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Regio- and Stereocontrolled Palladium-Catalyzed Allylic Substitution on *N*-Acetylneuraminic Acid Derivatives

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A process for highly effective regio- and stereoselective palladium-catalyzed allylic substitution of 2,3-unsaturated derivatives of *N*-acetylneuraminic acid (Neu5Ac2en) has been developed. We show that the efficiency of the allylation reaction depends on suitable protecting groups on the starting material and that, with sodium malonate anion as a nucleophile, the regioselectivity can be fine-tuned by the nature of the ligands associated with the palladium complex. These results are explained by the stoichiometric preparation and study of the highly probable complexes involved in the catalytic reaction. Reactions of this type were also applied to other nucleophiles for the construction of C–C, C–N, and C–O bonds, leading to the major formation of the C-4 regioisomers. The selective transformation of some of the substitution products provided easy access to a variety of modified sialic acid derivatives that might serve as useful sialyl building blocks for biological research.

Introduction

Palladium(0)-catalyzed allylic substitution is a powerful synthetic methodology that has attracted enormous interest because of its broad scope and versatility.[1] With soft nucleophiles, it provides a very efficient method for the construction of carbon–carbon or carbon–heteroatom bonds. One of the most interesting aspects of this type of chemistry is the potential to control the regio- and stereoselectivity in the allylic moiety. Both sterics and electronics play a role in determining the outcome of the reaction, and the regiochemistry of the nucleophilic attack can be affected by, among other factors, the nucleophile,[2] the nature of the ligand associated with the allylpalladium complex,[3] or the substituents in the substrate.[4] In our ongoing involvement in the synthesis of new sialic acid constructs[5] we have been interested in their preparation through Pd^0-catalyzed allylic substitution of 2,3-unsaturated *N*-acetylneuraminic acids.[6] Indeed, the development of efficient synthetic methods for the preparation of *N*-acetylneuraminic acid (Neu5Ac) conjugates and modified structures for biological research has been a major focus in carbohydrate chemistry, due to their central role in physiological processes and diseases.[7,8] This has led to intense research in sialic acid chemistry[9] including the design of potent chemotherapeutic agents against the influenza virus.[10] The 2,3-unsaturated *N*-acetylneuraminic acid **2** (5-acetamido-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enoic acid, Neu5Ac2en, Figure 1), a neuraminidase inhibitor,[11] has been a highly useful guide in this area as it has served as a structural platform for the discovery and development of two antiinfluenza drugs currently used to treat infected patients: Zanamivir (**3**, Relenza®) and Oseltamivir phosphate (**4**, Tamiflu®). They are both very potent inhibitors of the influenza neuraminidase, mimicking the putative high-energy oxycarbenium intermediate **1** (Figure 1) generated during the neuraminidase cleavage of the glycosidic bond.[10,12] Recent reports on the emergence of drug resistance[13] have, however, accentuated the

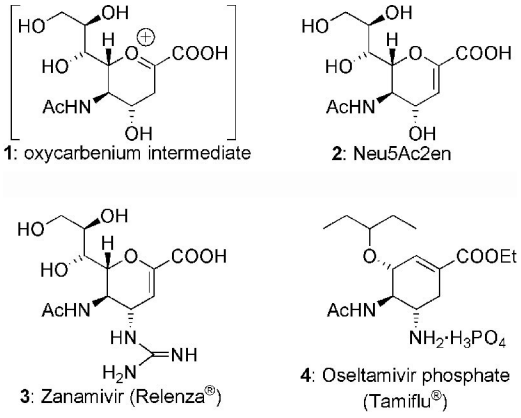

Figure 1. Potent neuraminidase inhibitors believed to mimick the putative high-energy oxycarbenium intermediate **1** during the neuraminidase cleavage of the α-sialyl glycosides.

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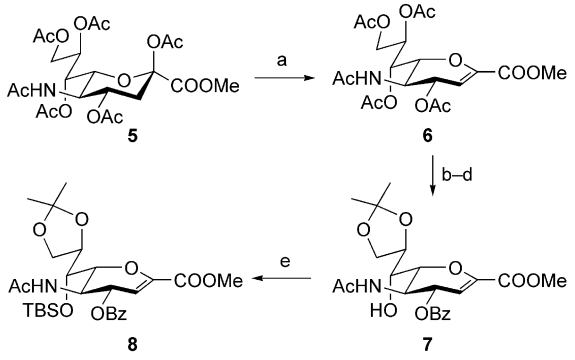
need for the development of additional antiinfluenza molecules through the use of rapid and efficient procedures to access new constructs based on the readily available Neu5Ac.[14] Furthermore, the design and synthesis of selective human neuraminidase inhibitors is also highly desirable.[15] In this article we wish to report in full the successful Pd-catalyzed selective modification of simple Neu5Ac2en derivatives at C-2 and C-4, which provides easy access to a variety of modified sialic acid derivatives.

Results and Discussion

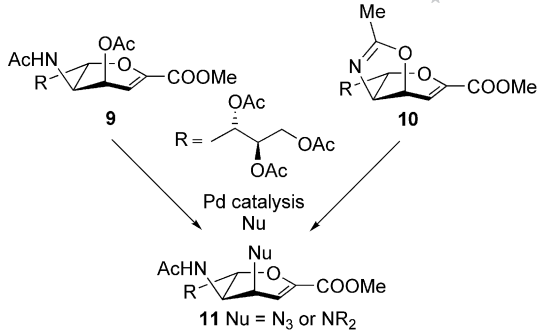
We started our investigation by studying the Pd^0-catalyzed allylic substitution of compound **6**, which was readily prepared from **5**[16] by treatment with TMSOTf in ethyl acetate (Scheme 1).



Scheme 1. Reagents and conditions for the preparation of Neu5Ac2en derivatives **7** and **8**. (a) TMSOTf, AcOEt, 0 °C to room temp. 4 h, 89%; (b) NaOMe, MeOH; (c) CSA, 2,2-dimethoxypropane, acetone; (d) BzCl, pyridine, CH_2Cl_2, 72% for the three steps; (e) TBSOTf, CH_2Cl_2, lutidine, room temp., 88%.

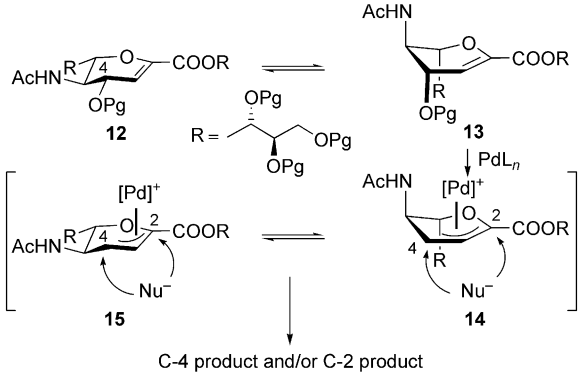
With dimethyl malonate sodium salt as a nucleophile, however, the acetate **6** failed to yield any alkylation product, as had also previously been reported for this substrate bearing an equatorial allylic substituent at C-4.[17] This chemistry was instead developed with the C-4 isomeric substrate **9** (Scheme 2), which underwent easy formation of a (π-allyl)-palladium complex thanks to its axially disposed leaving group,[18] thus providing the C-4 products with overall retention of configuration on treatment with azide ion (**11**; Nu = N_3).[17,19]

Similarly, the palladium-promoted allylic amination of the oxazoline **10** was also performed very recently[20] with simple amines (**11**; Nu = NR_2). We thought, however, that the half-chair conformational flexibility in glycals[21] and the electronic effects in substrates such as **12** might be modulated by a simple change in the protecting groups (Pg, Scheme 3).[22] This would facilitate the initial oxidative addition on the $^5H_6$ conformer **13**, with a pseudoaxial allylic substituent at C-4, to afford the (π-allyl)palladium complex **14**, possibly in equilibrium with the inverted half-chair complex **15**. Additionally, it was expected that the regioselectivity of the nucleophilic attack might be influenced by the



Scheme 2. Palladium-catalyzed allylic azidation or amination of the C-4 stereomer of Neu5Ac2en **9** and the oxazoline **10**.

nature of the nucleophile[2] as well as the ligands associated with the allylpalladium complex,[3] most likely then providing a selective route to the C-2 or the C-4 products.

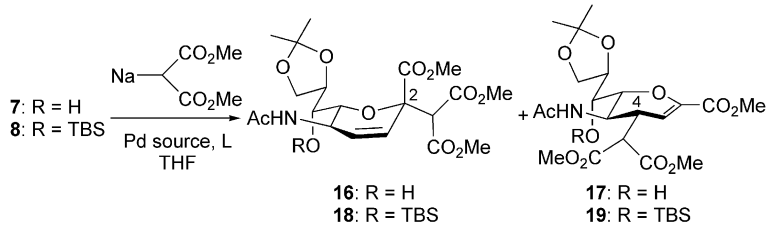


Scheme 3. Palladium-catalyzed substitution of 2,3-unsaturated sialic acid derivatives. Pg = protecting group; L = ligand.

For this purpose, we turned our attention to the allylic alkylation of compounds **7** and **8** (Scheme 1). The Neu5Ac2en derivative **7** was synthesized after Zemplén de-*O*-acetylation of **6** followed by 8,9-isopropylidenation[23] to furnish a diol, which was selectively benzoylated at the allylic position. Treatment of **7** with TBSOTf in the presence of lutidine in DCM led to the 7-*O*TBS derivative **8** in 88% yield.[24]

Compound **7** was then allowed to react with dimethyl malonate sodium salt in the presence of a catalytic amount of Pd^0 in THF. After several sets of conditions had been examined, it was found that the use of $Pd(OAc)_2$ (20 mol-%) in combination with PPh_3 (40 mol-%) gave the best results (Scheme 4). In this case the reaction was carried out at 50 °C and had led after 18 h to a mixture of regioisomeric compounds **16** and **17** in an 81:19 ratio and 66% yield. Different palladium sources {$Pd_2(dba)_3$·$CHCl_3$, [allylPdCl]$_2$, ...} associated with different ligands (PPh_3, PBu_3, dppb, ...) did not significantly improve the chemical yield and led stereoselectively to the C-2 adduct as the major regioisomer.

Synthetically much more useful results were obtained in the case of the palladium-catalyzed reaction between the benzoate **8** and dimethyl malonate sodium salt. Unexpectedly, a reversal in the regioselectivity as a function of the



Scheme 4. Allylic substitution of Neu5Ac2en derivatives **7** and **8** with dimethyl malonate sodium salt.

ligand used was observed. As can be seen in Table 1 (Entries 1–5), the C-4 adduct became the major regioisomer when the reaction was carried out in the presence of a monophosphane. Similar results were obtained with different palladium sources {$Pd(OAc)_2$, $PdCl_2(PhCN)_2$, [allylPdCl]$_2$}, but use of $Pd_2(dba)_3$·$CHCl_3$ was found to be preferable. In the presence of 10 mol-% of this catalyst associated to PPh_3 (20 mol-%), **18** and **19** were obtained in a 25:75 ratio and 98% yield at 50 °C in THF after 0.5 h (Entry 1). The best levels of selectivity were observed with PCy_3 (9:91; Entry 3) and PBu_3 (5:95; Entry 4), both of which gave alkylation products **18** and **19** in excellent yields. With PBu_3 the catalyst loading could be decreased to 5 mol-% (Entry 5), affording the desired **18** and **19** in 95% yield with a slight decrease in the regioselectivity (13:87). It is worth noting that with PPh_3, a 1:1 ratio of Pd/phosphane had to be used to preserve the regioselectivity (see Entries 1 and 2). This was not the case with PBu_3 or PCy_3, in which 1:2 ratios of Pd/phosphane were employed.

Table 1. Regio- and stereoselective allylic substitution of the 7-*O*-silylated Neu5Ac2en derivative **8** with dimethyl malonate sodium salt. dppb = 1,4-bis(diphenylphosphanyl)butane; dppe = 1,2-bis(diphenylphosphanyl)ethane; dppf = 1,1′-bis(diphenylphosphanyl)ferrocene.

Entry	Mol-% of catalyst,[a] ligand (equiv.)[b]	*t* [h]	Yield[c] [%]	**18/19**[d]
1	10, PPh_3 (1)	3	98	25:75
2	10, PPh_3 (2)	3	43	42:58
3	10, PCy_3 (2)	2	91	9:91
4	10, PBu_3 (2)	2	95	5:95
5	5, PBu_3 (2)	3	95	13:87
6	10, dppb (2)	2	84	>95:5
7	10, dppb (1)	2	91	53:47
8	10, none	2	66	47:53
9	5, dppb (4)	2	92	>95:5
10	2.5, dppb (4)	3	87	93:7
11	10, dppe (2)	2	88	>95:5
12	10, dppf (2)	3	94	>95:5

[a] The reaction was carried out at 50 °C with $Pd_2(dba)_3$·$CHCl_3$ and dimethyl malonate sodium salt (2 equiv.) in degassed solvent at a concentration of 0.08 M in THF. [b] Equivalents relative to the palladium catalyst. [c] Isolated yield after chromatography. [d] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture.

The regioselectivity was dramatically changed when the reaction was performed in the presence of diphosphanes (dppe, dppb, dppf; Entries 6 and 11–12). With these ligands, the more substituted C-2 adduct **18** was favored independently of the palladium source tested. As seen above with the monophosphanes, the best results in terms of yield and selectivity were obtained with $Pd_2(dba)_3$·$CHCl_3$, for which the catalyst loading could be decreased to 2.5 mol-%. Once again, the proportion of the ligand proved important, with at least 2 equiv. of the diphosphane dppb per 1 equiv. of Pd being needed to attain the maximum selectivity (more than 95:5; Entries 6 and 9). With only 1 equiv. of diphosphane per 1 equiv. of Pd, the reaction led to a 53:47 ratio of **18/19** (Entry 7), almost the same as that obtained with no ligand (Entry 8). The reaction was also performed in other solvents such as DCM, CH_3CN, or toluene with similar trends. With triphenylphosphane as ligand, the reaction was inefficient in toluene, but in DCM or CH_3CN led to the C-4 major alkylation product in good yields but with a slightly lower regioselectivity than in THF. With dppb, the C-2 adduct was also favored in DCM with a very good yield and selectivity.

The structures of **16**–**19** were assigned by ^{1}H NMR spectral analysis. For the compounds alkylated at C-4 – compounds **17** and **19** – the vicinal coupling constants observed for the hydrogen atom 5-H ($^3J_{5\text{-H},4\text{-H}} = {}^3J_{5\text{-H},6\text{-H}} = 10.0$ Hz) indicate a *trans* diaxial relationship between 5-H and 4-H. In addition, for compound **18**, the strong NOE effects observed between 4-H and both 6-H and the hydrogen atom of the acetamido group confirm this relative configuration. For the C-2-alkylated compound **16**, the NMR spectroscopic data also provided the relative configuration of the newly formed stereocenter. Moreover, this was also unambiguously assigned by X-ray diffraction (Figure 2). For compound **16**, the relative configuration at C-2 was further established by treatment with TBSOTf, leading to a silylated compound identical to **18**, according to its ^{1}H NMR spectrum.

Interestingly, the bicyclic derivative **20** (Scheme 5) was formed in high yield by treatment of **7** with a palladium catalyst without an external nucleophile. This indicated a probable transitory (π-allyl)palladium complex in geometry close to **20** and therefore to conformer **14** (Scheme 3). In the catalytic process, the Pd^0 complexes reacted with the carbon–carbon double bond in **7** to form a π-allyl species with inversion of configuration at the carbon atom bearing the leaving group.[25] The resulting (π-allyl)palladium(II) complex **14** could therefore be formed, leading to the C-4 allylic terminus being hindered by the bulky glycerol side

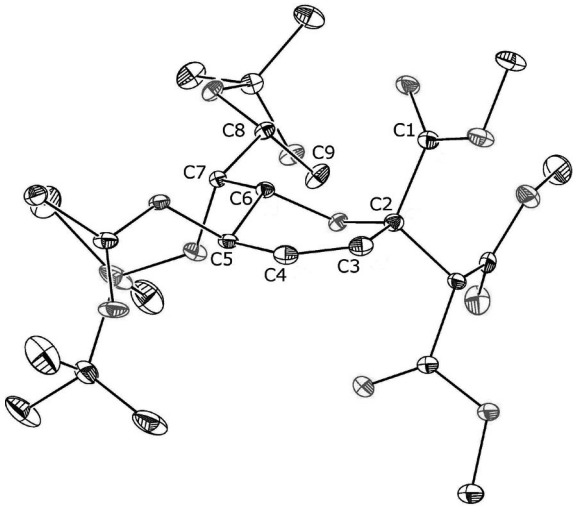
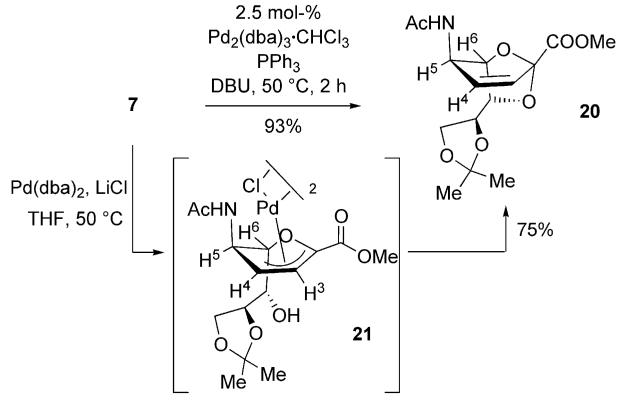


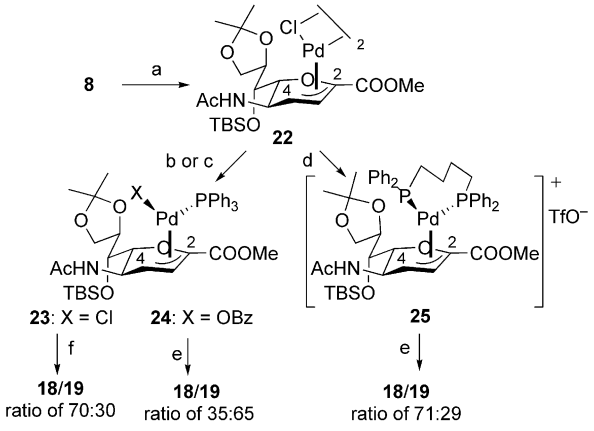
Figure 2. ORTEP drawing of **18**. Ellipsoids are drawn at the 50% probability level. The hydrogen atoms are omitted for the sake of clarity.

chain, which might explain the formation of the C-2 adduct as the major regioisomer. In order to verify this hypothesis, the isolation of the intermediate (π-allyl)palladium(II) complex **21** (Scheme 5) was attempted, with **7** being treated with a stoichiometric amount of $Pd(dba)_2$ in the presence of lithium chloride in THF at 50 °C. In this case, the expected chloro-bridged dimer **21** was not observed, and only the stable bicyclic compound **20** resulting from intramolecular alkylation at C-2 was isolated, in 75% yield. This result provides evidence in favor of an intermediate (π-allyl)palladium complex **14** and logically explains the selective formation of the C-2 adduct on steric grounds, with the bulky side chain at C-6 screening the C-4 attack of the incoming nucleophile.



Scheme 5. Formation of bicyclic acetal **20**.

For the alkylation of the 7-*O*TBS derivative **8**, the strong influence of the ligand/Pd molar ratio in affording good selectivity led us to believe that different (π-allyl)palladium species could be involved in the course of the reaction. Previous detailed mechanistic investigations had revealed that palladium(0)-catalyzed allylation of nucleophiles generally involves the intermediacy of cationic allylpalladium complexes, which were isolated and characterized by X-ray crystallography.[26] For our substrate with PPh_3, however, a Pd/phosphane ratio of 1:1 (or less phosphane) has to be respected to preserve selectivity at C-4. This led us to consider the intermediacy of a neutral complex with monophosphane ligands. In contrast, with diphosphanes, an excess of the ligand is recommended for a highly selective C-2 alkylation. For a better understanding of the variation of the regioselectivity according to the nature of the ligand in the allylic alkylation of **8**, we synthesized the differently defined complexes **23**, **24**, and **25** (Scheme 6).



Scheme 6. Preparation of the palladium complexes and their reaction with dimethyl malonate sodium salt. Reagents and conditions: (a) $Pd(dba)_2$, LiCl, THF, room temp., 72%; (b) PPh_3 (2 equiv.), $CDCl_3$; (c) PPh_3 (2 equiv.), $CDCl_3$ then AgOBz (2 equiv.); (d) dppb (3 equiv.), $CDCl_3$ then AgOTf (2.2 equiv.); (e) sodium malonate anion, THF, 50 °C; (f) sodium malonate anion, AgOTf, THF, 50 °C. dppb = 1,4-bis(diphenylphosphanyl)butane.

The chloro-bridged dimer **22** was first prepared by treatment of **8** with $Pd(dba)_2$ in the presence of LiCl in THF at room temp. for 4 h. This compound was stable enough to be purified on silica gel and was recrystallized from a mixture of pentane/ether (2:1) at –18 °C providing crystals suitable for X-ray analysis (Figure 3). Data were collected at 100 K because the crystal appeared to be unstable over extended periods of time, probably due to the presence of 1 equiv. of Et_2O associated with the dimer in the crystal structure. For this complex, we noticed a small distortion of the allyl–metal bonding in the (η^3-allyl)palladium complex, with the Pd(A)–C2(A) bond (2.162 Å) being longer than the Pd(A)–C4(A) bond (2.131 Å) by 0.03 Å.

The monomeric neutral complex **23** was then prepared from **22** by splitting the chloride bridge with PPh_3. After treatment with silver benzoate, **23** was transformed into **24**, whereas the cationic complex **25** was obtained after treatment of **22** with dppb and displacement of the chloride with silver triflate. Because of the moderate stabilities or difficulties in crystallization of the complexes, they were directly prepared in $CDCl_3$ solutions and completely characterized by ^1H, ^{13}C, and ^{31}P NMR spectroscopy, showing the formation of a single species for each complex. For complexes **23** and **24**, we were able to easily determine that the C-4 carbon atom of the allylic system was *trans* to the phosphane

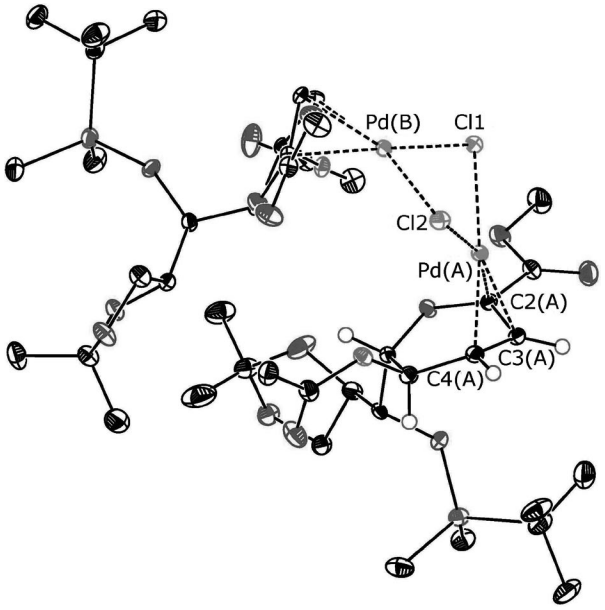


Figure 3. ORTEP drawing of complex **22**. Ellipsoids are drawn at the 50% probability level. The diethyl ether solvate molecule is omitted. The hydrogen atoms are omitted for the sake of clarity.

ligand, as shown by a shift of this carbon signal to a higher frequency and a larger $^2J_{P,C-4}$ coupling constant (Table 2).[3a,27] This could also be deduced from the ^{1}H NMR spectra of **23** and **24** through an important shift (about –0.7 ppm) of the methyl signal of the ester group to a lower frequency, probably because of its interaction with the phenyl groups of PPh_3. This was confirmed for **23** by the observation of a strong NOE between these two groups.

It was particularly interesting to compare the ^{13}C NMR shift values of the allylic terminal carbon atoms for **22**, **23**, and **24**. In **22** there is a large difference (41.9 ppm) between the shift values of C-2 (δ = 107.7 ppm) and C-4 (δ = 65.8 ppm) because of the inductive effect of the endocyclic oxygen atom. This difference tended to decrease in both **23** and **24**, for which very small differences in the shift values of the allylic terminal carbon atom were observed (2.1 ppm).

The two neutral complexes **23** and **24** were then engaged in the stoichiometric reaction with dimethyl malonate sodium salt as nucleophile in THF at 50 °C. Compound **23** failed to yield any alkylation product, probably because of an excessively high stability of the complex, whereas use of **24** led to a 35:65 mixture of **18**/**19**. The structure of **24** agrees well with the major formation of the C-4 adduct because it is generally accepted that the attack of an incoming nucleophile is favored at the carbon atom *trans* to the acceptor ligand.[28] With the cationic complex **25**, treatment with dimethyl malonate sodium salt in THF at 50 °C led as expected to the preferential formation of the C-2 alkylated compound (71:29 mixture of **18**/**19**). For this complex we noticed a shift of the C-2 carbon signal to a higher frequency, suggesting an increased olefin character at this position. This implies weaker allyl bonding to the Pd atom, leading to a longer Pd–C2 bond, which is preferentially attacked by the malonate anion.[29] The desymmetrization of the π-allyl system could be the result of a steric effect induced by the diphosphane ligand. However, it is noteworthy that treatment of **23** with dimethyl malonate sodium salt in THF at 50 °C in the presence of silver triflate produced a cationic species that also led to the major formation of the C-2 alkylated adduct (70:30 mixture of **18**/**19**).

A set of different nucleophiles was also surveyed in the allylic substitution of **8**. As above, we were able to control the regioselectivity of the nucleophilic attack of the anion of benzyl methyl malonate on the allylic system according to the ligand. Indeed, with PBu_3 or dppb as ligands, we could obtain the C-4 adduct **29** or the C-2 adduct **28** selectively in 75 and 80% yields, respectively, as mixtures of the diastereomers (Table 3, Entries 1 and 2). However, with the other tested nucleophiles, the reaction led to the C-4 adduct as the major regioisomer, whatever the ligand used. Various conditions for each nucleophile were tested, and the best are reported in Table 3.

With the sterically hindered sodium anion of bis(phenylsulfonyl)methane a higher temperature (80 °C) was required in order to speed up the reaction, and compound **30** was obtained after purification in a moderate 46% yield (Entry 3). In this case the steric factors dominate in the preferential formation of the alkylated compound at the less hindered position of the system, as previously noted by Trost and Verhoeven in the catalytic reaction of the allylic acetates.[2a,30]

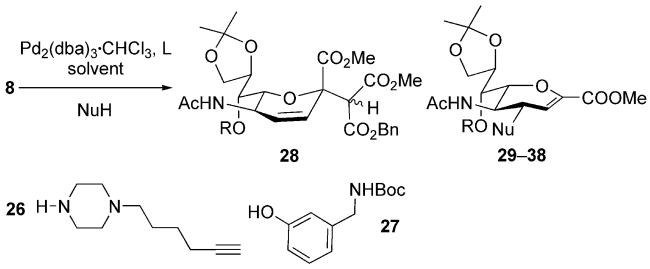
We then turned our attention to the azidation of the allylic moiety (Entry 4). With sodium azide, the best conditions were obtained with Pd^0 in combination with dppb in the presence of tetrabutylammonium bromide in a THF/water (4:1) mixture at 60 °C. A longer reaction time resulted in a poorer yield, so the reaction was stopped after 8 h and afforded the C-4 adduct **31** in a 65% yield. The formation of this regioisomer was expected because a [3,3]-sigmatropic rearrangement of the 2-azido-3,4-didehydrosialic acid intermediate to the corresponding 4-azido isomer had been reported.[17,31]

Table 2. Selected NMR spectroscopic data for the complexes **22**–**25**.

Entry	Complex	Selected ^{13}C NMR data, J [Hz]	$\Delta\delta(^{13}C)$ [ppm][a]	^{31}P NMR
1	**22**	107.7 (C-2), 88.4 (C-3), 65.8 (C-4)	41.9	–
2	**23**	105.9 (C-2), 95.0 (C-3), 86.0 (C-4); $^2J_{P,C-2}$ = 5, $^2J_{P,C-4}$ = 42	19.9	22.3 (s)
3	**24**	96.2 (C-2), 95.4 (C-3), 94.1 (C-4); $^2J_{P,C-2}$ = 5, $^2J_{P,C-4}$ = 28	2.1	25.9 (s)
4	**25**	120.3 (C2), 94.9 (C3), 78.9 (C4)	41.4	25.8 (d, J = 61.5), 11.6 (d, J = 61.5)

[a] Difference between the δ values of C-2 and C-4.

Table 3. Conditions for the regioselective allylic substitution of **8** with various nucleophiles.

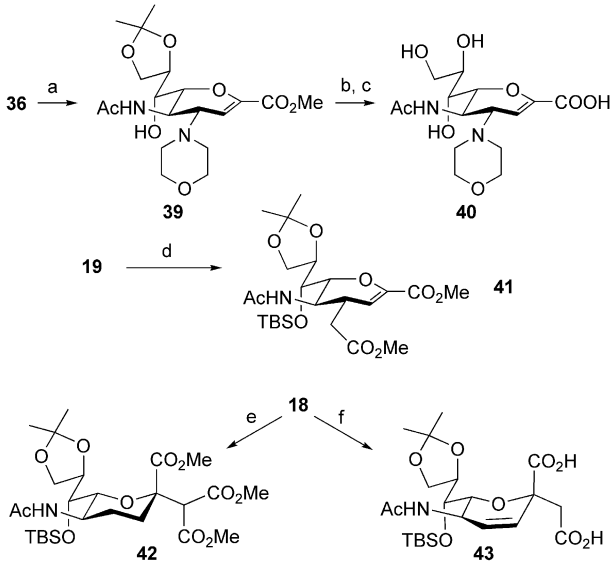


Entry	Nucleophile[a]	Solvent	*T* [°C]	*t* [h]	Ligand (equiv.)[b]	Additive (equiv.)[c]	Product, yield [%][d]
1	$NaCH(CO_2Me)(CO_2Bn)$[e]	THF	60	2	dppb (2)	–	**28**, 75
2	$NaCH(CO_2Me)(CO_2Bn)$[e]	THF	60	18	PBu_3 (1)	–	**29**, 80
3	$NaCH(SO_2Ph)_2$	THF	80	15	PBu_3 (1)	–	**30**, 46
4	NaN_3	THF/water[f]	60	8	dppb (1)	Bu_4NBr (0.1)	**31**, 65
5	aniline	CH_2Cl_2	60	15	dppb (2)	Et_3N (7)	**32**, 74
6	benzylamine	CH_2Cl_2	60	15	dppb (2)	Et_3N (7)	**33**, 89
7	*N*-methylbenzylamine	CH_2Cl_2	80	15	dppb (2)	Et_3N (5)	**34**, 83
8	**26**	CH_2Cl_2	80	15	dppb (2)	Et_3N (7)	**35**, 63
9	morpholine	CH_2Cl_2	80	15	dppb (2)	Et_3N (2.5)	**36**, 93
10	phenol	CH_2Cl_2	80	15	dppb (2)	Cs_2CO_3 (2)	**37**, 88
11	3-cyanophenol	CH_2Cl_2	70	8	dppb (2)	Cs_2CO_3 (2)	**38**, 61
12	**27**	CH_2Cl_2	70	4	dppb (2)	Cs_2CO_3 (2)	**39**, 73

[a] The reactions were carried out in a degassed solvent at a concentration of 0.07 M with $Pd_2(dba)_3$·$CHCl_3$ (20 mol-%) and the nucleophile (3 equiv.), until TLC showed conversion of the starting material. [b] Equivalents relative to the palladium catalyst. [c] Equivalents relative to the substrate. [d] Isolated yield after chromatography. [e] The reactions were carried out with $Pd_2(dba)_3$·$CHCl_3$ (10 mol-%) and the nucleophile (2 equiv.). [f] As a 4:1 mixture.

The formation of allylamines with primary or secondary amines was investigated (Entries 5–9). The reactions were best performed with palladium(0) associated with dppb in DCM in the presence of NEt_3. In contrast with the selectivity obtained in the case of the malonate anion with diphosphane ligands, the reactions led to the compounds alkylated at C-4 in good yields (63–90%). The reactions were also performed with phenol derivatives as nucleophiles (Entries 10–12) and also led, with dppb, to the C-4 adducts as the major isomers in 61–88% yields. A possible explanation for the reversed selectivity observed in these reactions is the change in the "hard/soft" character of the nucleophile. Because (π-allyl)palladium species are relatively soft, the change from a softer malonate carbanion to a hard phenoxide or amine nucleophile could result in different regioselectivities. In the amine case, however, one cannot exclude a palladium-catalyzed isomerization process of the more substituted kinetic product to the less substituted thermodynamic adduct, as has already been described.[32]

The possibility of further transformations was also briefly investigated with selected derivatives. Straightforward deprotection of these derivatives is shown with the morpholine derivative **36**. Desilylation afforded the alcohol **39** (Scheme 7; 90% yield) which was saponified and completely deprotected to afford the triol **40**. A variety of transformations with the malonyl derivatives were also possible. Hydrogenation of the C–C double bond in the unsaturated derivative **19** provided the corresponding 4-deoxy-*C*-glycosyl analogue **42** (Scheme 7).



Scheme 7. Selective transformations of the allylic substitution products. Reagents and conditions: (a) TBAF, THF, room temp., 2 h, 90%; (b) aq. NaOH, MeOH, room temp., 19 h; (c) AcOH (80%), room temp., 36 h, 91% for the two steps; (d) DMSO, H_2O, NaCl, 150 °C, 3 h, 62%; (e) Pd/C (10%), H_2, AcOEt, room temp., 24 h, 86%; (f) aq. NaOH, MeOH, 140 °C, 3 h, 74%.

In addition, decarboxylation[33] of the methyl malonates **18** and **19** opened an efficient route to C-2- and C-4-branched modified sialoacetic acids. Deethoxycarbonylation of the malonate **19** under Krapcho conditions gave

the fully protected diester **41**, whereas aqueous conditions provided the diacid **43** (Scheme 7). These derivatives represent suitable precursors for the elaboration of sialo clusters useful for biological studies.

Conclusion

We have developed a technique for stereo- and regioselective allylic substitution on simple Neu5Ac2en derivatives with high efficiency, based on suitable protecting groups in the starting material. In the malonylation reaction, the regioselectivity is controlled by the ligands (monodentate or bidentate) associated with the palladium complex, leading selectively to the C-4 or the C-2 adducts. This behavior was attributed to the formation of different (π-allyl)palladium species in the course of the reaction (i.e., neutral complexes in the case of monophosphane ligands and cationic complexes with diphosphanes). The reaction was also applied to other nucleophiles for the construction of C–C, C–N, and C–O bonds and led to the major formation of the C-4 regioisomers. Selective transformations of these products provided an easy route to a variety of modified sialic acid derivatives, which can serve as sialyl building blocks for the preparation of useful constructs in biological applications.

Experimental Section

General: Unless otherwise stated, all reactions were carried out under argon. THF and DCM were purified with the aid of a PureSolv solvent purification system (Innovative Technology Inc.). Reactions were monitored by analytical thin-layer chromatography (TLC) on silica gel plates (60 F_{254}) with visualization under UV (254 nm) and/or by staining with $KMnO_4$. Silica gel (SDS 60 ACC 35–70 mm) was used for column chromatography. NMR spectra were recorded with Bruker AM 300, AVANCE 300, and AVANCE 500 spectrometers. Chemical shifts are given in parts per million, referenced to the solvent peaks of $CDCl_3$, defined at δ = 77.0 (^{13}C NMR) and 7.26 ppm (^1H NMR). Melting points (uncorrected) were determined with the aid of a Büchi B-540 apparatus. IR spectra were recorded with a Perkin–Elmer Spectrum BX instrument with an FT-IR system. Optical rotations were measured with a JASCO-810 polarimeter in a cell of 1 dm pathlength.

Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-2,6-anhydro-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-enoate (6): TMSOTf (2.68 mL, 14.82 mmol) was added dropwise to a solution of **5**[16] (3.5 g, 6.67 mmol) in ethyl acetate (30 mL) at 0 °C over a period of 5 min. The solution was allowed to warm to room temperature and stirred for another 4 h. The reaction was monitored by TLC, quenched with Et_3N (5 mL) at 0 °C and water (50 mL), and then the mixture was extracted with ethyl acetate (2 × 30 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), and concentrated to obtain the crude product, which was purified by silica gel chromatography (DCM/MeOH, 97:3) to afford Neu5Ac2en (2.73 g, 5.84 mmol, 89%) as a white solid.

Methyl 5-Acetamido-2,6-anhydro-4-*O*-benzoyl-3,5-dideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (7): The Neu5Ac2en derivative **6** (5.9 g, 12.63 mmol) was dissolved in freshly distilled methanol (100 mL), and sodium (38 mg, 0.61 mmol) was added at room temperature. When the clear solution had turned cloudy (1 h), the reaction was complete. Dowex 50 (H^+) resin was added, and the reaction mixture was filtered and washed with hot methanol. The filtrates were concentrated in vacuo to give a white solid (3.85 g), which was used directly for the next step. 2,2-Dimethoxypropane (12 mL) was added to the crude mixture of deacetylated product (3.85 g) and CSA (0.15 g, 0.73 mmol) in anhydrous acetone (200 mL). The reaction mixture was heated to reflux for 1 h. After cooling, the solvent was evaporated to give the crude product (4.50 g). Pyridine (10 mL) was then added to a solution of the crude product (4.50 g) in DCM (100 mL), followed by dropwise addition of BzCl (2.14 mL, 18.50 mmol) at 0 °C. The reaction was complete after 1–2 h (monitoring by TLC), and the mixture was co-evaporated with toluene (3 × 50 mL). The residue was diluted with DCM (200 mL) and washed with HCl (0.5% in water, 3 × 10 mL), water (10 mL), and saturated aqueous $NaHCO_3$ solution (2 × 10 mL). After evaporation of the solvents, the crude residue was purified by silica gel chromatography (DCM/MeOH, 100:0 to 98:2) to give the expected product **8** (4.09 g, three steps 72%) as a white solid; m.p. 230–232 °C. $[\alpha]_D^{25}$ = +69.8 (c = 1.05 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.02 (d, $^3J_{H,H}$ = 7.0 Hz, 2 H, H-Ph), 7.60 (dd, $^3J_{H,H}$ = 7.4, $^3J_{H,H}$ = 8.4 Hz, 1 H, H-Ph), 7.45 (dd, $^3J_{H,H}$ = 7.3, $^3J_{H,H}$ = 8.4 Hz, 2 H, H-Ph), 6.07 (d, $^3J_{NH,5\text{-}H}$ = 7.0 Hz, 1 H, NH), 5.96 (d, $^3J_{3\text{-}H,4\text{-}H}$ = 2.6 Hz, 1 H, 3-H), 5.95 (dd, $^3J_{4\text{-}H,3\text{-}H}$ = 2.6, $^3J_{4\text{-}H,5\text{-}H}$ = 11.5 Hz, 1 H, 4-H), 4.78 (d, $^3J_{OH,7\text{-}H}$ = 4.5 Hz, 1 H, OH), 4.44–4.31 (m, 2 H, 5-H, 8-H), 4.19–4.08 (m, 3 H, 6-H, 9-H, 9′-H), 3.79 (s, 3 H, OCH_3), 3.50 (dd, $^3J_{OH,7\text{-}H}$ = 4.5, $^3J_{H,H}$ = 8.3 Hz, 1 H, 7-H), 1.99 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 173.2 (*C*O), 167.5 (*C*O), 161.9 (*C*O), 146.6 (C-2), 133.9 (Ph), 129.9 (Ph), 128.7 (Cq-Ph), 128.6 (Ph), 109.2 (Cq-acetonide), 106.7 (C-3), 77.9 (C-6), 74.0 (C-8), 69.7 (C-7), 69.1 (C-4), 67.3 (C-9), 52.4 (O*C*H_3), 49.4 (C-5), 27.1 (*C*H_3), 25.2 (*C*H_3), 23.1 (NHCO*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 3280, 3093, 2924, 1727, 1667, 1638, 1562, 1556, 1454, 1439, 1390, 1250, 1127, 1067, 1043, 975, 860, 801 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{27}O_9NNa$ $[M + Na]^+$ 472.1578; found 472.1589. $C_{22}H_{27}NO_9$ (449.45): calcd. C 58.79, H 6.06, N 3.12, O 32.04; found C 59.01, H 6.08, N 3.05, O 31.99.

Methyl 5-Acetamido-2,6-anhydro-4-*O*-benzoyl-7-*O*-(*tert*-butyldimethylsilyl)-3,5-dideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (8): 2,6-Lutidine (0.22 mL, 1.89 mmol) was added to a solution of **7** (168 mg, 0.37 mmol) in anhydrous DCM (1.5 mL), followed by slow addition of TBSOTf (0.30 mL, 1.31 mmol) at room temperature. After the mixture had been stirred overnight, the reaction was quenched with Et_3N and the mixture poured into water, washed with HCl (0.5% in water, 3 × 3 mL), water (3 mL), saturated aqueous $NaHCO_3$ solution (3 mL), and brine (3 mL), and dried ($MgSO_4$). After concentration under reduced pressure, the residue was purified by silica gel chromatography (DCM/MeOH, 100:0 to 97.5:1.5) to furnish **8** (185 mg, 88%) as a white solid; m.p. 152–154 °C. $[\alpha]_D^{25}$ = +103.5 (c = 0.8 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.02 (d, $^3J_{H,H}$ = 7.9 Hz, 1 H, H-Ph), 7.57 (dd, $^3J_{H,H}$ = 7.6, $^3J_{H,H}$ = 8.0 Hz, 1 H, H-Ar), 7.44 (dd, $^3J_{H,H}$ = 7.6, $^3J_{H,H}$ = 7.9 Hz, 2 H, H-Ph), 6.13 (d, $J_{3\text{-}H,4\text{-}H}$ = 4.0 Hz, 1 H, 3-H), 5.70 (dd, $^3J_{4\text{-}H,3\text{-}H}$ = 4.0, $^3J_{4\text{-}H,5\text{-}H}$ = 5.4 Hz, 1 H, 4-H), 5.55 (d, $^3J_{NH,5\text{-}H}$ = 7.7 Hz, 1 H, NH), 4.49–4.32 (m, 4 H, 5-H, 6-H, 7-H, 8-H), 4.06 (dd, $^3J_{9\text{-}H,8\text{-}H}$ = 6.4, $^2J_{9\text{-}H,9'\text{-}H}$ = 7.7 Hz, 1 H, 9-H), 3.93 (t, $^3J_{9'\text{-}H,9\text{-}H}$ = $^3J_{9'\text{-}H,8\text{-}H}$ = 7.6 Hz, 1 H, 9′-H), 3.79 (s, 3 H, OCH_3), 1.93 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 0.90 (s, 9 H, CH_3), 0.11 (s, 3 H, CH_3), 0.06 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 169.7 (*C*O), 165.9 (*C*O), 162.1 (*C*O), 145.2 (C-2), 133.4 (Ph), 129.9 (Ph), 129.3 (Cq-Ph), 128.5 (Ph), 108.6 (Cq-acetonide), 106.7 (C-3), 79.0 (C-6), 75.6 (C-7), 70.0 (C-8), 67.7 (C-4), 64.9 (C-9), 52.4 (O*C*H_3), 47.5 (C-5),

26.6 (CH_3), 25.9 [SiC(CH_3)$_3$], 25.2 (CH_3), 23.3 (NHCOCH_3), 18.3 (Si*C*), –3.6 (SiCH_3), –4.5 (SiCH_3) ppm. IR (neat): $\tilde{\nu}$ = 2929, 2854, 2870, 1746, 1734, 1725, 1643, 1530, 1450, 1370, 1249, 1225, 1058, 1093, 1024, 918, 851, 834, 772, 711 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{41}O_9NNaSi$ [M + Na]$^+$ 586.2443; found 586.2455. $C_{28}H_{41}NO_9Si$ (563.71): calcd. C 59.66, H 7.33, N 2.48; found C 59.69, H 7.35, N 2.44.

General Procedures for the Palladium-Mediated Allylic Substitution

(A) With Sodium Malonate as Nucleophile: In a Schlenk tube, a solution of the palladium source and the appropriate ligand in degassed THF (0.25 M) was added to **7** or **8**. After stirring for 10 min, a solution of freshly prepared dimethyl malonate sodium salt in THF (0.33 M) was added, and the resulting mixture was heated at 50 °C for 0.5–18 h. After cooling, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel.

(B) With Other Nucleophiles: In a Schlenk tube, a mixture of **8**, $Pd_2(dba)_3$·$CHCl_3$, the appropriate ligand, the nucleophile, and the base or the additive in degassed solvent (0.07 M) was heated at the indicated temperature. After cooling, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel.

Methyl 5-Acetamido-2,6-anhydro-2-*C*-[bis(methoxycarbonyl)-methyl]-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-3-enonate (16) and Methyl 5-Acetamido-2,6-anhydro-4-*C*-[bis-(methoxycarbonyl)methyl]-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (17): The reaction was carried out as described under General Procedure (A) at 50 °C for 18 h on **7** (18 mg, 40 μmol) with $Pd(OAc)_2$ (2 mg, 8 μmol), PPh_3 (4 mg, 16 μmol), and dimethyl malonate sodium salt [prepared from dimethyl malonate (9 μL, 80 μmol) and sodium (60% in mineral oil, 3 mg, 80 μmol)]. Purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 1:0 to 97:3) afforded **16** (11 mg, 54%) and **17** (2 mg, 12%).

Compound 16: M.p. 158–160 °C. $[\alpha]_D^{25}$ = –1.7 (*c* = 0.4 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.04 (dd, $^3J_{3\text{-H},4\text{-H}}$ = 9.5, $^4J_{3\text{-H},5\text{-H}}$ = 2.0 Hz, 1 H, 3-H), 5.92 (dd, $^3J_{4\text{-H},5\text{-H}}$ = 2.0, $^3J_{4\text{-H},3\text{-H}}$ = 9.5 Hz, 1 H, 4-H), 5.56 (d, $^3J_{NH,5\text{-H}}$ = 9.5 Hz, 1 H, NH), 4.66 (tt, $^3J_{5\text{-H},4\text{-H}}$ = $^4J_{5\text{-H},3\text{-H}}$ = 2.0, $^3J_{5\text{-H,NH}}$ = $^3J_{5\text{-H},6\text{-H}}$ = 9.5 Hz, 1 H, 5-H), 4.25 (q, $^3J_{8\text{-H},9\text{-H}}$ = $J_{8\text{-H},9'\text{-H}}$ = 6.5 Hz, 1 H, 8-H), 4.09 (s, 1 H, H-malonyl), 4.05 (dd, $^3J_{9\text{-H},8\text{-H}}$ = 6.5, $^2J_{9\text{-H},9'\text{-H}}$ = 8.5 Hz, 1 H, 9-H), 3.99 (dd, $^3J_{9'\text{-H},8\text{-H}}$ = 6.5, $^2J_{9'\text{-H},9\text{-H}}$ = 8.5 Hz, 1 H, 9′-H), 3.75–3.77 (m, 1 H, 6-H), 3.74 (s, 3 H, OCH_3), 3.72 (s, 6 H, OCH_3), 3.65–3.67 (m, 1 H, 7-H), 3.54–3.58 (br., 1 H, OH), 1.99 (s, 3 H, NHCOCH_3), 1.37 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.4 (CO), 170.1 (CO), 166.6 (CO), 166.4 (CO), 131.7 (C-4), 127.0 (C-3), 108.5 (Cq), 78.7 (C-2), 76.4 (C-8), 75.3 (C-6), 69.5 (C-7), 66.0 (C-9), 58.6 (C-malonyl), 53.0 (OCH_3), 52.9 (OCH_3), 41.3 (C-5), 26.8 (CH_3), 25.7 (CH_3), 23.3 (NHCOCH_3) ppm. IR (neat): $\tilde{\nu}$ = 3476 (br.), 3267 (br.), 2957, 2358, 1735, 1643, 1550, 1433, 1370, 1331, 1246, 1155, 1111, 1058, 1012, 890, 853, 757, 710 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{29}NO_{11}Na$ [M + Na]$^+$ 482.1638; found 482.1642. $C_{20}H_{29}NO_{11}$ (459.44): calcd. C 52.28, H 6.36, N 3.05, O 38.31; found C 51.99, H 6.32, N 3.01, O 38.05.

Compound 17: M.p. 191–193 °C. $[\alpha]_D^{25}$ = +20.2 (*c* = 0.43 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 5.97 (d, $^3J_{NH,5\text{-H}}$ = 8.0 Hz, 1 H, NH), 5.88 (d, $^3J_{3\text{-H},4\text{-H}}$ = 2.5 Hz, 1 H, 3-H), 4.67–4.58 (br. s, 1 H, O*H*), 4.39 (m, 1 H, 8-H), 4.18 (dd, $^2J_{9\text{-H},9'\text{-H}}$ = 8.5, $^3J_{9\text{-H},8\text{-H}}$ = 6.0 Hz, 1 H, 9-H), 4.12 (dd, $^3J_{9'\text{-H},8\text{-H}}$ = 5.0, $^2J_{9'\text{-H},9\text{-H}}$ = 8.5 Hz, 1 H, 9′-H), 4.05 (td, $^3J_{5\text{-H,NH}}$ = $^3J_{5\text{-H},4\text{-H}}$ = 8.0, $^3J_{5\text{-H},6\text{-H}}$ = 10.5 Hz, 1 H, 5-H), 3.85 (d, $^3J_{6\text{-H},5\text{-H}}$ = 10.5 Hz, 1 H, 6-H), 3.81 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 3.59 (d, $^3J_{\text{H-malonyl},4\text{-H}}$ = 5.5 Hz, 1 H, H-malonyl), 3.55 (d, $J_{7\text{-H},8\text{-H}}$ = 8.0 Hz, 1 H, 7-H), 3.30 (ddd, $^3J_{4\text{-H},3\text{-H}}$ = 2.5, $^3J_{\text{H-malonyl},4\text{-H}}$ = 5.5, $^3J_{4\text{-H},5\text{-H}}$ = 8.0 Hz, 1 H, 4-H), 2.06 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 172.8 (*C*O), 168.7 (*C*O), 168.3 (*C*O), 162.3 (*C*O), 145.3 (C-2), 109.1 (Cq), 108.9 (C-3), 77.9 (C-6), 74.4 (C-8), 69.5 (C-7), 67.2 (C-9), 53.9 (OCH_3), 53.1 (C-malonyl, OCH_3), 52.3 (OCH_3), 46.7 (C-5), 37.9 (C-4), 27.0 (CH_3), 25.3 (CH_3), 23.0 (NHCOCH_3) ppm. IR (neat): $\tilde{\nu}$ = 3271 (br.), 2955, 2359, 1754, 1726, 1641, 1556, 1435, 1370, 1311, 1256, 1227, 1158, 1043, 920, 862, 777, 731 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{29}NO_{11}Na$ [M + Na]$^+$ 482.1638; found 482.1634. $C_{20}H_{29}NO_{11}$ (459.44): calcd. C 52.28, H 6.36, N 3.05, O 38.31; found C 52.17, H 6.36, N 3.11, O 38.05.

Methyl 5-Acetamido-2,6-anhydro-2-*C*-[bis(methoxycarbonyl)-methyl]-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-3-enoate (18): The reaction was carried out as described under General Procedure (A) at 50 °C for 3 h on **8** (28 mg, 50 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (5 mg, 5 μmol), dppb (8 mg, 20 μmol), and dimethyl malonate sodium salt [prepared from dimethyl malonate (11 μL, 100 μmol) and sodium (60% in mineral oil, 4 mg, 100 μmol)]. Purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 1:0 to 49:1) afforded **18** (24 mg, 84%); m.p. 142–144 °C. $[\alpha]_D^{25}$ = –3.3 (*c* = 1.3 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.02 (dd, $^3J_{3\text{-H},5\text{-H}}$ = 1.5, $^3J_{3\text{-H},4\text{-H}}$ = 10.4 Hz, 1 H, 3-H), 5.99 (dd, $^3J_{4\text{-H},5\text{-H}}$ = 1.5, $^3J_{4\text{-H},3\text{-H}}$ = 10.4 Hz, 1 H, 4-H), 5.48 (d, $^3J_{NH,5\text{-H}}$ = 7.5 Hz, 1 H, NH), 4.36 (ddt, $^3J_{5\text{-H},3\text{-H}}$ = $^3J_{5\text{-H},4\text{-H}}$ = 1.5, $^3J_{5\text{-H,NH}}$ = 7.5, $^3J_{5\text{-H},6\text{-H}}$ = 9.3 Hz, 1 H, 5-H), 4.25 (td, $^3J_{8\text{-H},7\text{-H}}$ = 3.0, $^3J_{8\text{-H},9\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = 7.5 Hz, 1 H, 8-H), 4.15 (dd, $^3J_{7\text{-H},6\text{-H}}$ = 1.5, $^3J_{7\text{-H},8\text{-H}}$ = 3.0 Hz, 1 H, 7-H), 3.96 (t, $J_{9\text{-H},9'\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = 7.5 Hz, 1 H, 9-H), 3.95 (s, 1 H, H-malonyl), 3.88 (dd, $^3J_{6\text{-H},7\text{-H}}$ = 1.5, $^3J_{6\text{-H},5\text{-H}}$ = 9.3 Hz, 1 H, 6-H), 3.82 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 7.5 Hz, 1 H, 9′-H), 3.74 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 1.94 (s, 3 H, NHCOCH_3), 1.40 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3), 0.89 (s, 9 H, CH_3), 0.12 (s, 3 H, CH_3), 0.11 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.1 (*C*O), 169.8 (*C*O), 166.2 (*C*O), 166.0 (*C*O), 132.3 (C-4), 125.1 (C-3), 107.7 (Cq), 78.9 (C-2), 77.4 (C-8), 76.6 (C-6), 70.8 (C-7), 64.7 (C-9), 59.0 (C-malonyl), 52.7 (OCH_3), 52.5 (OCH_3), 44.3 (C-5), 26.3 (CH_3), 26.0 [SiC(CH_3)$_3$], 24.8 (CH_3), 23.3 (CH_3 NHCOCH_3), 18.2 (Si*C*), –4.9 (SiCH_3), –3.9 (q, SiCH_3) ppm. IR (neat): $\tilde{\nu}$ = 2951, 1740, 1646, 1542, 1433, 1243, 1156, 1015, 835, 776, 714 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{43}NO_{11}SiNa$ [M + Na]$^+$ 596.2503; found 596.2500. $C_{26}H_{43}NO_{11}Si$ (573.71): calcd. C 54.43, H 7.55, N 2.44; found C 54.51, H 7.53, N 2.36.

Methyl 5-Acetamido-2,6-anhydro-4-*C*-[bis(methoxycarbonyl)-methyl]-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (19): The reaction was carried out as described under General Procedure (A) at 50 °C for 15 h on **8** (281 mg, 500 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (51 mg, 50 μmol), PBu_3 (50 μL, 200 μmol), and dimethyl malonate sodium salt [prepared from dimethyl malonate (114 μL, 1 mmol) and sodium (60% in mineral oil, 40 mg, 1 mmol)]. Purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 1:0 to 99:1) afforded **19** (261 mg, 92%); m.p. 78 °C. $[\alpha]_D^{25}$ = +30.2 (*c* = 1 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.02 (d, $^3J_{3\text{-H},4\text{-H}}$ = 2.5 Hz, 1 H, 3-H), 5.62 (d, $^3J_{NH,5\text{-H}}$ = 8.0 Hz, 1 H, N*H*Ac), 4.38 (dd, $^3J_{6\text{-H},7\text{-H}}$ = 1.2, $^3J_{6\text{-H},5\text{-H}}$ = 10.0 Hz, 1 H, 6-H), 4.29 (td, $^3J_{8\text{-H},7\text{-H}}$ = 5.0, $^3J_{8\text{-H},9\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = 6.6 Hz, 1 H, 8-H), 4.14 (dd, $^3J_{7\text{-H},6\text{-H}}$ = 1.2, $^3J_{7\text{-H},8\text{-H}}$ = 5.0 Hz, 1 H, 7-H), 4.09 (dd, $^3J_{9\text{-H},8\text{-H}}$ = 6.6, $^3J_{9\text{-H},9'\text{-H}}$ = 8.1 Hz, 1 H, 9-H), 3.96 (dd, $^3J_{9'\text{-H},8\text{-H}}$ =

6.6, $^2J_{9'\text{-H},9\text{-H}}$ = 8.1 Hz, 1 H, 9′-H), 3.83 (td, $^3J_{5\text{-H,NH}}$ = 8.0, $^3J_{5\text{-H},6\text{-H}}$ = $^3J_{5\text{-H},4\text{-H}}$ = 10.0 Hz, 1 H, 5-H), 3.78 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.72 (d, $^3J_{\text{H-malonyl},4\text{-H}}$ = 4.5 Hz,1 H, H-malonyl), 3.54 (ddd, $^3J_{4\text{-H},3\text{-H}}$ = 2.5, $^3J_{4\text{-H,H-malonyl}}$ = 4.5, $^3J_{4\text{-H},5\text{-H}}$ = 10.0 Hz, 1 H, 4-H), 1.96 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 0.87 (s, 9 H, 3 × CH_3), 0.12 (s, 3 H, CH_3), 0.11 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.2 (CO), 168.7 (CO), 167.9 (CO), 162.3 (CO), 144.1 (C-2), 109.9.1 (C-3), 108.3 (Cq), 77.5 (C-6), 76.3 (C-8), 71.5 (C-7), 65.6 (C-9), 52.8 (OCH_3), 52.6 (OCH_3), 52.1 (C-malonyl, OCH_3), 47.7 (C-5), 38.2 (C-4), 26.6 (CH_3), 26.0 [SiC(CH_3)$_3$], 24.9 (CH_3), 23.6 (CH_3), 18.4 (SiC), –3.3 (SiCH_3), –4.3 (SiCH_3) ppm. IR (neat): $\tilde{\nu}$ = 3476 (br.), 3267 (br.), 2957, 2358, 1735, 1643, 1550, 1433, 1370, 1331, 1246, 1155, 1111, 1058, 1012, 890, 853, 757, 710 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{43}NO_{11}SiNa$ [M + Na]$^+$ 596.2503; found 596.2503. $C_{26}H_{43}NO_{11}Si$ (573.71): calcd. C 54.43, H 7.55, N 2.44; found C 54.31, H 7.54, N 2.38.

Bicyclic Compound 20: The reaction was carried out as described under General Procedure (B) at 50 °C for 3 h on **7** (240 mg, 530 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (16 mg, 16 μmol), PPh_3 (8 mg, 32 μmol), and DBU (96 μL, 640 μmol) in CH_2Cl_2 (2 mL). Purification by flash column chromatography on silica gel (heptane/EtOAc, 6:4 to 3:7) afforded **20** (162 mg, 93%). $[\alpha]_D^{25}$ = –133.6 (c = 1 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.33 (dd, $^4J_{3\text{-H},5\text{-H}}$ = 1.0, $^3J_{3\text{-H},4\text{-H}}$ = 10.0 Hz, 1 H, 3-H), 5.95 (d, $^3J_{\text{NH},5\text{-H}}$ = 9.5 Hz, 1 H, NH), 5.87 (ddd, $^3J_{4\text{-H},3\text{-H}}$ = 10.0, $^3J_{4\text{-H},5}$ = 4.5, $^4J_{4\text{-H},6\text{-H}}$ = 1.0 Hz, 1 H, 4-H), 4.65 (q, $^3J_{6\text{-H},7\text{-H}}$ = $^3J_{6\text{-H},5\text{-H}}$ = $^4J_{6\text{-H},4\text{-H}}$ = 1.0 Hz, 1 H, 6-H), 4.41 (ddt, $^4J_{5\text{-H},3\text{-H}}$ = $^3J_{5\text{-H},6\text{-H}}$ = 1.0, $^3J_{5\text{-H},4\text{-H}}$ = 4.5, $^3J_{5\text{-H,NH}}$ = 10.0 Hz, 1 H, 5-H), 4.16–4.02 (m, 2 H, 9-H, 8-H), 3.94 (dd, $^2J_{9'\text{-H},9\text{-H}}$ = 8.0, $^3J_{9'\text{-H},8\text{-H}}$ = 4.0 Hz, 1 H, 9′-H), 3.91 (s, 3 H, CO_2CH_3), 3.82 (dd, $^3J_{7\text{-H},6\text{-H}}$ = 1.5, $^3J_{7\text{-H},8\text{-H}}$ = 8.0 Hz, 1 H, 7-H), 2.02 (s, 3 H, COCH_3), 1.45 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 169.1 (COCH$_3$), 165.9 (CO_2CH_3), 129.9.4 (C-3), 126.4.3 (C-4), 109.9 [C(CH$_3$)$_2$], 99.7 (C-2), 80.1 (C-8), 77.8 (C-7), 75.7 (C-6), 67.0 (C-9), 53.3 (CO_2CH_3), 46.6 (C-5), 26.9 [C(CH$_3$)$_2$], 25.2 [C(CH$_3$)$_2$], 23.1 (COCH$_3$) ppm. IR (neat): $\tilde{\nu}$ = 3272, 2986, 2932, 1752, 1651, 1530, 1371, 1200, 1107, 1059, 983, 842, 731 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{21}NO_7Na$ [M + Na]$^+$ 350.1216; found 350.1211. $C_{15}H_{21}NO_7$ (327.33): calcd. C 55.04, H 6.47, N 4.28, O 34.21; found C 55.31, H 6.62, N 4.02, O 33.97.

Methyl 5-Acetamido-2,6-anhydro-2-*C*-[(benzyloxycarbonyl)(methoxycarbonyl)methyl]-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-3-enoate (28; 1:1 Mixture of Two Diastereoisomers): The reaction was carried out as described under General Procedure (A) at 60 °C for 2 h on **8** (28 mg, 50 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (5 mg, 5 μmol), dppb (6 mg, 15 μmol), and benzyl methyl malonate sodium salt [prepared from benzyl methyl malonate (18 μL, 100 μmol) and sodium (60% in mineral oil, 4 mg, 100 μmol)]. Purification by flash column chromatography on silica gel (heptane/EtOAc, 6:4 to 4:6) afforded **28** (24 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.30–7.10 (m, 5 H, Ph), 5.95–5.80 (m, 2 H, 3-H, 4-H), 5.38 (d, $^3J_{\text{NH},5\text{-H}}$ = 9.5 Hz, 1 H, NH), 5.10–4.95 (m, 2 H, CH_2Ph), 4.25–4.20 (m, 1 H, 5-H), 4.20–4.06 (m, 1 H, 8-H), 4.05–4.0 (m, 1 H, 7-H), 3.90–3.65 (m, 4 H, H-malonyl, 6-H, 9-H, 9′-H), 3.56 (m, 4.5 H, OCH_3), 3.48 (s, 1.5 H, OCH_3), 1.83 (s, 3 H, NHCOCH_3), 1.29 (s, 3 H, CH_3), 1.19 (s, 3 H, CH_3), 0.78 [s, 9 H, SiC(CH_3)$_3$], 0.01 (s, 6 H, SiCH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.1 (CO), 169.8 (CO), 166.1 (CO), 165.9 (CO), 165.5 (CO), 165.4 (CO), 135.1 (Cq-Ph), 133.5 (Cq-Ph), 132.5 (C-4), 132.4 (C-4), 130.1 (Ph), 128.5 (Ph), 128.4 (Ph), 128.3 (Ph), 128.2 (Ph), 128.1 (Ph), 125.1 (C-3), 125.0 (C-3), 107.7 (Cq), 107.6 (Cq), 78.9 (C-2), 78.8 (C-2), 77.2 (C-8), 77.0 (C-8), 75.2 (C-6), 75.1 (C-6), 71.0 (C-7), 70.9 (C-7), 67.4 (CH$_2$Ph), 67.3 (CH$_2$Ph), 64.7 (C-9), 64.5 (C-9), 59.2 (C-malonyl), 59.0 (C-malonyl), 52.7 (OCH$_3$), 52.5 (OCH$_3$), 52.4 (OCH$_3$), 44.6 (C-5), 44.5 (C-5), 26.3 (CH$_3$), 26.0 [SiC(CH$_3$)$_3$], 24.8 (CH$_3$), 23.3 (NHCOCH$_3$), 18.2 (Cq), –3.9 (SiCH$_3$), –4.9 (SiCH$_3$) ppm. IR (neat): $\tilde{\nu}$ = 3278, 2953, 1738, 1649, 1538, 1434, 1372, 1249, 1150, 1079, 1017, 833, 778, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{32}H_{47}NO_{11}NaSi$ [M + Na]$^+$ 672.2816; found 672.2825. $C_{32}H_{47}NO_{11}Si$ (649.80): calcd. C 59.15, H 7.29, N 2.16; found C 59.41, H 7.57, N 2.05.

Methyl 5-Acetamido-2,6-anhydro-4-*C*-[(benzyloxycarbonyl)(methoxycarbonyl)methyl]-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (29; 1:1 Mixture of Two Diastereoisomers): The reaction was carried out as described under General Procedure (A) at 60 °C for 18 h on **8** (56 mg, 100 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (10 mg, 10 μmol), PBu_3 (10 μL, 40 μmol), and benzyl methyl malonate sodium salt [prepared from benzyl methyl malonate (36 μL, 200 μmol) and sodium (60% in mineral oil, 8 mg, 200 μmol)]. Purification by flash column chromatography on silica gel (heptane/EtOAc, 1:0 to 3:7) afforded **29** (42 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 5.88 (d, $^3J_{3\text{-H},4\text{-H}}$ = 2.0 Hz, 0.5 H, 3-H), 5.86 (d, $^3J_{3\text{-H},4\text{-H}}$ = 2.5 Hz, 0.5 H, 3-H), 5.44 (d, $^3J_{\text{NH},5\text{-H}}$ = 8.0 Hz, 0.5 H, NH), 5.48 (d, $^3J_{\text{NH},5\text{-H}}$ = 7.5 Hz, 0.5 H, NH), 5.09 (d, $^2J_{\text{H,H}}$ = 12.5 Hz, 0.5 H, CH_2Ph), 5.06 (s, 1 H, CH_2Ph), 4.97 (d, $^2J_{\text{H,H}}$ = 12.5 Hz, 0.5 H, CH_2Ph), 4.25–4.21 (m, 1 H, 6-H), 4.17–4.11 (m, 1 H, 8-H), 4.01–3.97 (m, 1 H, 7-H), 3.96–3.91 (m, 1 H, 9-H), 3.83–3.78 (m, 1 H, 9′-H), 3.76–3.71 (m, 1 H, 5-H), 3.63–3.53 (m, 7 H, H-malonyl, OCH_3), 3.43–3.36 (m, 1 H, 4-H), 1.82 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 0.76 [s, 9 H, SiC(CH_3)$_3$], –0.00 (s, 6 H, SiCH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.2 (CO), 168.6 (CO), 168.0 (CO), 167.8 (CO), 167.3 (CO), 162.3 (CO), 162.2 (CO), 144.2 (C-2), 144.1 (C-2), 135.2 (Cq-Ph), 135.1 (Cq-Ph), 128.6 (Ph), 128.5 (Ph), 128.4 (Ph), 128.3 (Ph), 128.2 (Ph), 128.1 (Ph), 110.0 (C-3), 109.9 (C-3), 108.3 (Cq), 108.2 (Cq), 77.6 (C-6), 77.5 (C-6), 76.4 (C-8), 76.3 (C-8), 71.5 (C-7), 71.4 (C-7), 67.5 (CH$_2$Ph), 67.4 (CH$_2$Ph), 65.6 (C-9), 65.5 (C-9), 52.7 (OCH$_3$), 52.5 (OCH$_3$), 52.4 (OCH$_3$), 52.1 (C-malonyl), 52.0 (C-malonyl), 47.9 (C-5), 47.7 (C-5), 38.2 (C-4), 38.1 (C-4), 26.6 (CH$_3$), 26.0 [SiC(CH$_3$)$_3$], 24.9 (CH$_3$), 23.5 (NHCOCH$_3$), 18.4 (Cq), –3.4 (SiCH$_3$), –4.3 (SiCH$_3$) ppm. IR (neat): $\tilde{\nu}$ = 2931, 2856, 1731, 1660, 1538, 1436, 1371, 1252, 1207, 1156, 1131, 1070, 1040, 832, 778, 748, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{32}H_{47}NO_{11}SiNa$ [M + Na]$^+$ 672.2816; found 672.2819.

Methyl 5-Acetamido-2,6-anhydro-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-4-*C*-[bis(phenylsulfonyl)methyl]-D-*glycero*-D-*galacto*-non-2-enoate (30): The reaction was carried out as described under General Procedure (A) at 80 °C for 15 h on **8** (28 mg, 50 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (10 mg, 10 μmol), PBu_3 (6 μL, 40 μmol), and sodium bis(phenylsulfonyl)methane anion [prepared from bis(phenylsulfonyl)methane (44 mg, 150 μmol) and sodium (60% in mineral oil, 6 mg, 150 μmol)]. Purification by flash column chromatography on silica gel (toluene/acetone, 1:0 to 8:2) afforded **30** (17 mg, 46%); m.p. 177–179 °C. $[\alpha]_D^{25}$ = +2.3 (c = 0.3 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.05 (d, $^3J_{\text{H,H}}$ = 7.8 Hz, 2 H, Ph), 7.80 (d, $^3J_{\text{H,H}}$ = 7.7 Hz, 2 H, Ph), 7.67–7.56 (m, 2 H, Ph), 7.45–7.54 (m, 4 H, Ph), 6.18 (d, $^3J_{3\text{-H},4\text{-H}}$ = 2.1 Hz, 1 H, 3-H), 5.68 (d, $^3J_{\text{NH},5\text{-H}}$ = 7.8 Hz, 1 H, NH), 5.65 [s, 1 H, $HC(SO_2Ph)_2$], 4.71 (td, $^3J_{5\text{-H,NH}}$ = 7.8, $^3J_{5\text{-H},4\text{-H}}$ = $^3J_{5\text{-H},6\text{-H}}$ = 9.5 Hz, 1 H, 5-H), 4.28–4.18 (m, 2 H, 7-H, 8-H), 4.05 (dd, $^3J_{9\text{-H},8\text{-H}}$ = 5.8, $^2J_{9\text{-H},9'\text{-H}}$ = 7.5 Hz, 1 H, 9-H), 3.94 (d, $^3J_{6\text{-H},5\text{-H}}$ = 9.5 Hz, 1 H, 6-H), 3.88 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9'\text{-H},9\text{-H}}$ = 7.5 Hz, 1 H, 9′-H), 3.77 (s, 3 H, CH_3), 3.58 (dd, $J_{4\text{-H},3\text{-H}}$ = 2.1, $^3J_{4\text{-H},5\text{-H}}$ = 9.5 Hz, 1 H, 4-H), 1.86 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3), 1.23 (s, 3 H,

CH_3), 0.89 (s, 9 H, 3 × CH_3),0.14 (s, 6 H, 2 × CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 171.3 (CO), 161.8 (CO), 144.9 (C-2), 140.0 (Cq Ph), 137.2 (Cq Ph), 134.7 (Ph), 134.1 (Ph), 129.7 (Ph), 129.4 (Ph), 129.3 (Ph), 108.3 (Cq), 107.6 (C-3), 80.7 [*C*(SO_2Ph)$_2$], 78.1 (C-7), 75.9 (C-8), 71.9 (C-6), 65.2 (C-9), 52.3 (O*C*H_3), 47.5 (C-5), 41.4 (C-5), 26.5 (*C*H_3), 26.0 [SiC(*C*H_3)$_3$], 25.0 (*C*H_3), 23.5 (NHCO*C*H_3), 18.3 (Si*C*), –3.8 (Si*C*H_3), –4.5 (Si*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 2927, 1730, 1666, 1650, 1536, 1309, 1277, 1253, 1145, 1078, 832, 745, 727, 625 cm^{-1}. HRMS (ESI) for $C_{34}H_{47}NO_{11}S_2$SiNa; found 760.2247: calcd. for 760.2258.

Methyl 5-Acetamido-2,6-anhydro-4-azido-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (31): The reaction was carried out as described under General Procedure (B) at 60 °C for 8 h on **8** (28 mg, 50 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (10 mg, 10 μmol), dppb (16 mg, 20 μmol), *n*Bu_4NBr (1.6 mg, 5 μmol), and NaN_3 (10 mg, 150 μmol) in THF/water (4:1; 1.6 mL). Purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 1:0 to 99:1) afforded **31** (16 mg, 65%). $[\alpha]_D^{25}$ = +65.6 (*c* = 1.2 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 5.97 (d, $J_{3\text{-H},4\text{-H}}$ = 2.5 Hz, 1 H, 3-H), 5.69 (d, $^3J_{NH,5\text{-H}}$ = 8.5 Hz, 1 H, N*H*), 4.68 (dd, $^3J_{6\text{-H},7\text{-H}}$ = 3, $^3J_{6\text{-H},5\text{-H}}$ = 8.5 Hz, 1 H, 6-H), 4.65 (dd, $^3J_{4\text{-H},3\text{-H}}$ = 2.5, $J_{4\text{-H},5\text{-H}}$ = 8.5 Hz, 1 H, 4-H), 4.29 (q, $^3J_{8\text{-H},9\text{-H}}$ = $J_{8\text{-H},9'\text{-H}}$ = $^3J_{8\text{-H},7\text{-H}}$ = 7.0 Hz, 1 H, 8-H), 4.18–4.14 (m, 1 H, 7-H), 4.11 (t, $^3J_{9\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 7.0 Hz, 1 H, 9-H), 3.94 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9'\text{-H},9\text{-H}}$ = 7.0 Hz, 1 H, 9′-H), 3.82 (s, 3 H, O*C*H_3), 3.61 (q, $^3J_{5\text{-H},4\text{-H}}$ = $^3J_{5\text{-H,NH}}$ = $^3J_{5\text{-H},6\text{-H}}$ = 8.5 Hz, 1 H, 5-H), 2.04 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 0.91 (s, 9 H, 3 × CH_3), 0.16 (s, 3 H, CH_3), 0.14 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.4 (*C*O), 161.8 (*C*O), 145.3 (C-2), 108.5 (Cq), 106.7 (C-3), 77.5 (C-6), 76.3 (C-8), 70.7 (C-7), 65.5 (C-9), 56.6 (C-4), 52.4 (O*C*H_3), 50.5 (C-5), 26.5 (*C*H_3), 26.0 [SiC(*C*H_3)$_3$], 24.9 (*C*H_3), 23.5 (NHCO*C*H_3), 18.5 (Si*C*), –3.2 (Si*C*H_3), –4.3 (Si*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 2927, 2854, 2357, 2096, 1731, 1650, 1659, 1537, 1438, 1370, 1249, 1129, 1070, 832, 776, 712 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{36}N_4O_7$SiNa 507.2251; found 507.2271.

Methyl 5-Acetamido-2,6-anhydro-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-4-(phenylamino)-D-*glycero*-D-*galacto*-non-2-enoate (32): The reaction was carried out as described under General Procedure (B) at 60 °C for 15 h on **8** (28 mg, 50 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (10 mg, 10 μmol), dppb (16 mg, 20 μmol), aniline (13 μL, 150 μmol), and NEt_3 (50 μL, 350 μmol) in CH_2Cl_2 (0.7 mL). Purification by flash column chromatography on silica gel (heptane/EtOAc/NEt_3, 90:10:1 to 30:70:1) afforded **32** (20 mg, 74%). $[\alpha]_D^{25}$ = +31.6 (*c* = 0.6 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.21 (dd, $^3J_{H,H}$ = 8.0, $^3J_{H,H}$ = 8.5 Hz, 2 H, Ph), 6.76 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, Ph), 6.66 (d, $^3J_{H,H}$ = 8.0 Hz, 2 H, Ph), 6.10 (d, $^3J_{3\text{-H},4\text{-H}}$ = 2.5 Hz, 1 H, 3-H), 5.89 (d, $^3J_{NH,5\text{-H}}$ = 8.5 Hz, 1 H, N*H*), 4.61 (d, $J_{NH,4\text{-H}}$ = 6.5 Hz, 1 H, NH), 4.30 (dd, $^3J_{6\text{-H},7\text{-H}}$ = 2.0, $^3J_{6\text{-H},5\text{-H}}$ = 8.5 Hz, 1 H, 6-H), 4.30–4.23 (m, 3 H, 4-H, 7-H, 8-H), 4.10 (q, $^3J_{5\text{-H,NH}}$ = $^3J_{5\text{-H},4\text{-H}}$ = $^3J_{5\text{-H},6\text{-H}}$ = 8.5 Hz, 1 H, 5-H), 4.06–4.02 (m, 1 H, 9-H), 3.92–3.88 (m, 1 H, 9′-H), 3.79 (s, 3 H, O*C*H_3), 1.97 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 0.93 (s, 9 H, 3 × CH_3), 0.18 (s, 3 H, CH_3), 0.17 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 171.2 (*C*O), 162.4 (*C*O), 146.7 (Cq), 143.5 (C-2), 129.5 (Ph), 118.1 (Ph), 113.2 (Ph), 110.7 (C-3), 108.5 (Cq), 78.4 (C-8), 75.6 (C-6), 71.8 (C-7), 65.3 (C-9), 53.5 (C-4), 52.2 (O*C*H_3), 49.4 (C-5), 26.5 (*C*H_3), 25.7 [SiC(*C*H_3)$_3$], 25.1 (*C*H_3), 23.4 (NHCO*C*H_3), 18.3 (Si*C*), –3.7 (Si*C*H_3), –4.5 (Si*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 3284, 2929, 2855, 1731, 1650, 1601, 1504, 1435, 1370, 1307, 1249, 1143, 1069, 835, 748, 730 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{42}N_2O_7$SiNa 557.2659; found 557.2695.

Methyl 5-Acetamido-2,6-anhydro-4-(benzylamino)-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (33): The reaction was carried out as described under General Procedure (B) at 60 °C for 15 h on **8** (28 mg, 50 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (10 mg, 10 μmol), dppb (16 mg, 20 μmol), benzylamine (38 μL, 360 μmol), and NEt_3 (50 μL, 350 μmol) in CH_2Cl_2 (0.5 mL). Purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 99:1 to 98:2) afforded **33** (24 mg, 88%); m.p. 90–92 °C. $[\alpha]_D^{25}$ = +41.1 (*c* = 0.5 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.37–7.27 (m, 5 H, Ph), 6.11 (d, $^3J_{3\text{-H},4\text{-H}}$ = 3.0 Hz, 1 H, 3-H), 5.57 (d, $^3J_{NH,5\text{-H}}$ = 6.0 Hz, 1 H, N*H*), 4.29 (td, $^3J_{8\text{-H},7\text{-H}}$ = 3.5, $^3J_{8\text{-H},9\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = 6.5 Hz, 1 H, 8-H), 4.25 (t, $^3J_{7\text{-H},6\text{-H}}$ = $^3J_{7\text{-H},8\text{-H}}$ = 3.5 Hz, 1 H, 7-H), 4.19 (dd, $^3J_{6\text{-H},7\text{-H}}$ = 3.5, $^3J_{6\text{-H},5\text{-H}}$ = 8.5 Hz, 1 H, 6-H), 4.03 (dd, $^3J_{9\text{-H},8\text{-H}}$ = 6.5, $^2J_{9\text{-H},9'\text{-H}}$ = 8.0 Hz, 1 H, 9-H), 3.95–3.86 (m, 3 H, 5-H, 9′-H, NCH_2Ph), 3.80–3.74 (m, 5 H, NH, NCH_2Ph, O*C*H_3), 3.48 (dd, $^3J_{4\text{-H},3\text{-H}}$ = 3.0, $^3J_{4\text{-H},5\text{-H}}$ = 7.0 Hz, 1 H, 4-H), 1.93 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 0.88 (s, 9 H, 3 × CH_3), 0.10 (s, 3 H, CH_3), 0.07 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.2 (CO), 162.7 (CO), 143.6 (C-2), 140.0 (Cq), 128.6 (Ph), 128.5 (Ph), 128.3 (Ph), 127.1 (Ph), 126.8 (Ph), 110.9 (C-3), 108.4 (Cq), 78.8 (C-6), 76.0 (C-8), 70.8 (C-7), 65.3 (C-9), 54.6 (C-4), 52.2 (O*C*H_3), 50.4 (N*C*H_2Ph), 48.8 (C-5), 26.6 (*C*H_3), 26.0 [SiC(*C*H_3)$_3$], 25.2 (*C*H_3), 23.5 (NHCO*C*H_3), 18.3 (Si*C*), –3.4 (Si*C*H_3), –4.4 (Si*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 3320 (br.), 2930, 2854, 1713, 1650, 1537, 1436, 1370, 1252, 1138, 1027, 832, 776, 742, 695 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{44}N_2O_7$SiNa 549.2996; found 549.2997.

Methyl 5-Acetamido-2,6-anhydro-4-[(benzyl)(methyl)amino]-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (34): The reaction was carried out as described under General Procedure (B) at 80 °C for 15 h on **8** (56 mg, 100 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (20 mg, 20 μmol), dppb (34 mg, 80 μmol), *N*-methylbenzylamine (50 μL, 200 μmol), and NEt_3 (100 μL, 700 μmol) in CH_2Cl_2 (1 mL). Purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 99:1 to 98:2) afforded **33** (47 mg, 83%); m.p. 95–97 °C. $[\alpha]_D^{25}$ = +59.8 (*c* = 0.65 in THF). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.33–7.27 (m, 5 H, Ph), 6.14 (s, 1 H, 3-H), 5.31 (br. s, 1 H, N*H*), 4.36 (d, $^3J_{6\text{-H},5\text{-H}}$ = 7.0 Hz, 1 H, 6-H), 4.29 (q, $^3J_{8\text{-H},7\text{-H}}$ = $^3J_{8\text{-H},9\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = 6.5 Hz, 1 H, 8-H), 4.14 (d, $^3J_{7\text{-H},8\text{-H}}$ = 6.5 Hz, 1 H, 7-H), 4.12 (dd, $^3J_{9\text{-H},8\text{-H}}$ = 6.5, $^2J_{9\text{-H},9'\text{-H}}$ = 8.0 Hz, 1 H, 9-H), 3.99 (dd, $^3J_{9\text{-H},8\text{-H}}$ = 6.5, $^2J_{9\text{-H},9'\text{-H}}$ = 8.0 Hz, 1 H, 9-H), 3.97–3.91 (m, 1 H, 5-H), 3.84–3.74 (m, 4 H, NCH_2Ph, O*C*H_3), 3.72–3.66 (m, 1 H, 4-H), 3.59 (d, $^2J_{H,H}$ = 13.0 Hz,1 H, NCH_2Ph), 2.25 (s, 3 H, CH_3), 1.94 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 0.87 (s, 9 H, 3 × CH_3), 0.11 (s, 3 H, CH_3), 0.10 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.0 (*C*O), 162.4 (*C*O), 145.5 (C-2), 139.2 (Cq), 128.7 (Ph), 128.4 (Ph), 127.2 (Ph), 109.0 (Cq), 108.3 (C-3), 78.2 (C-8), 76.3 (C-6), 71.1 (C-7), 65.8 (C-9), 59.3 (C-4), 58.6 (N*C*H_2Ph), 52.1 (O*C*H_3), 46.6 (C-5), 37.7 (N*C*H_3), 26.6 (*C*H_3), 26.0 [SiC(*C*H_3)$_3$], 25.0 (*C*H_3), 23.7 (NCO*C*H_3), –3.1 (Si*C*H_3), 18.5 (Si*C*), –4.1 (Si*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 2927, 2854, 1736, 1650, 1547, 1454, 1369, 1250, 1133, 1071, 832, 776, 741, 697 cm^{-1}. HRMS (ESI): calcd. for $C_{29}H_{47}N_2O_7$Si 563.3152; found: 563.3156. $C_{29}H_{46}N_2O_7$Si (562.77): calcd. C 61.89, H 8.24, N 4.98; found C 62.19, H 8.45, N 4.31.

Methyl 5-Acetamido-2,6-anhydro-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-4-[4-(hex-5-ynyl)piperazin-1-yl]-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (35): The reaction was carried out as described under General Procedure (B) at 80 °C for 15 h on **8** (22 mg, 40 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (8 mg, 8 μmol), dppb (13 mg, 32 μmol), **26** (13 mg, 80 μmol), and NEt_3 (40 μL,

280 μmol) in CH_2Cl_2 (0.8 mL). Purification by flash column chromatography on silica gel (heptane/EtOAc/NEt_3, 6:4:0.15) afforded **35** (15.2 mg, 63%); m.p. 55–56 °C. $[\alpha]_D^{25}$ = +53.2 (*c* = 0.9 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.08 (d, $^3J_{3\text{-H},4\text{-H}}$ = 3.0 Hz 1 H, 3-H), 5.52 (d, $^3J_{NH,5\text{-H}}$ = 7.0 Hz, 1 H, N*H*), 4.36–4.31 (m, 1 H, 8-H), 4.31–4.26 (m, 1 H, 7-H), 4.24–4.18 (m, 1 H, 6-H), 4.01 (t, $^3J_{9\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 7.0 Hz, 1 H, 9-H), 3.98–3.92 (m, 1 H, 5-H), 3.91 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9'\text{-H},9\text{-H}}$ = 7.0 Hz, 1 H, 9′-H), 3.76 (s, 3 H, OCH_3), 3.44–3.40 (m, 1 H, 4-H), 2.75–2.62 (m, 4 H, NCH_2), 2.52–2.39 (m, 4 H, NCH_2), 2.38–2.32 (m, 2 H, CH_2), 2.24–2.20 (m, 2 H, CH_2), 1.95 (s, 3 H, CH_3), 1.91 (s, 1 H, C*H*-alkyne), 1.72–1.48 (m, 6 H, CH_2), 1.40 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3), 0.88 (s, 9 H, CH_3), 0.09 (s, 3 H, CH_3), 0.06 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.0 (*C*O), 162.4 (*C*O), 144.3 (C-2), 108.7 (Cq), 108.3 (C-3), 84.3 (*C*-alkyne), 79.1 (C-6), 76.1 (C-8), 70.0 (C-7), 68.5 (*C*H-alkyne), 64.8 (C-9), 60.2 (C-4), 58.0 (*C*H_2), 53.5 (*C*H_2), 52.2 (O*C*H_3), 49.4 (*C*H_2), 45.9 (C-5), 26.5 (*C*H_3), 26.4 (*C*H_2), 26.0 (*C*H_3), 25.9 (*C*H_2), 25.4 (*C*H_3), 23.5 (NHCO*C*H_3), 18.3 (Si*C*, *C*H_2), –3.0 (Si*C*H_3), –4.5 (Si*C*H_3) ppm. IR (neat): ṽ = 3268, 2930, 1731, 1650, 1436, 1369, 1251, 1119, 1070, 1006, 833, 776, 695 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{54}N_3O_7Si$ 608.3731; found 608.3730.

Methyl 5-Acetamido-2,6-anhydro-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-4-morpholino-D-*glycero*-D-*galacto*-non-2-enoate (36): The reaction was carried out as described under General Procedure (B) at 80 °C for 15 h on **8** (113 mg, 200 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (40 mg, 40 μmol), dppb (68 mg, 100 μmol), morpholine (53 μL, 460 μmol), and NEt_3 (70 μL, 500 μmol) in CH_2Cl_2 (1.5 mL). Purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 99:1 to 98:2) afforded **36** (98 mg, 93%); m.p. 61–63 °C. $[\alpha]_D^{25}$ = +45.8 (*c* = 1.5 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.07 (d, $J_{3,4}$ = 3.6 Hz, 1 H, 3-H), 5.46 (d, $^3J_{NH,5}$ = 7.2 Hz, 1 H, N*H*), 4.38–4.24 (m, 3 H, 6-H, 7-H, 8-H), 4.07 (q, $^3J_{5\text{-H},6\text{-H}}$ = $^3J_{5\text{-H},NH}$ = $^3J_{5\text{-H},4\text{-H}}$ = 7.2 Hz, 1 H, 5-H), 4.06 (t, $^3J_{9\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 7.3 Hz, 1 H, 9-H), 3.95 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9'\text{-H},9\text{-H}}$ = 7.3 Hz, 1 H, 9′-H), 3.81 (s, 3 H, OCH_3), 3.72–3.68 (m, 4 H, 2×CH_2), 3.34 (dd, $^3J_{4\text{-H},3\text{-H}}$ = 3.6, $^3J_{4\text{-H},5\text{-H}}$ = 7.2 Hz, 1 H, 4-H), 2.76–2.58 (m, 4 H, 2×CH_2), 1.96 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3), 0.87 (s, 9 H, 3×CH_3), 0.08 (s, 3 H, CH_3), 0.04 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.1 (*C*O), 162.5 (*C*O), 144.9 (C-2), 108.6 (Cq), 108.1 (C-3), 79.2 (C-8), 76.2 (C-6), 70.5 (C-7), 67.5 (*C*H_2O), 65.2 (C-9), 61.3 (C-4), 52.4 (O*C*H_3), 50.2 (*C*H_2N), 45.6 (C-5), 26.8 (CH_3), 26.2 [SiC(*C*H_3)$_3$], 25.4 (CH_3), 23.7 (NHCO*C*H_3), 18.6 (Si*C*), –3.1 (Si*C*H_3), –4.2 (Si*C*H_3) ppm. IR (neat): ṽ = 2929, 2854, 1731, 1650, 1537, 1437, 1369, 1250, 1152, 1114, 1004, 832, 776, 692 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{44}N_2O_8SiNa$ 551.2765; found 551.2767. $C_{25}H_{44}N_2O_8Si$ (528.71): calcd. C 56.79, H 8.39, N 5.30; found C 56.67, H 8.51, N 5.07.

Methyl 5-Acetamido-2,6-anhydro-7-*O*-(*tert*-butyldimethylsilyl)-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-phenyl-D-*glycero*-D-*galacto*-non-2-enoate (37): The reaction was carried out as described under General Procedure (B) at 80 °C for 15 h on **8** (22 mg, 40 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (8 mg, 8 μmol), dppb (15 mg, 32 μmol), phenol (10 μL, 100 μmol), and Cs_2CO_3 (26 mg, 80 μmol) in CH_2Cl_2 (0.5 mL). Purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 99.5:0.5 to 99:1) afforded **37** (19 mg, 88%); m.p. 87–89 °C. $[\alpha]_D^{25}$ = +62.0 (*c* = 0.9 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.28 (dd, $^3J_{H,H}$ = 7.2, $^3J_{H,H}$ = 7.2 Hz, 2 H, 8.7 Hz, Ph), 7.02–6.95 (m, 3 H, Ph), 6.16 (d, $J_{3\text{-H},4\text{-H}}$ = 3.9 Hz, 1 H, 3-H), 5.72 (d, $^3J_{NH,5\text{-H}}$ = 6.0 Hz, 1 H, N*H*), 5.19 (dd, $^3J_{4\text{-H},3\text{-H}}$ = 3.9, $^3J_{4\text{-H},5\text{-H}}$ = 6.0 Hz, 1 H, 4-H), 4.55 (t, $^3J_{6\text{-H},5\text{-H}}$ = $^3J_{6\text{-H},7\text{-H}}$ = 6.0 Hz, 1 H, 6-H), 4.38 (dd, $^3J_{7\text{-H},8\text{-H}}$ = 3.9, $^3J_{7\text{-H},6\text{-H}}$ = 6.0 Hz, 1 H, 7-H), 4.21 (ddd, $^3J_{8\text{-H},7\text{-H}}$ = 3.9, $^3J_{8\text{-H},9\text{-H}}$ = 6.6, $^3J_{8\text{-H},9'\text{-H}}$ = 7.8 Hz, 1 H, 8-H), 4.15 (q, $^3J_{5\text{-H},6\text{-H}}$ = $^3J_{5\text{-H},NH}$ = $^3J_{5\text{-H},4\text{-H}}$ = 6.0 Hz, 1 H, 5-H), 3.96 (dd, $^3J_{9\text{-H},8\text{-H}}$ = 6.6, $^2J_{9\text{-H},9'\text{-H}}$ = 7.8 Hz, 1 H, 9-H), 3.93 (t, $^2J_{9'\text{-H},9\text{-H}}$ = $^3J_{9'\text{-H},8\text{-H}}$ = 7.8 Hz, 1 H, 9′-H), 3.82 (s, 3 H, OCH_3), 1.93 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 0.90 (s, 9 H, 3×CH_3), 0.11 (s, 3 H, CH_3), 0.06 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.2 (*C*O), 162.4 (*C*O), 156.9 (Ph), 144.5 (C-2), 129.8 (Ph), 121.8 (Ph), 115.7 (Ph), 108.4 (Cq), 106.9 (C-3), 79.1 (C-6), 76.1 (C-8), 69.3 (C-7), 68.9 (C-4), 64.4 (C-9), 52.4 (O*C*H_3), 48.8 (C-5), 26.4 (*C*H_3), 26.0 [SiC(*C*H_3)$_3$], 25.0 (CH_3), 23.4 (NHCO*C*H_3), 18.4 (SiC), –3.4 (Si*C*H_3), –4.6 (Si*C*H_3) ppm. IR (neat): ṽ = 2928, 2854, 1731, 1705, 1650, 1537, 1370, 1251, 1219, 1114, 1069, 1004, 834, 776, 691 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{41}NO_8SiNa$ 558.2499; found 558.2491. $C_{27}H_{41}NO_8Si$ (535.70): calcd. C 60.54, H 7.71, N 2.61; found C 60.35, H 7.82, N 2.51.

Methyl 5-Acetamido-2,6-anhydro-7-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(3-cyanophenyl)-3,5-dideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (38): The reaction was carried out as described under General Procedure (B) at 70 °C for 8 h on **8** (56 mg, 100 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (20 mg, 20 μmol), dppb (34 mg, 40 μmol), phenol (30 mg, 250 μmol), and Cs_2CO_3 (65 mg, 200 μmol) in CH_2Cl_2 (1 mL). Purification by flash column chromatography on silica gel (heptane/EtOAc, 8:2 to 4:6) afforded **38** (34 mg, 61%); m.p. 74–76 °C. $[\alpha]_D^{25}$ = +79.8 (*c* = 1.3 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.39 (t, $^3J_{H,H}$ = 8.0 Hz, 1 H, Ph), 7.35–7.25 (m, 3 H, Ph), 6.05 (d, $^3J_{3\text{-H},4\text{-H}}$ = 4.5 Hz, 1 H, 3-H), 5.72 (d, $^3J_{NH,5\text{-H}}$ = 7.0 Hz, 1 H, N*H*), 5.18 (t, $^3J_{4\text{-H},3\text{-H}}$ = $^3J_{4\text{-H},5\text{-H}}$ = 4.5 Hz, 1 H, 4-H), 4.50 (t, $^3J_{6\text{-H},5\text{-H}}$ = $^3J_{6\text{-H},7\text{-H}}$ = 5.0 Hz, 1 H, 6-H), 4.32 (t, $^3J_{7\text{-H},6\text{-H}}$ = $^3J_{7\text{-H},8\text{-H}}$ = 5.0 Hz, 1 H, 7-H), 4.15–4.08 (m, 1 H, 5-H, 8-H), 3.94 (t, $^3J_{9\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 7.5 Hz, 1 H, 9-H), 3.87 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9'\text{-H},9\text{-H}}$ = 7.5 Hz, 1 H, 9′-H), 3.78 (s, 3 H, OCH_3), 1.94 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.17 (s, 3 H, CH_3), 0.99 (s, 9 H, 3×CH_3), 0.11 (s, 3 H, CH_3), 0.04 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 170.3 (*C*O), 162.1 (*C*O), 157.1 (Cq-Ph), 145.0 (C-2), 130.8 (Ph), 125.4 (Ph), 120.0 (Ph), 119.4 (Ph), 118.3 (*C*N), 113.7 (Cq-Ph), 108.6 (Cq), 105.6 (C-3), 79.0 (C-6), 76.1 (C-8), 69.4 (C-7, C-4), 64.7 (C-9), 52.5 (O*C*H_3), 48.6 (C-5), 26.3 (*C*H_3), 26.0 [SiC(*C*H_3)$_3$], 25.0 (CH_3), 23.4 (NHCO*C*H_3), 18.4 (SiC), –3.4 (Si*C*H_3), –4.5 (Si*C*H_3) ppm. IR (neat): ṽ = 2931, 2231, 1735, 1654, 1578, 1541, 1480, 1432, 1370, 1248, 1127, 1057, 1013, 834, 777, 681 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{40}N_2O_8SiNa$ [M + Na]$^+$ 583.2452; found 583.2451. $C_{28}H_{40}N_2O_8Si$ (560.71): calcd. C 59.98, H 7.19, N 5.00; found C 59.99, H 7.13, N 4.75.

Methyl 5-Acetamido-2,6-anhydro-4-*O*-(3-{[(*tert*-butoxycarbonyl)-amino]methyl}phenyl)-7-*O*-(*tert*-butyldimethylsilyl)-3,5-dideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-2-enoate (39): The reaction was carried out as described under General Procedure (B) at 70 °C for 4 h on **8** (35 mg, 62 μmol) with $Pd_2(dba)_3$·$CHCl_3$ (13 mg, 12 μmol), dppb (11 mg, 25 μmol), phenol (42 mg, 186 μmol), and Cs_2CO_3 (40 mg, 124 μmol) in CH_2Cl_2 (0.6 mL). Purification by flash column chromatography on silica gel (heptane/EtOAc, 6:4 to 4:6) afforded **39** (30 mg, 73%); m.p. 58–60 °C. $[\alpha]_D^{25}$ = +54.7 (*c* = 0.7 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.23–7.21 (m, 1 H, Ph), 6.93–6.86 (m, 3 H, Ph), 6.01 (d, $^3J_{3\text{-H},4\text{-H}}$ = 4.5 Hz, 1 H, 3-H), 5.72 (d, $^3J_{NH,5\text{-H}}$ = 7.0 Hz, 1 H, N*H*), 5.13 (t, $^3J_{4\text{-H},3\text{-H}}$ = $^3J_{4\text{-H},5\text{-H}}$ = 4.5 Hz, 1 H, 4-H), 4.99–4.88 (m, 1 H, N*H*), 4.49 (t, $^3J_{6\text{-H},5\text{-H}}$ = $^3J_{6\text{-H},7\text{-H}}$ = 5.0 Hz, 1 H, 6-H), 4.35 (t, $^3J_{7\text{-H},6\text{-H}}$ = $^3J_{7\text{-H},8\text{-H}}$ = 5.0 Hz, 1 H, 7-H), 4.20–4.13 (m, 2 H, CH_2NHBoc), 4.09–3.94 (m, 1 H, 5-H, 8-H), 3.94 (t, $^3J_{9\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 7.5 Hz, 1 H, 9-H), 3.87 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9'\text{-H},9\text{-H}}$ = 7.5 Hz, 1 H, 9′-H), 3.77 (s, 3 H, OCH_3), 1.92 (s, 3 H, CH_3), 1.43 [s, 9 H, C(CH_3)$_3$], 1.34 (s,

3 H, CH_3), 1.17 (s, 3 H, CH_3), 0.89 (s, 9 H, 3 × CH_3), 0.11 (s, 3 H, CH_3), 0.06 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 170.5 (*C*O), 162.6 (*C*O), 157.1 (Cq-Ph), 144.6 (C-2), 130.0 (Ph), 120.7 (Ph), 114.3 (Ph), 118.3 (Cq-Ph), 108.4 (Cq), 106.7 (C-3), 79.0 (C-6), 76.1 (C-8), 69.3 and 69.0 (C-7, C-4), 64.5 (C-9), 52.4 (O*C*H$_3$), 48.7 (C-5), 44.5 [*C*(CH$_3$)$_3$], 29.7 (*C*H$_2$NH), 28.4 [C(*C*H$_3$)$_3$], 26.4 (*C*H$_3$), 26.0 [SiC(*C*H$_3$)$_3$], 25.0 (CH$_3$), 23.4 (NHCO*C*H$_3$), 18.4 (SiC), –3.4 (Si*C*H$_3$), –4.5 (Si*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 3318, 2952, 2929, 2855, 1713, 1693, 1681, 1659, 1537, 1530, 1366, 1249, 1159, 1127, 1024, 835, 776 cm^{-1}. HRMS (ESI): calcd. for $C_{33}H_{52}N_2O_{10}SiNa$ [M + Na]$^+$ 687.3259; found 687.3289.

Chloro-Bridged Dimer 22: Degassed THF (1.2 mL) was added to a mixture of **8** (112 mg, 0.199 mmol), LiCl (34 mg, 0.8 mmol), and Pd(dba)$_2$ (103 mg, 0.179 mmol). After 4 h at room temp., the reaction mixture was concentrated and purified by flash chromatography on silica gel (heptane/AcOEt, 7:3 to 0:1) followed by recrystallization (Et$_2$O/pentane, 1:2) to afford **22** as a yellow solid (76 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.87 (br. s, 1 H, N*H*), 5.79 (d, $^3J_{3\text{-H},4\text{-H}}$ = 6.5 Hz, 1 H, 3-H), 4.95 (t, $^3J_{4\text{-H},3\text{-H}}$ = $^3J_{4\text{-H},5\text{-H}}$ = 6.5 Hz, 1 H, 4-H), 3.95–3.90 (m, 3 H, 6-H, 7-H, 8-H), 3.87 (dd, $^3J_{5\text{-H},4\text{-H}}$ = 6.5, $^3J_{5\text{-H},6\text{-H}}$ = 11.0 Hz, 1 H, 5-H), 3.84 (t, $^2J_{9\text{-H},9'\text{-H}}$ = $^3J_{9\text{-H},8\text{-H}}$ = 6.5 Hz, 1 H, 9-H), 3.71 (s, 3 H, CO$_2$CH_3), 3.58 (t, $^2J_{9'\text{-H},9\text{-H}}$ = $^3J_{9'\text{-H},8\text{-H}}$ = 6.5 Hz, 1 H, 9′-H), 1.97 (s, 3 H, COCH_3), 1.23 (s, 3 H, OCH_3), 1.15 (s, 3 H, OCH_3), 0.72 [s, 9 H, SiC(CH_3)$_3$], 0.01, –0.0 (s, 6 H, SiCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 170.5 (*C*OCH$_3$), 164.1 (*C*O$_2$CH$_3$), 108.7 [*C*(CH$_3$)$_2$], 107.7 (C-2), 88.4 (C-3), 82.2 (C-5), 76.2 (C-8), 75.2 (C-7), 70.3 (C-4), 65.8 (C-9), 53.2 (CO$_2$*C*H$_3$), 48.9 (C-6), 26.4 [C(*C*H$_3$)$_2$], 25.9 [SiC(*C*H$_3$)$_3$], 25.0 [C(*C*H$_3$)$_2$], 22.6 (CO*C*H$_3$), 18.1 [Si*C*(CH$_3$)$_3$], –3.3, –4.4 [Si(*C*H$_3$)$_2$] ppm. IR (neat): $\tilde{\nu}$ = 2931, 1750, 1733, 1664, 1491, 1304, 1256, 1076, 1041, 835, 808 cm^{-1}. MS (ESI): *m*/*z* = 1190.2 (73) [M + Na]$^+$, 1191.2 (100) [M + Na]$^+$, 1192.2 (46) [M + Na]$^+$, 1193.2 (73) [M + Na]$^+$. HRMS (ESI): calcd. for $C_{42}H_{72}{}^{35}Cl_2N_2O_{14}{}^{106}Pd^{108}PdSi_2Na$ 1191.1871; found 1191.1914.

Complex 23: A solution of **20** (5.1 mg, 4.4 μmol) and PPh$_3$ (2.3 mg, 8.7 μmol) in CH_2Cl_2 (0.5 mL) was stirred at room temp. for 1 h; AgOBz (2 mg, 8.7 μmol) was then added, and, after stirring for further 1 h, the reaction mixture was filtered through a pad of Celite and concentrated. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 8.90 (d, $^3J_{\text{NH},5\text{-H}}$ = 9.0 Hz, 1 H, N*H*), 7.45–6.92 (m, 20 H, Ph), 5.86 (d, $^3J_{3\text{-H},4\text{-H}}$ = 8.0 Hz, 1 H, 3-H), 5.47 (td, *J* = 3.0, $^3J_{4\text{-H},3\text{-H}}$ = $^3J_{4\text{-H},5\text{-H}}$ = 8.0 Hz, 1 H, 4-H), 4.30 (d, ^3J = 8.5 Hz, 1 H, 6-H), 4.20–4.12 (m, 1 H, 5-H), 3.90 (q, $^3J_{8\text{-H},7\text{-H}}$ = $^3J_{8\text{-H},9\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = 5.5 Hz, 1 H, 8-H), 3.77–3.72 (m, 2 H, 7-H, 9-H), 3.57–3.50 (m, 1 H, 9′-H), 2.67 (m, 3 H, CO$_2$CH_3), 1.72 (s, 3 H, COCH_3), 1.11 (s, 3 H, OCH_3), 1.07 (s, 3 H, OCH_3), 0.61 [s, 9 H, SiC(CH_3)$_3$], –0.01, –0.15 (s, 6 H, SiCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 171.0 (*C*OCH$_3$), 166.9 (*C*O$_2$CH$_3$), 134.0, 133.9, 132.2, 132.1, 132.0, 130.6, 130.0, 129.6, 129.5, 128.6, 128.5, 128.4, 127.5, 108.3 [*C*(CH$_3$)$_2$], 96.2 (d, *J* = 5 Hz, C-2), 95.4 (d, *J* = 4 Hz, C-3), 94.2 (d, *J* = 27.5 Hz, C-4), 81.4 (C-6), 76.8 (C-8), 71.5 (C-7), 66.1 (C-9), 52.0 (CO$_2$*C*H$_3$), 44.6 (d, *J* = 5 Hz, C-5), 26.6 [C(*C*H$_3$)$_2$], 26.1 [SiC(*C*H$_3$)$_3$], 25.6 [C(*C*H$_3$)$_2$], 25.5 [C(*C*H$_3$)$_2$], 23.1 (CO*C*H$_3$), 18.4 [Si*C*(CH$_3$)$_3$], –3.5, –4.2 [Si(*C*H$_3$)$_2$] ppm. ^{31}P NMR (202 MHz, $CDCl_3$): δ = 25.9 ppm. MS (ESI): *m*/*z* = 954.2 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{46}H_{56}NO_9P^{106}PdSiNa$ 954.2394; found 954.2384.

Complex 24: A solution of **19** (4.8 mg, 4.1 μmol) and PPh$_3$ (2.2 mg, 8.2 μmol) in $CDCl_3$ (0.5 mL) was stirred at room temp. for 1 h. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 8.02 (d, $^3J_{\text{NH},5\text{-H}}$ = 8.4 Hz, 1 H, N*H*), 7.80–7.35 (m, 15 H, Ph), 6.02 (d, $^3J_{3\text{-H},4\text{-H}}$ = 8.0 Hz, 1 H, 3-H), 5.55–5.45 (m, 1 H, 4-H), 4.51–4.38 (m, 1 H, 5-H), 4.31 (d, $^3J_{5\text{-H},6\text{-H}}$ = 7.0 Hz, 1 H, 6-H), 4.13 (q, $^3J_{8\text{-H},7\text{-H}}$ = $^3J_{8\text{-H},9\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = 6.5 Hz, 1 H, 8-H), 4.08–3.98 (m, 2 H, 7-H, 9-H), 3.83 (t, $^2J_{9'\text{-H},9\text{-H}}$ = $^3J_{9'\text{-H},8\text{-H}}$ = 6.5 Hz, 1 H, 9′-H), 2.99 (m, 3 H, CO$_2$CH_3), 2.03 (s, 3 H, COCH_3), 1.34 (s, 6 H, CH_3), 0.88 [s, 9 H, SiC(CH_3)$_3$], 0.20, 0.13 (s, 6 H, SiCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 170.5 (*C*OCH$_3$), 165.3 (*C*O$_2$CH$_3$), 134.7, 134.0, 130.8, 130.6, 130.4, 128.6, 128.4, 108.6 [*C*(CH$_3$)$_2$], 105.9 (d, $^2J_{\text{P,C-2}}$ = 6 Hz, C-2), 95.4 (d, $^2J_{\text{P,C-3}}$ = 4 Hz, C-3), 86.0 (d, $^2J_{\text{P,C-4}}$ = 31 Hz, C-4), 81.7 (C-6), 76.2 (C-8), 73.3 (C-7), 66.4 (C-9), 52.2 (CO$_2$*C*H$_3$), 46.7 (d, $^3J_{\text{P,C-5}}$ = 5 Hz, C-5), 26.6 [C(*C*H$_3$)$_2$], 26.0 [SiC(*C*H$_3$)$_3$], 25.5 [C(*C*H$_3$)$_2$], 22.9 (CO*C*H$_3$), 18.3 [Si*C*(CH$_3$)$_3$], –3.6, –4.0 [Si(*C*H$_3$)$_2$] ppm. ^{31}P NMR (202 MHz, $CDCl_3$): δ = 22.3 ppm. HRMS (ESI): calcd. for $C_{39}H_{51}{}^{37}ClNO_7P^{106}PdSiNa$ [M + Na]$^+$ 870.1764; found 870.1747.

Complex 25: dppb (6.5 mg, 15 μmol) and AgOTf (2.9 mg, 11.3 μmol) were added successively to a solution of **20** (6 mg, 5.1 μmol) in $CDCl_3$ (0.5 mL). After 1 h at room temp., the reaction mixture was filtered through a pad of Celite. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.80–7.15 (m, 20 H, Ph), 7.03 (d, $^3J_{\text{NH},5\text{-H}}$ = 7.0 Hz, 1 H, N*H*), 5.74 (d, $^3J_{3\text{-H},4\text{-H}}$ = 7.0 Hz, 1 H, 3-H), 5.05–4.95 (m, 1 H, 4-H), 4.30–4.20 (m, 1 H, 5-H), 4.10 (dd, $^3J_{6\text{-H},7\text{-H}}$ = 3.0, $^3J_{6\text{-H},5\text{-H}}$ = 10.5 Hz, 1 H, 6-H), 3.94 (br. s, 1 H, 7-H), 3.84 (td, $^3J_{8\text{-H},7\text{-H}}$ = 2.0, $^3J_{8\text{-H},9\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = 8.0 Hz, 1 H, 8-H), 3.46 (t, $^3J_{9\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 8.0 Hz, 1 H, 9′-H), 3.38–3.31 (m, 4 H, 9′-H, CO$_2$CH_3), 3.29–3.20 (m, 1 H, PCH_2), 3.17–3.07 (m, 1 H, PCH_2), 2.66–2.55 (m, 1 H, PCH_2), 2.32–2.22 (m, 1 H, PCH_2), 1.98–1.88 (m, 1 H, CH_2), 1.75–1.65 (m, 1 H, CH_2), 1.53 (s, 3 H, COCH_3), 1.45–1.25 (m, 8 H, 2 × OCH_3, 2 × CH_2), 0.76 [s, 9 H, SiC(CH_3)$_3$], 0.00, –0.09 (s, 6 H, SiCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 171.5 (*C*OCH$_3$), 164.5 (d, $^3J_{\text{P,C-1}}$ = 5 Hz, *C*O$_2$CH$_3$), 135.1, 134.8, 134.7, 134.6, 133.8, 133.5, 133.3, 133.2, 133.1, 133.0, 132.8, 132.6, 132.5, 132.4, 132.3, 132.1, 132.0, 131.8, 131.7, 131.6, 131.4, 130.6, 130.9, 130.8, 130.7, 130.4, 130.1, 129.5, 129.4, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 127.7, 127.3, 120.4 (m, C-2), 107.3 [*C*(CH$_3$)$_2$], 94.9 (m, C-3), 78.9 (C-4, C-6), 77.5 (C-8), 69.0 (C-7), 64.3 (C-9), 52.7 (CO$_2$*C*H$_3$), 45.9 (m, C-5), 26.4 [C(*C*H$_3$)$_2$], 26.3 (d, $^1J_{\text{P,C}}$ = 24 Hz, P*C*H$_2$), 26.1 [SiC(*C*H$_3$)$_3$], 25.5 [C(*C*H$_3$)$_2$], 25.3 (d, $^1J_{\text{P,C}}$ = 22 Hz, P*C*H$_2$), 23.3 (CO*C*H$_3$), 22.9 (d, $^2J_{\text{P,C}}$ = 4 Hz, *C*H$_2$), 22.0 (d, $^2J_{\text{P,C}}$ = 6 Hz, *C*H$_2$), 18.3 [Si*C*(CH$_3$)$_3$], –3.0, –5.5 [Si(*C*H$_3$)$_2$] ppm. ^{31}P NMR (202 MHz, $CDCl_3$, 25 °C): δ = 25.5 (d, *J* = 61.5 Hz), 11.1 (d, *J* = 61.5 Hz) ppm. MS (ESI): *m*/*z* = 974.3 [M + H]$^+$. HRMS (ESI): calcd. for $C_{49}H_{64}NO_7P_2{}^{106}PdSi$ 974.2962; found 974.2885.

5-Acetamido-2,6-anhydro-3,4,5-trideoxy-4-morpholino-D-*glycero*-D-*galacto*-non-2-enoate (40): TBAF (1 M in THF, 240 μL) was added to a solution of **36** (43 mg, 81 μmol) in THF (1 mL), and the mixture was stirred at room temp. for 2 h. After evaporation of the solvents, the residue was purified by flash column chromatography on silica gel (EtOAc/EtOH, 98:2 to 95:5) to give the expected compound **35** (30 mg, 90%). This was then diluted with MeOH (2 mL) and treated with NaOH (1N, 200 μL) at room temp. for 24 h. The mixture was neutralized with Dowex H$^+$ and filtered, and the solvents were removed under reduced pressure. AcOH (80% in water, 0.5 mL) was added to the crude residue, and the mixture was stirred at room temp. for 3 d. After evaporation of the solvents, the residue was chromatographed on Sephadex LH20 (MeOH) to give the expected **40** as a white solid (23 mg, 91%); m.p. 224–226 °C. $[\alpha]_D^{25}$ = +31.5 (*c* = 1.0 in MeOH). ^{1}H NMR (500 MHz, D_2O, 25 °C): δ = 5.72 (d, $^3J_{3\text{-H},4\text{-H}}$ = 2.5 Hz, 1 H, 3-H), 4.34 (t, $^3J_{5\text{-H},6\text{-H}}$ = $^3J_{5\text{-H},4\text{-H}}$ = 9.5 Hz, 1 H, 5-H), 4.14 (d, $^3J_{6\text{-H},5\text{-H}}$ = 9.5 Hz, 1 H, 6-H), 3.88 (ddd, $^3J_{8\text{-H},9\text{-H}}$ = 2.5, $^3J_{8\text{-H},9'\text{-H}}$ = 6.0, $^3J_{8\text{-H},7\text{-H}}$ = 9.5 Hz,1 H, 8-H), 3.82 (dd, $^3J_{9\text{-H},8\text{-H}}$ = 2.5, $^2J_{9\text{-H},9'\text{-H}}$ = 12.0 Hz, 1 H, 9-H), 3.78–3.68 (m, 4 H, CH_2N), 3.64 (dd, $^3J_{4\text{-H},3\text{-H}}$ = 2.5, $^3J_{4\text{-H},5\text{-H}}$ = 9.5 Hz, 1 H, 4-H), 3.59 (dd, $^3J_{9'\text{-H},8\text{-H}}$ = 6.0, $^2J_{9'\text{-H},9\text{-H}}$ = 12.0 Hz, 1 H, 9′-H),

3.57 (d, $^3J_{7\text{-H},8\text{-H}}$ = 9.5 Hz, 1 H, 7-H), 2.89–2.81 (m, 2 H, CH_2O), 2.77–2.68 (m, 2 H, CH_2O), 1.99 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, D_2O, 25 °C): δ = 174.2 (*C*O), 150.3 (C-2), 102.9 (C-3), 75.9 (C-6), 69.9 (C-8), 68.6 (C-7), 66.2 (*C*H_2N), 63.1 (C-9), 61.9 (C-4), 48.4 (*C*H_2O), 42.9 (C-5), 22.2 (*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 3257, 2923, 1556, 1404, 1325, 1288, 1162, 1108, 1068, 1041, 999, 935, 856, 772, 651 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{23}N_2O_8$ [M – H]$^+$ 359.1454; found 359.1454.

Methyl 5-Acetamido-2,6-anhydro-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-4-[(methoxycarbonyl)methyl]-D-*glycero*-D-*galacto*-non-2-enoate (41): H_2O (3 μL, 166 μmol) and NaCl (4 mg, 68 μmol) were added to a solution of **19** (38 mg, 66 μmol) in DMSO (136 mL), and the mixture was heated at 150 °C for 3 h. After addition of water (1 mL), the aqueous phase was extracted with EtOAc (3 × 2 mL), and the combined organic phases were washed with brine (5 mL) and dried (Na_2SO_4). After filtration, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel (heptane/EtOAc, 45:55) to give **41** as an amorphous solid (21 mg, 62%). $[\alpha]_D^{25}$ = +19.1 (*c* = 1.3 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 5.76 (d, $J_{3,4}$ = 2.5 Hz, 1 H, 3-H), 5.72 (d, $^3J_{\text{NH},5\text{-H}}$ = 9.0 Hz, 1 H, N*H*), 4.13 (q, $^3J_{8\text{-H},9\text{-H}}$ = $^3J_{8\text{-H},9'\text{-H}}$ = $^3J_{8\text{-H},7\text{-H}}$ = 6.0 Hz, 1 H, 8-H), 3.96 (dd, $^3J_{6\text{-H},5\text{-H}}$ = 9.0, $^3J_{6\text{-H},7\text{-H}}$ = 1.0 Hz, 1 H, 6-H), 3.95–3.90 (m, 2 H, 7-H, 9-H), 3.78 (dd, $^3J_{9'\text{-H},8\text{-H}}$ = 6.0, $^2J_{9'\text{-H},9\text{-H}}$ = 8.0 Hz, 1 H, 9′-H), 3.71 (q, $^3J_{5\text{-H},6\text{-H}}$ = $^3J_{5\text{-H,NH}}$ = $^3J_{5\text{-H},4\text{-H}}$ = 9.0 Hz, 1 H, 5-H), 3.62 (s, 3 H, OCH_3), 3.55 (s, 3 H, OCH_3), 2.86–2.82 (m, 1 H, 4-H), 2.53 (dd, $^3J_{\text{H,H}}$ = 5.0, $^2J_{\text{H,H}}$ = 16.0 Hz, 1 H, CH_2CO$_2$Me), 2.21 (dd, $^3J_{\text{H,H}}$ = 9.0, $^2J_{\text{H,H}}$ = 16.0 Hz, 1 H, CH_2CO$_2$Me), 1.84 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 0.75 (s, 9 H, 3 × CH_3), 0.01 (s, 3 H, CH_3), –0.02 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 172.5 (*C*O), 169.8 (*C*O), 162.4 (*C*O), 143.5 (C-2), 112.0 (C-3), 108.6 (Cq), 77.9 (C-6), 75.7 (C-8), 72.2 (C-7), 66.1 (C-9), 52.1 (O*C*H_3), 51.8 (O*C*H_3), 48.6 (C-5), 36.9 (*C*H_2CO$_2$Me), 36.4 (C-4), 26.7 (*C*H_3), 26.0 [SiC(*C*H_3)$_3$], 25.1 (CH_3), 23.5 (NHCO*C*H_3), 18.4 (SiC), –3.5 (Si*C*H_3), –4.1 (Si*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 2928, 2854, 1731, 1658, 1538, 1251, 1159, 1132, 1069, 830, 776 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{41}NO_9SiNa$ 558.2448; found 538.2468.

Methyl 5-Acetamido-2,6-anhydro-2-[bis(methoxycarbonyl)methyl]-7-*O*-(*tert*-butyldimethylsilyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-nonanoate (42): A solution of **18** (21 mg, 37 μmol) and Pd/C (10 wt.-%, 10 mg) in EtOAc (1 mL) was stirred at room temp. for 24 h. After filtration, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel (DCM/MeOH, 98:2 to 93:7) to give **42** as an amorphous solid (18 mg, 86%); m.p. 62–64 °C. $[\alpha]_D^{25}$ = –2.3 (*c* = 0.5 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 5.57 (d, $^3J_{\text{NH},5\text{-H}}$ = 6.0 Hz, 1 H, N*H*), 4.16–4.09 (m, 2 H, 7-H, 8-H), 3.91 (dd, $^3J_{6\text{-H},5\text{-H}}$ = 10.5, $^3J_{6\text{-H},7\text{-H}}$ = 1.0 Hz, 1 H, 6-H), 3.86 (t, $^3J_{9\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 8.0 Hz,1 H, 9-H), 3.81 (s, 1 H, H-malonyl), 3.76 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9'\text{-H},9\text{-H}}$ = 8.0 Hz, 1 H, 9′-H), 3.73 (s, 3 H, OCH_3), 3.70 (s, 6 H, 2 × OCH_3), 3.61–3.51 (m, 1 H, 5-H), 2.39–2.32 (m, 1 H, 4-H), 2.24–2.16 (m, 2 H, 3-H), 1.89 (s, 3 H, NHCOCH_3), 1.38 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 1.27–1.20 (m, 1 H, 4′-H), 0.90 (s, 9 H, 3 × CH_3), 0.11 (s, 3 H, CH_3), 0.10 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 171.5 (*C*O), 169.6 (*C*O), 166.3 (*C*O), 107.5 (Cq), 79.1 (C-2), 76.9 (C-7), 76.8 (C-6), 71.7 (C-8), 64.2 (C-9), 59.3 (C-malonyl), 52.6 (O*C*H_3), 52.4 (O*C*H_3), 47.2 (C-5), 28.6 (C-3), 26.7 (C-4), 26.3 (*C*H_3), 26.0 [SiC(*C*H_3)$_3$], 24.9 (CH_3), 23.5 (NHCO*C*H_3), 18.2 (Si*C*), –3.9 (Si*C*H_3), –5.0 (Si*C*H_3) ppm. IR (neat): $\tilde{\nu}$ = 3283, 2953, 1736, 1648, 1546, 1436, 1368, 1307, 1250, 1210, 1158, 1094, 1026, 830, 778 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{45}NO_{11}SiNa$ [M + Na]$^+$ 558.2660; found 598.2656.

5-Acetamido-2,6-anhydro-7-*O*-(*tert*-butyldimethylsilyl)-2-(carboxymethyl)-3,4,5-trideoxy-8,9-*O*-isopropylidene-D-*glycero*-D-*galacto*-non-3-enoic Acid (43): NaOH in H_2O (1 M, 0.21 mL, 210 μmol) was added to a solution of **18** (40 mg, 70 μmol) in MeOH (1.5 mL) and the mixture was heated at 140 °C for 3 h. After addition of Dowex H^+ and filtration, the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel (EtOAc/*i*PrOH/H_2O, 22:2:1 to 10:2:1) to give **43** as a solid (25 mg, 74%); m.p. 179–181 °C. $[\alpha]_D^{25}$ = –2.7 (*c* = 0.6 in MeOH). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ = 5.99 (dd, $^4J_{3\text{-H},5\text{-H}}$ = 2.5, $^3J_{3\text{-H},4\text{-H}}$ = 10.0 Hz, 1 H, 3-H), 5.76 (dd, $^3J_{4\text{-H},5\text{-H}}$ = 1.5, $^3J_{4\text{-H},3\text{-H}}$ = 10.0 Hz, 1 H, 4-H), 4.55–4.42 (m, 2 H, 5-H, 8-H), 4.26 (br. s, 1 H, 7-H), 4.16 (t, $^3J_{9\text{-H},8\text{-H}}$ = $^2J_{9\text{-H},9'\text{-H}}$ = 8.0 Hz, 1 H, 9-H), 4.01 (d, $^3J_{6\text{-H},5\text{-H}}$ = 10.0 Hz, 1 H, 6-H), 3.97 (t, $^3J_{9'\text{-H},8\text{-H}}$ = $^2J_{9'\text{-H},9\text{-H}}$ = 8.0 Hz, 1 H, 9′-H), 2.81 (d, $^2J_{\text{H,H}}$ = 15.0 Hz, 1 H, CH_2CO$_2$H), 2.66 (d, $^2J_{\text{H,H}}$ = 15.0 Hz, 1 H, CH_2CO$_2$H), 1.95 (s, 3 H, NHCOCH_3), 1.42 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 0.94 (s, 9

Table 4. Crystallographic data for complex **22** and compound **18**.

	Complex **22**	Compound **18**
Empirical formula	$C_{42}H_{72}Cl_2N_2O_{14}Pd_2Si_2 \cdot C_4H_{10}O$	$C_{26}H_{43}NO_{11}Si$
Formula mass	1243.06	573.70
T [K]	100(1)	100(1)
λ [Å]	0.71073	0.71073
Crystal system	monoclinic	orthorhombic
Space group	$P2_1$	$P2_12_12_1$
a [Å]	11.8812(8)	9.7519(4)
b [Å]	11.9948(8)	14.8028(8)
c [Å]	20.1926(14)	21.8450(13)
β [°]	90.879(2)	90
V [Å^3]	2877.4(3)	3153.4(3)
Z	2	4
$\rho_{\text{calcd.}}$ [g cm^{-3}]	1.435	1.208
μ [mm^{-1}]	0.820	0.128
Reflections collected	39926	51453
Independent reflections	17541 (R_{int} = 4.49%)	9585 (R_{int} = 4.75%)
Final *R* indices [$I > 2\sigma(I)$]	0.0417	0.0795
Final *wR* indices [$I > 2\sigma(I)$]	0.0807	0.2071
Flack parameter	0.021(15)	0.09(3)

H, 3 × CH_3), 0.14 (s, 3 H, CH_3), 0.09 (s, 3 H, CH_3) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 173.2 (NH*C*OCH$_3$), 130.6 (C-3), 129.5 (C-4), 108.5 (Cq), 80.0 (C-8), 79.1 (C-2), 76.0 (C-6), 71.1 (C-7), 65.8 (C-9), 46.3 (*C*H$_2$CO$_2$H), 45.0 (C-5), 26.8 [SiC(*C*H$_3$)$_3$], 26.7 (*C*H$_3$), 25.0 (CH$_3$), 22.7 (NHCO*C*H$_3$), 19.4 (Si*C*), –2.8 (Si*C*H$_3$), –4.7 (Si*C*H$_3$) ppm. IR (neat): $\tilde{\nu}$ = 3266, 2922, 1556, 1404, 1325, 1287, 1162, 1108, 1067, 1042, 998, 935, 855, 772, 652 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{36}NO_9Si$ [M – H]$^+$ 486.2165; found 486.2159.

X-ray Crystallography: X-ray diffraction data (Tables 4 and 5) were collected with a Kappa X8 APPEX II Bruker diffractometer with use of graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). The temperature of the crystal was maintained at the selected value (100 K) to within an accuracy of ±1 K with the aid of a 700 series Cryostream cooling device. The data were corrected for Lorentz polarization and absorption effects. The structures were solved by direct methods with SHELXS-97[34] and refined against F^2 by full-matrix least-squares techniques with SHELXL-97[35] with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were located on a difference Fourier map and introduced into the calculations as a riding model with isotropic thermal parameters. All calculations were performed with the aid of the Crystal Structure crystallographic software package WINGX.[36] The absolute configurations were determined by refinement of the Flack[37] parameters with use of a large number of Friedel's pairs. CCDC-725899 (for **22**) and -725900 (for **18**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table 5. Selected average bond lengths [Å] for palladium complex **22**.

Pd(A)–Cl1	2.4222(8)	Pd(B)–Cl1	2.4110(8)
Pd(A)–Cl2	2.4035(8)	Pd(B)–Cl2	2.4163(8)
Pd(A)–C2(A)	2.162(3)	Pd(B)–C2(B)	2.168(3)
Pd(A)–C3(A)	2.091(3)	Pd(B)–C3(B)	2.088(3)
Pd(A)–C4(A)	2.131(3)	Pd(B)–C4(B)	2.129(3)
Pd(A)–Pd(B)	3.062(4)		

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