A Convergent Synthetic Route to the Tunicamycin Antibiotics. Synthesis of (+)-Tunicamycin V.

Thesis by

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To my mother and father,

for their undying love and support.

Acknowledgments

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Abstract

A concise synthetic route to the tunicamycin antibiotics is described, illustrated by the preparation of (+)-tunicamycin-V (**1-V**). Key features of the synthesis include: (1) the development and application of a silicon-mediated reductive coupling of aldehydes and allylic alcohols to construct the undecose core of the natural product; and (2) the development of an efficient procedure for the synthesis of the trehalose glycosidic bond within the antibiotic. These innovations allow for the coupling of a uridine-derived aldehyde fragment with a preformed trehalose-linked disaccharide allylic alcohol to form the carbohydrate core (**1**) of the natural product in a highly convergent manner. The resultant amino polyol is a versatile intermediate for the synthesis of any of the homologous tunicamycin antibiotics.

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List of Abbreviations

$[\alpha]_D^{25}$	optical rotation (589 nm, 25 °C)
Å	angstrom
Ac	acetyl
AIBN	2,2'-azobis(isobutyronitrile)
Aoc	allyloxy carbonate
arom.	aromatic
Boc	*tert*-butyl carbamate
BOM	benzyloxy methyl
Bu	butyl
Bz	benzoyl
c	grams per 100 mL of solution
°C	degrees Celsius
CI	chemical ionization
CAN	ceric ammonium nitrate
cat.	catalyst
Cbz	benzyl carbamate
cm^{-1}	reciprocal centimeters
CSA	camphorsulfonic acid
δ	chemical shift
DBU	1,8-diazobicylo[5.4.0]undec-7-ene
DCC	1,3-dicyclohexylcarbodiimide
DMAP	4-(*N,N*-dimethylamino)pyridine
DME	dimethoxyethane

DMF	*N,N*-dimethylformamide
DMS	dimethyl sulfide
DMSO	dimethyl sulfoxide
DMT	*para*-dimethoxytrityl
Dol	dolichol
EI	electron impact
equiv	equivalent
Et	ethyl
FAB	fast atom bombardment
FT	Fourier transform
g	gram
GDP	guanosine diphosphate
Glc	glucose
GlcNAc	*N*-acetylglucosamine
h	hour
Hal^-	halide
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectroscopy
Hz	Hertz
i	iso
IR	infrared
J	coupling constant
L	liter
LDA	lithium diisopropylamide
m	meta

M	molar
M^+	molecular ion
m-CPBA	*meta*-chloroperoxybenzoic acid
Man	mannose
Me	methyl
MEM	methoxyethoxy methyl
MeOH	methyl alcohol
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mM	millimolar
mmol	millimole
mol	mole
mol. sieves	molecular sieves
MOM	methoxy methyl
mp	melting point
MS	mass spectroscopy
MurNAc	*N*-acetylmuramic acid
μL	microliter
n	normal
N	normal (concentration)
NBS	*N*-bromosuccinimide
nm	nanometer
NMR	nuclear magnetic resonance

o	ortho
p	para
P	phosphate
P	protecting group
pep	peptide
Ph	phenyl
PMB	*para*-methoxybenzyl
ppm	parts per million
Pr	propyl
PhthN	phthalimide
Py	pyridine
R, Re	rectus
R_f	retention factor
S, Si	sinister
SEM	trimethylsilylethoxymethyl
t	tertiary
TBAF	tetrabutylammonium fluoride
TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
UDP	uridine diphosphate
UMP	uridine monophosphate
v/v	volume-to-volume ratio

W	Watt
w/w	weight-to-weight ratio

Chapter 1

Introduction

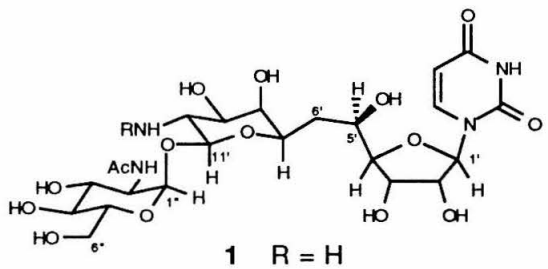
The Tunicamycin Antibiotics

The tunicamycins, corynetoxins, and streptovirudins make up a unique class of microbial metabolites that inhibit various enzymatic processes involving the formation of phospholipid-linked intermediates. As a consequence, they elicit a range of biological responses, to include potent antimicrobial, antiviral, and antitumor activities.[1] Structurally, the more than thirty members of the class may be categorized as long-chain *N*-acyl derivatives of the core substructure **1** or, in the case of certain streptovirudins, its dihydrouracil analog. The *N*-acyl appendages vary in length and in degree of unsaturation, branching, and hydroxylation. Representative examples are depicted below (Figure 1).

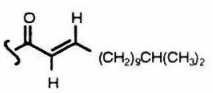
Consideration of these antibiotic structures has led to the proposal that they function as bisubstrate analogs for the enzymes they inhibit.[2] In prokaryotic systems, for example, the tunicamycins block the exchange of uridine diphosphate *N*-acetylmuramic acid-pentapeptide (UDP-MurNAc-pep$_5$) with a phospholipid carrier (Lipid-P, Scheme I), thus inhibiting cell wall biosynthesis.[3] In eukaryotic systems, they block the transfer of *N*-acetylglucosamine-1-phosphate from its UDP-activated precursor uridine diphosphate *N*-acetylglucosamine (UDP-GlcNAc) to the phospholipid dolichol phosphate (Dol-P, Scheme II), thereby inhibiting oligosaccharide biosynthesis.[4]

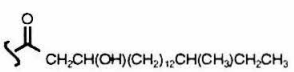
Given the substantial structural differences between the substrates of these enzymatic transformations, it is reasonable to propose that these processes might respond differently to variations in antibiotic structure, and that the relative inhibitory activities of different tunicamycins might differ as a consequence. An ambiguity in most biological studies of the tunicamycins conducted thus far is that complex and varying mixtures of tunicamycins, as obtained by fermentation, are typically assayed. Separation of these mixtures is tedious, requiring the use of reverse-phase HPLC; thus, in practical terms, only

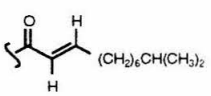
Figure 1



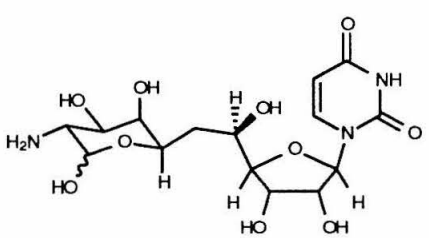
1 R = H

Tunicamycin–V (**1–V**) R = 

Corynetoxin–H19a* R = 

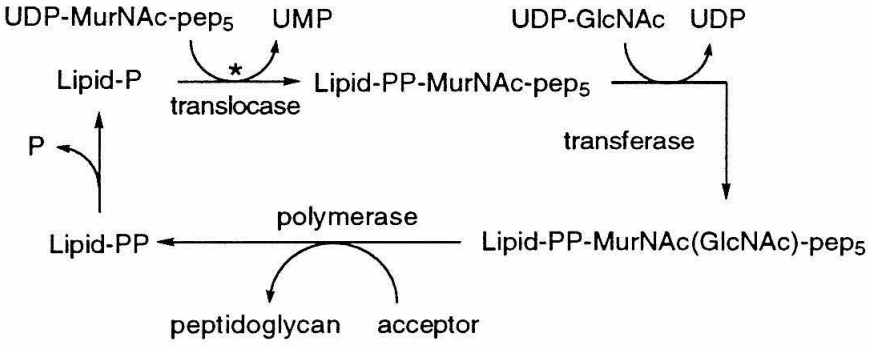
Streptovirudin–A_1 R = 

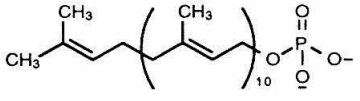
* Stereochemistry of acyl appendage undetermined.



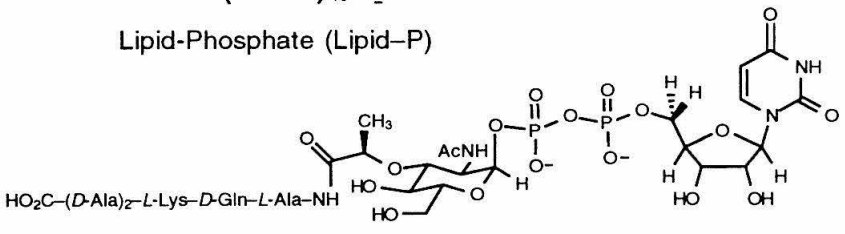
Tunicaminyluracil (**2**)

Scheme I **Tunicamycin Inhibition of the Lipid Cycle in Peptidoglycan Biosynthesis**



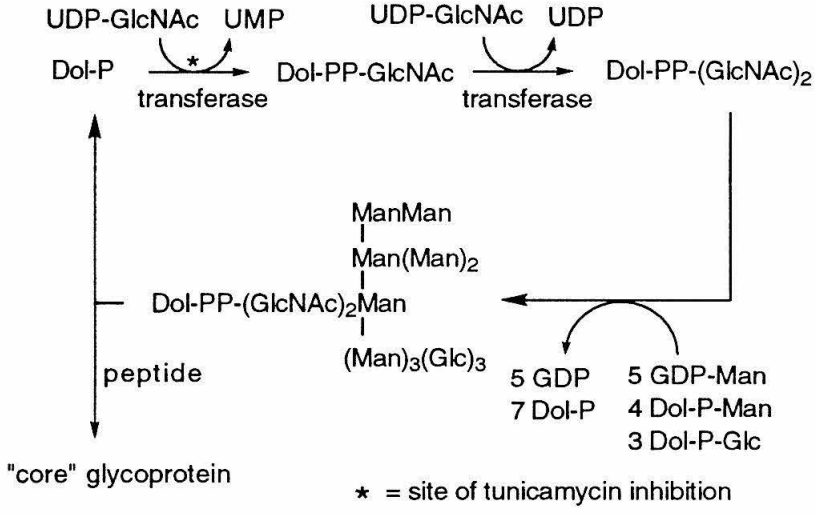


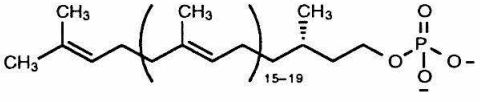
Lipid-Phosphate (Lipid–P)



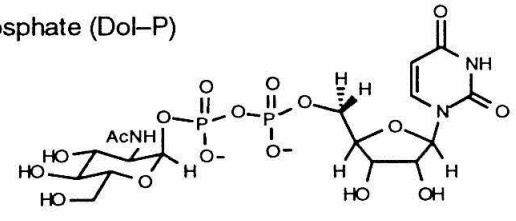
Uridine Diphosphate*N*-Acetylmuramic Acid-Pentapeptide (UDP-MurNAc-pep$_5$)

Scheme II **Tunicamycin Inhibition of Asparagine-Linked Glycoprotein Biosynthesis**





Dolichol Phosphate (Dol–P)



Uridine Diphosphate
N-Acetylglucosamine (UDP-GlcNAc)

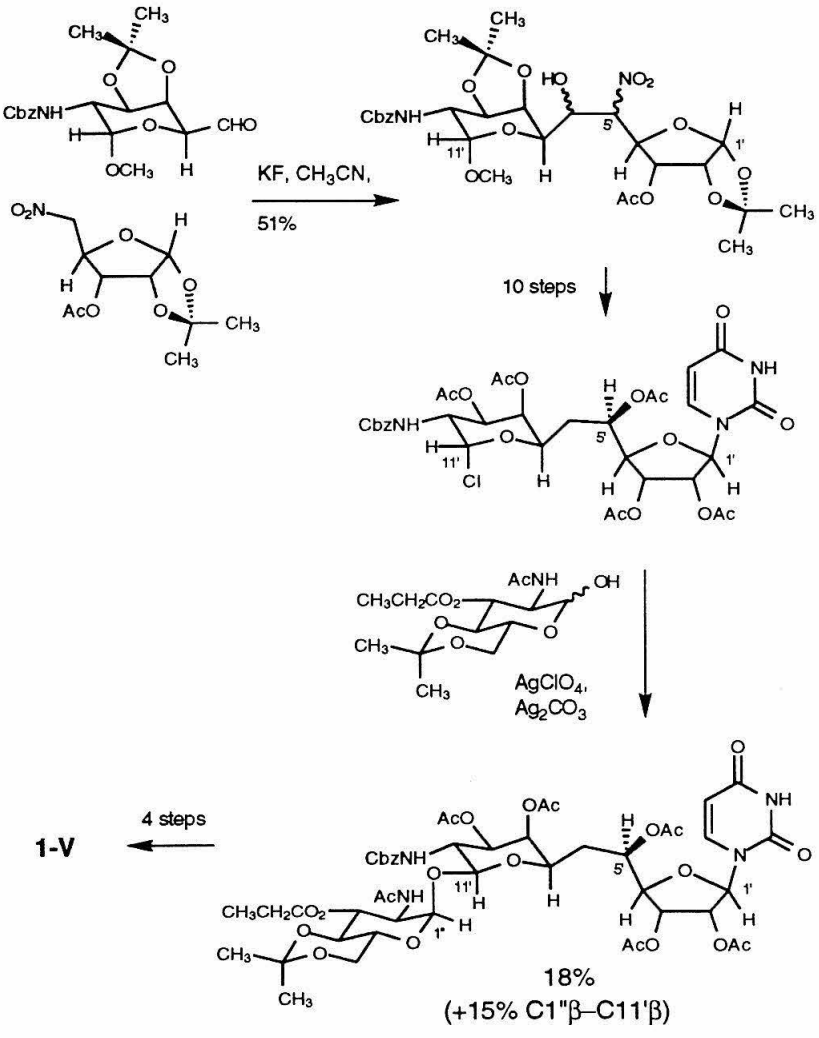
milligram quantities of any given pure tunicamycin are available.[5] For this reason, and in light of the potent biological activity of the tunicamycins, we have developed an efficient synthetic route to the tunicamycin antibiotics,[6] described in full herein.

Synthetic Plan

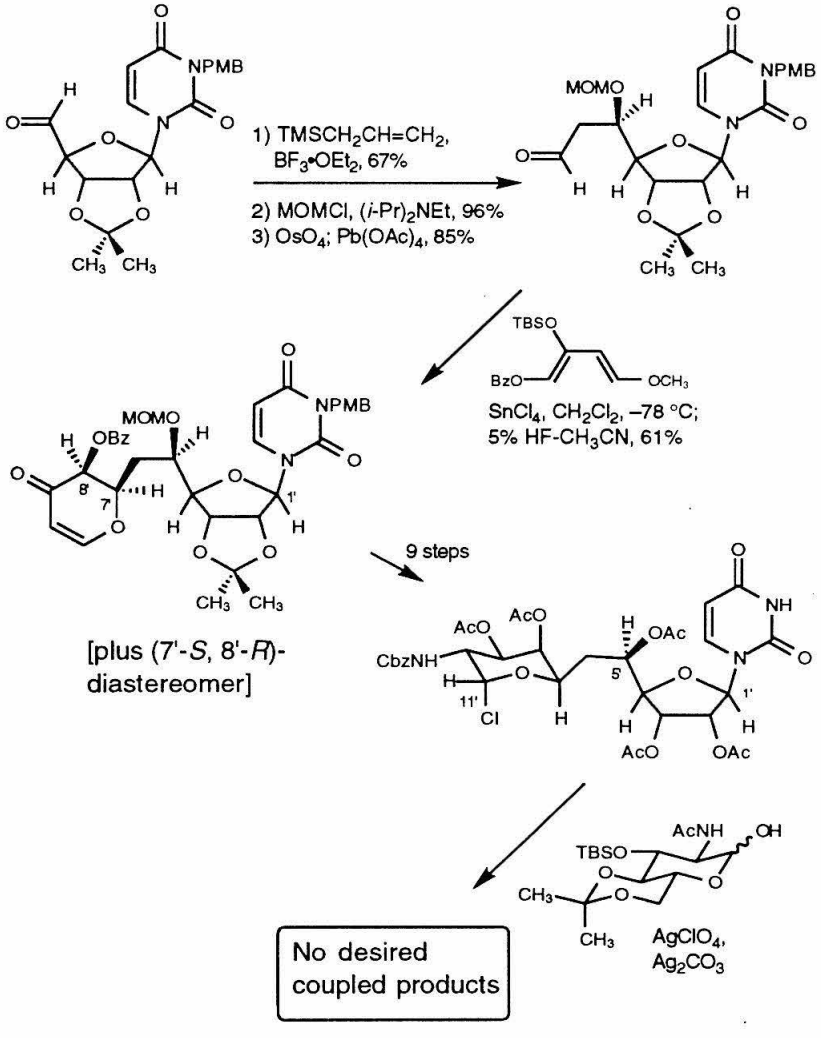
Retrosynthetic analysis of the tunicamycins as a class suggests that one highly versatile strategy for their preparation would involve the selective *N*-acylation of the precursor **1** as the final synthetic step. Two challenges emerge upon consideration of the simplified precursor **1** as a synthetic target: (1) the construction of the undecose fragment, tunicaminyluracil (**2**), from readily available precursors; and (2) the efficient formation of the trehalose disaccharide linkage with proper stereochemistry.

Given the complexity of the tunicaminyluracil substructure (**2**) in terms of stereochemistry and functionality, it is not surprising that previous efforts to synthesize the tunicamycins have focused initially on the preparation of **2**, deferring formation of the trehalose disaccharide linkage to a later stage.[7,8] These same studies have shown, however, that the latter problem is perhaps as difficult as the former. In the single reported synthesis of a natural tunicamycin prior to studies described herein, Suami *et al.*[7] described the successful late-stage formation of the trehalose linkage via a modified Koenigs-Knorr carbohydrate construction, albeit proceeding in poor yield (18%, Scheme III). In a detailed study, Danishefsky and co-workers[8] noted that a similar coupling reaction involving nearly identical precursors did not proceed according to precedent (Scheme IV); these authors point out that the earlier successful coupling had been achieved with retrosynthetically-derived material and was conducted on relatively large scale. These observations proved invaluable in the development of our synthetic plan, where it was determined to conduct the trehalose bond-forming step at an early stage in the synthesis.

Scheme III Previous Synthetic Studies: Suami *et al.*



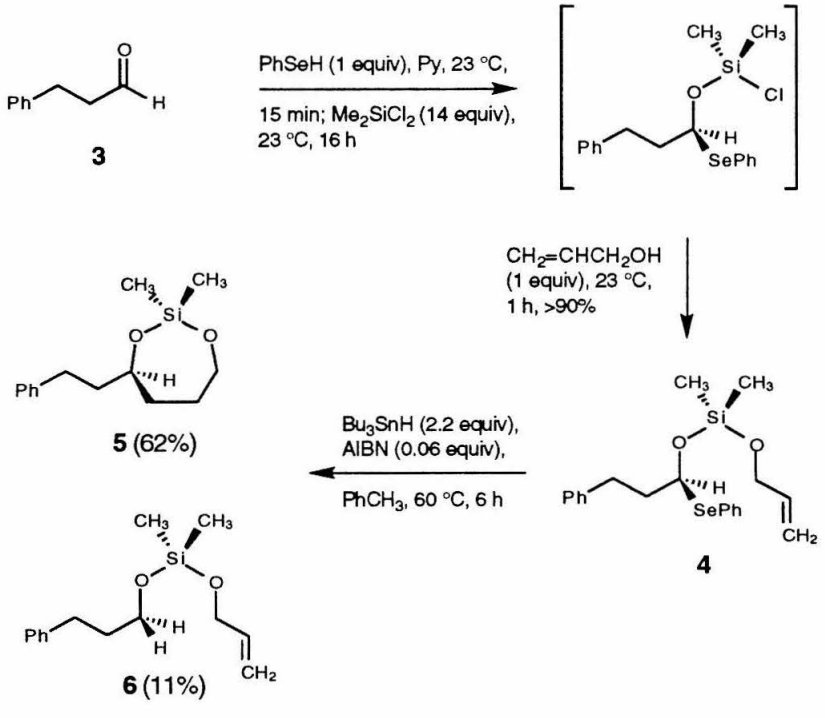
Scheme IV Previous Synthetic Studies: Danishefsky *et al.*



The undecose substructure within **1** may be viewed as the product of the coupling of uridine and galactosamine residues through carbons C5' and C6, respectively. Suami *et al.* employed a related coupling reaction in their synthesis of tunicaminyluracil (**2**) (Scheme III),[7c] while Danishefsky *et al.* established this bond by an organometallic addition reaction with subsequent development of the galactosamine fragment by de novo construction (Scheme IV).[8] Our retrosynthetic analysis of **1** also targeted the C5'-C6' bond for disconnection; however, we planned to employ a new method for this bond formation that allowed for the use of simple precursors derived from uridine and galactosamine.[6b]

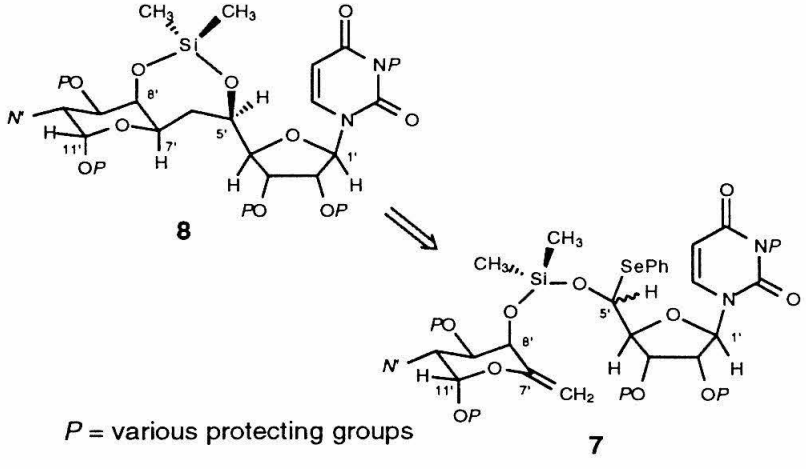
Exploratory studies had shown (Scheme V) that when a solution of dihydrocinnamaldehyde (**3**, 1 equiv) in pyridine was treated sequentially with benzeneselenol[9] (1.0 equiv, 23 °C, 15 min), excess dichlorodimethylsilane (14 equiv, 23 °C,

Scheme V



16 h, excess reagent removed in vacuo), and allyl alcohol (1.0 equiv, 23 °C, 1 h), the *O*-silylhemiselenoacetals **4** were formed in high yield (>90%).[10] Subsequent exposure of *O*-silylhemiselenoacetals **4** to tributyltin hydride (2.2 equiv) at 60 °C in toluene in the presence of the radical initiator 2,2'-azobis(isobutyronitrile) (AIBN, 0.06 equiv) led to a 7-*endo*-trig ring closure to form the siloxane **5** (62%) together with a small amount of non-cyclized reduction product **6** (11%). No product arising from 6-*exo*-trig cyclization was observed, perhaps a consequence of the length of the Si–O bonds.[11] This procedure allowed for the mild and efficient coupling of aldehydes and allylic alcohols and generated a siloxane-protected 1,4-diol functionality, a retron that maps onto the C5'-C8' substructure within **1** (Scheme VI). A substrate such as the *O*-silylhemiselenoacetal **7**, prepared from an

Scheme VI



appropriate uridine 5'-aldehyde derivative and a galactosamine-derived allylic alcohol, was thus envisioned to undergo a similar silicon-mediated reductive coupling to form the siloxane **8**. For the proposed retrosynthetic disconnection to be valid, it was critical that the newly-formed stereogenic centers at C5' and C7' be established with correct

stereochemistry. The stereochemical outcome at C7' was predicted to be the desired *R* configuration for the following reasons: (1) glycosyl radicals are known to react to form axial bonds preferentially,[12] and (2) equatorial C–H bond formation would result in a prohibitively strained ring system. The stereochemistry of C5', on the other hand, was less easily predicted (vide infra). To investigate the feasibility of the proposed bond formation and its potential application in a synthesis **1**, the reductive coupling procedure was first examined in the context of a synthesis of tunicaminyluracil (**2**).

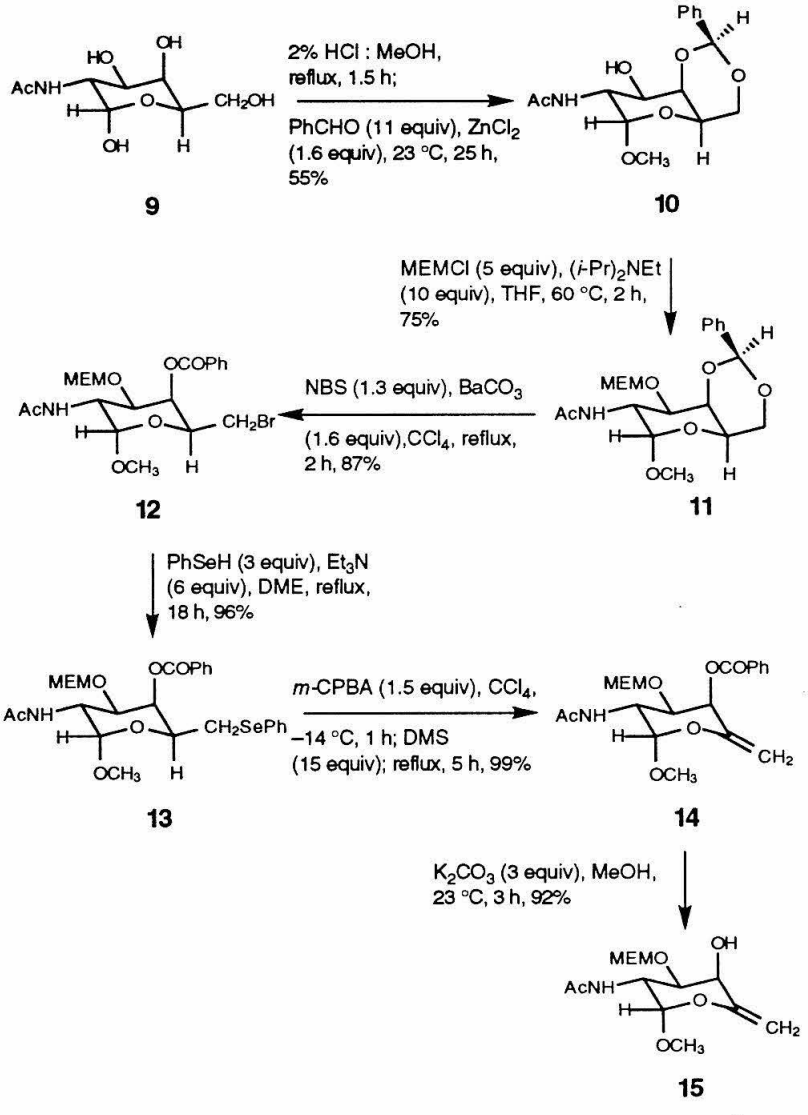
Chapter 2

Synthesis of Tunicaminyluracil

Synthesis of (+)-Tunicaminyluracil (2)

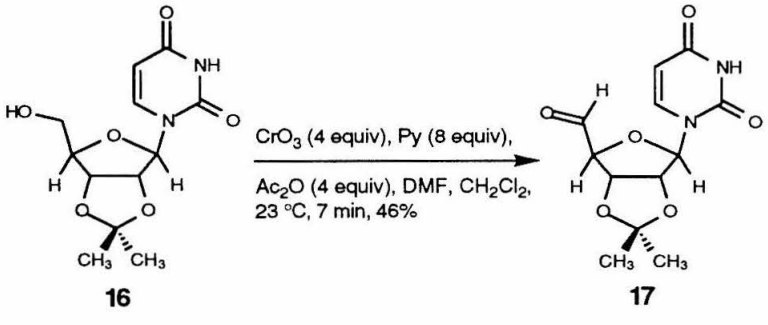
To apply the hemiselenoacetal reductive coupling methodology described above in a synthesis of tunicaminyluracil (**2**), the allylic alcohol **15** was synthesized, employing commercially available *N*-acetylgalactosamine (**9**) as the starting material (Scheme VII). Heating a solution of **9** and hydrochloric acid in methyl alcohol at reflux for 1.5 h provided the corresponding α-methylgalactopyranoside which, without purification, was treated with benzaldehyde (11 equiv) and zinc chloride (1.6 equiv) at 23 °C for 25 h to provide the 4,6-*O*-benzylidene-α-methylgalactopyranoside **10**[13] as a single anomer in 55% yield (mp 165.0-166.3 °C, ethyl alcohol). In initial investigations, alcohol **10** was protected as the corresponding 3-*O*-*t*-butyldimethylsilyl ether derivative; however, the silyl protecting group was later shown to be inappropriate due its propensity to migrate upon deprotection of the C4-hydroxyl functionality. Consequently, **10** was protected as the 3-*O*-methoxyethoxymethyl (MEM) ether[14] **11** (MEM chloride (5.0 equiv), diisopropylethylamine (10 equiv), tetrahydrofuran (THF), 60 °C, 2 h, 75%). Generation of the C6-*exo*-methylene functional group from **11** was initiated by oxidative cleavage of the 4,6-*O*-benzylidene acetal. Thus, exposure of **11** to *N*-bromosuccinimide (NBS, 1.3 equiv) and barium carbonate (1.6 equiv) in refluxing carbon tetrachloride for 2 h[15] efficiently formed the bromide **12** (87%). It was necessary to employ the anomeric methyl galactopyranoside in the latter transformation because the corresponding benzyl galactopyranoside underwent competitive oxidation of the benzyl group. In efforts to generate the C6-*exo*-methylene functionality from **12** by the direct elimination of hydrogen bromide (*e.g.*, silver fluoride, pyridine;[16] triethylamine, benzene, reflux; silver carbonate, isooctane, reflux), **12** was found to be unreactive, presumably a consequence of steric shielding of the C5-hydrogen by the axial C1-methoxyl substituent. Elimination was therefore induced in a two-step procedure involving the initial treatment of the bromide **12**

Scheme VII


2% HCl : MeOH, reflux, 1.5 h;
PhCHO (11 equiv), ZnCl2 (1.6 equiv), 23 °C, 25 h, 55%
9
10
MEMCl (5 equiv), (i-Pr)2NEt (10 equiv), THF, 60 °C, 2 h, 75%
NBS (1.3 equiv), BaCO3
(1.6 equiv),CCl4, reflux, 2 h, 87%
12
11
PhSeH (3 equiv), Et3N (6 equiv), DME, reflux, 18 h, 96%
m-CPBA (1.5 equiv), CCl4, −14 °C, 1 h; DMS (15 equiv); reflux, 5 h, 99%
13
14
K2CO3 (3 equiv), MeOH, 23 °C, 3 h, 92%
15

with benzeneselenol (3.0 equiv) in the presence of triethylamine (6.0 equiv) in refluxing dimethoxyethane (DME) for 18 h to generate the phenylselenide **13** (96%). Oxidation of the phenylselenide **13** with *m*-chloroperoxybenzoic acid (*m*-CPBA, 1.5 equiv) in carbon tetrachloride at –14 °C for 1 h, followed by thermal elimination of the resulting selenoxide (carbon tetrachloride, reflux, 5 h),[17] afforded the allylic acetate **14** in 99% yield. Removal of the C4-benzoyl ester group of **14** was accomplished by transesterification with potassium carbonate (3.0 equiv) in methyl alcohol at 23 °C for 3 h to yield the allylic alcohol **15** (92%).

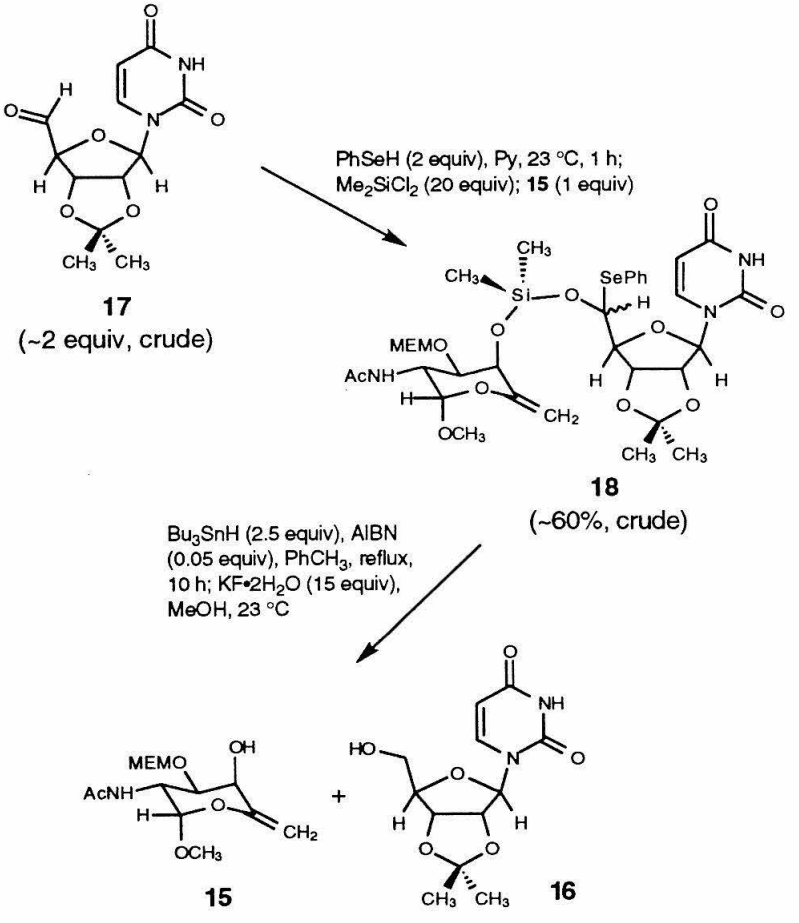
The uridine 5'-aldehyde derivative **17** was prepared as the initial coupling partner for the allylic alcohol **15** and was synthesized from commercially available 2',3'-isopropylidene uridine (**16**). Oxidation of **16** following the procedure of Corey and Samuelsson (chromium trioxide (4.0 equiv), pyridine (8.0 equiv), acetic anhydride (4.0 equiv), dichloromethane, *N,N*-dimethylformamide (DMF), 23 °C, 20 min)[18] afforded **17** in 55% yield. The aldehyde **17**, like many others synthesized during the course of our investigations, underwent ready hydration and was unstable to purification by conventional chromatography on silica gel. Aldehyde **17** was partially purified in its hydrated form by flash chromatography on silica gel at –14 °C. Regeneration of the aldehyde was readily accomplished by the azeotropic removal (toluene) of water from the hydrate.



16 **17**

Initial attempts to construct the *O*-silylhemiselenoacetal **18** (Scheme VIII) from **17** and the allylic alcohol **15** employed the procedure developed for the coupling of hydrocinnamaldehyde and allyl alcohol (see above). Thus, treatment of the aldehyde **17** (2.0 equiv) with benzeneselenol (2.0 equiv, 8 h) in pyridine at 23 °C for 1 h, addition of dichlorodimethylsilane (20 equiv), removal of excess dichlorodimethylsilane in vacuo, and addition of a solution of allylic alcohol **15** (1 equiv) in pyridine at 23 °C produced the

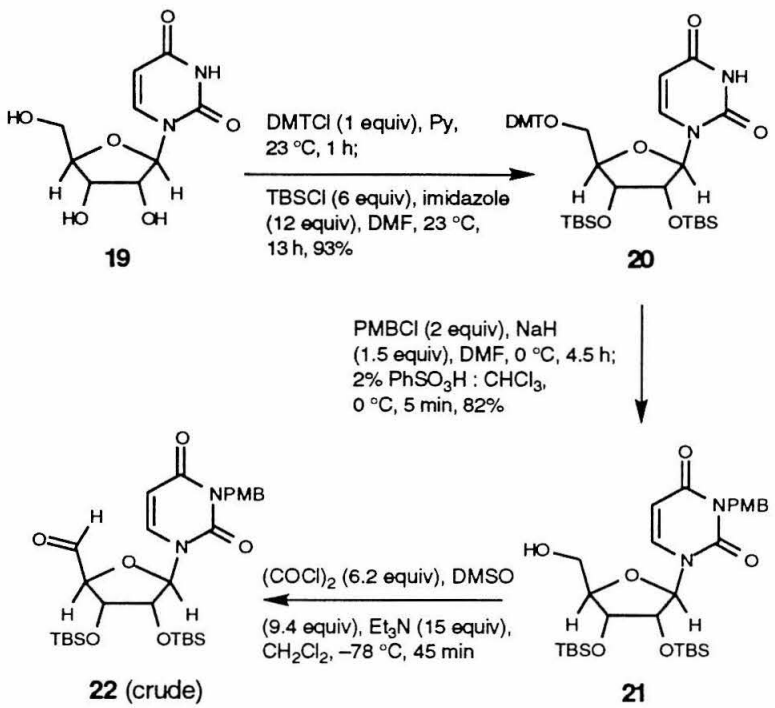
Scheme VIII



adducts **18** in modest yield as a 1:1 mixture of diastereomers at C5'. Purification of the diastereomers **18** proved to be difficult due to their instability to column chromatography; as a result, the crude adducts (approximately 60% pure) were subjected directly to conditions conducive to free radical cyclization. Addition of a solution of tributyltin hydride (2.5 equiv, 10 mM) and 2,2'-azobis(isobutyronitrile) (0.05 equiv) in toluene over a period of 10 h to a solution of diastereomers **18** in refluxing toluene (1 mM), followed by treatment of the crude product mixture with potassium fluoride hydrate in methyl alcohol, afforded only the reduction product **16** and recovered allylic alcohol **15**, indicating that trapping of the C5'-radical with tributyltin hydride was faster than cyclization.

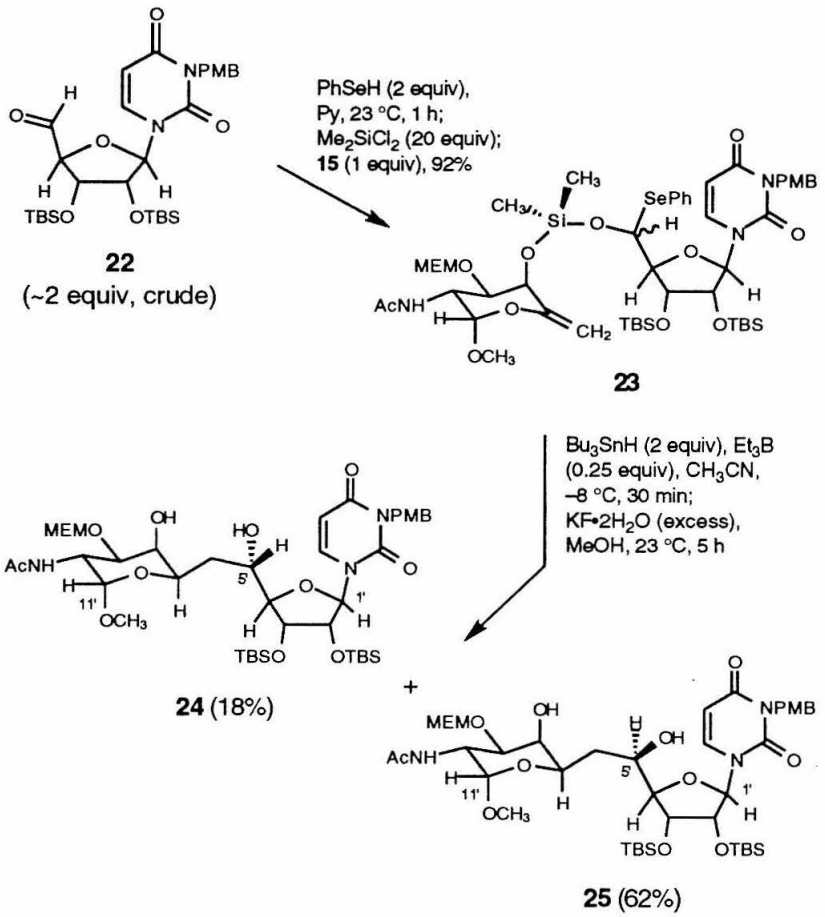
This unfavorable result in the initial cyclization attempt prompted the preparation of a second *O*-silylhemiselenoacetal derivative (**23**, Scheme X). This derivative incorporated a protecting group for the imido functionality and, with the greater steric bulk of the 2'-*O*- and 3'-*O*-silyl ethers, was felt to be better disposed toward intramolecular cyclization through shielding of the C5'-radical intermediate from bimolecular trapping. Preparation of **23** began with the treatment of uridine (**19**) with dimethoxytrityl chloride (1.0 equiv) in pyridine at 23 °C for 12 h (Scheme IX).[19] The resultant dimethoxytrityl ether was combined with excess *t*-butyldimethylsilyl chloride (6.0 equiv) and imidazole (12 equiv) in DMF at 23 °C for 13 h to afford the bis(*t*-butyldimethylsilyl) ether **20** in 93% yield from uridine. Exposure of **20** to *p*-methoxybenzyl chloride (2.0 equiv) and sodium hydride (1.5 equiv) in DMF at 0 °C for 4.5 h afforded the corresponding *N*-(*p*-methoxybenzyl) derivative. Subsequent removal of the dimethoxytrityl protecting group with a solution of benzenesulfonic acid in chloroform (2% (w/w)) at 0 °C for 5 min[20] provided the alcohol **21** in 82% yield for the two steps. The use of the *p*-methoxybenzyl protecting group for the imido functionality of uracil is precedented in the work of Danishefsky and co-workers in their synthesis of tunicaminyluracil.[8] Efforts to oxidize **21** to the corresponding aldehyde

Scheme IX



(**22**) employing a number of standard reagents (pyridinium dichromate, chromium trioxide in pyridine, or 1,3-dicyclohexylcarbodiimide and dimethyl sulfoxide) were complicated by the formation of by-products that could not be readily separated from **22**. Only the Swern oxidation[21] (oxalyl chloride (6.2 equiv), dimethylsulfoxide (9.4 equiv), triethylamine (15 equiv), dichloromethane, –78 °C, 45 min) afforded product **22** of sufficient purity (~90%) to carry on with the reductive cyclization procedure. Subjection of the crude aldehyde **22** (2.0 equiv) to the coupling conditions described above (benzeneselenol (2.0 equiv), pyridine, 23 °C; dichlorodimethylsilane (20 equiv); **15** (1 equiv)) afforded the *O*-silylhemiselenoacetals **23** in 92% yield as a 1:1 mixture of C5'-diastereomers after purification by flash column chromatography (Scheme X). The stability of *O*-silylhemiselenoacetals **23** to silica gel is notable in light of the lability of the hemiselenoacetals **13** previously encountered.

Scheme X



A series of experiments was performed to evaluate the feasibility of carbon-carbon bond formation within the hemiselenoacetals **23** (Table I). Treatment of a solution of the hemiselenoacetals **23** with tributyltin hydride in the presence of a free radical initiator led to efficient intramolecular cyclization to form a mixture of epimeric adducts whose diastereomeric ratio varied markedly with the choice of solvent. Direct treatment of the

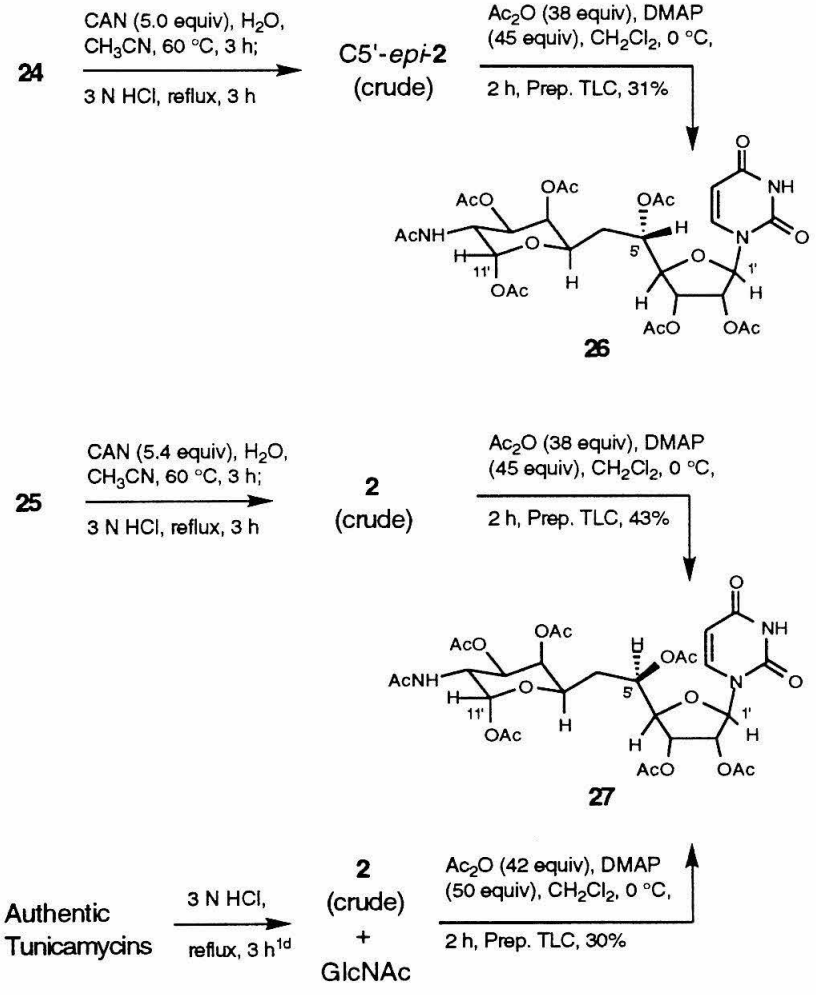
Table I **Reductive Coupling of 23: Solvent and Temperature Effects**[a]

Solvent	Temperature[b] (°C)	Product Ratio[c] **25**(desired) : **24**(undesired)
$PhCH_3$	110	1.0 : 3.0
$PhCH_3$	60	1.0 : 3.2
$PhCH_3$	50	1.0 : 4.2
$PhCH_3$	$-78 \rightarrow 23$	1.0 : 5.3
THF	60	1.0 : 2.2
10% H_2O : THF	60	1.0 : 2.0
10% DMF : THF	60	1.0 : 3.0
CH_3CN	23	1.9 : 1.0
CH_3CN	0	2.4 : 1.0
CH_3CN	–5	2.9 : 1.0
CH_3CN	$-14 \rightarrow 0$	3.1 : 1.0
$(CH_3)_2CHOH$	0	1.9 : 1.0
$(CH_3)_2CHOH$	$-78 \rightarrow 23$	1.9 : 1.0
CH_3CH_2OH	65	1.0 : 1.0
CH_3CH_2OH	0	1.7 : 1.0
CH_3OH	0	3.7 : 1.0
0.06% H_2O : CH_3CN	0	2.4 : 1.0
0.06% H_2O : CH_3CN	$-14 \rightarrow 23$	2.3 : 1.0
20% CH_3OH : CH_3CN	0	2.9 : 1.0
20% CH_3OH : CH_3CN	$-20 \rightarrow 23$	2.1 : 1.0

[a] Reactions were performed employing 3-5 mg **23** (1 equiv, 1 mM) and 10 equiv Bu_3SnH. [b] Reactions performed at or below 23 °C were initiated with Et_3B and oxygen. Reactions conducted at temperatures >23 °C were initiated by the slow addition of a solution of Bu_3SnH (10 equiv) and AIBN (0.05 equiv) at 23 °C. [c] Yields were generally >70%, except for those reactions carried out in protic solvents, which afforded yields of ~40%. The major by-product in all cases was that of hydrogen-atom addition to the radical site.

crude product mixture with potassium fluoride hydrate in methyl alcohol produced the diastereomeric diols **24** and **25** in 40-80% yield from **23**. These diastereomers could be separated by preparative thin-layer chromatography or radial chromatography to afford each C5'-diastereomer in pure form. To establish the stereochemistry of the cyclization products, each of the diols **24** and **25** was separately deprotected (ceric ammonium nitrate, acetonitrile,

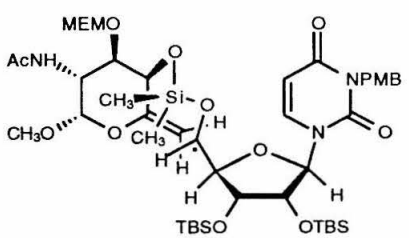
Scheme XI



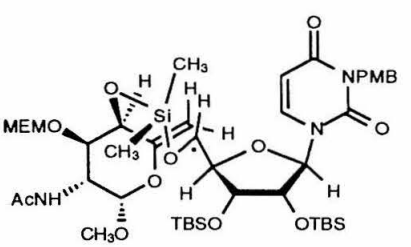
water, 60 °C, 3 h;[22] 3 N hydrochloric acid, reflux, 3 h) and was peracetylated (acetic anhydride, 4-(*N,N*-dimethylamino)pyridine (DMAP), dichloromethane, 0 °C, 2 h) to give α-heptaacetyl-5'-*epi*-tunicaminyluracil (**26**) from **24** and α-heptaacetyltunicaminyluracil (**27**) from **25** after preparative thin layer chromatography (Scheme XI). These products were compared with an authentic sample of α-heptaacetyltunicaminyluracil (**27**), prepared from a mixture of tunicamycins according to the procedure of Tamura *et al.*[1d]

In general, the use of nonpolar solvents (toluene, THF) in the free-radical cyclization was found to favor the formation of the undesired epimer (**24**) from **23**, whereas polar solvents (acetonitrile, methyl alcohol) favored the formation of the desired isomer **25**. Hypothetical transition structures **28** and **29** leading to these isomers, respectively, are depicted in Figure 2. In both structures, attack of the C5'-radical is invoked to occur opposite the bulky *t*-butyldimethylsilyl ether substituents. The manner in which the solvent polarity apparently influences the stereochemical outcome of the cyclization reaction is not at all evident, and the validity of transition structures **28** and **29** is certainly open to question.

Figure 2



28



29

Nevertheless, the role of the solvent in the reaction provides a useful device for practical syntheses of either stereoisomer. The optimal protocol for the preparation of the desired stereoisomer (**25**) involved the addition of tributyltin hydride (2.0 equiv) and triethylborane[23] (0.25 equiv) to a solution of *O*-silylhemiselenoacetals **23** (1 mM, 1 equiv) in acetonitrile at –8 °C. Treatment of the crude product mixture with potassium fluoride hydrate in methyl alcohol and purification of the resulting diol mixture by radial chromatography afforded the pure diol **25** in 62% yield and the pure diol **24**, isolated in separate fractions, in 18% yield. Although reactions conducted in methyl alcohol produced an increased proportion of **25** relative to reactions conducted in acetonitrile, the increased formation of the reduction product **21** in methyl alcohol led to a lower absolute yield.

Deprotection of the synthetic diol **25** (ceric ammonium nitrate (5.4 equiv), acetonitrile-water, 60 °C, 3 h; 3 N hydrochloric acid, reflux, 3 h) furnished synthetic tunicaminyluracil (**2**) in crude form. Peracetylation of synthetic **2** with excess acetic anhydride and DMAP in dichloromethane at 0 °C afforded, after preparative thin-layer chromatography, α-heptaacetyltunicaminyluracil (**27**, 43%), which was shown to be identical in all respects (^{1}H NMR, ^{13}C NMR, mp, FTIR, MS, HRMS, TLC, HPLC, optical rotation) with an authentic sample.

Chapter 3

Synthesis of Tunicamycin-V

Synthesis of (+)-Tunicamycin-V (1-V)

The establishment of an efficient method for the formation of the C5'-C6' carbon-carbon bond of tunicaminyluracil has provided the basis for a highly convergent synthesis of the tunicamycin antibiotics. In addition to the preparation of the undecose core, the latter endeavor required the development of a method for the construction of the β,α-trehalose linkage within **1**, a crucial problem that previously had been met with only modest success. In contrast to prior work, in which the trehalose bond was formed as a late-stage synthetic operation,[7,8] the approach described herein focused on glycosidic bond formation early in the synthesis, as the initial convergent step. Construction of the C5'-C6' bond of the tunicaminyluracil core was deferred to a later stage in the synthesis, where the mild conditions of the silicon-mediated reductive coupling methodology projected to form this bond (see above) were anticipated to be compatible with the trehalose linkage. An advantage of this strategy was that it permitted the use of relatively simple carbohydrate precursors for the synthesis of the trehalose-linked disaccharide.

Synthesis of the β,α-Trehalose Linkage

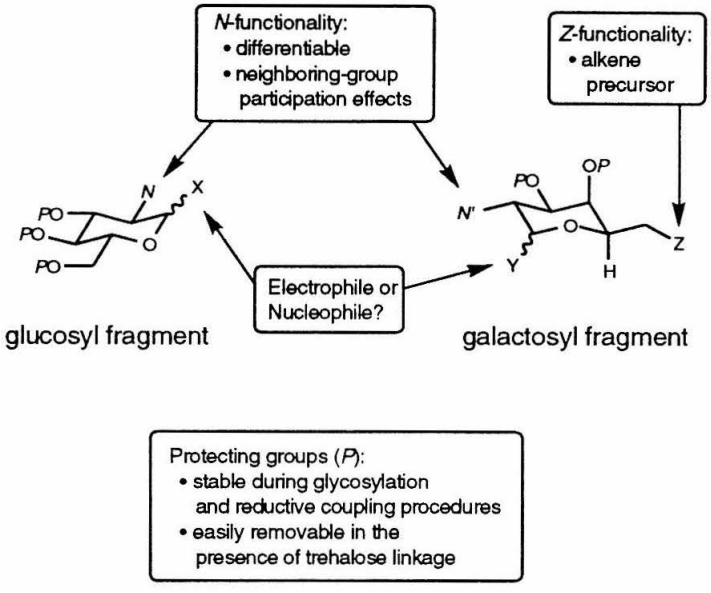
Although the stereocontrolled synthesis of any glycosidic bond is inherently challenging, the preparation of disaccharides containing an ether linkage between anomeric carbons (trehalose linkage) is particularly so. Any such linkage is potentially disconnected retrosynthetically in two ways; in both disconnections the glycosyl acceptor (nucleophilic component) contains an anomeric hydroxyl group as the nucleophile. This compounds the difficulty of glycosidic bond formation by virtue of the poorer nucleophilicity of the anomeric hydroxyl group as compared with other alcohols, and because the orientation of the anomeric hydroxyl group is ambiguous. As a consequence, trehalose-linked saccharides are seldom prepared efficiently.

The traditional method of glycosidic bond formation, originating with Koenigs and Knorr in 1901,[24] suffers from several disadvantages, to include:[25] (1) the difficulty of stereocontrolled synthesis of the glycosyl halide coupling partners; (2) the thermal and hydrolytic instability of these halides; (3) the use of toxic or potentially explosive heavy-metal salts in the coupling reaction; and (4) the frequently poor efficiency of the coupling reactions, particularly with hydroxyl groups of low nucleophilicity.

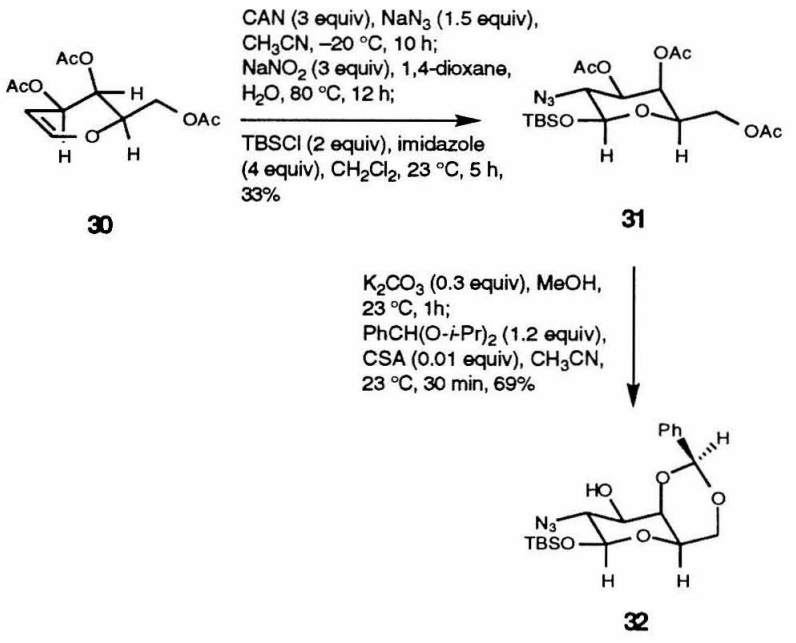
For these reasons, and given the documented poor performance of the Koenigs-Knorr methodology in the context of synthesis of the tunicamycin trehalose linkage,[7,8] our studies focused on the methodology of Schmidt *et al.* for glycosidic bond formation. Also known as the trichloroacetimidate method,[26] the Schmidt protocol entails the coupling of an anomeric trichloroacetimidate (glycosyl donor) with the nucleophilic hydroxyl group of a glycosyl acceptor. Advantages of this method include: (1) the ease of synthesis of trichloroacetimidates of either α- or β-configuration; (2) the thermal and hydrolytic stability of the glycosyl trichloroacetimidates; (3) mild conditions for glycosidic bond formation, typically catalyzed by Lewis acids; and (4) the efficiency and stereoselectivity of these coupling reactions. The trichloroacetimidate methodology has seen limited use in the synthesis of disaccharides containing the trehalose linkage.[27]

In retrosynthetic analysis of the tunicamycin trehalose-linked disaccharide, primary consideration must be given to the assignment of the roles of electrophile and nucleophile to the galactosamine and glucosamine components (Figure 3). In addition, careful consideration must be given to the choice of protective groups for each C2-amino functionality and to the potential role of that protective group in the glycosylation reaction. Similar considerations apply to the hydroxyl groups of each sugar. In addition, the C6-substituent ("*Z*") of the galactosamine residue must function as a precursor to an *exo*-methylene group (C5-C6).

Figure 3

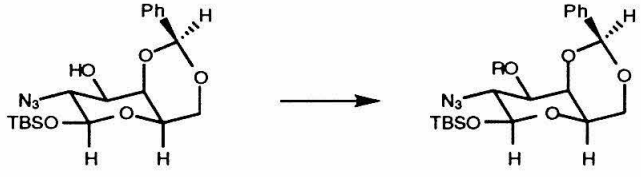


After extensive experimentation, the coupling partners **38** and **44** were found to serve as optimal substrates in an acid-promoted trichloroacetimidate glycosylation reaction to form the desired β,α-trehalose linkage (see below). This approach employed the galactosamine derivative **38** as the nucleophilic component in the reaction. This component was synthesized from tri-*O*-acetyl-D-galactal (**30**)[28] in a sequence initiated by the azido nitration procedure of Lemieux *et al.* (ceric ammonium nitrate (3.0 equiv), sodium azide (1.5 equiv), acetonitrile, –20 °C, 10 h).[29] Hydrolysis of the product anomeric nitrate esters with sodium nitrite (3.0 equiv) in a mixture of water and 1,4-dioxane at 80 °C for 12 h afforded the corresponding azido sugar as a mixture of anomers. The azido nitration procedure proved to be extremely valuable in the synthesis as it allowed for the facile incorporation of a masked amino group at C2 of galactose from a readily available carbohydrate precursor. Protection of the anomeric hydroxyl group of the intermediate azido sugar with *t*-



butyldimethylsilyl chloride (2.0 equiv) and imidazole (4.0 equiv) in dichloromethane provided the *t*-butyldimethylsilyl ether **31** as a single anomer (β) in 33% yield from tri-*O*-acetyl-D-galactal (**30**). Methanolysis of triester **31** with potassium carbonate (0.3 equiv) in methyl alcohol (23 °C, 1 h) and selective protection of the C4- and C6-hydroxyl groups of the resulting triol with diisopropoxybenzyl acetal (1.2 equiv) and camphorsulfonic acid (0.01 equiv) in acetonitrile (23 °C, 30 min) furnished the galactopyranoside **32**[30] in 69% yield. The 4,6-*O*-benzylidene acetal not only served to protect the C4- and C6-hydroxyl groups, but also functioned as a precursor to the allylic alcohol functionality necessary for the reductive coupling that would form the undecose core of the tunicamycins (see Scheme VII). Because of concerns that the benzylidene acetal would not be stable under the acidic conditions of the glycosidic coupling procedure, the oxidative cleavage of this group was performed prior to the glycosidic coupling. Initially, it was deemed prudent to protect the C3-hydroxyl group before oxidative cleavage of the benzylidene acetal; however, after

Table II. Screening of 3-*O*-Protective Groups (R) for 32[a]



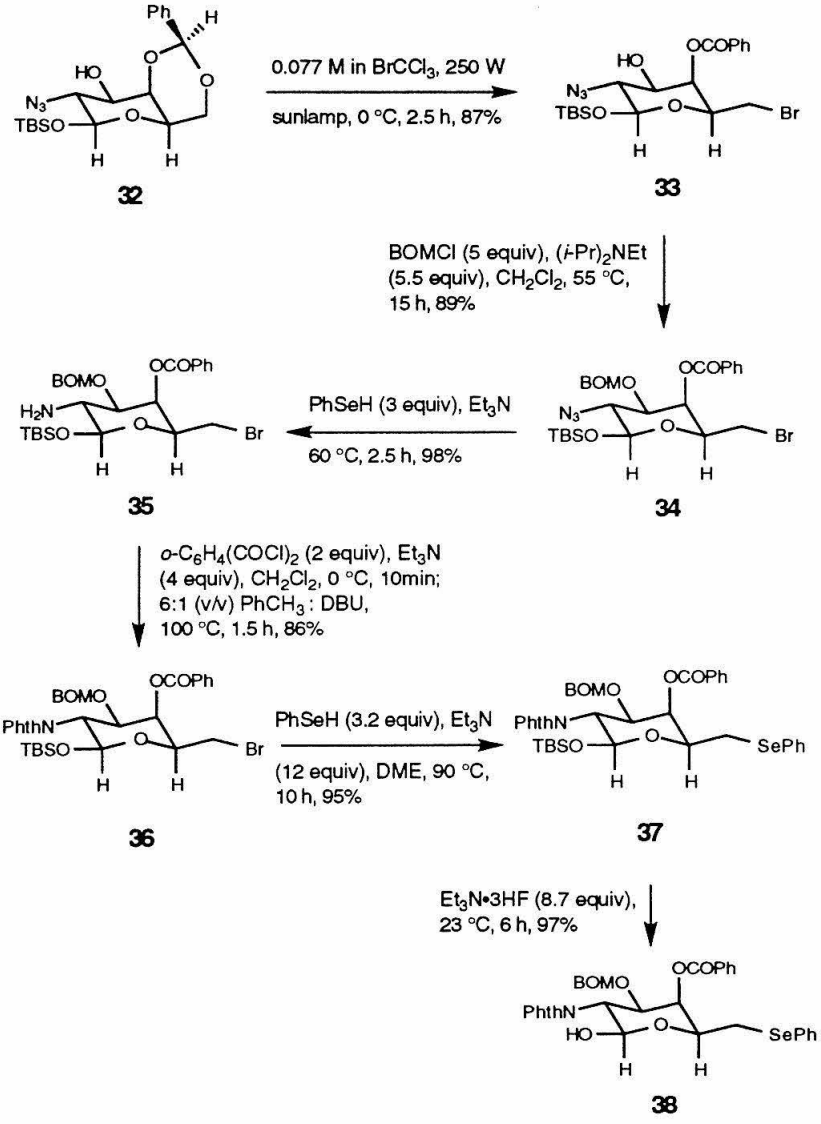
32

R	Reagent	Yield (%)	Incompatibility
Benzyl	Benzyl bromide	84	Removal during NBS-cleavage of benzylidene
SEM	SEMCl	95	Removal during acid-catalyzed glycosylation
TBS	TBSCl	92	Migration upon deprotection of C4-OH
Acetyl	acetic anhydride	quantitative	Migration to form C2-acetamide on azide reduction

[a] SEM = trimethylsilylethoxymethyl, TBS = *t*-butyldimethylsilyl, NBS = *N*-bromosuccinimide.

serious difficulties were encountered with four different types of protective groups (Table II), the direct oxidative cleavage of **32**, with a free C3-hydroxyl group, was examined. Irradiation of a solution of **32** (0.077 M) in bromotrichloromethane with a 250-W sunlamp at 0 °C for 2.5 hours[31] afforded the bromide **33** in 87% yield (Scheme XII). The C3-

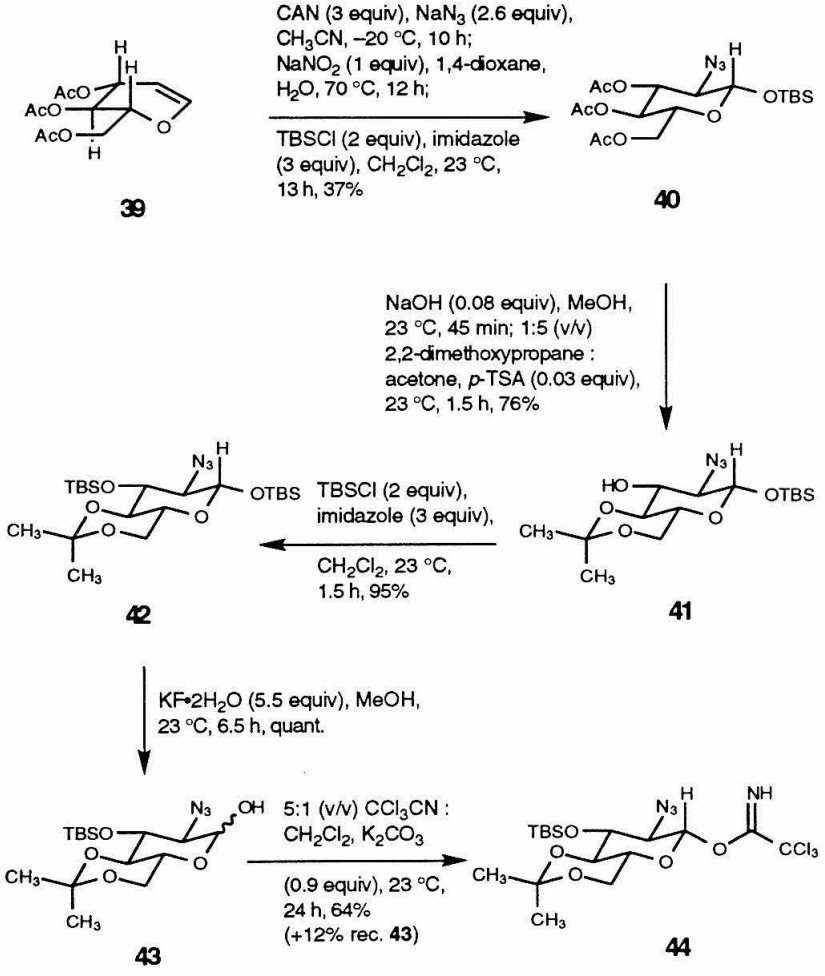
Scheme XII


0.077 M in BrCCl3, 250 W
sunlamp, 0 °C, 2.5 h, 87%
32
33
BOMCl (5 equiv), (i-Pr)2NEt
(5.5 equiv), CH2Cl2, 55 °C,
15 h, 89%
PhSeH (3 equiv), Et3N
60 °C, 2.5 h, 98%
35
34
o-C6H4(COCl)2 (2 equiv), Et3N
(4 equiv), CH2Cl2, 0 °C, 10min;
6:1 (v/v) PhCH3 : DBU,
100 °C, 1.5 h, 86%
PhSeH (3.2 equiv), Et3N
(12 equiv), DME, 90 °C,
10 h, 95%
36
37
Et3N•3HF (8.7 equiv),
23 °C, 6 h, 97%
38

hydroxyl group of **33** was then protected as the corresponding benzyloxymethyl (BOM) ether[32] (**34**, BOM chloride (5.0 equiv), diisopropylethylamine (5.5 equiv), dichloromethane, 55 °C, 15 h, 98%). The BOM ether **34** was found to be unreactive toward a variety of standard reagents developed for the reduction of azides,[33] presumably a consequence of steric shielding of the azido group by the adjacent *t*-butyldimethylsilyloxy group. Only the treatment of **34** with benzeneselenol (3.0 equiv) in triethylamine at 60 °C for 2.5 h[34] efficiently formed the corresponding amine (**35**, 98%). Protection of the amine **35** with phthaloyl dichloride (2.0 equiv) in a mixture of toluene and 1,8-diazabicylo[5.4.0]undec-7-ene (DBU) at 100 °C for 1.5 h afforded the phthalimide **36** in 86% yield. Displacement of the primary bromide within **36** using benzeneselenol (3.2 equiv) and triethylamine (12 equiv) in refluxing dimethoxyethane for 10 h efficiently furnished the phenylselenide **37** (95%). It was also possible to both reduce the azido group and displace the bromide by the treatment of **34** with benzeneselenol and triethylamine; however, the two-step procedure outlined above proceeded in higher yield. The phenylseleno group served as a masked form of the *exo*-methylene functionality necessary for the planned reductive coupling protocol. Cleavage of the anomeric *t*-butyldimethylsilyl ether **37** with triethylamine trihydrofluoride (8.7 equiv) in acetonitrile (23 °C, 6 h, 97%) produced the hemiacetal **38** as a 10:1 (β:α) mixture of anomers. The C2-phthalimido substituent is believed to favor the equatorial or β-orientation of the anomeric hydroxyl group, by virtue of a non-bonding steric interaction between a phthalimido carbonyl group and the anomeric hydroxyl group within the axial or α-anomer.[35] The β-orientation is required to prepare the trehalose linkage within the tunicamycins.

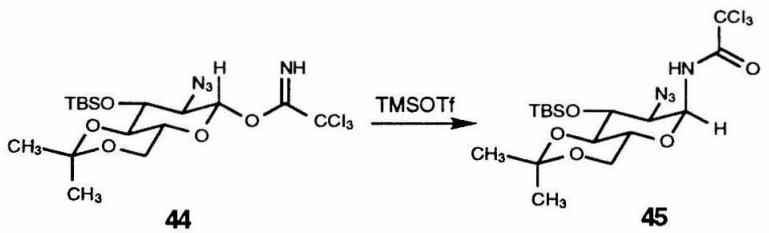
The preparation of the coupling partner **44** was initiated in a manner similar to that of **38**, by the azido nitration[29] of commercially available triacetoxy-D-glucal (**39**, Scheme XIII) with ceric ammonium nitrate (3.0 equiv) and sodium azide (2.6 equiv) in acetonitrile at

Scheme XIII

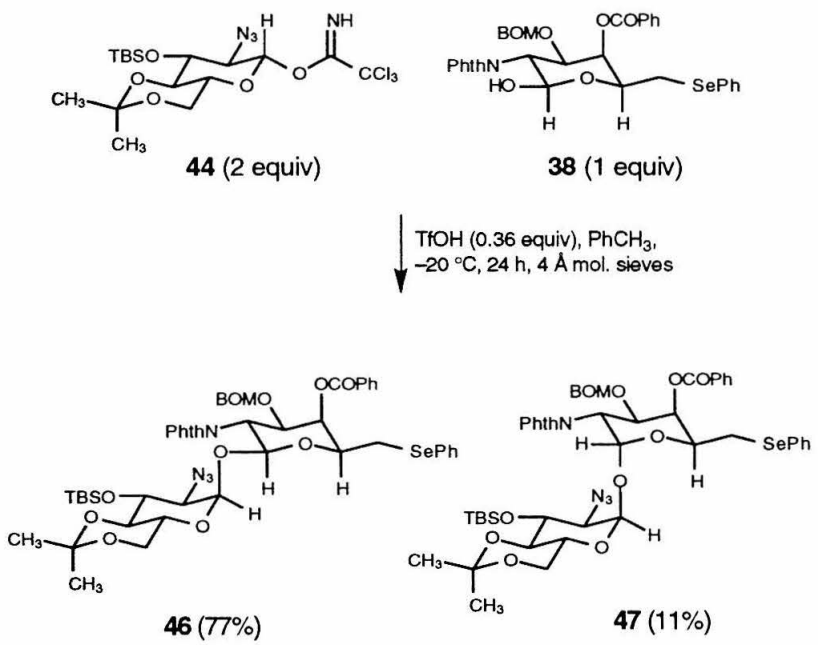

CAN (3 equiv), NaN_3 (2.6 equiv),
CH_3CN, –20 °C, 10 h;
$NaNO_2$ (1 equiv), 1,4-dioxane,
H_2O, 70 °C, 12 h;
TBSCl (2 equiv), imidazole
(3 equiv), CH_2Cl_2, 23 °C,
13 h, 37%
39
40
NaOH (0.08 equiv), MeOH,
23 °C, 45 min; 1:5 (v/v)
2,2-dimethoxypropane :
acetone, p-TSA (0.03 equiv),
23 °C, 1.5 h, 76%
TBSCl (2 equiv),
imidazole (3 equiv),
CH_2Cl_2, 23 °C,
1.5 h, 95%
41
42
$KF•2H_2O$ (5.5 equiv), MeOH,
23 °C, 6.5 h, quant.
5:1 (v/v) CCl_3CN :
CH_2Cl_2, K_2CO_3
(0.9 equiv), 23 °C,
24 h, 64%
(+12% rec. 43)
43
44

–20 °C for 10 h. The resulting 1-nitrato-2-azidosugar was readily hydrolyzed with sodium nitrite (1 equiv) in aqueous 1,4-dioxane at 70 °C for 12 h. Protection of the resulting anomeric hydroxyl group with *t*-butyldimethylsilyl chloride (2.0 equiv) and imidazole (3.0 equiv) in dichloromethane at 23 °C for 13 h produced the β-oriented silyl ether **40** in 37% yield from **39**. Methanolysis of the acetoxy substituents with a catalytic amount of sodium hydroxide (0.08 equiv) in methyl alcohol at 23 °C for 45 min, followed by selective protection of the C4- and C6-hydroxyl groups with excess 2,2-dimethoxypropane and *p*-toluenesulfonic acid (0.03 equiv) in acetone at 23 °C for 1.5 h afforded the acetonide **41** in 76% yield. Treatment of **41** with *t*-butyldimethylsilyl chloride (2.0 equiv) and imidazole (3.0 equiv) in dichloromethane at 23 °C for 1.5 h produced the bis(silyl) ether **42** in 95% yield.[36] Quantitative and selective cleavage of the anomeric silyl ether was accomplished by the treatment of **42** with potassium fluoride hydrate (5.5 equiv) in methyl alcohol at 23 °C for 6.5 h. Exposure of the hemiacetal **43** to a suspension of potassium carbonate (0.9 equiv) in trichloroacetonitrile and dichloromethane at 23 °C for 24 h provided the β-trichloroacetimidate **44** (64%) as well as recovered starting material (12%), after flash chromatography using triethylamine-treated silica gel.

Literature procedures for the Schmidt coupling of anomeric trichloroacetimidates with alcohols typically involve the use of the Lewis acids boron trifluoride etherate or trimethylsilyltrifluoromethane sulfonate (TMSOTf).[26] Treatment of the coupling partners **38** and **44** with boron trifluoride etherate under a variety of conditions led only to the decomposition of **44**. The use of TMSOTf as catalyst did produce the coupled products **46** and **47** in low yield (<30% combined yield); the competitive rearrangement of **44** to the amide **45** accompanied this transformation. The latter coupling reaction appeared to exhibit induction periods of varying length, suggesting that trifluoromethanesulfonic acid (TfOH) might function as the actual catalyst in the reaction.[37] Indeed, coupling reactions employing

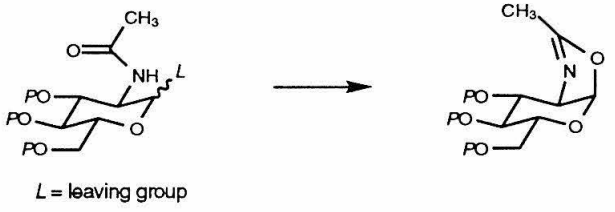


TfOH as the catalyst were found to be both rapid and efficient. In the optimum procedure, slow addition of a solution of TfOH (5% in toluene (v/v), 0.36 equiv total) to a solution of hemiacetal **38** (1 equiv) and trichloroacetimidate **44** (2.0 equiv) in dry toluene at 4-h intervals over a 24-h period at –20 °C produced the β,α-linked trehalose **46** in 77% yield after flash column chromatography. The α,α-diastereomer (**47**) was also isolated as a minor product (11%) in separate fractions. This procedure was found to be equally efficient on the milligram to 10-gram scale and represents a highly practical solution to the problem of stereocontrolled formation of the trehalose linkage within **1**.

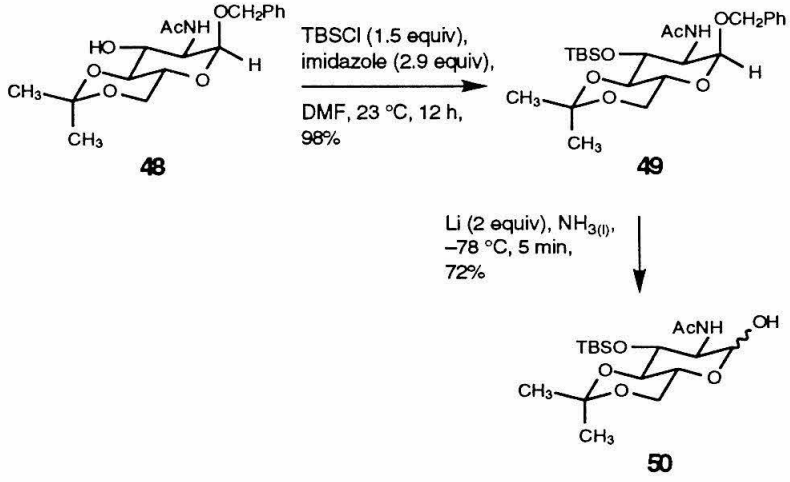


Other Glycosylation Attempts

Prior to the development of the glycosylation procedure described above, early investigations into trehalose construction centered on a reversal of the roles of the galactosamine- and glucosamine-derived coupling partners. Initial efforts employed the *N*-acetylglucosamine derivative **50**[8] as the nucleophilic component in the glycosylation reaction. This was a logical strategy to follow given that the tunicamycins contain an *N*-

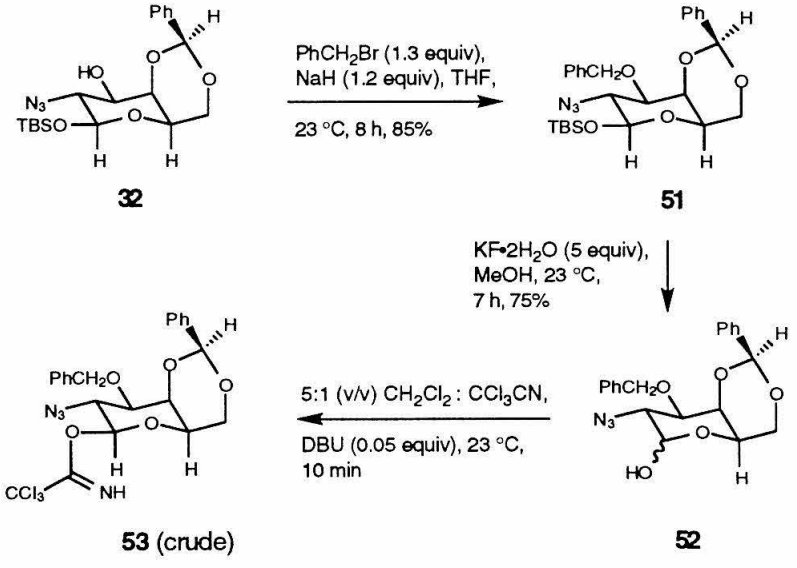


acetylglucosamine residue. The incompatibility of the C2-acetamido group with a leaving group at C1 (oxazoline formation) mandated that the *N*-acetylglucosamine residue serve as the nucleophilic component in the coupling reaction, if it were to be used at all. Protection of the known benzylgalactopyranoside **48**[38] with *t*-butyldimethylsilyl chloride (1.5 equiv)



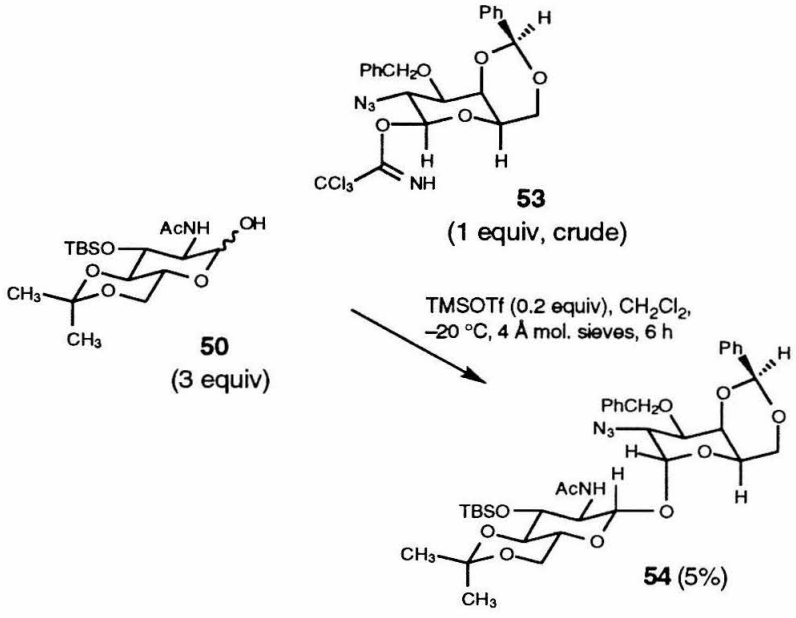
and imidazole (2.9 equiv) in DMF at 23 °C for 12 h furnished the silyl ether **49** in 98% yield. Reduction of **49** with lithium (2.0 equiv) in liquid ammonia at –78 °C produced the *N*-acetylglucosamine derivative **50** as a 2:1 (α:β) mixture of anomers in 72% yield.

The galactose-derived trichloroacetimidate **53**, with a C2-azido substituent, was synthesized for initial coupling studies with **50**. The azido alcohol **32**, described above, was protected as its benzyl ether (**51**) using sodium hydride (1.2 equiv) and benzyl bromide (1.3 equiv) in THF at 23 °C for 8 h. Cleavage of the anomeric silyl ether with potassium fluoride hydrate in methyl alcohol at 23 °C furnished the anomeric alcohols **52** (1.5:1, α:β) in 75% yield. Treatment of the anomers **52** with excess trichloroacetonitrile and a catalytic quantity of DBU (0.05 equiv) in dichloromethane at 23 °C for 10 min afforded the β-trichloroacetimidate **53**, which was used in the coupling reaction without purification.

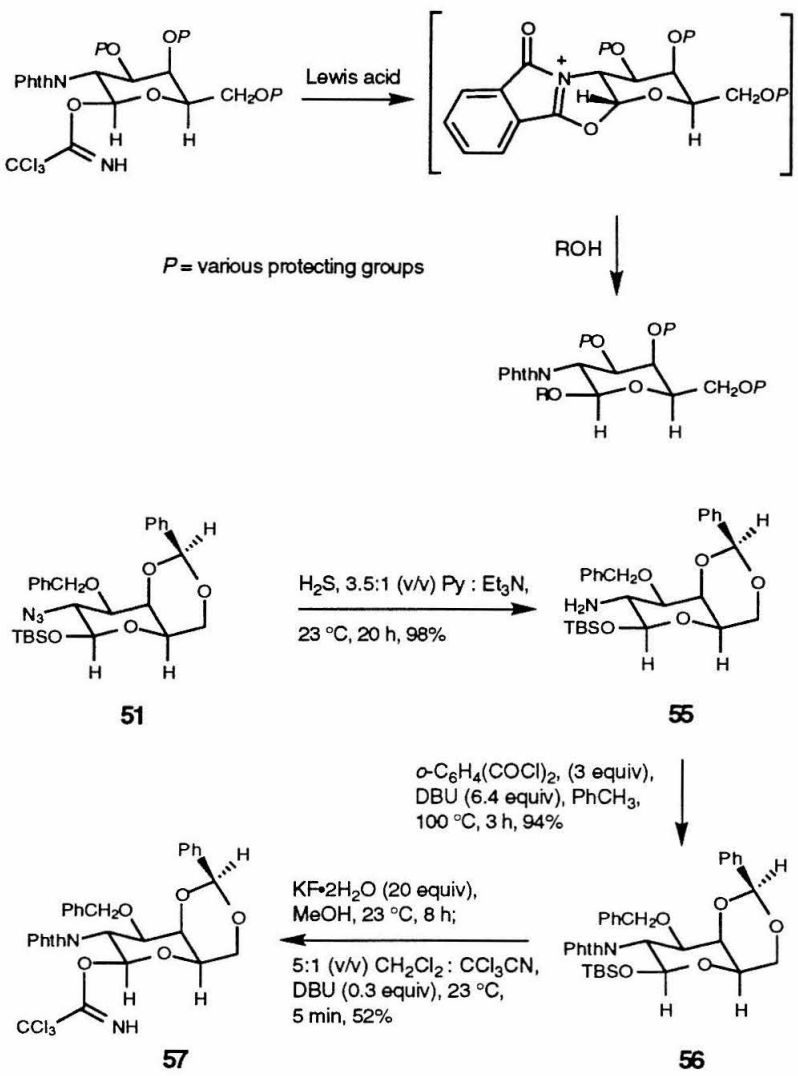


32 **51** **52** **53** (crude)

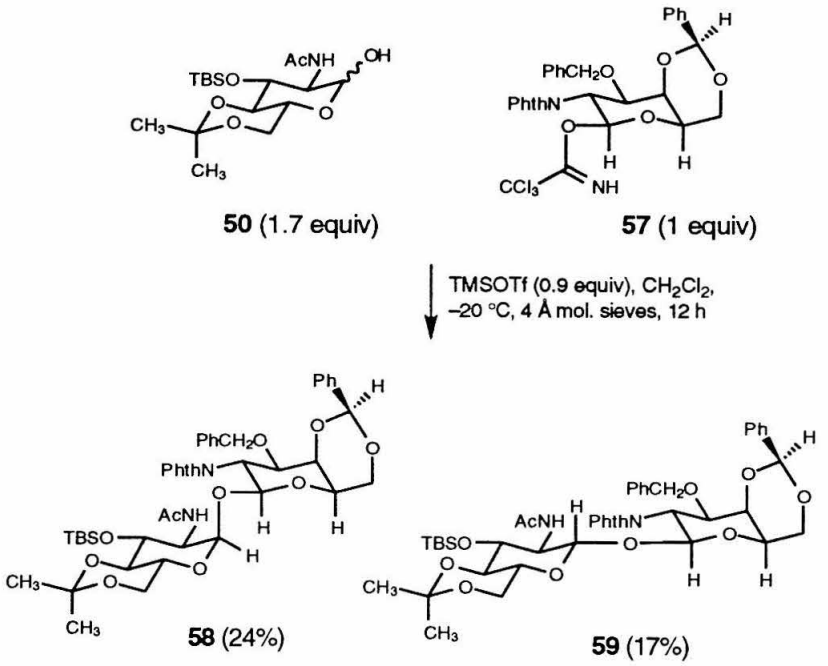
Exposure of a mixture of anomers **50** (3.0 equiv) and the trichloroacetimidate **53** (1 equiv) to TMSOTf (0.2 equiv) in dry dichloromethane at –20 °C for 6 h provided only trace



quantities of coupling products; the anomeric alcohols **50** and **52** were the primary components of the reaction mixture. The disaccharide **54**, containing the undesired α,β-trehalose configuration, was isolated in ~5% yield. It should be noted that this product was formed with the incorrect stereochemistry at both anomeric positions. Although the configuration of the anomeric nucleophile (**50**) could not be controlled in any obvious way, there was ample precedent for the use of a C2-phthalimido group within the electrophilic component to direct nucleophilic attack in the desired (β) sense.[35] Toward this end, the glycosyl donor **57** was prepared, initiated by the reduction of the azido group of **51** with hydrogen sulfide in a mixture of pyridine and triethylamine (3.5:1 (v/v), 23 °C, 20 h) to furnish the amine **55** in 98% yield. Introduction of the phthalimido protecting group was accomplished by the treatment of **55** with phthaloyl dichloride (3 equiv) and DBU (6.4 equiv) in toluene at 100 °C for 3 h to provide the phthalimide **56** in 94% yield. Cleavage of the anomeric silyl ether of **56** with potassium fluoride hydrate (20 equiv) in methyl alcohol



at 23 °C for 8 h and activation of the resultant hemiacetal with excess trichloroacetonitrile in methylene chloride in the presence of a catalytic amount of DBU (0.3 equiv) at 23 °C for 5 min afforded the β-trichloroacetimidate **57** in 52% yield from **56**. Treatment of a solution of the coupling partners **50** (1.7 equiv) and **57** (1 equiv) in dry dichloromethane with TMSOTf (0.9 equiv) at –20 °C for 12 h produced the desired β,α-trehalose **58** as the major



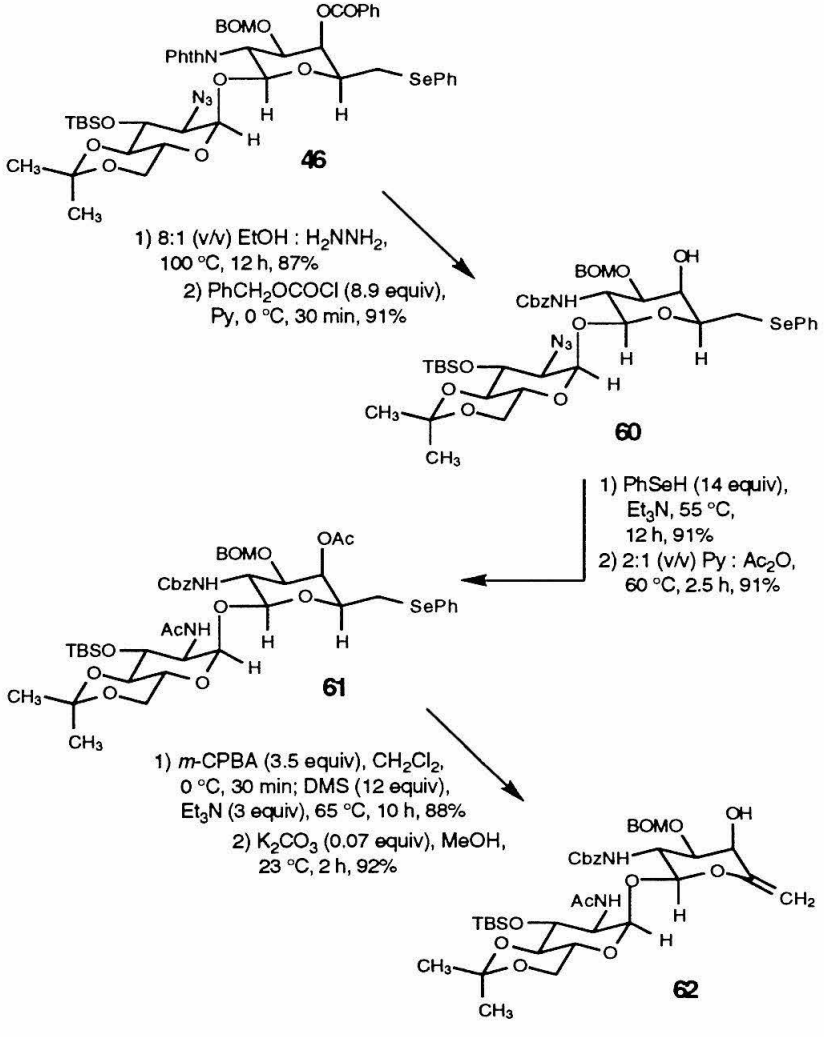
product (24%) along with a significant amount of the β,β-linked diastereomer **59** (17%). Although the problem of stereochemical control at the anomeric center of the galactosamine residue appears to have been solved with the introduction of the phthalimido group, the anomeric center of the nucleophilic *N*-acetylglucosamine residue was poorly controlled. In addition, the coupling yield was unacceptable for preparative purposes. For these reasons, this glycosylation approach was abandoned in favor of one in which the roles of electrophile and nucleophile in the coupling reaction were interchanged—an approach that evolved into the optimized glycosylation procedure with the substrates **44** and **38** described above.

Carbon-Carbon Bond Formation—Construction of the Trisaccharide Core.

With the establishment of an efficient procedure for the synthesis of the β,α-trehalose-linked disaccharide **46**, efforts turned toward the development of a procedure for its transformation to the allylic alcohol **62**, required for reductive coupling with a uridine-derived

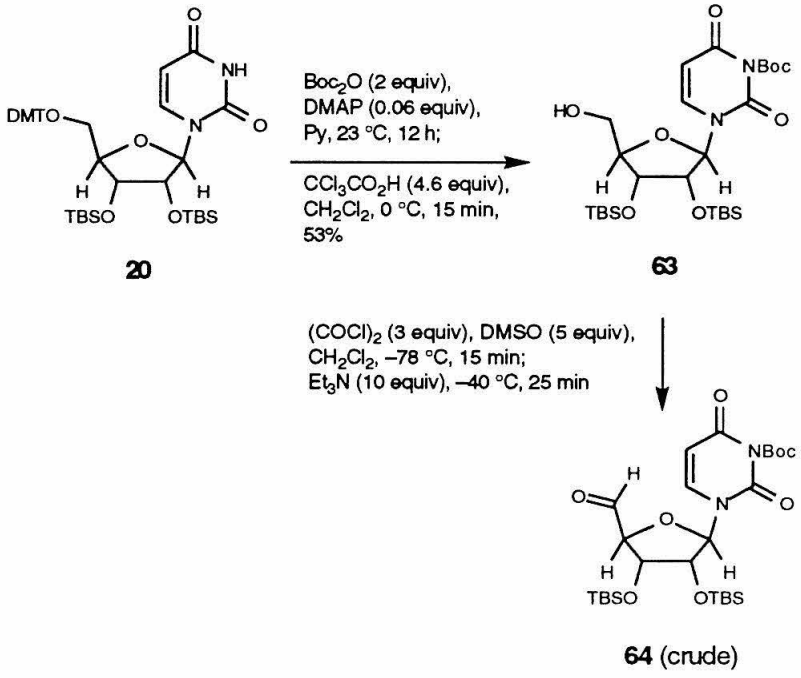
5'-aldehyde. Because of the lability of the phthalimido substituent, we first elected to replace this protective group with the more stable benzyl carbamate group (Scheme XIV). Treatment of **46** with a mixture of hydrazine hydrate and ethyl alcohol (1:8 (v/v)) at 100 °C in a sealed tube for 12 h led to cleavage of both the phthalimido and benzoyl substituents to afford the

Scheme XIV



corresponding amino alcohol in 87% yield. Selective protection of the amino group as the benzyl carbamate was accomplished by the treatment of the amino alcohol with benzyl chloroformate (8.9 equiv) in pyridine at 0 °C for 30 min, furnishing the disaccharide **60** in 91% yield. The hindered azido group of **60** was smoothly reduced with benzeneselenol[34] (14 equiv) in triethylamine at 55 °C for 12 h (91%), and the resultant amino alcohol was directly acetylated with acetic anhydride and pyridine (60 °C, 2.5 h, 91%), providing the diacetyl derivative **61**. Transformation of **61** to the allylic alcohol **62** proceeded efficiently in a two-step procedure involving the initial oxidation of **61** to the selenoxide (*m*-CPBA (3.5 equiv), carbon tetrachloride, 0 °C, 30 min) followed by thermolysis of the selenoxide at 65 °C for 10 h. Exposure of the resulting allylic acetate to potassium carbonate (0.07 equiv) in methyl alcohol at 23 °C for 2 h produced the allylic alcohol **62** in 81% yield from **61**.

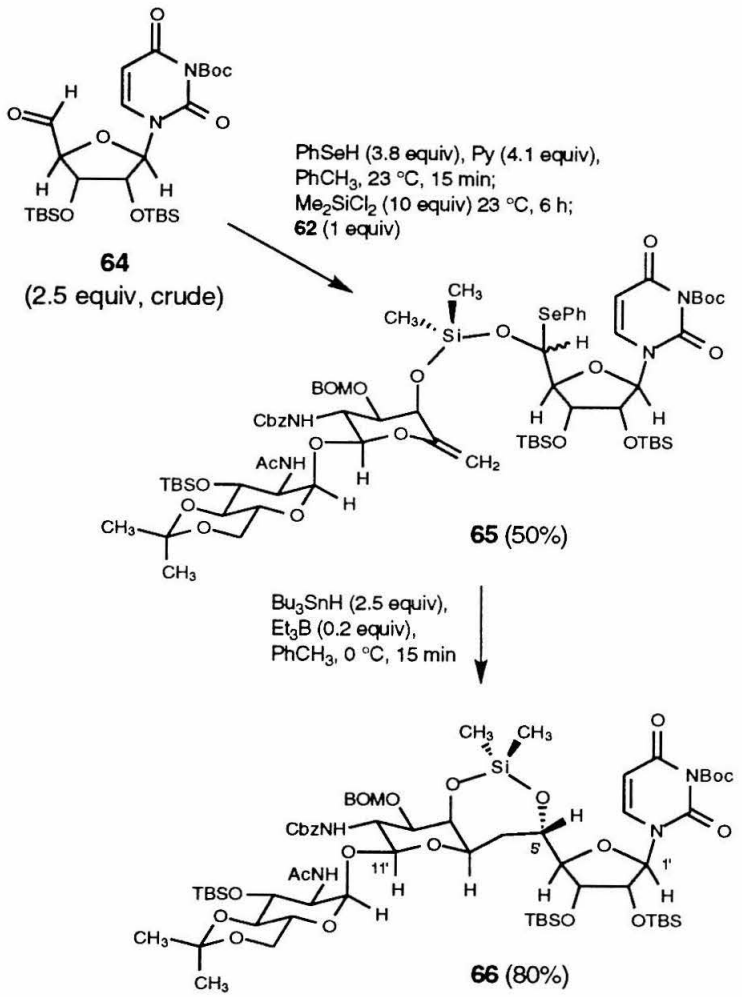
The silicon-mediated reductive coupling of the allylic alcohol **62** with a uridine-derived 5'-aldehyde coupling partner represented the final convergent step in the construction of the core structure (**1**) of the tunicamycins. The aldehyde **64** was chosen as the initial substrate for coupling. Unlike the aldehyde **22**, used in the synthesis of tunicaminyluracil (**2**), **64** does not incorporate the *p*-methoxybenzyl group for protection of the uracil imide. Although the latter protective group functioned adequately in two previous syntheses of tunicaminyluracil, the rather harsh oxidative conditions necessary for its removal[22] were believed to be incompatible with the trehalose linkage of **1**. The *t*-butyl carbamate protective group was chosen as an alternative that was anticipated to undergo facile deprotection under mildly acidic conditions. Treatment of uridine derivative **20** with di-*t*-butyl dicarbonate (2.0 equiv) and DMAP (0.06 equiv) in pyridine at 23 °C for 12 h, and exposure of the resulting *t*-butyl carbamate to trichloroacetic acid (4.6 equiv) in dichloromethane at 0 °C for 15 min furnished the alcohol **63** in 53% yield from **20**. Efficient oxidation of **63** to the corresponding aldehyde (**64**) was accomplished, as before,



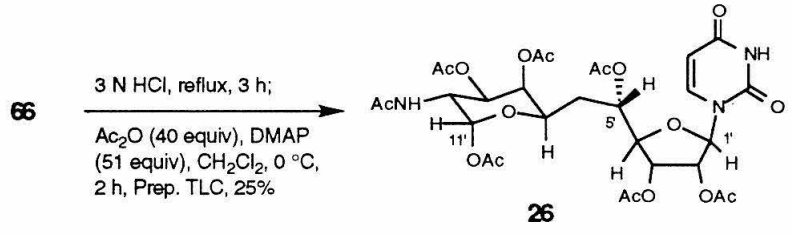
employing the Swern oxidation protocol (oxalyl chloride (3.0 equiv), dimethyl sulfoxide (5.0 equiv), triethylamine (10 equiv), dichloromethane, –40 °C, 25 min). Like uridine-5'-aldehyde derivatives previously prepared, **64** was found to be unstable toward chromatography on silica gel and was therefore used in crude form for the formation of the *O*-silylhemiselenoacetal in the next step.

The procedure for hemiselenoacetal adduct formation (Scheme XV) was similar to that used for the preparation of **23** (see Scheme X). Thus, a deoxygenated solution of the aldehyde **64** (2.5 equiv) in toluene was treated with benzeneselenol (3.8 equiv) and pyridine (4.1 equiv) at 23 °C for 15 min, followed by a solution of dichlorodimethylsilane (10 equiv) in pyridine at 23 °C for 6 h; excess dichlorodimethylsilane and solvents were removed in vacuo and a solution of the allylic alcohol **62** (1 equiv) in pyridine was added at 23 °C to form, within 5 min, the adduct **65** as a 5:1 mixture of C5'-epimers (50%). Free-radical cyclization

Scheme XV


PhSeH (3.8 equiv), Py (4.1 equiv),
PhCH3, 23 °C, 15 min;
Me2SiCl2 (10 equiv) 23 °C, 6 h;
62 (1 equiv)
64
(2.5 equiv, crude)
65 (50%)
Bu3SnH (2.5 equiv),
Et3B (0.2 equiv),
PhCH3, 0 °C, 15 min
66 (80%)

of **65** was induced by the dropwise addition of a solution of triethylborane in THF (1 M , 0.2 equiv) over a 15-min period to a solution of **65** and tributyltin hydride (2.5 equiv) in toluene (1 mM) at 23 °C. The cyclic siloxane **66** was isolated in 80% yield after chromatography on silica gel. Although carbon-carbon bond formation was highly efficient, the reaction produced exclusively the *S*-configuration at C5'—the configuration opposite to that of the desired product. This stereochemical assignment was determined by degradation of **66** with aqueous hydrochloric acid (3 N, reflux, 3 h) followed by peracetylation of the resulting amino polyol with acetic anhydride (40 equiv) and DMAP (51 equiv) in dichloromethane at 0 °C for 2 h, and comparison of the product with authentic samples of peracetyl α-tunicaminyluracil (**27**) and peracetyl C5'-*epi*-α-tunicaminyluracil (**26**). The observed preference for the formation of the undesired C5'-*S* diastereomer in this transformation paralleled our earlier

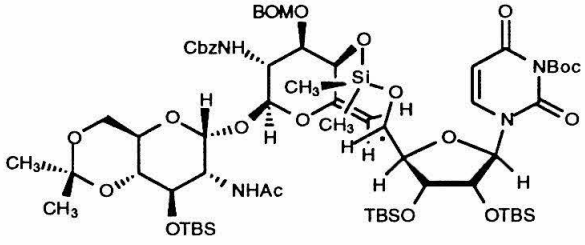


26

results in studies leading to a synthesis of tunicaminyluracil. Unfortunately, the use of polar solvents in the cyclization of substrate **65**, a procedure which led to a reversal of selectivity in the previous study, failed to produce the desired diastereomer; cyclizations of **65** conducted in acetonitrile, methyl alcohol, and aqueous methyl alcohol all produced **66** exclusively.

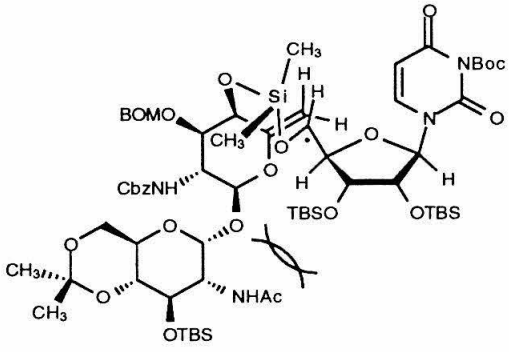
The high stereoselectivity of this free-radical cyclization reaction was rationalized by invoking the two hypothetical transition structures **67** and **68** (Figure 4). These structures, similar to structures **28** and **29** previously invoked (Figure 2), depict the olefin approaching the carbon-centered radical from the side opposite to that of the bulky *t*-butyldimethylsilyl

Figure 4



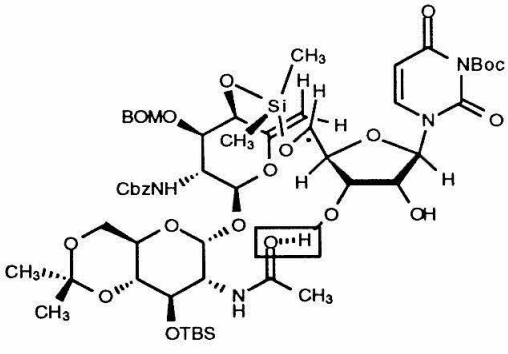
67

Hypothetical transition structure leading to undesired product. (Observed).



68

Hypothetical transition structure leading to desired product. (Not observed).

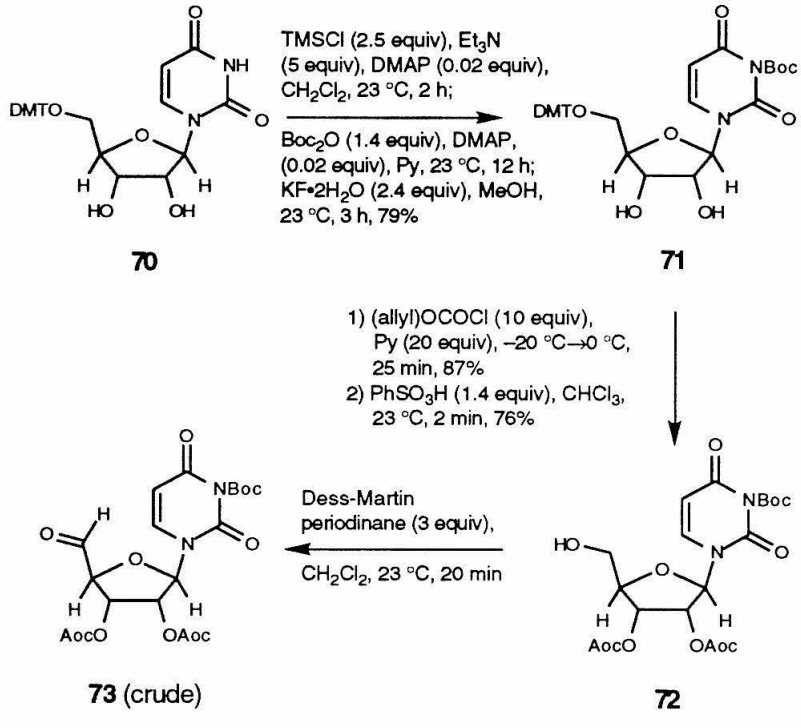


69

ethers on the furanose ring. Structure **68**, which leads to the formation of the desired C5'-*R* configuration in the product, is believed to possess a destabilizing steric interaction between the disaccharide and the 3'-*O*-*t*-butyldimethylsilyl ether. This destabilizing interaction is diminished in structure **67**. The proposed steric interaction is believed to be exacerbated in **68** relative to **29** by the additional steric shielding of the *N*-acetylglucosamine residue. Further consideration of structures **67** and **68** suggested that the replacement of the bulky silyloxy groups of the uridine-derived fragment with hydroxyl groups would not only eliminate the disfavorable steric interaction, but might also induce an associative interaction that draws the *N*-acetylglucosamine residue closer to the furanose ring by virtue of an intramolecular hydrogen bond between the acetamide carbonyl group and the C3'-hydroxyl group. The proposed transition structure (**69**) should favor formation of the desired C5'-*R* stereochemistry in the cyclized product.

In order to test this hypothesis, it was necessary to devise a synthesis of the diol *O*-silylhemiselenoacetal **75** (Scheme XVII). This required a protective group for the 2'- and 3'-hydroxyl groups of the uridine moiety that could be removed in the presence of the sensitive *O*-silylhemiselenoacetal functional group. Toward this end, the aldehyde **73**, incorporating allyloxy carbonate (Aoc) protective groups[39] on the C2'- and C3'-hydroxyl groups, was prepared in a five-step sequence from 5'-*O*-dimethoxytrityl uridine (**70**) (Scheme XVI). Transient protection of the C2'- and C3'-hydroxyl groups within **70** (trimethylsilyl chloride (2.5 equiv), triethylamine (5.0 equiv), DMAP (0.02 equiv), dichloromethane, 23 °C, 2 h), followed by the sequential treatment of the resulting bis(trimethylsilyl) ether with di-*t*-butyl dicarbonate (1.4 equiv) and DMAP (0.02 equiv) in pyridine at 23 °C for 12 h and then potassium fluoride hydrate (2.4 equiv) in methyl alcohol at 23 °C for 3 h, afforded the diol **71** in 79% yield. Exposure of the diol **71** to allylchloroformate (10 equiv) in pyridine (–20 °C → 0 °C) produced the diallyloxycarbonate derivative (87%). Subjection of the latter to

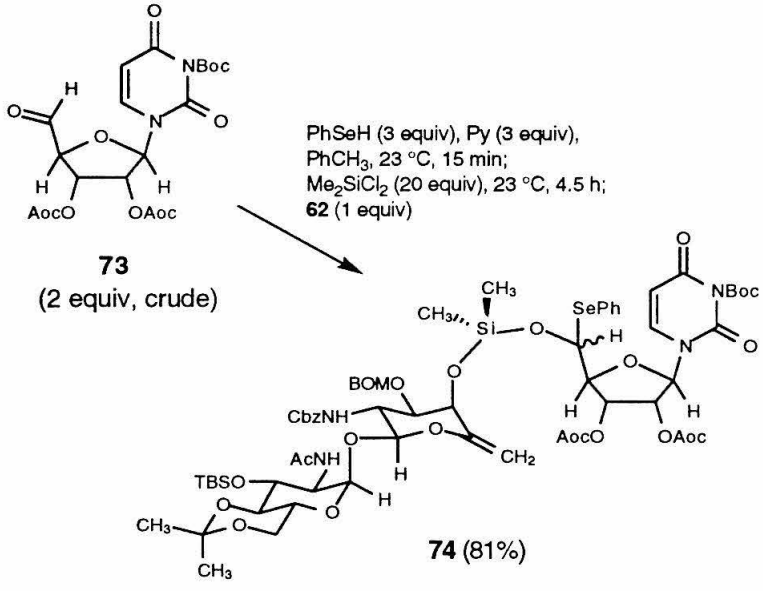
Scheme XVI



benzenesulfonic acid (1.4 equiv) in chloroform at 23 °C for 2 min afforded the alcohol **72** in 76% yield. Swern oxidation of **72**, as previously conducted, produced multiple products, presumably a consequence of the greater lability of the aldehyde **73** due to the electron-withdrawing character of the C2'- and C3'-substituents. Oxidation of **72** with the Dess-Martin periodinane[44] (3.0 equiv) in dichloromethane at 23 °C for 20 min, by contrast, was found to furnish the desired aldehyde (**73**), isolated as a mixture with its hydrated form. Regeneration of the aldehyde from its hydrated form was readily accomplished prior to siloxane adduct formation by azeotropic drying with toluene.

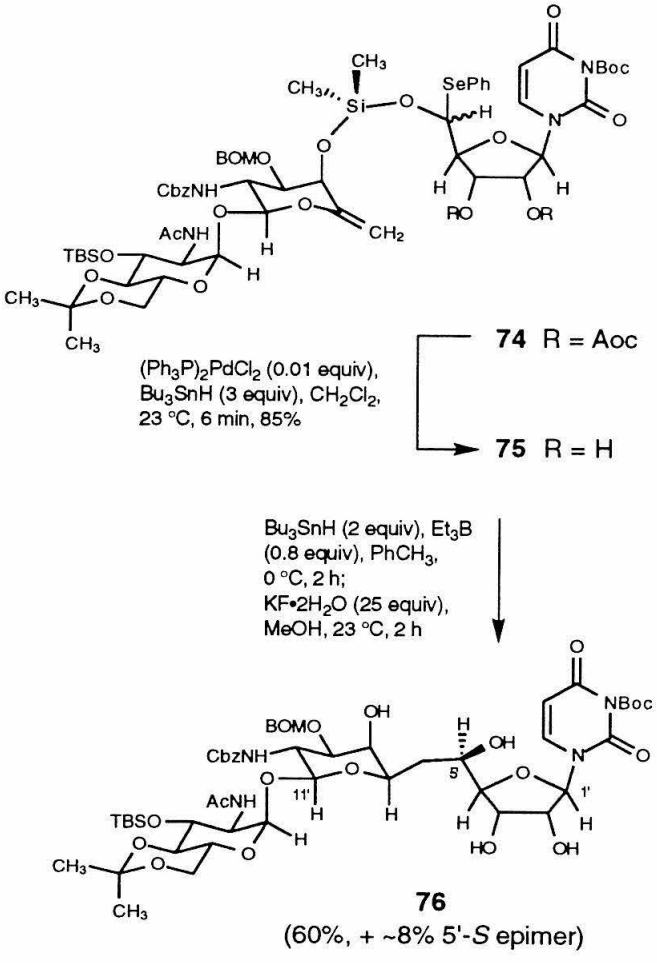
The coupling of the aldehyde **73** with the allylic alcohol **62** proceeded according to procedures described above, involving (1) the treatment of the aldehyde **73** (2.0 equiv) with

benzeneselenol (3.0 equiv) and pyridine (3.0 equiv) in dry toluene at 23 °C for 15 min, (2) exposure of the resulting solution to dichlorodimethylsilane (20 equiv) at 23 °C for 4.5 h, (3) removal of excess dichlorodimethylsilane and solvents in vacuo, and (4) treatment of the residue with a solution of the allylic alcohol **62** (1 equiv) in pyridine at 23 °C for 5 min. The



siloxane adducts **74** were isolated as an inseparable mixture of C5'-diastereomers (2:1, stereochemistry not determined) in 81% combined yield. Selective removal of the allyloxy carbonate protective groups (Scheme XVII) proceeded efficiently employing a catalytic quantity of dichlorobis(triphenylphosphine) palladium (0.01 equiv) and tributyltin hydride (3.0 equiv) in moist dichloromethane at 23 °C for 6 min to afford the diols **75** in 85% yield.[39] Free-radical cyclization of the diols **75** was initiated by the addition of aliquots of a solution of triethylborane (1 M, hexanes, 0.1 equiv each) at 15-min intervals to a solution of the diols **75** (1 mM) and tributyltin hydride (2.0 equiv) in toluene at 0 °C over 2 h. Subsequent treatment of the crude cyclization products with potassium fluoride hydrate (25

Scheme XVII

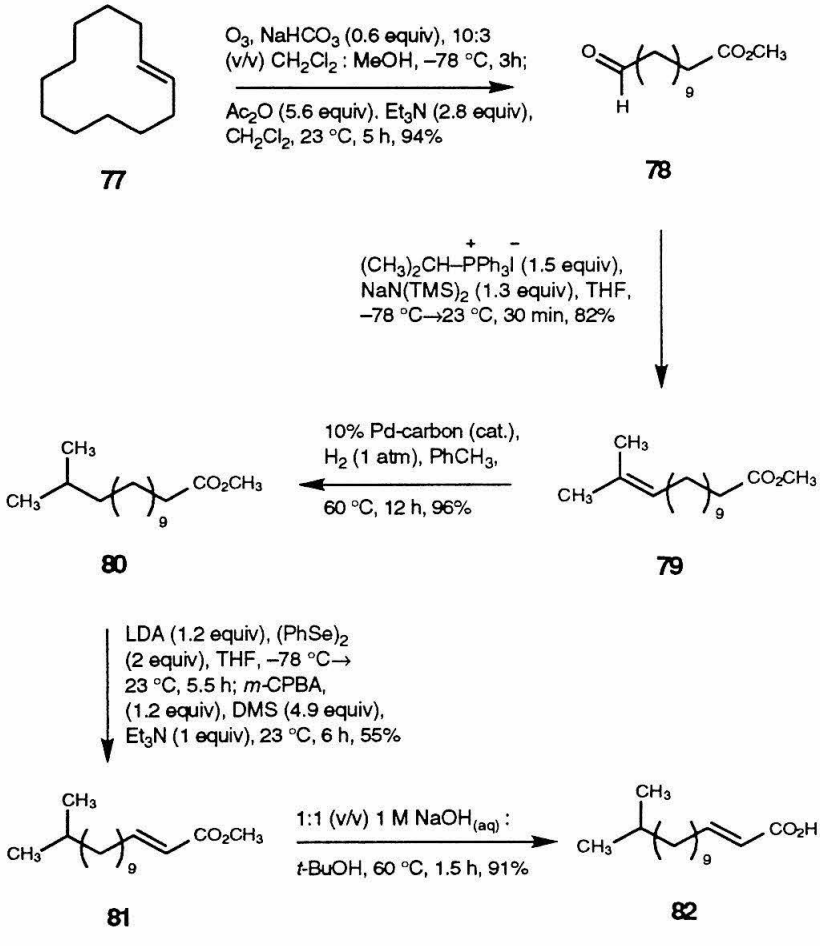

74 R = Aoc
75 R = H
(Ph3P)2PdCl2 (0.01 equiv), Bu3SnH (3 equiv), CH2Cl2, 23 °C, 6 min, 85%
Bu3SnH (2 equiv), Et3B (0.8 equiv), PhCH3, 0 °C, 2 h; KF•2H2O (25 equiv), MeOH, 23 °C, 2 h
76
(60%, + ~8% 5'-S epimer)

equiv) in methyl alcohol to remove the siloxane tether produced a mixture of tetraols epimeric at C5' in a ratio of 7.5:1. The major product was determined to possess the desired C5'-*R* configuration by its transformation to peracetyl α-tunicaminyluracil (**27**) and comparison with an authentic sample as above. The diastereomer **76** could be separated by careful column chromatography on silica gel eluting with benzene:acetonitrile:isopropyl alcohol (12:4:1); the desired 5'-*R* diastereomer **76** was isolated in pure form in 60% yield. This observed reversal of stereoselectivity compared to that of the cyclization of **65** supports the proposed transition structure **69**. In further support of this hypothesis, it was found that the cyclization of **75** in a protic solvent (methyl alcohol) led to an erosion in the stereoselectivity in the carbon-carbon bond forming process (1.6:1, C5'-*R* : C5'-*S*), presumably due to disruption of the proposed intramolecular hydrogen bond. Given the complexity of the system, however, it is certainly possible that other factors may be involved.

Final Stages

Having constructed the carbon framework of the tunicamycin antibiotics, there remained the deprotection steps and the attachment of the lipophilic *N*-acyl substituent to complete the synthesis. Tunicamycin-V, a major constituent of most fermentation broths of the natural tunicamycins, was selected for preparation, thus necessitating that the (*E*)-14-methyl-2-tetradecenoic acid side chain be synthesized (Scheme XVIII). Ozonolysis of a commercial sample of cyclododecene (**77**) in a mixture of dichloromethane and methyl alcohol in the presence of sodium bicarbonate (0.6 equiv) at –78 °C for 3 h and treatment of the crude product mixture with triethylamine (2.8 equiv) and acetic anhydride (5.6 equiv) in dichloromethane at 23 °C for 6 h afforded the aldehyde **78** in 94% yield.[40] Olefination of **78** with isopropylidene triphenylphosphorane afforded the corresponding trisubstituted

Scheme XVIII

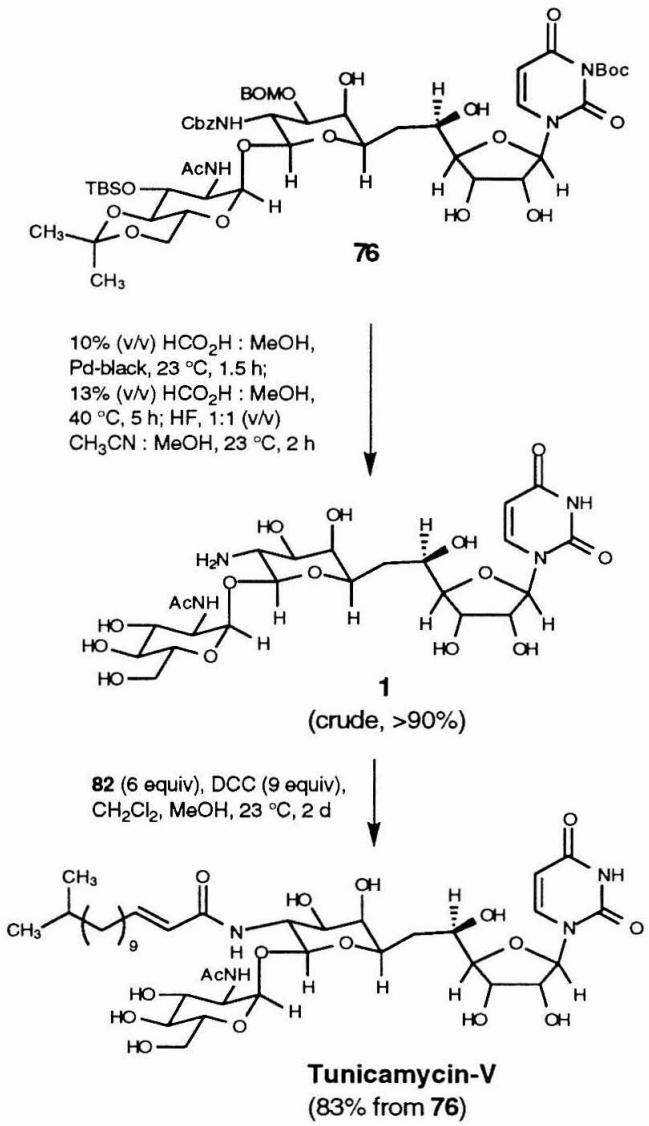


olefin **79** (82%), which, upon hydrogenation under one atmosphere of hydrogen with 10% palladium on carbon as catalyst in toluene at 60 °C for 12 h, furnished the methyl ester **80** in 96% yield. Introduction of α,β-unsaturation in the acyl chain was accomplished by the formation of the α-phenylselenide (lithium diisopropylamide (1.2 equiv), THF, –78 °C, 25 min; diphenyldiselenide (2 equiv), –78 °C —> 23 °C, 5.5 h) and oxidation of the crude selenide with *m*-CPBA (1.2 equiv) in dichloromethane at –78 °C for 2 h. Treatment of the oxidation mixture with dimethyl sulfide (4.9 equiv) and Et_3N (1.0 equiv) at 23 °C for 6 h induced elimination of the selenoxide to form the (*E*)-α,β-unsaturated ester **81** in 55% yield. Saponification of **81** with aqueous sodium hydroxide in *t*-butyl alcohol (60 °C, 1.5 h) produced the crystalline fatty acid **82** (91%).

In the final stages of the synthesis, deprotection of the tetraol **76** (Scheme XIX) by catalytic transfer hydrogenolysis of both the benzyl carbamate and the benzyloxymethyl ether groups was performed with 10% formic acid in methyl alcohol in the presence of a catalytic amount of palladium black at 23 °C for 1.5 h. Subsequent treatment of the crude amino pentaol with 13% formic acid in methyl alcohol at 40 °C for 5 h led efficiently to hydrolysis of the isopropylidene ketal and the *t*-butyl carbamate groups. Further treatment of the crude product from the latter reaction with excess hydrofluoric acid in a mixture of acetonitrile and methyl alcohol (1:1) at 23 °C for 2 h furnished the amino polyol **1**. Purification of **1** was achieved by chromatography with RP-18 reverse-phase silica gel eluting with pyridine:methyl alcohol:water (1:1:1.5); **1** was obtained in greater than 90% yield over the entire deprotection sequence.

N-Acylation of **1** was accomplished under conditions similar to those described by Suami *et al.*[7] The fatty acid (6.0 equiv) was activated by stirring **82** with 1,3-dicyclohexylcarbodiimide (9.0 equiv) in dichloromethane at 23 °C for 30 min. Aliquots of the latter solution were added (1.0 equiv each) to a solution of **1** in methyl alcohol at 8-h

Scheme XIX

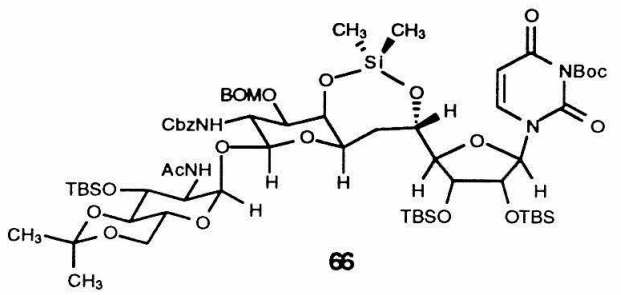

BOMO
CbzNH
AcNH
TBSO
NBoc
OH
HO
76
10% (v/v) HCO2H : MeOH,
Pd-black, 23 °C, 1.5 h;
13% (v/v) HCO2H : MeOH,
40 °C, 5 h; HF, 1:1 (v/v)
CH3CN : MeOH, 23 °C, 2 h
H2N
NH
1
(crude, >90%)
82 (6 equiv), DCC (9 equiv),
CH2Cl2, MeOH, 23 °C, 2 d
Tunicamycin-V
(83% from 76)

intervals over 2 days to afford, after flash column chromatography through RP-18 reverse-phase silica gel eluting with methyl alcohol:pyridine:water (1:1:1) and trituration with chloroform, pure tunicamycin-V. It should be noted that the judicious selection of the protecting groups on the trisaccharide core (**76**) allowed for a highly efficient deprotection sequence. Thus, the entire deprotection procedure was performed without purification of any intermediate and provided, after fatty acid coupling, purified tunicamycin-V (88 mg) in 83% yield from the tetraol **76**. Synthetic **1-V** was shown to be identical in all respects (^{1}H NMR, ^{13}C NMR, melting point, mixed melting point, FTIR, HPLC, MS, HRMS, optical rotation) to that of a purified authentic sample. The route described for the synthesis of **1-V** is potentially applicable to the preparation of any of the homologous tunicamycin antibiotics by the attachment of the appropriate fatty acid side chain in the final step.

Preparation of C5'-*epi*-Tunicamycin-V

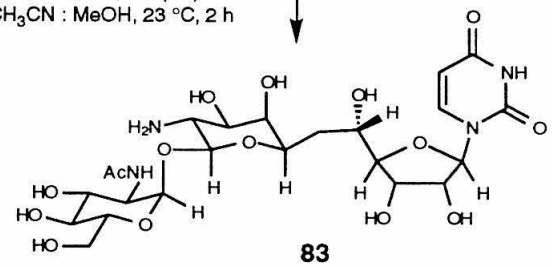
Using the synthetic route described for the preparation of tunicamycin-V (**1-V**), the C5'-*S* diastereomer **66** was transformed efficiently into the nonnatural tunicamycin isomer C5'-*epi*-tunicamycin-V (**84**), outlined in Scheme XX. Thus, using the chemistry described, this stereoisomeric series of tunicamycins is also available for biological evaluation .

Scheme XX



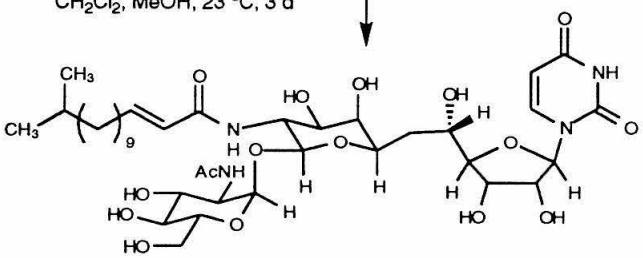
66

10% (v/v) HCO_2H : MeOH,
Pd-black, 23 °C, 30 min;
13% (v/v) HCO_2H : MeOH,
40 °C, 4 h; HF, 1:1 (v/v)
CH_3CN : MeOH, 23 °C, 2 h



83
(crude, >90%)

82 (9 equiv), DCC (13.5 equiv),
CH_2Cl_2, MeOH, 23 °C, 3 d



C5'-*epi*-Tunicamycin-V (84)
(74% from **66**)

Summary

A convergent, stereoselective synthesis of tunicamycin-V (**1-V**) and its C5'-epimer is described. Within this synthetic route, an efficient method for carbon-carbon bond formation was developed, involving the silicon-mediated reductive coupling of aldehydes and allylic alcohols. This protocol forms the basis for the stereoselective preparation of tunicaminyluracil (**2**) and its C5'-epimer, employing the uridine derivative **22** and the galactosamine derivative **15** as the coupling partners. An attractive feature of this reductive coupling procedure is its compatibility with the sensitive trehalose glycosidic linkage within the tunicamycins. This allowed for the synthesis of the carbohydrate core (**1**) by carbon-carbon bond formation between a uridine 5'-aldehyde derivative and a trehalose-linked disaccharide allylic alcohol. Implementation of this synthetic plan led to the development of an efficient procedure for the previously problematic preparation of the β,α-trehalose linkage within the natural product, using the glycosidic coupling partners **38** and **44** in a variation of the trichloroacetimidate glycosylation method. Subsequent reductive coupling of the trehalose-linked disaccharide allylic alcohol **62** with uridine 5'-aldehyde derivatives **73** or **64** allowed for the highly convergent and selective preparation of **1** or its C5'-epimer (**83**), respectively. The synthesis of the amino polyol intermediates **1** and **83** should allow for the preparation of any of the homologous tunicamycin antibiotics in pure form, as well as of related structures of potential utility as biochemical probes.

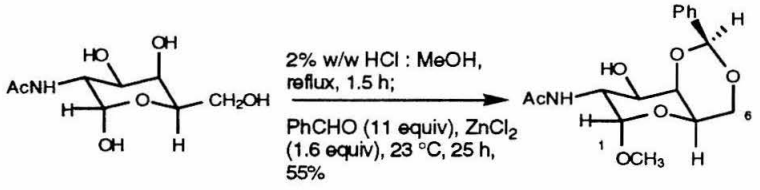
Experimental Section

General Procedures. All reactions were performed in flame-dried round bottom or modified Schlenk (Kjeldahl shape) flasks fitted with rubber septa under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Where necessary (so noted), solutions were deoxygenated by alternate evacuation/argon flush cycles (greater than three iterations). Organic solutions were concentrated by rotary evaporation below 30 °C at *ca.* 25 Torr (water aspirator). Flash column chromatography was performed as described by Still *et al.* employing 230-400 mesh silica gel.[41] Thin-layer chromatography (analytical and preparative) was performed using glass plates pre-coated to a depth of 0.25 mm with 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm).

Materials. Commercial reagents and solvents were used as received with the following exceptions. Tetrahydrofuran, ethyl ether, and dimethoxyethane were distilled from sodium benzophenone ketyl. Dichloromethane, *N,N*-diisopropylethylamine, diisopropylamine, triethylamine, pyridine, toluene, and acetonitrile were distilled from calcium hydride at 760 Torr. Dimethyl sulfoxide was distilled from calcium sulfate at 40 Torr and was stored over 4Å molecular sieves. Carbon tetrachloride was distilled from phosphorous pentoxide at 760 Torr. Oxalyl chloride was distilled at 760 Torr immediately prior to use. The molarity of *n*-butyllithium solutions was determined by titration using diphenyacetic acid as an indicator (average of three determinations).[42]

Instrumentation. Infrared (IR) spectra were obtained using a Perkin-Elmer 1600 FT-IR spectrophotometer referenced to a polystyrene standard. Data are presented as follows: frequency of absorption (cm^{-1}), and intensity of absorption (s = strong, m=

medium, w = weak). Proton and carbon-13 nuclear magnetic resonance (^{1}H NMR or ^{13}C NMR) spectra were recorded with a JEOL JX-400 (400 MHz) or a GE QE-300-Plus (300 MHz) NMR spectrometer; chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ 7.26, C_6HD_5: δ 7.20, CD_3COCD_2H: δ 2.04, CD_2HOD: δ 3.30). Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = quartet, m = multiplet and/or multiple resonances), integration, coupling constant in Hertz (Hz), and assignment. High performance liquid chromatography (HPLC) was conducted with a Waters 501 HPLC equipped with a Beckman ODS C18 standard reverse phase column and an Isco V^4 Absorbance detector set at 255 nm. Optical rotations were determined with a JASCO-DIP-181 polarimeter equipped with a sodium lamp source. High resolution mass spectra were obtained from the University of California, Riverside Mass Spectrometry Facility. Melting points were recorded with a Büchi SMP-20 melting point apparatus and are uncorrected.



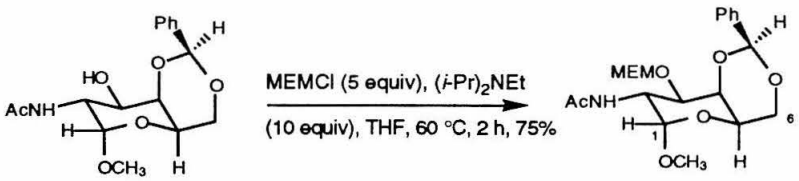
9 **10**

α-Methyl Galactopyranoside **10**.

N-Acetylgalactosamine (**9**) (5.0 g, 22.6 mmol, 1 equiv) was dissolved in methanolic hydrochloric acid (2% (w/w), 250 mL), and the resulting solution was heated at reflux for 1.5 h. The reaction mixture was allowed to cool to 23 °C, whereupon solid silver carbonate (15.0 g, 54.4 mmol, 2.4 equiv) was added slowly to neutralize the acid catalyst. The solids were removed by filtration, and the filtrate was concentrated in vacuo. The residue, benzaldehyde (25.0 mL, 245.9 mmol, 10.9 equiv), and fused zinc chloride (5.0 g, 36.7 mmol, 1.6 equiv) were combined, and the resulting suspension was stirred vigorously at 23 °C for 25 h. The reaction mixture was shaken with a mixture of water and pentane (1:1 (v/v), 160 mL) to afford a white precipitate that was isolated by filtration. The crude, solid product was washed well with ice-cold pentane (100 mL), then was recrystallized from 95% ethyl alcohol to afford pure **10** as white crystals (4.0 g, 55%) (mp 165.0–166.3 °C).

^{1}H NMR (400 MHz, acetone-d_6) δ: 7.53 (m, 2 H, arom) 7.34 (m, 3 H, arom) 6.95 (s, 1 H, NH), 5.63 (s, 1 H, benzylidene acetal) 4.75 (d, 1 H, J = 3.5 Hz, H 1), 4.31 (ddd, 1 H, J = 3.5, 8.8, 11.4 Hz, H 2), 4.26 (d, 1 H, J = 3.5 Hz, H 4), 4.13 (m, 2 H, H 6), 3.84 (m, 1 H, H 3), 3.73 (d, 1

	H, J = 9.4 Hz, OH), 3.70 (d, 1 H, J = 1.2 Hz, H 5), 3.33 (s, 3 H, OCH_3), 1.89 (s, 3 H, Ac).
FTIR (neat film) cm^{-1}:	3320 (w, br), 2908 (w), 1614 (s), 1557 (m), 1455 (m), 1097 (s), 1045 (s), 994 (m), 773 (m), 700 (s).
MS (FAB) *m/z*:	324 $(MH)^+$, 292 (M^+ - CH_3O), 186 (M^+ - PhCHO, CH_3O).
HRMS (FAB) *m/z*:	Calcd for $C_{16}H_{22}NO_6$ $(MH)^+$: 324.1447. Found: 324.1460.
TLC R_f (33% PhH in acetone):	0.42



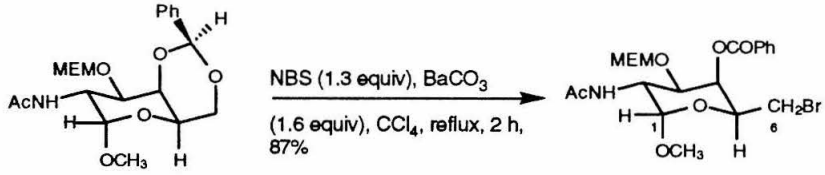
10 **11**

Methoxyethoxymethyl Ether **11.**

Methoxyethoxymethyl chloride (4.4 mL, 30.7 mmol, 5.0 equiv) was added to a solution of **10** (2.5 g, 7.7 mmol, 1 equiv) and diisopropylethylamine (13.5 mL, 77.3 mmol, 10.0 equiv) in tetrahydrofuran (20 mL), and the resulting solution was heated at 60 °C for 2 h. The reaction mixture was partitioned between water (600 mL) and ethyl acetate (4 x 200 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. The residue was purified by flash column chromatography (20% acetone in ethyl acetate) to give the methoxyethoxymethyl ether **11** (2.37 g, 75%) as a white solid (mp 53.5–54.0 °C).

^{1}H NMR (400 MHz, acetone-d_6) δ: 7.51 (m, 2 H, arom), 7.34 (m, 3 H, arom), 6.98 (s, 1 H, NH), 5.65 (s, 1 H, benzylidene acetal), 4.79 (d, 1 H, J = 7.0 Hz, MEM CH_2), 4.74 (d, 1 H, J = 3.5 Hz, H 1), 4.67 (d, 1 H, J = 7.0 Hz, MEM CH_2), 4.51 (d, 1 H, J = 3.2 Hz, H 4), 4.48 (m, 1 H, H 2), 4.12 (m, 2 H, H 6), 3.99 (dd, 1 H, J = 3.5, 11.4 Hz, H 3), 3.75 (m, 1 H, H 5), 3.69 (m, 2 H, MEM CH_2), 3.54 (m, 2 H, MEM CH_2), 3.35 (s,

	3 H, CH_3O), 3.34 (s, 3 H, CH_3O), 1.85 (s, 3 H, Ac).
FTIR (neat film) cm^{-1}:	3300 (w, br), 2898 (m), 1659 (s), 1548 (m), 1453 (w), 1370 (w), 1199 (w), 1134 (m), 1112 (m), 1050 (s), 984 (m), 792 (w), 748 (w), 760 (m).
MS (FAB) *m/z*:	412 $(MH)^+$, 336 (M^+ - $CH_3OCH_2CH_2O$).
HRMS (FAB) *m/z*:	Calcd for $C_{20}H_{30}NO_8$ $(MH)^+$: 412.1971. Found: 412.1970.
TLC R_f (25% acetone in EtOAc):	0.32



11 **12**

Bromobenzoate **12**.

Solid barium carbonate (1.80 g, 9.1 mmol, 1.6 equiv) and *N*-bromosuccinimide (1.32 g, 7.4 mmol, 1.3 equiv) were added sequentially to a solution of the methoxyethoxymethyl ether **11** (2.34 g, 5.7 mmol, 1 equiv) in carbon tetrachloride (47 mL). The resulting suspension was deoxygenated and was heated at reflux for 2 h, during which time the reaction mixture turned orange and then yellow. After allowing the reaction mixture to cool to 23 °C, the solvent was removed in vacuo, and the residue was diluted with dichloromethane (500 mL). Solids were removed by filtration, and the filtrate was washed sequentially with 5% aqueous sodium bisulfate solution (500 mL) and saturated aqueous sodium chloride solution (300 mL). The organic layer was dried (magnesium sulfate) and concentrated, and the residue was purified by flash column chromatography (100% ethyl acetate) to afford **12** (2.42 g, 87%) as a white solid (mp 57.0–57.5 °C).

^{1}H NMR (400 MHz, acetone-d_6) δ: 8.06 (m, 2 H, arom), 7.67 (m, 1 H, arom), 7.55 (m, 2 H, arom), 7.10 (d, 1 H, J = 9.4 Hz, NH), 5.82 (d, 1 H, J = 2.0 Hz, H 4), 4.83 (d, 1 H, J = 3.5 Hz, H 1), 4.81 (d, 1 H, 7.3 Hz, MEM CH_2), 4.47 (d, 1 H, J = 7.3 Hz, MEM CH_2), 4.47 (m, 1 H, H 2),

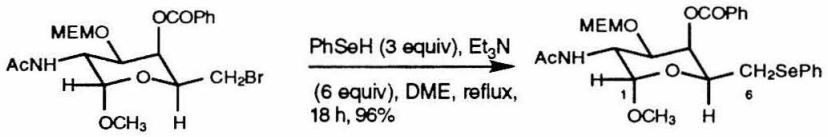
4.25 (m, 2 H, H 3, 5), 3.81-3.50 (m, 6 H, H 6, MEM CH_2), 3.44 (s, 3 H, CH_3O), 3.37 (s, 3 H, CH_3O), 1.87 (s, 3 H, Ac).

FTIR (neat film) cm^{-1}: 3314 (w), 2924 (w), 1723 (s), 1670 (m), 1543 (m), 1451 (w), 1370 (w), 1268 (s), 1116 (s), 1038 (s), 981 (w), 942 (w), 846 (w), 711 (m).

MS (FAB) *m/z*: 490 $(MH)^+$, 414 (M^+ - $CH_3OCH_2CH_2O$), 307 (M^+ - MEMO, C_6H_5).

HRMS (FAB) *m/z*: Calcd for $C_{20}H_{29}BrNO_8$ $(MH)^+$: 490.1077. Found: 490.1091.

TLC R_f (50% acetone in EtOAc): 0.50



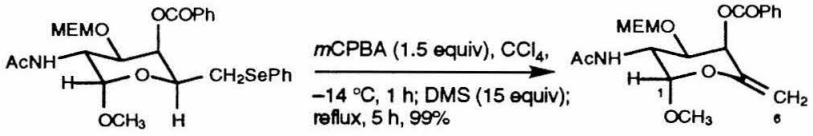
12 **13**

Phenyl Selenide **13.**

Benzeneselenol (1.81 mL, 16.5 mmol, 3.0 equiv) was added to a solution of **12** (2.70 g, 5.5 mmol, 1 equiv) and triethylamine (4.60 mL), 33.0 mmol, 6.0 equiv) in dimethoxyethane (40 mL), and the resulting mixture was heated at reflux for 18 h. The reaction solution was partitioned between saturated aqueous sodium bicarbonate solution (300 mL) and ethyl acetate (4 x 200 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. The residue was purified by flash column chromatography (100% ethyl acetate) to give **13** (2.98 g, 96%) as a white solid (mp 44.0 °C).

^{1}H NMR (400 MHz, acetone-d_6) δ: 8.07 (m, 2 H, Bz arom), 7.67 (m, 1 H, Bz arom), 7.55 (m, 4 H, Bz arom, PhSe arom), 7.25 (m, 3 H, PhSe arom), 7.06 (s, 1 H, NH), 5.80 (d, 1 H, J = 2.0 Hz, H 4), 4.80 (m, 2 H, H 1, MEM CH_2), 4.47 (m, 1 H, H 2), 4.46 (d, 1 H, J = 7.3 Hz, MEM CH_2), 4.21 (m, 2 H, H 3, 5), 3.78 (m, 1 H, MEM CH_2), 3.55 (m, 3 H, MEM CH_2), 3.38 (s, 3 H, CH_3O), 3.35 (s, 3 H, CH_3O), 3.18 (dd, 1 H, J =

	8.8, 12.6 Hz, H 6), 3.04 (dd, 1 H, J = 5.0, 12.6 Hz, H 6), 1.86 (s, 3 H, Ac).
FTIR (neat film) cm^{-1}:	3316 (w), 2934 (w), 2896 (w), 1722 (s), 1674 (m), 1539 (m), 1452 (w), 1371 (w), 1269 (s), 1116 (s), 1040 (s), 981 (w), 941 (w), 711 (m).
MS (FAB) *m/z*:	568 $(MH)^+$, 536 (M^+ - CH_3O), 492 (M^+ - $CH_3OCH_2CH_2O$).
HRMS (FAB) *m/z*:	Calcd for $C_{26}H_{34}NO_8Se$ $(MH)^+$: 568.1450. Found: 568.1437.
TLC R_f (100% EtOAc):	0.24



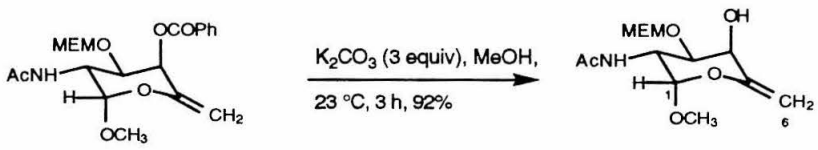
13 **14**

Alkene **14.**

Solid *m*-chloroperoxybenzoic acid (*ca.* 60% (w/w), 2.22 g, 7.7 mmol, 1.5 equiv) was added to a solution of the selenide **13** (2.91 g, 5.14 mmol, 1 equiv) in carbon tetrachloride (40 mL) at −14 °C, and the resulting suspension was stirred at this temperature for 1 h. Excess oxidant was quenched by the addition of dimethyl sulfide (5.66 mL, 77.1 mmol, 15.0 equiv) and triethylamine (1.51 mL, 10.3 mmol, 2.0 equiv), and the mixture was heated at reflux for 5 h. The resulting yellow solution was partitioned between saturated aqueous sodium bicarbonate solution (400 mL) and ethyl acetate (3 x 200 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. The crude product was purified by flash column chromatography (100% ethyl acetate) to give **14** (2.07 g, 99%) as a white solid (mp 44.0–44.5 °C).

^{1}H NMR (400 MHz, acetone-d_6) δ: 8.04 (m, 2 H, arom), 7.65 (m, 1 H, arom), 7.54 (m, 2 H, arom), 7.19 (d, 1 H, J = 8.1 Hz, NH), 6.02 (d, 1 H, J = 3.4 Hz, H 4), 4.91 (d, 1 H, J = 3.4 Hz, H 1), 4.83 (s, 1 H, H 6), 4.81 (d, 1 H, J = 7.3 Hz, MEM CH_2), 4.78 (s, 1 H, H 6), 4.70 (m, 1 H, H 2), 4.57 (d, 1 H, J = 7.3 Hz, MEM CH_2), 4.26 (dd, 1 H, J = 3.4, 11.2 Hz, H 3), 3.75 (m, 1 H, MEM

	CH_2), 3.55 (m, 3 H, MEM CH_2), 3.43 (s, 3 H, CH_3O), 3.34 (s, 3 H, CH_3O), 1.89 (s, 3 H, Ac).
FTIR (neat film) cm^{-1}:	3287 (w), 2933 (w), 17196 (s), 1663 (s), 1543 (m), 1451 (w), 1369 (w), 1266 (s), 1197 (w), 1132 (m), 1111 (s), 1025 (s), 950 (m), 884 (w), 713 (m).
MS (FAB) *m/z*:	410 $(MH)^+$, 378 (M^+ - CH_3O), 334 (M^+ - $CH_3CH_2CH_2O$), 105 $(MEMO)^+$.
HRMS (FAB) *m/z*:	Calcd for $C_{20}H_{28}NO_8$ $(MH)^+$: 410.1815. Found: 410.181.
TLC R_f (100% EtOAc):	0.20



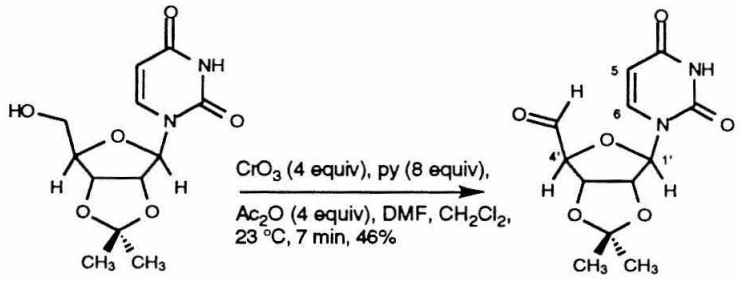
14 **15**

Allylic Alcohol **15.**

Potassium carbonate (2.0 g, 14.5 mmol, 3.0 equiv) was added to a solution of alkene **14** (2.00 g, 4.9 mmol, 1 equiv) in methyl alcohol (35 mL), and the resulting suspension was stirred at 23 °C for 3 h. The reaction mixture was partitioned between saturated aqueous sodium chloride solution (200 mL) and dichloromethane (4 x 200 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. Flash column chromatography of the residue afforded **15** (1.37 g, 92%) as a white solid (mp 102.5 °C).

^{1}H NMR (400 MHz, C_6D_6) δ: 5.97 (d, 1 H, J = 8.6 Hz, NH), 5.12 (ddd, 1 H, J = 3.6, 8.6, 10.0 Hz, H 2), 4.95 (d, 1 H, J = 3.6 Hz, H 1), 4.77 (s, 1 H, H 6), 4.63 (s, 1 H, H 6), 4.49 (d, 1 H, J = 7.7 Hz, MEM CH_2), 4.47 (d, 1 H, J = 3.8 Hz, H 4), 4.42 (d, 1 H, J = 7.7 Hz, MEM CH_2), 4.08 (dd, 1 H, J = 3.8, 10.0 Hz, H 3), 3.48 (m, 1 H, MEM CH_2), 3.39 (d, 1 H, J = 4.1 Hz, OH), 3.34 (m, 1 H, MEM CH_2), 3.12 (s, 3 H, CH_3O), 3.11 (m, 2 H, MEM CH_2), 3.03 (s, 3 H, CH_3O), 1.68 (s, 3 H, Ac).

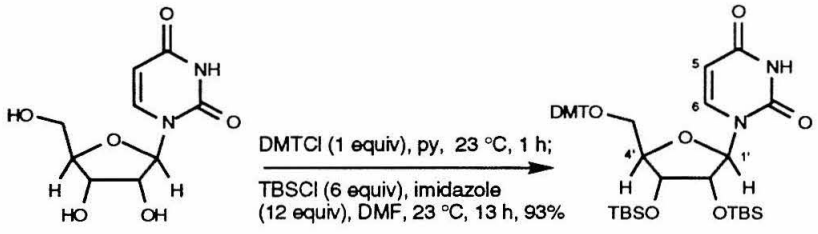
FTIR (neat film) cm^{-1}:	3589-3096 (m), 2930 (m), 1660 (s), 1649 (s), 1556 (m), 1373 (w), 1249 (w), 1196 (w), 1138 (m), 1104 (s), 1038 (s), 973 (w), 944 (w).
MS (FAB) *m/z*:	306 $(MH)^+$, 289 ($M^+ - CH_3$), 274 ($M^+ - CH_3O$), 230 ($M^+ - CH_3OCH_2CH_2O$).
HRMS (FAB) *m/z*:	Calcd for $C_{13}H_{24}NO_7$ $(MH)^+$: 306.1553. Found: 306.1550.
TLC R_f (50% acetone in PhH):	0.20



16 **17**

Uridine-5'-Aldehyde **17.**

Pyridine (645 μL, 8.0 mmol, 8.0 equiv) was added dropwise to a solution of chromium trioxide (400 mg, 4.0 mmol, 4.0 equiv) in a mixture of dichloromethane and *N,N*-dimethylformamide (4:1 (v/v), 5 mL) at 23 °C, and the resulting solution was stirred at 23 °C for 15 min. To this solution were added sequentially a solution of **16** (284 mg, 1.0 mmol, 1 equiv) in a mixture of dichloromethane and *N,N*-dimethylformamide (4:1 (v/v), 4 mL), and acetic anhydride (378 μL, 4.0 mmol, 4.0 equiv). After stirring the reaction mixture at 23 °C for 7 min, excess oxidant was quenched by the addition of anhydrous ethyl alcohol (0.50 mL). The product solution was diluted with ethyl acetate (250 mL) and was filtered through a short column of silica gel topped with sodium sulfate to remove chromium salts. The filtrate was concentrated, and the residue was passed through a column of silica gel at –14 °C (5% hexanes in ethyl acetate) to afford crude **17** (130 mg) as a white solid, which was used without further purification in the coupling attempt with allylic alcohol **15**.



19 **20**

Hydroxy-protected Uridine **20**.

Uridine (**19**) (1.00 g, 4.1 mmol, 1 equiv), dimethoxytrityl chloride (1.40 g, 4.10 mmol, 1 equiv), and pyridine (7 mL) were combined, and the resulting solution was stirred at 23 °C for 12 h. The orange mixture was poured into vigorously stirred ice-water (100 mL), and the resulting yellow precipitate was isolated by filtration. The solid was dried by azeotropic removal of residual water (toluene, 3 x 3 mL) and was dissolved in *N,N*-dimethylformamide (3 mL). Imidazole (3.33 g, 49.0 mmol, 12.0 equiv) and *t*-butyldimethylsilyl chloride (3.70 g, 24.5 mmol, 6.0 equiv) were added sequentially, and the resulting viscous solution was stirred at 23 °C for 13.5 h at which point excess silyl chloride was quenched by the slow addition of methyl alcohol (10 mL). The product mixture was partitioned between water (500 mL) and ethyl acetate (3 x 200 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. The residue was purified by flash chromatography (33% ethyl acetate in hexanes) to afford **20** (2.95 g, 93%) as a pale yellow solid (mp 118.0–122.0 °C).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.47 (s, 1 H, NH), 8.19 (d, 1 H, J = 8.2 Hz, H 6), 7.4-7.2 (m, 9 H, arom), 6.85 (m, 4 H, arom), 5.84 (d, 1 H, J = 1.8 Hz, H 1'), 5.29 (dd, 1 H, J = 2.3,

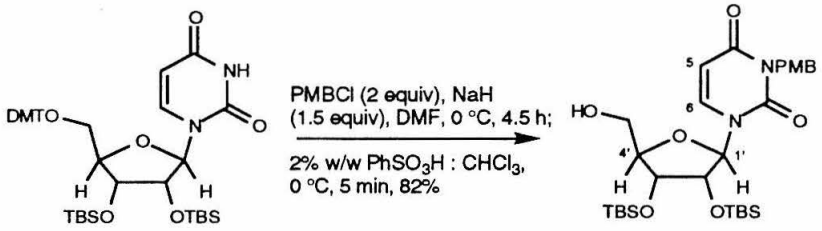
8.2 Hz, H 5), 4.17 (m, 3 H, H 2', 3', 4'), 3.79 (s, 6 H, CH_3O), 3.71 (dd, 1 H, J = 1-2, 9.4 Hz, H 5'), 3.34 (dd, 1 H, J = 1-2, 10.6 Hz, H 5'), 0.90 (s, 9 H, *t*-butyl), 0.77 (s, 9 H, *t*-butyl), 0.18 (s, 3 H, $SiCH_3$), 0.10 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$), -0.06 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3184 (m), 3058 (m), 2930 (s), 2856 (s), 1684 (s), 1608 (m), 1509 (s), 1463 (s), 1253 (s), 1175 (m), 836 (s).

MS (FAB) *m/z*: 775 $(MH)^+$, 718 (MH^+ - *t*-butyl), 303 $(DMT)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{42}H_{59}N_2O_8Si_2$ $(MH)^+$: 775.3810. Found: 775.3774.

TLC R_f (50% EtOAc in hexanes): 0.45



20 **21**

Uridine-5'-Alcohol **21.**

A solution of the imide **20** (2.90 g, 3.7 mmol, 1 equiv) in *N,N*-dimethylformamide (5 mL) and neat *p*-methoxybenzyl chloride (1.01 mL, 7.5 mmol, 2.0 equiv) were added sequentially to a suspension of sodium hydride (135 mg, 5.6 mmol, 1.5 equiv) in *N,N*-dimethylformamide (4 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 4.5 h, whereupon excess base was neutralized by the slow addition of methyl alcohol (5 mL). The resulting solution was partitioned between water (500 mL) and ethyl acetate (3 x 200 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. The residue was dissolved in a solution of benzenesulfonic acid in chloroform (2% (w/w), 20 mL) at 0 °C, and the resulting orange solution was stirred at 0 °C for 5 min. The product solution was partitioned between saturated aqueous sodium bicarbonate solution (500 mL) and ethyl acetate (3 x 200 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. Flash column chromatography of the residue (50% ethyl acetate in hexanes) afforded **21** contaminated with residual *p*-methoxybenzyl alcohol. The product was purified by flash column chromatography (gradient elution: dichloromethane → 50% ethyl acetate in dichloromethane) to give pure **21** (1.82 g, 82%) as a white solid (mp 84.0 °C).

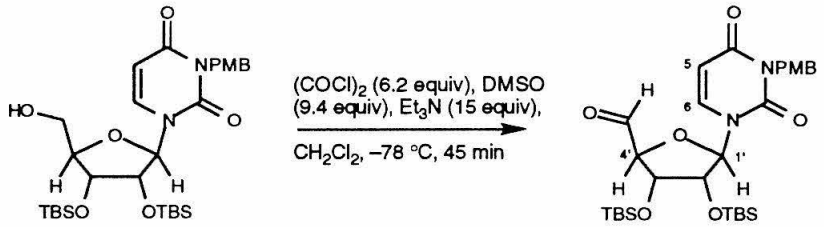
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (d, 2 H, J = 8.8 Hz, arom), 7.39 (d, 1 H, J = 8.1 Hz, H 6), 6.80 (d, 2 H, J = 8.8 Hz, arom), 5.77 (d, 1 H, J = 8.1 Hz, H 5), 5.40 (d, 1 H, J = 6.3 Hz, H 1'), 5.07 (d, 1 H, J = 13.4 Hz, PMB CH_2), 4.99 (d, 1 H, J = 13.4 Hz, PMB CH_2), 4.62 (dd, 1 H, J = 4.6, 6.3 Hz, H 2'), 4.15 (dd, 1 H, J = 2.7, 4.6 Hz, H 3'), 4.06 (m, 1 H, H 4'), 3.91 (m, 1 H, H 5'), 3.77 (s, 3 H, CH_3O), 3.68 (m, 1 H, H 5'), 3.34 (dd, 1 H, J = unres., 5.9 Hz, OH), 0.90 (s, 9 H, *t*-butyl), 0.80 (s, 9 H, *t*-butyl), 0.08 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), -0.03 (s, 3 H, $SiCH_3$), -0.19 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3456 (w, br), 2930 (m), 2857 (m), 1710 (m), 1667 (s), 1513 (m), 1462 (m), 1250 (s), 1162 (w), 1097 (w), 836 (m), 776 (m).

MS (FAB) *m/z*: 593 $(MH)^+$, 535 (M^+ - *t*-butyl), 121 $(PMB)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{29}H_{49}N_2O_7Si_2$ $(MH)^+$: 593.3078. Found: 593.3088.

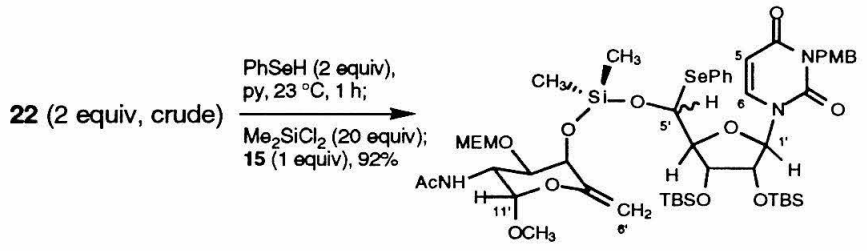
TLC R_f (50% EtOAc in hexanes): 0.43



21 **22** (crude)

Uridine-5'-Aldehyde **22**.

Dimethyl sulfoxide (204 μL, 2.9 mmol, 4.7 equiv) was added dropwise to a solution of oxalyl chloride (167 μL, 1.9 mmol, 3.1 equiv) in dichloromethane (4 mL) at –78 °C, and the resulting solution was stirred at –78 °C for 5 min. To this solution was added dropwise via cannula a solution of **21** (365 mg, 0.62 mmol, 1 equiv) in dichloromethane (4 mL), and the mixture was stirred at –78 °C for 15 min. Triethylamine (669 μL, 4.8 mmol, 7.5 equiv) was added at –78 °C and, after 30 min, the cold reaction mixture was poured into saturated aqueous sodium bicarbonate solution (150 mL). The aqueous layer was extracted with ethyl acetate (2 x 100 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated to afford the uridine 5'-aldehyde derivative **22** (375 mg) as a pale yellow solid. Due to the lability of the product and its susceptibility to hydration, the uridine 5'-aldehyde derivative **22** was used in its crude form in the following experiment.



23

O-Silylhemiselenoacetal Adduct **23**.

Freshly distilled benzeneselenol (68 μL, 0.62 mmol, 2.0 equiv) was added to a solution of the aldehyde **22** (375 mg, *ca.* 0.62 mmol, *ca.* 2 equiv, azeotropically dried with two 3-mL portions of toluene) in pyridine (6 mL), and the resulting solution was deoxygenated. After stirring at 23 °C for 1 h, the reaction mixture was transferred via cannula to a solution of dichlorodimethylsilane (752 μL, 6.2 mmol, 20 equiv) in pyridine (6 mL). The resulting solution was deoxygenated and was to stirred at 23 °C for 10 h. The cloudy yellow suspension was concentrated in vacuo at 23 °C, and the residue was suspended in toluene (3 mL). Volatiles were removed in vacuo, and the residue was diluted with a mixture of toluene and pyridine (10:1 (v/v), 6.6 mL). To the suspension was added via cannula a solution of the allylic alcohol **15** (94 mg, 0.31 mmol, 1 equiv) in pyridine (2 mL), and the resulting reaction mixture was stirred at 23 °C for 10 min. The product was partitioned between a mixture of ethyl acetate and pentane (1:1 (v/v), 200 mL) and water (100 mL). The organic layer was washed with water (100 mL), then was dried (magnesium sulfate) and concentrated. Flash column chromatography (ethyl acetate) of the residue afforded a 1:1 mixture of the C5'-diastereomers **23** (314 mg, 92%). For analytical

purposes, the diastereomers could be separated by preparative thin layer chromatography (1:1 ethyl acetate in hexanes).

23a:

^{1}H NMR (400 MHz, C_6D_6) δ: 8.04 (d, 1 H, *J* = 8.2 Hz, H 6), 7.76 (d, 2 H, *J* = 8.5 Hz, PMB arom.), 7.72 (d, 2 H, *J* = 7.0 Hz, PhSe arom), 7.10 (t, 2 H, *J* = 7.0 Hz, PhSe arom), 7.04 (d, 1 H, *J* = 7.3 Hz, PhSe arom), 6.78 (d, 2 H, *J* = 8.5 Hz, PMB arom), 6.71 (d, 1 H, *J* = 8.4 Hz, NH), 6.61 (d, 1 H, *J* = 6.2 Hz, H 1'), 5.90 (d, 1 H, *J* = 7.9 Hz, H 5), 5.90 (d, 1 H, *J* = 2.3 Hz, H 5'), 5.28 (d, 1 H, *J* = 13.2 Hz, PMB CH_2), 5.11 (d, 1 H, *J* = 13.2 Hz, PMB CH_2), 5.11 (m, 1 H, H 10'), 5.09 (d, 1 H, *J* = 3.5 Hz, H 11'), 4.67 (t, 1 H, *J* = 2.4 Hz, H 4'), 4.59 (s, 1 H, H 6'), 4.56 (d, 1 H, *J* = 7.0 Hz, MEM CH_2), 4.46 (m, 1 H, H 2'), 4.41 (d, 1 H, *J* = 7.0 Hz, MEM CH_2), 4.41 (d, 1 H, *J* = 2.9 Hz, H 8'), 4.35 (m, 1 H, H 3'), 4.31 (s, 1 H, H 6'), 4.25 (dd, 1 H, *J* = 2.9, 10.8 Hz, H 9'), 3.79 (m, 1 H, MEM CH_2), 3.29 (s, 3 H, CH_3O), 3.17 (m, 2 H, MEM CH_2), 3.14 (s, 3 H, CH_3O), 3.03 (m, 1 H, MEM CH_2), 3.00 (s, 3 H, CH_3O), 1.84 (s, 3 H, Ac), 1.02 (s, 9 H, *t*-butyl), 0.99 (s, 9 H, *t*-butyl), 0.33 (s, 3 H, $SiCH_3$), 0.24 (s, 3 H,

$SiCH_3$), 0.23 (s, 6 H, $SiCH_3$), 0.20 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3332 (w), 2929 (m), 2856 (w), 1713 (m), 1670 (s), 1513 (m), 1455 (m), 1390 (w), 1251 (m), 1108 (m), 1038 (m), 839 (m), 777 (w), 742 (w).

MS (FAB) *m/z*: 1111 $(MH)^+$, 121 $(PMB)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{50}H_{80}N_3O_{14}SeSi_3$ $(MH)^+$: 1110.4113. Found: 1110.4136.

mp: 57.0–59.0 °C.

TLC R_f (100% EtOAc): 0.38

23b:

^1H NMR (400 MHz, C_6D_6) δ: 7.75 (m, 5 H, H 6, PMB arom, PhSe arom), 7.12 (m, 2 H, PhSe arom), 7.07 (m, 1 H, PhSe arom), 6.78 (d, 2 H J = 8.5 Hz, PMB arom), 6.68 (d, 1 H, J = 7.3 Hz, H 1'), 6.59 (d, 1 H, J = 8.5 Hz, NH), 6.11 (d, 1 H, J = 8.2 Hz, H 5), 6.00 (d, 1 H, J = 4.7 Hz, H 5'), 5.30 (d, 1 H, J = 13.2 Hz, PMB CH_2), 5.15 (m, 1 H, H 10'), 5.12 (d, 1 H, J = 13.2 Hz, PMB CH_2), 5.01 (d, 1 H, J = 3.2 Hz, H 11'),

4.60 (m, 4 H, H 2', 3', 6', MEM CH_2), 4.52 (d, 1 H, J = 2.9 Hz, H 8'), 4.49 (m, 1 H, H 4'), 4.42 (d, 1 H, J = 7.0 Hz, MEM CH_2), 4.36 (s, 1 H, H 6'), 4.26 (dd, 1 H, J = 2.9, 11.4 Hz, H 9'), 3.72 (m, 1 H, MEM CH_2), 3.29 (s, 3 H, CH_3O), 3.20 (m, 2 H, MEM CH_2), 3.11 (s, 3 H, CH_3O), 3.07 (m, 1 H, MEM CH_2), 3.02 (s, 3 H, CH_3O), 1.79 (s, 3 H, Ac), 1.04 (s, 9 H, *t*-butyl), 0.97 (s, 9 H, *t*-butyl), 0.39 (s, 3 H, $SiCH_3$), 0.28 (s, 3 H, $SiCH_3$), 0.27 (s, 3 H, $SiCH_3$), 0.24 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.06 (s, 3 H, $SiCH_3$).

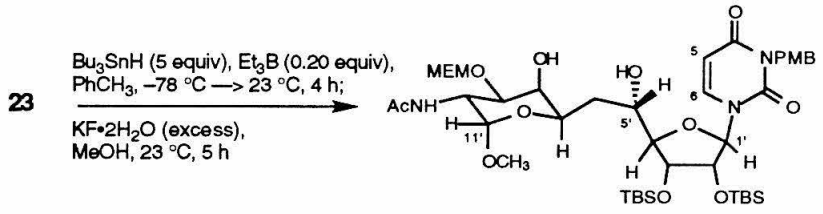
FTIR (neat film) cm^{-1}: 3335 (w), 2830 (m), 2856 (w), 1713 (m), 1668 (s), 1513 (w), 1455 (w), 1390 (w), 1251 (m), 1108 (m), 1039 (m), 837 (m), 775 (w), 743 (w).

MS (FAB) *m/z*: 1111 $(MH)^+$, 121 $(PMB)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{50}H_{80}N_3O_{14}SeSi_3$ $(MH)^+$: 1110.4113. Found: 1110.4111.

mp: 59.5–61.0 °C.

TLC R_f (100% EtOAc): 0.35



24 (59%)

Diol **24.**

A solution of triethylborane (30 μL, 1.0 M in hexanes, 0.03 mmol, 0.2 equiv) was added to a deoxygenated solution of the siloxanes **23** (153 mg, 0.14 mmol, 1 equiv) and tributyltin hydride (185 μL, 0.69 mmol, 5.0 equiv) in toluene at –78 °C, and the resulting solution was allowed to warm to 23 °C over 4 h. Volatiles were removed in vacuo, and the residue was diluted with methyl alcohol (25 mL). Potassium fluoride hydrate (300 mg, 3.2 mmol, 16.0 equiv) was added, and the resulting suspension was stirred at 23 °C for 9 h. After dilution with dichloromethane (50 mL), the suspension was filtered, and the filtrate was concentrated. Flash column chromatography of the residue (25% acetone in ethyl acetate) afforded a 5:1 mixture of the diastereomers **24** and **25**, respectively (88 mg combined, 71%) as a white solid.

24:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (d, 1 H, J = 8.8 Hz, H 6), 7.44 (d, 2 H, J = 9.1 Hz, arom), 6.80 (d, 2 H, J = 9.1 Hz, arom), 6.21 (d, 1 H, J = 9.4 Hz, NH), 5.79 (d, 1 H, J = 4.5 Hz, H 1'), 5.75 (d, 1 H, J = 8.8 Hz, H 5), 5.03 (s, 2 H, PMB CH_2), 4.80 (d, 1 H, J = 7.9 Hz,

MEM CH_2), 4.79 (d, 1 H, J = 3.8 Hz, H 11'), 4.67 (d, 1 H, J = 7.9 Hz, MEM CH_2), 4.50 (m, 1 H, H 10'), 4.20 (t, 1 H, J = 4.4 Hz, H 2'), 4.12 (t, 1 H, J = 4.4 Hz, H 3'), 3.95 (m, 3 H, H 5', 7', 8'), 3.89 (m, 2 H, H 4', 9'), 3.84 (m, 1 H, MEM CH_2), 3.75 (s, 3 H, CH_3O), 3.72 (m, 1 H, MEMCH_2), 3.57 (m, 3 H, OH, MEM CH_2), 3.41 (s, 3 H, CH_3O), 3.37 (s, 4 H, OH CH_3O), 2.26 (m, 1 H, H 6'), 1.98 (s, 3 H, Ac), 1.79 (m, 1 H, H 6'), 0.87 (s, 9 H, *t*-butyl), 0.83 (s, 9 H, *t*-butyl), 0.07 (s, 3 H, $SiCH_3$), 0.06 (s, 3 H, $SiCH_3$), 0.02 (s, 3 H, $SiCH_3$), -0.02 (s, 3 H, $SiCH_3$).

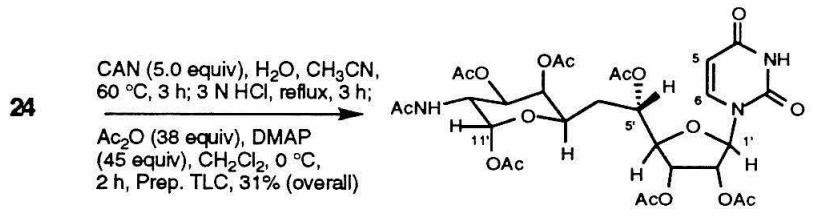
FTIR (neat film) cm^{-1}: 3600-3213 (w, br), 2930 (m), 2857 (m), 1712 (m), 1668 (s), 1514 (m), 1455 (m), 1392 (w), 1249 (m), 1109 (m), 1052 (m), 837 (m), 778 (m).

MS (FAB) *m/z*: 898 $(MH)^+$, 866 (M^+ - CH_3O), 840 (M^+ - *t*-butyl), 822 (M^+ - $CH_3OCH_2CH_2O$), 121 $(PMB)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{42}H_{72}N_3O_{14}Si_2$ $(MH)^+$: 898.4553. Found: 898.4551.

mp: 100.5–102.0 °C.

TLC R_f (10% MeOH in CH_2Cl_2): 0.50

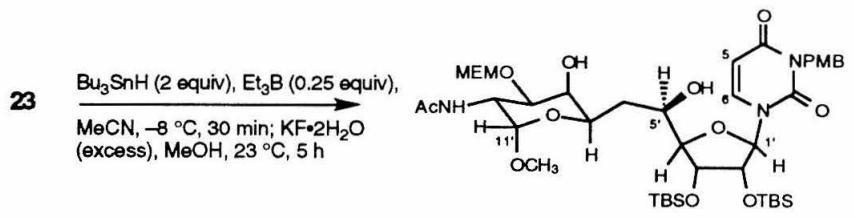


26

C5'-*epi*-α-Heptaacetyl Tunicaminyluracil **26.**

Ceric ammonium nitrate (60 mg, 0.11 mmol, 5.0 equiv) was added to a solution of the diol **24** (20 mg, 0.022 mmol, 1 equiv) in a mixture of acetonitrile and water (10:1 (v/v), 3.3 mL), and the resulting solution was heated at 60 °C for 3 h. The reaction mixture was partitioned between saturated aqueous sodium chloride solution (50 mL) and ethyl acetate (3 x 50 mL), and the combined organic layers were dried (sodium sulfate) and concentrated. The residue was diluted with aqueous hydrochloric acid (3 N, 2 mL), and the resulting suspension was heated at reflux for 3 h, at which time volatiles were removed in vacuo at 23 °C. The solid residue of 5'-*epi*-tunicaminyluracil was diluted with dichloromethane (5 mL), and to the resulting solution was cooled to 0 °C and treated sequentially with DMAP (120 mg, 1.0 mmol, 45 equiv) and acetic anhydride (80 μL, 0.84 mmol, 38 equiv). The reaction mixture was stirred at 0 °C for 2 h, then was diluted with ethyl acetate (50 mL). The product solution was washed sequentially with 0.5 N aqueous hydrochloric acid solution (40 mL), saturated aqueous sodium bicarbonate solution (40 mL), and saturated aqueous sodium chloride solution (40 mL). The organic layer dried (sodium sulfate), and concentrated, and the residue was purified by preparative thin layer chromatography (7% methyl alcohol in dichloromethane) to afford **26** as the major product (6.5 mg, 31%).

^{1}H NMR (400 MHz, $CDCl_3$) δ:	8.42 (s, 1 H, imide NH), 7.53 (d, 1 H, *J* = 8.6 Hz, H 6), 6.17 (d, 1 H, *J* = 3.7 Hz, H 11'), 6.13 (d, 1 H, *J* = 5.6 Hz, H 1'), 5.85 (d, 1 H, *J* = 8.6 Hz, H 5), 5.44 (d, 1 H, *J* = 9.9 Hz, amide NH), 5.28 (d, 1 H, *J* = 2.9 Hz, H 8'), 5.26 (m, 1 H, H 5'), 5.22 (t, 1 H, *J* = 5.6 Hz, H 2'), 5.19 (dd, 1 H, *J* = 2.9, 12.0 Hz, H 9'), 5.11 (dd, 1 H, *J* = 4.0, 5.6 Hz, H 3'), 4.69 (ddd, 1 H, *J* = 3.7, 9.9, 12.0 Hz, H 10'), 4.22 (d, 1 H, *J* = 8.3 Hz, H 7'), 4.10 (d, 1 H, *J* = 4.0 Hz, H 4'), 2.19 (s, 6 H, Ac), 2.11 (s, 3 H, Ac), 2.11 (m, 1 H, H 6'), 2.08 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.94 (s, 3 H, Ac), 1.62 (m, 1 H, H 6').
FTIR (neat film) cm^{-1}:	3289 (w, br), 2925 (w), 1747 (s), 1693 (s) 1546 (w), 1458 (w), 1370 (m), 1223 (s), 1123 (w), 1041 (m), 929 (w).
MS (FAB) *m/z*:	700 $(MH)^+$, 640 (M^+ - AcO).
HRMS (FAB) *m/z*:	Calculated for $C_{29}H_{38}N_3O_{17}$ $(MH)^+$: 700.2201. Found: 700.2231.
TLC R_f (10% MeOH in CH_2Cl_2):	0.33



25 (62%)

Diol **25**.

A solution of triethylborane (15 μL, 1.0 M in hexanes, 0.015 mmol, 0.2 equiv) was added to a deoxygenated solution of the siloxane adducts **23** (110 mg, 0.099 mmol, 1 equiv) and tributyltin hydride (53 μL, 0.20 mmol, 2.0 equiv) in acetonitrile (110 mL) at –8 °C. After 10 min, a second aliquot of triethylborane solution (5 μL, 0.005 mmol, 0.05 equiv) was added. The reaction mixture was stirred at –8 °C for 20 min, and volatiles were removed in vacuo. The residue was diluted with methyl alcohol (30 mL), and potassium fluoride hydrate (1.0 g) was added to the resulting solution. After stirring at 23 °C for 5 h, the reaction solution was concentrated, and the residue was partitioned between saturated aqueous sodium chloride solution (70 mL) and ethyl acetate (6 x 50 mL). The combined organic layers were dried (sodium sulfate) and concentrated, and the products were isolated by radial chromatography (5% methyl alcohol in dichloromethane) to afford separate fractions of **25** (55 mg, 62%) and **24** (16 mg, 18%) as white solids.

25:

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, 2 H, J = 7.5 Hz, arom), 7.22 (d, 1 H, J = 8.3 Hz, H 6), 6.77 (d, 2 H, J = 7.5 Hz, arom), 6.16 (d, 1 H, J = 8.8 Hz, NH), 5.79 (d, 1 H, J = 8.3 Hz,

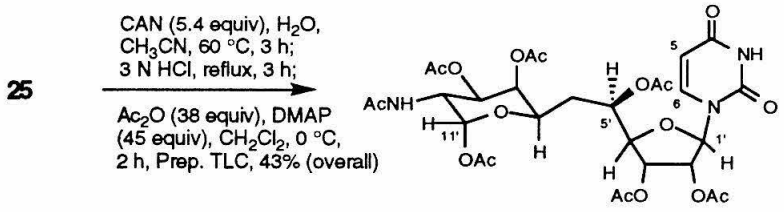
H 5), 5.26 (d, 1 H, J = 7.9 Hz, H 1'), 5.06 (d, 1 H, J = 13.9 Hz, PMB CH_2), 4.95 (d, 1 H, J = 13.9 Hz, PMB CH_2), 4.81 (m, 2 H, H 2', MEM CH_2), 4.74 (d, 1 H, J = 3.8 Hz, H 11'), 4.70 (s, 1 H, OH), 4.68 (d, 1 H, J = 7.3 Hz, MEM CH_2), 4.49 (m, 1 H, H 10'), 4.13 (d, 1 H, J = 4.4 Hz, H 2'), 4.06 (m, 2 H, H 5', 7'), 3.98 (m, 1 H, H 4'), 3.90 (m, 2 H, H 8', 9'), 3.82 (m, 1 H, MEM CH_2), 3.75 (s, 3 H, CH_3O), 3.74 (m, 1 H, MEM CH_2), 3.58 (m, 2 H, MEM CH_2), 3.40 (s, 3 H, CH_3O), 3.38 (s, 3 H, CH_3O), 3.10 (s, 1 H, OH), 2.04 (m, 1 H, H 6'), 1.98 (s, 3 H, Ac), 1.57 (m, 1 H, H 6'), 0.89 (s, 9 H, *t*-butyl), 0.72 (s, 9 H, *t*-butyl), 0.09 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), -0.10 (s, 3 H, $SiCH_3$), -0.31 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3624-3178 (w, br), 2930 (m), 2860 (w), 1713 (m), 1667 (s), 1514 (m), 1456 (m), 1390 (w), 1250 (m), 1108 (m), 1052 (s), 876 (w), 838 (m), 775 (m).

MS (FAB) *m/z*: 898 $(MH)^+$, 866 (M^+ - CH_3O), 840 (M^+ - *t*-butyl), 822 (M^+ - $CH_3OCH_2CH_2O$), 121 $(PMB)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{42}H_{72}N_3O_{14}Si_2$ $(MH)^+$: 898.4553. Found: 898.4528.

mp:	100.5–101.5 °C.
TLC R_f (10% MeOH in CH_2Cl_2):	0.53



27

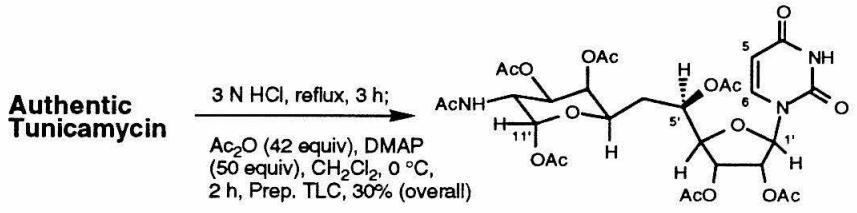
Synthetically-Derived α-Heptaacetyl Tunicaminyluracil **27.**

Ceric ammonium nitrate (165 mg, 0.30 mmol, 5.4 equiv) was added to a solution of the diol **25** (50 mg, 0.056 mmol, 1 equiv) in a mixture of acetonitrile and water (10:1 (v/v), 5.5 mL), and the resulting solution was heated at 60 °C for 3 h. The reaction mixture was partitioned between saturated aqueous sodium chloride solution (50 mL) and ethyl acetate (3 x 50 mL), and the combined organic layers were dried (sodium sulfate) and concentrated. The residue was diluted with aqueous hydrochloric acid (3 N, 3 mL), and the resulting suspension was heated at reflux for 3 h, at which time volatiles were removed in vacuo at 23 °C. The solid residue of crude tunicaminyluracil was diluted with dichloromethane (5 mL), and the resulting solution was cooled to 0 °C and was treated sequentially with DMAP (300 mg, 2.5 mmol, 45 equiv) and acetic anhydride (200 μL, 2.1 mmol, 38 equiv). The reaction mixture was stirred at 0 °C for 2 h, then was diluted with ethyl acetate (50 mL). The product solution was washed sequentially with 0.5 N aqueous hydrochloric acid solution (40 mL), saturated aqueous sodium bicarbonate solution (40 mL), and saturated aqueous sodium chloride solution (40 mL). The organic layer was dried (sodium sulfate), and concentrated, and the residue was purified by preparative thin layer chromatography (7% methyl alcohol in dichloromethane) to afford **27** as the major product (17 mg, 43%) (mp 174.5 °C (decomp)).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (s. 1 H, imide NH), 7.21 (d, 1 H, *J* = 8.4 Hz, H 6), 6.12 (d, 1 H, *J* = 3.5 Hz, H 11'), 5.90 (d, 1 H, *J* = 5.9 Hz, H 1'), 5.80 (d, 1 H, *J* = 8.4 Hz, H 5), 5.46 (d, 1 H, *J* = 9.8 Hz, amide NH), 5.35 (t, 1 H, *J* = 5.9 Hz, H 3'), 5.27 (t, 1 H, *J* = 5.9 Hz, H 2'), 5.24 (d, 1 H, *J* = 3.3 Hz, H 8'), 5.20 (dd, 1 H, *J* = 3.3, 11.6 Hz, H 9'), 5.10 (m, 1 H, H 5'), 4.71 (ddd, 1 H, *J* = 3.5, 9.8, 11.6 Hz, H 10'), 4.07 (m, 2 H, H 4', 7'), 2.19 (s, 3 H, Ac), 2.17 (s, 3 H, Ac), 2.12 (s, 3 H, Ac), 2.10 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 1.95 (s, 3 H, Ac), 1.95 (obscured, 1 H, H 6'), 1.55 (ddd, 1 H, *J* = 1.9, 8.3, 9.9 Hz, H 6').

^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.2, 170.6, 170.0, 170.0, 169.6, 169.3, 169.1 (6 x CH_3CO_2, CH_3CONH), 162.2 (C 4), 149.9 (C 2), 139.7 (C 6), 103.5 (C 5), 91.1, 88.0, 82.6 (C 1', 4', 11'), 72.4, 69.6, 69.6, 69.4, 68.2, 67.7 (C 2', 3', 5', 8', 9', 10'), 46.8, 32.6 (C 6', 7'), 23.2 (CH_3CONH), 20.9, 20.9, 20.8, 20.7, 20.5, 20.4 (6 x CH_3CO_2).

FTIR (neat film) cm^{-1}:	3295 (w, br), 3013 (w), 1746 (s), 1694 (s), 1543 (w), 1455 (w), 1431 (w), 1373 (m), 1222 (s), 1046 (m), 933 (w), 756 (w).
MS (FAB) *m/z*:	700 $(MH)^+$, 640 (M^+ - AcO).
HRMS (FAB) *m/z*:	Calcd for $C_{29}H_{38}N_3O_{17}$ $(MH)^+$: 700.2201. Found: 700.2177.
$[\alpha]_D^{25}$:	+65.9° (c = 1.67, $CHCl_3$).
HPLC	See Appendix.
TLC R_f (10% MeOH in CH_2Cl_2):	0.31



27

Authentically-Derived α-Heptaacetyl Tunicaminyluracil **27.**

A solution of commercial tunicamycin (20 mg, 0.024 mmol, 1 equiv) in aqueous hydrochloric acid (3 N, 1.5 mL) was heated at reflux for 3 h, and volatiles were removed in vacuo at 23 °C. The residue was diluted with dichloromethane (3 mL), and to this solution were added DMAP (150 mg, 1.2 mmol, 50 equiv) and acetic anhydride (100 μL, 1.0 mmol, 42 equiv) in sequence, at 0 °C. The resulting solution was stirred at 0 °C for 2 h, then was diluted with ethyl acetate (50 mL). The product solution was washed sequentially with 0.5 N aqueous hydrochloric acid solution (40 mL), saturated aqueous sodium bicarbonate solution (40 mL), and saturated aqueous sodium chloride solution (40 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by preparative thin layer chromatography (7% methyl alcohol in dichloromethane) to afford **27** as the major product (5 mg, 30%) (mp 175.0 °C (decomp)).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.34 (s. 1 H, imide NH), 7.21 (d, 1 H, J = 8.4 Hz, H 6), 6.12 (d, 1 H, J = 3.4 Hz, H 11'), 5.90 (d, 1 H, J = 5.9 Hz, H 1'), 5.80 (d, 1 H, J = 8.4 Hz, H 5), 5.47 (d, 1 H, J = 10.0 Hz, amide NH), 5.35 (t, 1 H, J = 5.9 Hz, H 3'), 5.27 (t, 1 H, J = 5.9 Hz, H

2'), 5.24 (d, 1 H, J = 3.3 Hz, H 8'), 5.20 (dd, 1 H, J = 3.3, 11.4 Hz, H 9'), 5.10 (m, 1 H, H 5'), 4.71 (ddd, 1 H, J = 3.4, 10.0, 11.4 Hz, H 10'), 4.07 (m, 2 H, H 4', 7'), 2.19 (s, 3 H, Ac), 2.17 (s, 3 H, Ac), 2.12 (s, 3 H, Ac), 2.10 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 1.95 (s, 3 H, Ac), 1.95 (obscured, 1 H, H 6'), 1.55 (ddd, 1 H, J = 2.0, 8.2, 9.9 Hz, H 6').

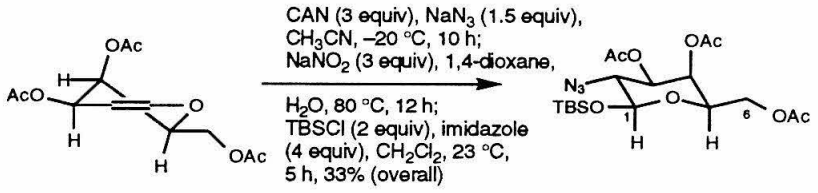
^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.2, 170.6, 170.0, 170.0, 169.6, 169.3, 169.1 (6 x CH_3CO_2, CH_3CONH), 162.1 (C 4), 149.8 (C 2), 139.7 (C 6), 103.5 (C 5), 91.1, 88.0, 82.6 (C 1', 4', 11'), 72.4, 69.7, 69.6, 69.4, 68.2, 67.7 (C 2', 3', 5', 8', 9', 10'), 46.8, 32.6 (C 6', 7'), 23.2 (CH_3CONH), 20.9, 20.9, 20.8, 20.7, 20.5, 20.4 (6 x CH_3CO_2).

FTIR (neat film) cm^{-1}: 3307 (w, br), 3023 (w), 1747 (s), 1694 (s), 1538 (w), 1455 (w), 1431 (w), 1373 (m), 1223 (s), 1046 (m), 933 (w), 756 (w).

MS (FAB) *m/z*: 700 $(MH)^+$, 640 (M^+ - AcO).

HRMS (FAB) *m/z*: Calcd for $C_{29}H_{38}N_3O_{17}$ $(MH)^+$: 700.2201. Found: 700.2229.

$[\alpha]_D^{25}$:	+63.4° (c = 1.33, $CHCl_3$).
HPLC	See Appendix.
TLC R_f (10% MeOH in CH_2Cl_2):	0.31



30 **31**

2-Deoxy-2-azidogalactopyranoside **31.**

A solution of triacetoxy-D-galactal (**30**) (5.0 g, 18.2 mmol, 1 equiv) in acetonitrile (100 mL) at –40 °C was added via cannula to a powdered mixture of ceric ammonium nitrate (30 g, 54.7 mmol, 3.0 equiv) and sodium azide (1.78 g, 27.4 mmol, 1.5 equiv) at –20 °C over a 20-min period. The resulting orange slurry was stirred at –20 °C for 8 h, at which time the reaction mixture was diluted with water (400 mL). The product solution was extracted with ethyl ether (2 x 250 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated in vacuo. The residue was dissolved in a mixture of 1,4-dioxane (100 mL) and water (15 mL), and sodium nitrite (1.60 g, 23.0 mmol, 1.3 equiv) was added. After heating at 80 °C for 12 h, the reaction mixture was partitioned between water (250 mL) and ethyl ether (250 mL), and the organic layer was washed sequentially with water (200 mL) and saturated aqueous sodium chloride solution (200 mL). The ethereal solution was dried (sodium sulfate) and concentrated, and the residue was subjected to flash column chromatography (50% ethyl acetate in hexanes) to afford the azido sugar intermediate. The anomeric mixture of galactopyranosides was dissolved in dichloromethane (50 mL), and imidazole (3.46 g, 50.8 mmol, 2.8 equiv) and *t*-butyldimethylsilyl chloride (3.83 g, 25.4 mmol, 1.4 equiv) were added to the resulting solution in sequence. After stirring at 23 °C for 5.5 h, excess silyl chloride was quenched by the slow addition of methyl alcohol (10

mL). The product mixture was partitioned between water (200 mL) and dichloromethane (2 x 150 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. Purification of the residue by flash column chromatography (25% ethyl acetate in hexanes) afforded the pure β-*O*-*t*-butyldimethylsilyl ether **31** as a viscous oil (2.7 g) in 33% overall yield from **30**.

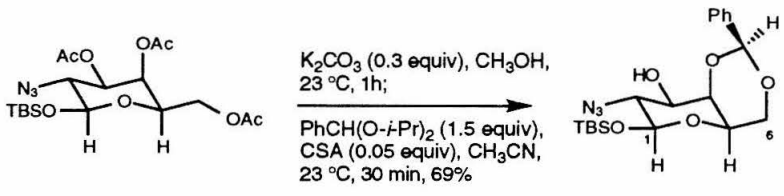
^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.31 (dd, 1 H, J = 1.12, 3.4 Hz, H 4), 4.75 (dd, 1 H, J = 3.4, 11.0 Hz, H 3), 4.58 (d, 1 H, J = 7.6 Hz, H 1), 4.15 (dd, 1 H, J = 7.2, 11.3 Hz, H 6), 4.07 (dd, 1 H, J = 5.9, 11.3 Hz, H 6), 3.84 (m, 1 H, H 5), 3.60 (dd, 1 H, J = 7.6, 11.0 Hz, H 2), 2.15 (s, 3 H, Ac), 2.04 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 0.94 (s, 9 H, *t*-butyl), 0.17 (s, 6 H, 2 x $SiCH_3$).

FTIR (neat film) cm^{-1}: 2932 (w), 2559 (w), 2114 (s), 1750 (s), 1368 (m), 1236 (s), 1179 (w), 1158 (w), 1115 (w), 1078 (m), 1046 (m), 840 (m), 784 (w).

MS (CI (NH_3)) *m/z*: 463 $(MNH_4)^+$, 388 (M^+ - *t*-butyl), 314 (M^+ - OTBS).

HRMS (CI (NH_3)) *m/z*: Calcd for $C_{18}H_{35}N_4O_8Si$ $(MNH_4)^+$: 463.2224 Found: 463.2210.

TLC R_f (20% EtOAc in hexanes): 0.21

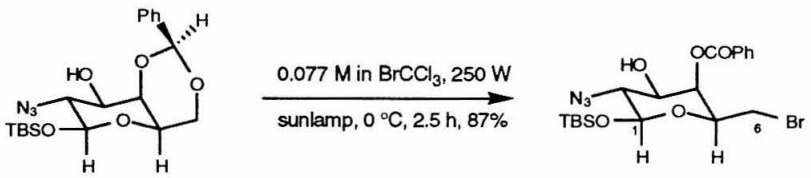


31 **32**

4,6-*O*-Benzylidene-galactopyranoside **32.**

Solid potassium carbonate (0.5 g, 3.62 mmol, 0.3 equiv) was added to a solution of **31** (5.2 g, 11.7 mmol, 1 equiv) in methyl alcohol (50 mL), and the resulting solution was stirred at 23 °C for 1 h, whereupon strongly acidic Amberlite IR-120 resin (1 g) was added to neutralize the base catalyst. The suspension was filtered, and the filtrate was concentrated in vacuo. The residue was passed through a short column of silica gel eluting with 5% methyl alcohol in ethyl acetate to afford the crude triol intermediate. Acetonitrile (150 mL), diisopropoxybenzyl acetal (2.98 g, 13.7 mmol, 1.2 equiv), the crude triol intermediate, and crushed 4Å molecular sieves (9 g) were combined, and the resulting suspension was stirred at 23 °C for 1 h. (±)-Camphorsulfonic acid (20 mg, 0.10 mmol, 0.01 eq) was added to the reaction mixture, and the whole was stirred at 23 °C for 30 min. After neutralization of acid catalyst by the addition of excess triethylamine (3 mL), the reaction mixture was diluted with ethyl ether (300 mL), and the solids were removed by filtration. The ethereal solution was washed with water (300 mL), dried (magnesium sulfate), and concentrated, and the residue was purified by flash column chromatography (2.5% ethyl acetate in dichloromethane) providing **32** (3.24 g, 69%) as a viscous oil.

^{1}H NMR (300 MHz, C_6D_6) δ:	7.51 (m, 2 H, arom), 7.40 (m, 3 H, arom), 5.56 (s, 1 H, benzylidene acetal), 4.56 (d, 1 H, *J* = 7.0 Hz, H 1), 4.29 (dd, 1 H, *J* = 1.4, 12.4 Hz, H 6), 4.16 (dd, 1 H, *J* = 3.2, 0.6 Hz, H 4), 4.06 (dd, 1 H, *J* = 12.4, 1.8 Hz, H 6), 3.51 (m, 2 H, H 2,3), 3.42 (d, 1 H, *J* = 1.4 Hz, H 5), 2.51 (d, 1 H, *J* = 8.9 Hz, OH), 0.96 (s, 9 H, *t*-butyl), 0.20 (s, 3 H, $SiCH_3$), 0.18 (s, 3 H, $SiCH_3$).
FTIR (neat film) cm^{-1}:	3401 (w, br), 2929 (w), 2858 (w), 2112 (s), 1396 (w), 1365 (w), 1252 (m), 1171 (m), 1088 (m), 1055 (m), 995 (m), 837 (m), 820 (w), 783 (w), 733 (w), 698 (w).
MS (FAB) *m/z*:	408 $(MH)^+$, 365 (M^+ - N_3), 350 (M^+ - *t*-butyl), 330 (M^+ - C_6H_5).
HRMS (FAB) *m/z*:	Calcd for $C_{19}H_{30}N_3O_5Si$ $(MH)^+$: 408.1955. Found: 408.1977.
TLC R_f (EtOAc in hexanes):	0.50



32 **33**

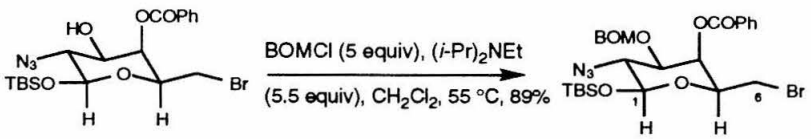
Bromide **33.**

A solution of galactopyranoside **32** (4.70 g, 11.6 mmol, 1 equiv) in bromotrichloromethane (150 mL) was divided equally among 10 sealed Pyrex tubes (10 x 1.5 cm) and the tubes were irradiated with a 275-watt sunlamp at 0 °C for 2.5 h. The reaction mixtures were combined and concentrated, and the residue was purified by flash column chromatography (25% ethyl acetate in hexanes) to give the bromide **33** (4.88 g, 87%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (m, 2 H, arom), 7.63 (m, 1 H, arom), 7.50 (m, 2 H, arom), 5.63 (dd, 1 H, J = 3.4, 1.0 Hz, H 4), 4.63 (d, 1 H, J = 7.5 Hz, H 1), 3.87 (ddd, 1 H, J = 7.6, 5.9, 1.0 Hz, H 5), 3.71 (m, 1 H, H 3), 3.57 (dd, 1 H, J = 10.3, 7.5 Hz, H 2), 3.41 (m, 2 H, H 6), 2.45 (s(br), 1 H, OH), 0.98 (s, 9 H, *t*-butyl), 0.24, 0.22 (2 x s, 2 x 3H, $Si(CH_3)_2$).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.4, 133.5-128.4 (arom), 97.4, 74.0, 70.5, 70.4, 66.0, 29.1, 25.6, 25.6, 25.5, 17.8, -4.2, -5.2.

FTIR (neat film) cm^{-1}:	3624-3248 (m, br), 2930 (m), 2858 (m), 2115 (s), 1725 (s), 1452 (w), 1362 (w), 1273 (s), 1115 (s), 1071 (s), 836 (s), 708 (s).
MS (FAB) *m/z*:	486 $(MH)^+$, 354 (M^+ - OTBS), 105 $(C_6H_5CO)^+$.
HRMS (FAB) *m/z*:	Calcd for $C_{19}H_{29}N_3O_5BrSi$ $(MH)^+$: 486.1077. Found: 486.1060.
TLC R_f (33% EtOAc in hexanes):	0.40



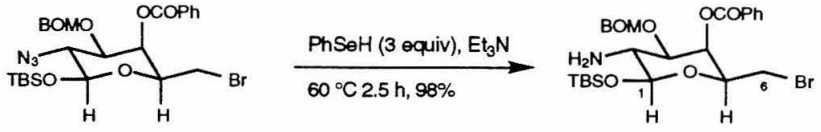
33 **34**

C3-*O*-Benzyloxymethyl Ether **34.**

Benzyloxymethyl chloride (26.0 mL, 188 mmol, 5.0 equiv) was added to a solution of the bromide **33** (18.3 g, 37.6 mmol, 1 equiv) and diisopropylethylamine (36.0 mL, 207 mmol, 5.5 equiv) in dichloromethane (150 mL), and the resulting solution was heated at 55 °C for 15 h. The reaction mixture was diluted with dichloromethane (200 mL), and the resulting solution was washed sequentially with water (50 mL) and saturated aqueous sodium chloride solution (50 mL). The organic layer was dried (sodium sulfate) and concentrated, and the residue was filtered through a short column of silica gel (17% ethyl acetate hexanes) providing the corresponding benzyloxymethyl ether **34** (20.2 g, 89%) as a viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (m, 2 H, arom), 7.62 (m, 1 H, arom), 7.50 (m, 2 H, arom), 7.41-7.28 (m, 5 H, arom), 5.71 (dd, 1 H, *J* = 3.2, 1.0 Hz, H 4), 4.93 (d, 1 H, *J* = 7.3 Hz, OCH_2O), 4.75 (d, 1 H, *J* = 6.6 Hz, $PhOCH_2O$), 4.74 (d, 1 H, *J* = 7.3 Hz, OCH_2O), 4.64 (d, 1 H, *J* = 7.6 Hz, H 1), 4.60 (d, 1 H, *J* = 6.6 Hz, $PhCH_2O$), 3.83 (m, 1 H, H 5), 3.78 (dd, 1 H, *J* = 10.5, 3.2 Hz, H 3), 3.66 (dd, 1 H, 10.5, 7.6 Hz, H

	2), 3.40 (m, 2 H, H 6), 1.00 (s, 9 H, *t*-butyl), 0.25 (s, 3 H, $SiCH_3$), 0.24 (s, 3 H, $SiCH_3$).
FTIR (neat film) cm^{-1}:	2930 (m), 2858 (m), 2113 (s), 1728 (s), 1602 (w), 1454 (w), 1267 (s), 1113 (s), 1027 (s), 836 (s), 784 (m), 709 (s).
MS (FAB) *m/z*:	604 (M^+ - H), 526 (M^+ - Br).
HRMS (FAB) *m/z*:	Calcd for $C_{27}H_{35}N_3O_6BrSi$ (M^+ - H): 604.1511. Found: 604.1479.
TLC R_f (33% EtOAc in hexanes):	0.60



34 **35**

Amine **35.**

A solution of the benzyloxymethyl ether **34** (20.2 g, 33.4 mmol, 1 equiv) in triethylamine (50 mL) was added dropwise to a solution of benzeneselenol (10.2 mL, 96 mmol, 2.9 equiv) in triethylamine (150 mL) at 0 °C. The resulting solution was stirred at 0 °C for 5 min, then at 23 °C for 5 min, and finally at 60 °C for 2.5 h. The reaction mixture was concentrated in vacuo, and the yellow residue was dissolved in ethyl acetate (250 mL). The latter solution was washed sequentially with water (2 x 100 mL) and saturated aqueous sodium chloride solution (50 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (gradient elution: 20 → 33% ethyl acetate in hexanes) to furnish the amine **35** (18.9 g, 98%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (m, 2 H, arom), 7.60 (m, 1 H, arom), 7.47 (m, 2 H, arom), 7.34-7.27 (m, 5 H, arom), 5.68 (d(br), 1 H, J = 2.6 Hz, H 4), 4.96 (d, 1 H, J = 7.1 Hz, OCH_2O), 4.74 (d, 1 H, J = 7.1 Hz, OCH_2O), 4.66 (d, 1 H, J = 11.7 Hz, $PhCH_2O$), 4.58 (d, 1 H, J = 7.6 Hz, H 1), 4.56 (d, 1 H, J = 11.7 Hz, $PhCH_2O$), 3.87 (dd(br), 1 H, J = 7.8, 5.6 Hz, H 5), 3.81 (dd, 1 H, J = 10.3, 2.6 Hz, H 3), 3.43 (dd,

1 H, J = 10.7, 5.4 Hz, H 6), 3.38 (dd, 1 H, J = 10.7, 7.8 Hz, H 6), 3.21 (dd, 1 H, J = 10.3, 7.6 Hz, H 2), 1.79 (m, 2 H, NH_2), 0.96 (s, 9 H, *t*-butyl), 0.22, 0.20 (2 x s, 2x 3 H, $Si(CH_3)_2$).

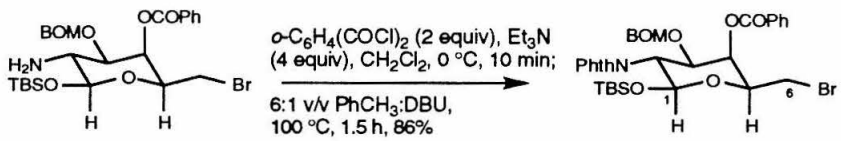
^{13}C NMR (300 MHz, $CDCl_3$) δ: 166.5, 137.3-127.8 (arom), 99.4, 93.1, 77.0, 74.3, 70.0, 67.6, 54.7, 29.7, 25.8, 17.0, -3.8, -5.1.

FTIR (neat film) cm^{-1}: 2928 (m), 2857 (m), 1722 (s), 1452 (w), 1271 (s), 1170 (m), 1109 (s), 1044 (s), 837 (s), 783 (m), 708 (m).

MS (FAB) *m/z*: 580 $(MH)^+$, 502 (M^+ - Br).

HRMS (FAB) *m/z*: Calcd for $C_{27}H_{39}NO_6BrSi$ $(MH)^+$: 580.1739. Found: 580.1730.

TLC R_f (50% EtOAc in hexanes): 0.20



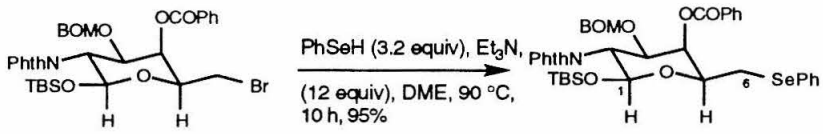
35 **36**

Phthalimide **36.**

A solution of the amine **35** (21.0 g, 36.5 mmol, 1 equiv) and triethylamine (20.0 mL, 146 mmol, 4.0 equiv) in dichloromethane (240 mL) at 0 °C was treated with phthaloyl dichloride (10.5 mL, 72.9 mmol, 2.0 equiv), then was stirred at 0°C for 10 min. The reaction solution was concentrated in vacuo, and the residue was diluted with a mixture of toluene and DBU (6:1 (v/v), 280 mL). The resulting green solution was heated at 100 °C for 1.5 h, then was cooled to 23 °C. Ethyl acetate (300 mL) was added, and the product solution was washed sequentially with water (2 x 100 mL) and saturated aqueous sodium chloride solution (100 mL). The organic layer was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (33% ethyl acetate in hexanes) to afford phthalimide **36** (22.1 g, 86%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (m, 2 H, ArH), 7.84-6.98 (m, 12 H, ArH), 5.85 (d(br), 1 H, J = 4.4 Hz, H 4), 5.52 (d, 1 H, J = 8.0 Hz, H 1), 4.88 (dd, 1 H, J = 11.5, 4.4 Hz, H 3), 4.84 (d, 1 H, J = 7.3 Hz, OCH_2O), 4.56 (dd, 1 H, J = 11.5, 8.0 Hz, H 2), 4.53 (d, 1 H, J = 7.3 Hz, OCH_2O), 4.18 (s, 2 H, Ph**C**$\mathbf{H_2}$O), 4.08 (m,

	1 H, H 5), 3.47 (m, 2 H, H 6), 0.72 (s, 9 H, *t*-butyl), 0.14, 0.01 (2 x s, 2 x 3 H, $Si(CH_3)_2$);
^{13}C NMR (400 MHz, $CDCl_3$) δ:	168.2, 167.5, 166.1, 137.2-123.1 (arom), 94.0, 94.0, 93.3, 74.4, 71.7, 69.7, 68.3, 54.9, 29.4, 25.4, 17.6, -4.0, -5.4.
FTIR (neat film) cm^{-1}:	2955 (m), 2858 (m), 1775 (m), 1715 (s), 1267 (s), 1175 (m), 1110 (s), 1039 (s), 837 (s), 783 (m), 721 (m).
MS (FAB) *m/z*:	708 $(M - H)^+$, 652 $(M - t\text{-butyl})^+$.
HRMS (FAB) *m/z*:	Calcd for $C_{35}H_{39}BrNO_8Si$ $(M^+ - H)$: 708.1628. Found: 708.1595.
TLC R_f (50% EtOAc in hexanes):	0.45



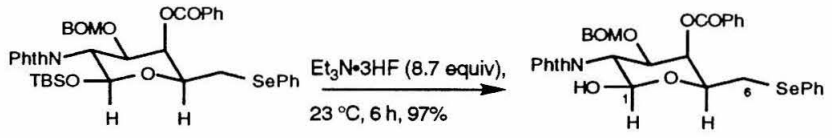
36 **37**

Phenylselenide **37.**

Benzeneselenol (10.6 mL, 100 mmol, 3.2 equiv) was added to a deoxygenated solution of bromide **36** (22.0 g, 31.2 mmol, 1 equiv) and triethylamine (50.0 mL, 359 mmol, 11.5 equiv) in anhydrous dimethoxyethane (280 mL), and the resulting solution was heated at 90 °C for 10 h. The reaction mixture was cooled to 23 °C, then was diluted with ethyl ether (300 mL). The resulting solution was washed sequentially with water (100 mL) and saturated aqueous sodium chloride solution (100 mL). The organic layer was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (25% ethyl acetate in hexanes) to afford the phenylselenide **37** (23.3 g, 95%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (m, 2 H, arom), 7.84-6.98 (m, 17 H, arom), 5.78 (d(br), 1 H, J = 3.4 Hz, H 4), 5.74 (d, 1 H, J = 8.1 Hz, H 1), 4.84 (dd, 1 H, J = 11.2, 3.4 Hz, H 3), 4.82 (d, 1 H, J = 7.6 Hz, OCH_2O), 4.57 (dd, 1 H, J = 11.2, 8.1 Hz, H 2), 4.51 (d, 1 H, J = 7.6 Hz, OCH_2O), 4.17 (s, 2 H, Ph$\mathbf{CH_2}$O), 3.98 (ddd, 1 H, J = 8.6, 5.1, 1.0 Hz, H 5), 3.21 (dd, 1 H, J = 12.9, 8.6 Hz, H 6), 3.01 (dd, 1 H, J = 12.9,

	5.1 Hz, H 6), 0.71 (s, 9 H, *t*-butyl), 0.15, 0.02 (2 x s, 2 x 3 H, $Si(CH_3)_2$).
^{13}C NMR (300 MHz, $CDCl_3$) δ:	168.6, 168.0, 166.2, 137.1-123.0 (arom), 93.9, 93.0, 73.6, 71.6, 69.6, 54.9, 28.1, 25.4, 17.5, -3.9, -5.5; IR (neat film) 2928 (m), 2849 (m), 1775 (m), 1715 (s), 1469 (w), 1389 (s), 1266 (s), 1173 (m), 1113 (s), 1038 (s), 839 (s), 783 (m), 721 (m).
MS (FAB) *m/z*:	786 (M^+ - H), 730 (M^+ - *t*-butyl).
HRMS (FAB) *m/z*:	Calcd for $C_{41}H_{44}NO_8SeSi$ (M^+ - H): 786.2001. Found: 786.2013.
TLC R_f (25% EtOAc in hexanes):	0.40



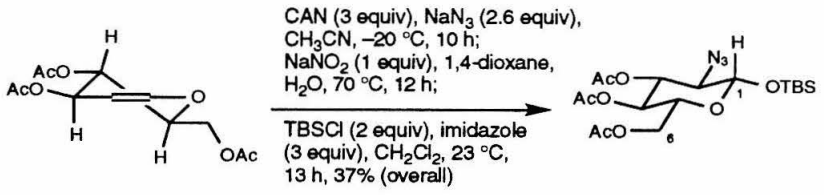
37 **38**

Hemiacetals **38.**

Triethylamine trihydrofluoride (40.0 mL, 250 mmol, 8.7 equiv) was added to a solution of the phenylselenide **37** (22.5 g, 28.6 mmol, 1 equiv) in acetonitrile (120 mL) contained in a 300-mL polyethylene reaction vessel. The resulting solution was stirred at 23 °C for 6 h, then was partitioned between ethyl acetate (200 mL) and water (100 mL). The organic phase was washed sequentially with water (100 mL) and saturated aqueous sodium chloride solution (100 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (gradient elution: 25 → 50% ethyl acetate in hexanes) to afford **38** as a mixture of anomers (>10:1; β:α, 18.6 g, 97%) as a colorless oil. The β-anomer could be fractionally crystallized (ethyl acetate in hexanes) to give white needles (mp 69.0–71.0 °C).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (m, 2 H, arom), 7.83-6.97 (m, 17 H, arom), 5.88 (d(br), 1 H, J = 2.9 Hz, H 4), 5.53 (t(br), 1 H, J ~ 8.1 Hz, H 1), 4.87 (dd, 1 H, J = 11.0, 3.2 Hz, H 3), 4.84 (d, 1 H, J = 7.3 Hz, OCH_2O), 4.56 (dd, 1 H, J = 11.2, 8.5 Hz, H 2), 4.52 (d, 1 H, J = 7.3 Hz, OCH_2O), 4.16 (s, 2 H, Ph**C**$\mathbf{H_2}$O), 4.02 (t(br), 1 H, J ~ 6.8 Hz, H 5), 4.74 (d(br), 1 H, J =

	7.5 Hz, OH), 3.19 (dd, 1 H, J = 12.9, 7.3 Hz, H 6), 3.02 (dd, 1 H, J = 12.9, 6.3 Hz, H 6).
^{13}C NMR (400 MHz, C_6D_6) δ:	169.0, 168.2, 166.3, 137.9-123.2 (arom), 93.9, 93.4, 74.3, 72.5, 69.8, 54.9, 28.6.
FTIR (neat film) cm^{-1}:	3600-3300 (s), 3062 (m), 2857 (m), 1773 (m), 1714 (s), 1602 (w), 1453 (w), 1392 (s), 1268 (s), 1176 (m), 1114 (s), 1025 (s), 720 (m).
MS (FAB) *m/z*:	673 $(M)^+$, 626 (M^+ - OH), 566 (M^+ - $C_6H_5CH_2O$).
HRMS (FAB) *m/z*:	Calcd for $C_{35}H_{31}NO_8Se$ $(M)^+$: 673.1191. Found: 673.1215.
TLC R_f (33% EtOAc in hexanes):	0.40



39 **40**

2-Deoxy-2-azidoglucopyranoside **40.**

A solution of triacetoxy-D-glucal (**39**) (25.0 g, 91.9 mmol, 1 equiv) in acetonitrile (500 mL) at –40 °C was added via cannula to a powdered mixture of ceric ammonium nitrate (150 g, 274 mmol, 3 equiv) and sodium azide (10 g, 154 mmol, 2.6 equiv) at –20 °C over a 20-min period. The resulting orange slurry was stirred at –20 °C for 1.5 h, whereupon a second portion of sodium azide (4.7 g, 72.3 mmol, 0.8 equiv) was added to the reaction mixture. The resulting suspension was stirred for 3 h at –20 °C, and a third portion of sodium azide (4.7 g, 72.3 mmol, 0.8 equiv) was added, and the whole was stirred for an additional 5 h. Ethyl ether (2 L) was added, and the product solution was washed sequentially with water (2 x 1 L) and saturated aqueous sodium chloride solution (1 L). The combined organic layers were dried (magnesium sulfate) and concentrated. The residue was dissolved in a solution of 1,4-dioxane in water (3.5:1 (v/v), 450 mL), and sodium nitrite (6.5 g, 94.2 mmol, 1.0 equiv) was added. The resulting solution was heated at 80 °C 12 h, then was concentrated in vacuo to a volume of 100 mL. The product was extracted with three 200-mL portions of ethyl ether, and the combined organic layers were dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (33% ethyl acetate in hexanes), and the purified anomeric alcohols were dissolved in dichloromethane (130 mL). The resulting solution was treated sequentially

with imidazole (12.3 g, 181 mmol, 2 equiv) and *t*-butyldimethylsilyl chloride (18.2 g, 121 mmol, 1.3 equiv). After stirring at 23 °C for 13 h, the reaction mixture was partitioned between water (500 mL) and dichloromethane (500 mL), and the combined organic layers were dried (magnesium sulfate) and concentrated. Purification of the residue by flash column chromatography (25% ethyl acetate in hexanes) afforded the pure β-*O*-*t*-butyldimethylsilyl ether **40** as a viscous oil (14.7 g) in 37% yield from **39**.

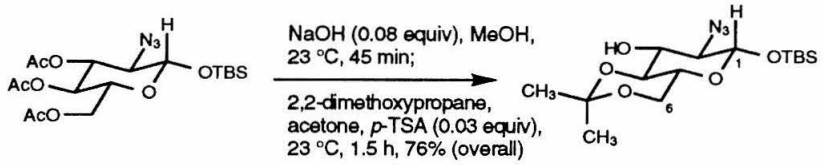
^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.07 (m, 2 H, H 3,4), 4.64 (d, 1 H, J = 7.7 Hz, H 1), 4.20 (dd, 1 H, J = 12.1, 6.0 Hz, H 6), 4.12 (dd, 1 H, J = 12.1 2.6 Hz, H 6), 3.68 (m, 1 H, H 5), 3.44 (dd, 1 H, J = 10.3, 7.7 Hz, H 2), 2.09 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 0.94 (s, 9 H, *t*-butyl), 0.17 (s, 6 H, 2 x $SiCH_3$).

FTIR (neat film) cm^{-1}: 2932 (w), 2859 (w), 2113 (s), 1755 (s), 1366 (m), 1228 (s), 1051 (s), 841 (s), 785 (m).

MS (FAB) *m/z*: 446 $(MH)^+$, 430 (M^+ - CH_3), 388 (M^+ - *t*-butyl), 314 (M^+ - OTBS).

HRMS (FAB) *m/z*: Calcd for $C_{18}H_{32}N_3O$-8Si $(MH)^+$: 446.1959. Found: 446.1970.

TLC R_f (25% EtOAc in hexanes): 0.26



40 **41**

4,6-*O*-Isopropylidene Glucopyranoside **41**.

Sodium hydroxide (100 mg, 2.50 mmol, 0.08 equiv) was added to a solution of triacetate **40** (14.50 g, 32.6 mmol, 1 equiv) in methyl alcohol (100 mL), and the resulting solution was stirred at 23 °C for 45 min. The base catalyst was neutralized by the addition of Amberlyst IR-45 acidic ion-exchange resin (2.5 g); after stirring for 5 min, the solids were removed by filtration. The filtrate was concentrated, and the residue, together with crushed activated 5Å molecular sieves (9.5 g), was diluted with a solution of acetone and 2,2-dimethoxypropane (5:1 (v/v), 120 mL). The resulting suspension was stirred at 23 °C for 40 min, then solid *p*-toluenesulfonic acid monohydrate (200 mg, 1.05 mmol, 0.03 equiv) was added, and the reaction mixture was stirred at 23 °C for 1.5 h. The acid catalyst was quenched by the addition of triethylamine (2.0 mL), and the solids were removed by filtration. The filtrate was concentrated, and the residue was purified by flash column chromatography (25% ethyl acetate in hexanes) to afford **41** (8.90 g, 76%) as a viscous oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.58 (d, 1 H, J = 10.2 Hz, H 1), 3.86 (dd, 1 H, J = 7.0, 14.8 Hz, H 6), 3.76 (t, 1 H, J = 14.8 Hz, H 6), 3.57 (t, 1 H, J = 12.5 Hz, H 4), 3.45 (ddd, 1 H, J = 3.6, 10.2, 12.5 Hz, H 3), 3.26 (dd, 1 H, J = 10.2, 12.5 Hz, H 2), 3.23 (m, 1 H, H 5), 2.89 (d, 1 H, J

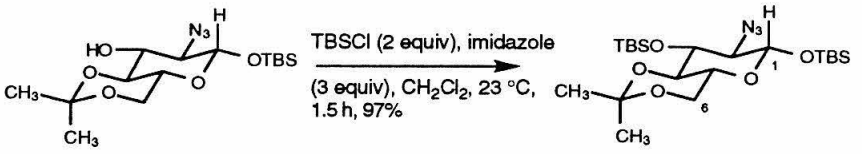
= 3.6 Hz, OH), 1.50 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 0.90 (s, 9 H, *t*-butyl), 0.15 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3458 (m, br), 2931 (m), 2860 (m), 2112 (s), 1473 (w), 1382 (m), 1267 (m), 1198 (m), 1181 (m), 1096 (s), 1039 (m), 966 (m), 842 (s), 784 (m), 682 (w).

MS (FAB) *m/z*: 360 $(MH)^+$, 344 (M^+ - CH_3), 302 (M^+ - *t*-butyl), 228 (M^+ - OTBS).

HRMS (FAB) *m/z*: Calcd for $C_{15}H_{30}N_3O_6Si$ $(MH)^+$: 360.1955. Found: 360.1974.

TLC R_f (50% EtOAc in hexanes): 0.59



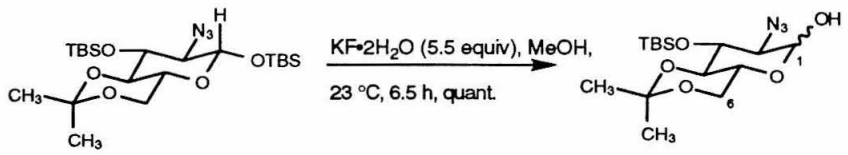
41 **42**

Bis(TBS) Glucopyranoside **42**.

Solid *t*-butyldimethylsilyl chloride (7.45 g, 49.4 mmol, 2.0 equiv) was added to a solution of the glucopyranoside **41** (8.87 g, 24.7 mmol, 1 equiv) and imidazole (5.04 g, 74.1 mmol, 3.0 equiv) in dichloromethane (100 mL) at 23 °C. The reaction mixture was stirred at 23 °C for 1.5 h, then was partitioned between dichloromethane (100 mL) and water (100 mL). The organic layer was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (10% ethyl acetate in hexanes) to give **42** (11.10 g, 95%) as clear, colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.52 (d, 1 H, *J* = 10.3 Hz, H 1), 3.85 (dd, 1 H, *J* = 7.1, 14.1 Hz, H 6), 3.75 (t, 1 H, *J* = 14.1 Hz, H 6), 3.48 (t, 1 H, *J* = 12.1 Hz, H 4), 3.38 (t, 1 H, *J* = 12.1 Hz, H 3), 3.16 (dd, 1 H, *J* = 10.3, 12.1 Hz, H 2), 3.16 (m, 1 H, H 5), 1.45 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 0.93 (s, 9 H, *t*-butyl), 0.90 (s, 9 H, *t*-butyl), 0.14 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.10 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}:	2931 (m), 2859 (m), 2111 (s), 1472 (w), 1380 (w), 1258 (m), 1126 (s), 1094 (s), 968 (w), 836 (s), 781 (m).
MS (FAB) *m/z*:	474 $(MH)^+$, 472 $(M^+ - H)$, 458 $(M^+ - CH_3)$, 416 $(M^+$ - *t*-butyl).
HRMS (FAB) *m/z*:	Calcd for $C_{21}H_{42}N_3O_5Si_2$ $(MH)^+$: 472.2663,. Found: 472.2675.
TLC R_f (25% EtOAc in hexanes):	0.67



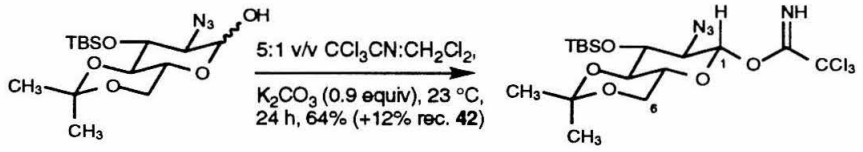
42 **43**

Glucosyl Hemiacetal **43.**

Solid potassium fluoride hydrate (12.0 g, 127.5 mmol, 5.5 equiv) was added to a solution of **42** (11.0 g, 23.3 mmol, 1 equiv) in methyl alcohol (100 mL), and the resulting solution was stirred at 23 °C for 6.5 h. The reaction mixture was partitioned between ethyl acetate (700 mL) and water (300 mL). The organic layer was washed with saturated aqueous sodium chloride solution (300 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (25% ethyl acetate in hexanes) to afford a mixture of the hemiacetals **43** (α:β 2:1, 8.49 g, quantitative) as a clear, colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.30 (t, 1 H, *J* = 3.6 Hz, H 1α), 5.11 (d, 1 H, *J* ~ 1 Hz, OHβ), 4.62 (dd, 1 H, *J* = 1, 8.0 Hz, H 1β), 4.19 (dd, 1 H, *J* = 4.0, 8.4 Hz, H 6β), 4.0 - 3.6 (m, H 6α&β, OHα), 3.55 - 3.40 (m, H 3, 4α&β), 3.30 - 3.10 (m, H 5, 2 α&β), 1.47 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 0.92 (s, 9 H, *t*-butyl), 0.90 (s, 9 H, *t*-butyl), 0.16 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H,

	$SiCH_3$), 0.11 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$).
FTIR (neat film) cm^{-1}:	3391 (w, br), 2930 (m), 2859 (m), 2111 (s), 1472 (w), 1383 (w), 1267 (m), 1124 (m), 1088 (s), 838 (s).
MS (FAB) *m/z*:	360 $(MH)^+$, 344 (M^+ - CH_3), 302 (M^+ - *t*-butyl), 228 (M^+ - OTBS).
HRMS (FAB) *m/z*:	Calcd for $C_{15}H_{30}N_3O_5Si$: $(MH)^+$ 360.1955. Found: 360.1960.
TLC R_f (50% EtOAc in hexanes):	0.57



43 **44**

β-Trichloroacetimidate **44.**

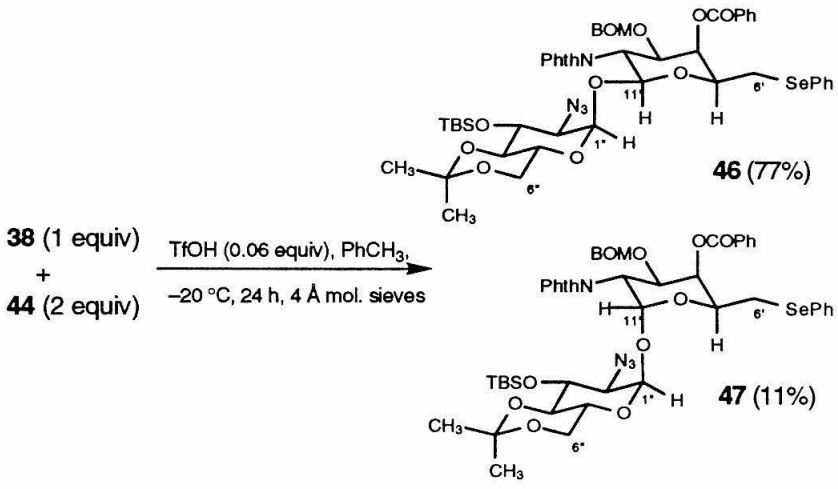
Potassium carbonate (3.0 g, 21.7 mmol, 0.9 equiv) was added to a solution of the hemiacetals **43** (8.40 g, 23.4 mmol, 1 equiv) in a mixture of dichloromethane and trichloroacetonitrile (5:1 (v/v), 120 mL), and the resulting solution was stirred at 23 °C for 24 h. Precipitated solids were removed by filtration, and the filtrate was concentrated. The residue was purified by flash column chromatography (10% ethyl acetate in hexanes containing 2% triethylamine) to afford **44** (7.53 g, 64%). Unreacted starting material **43**, (1.0 g, 12%) was recovered in separate fractions.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.73 (s, 1 H, NH), 5.67 (d, 1 H, J = 6.7 Hz, H 1), 3.97 (dd, 1 H, J = 4.8, 12.1 Hz, H 6), 3.79 (t, 1 H, J = 12.1 Hz, H 6), 3.55 (m, 3 H, H 2, 3, 4), 3.35 (m, 1 H, H 5), 1.48 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 0.90 (s, 9 H, *t*-butyl), 0.14 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3347 (w), 2930 (m), 2858 (m), 2113 (s), 1679 (s), 1472 (w), 1373 (m), 1267 (s), 1203 (m), 1173 (m),

1065 (s), 971 (m), 835 (s), 798 (s), 781 (s), 647 (m).

TLC R_f (20% EtOAc in hexanes): 0.30



β,α-Trehalose Disaccharide **46.**

Hemiacetal **38** (0.90 g, 1.34 mmol, 1 equiv), imidate **44** (1.33 g, 2.64 mmol, 2.0 equiv), crushed 4 Å molecular sieves (2 g), and toluene (10 mL) were combined, and the mixture was stirred at 23 °C for 2 h. The suspension was cooled to –20 °C, and 6 aliquots of a solution of trifluoromethanesulfonic acid in toluene (5% (v/v), 300 μL-aliquots, 0.17 mmol each, 0.06 equiv each) were added dropwise at 4-hour intervals over a 24-hour period. The acid catalyst was neutralized by the addition of triethylamine (100 μL), and the reaction mixture was diluted with ethyl acetate (50 mL). The product solution was filtered through a pad of Celite and was concentrated. The residue was purified by flash column chromatography (25% ethyl acetate in hexanes) to provide disaccharide **46** (1.04 g, 77%), as well as the α,α-trehalose coupling product **47** (149 mg, 11%) in separate fractions, both as colorless oils.

46:

^{1}H NMR (400 MHz, C_6D_6) δ: 8.24 (m, 2 H, arom), 7.64 (m, 1 H, arom), 7.57 (m, 1 H, arom), 7.48 (m, 2 H, arom), 7.08-6.87 (m, 13 H, arom), 5.67 (d(br), 1 H, *J* = 3.2 Hz, H 8'), 5.64 (d, 1 H, *J* = 8.8 Hz, H 11'), 5.24 (dd, 1 H, *J* = 11.0, 8.8 Hz, H 10'), 4.94 (dd, 1 H, *J* = 11.0, 3.2 Hz, H 9'), 4.83 (d, 1 H, *J* = 3.7 Hz, H 1''), 4.81 (d, 1 H, *J* = 7.3 Hz, OCH_2O), 4.43 (d, 1 H, *J* = 7.3 Hz, OCH_2O-, 4.27 (d, 1 H, *J* = 12.2 Hz, $PhCH_2O$), 4.26 (m, 2 H, H 6''), 4.10 (d, 1 H, *J* = 12.2 Hz, $PhCH_2O$), 3.98 (t, 1 H, *J* = 9.0 Hz, H 3''), 3.65 (m, 2 H, H 5, H 5''), 3.29 (t, 1 H, *J* = 9.6, H 4''), 3.25 (dd, 1 H, *J* = 12.5, 9.0 Hz, H 6'), 2.88 (dd, 1 H, *J* = 12.5, 4.4 Hz, H 6'), 2.82 (dd, 1 H, *J* = 9.5, 3.7 Hz, H 2''), 1.39, 1.24 (2 x s, 2 x 3 H, $C(CH_3)_2$), 0.97 (s, 9 H, *t*-butyl), 0.08, 0.06 (2 x s, 2 x 3 H, $Si(CH_3)_2$).

^{13}C NMR (100 MHz, C_6D_6) δ: 169.2, 167.7, 166.2, 137.8-123.0 (arom), 101.3, 101.1, 99.4, 93.3, 74.8, 74.5, 72.3, 71.2, 69.7, 69.4, 66.4, 65.2, 62.5, 53.2, 29.1, 26.1, 25.9, 19.0, 18.3, -4.2, -5.1.

FTIR (neat film) cm^{-1}: 2952 (s), 2856 (s), 2107 (s), 1778 (m), 1714 (s), 1580 (w), 1470 (m), 1392 (s), 1265 (s), 1125 (s), 1025 (s), 970 (m), 865 (s), 720 (s).

MS (FAB) *m/z*: 957 (M^+ - *t*-butyl), 156 $(PhSe)^+$.

Elemental Analysis: Calcd for $C_{50}H_{58}N_4O_{12}SeSi$: C, 59.22; H, 5.77; N, 5.52.
Found: C, 59.13; H, 5.79; N, 5.71.

TLC R_f (25% EtOAc in hexanes): 0.36

47:

^1H NMR (400 MHz, C_6D_6) δ: 8.33 (m, 2 H, arom), 7.67 (m, 1 H, arom), 7.57 (m, 2 H, arom), 7.48 (m, 1 H, arom), 7.17-6.86 (m, 13 H, arom), 6.09 (d, 1 H, *J* = 3.2 Hz, H 8'), 5.92 (dd, 1 H, *J* = 11.5, 3.2 Hz, H 9'), 5.69 (d, 1 H, *J* = 3.9 Hz, H 11'), 5.48 (dd, 1 H, *J* = 11.5, 3.9 Hz, H 10'), 5.38 (d, 1 H, *J* = 3.4 Hz, H 1"), 4.87 (d, 1 H, *J* = 7.0 Hz, OCH_2O), 4.83 (d, 1 H, *J* = 7.0 Hz, OCH_2O), 4.82 (m, 1 H, H 6"), 4.46 (d, 1 H, *J* = 12.2 Hz, $PhCH_2O$), 4.38 (d, 1 H, *J* = 12.2 Hz, $PhCH_2O$), 4.27 (dd, 1 H, *J* = 9.5, 8.8 Hz, H 6"), 3.32 (dd, 1 H, *J* = 12.9, 9.5 Hz, H 3"), 3.26 (m, 2 H, H 6', 7'), 3.19 (t, 1 H, *J* = 9.5 Hz, H 4"), 3.12

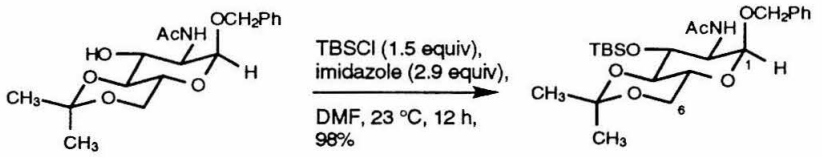
(m, 1 H, H 5"), 2.99 (dd, 1 H, J = 12.9, 3.4 Hz, H 2"), 2.96 (dd, 1 H, J = 9.8, 3.4 Hz, H 6'), 1.18 (s, 9 H, *t*-butyl), 1.08 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.57 (s, 3 H, $SiCH_3$), 0.42 (s, 3 H, $SiCH_3$).

^{13}C NMR (100 MHz, C_6D_6) δ: 168.7, 167.9, 166.1, 138.3-123.4 (arom), 99.0, 94.8, 94.1, 93.1, 74.7, 71.9, 71.7, 70.7, 70.4, 70.3, 65.2, 65.1, 62.0, 52.1, 29.0, 28.9, 26.1, 18.7, 18.6, -3.9, -4.6.

FTIR (neat film) cm^{-1}: 2950 (w), 2856 (w), 2108 (s), 1775 (w), 1722 (s), 1470 (w), 1386 (m), 1267 (s), 1135 (m), 1071 (m), 970 (m), 869 (m), 711 (m).

MS (FAB) *m/z*: 656 (galactosyl hemiacetal **37** - OH)$^+$, 156 (PhSe)$^+$, 131 (OTBS)$^+$.

TLC R_f (25% EtOAc in hexanes): 0.22



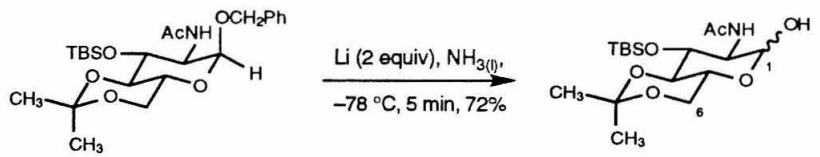
48 **49**

N-Acetylglucopyranoside **49**.

Imidazole (3.90 g, 57.4 mmol, 2.9 equiv) and *t*-butyldimethylsilyl chloride (4.53 g, 29.9 mmol, 1.5 equiv) were added sequentially to a solution of *N*-acetylglucosamine derivative **48** (7.00 g, 19.9 mmol, 1 equiv) in *N,N*-dimethylformamide (50 mL), and the resulting solution was stirred at 23 °C for 12 h. The reaction mixture was partitioned between water (100 mL) and ethyl acetate (100 mL). The organic layer was washed with saturated aqueous sodium chloride solution (50 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (gradient elution: 33% → 50% ethyl acetate in hexanes) to afford **49** (9.13 g, 98%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 (m, 5 H, arom), 5.50 (d, 1 H, J = 9.8 Hz, NH), 4.83 (d, 1 H, J = 3.9 Hz, H 1), 4.68 (d, 1 H, J = 12.0 Hz, PhC**H**$_2$), 4.44 (d, 1 H, J = 12.0 Hz, PhC**H**$_2$), 4.23 (dt, 1 H, J = 9.8, 3.9 Hz, H 2), 3.82 (dd, 1 H, J = 10.0, 4.9 Hz, H 6), 3.74 (t, 1 H, J = 10.0 Hz, H 6), 3.68 (t, 1 H, J = 9.8 Hz, H 3), 3.67 (m, 1 H, H 5), 3.57 (t, 1 H, J = 9.8 Hz, H 4), 1.93 (s, 3 H, Ac), 1.47 (s, 3 H, CH_3), 1.40 (s, 3 H,

	CH_3), 0.84 (s, 9 H, *t*-butyl), 0.04 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$).
^{13}C NMR (100 MHz, $CDCl_3$) δ:	169.3, 136.9, 128.4, 128.1, 128.0, 99.2, 97.6, 74.7, 71.0, 69.5, 63.8, 62.2, 53.8, 28.9, 25.5, 23.2, 18.8, 18.0, -4.2, -5.1.
FTIR (neat film) cm^{-1}:	3291 (m), 2928 (s), 2856 (m), 1653 (s), 1552 (m), 1374 (m), 1200 (m), 1131 (s), 1042 (s), 838 (s).
MS (FAB) *m/z*:	466 $(MH)^+$, 450 (M^+ - CH_3), 408 (M^+ - *t*-butyl), 350 (M^+ - $PhCH_2O$).
HRMS (FAB) *m/z*:	Calcd for $C_{24}H_{40}NO_6Si$ $(MH)^+$: 466.2625. Found: 466.2604.
TLC R_f (33% EtOAc in hexanes):	0.39



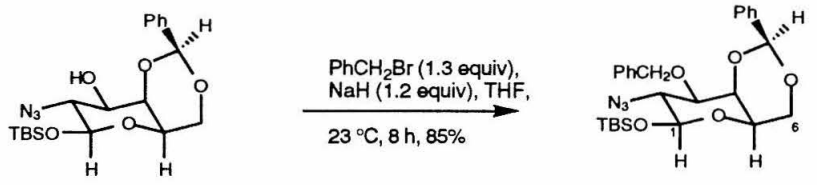
49 **50**

N-Acetylglucosyl Hemiacetal **50**.

A solution of **49** (0.98 g, 2.1 mmol, 1 equiv) in tetrahydrofuran (15 mL) was added dropwise via cannula to a solution of lithium metal (30 mg, 4.3 mmol, 2 equiv) in freshly distilled liquid ammonia (75 mL) at –78 °C. The resulting solution was stirred at –78 °C for 5 min, whereupon excess solid ammonium chloride (3 g) was added. The reaction mixture was allowed to warm slowly to 23 °C and was stirred at this temperature for 2 h to allow the solvent ammonia to evaporate. The residue was further concentrated in vacuo, then was purified by flash column chromatography (100% ethyl acetate) to afford an anomeric mixture of hemiacetals **50** (2:1 α:β, 0.60 g, 72%) as a viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.72 (d, 1 H, *J* = 9.5 Hz, NHα), 5.68 (d, 1 H, *J* = 5.9 Hz, NHβ), 5.19 (d, 1 H, *J* = 3.7 Hz, H 1α), 4.62 (d, 1 H, *J* = 8.0 Hz, H 1β), 4.14 (m, 2 H, H 2α,2b), 3.94 (dd, 1 H, *J* = 11.0, 5.4 Hz, H 6β), 3.8-3.5 (m), 3.24 (m, 1 H, H 5β), 2.05 (s, 3 H, Acβ), 2.00 (s, 3 H, Acα), 1.47 (s, 6 H, CH_3α&β), 1.40 (s, 6 H, CH_3α&β), 0.87 (s, 9 H, *t*-butylβ), 0.85 (s, 9 H, *t*-butylα), 0.10 (s, 3 H, $SiCH_3$β),

	0.09 (s, 3 H, $SiCH_3\beta$), 0.06 (s, 3 H, $SiCH_3\alpha$), 0.05 (s, 3 H, $SiCH_3\alpha$).
FTIR (neat film) cm^{-1}:	3300 (m, br), 2930 (m), 2856 (m), 1654 (s), 1534 (m), 1377 (s), 1200 (s), 1130 (s), 965 (w), 868 (s).
MS (FAB) *m/z*:	376 $(MH)^+$, 318 (M^+ - *t*-butyl), 268 (M^+ - $PhCH_2O$), 244 (M^+ - OTBS).
HRMS (FAB) *m/z*:	Calcd for $C_{17}H_{35}NO_6Si$ $(MH)^+$: 376.2155. Found: 376.2144.
TLC R_f (100% EtOAc):	0.40



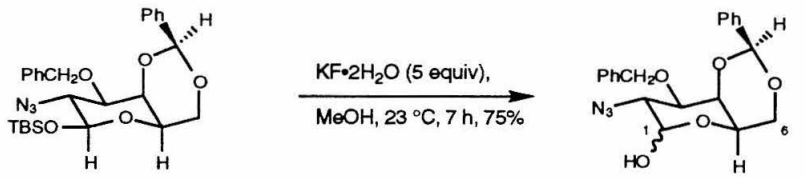
32 **51**

2-Azido-2-deoxygalactopyranoside **51.**

A solution of alcohol **32** (1.66 g. 4.1 mmol, 1 equiv) in tetrahydrofuran (25 mL) was added via cannula to a suspension of sodium hydride (120 mg, 4.9 mmol, 1.2 equiv) in tetrahydrofuran (10 mL), and the resulting mixture was stirred at 23 °C for 15 min. Benzyl bromide (630 μL, 5.3 mmol, 1.3 equiv) was added, and the heterogeneous reaction mixture was heated at 60 °C for 10 h. The suspension was diluted with ethyl ether (200 mL), and the resulting ethereal solution was filtered through a short column of Celite. The filtrate was concentrated, and the residue was purified by flash column chromatography (15% ethyl acetate in hexanes) to provide **51** (1.72 g, 85%) as a pale yellow viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (m, 2 H, arom), 7.37 (m, 8 H, arom), 5.47 (s, 1 H, benzylidene acetal), 4.74 (s, 2 H, $PhCH_2$), 4.52 (d, 1 H, J = 7.8 Hz, H 1), 4.24 (dd, 1 H, J = 12.2, 1.2 Hz, H 6), 4.06 (d(br), 1 H, J = 3.7 Hz, H 4), 4.00 (dd, 1 H, J = 12.2, 1.7 Hz, H 6), 3.78 (dd, 1 H, J = 10.5, 7.8 HZ, H 2), 3.32 (dd, 1 H, J = 10.5, 3.7 Hz, H 3), 3.28 (s(br), 1 H, H 5), 0.97 (s,

	9 H, *t*-butyl), 0.19 (s, 3 H, $SiCH_3$), 0.17 (s, 3 H, $SiCH_3$).
FTIR (neat film) cm^{-1}:	2929 (w), 2857 (w), 2112 (s), 1454 (w), 1402 (w), 1365 (w), 1284 (w), 1253 (w), 1174 (m), 1108 (s), 1059 (m), 997 (m), 837 (s), 783 (w), 697 (m).
MS (FAB) *m/z*:	496 (M^+ - H), 440 (M^+ - *t*-butyl), 420 (M^+ - C_6H_5).
HRMS (FAB) *m/z*:	Calcd for $C_{26}H_{34}N_3O_5Si$ (M^+ - H): 496.2268. Found: 496.2289.
TLC R_f (25% EtOAc in hexanes):	0.44



51 **52**

Galactosyl Hemiacetal **52.**

Solid potassium fluoride hydrate (0.93 g, 9.9 mmol, 5.0 equiv) was added to a solution of **51** (0.98 g, 1.97 mmol, 1 equiv) in methyl alcohol (40 mL), and the resulting solution was stirred at 23 °C for 7 h. Ethyl acetate (100 mL) was added, and the resulting solution was washed sequentially with water (2 x 100 mL) and saturated aqueous sodium chloride solution (100 mL). The organic phase was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (50% ethyl acetate in hexanes) to afford an anomeric mixture of hemiacetals **52** (1.5:1 α:β, 0.57 g, 75%) as a colorless oil.

^{1}H NMR (300 MHz, C_6D_6) δ: 7.8-7.2 (m, arom), 5.26 (s, 2 H, benzylidene acetal α&β), 4.86 (t(br), 1 H, J = 3.3 Hz, H 1α), 4.54 (s, 2 H, PhC**H**$_2$ β), 4.52 (s, 2 H, PhC**H**$_2$ α), 4.16 (t, 1 H, J = 9.2 Hz, H 1β), 4.07 (d(br), 1 H, J = 11.8 Hz, H 3α), 4.05 (d(br), 1 H, J = 12.3 Hz, H 6β), 3.89 (s,(br), 2 H, H 6α), 3.74 (s(br), 1 H, H 4α), 3.70 (dd, 1 H, J = 10.2, 9.2 Hz, H 2β), 3.51 (d, 1 H, J = 3.0 Hz, H 4β), 3.42 (d(br), 1 H, J = 11.8

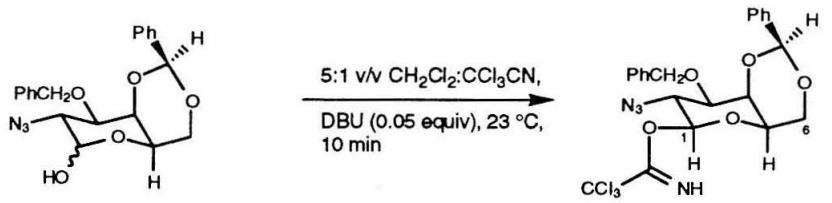
Hz, H 2α), 3.32 (d(br), 1 H, J = 12.3 Hz, H 6β), 3.28 (s(br), 1 H, H 5α), 3.01 (dd, 1 H, J = 10.2, 3.0 Hz, H 3β), 2.59 (d, 1 H, J = 9.2 Hz, OHβ), 2.31 (s, 1 H, H 5β), 2.00 (d, 1 H, J = 3.8 Hz, OHα).

FTIR (neat film) cm^{-1}: 3420 (w, br), 3049 (w), 2867 (w), 2112 (s), 1454 (w), 1363 (w), 1249 (w), 1170 (w), 1099 (m), 1049 (m), 995 (m), 744 (m), 698 (m).

MS(FAB) *m/z*: 384 $(MH)^+$, 366 (M^+ - OH), 341 (M^+ - N_3).

HRMS (FAB) *m/z*: Calcd for $C_{20}H_{22}N_3O_5$ $(MH)^+$: 384.1559. Found: 384.1548.

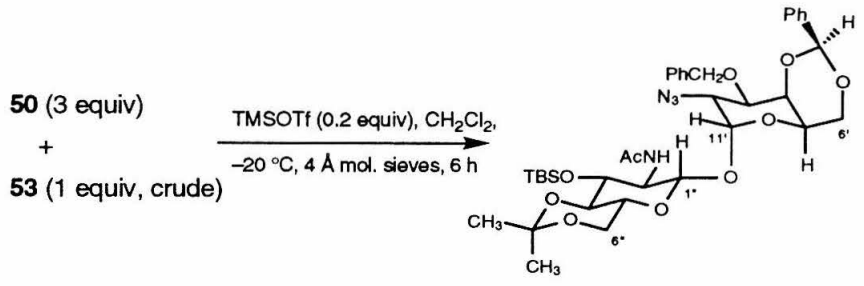
TLC R_f (50% EtOAc in hexanes): 0.34



52 **53** (crude)

Galactosyl Trichloroacetimidate **53.**

DBU (10 μL, 0.07 mmol, 0.05 equiv) was added to a solution of hemiacetals **52** (500 mg, 1.31 mmol, 1 equiv) in a mixture of trichloroacetonitrile and dichloromethane (1:5 (v/v), 12 mL). The resulting solution was stirred at 23 °C for 10 min, then volatiles were removed in vacuo. The residue was filtered through a short column of silica gel, eluting with 33% ethyl acetate in hexanes containing 2% triethylamine to afford the trichloroacetimidate **53**, which was used in the following glycosylation reaction without further purification.



54 (5%)

α,β-Disaccharide **54**.

The crude trichloroacetimidate from the previous experiment (**53**, 137 mg, ~0.26 mmol, ~1 equiv), hemiacetals **50** (308 mg, 0.79 mmol, 3.0 equiv), dichloromethane (2 mL), and crushed, activated 4Å molecular sieves (200 mg) were combined, and the resulting suspension was stirred at 23 °C for 2 h. The suspension was cooled to –20 °C, and a solution of trimethylsilyltrifluormethane sulfonate (5% (v/v) in dichloromethane, 250 μL, 0.14 mmol, 0.2 equiv total) was added portion-wise at 1-hour intervals over a 5-h period. The suspension was diluted with ethyl ether (10 mL) and was allowed to warm to 23 °C. Solids were removed by filtration through a short column of Celite, and the filtrate was concentrated. The residue was purified by flash column chromatography (50% ethyl acetate in hexanes) to provide disaccharide **54** (12 mg, 5%) and recovered **52** (76 mg, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.5-7.2 (m, 10 H, arom), 5.62 (d, 1 H, J = 7.8 Hz, NH), 5.44 (s, 1 H, benzylidene acetal), 5.16 (d, 1 H, J = 3.2 Hz, H 11'), 5.15 (d, 1 H, J = 8.5 Hz, H 1"), 4.71 (s, 2 H, PhC**H**$_2$), 4.17 M, 2 H, H 6', 8'), 4.14 (dd, 1 H, J = 10.3, 9.5 Hz, H 3"), 3.95

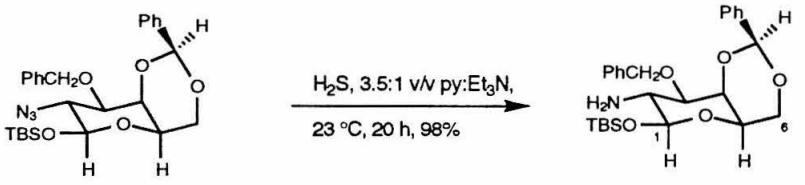
(m, 3 H, H 6', 9', 10'), 3.83 (m, 2 H, H 6", 7'), 3.69 (t, 1 H, J = 10.3 Hz, H 4"), 3.40 (t, 1 H, J = 10.4 Hz, H 6"), 3.33 (m, 1 H, H 5"), 3.22 (m, 1 H, H 2"), 1.98 (s, 3 H, Ac), 1.45 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 0.87 (s, 9 H, *t*-butyl), 0.06 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3286 (w), 2928 (w), 2856 (w), 2113 (s), 1657 (s), 1556 (w), 1372 (m), 1249 (m), 1099 (s), 1040 (s), 860 (m), 697 (m).

MS (FAB) *m/z*: 741 $(MH)^+$, 683 (M^+ - *t*-butyl).

HRMS (FAB) *m/z*: Calcd for $C_{37}H_{53}N_4O_{10}Si$ $(MH)^+$: 741.3531. Found: 741.3550.

TLC R_f (50% EtOAc in hexanes): 0.28



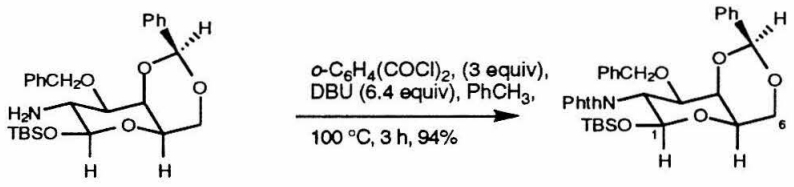
51 **55**

Galactosamine **55.**

Hydrogen sulfide gas was bubbled through a solution of azido sugar **51** (500 mg, 1.01 mmol, 1 equiv) in a mixture if pyridine and triethylamine (3.5:1 (v/v), 40 mL) at 23 °C for 20 h. Volatiles were removed in vacuo at 23 °C, and the residue was partitioned between water (100 mL) and ethyl ether (100 mL). The organic layer was washed with saturated aqueous sodium chloride solution (100 mL), then was dried (magnesium sulfate) and concentrated. The residue was purified by flash column chromatography (67% ethyl acetate in hexanes) to afford the amine **55** (465 mg, 98%) as a viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 (m, 2 H, arom), 7.30 (m, 8 H, arom), 5.45 (s, 1 H, benzylidene acetal), 4.71 (d, 1 H, J = 12.0 Hz, PhC**H**$_2$), 4.63 (d, 1 H, J = 12.0 Hz, PhC**H**$_2$), 4.51 (d, 1 H, J = 7.3 Hz, H 1), 4.25 (d(br), 1 H, J = 12.2 Hz, H 6), 4.08 (d, 1 H, J = 2.7 Hz, H 4), 4.03 (dd, 1 H, J = 12.2, 1.9 Hz, H 6), 3.43 (dd, 1 H, J = 10.3, 2.7 Hz, H 3), 3.35 (s(br), 1 H, H 5), 3.27 (dd, 1 H, J = 10.3, 7.3 Hz, H 2), 0.92 (s, 9 H, *t*

	-butyl), 0.17 (s, 3 H, $SiCH_3$), 0.14 (s, 3 H, $SiCH_3$).
FTIR (neat film) cm^{-1}:	2927 (m), 2856 (m), 1454 (w), 1405 (w), 1366 (w), 1251 (w), 1172 (m), 1105 (s), 1059 (s), 1027 (m), 1002 (m), 880 (w), 836 (s), 782 (m).
MS (FAB) *m/z*:	472 $(MH)^+$, 414 (M^+ - *t*-butyl), 340 (M^+ - OTBS).
HRMS (FAB) *m/z*:	Calcd for $C_{26}H_{38}NO_5Si$ $(MH)^+$: 472.2519. Found: 472.2532.
TLC R_f (50% EtOAc in hexanes):	0.13



55 **56**

Phthalimide **56.**

DBU (2.64 mL, 17.7 mmol, 6.4 equiv) and phthaloyl dichloride (1.20 mL, 8.26 mmol, 3 equiv) were added sequentially to a solution of amine **55** in toluene (15 mL), and the mixture was heated at 100 °C for 3 h. The reaction mixture was allowed to cool to 23 °C, then was diluted with ethyl ether (100 mL). The ethereal solution was washed sequentially with water (2 x 50 mL) and saturated aqueous sodium chloride solution (50 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (33% ethyl acetate in hexanes) to provide **56** (1.56 g, 94%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.86 (m, 1 H, arom), 7.71 (m, 3 H, arom), 7.60 (m, 2 H, arom), 7.39 (m, 3 H, arom), 7.10 (m, 5 H, arom), 5.51 (s, 1 H, benzylidene acetal), 5.38 (d, 1 H, J = 8.1 Hz, H 1), 4.64 (dd, 1 H, J = 11.2, 8.1 Hz, H 2), 4.62 (d, 1 H, J = 12.4 Hz, PhC**H**$_2$), 4.49 (d, 1 H, J = 12.4 Hz, PhC**H**$_2$), 4.46 (dd, 1 H, J = 11.2, 3.4 Hz, H 3), 4.3 (d, 1 H, J = 12.2 Hz, H 6), 4.20 (d, 1 H, J = 3.4 Hz, H 4), 4.08 (d, 1 H, J =

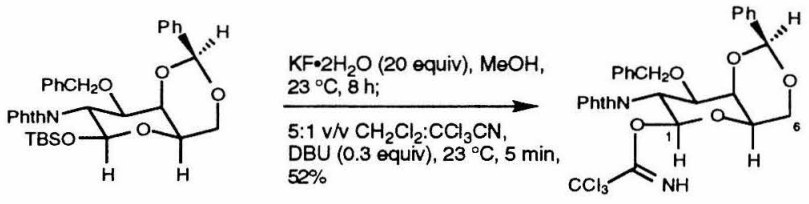
12.2 Hz, H 6), 3.50 (s(br), 1 H, H 5), 0.68 (s, 9 H, *t*-butyl), 0.09 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 2929 (w), 2857 (w), 1775 (w), 1714 (s), 1470 (w), 1389 (m), 1251 (w), 1172 (w), 1087 (m), 838 (m), 720 (w), 700 (w).

MS (FAB) *m/z*: 600 (M^+ - H), 544 (M^+ - *t*-butyl), 470 (M^+ - OTBS).

HRMS (FAB) *m/z*: Calcd for $C_{34}H_{38}NO_7Si$ (M^+ - H): 600.2418. Found: 600.2422.

TLC R_f (50% EtOAc in hexanes): 0.57



56 **57**

β–Trichloroacetimidate **57.**

Solid potassium fluoride hydrate (4.80 g, 52 mmol, 20 equiv) was added to a solution of phthalimide **56** (1.55 g, 2.58 mmol, 1 equiv) in methyl alcohol (90 mL), and the resulting solution was stirred at 23 °C for 8 h. The reaction mixture was diluted with ethyl acetate (100 mL), and the resulting solution was washed sequentially with water (2 x 100 mL) and saturated aqueous sodium chloride solution (100 mL). The organic phase was dried (sodium sulfate) and concentrated, and the residue was dissolved in a mixture of dichloromethane and trichloroacetonitrile (5:1 (v/v), 24 mL). DBU (100 μL, 0.70 mmol, 0.3 equiv) was added, and the mixture was stirred at 23 °C for 5 min. Volatiles were removed in vacuo, and the residue was purified by flash column chromatography (50% ethyl acetate in hexanes with 3% triethylamine) to afford trichloroacetimidate **57** (876 mg, 52% from **56**) as a white solid (mp 154-157 °C).

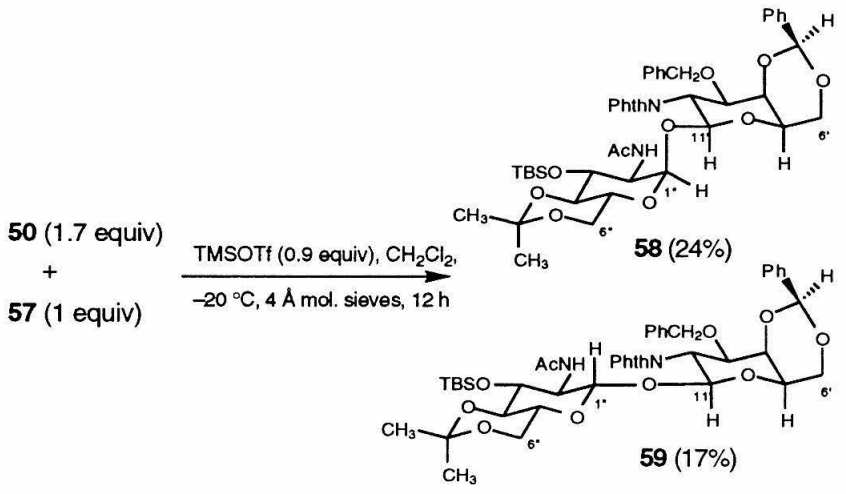
^{1}H NMR (400 MHz, C_6D_6) δ: 7.70 (m, 2 H, arom), 7.49 (m, 1 H, arom), 7.40 (m, 1 H, arom), 7.19-6.75 (m, 11 H, arom, H 1), 5.61 (dd, 1 H, J = 11.0, 8.8 Hz, H 2), 5.28 (s, 1 H, benzylidene acetal), 4.76 (dd, 1 H, J = 11.0, 3.4 Hz, H 3), 4.57 (d, 1 H, J = 12.4 Hz, $PhCH_2$), 4.42

(d, 1 H, J = 12.4 Hz, PhC**H**$_2$), 4.15 (dd, 1 H, J = 12.4, 1.5 Hz, H 6), 3.79 (d(br), 1 H, J = 3.4 Hz, H 4), 3.37 (dd, 1 H, J = 12.4, 1.7 Hz, H 6), 2.89 (s(br), 1 H, H 5).

FTIR (neat film) cm^{-1}: 3336 (w), 2871 (w), 1777 (w), 1715 (s), 1677 (m), 1455 (w), 1389 (s), 1297 (m), 1060 (s), 795 (m), 721 (m).

MS (FAB) *m/z*: 471 (M^+ - $OC(NH)CCl_3$).

TLC R_f (50% EtOAc in hexanes): 0.24



Trehalose Disaccharides **58** and **59**.

Hemiacetals **50** (110 mg, 0.28 mmol, 1.7 equiv), trichloroacetimidate **57** (104 mg, 0.16 mmol, 1 equiv), crushed, activated 4Å molecular sieves (200 mg), and dichloromethane (1.5 mL) were combined, and the resulting suspension was stirred at 23 °C for 2 h. The reaction mixture was cooled to –20 °C, and trimethylsilyltrifluormethane sulfonate (50 μL, 0.26 mmol, 0.9 equiv total) was added portion-wise at 4-h intervals over a 12-h period. The suspension was diluted with ethyl ether (20 mL) and was allowed to warm to 23 °C. Solids were removed by filtration through a short column of Celite, and the filtrate was washed sequentially with water (10 mL) and saturated aqueous sodium chloride solution (10 mL). The ethereal layer was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (25% ethyl acetate in hexanes) providing the disaccharides **58** (34 mg, 24%) and **59** (23 mg, 17%), as colorless oils.

58:

^{1}H NMR (400 MHz, $CDCl_3$) δ:	7.83-7.03 (m, 14 H, arom), 5.54 (s, 1 H, benzylidene acetal), 5.25 (d, 1 H, *J* = 8.6 Hz, H 11'), 5.24 (d, 1 H, *J* = 10.5 Hz, NH), 4.75 (dd, 1 H, *J* = 11.2, 8.6 Hz, H 10'), 4.72 (d, 1 H, *J* = 3.9 Hz, H 1"), 4.63 (d, 1 H, *J* = 12.4 Hz, PhC**H**$_2$), 4.51 (dd, 1 H, *J* = 11.2, 3.4 Hz, H 9'), 4.46 (d, 1 H, *J* = 12.4 Hz, PhC**H**$_2$), 4.30 (d, 1 H, *J* = 12.0 Hz, H 6'), 4.24 (d, 1 H, *J* = 3.4 Hz, H 8'), 4.11 (d, 1 H, *J* = 12.0 Hz, H 6'), 4.04 (m, 2 H, H 2", 5"), 3.73-3.60 (m, 3 H, H 6", 3"), 3.58 (s(br), 1 H, H 7'), 3.47 (t, 1 H, *J* = 9.3 Hz, H 4"), 1.43 (s, 3 H, Ac), 1.41 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 0.79 (s, 9 H, *t*-butyl), 0.03 (s, 6 H, $SiCH_3$).
FTIR (neat film) cm^{-1}:	3446 (w), 2928 (w), 2856 (w), 1774 (w), 1715 (s), 1507 (w), 1387 (m), 1174 (w), 1072 (s), 1028 (s), 868 (m), 723 (m).
MS (FAB) *m/z*:	845 $(MH)^+$, 787 (M^+ - *t*-butyl).
HRMS (FAB) *m/z*:	Calcd for $C_{45}H_{57}N_2O_{12}Si$ $(MH)^+$: 845.3681. Found: 845.3671.
TLC R_f (15% EtOAc in CH_2Cl_2):	0.11

59:

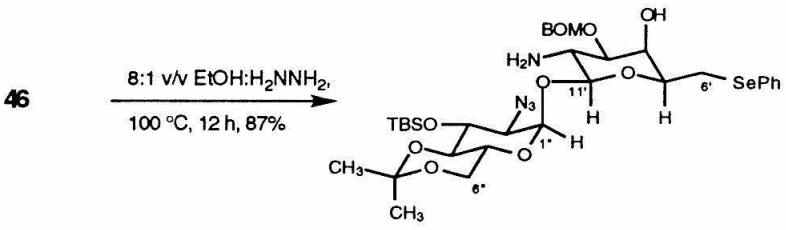
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.86-7.05 (m, 14 H, arom), 5.74 (d, 1 H, *J* = 7.1 Hz, NH), 5.49 (s, 1 H, benzylidene acetal), 5.22 (d, 2 H, *J* = 8.3 Hz, H 11', 1"), 4.62 (m, 2 H, H 10', $PhCH_2$), 4.56 (dd, 1 H, *J* = 11.2, 3.4 Hz, H 9'), 4.51 (d, 1 H, *J* = 12.4 Hz, $PhCH_2$), 4.40 (t, 1 H, *J* = 8.6 Hz, H 3"), 4.25 (d, 1 H, *J* = 12.2 Hz, H 6'), 4.18 (d, 1 H, *J* = 3.4 Hz, H 8'), 4.05 (d(br), 1 H, *J* = 12.2 Hz, H 6'), 3.50 (s(br), 1 H, H 7'), 3.31 (dd, 1 H, *J* = 10.2, 4.6 Hz, H 6"), 3.10 (m, 2 H, H 4", 5"), 2.82 (t, 1 H, *J* = 10.2 Hz, H 6"), 2.68 (m, 1 H, H 2"), 1.93 (s, 3 H, Ac), 1.28 (s, 3 H, CH_3), 1.21 (s, 3 H, CH_3), 0.80 (s, 9 H, *t*-butyl), -0.04 (s, 6 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3260 (w), 2926 (w), 2849 (w), 1772 (w), 1715 (s), 1652 (m), 1393 (m), 1167 (w), 1108 (m), 1073 (s), 857 (m), 714 (m).

MS (FAB) *m/z*: 845 $(MH)^+$, 787 (M^+ - *t*-butyl).

HRMS (FAB) *m/z*: Calcd for $C_{45}H_{57}N_2O_{12}Si$ $(MH)^+$: 845.3681. Found: 845.3692.

TLC R_f (15% EtOAc in CH_2Cl_2): 0.05



C10'-Amino-disaccharide.

A 25-mL heavy-walled Pyrex tube containing a solution of disaccharide **46** (0.81 g, 0.79 mmol, 1 equiv) in a mixture of ethyl alcohol and hydrazine hydrate (8:1 (v/v), 22.5 mL) was placed under static vacuum and was sealed, then was immersed in an oil bath at 100 °C for 12 h. The reaction mixture was cooled to 23 °C, and the product was partitioned between ethyl acetate (75 mL) and water (50 mL). The organic layer was washed sequentially with water (50 mL) and saturated aqueous sodium chloride solution (50 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (50% ethyl acetate in hexanes) to afford the intermediate amino alcohol (0.54 g, 87%) as a colorless oil.

^{1}H NMR (400 MHz, C_6D_6) δ: 7.47 (m, 3 H, arom), 7.30 (m, 2 H, arom), 7.23-6.99 (m, 5 H, arom), 5.00 (d, 1 H, *J* = 3.7 Hz, H 1"), 4.54, 4.48 (2 x d, 2 x 1 H, *J* = 6.8 Hz, OCH_2O), 4.44 (m, 2 H, $PhCH_2O$), 4.33 (m, 2 H, H 5', H 6"), 4.21 (t, 1 H, *J* = 9.5 Hz, H 3"), 4.17 (d, 1 H, *J* = 7.8 Hz, H 11'), 3.79 (d(br), 1 H, *J* = 2.9 Hz, H 8'), 3.70 (m, 1 H, H 6"), 3.43 (t, 1 H, *J* = 9.5 Hz, H 4"), 3.32 (m, 2 H, H 6'), 3.27 (dd, 1

H, J = 11.0, 7.8 Hz, H 10'), 3.22 (dd, 1 H, J = 11.0, 2.9 Hz, H 9'), 3.08 (m, 1 H, H 7'), 3.01 (dd, 1 H, J = 9.5, 3.7 Hz, H 2"), 1.91 (m(br), 1 H, OH), 1.45, 1.32 (2 x s, 2 x 3 H, $C(CH_3)_2$), 1.11 (s, 9 H, *t*-butyl), 0.50 (m(br), 2 H, NH_2), 0.28, 0.21 (2 x s, 2 x 3 H, $Si(CH_3)_2$).

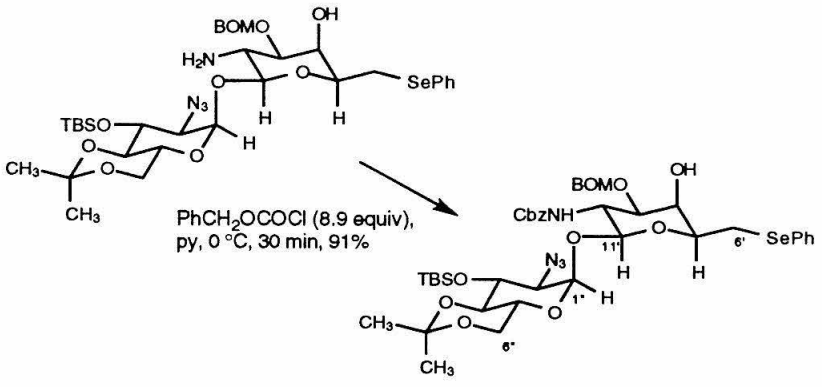
^{13}C NMR (100 MHz, C_6D_6) δ: 138.0-127.0 (arom), 105.9, 100.6, 99.5, 94.0, 81.0, 75.2, 75.0, 71.2, 70.1, 67.2, 66.2, 64.7, 62.6, 52.6, 29.2, 28.4, 26.0, 19.0, 18.5, -3.9, -4.9.

FTIR (neat film) cm^{-1}: 3600-2900 (m, br), 2930 (s), 2857 (s), 2107 (s), 1580 (w), 1472 (w), 1383 (m), 1265 (m), 1128 (s), 1024 (s), 970 (m), 856 (s), 737 (s).

MS (FAB) *m/z*: 781 $(MH)^+$, 723 (M^+ - *t*-butyl), 624 (M^+ - SePh).

HRMS (FAB) *m/z*: Calcd for $C_{35}H_{53}N_4O_9SeSi$ $(MH)^+$: 781.2747. Found: 781.2731.

TLC R_f (50% EtOAc in hexanes): 0.18



60

Benzylcarbamate **60**.

To a solution of the intermediate amino alcohol (1.35 g, 1.73 mmol, 1 equiv) in pyridine (25 mL) at 0 °C was added benzyl chloroformate (2.30 mL, 15.0 mmol, 8.9 equiv), and the resulting mixture was stirred at 0 °C for 30 min. The reaction mixture was diluted with ethyl ether (150 mL), and the resulting solution was washed sequentially with water (3 x 75 mL) and saturated aqueous sodium chloride solution (50 mL). The ethereal solution was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (33% ethyl acetate in hexanes) to provide **60** (1.35 g, 91%) as white needles (mp 114.0–115.0 °C).

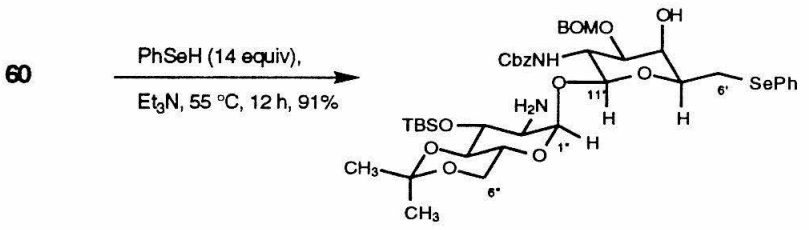
^{1}H NMR (400 MHz, C_6D_6) δ: 7.50-6.98 (m, 10 H, arom), 5.15 (d, 1 H, J = 12.2 Hz, PhC**H**$_2$OCO), 5.06 (m(br), 1 H, PhC**H**$_2$OCO), 5.05 (d, 1 H, J = 3.9 Hz, H 1"), 5.00 (d(br), 1 H, J = 7.8 Hz, H 11'), 4.95 (m, 1 H, NH), 4.60 (d, 1 H, J = 6.8 Hz, OC**H**$_2$O), 4.57 (d, 1 H, J = 6.8 Hz,

OCH_2O), 4.47 (d, 1 H, J = 12.1 Hz, $PhCH_2O$), 4.45 (d, 1 H, J = 12.1 Hz, $PhCH_2O$), 4.25 (m, 2 H, H 5', H 6"), 4.16 (dd, 1 H, J = 9.5, 9.0 Hz, H 3"), 4.02 (m(br), 1 H, H 10'), 3.87 (m, 1 H, H 8'), 3.67 (m, 1 H, H 6"), 3.59 (m(br), 1 H, H 9'), 3.46 (dd(br), 1 H, J = 7.3, 6.5 Hz, H 7'), 3.45 (dd, 1 H, J = 9.8, 9.0 Hz, H 4"), 3.30 (dd, 1 H, J = 12.5, 7.3 Hz, H 6'), 3.10 (dd, 1 H, J = 12.5, 6.5 Hz, H 6'), 3.03 (dd, 1 H, J = 9.8, 3.7 Hz, H 2"), 2.19 (m(br), 1 H, OH), 1.43, 1.33 (2 x s, 2 x 3 H, $C(CH_3)_2$), 1.08 (s, 9 H, *t*-butyl), 0.28, 0.22 (2 x s, 2 x 3 H, $Si(CH_3)_2$).

^{13}C NMR (100 MHz, C_6D_6) δ: 155.5, 141.9-127.0 (arom), 100.2, 99.6, 93.8, 75.3, 74.9, 70.8, 70.0, 69.6, 68.0, 67.0, 65.8, 65.0, 64.8, 62.7, 54.1, 29.2, 28.4, 26.0, 19.0, 18.5, -3.8, -4.9.

FTIR (neat film) cm^{-1}: 3650-3175 (m, br), 3309 (s), 2930 (s), 2857 (s), 2107 (s), 1694 (s), 1556 (s), 1455 (m), 1384 (m), 1248 (s), 1023 (s), 949 (m), 860 (s), 696 (s).

Elemental Analysis:	Calcd for $C_{43}H_{57}N_4O_{11}SeSi$: C, 56.52; H, 6.29; N, 6.14.
	Found: C, 56.17; H, 6.29; N, 6.11.
TLC R_f (33% EtOAc in hexanes):	0.63



C2"-Amino-Disaccharide.

Benzeneselenol (2.50 mL, 24.0 mmol, 14.0 equiv) was added to a deoxygenated solution of benzylcarbamate **60** (1.52 g, 1.66 mmol, 1 equiv) in triethylamine (50 mL), and the resulting mixture was heated at 55 °C for 12 h. The product was partitioned between dichloromethane (150 mL) and water (150 mL), and the organic phase was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (33% ethyl acetate in hexanes) to afford the intermediate C2"-amino disaccharide (1.35 g, 91%) as white needles (mp 172.0–174.0 °C).

^{1}H NMR (400 MHz, C_6D_6) δ: 7.49-6.99 (m, 10 H, arom), 5.17 (d, 1 H, *J* = 12.3 Hz, PhC**H**$_2$OCO), 5.14 (d, 1 H, *J* = 3.7 Hz, H 1"), 5.11 (d, 1 H, *J* = 12.3 Hz, PhC**H**$_2$OCO), 4.96 (m(br), 1 H, H 11'), 4.61 (d, 1 H, J = 7.1 Hz, OC**H**$_2$O), 4.59 (d, 1 H, *J* = 7.1 Hz, OC**H**$_2$O), 4.54 (d, 1 H, *J* = 12.1 Hz, PhOC**H**$_2$), 4.47 (d, 1 H, *J* = 12.1 Hz, PhOC**H**$_2$), 4.45 (d(br), 1 H, *J* = 8.3 Hz, NH), 4.31 (m, 2 H, H 5", H 6"), 4.00 (q(br), 1 H, *J* ~ 10.5 Hz, H 10'), 3.88 (d(br), 1 H, *J* = 2.9 Hz, H 8'), 3.79 (t, 1 H, *J* = 9.0 Hz, H 3"), 3.74 (t,

1 H, J = 10.0 Hz, H 6"), 3.52 (d(br), 1 H (obscured), H 3), 3.50 (dd, 1 H, J = 9.3, 8.7 Hz, H 4"), 3.43 (dd(br), 1 H, J = 7.3, 6.6 Hz, H 7'), 3.28 (dd, 1 H, J = 12.5, 6.6 Hz, H 6'), 3.13 (dd, 1 H, J = 12.5, 7.3 Hz, H 6'), 2.80 (dd, 1 H, J = 9.0, 3.7 Hz, H 2"), 2.61 (m(br), 1 H, OH), 1.46, 1.36 (2 x s, 2 x 3 H, $C(CH_3)_2$), 1.02 (s, 9 H, *t*-butyl), 0.18, 0.15 (2 x s, 2 x 3 H, $Si(CH_3)_2$).

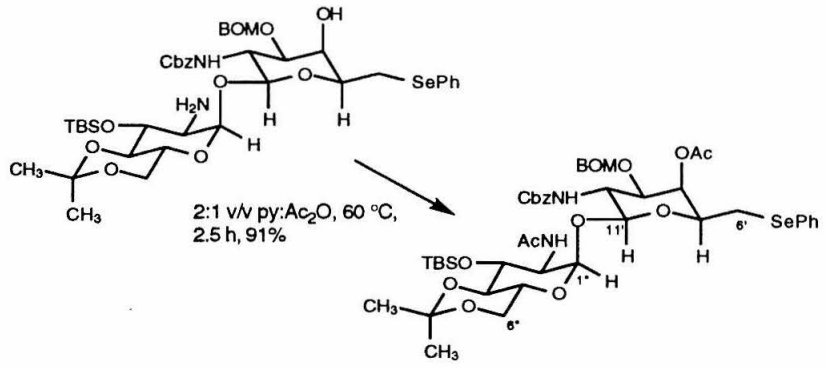
^{13}C NMR (100 MHz, C_6D_6) δ: 157.0, 138.1-126.9 (arom), 102.8, 99.3, 93.7, 75.2, 75.2, 74.7, 70.1, 67.7, 67.1, 65.2, 64.8, 63.0, 58.7, 53.5, 29.4, 28.2, 26.3, 19.1, 18.6, -3.7, -4.4.

FTIR (neat film) cm^{-1}: 3516-3100 (m, br), 3308 (m), 2928 (s), 2858 (m), 1700 (s), 1544 (s), 1478 (w), 1382 (m), 1248 (s), 1097 (s), 1038 (s), 945 (m), 864 (m), 735 (m).

MS (FAB) *m/z*: 889 (MH^+), 556 $(galactopyranoside)^+$, 316 $(glucopyranoside)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{43}H_{61}N_2O_{11}SeSi$: $(MH)^+$: 889.3210. Found: 889.3210.

TLC R_f (50% EtOAc in hexanes): 0.28



61

Diacetyl-Disaccharide **61.**

The intermediate C2"-amino disaccharide (1.35 g, 1.52 mmol, 1 equiv) was dissolved in a mixture of pyridine and acetic anhydride (2:1 (v/v), 30 mL), and the resulting solution was heated at 60 °C for 2.5 h. The reaction mixture was diluted with ethyl ether (100 mL), and the resulting solution was washed sequentially with water (50 mL) and saturated aqueous sodium chloride solution (30 mL). The ethereal solution was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (33% ethyl acetate in hexanes) to afford **61** (1.35 g, 91%) as a colorless oil.

^{1}H NMR (400 MHz, C_6D_6) δ: 7.45-6.95 (m, 10 H, arom), 6.00 (m(br), 1 H, N**H**Ac), 5.30 (d, 1 H, *J* = 3.2 Hz, H 8'), 5.24 (d(br), 1 H, *J* = 12.5 Hz, PhC**H**$_2$OCO), 5.13 (m(br), 1 H, N**H**CO$_2$R), 5.08 (d, 1 H, *J* = 3.2 Hz, H 1"), 4.92 (d(br), 1 H, *J* = 12.5 Hz, PhC**H**$_2$OCO),

4.70 (d, 1 H, J = 7.3 Hz, OCH_2O), 4.55 (dt, 1 H, J = 9.3, 3.2 Hz, H 2"), 4.54 (d, 1 H, J = 12.5 Hz, PhCH_2O), 4.50 (d, 1 H, J = 7.3 Hz, OCH_2O), 4.32 (m, 2 H, H 5", H 6"), 4.31 (d, 1 H, J = 12.5 Hz, PhCH_2O), 4.13 (q(br), 1 H, J = obscured, H 10'), 3.90 (t, 1 H, J = 9.3 Hz, H 3"), 3.74 (m, 1 H, H 6"), 3.58 (t, 1 H, J = 9.3 Hz, H 4"), 3.50 (dd, 1 H, J = 11.0, 3.2 Hz, H 9'), 3.37 (dd(br), 1 H, J = 8.1, 6.4 Hz, H 7'), 3.03 (dd, 1 H, J = 13.5, 8.1 Hz, H 6'), 2.79 (dd, 1 H, J = 13.5, 6.4 Hz, H 6'), 2.04 (s, 3 H, NHCOCH_3), 1.57 (s, 3 H, $OCOCH_3$), 1.39, 1.32 (2 x s, 2 x 3 H, $C(CH_3)_2$), 0.96 (s, 9 H, *t*-butyl), 0.08, 0.04 (2 x s, 2 x 3 H, $Si(CH_3)_2$).

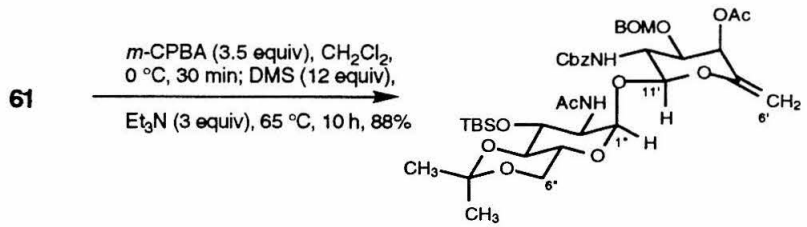
^{13}C NMR (100 MHz, C_6D_6) δ: 170.1, 157.2, 138.1-127.3 (arom), 101.2, 99.5, 92.8, 75.3, 74.6, 73.3, 71.8, 69.9, 67.7, 67.1, 65.2, 62.8, 54.5, 54.2, 29.3, 28.2, 26.0, 23.6, 20.2, 19.2, 18.4, -3.9, -4.7.

FTIR (neat film) cm^{-1}: 3525-3100 (m, br), 2929 (s), 2856 (m), 1722 (s), 1667 (s), 1538 (s), 1373 (s), 1296 (w), 1231 (s), 1117 (s), 1068 (s), 1027 (s), 864 (m), 737 (m).

MS (FAB) *m/z*: 973 (MH^+), 915 (M^+ - *t*-butyl).

HRMS (FAB) *m/z*: Calcd for $C_{47}H_{65}N_2O_{13}SeSi$: $(MH)^+$: 973.3437.
Found: 973.3421.

TLC R_f (50% EtOAc in hexanes): 0.63



Allylic Acetate Disaccharide.

Solid *m*-chloroperoxybenzoic acid (~60% (w/w), 1.38 g, 4.8 mmol, 3.5 equiv) was added to a solution of selenide **61** (1.35 g, 1.39 mmol, 1 equiv) in carbon tetrachloride (10 mL) at –15 °C. The resulting suspension was stirred at –15 °C for 20 min, and then at 0 °C for 30 min. Excess oxidant was quenched by the sequential addition of dimethyl sulfide (1.20 mL, 16.0 mmol, 12.0 equiv) and triethylamine (0.5 mL, 4.0 mmol, 3.0 equiv), and the resulting solution then was heated at 65 °C for 10 h. The product was partitioned between ethyl acetate (100 mL) and saturated aqueous sodium bicarbonate solution (40 mL). The organic layer was washed sequentially with water (40 mL) and saturated aqueous sodium chloride solution (40 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (gradient elution: 33 → 50% ethyl acetate in hexanes) to provide the intermediate allylic acetate disaccharide (1.09 g, 88%) as a colorless oil.

^{1}H NMR (400 MHz, C_6D_6) δ: 7.26-7.06 (m, 10 H, arom), 6.25 (d(br), 1 H, *J* = 9.8 Hz, NHAc), 5.86 (d, 1 H, *J* = 3.2 Hz, H 8'), 5.18 (d, 1 H, *J* = 12.2 Hz, PhC**H**$_2$OCO), 5.10 (d(br), 1 H, *J* = 7.0 Hz, N**H**CO$_2$R), 5.04 (d, 1 H, *J* = 3.7 Hz, H 1"), 4.97 (d(br), 1 H, *J* = 12.2 Hz,

PhC**H**$_2$OCO), 4.69 (d, 1 H, *J* = 1.0 Hz, H 6'), 4.65 (ddd, 1 H, *J* = 9.8, 9.8, 3.7 Hz, H 2"), 4.62 (d, 1 H, *J* = 7.1 Hz, OC**H**$_2$O), 4.61 (d, 1 H, *J* = 6.1 Hz, H 11'), 4.54 (d, 1 H, *J* = 7.1 Hz, OC**H**$_2$O), 4.53 (d, 1 H, *J* = 1.0 Hz, H 6'), 4.52 (d, 1 H, *J* = 12.3 Hz, PhC**H**$_2$O), 4.42 (ddd, 1 H, *J* = 10.5, 7.0, 6.1 Hz, H 10'), 4.41 (d, 1 H, *J* = 12.3 Hz, PhC**H**$_2$O), 4.24 (ddd, 1 H, *J* = 10.5, 10.5, 5.3 Hz, H 5"), 3.96 (dd, 1 H, *J* = 9.8, 9.7 Hz, H 3"), 3.94 (dd, 1 H, *J* = 10.5, 5.3 Hz, H 6"), 3.73 (t, 1 H, *J* = 10.5 Hz, H 6"), 3.60 (td, 1 H, *J* = 10.0, 9.7 Hz, H 4"), 3.59 (dd, 1 H, *J* = 10.5, 3.2 Hz, H 9'), 2.13 (s, 3 H, NHCOC**H**$_3$), 1.77 (s, 3 H, OCOC**H**$_3$), 1.43, 1.34 (s, 9 H, *t*-butyl), 0.17, 0.15 (2 x s, 2 x 3 H, Si(C**H**$_3$)$_2$).

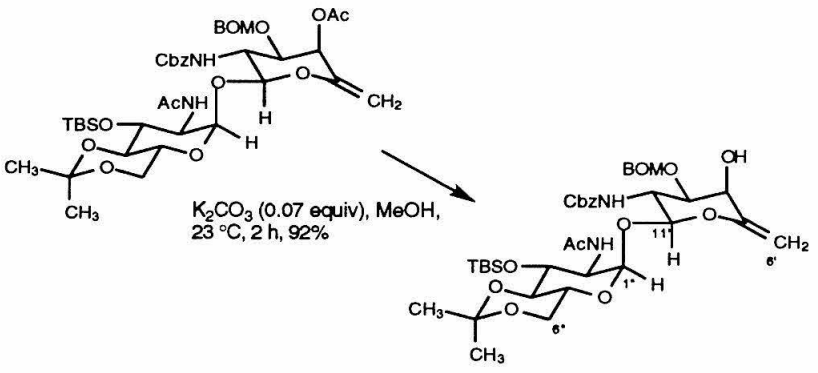
^{13}C NMR (100 MHz, C_6D_6) δ: 169.8, 169.7, 157.2, 152.2, 137.9-127.6 (arom), 103.8, 101.2, 99.5, 93.7, 75.1, 73.9, 72.0, 70.0, 68.0, 67.2, 65.3, 62.5, 54.4, 54.2, 53.5, 29.3, 26.0, 23.5, 20.5, 19.1, 18.5, -3.9, -4.7.

FTIR (neat film) cm^{-1}: 3530-3125 (m, br), 2952 (s), 1745 (s), 1715 (s), 1666 (s), 1523 (s), , 1372 (s), 1230 (s), 1113 (s), 1023 (s), 864 (m), 698 (m).

MS (FAB) *m/z*: 815 $(MH)^+$, 757 (M^+ - *t*-butyl).

HRMS (FAB) *m/z*: Calcd for $C_{41}H_{59}N_2O_{13}Si$ $(MH)^+$: 815.3820.
Found: 815.3786.

TLC R_f (50% EtOAc in hexanes): 0.46



62

Allylic Alcohol Disaccharide **62.**

Solid potassium carbonate (10 mg, 0.07 mmol, 0.07 equiv) was added to a solution of the intermediate allylic acetate disaccharide (0.81 g, 1.0 mmol, 1 equiv) in methyl alcohol (25 mL), and the resulting suspension was stirred at 23 °C for 2 h. The product was partitioned between ethyl acetate (100 mL) and water (40 mL). The organic layer was washed sequentially with water (40 mL) and saturated aqueous sodium chloride solution (40 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (50% ethyl acetate in hexanes) to afford allylic alcohol **62** (703 mg, 92%) as a colorless oil.

^{1}H NMR (400 MHz, C_6D_6) δ: 7.29-7.08 (m, 10 H, arom), 6.06 (d(br), 1 H, J ~ 8.6 Hz, N**H**Ac), 5.17 (d, 1 H, J = 12.2 Hz, Ph**CH**$_2$OCO), 5.12 (d, 1 H, J = 3.7 Hz, H 1"), 5.08 (d(br), 1 H, J ~ 8.3 Hz, N**H**CO$_2$CH$_2$Ph), 5.04 (d(br), 1 H, J = 12.2 Hz, Ph**CH**$_2$OCO), 4.71 (s, 1

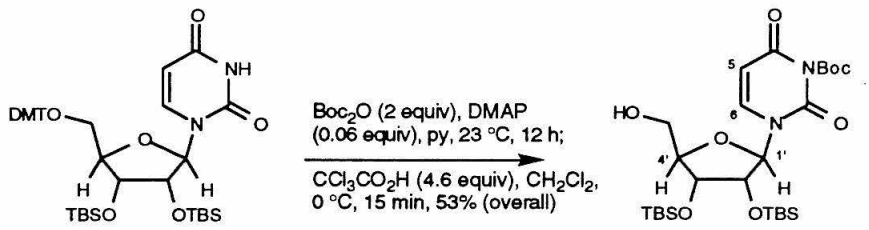
H, H 6'), 4.70 (d, 1 H, J = 6.5 Hz, H 11'), 4.63 (dt, 1 H, J = 10.8, 3.7 Hz, H 2"), 4.57 (m, 2 H, OCH_2O), 4.49 (s, 2 H, $PhCH_2O$), 4.45 (s, 1 H, H 6'), 4.33 (dt, 1 H, J = 8.6, 6.5 Hz, H 10'), 4.28 (dt, 1 H, J = 10.3, 5.4 Hz, H 5"), 4.23 (m, 1 H, H 8'), 4.02 (dd, 1 H, J = 10.3, 5.4 Hz, H 6"), 3.97 (dd, 1 H, J = 11.2, 10.8 Hz, H 3"), 3.75 (t, 1 H, J = 10.3 Hz, H 6"), 3.60 (dd, 1 H, J = 11.2, 10.3 Hz, H 4"), 3.58 (dd, 1 H, J = 8.6, 3.4 Hz, H 9'), 2.58 (m, 1 H, OH), 2.06 (s, 3 H, Ac), 1.47, 1.35 (2 x s, 2 x 3 H, $C(CH_3)_2$), 1.06 (s, 9 H, *t*-butyl), 0.21, 0.18 (2 x s, 2 x 3 H, $Si(CH_3)_2$).

^{13}C NMR (100 MHz, C_6D_6) δ: 170.3, 157.1, 155.9, 138.0-127.8 (arom), 102.7, 100.6, 99.6, 98.3, 94.4, 77.4, 75.2, 71.9, 70.2, 67.7, 67.2, 65.1, 62.6, 54.8, 53.8, 29.3, 26.1, 23.4, 19.2, 18.5, -3.8, -4.6.

FTIR (neat film) cm^{-1}: 3650-3100 (s), 2928 (s), 2856 (m), 1709 (s), 1662 (s), 1534 (s), 1375 (s), 1247 (s), 1116 (s), 1026 (s), 861 (m), 780 (m), 698 (m).

MS (FAB) *m/z*: 773 $(MH)^+$, 398 (galactopyranoside)$^+$, 358 (glucopyranoside)$^+$.

HRMS (FAB) *m/z*:	Calcd for $C_{39}H_{57}N_2O_{12}Si$ $(MH)^+$: 773.3676. Found: 773.3681.
Elemental Analysis:	Calcd for $C_{39}H_{56}N_2O_{12}Si$: C, 60.60; H, 7.30; N, 3.62. Found: C, 60.28; H, 7.13; N, 3.90.
TLC R_f (50% EtOAc in hexanes):	0.44



20 **63**

Uridine-5'-Alcohol **63.**

DMAP (50 mg, 0.4 mmol, 0.06 equiv) and di-*t*-butyl dicarbonate (2.90 g, 13 mmol, 2 equiv) were added sequentially to a solution of uridine derivative **20** (5.1 g, 6.5 mmol, 1 equiv) in pyridine (50 mL) at 0 °C, and the resulting solution was stirred at 23 °C for 12 h. Volatiles were removed in vacuo, and the residue was dissolved in dichloromethane (100 mL). A solution of trichloroacetic acid (5.0 g, 30 mmol, 4.6 equiv) in dichloromethane (45 mL) was added dropwise over a 5-min period at 0 °C, and the resulting orange solution was stirred at 0 °C for 15 min. The product was partitioned between dichloromethane (150 mL) and saturated aqueous sodium bicarbonate solution (80 mL). The organic layer was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (50% ethyl acetate in hexanes) to afford the product **63** (2.01 g, 53%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 (d, 1 H, J = 8.3 Hz, H 6), 5.64 (d, 1 H, J = 8.3 Hz, H 5), 5.42 (d, 1 H, J = 5.4 Hz, H 1'), 4.43 (dd, 1 H, J = 5.4, 4.4 Hz, H 2'), 4.05 (dd, 1 H, J = 4.4, 2.9 Hz, H 3'), 3.97 (m, 1 H, H 4'), 3.82 (m, 1 H, J = 12.2 Hz, H 5'), 3.60 (m, 1 H, J = 12.2 Hz,

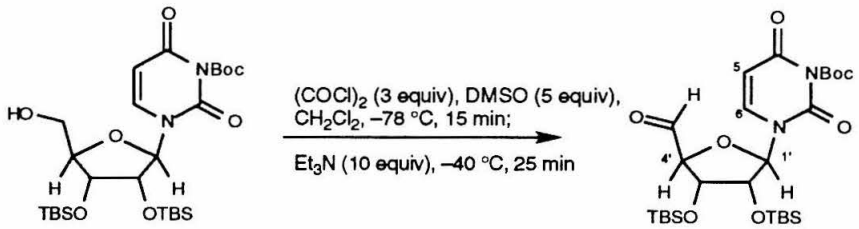
H 5'), 2.93 (m, 1 H, OH), 1.49 (s, 9 H, *t*-Boc), 0.81 (s, 9 H, *t* -butyl), 0.77 (s, 9 H, *t* -butyl), -0.01, -0.02, -0.05, -0.08 (4 x s, 4 x 4 H, 4 x $SiCH_3$)

FTIR (neat film) cm^{-1}: 3495 (w), 2930 (m), 2857 (m), 1788 (s), 1722 (s), 1678 (s), 1449 (m), 1372 (m), 1253 (s), 1151 (s), 837 (s), 778 (s).

MS (FAB) *m/z*: 515 (M^+ - *t*-butyl), 471 (M^+ - *t*-Boc), 457 (M^+ - TBS).

HRMS (FAB) *m/z*: Calcd for $C_{26}H_{49}N_2O_8Si_2$ $(MH)^+$: 573.3027. Found: 573.3032.

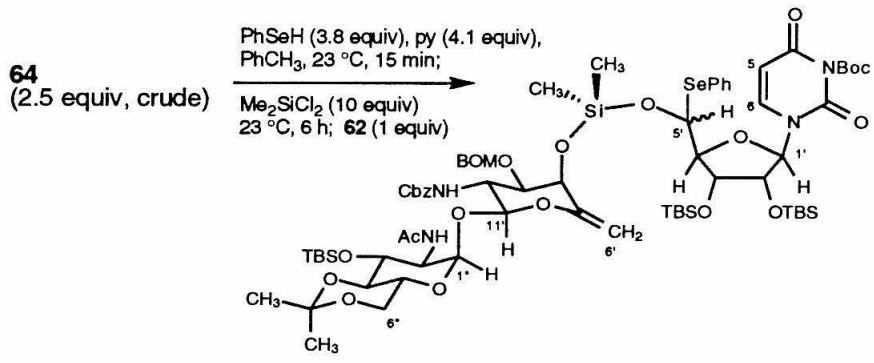
TLC R_f (50% EtOAc in hexanes): 0.43



63 **64** (crude)

Uridine-5'-Aldehyde **64.**

Dimethylsulfoxide (311 μL, 4.3 mmol, 5 equiv) was added dropwise to a solution of oxalyl chloride (224 μL, 2.6 mmol, 3 equiv) in dichloromethane (12 mL) at –78 °C, and the resulting solution was stirred at –78 °C for 5 min. A solution of uridine derivative **63** (500 mg, 0.87 mmol, 1 equiv) in dichloromethane (10 mL) was added via cannula, and the resulting solution was stirred at –78 °C for 15 min. Triethylamine (1.21 mL, 8.7 mmol, 10 equiv) was added, and the resulting suspension was stirred at –78 °C for an additional 25 min. The reaction mixture was poured into saturated aqueous sodium bicarbonate solution (150 mL), the aqueous layer was extracted with ethyl acetate (2 x 100 mL), and the combined organic layers were dried (sodium sulfate) and concentrated to provide crude (**64**, 513 mg) as a pale yellow solid. Due to the lability of the product and its susceptibility to hydration, the uridine 5'-aldehyde derivative **64** was used in its crude form in the following experiment.



65 (50%)

O-Silylhemiselenoacetal Adduct **65**.

Benzeneselenol (56 μL, 0.51 mmol, 3.8 equiv) and pyridine (45 μL, 0.55 mmol, 4.1 equiv) were added sequentially to a freshly prepared, deoxygenated solution of aldehyde **64** (190 mg, ~0.34 mmol, ~2.5 equiv, azeotropically dried with 1.5 mL of toluene), and the resulting solution was deoxygenated. After stirring at 23 °C for 15 min, the reaction mixture was transferred via cannula to a solution of dichlorodimethylsilane (340 μL, 3.4 mmol, 10 equiv) in pyridine (2 mL). The resulting suspension was deoxygenated and was stirred in the dark at 23 °C for 6 h. The reaction mixture was concentrated in vacuo at 23 °C, and the residue was suspended in toluene (2 mL). Volatiles were removed at 23 °C, and the residue was diluted with toluene (3 mL). To the mixture was added via cannula a solution of allylic alcohol **62** (104 mg, 0.13 mmol, 1 equiv) in pyridine (2 mL), and the resulting suspension was stirred at 23 °C for 5 min. The product was partitioned between ethyl acetate (100 mL) and water (100 mL). The organic layer was dried (sodium sulfate) and concentrated, and the residue was purified by flash column chromatography (gradient elution: 33% → 50% ethyl acetate in hexanes) to afford a 5:1 mixture of C5'-diastereomers **65** (106 mg, 50%) as

a colorless oil. Preparative thin layer chromatography (50% ethyl acetate in hexanes) provided analytical samples of each diastereomer.

65a:

^{1}H NMR (400 MHz, C_6D_6) δ: 7.78 (d, 1 H, *J* = 8.6 Hz, H 6), 7.7-7.0 (m, 15 H, arom), 6.46 (d, 1 H, *J* = 9.8 Hz, NH), 6.21 (d, 1 H, *J* = 5.9 Hz, H 1'), 5.94 (d, 1 H, *J* = 8.6 Hz, H 5), 5.78 (d, 1 H, *J* = 3.7 Hz, H 5'), 5.23 (d, 1 H, *J* = 12.2 Hz, PhC**H**$_2$OCO), 5.12 (d, 1 H, *J* = 3.9 Hz, H 1"), 5.08 (d, 1 H, *J* = 12.2 Hz, PhC**H**$_2$OCO), 4.8-4.5 (m), 4.45 (m, 2 H), 4.32 (s, 1 H, H 6'), 4.31 (m, 1 H), 4.25 (dd, 1 H, *J* = 4.4, 2.9 Hz, H 3'), 4.22 (m, 1 H, H 2"), 3.98 (m, 2 H), 3.75 (t, 1 H, *J* = 10.2 Hz, H 3"), 5.90 (m, 2 H)2.16 (s, 3 H, Ac), 1.51 (s, 9 H, *t*-Boc), 1.46, 1.35 (2 x s, 2 x 3 H, 2 x CH_3), 1.11, 1.03, 0.98 (3 x s, 3 x 9 H, 3 x *t*-butyl), 0.31, 0.28, 0.27, 0.25, 0.21, 0.16, 0.15, 0.10 (8 x s, 8 x 3 H, 8 x $SiCH_3$).

FTIR (neat film) cm^{-1}: 3324 (w), 2929 (m), 2850 (m), 1789 (s), 1724 (s), 1680 (s), 1535 (w), 1448 (m), 1371 (m), 1257 (s), 1150 (s), 1063 (s), 972 (m), 838 (s).

MS (FAB) *m/z*: 1549 (M^+ - *t*-butyl), 1425 (M^+ - OTBS), 1400 (M^+ - PhSe).

TLC R_f (50% EtOAc in hexanes): 0.36

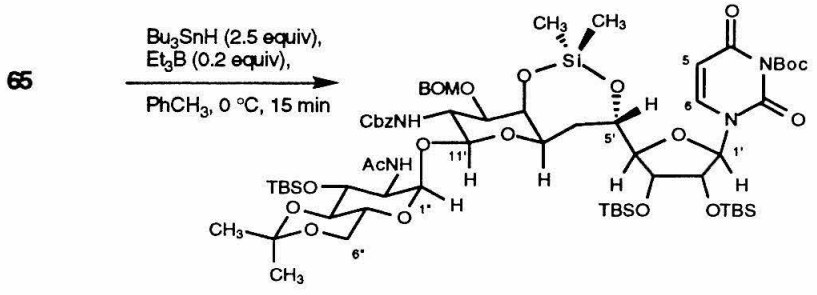
65b:

^{1}H NMR (400 MHz, C_6D_6) δ: 7.81 (d, 1 H, J = 7.6 Hz, H 6), 7.5-7.0 (m, 15 H, arom), 6.56 (d, 1 H, J = 7.6 Hz, NH), 6.40 (d, 1 H, J = 8,3 Hz, H 5), 5.83 (d, 1 H, J = 2.4 Hz, H 1"), 5.32 (d, 1 H, J = 4.15 Hz, H 5'), 5.21 (d(br), 2 H, NH), 4.67 (m, 1 H, H 2"), 4.65-4.15 (m), 4.00 (dd, 1 H, J = 10.7, 5.4 Hz, H 6"), 3.78 (t, 1 H, J = 10.7 Hz, 3.63 (dd, 1 H, J = 9.8, 8.6 Hz, H 3"), 3.56 (m, 1 H), 2.23 (s, 3 H, Ac), 1.51 (s, 9 H, *t*-Boc), 1.44, 1.36 (2 x s, 2 x 3 H, 2 x CH_3), 1.16, 1.06, 1.05 (3 x s, 3 x 9 H, 3 x *t*-butyl), 0.40, 0.32, 0.31, 0.29, 0.28, 0.25, 0.17, 0.16 (8 x s, 8 x 3 H, 8 x $SiCH_3$).

FTIR (neat film) cm^{-1}: 3320 (w), 2929 (m), 2857 (m), 1789 (m), 1724 (s), 1684 (s), 1527 (w), 1448 (w), 1372 (m), 1257 (s), 1114 (s), 1023 (s), 838 (s), 779 (m).

MS (FAB) *m/z*: 1549 (M^+ - *t*-butyl), 1400 (M^+ - PhSe).

TLC R_f (50% EtOAc in hexanes): 0.32



66 (80%)

Siloxane **66.**

A solution of triethylborane (5 μL, 1.0 M solution in hexanes, 0.005 mmol, 0.2 equiv) was added to a deoxygenated solution of *O*-silylhemiselenoacetals **65** (50 mg, 0.03 mmol, 1 equiv) and tributyltin hydride (20 μL, 0.07 mmol, 2.5 equiv) in toluene at 0 °C, and the resulting solution was stirred at 0 °C for 15 min. The solvent was removed in vacuo at 0 °C, and flash column chromatography of the residue (gradient elution: 33% → 100% ethyl acetate in hexanes) afforded siloxane **66** (36 mg, 80%) as a colorless film.

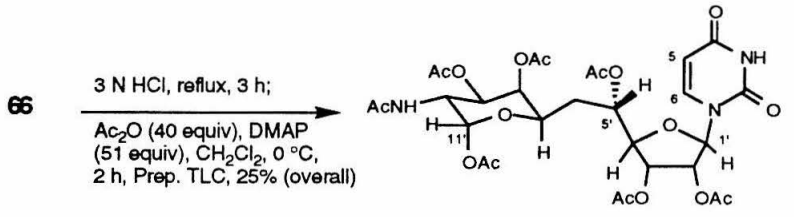
^{1}H NMR (400 MHz, C_6D_6) δ: 7.90 (d, 1 H, *J* = 8.3 Hz, H 6), 6.50 (d, 1 H, *J* = 6.8 Hz, H 1'), 5.86 (d, 1 H, *J* = 9.8 Hz, NH), 5.64 (d, 1 H, *J* = 8.3 Hz, H 5), 5.29 (d, 1 H, *J* = 12.4 Hz, PhC**H**$_2$OCO), 5.17 (d, 1 H, *J* = 3.7 Hz, H 1"), 5.00 (d, 1 H, *J* = 12.4 Hz, PhC**H**$_2$OCO), 4.83 (d, 1 H, *J* = 8.6 Hz, NH), 4.70-4.44 (m, 7 H), 4.42 (dd, 1 H, *J* = 6.8, 4.4 Hz, H 2'), 4.28 (m, 1 H, *J* = 8.8 Hz, H 10'), 4.15 (m, 1 H, H 2"), 4.13 (m, 1 H, H5'), 4.08 (m, 1 H, H 4'), 3.93 (d, 1 H, *J* = H 8'),

3.88 (m, 2 H, H 4", 6"), 3.74 (t, 1 H, J = 10.5 Hz, H 3"), 3.57 (t, 1 H, J = 9.8 Hz, H 6"), 3.49 (dd, 1 H, J = 8.8, 2.7 Hz, H 9'), 3.16 (m, 1 H, H 7'), 2.07 (s, 3 H, Ac), 1.90 (m, 2 H, H 6'), 1.51 (s, 9 H, *t*-Boc), 1.50, 1.34 (2 x s, 2 x 3 H, 2 x CH_3), 1.07, 1.06, 0.99 (3 x s, 3 x 9 H, 3 x *t*-butyl), 0.24, 0.22, 0.17, 0.12, 0.12, 0.09, 0.06, 0.04 (8 x s, 8 x 3 H, 8 x $SiCH_3$).

FTIR (neat film) cm^{-1}: 3329 (w), 2930 (m), 2858 (m), 1789 (m), 1726 (s), 1688 (s), 1532 (w), 1447 (m), 1372 (m), 1258 (s), 1151 (s), 1029 (s), 838 (s), 779 (m).

MS (FAB) *m/z*: 1346 (M^+ - *t*-butyl).

TLC R_f (50% EtOAc in hexanes): 0.22



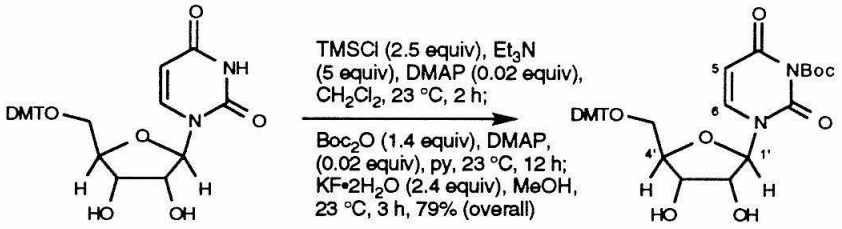
26

C5'-*epi*-α-Heptaacetyl Tunicaminyluracil **26.**

A solution of siloxane **66** (23 mg, 0.02 mmol, 1 equiv) in 3 N aqueous hydrochloric acid (1.5 mL) was heated at reflux for 3 h, at which time the solvent was removed *in vacuo* at 23 °C. The residue then was diluted with dichloromethane (2 mL), and to this solution at 0 °C was added sequentially 4-(*N,N*-dimethylamino)pyridine (50 mg, 0.4 mmol, 20 equiv) and acetic anhydride (33 μL, 0.3 mmol, 15 equiv). The resulting reaction mixture was stirred at this temperature for 2 h before it was diluted with ethyl acetate (50 mL). The product solution then was washed sequentially with 0.5 N aqueous hydrochloric acid solution (40 mL), saturated aqueous sodium bicarbonate solution (40 mL), and saturated aqueous sodium chloride solution (40 mL), and the organic layer was dried (sodium sulfate) and concentrated. The residue was purified by preparative thin layer chromatography (7% methanol in dichloromethane) to yield **26** as the major product (4 mg, 36%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.42 (s, 1 H, imide NH), 7.53 (d, 1 H, J = 8.6 Hz, H 6), 6.17 (d, 1 H, J = 3.7 Hz, H 11'), 6.13 (d, 1 H, J = 5.6 Hz, H 1'), 5.85 (d, 1 H, J = 8.6 Hz, H 5), 5.44 (d, 1 H, J = 9.9 Hz, amide NH), 5.28 (d, 1 H, J = 2.9 Hz, H 8'), 5.26 (m, 1 H, H 5'), 5.22 (t,

	1 H, J = 5.6 Hz, H 2'), 5.19 (dd, 1 H, J = 2.9, 12.0 Hz, H 9'), 5.11 (dd, 1 H, J = 4.0, 5.6 Hz, H 3'), 4.69 (ddd, 1 H, J = 3.7, 9.9, 12.0 Hz, H 10'), 4.22 (d, 1 H, J = 8.3 Hz, H 7'), 4.10 (d, 1 H, J = 4.0 Hz, H 4'), 2.19 (s, 6 H, Ac), 2.11 (s, 3 H, Ac), 2.11 (m, 1 H, H 6'), 2.08 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.94 (s, 3 H, Ac), 1.62 (m, 1 H, H 6').
FTIR (neat film) cm^{-1}:	3289 (w, br), 2925 (w), 1747 (s), 1693 (s) 1546 (w), 1458 (w), 1370 (m), 1223 (s), 1123 (w), 1041 (m), 929 (w).
MS (FAB) *m/z*:	700 $(MH)^+$, 640 (M^+ - AcO).
HRMS (FAB) *m/z*:	Calculated for $C_{29}H_{38}N_3O_{17}$ $(MH)^+$: 700.2201. Found: 700.2231.
TLC R_f (10% MeOH in CH_2Cl_2):	0.33



70 **71**

Uridine Diol **71.**

Chlorotrimethylsilane (3.47 mL, 27.40 mmol, 2.5 equiv) was added to a solution of 5'-*O*-dimethoxytrityl uridine (**70**) (5.98 g, 10.94 mmol, 1 equiv), DMAP (30 mg, 0.25 mmol, 0.02 equiv), and triethylamine (7.62 mL, 54.70 mmol, 5.0 equiv) in dichloromethane (20.0 mL). The resulting white slurry was stirred at 23 °C for 2 h and then was filtered. The filtrate was concentrated, and the residual oil was passed through flash grade silica gel (33% ethyl acetate in hexanes) to yield a viscous, yellow oil (6.95 g). The intermediate bis(trimethylsilyl) ether was dissolved in pyridine (25.0 mL), and DMAP (30 mg, 0.25 mmol, 0.02 equiv) and di-*t*-butyl dicarbonate (3.47 mL, 15.10 mmol, 1.4 equiv) were added sequentially. The resulting mixture was stirred at 23 °C for 12 h. Volatiles were removed in vacuo, and the residue was diluted with methyl alcohol (20 mL). Potassium fluoride hydrate (2.50 g, 26.56 mmol, 2.4 equiv) was added to the resulting solution, and the reaction mixture was stirred at 23 °C for 3 h. The product was partitioned between ethyl acetate (600 mL) and water (200 mL). The organic layer was washed with saturated aqueous sodium chloride solution (200 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (40% ethyl acetate in hexanes) to provide **71** (5.58 g, 79%) as a white solid (mp 93.0 °C).

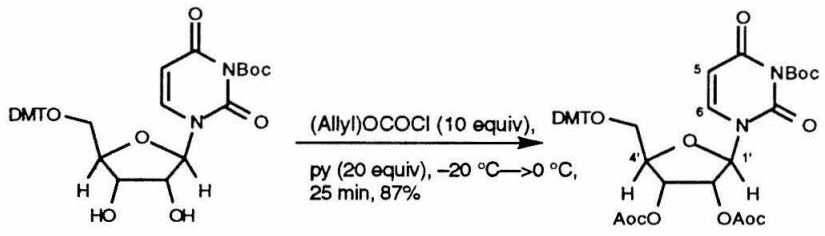
^{1}H NMR (400 MHz, Acetone-d_6) δ: 7.97 (d, 1 H, J = 8.2 Hz, H 6), 7.47 (m, 2 H, arom), 7.33 (m, 6 H, arom), 7.26 (m, 1 H, arom), 6.90 (m, 4 H, arom), 5.89 (d, 1 H, J = 4.1 Hz, H 1'), 5.33 (d, 1 H, J = 8.2 Hz, H 5), 4.84 (d, 1 H, J = 5.5 Hz, OH), 4.49 (m, 1 H, H 3'), 4.37 (m, 2 H, H 4' and OH), 4.13 (m, 1 H, H 2'), 3.78 (s, 6 H, OCH_3), 3.50 (dd, 1 H, J = 3.0, 12.1 Hz, H 5'), 3.43 (dd, 1 H, J = 2.7, 12.1 Hz, H 5'), 1.55 (s, 9 H, *t*-butyl).

FTIR (neat film) cm^{-1}: 3436 (w, br), 2932 (w), 1784 (s), 1716 (s), 1668 (s), 1608 (m), 1509 (m), 1446 (m), 1392 (m), 1252 (s), 1177 (w), 1147 (m).

MS (FAB) *m/z*: 646 $(M)^+$, 303 $(DMT)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{35}H_{38}N_2O_{10}$ $(M)^+$: 646.2526. Found: 646.2498.

TLC R_f (67% EtOAc in hexanes): 0.46



71

2',3'-Bis(Aoc) Uridine.

Allyl chloroformate (10.20 mL, 95.80 mmol, 10.0 equiv) was added dropwise over a 10-min interval to a solution of diol **71** (6.20 g, 9.58 mmol, 1 equiv) in pyridine (15.50 mL, 191.6 mmol, 20.0 equiv) at –20 °C. The resulting slurry was allowed to warm to 23 °C and was stirred at this temperature for 25 min. Volatiles were removed in vacuo, and the residue was dissolved in dichloromethane (30 mL). The product was partitioned between ethyl acetate (500 mL) and water (300 mL). The organic layer was washed with saturated aqueous sodium chloride solution (300 mL), then was dried (sodium sulfate) and concentrated. The crude product was purified by flash column chromatography (33% ethyl acetate in hexanes) to yield 2',3'-*O*-di(allyloxycarbonyl)-5'-*O*-dimethoxytrityl-3-*N*-*t*-butylcarbamate uridine (6.78 g, 87%) as a white solid (mp 77.0 - 78.0 °C).

^{1}H NMR (300 MHz, C_6D_6) δ: 7.57 (m, 2 H, arom), 7.40 (m, 4 H, arom), 7.36 (d, 1 H, J = 8.2 Hz, H 6), 7.20 (m, 2 H, arom), 7.07 (m, 1 H, arom), 6.80 (m, 4 H, arom), 6.26 (d, 1 H, J = 3.7 Hz, H 1'), 5.73 (m, 3 H, Aoc), 5.67 (m, 1 H, H 3'), 5.62 (m, 1 H, H 2'), 5.19 (d, 1 H, J = 8.2 Hz, H 5), 5.14 (m, 1 H, Aoc), 5.08 (m, 1 H,

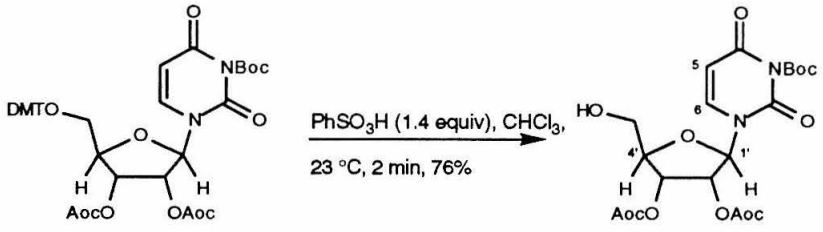
Aoc), 4.98 (m, 1 H, Aoc), 4.96 (m, 1 H, Aoc), 4.43 (m, 1 H, Aoc), 4.40 (m, 1 H, Aoc), 4.31 (m, 1 H, Aoc), 4.10 (m, 1 H, H 4'), 3.44 (dd, 1 H, J = 2.9, 11.5 Hz, H 5'), 3.35 (dd, 1 H, J = 2.9, 11.5 Hz, H 5'), 3.33 (s, 6 H, OCH_3), 1.45 (s, 9 H, *t*-butyl).

FTIR (neat film) cm^{-1}: 2935 (w), 1787 (s), 1759 (s), 1724 (s), 1682 (s), 1608 (w), 1509 (m), 1440 (m), 1372 (m), 1256 (s), 1148 (m), 1033 (w), 833 (w).

MS (FAB) *m/z*: 814 $(M)^+$, 303 $(DMT)^+$.

HRMS (FAB) *m/z*: Calcd for $C_{43}H_{46}N_2O_{14}$ $(M)^+$: 814.2949. Found: 814.2900.

TLC R_f (50% EtOAc in hexanes): 0.53



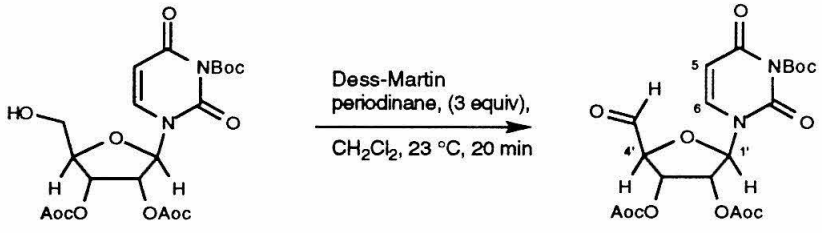
72

Uridine-5'-Alcohol **72.**

A solution of benzenesulfonic acid (1.80 g, 11.38 mmol, 1.4 equiv) in chloroform (60.0 mL) was poured onto 2',3'-*O*-di(allyloxycarbonyl)-5'-*O*-dimethoxytrityl-3-*N*-*t*-butylcarbamate uridine (6.78 g, 8.33 mmol, 1 equiv), and the resulting orange solution was stirred at 23 °C for 2 min. The product was partitioned between ethyl acetate (500 mL) and saturated aqueous sodium bicarbonate solution (300 mL). The organic layer was washed with saturated aqueous sodium chloride solution (300 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (67% ethyl acetate in hexanes) to afford **72** (3.26 g, 76%) as a white solid (mp 62.0 °C).

^{1}H NMR (300 MHz, C_6D_6) δ: 7.01 (d, 1 H, *J* = 10.1 Hz, H 6), 5.96 (d, 1 H, *J* = 6.7 Hz, H 1'), 5.73 (m, 1 H, Aoc), 5.72 (m, 1 H, H 3'), 5.68 (m, 1 H, Aoc), 5.62 (m, 1 H, Aoc), 5.48 (dd, 1 H, *J* = 5.3, 6.7 Hz, H 2'), 5.34 (d, 1 H, *J* = 10.1 Hz, H 5), 5.20 - 4.94 (m, 4 H, Aoc), 4.45 - 4.28 (m, 3 H, Aoc), 3.95 (m, 1 H, H 4'), 3.53 (m, 1 H, H 5'), 3.30 (m, 1 H, H 5'), 2.57 (t(br), 1 H, OH), 1.45 (s, 9 H, *t*-butyl).

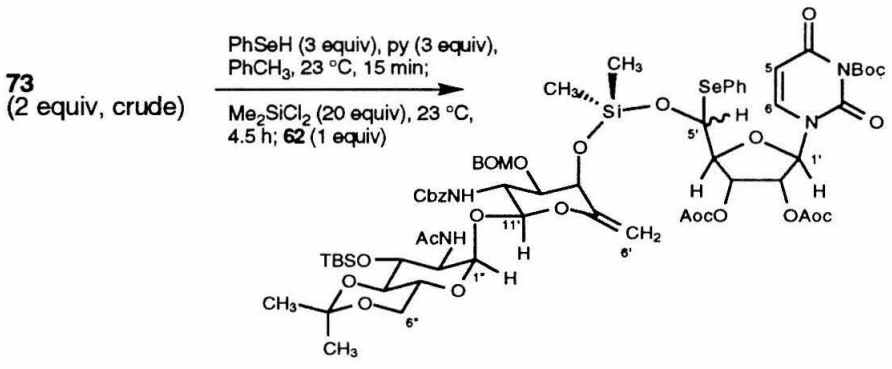
FTIR (neat film) cm^{-1}:	3499 (w, br), 2986 (w), 1784 (s), 1756 (s), 1722 (s), 1682 (s), 1451 (m), 1372 (m), 1265 (s), 1147 (m), 1100 (w), 951 (w), 786 (w).
MS (FAB) *m/z*:	513 $(MH)^+$, 413 (MH^+ - *t*-Boc).
HRMS (FAB) *m/z*:	Calcd for $C_{22}H_{29}N_2O_{12}$ $(MH)^+$: 513.1720. Found: 513.1739.
TLC R_f (67% EtOAc in hexanes):	0.42



72 **73** (crude)

Aldehyde **73.**

A solution of alcohol **72** (355 mg, 0.693 mmol, 1 equiv) in dichloromethane (4.0 mL) was added via cannula to a suspension of the Dess-Martin periodinane (882 mg, 2.08 mmol, 3.0 equiv) in dichloromethane (4.0 mL), and the resulting suspension was stirred at 23 °C for 20 min. The product was partitioned between ethyl acetate (130 mL) and a mixture of saturated aqueous sodium bicarbonate solution and saturated aqueous sodium thiosulfate solution (4:1 (v/v), 50 mL). The organic layer was washed with saturated aqueous sodium chloride solution (50 mL), then was dried (sodium sulfate) and concentrated. The residue was filtered through a short column of silica gel (67% ethyl acetate in hexanes) to afford the crude aldehyde **73** (250 mg). Due to the extreme lability of the product and its high susceptibility to hydration, the crude uridine 5'-aldehyde derivative **73** was immediately used without further purification in the following experiment.



74 (81%)

O-Silylhemiselenoacetal **74.**

Benzeneselenol (81 μL, 0.74 mmol, 3.0 equiv) and pyridine (59 μL, 0.74 mmol, 3.0 equiv) were added sequentially to a deoxygenated solution of freshly prepared aldehyde **73** from the previous experiment (250 mg, ~0.5 mmol, ~2 equiv, azeotropically dried with 1.5 mL of toluene), and the resulting solution was deoxygenated. After stirring at 23 °C for 15 min, the reaction mixture was transferred via cannula to a solution of dichlorodimethylsilane (594 μL, 4.9 mmol, 20 equiv) in pyridine (2 mL). The resulting suspension was deoxygenated and was stirred in the dark at 23 °C for 6 h. The reaction mixture was concentrated in vacuo at 23 °C, and the residue was suspended in toluene (2 mL). The volatiles were removed at 23 °C, and the residue was diluted with toluene (3 mL). To the mixture was added via cannula a solution of allylic alcohol **62** (189 mg, 0.24 mmol, 1 equiv) in pyridine (2.5 mL), and the resulting suspension was stirred at 23 °C for 5 min. The product was partitioned between ethyl acetate (100 mL) and water (100 mL). The organic phase was dried (sodium sulfate) and concentrated, and the residue was purified by flash

column chromatography (50% ethyl acetate in hexanes) to afford an inseparable mixture of diastereomers **74** (1.5:1) (296 mg, 81% total) as a white solid (mp 78.0–80.5 °C).

^{1}H NMR (400 MHz, C_6D_6, 50 °C) δ: 7.69 (m, arom), 7.60 (m, arom), 7.30 (m, arom), 7.14 (m, arom), 7.10-7.03 (m, arom), 6.36 (d, 1 H, *J* = 10.1 Hz, H 1'), 6.27 (m, 2 H, NH, H 1'), 5.97 (m), 5.91 (m, 1 H, NH), 5.85 (m, H 5'), 5.78-5.54 (m, Aoc, H 11', H 1', H 2', H 3'), 5.25-4.95 (m), 4.74-4.53 (m), 4.50-4.20 (m), 4.14 (t, 1 H, *J* = 9.75 Hz, H 6"), 4.07-3.95 (m), 3.77 (t, 1 H, *J* = 9.75 Hz, H 4"), 3.65-3.56 (m), 2.18 (s, 3 H, Ac), 2.13 (s, 3 H, Ac), 1.49 (s, *t*-Boc), 1.45 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.12 (s, 9 H, *t*-butyl), 1.09 (s, 9 H, *t*-butyl), 0.31 (s, 3 H, $SiCH_3$), 0.28 (s, 3 H, $SiCH_3$), 0.24 (s, 3 H, $SiCH_3$), 0.21 (s, $SiCH_3$), 0.20 (s, $SiCH_3$), 0.19 (s, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3331 (w, br), 2943 (w), 1784 (m), 1760 (m), 1723 (m), 1682 (s), 1527 (w), 1450 (w), 1373 (m), 1262 (s), 1147 (m), 1079 (m), 1023 (m), 842 (w).

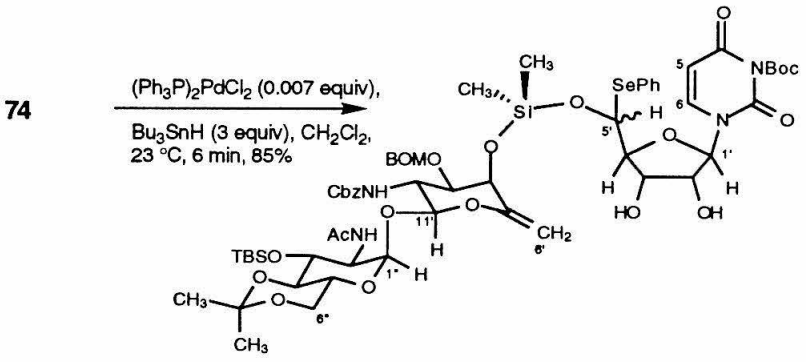
MS (FAB) *m/z*: 1498$(MH)^+$, 772 (allylic alcohol disaccharide)$^+$.

Elemental Analysis: Calcd for $C_{69}H_{92}N_4O_{24}SeSi_2$: C, 55.37; H, 6.20;

N, 3.74.

Found: C, 55.70; H, 6.18; N, 3.82.

TLC R_f (67% EtOAc in hexanes): 0.59



75

Diol **75.**

Tributyltin hydride (503 μL, 1.9 mmol, 3.0 equiv) was added to a deoxygenated solution of *O*-silylhemiselenoacetals **74** (931 mg, 0.62 mmol, 1 equiv) and bis(triphenylphosphine)palladium(II) chloride chloride (3 mg, 4 μmol, 0.007 equiv) in a mixture of water in dichloromethane (2% (v/v), 6 mL), and the resulting brown solution was stirred at 23 °C for 6 min. The reaction mixture immediately was subjected to flash column chromatography (gradient elution: 50 → 67% ethyl acetate in hexanes) to afford diol **75** (700 mg, 85%) as a white solid (mp 94.0–95.5 °C).

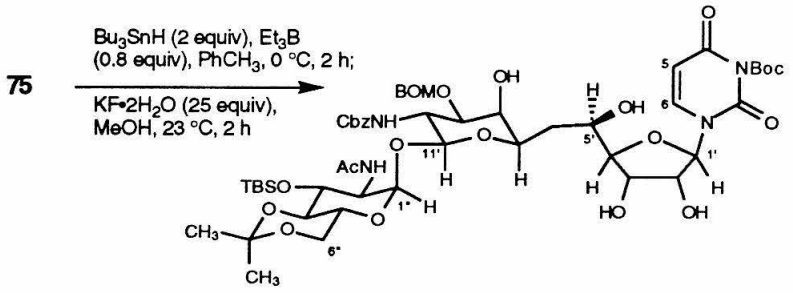
^{1}H NMR (400 MHz, C_6D_6, 50 °C) δ: 9.70 (d, 1 H, *J* = 9.7 Hz, H 6), 7.68-7.60 (m, arom), 6.16 (d, 1 H, *J* = 3.33 Hz, H 1'), 6.11 (d, 1 H, *J* = 10.0 Hz, NH), 6.01 (d, 1 H, *J* = 5.67 Hz, H 11'), 5.80 (m, 2 H, NH, H 1''), 5.70 (d, 1 H, *J* = 2.0 Hz, H 5'), 5.53 (d, 1 H, *J* = 8.67 Hz, H 5), 5.51 (d, 1 H, *J* = 10.0 Hz, NH), 5.27-5.15 (m),

4.73-3.95 (m), 3.84-3.73 (m), 3.64-3.55 (m), 2.13 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 1.51 (s, 9 H, *t*-Boc), 1.47 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.09 (s, 9 H, *t*-butyl), 1.06 (s, 9 H, *t*-butyl), 0.28 (s, 3 H, $SiCH_3$), 0.25 (s, 3 H, $SiCH_3$), 0.23 (s, $SiCH_3$), 0.22 (s, $SiCH_3$), 0.16 (s, $SiCH_3$), 0.15 (s, $SiCH_3$), 0.05 (s, $SiCH_3$), -0.17 (s, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3334 (w, br), 2931 (w), 1786 (m), 1719 (s), 1667 (s), 1540 (w), 1452 (w), 1374 (m), 1256 (s), 1120 (s), 1022 (s), 861 (m), 840 (m).

MS (FAB) *m/z*: 1329 $(MH)^+$, 358 $(glucopyranoside)^+$.

TLC R_f (67% EtOAc in hexanes): 0.44



76 (60%)

Tetraol **76.**

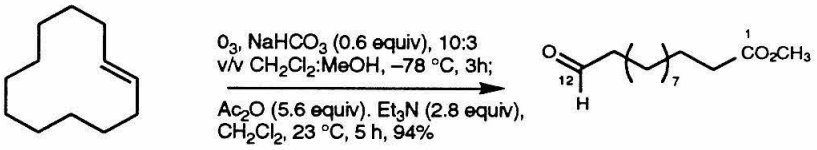
Aliquots of a solution of triethylborane (25 μL each, 1.0 M in hexanes, 0.025 mmol, 0.1 equiv each) were added to a deoxygenated solution of diol **75** (340 mg, 0.26 mmol, 1 equiv) and tributyltin hydride (138 μL, 0.51 mmol, 2.0 equiv) in toluene (300 mL) at 0 °C at 15-min intervals over a 2-hour period. The resulting solution was concentrated at 0 °C, and the residue was diluted with methyl alcohol (10 mL). To this solution was added potassium fluoride hydrate (600 mg, 6.4 mmol, 25 equiv), and the resulting mixture was stirred at 23 °C for 2 h. The product was partitioned between ethyl acetate (300 mL) and saturated aqueous sodium chloride solution (150 mL). The organic layer was separated, and the aqueous layer was extracted further with ethyl acetate (100 mL). The combined organic layers were dried (sodium sulfate) and concentrated, and the residue, containing a 7.5:1 mixture of C5' diastereomers, was purified by careful flash column chromatography (12:4:1 benzene:acetonitrile:isopropanol) to afford pure **76** (172 mg, 60%) as a white solid (mp 223.0 °C).

^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ: 7.52 (d, 1 H, *J* = 8.1 Hz, H 6), 7.35-7.20 (m, 10 H, arom), 5.83 (d, 1 H, *J* = 8.6 Hz, NH), 5.74 (d, 1 H, *J* = 8.1 Hz, H 5), 5.65 (d, 1 H, *J* = 4.0 Hz, H 1'), 5.18 (d, 1 H, *J* = 12.1 Hz, $PhCH_2OCO$), 5.03 (m, 2 H, H 1", H 11'), 4.98 (d, 1 H, *J* = 12.1 Hz, $PhCH_2OCO$), 4.79 (d, 1 H, *J* = 6.3 Hz, OCH_2O), 4.73 (d, 1 H, *J* = 6.3 Hz, OCH_2O), 4.62 (d, 1 H, *J* = 7.5 Hz, NH), 4.56 (d, 1 H, *J* = 11.8 Hz, $PhCH_2$), 4.52 (d, 1 H, *J* = 11.8 Hz, $PhCH_2$), 4.32 (m, 2 H), 4.20-4.05 (m, 2 H, 3.96 (t, 1 H, *J* = 3.5 Hz, H 3'), 3.94 (m, 1 H, H6"), 3.84 (m, 1 H, H 4'), 3.82-3.71 (m, 3 H), 3.66 (t, 1 H, *J* = 10.1 Hz, H 6"), 3.55 (t, 1 H, *J* = 9.2 Hz, H 4"), 3.43 (s-br, 1 H), 3.27 (s-br, 1 H), 2.62 (s-br, 1 H), 2.20 (m, 1 H, H 6'), 1.91 (s, 3 H, Ac), 1.74 (m, 1 H, H 6'), 1.58 (s, 9 H, *t*-Boc), 1.45 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 0.85 (s, 9 H, *t*-butyl), 0.08 (s, 6 H, $SiCH_3$).

FTIR (neat film) cm^{-1}: 3354 (m, br), 2933 (m), 1784 (m), 1713 (s), 1667 (s), 1544 (m), 1449 (w), 1374 (m), 1253 (m), 1120 (s), 1079 (m), 1026 (s), 867 (w), 838 (w), 726 (m).

MS (FAB) *m/z*: 908 (MH^+ - uracil(Boc)), 211 (uracil(Boc))$^+$.

TLC R_f (10% MeOH in CH_2Cl_2): 0.34

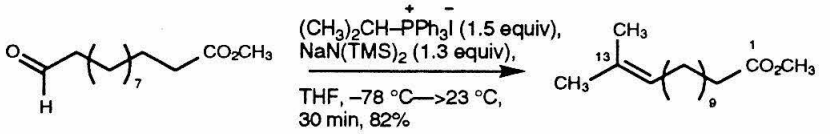


77 **78**

Aldehyde **78.**

Ozone was bubbled through a mixture of sodium bicarbonate (1.60 g, 19.0 mmol, 0.6 equiv) and cyclododecene (**77**) (5.00 g, 30.1 mmol, 1 equiv) in a mixture of dichloromethane and methyl alcohol (10:3 (v/v), 130 mL) at –78 °C for 3 h until the solution became deep blue. To remove excess ozone, nitrogen was bubbled through the solution at –78 °C for 15 min until the solution became colorless; the reaction mixture was then allowed to warm to 23 °C. After filtration of the suspension, benzene (80 mL) was added to the filtrate, and the resulting solution was concentrated to a volume of 40 mL. The concentrate was diluted with dichloromethane (160 mL), and triethylamine (12.0 mL, 86.1 mmol, 2.8 equiv) and acetic anhydride (16.0 mL, 169.6 mmol, 5.6 equiv) were added sequentially at 23 °C over a 10-min period. After stirring for 5 h, the reaction mixture was diluted further with dichloromethane (150 mL). The solution was washed sequentially with 0.1 N aqueous hydrochloric acid (300 mL), saturated aqueous sodium bicarbonate solution (300 mL), and saturated aqueous sodium chloride solution (300 mL). The organic layer was dried (sodium sulfate) and concentrated, and the pale yellow residue was purified by flash column chromatography (10% ethyl acetate in hexanes) to give the aldehyde **78** (6.10 g, 94%) as a clear, colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ:	9.75 (s, 1 H, H 12), 3.62 (s, 3 H, OCH_3), 2.41 (dt, 1 H, J = 2.1, 7.5 Hz, H 2), 2.30 (t, 1 H, J = 7.5 Hz, H 2), 1.62 (m, 2 H, H 11), 1.29 (m, 16 H, CH_2).
FTIR (neat film) cm^{-1}:	2926 (s), 2853 (s), 1739 (s), 1436 (w), 1172 (m).
MS (EI) *m/z*:	227 (M^+ - H), 213 (M^+ - CH_3).
HRMS (EI) *m/z*:	Calcd for $C_{13}H_{23}O_3$ (M^+ - H): 227.1647, Found: 227.1641.
TLC R_f (20% EtOAc in hexanes):	0.39



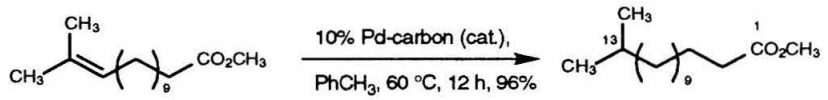
78 **79**

Alkenyl Methyl Ester **79.**

A solution of sodium bis(trimethysilyl)amide (12.0 mL, 1.0 M in tetrahydrofuran, 12.0 mmol, 1.3 equiv) was added to a suspension of isopropyl-triphenyl-phosphonium iodide (6.00 g, 13.9 mmol, 1.5 equiv) in tetrahydrofuran (100 mL) at –78 °C. The resulting red suspension was stirred at –78 °C for 5 min, then at 23 °C for 25 min, and finally at 0 °C for 5 min. A solution of aldehyde **78** (2.00 g, 9.25 mmol, 1 equiv) in tetrahydrofuran (25 mL) was added via cannula to the ylide solution at 0 °C, and the resulting suspension was stirred at 23 °C for 1 h. The product was partitioned between ethyl ether (500 mL) and water (300 mL). The organic layer was washed with saturated aqueous sodium chloride solution (300 mL), then was dried (sodium sulfate) and concentrated. The resulting oil was purified by flash column chromatography (gradient elution: 3 → 5% ethyl acetate in hexanes) to afford the methyl ester **79** (1.92 g, 82%) as a clear, colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.11 (m, 1 H, H 12), 3.66 (s, 3 H, OCH_3), 3.30 (d, 2 H, J = 7.7 Hz, H 2), 1.93 (m, 1 H, H 11), 1.65 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 1.60 (m, 1 H, H 11), 1.27 (m, 16 H, CH_2).

FTIR (neat film) cm^{-1}:	2925 (s), 2854 (s), 1743 (s), 1436 (m), 1376 (w), 1171 (m).
MS (EI) *m/z*:	254 $(M)^+$, 223 (M^+ - OCH_3).
HRMS (EI) *m/z*:	Calcd for $C_{16}H_{30}O_2$ $(M)^+$: 254.2246, Found: 254.2246.
TLC R_f (10% EtOAc in hexanes):	0.57



79 **80**

Methyl Ester **80.**

A solution of the methyl ester **79** (2.02 g, 7.87 mmol, 1 equiv) in toluene (20 mL) was heated at 60 °C in the presence of 10% palladium on activated carbon (300 mg) under a hydrogen atmosphere (1 atm) for 12 h. The reaction mixture was filtered through a pad of Celite, washing well with ethyl ether (150 mL). The filtrate was concentrated to afford pure **80** (1.94 g, 96%) as a clear, colorless oil.

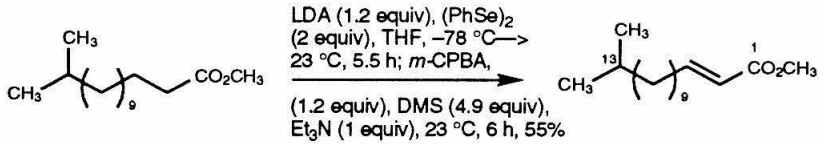
^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.64 (s, 3 H, OCH_3), 2.29 (t, 2 H, J = 7.5 Hz, H 2), 1.52 (m, 1 H, H 13), 1.61 - 1.16 (m, 20 H, CH_2), 0.84 (d, 6 H, J = 8.3 Hz, CH_3).

FTIR (neat film) cm^{-1}: 2925 (s), 2853 (s), 1743 (s), 1461 (w), 1436 (w), 1170 (m).

MS (EI) *m/z*: 256 $(M)^+$, 225 (M^+ - OCH_3).

HRMS (EI) *m/z*: Calcd for $C_{16}H_{32}O_2$ $(M)^+$: 256.2402, Found: 256.2382.

TLC R_f (10% EtOAc in hexanes): 0.57



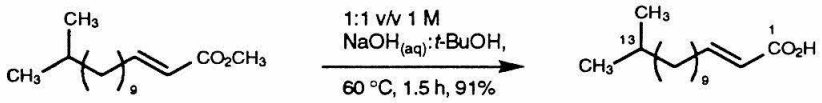
80 **81**

α,β-Unsaturated Methyl Ester **81.**

n-Butyllithium (8.15 mL, 1.3 M in hexanes, 10.6 mmol, 1.2 equiv) was added to a solution of diisopropylamine (1.86 mL, 13.3 mmol, 1.5 equiv) in tetrahydrofuran (40 mL) at –78 °C. The reaction flask was transferred briefly to an ice bath (<10 min), and then was recooled to –78 °C. A solution of **80** (2.26 g, 8.83 mmol, 1 equiv) in tetrahydrofuran (20 mL) was transferred by cannula to the cold solution of lithium diisopropylamide, and the resulting solution was stirred at –78 °C for 25 min. Solid diphenyldiselenide was added to the reaction mixture in one portion, and the resulting suspension was allowed to warm to 23 °C. The deep yellow solution was stirred at 23 °C for 5.5 h. The product was partitioned between ethyl ether (700 mL) and water (300 mL). The organic layer was washed sequentially with water (300 mL) and saturated aqueous sodium chloride solution (300 mL), then was dried (sodium sulfate) and concentrated. Excess diphenyldiselenide was removed from the residue by flash column chromatography (gradient elution: 20 → 25% dichloromethane in hexanes). Solid *m*-chloroperoxybenzoic acid (3.13 g, 60% (w/w), 10.9 mmol, 1.2 equiv) was added to a solution of the crude selenide residue in dichloromethane (100 mL) at –78 °C, and the resulting suspension was stirred at –78 °C for 2 h. Excess oxidant was quenched by the addition of dimethyl sulfide (3.20 mL, 43.6 mmol, 4.9 equiv) and triethylamine (1.22 mL, 8.83 mmol, 1 equiv). The resulting solution was stirred at 23 °C for 6 h, and the product was partitioned between ethyl ether (500 mL) and water (300

mL). The organic layer was washed with saturated aqueous sodium chloride solution (300 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (5% dichloromethane in benzene) to afford methyl ester **81** (1.11 g, 55%) as a clear, colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ:	6.97 (dt, 1 H, J = 6.9, 15.5 Hz, H 3), 5.81 (dt, 1 H, J = 1.4, 15.5 Hz, H 2), 3.73 (s, 3 H, OCH_3), 2.20 (m, 2 H, H 4), 1.50 (m, 1 H, H 13), 1.45 - 1.17 (m, 16 H, CH_2), 0.82 (d, 6 H, J = 6.9 Hz, CH_3).
FTIR (neat film) cm^{-1}:	2926 (s), 2854 (s), 1729 (s), 1658 (m), 1436 (w), 1269 (m), 1173 (w), 1042 (w).
MS (EI) *m/z*:	255 $(MH)^+$, 223 (M^+ - OCH_3).
HRMS (EI) *m/z*:	Calcd for $C_{16}H_{31}O_2$ $(MH)^+$: 255.2113, Found: 255.2313.
TLC R_f (5% EtOAc in hexanes):	0.28



81 **82**

α,β-Unsaturated Fatty Acid **82.**

Methyl ester **81** (364 mg, 1.43 mmol, 1 equiv) was dissolved in a mixture of 1 M aqueous sodium hydroxide solution and *t*-butyl alcohol (1:1 (v/v), 8 mL), and the resulting solution was heated at 60 °C for 1.5 h. The product was partitioned between ethyl acetate (100 mL) and 0.5 N aqueous hydrochloric acid solution (100 mL). The organic layer was washed with saturated aqueous sodium chloride solution (100 mL), then was dried (sodium sulfate) and concentrated. The residue was purified by flash column chromatography (50% ethyl acetate in hexanes) to afford **82** (312 mg, 91%) as a white solid (mp 41.5 °C).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.09 (dt, 1 H, J = 7.1, 15.3 Hz, H 3), 5.82 (dt, 1 H, J = 1.2, 15.3 Hz, H 2), 2.22 (m, 2 H, H 4), 1.50 (m, 1 H, H 13), 1.47 - 1.12 (m, 16 H, CH_2), 1.86 (d, 6 H, J = 7.0 Hz, CH_3).

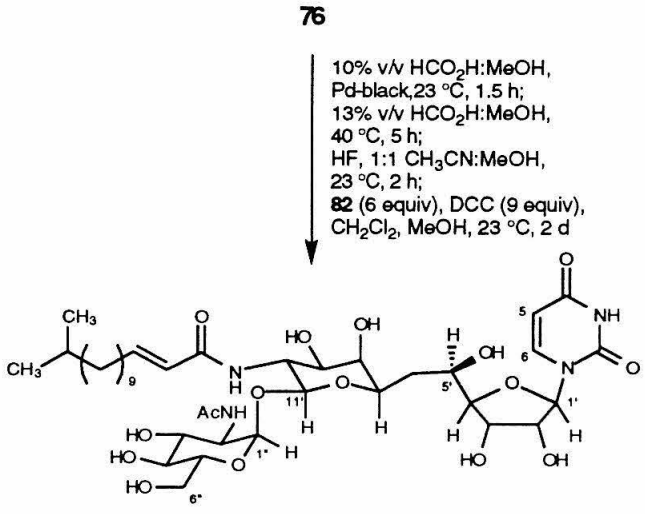
FTIR (neat film) cm^{-1}: 3300 - 2300 (w, br), 2922 (s), 2849 (s), 1691 (s), 1651 (m), 1668 (w), 1420 (w), 1284 (w).

MS (EI) *m/z*: 241 $(MH)^+$, 223 $(M^+ - OH)$.

HRMS (EI) *m/z*: Calcd for $C_{15}H_{29}O_2$ $(MH)^+$: 241.2168,

Found: 241.2178.

TLC R_f (25% EtOAc in hexanes): 0.35



Tunicamycin-V (1-V) (83% from **76**)

Tunicamycin V (**1-V**).

Palladium black (60 mg) was added to a solution of tetraol **76** (140 mg, 0.13 mmol, 1 equiv) in a mixture of formic acid in methyl alcohol (10% (v/v), 10 mL), and the resulting suspension was stirred at 23 °C for 1.5 h. After filtration of the reaction mixture and concentration of the filtrate, the residue was diluted with a mixture of of formic acid in methyl alcohol (13% (v/v), 10 mL), and the resulting solution was heated at 40 °C for 5 h. Following removal of volatiles in vacuo, the residue was dissolved in a mixture of methyl alcohol and acetonitrile (1:1 (v/v), 15 mL), and an aqueous solution of hydrofluoric acid (48% (w/w), 300 μL) was added. The resulting solution was stirred at 23 °C for 2 h. Concentration of the reaction mixture at 23 °C and filtration of the residue through a short column of RP–18 reverse phase silica gel (1:1:1.5 methyl alcohol :pyridine:water) afforded the corresponding crude amino heptaol **1** (81 mg), which was used without further purification.

Solutions of the activated fatty acid **82** were prepared as follows: dichloromethane (3 mL) was added to a solid mixture of fatty acid **82** (31 mg, 0.13 mmol, 1 equiv) and 1,3-dicyclohexylcarbodiimide (40 mg, 0.19 mmol, 1.5 equiv), and the resulting suspension was stirred at 23 °C for 30 min. Freshly prepared solutions of activated **82** (1 equiv each, 6 equiv total) were added to a solution of the crude amino heptaol **1** (81 mg) in methyl alcohol (4 mL) at 8-h intervals over a period of 2 days. The reaction mixture was concentrated at 23 °C, and the residue was purified by flash column chromatography through RP–18 reverse phase silica gel (1:1:1 methyl alcohol pyridine:water) followed by trituration of the residue with chloroform to afford pure **1-V** (88 mg, 83% from tetraol **76**) as a white solid (mp 235–236 °C (decomp)).

^{1}H NMR (400 MHz, CD_3OD) δ: 7.91 (d, 1 H, *J* = 8.0 Hz, H 6), 6.81 (dt, 1 H, *J* = 6.9, 15.5 Hz, fatty acid Hβ,), 5.93 (d, 1 H, *J* = 15.5 Hz, fatty acid Hα), 5.92 (d, 1 H, *J* = 5.6 Hz, H 1'), 5.74 (d, 1 H, *J* = 8.0 Hz, H 5), 4.92 (d, 1 H, *J* = 3.9 Hz, H 1"), 4.58 (d, 1 H, *J* = 8.8 Hz, H 11'), 4.20 (m, 2 H, H 3', H 2'), 4.07 (m, 1 H, H 10'), 4.01 (m, 2 H, H 5', H 5"), 3.84 (m, 3 H, H 3", H 4', H 8'), 3.77 (m, 1 H, H 7'), 3.64 (m, 4 H, H 3", H 6", H 9'), 3.33 (t, 1 H, *J* = 9.1 Hz, H 4"), 2.19 (m, 2 H, fatty acid Hγ), 2.09 (m, 1 H, H 6'), 1.92 (s, 3 H, Ac), 1.57-1.40 (m, 3 H, H 6', *i*-Pr-CH, fatty acid Hδ), 1.28 (s-br, 12 H, CH_2), 1.16 (m, 2 H, CH_2), 0.87 (d, 1 H, *J* = 6.7 Hz, *i*-Pr-CH_3).

^{13}C NMR (100 MHz, CD_3OD) δ:	173.5 (acetamide C=O), 169.8 (fatty acid amide C=O), 166.1 (C4), 152.6 (C2), 146.5 (C6), 142.8 (fatty acid Cβ), 125.0 (fatty acid Cα), 103.1, 102.1 (C5), 100.3 (C11'), 90.1 (C1"), 90.1, 89.6 (C1'), 75.5, 74.3, 73.3, 72.9, 72.7, 72.6, 72.1, 70.9, 68.4, 63.2, 55.0, 54.5, 40.2, 35.9, 33.0, 31.0, 30.7, 30.6, 30.5, 30.3, 29.5, 29.1, 28.5, 23.2, 23.0.
FTIR (neat film) cm^{-1}:	3329 (s, br), 2924 (s), 2849 (m), 1667 (s, br), 1468 (m), 1267 (w), 1096 (s), 1020 (s).
MS (FAB) *m/z*:	831 $(MH)^+$, 223 (fatty acid acyl fragment)$^+$.
HRMS (FAB) *m/z*:	Calcd for $C_{38}H_{63}N_4O_{16}$ $(MH)^+$: 831.4239. Found: 831.4229.
$[\alpha]_D^{24}$:	+60.5 ° (c = 0.515, pyridine).
HPLC	See Appendix.

TLC R_f (2:1:1 *n*-BuOH:AcOH:H_2O): 0.60

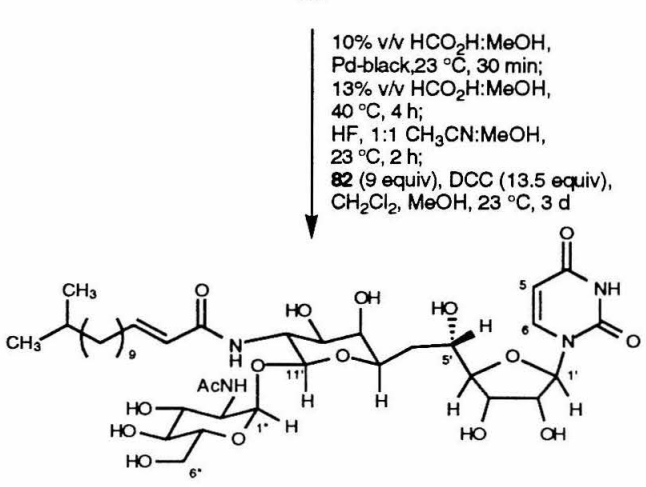
Authentic **1-V.**

A sample of authentic tunicamycins (25 mg, Sigma) was dissolved in methyl alcohol (5 mL) at 40 °C. The solution of authentc **1-V**, in ten separate 500-μL injections, was loaded onto a Beckman Ultrasphere ODS (C_{18}, 5 μm) rp-HPLC column (10 x 250 mm, as part of a Waters 501 HPLC system, flow = 2.00 mL/min), eluting with 85:15 (v/v) methyl alcohol:water. Fractions containing authentic **1-V** were collected and pooled. The combined fractions were concentrated to afford authentic tunicamycin-V (4 mg) as a white solid.

^{1}H NMR (400 MHz, CD_3OD) δ: 7.91 (d, 1 H, *J* = 8.1 Hz, H 6), 6.81 (dt, 1 H, *J* = 6.9, 15.5 Hz, fatty acid Hβ,), 5.93 (d, 1 H, *J* = 15.5 Hz, fatty acid Hα), 5.92 (d, 1 H, *J* = 5.6 Hz, H 1'), 5.74 (d, 1 H, *J* = 8.1 Hz, H 5), 4.92 (d, 1 H, *J* = 3.9 Hz, H 1"), 4.58 (d, 1 H, *J* = 8.6 Hz, H 11'), 4.20 (m, 2 H, H 3', H 2'), 4.07 (m, 1 H, H 10'), 4.01 (m, 2 H, H 5', H 5"), 3.84 (m, 3 H, H 3", H 4', H 8'), 3.77 (m, 1 H, H 7'), 3.64 (m, 4 H, H 3", H 6", H 9'), 3.33 (t, 1 H, *J* = 9.1 Hz, H 4"), 2.19 (m, 2 H, fatty acid Hγ), 2.09 (m, 1 H, H 6'), 1.92 (s, 3 H, acetamide), 1.57-1.40 (m, 3 H, H 6', *i*-Pr-CH, fatty acid Hδ), 1.28 (s-br, 12 H, CH_2), 1.16 (m, 2 H, CH_2), 0.87 (d, 1 H, *J* = 6.7 Hz, *i*-Pr-CH_3).

^{13}C NMR (100 MHz, CD_3OD) δ:	173.5 (acetamide C=O), 169.8 (fatty acid amide C=O), 166.1 (C4), 152.6 (C2), 146.5 (C6), 142.8 (fatty acid Cβ), 125.0 (fatty acid Cα), 103.1, 102.1 (C5), 100.3 (C11'), 90.1 (C1"), 90.1, 89.6 (C1'), 75.5, 74.3, 73.3, 72.9, 72.7, 72.6, 72.1, 70.9, 68.4, 63.2, 55.0, 54.5, 40.2, 35.9, 33.0, 31.0, 30.7, 30.6, 30.5, 30.3, 29.5, 29.1, 28.5, 23.2, 23.0.
FTIR (neat film) cm^{-1}:	3328 (s, br), 2924 (s), 2849 (m), 1666 (s, br), 1465 (m), 1267 (w), 1096 (s), 1020 (s).
MS (FAB) *m/z*:	831 $(MH)^+$.
HRMS (FAB)*m/z*:	Calcd for $C_{38}H_{63}N_4O_{16}$ $(MH)^+$: 831.4239. Found: 831.4250.
$[\alpha]_D^{24}$:	+59.1 ° (c = 0.501, pyridine).
mp:	233–235 °C (decomp).
HPLC	See Appendix.

TLC R_f (2:1:1 *n*-BuOH:AcOH:H_2O): 0.60



C5'-*epi*-Tunicamycin-V (84) (74% from **66**)

C5'-*epi*-Tunicamycin V (**84**).

Palladium black (45 mg) was added to a solution of tetraol **66** (55 mg, 0.039 mmol, 1 equiv) in a mixture of formic acid in methyl alcohol (10% (v/v), 10 mL), and the resulting suspension was stirred at 23 °C for 30 min. After filtration of the reaction mixture and concentration of the filtrate, the residue was diluted with a mixture of of formic acid in methyl alcohol (13% (v/v), 7 mL), and the resulting solution was heated at 40 °C for 4 h. Following removal of volatiles in vacuo, the residue was dissolved in a mixture of methyl alcohol and acetonitrile (1:1 (v/v), 10 mL), and an aqueous solution of hydrofluoric acid (48% (w/w), 200 μL) then was added. The resulting solution was stirred at 23 °C for 2 h. Concentration of the reaction mixture at 23 °C and filtration of the residue through a short column of RP–18 reverse phase silica gel (1:1:1.5 methyl alcohol :pyridine:water) afforded the corresponding crude amino heptaol **83** (22 mg), which was used without further purification.

Solutions of the activated fatty acid **82** were prepared in a manner similar to that described above: dichloromethane (1 mL) was added to a solid mixture of fatty acid **82** (14 mg, 0.06 mmol, 1.5 equiv) and 1,3-dicyclohexylcarbodiimide (20 mg, 0.10 mmol, 2.6 equiv), and the resulting suspension was stirred at 23 °C for 30 min. Freshly prepared solutions of activated **82** (1.5 equiv each, 9 equiv total) were added to a solution of the crude amino heptaol **83** (22 mg) in methyl alcohol (2 mL) at 12-hour intervals over a period of 3 days. The reaction mixture was concentrated at 23 °C, and the residue was purified by flash column chromatography through RP–18 reverse phase silica gel (1:1:1 methyl alcohol :pyridine:water) followed by trituration of the residue with chloroform to afford pure **84** (24 mg, 74% from siloxane **66**).

^{1}H NMR (400 MHz, CD_3OD) δ: 8.11 (d, 1 H, *J* = 8.1 Hz, H 6), 6.81 (dt, 1 H, *J* = 15.2, 7.0 Hz, fatty acid Hβ), 5.95 (d, 1 H, *J* = 15.2 Hz, fatty acid Hα), 5.93 (d, 1 H, *J* = 5.0 Hz, H 1'), 5.72 (d, 1 H, *J* = 8.1 Hz, H 5), 4.96 (d, 1 H, *J* = 3.5 Hz, H 1''), 4.56 (d, 1 H, *J* = 8.4 Hz, H 11'), 4.20 (m, 2 H, H 2', 3'), 4.05 (dd, 1 H, *J* = 10.7, 8.4 Hz, H 10'), 4.00-3.60 (m, 10 H), 3.42 (t, 1 H, *J* = 9.8 Hz), 2.20 (m, 2 H, fatty acid Hγ), 2.09 (m, 1 H, H 6'), 1.91 (s, 3 H, Ac), 1.88 (m, 1 H, H 6'), 1.60-1.15 (m, 16 H), 0.88 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, CD_3OD) δ: 173.4 (acetamide C=O), 169.7 (fatty acid amide C=O), 166.3 (C4), 152.6 (C2), 146.6 (C6), 142.9

(fatty acid Cβ), 124.9 (fatty acid Cα), 102.8, 102.5 (C5), 100.4 (C11'), 90.1 (C1"), 90.1, 87.8 (C1'), 75.6, 74.3, 74.1, 73.1, 72.8, 72.5, 71.8, 70.8, 68.8, 62.3, 55.0, 54.4, 40.3, 35.9, 33.1, 31.1, 30.8, 30.7, 30.6, 30.4, 29.5, 29.2, 28.6, 23.3, 23.1.

FTIR (neat film) cm^{-1}: 3399 (s, br), 2919 (m), 2849 (w), 1666 (s), 1631 (m), 1561 (w), 1461 (w), 1414 (m), 1349 (m), 1094 (m), 1023 (m).

MS (FAB) *m/z*: 853 $(MNa)^+$, 223 (fatty acid acyl fragment)$^+$.

HRMS (FAB) *m/z*: Calcd for $C_{38}H_{62}N_4O_{16}$ $(MNa)^+$: 853.4059. Found: 853.4036.

TLC R_f (2:1:1 *n*-BuOH:AcOH:H_2O): 0.60

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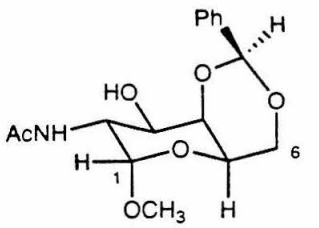
Appendix

Catalog of Spectra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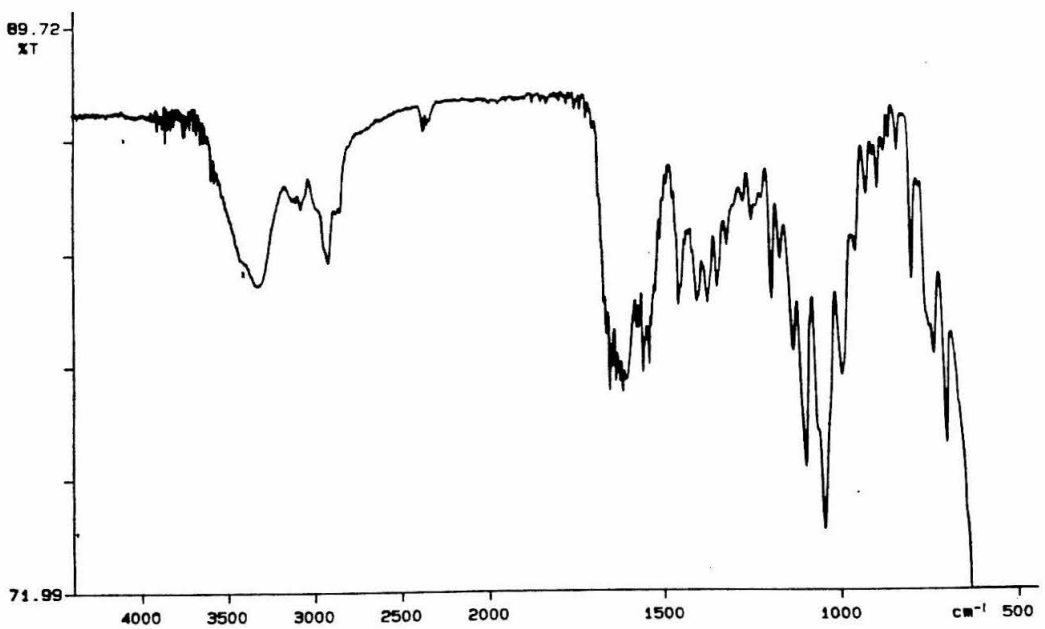
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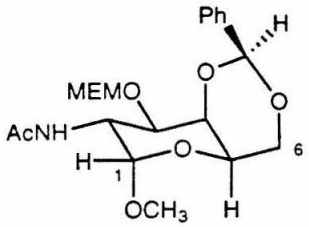
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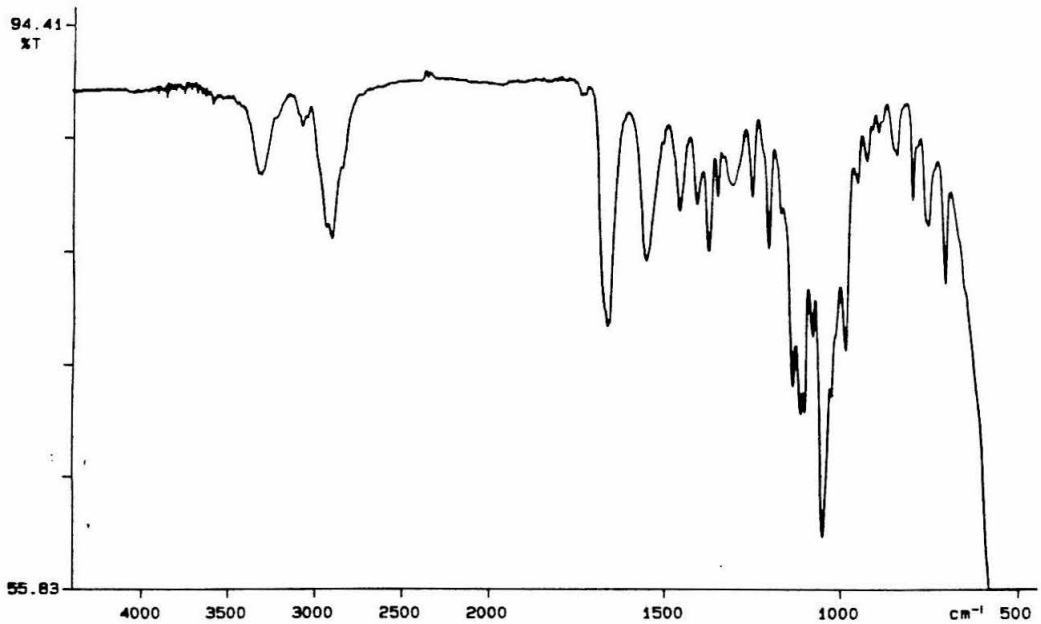
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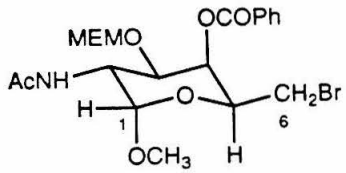
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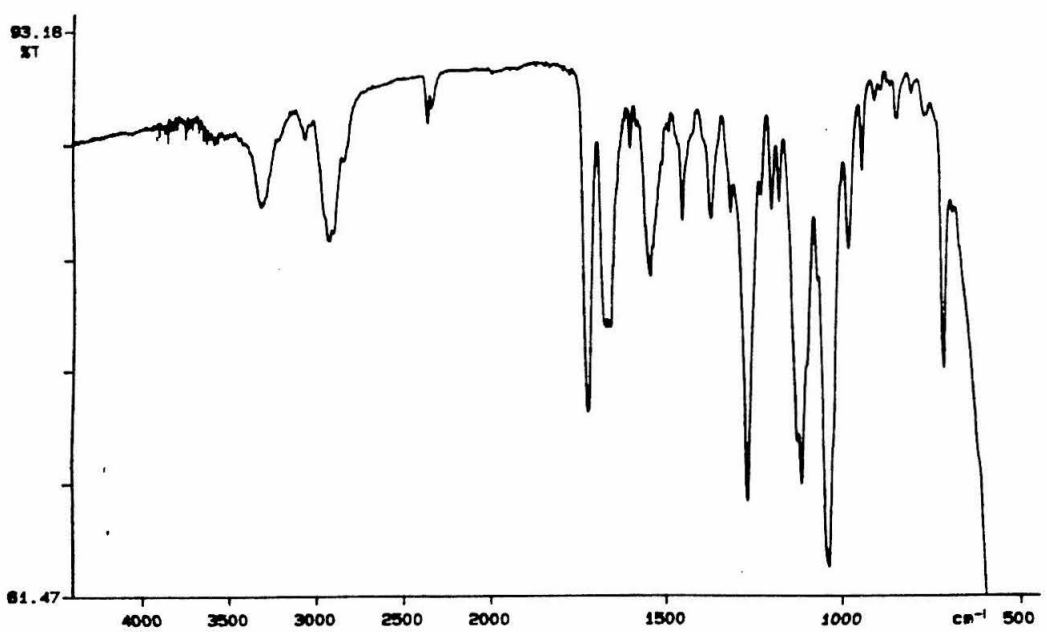
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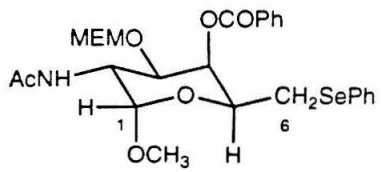
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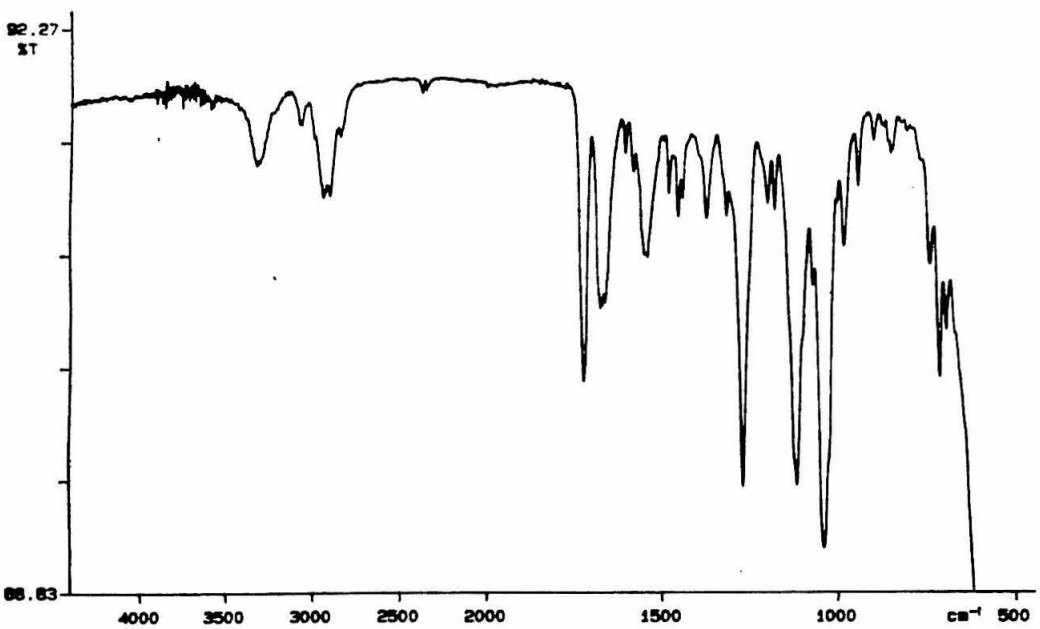
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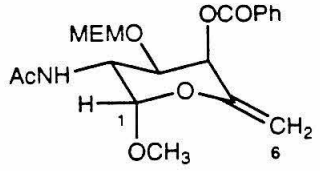
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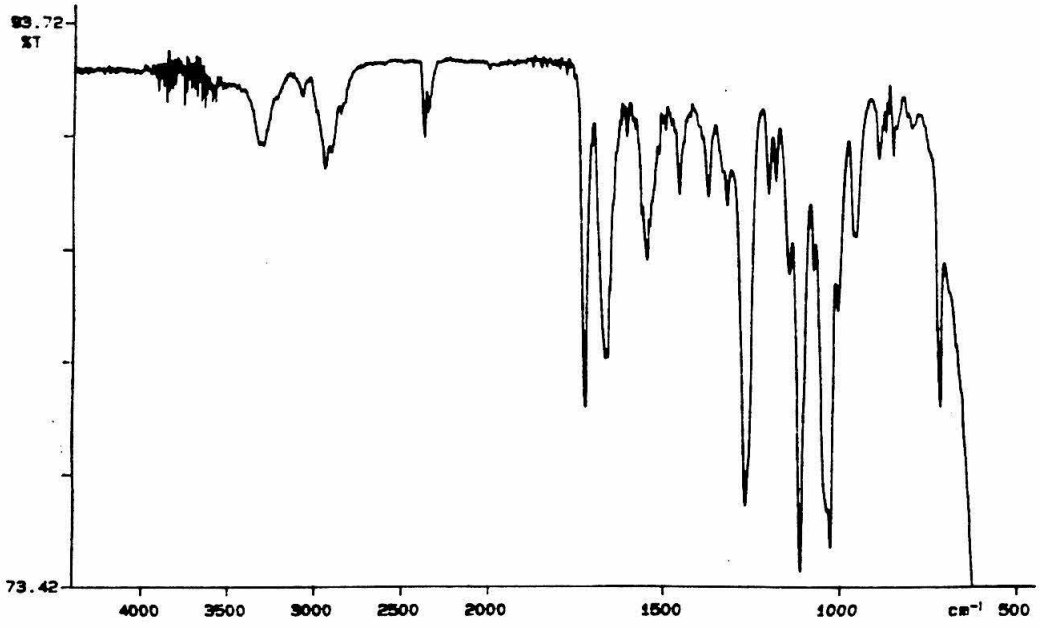
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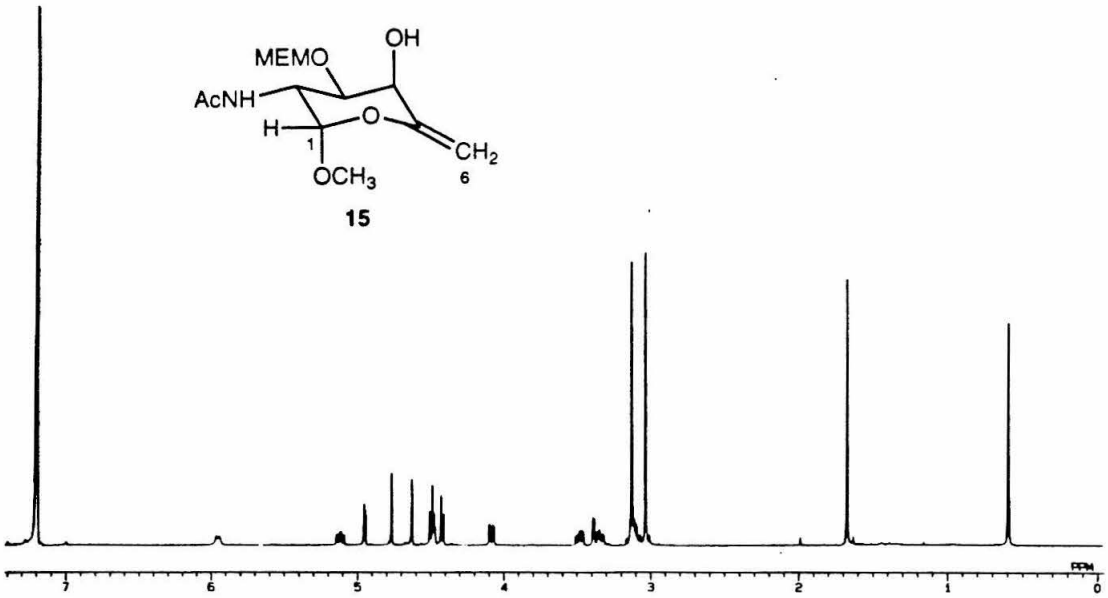
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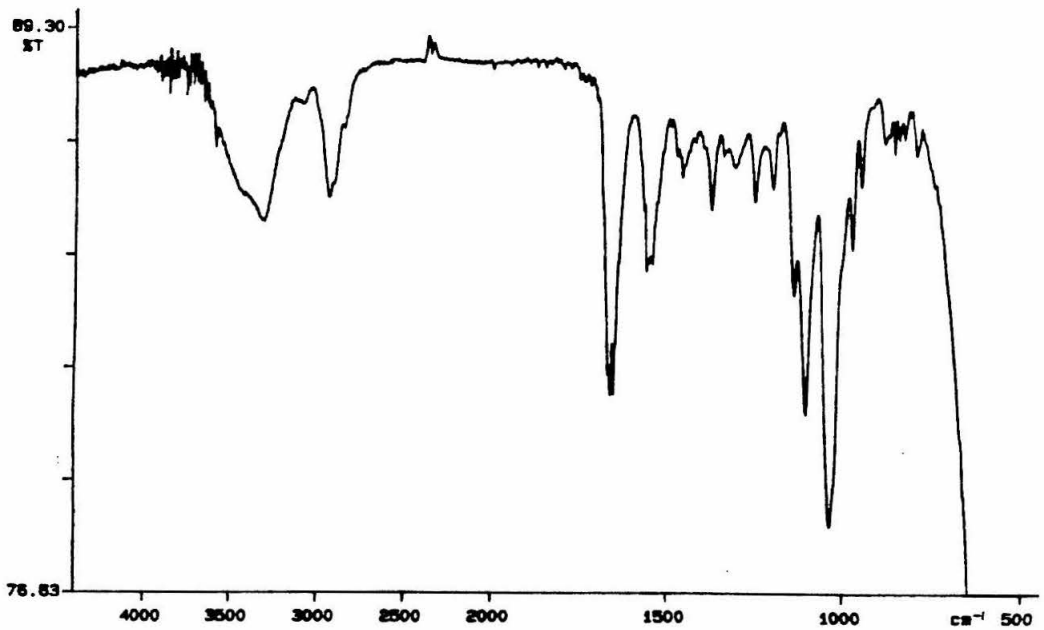
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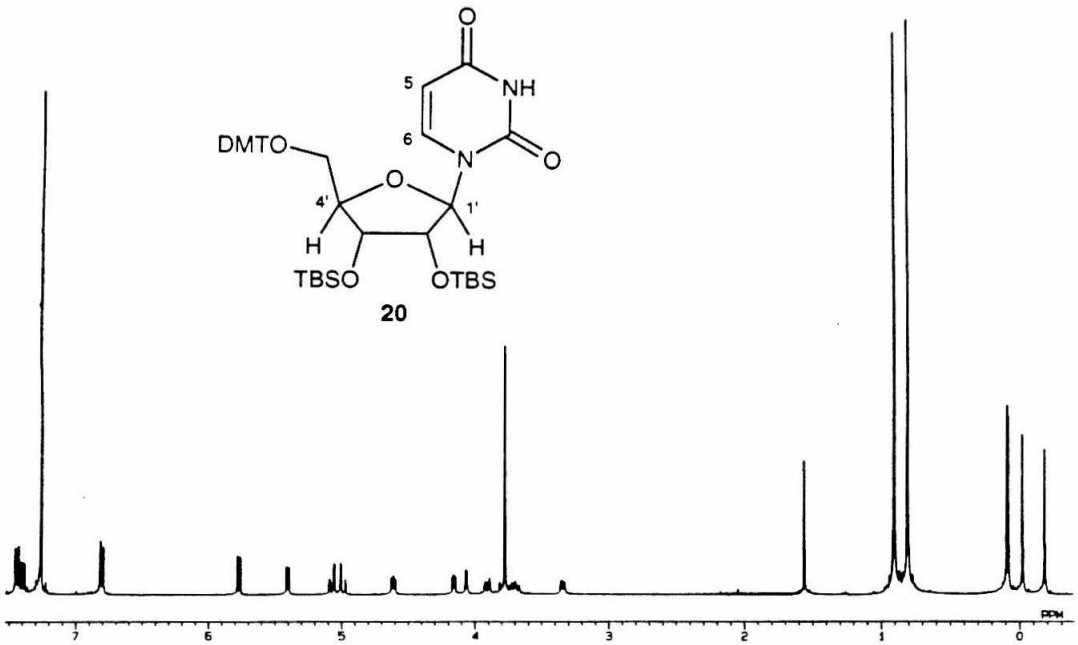
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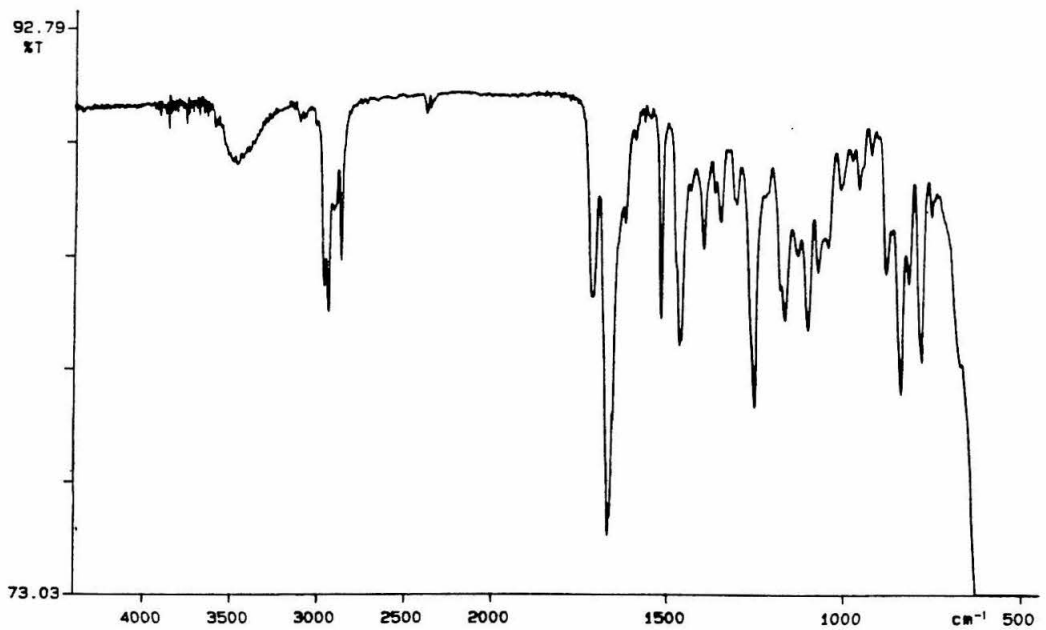
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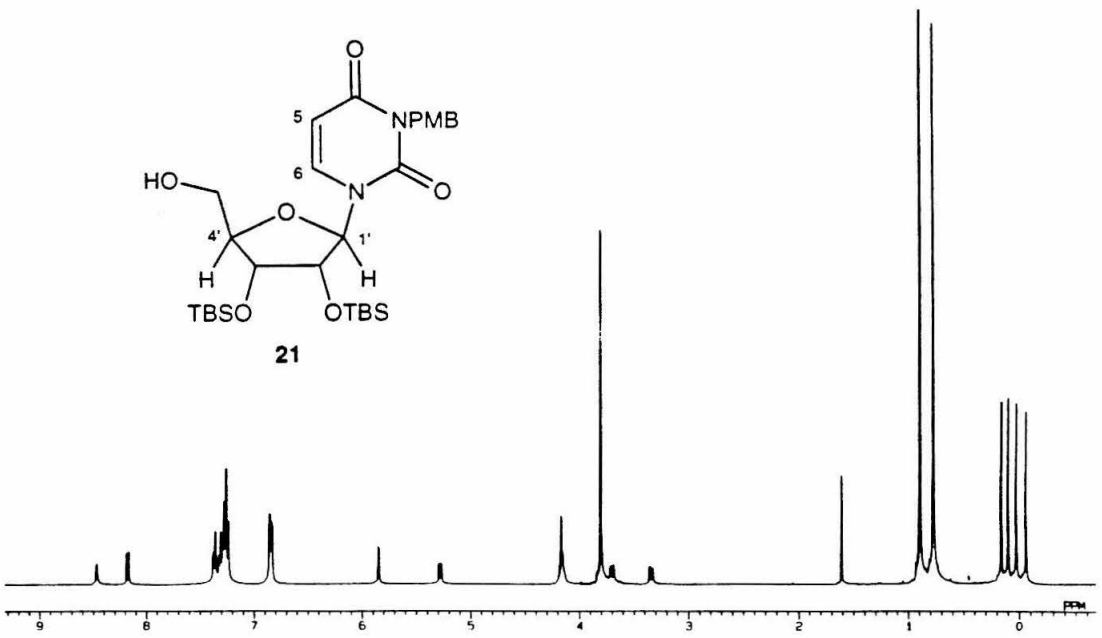
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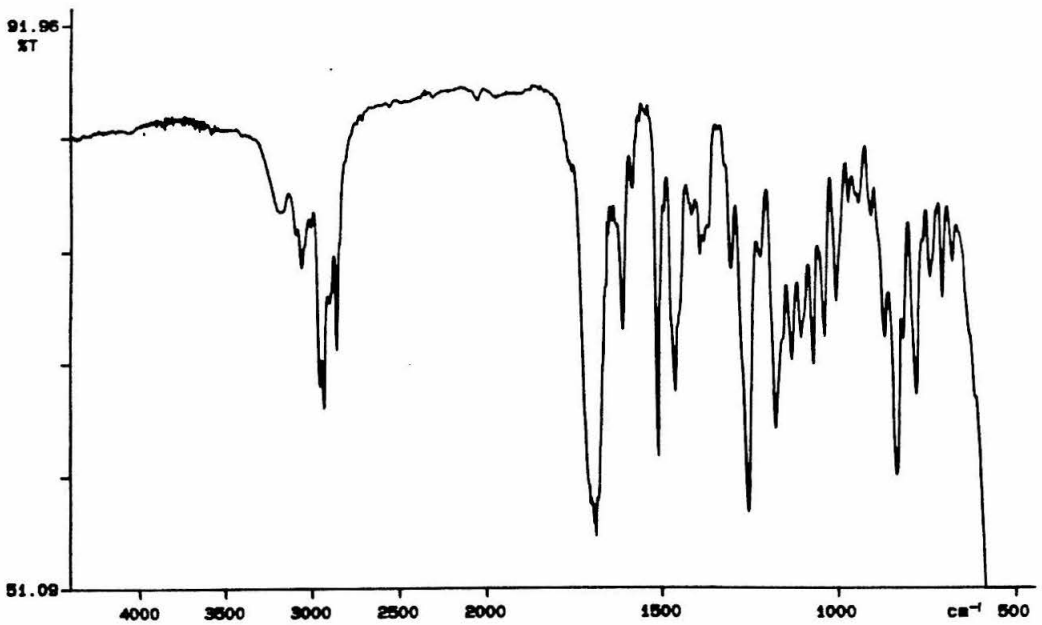
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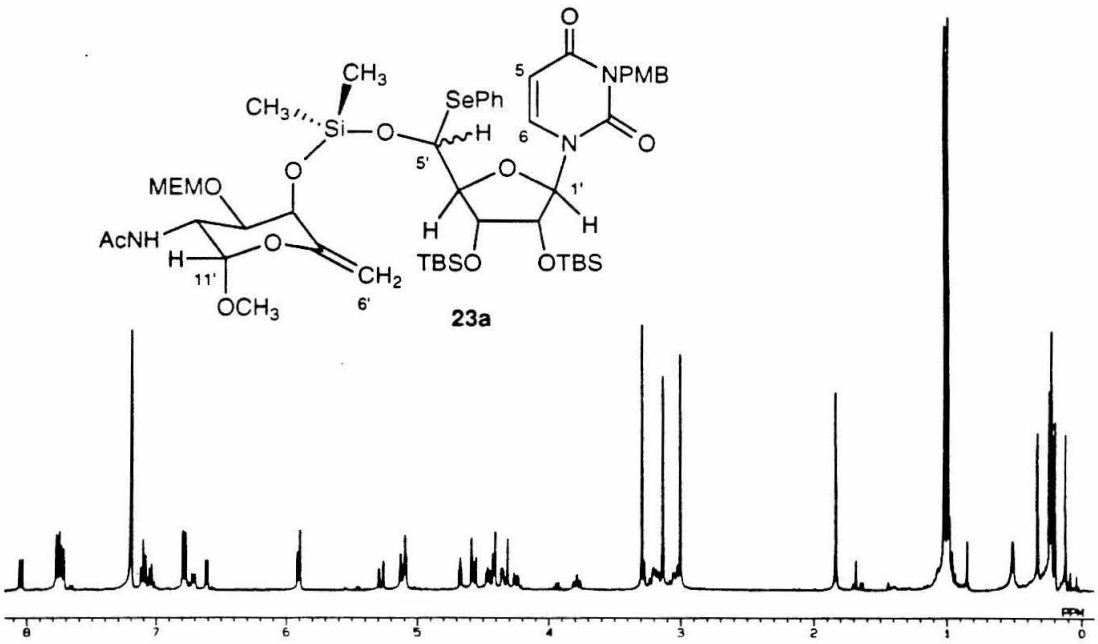
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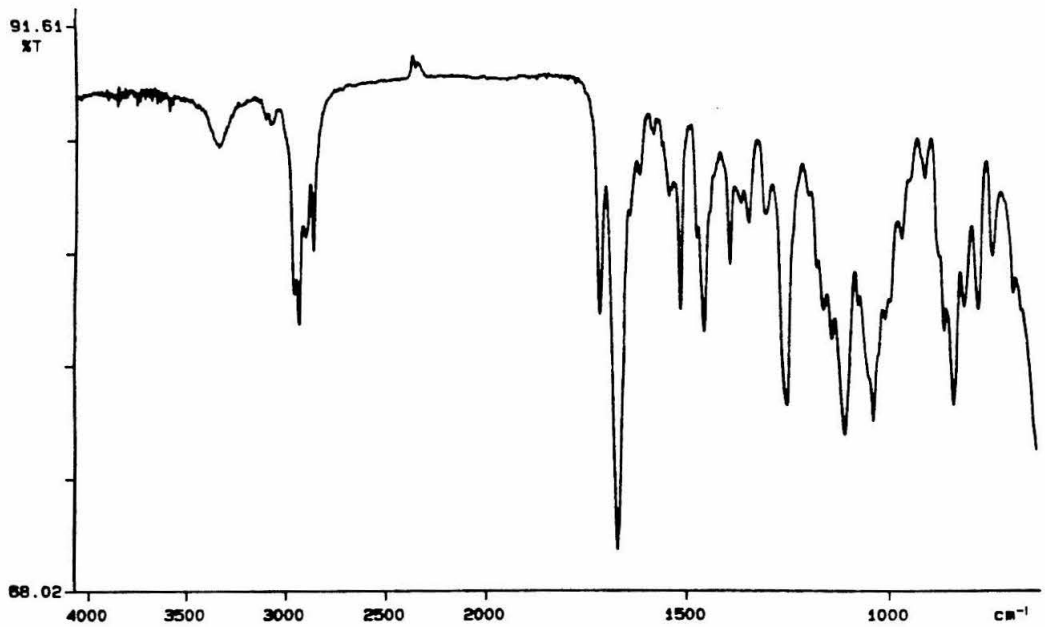
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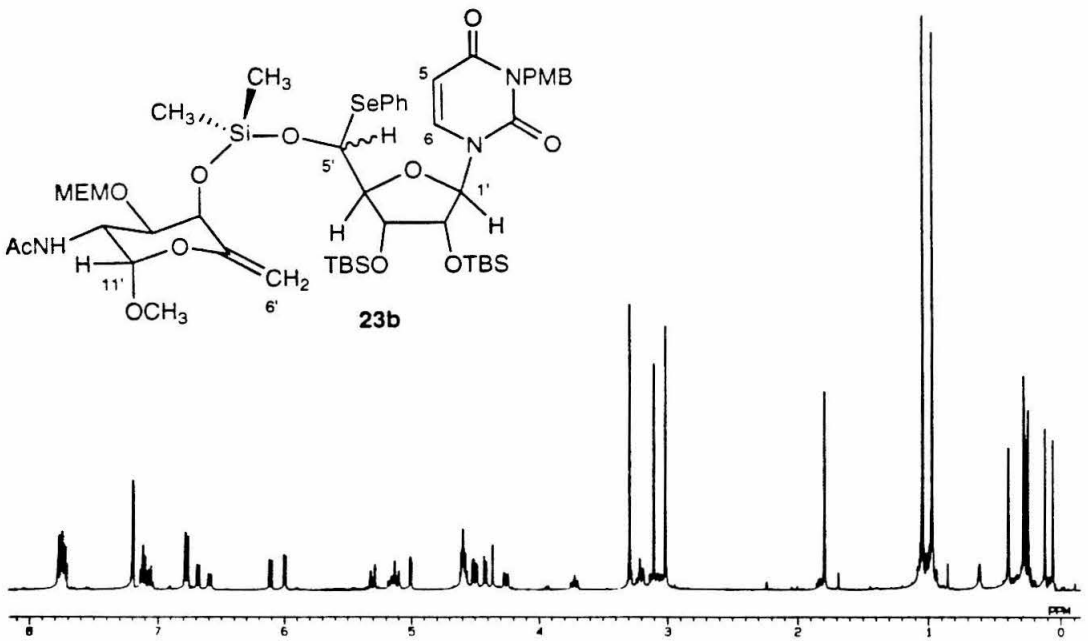
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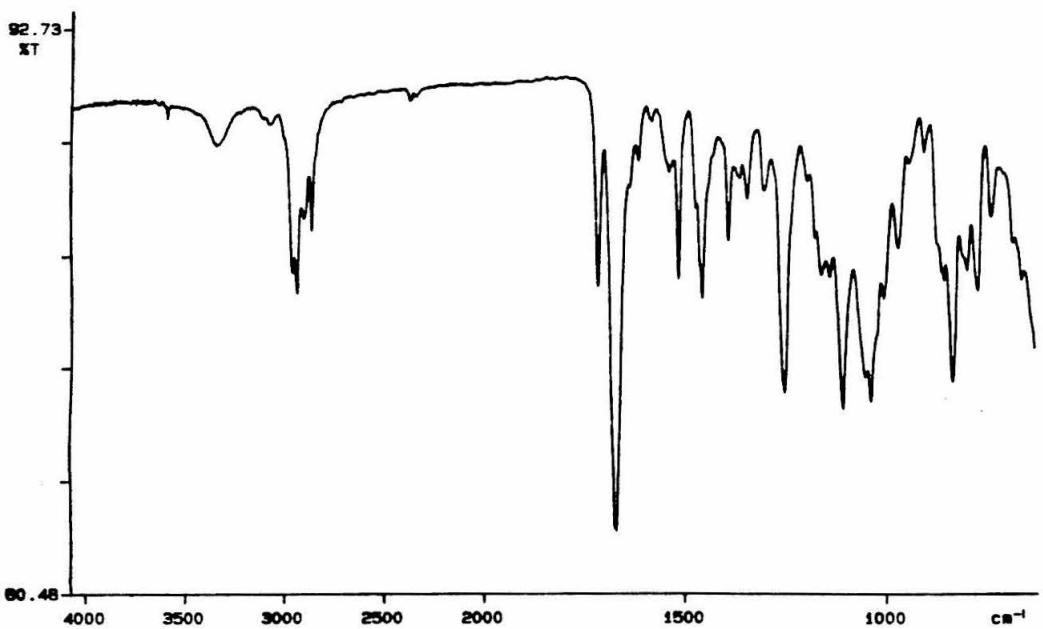
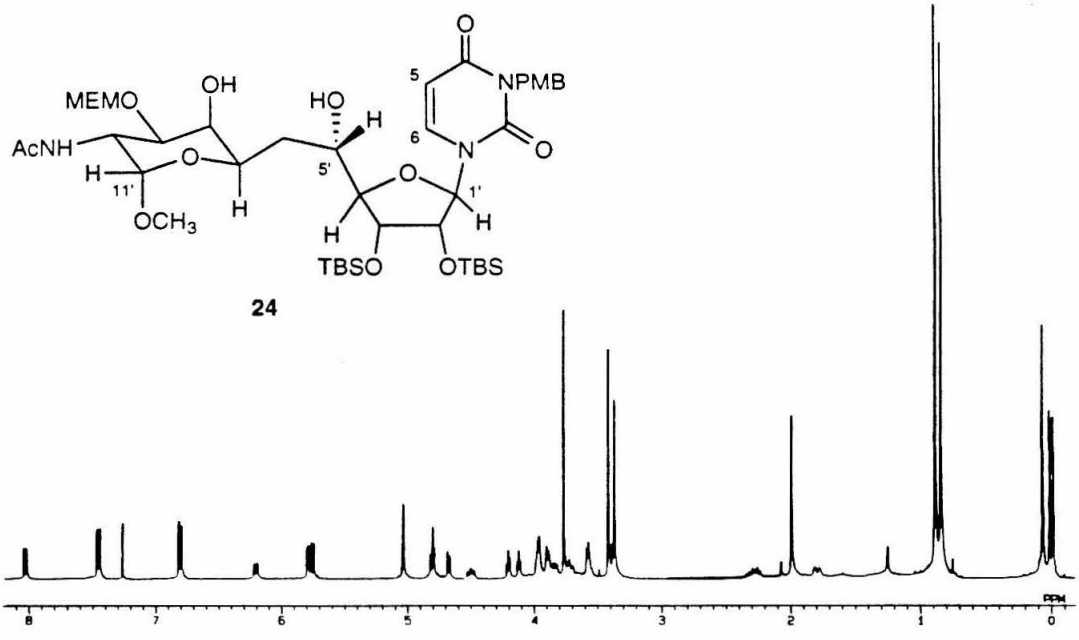
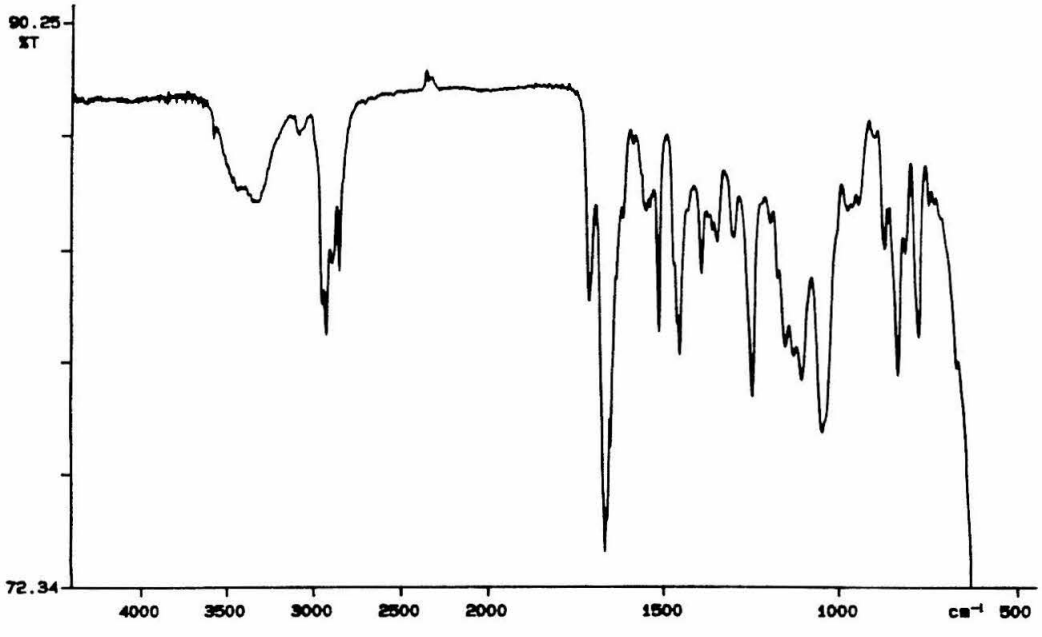
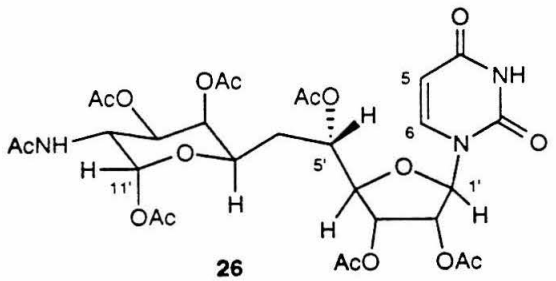
H
H
TBSO
OTBS
23b
PPM


92.73
%T
60.48
4000
3500
3000
2500
2000
1500
1000
cm-1


MEMO
OH
HO
H
AcNH
H
11'
O
OCH3
H
5'
5
6
NPMB
O
N
O
O
1'
H
H
TBSO
OTBS
PPM
8
7
6
5
4
3
2
1
0

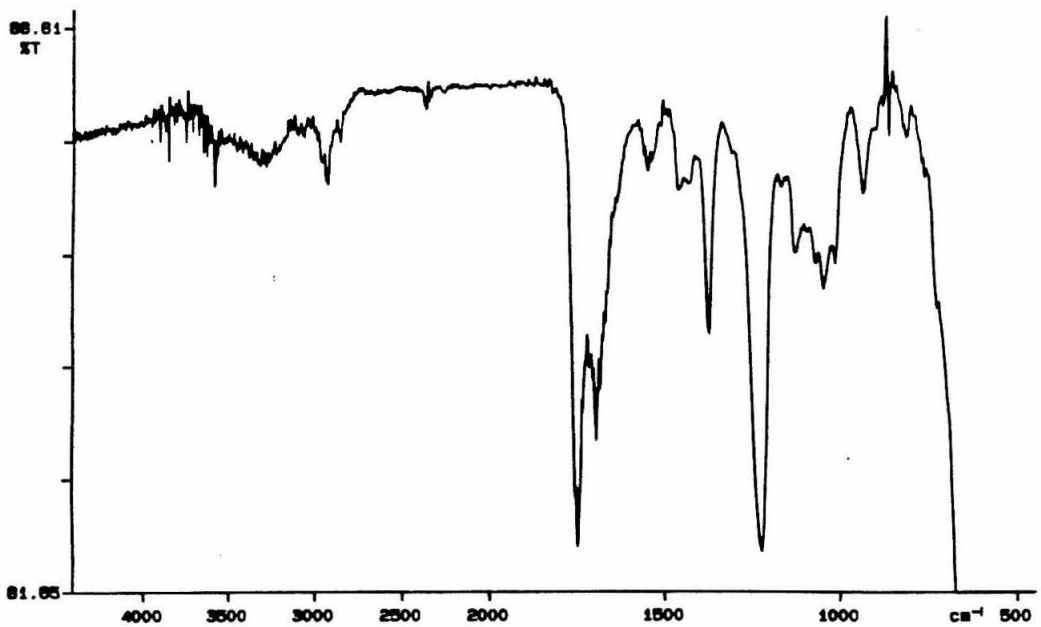
24

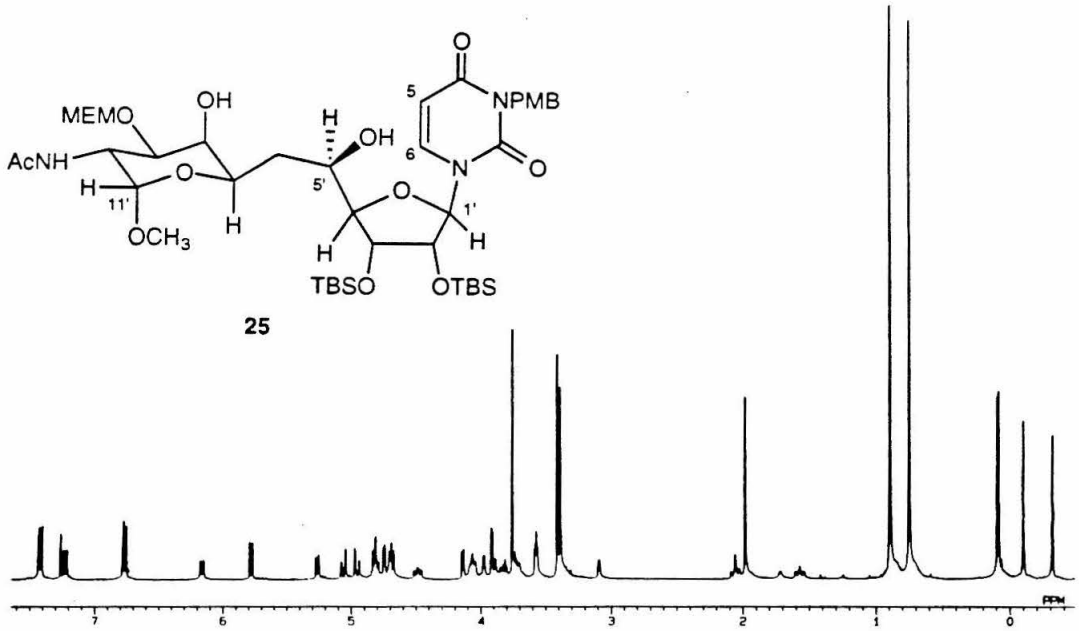

90.25
%T
72.34
4000
3500
3000
2500
2000
1500
1000
cm-1
500


AcO
OAc
AcO
AcNH
H
11'
OAc
H
5'
H
O
NH
5
6
N
O
1'
H
H
AcO
OAc

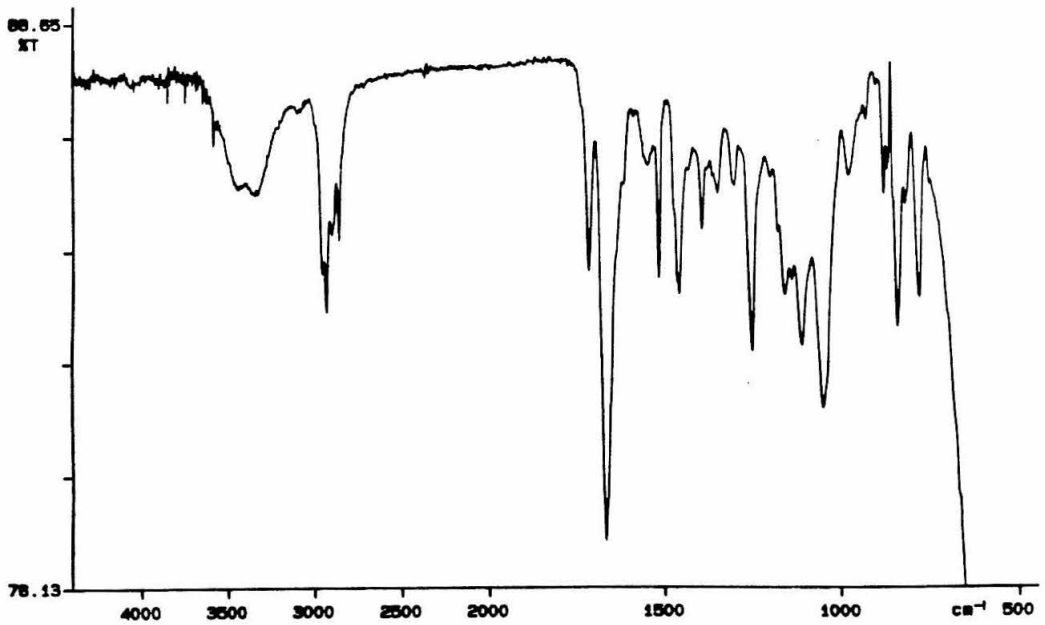
26

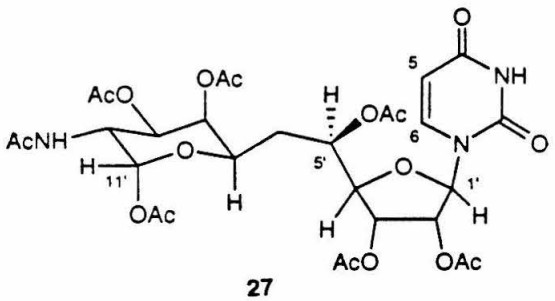
8
7
6
5
4
3
2
1
0
PPM


88.61
%T
81.65
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


MEMO
OH
AcNH
H
11'
OCH3
O
H
H
5'
OH
O
5
NPMB
6
N
O
1'
H
H
TBSO
OTBS
PPM

25

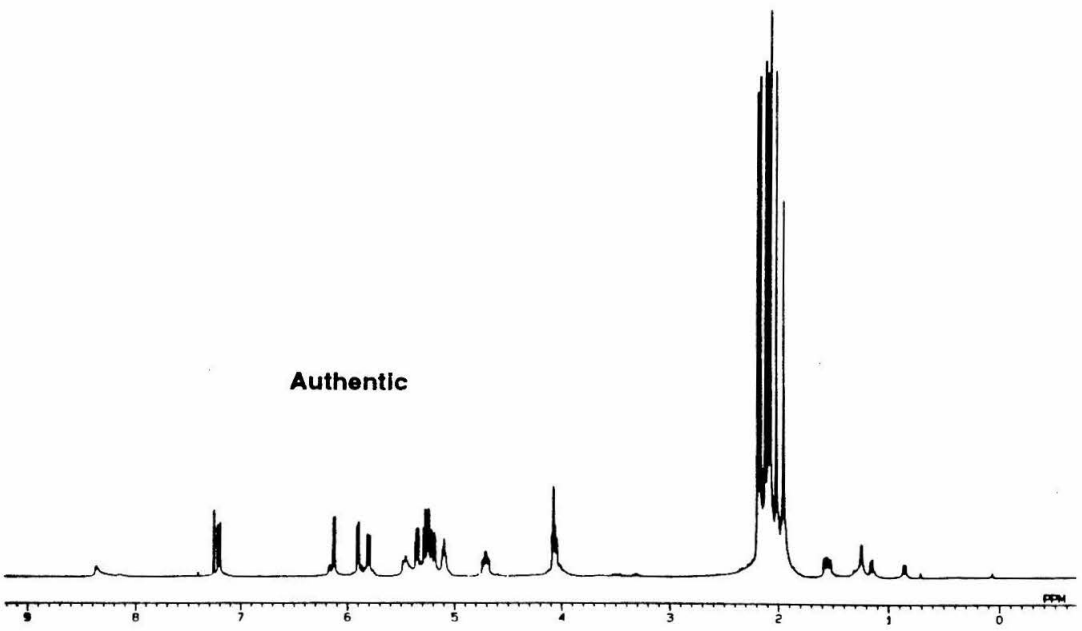

88.65
%T
78.13
4000
3500
3000
2500
2000
1500
1000
cm-1
500

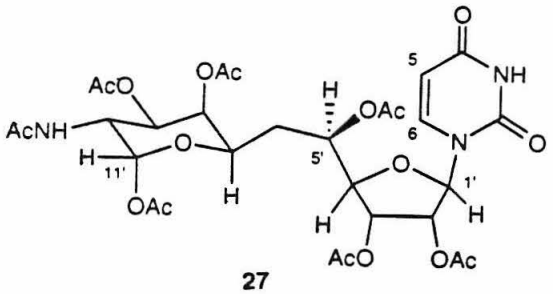


27

Synthetic

Authentic

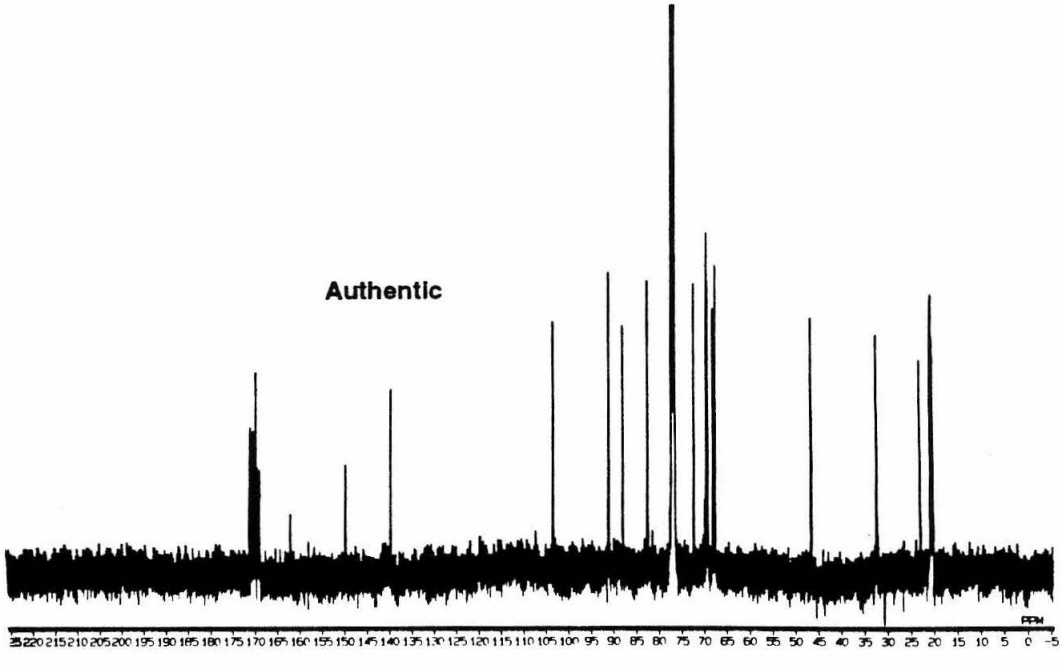


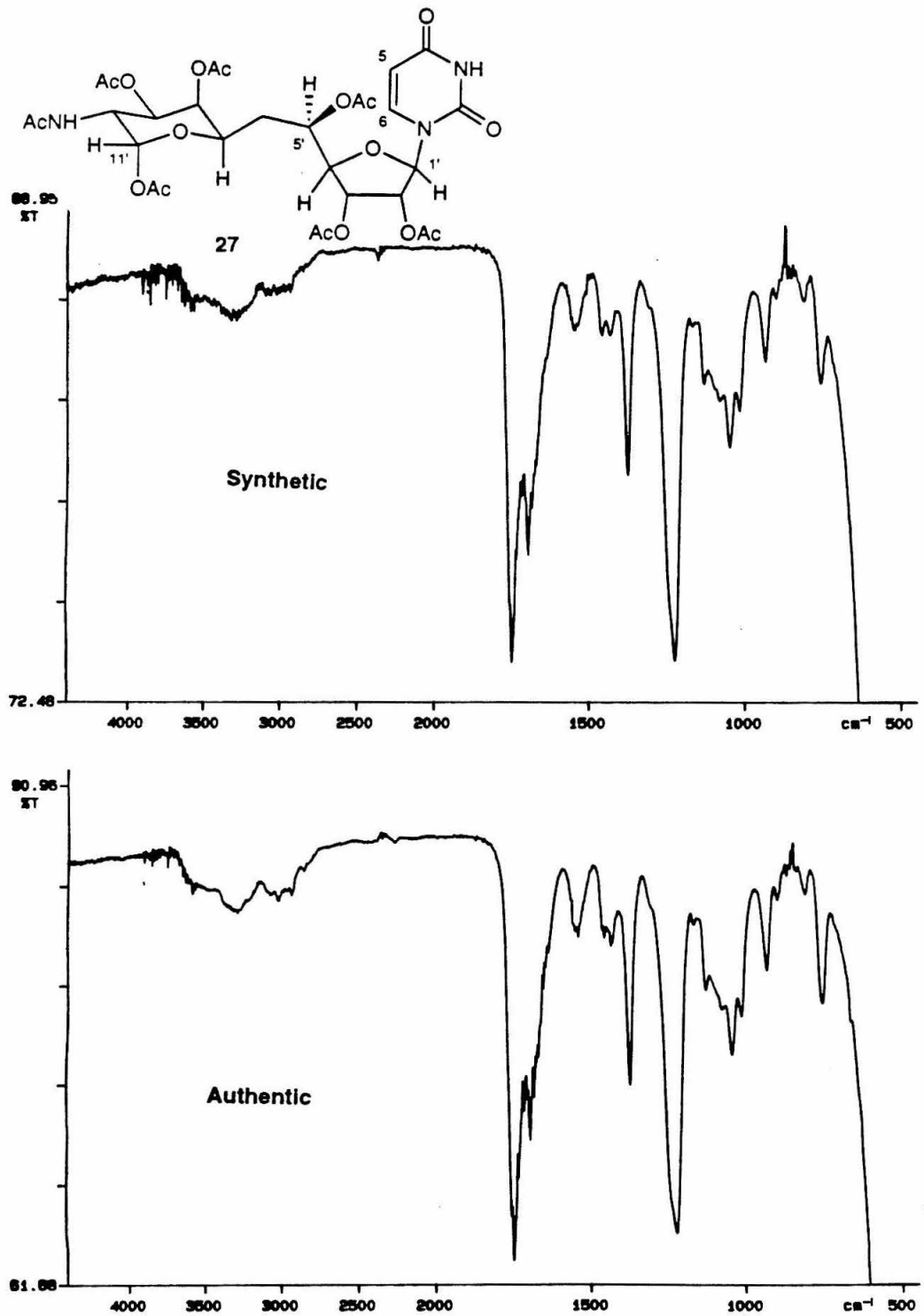


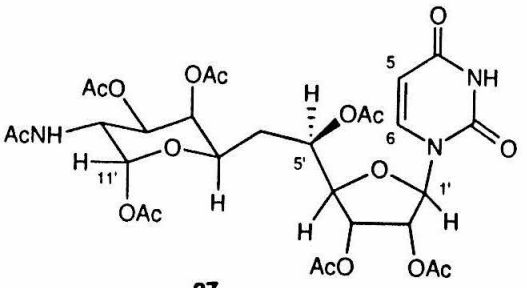
27

Synthetic

Authentic

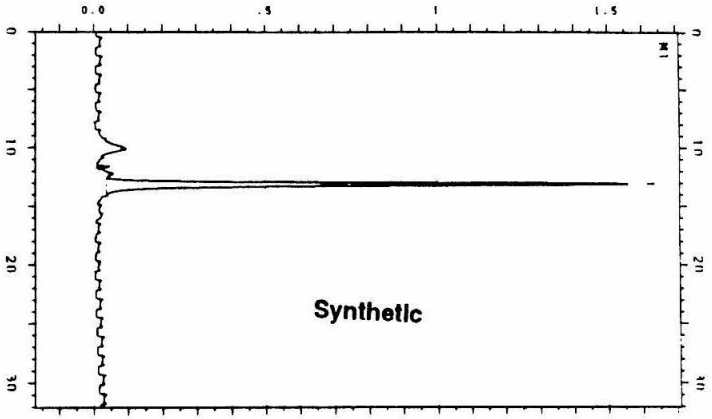


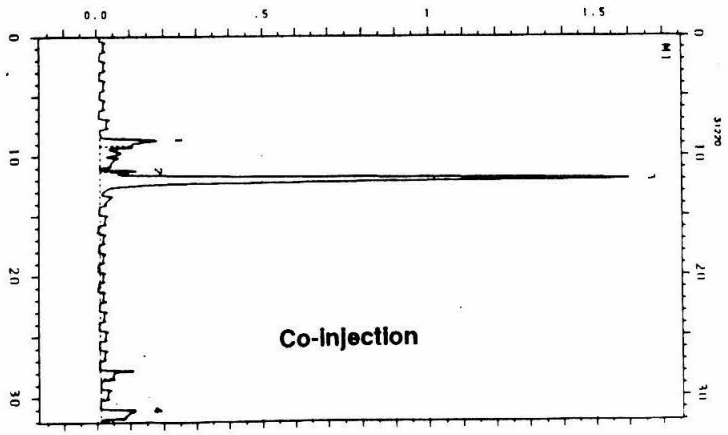

27
Synthetic
Authentic
%T
cm⁻¹
4000
3500
3000
2500
2000
1500
1000
500

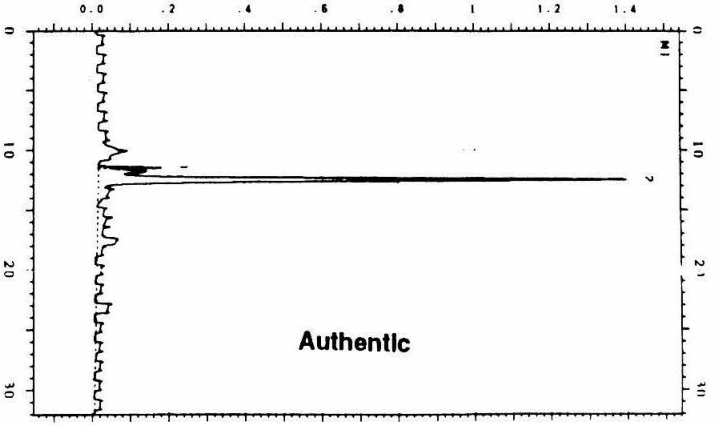


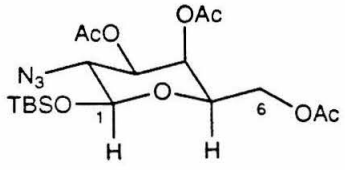
27

Waters 994	< I N T E G R A T O R >		Stop at 32.02 min		
Date	: Jul/12/91 14:19:14	FILE NAME	: TEST1		
Wavelength	: M1				
Time range	: 0.00 --- 32.02 min	Smoothing	: 7	points	
Interval	: NORMAL	Minimum area	: 0.001	AU*min	
Time double	: 183 min	Slope	: 0.001	AU/min	
Minus peak	: OFF	Drift	: 0.001	AU/min	
Paper speed	: 3.0 mm/min	Height	: 0.1	AU	
Baseline correct	: OFF	Width	: 0.01	min	
Sample name	: CO-INJECT A-AC	Packing material	: SILICA GEL		
Column	: 3.9mmID* 30.0cm	Mobile phase	: 90/10 DCM/MEOH		
Flow rate	: 0.50 ml/min	Pressure	: 1200.0	PSI	
Temperature	: 25.0 °C	Injection volume	: 50	µl	
Flow cell	: 10.00 mm				



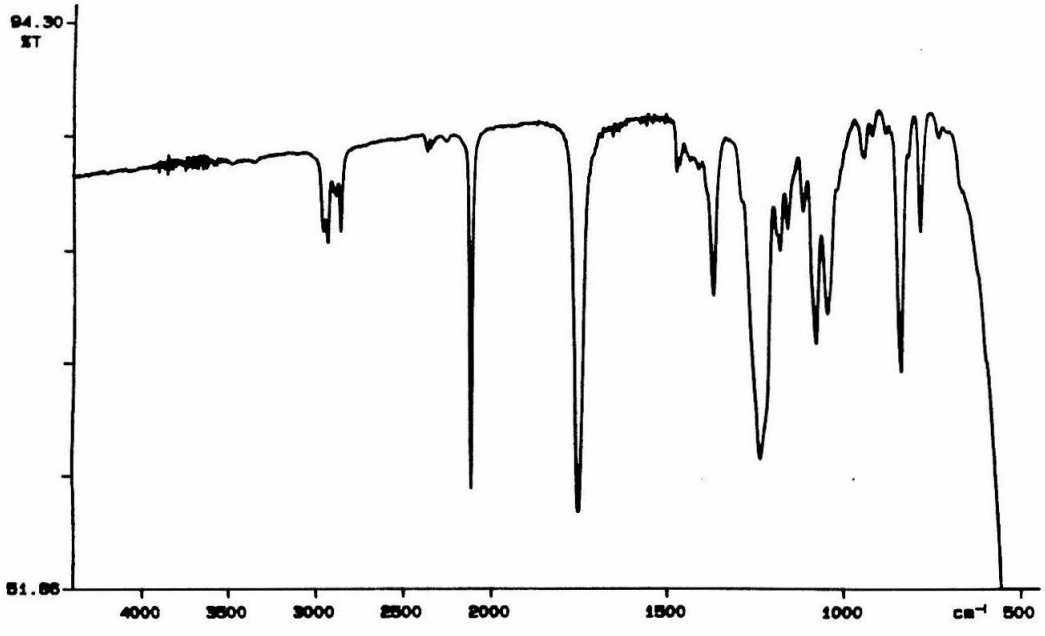


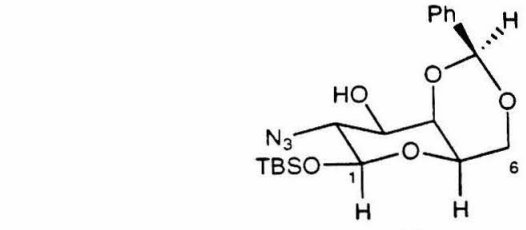



OAc
AcO
N_3
TBSO
1
O
6
OAc
H
H

31

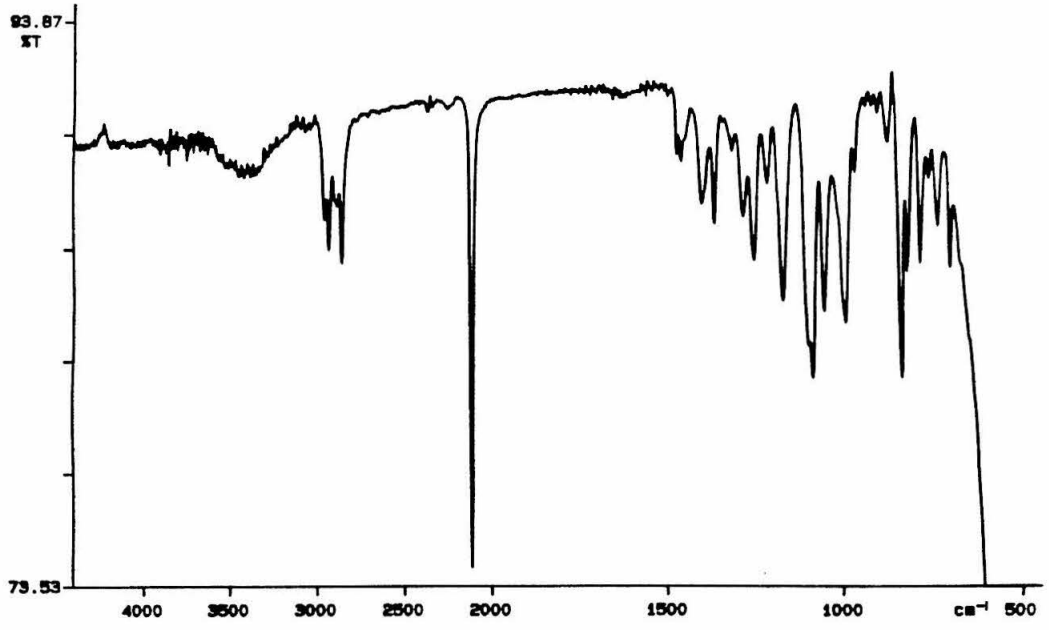
8
6
4
2
0
PPM

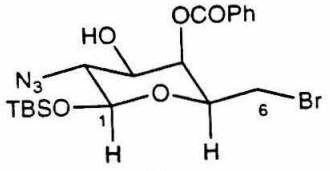

94.30
%T
51.86
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


Ph
H
O
O
HO
N_3
TBSO
O
1
6
H
H

32

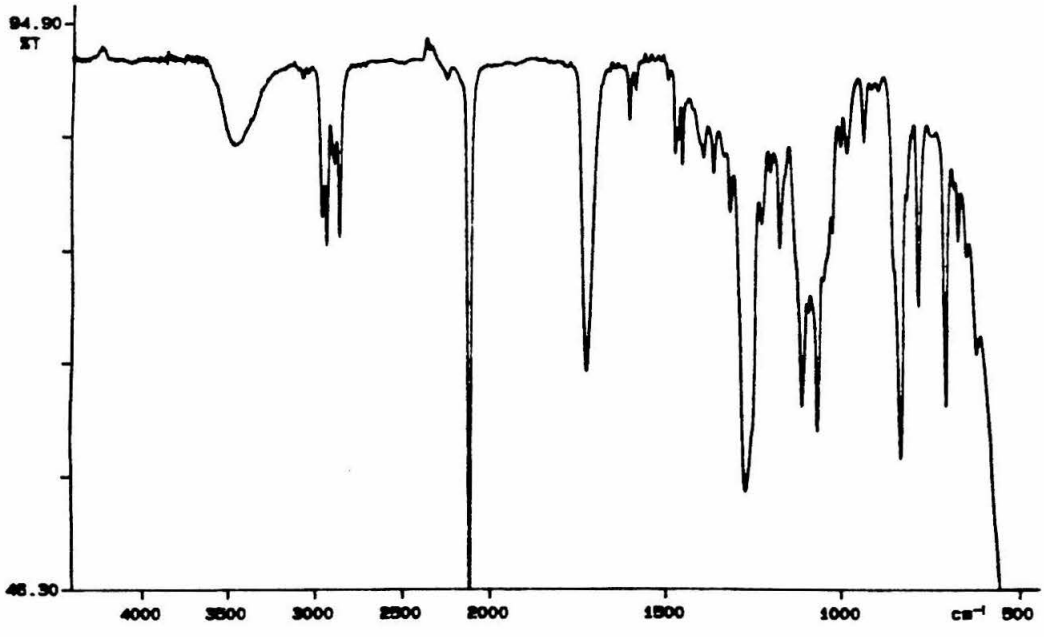
8
6
4
2
0
PPM

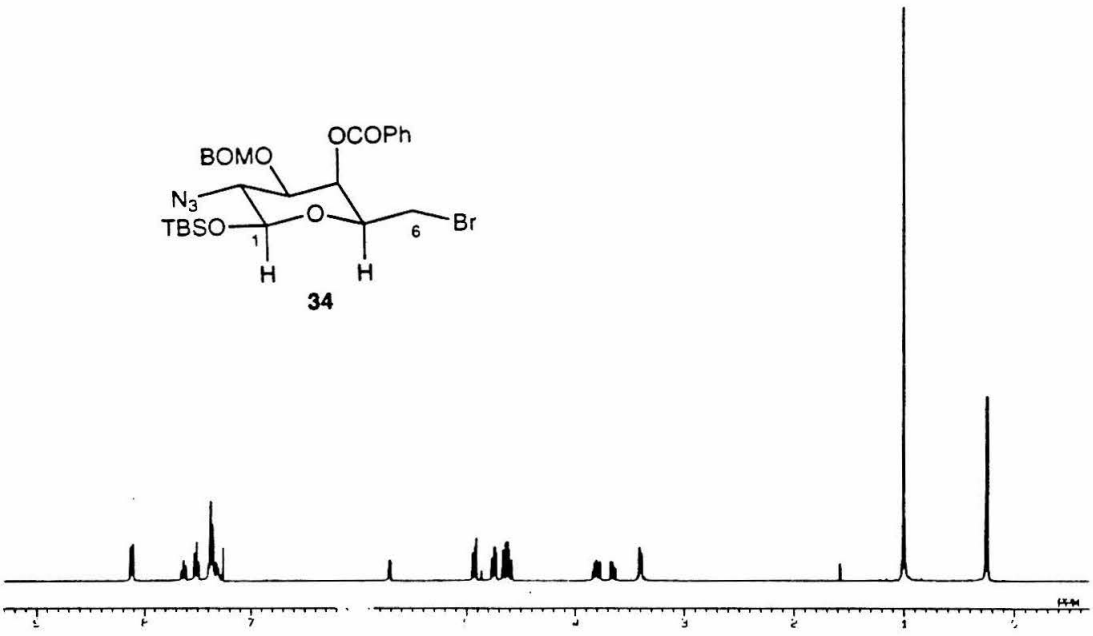

93.87
%T
79.53
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


OCOPh
HO
N3
TBSO
O
Br
1
6
H
H

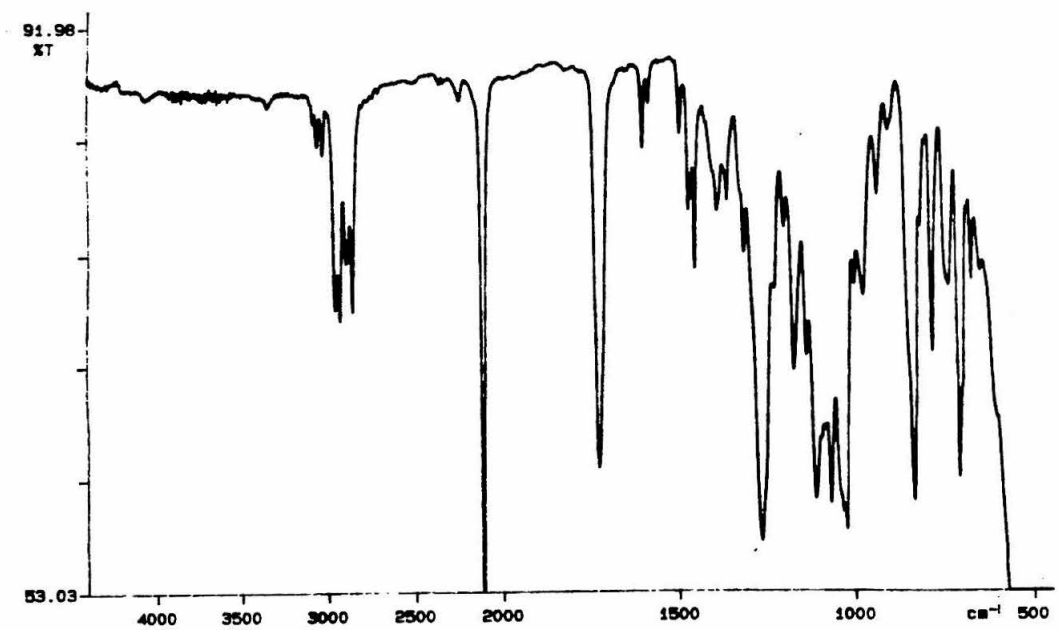
33

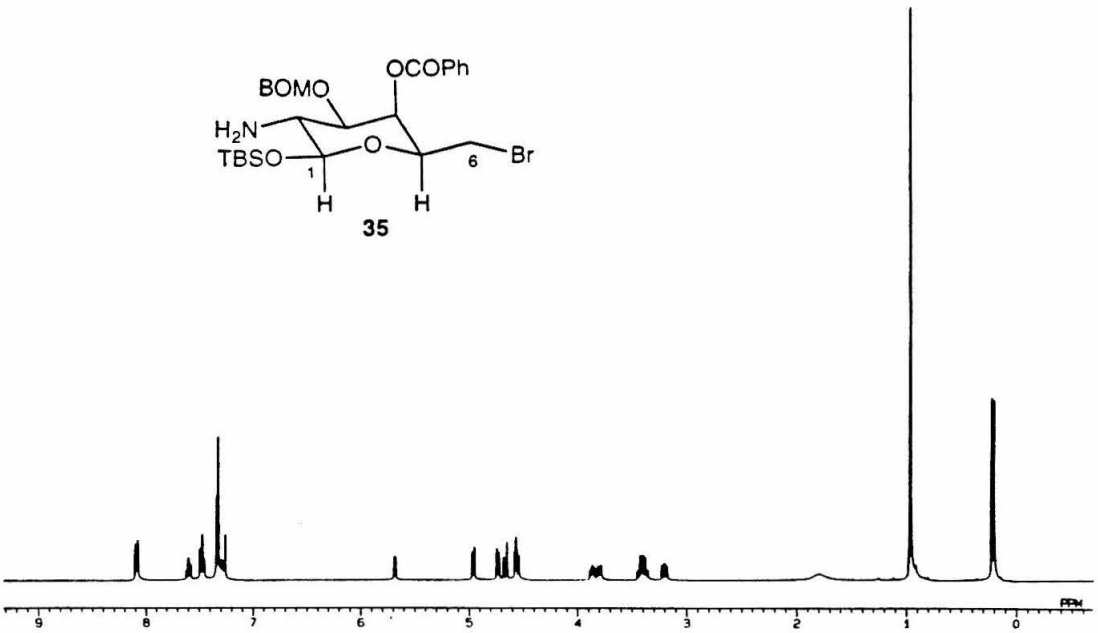
PPM
9
8
7
6
5
4
3
2
1
0

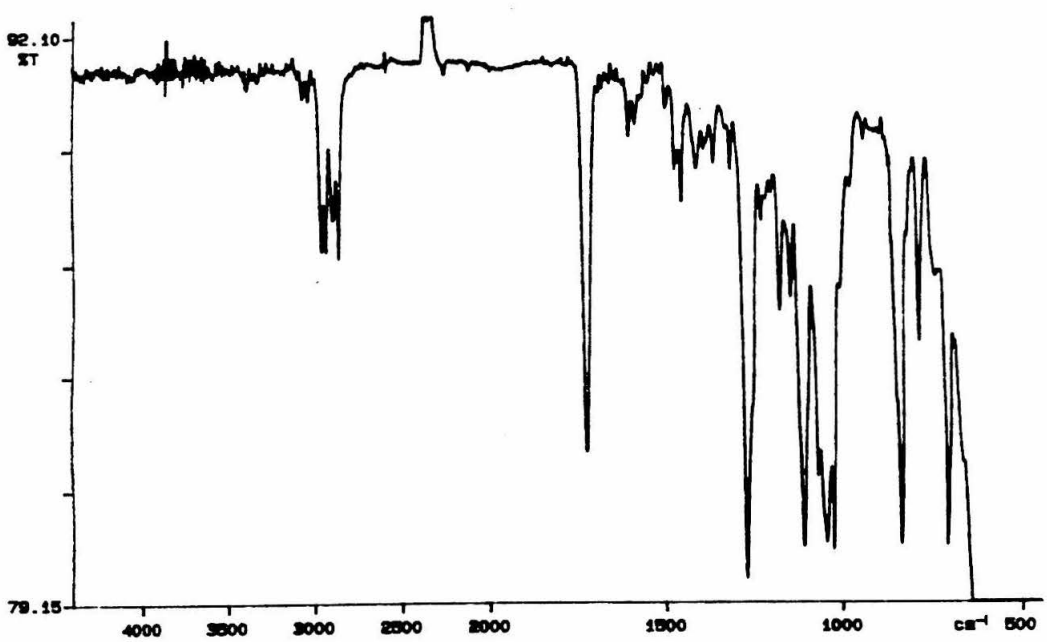

94.90
%T
46.30
4000
3500
3000
2500
2000
1500
1000
cm-1
500

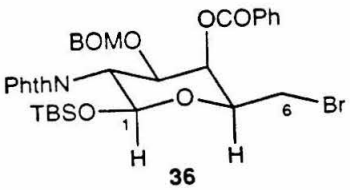

OCOPh
BOMO
N3
TBSO
O
Br
1
6
H
H

34


91.98
%T
53.03
4000
3500
3000
2500
2000
1500
1000
cm-1
500

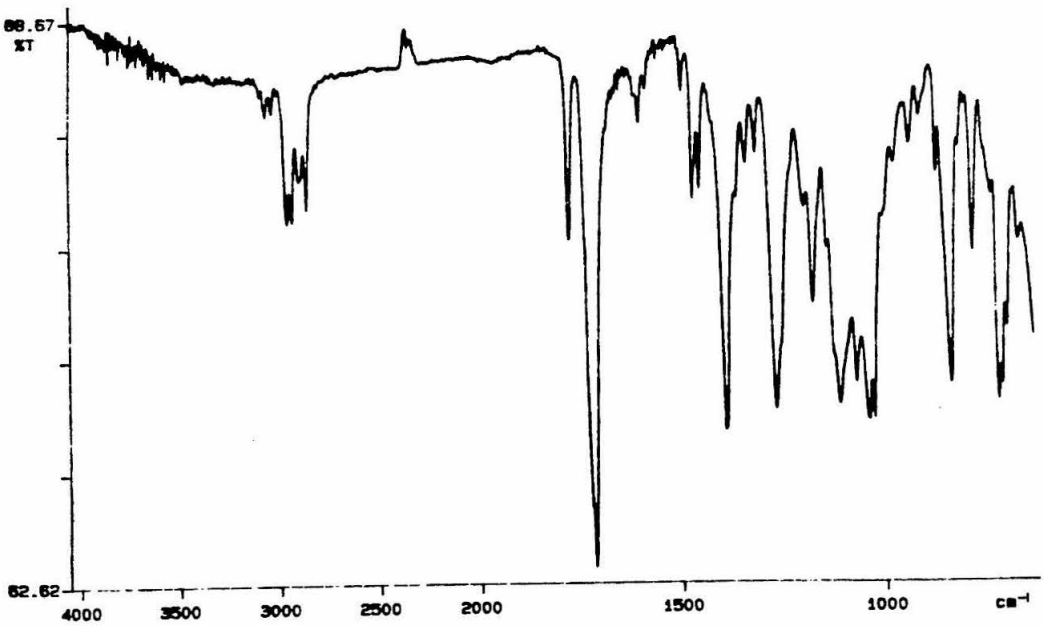

OCOPh
BOMO
H_2N
TBSO
O
1
6
Br
H
H
35
9
8
7
6
5
4
3
2
1
0
PPM

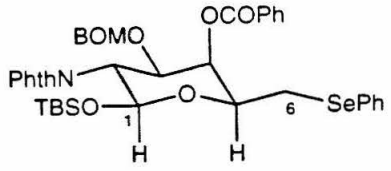

92.10
%T
79.15
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


OCOPh
BOMO
PhthN
TBSO
O
1
6
Br
H
H

36

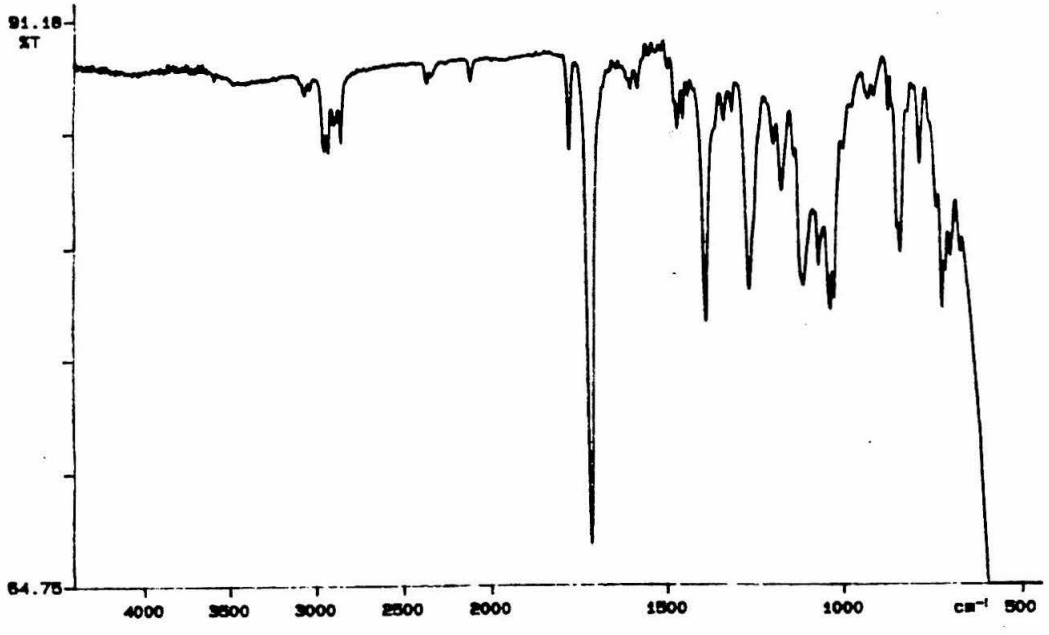
9
8
7
6
5
4
3
2
1
0
PPM

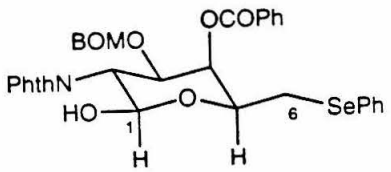

88.67
%T
62.62
4000
3500
3000
2500
2000
1500
1000
cm-1


OCOPh
BOMO
PhthN
TBSO
O
1
6
SePh
H
H

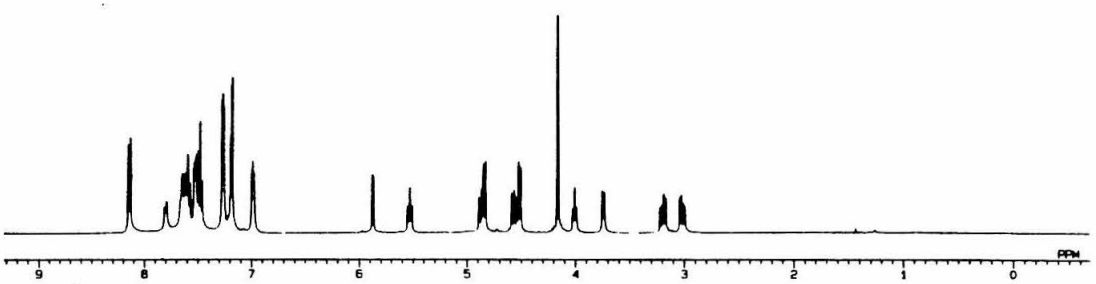
37

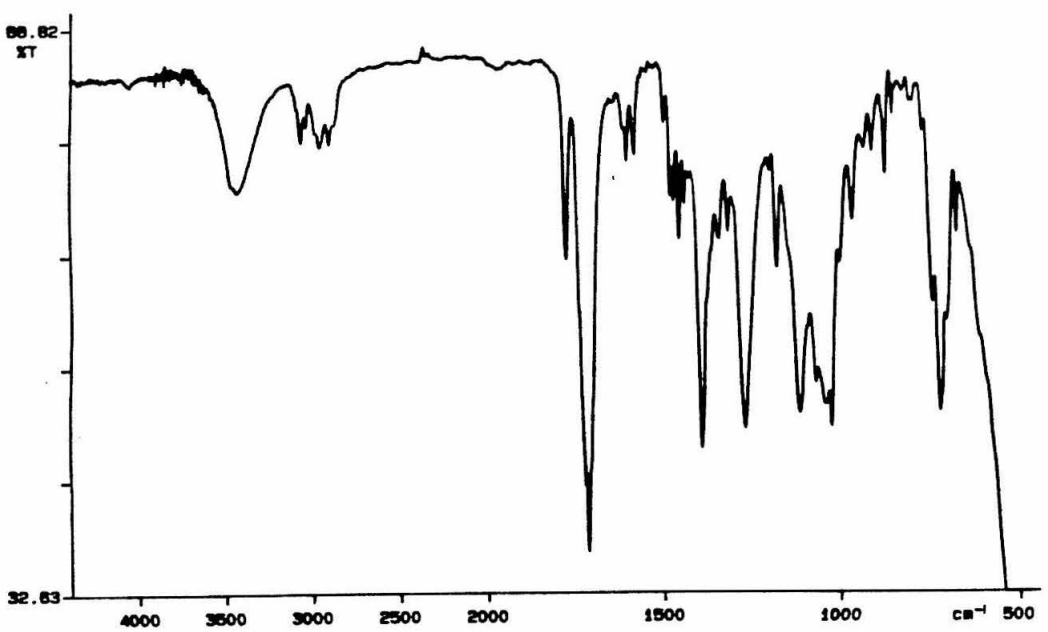
9
8
7
6
5
4
3
2
1
0
PPM

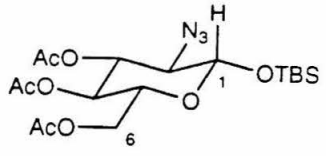

91.18
%T
64.75
4000
3500
3000
2500
2000
1500
1000
cm-1
500


OCOPh
BOMO
PhthN
HO
O
SePh
1
6
H
H

38

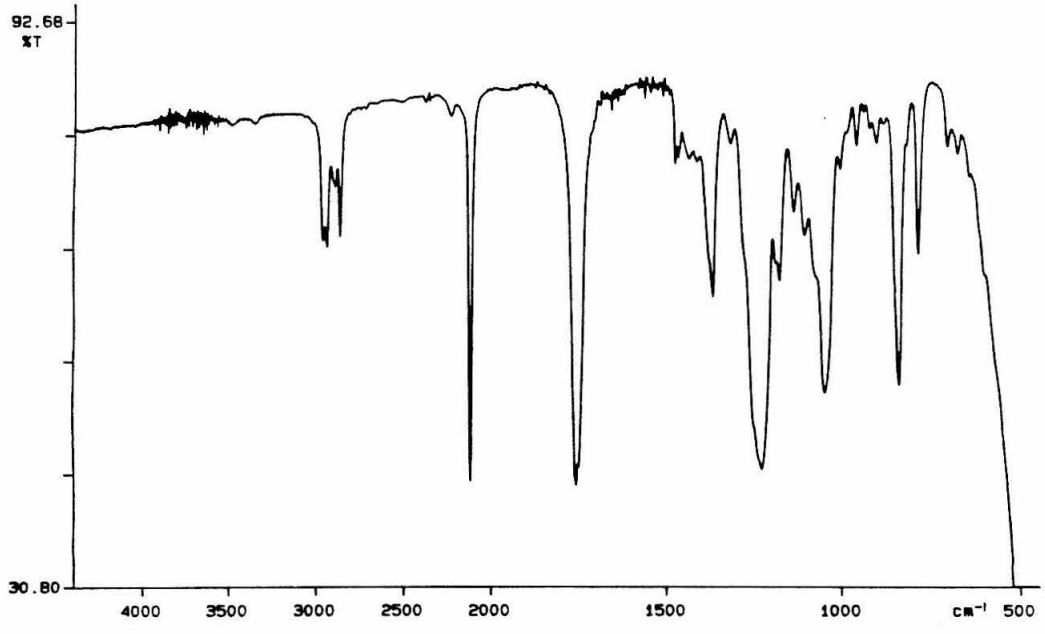

9
8
7
6
5
4
3
2
1
0
PPM

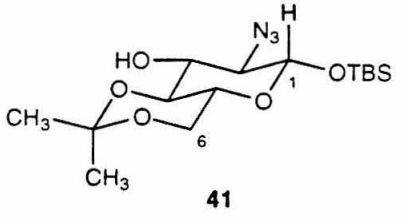

88.82
%T
32.63
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


H
N3
AcO
AcO
AcO
OTBS
1
O
6

40

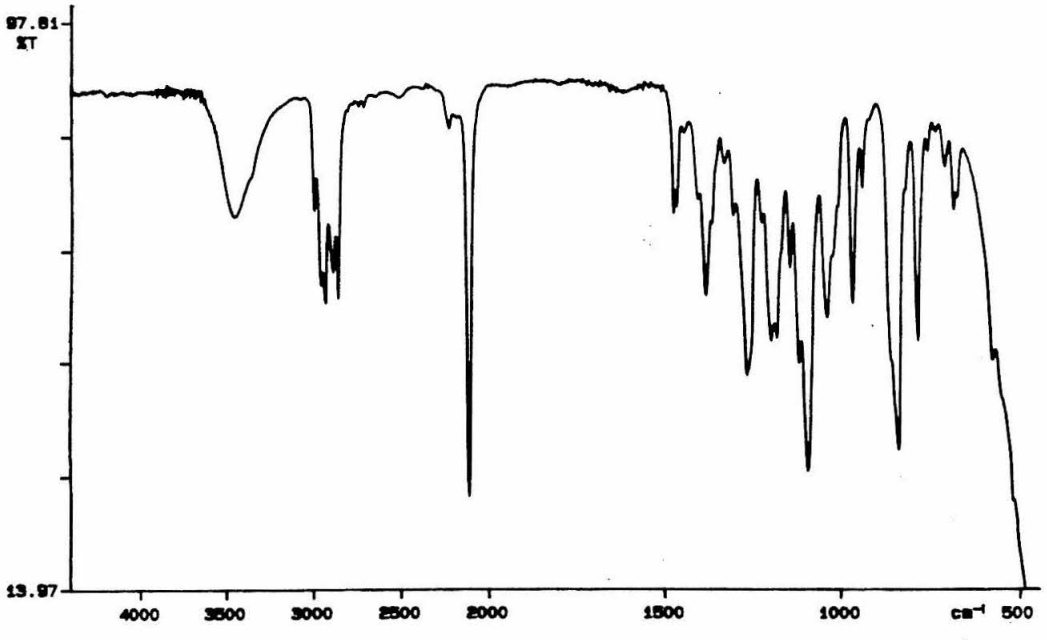
8
6
4
2
0
PPM

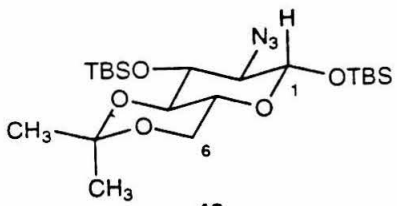

92.68
%T
30.80
4000
3500
3000
2500
2000
1500
1000
cm-1
500


H
N_3
HO
OTBS
1
O
O
CH_3
O
6
CH_3

41

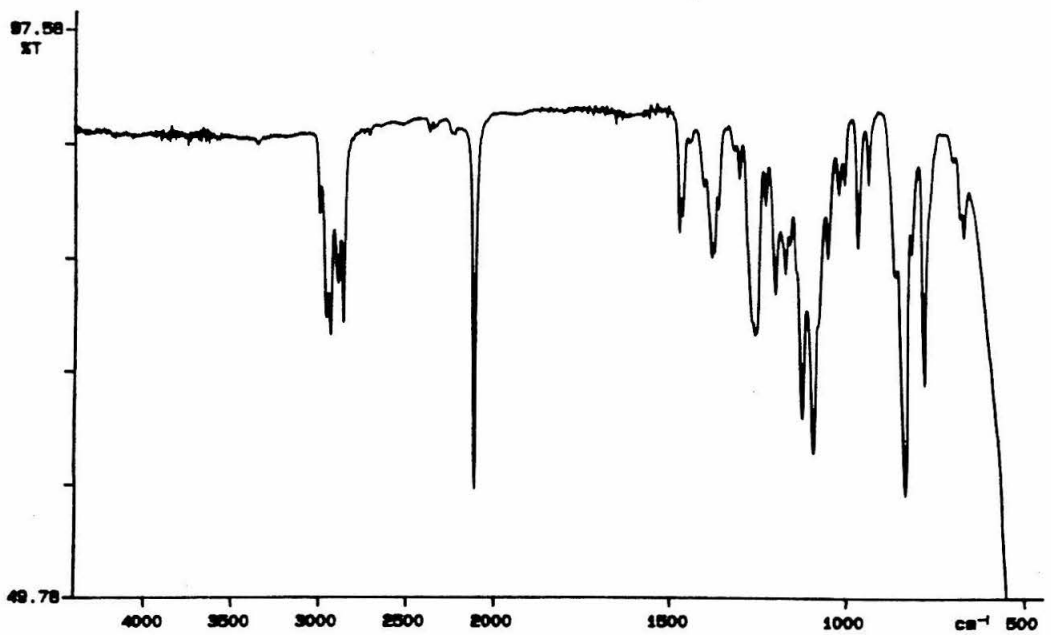
9
8
7
6
5
4
3
2
1
0
PPM

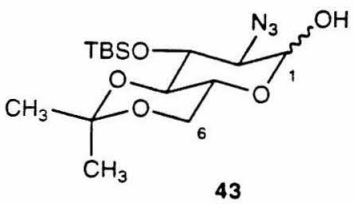

97.81
%T
13.97
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


H
N_3
TBSO
OTBS
1
O
O
O
CH_3
6
CH_3

42

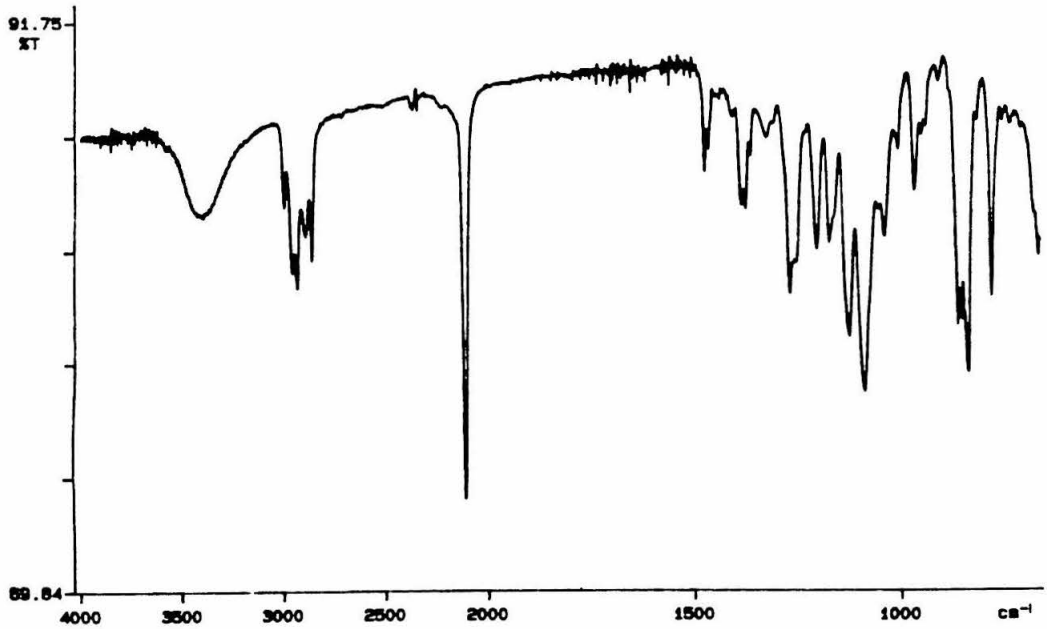
9
8
7
6
5
4
3
2
1
0
PPM

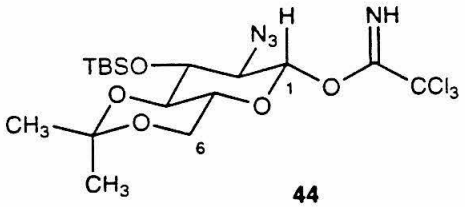

97.58
%T
49.78
4000
3500
3000
2500
2000
1500
1000
cm^{-1}
500


TBSO
N_3
OH
O
O
O
1
6
CH_3
CH_3

43

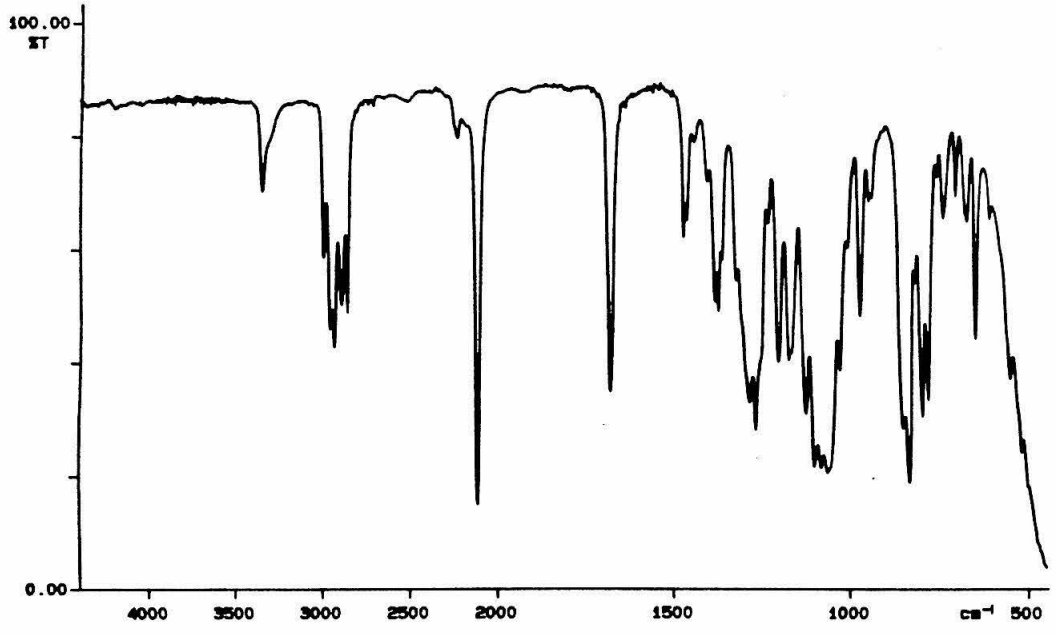
8
6
4
2
0
PPM

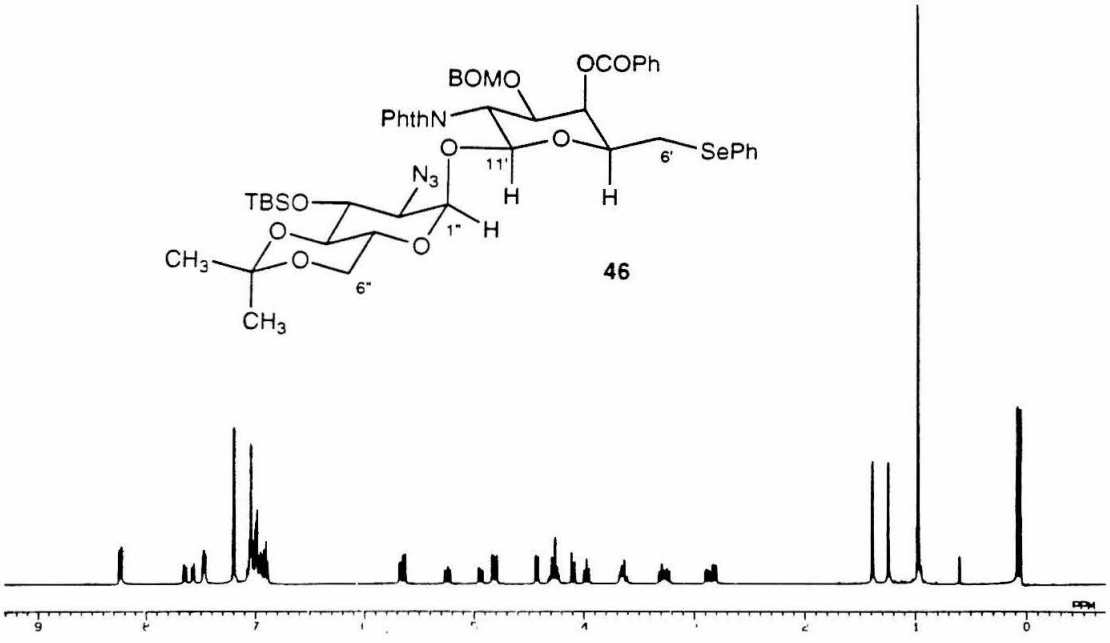

91.75
%T
69.84
4000
3500
3000
2500
2000
1500
1000
cm⁻¹

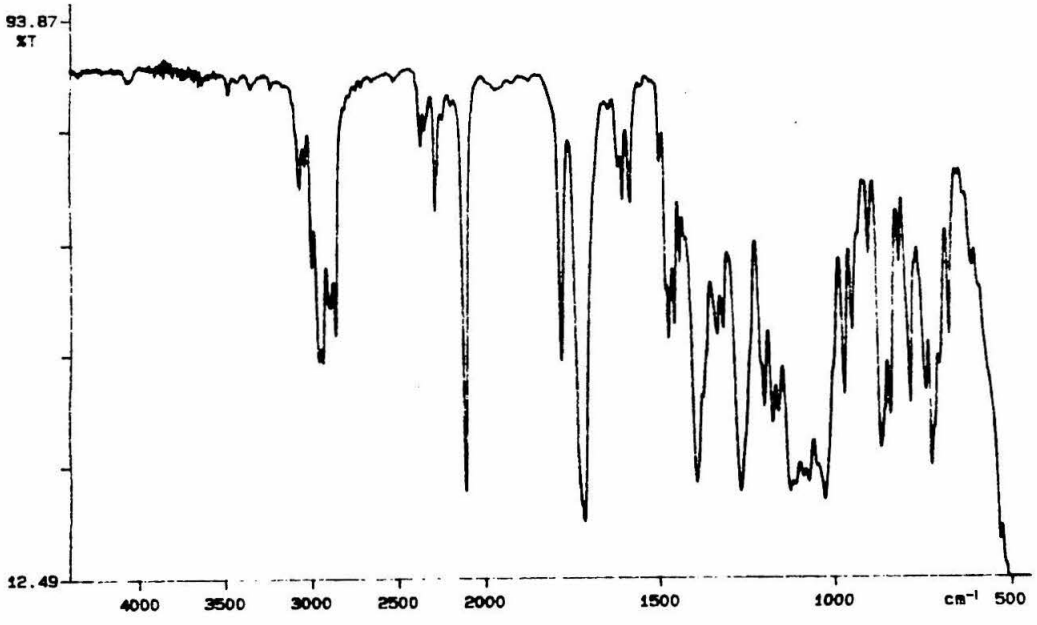

TBSO
N_3
H
NH
O
O
O
O
1
6
CH_3
CH_3
CCl_3

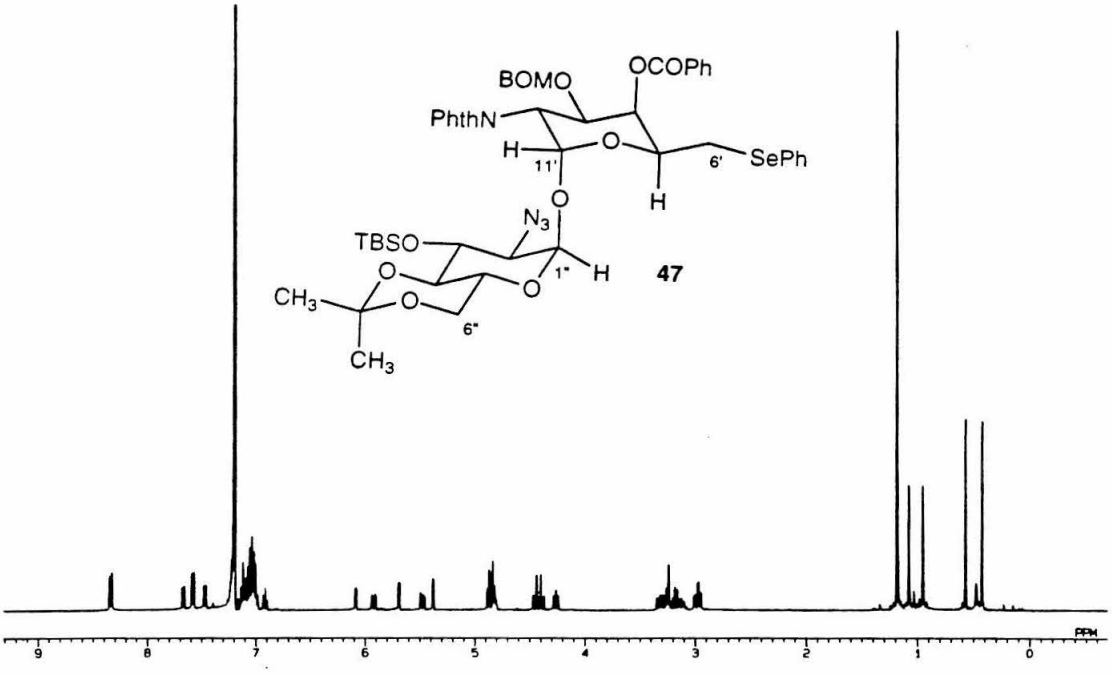
44

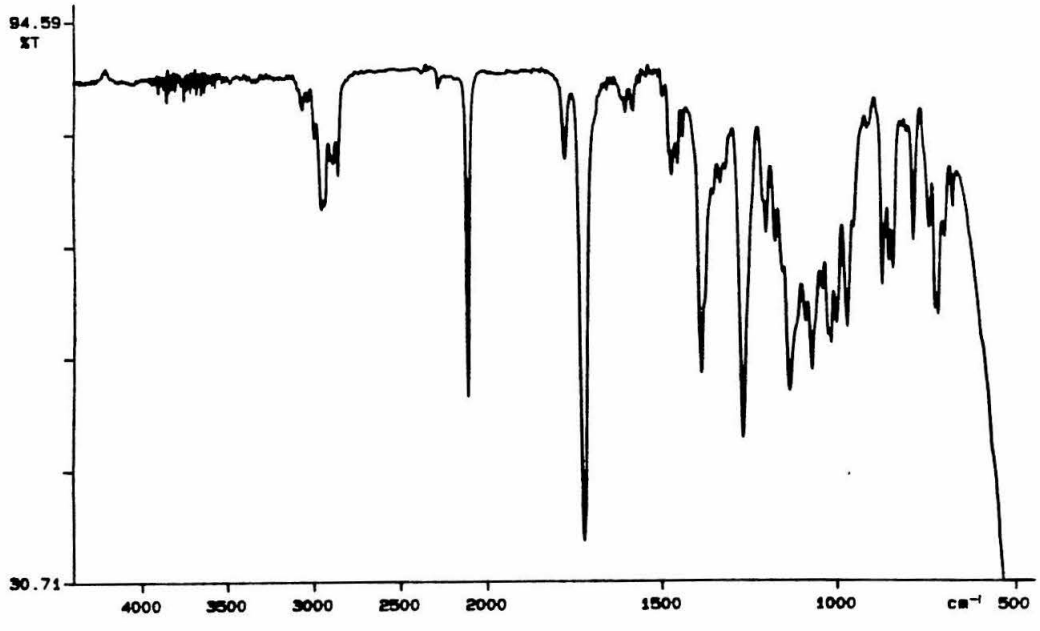
PPM

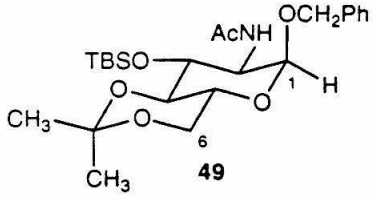

100.00
%T
0.00
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


BOMO
OCOPh
PhthN
O
O
SePh
6'
11'
H
H
N3
TBSO
O
1"
H
O
CH3
O
6"
CH3
46
PPM

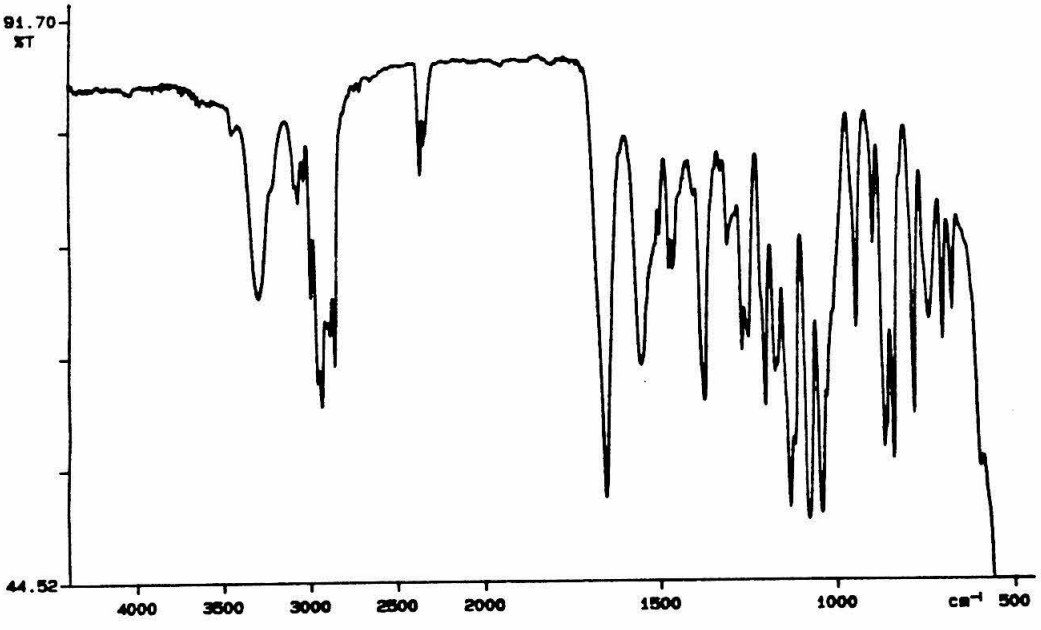

93.87
%T
12.49
4000
3500
3000
2500
2000
1500
1000
cm-1
500

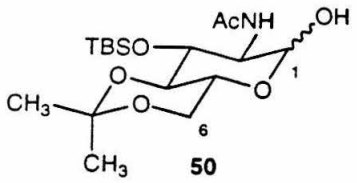

BOMO
OCOPh
PhthN
H
O
11'
6'
SePh
H
O
N3
TBSO
O
1"
H
47
CH3
O
O
6"
CH3
PPM
9
8
7
6
5
4
3
2
1
0


94.59
%T
30.71
4000
3500
3000
2500
2000
1500
1000
cm-1
500

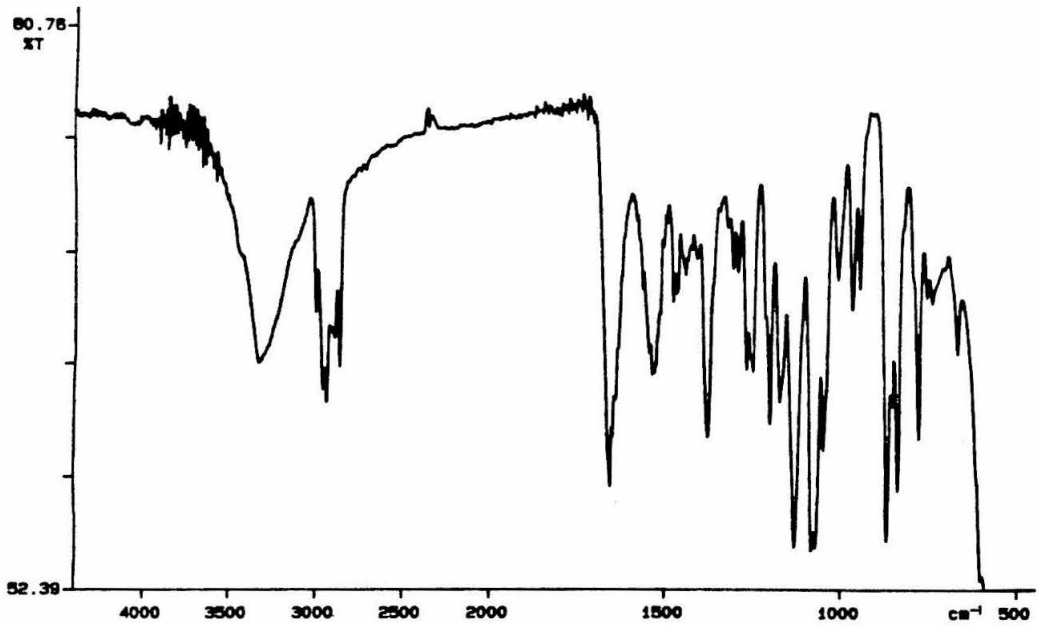

OCH2Ph
AcNH
TBSO
O
1
H
O
CH3
O
6
CH3

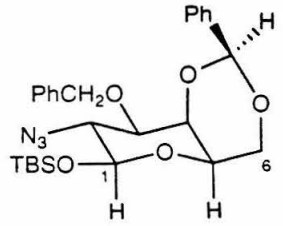
49


91.70
%T
44.52
4000
3500
3000
2500
2000
1500
1000
cm-1
500


AcNH
OH
TBSO
O
1
O
O
CH3
O
6
CH3

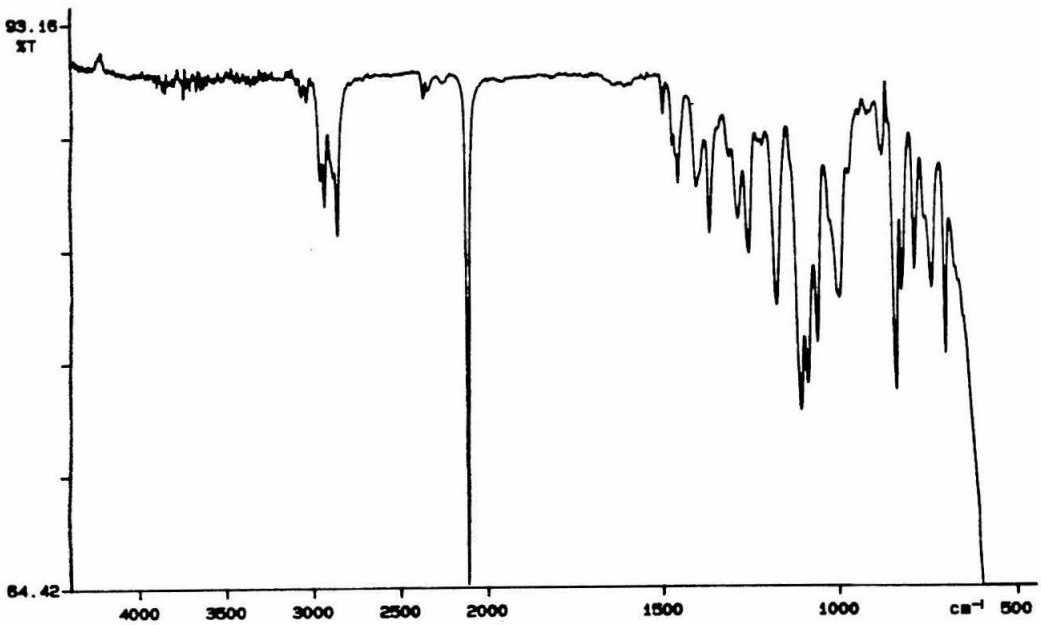
50

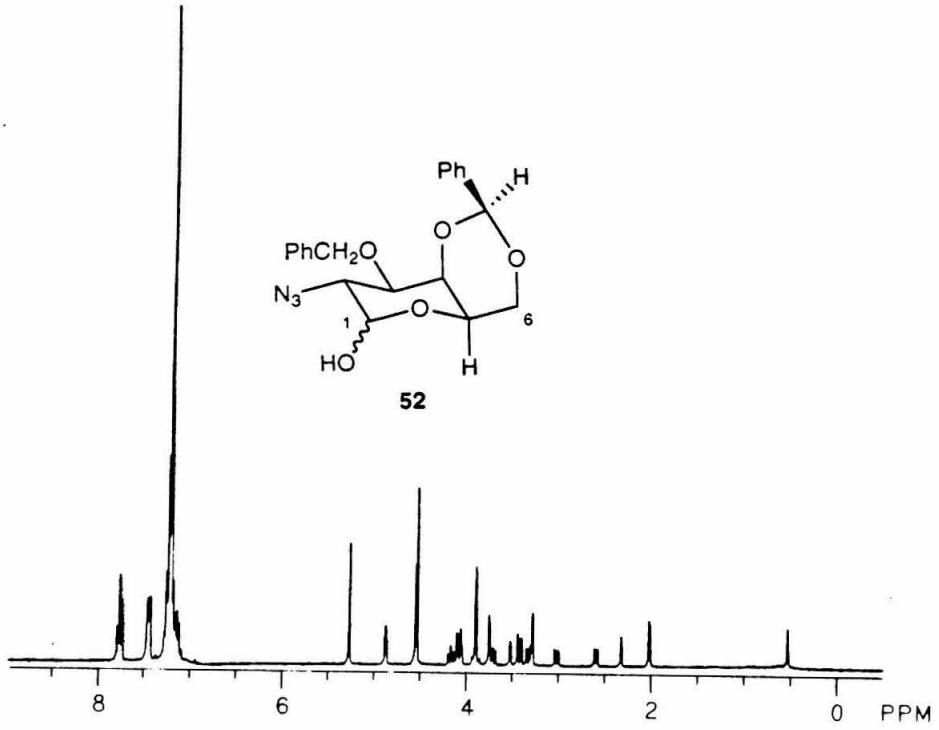

80.76
%T
52.39
4000
3500
3000
2500
2000
1500
1000
cm-1
500


Ph
H
O
O
PhCH2O
N3
TBSO
O
1
6
H
H

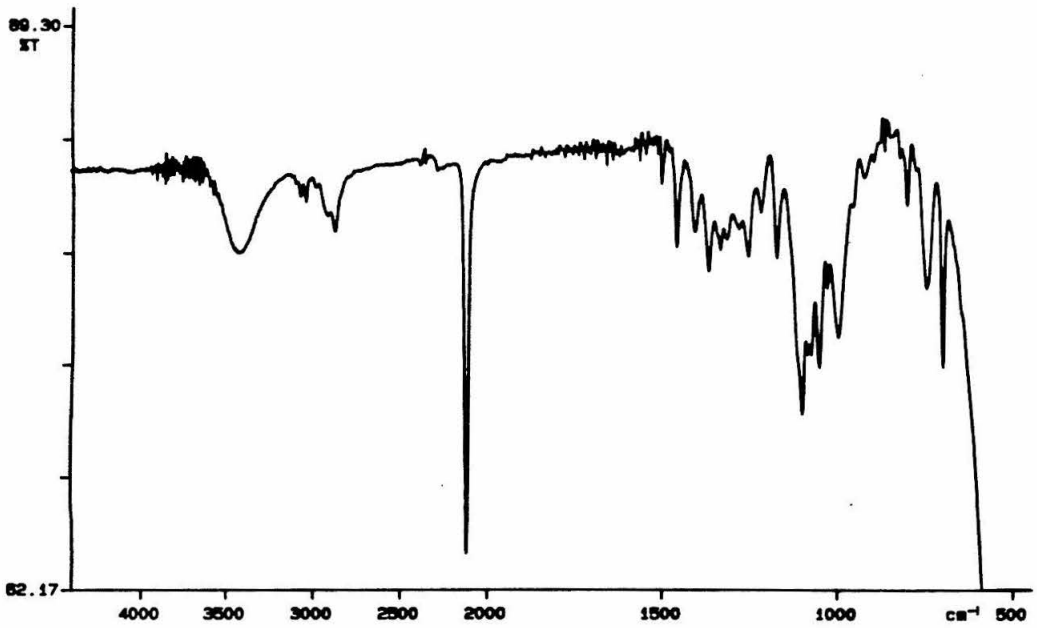
51

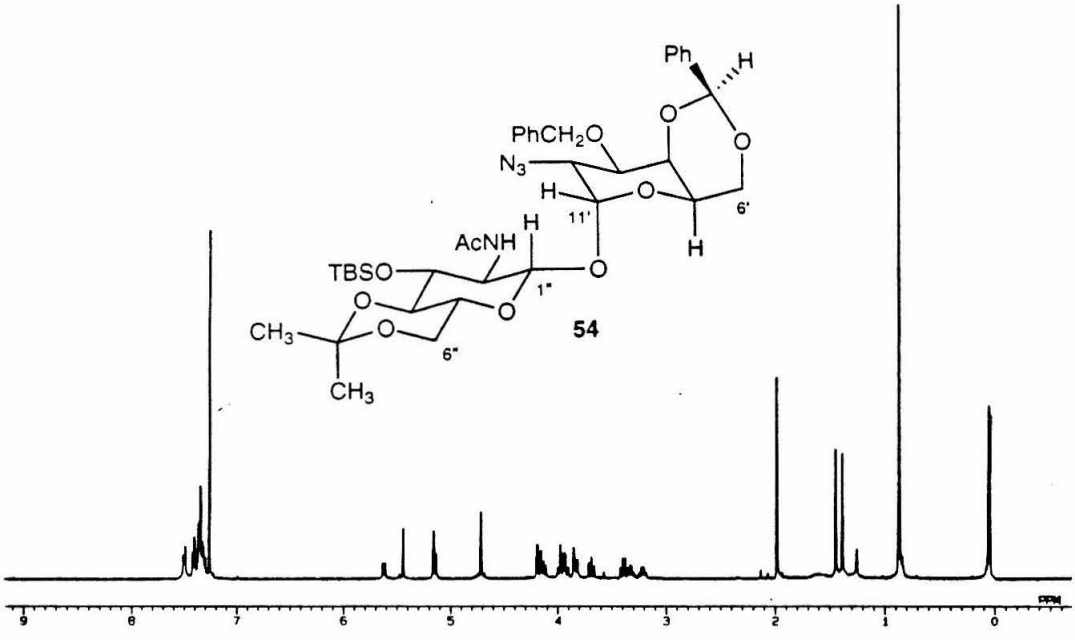
9
8
7
6
5
4
3
2
1
0
PPM

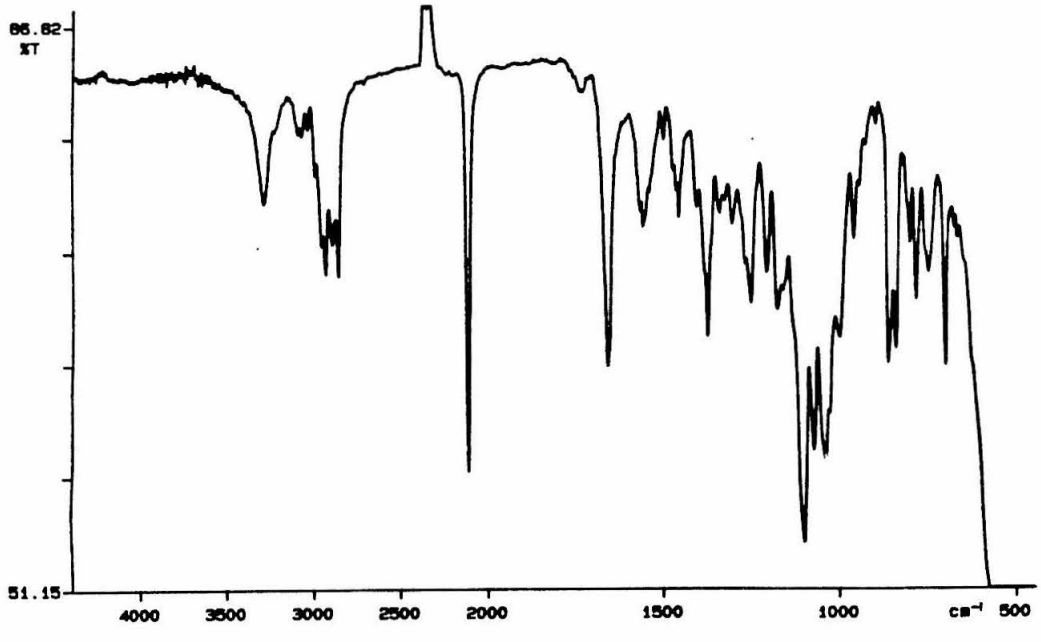

93.16
%T
84.42
4000
3500
3000
2500
2000
1500
1000
cm-1
500

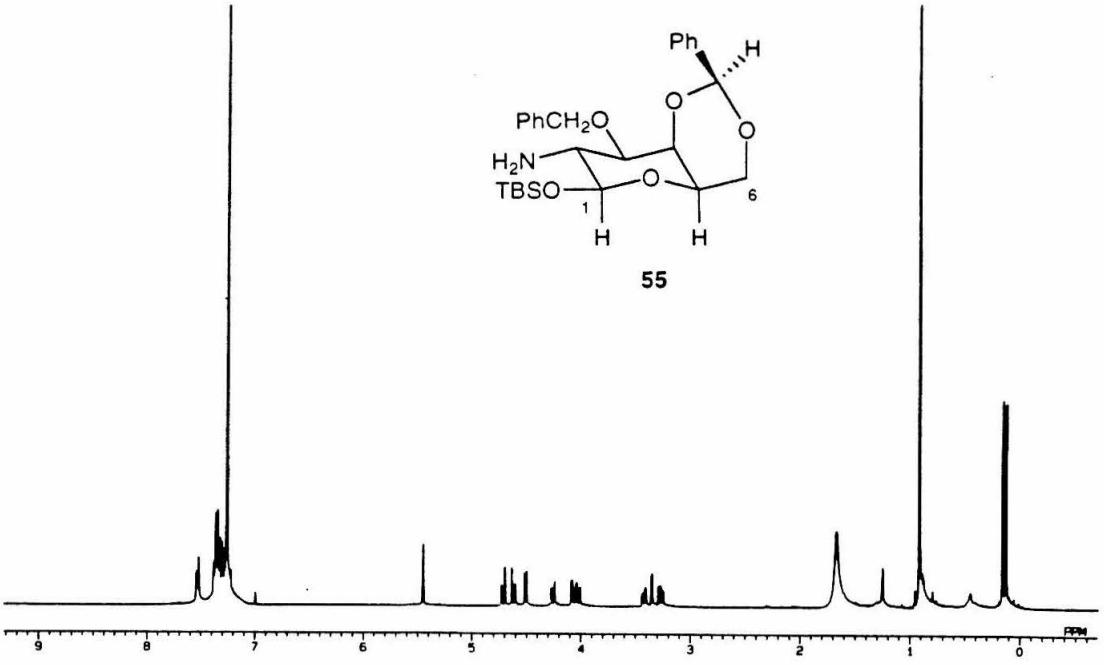

Ph
H
O
O
PhCH2O
N3
O
1
6
HO
H
8
6
4
2
0
PPM

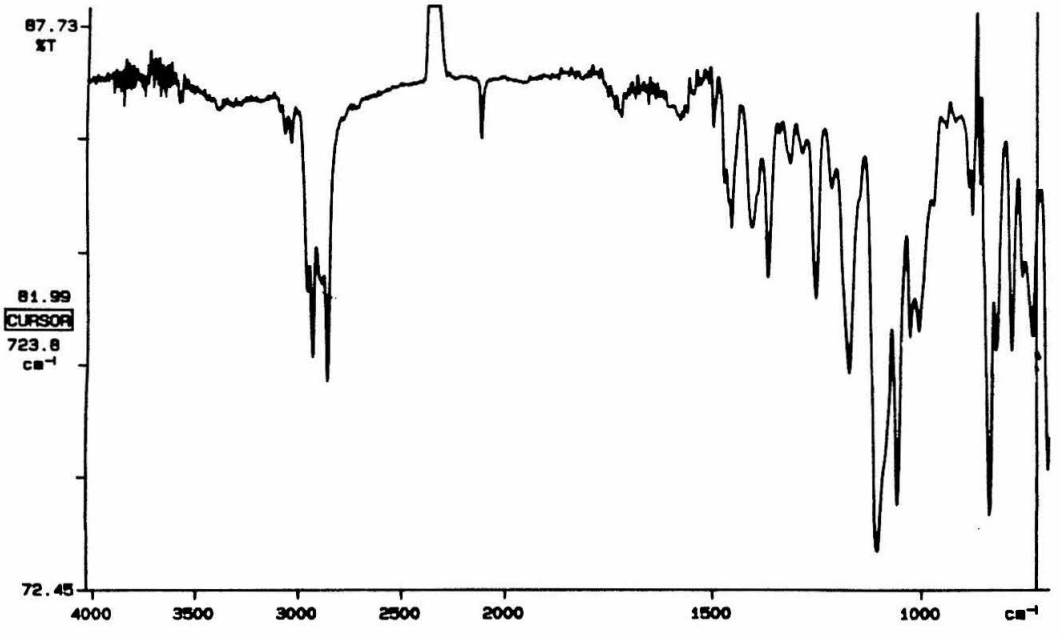
52

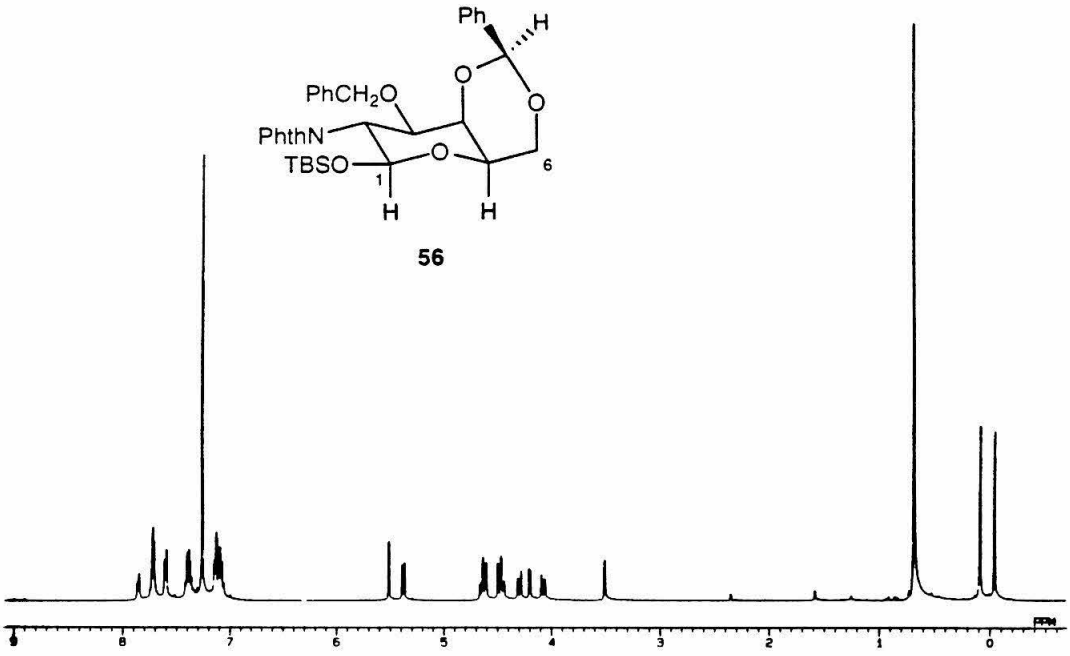

89.30
%T
82.17
4000
3500
3000
2500
2000
1500
1000
cm-1
500


Ph
H
O
O
PhCH2O
N3
H
O
11'
6'
H
AcNH
H
TBSO
O
1"
O
O
CH3
O
6"
CH3
54
9
8
7
6
5
4
3
2
1
0
PPM


86.82
%T
51.15
4000
3500
3000
2500
2000
1500
1000
cm-1
500

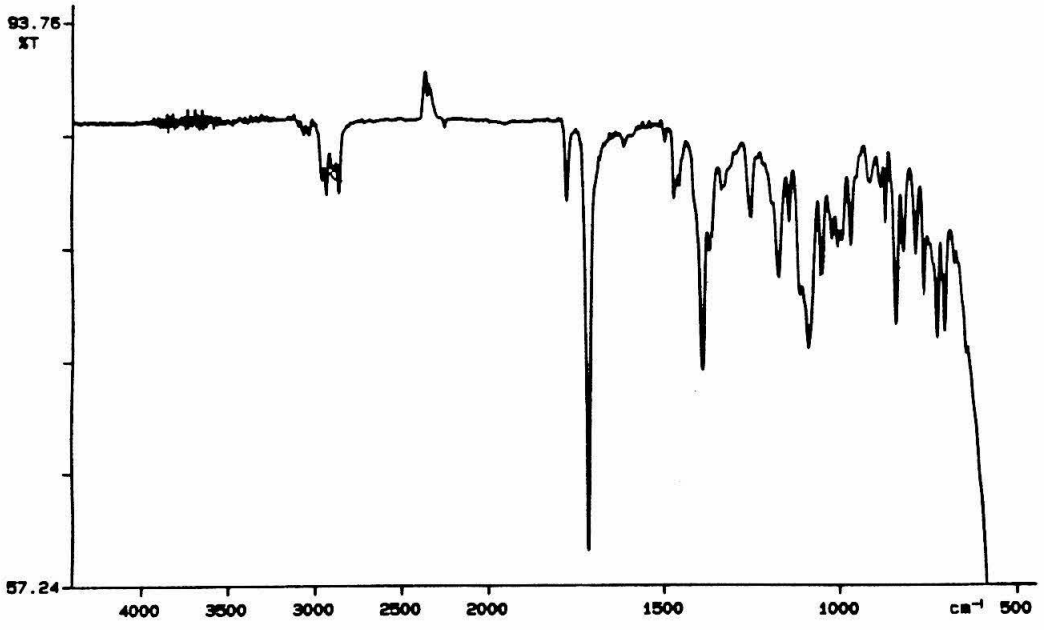

Ph
H
O
O
PhCH2O
H2N
TBSO
O
1
6
H
H
55
9
8
7
6
5
4
3
2
1
0
PPM

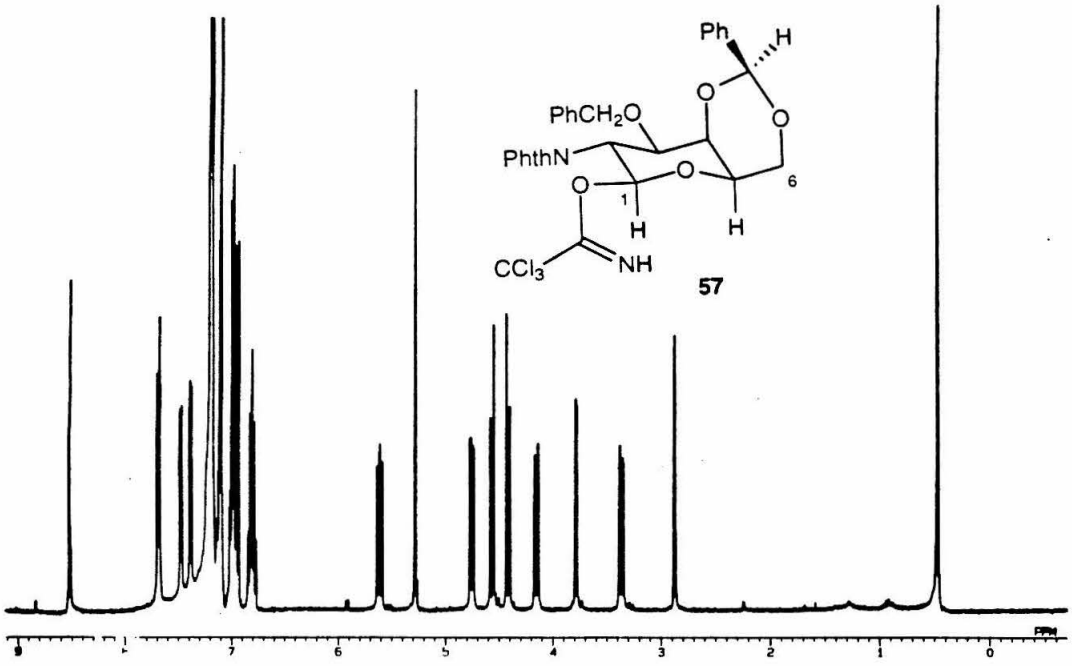

87.73
%T
81.99
CURSOR
723.8
cm-1
72.45
4000
3500
3000
2500
2000
1500
1000
cm-1

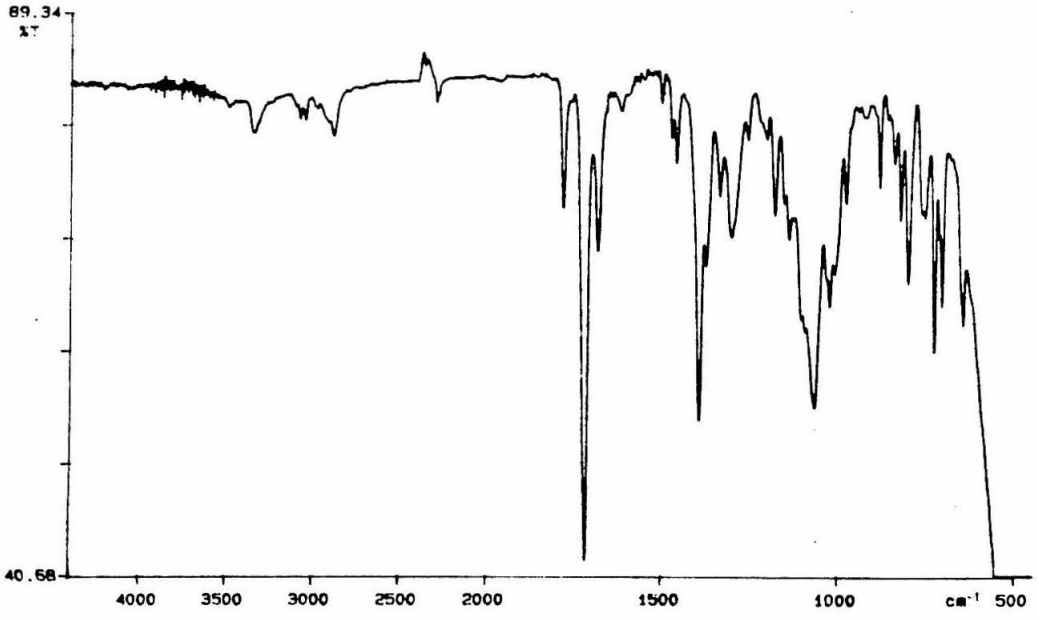

Ph
H
O
O
PhCH2O
PhthN
TBSO
O
1
6
H
H

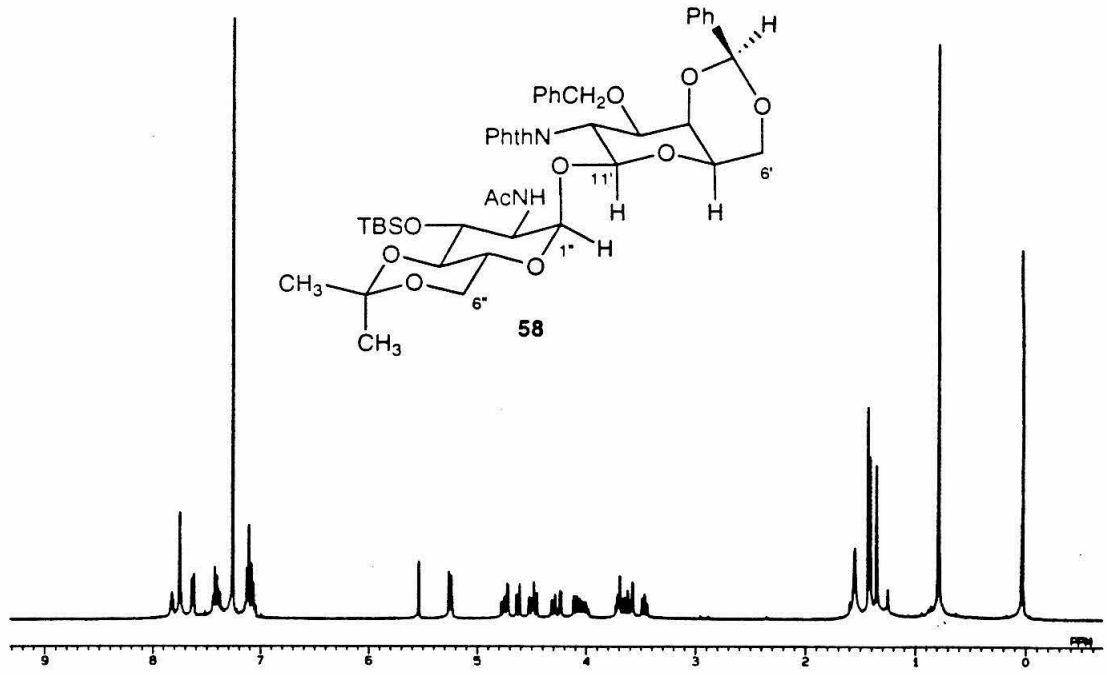
56

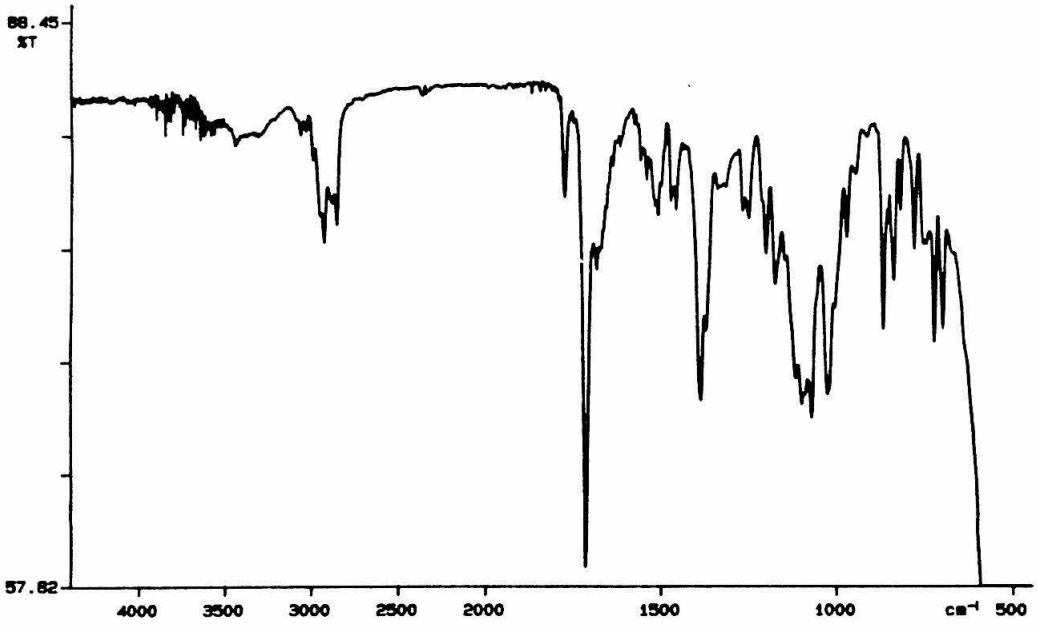
PPM
9
8
7
6
5
4
3
2
1
0

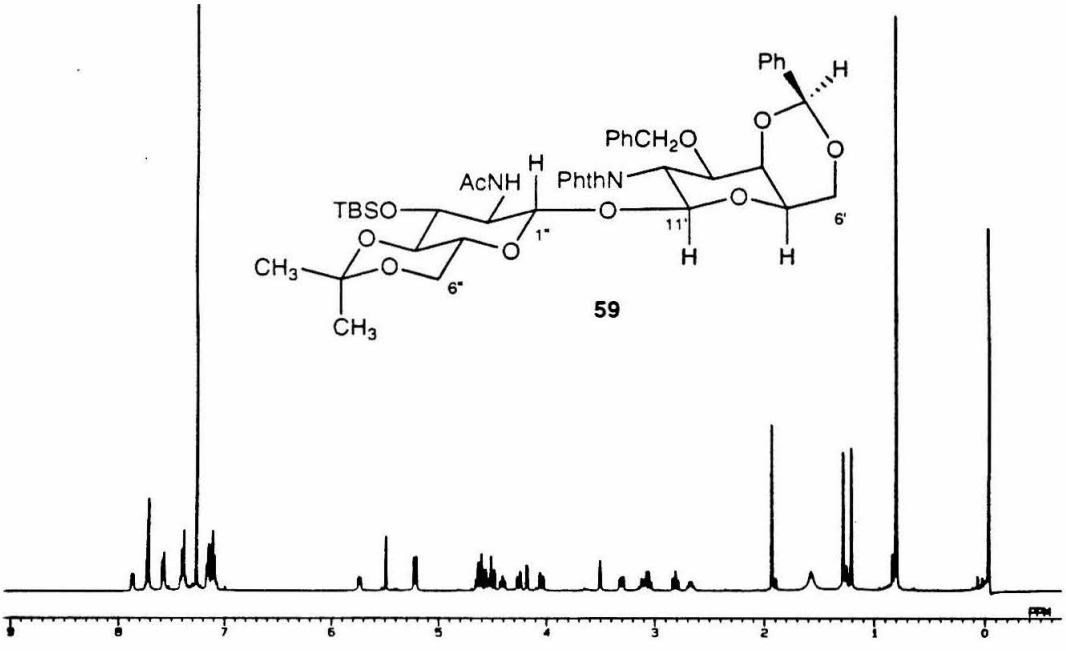

93.76
%T
57.24
4000
3500
3000
2500
2000
1500
1000
cm-1
500


Ph
H
O
O
PhCH2O
PhthN
O
O
6
1
H
H
CCl3
NH
57
9
8
7
6
5
4
3
2
1
0
PPM


89.34
%T
40.68
4000
3500
3000
2500
2000
1500
1000
cm-1
500

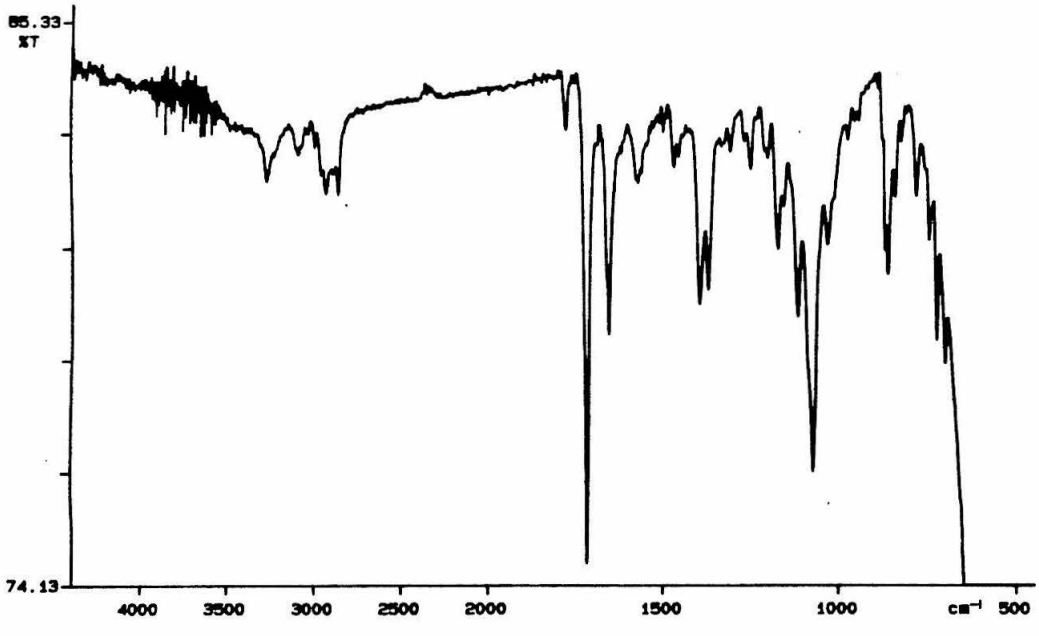

Ph
H
PhCH2O
PhthN
AcNH
TBSO
CH3
CH3
11'
6'
1"
6"
H
H
H
O
58
9
8
7
6
5
4
3
2
1
0
PPM

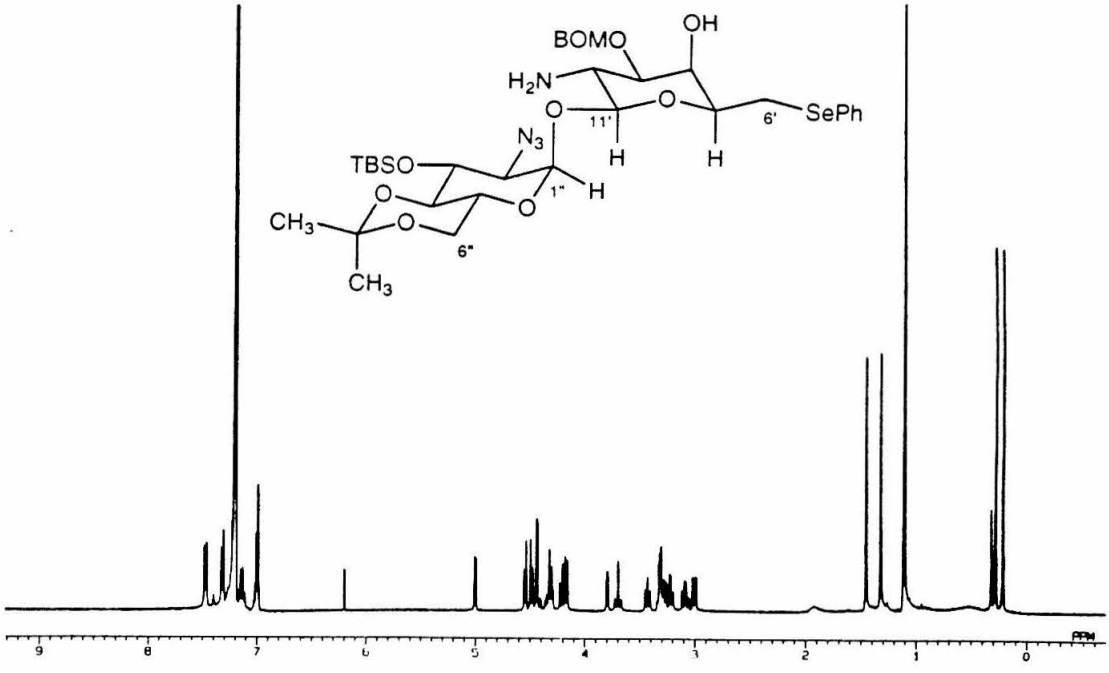

88.45
%T
57.82
4000
3500
3000
2500
2000
1500
1000
cm-1
500

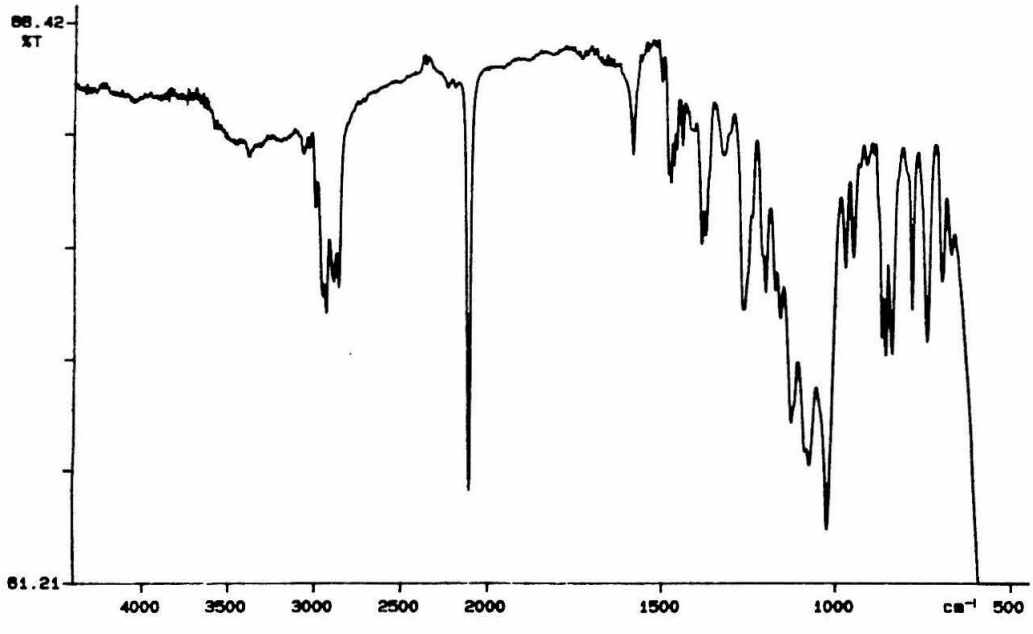

Ph
H
PhCH2O
AcNH
H
PhthN
TBSO
O
1"
11'
6'
CH3
O
6"
CH3
H
H

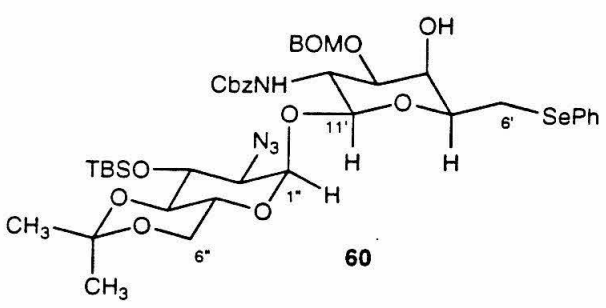
59

PPM


85.33
%T
74.13
4000
3500
3000
2500
2000
1500
1000
cm-1
500

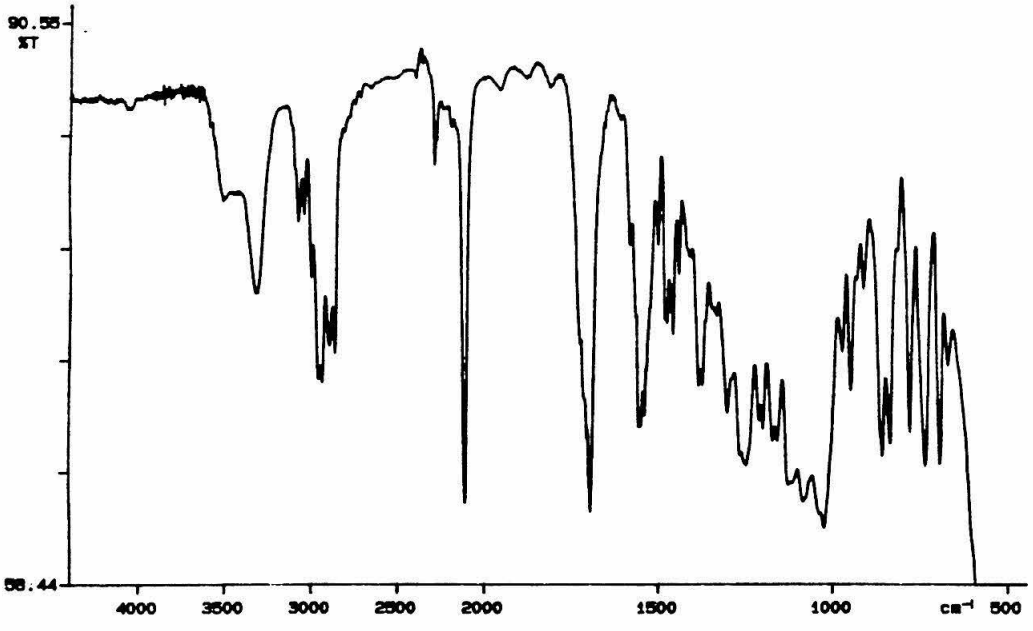

BOMO
OH
H_2N
O
11'
O
6'
SePh
N_3
H
H
TBSO
O
1"
H
O
CH_3
O
6"
CH_3
9
8
7
6
5
4
3
2
1
0
PPM

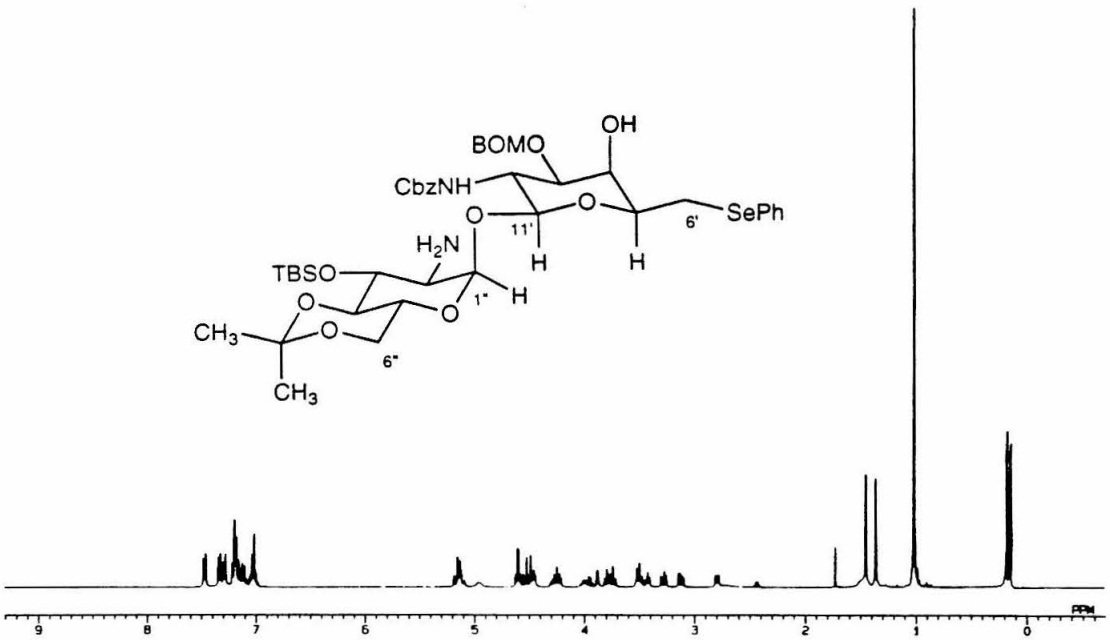

88.42
%T
61.21
4000
3500
3000
2500
2000
1500
1000
cm^{-1}
500

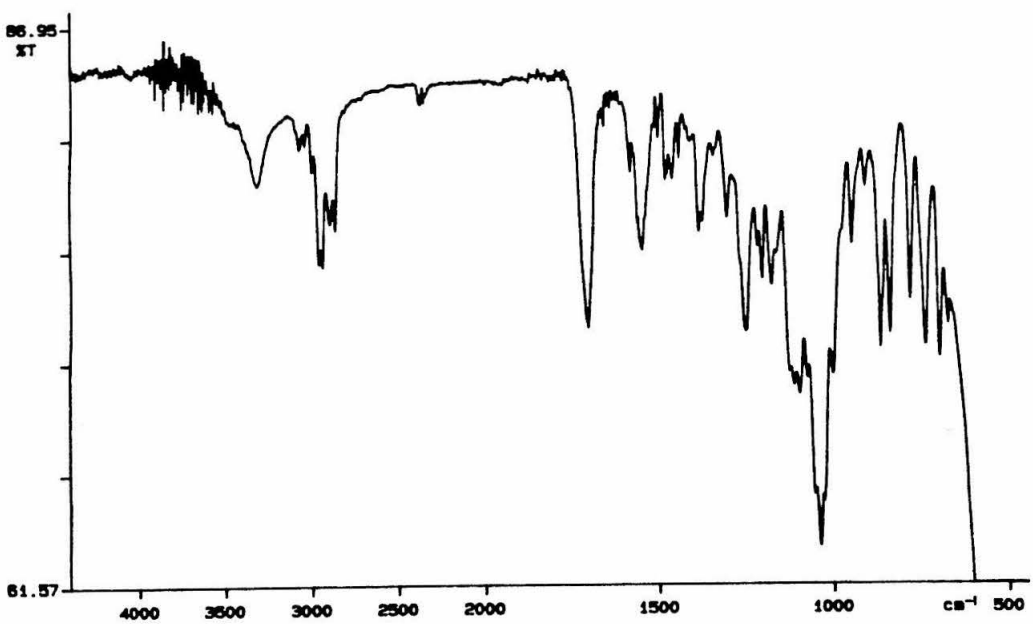

BOMO
OH
CbzNH
O
11'
O
6'
SePh
N3
TBSO
H
H
O
1"
H
O
CH3
O
6"
CH3

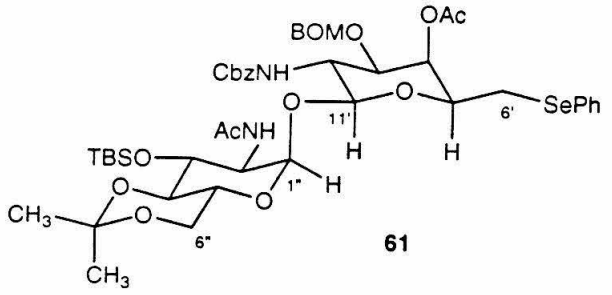
60

9
8
7
6
5
4
3
2
1
0
PPM


90.55
%T
58.44
4000
3500
3000
2500
2000
1500
1000
cm-1
500

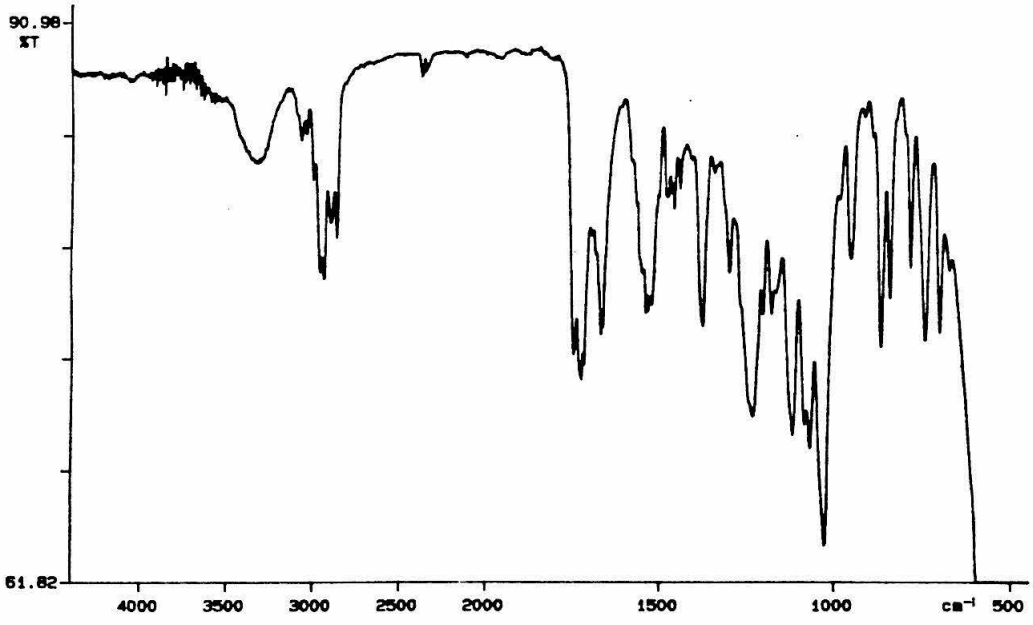

BOMO
OH
CbzNH
O
11'
O
6'
SePh
H
H
H_2N
TBSO
O
1"
H
O
O
CH_3
6"
CH_3
9
8
7
6
5
4
3
2
1
0
PPM

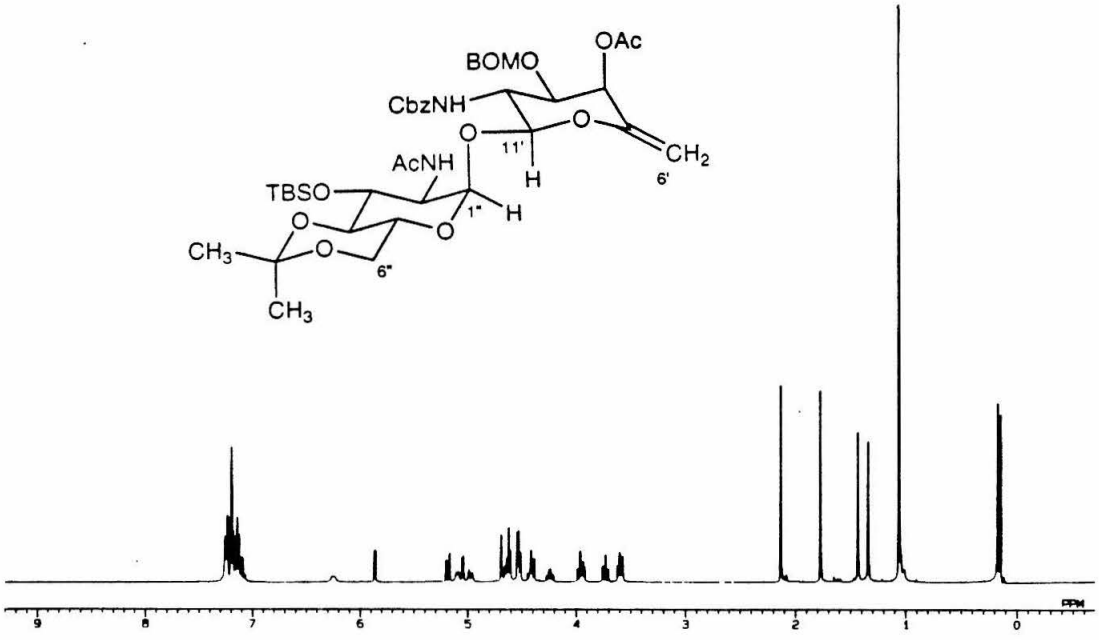

86.95
%T
61.57
4000
3500
3000
2500
2000
1500
1000
cm^{-1}
500

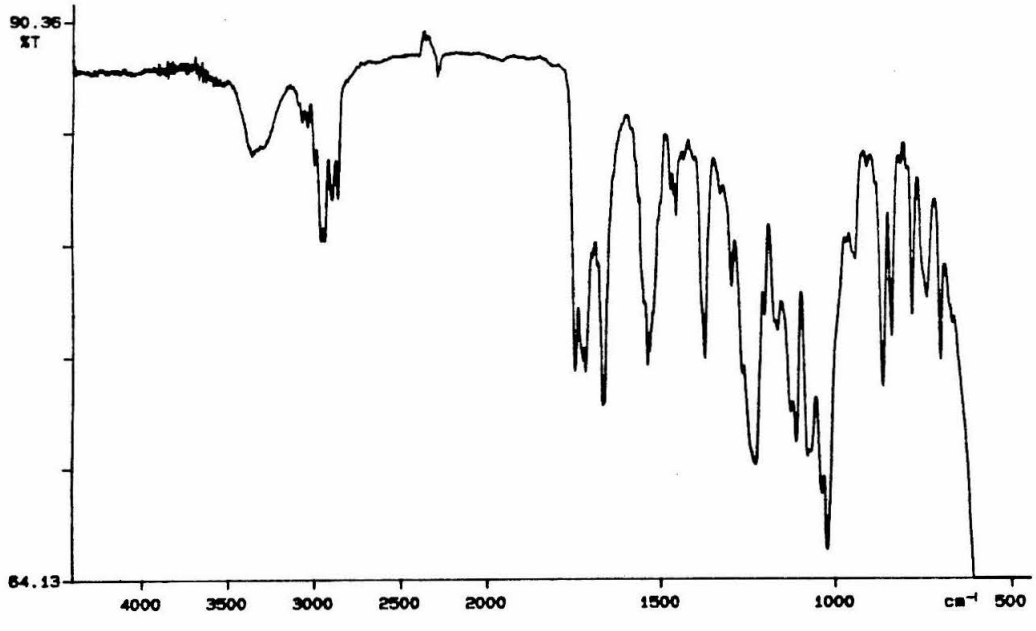

BOMO
OAc
CbzNH
O
11'
O
6'
SePh
AcNH
H
H
TBSO
O
1"
H
CH3
O
O
6"
CH3

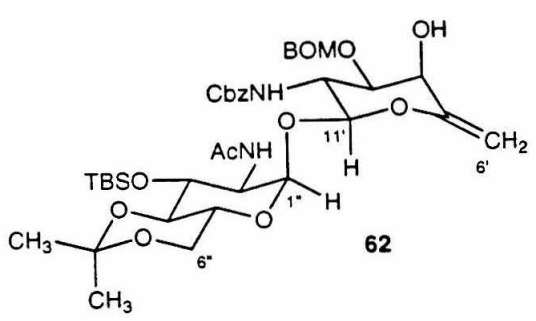
61

9
8
7
6
5
4
3
2
1
0
PPM


90.98
%T
61.82
4000
3500
3000
2500
2000
1500
1000
cm-1
500

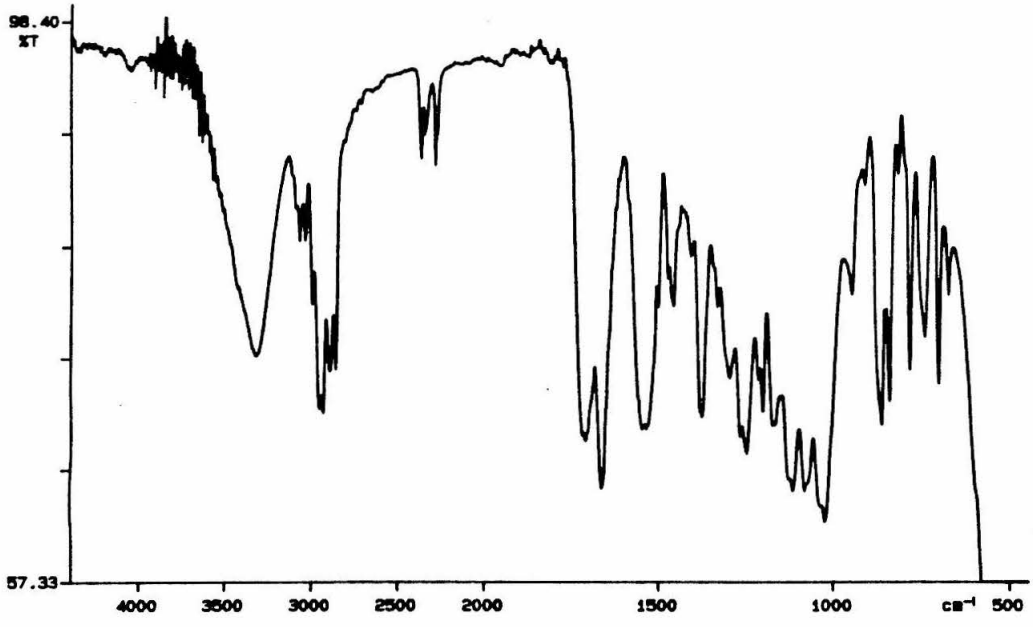

BOMO
OAc
CbzNH
AcNH
TBSO
CH2
6'
11'
H
1"
H
6"
CH3
CH3
PPM

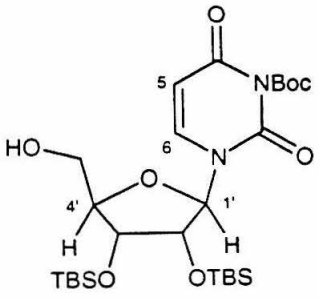

90.36
%T
64.13
4000
3500
3000
2500
2000
1500
1000
cm-1
500


BOMO
OH
CbzNH
O
11'
O
CH2
6'
AcNH
H
TBSO
1"
H
O
O
CH3
O
6"
CH3

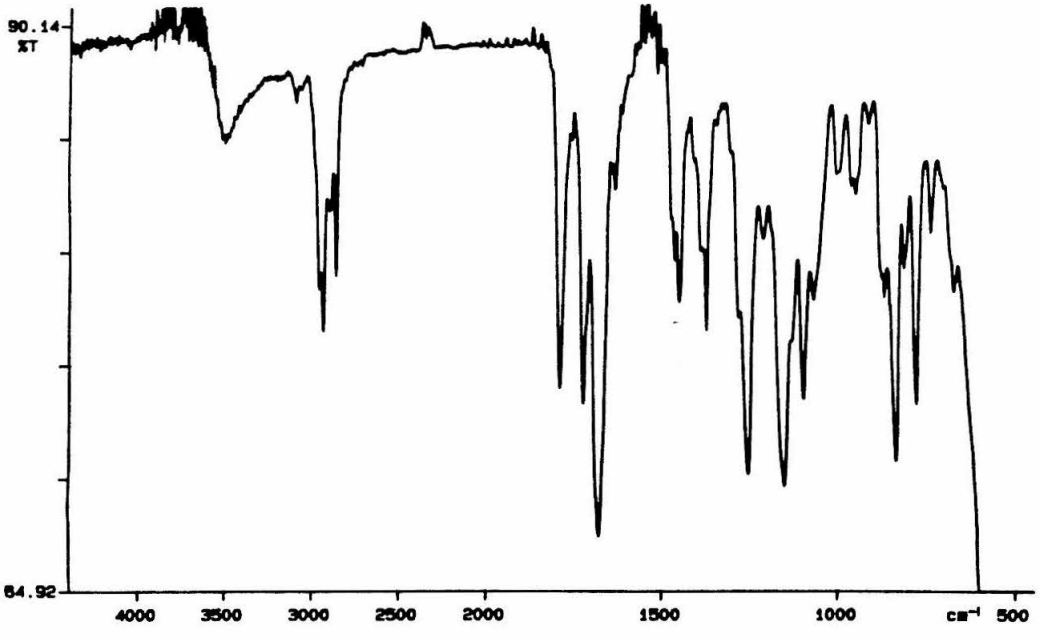
62

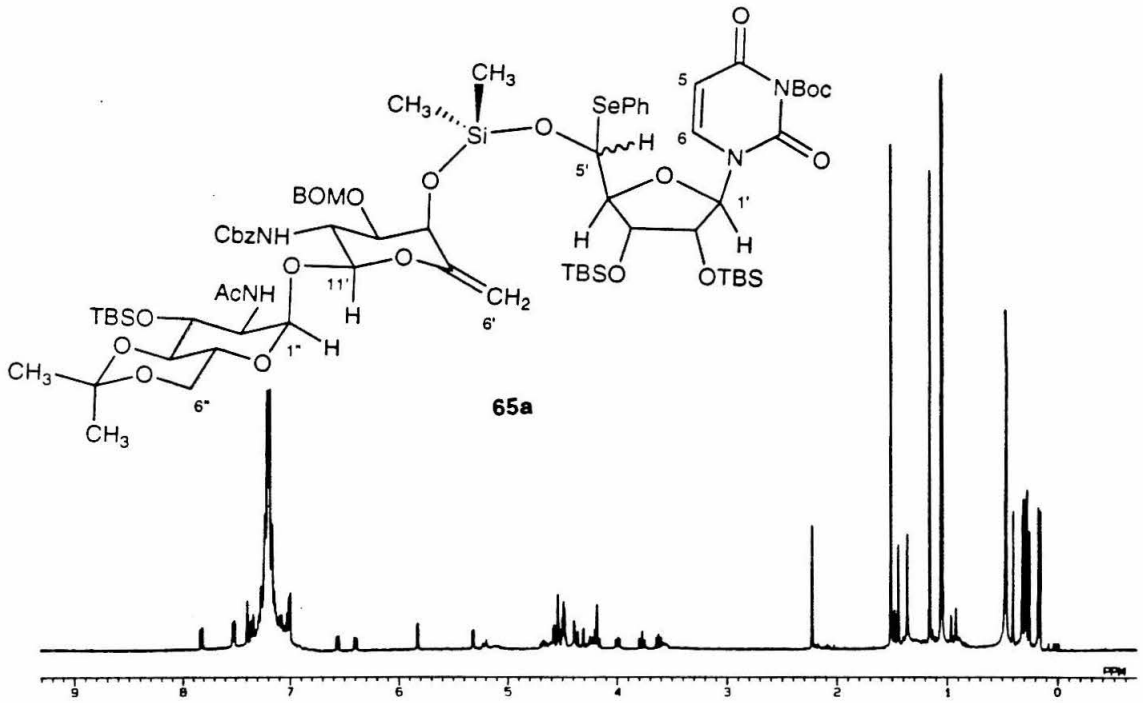
9
8
7
6
5
4
3
2
1
0
PPM

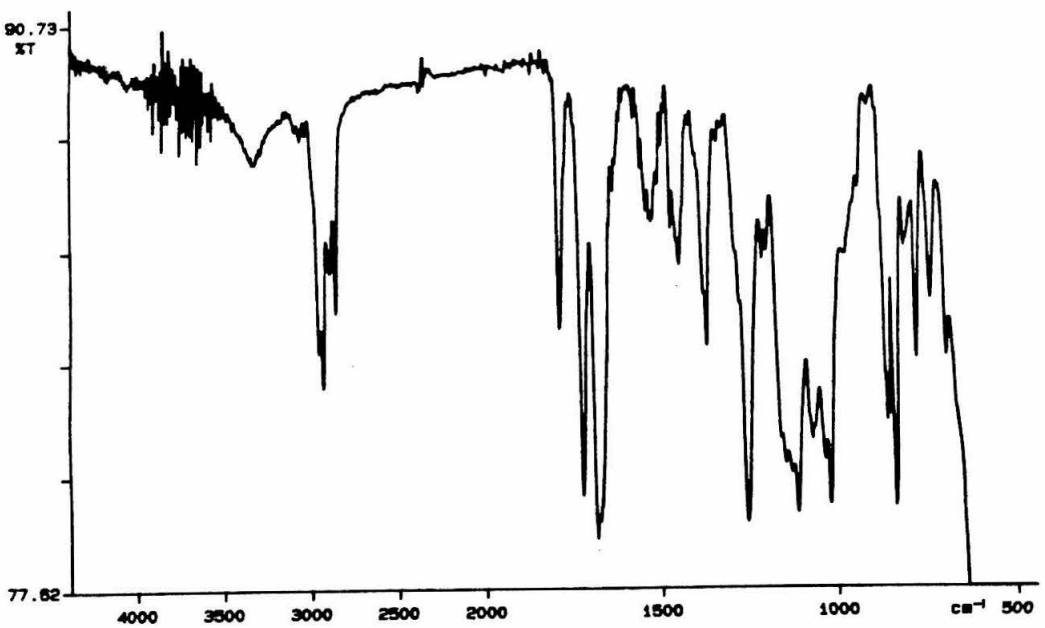

98.40
%T
57.33
4000
3500
3000
2500
2000
1500
1000
cm-1
500

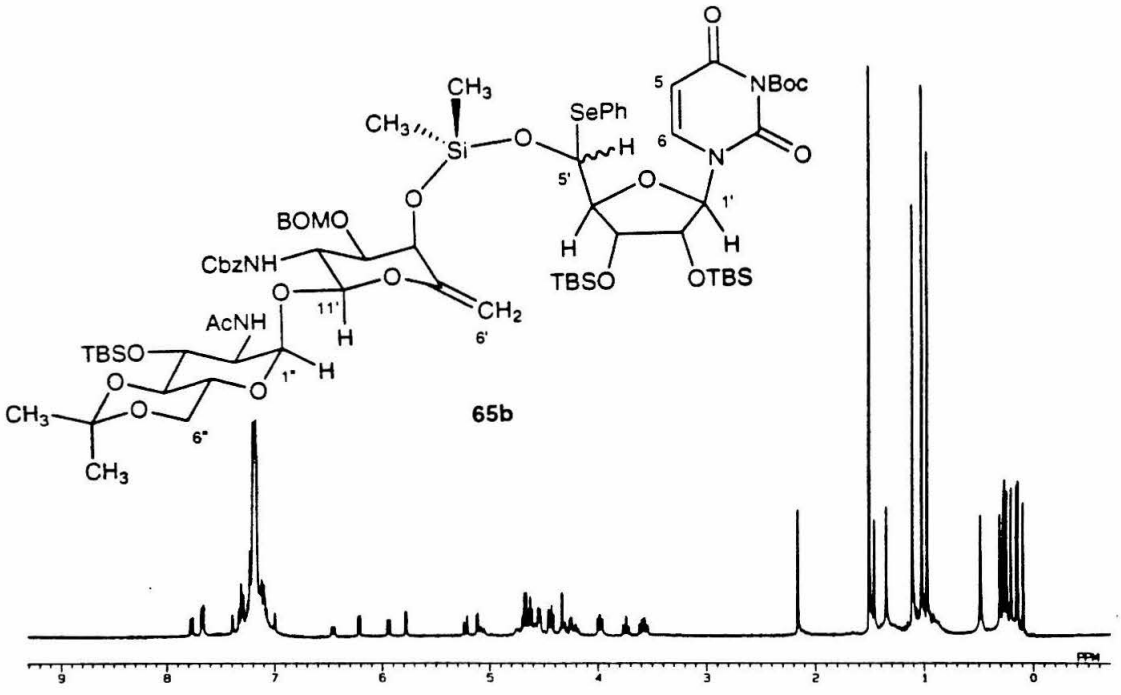

O
5
NBoc
6
N
O
HO
O
4'
1'
H
H
TBSO
OTBS

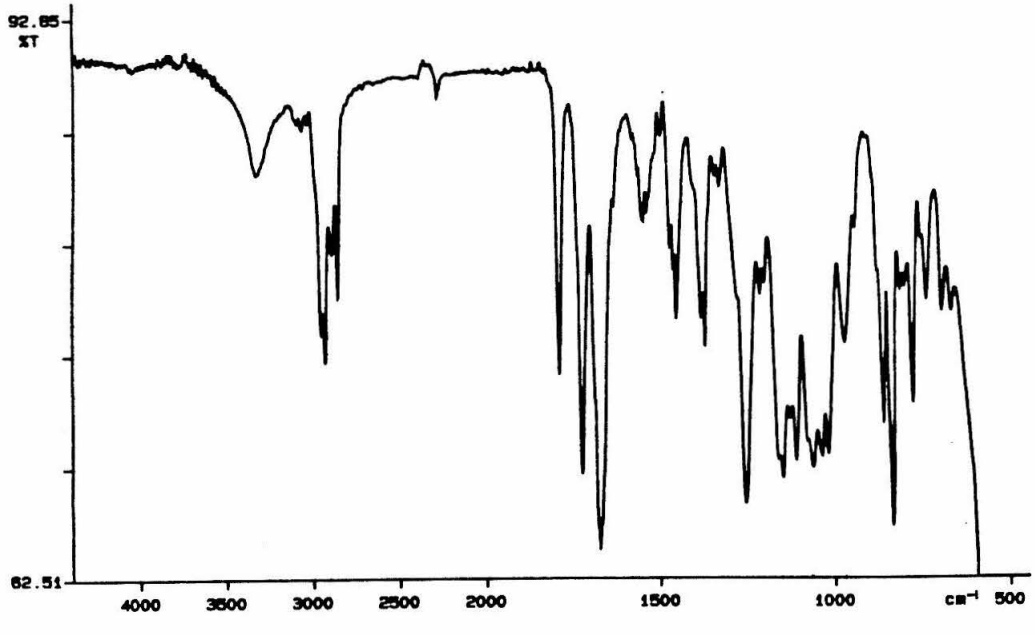
63

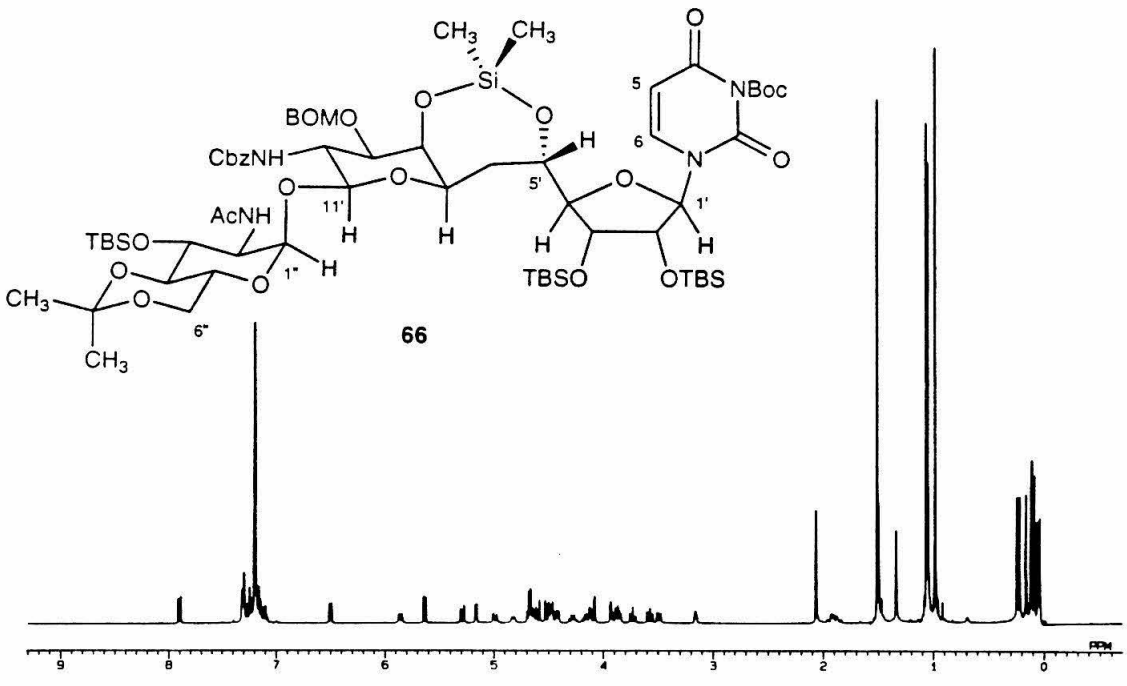

90.14
%T
64.92
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500

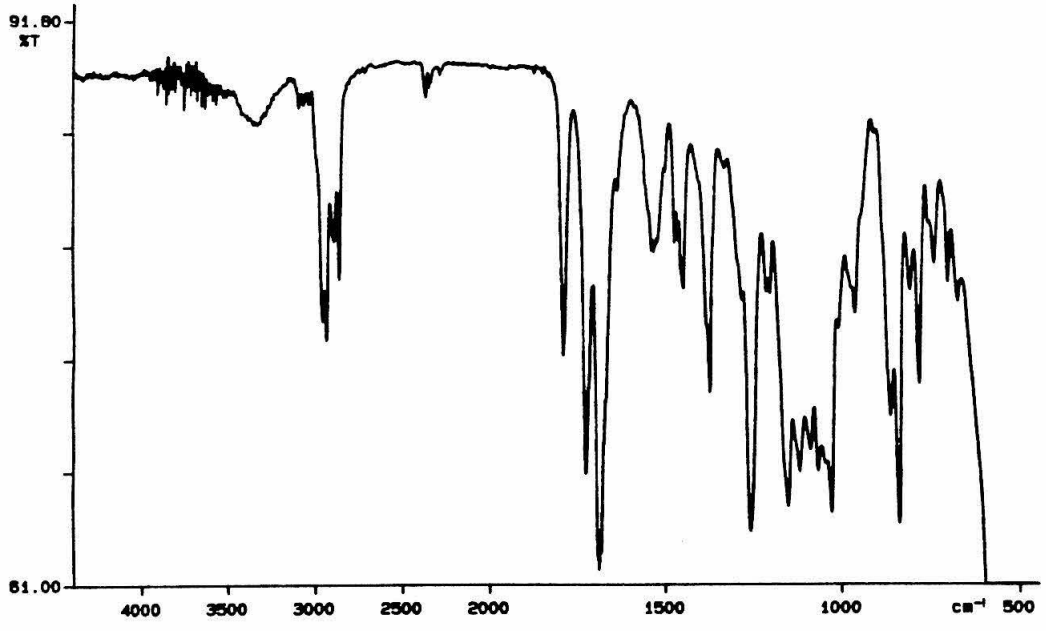

CH3
CH3
Si
O
SePh
H
5'
O
O
5
NBoc
6
N
O
1'
BOMO
CbzNH
O
11'
O
CH2
6'
H
H
TBSO
OTBS
AcNH
TBSO
O
1"
H
O
O
CH3
6"
CH3
65a
PPM

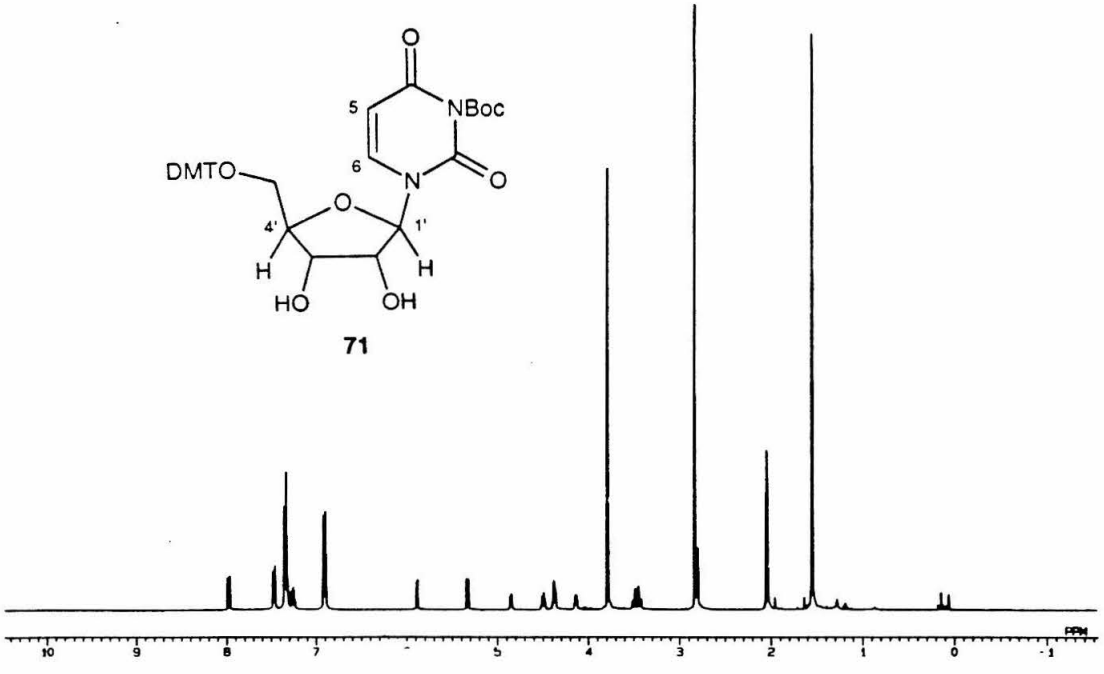

90.73
%T
77.62
4000
3500
3000
2500
2000
1500
1000
cm-1
500

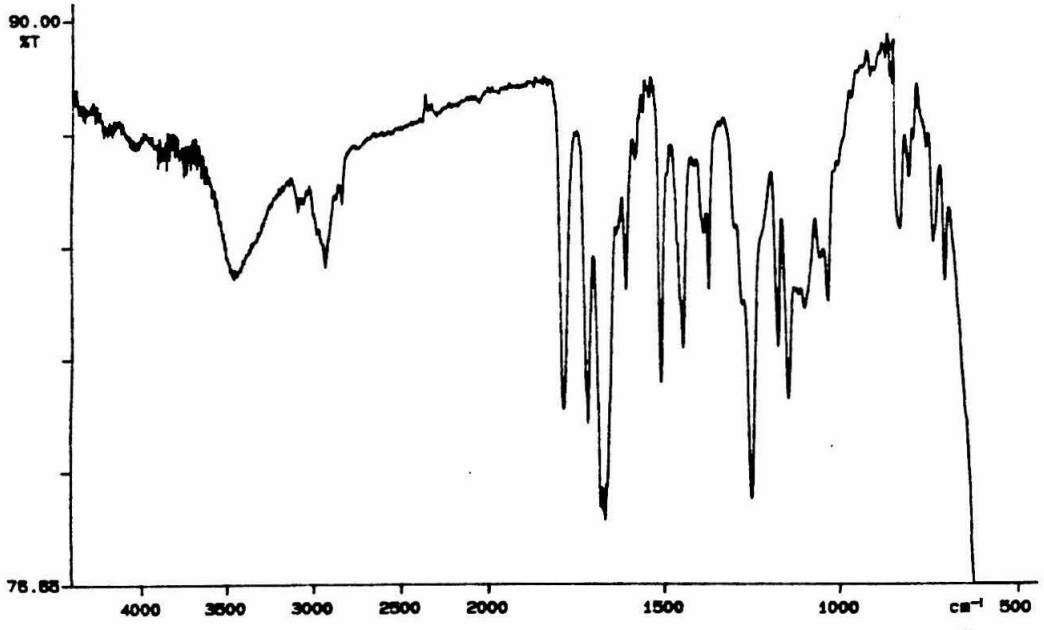

CH3
CH3
Si
O
SePh
H
5'
O
1'
5
NBoc
6
N
O
O
BOMO
CbzNH
O
11'
H
O
CH2
6'
AcNH
TBSO
O
1"
H
O
CH3
O
6"
CH3
H
H
TBSO
OTBS
65b
PPM
9
8
7
6
5
4
3
2
1
0

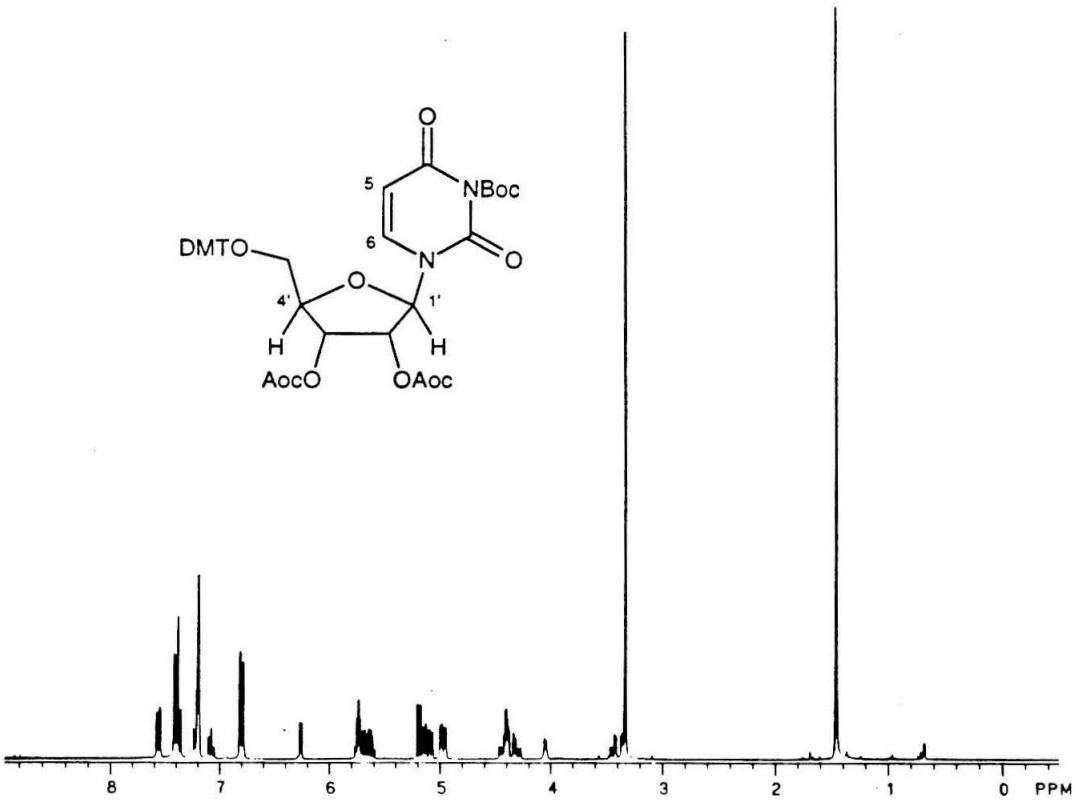

92.65
%T
62.51
4000
3500
3000
2500
2000
1500
1000
cm-1
500

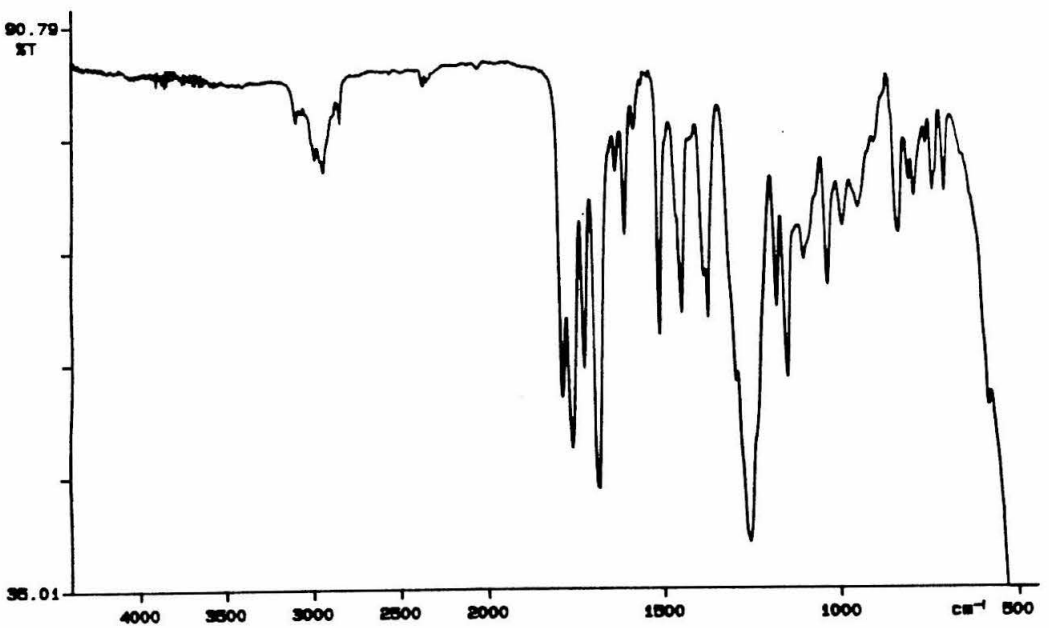

CH3
CH3
Si
O
O
BOMO
CbzNH
AcNH
TBSO
O
O
O
CH3
CH3
6"
1"
H
11'
H
H
5'
H
O
O
5
6
NBoc
N
O
O
1'
H
H
TBSO
OTBS
66
9
8
7
6
5
4
3
2
1
0
PPM

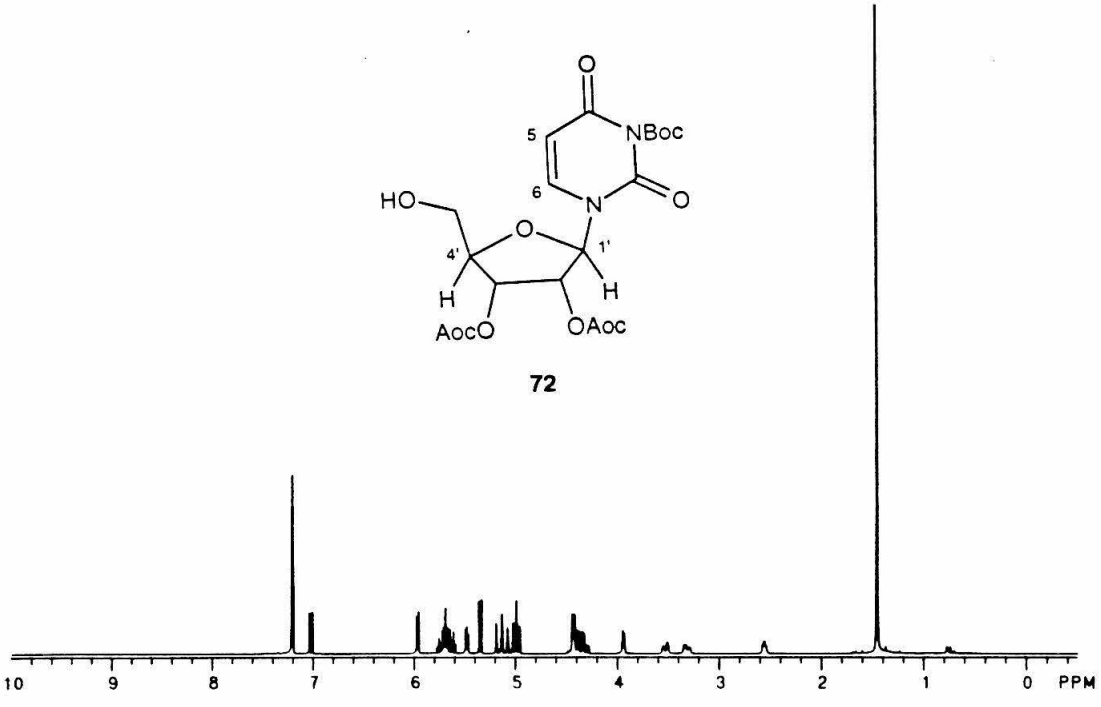

91.80
%T
61.00
4000
3500
3000
2500
2000
1500
1000
cm-1
500


O
5
NBoc
6
N
O
DMTO
O
4'
1'
H
H
HO
OH
71
10
9
8
7
5
4
3
2
1
0
-1
PPM

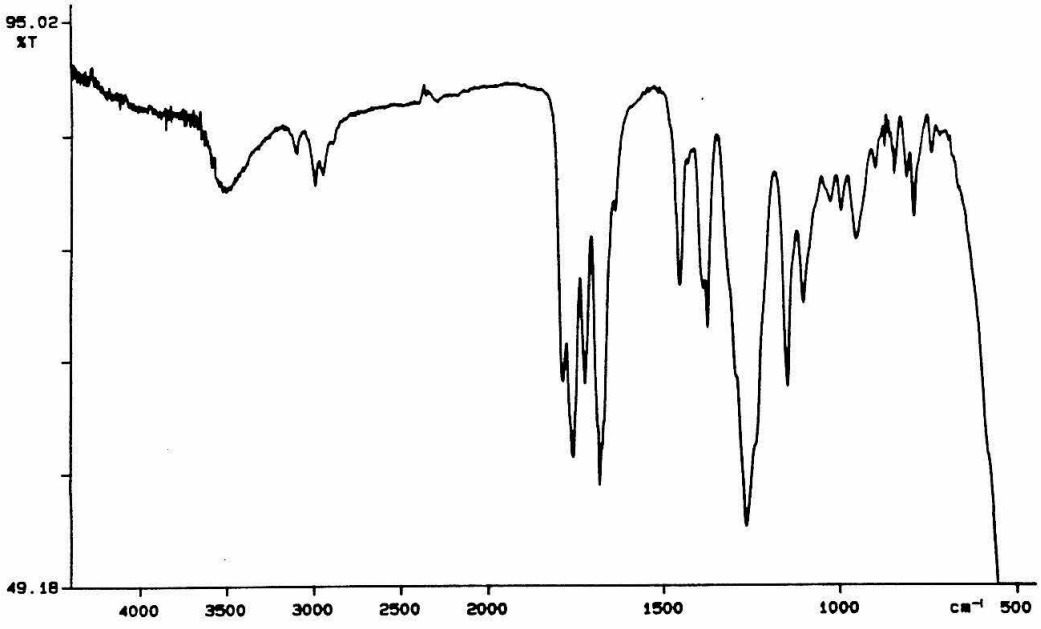

90.00
%T
76.65
4000
3500
3000
2500
2000
1500
1000
cm-1
500

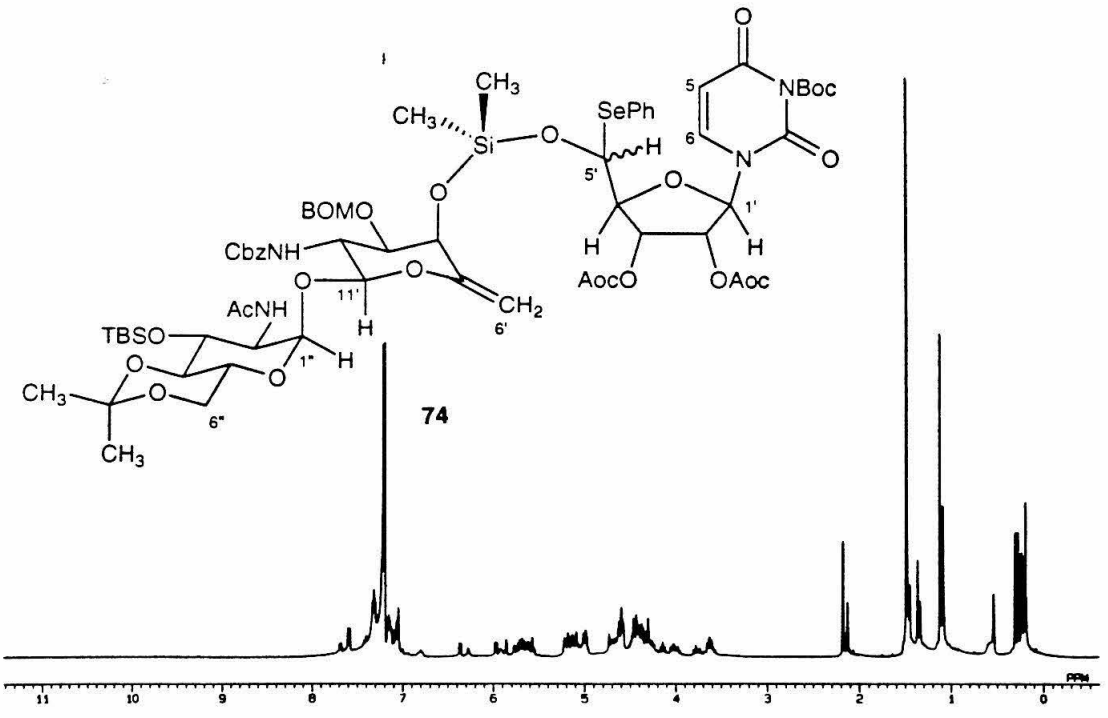

O
5
NBoc
6
N
O
DMTO
O
4'
1'
H
H
AocO
OAoc
8
7
6
5
4
3
2
1
0
PPM

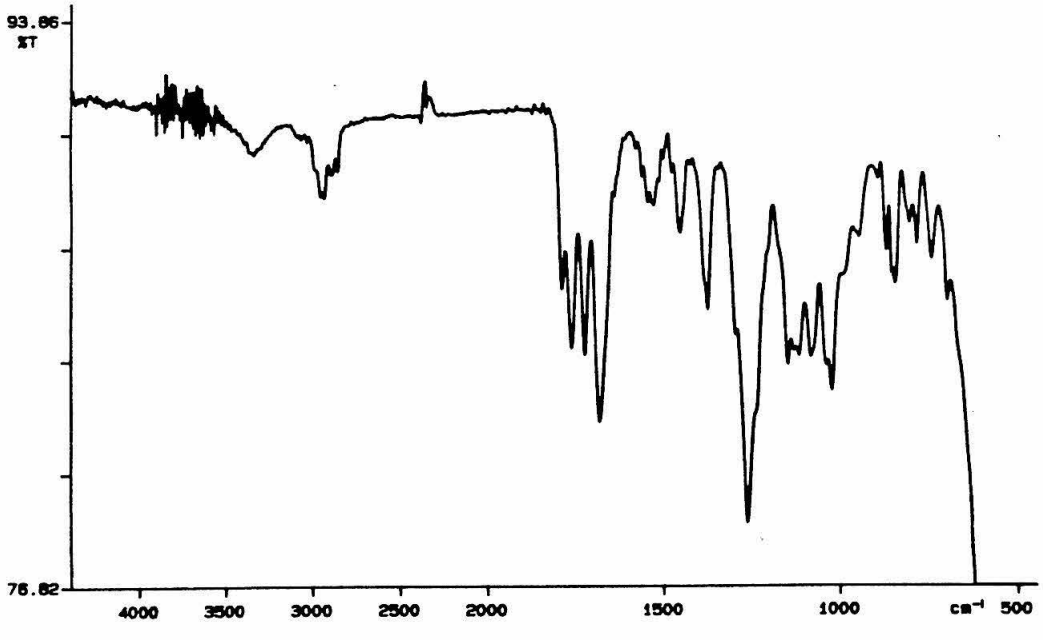

90.79
%T
35.01
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500

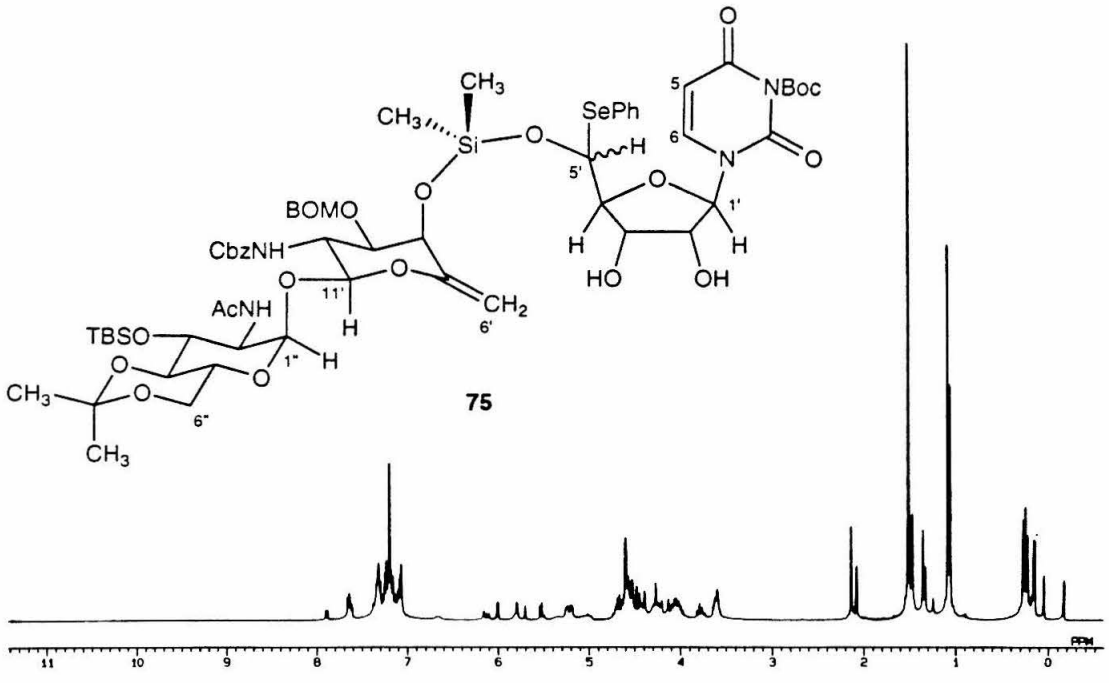

O
NBoc
5
6
N
O
HO
O
4'
1'
H
H
AocO
OAoc
10
9
8
7
6
5
4
3
2
1
0
PPM

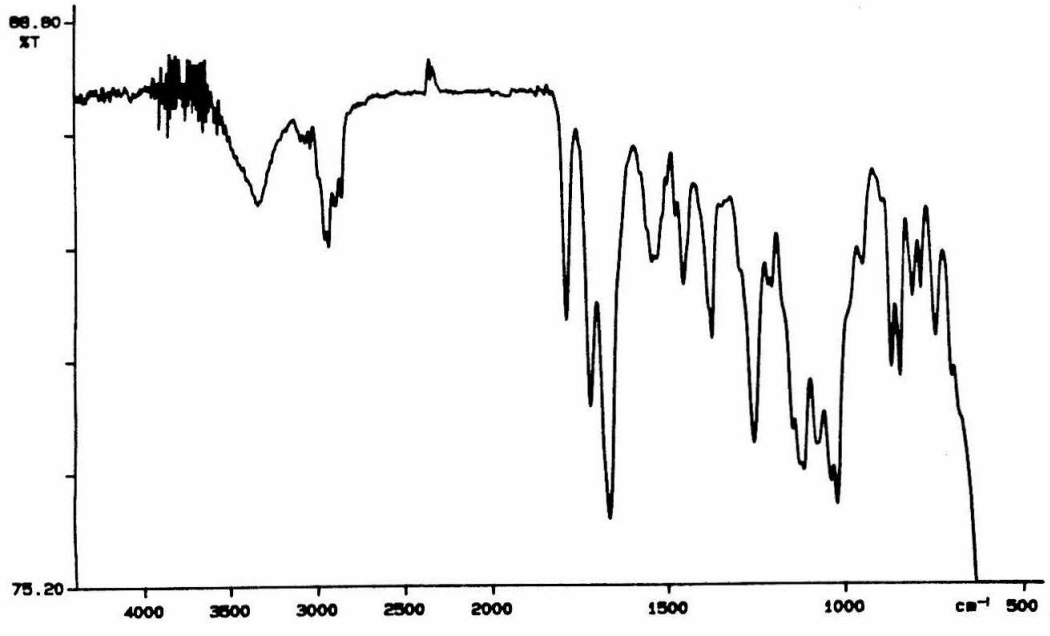
72

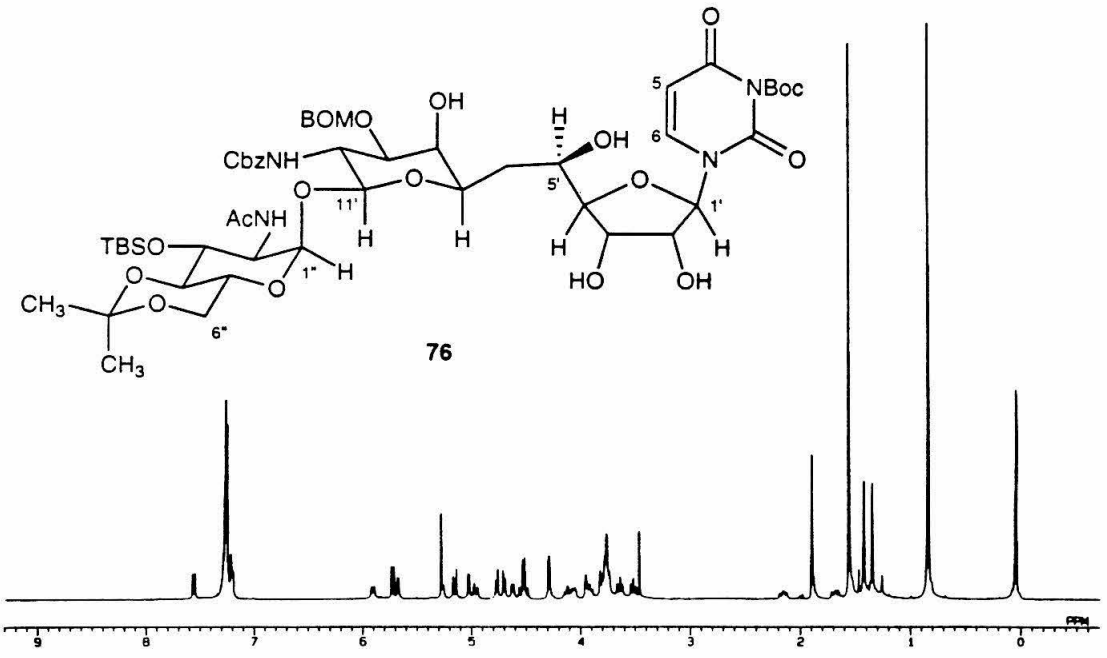

95.02
%T
49.18
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


CH3
CH3
Si
O
SePh
H
5'
O
5
NBoc
6
N
O
O
1'
BOMO
CbzNH
O
11'
O
CH2
6'
H
H
AocO
OAoc
AcNH
TBSO
O
1"
H
O
O
CH3
6"
CH3
74
11
10
9
8
7
6
5
4
3
2
1
0
PPM

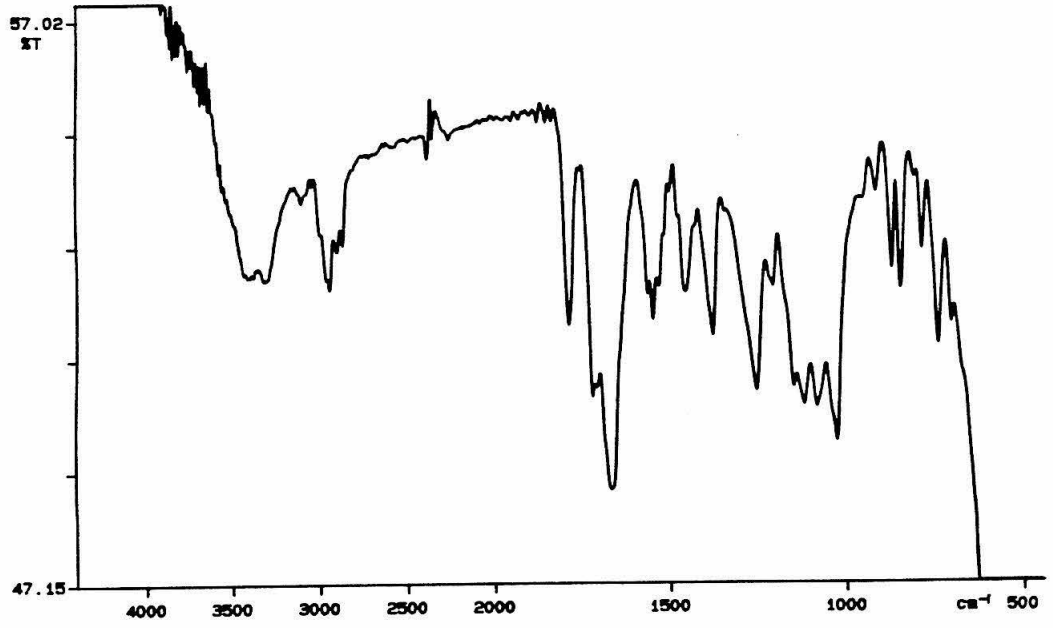

93.86
%T
76.82
4000
3500
3000
2500
2000
1500
1000
cm-1
500

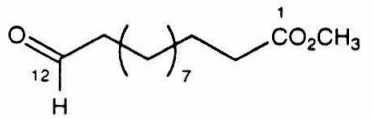

CH3
CH3
Si
O
SePh
H
5'
O
5
NBoc
6
N
O
O
1'
BOMO
CbzNH
O
11'
O
CH2
6'
H
H
HO
OH
AcNH
TBSO
O
1"
H
O
CH3
O
6"
CH3
75
11
10
9
8
7
6
5
4
3
2
1
0
PPM


88.80
%T
75.20
4000
3500
3000
2500
2000
1500
1000
cm-1
500


BOMO
OH
CbzNH
AcNH
TBSO
CH3
CH3
11'
1"
6"
5'
1'
5
6
NBoc
HO
OH
PPM

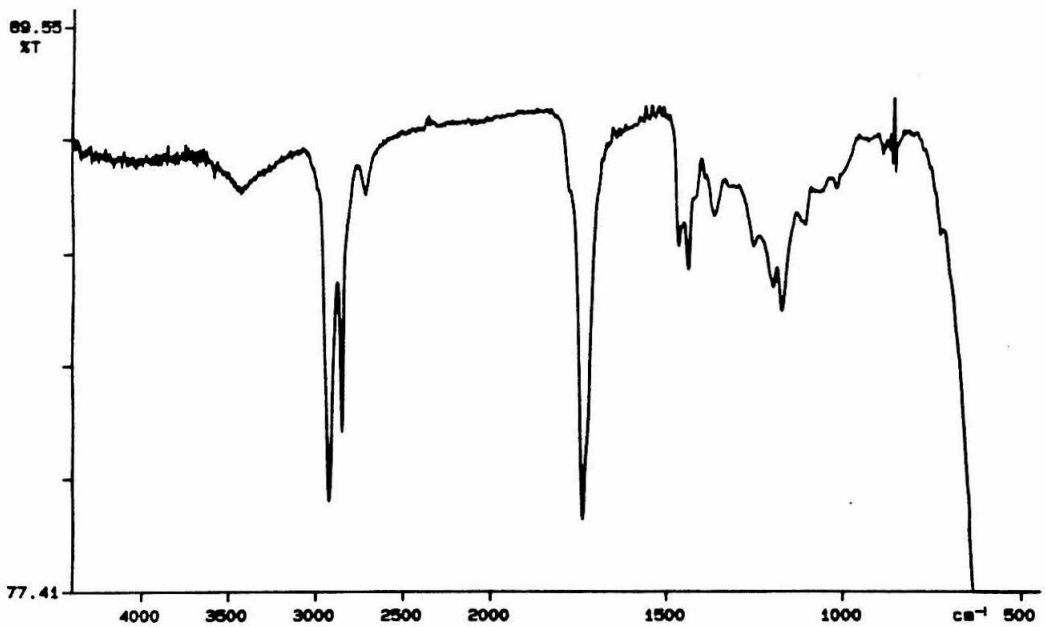
76

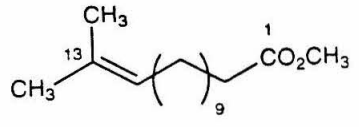

57.02
%T
47.15
4000
3500
3000
2500
2000
1500
1000
cm-1
500


O
12
H
7
1
CO2CH3

78

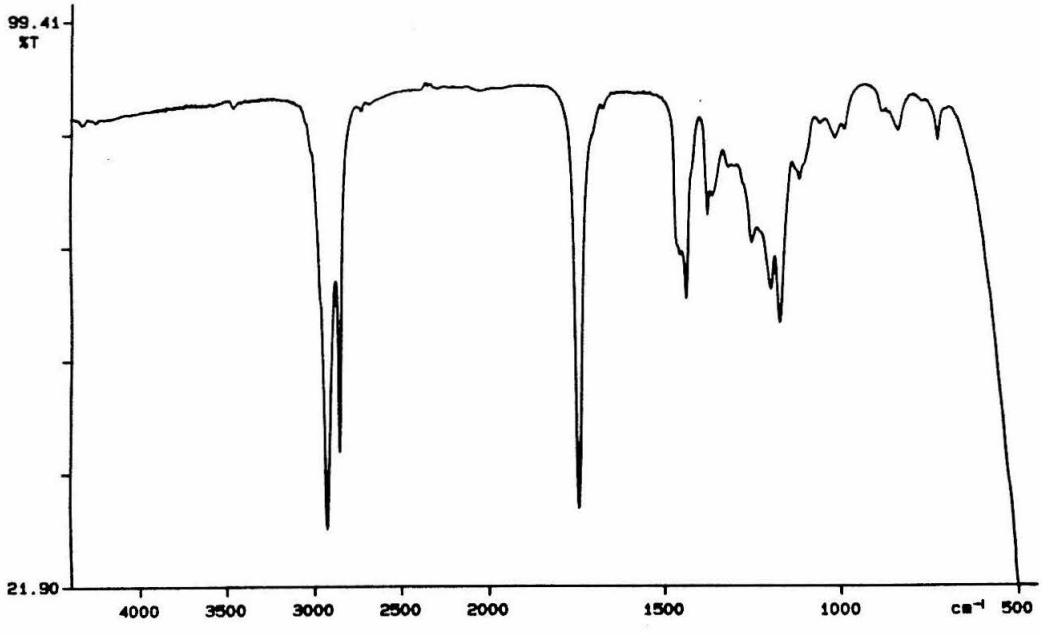
10
8
6
4
2
0
PPM

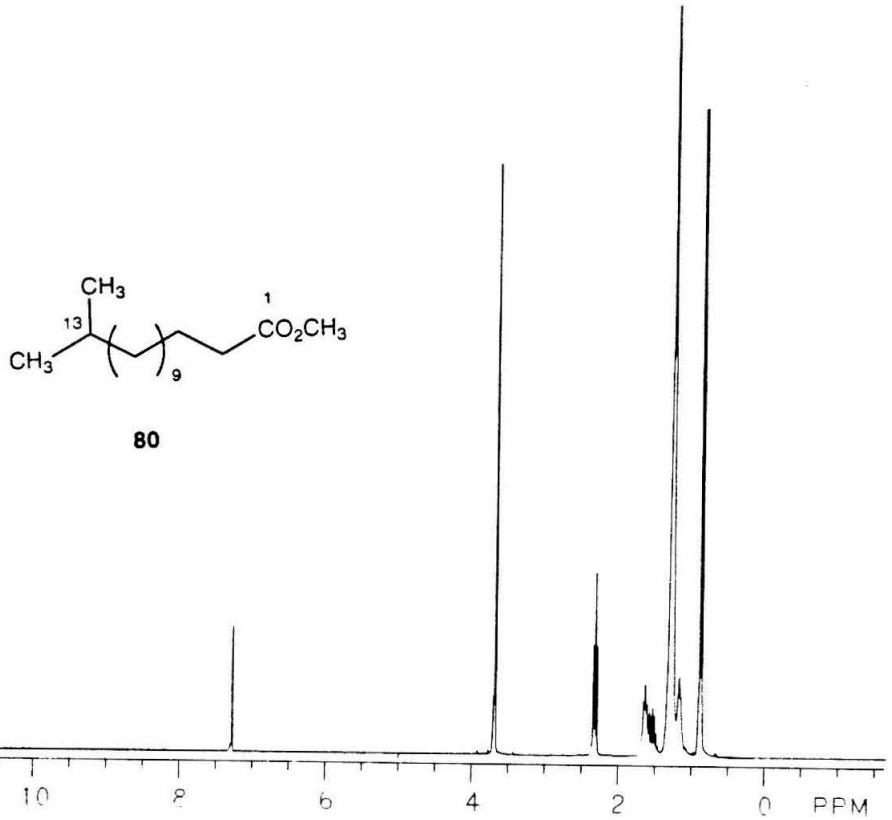

89.55
%T
77.41
4000
3500
3000
2500
2000
1500
1000
cm-1
500


CH3
13
1
CO2CH3
CH3
9

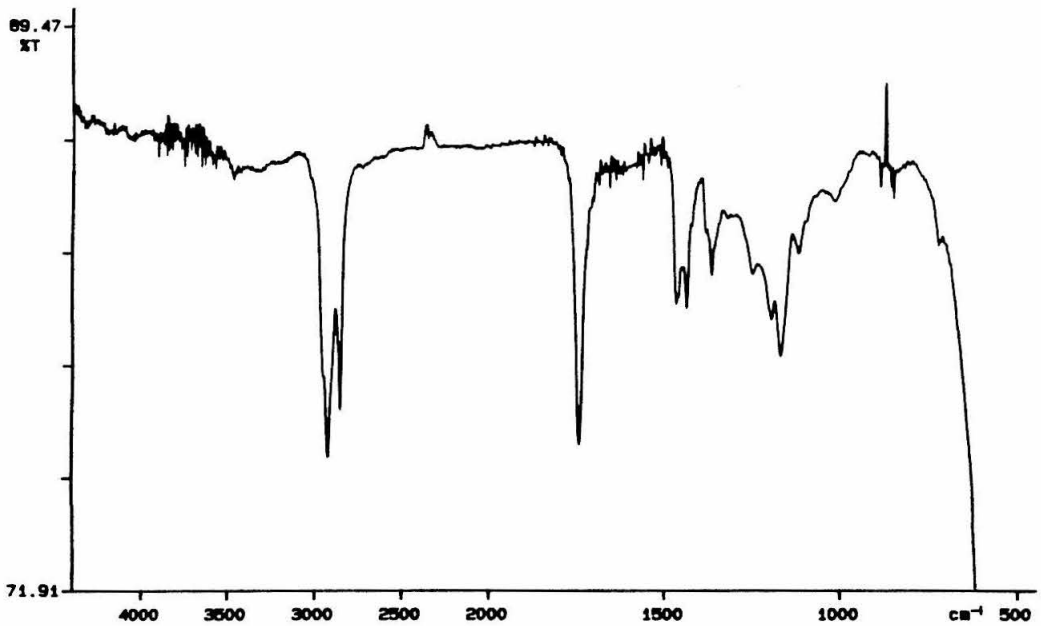
79

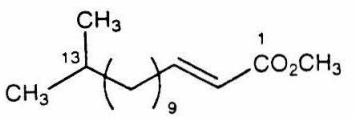
9
8
7
6
5
4
3
2
1
0
PPM


99.41
%T
21.90
4000
3500
3000
2500
2000
1500
1000
cm-1
500


CH3
13
CH3
1
CO2CH3
9
10
8
6
4
2
0
PPM

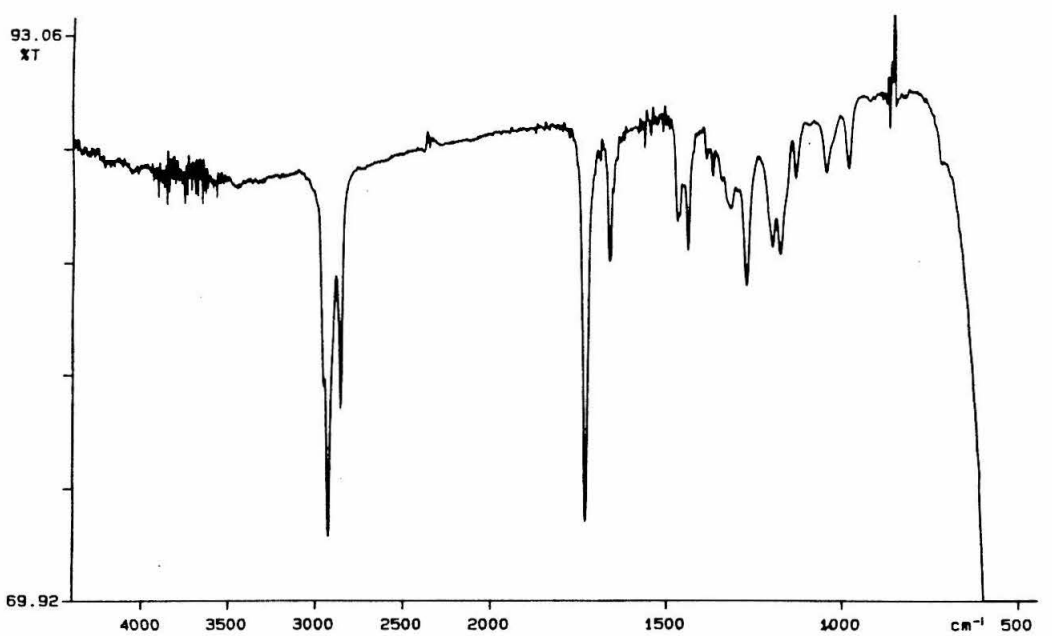
80

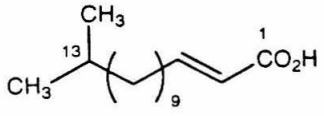

89.47
%T
71.91
4000
3500
3000
2500
2000
1500
1000
cm-1
500


CH3
13
CH3
1
CO2CH3
9

81

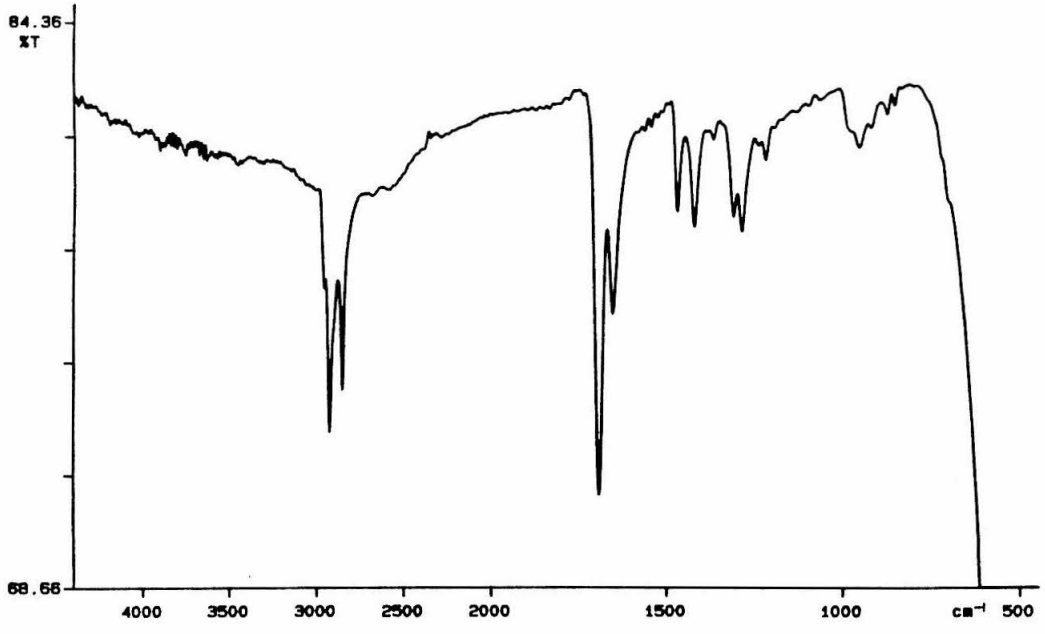
10
8
6
4
2
0
−2
PPM

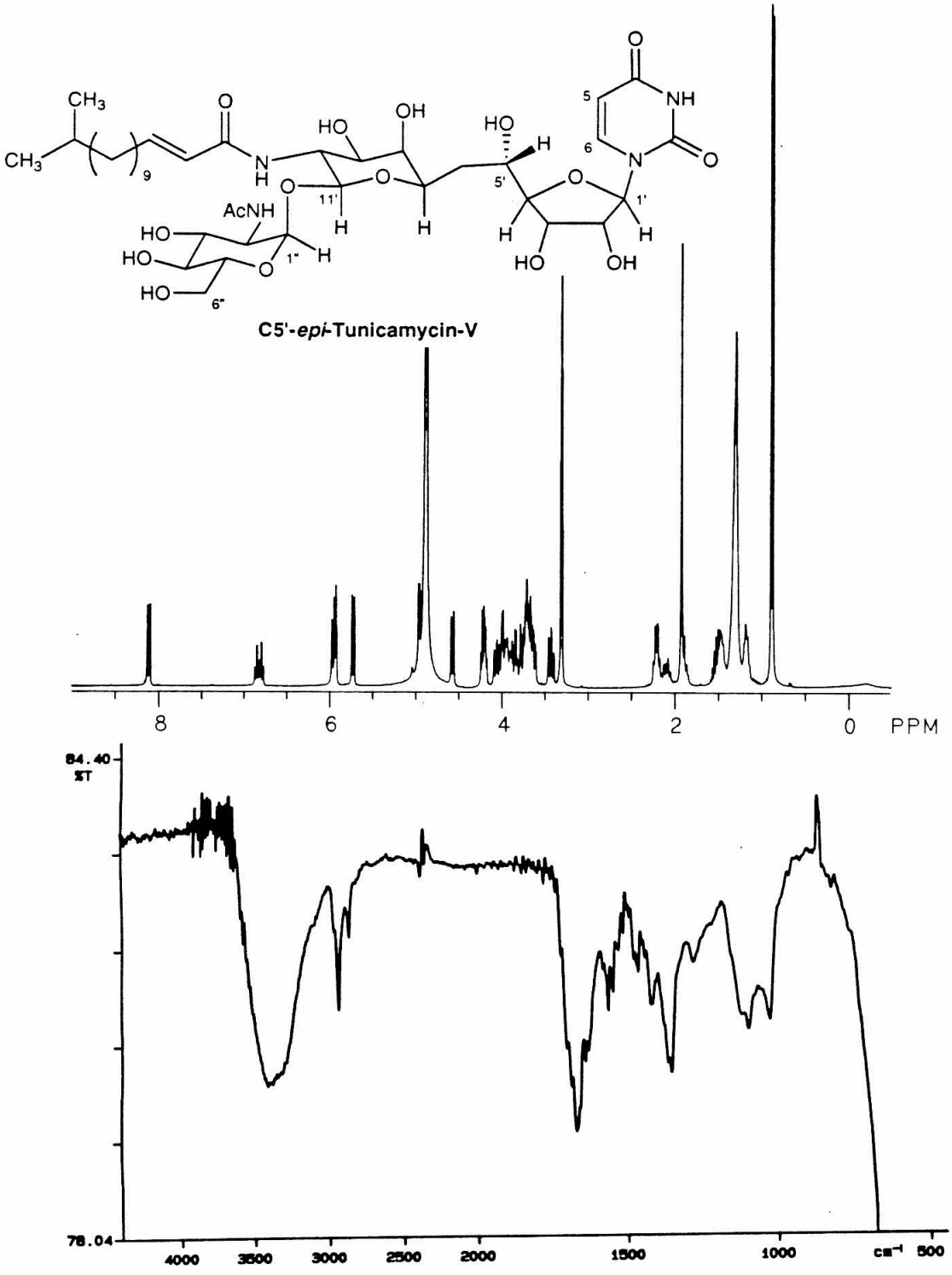

93.06
%T
69.92
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500

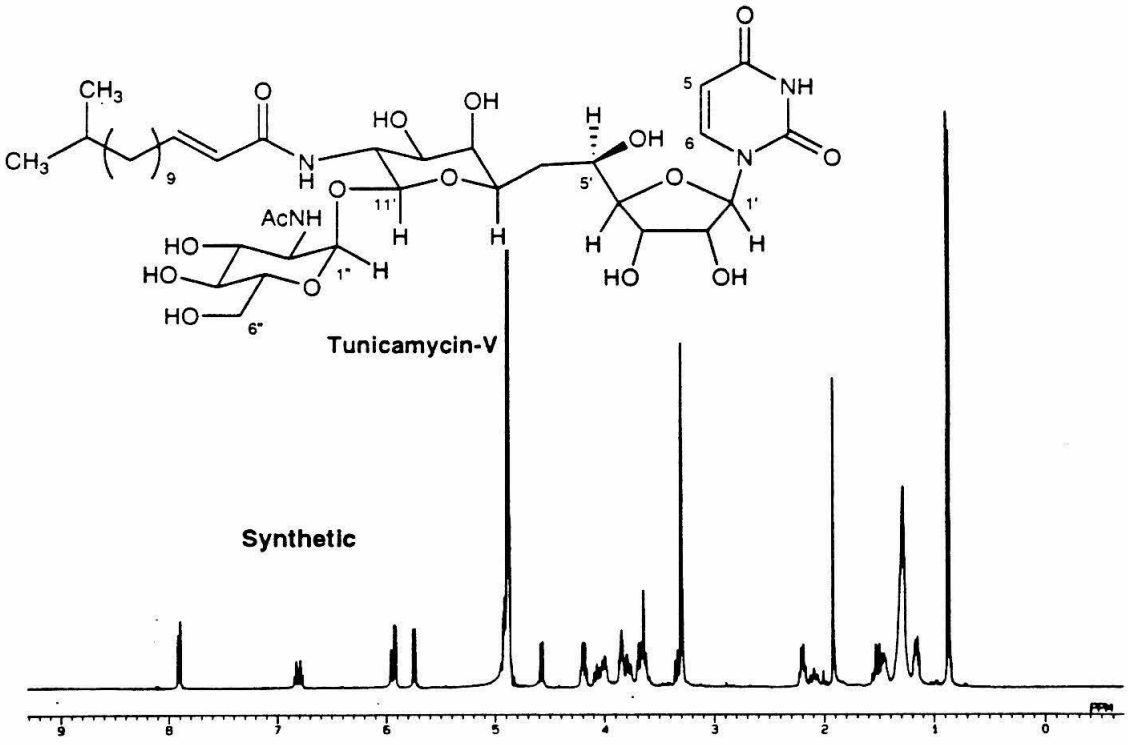

CH3
13
1
CO2H
CH3
9

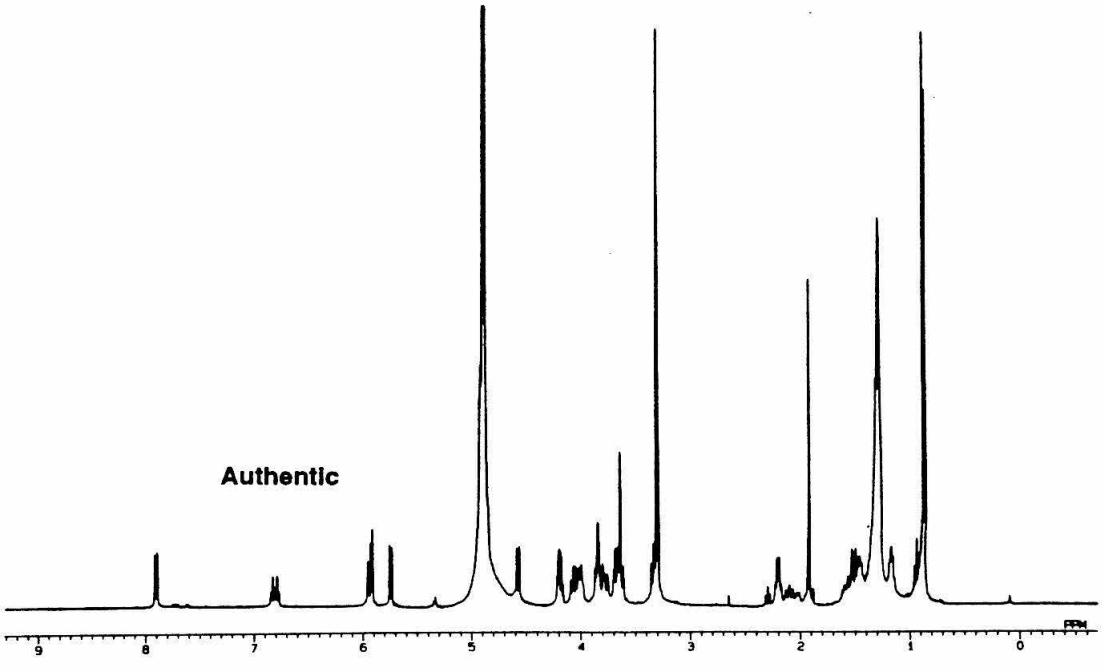
82

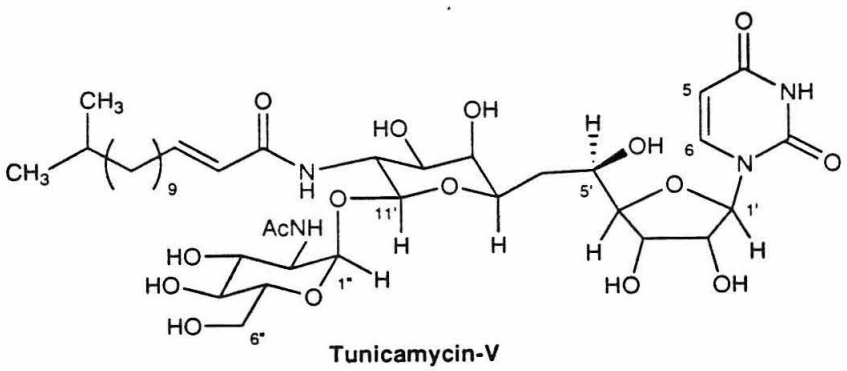
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
PPM


84.36
%T
68.66
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500


C5'-epi-Tunicamycin-V
8
6
4
2
0
PPM
84.40
%T
78.04
4000
3500
3000
2500
2000
1500
1000
cm⁻¹
500

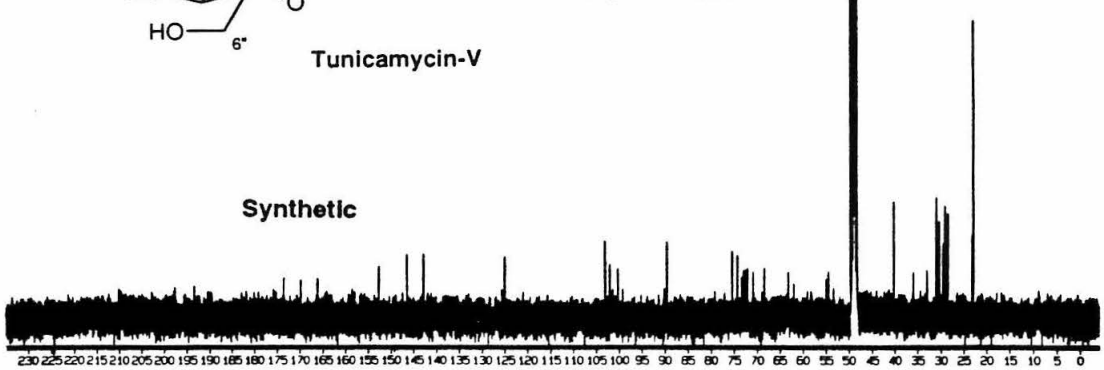

Tunicamycin-V
Synthetic


Authentic

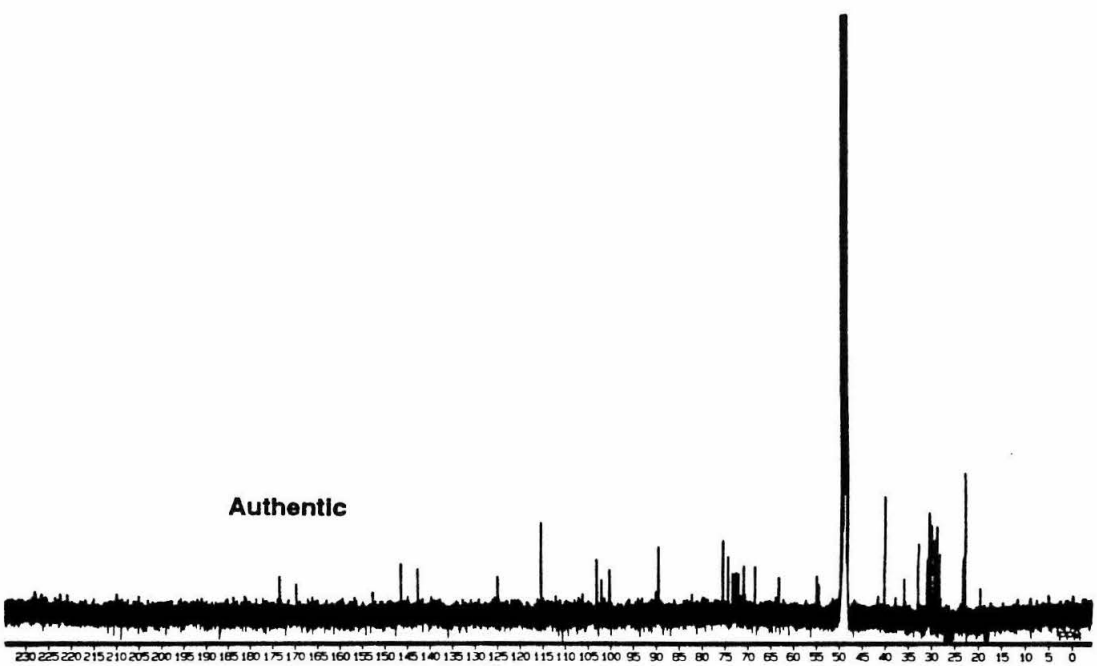


Tunicamycin-V

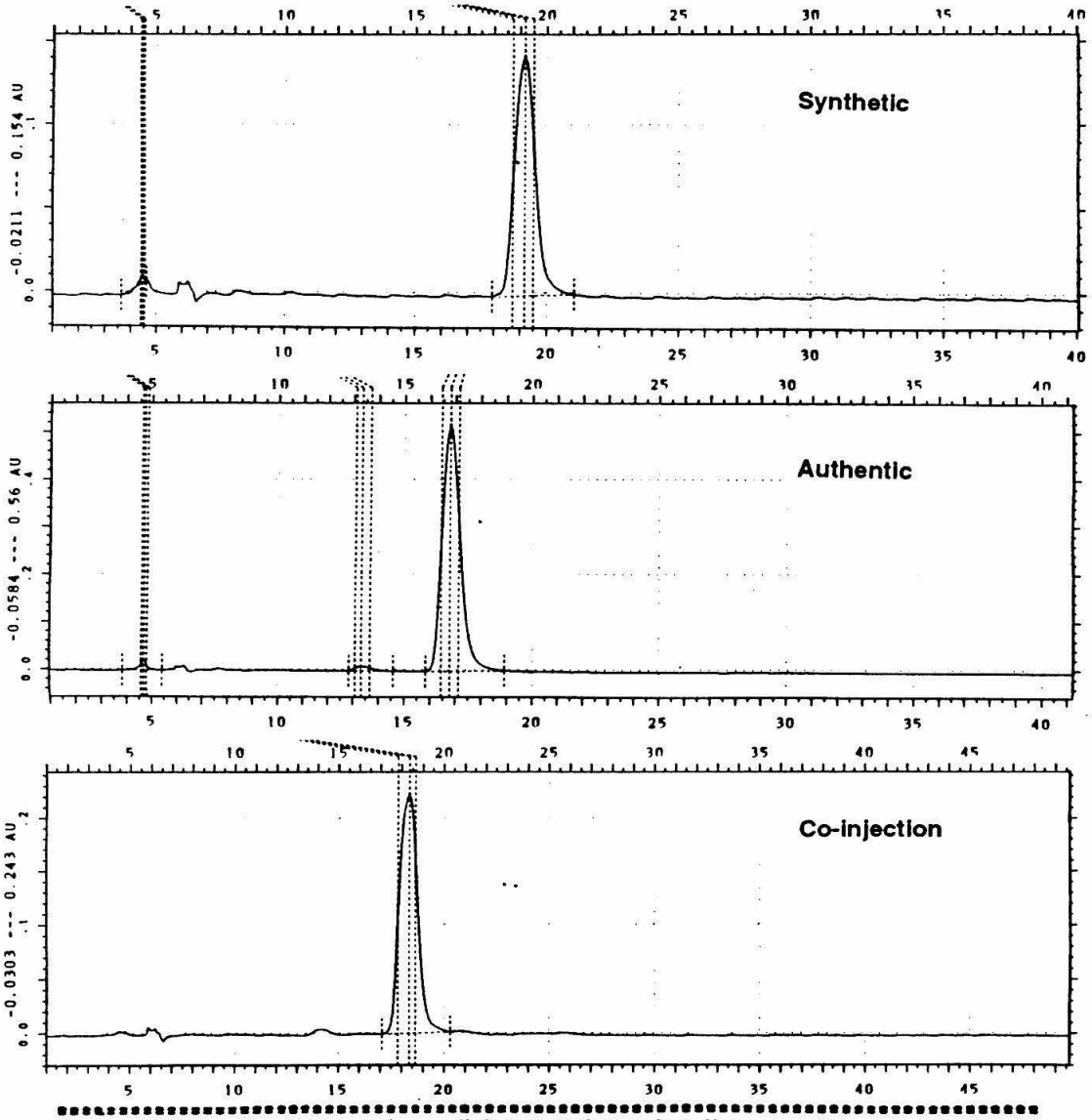
Synthetic



Authentic



Tunicamycin-V



Waters 994	< M U L T I - C H R O M A T O G R A M >		Stop at 49.65 min
Date	: Oct/16/92 13:18:27	FILE NAME	: TEST1
Time range	: 1.00 --- 40.00 min		
Baseline correct	: OFF	Paper speed	: 7.0 mm/min
Interval	: NORMAL	Scale M1	: AUTO SCALE
		M2	: AUTO SCALE
Sample name	: T-V CO-INJECT	Packing material	: BECKMAN ODS
Column	: 4.5mmID× 25.0cm	Mobile phase	: 85/15 CH3OH/H2O
Flow rate	: 0.40 ml/min	Pressure	: 1500.0 PSI
Temperature	: 25.0 °C	Injection volume	: 50 µl
Flow cell	: 10.00 mm		

Tunicamycin-V