 45 min, than the reaction mixture was poured into an aqueous ammonium chloride solution and extracted twice with ethyl acetate. The combined organic

layers were dried (MgSO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography with light petroleum / ethyl acetate (1:3) to yield 167 mg (88%) of **10** as a colorless foam. TLC (light petroleum / ethyl acetate, 1:3): $R_f=0.32$. $[\alpha]_D^{22}=-18$ (c=1, chloroform). $^1\text{H-NMR}$: $\delta = 1.89\text{-}2.14$ (5s, 15H, 5 COCH_3), 2.03 (under an COCH_3 signal is 1H, H-3' $_{ax}$), 2.51 (dd, $J_{3'_{ax},3'_{eq}} = 12.9$ Hz, $J_{3'_{eq},4'} = 4.6$ Hz, 1H, H-3' $_{eq}$), 2.79 (bd, $J_{2,3} = 6.3$ Hz, $J_{3,4}$ and $J_{3,3''} < 0.5$ Hz, 1H, H-3), 3.45 (s, 3H, OCH_3), 3.57 - 3.58 (m, 2H, 2 H-6), 3.87 (bs, $J_{3'',OH} = J_{3'',3} < 0.5$ Hz, 1H, H-3''), 3.90 (dd, $J_{5',6'} = 10.7$ Hz, $J_{6',7'} = 2.1$ Hz, 1H, H-6'), 3.97 - 4.01 (m, 2H, H-2 and H-5'), 4.05 (dd, $J_{8',9'_A} = 6.1$ Hz, $J_{9'_A,9'_B} = 12.3$ Hz, 1H, H-9' $_A$), 4.31 (dd, $J_{8',9'_B} = 3.9$ Hz, 1H, H-9' $_B$), 4.39 (m, 2H, H-5 and OH), 4.41 - 4.66 (m, 7H, 3 CH_2Ph and H-4 at $\delta = 4.55$), 4.90 (ddd, $J_{3'_{ax},4'} = J_{4',5'} = 11.6$ Hz, 1H, H-4'), 5.15 (bd, $J_{NH,5'} = 9.8$ Hz, 1H, NH), 5.28 (dd, $J_{7',8'} = 7.7$ Hz, 1H, H-7'), 5.42 (ddd, 1H, H-8'), 7.12 - 7.42 (m, 15H, 3 Ph).

Anal. Calcd for $\text{C}_{49}\text{H}_{61}\text{N}_1\text{O}_{18}$ (952.02): C, 61.82; H, 6.46; N, 1.47. Found: C, 61.47; H, 6.53; N, 1.26.

Synthesis of Methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-2-C [hydroxy-4-(tert-butylcyclohexyl)] -D-erythro-L-manno-nononate (II).

To a vigorously stirred neat mixture of 120 mg (0.2 mmol) [methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy- α -D-glycero-D-galacto-2-nonulopyranosyl)onate] 2-pyridyl sulfone (**8**) and 83.0 mg (0.6 mmol) 4-*tert*-butylcyclohexanone under argon a 0.1M solution of freshly prepared SmI_2 in THF (7 mL, 0.7 mmol) was added dropwise at 20°C. Stirring was continued for 45 min, then the reaction mixture was poured into an aqueous ammonium chloride solution and extracted twice with ethyl acetate. The combined organic layers were dried (MgSO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography with light petroleum / ethyl acetate (1:3) to yield 167 mg (90%) of **11** as a colorless oil. TLC (light petroleum / ethyl acetate, 1:3): $R_f=0.6$. $[\alpha]_D^{22} = -12$ (c=1, chloroform). $^1\text{H-NMR}$: $\delta = 0.88$ (s, 9H), 1.19 (dt, $J=13.1$ Hz, $J=3,3$ Hz), 1.42 (m, 3H), 1.60 (m, 3H), 1.78 (m, 1H), 1.85 (m, 3H), 1.87 (s, 3H), 1.96 (t, $J=12.4$ Hz), 2.02 (s,

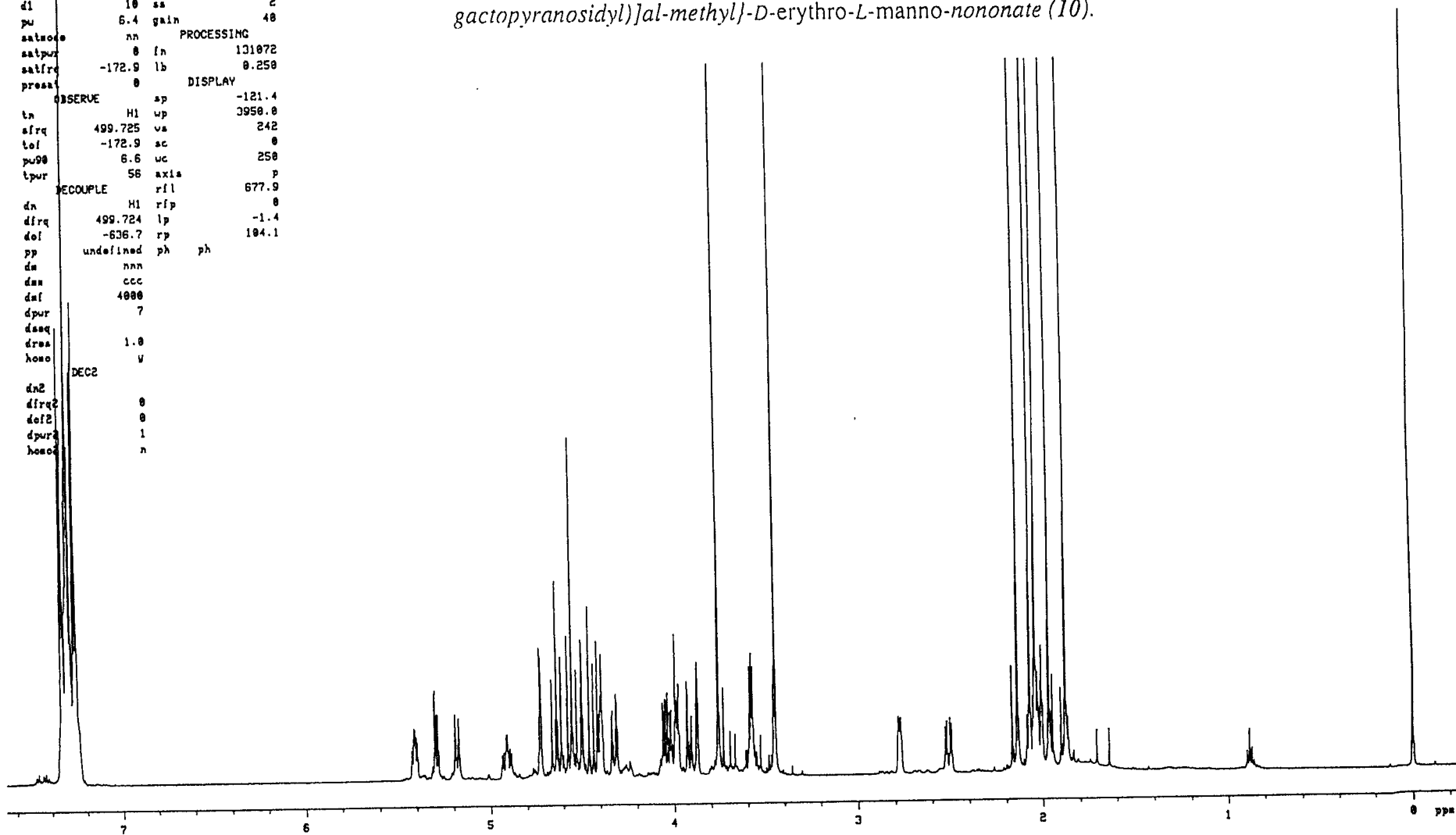
3H), 2.05 (s, 3H), 2.12 (s, 3H), 2.16 (s, 3H), 2.46 (dd, $J=12.4$ Hz, $J=4.5$ Hz), 2.57 (s, 1H), 3.79 (s, 3H), 3.99 (m, 2H), 4.07 (dd, 1H, $J=12.3$ Hz, $J=6.2$ Hz), 4.32 (dd, 1H, $J=12.3$ Hz, $J=2.5$ Hz), 4.76 (m, 1H), 5.16 (bd, 1H, $J=8.8$ Hz), 5.30 (d, 1H, $J=6.1$ Hz), 5.42 (dt, $J=6.1$ Hz, $J=2.4$ Hz). Anal. Calcd for $C_{30}H_{47}N_1O_{13}$ (629.70): C, 57.22; H, 7.52; n, 2.22. Found: C, 56.94; H, 7.63; N, 1.94.

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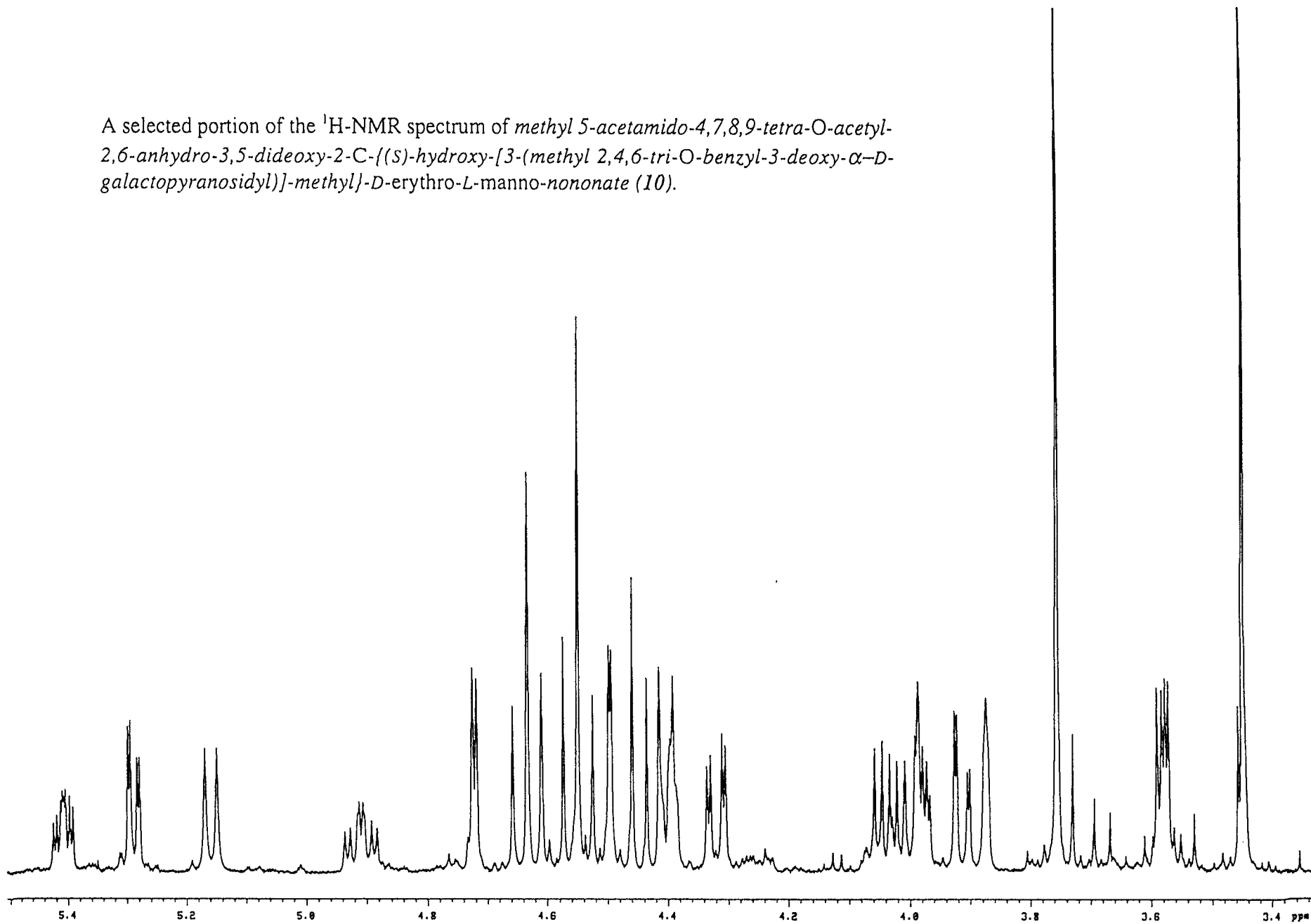
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temp 25.0 fb 5500
solvent CDCl3 at 4.000
PULSE SEQUENCE np 48000
pad 0 ct 16
d1 10 ss 2
pu 6.4 gain 40
satp00 nn PROCESSING
satp01 0 fn 131072
satf01 -172.9 lb 0.250
prea01 0 DISPLAY
OBSERVE ap -121.4
tn H1 up 3950.0
sfrq 499.725 va 242
tol -172.9 ac 0
pu00 6.6 uc 250
tpur 56 axia p
DECOUPLE H1 ril 677.9
dn H1 rip 0
dfrq 499.724 lp -1.4
dof -636.7 rp 104.1
pp undefined ph ph
dn nnn
das ccc
daf 4000
dpu 7
dsq 1.0
das v
DECE
dn2 0
dfrq2 0
dof2 0
dpu2 1
hono n

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¹H-NMR spectrum of *methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-2-C-((S)-hydroxy-[3-(methyl 2,4,6-tri-O-benzyl-3-deoxy- α -D-gactopyranosidyl)]al-methyl)-D-erythro-L-manno-nononate (10)*.



A selected portion of the $^1\text{H-NMR}$ spectrum of *methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-2-C-[(S)-hydroxy-[3-(methyl 2,4,6-tri-O-benzyl-3-deoxy- α -D-galactopyranosidyl)]-methyl]-D-erythro-L-manno-nononate (10)*.

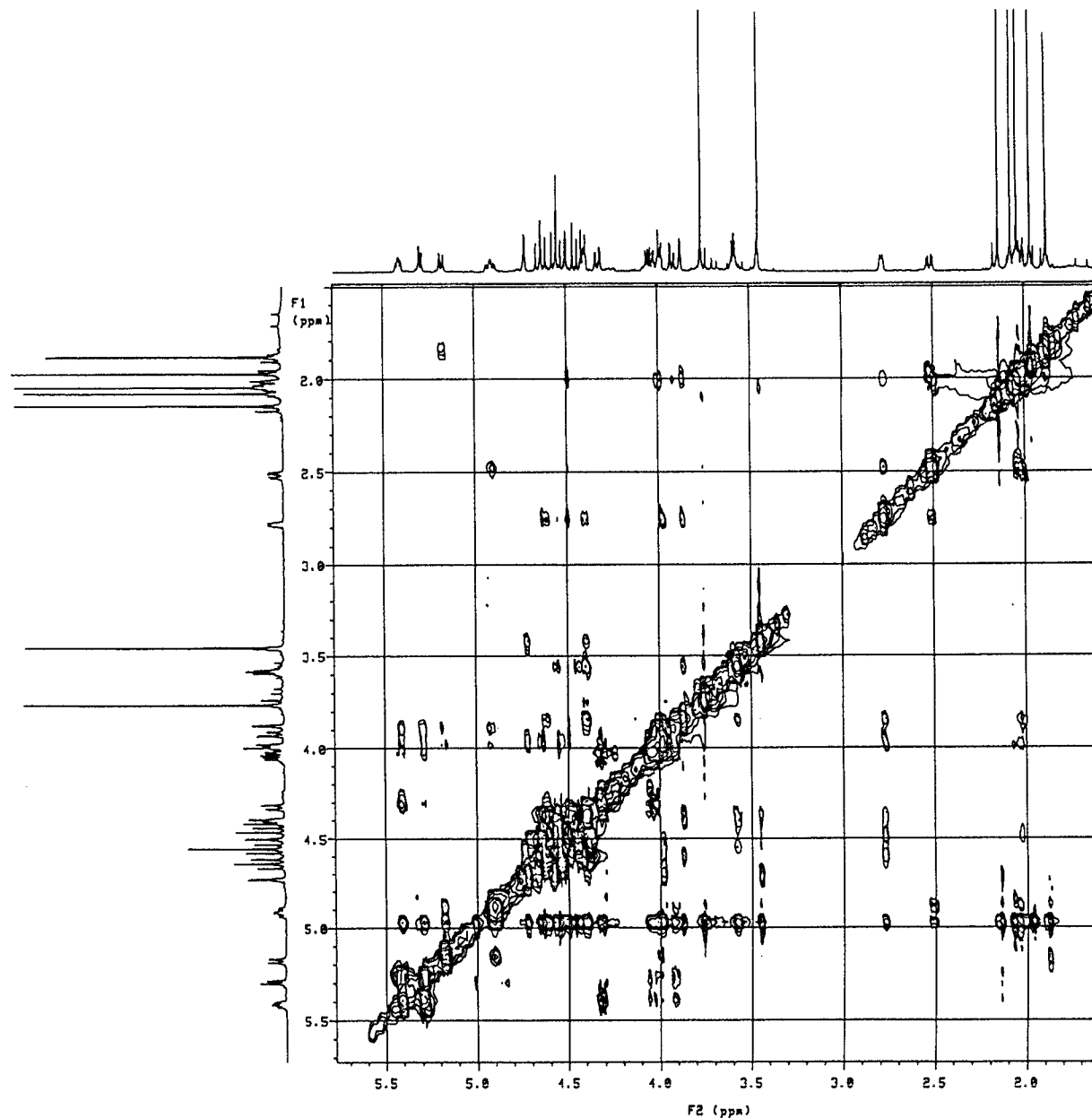


new experiment

exp2 pulse sequence: roesy

SAMPLE		2D SPECTRUM		ACQUISITION ARRAYS	
date	Jul 15 96	au1	5999.7	array	phase
temp	25.0	n1	256	arraydim	512
solvent	CDC13	phase	arrayed		
PULSE SEQUENCE		PROCESSING		1	phase
d1	3	fn	2048	1	1
p1	6.5	gf	0.079	2	2
plvl	56	gfa	not used		
pw	4.3	2D PROCESSING			
mix	0.100	fn1	512		
ratio	2.000	gf1	0.020		
rocomp	n	gfa1	not used		
sapul	n	DISPLAY			
hs	nn	ap	785.3		
salmode	n	up	2099.6		
OBSERVE		us	100		
tn	H1	sc	10		
dirq	499.725	uc	115		
tof	0	axia	pp		
pu90	6.6	rfl	505.0		
tpur	44	rfp	0		
DECOUPLE		lp	28.8		
dn	H1	rp	720.7		
dirq	499.724	ai	cdc ph		
dof	-788.9	2D DISPLAY			
dpur	7	ap1	742.0		
homo	v	up1	2117.5		
DEC2		th	0		
dn2	sc2		0		
dirq2	0	uc2	115		
dof2	0	rfl1	505.0		
dpur2	1	rfl1	0		
homo2	n	lp1	2.0		
SPECTRUM		rp1	5.4		
su	5999.7				
fb	3300				
at	0.171				
np	2048				
nt	4				
ss	8				
gain	40				

A selected portion of the ^1H - ^1H ROESY ($\tau_m=100$ ms) spectrum of *methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-2-C-[(S)-hydroxy-[3-(methyl 2,4,6-tri-O-benzyl-3-deoxy- α -D-galactopyranosidyl)]-methyl]-D-erythro-L-manno-nononate (10)*.



exp7 pulse sequence: roesy

SAMPLE		2D SPECTRUM		ACQUISITION ARRAYS	
date	Jul 16 96	swl	5999.7	array	phase
temp	25.0	ni	256	arraydim	512
solvent	CDC13	phase	arrayed		
PULSE SEQUENCE		PROCESSING		1	phase
d1	3	fn	2048	1	1
p1	6.5	gf	0.079	2	2
pilvl	56	gfs	not used		
pw	4.3	2D PROCESSING			
mix	0.700	fn1	512		
ratio	2.000	gfi	0.020		
rocomp	n	gfal	not used		
aspul	n	DISPLAY			
hs	nn	sp	746.8		
satmode	n	up	2099.6		
OBSERVE		vs	111		
tn	H1	ac	10		
afreq	499.725	uc	115		
tof	0	axis	pp		
pu00	6.6	rfl	496.6		
tpur	44	rfp	0		
DECOUPLE		lp	26.5		
dn	H1	rp	1.3		
dfrq	499.724	ai	cdc ph		
dof	-788.9	2D DISPLAY			
dpr	7	sp1	723.5		
homo	v	up1	2094.0		
DEC2		th	1		
dn2	0	sc2	0		
dfrq2	0	uc2	115		
dof2	0	rfl1	500.0		
dpr2	1	rfpl	0		
homo2	n	lp1	-1.2		
SPECTRUM		rp1	6.5		
aw	5999.7				
fb	3300				
at	0.171				
np	2048				
ct	4				
sa	8				
gain	40				

A selected portion of the ^1H - ^1H ROESY ($\tau_m=700$ ms) spectrum of *methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-2-C-((S)-hydroxy-[3-(methyl 2,4,6-tri-O-benzyl-3-deoxy- α -D-galactopyranosidyl)]-methyl)-D-erythro-L-manno-nononate (10)*.

