Synlett D. Wiegmann et al. Letter

Thieme Chemistry Journals Awardees – Where Are They Now? Ribosylation of an Acid-Labile Glycosyl Acceptor as a Potential Key Step for the Synthesis of Nucleoside Antibiotics

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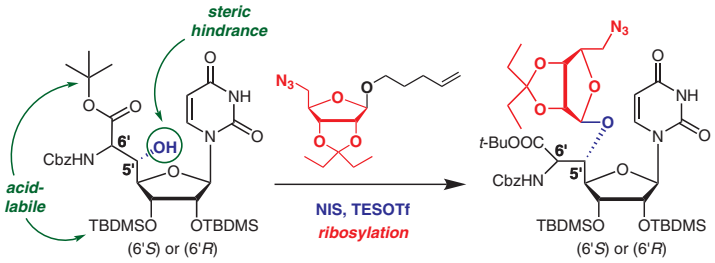
Dedicated to Professor Joachim Thiem on the occasion of his birthday.



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Abstract Naturally occurring nucleoside antibiotics (e.g., muraymycins and caprazamycins) represent attractive lead structures for the development of urgently needed novel antibacterial agents. One major challenge in the total synthesis of muraymycins, caprazamycins, and their analogues is the efficient construction of the densely functionalized aminoribosylated uridine-derived core unit. In order to avoid tedious protecting-group manipulations, we have aimed to conduct the aminoribosylation step with an acid-labile glycosyl acceptor. Therefore, different glycosylation approaches have been studied, with pentenyl glycosides giving the best results.

Key words natural products, antibiotics, nucleosides, glycosylation, ribosylation, pentenyl glycosides

Spreading resistances of bacteria against a variety of clinically used antibiotics cause an urgent need for new antibacterial drugs.[1] In order to avoid the formation of cross resistances, these substances should address new targets and display novel modes of action. Since there is no equivalent biochemical process in eukaryotic cells, bacterial cell wall biosynthesis furnishes valuable drug targets for antibacterial agents, with multiple established antibiotics inhibiting the late extracellular steps of peptidoglycan formation.[2] However, the early intracellular steps of this biosynthetic pathway are only scarcely targeted by drugs.[2] The transmembrane enzyme MraY represents such an emerging intracellular drug target.[3] MraY catalyzes the transfer of the peptidoglycan precursor UDP-Mur*N*Ac-pentapeptide ('Park's nucleotide') to the membrane-bound undecaprenyl phosphate lipid carrier on the cytosolic side of the bacterial membrane (not displayed).[4] The formation of the resultant biosynthetic intermediate 'lipid I' is inhibited by nucleoside antibiotics, i.e., a class of uridine-derived natural products functioning as MraY inhibitors.[5] We are particularly inter-

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ested in the muraymycin[6] and caprazamycin[7] subclasses of naturally occurring nucleoside antibiotics, which share an identical aminoribosylated glycyluridine (GlyU)[8] core motif (Figure 1).

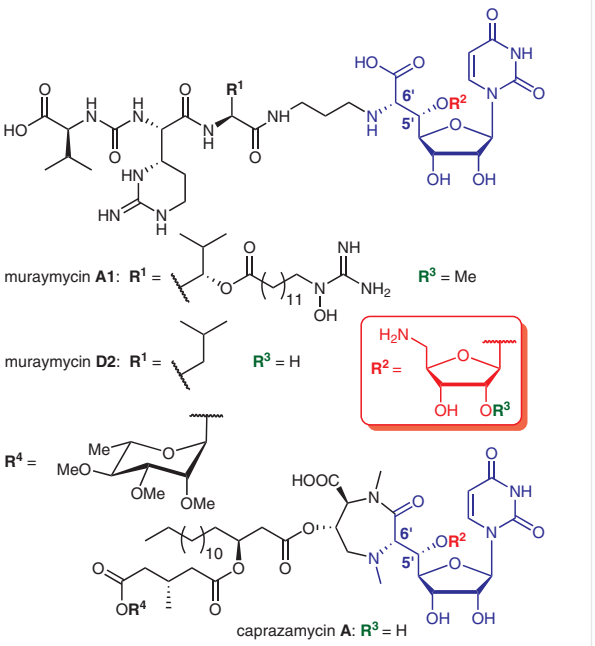
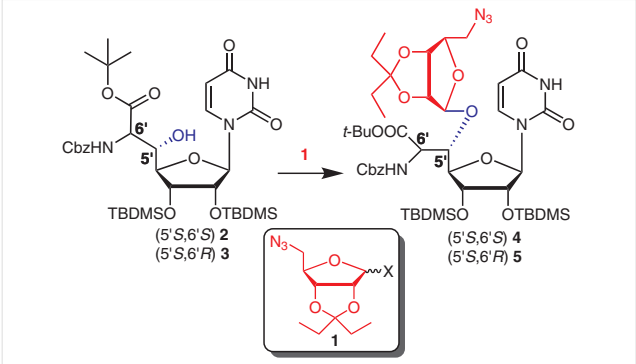


Figure 1 Selected naturally occurring muraymycin and caprazamycin antibiotics (blue: GlyU unit; red: aminoribosyl moiety)

Initial structure–activity relationship (SAR) studies of muraymycins[9] and caprazamycins[10] have already been performed. For such investigations, efficient synthetic access to the complex target structures is indispensable. Hence, different synthetic strategies towards muraymycin[5c,9c,11] and caprazamycin[12] nucleoside antibiotics have been developed. Most of these total syntheses employed acid-labile protecting groups, which were then cleaved in a final global acidic deprotection step.

Particular attention has been given to the preparation of the β-configured aminoribosylated GlyU core structure.[11b,c,12a,13] Establishing the aminoribosylation of GlyU with high β-selectivity is challenging as the overall protecting-group strategy precluded the use of neighboring-group participation. Ichikawa, Matsuda, and coworkers provided an approach using ribosyl fluoride donors which were sterically shielded on the α-face.[13a] However, such ribosylation reactions require rather harsh Lewis acidic conditions which are incompatible, e.g., with the presence of *tert*-butyl esters in the glycosyl acceptor, thus requiring subsequent protecting-group manipulations in the total synthesis of muraymycins and their analogues.[9a,b,11a] Kurosu and coworkers established a different strategy involving a thioriboside donor and an uridine-derived propargyl alcohol acceptor, which was transformed into the GlyU core motif over several steps after the ribosylation reaction.[11c] However, their method furnished a product bearing the 2-*O*-methylated aminoribosyl unit (R^3 = Me in Figure 1) that is found in some naturally occurring muraymycins. Hence, it does not furnish the target structures of this work (*vide infra*). Furthermore, Kurosu's method requires protection of the uracil nucleobase and the use of toxic heavy metals in the transformations towards the GlyU core structure.

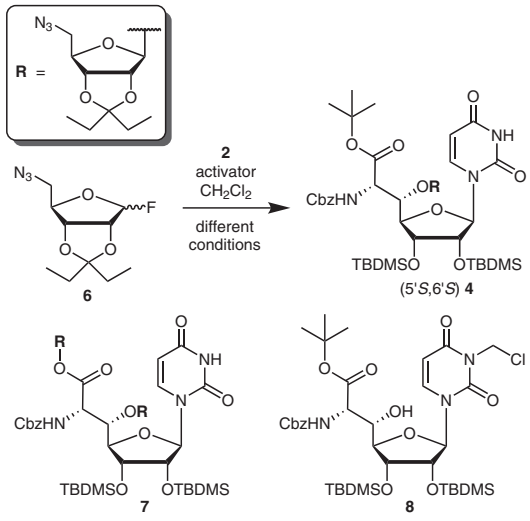
Our goal in this work was to establish a mild ribosylation methodology with glycosyl donors of type **1**, which should be compatible with glycosyl acceptors **2** and **3** containing acid-labile protecting groups (*tert*-butyl ester, TBDMS ethers, Scheme 1). This would then furnish ribosylated target structures **4** and **5**, which are protected derivatives of the native aminoribosylated (5′*S*,6′*S*)-GlyU core and its non-natural (6′*R*)-epimer, respectively. Such a mild ribosylation reaction will facilitate the total synthesis of muraymycins and their analogues, and it will also generally contribute to glycosylation methodology with acid-labile acceptor structures.



Scheme 1 Attempted ribosylation reaction of acid-labile glycosyl acceptors

Initially, we tested Ichikawa's and Matsuda's originally reported glycosyl fluoride donor **6**[13a] (α- and/or β-configured) in transformations with acceptor **2** (see below for its synthesis) under various conditions (Table 1). Formation of product **4** was generally only observed in negligible amounts at best, while byproducts **7** and **8** were obtained in varying ratios. Compound **7** apparently resulted from cleavage of the *tert*-butyl ester under the Lewis acidic conditions with subsequent ribosylation of the resultant carboxylic acid moiety. Compound **8** was obviously formed in a reaction of the nonribosylated acceptor with the solvent dichloromethane. The notable exception in this series of experiments was the transformation of **2** and α-**6** in the presence of AgOTf and Cp_2HfCl_2 at low temperatures, which afforded the desired product **4** in 25% yield (Table 1, entry 5). However, besides its rather moderate yield, this method suffered from limited reproducibility. Attempts to repeat the reaction with a similar outcome failed, although the quality of all reagents was checked carefully and the previously employed protocol was strictly followed.

Table 1 Initial Ribosylation Studies with Fluoride Donor **6** and Acid-Labile Acceptor **2**

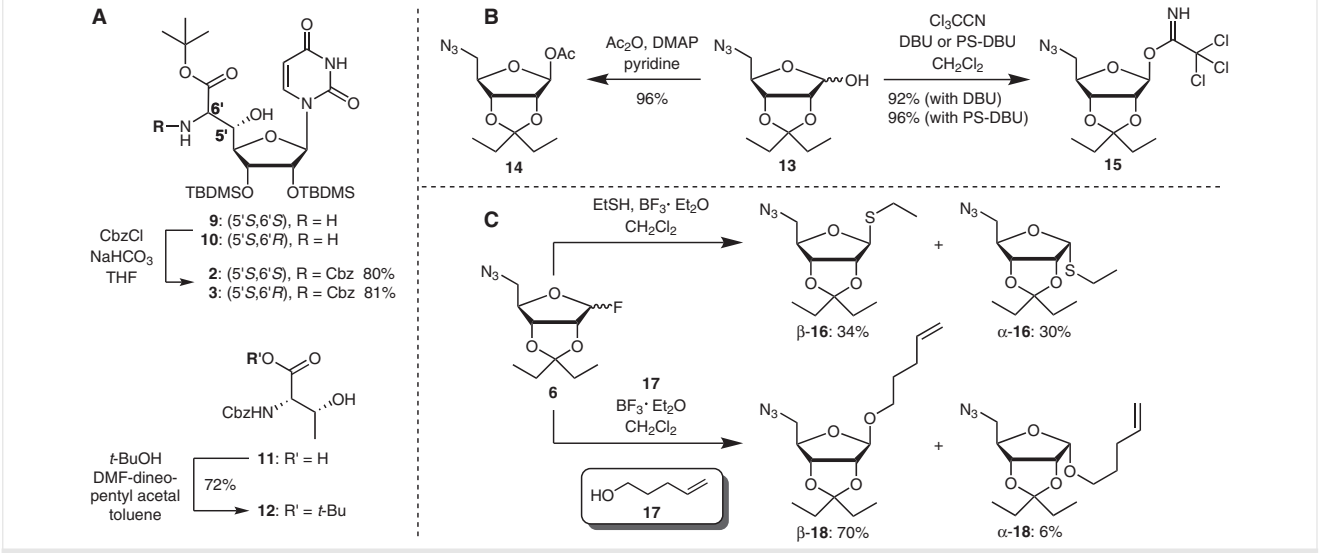


Entry	Donor	Activator	Conditions	Product(s)
1	α/β-**6**	$BF_3{\cdot}Et_2O$[a]	–45 °C to r.t., 9 h	**4** (traces)
2	β-**6**	$BF_3{\cdot}Et_2O$[a]	–24 °C to 0 °C, 3 d	**4** + **7**[b]
3	α-**6**	$BF_3{\cdot}Et_2O$[a]	0 °C, 3 h	decomposition
4	α-**6**	Bu_4NClO_4, CsF	r.t., 16 h	**8** (36%)
5	α-**6**	AgOTf, Cp_2HfCl_2	–45 °C to r.t., 9 h	**4** (25%)
6	α-**6**	AgOTf, Cp_2HfCl_2	r.t., 18 h	**4** + **7**[b]
7	β-**6**	AgOTf, Cp_2HfCl_2	r.t., 18 h	**4** + **7**[b]

[a] With addition of freshly activated molecular sieves (4 Å).
[b] Nonseparable mixture.

The aforementioned formation of bisribosylated by-product **7** with only limited amounts of desired **4** indicated that the transformations with glycosyl fluoride **6** suffered from the relatively harsh activation conditions. Therefore, it has been decided to investigate a range of alternative glycosyl donors with milder activators. Acceptor **2** had been obtained by standard Cbz protection of previously reported amine **9**[9c,11b] in 80% yield (Scheme 2, A). Furthermore, 6′-epimer **3** was also used as an alternative glycosyl acceptor additionally allowing for investigation of any potential influence of the stereochemistry in 6′-postion on the ribosylation reaction (see Scheme 1). Isomer **3** was be obtained from the previously reported readily accessible amine precursor **10**[14] in 81% yield (Scheme 2, A). The respective 6′-epimeric ribosylated product **5** will also be particularly relevant for further SAR studies on muraymycins and caprazamycins. As a structurally simplified model glycosyl acceptor, *tert*-butyl ester **12** was obtained from commercially available *N*-Cbz-threonine **11** using Eschenmoser's method[15] (72% yield, Scheme 2, A). Compound **12** represents a truncated analogue of acceptor **2** lacking the nucleoside moiety. Our general approach was to first identify a suitable ribosylation method using acceptor **12** in model reactions. The thus obtained most promising method was then envisioned to be applied on the transformation of **3** into **5**, and finally also on the transformation of **2** into ribosylated **4**. Compound **4** should then be used for the synthesis of an aminoribosylated GlyU building block.

Following the synthesis of glycosyl acceptors, a range of azidoribosyl donors were prepared. Protected 5′-azido-5′-deoxyribose **13**[13a] was acetylated to give **14** in 96% yield (Scheme 2, B), which was envisioned to serve as a precursor for Koenigs–Knorr glycosyl halides. The trichloroacetimidate donor **15** was also synthesized from hemiacetal **13** us-



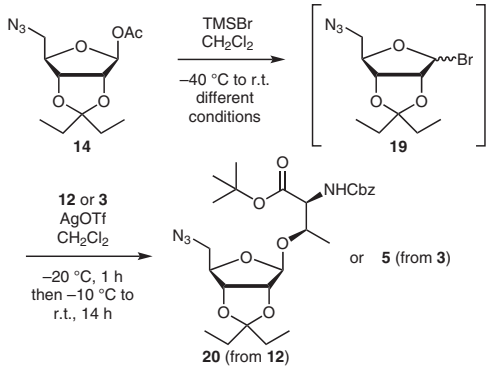
Scheme 2 Synthesis of glycosyl acceptors **2**, **3**, and **12** (A) as well as of glycosyl donors **14**–**16** and **18** (B, C) for studies on the ribosylation reaction

ing trichloroacetonitrile with either DBU[16] or polystyrene-supported DBU (PS-DBU)[17] as base (Scheme 2, B). With PS-DBU, no further purification was necessary, but yields were high with both forms of DBU (92% and 96%, respectively). Thioglycoside **16** was obtained from ribosyl fluoride **6** using BF_3-Et_2O as activator, with anomers chromatographically separated to afford β-**16** in 34% yield and α-**16** in 30% yield (Scheme 2, C). Finally, the reaction of **6** with 4-pentene-1-ol **17** under similar conditions furnished *n*-pentenyl glycoside **18** in anomerically pure form after separation (β-**18**: 70% yield, α-**18**: 6% yield, Scheme 2, C). The anomeric purity of the glycosyl donors was not considered to have significant impact on the reaction outcome as the ribosylation reactions were expected to largely proceed via an S_N1-type mechanism. For all donors, the respective β-product was favored due to the steric shielding of the α-face resulting from the bulky isopentylidene protecting group.[13a]

In the next set of experiments, we aimed to implement a modified version of the Koenigs–Knorr ribosylation method reported by Gravier–Pelletier et al.[18] The ribosyl bromide **19** was freshly generated from **14** and then directly reacted with acceptors **12** or **3**, respectively, in a one-pot manner (Table 2). The conversion of the acetylated precursor **14** into **19** was accomplished using trimethylsilyl bromide (TMSBr), and the subsequent activation of resultant bromide **19** was achieved with silver(I) triflate (AgOTf). Under different reaction conditions, only limited amounts of the desired products **20** (from **12**) or **5** (from **3**), respectively, were obtained (Table 2). In several cases, the products still contained major amounts of the unreacted precursor **14**. Therefore, we concluded that the transformation into bromide **19** was problematic, and that the ribosylation of the sterically hindered alcohols probably proceeded slowly. Hence, this method was discarded.

The next glycosylation approach to be studied was Schmidt's trichloroacetimidate method, for which some precedent with furanose donors exists.[19] Again, threonine-derived model compound **12** and the protected GlyU epimer **3** were used as acceptors. Glycosyl donor **15** was mildly activated with catalytic amounts of trimethylsilyl triflate (TMSOTf) under different reaction conditions (Table 3). This method gave encouraging initial results for the transformation of **12** into **20** (Table 3, entries 1 and 2), and it also furnished the ribosylated protected GlyU epimer **5** (from **3**) in 44% yield (69% brsm, Table 3, entry 3). Remarkably, all attempts to reproduce the latter synthesis of **5** failed, when the reaction was performed again under identical conditions. Portionwise addition of the donor was presumed to avoid unwanted side reactions, but according further variations of the reaction protocol were not successful either (Table 3, entries 4–6). It was therefore concluded that this method also did not furnish robust and reproducible results.

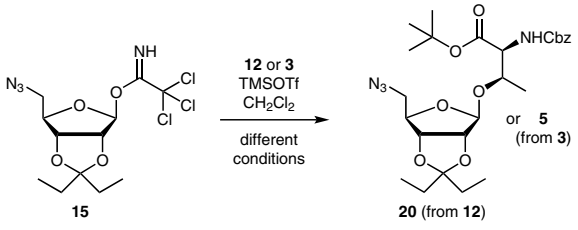
Table 2 Ribosylation Studies Using Koenigs–Knorr Glycosylation



Entry	Acceptor	TMSBr/activation[a]	**14**[b]	Product(s) (yield)
1	**12**	1 × 4 equiv (2 h), 2 × 8 equiv (2 h each)	0.77 equiv	**20**/**14** 1.0:2.5 (14% **20** calcd)[c]
2	**12**	1 × 4 equiv (2 h), 3 × 8 equiv (2 h each)	1.25 equiv	**20**/**14** 1.0:1.2 (23% **20** calcd)[c]
3	**12**	1 × 4 equiv (2 h), 4 × 8 equiv (2/2/12/2 h)	1.25 equiv	**20** (14%)
4	**12**	5 × 8 equiv (1 h each)	1.25 equiv	**20**/**14** 1.0:3.0 (12% **20** calcd)[c]
5	**3**	1 × 4 equiv (2 h), 3 × 8 equiv (2 h each)	4.2 equiv	**5** (13%)

[a] Activation step (**14** to **19**): equivalents of TMSBr (added portionwise) with respect to precursor **14** as well as (in parentheses) subsequent reaction time(s) after each addition of TMSBr.
[b] Glycosylation step (**19** to **20** or **5**): equivalents of precursor **14** with respect to the acceptor **12** or **3**.
[c] Yield calculated from the NMR spectra of the product mixture.

Table 3 Ribosylation Studies Using Schmidt's Tricholoracetimidate Method



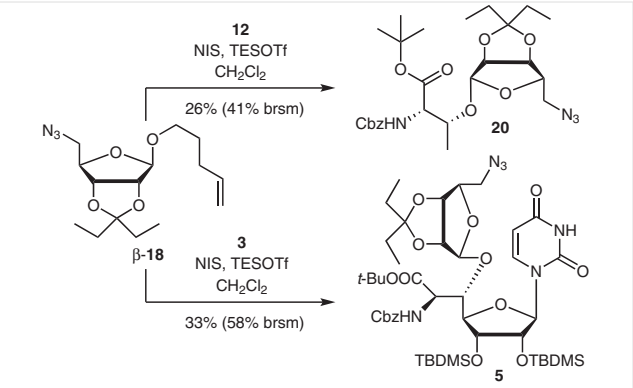
Entry	Acceptor	**15**	TMSOTf	Conditions	Product(s) (yield)
1	**12**	1.0 equiv	2 × 0.05 equiv[a]	0 °C to r.t., 2 h	**20** (44%)
2	**12**	2.0 equiv	0.06 equiv	0 °C, 30 min	**20** (72%), α-**20** (5%)
3	**3**	2.3 equiv	2 × 0.07 equiv[a]	0 °C, 1.5 h	**5** (44%, 69% brsm), α-**5** (<15%)
4	**3**	2.1 equiv	4 × 0.06 equiv[a]	–10 °C, 4 h	rsm **3** (34%), decomposition

Entry	Acceptor	15	TMSOTf	Conditions	Product(s) (yield)
5	**3**	5.6 equiv	4 × 0.17 equiv[a]	–10 °C to 35 °C, 31 h	**5** (traces), decomposition
6	**3**	4.0 equiv	2 × 0.2 equiv[a]	0 °C, 1.5 h	decomposition

[a] TMSOTf added portionwise (n × the listed equivalents).

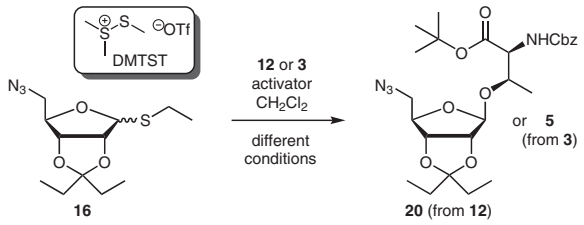
We then explored ribosylation reactions with the thioglycoside **16** as donor.[20] In general, thioglycosides can serve as stable glycosyl donors with different pathways to activate them for glycosyl transfer. A very mild activation method is the treatment with dimethyl(methylthio)-sulfonium triflate (DMTST)[21a] (Table 4, entries 1–8).[21b] Using the sterically less hindered threonine-derived model acceptor **12**, the product **20** was obtained in yields up to 36% (60% brsm, entry 2). However, all attempts to apply this method to the protected GlyU epimer **3** as acceptor gave the respective product **5** only in very low yields (ca. 5%, Table 4, entries 4–8). Thus, activation with Cu(II) bromide and tetrabutylammonium bromide was studied as an even milder option (Table 4, entries 9–11).[22] However, this method turned out to be too mild for the secondary acceptor alcohols **12** and **3**, respectively. The starting materials were either re-isolated or decomposed at elevated temperatures, which were applied in order to force the reactions to proceed. In principle, the unwanted glycosylation of the uracil ring might be a competing side reaction in the ribosylation of acceptor **3**. Zhang and Knapp have recently reported an indium(III) triflate promoted glycosylation of uridine derivatives with thioglycoside donors, which overcame this hurdle.[23] We have applied identical conditions to the attempted ribosylation of **3**, but poor conversion and decomposition products were observed (Table 4, entry 12).

Following the results using the thioglycoside approach, Fraser–Reid's *n*-pentenyl glycoside method was studied next.[24] Thus, pentenyl glycoside β-**18** was mildly activated with *N*-iodosuccinimide (NIS) and catalytic amounts of triethylsilyl triflate (TESOTf) to enable the ribosylation reaction. Conversions were observed both with the threonine-derived model acceptor **12** as well as with the 6′-*epi*-GlyU acceptor **3**



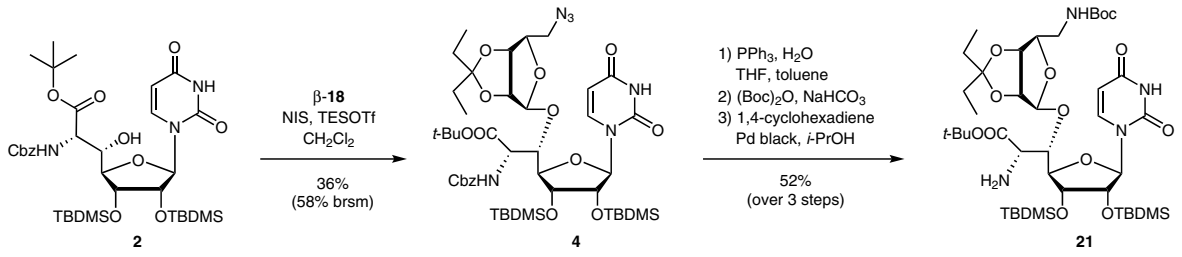
Scheme 3 Ribosylation with *n*-pentenyl glycoside **18**

Table 4 Ribosylation Studies Using Thioglycoside Donor **16**



Entry	Acceptor	16	Activator	Conditions	Product(s) (yield)
1	**12**	1.25 equiv	5.0 equiv DMTST	–15 °C, 4 h, then r.t., 1 h	decomposition
2	**12**	1.4 equiv	5.7 equiv DMTST	–15 °C, 3.5 h, then 10 °C, 1.5 h	**20** (36%, 60% brsm), α-**20** (traces)
3	**12**	2.0 equiv	2.7 equiv DMTST	–15 °C, 2 h	**20** (32%, 44% brsm)
4	**3**	2.5 equiv	3.75 equiv DMTST	–15 °C, 2 h, then 5 °C, 30 min	**5** (5%, 13% brsm)
5	**3**	2.8 equiv	3 × 2.8 equiv DMTST[a]	–15 °C, 2 h, then r.t., 1 h	decomposition
6	**3**	2.1 equiv	8 × 0.43 equiv DMTST[a]	–15 °C, 2 h, then 0 °C, 1.5 h	**5** (5%, 14% brsm)
7	**3**	2.4 equiv	3.6 equiv DMTST[b]	0 °C, 3 h	**5** (5%, 12% brsm)
8	**3**	2.2 equiv	6.7 equiv DMTST[b]	10 °C, 5 h	**5** (ca. 5%, impure)
9	**12**	1.2 equiv	3.4 equiv $CuBr_2$ + 3.2 equiv Bu_4NBr	r.t., 25 h	rsm **12** (96%)
10	**12**	2.0 equiv	3.4 equiv $CuBr_2$ + 3.2 equiv Bu_4NBr	r.t. to 150 °C, 4 d	decomposition
11	**3**	2.0 equiv	4.0 equiv $CuBr_2$ + 4.0 equiv Bu_4NBr	r.t. to 140 °C, 3 d	rsm **3** (66%)
12[c]	**3**	1.5 equiv	1.5 equiv $In(OTf)_3$ + 1.5 equiv NIS	0 °C to r.t., 14 h	rsm **3** (crude), decomposition

[a] DMTST added portionwise (n × the listed equivalents).
[b] DMTST added steadily over the reaction period.
[c] 1,2-Dichloroethane used as solvent.



Scheme 4 Synthesis of the aminoribosylated (5′*S*,6′*S*)-GlyU core structure **21** as a building block for the total synthesis of muraymycin antibiotics

(Scheme 3) to furnish products **20** and **5** in isolated yields of 26% and 33%, respectively. While these yields were moderate, the yields based on recovered acceptor starting material were acceptable (41% yield brsm for **20**, 58% yield brsm for **5**). Hence, this approach allowed for significant amounts of both acceptors to be recovered and then converted within a second transformation with glycosyl donor **18**.

Attempts to further improve the yields of these ribosylations with pentenyl glycoside **18** by optimization of the reaction conditions (temperature, time, protocol of addition) were not successful. However, in contrast to other methods (*vide supra*) the reaction could be repeated several times with identical results. Thus, the reliability and robustness of this method provide unquestionable advantages over all other ribosylation approaches studied within this work. The *n*-pentenyl glycoside strategy was therefore also applied for the corresponding transformation of protected (5′*S*,6′*S*)-GlyU **2**. The reaction worked as for the epimeric acceptor **3** and gave the desired azidoribosylated (5′*S*,6′*S*)-GlyU **4** in 36% isolated yield (58% brsm, Scheme 4).[25] Again, recovery of significant amounts of the acceptor allowed for its potential conversion within a subsequent second transformation with donor **18**. Product **4** was then subjected to a sequence consisting of Staudinger reduction of the azido group, Boc protection of the resultant amine, and subsequent Cbz hydrogenolysis to afford **21** in 52% yield over three steps. The aminoribosylated GlyU derivative **21** can serve as a valuable building block for the total synthesis of muraymycin antibiotics and their analogues, as it shows significant similarity to an according synthetic intermediate employed by Ichikawa and Matusda in their syntheses of muraymycins.[9a,b,11a] Furthermore, the successful use of silylated nonribosylated GlyU derivatives in the synthesis of muraymycin analogues has been demonstrated by us before.[9c,14]

In summary, we report a robust method for the challenging ribosylation reaction of protected uridine-derived nucleosyl amino acids. Glycosyl acceptors **2** and **3** were decorated with acid-labile protecting groups, in line with general synthetic strategies towards nucleoside antibiotics such as muraymycins. However, this protecting group pattern rules out harshly acidic glycosylation conditions. A comparative study including ribosyl fluoride, bromide, and trichloroacetimidate donors as well as thioglycosides and *n*-pentenyl glycosides revealed the latter to provide the best results in terms of both reproducibility and yield. These findings will aid to facilitate the total synthesis of muraymycin and caprazamycin nucleoside antibiotics and their analogues. Furthermore, they are also relevant in a more general context as precedent for glycosylation reactions with *n*-pentenyl furanosides is rather limited, including few examples of according arabinosylation reactions.[26] Our results therefore complement the toolbox for synthetic ribosylation reactions, in particular for densely functionalized, sterically hindered, acid-labile glycosyl acceptor moieties.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591517.

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(25) **Synthesis of Protected Ribosylated (5′*S*,6′*S*)-GlyU 4**

To a solution of the glycosyl donor β-**18** (20.1 mg, 64.5 µmol) and the (5′*S*,6′*S*)-GlyU-derived acceptor **2** (35.6 mg, 48.4 µmol) in CH_2Cl_2 (3 mL) with freshly activated molecular sieves (4 Å), NIS (18.9 mg, 83.9 µmol) was added at r.t. under exclusion of light. Over 10 min, TESOTf (5.8 µL, 26 µmol, 1% solution in CH_2Cl_2) was added dropwise. The reaction mixture was stirred at r.t. for 15 min before ice (5 g) was added and the mixture was allowed to warm to r.t. again. It was then diluted with CH_2Cl_2 (70 mL) and the organic layer was washed with 10% $Na_2S_2O_3$ solution (1 × 70 mL), sat. $NaHCO_3$ solution (1 × 70 mL), and brine (1 × 70 mL). The organic layer was dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The resultant crude product was purified by column chromatography (PE–EtOAc, 75:25 → 70:30) to give **4** (16.6 mg, 36%, 58% brsm) as a colorless solid; mp 72 °C. TLC: R_f = 0.28 (*i*-hexane–EtOAc, 7:3). $[\alpha]_D^{20}$ –7.0 (*c* 0.7, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.07 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$), 0.13 (s, 3 H, $SiCH_3$), 0.83 (t, *J* = 7.5 Hz, 3 H, 1^{iv}-H), 0.88 (t, *J* = 7.5 Hz, 3 H, 5^{iv}-H), 0.90 (s, 9 H, $SiC(CH_3)_3$), 0.90 (s, 9 H, $SiC(CH_3)_3$), 1.45 (s, 9 H, $OC(CH_3)_3$), 1.53 (q, *J* = 7.4 Hz, 2 H, 2^{iv}-H), 1.66 (dq, *J* = 7.4, 1.8 Hz, 2 H, 4^{iv}-H), 3.55 (dd, *J* = 13.0, 4.0 Hz, 1 H, 5‴-H_a), 3.72 (dd, *J* = 13.0, 3.9 Hz, 1 H, 5‴-H_b), 3.94 (dd, *J* = 5.7, 4.1 Hz, 1 H, 3′-H), 4.13 (dd, *J* = 5.7, 2.3 Hz, 1 H, 4′-H), 4.16 (dd, *J* = 4.1, 3.6 Hz, 1 H, 2′-H), 4.31–4.34 (m, 1 H, 4‴-H), 4.39 (dd, *J* = 2.3, 1.9 Hz, 1 H, 5′-H), 4.48 (d, *J* = 6.3 Hz, 1 H, 2‴-H), 4.51 (dd, *J* = 9.2, 1.9 Hz, 1 H, 6′-H), 4.64 (dd, *J* = 6.3, 1.4 Hz, 1 H, 3‴-H), 4.97 (d, *J* = 12.1 Hz, 1 H, 1″-H_a), 5.14 (s, 1 H, 1‴-H), 5.24 (d, *J* = 12.1 Hz, 1 H, 1″-H_b), 5.44 (d, *J* = 3.6 Hz, 1 H, 1′-H), 5.60 (dd, *J* = 8.2, 2.1 Hz, 1 H, 5-H), 6.15 (d, *J* = 9.2 Hz, 1 H, 6′-NH), 7.24–7.36 (m, 5 H, aryl-H), 7.82 (d, *J* = 8.2 Hz, 1 H, 6-H), 8.02 (d, *J* = 2.1 Hz, 1 H, 3-NH). ^{13}C NMR (126 MHz, $CDCl_3$): δ = –4.9, –4.8, –4.2, –3.9, 7.6, 8.5, 18.1, 18.2, 26.0, 26.0, 28.1, 28.9, 29.4, 53.5, 56.5, 67.0, 71.5, 74.8, 77.8, 81.8, 82.7, 85.3, 86.0, 86.4, 90.6, 101.1, 112.3, 117.9, 128.3, 128.4, 127.7, 136.8, 140.8, 149.9, 156.4, 162.9, 168.8. HRMS (ESI$^+$): *m/z* calcd for $C_{45}H_{73}N_6O_{13}Si_2$: 961.4769 [M + H]$^+$; found: 961.4778. IR (ATR): ν = 2930, 2857, 2104, 1685, 1457, 1253, 1160, 1059, 835, 775 cm^{-1}. UV (MeCN): λ_{max} = 261 nm.

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