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The use of anhydroiminocyclitols as glycosyl donors in glycosidation reactions

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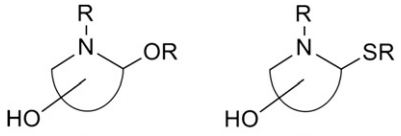
ABSTRACT

High yielding synthesis of six- and five-membered *N*-substituted iminosugar glycosides and of five-membered iminosugar thioglycosides by nucleophilic opening of both new and previously described *N*-diethoxycarbonylvinyl anhydroiminosugar derivatives (glycosyl donors) with primary alcohols, primary thiols, and thiophenol (glycosyl acceptors) is reported. The reactions are highly stereoselective, with anomeric ratios better than 4:1.

1. Introduction

In the past decade the stereoselective syntheses of highly functionalized molecules, such as natural and pharmaceutically important compounds, have been a challenge in organic chemistry.[1] Carbohydrate derivatives, due to their numerous stereogenic centers, anomeric reactivity, and conformational properties, play an important role in these syntheses, where can be considered as targets or as key chiral intermediates.[2] Particularly, iminocyclitols, also known as iminosugars, are glycosidase and glycosyltransferase inhibitors and consequently they can be useful in the treatment of metabolic disorders and inflammatory processes.[3,4] It is not surprising that this therapeutical potential has generated a huge interest in the syntheses and structural modifications of iminosugars, and many short and stereoselective routes have been reported.[5] We have described a versatile procedure to prepare five[6]-, six[7]-, and seven[8]-membered iminosugars, starting from glycosylenamines and being the key chiral intermediate an anhydroiminosugar.

The data on the preparation of iminosugar glycosides (**1**) and iminosugar thioglycosides (**2**) are limited. Multistep, low-yielding syntheses of 2-alkoxy polyhydroxypiperidines have been reported.[9,10] Six-membered iminosugar glycosides have been used as intermediates to prepare monocyclic[11–13] and bicyclic azasugars.[14] A method for the synthesis of six-membered azasugar glycosides and thioglycosides starting from 1,2-*O*-isopropylidene furanosyl derivatives has been reported by Schmidt.[15] The author has used the glycosidation reaction, with trichloroacetimidates as glycosyl donors, to prepare nojirimycin thioglycosides.[16] Hashimoto[17] has reported the first synthesis of an ethyl thioglycoside of a thiodisaccharide having one iminosugar moiety. Later, we have described[18] the synthesis of six-membered iminosugar thioglycosides starting from an anhydroiminosugar with D-*ribo* configuration.



Regarding the preparation of five-membered iminosugar glycosides, Schmidt[19] has described a multistep synthesis of a methyl iminoriboside, and we have reported[20] the preliminary data on the use of an anhydroiminocyclitol, particularly with D-*galacto* configuration, as glycosyl donor in glycosidation reactions, but only methanol was used as glycosyl acceptor. The bibliographic data on five-membered iminocyclitol derivatives having a thioalkoxy group on the pseudoanomeric carbon atom are very scarce, and limited to thioanalogues of the indolizidine alkaloid castanospermine having the sulfur atom taking part in the five-membered ring.[21]

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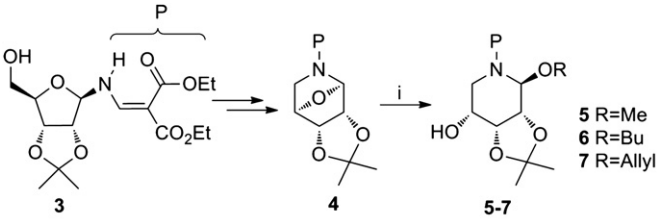
In a recent letter[22] we have communicated our preliminary results on the use of iminosugar thioglycosides as glycosyl donors in glycosidation reactions. Continuing our work on the chemistry of iminosugars,[18,23] herein we present the preparation of a new anhydroiminosugar (**13**) and the use of this type of compounds to prepare six-(**5**–**7**) and five-(**14**–**19**)-membered iminosugar glycosides, and five-membered (**21**–**27**) iminosugar thioglycosides.[24]

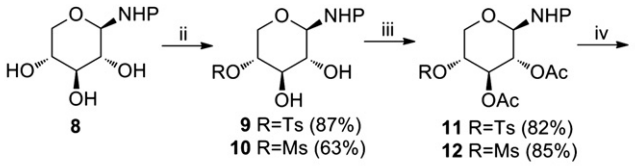
2. Results and discussion

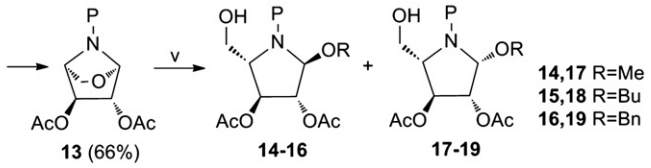
2.1. Synthesis of six- and five-membered iminosugar glycosides

The starting material to prepare the six-membered iminosugar glycosides **5**–**7** (pyranoside analogues) is the anhydroiminosugar **4**[18] (Scheme 1), which was easily prepared from the furanosylenamine **3**, using the capability of the alkoxycarbonylvinyl group to stabilize a negative charge on the nitrogen atom, and to produce an internal substitution[8] (see Fig. 3). Reaction of the glycosyl donor **4** with methanol, butanol, and allyl alcohol as glycosyl acceptors, in the presence of $BF_3{\cdot}OEt_2$ produced the corresponding iminosugar glycoside (**5**–**7**) in almost quantitative yield and only as β-anomer. Probably, the coordination of **4** with BF_3 produce an oxocation (Fig. 1) facilitating the attack of the alcohol. The stereoselectivity for the formation of the β-anomer, is due to the steric hindrance of the α-attack caused by the isopropylidene group.



Compound	5	6	7
Yield (%)	81	80	85





Compound	14	17	15	18	16	19
Yield (%)	52	34	50	34	62	20

Reagents and conditions. (i) ROH, 4 Å molecular sieves, $BF_3.OEt_2$, 0°C, 45 min; (ii) Bu_2SnO, toluene, reflux, 3h; Ts(Ms)Cl, DMAP, dioxane, rt, 4 h; (iii)Ac_2O, Py, rt, 4h; (iv) NaOMe, HMPA, 40 °C, vacuum, 40 min; (v) $BF_3.OEt_2$, ROH, 4 Å molecular sieves, rt, 1h.

Scheme 1. Synthesis of glycosides.

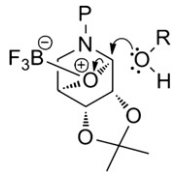


Fig. 1. Intermediate cation in the formation of **5**–**7**.

The chemical shift (see Experimental) for the resonances of H-2 and C-2 (pseudoanomeric position) in **5**–**7** and the appearance of a doublet at 2.07–2.15 ppm for the OH group support the ring opening and the formation of a new glycosidic bond. A double pulsed field gradient spin echo (DPFGSE-NOE) experiment,[25] performed on H-5, was used to assess the configuration of C-2. NOE spectra data (Fig. 2) revealed important correlations between the *endo*-methyl protons of the isopropylidene group an H-6b, and between the methyl group of the aglycone and H-6a. All data were in agreement with S-configuration for C-2.

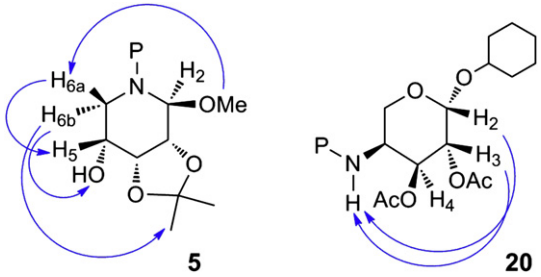


Fig. 2. Diagnostic NOE observation for compounds **5** and **20**.

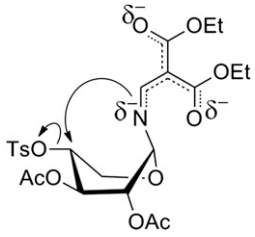


Fig. 3. Intermediate amide ion for the formation of **13**.

We have carried out several attempts of glycosidation of cyclohexanol, a secondary alcohol, with **4** but the reaction was unsuccessful, probably due to the steric hindrance. The corresponding cyclohexyl iminosugar glycoside could be obtained using a thioglycoside as glycosyl donor, as we have reported in a previous communication.[22]

The key chiral intermediate to prepare the five-membered iminosugar glycosides **14**–**19** (furanoside analogues) was the anhydroiminocyclitol **13** (Scheme 1), which was prepared from the D-xylopyranosylenamine **8**,[26] following a modification of the reported method for the synthesis of other anhydroiminocyclitols.[6] Dibutyltin oxide derivatives have been extensively employed as intermediates in the regioselective derivatization of carbohydrates.[27] At the same time, the tosyl group is useful in the field of carbohydrate chemistry as activating group[28] for substitution reactions. However, the preparation of a particular mono-*O*-tosyl derivative often requires multistep and low-yielding syntheses. The regioselective benzoylation[29] and tosylation[30] of various non-protected monosaccharide derivatives after activation of a hydroxyl group with dibutyltin oxide have been reported.[31]

The treatment of **8** with dibutyltin oxide in the presence of dimethylaminopyridine (DMAP), followed by the addition of tosyl

chloride selectively produced the 4-*O*-tosyl derivative **9**. When the same reaction was performed using mesyl chloride instead of tosyl chloride, compound **10** was the major product but the yield was low and other regioisomers were detected. The presence of the 4-*O*-sulfonyloxy group in **9** and **10** was confirmed by NMR spectra (see Experimental), which showed the described[32] downfield shifts for the resonances of H-4 ($\Delta\delta$, 0.80–0.94 ppm) and C-4 ($\Delta\delta$, 7.6), and the upfield shifts for the resonances of C-3 ($\Delta\delta$, −2.1 ppm) and C-5 ($\Delta\delta$, −2.4 to −1.8 ppm) with respect to the same signals for **8**.

Conventional acetylation[23] of **9** and **10** yielded, respectively, **11** and **12** whose spectroscopic data also confirmed the structures of **9** and **10**.

Treatment of **11** with 1 equiv of sodium methoxide in hexamethyl phosphoramide (HMPA) afforded the 1,4-anhydro-α-L-arabinopyranosylamine **13**, whose formation could be explained through the formation of a stabilized amide ion (Fig. 3).

When the ^{1}H NMR spectrum of **13** is compared with that for **11**, the disappearance of the NH signal, and the resonance for the HC=, of the enamino moiety, as a singlet was observed. Additionally, the signal for H-1 was downfield shifted, whereas the resonance for H-4 was upfield shifted, which is in agreement with the substitution of the *C*-tosyloxy group by the enamino group. Also important changes in the coupling constant values for the sugar ring were observed.

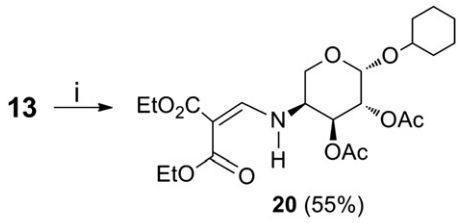
Reaction of 1,4-anhydroiminosugar **13** with methanol, butyl alcohol, and benzyl alcohol in the presence of boron trifluoride diethyl etherate afforded (Scheme 1) the five-membered iminosugar glycosides (furanoside analogues) **14**–**19** as resoluble pairs of anomers (**14**, **17**; **15**, **18**; and **16**, **19**, respectively). The alcohols were used as reagents and solvents, except in the case of **16** and **19** where ether was used as solvent. The substitution reaction occurred rapidly and the products were formed within 30 min at rt. When the reaction mixtures of butanol and benzyl alcohol were left for longer times, some transacetylations (from C-4 to C-6) were observed and confirmed by NMR spectroscopy. Table 1 shows the reaction conditions, yields, and anomeric ratios, which were determined by ^{1}H NMR spectroscopy. The mixtures of anomers were chromatographically resolved.

Table 1
Reaction conditions for compounds **14**–**19**

Nucleophile	Solvent	Temperature	Products	α:β ratio	Yield (%)
MeOH	Methanol	rt	**14** and **17**	3:2	86
BuOH	Butanol	rt	**15** and **18**	3:2	84
BnOH	Ether	rt	**16** and **19**	3:1	82

The NMR data (see Experimental) for the sugar ring nuclei of compounds **14**–**19** were similar to those for the corresponding anomers of methyl α- and β-L-furanosides.[33,34] The NMR spectra of compounds **14**–**16** were very similar; in the three cases the signal for H-2 was a broad singlet ($J_{2,3}$<0.5 Hz) in accord with the data of α-L-furanosides. However, the same proton for compounds **17**–**19** resonated as a doublet ($J_{2,3}$=4.8–5.0 Hz) as is reported for β-L-furanosides.

When the reaction of **13** was attempted with a secondary alcohol, such as cyclohexanol, as glycosyl donor a mixture of compounds was obtained, from which only the 5-aminoglycoside **20** was isolated in medium yield (Scheme 2). The formation of **20** involves a rearrangement of the enamino moiety from the position 2 to the position 5. A similar reaction has been reported for related compounds.[20] The resonances for the NH of **20** was a double doublet and the proton =CH resonated as a doublet. NOE experiments (Fig. 2) revealed correlations in the space between protons NH and H-3, and also between NH and H-2, supporting the β-L-anomeric configuration.

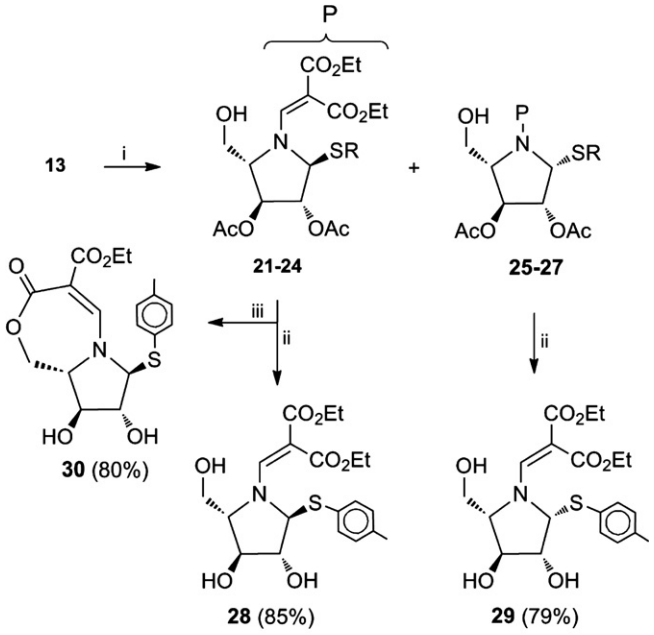


Reagents and conditions. (i) Cyclohexanol, 4 Å molecular sieves, $BF_3.OEt_2$, 0°C, 1 h.

Scheme 2. Formation of compound **20**.

2.2. Synthesis of five-membered iminosugar thioglycosides

The starting material to prepare the five-membered iminosugar thioglycosides **21**–**27** was the 1,4-anhydro-L-arabinopyranosylamine **13** (Scheme 3). Thus, reaction of **13**, as glycosyl donor, and thiols (ethanethiol, butanethiol, *p*-tolylphenol, and 1,4-butanedithiol) as glycosyl acceptors, in the presence of $BF_3\cdot OEt_2$, produced **21**–**27** as resoluble pairs of anomers, except in the case of the butanedithiol where only the α anomer **24** was isolated.



Compound	21	22	23	24	25	26	27
R	Et	Bu	*p*-Tol	$(CH_2)_4SH$	Et	Bu	*p*-Tol
Yield (%)	58	54	63	44	12	14	13

Reagents and conditions. (i) RSH, 4 Å molecular sieves, $BF_3.OEt_2$, Et_2O, rt, 1h; (ii) Amberlite IR-400(HO^-), MeOH, rt, 12h; (iii) Amberlite IR-400(HO^-), MeOH, rt, 7 days.

Scheme 3. Synthesis of thioglycosides.

Different experiments, performed on the synthesis of ethyl (**21**, **25**) and butyl (**22**, **26**) derivatives, were carried out to establish the optimal reaction conditions (see Table 2). The best results (high yields without side products, and high anomeric selectivities) were obtained under the conditions of entries 2 and 9, that is, using ether as solvent and rt.

The ^{1}H NMR spectra (see Experimental) of **21**–**27** showed a singlet at ≈7.50 ppm, which corresponds to the HC=group of the enamino moiety, and a broad signal in the range 2.4–2.3 ppm

Table 2
Optimization conditions for the reactions of **13** with thiols

Entry	Nucleophile	Solvent	Temperature	Products	α:β ratio
1	EtSH	DMF[a]	0 °C	**25** and side products	1:0
2	EtSH	Ether	rt	**21**, **25**	5:1
3	EtSH	Ether	0 °C	**21**, **25**	4:1
4	EtSH	Ether	−5 °C	**21**, **25**	5:3
5	EtSH	Ether	−35 °C	**21**, **25**	5:3
6	EtSH	Ether	−75 °C	**21**, **25**	4:3
7	BuSH	Toluene[a]	rt	**22**, **26**, and side products	4:1
8	BuSH	CH_3CN[a]	rt	**22**, **26**, and side products	4:1
9	BuSH	Ether	rt	**22**, **26**	4:1
10	BuSH	Toluene[a]	45 °C	**22**, **26**, and side products	4:1

[a] The total yield was low or very low due, in part, to the formation of side-products.

corresponding to the OH group; both signals are indicative of ring opening by cleavage of the C–O bond. In the ^{13}C NMR spectra the signals for C-2 appeared upfield shifted with respect to the same resonances for the glycosides **14**–**19**, as corresponds to the substitution of an oxygen atom by a sulfur atom.[35] The β configuration of compound **27** was deduced from the $J_{2,3}$ value (5.8 Hz), similar to that for **17**–**19**. However, for compounds **21**–**26**, resonances of the protons H-2 and H-3 appeared very close, and NOE experiments were necessary to confirm the anomeric configurations. In every case appeared correlations confirming the configurations indicated in Scheme 3. As examples, Fig. 4 shows the NOE contacts in ethyl thioglycosides **21** and **25**. The α configuration of **21** is supported by correlations between H-5 and S–CH_2, between H-2 and H-4, and between H-2 and H-6. The β configuration of **25** is in agreement with NOE contacts between H-2 and H-5 and between H-4 and S–CH_2.

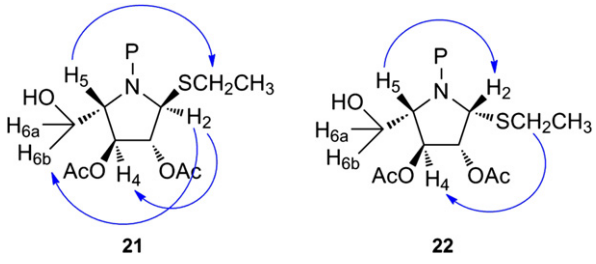


Fig. 4. Diagnostic NOE observations for compounds **21** and **25**.

Treatment of compounds **23** and **27** with resin Amberlite IRA-400 (OH) for 12 h produced de-*O*-acetylation with formation of **28** and **29**, respectively, in high yield (Scheme 3). Longer reaction time (tested on **28**) produced transesterification and the bicyclic derivative **30** was isolated. No N-deprotection[36] was observed. Several attempts of N-deprotection using other described procedures[26] for *N*-dialcoxycarbonyl-2-aminosugars, only gave irresolvable mixtures of decompositions products.

3. Conclusions

Six- and five-membered *N*-diethoxycarbonylvinyl iminosugar glycosides, and five-membered *N*-diethoxycarbonylvinyl iminosugar thioglycosides are obtained in good yields through glycosidation reactions using anhydro-iminosugars as glycosyl donors and primary alcohols or thiols (*p*-tolylthiophenol) as glycosyl acceptors. The glycosidations were completely stereoselective in the pseudoanomeric position for piperidine derivatives (pyranoid analogues), whereas in the case of pyrrolidine derivatives (furanoid analogues) resoluble mixtures of anomers were obtained. When the glycosidation reaction was tried using cyclohexanol (a secondary alcohol) as an acceptor a rearrangement of the enamino moiety took place and a 4-amino-4-deoxy-L-arabinoside derivative was obtained.

4. Experimental

4.1. General methods

Unless otherwise noted, starting materials were obtained for commercial suppliers and used without purification. All manipulations of air-sensitive compounds were carried out in an inert atmosphere under recirculation of nitrogen or argon. The following reaction solvents were distilled under nitrogen immediately before use: THF and Et_2O from Na/benzophenone; CH_2Cl_2 from CaH_2; toluene from Na; and MeOH from Mg. Et_2O and petroleum ether for column chromatography were also distilled under nitrogen from Na/benzophenone before use. TLC were performed on silica gel HF_{254}, with visualization by UV light or charring with 10% H_2SO_4 (EtOH) or 1% $Ce(SO_4)_2\cdot 4H_2O$-5% ammonium molybdate-6% H_2SO_4. Silica gel 60 (Merck, 70–230 or 230–400 mesh) was used for preparative chromatography. A Perkin–Elmer model 141 MC polarimeter, tubes of 1 cm, and solutions in CH_2Cl_2, unless other stated, at 589 nm, were used for measurements of specific rotations. IR spectra were recorded for KBr discs or films on a Bomen Michelson MB 120 FTIR spectrophotometer. Mass spectra (EI, CI, and FAB) were recorded with a Kratos MS-80RFA or a Micromass AutoSpecQ instrument with a resolution of 1000 or 60,000 (10% valley resolution). For the FAB spectra; ions were produced by a beam of xenon atoms (6–7 KeV), using 3-nitrobenzyl alcohol or thioglycerol as matrix and NaI as salt. A Waters 2690 instrument, with a PDA 996 detector, and a μBondpack C18 column (7.8×300 mm) was used for HPLC. NMR experiments were recorded on a Bruker AMX 500 (500.13 MHz for ^1H and 125.75 MHz for ^{13}C) or on a Bruker AMX300 (300.5 MHz for ^1H and 75.50 MHz for ^{13}C). Sample concentrations were typically in the range 10–15 mg per 0.5 mL of solvent. Chemical shifts are given in parts per million, and tetramethylsilane was the internal standard. 2D COSY, HMQC, TOCSY, HMBC, and 1D NOESY experiments were carried out to assist in NMR signal assignments.

Compounds **3**,[35] **4**,[18] and **8**[26] were prepared according to the described literature procedures.

4.2. General procedure for the synthesis of glycosides 5–7

To a stirred solution of compound **4** (*x* mg) in the corresponding dry alcohol (methanol for **5**, butanol for **6**, and allyl alcohol for **7**) (*y* mL), over 4 Å molecular sieves, at 0 °C, boron trifluoride diethyl etherate (*z* μl) was added. The reaction mixture was stirred for 45 min, then neutralized with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with water, dried over $MgSO_4$, and concentrated to dryness. The residue was purified by column chromatography (ether/hexane 1:2).

*4.2.1. (2S,3R,4R,5R)-N-(2,2-Diethoxycarbonylvinyl)-3,4,5-trihydroxy-3,4-O-isopropylidene-2-methoxypiperidine (**5**).* *x*=150 mg (0.44 mmol); *y*=10 mL; *z*=250 μl. Solid (133 mg; 81%). $[\alpha]_D^{22}$ −32 (*c* 1.0, CH_2Cl_2); IR: ν_{max} 3447, 2884, 2935, 1692, 1598, 1383, 1268, 1171, 1091, 905 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 7.44 (s, 1H, HC=), 4.48 (dd, $J_{2,3}$=2.4, $J_{3,4}$=7.8, 1H, H-3), 4.39 (d, 1H, H-4), 4.37 (m, 2H, H-2, H-5), 4.26, 4.16 (each q, each 2H, $J_{H,H}$=7.0, 2COO$CH_2$$CH_3$), 3.37 (dd, 1H, $J_{5,6a}$=6.0, $J_{6a,6b}$=11.4, H-6a), 3.30 (s, 3H, OCH_3), 3.11 (t, 1H, $J_{5,6b}$=11.4, H-6b), 2.07 (d, 1H, $J_{5,OH}$=10.4, OH-5), 1.43, 1.33 [each s, each 3H, $(CH_3)_2$C], 1.32, 1.24 (each t, each 3H, 2COOCH$_2$$CH_3$); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 167.6, 167.0 (2C=O),149.5 (HC=), 110.8 (*C*(CH_3), 96.7 (=C), 93.4 (C-2), 74.7 (C-4), 73.4 (C-3), 63.5 (C-5), 61.2, 60.4 (2COO$CH_2$$CH_3$), 55.6 (O$CH_3$), 45.3 (C-6), 26.2, 24.6 [2 (CH_3)$_2$C)], 14.7, 14.3 (2COOCH$_2$$CH_3$). Anal. Calcd for $C_{17}H_{27}NO_8$: C, 54.68; H, 7.29; N, 3.75. Found: C, 54.88; H, 7.17; N, 3.74.

*4.2.2. (2S,3R,4R,5R)-2-Butoxy-N-(2,2-diethoxycarbonylvinyl)-3,4,5-trihydroxy-3,4-O-isopropylidenepiperidine (**6**).* *x*=77 mg (0.41 mmol); *y*=8 mL; *z*=250 μl. Syrup (136 mg; 80%). $[\alpha]_D^{22}$ −11 (*c* 1.0, CH_2Cl_2); IR:

ν_{max} 3447, 2929, 1682, 1593, 1376, 1276, 1206, 1164, 1082, 946, 899 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 7.44 (s, 1H, HC=), 4.54 (dd, $J_{5,6}$=7.8, $J_{4,5}$=2.8, 1H, H-5), 4.41 (d, 1H, $J_{2,3}$=1.5, H-2), 4.41 (br s, 1H, H-3), 4.39 (d, 1H, $J_{3,4}$=1.5 Hz, H-4) 4.29, 4.19 (each q, each 2H, $J_{H,H}$=7.0, $2COOCH_2CH_3$), 3.58 (dd, 1H, $J_{5,6a}$=6.5, $J_{6a,6b}$=12.0, H-6a), 3.36 [m, 2H, $OCH_2(CH_2)_2CH_3$], 3.12 (t, 1H, $J_{5,6b}$=10.8, H-6b), 2.14 (d, 1H, $J_{5,OH}$=10.5, OH-5), 1.53 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.45, 1.36 [each s, each 3H, $(CH_3)_2C$], 1.31, 1.26 (each t, each 3H, $2COOCH_2CH_3$), 0.934 (m, 5H, $OCH_2CH_2CH_2CH_3$); ^{13}C NMR: (125.7 MHz, $CDCl_3$): δ 167.5, 166.9 (2C=O), 149.4 (HC=), 110.7 [$C(CH_3)_2$], 96.1 (=C), 92.0 (C-2), 74.7 (C-4), 73.2 (C-3), 67.9 [$OCH_2(CH_2)_2CH_3$], 63.5 (C-5), 61.1, 60.3 ($2COOCH_2CH_3$), 45.28 (C-6), 31.27 ($OCH_2CH_2CH_2CH_3$), 26.0, 24.4 [2 $(CH_3)_2C$], 19.32 ($OCH_2CH_2CH_2CH_3$), 14.3, 14.1 ($2COOCH_2CH_3$), 13.7 ($OCH_2CH_2CH_2CH_3$); HRFABMS: calcd for $C_{13}H_{25}N_2O_5Na$: 311.1583. Found: 311.1589.

*4.2.3. (2S,3R,4R,5R)-2-Allyloxy-N-(2,2-diethoxycarbonylvinyl)-3,4,5-trihydroxy-3,4-O-isopropylidenepiperidine (**7**).* x=110 mg (0.32 mmol); y=8 mL; z=100 μl. Syrup (110 mg; 85%). $[\alpha]_D^{22}$ −33.0 (c 1.0, CH_2Cl_2); IR: ν_{max} IR: 3433, 2917, 1623, 1376, 1206, 1164, 1088, 864 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$): δ 7.43 (s, 1H, NCH=), 5.82 (m, 1H, OCH_2CH=CH_2), 5.29 (t, 2H, $J_{=CH,=CH2}$=14.7, OCH_2CH=CH_2), 4.57 (dd, $J_{5,4}$=2.7, $J_{5,6}$=9.4 1H, H-5), 4.47 (d, 1H, $J_{2,3}$=1.5, H-2), 4.44 (br s, 1H, H-4), 4.40 (d, 1H, H-3), 4.29, 4.19 (each q, each 2H, $J_{H,H}$=7.2, $2COOCH_2CH_3$), 4.09 (d, 1H, $J_{OCHa,=CH}$=4.8, OCH_aH_b), 3.94 (dd, 1H, $J_{OCHb,=CH}$=6.6, $J_{Ha,Hb}$=14.8, OCH_aH_b), 3.40 (dd, 1H, $J_{5,6a}$=6.0, $J_{6a,6b}$=11.4, H-6a), 3.17 (t, 1H, $J_{5,6b}$=11.1, H-6b), 2.15 (d, 1H, $J_{5,OH}$=10.2, OH-5), 1.44, 1.32 (each s, each 3H, $[(CH_3)_2C]$), 1.31, 1.26 (each t, each 3H, $2COOCH_2CH_3$); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 167.5, 166.8 (2C=O), 149.3 (HC=), 132.7 (CH_2CH=CH_2), 119.0 (OCH_2CH=CH_2) 110.7 [$C(CH_3)_2$], 96.5 (=C), 90.4 (C-2), 74.7 (C-4), 73.2 (C-3), 68.3 (OCH_2CH=CH_2), 63.4 (C-5), 61.1, 60.2 ($2COOCH_2CH_3$), 45.28 (C-6), 26.0, 24.4 (2 $[(CH_3)_2C)]$, 14.3, 14.1 ($2COOCH_2CH_3$); HRFABMS: calcd for $C_{19}H_{29}NO_8Na$: 422.1791. Found: 422.1783.

4.3. General procedure for the synthesis of compounds 9 and 10

A mixture of **8** (x g) and dibutyltin oxide (y g) was heated under reflux in dry toluene (100 mL) for 3 h. The solution was evaporated to dryness and the dark brown residue obtained was dissolved in dioxane (50 mL). Then, *p*-toluenesulfonyl chloride (TsCl) for **9**, or methanesulfonyl chloride (MsCl) for **10** (z g or mL), and DMAP (catalytic amount) were added. The reaction mixture was stirred at rt for 4.0 h. Water (10 mL) was added and the mixture was extracted by CH_2Cl_2 (2×50 mL). The organic layer was washed by saturated aqueous $NaHCO_3$ (30 mL) and water (30 mL), dried over $MgSO_4$, and evaporated to dryness. The crude product was purified by column chromatography (ethyl acetate/hexane 2:3).

*4.3.1. N-(2,2-Diethoxycarbonylvinyl)-4-O-tosyl-β-D-xylopyranosylamine (**9**).* x=4.00 g (12.5 mmol); y=3.70 g (15.0 mmol); z=2.90 g (15.0 mmol). Syrup (4.10 g; 87%). $[\alpha]_D^{22}$ +10.7 (c 1.0, CH_2Cl_2); IR: ν_{max} 3848, 3737, 3649, 3568, 3649, 3451, 2332, 1865, 1842, 1737, 1713, 1690, 1655, 1556, 1504, 1451 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 9.30 (dd, $J_{NH,=CH}$=13.4, $J_{NH,1}$=8.3, 1H, NH), 8.0 (d, 1H, HC=), 7.83, 7.81, 7.37, 7.35 (4H, Ph), 4.38 (m, 1H, H-4), 4.31 (t, J=8.3, 1H, H-1), 4.24–4.14 (m, $2COOCH_2CH_3$), 3.96 (dd, $J_{5a,5b}$=11.8, $J_{4,5a}$=5.4, 1H, H-5a), 3.72 (t, $J_{2,3}$=$J_{3,4}$=8.5, H-3), 3.47 (t, 1H, H-2), 3.41 (dd, $J_{4,5b}$=1.5 Hz, 1H, H-5b), 2.45 (s, 3H, Ph−CH_3) 1.30, 1.27 (each t, each 3H, $2COOCH_2CH_3$); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 168.7, 165.8 (2C=O), 158.1 (HC=), 145.8, 133.0, 130.2, 128.2 (Ph), 93.8 (=C), 88.4 (C-1), 77.0 (C-4), 74.4 (C-3), 73.1 (C-2), 64.8 (C-5), 60.5, 60.2 ($2COOCH_2CH_3$), 21.8 (Ph−CH_3) 14.5, 14.3 ($2COOCH_2CH_3$); HRFABMS: calcd for $C_{20}H_{27}NO_{10}SNa$: 496.1253. Found: 496.1276. Anal. Calcd for $C_{20}H_{27}NO_{10}S$: C, 50.73; H, 5.75; N, 2.96; S, 6.77. Found: C, 50.32; H, 5.78; N, 2.99; S, 6.20%.

*4.3.2. N-(2,2-Diethoxycarbonylvinyl)-4-O-mesyl-β-D-xylopyranosylamine (**10**).* x=5.00 g (15.6 mmol); y=4.70 g (18.7 mmol); z=2,00 mL (17.5 mmol). Syrup (3.92 g; 63%). $[\alpha]_D^{22}$ +40.2 (c 1.0, CH_2Cl_2); IR: ν_{max} 3901, 3837, 3750, 3674, 3648, 3566, 3617, 1942, 1918, 1733, 1670, 1575, 1361, 1071, 961, 669 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 9.26 (dd, $J_{NH,=CH}$=13.6, $J_{NH,1}$=8.3, 1H, N−H), 8.02 (d, 1H, HC=), 4.54 (m, 1H, H-4), 4.34 (t, $J_{1,2}$=8.3 Hz, 1H, H-1), 4.24–4.08 (m, 3H, $2COOCH_2CH_3$, H-5b), 3.74 (t, $J_{2,3}$=8.9, H-3), 3.55–3.47 (m, 2H, H-2, H-5b), 3.15(s, 3H, OSO_2CH_3), 1.30, 1.27 (each t, each 3H, $2COOCH_2CH_3$); ^{13}C NMR: (125.7 MHz, CDCl3) δ 168.7, 166.2 (2C=O), 158.3 (HC=), 93.5 (=C), 88.7 (C-1), 77.0 (C-4), 74.4 (C-3), 73.5 (C-2), 65.4 (C-5), 60.6, 60.4 ($2COOCH_2CH_3$), 38.4 ($OSO2CH_3$) 14.4, 14.3 ($2COOCH_2CH_3$); HRFABMS: calcd for $C_{14}H_{24}NO_{10}S$: 398.1094. Found: 398.1121.

4.4. General procedure for the synthesis of compounds 11 and 12

To a stirred solution of **8** or **9** (x g) in pyridine (50 mL) at rt, acetic anhydride (10 mL) was added. The reaction mixture was stirred at rt for 4.0 h and then was added over ice-water (200 mg) and extracted with CH_2Cl_2 (2×100 mL). The organic layer was washed successively with H_2SO_4 (20 mL, 1 M), saturated aqueous $NaHCO_3$ (20 mL) and H_2O (20 mL), dried over $MgSO_4$, and evaporated to dryness. The dark residue obtained was purified by column chromatography (ethyl acetate/hexane 1:2).

*4.4.1. 2,3-Di-O-acetyl-N-(2,2-diethoxycarbonylvinyl)-4-O-tosyl-β-D-xylopyranosylamine (**11**).* From **8**; x=3.60 g (7.6 mmol). Syrup (3.50 g; 82%). $[\alpha]_D^{22}$ −56.5 (c 1.0, CH_2Cl_2); IR: ν_{max} 3848, 3737, 3649, 3557, 2985, 2367, 2332, 1749, 1707, 1649, 1370, 1212, 1060 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 9.25 (dd, $J_{NH,=CH}$=13.1, $J_{NH,1}$=8.8, 1H, NH), 7.90 (d, 1H, HC=), 7.78, 7.76, 7.37, 7.35 (4H, Ph), 5.21 (t, $J_{2,3}$=$J_{3,4}$=8.5, 1H, H-3), 4.90 (t, $J_{1,2}$=8.5, 1H, H-2), 4.52 (m, 1H, H-4), 4.48 (t, 1H, H-1), 4.26–4.10 (m, 3H, $2COOCH_2CH_3$, H-5a), 3.52 (dd, $J_{5a,5b}$=12.0, $J_{4,5b}$=9.7, 1H, H-5b), 2.45 (s, 3H, Ph−CH_3), 1.99, 1.84 (each s, each 3H, $2COCH_3$), 1.30, 1.27 (each t, each 3H, $2COOCH_2CH_3$); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 169.6, 169.4, 167.9, 165.4 (4C=O), 157.2 (HC=), 145.6, 133.1, 130.2, 128.0 (Ph), 95.1 (=C), 86.9 (C-1), 74.1 (C-4), 70.8 (C-3), 70.3 (C-2), 64.7 (C-5), 60.5, 60.3 ($2COOCH_2CH_3$), 21.8 (Ph−CH_3), 20.5, 20.4 ($COCH_3$), 14.5, 14.3 ($2COOCH_2CH_3$); HRFABMS: calcd for $C_{24}H_{31}NO_{12}SNa$: 580.1465. Found: 580.1465. Anal. Calcd for $C_{24}H_{31}NO_{12}S$: C, 51.70; H, 5.60; N, 2.51; S, 5.75. Found: C, 51.41; H, 5.39; N, 2.58; S, 5.47%.

*4.4.2. 2,3-Di-O-acetyl-N-(2,2-diethoxycarbonylvinyl)-4-O-mesyl-β-D-xylopyranosylamine (**12**).* From **9**; x=4.60 g (10.1 mmol). Syrup (4.13 g; 85%). $[\alpha]_D^{22}$ −35.7 (c 1.0, CH_2Cl_2); IR: ν_{max} 3901, 3801, 3689, 3566, 1868, 1828, 1792, 1750, 1733, 1716, 1670, 1652, 1635, 1456, 1418, 1363, 1225, 1178, 1069 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 9.29 (dd, $J_{NH,=CH}$=13.0, $J_{NH,1}$=8.8 1H, NH), 8.0 (d, 1H, HC=), 5.28 (t, $J_{2,3}$=$J_{3,4}$=8.0, 1H, H-3), 4.97 (t, $J_{1,2}$=8.0, 1H, H-2), 4.71 (m, 1H, H-4), 4.54 (t, 1H, H-1), 4.26–4.16 (m, $2COOCH_2CH_3$, H5a), 3.60 (dd, $J_{5a,5b}$=12.0, $J_{4,5b}$=2.5, 1H, H-5b), 3.04 (s, 3H, OSO_2CH_3), 2.11, 2.03 (each s, each 3H, $2COCH_3$), 1.31, 1.28 (each t, each 3H, $2COOCH_2CH_3$); ^{13}C NMR: (125.7 MHz, CDCl3) δ 169.7, 169.6, 167.9, 165.4 (4C=O), 157.4 (HC=), 95.2 (=C), 87.0 (C-1), 73.2 (C-4), 71.0 (C-3), 70.2 (C-2), 64.6 (C-5), 60.5, 60.3 ($2COOCH_2CH_3$), 38.5 (OSO_2CH_3), 20.7, 20.6 ($2COCH_3$), 14.5, 14.3 ($2COOCH_2CH_3$); HRFABMS: calcd for $C_{18}H_{28}NO_{12}S$=482.1332. Found: 482.1324.

*4.4.3. 3,4-Di-O-acetyl-1,4-anhydro-N-(2,2-diethoxycarbonylvinyl)-α-L-arabinopyranosylamina (**13**).* To a stirred solution of the tosyl

derivative **11** (3.00 g, 5.38 mmol) in hexamethyl phosphoramide (HMPA) (25 mL) at 40 °C in vacuum (20 mmHg), sodium methoxide (0.35 g; 6.36 mmol) was added. After 40 min, the mixture was poured into ice water (200 g) and extracted with ether (3×70 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated to dryness. The residue was purified by column chromatography (ether/hexane 3:2) to afford compound **13** as an amorphous solid (1.40 g; 66%). $[\alpha]_D^{22}$ +138 (*c* 1.0, CH_2Cl_2); IR: ν_{max} 3854, 3731, 3638, 2985, 2378, 2355, 2326, 1871, 1854, 1731, 1690, 1544, 1370, 1223, 1066 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.51 (s, 1H, HC=), 5.53 (d, $J_{1,2}$=2.5, 1H, H-1), 4.78 (m, 1H, H-2), 4.58 (d, $J_{2,3}$=1.3, 1H, H-3), 3.82 (d, $J_{4,5a}$=3.8, 1H, H-4), 4.25, 4.19 (each q, each 2H, $J_{H,H}$=7.0, 2COOCH_2CH$_3$), 3.68 (dd, 1H, $J_{5a,5b}$=7.9, H-5a), 3.63 (d, 1H, H-5b), 2.12, 2.09 (2s, COCH_3), 1.30, 1.25 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.7, 170.2, 166.3, 165.7 (4C=O), 146.0 (HC=), 103.1 (=C), 88.5 (C-1), 79.5 (C-2), 76.6 (C-3), 65.1 (C-5), 63.6 (C-4), 61.3, 60.8 (2COOCH_2CH$_3$), 20.9, 20.7 (COCH_3), 14.4, 14.2 (2COOCH$_2$CH_3); HRFABMS: calcd for $C_{17}H_{24}NO_9$=386.1451. Found: 386.1439.

4.5. General procedure for the synthesis of compounds 14–20

To a stirred solution of compound **13** (*x* mg) in the corresponding dry alcohol (methanol for **14** and **17**, and butanol for **15** and **18**) (*y* mL), over 4 Å molecular sieves at rt, boron trifluoride diethyl etherate (*z* μl) was added. After 1.0 h, the reaction mixture was neutralized by saturated aqueous $NaHCO_3$ and then extracted with ethyl acetate (2×50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated to dryness. The residue was purified by column chromatography (ethyl acetate/hexane 1:2).

*4.5.1. (2S,3R,4R,5S)-3,4-Di-acetoxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethyl-2-methoxypyrrolidine (**14**) and (2R,3R,4R,5S)-3,4-di-acetoxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethyl-2-methoxy pyrrolidine (**17**).* *x*=180 mg (0.47 mmol); *y*=10.0 mL; *z*=200 μl. Data for **14**: syrup (102 mg, 52%). $[\alpha]_D^{22}$ +24 (*c* 1.1, CH_2Cl_2); IR: ν_{max} 3861, 3742, 2984, 1868,1791, 1742, 1693, 1605, 1372, 1230, 1716, 1074 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.56 (s, 1H, HC=), 5.20 (br s, 1H, H-3), 5.03 (br s, 1H, H-4), 4.93 (br s, 1H, H-2), 4.38–4.14 (m, 4H, 2COOCH_2CH$_3$), 4.02 (t, *J*=6.0, 1H, H-5), 3.72 (m, 2H, H-6a, H-6b), 3.30 (s, 3H, OCH_3), 2.60 (1H, OH), 2.11, 2.10 (each s, each 3H, 2COCH_3), 1.31, 1.25 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.5, 169.4, 166.9, 166.7 (4C=O), 145.9 (HC=), 99.7 (=C), 94.6 (C-2), 77.15 (C-3), 75.8 (C-4), 70.5 (C-5), 62.0 (C-6), 61.1, 60.6 (2COOCH_2CH$_3$), 53.9 (OCH_3), 21.0, 20.9 (2COCH_3), 14.5, 14.2 (2COOCH$_2$CH_3); HRFABMS: calcd for $C_{18}H_{28}NO_{10}$=418.1713. Found: 418.1721.

Data for **17**: syrup (67 mg, 34%). $[\alpha]_D^{22}$ +115 (*c* 1.0, CH_2Cl_2); IR: ν_{max} 3853, 3749, 3674, 3648, 1733, 1698, 1652, 1635, 1616, 1558, 1540, 1520, 1507, 1456, 1418, 1236 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.51 (s, 1H, HC=), 5.20 (dd, $J_{3,4}$=6.6, $J_{4,5}$=3.6, 1H, H-4), 5.04 (d, $J_{2,3}$=4.8, 1H, H-2), 4.96 (dd, 1H, H-3), 4.30–4.13 (m, 4H, 2COOCH_2CH$_3$), 3.93 (dd, $J_{5,6a}$=9.7, 1H, H-5), 3.73–3.64 (m, 2H, H-6a, H-6b), 3.36 (s, 3H, OCH_3), 2.95 (d, *J*=7.2, 1H, OH), 2.11, 2.10 (each s, each 1H, 2COCH_3), 1.30, 1.25 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 171.3, 170.4, 167.2, 166.6 (4C=O), 145.6 (HC=), 98.1 (=C), 93.2 (C-2), 77.9 (C-4), 75.5 (C-3), 64.5 (C-5), 62.5 (C-6), 61.7, 60.8 (2COOCH_2CH$_3$), 56.0 (OCH_3), 21.0, 20.7 (2COCH_3), 14.4, 14.1 (2COOCH$_2$CH_3); HRFABMS: calcd for $C_{18}H_{28}NO_{10}Na$=440.1532. Found: 440.1548.

*4.5.2. (2S,3R,4R,5S)-3,4-Di-acetoxy-2-butoxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethylpyrrolidine (**15**) and (2R,3R,4R,5S)-3,4-di-acetoxy-2-butoxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethylpyrrolidine (**18**).* *x*=100 mg (0.26 mmol); *y*=10.0 mL; *z*=170 μl. Data for **15**: syrup (60 mg, 50%). $[\alpha]_D^{22}$ +87 (*c* 1.1, CH_2Cl_2); IR: ν_{max} 3901, 3869, 3853, 3837, 3819, 2960, 1918, 1868, 1844, 1828, 1791, 1748, 1716, 1698, 1684, 1652, 1635, 1601, 1558, 1540, 1520, 1497, 1488, 1473, 1456, 1418, 1372, 1170, 1076 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.57 (s, 1H, HC=), 5.16 (br s, 1H, H-3), 5.04 (br s, 1H, H-4), 5.00 (br s, 1H, H-2), 4.36–4.08 (m, 4H, 2COOCH_2CH$_3$), 4.05 (t, *J*=5.9 Hz, 1H, H-5), 3.76–3.62 (m, 2H, H-6a, H6b), 3.44 (m, 2H, OCH_2(CH$_2$)$_2$CH$_3$), 2.57 (br s, 1H, OH), 2.10, 2.09 (each s, each 3H, COCH_3), 1.51 (m, 2H, OCH$_2$CH_2CH$_2$CH$_3$), 1.36 (m, 2H, OCH$_2$CH$_2$CH_2CH$_3$), 1.30, 1.25 (each t, each 3H, 2COOCH$_2$CH_3), 0.89 (t, O(CH$_2$)$_3$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.5, 169.4, 167.9, 166.8 (4C=O), 146.3 (HC=), 99.3 (=C), 94.0 (C-2), 77.15 (C-3), 76.0 (C-4), 69.8 (C-5), 66.6 (OCH$_2$(CH$_2$)$_2$CH$_3$), 61.9 (C-6), 61.1, 60.6 (2COOCH$_2$CH$_3$), 31.6 (OCH$_2$CH$_2$CH$_2$CH$_3$), 20.95, 20.93 (2COCH$_3$), 19.3 (OCH$_2$CH$_2$CH$_2$CH$_3$), 14.4, 14.2 (2COOCH$_2$CH$_3$), 13.9 (O(CH$_2$)$_3$CH$_3$); HRFABMS: calcd for $C_{21}H_{33}NO_{10}Na$: 482.4981. Found: 482.4986.

Data for **18**: (from a mixture 1:9 of compounds **15** and **18**): syrup (40 mg, 34%); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.51 (s, 1H, HC=), 5.38 (dd, $J_{3,4}$=6.4, $J_{4,5}$=3.4, 1H, H-4), 5.13 (d, $J_{2,3}$=5.0 1H, H-2), 4.96 (dd, 1H, H-3), 4.30–3.95 (m, 4H, 2COOCH_2CH$_3$), 3.73–3.60 (m, 3H, H-5, H6a, H6b), 3.40–3.25 (m, 2H, OCH_2(CH$_2$)$_2$CH$_3$), 2.97 (dd, $J_{OH,6a}$=4.2, $J_{OH,6b}$=8.6, 1H, OH), 2.10, 2.09 (each s, each 3H, 2COCH_3), 1.52 (m, 2H, OCH$_2$CH_2CH$_2$CH$_3$), 1.40 (m, 2H, OCH$_2$CH$_2$CH_2CH$_3$), 1.30, 1.25 (each t, each 3H, 2COOCH$_2$CH_3), 0.98 (t, 3H, O(CH$_2$)$_3$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 171.3, 170.4, 167.2, 166.7 (4C=O), 145.6 (HC=), 98.0 (=C), 92.3 (C-2), 78.3 (C-4), 75.6 (C-3), 70.0 (OCH_2(CH$_2$)$_2$CH$_3$), 64.4 (C-5), 62.3 (C-6), 61.7, 60.7 (2COOCH_2CH$_3$), 31.5 (OCH$_2$CH$_2$CH$_2$CH$_3$), 21.0, 20.6 (2COCH_3), 19.3 (OCH$_2$CH$_2$CH_2CH$_3$), 14.4, 14.1 (2COOCH$_2$CH_3), 13.8 [O(CH$_2$)$_3$CH_3].

*4.5.3. (2S,3R,4R,5S)-3,4-Di-acetoxy-2-benzyloxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethylpyrrolidine (**16**) and (2R,3R,4R,5S)-3,4-di-acetoxy-2-benzyloxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethylpyrrolidine (**19**).* To a stirred solution of compound **13** (100 mg; 0.26 mmol) in dry ether (10.0 mL), over 4 Å molecular sieves at 0 °C, boron trifluoride diethyl etherate (170 μl) was added. The color of the solution became white, and then benzyl alcohol (500 μl) was added. The reaction mixture was stirred at rt for 1.0 h, neutralized with saturated aqueous $NaHCO_3$, and extracted with ethyl acetate (2×50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated to dryness. The residue was purified by column chromatography (ethyl acetate/hexane 1:2).

Data for **16**: syrup (80 mg, 62%). $[\alpha]_D^{22}$ +89 (*c* 1.0, CH_2Cl_2); IR: ν_{max} 3901, 3819, 3710, 2982, 2918, 1868, 1844, 1791, 1748, 1716, 1684, 1652, 1635, 1602, 1558, 1488, 1473, 1418, 1371, 1232, 1168, 1071 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.57 (s, 1H, HC=), 7.32–7.25 (5H, Ph), 5.19 (br s, 1H, H-3), 5.16 (br s, 1H, H-2), 5.07 (br s, 1H, H-4), 4.60 (s, 2H, CH_2Ph), 4.30–3.90 (m, 4H, 2COOCH_2CH$_3$), 4.10 (t, *J*=5.6, 1H, H-5), 3.76–3.65 (m, 2H, H-6a, H6b), 2.56 (br s, 1H, OH), 2.10, 2.06 (each s, each 3H, 2COCH_3), 1.25, 1.20 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) 170.5, 169.5, 166.9, 166.7 (4C=O), 146.3 (HC=), 137.0, 128.5, 127.9, 127.7, 99.6 (=C), 93.8 (C-2), 77.6 (C-3), 76.2 (C-4), 69.7 (C-5), 68.7 (*C*H$_2$Ph) 61.8 (C-6), 61.1, 60.6 (2COOCH_2CH$_3$), 20.9 (2COCH_3), 14.4, 14.0 (2COOCH$_2$CH_3); HRFABMS: calcd for $C_{24}H_{31}NO_{10}Na$=516.1846. Found: 516.1857.

Data for **19**: syrup (26 mg, 20%). $[\alpha]_D^{22}$ +11 (*c* 1.0, CH_2Cl_2); IR: ν_{max} 3853, 3837, 3749, 3628, 2982, 1868, 1844, 1828, 1792, 1748, 1698, 1652, 1602, 1558, 1540, 1507, 1488, 1473, 1456, 1366, 1069 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.49 (s, 1H, HC=), 7.37–7.27 (5H, Ph), 5.40 (dd, $J_{3,4}$=6.4, $J_{4,5}$=3.5, 1H, H-4), 5.24 (d, $J_{2,3}$=4.8, 1H, H-2), 5.00 (dd, 1H, H-3), 4.70 (d, $J_{a,b}$=11.6, 1H, C*H*HPh), 4.46 (d, *J*=11.6 Hz, 1H, CH*H*Ph), 4.31–4.13 (m, 4H, 2COOCH_2CH$_3$), 4.00 (m, 1H, H-5), 3.80–3.67 (m, 2H, H-6a, H6b), 2.90 (dd, $J_{OH,H6a}$=2.8, $J_{OH,H6b}$=9.6, 1H, OH), 2.11, 2.08 (each s, each 3H, 2COCH_3), 1.31, 1.27 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 171.1, 170.1, 167.0, 166.3 (4C=O), 145.3 (HC=), 135.6, 128.6, 128.3, 127.8, 97.8 (=C),

90.9 (C-2), 77.9 (C-4), 75.2 (C-3), 64.1 (C-5), 70.1 (CH_2Ph) 62.3 (C-6), 61.5, 60.2 (2COOCH_2CH_3), 20.8, 20.4 (2COCH_3), 14.2, 13.8 (2COOCH_2CH_3); FABMS: *m/e* 516 [(M+Na)$^+$]; HRFABMS: calcd for $C_{24}H_{31}NO_{10}Na$=516.1846. Found: 516.1857.

*4.5.4. Cyclohexyl 2,3-di-O-acetyl-4-deoxy-4-diethoxycarbonylvinylamino-β-L-arabinopyranoside (**20**).* To a stirred solution of **13** (0.10 g; 0.26 mmol) in dry ether (10.0 mL), over 4 Å molecular sieves at 0 °C, boron trifluoride diethyl etherate (220 μl) was added. The color of the solution became white, and then cyclohexanol (500 μl) was added. The reaction mixture was stirred at rt for 1.0 h, neutralized with saturated aqueous $NaHCO_3$, and extracted with ethyl acetate (2×50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated to dryness. The residue was purified by column chromatography (diethyl ether/hexane 1:1) to afford compound **20** as a syrup (70 mg; 55%). $[\alpha]_D^{22}$ +25 (*c* 1.0, CH_2Cl_2); IR: ν_{max} 3372, 1744, 1686, 1656, 1607, 1433, 1372, 1316, 1224, 1153, 1061, 1025, 901 cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 9.48 (dd, $J_{NH,5}$=9.8, $J_{NH,HC=}$=13.6, 1H, NH), 7.84 (d, 1H, HC=), 5.27 (d, $J_{2,3}$=3.8, 1H, H-2), 5.30 (dd, 1H, $J_{3,4}$=10.6, $J_{4,5}$=4.0, H-4), 4.83 (dd, 1H, H-3), 4.26 (q, 1H, COOCH_2CH_3), 4.21–4.14 (m, 3H, COO*CH*2CH3, H6a), 3.85 (ddd, $J_{5,6a}$=10.9, $J_{5,6b}$=1.9, 1H, H-5), 3.67 (dd, $J_{6a,6b}$=12.3, 1H, H6b), 3.55 (m, 1H, OC_6H_{11}), 2.08, 2.04 (2s, COCH_3), 1.82–1.68 (m, 5H, OC_6H_{11}), 1.51–130 (m, 5H, OC_6H_{11}), 1.31, 1.25 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.5, 170.3, 168.9, 166.0 (4C=O), 159.1 (HC=), 94.5 (C-2) 91.4 (=C), 76.4, 33.3, 31.4, 25.5, 23.8, 23.5 (OC_6H_{11}), 69.1 (C-3), 68.9 (C-4), 60.0 (C-6), 60.0, 59.7 (2COOCH_2CH_3), 57.4 (C-5), 20.7, 20.6 (COCH_3), 14.4, 14.3 (2COOCH_2CH_3); HRFABMS: calcd for $C_{23}H_{36}NO_{10}$=486.2339. Found: 486.2318.

4.6. General procedure for the synthesis of compounds 21–27

To a stirred solution of compound **13** (*x* mg) in dry ether (*y* mL), over 4 Å molecular sieves at rt, boron trifluoride diethyl etherate (*z* μl) was added. The color of solution became white, and then the corresponding thiol (ethanethiol for **21** and **25**, butanethiol for **22** and **26**, and butane-1,4-dithiol for **24**) (*w* μl) was added. After 1 h at rt, the reaction mixture was neutralized with saturated aqueous $NaHCO_3$, and extracted by ethyl acetate (2×50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated to dryness. The residue was purified by column chromatography (ethyl acetate/hexane 2:3).

*4.6.1. (2S,3R,4R,5S)-3,4-Di-acetoxy-N-(2,2-diethoxycarbonylvinyl)-2-ethylthio-5-hydroxymethylpyrrolidine (**21**) and (2R,3R,4R,5S)-3,4-di-acetoxy-N-(2,2-diethoxycarbonylvinyl)-2-ethylthio-5-hydroxymethylpyrrolidine (**25**).* *x*=180 mg (0.47 mmol); *y*=10.0 mL; *z*=200 μl; *w*=500 μl. Data for **21**: syrup (93 mg, 58%). $[\alpha]_D^{22}$ +129 (*c* 1.0, CH_2Cl_2); IR: ν_{max} 3901, 3819, 3710, 3628, 2928, 1918, 1868, 1844, 1771, 1683, 1576, 1520, 1507, 1456, 1396, 1373, 1034 cm^{-1}; ^{1}H NMR: (500 MHz, $CDCl_3$) δ 77.72 (s, 1H, HC=), 5.39 (br s, 1H, H-3), 5.10 (br s, 1H, H-4), 4.91 (br s, 1H, H-2), 4.38–4.14 (m, 4H, 2COOCH_2CH_3), 4.02 (t, *J*=5.2, 1H, H-5), 3.78 (m, 2H, H-6a, H6b), 2.60 (m, 2H, SCH_2CH_3), 2.28 (1H, OH), 2.12, 2.11 (each s, each 3H, 2COCH_3), 1.32, 1.27 (each t, each 3H, 2COOCH$_2$CH_3), 1.23 (t, 3H, SCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.4, 169.4, 166.9, 166.7 (4C=O), 147.0 (HC=), 98.3 (=C), 79.7 (C-3), 75.1 (C-4), 69.7 (C-5, C-2), 61.0 (C-6), 60.1, 59.6 (2COOCH_2CH_3), 24.7 (SCH_2CH_3), 20.7, 20.5 (COCH_3), 14.4, 14.2 (2COOCH_2CH_3), 13.3 (SCH$_2$CH_3); HRFABMS: calcd for $C_{19}H_{30}NO_9S$=448.1641. Found: 448.1628.

Data for **25** (from a mixture 1:8 of compounds 21 and 25): syrup (20 mg, 12%); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.59 (s, 1H, HC=), 5.38 (m, 1H, H-4), 5.33–5.30 (m, 2H, H-2, H-3), 4.30–4.17 (m, 4H, 2COOCH_2CH_3), 3.99 (m, 1H, H-5), 3.83 (m, 1H, H-6a), 3.72 (m, 1H, H-6b), 2.63 (m, 2H, SCH_2CH_3), 2.13, 2.10 (each s, each 3H, 2COCH_3), 1.34, 1.20 (each t, each 3H, 2COOCH$_2$CH_3), 1.20 (t, 3H, SCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.7, 169.8, 167.0, 166.5 (4C=O), 145.5 (HC=), 97.5 (=C), 76.9 (C-4), 74.9 (C-3), 71.6 (C-2), 65.1 (C-5), 61.3 (C-6), 60.4, 60.5 (2COOCH_2CH_3), 25.0 (SCH_2CH_3), 20.8, 20.6 (COCH_3), 14.4, 14.2 (2COOCH_2CH_3), 14.0 (SCH$_2$CH_3); HRFABMS: calcd for $C_{19}H_{30}NO_9SNa$=470.1460. Found: 470.1469.

*4.6.2. (2S,3R,4R,5S)-3,4-Di-acetoxy-2-butylthio-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethylpyrrolidine (**22**) and 3,4-di-acetoxy-2-butylthio-(2R,3R,4R,5S)-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethylpyrrolidine (**26**).* *x*=100 mg (0.26 mmol); *y*=8.0 mL; *z*=170 μl; *w*=300 μl. Data for **22**: syrup (66 mg, 54%). $[\alpha]_D^{22}$ +13 (*c* 0.8, CH_2Cl_2); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.72 (s, 1H, HC=), 5.38 (br s, 1H, H-3), 5.09 (br s, 1H, H-4), 4.89 (br s, 1H, H-2), 4.38–4.12 (m, 4H, 2COOCH_2CH_3), 4.02 (t, $J_{5,6a}$=$J_{5,6b}$=5.0 Hz, 1H, H-5), 3.76 (d, 2H, H-6a, H6b), 2.56 (t, 2H, SCH_2(CH$_2$)$_2$CH$_3$), 2.40 (br s, 1H, OH), 2.11, 2.10 (each s, each 3H, 2COCH_3), 1.55 (m, 2H, SCH$_2$CH_2CH$_2$CH$_3$), 1.37 (m, 2H, SCH$_2$CH$_2$CH_2CH$_3$), 1.32, 1.23 (each t, each 3H, 2COOCH$_2$CH_3), 0.9 (t, 3H, S(CH$_2$)$_3$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.4, 169.4, 166.9, 166.7 (4C=O), 147.0 (HC=), 99.3 (=C), 80.6 (C-3), 76.1 (C-4), 70.8 (C-2, C-5), 62.0 (C-6), 61.1, 60.6 (2COOCH_2CH_3), 31.6 (SCH$_2$CH$_2$CH$_2$CH$_3$), 30.1 (SCH$_2$(CH$_2$)$_2$CH$_3$), 22.2 (SCH$_2$CH$_2$CH_2CH$_3$), 20.7, 20.5 (2COCH_3), 14.4, 14.2 (2COOCH_2CH_3), 13.7 (S(CH$_2$)$_3$CH$_3$); HRFABMS: calcd for $C_{21}H_{33}NO_9SNa$=498.1804. Found: 498.1773.

Data for **26** (from a mixture 1:9 of compounds 22 and 26): syrup (17 mg, 14%); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.58 (s, 1H, HC=), 5.38 (m, 1H, H-4), 5.33 (m, 1H, H-3), 5.30 (m, 1H, H-2), 4.30–4.17 (m, 4H, 2COOCH_2CH_3), 3.99 (m, 1H, H-5), 3.83 (m, 1H, H-6a), 3.72 (m, 1H, H-6b), 2.60 (m, 2H, SCH_2(CH$_2$)$_2$CH$_3$), 2.30 (br s, 1H, OH), 2.13, 2.10 (each s, each 3H, 2COCH_3), 1.56 (m, 2H, SCH$_2$CH_2CH$_2$CH$_3$), 1.40 (m, 2H, SCH$_2$CH$_2$CH_2CH$_3$) 1.32, 1.24 (each t, each 3H, 2COOCH$_2$CH_3), 0.91 (t, 3H, S(CH$_2$)$_3$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.9, 169.9, 167.0, 166.0 (4C=O), 145.7 (HC=), 99.0 (=C), 77.1 (C-4), 75.1 (C-3), 72.0 (C-2), 65.3 (C-5), 61.5 (C-6), 61.6, 60.6 (2COOCH_2CH_3), 31.6 (SCH$_2$CH$_2$CH$_2$CH$_3$), 30.8 (SCH_2(CH$_2$)$_2$CH$_3$), 22.0 (SCH$_2$CH$_2$CH$_2$CH$_3$), 21.0, 20.5 (COCH_3), 14.4, 14.2 (2COOCH$_2$CH_3), 13.7 (S(CH$_2$)$_3$CH_3); FABMS: *m/e* 498 [(M+Na)$^+$].

*4.6.3. (2S,3R,4R,5S)-3,4-Di-acetoxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethyl-2-mercaptobutylpyrrolidine (**24**).* *x*=100 mg (0.26 mmol); *y*=8.0 mL; *z*=150 mL; *w*=300 mL. Syrup (58 mg, 44%). $[\alpha]_D^{22}$ +12 (*c* 1.0, CH_2Cl_2); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.70 (s, 1H, HC=), 5.37 (br s, 1H, H-3), 5.10 (br s, 1H, H-4), 4.90 (br s, 1H, H-2), 4.39–4.13 (m, 4H, 2COOCH_2CH_3), 4.01 (t, $J_{5,6a}$=$J_{5,6a}$=5.5, 1H, H-5), 3.76 (d, 2H, H-6a, H6b), 2.57 (t, 2H, SCH_2(CH$_2$)$_3$SH), 2.52 (m, 2H, SCH$_2$CH$_2$CH$_2$CH_2SH), 2.44 (1H, SH), 2.11, 2.10 (each s, each 3H, 2COCH_3), 1.68 (m, 4H, SCH$_2$(CH$_2$)$_2$CH$_2$SH), 1.37 (m, 2H, SCH$_2$CH$_2$CH$_2$CH_2CH$_3$), 1.32, 1.27 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.3, 169.5, 166.9, 166.7 (4C=O), 146.9 (HC=), 99.5 (=C), 80.7 (C-3), 76.1 (C-4), 70.8 (C-2, C-5), 62.0 (C-6), 61.2, 60.7 (2COOCH_2CH_3), 33.2 (HSCH$_2$(CH$_2$)$_3$S), 29.8 (HS(CH$_2$)$_3$CH$_2$S), 27.7, 24.2 (SCH$_2$CH$_2$CH$_2$CH$_2$SH, SCH$_2$CH$_2$CH$_2$CH$_2$SH), 21.1, 21.0 (2COCH_3), 14.5, 14.3 (2COOCH$_2$CH_3); HRFABMS: calcd for $C_{21}H_{33}NO_9S_2Na$=530.1494. Found: 530.1495.

*4.6.4. (2S,3R,4R,5S)-3,4-di-acetoxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethyl-2-p-tolylthiopyrrolidine (**23**) and (2R,3R,4R,5S)-3,4-di-acetoxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethyl-2-p-tolylthiopyrrolidine (**27**).* To a stirred solution of compound **13** (280 mg; 0.73 mmol) in dry ether (10.0 mL), over 4 Å molecular sieves at rt, boron trifluoride diethyl etherate (300 μl) was added. The color of solution became white, and then *p*-thiocresol (0.46; 3.7 mmol) in dry ether (2.0 mL) was added. After 1 h at rt, the reaction mixture was neutralized with saturated aqueous $NaHCO_3$ and extracted by ethyl acetate (2×50 mL). The organic layer was dried

over $MgSO_4$, filtered, and concentrated to dryness. The residue was purified by column chromatography (ethyl acetate/hexane 1:2).

Data for **23**: syrup (234 mg, 63%). $[\alpha]_D^{22}$ +7 (*c* 0.8, CH_2Cl_2); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.61 (s, 1H, HC=), 7.36, 7.35, 7.14, 7.12 (4H, C_6H_4), 5.43 (br s, 1H, H-3), 5.20 (br s, 1H, H-2), 5.07 (br s, 1H, H-4), 4.24–3.98 (m, 4H, 2COOCH_2CH$_3$), 3.90 (br s, 1H, H-5), 3.76 (d, *J*=5.0 Hz, 2H, H-6a, H6b), 2.42 (br s, 1H, OH), 2.32 (s, 3H, C_6H_4–CH_3), 2.08, 2.02 (each s, each 1H, 2COCH_3), 1.28–1.24 (m, 6H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.4, 169.3, 166.9, 166.6 (4C=O), 146.6 (HC=), 139.2, 134.8, 130.8, 127.6 (C_6H_4), 100.0 (=C), 79.5 (C-3), 76.1 (C-4), 73.4 (C-2), 69.7 (C-5), 61.6 (C-6), 61.1, 60.7 (2COOCH_2CH$_3$), 21.8 (C_6H_4–CH_3), 20.9, 20.7 (COCH_3), 14.4, 14.2 (2COOCH$_2$$CH_3$); HRFABMS: calcd for $C_{24}H_{31}NO_9SNa$=532.1617. Found: 532.1611.

Data for **27**: syrup (48 mg, 13%). $[\alpha]_D^{22}$ +22 (*c* 0.9, CH_2Cl_2); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.06 (s, 1H, HC=), 7.38, 7.37, 7.17, 7.16 (4H, C_6H_4), 5.47 (d, $J_{2,3}$=6.0, 1H, H-2), 5.40 (m, 1H, H-4), 5.34 (t, $J_{3,4}$=6.0, 1H, H-3), 4.23–4.03 (m, 4H, 2COOCH_2CH$_3$), 3.98 (br s, 1H, H-5), 3.84 (m, 1H, H-6a), 3.70 (m, 1H, H-6b), 2.34 (s, 3H, C_6H_4–CH_3), 2.11, 2.05 (each s, each 1H, 2COCH_3), 1.29, 1.17 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $CDCl_3$) δ 170.9, 169.9, 167.0, 166.0 (4C=O), 145.3 (HC=), 139.6, 135.0, 130.4, 126.8 (C_6H_4), 97.7 (=C), 76.7 (C-4), 74.9 (C-3), 76.1 (C-2), 64.7 (C-5), 61.3 (C-6), 61.4, 60.2 (2COOCH_2CH$_3$), 21.2 (C_6H_4–CH_3), 20.9, 20.5 (2COCH_3), 14.2, 14.0 (2COOCH$_2$$CH_3$); HRFABMS: calcd for $C_{24}H_{31}NO_9SNa$=532.1617. Found: 532.1635.

4.7. General procedure for the synthesis of compounds 28–30

To a solution of the corresponding *O*-protected thioglycoside (**23** for **28** and **27** for **29**) (*x* mg) in methanol (*y* mL), Amberlite IRA-400 (HO) resin (*z* mg) was added. The reaction mixture was stirred for 12 h at rt. The resin was collected and rinsed with methanol, and the combined filtrates were evaporated to dryness. The crude obtained was washed with ether (1 mL) and purified by column chromatography (CH_2Cl_2/MeOH 25:1).

*4.7.1. (2S,3R,4R,5S)-3,4-Dihydroxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethyl-2-p-tolylthiopyrrolidine (**28**).* *x*=150 mg (0.28 mmol); *y*=5.0 mL; *z*=1.5 g (10 equiv). Amorphous solid (100 mg; 85%). $[\alpha]_D^{22}$ −14 (*c* 1.0, CH_2Cl_2); ^1H NMR: (500 MHz, $(CD_3)_2SO$, 80 °C) δ 7.75 (s, 1H, HC=), 7.31–7.30 (m, 2H, C_6H_4), 7.20–7.18 (m, 2H, C_6H_4), 5.60 (d, $J_{3,OH\text{-}3}$=5.3, 1H, OH-3), 5.1 (d, $J_{4,OH\text{-}4}$=3.9, 1H, OH-4), 5.0 (d, $J_{2,3}$=3.9, 1H, H-2), 4.80 (br s, 1H, OH-5), 4.11–4.07 (m, 2H, COOCH_2CH$_3$), 4.0 (d, 1H, H-3), 3.90 (m, 2H, COOCH_2CH$_3$), 3.80 (br s, 1H, H-4), 3.60 (m, 1H, H-6a), 3.50–3.47 (m, 2H, H-5, H-6b), 2.3 (s, 3H, C_6H_4–CH_3), 1.22, 1.18 (each t, each 3H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $(CD_3)_2SO$, 80 °C) δ 166.7, 166.2 (2C=O), 147.3 (HC=), 138.0, 133.5, 130.1, 129.5 (C_6H_4), 97.7 (=C), 80.3 (C-3), 75.8 (C-4, C-2), 71.1 (C-5), 60.6 (C-6), 60.1, 59.7 (2COOCH_2CH$_3$), 21.0 (C_6H_4–CH_3), 14.7, 14.4 (2COOCH$_2$$CH_3$); HRFABMS: calcd for $C_{20}H_{28}NO_7S$=426.1586. Found: 426.1574.

*4.7.2. (2R,3R,4R,5S)-3,4-Dihydroxy-N-(2,2-diethoxycarbonylvinyl)-5-hydroxymethyl-2-p-tolylthiopyrrolidine (**29**).* *x*=80 mg (0.15 mmol); *y*=4.0 mL; *z*=1.0 g (10 equiv). Syrup (50 mg; 79%). $[\alpha]_D^{22}$ +8 (*c* 1.0, CH_2Cl_2); IR: ν_{max} 3901, 3801, 3749, 3648, 3628, 2981, 1942, 1918, 1828, 1716, 1683, 1636, 1576, 1507, 1473, 1418, 1339, 1201, 1151, 1069 cm^{-1}; ^1H NMR: (500 MHz, $CDCl_3$) δ 7.53 (s, 1H, HC=), 7.40–7.38 (2H, C_6H_4), 7.20–7.16 (2H, C_6H_4), 5.50 (d, $J_{3,OH\text{-}3}$=5.3, 1H, OH-3), 5.37 (d, $J_{2,3}$=5.5, 1H, H-2), 5.13 (d, $J_{4,OH\text{-}4}$=3.9 Hz, 1H, OH-4), 4.73 (br s, 1H, OH-5), 4.19–4.0 (m, 6H, 2COOCH_2CH$_3$, H-3, H-4), 3.67–3.61 (m, 2H, H-6a, H-5), 3.50–3.45 (m, 1H, H-6b), 2.31 (s, 3H, C_6H_4–CH_3), 1.20–1.18 (6H, 2COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, $(CD_3)_2SO$, 80 °C) δ 166.6, 166.1 (2 C=O), 146.0 (HC=), 132.9, 130.5, 130.1, 129.5 (C_6H_4), 95.7 (=C), 77.2 (C-2), 76.5 (C-3), 76.3 (C-4), 86.5 (C-5), 60.2 (C-6), 60.1, 60.0 (2COOCH$_2$CH$_3$), 20.9 (C_6H_4–CH_3), 14.3 (2COOCH$_2$$CH_3$); HRFABMS: calcd for $C_{20}H_{28}NO_7S$=426.1586. Found: 426.1571.

*4.7.3. (7S,8R,9R,10S) 1-Aza-3-ethoxycarbonyl-8,9-dihydroxy-5-oxa-4-oxo-10-(p-tolylthio)bicyclo[5,3,0]dec-2-ene (**30**).* To a solution of compound **23** (100 mg, 0.23 mmol) in methanol (*y* mL), Amberlite IRA-400(HO) resin (1.0 g, 10 equiv) was added. The reaction mixture was stirred for 72 h at 40 °C. The resin was collected and rinsed with methanol, and the combined filtrates were evaporated to dryness. The crude obtained was washed with ether (1 mL) and purified by column chromatography (CH_2Cl_2/MeOH 25:1). Amorphous solid (70 mg; 80%). $[\alpha]_D^{22}$ −105 (*c* 0.5, CH_2Cl_2); ^1H NMR: (500 MHz, CD_3OD) δ 7.93 (s, 1H, HC=), 7.42–7.45 (2H, C_6H_4), 7.19–7.27 (2H, C_6H_4), 4.82 (br s, 1H, H-10), 4.47 (dd, $J_{6a,\ 6b}$=13.0, $J_{6a,7}$=7.8, 1H, H-6a), 4.42 (dd, $J_{6b,7}$=2.7, 1H, H-6b), 4.15 (q, 2H, COOCH_2CH$_3$), 3.87 (dd, $J_{9,8}$=6.9, $J_{9,10}$=6.3, 1H, H-9), 3.70 (dd, $J_{7,8}$=8.9, 1H, H-8), (ddd, 1H, H-7), 2.38 (s, 3H, C_6H_4–CH_3), 1.24 (t, 3H, COOCH$_2$CH_3); ^{13}C NMR: (125.7 MHz, CD_3OD) δ 168.1, 166.7 (2C=O), 149.3 (HC=), 140.1, 135.7, 130.0, 126.3 (Ph), 91.3 (=C), 77.3 (C-9), 76.1 (C-10), 74.8 (C-8), 65.5 (C-7), 65.4 (C-6), 60.1 (OCH$_2$Ph), 19.8 (Ph–CH$_3$), 13.2 (COOCH$_2$CH$_3$); HRFABMS: calcd $C_{18}H_{22}NO_6S$=380.1168. Found: 380.1176.

Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.09.065.

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