Chiral 2-Thioxotetrahydro-1,3-*O,N*-heterocycles from Carbohydrates. 2. Stereocontrolled Synthesis of Oxazolidine Pseudo-*C*-nucleosides and Bicyclic Oxazine-2-thiones†

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Chiral, sugar-derived oxazolidine-2-thiones having a pseudo-*C*-nucleoside structure, as well as bicyclic 2-thioxotetrahydro-1,3-oxazines, have been prepared by intramolecular cyclization of 6-deoxy-6-isothiocyanatoaldoses or -aldopyranosides, respectively. The reaction proceeds with total regioselectivity and no need for protection of the secondary hydroxyl groups. A one-pot procedure for the synthesis of the five-membered heterocycles from the corresponding amino sugars is also reported. The six-membered analogs have a *cis*- or *trans*-decalin-type core depending on the configuration of the sugar precursor.

Introduction

The use of five-membered 2-oxo-[1] and 2-thioxo-heterocycles[2] as chiral auxiliaries has encouraged the syntheses of optically pure, substituted derivatives of them. Recently, the first example of a chiral auxiliary having an oxazinone structure has been reported,[3] and a similar application could be expected for suitable chiral thioxo analogs. A key method for the preparation of these chiral auxiliaries is the "chiral pool" approach, whereby carbohydrates (as well as terpenes and amino acids) are chemically modified.

The synthesis of sugar-derived fused oxazolidinones and oxazinones has been widely investigated in the past.[4] The intramoleclar cyclic carbamates have been used for simultaneous protection of amino and hydroxyl groups,[4c-e,5] for synthetic purposes, for spectroscopic studies in conformationally rigid carbohydrates,[6] and in biological studies related to antitumor carbohydrate-derived *N*-nitrosoureas.[7] Recently, some examples on the application of sugar-derived oxazolidinones for stereochemical control in organic reactions and in the resolution of racemic mixtures have been communicated.[8] Hitherto, no attention has been directed to the synthesis of their thioxo analogs and no examples of pseudo-*C*-nucleosides[9] derivatives of 1,3-*O,N*-heterocycles have been described.

2-Thioxotetrahydro-1,3-*O,N*-heterocycles are an important class of heterocyclic compounds which find many biological applications. Starting from 2-thioxo-1,3-heterocycles, a number of fused heterocycles can be prepared that are interesting from both chemical and pharmacological points of view.[10] In addition, the use of oxazolidine-2-thiones as chiral auxiliaries shows some advantages as compared with their 2-oxo-analogs: (a) the compounds should be more readily analyzable by a HPLC with a UV detector because these heterocycles have a strong UV absorption ($\pi \rightarrow \pi^*$) with a high ϵ value[2] and (b) the thiones have been claimed to be more efficient as chiral auxiliaries than oxones in aldol-type reactions involving complex molecules.[11] Moreover, the 2-oxo compounds can be readily prepared from their thioxo analogs.[12]

A few examples of the preparation of fused and spirooxazolidine-2-thiones from sugars have been reported. The procedures involve either the reaction of a free sugar with thiocyanic acid[13] or the reaction of an amino sugar with carbon disulfide.[14] In both cases the anomeric hydroxyl group is involved in the heterocyclic ring closure.

† Part 1 is ref 17. Presented, in part, at the XVIth Int. Carbohydr. Symp., Paris (France), July 5–10, 1992; Abstr. A116, p 151.

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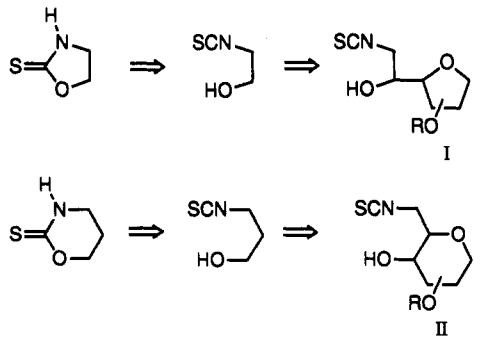


Figure 1. Stereostructures: I, aldohexofuranose; II, aldohexopyranose.

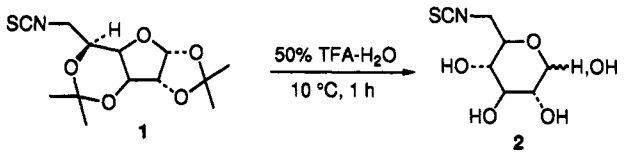
Different sugar tautomeric structures can thus react with the corresponding loss of product purity.

The classical procedures[2,15] for the preparation of this family of heterocycles start from the corresponding amino alcohols by condensation reaction with CS_2 or $CSCl_2$. The first route provides poor yields (30–40%) which can be raised to 60% by condensation of the salt intermediate (-NHCSS$^-$ HEt_3N^+) with ethyl chloroformate.[16] The second procedure leads to the formation of an isothiocyanate intermediate which, in the case of bearing the hydroxyl group at the β- or γ-position, undergoes spontaneous or base-induced cyclization to the heterocycle in virtually quantitative yield. Unprotected 6-deoxy-6-isothiocyanatoaldohexoses fulfill this structural requirement and, thus, can be used as chiral templates (stereostructures I and II) in the synthesis of oxazolidine-2-thiones or their six-membered analogs 2-thioxotetrahydro-1,3-oxazines, depending on the tautomeric form of the sugar involved in the cyclization process (Figure 1). This has been the subject of a preliminary account,[17] and we now report the full experimental details of the transformation. The synthesis of the deoxyisothiocyanato precursors, the mechanism of the reactions, and the scope and limitations of the methods are also discussed. A conformational study is also included.

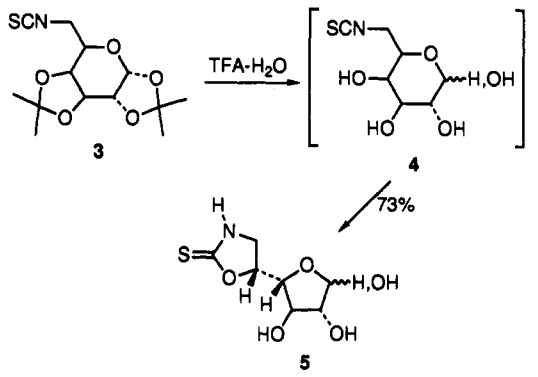
Results and Discussion

Although the synthesis of fully protected glycosyl isothiocyanates and 2-deoxy-2-isothiocyanatoaldoses is now routine,[18] there are only a few examples in the literature on stable sugar isothiocyanates bearing free hydroxyl groups,[19] in spite of their interest for enzymological and biomedical studies.[19a-f,20]

Scheme I



Scheme II



In 1977 Kahlenberg[21] reported a preparation of 6-deoxy-6-isothiocyanato-D-glucose (**2**) which was claimed as a stable photoaffinity reagent for the protein membrane of human erythrocytes involved in glucose transport. Compound **2** was obtained by deprotection of the di-*O*-isopropylidene derivative **1** with TFA–H_2O (Scheme I). Our preliminary results[17] showed that similar deprotection of the *galacto*-derivative **3** results in the direct formation of the oxazolidine-2-thione derivative **5**. The isothiocyanate intermediate **4** could be detected by infrared spectroscopy (IR) but not isolated from the reaction mixture (Scheme II).

We have now established the conditions for the preparation of oxazolidine-2-thione derivatives either from protected deoxyisothiocyanato or from fully unprotected 6-amino-6-deoxy sugars. The results have been extended to the synthesis of six-membered analogs 2-thioxotetrahydro-1,3-oxazines from the corresponding methyl 6-deoxy-6-isothiocyanatoaldopyranosides.

Synthesis of Sugar-Derived Oxazolidine-2-thiones. Compound **1** was treated with 50% TFA-H_2O under the conditions previously described.[21] Evaporation of the solvent was effected at two different ranges of temperature: (a) at $T < 20$ °C and (b) at T 40–50 °C.

Under conditions a, the resulting residue contained the mono-*O*-isopropylidene derivative **6** and a mixture of the isothiocyanate **2** and the cyclic thionocarbamate **7** (ν_{NCS} at 2114 cm^{-1} for **2** and δ_{NH} at 1535 cm^{-1} for **7** in the IR spectrum of this fraction). Compounds **2** and **7** could not be separated even after acetylation of the mixture. Nevertheless, the methyl glycosides **10** and **11** could be separated after treatment with methanol containing traces of TFA (Scheme III).

Using conditions b, a complete transformation of **6** into **7** was observed (TLC). Traces of the isothiocyanate **2** were still present in the reaction mixture (IR), but after repeated additions of water and evaporations, the heterocyclic derivative **7** was the sole reaction product.

(16) Fülöp, F.; Csirinyl, G.; Bernáth, G. *Synthesis* **1985**, 1149.
(17) García Fernández, J. M.; Ortiz Mellet, C.; Fuentes, J. *Tetrahedron Lett.* **1992**, *33*, 3931.
(18) (a) Witczak, Z. J. *Adv. Carbohydr. Chem. Biochem.* **1986**, *44*, 91. (b) Ortiz Mellet, C.; Jiménez Blanco, J. L.; García Fernández, J. M.; Fuentes, J. *J. Carbohydr. Chem.* **1993**, in press.
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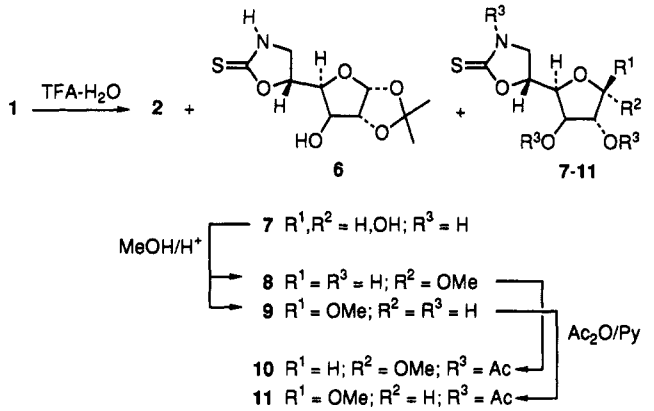
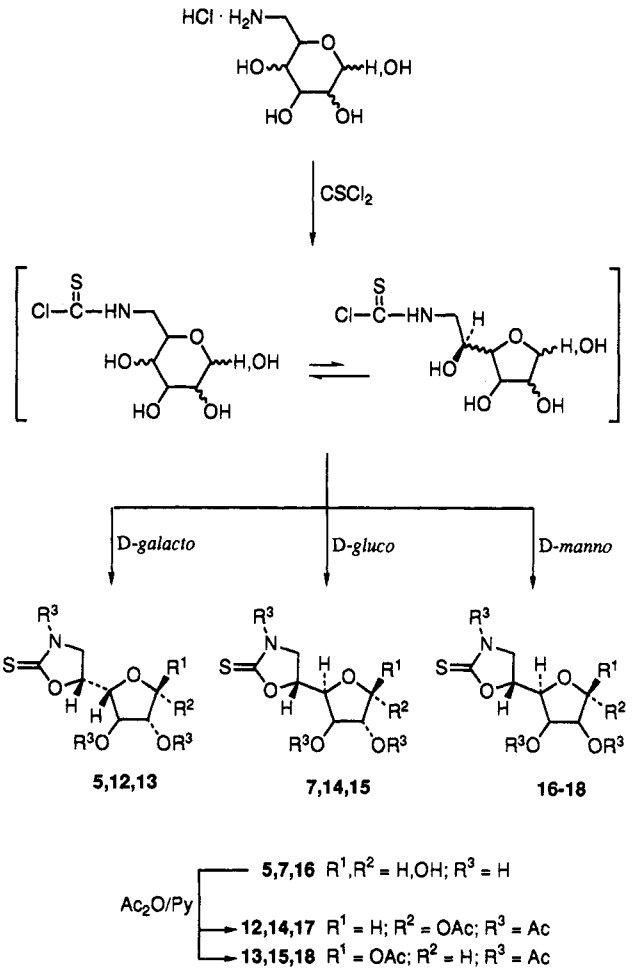
Scheme III



Scheme IV



The structure of **2** has been based[21] mainly on the ν_{NCS} absorption, microanalysis, and chromatographic homogeneity. However, the structures **2** and **7** are indistinguishable from analytical data, and their R_f chromatographical values for different systems are identical. The product obtained by Kahlenberg likely was a mixture of **2** and **7**.

It is noteworthy that compounds **5** and **7** possess a pseudo-*C*-nucleoside structure. This family of sugar derivatives finds many biomedical applications, and much effort has been devoted to their syntheses.[9,22] With the aim to develop a general route for the preparation of chiral oxazolidine-2-thiones having a pseudo-*C*-nucleoside structure, we have examined the reaction of 6-amino-6-deoxy aldoses with thiophosgene. Starting from the corresponding derivatives of D-galactose, D-glucose, and D-mannose, the (5*R*)-5-(L-tetrofuranos-4-yl)oxazoline-2-thiones **5**, **7**, and **16** were obtained in 82–88% yield. No formation of 6-deoxy-6-isothiocyanatoaldose intermediates could be detected in these reactions even at low temperatures. The mechanism likely involves chlorothioformamide intermediates which undergo subsequent, very rapid nucleophilic displacement of the chlorine atom by the β-located OH-5 of the furanose tautomer of the sugar (Scheme IV).

Previously reported results on the synthesis of 2-oxo-[4b] and 2-vinylidenetetrahydro-1,3-*O*,*N*-heterocycles[23] by intramolecular cyclization of unprotected 6-amino-6-deoxy sugar derivatives showed the formation of either the six-membered tetrahydrooxazine[4b] or a mixture of tetrahydrooxazine and oxazolidine.[23] Our results show that both 6-deoxy-6-isothiocyanato- and 6-[(chlorothiocarbonyl)amino]-6-deoxyaldoses act as stereostructures I (Figure 1). The cyclization reaction proceeds through the furanose tautomer leading to the formation of oxazolidine-2-thiones with total regioselectivity.

Structural proofs for the five-membered cyclic carbamate structure of compounds **5–9**, **16**, and the peracetylated derivatives **10–15**, **17**, and **18** were provided by both the proton (Table I) and carbon-13 NMR spectra (see Experimental Section).[24] The ^{13}C chemical shifts of C-5 and C-6 showed strong deshielding and shielding effects, respectively, as compared with the parent hexofuranoses,[25] indicative of the O-5–CSNH–C-6 bridge. The signal at δ 188.8–191.1 (unprotected derivatives) or 184.4–185.1 (peracetates) confirmed the presence of the thiocarbonyl group.[26] The coupling constants between H-5 and the *pro-R* and *pro-S* protons of the pseudo-*C*-aglyconic methylene group ($J_{5,6R}$ and $J_{5,6S}$, respectively) fit[27] with an almost planar five-membered ring, with H-5 and H-6_s in *syn*-disposition, in agreement with data reported for other oxazolidine-2-thiones.[2]

Although the relative disposition between the oxazolidine-2-thione ring and the tetrofuranos-4′-yl substituent cannot be unequivocally established from the ^1H NMR data, some useful information can be obtained from the value of $J_{4,5}$. The three possible staggered rotamers around the pseudoanomeric C-4–C-5 bond for 4′*R*- and 4′*S*-derivatives are shown in Figure 2. The average coupling value for two antiperiplanar vicinal protons in carbohydrate derivatives[28] is 8.6–11.5 Hz. Two *gauche* protons have a coupling of 0.6–5.8 Hz. The observed coupling constants (1.8 Hz for 4′*R*-derivatives **12** and **13** and 3.5–5.7 Hz for 4′*S*-derivatives **6**, **8–11**, **14**, **15**, **17** and **18**) indicate a marked preference for either conformers A or conformers

(22) (a) Rauter, A. P.; Ferreira, M. J.; Ismael, M. I.; Figuereido, J. A.; Saraia, L. M.; *XVIth Int. Carbohydr. Symp.* 1992, July 5–10, Paris, France; Abstr. A160, p 195. (b) Rauter, A. P.; Figuereido, J. A.; Ismael, I. M. *Carbohydr. Res.* **1989**, *188*, 19.

(23) Gries, P.; Kristen, H.; Vogel, C. *Carbohydr. Res.* **1987**, *167*, 87.

(24) For clarity of presentation, the authors choose not to use the numbers resulting from the nomenclature of the heterocyclic compounds (see Experimental Section) in the notation of atoms for NMR data. Instead, the notation was kept consistent with the parent compounds.

(25) Bock, K.; Pedersen, C. *Adv. Carbohydr. Chem. Biochem.* **1983**, *41*, 27.

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(27) Haasnot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783.

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Table I. Selected ^{1}H NMR Spectral Parameters (δ) and J (Hertz) of Oxazolidine-2-thione Derivatives (6, 8–15, 17, 18)

	compd										
parameter[a]	6[b,f]	8[c,f]	9[c,f]	10[d,f]	11[d,f]	12[d,e]	13[d,e]	14[d,g]	15[d,f]	17[d,f]	18[d,f]
$J_{4,5}$	4.5	3.6	3.5	4.3	5.7	1.8	1.8	5.0	5.2	3.5	4.7
$J_{5,6R}$		8.2	7.0	7.3	6.3	6.8	7.8	8.1	5.9	6.0	7.0
$J_{5,6S}$		9.2	10.5	9.2	9.3	9.1	7.8	8.1	9.1	9.3	9.2
NAc				2.83 s	2.83 s	2.78 s	2.70 s	2.81 s	2.80 s	2.81 s	2.81 s

[a] See ref 24. [b] In acetone-d_6. [c] In CD_3OD. [d] In $CDCl_3$. [e] At 200 MHz. [f] At 300 MHz. [g] At 500 MHz.

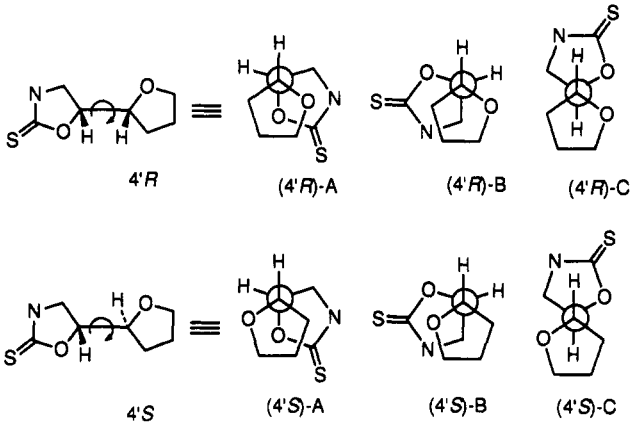


Figure 2. Pseudoanomeric staggered rotamers of (5*R*)-5-[(4′*R*)- and (4′*S*)-tetrofuranos-4′-yl]oxazolidine-2-thiones (substituents on the two rings are omitted).

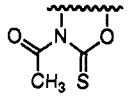


Figure 3.

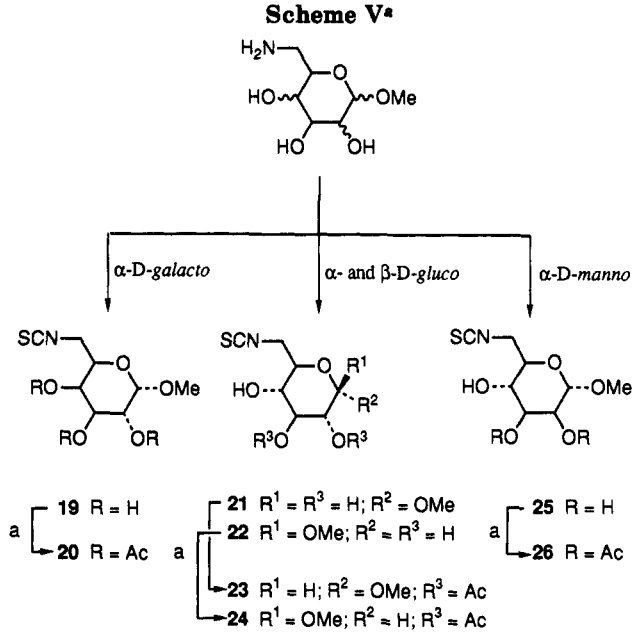
B, excluding a substantial contribution from the *exo*-conformers C.

Recently, it has been reported[29] that the preferred conformation of *C*-glycosides must be attributed predominantly to C–C *gauche* interactions, independently of the structure and stereochemistry of the substituents of the sugar ring, and a similar behavior could be expected for *C*-nucleosides and their pseudocounterparts. Following this reasoning, conformer A should be favored to conformer B in the 4′*R*-series, an *anti* C–C disposition being the most favorable arrangement.[29] However, in the case of 4′*S*-derivatives an analogous conformation having no C-4–C-6 *gauche* interaction (rotamer C) is ruled out from the experimental $J_{4,5}$ value (see above). Stereoelectronic effects between the oxazolidinethione and the furanose rings must play an important role in the preferred conformation of these molecules in contrast to that observed for *C*-glycosides.[29]

Unlike their oxo-analogs,[4b] compounds **5**, **7–9**, and **16** showed no differences of reactivity between the NH- and the OH- groups in acylation reactions. The ^{13}C and ^{1}H chemical shifts of the NAc group in the peracetates are indicative[14] of the conformation shown in Figure 3, where the methyl group is deshielded by the nearby C=S bond.

Synthesis of Sugar-Derived 2-Thioxotetrahydro-1,3-oxazines. To implement this strategy in the access of stereostructures II, it was necessary to anchor the pyranose form of the sugar precursors using glycosides as starting materials. The reactions of methyl 6-amino-6-deoxyaldopyranosides with thiophosgene yielded the corresponding 6-deoxy-6-isothiocyanato derivatives **19**, **21**, **22**, and **25** in high yield (Scheme V). These isothiocyanates were generally crystalline and stable compounds, as they could be stored as solids for several months and acetylated (to give **20**, **23**, **24**, and **26**) without any appreciable decomposition. Significantly, the FAB-mass spectra of these derivatives showed intense pseudomolecular peaks $(M + Na)^+$ and losses of CH_2NCS and MeNCS as the main primary fragmentations. An analogous fragmentation pathway was observed in the EI-mass spectra of the corresponding peracetates. These data probably reflect the higher stability of these compounds as compared to glycosyl isothiocyanates, for which no molecular peaks were observed and the losses of NCS and HNCS were much favored.[19g]

Scheme V[a]



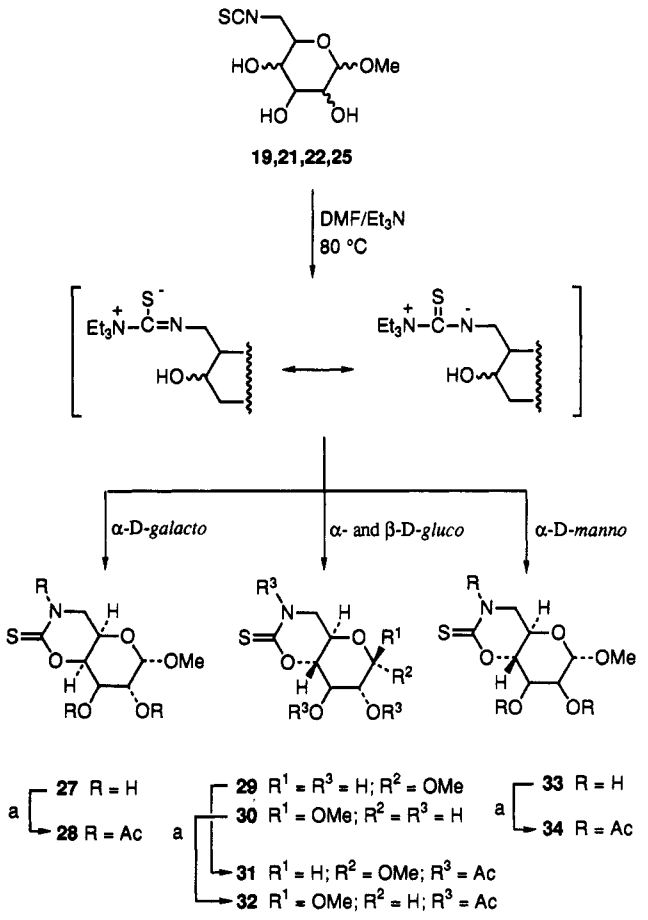
[a] Key: (a) Ac_2O/Py.

In the presence of a catalytic amount of Et_3N, compounds **19**, **21**, **22**, and **25** readily underwent intramolecular cyclization to give the bicyclic (5*R*)-(4-deoxy-1-*O*-methylglycopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thiones **27**, **29**, **30**, and **33**. The formation of a zwitterionic complex between the amine and the isothiocyanate[15a] which undergoes nucleophilic displacement by the γ-located OH-4 of the glycopyranose ring may explain this result (Scheme VI).

The reaction was monitored by IR (disappearance of the NCS band at 2100 cm^{-1}) and ^{13}C NMR spectroscopy (δ_{NCS} at 130.9–134.2; δ_{NHCSO} at 187.8–188.5 ppm). A strong deshielding effect was observed for the resonance of C-4 as compared to the isothiocyanato precursors ($\Delta\delta$ = 6.9–11.6 ppm) in agreement with the 6,4-cyclic thiocarbamate structure. No formation of intermolecular or higher-membered cyclic carbamates was detected.

(29) Goekjian, P. G.; Wu, T. Ch.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6412.

Scheme VI[a]



[a] Key: (a) Ac_2O/Py.

Table II. Selected ^1H NMR Spectral Parameters (δ) and J (Hertz) of Tetrahydroxazazine-2-thione Derivatives (27–34)

parameter[a]	compd							
	27[c,e]	28[b,e]	29[c,d]	30[b,d]	31[b,d]	32[b,d]	33[c,e]	34[b,d]
$J_{5,6e}$	1.1	2.5	5.7	5.8	7.4	6.5	6.0	7.3
$J_{5,6a}$	3.5	5.3	9.8	9.7	9.8	8.5	10.3	9.0
H-4	4.60 d	4.68 d	3.83 m	3.73 t	4.04 t	4.10 t	4.18 t	4.33 t
NAc		2.73 s			2.78 s	2.69 s		2.71 s

[a] See ref 24. [b] In $CDCl_3$. [c] In CD_3OD. [d] At 200 MHz. [e] At 300 MHz.

The $^3J_{H,H}$ coupling constants around the pyranose ring indicate that it adopts the expected chair conformation in both isothiocyanates and oxazinethiones. The coupling constant values between H-5 and the neighboring methylene group (Table II) for the L-*arabino* derivative **27** agree with reported values[28] for axial–equatorial and equatorial–equatorial *gauche* dispositions, supporting the *cis*-decalin-type structure. In the D-*xylo* (**29**, **30**) and D-*lyxo* (**33**) derivatives these J values are in accord with axial–axial and axial–equatorial relationships in a *trans*-decalin-type system.

Compounds **27**, **29**, **30**, and **33** showed a behavior in acylation reactions similar to that of their five-membered analogs (see above). Similar to the peracetates of the five-membered analogs, the NAc group in the peracetates **28**, **31**, **32**, and **34** adopts the conformation shown in Figure 3 to avoid dipole–dipole interaction between the C=S and C=O bonds. Additional support for the proposed structures was obtained from the ^1H NMR spectra of the peracetates (Table II). No deshielding effect was observed for the resonance of H-4 as compared to that for the corresponding unprotected derivatives, in agreement with the involvement of O-4 in the tetrahydrooxazine ring.

Conclusions

For the preparation of chiral, sugar-derived oxazolidine-2-thiones two types of reactions were used: (a) deprotection of 6-deoxydi-*O*-isopropylidene-6-isothiocyanatoaldoses and (b) reaction of 6-amino-6-deoxy sugars with thiophosgene. Both reactions proceed with total regioselectivity leading to intramolecular 6,5-cyclic thiocarbamates *via* transient 6-deoxy-6-isothiocyanato- or 6-(chlorothioformamido)-6-deoxy aldoses, respectively. It is also noteworthy that the oxazolidine-2-thiones thus obtained have a pseudo-*C*-nucleoside structure.

In contrast, the reaction of 6-amino-6-deoxyaldopyranosides with thiophosgene led to stable 6-deoxy-6-isothiocyanatoaldopyranosides. Subsequent base-induced intramolecular cyclization provided bicyclic 2-thioxotetrahydro-1,3-oxazines.

Experimental Section

General Methods. Melting points were determined with a Gallenkamp apparatus and are uncorrected. A Perkin-Elmer Model 141 MC polarimeter, 1-cm tubes, and room temperature were used for measurement of specific rotations. UV spectra were obtained on a Philips PU 8710 spectrophotometer. IR spectra were recorded on a Bomen Michelson MB-120 FTIR spectrophotometer. ^1H (and ^{13}C NMR) spectra were recorded at 500 (125.7), 300 (75.5), and 200 (50.3) MHz with, respectively, Brüker 500 AMX, Brüker 300 AMX, and Varian XL-200 spectrometers. Chemical shifts are given in ppm, and tetramethylsilane was the internal standard. Proton assignments were confirmed by decoupling experiments. Proton-decoupled APT[30] and 2D HETCOR spectra were used to assist in carbon signal assignments. Mass spectra were taken on a Kratos MS-80 RFA instrument. In the EI mode, operating conditions were as follows: ionizing energy 35 eV, ionizing current 100 μA, accelerating voltage 4 kV, resolution 1000 (10% valley definition). In the FAB mode, the primary beam consisted of xenon atoms with a maximum energy of 8 keV. The samples were dissolved in thioglycerol (unprotected derivatives) or *m*-nitrobenzyl alcohol (peracetates), and the positive ions were separated and accelerated over a potential of 7 kV. NaI was added as cationizing agent. TLC was performed with E. Merck precoated TLC plates, silica gel 30F-245, with visualization by UV light and by charring with 10% sulfuric acid. Flash and column chromatography was carried out with silica gel 60 (E. Merck, 230–400 mesh). Microanalyses were performed by the Departamento de Química Analítica (University of Sevilla) and by the Instituto de Química Orgánica General (CSIC) in Madrid. For unprotected derivatives, the analyses were run under argon using samples prepared in sealed tubes after drying over P_4O_{10}. The term "conventional acetylation" means treatment with Ac_2O–pyridine (1:1 v/v, 10 mL for 1 g of sample) overnight. The reaction mixture is then poured into ice–water and extracted with CH_2Cl_2 and the organic layer washed with 2 N H_2SO_4 and saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated.

Materials. 6-Deoxy-1,2:3,5-di-*O*-isopropylidene-6-isothiocyanato-α-D-glucofuranose was prepared as reported previously.[21] 6-Amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose hydrochloride,[31] methyl 6-amino-6-deoxy-α-D-galactopyranoside,[32] methyl 6-amino-6-deoxy-α-D-glucopyranoside,[33] methyl 6-amino-6-deoxy-β-D-glucopyranoside,[34] and methyl 6-amino-6-deoxy-α-D-mannopyranoside[34,35] were prepared from, respectively, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[36] and the corresponding commercial-grade methyl glycopyranosides in

(30) Patt, S. L.; Shoolery, J. N. *J. Magn. Reson.* **1982**, *46*, 535.
(31) (a) Reitz, A. B.; Tuman, R. N.; Marchione, C. S.; Jordan, A. D.; Bowden, C. R.; Maryanoff, B. E. *J. Med. Chem.* **1989**, *32*, 2110. (b) Coxon, B. C.; Reynolds, R. C. *Carbohydr. Res.* **1980**, *78*, 1. (c) Szarek, W. A.; Jones, J. K. N. *Can. J. Chem.* **1965**, *43*, 2345.
(32) Lee, R. T.; Myers, R. W.; Lee, Y. Ch. *Biochemistry* **1982**, *21*, 6292.

three steps, by direct replacement of the primary OH-6 by iodine,[37] nucleophilic displacement by NaN_3 in DMF,[38] and Staudinger reduction[39] of the 6-azido derivative with triphenylphosphine in dioxane–MeOH followed by in situ hydrolysis of the resulting phosphinimine (R—N=PPh_3) with ammonium hydroxide.[40] The overall yields varied from 60 to 80%, the last three reactions providing clean conversions as seen from ^{13}C NMR spectra of the crude reaction mixtures. 6-Amino-6-deoxy-D-galactose[41] and 6-amino-6-deoxy-D-glucose[34b] were prepared by deprotection of their 1,2:3,4- and 1,2:3,5-di-*O*-isopropylidene derivatives, respectively, with TFA–H_2O (9:1) at room temperature. They were used as hydrochlorides. 6-Amino-6-deoxy-D-mannose hydrochloride was obtained from the corresponding methyl glycoside as reported previously.[34]

Solvents were commercial grade and were used as supplied, with the following exceptions. DMF was distilled from BaO. Dioxane and toluene were distilled from metallic sodium. Methanol was distilled from methylmagnesium iodide. Pyridine was distilled from KOH. Acetic anhydride was distilled from freshly melted sodium acetate.

6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-isothiocyanato-α-D-galactopyranose (3). To a heterogeneous mixture of 6-amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose hydrochloride (1.5 g, 5.07 mmol) in $CHCl_3$ (15 mL), water (15 mL), and $CaCO_3$ (1.52 g, 15.2 mmol) was added thiophosgene (0.87 g, 0.58 mL, 7.6 mmol). The mixture was vigorously stirred for 3 h and then filtered. The organic layer was separated, washed with water, dried over $MgSO_4$, and concentrated. The crude product was chromatographed (hexanes–AcOEt (5:1)), giving pure **3** (1.31 g, 86%) as an oil: R_f 0.4, $[\alpha]_D$ −83° (*c* 1.4, $CHCl_3$); EIMS *m/z* 301 ($M^{\bullet+}$); IR (film) 2101 cm^{-1}; ^1H NMR ($CDCl_3$, 50.3 MHz) δ 5.52 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 4.64 (dd, 1H, $J_{2,3}$ = 2.5 Hz, $J_{3,4}$ = 8.5 Hz, H-3), 4.33 (dd, 1H, H-2),4.24 (dd, 1H, $J_{4,5}$ = 2.0 Hz, H-4), 3.97 (td, 1H, $J_{5,6}$ = $J_{5,6'}$ = 6.6 Hz, H-5), 3.69 (d, 2H, H-6,6'), 1.56, 1.46, 1.35, 1.33 (4s, each 3H, 4Me); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 132.4 (NCS), 96.0 (C-1), 70.4, 70.3, 70.2 (C-2 to C-4), 66.4 (C-5), 44.7 (C-6), 25.8, 25.6, 24.6, 24.1 (4 Me). Anal. Calcd for $C_{13}H_{19}NO_5S$: C, 51.81; H, 6.36; N, 4.65; S, 10.64. Found: C, 51.70; H, 6.36; N, 4.51; S, 10.50.

Reaction of 6-Deoxy-1,2:3,5-di-*O*-isopropylidene-6-isothiocyanato-α-D-glucofuranose (1) with TFA–H_2O. Compound **1** (0.4 g, 1.3 mmol) was treated with 50% TFA–H_2O (10 mL) at 10 °C as reported previously.[21] After 1 h, the reaction mixture, which showed two spots on TLC ($CHCl_3$–MeOH (4:1)), was concentrated at $T < 20$ °C under vacuum (0.1 Torr) over a period of 30 min. TLC of the syrupy residue showed a decrease of the relative proportion in the faster running product over this period. The residue was then dissolved in methanol (5 mL) and kept at 5 °C overnight to give the partially deprotected derivative **6** (0.051 g, 15%) as white crystals.

(5*R*)-5-[(4′*R*)-1′,2′-*O*-Isopropylidene-α-D-threofuranos-4′-yl]oxazolidine-2-thione (6): R_f 0.81; mp 225–227 °C dec (from methanol); $[\alpha]_D$ −51° (*c* 0.7, acetone); UV (MeOH) 242 nm (ϵ_{mM} 18.7); FABMS *m/z* 284 [(M + Na)$^+$]; IR (KBr) 3339, 1532, 1175 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) Table I and supplementary material (Table III); ^{13}C NMR (75.5 MHz, CD_3OD) δ 189.7 (C=S), 112.3 (*C*Me_2), 106.2 (C-1), 86.3 (C-2), 81.1, 80.8 (C-4,5), 75.0 (C-3), 46.2 (C-6), 27.1, 26.4 (2 Me). Anal. Calcd for $C_{10}H_{15}NO_5S$: C, 45.97; H, 5.79; N, 5.36; S, 12.27. Found: C, 46.00; H, 5.74; N, 5.50; S, 12.04.

Column chromatography ($CHCl_3$–MeOH (4:1)) of the mother liquor provided three fractions (fractions 1–3). Fraction no. 1 (0.04 g, 12%) consisted of additional **6**. Fraction no. 2 (R_f 0.62, 0.055 g, 18%) was a mixture of the methyl β- and α-threofuranosides **8** and **9**, as seen from ^{13}C NMR. Fraction no. 3 (R_f 0.47, 0.121 g, 44%) contained 6-deoxy-6-isothiocyanato-D-glucose (**2**) and (5*R*)-5-[(4′*S*)-L-threofuranos-4′-yl]oxazolidine-2-thione (**7**), as shown by IR. Compounds **8** and **9** could be obtained in pure form after acetylation of fraction no. 2, preparative TLC (CCl_4–acetone (4:1), two elutions) of the mixture of peracetates **10** and **11** (order of elution: **10** and **11**), and subsequent deacetylation (sodium methoxide).

(5*R*)-5-[(4′*S*)-1′-*O*-Methyl-β-L-threofuranos-4′-yl]oxazolidine-2-thione (8): syrup; $[\alpha]_D$ +108° (*c* 1, MeOH); UV (MeOH) 243 nm (ϵ_{mM} 13.9); FABMS *m/z* 258 [(M + Na)$^+$]; IR (film) 3341, 1545, 1175 cm^{-1}; ^1H NMR (CD_3OD) Table I and supplementary material (Table III); ^{13}C NMR (125.7 MHz, CD_3OD) δ 190.4 (C=S), 104.3 (C-1), 82.9 (C-5), 79.8 (C-4), 79.2 (C-2), 76.6 (C-3), 56.1 (Me), 46.4 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.79; H, 5.51; N, 6.10; S, 13.50.

(5*R*)-5-[(4′*S*)-1′-*O*-Methyl-α-L-threofuranos-4′-yl]oxazolidine-2-thione (9): syrup; $[\alpha]_D$ −41° (*c* 1.2, MeOH); UV (MeOH) 242 nm (ϵ_{mM} 14.2); FABMS *m/z* 258 [(M + Na)$^+$]; IR (film) 3340, 1541, 1175 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) Table I and supplementary material (Table III); ^{13}C NMR (75.5 MHz, CD_3OD) δ 190.2 (C=S), 111.7 (C-1), 84.3 (C-5), 83.1 (C-4), 82.0 (C-2), 76.9 (C-3), 55.9 (Me), 47.0 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.60; H, 5.38; N, 5.86; S, 13.36.

***N*-Acetyl-(5*R*)-5-[(4′*S*)-2′,3′-di-*O*-acetyl-1′-*O*-methyl-β-L-threofuranos-4′-yl]oxazolidine-2-thione (10):** syrup; $[\alpha]_D$ +111° (*c* 1, $CHCl_3$); UV ($CHCl_3$) 267 nm (ϵ_{mM} 11.7); EIMS *m/z* 361 ($M^{\bullet+}$); IR (film) 1759, 1703, 1256, 1230 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) Table I and supplementary material (Table III); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 184.6 (C=S), 171.3 (CO amide), 170.0, 169.5 (2 CO ester), 100.4 (C-1), 77.4 (C-4), 75.6 (C-5), 74.6, 74.5 (C-2,3), 55.8 (OMe), 47.9 (C-6), 25.9 (NCO*C*H_3), 20.7, 20.4 (3 CO*C*H_3). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.53, H, 5.30; N, 3.88; S, 8.87. Found: C, 46.27; H, 5.12; N, 3.79; S, 8.85.

***N*-Acetyl-(5*R*)-5-[(4′*S*)-2′,3′-di-*O*-acetyl-1′-*O*-methyl-α-L-threofuranos-4′-yl]oxazolidine-2-thione (11):** syrup; $[\alpha]_D$ −16° (*c* 0.9, $CHCl_3$); UV ($CHCl_3$) 268 nm (ϵ_{mM} 14.7); EIMS *m/z* 361 ($M^{\bullet+}$); IR (film) 1758, 1705, 1256, 1227 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) Table I and supplementary material (Table III); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 184.7 (C=S), 171.2 (CO amide), 169.3, 169.2 (2 CO ester), 107.6 (C-1), 80.3 (C-4), 79.8 (C-2), 76.1, (C-5), 74.4 (C-3), 55.9 (OMe), 48.4 (C-6), 25.9 (NCO*C*H_3), 20.7, 20.6 (2 CO*C*H_3). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.53, H, 5.30; N, 3.88; S, 8.87. Found: C, 46.38; H, 5.00; N, 3.54; S, 8.59.

General Procedure for the Preparation of 5-(Glycofuranos-4′-yl)oxazolidine-2-thiones. These compounds were obtained by reactions of 6-amino-6-deoxyhexopyranoses with $CSCl_2$ following the protocol later described for the preparation of 6-deoxy-6-isothiocyanatoaldopyranosides.

Conventional acetylation led to mixtures of α- and β-anomers with virtually quantitative recovery. Pure samples of both peracetylated anomers could be obtained in all cases after preparative TLC.

(5*R*)-5-[(4′*R*)-L-Threofuranos-4′-yl]oxazolidine-2-thione (5): syrup; 82%; β:α ratio 1:2 (C-1 integration); $[\alpha]_D$ −69° (*c* 1.2, water); UV (MeOH) 243 nm (ϵ_{mM} 8.5); FABMS *m/z* 244 [(M + Na)$^+$]; IR (film) 3349, 1680, 1545, 1187 cm^{-1}; ^{13}C NMR (50.3 MHz, CD_3OD) β anomer δ 190.5 (C=S), 97.2 (C-1), 84.2 (C-4), 82.2 (C-5), 78.4 (C-2), 75.9 (C-3), 47.0 (C-6); α anomer δ 190.4 (C=S), 103.1 (C-1), 83.6 (C-4), 83.3 (C-2), 82.7 (C-5), 77.3 (C-3), 46.9 (C-6). Anal. Calcd for $C_7H_{11}NO_5S$: C, 38.00; H, 5.01; N, 6.00; S, 14.49. Found: C, 38.12; H, 5.24; N, 6.33; S, 14.62.

Compound **5** was also prepared in 85% yield from 6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-isothiocyanato-α-D-galactopyranose (**3**, 0.4 g, 1.3 mmol) by treatment with TFA–H_2O (9:1, 15 mL) at 25 °C for 20 min under reduced pressure (water pump) and evaporation of the solvent at 40 °C.

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(37) (a) Garegg, P. J.; Samuelson, B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2866. (b) Garegg, P. J.; Johansonn, R.; Ortega, C.; Samuelsonn, B. *J. Chem. Soc., Perkin Trans. 1* **1982**, 681.

(38) For methylaldopyranoside derivatives the reaction conditions were: 3 equiv of NaN_3, *T* 90 °C, overnight. For the diisopropylidenegalactose derivative, more strenuous conditions were needed: 5 equiv of NaN_3, *T* 120 °C, 48 h.

(39) (a) Vaultier, M.; Knouzi, N.; Carrié, R. *Tetrahedron Lett.* **1983**, *24*, 763. (b) Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.

(40) For a typical procedure see: Boger, J.; Corcorand, R. J.; Lehn, J.-M. *Helv. Chim. Acta* **1978**, *61*, 2190.

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***N*-Acetyl-(5*R*)-5-[(4′*R*)-1′,2′,3′-tri-*O*-acetyl-β- and -α-L-threofuranos-4′-yl]oxazolidine-2-thione (12 and 13)**: β:α ratio 5:4; eluent hexanes–AcOEt (2:3).

Compound **12**: higher R_f; syrup; $[\alpha]_D$ −102° (*c* 1.1, $CHCl_3$); UV (CH_2Cl_2) 266 nm (ϵ_{mM} 11.4); EIMS *m/z* 389 ($M^{\bullet+}$); IR (film) 1748, 1703, 1254, 1223 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) Table I and supplementary material (Table III); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 185.1 (C=S), 171.0 (CO amide), 170.2, 169.7, 169.6 (3 CO ester), 92.1 (C-1), 80.2 (C-4), 75.5 (C-5), 74.3 (C-2), 72.7 (C-3), 48.1 (C-6) 25.8 ($NCOCH_3$) 21.2, 20.5, 20.2 (3 $COCH_3$). Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.23. Found: C, 46.10; H, 4.86; N, 3.36; S, 8.11.

Compound **13**: lower R_f; syrup; $[\alpha]_D$ +11° (*c* 1.1, $CHCl_3$); UV (CH_2Cl_2) 267 nm (ϵ_{mM} 9.2); EIMS *m/z* 389 ($M^{\bullet+}$); IR (film) 1748, 1703, 1254, 1223 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) Table I and supplementary material (Table III); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 184.9 (C=S), 171.0 (CO amide), 170.4, 169.9, 168.7 (3 CO ester), 98.9 (C-1), 85.5 (C-4), 79.5 (C-5), 76.7 (C-2), 75.6 (C-3), 48.2 (C-6) 25.8 ($NCOCH_3$) 20.8, 20.7, 20.5 (3 $COCH_3$). Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.23. Found: C, 46.27; H, 4.95; N, 3.51; S, 8.38.

(5*R*)-5-[(4′*S*)-L-Threofuranos-4′-yl]oxazolidine-2-thione (7): amorphous solid; 85%; β:α ratio 3:4 (C-1 integration); $[\alpha]_D$ +5.1° (*C* 1.2, MeOH); UV (MeOH) 242 nm (ϵ_{mM} 12.8); FABMS *m/z* 244 [(M + Na)$^+$]; IR (film) 3325, 1680, 1539, 1173 cm^{-1}; ^{13}C NMR (75.5 MHz, CD_3OD) β anomer δ 191.1 (C=S), 99.7 (C-1), 85.2 (C-5), 80.5 (C-4), 79.3 (C-2), 77.8 (C-3), 47.6 (C-6); α anomer δ 191.1 (C=S), 105.6 (C-1), 83.9 (C-4), 83.2 (C-2), 77.7 (C-3), 47.9 (C-6). Anal. Calcd for $C_7H_{11}NO_5S$: C, 38.00; H, 5.01; N, 6.33; S, 14.49. Found: C, 38.07; H, 4.95; N, 5.86; S, 14.24.

Compound **7** was also prepared in 81% yield from 6-deoxy-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (**1**) by treatment with TFA–H_2O as described above for its (4′*R*)-isomer **5**.

***N*-Acetyl-(5*R*)-5-[(4′*S*)-1′,2′,3′-tri-*O*-acetyl-β- and -α-L-threofuranos-4′-yl]oxazolidine-2-thione (14 and 15)**: β:α ratio 3:2; eluent hexanes–AcOEt (1:2).

Compound **14**: higher R_f; amorphous solid; $[\alpha]_D$ +90° (*c* 0.8, $CHCl_3$); UV ($CHCl_3$) 267 nm (ϵ_{mM} 14.2); EIMS *m/z* 389 ($M^{\bullet+}$); IR (KBr) 1751, 1688, 1260, 1220 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) Table I and supplementary material (Table III); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 184.3 (C=S), 171.2 (CO amide), 169.1, 168.9, 168.8 (3 CO ester), 92.9 (C-1), 76.5 (C-4), 75.8 (C-5), 75.1 (C-3), 73.8 (C-2), 48.0 (C-6), 25.7 ($NCOCH_3$), 20.8, 20.4, 20.1 (3 $COCH_3$). Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.23. Found: C, 46.24; H, 4.94; N, 3.41; S, 8.11.

Compound **15**: lower R_f; syrup $[\alpha]_D$ −18° (*c* 0.9, $CHCl_3$); UV ($CHCl_3$) 268 nm (ϵ_{mM} 14.8); EIMS *m/z* 389 ($M^{\bullet+}$); IR (film) 1755, 1709, 1258, 1223 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) Table I and supplementary material (Table III); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 184.4 (C=S), 171.0 (CO amide), 170.8, 168.8, 168.7 (3 CO ester), 98.6 (C-1), 81.6 (C-4), 78.9 (C-2), 75.5 (C-5), 73.9 (C-3), 48.2 (C-6), 25.7 ($NCOCH_3$), 20.6, 20.1 (2C) (3 $COCH_3$). Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.23. Found: C, 46.36; H, 5.01; N, 3.57; S, 8.33.

(5*R*)-5-[(4′*S*)-L-Erythrofuranos-4′-yl]oxazolidine-2-thione (16): syrup; 88%; $[\alpha]_D$ +7.5° (*c* 0.8, MeOH); UV (MeOH) 243 nm (ϵ_{mM} 10.5); FABMS *m/z* 244 [(M + Na)$^+$]; IR (film) 3333, 1690, 1543, 1171 cm^{-1}; ^{13}C NMR (125.7 MHz, CD_3OD) α anomer δ 188.8 (C=S), 96.1 (C-1), 82.6 (C-4), 81.5 (C-5), 71.5 (C-2), 70.9 (C-3), 46.1 (C-6); no signals for the β anomer were observed. Anal. Calcd for $C_7H_{11}NO_5S$: C, 38.00; H, 5.01; N, 6.00; S, 14.49. Found: C, 37.90; H, 5.02; N, 5.98; S, 14.00.

***N*-Acetyl-(5*R*)-5-[(4′*S*)-1′,2′,3′-tri-*O*-acetyl-β- and -α-L-erythrofuranos-4′-yl]oxazolidine-2-thione (17 and 18)**: β:α ratio 1:5, eluent hexanes–EtOAc (2:3).

Compound **17**: lower R_f; syrup; $[\alpha]_D$ −5.0° (*c* 0.8, $CHCl_3$); UV (CH_2Cl_2) 268 nm (ϵ_{mM} 14.2); EIMS *m/z* 389 ($M^{\bullet+}$); IR (film) 1755, 1703, 1252, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) Table I and supplementary material (Table III); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 184.4 (C=S), 171.2 (CO amide), 169.1, 168.9, 168.8 (3 CO ester), 92.8 (C-1), 79.5 (C-4), 75.9 (C-5), 69.9 (C-2), 68.6 (C-3), 47.9 (C-6), 25.7 ($NCOCH_3$), 20.8, 20.4, 20.1 (3 $COCH_3$). Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.23. Found: C, 46.25; H, 4.90; N, 3.31; S, 8.17.

Compound **18**: higher R_f; syrup; $[\alpha]_D$ +74.2° (*c* 1, $CHCl_3$); UV (CH_2Cl_2) 267 nm (ϵ_{mM} 13.1); EIMS *m/z* 389 ($M^{\bullet+}$); IR (film) 1753, 1709, 1250, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) Table I and supplementary material (Table III); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 184.4 (C=S), 171.0 (CO amide), 170.8, 168.8, 168.7 (3 CO ester), 97.6 (C-1), 77.4 (C-4), 75.5 (C-5), 74.0 (C-3), 69.9 (C-2), 47.6 (C-6), 25.7 ($NCOCH_3$), 20.6, 20.1, (2C)(3 $COCH_3$). Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.23. Found: C, 46.28; H, 5.00; N, 3.35; S, 8.46.

General Procedure for the Preparation of Methyl 6-Deoxy-6-isothiocyanatoaldopyranosides. To a heterogeneous mixture of the corresponding methyl 6-amino-6-deoxyaldopyranoside (1 g, 5.17 mmol) in water–acetone (3:2, 20 mL) and $CaCO_3$ (1.55 g, 15.51 mmol) was added thiophosgene (0.6 mL, 7.76 mmol). The mixture was vigorously stirred for 2 h and then filtered and the filtrate concentrated to dryness.

Peracetylated derivatives were obtained by conventional acetylation in virtually quantitative yields.

Methyl 6-deoxy-6-isothiocyanato-α-D-galactopyranoside (19): 86%; mp 120–122 °C (from MeOH); R_f 0.58 ($CHCl_3$–MeOH (3:1)); $[\alpha]_D$ +110° (*c* 1, MeOH); FABMS *m/z* 258 [(M + Na)$^+$]; IR (KBr) 3270, 2087 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) supplementary material (Table IV); ^{13}C NMR (50.3 MHz, CD_3OD) δ 134.2 (NCS), 101.7 (C-1), 71.1 (C-3), 70.9 (C-4), 70.7 (C-5), 69.8 (C-2), 56.1 (Me), 47.0 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.67; H, 5.36; N, 5.95; S, 13.38.

Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-galactopyranoside (20): syrup; R_f 0.30 (hexanes–AcOEt (1:2)); $[\alpha]_D$ +105° (*c* 1, $CHCl_3$); EIMS *m/z* 361 ($M^{\bullet+}$); IR (film) 2103, 1759, 1227 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) supplementary material (Table IV); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 170.1, 169.9, 169.6 (3CO), 134.3 (NCS), 97.1 (C-1), 68.4 (C-4), 67.7 (C-2), 67.2 (C-3), 66.9 (C-5), 55.8 (OMe), 45.2 (C-6), 20.6, 20.4 (2C) (3 $COCH_3$). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.50; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.50; H, 5.10; N, 3.71; S, 8.50.

Methyl 6-deoxy-6-isothiocyanato-α-D-glucopyranoside (21): 92%; mp 52–53 °C (from ether); R_f 0.41 ($CHCl_3$–MeOH (4:1)); $[\alpha]_D$ +117° (*c* 1, acetone); FABMS *m/z* 258 [(M + Na)$^+$]; IR (KBr) 3405, 2101 cm^{-1}; ^1H NMR (200 MHz, acetone-d_6) supplementary material (Table IV); ^{13}C NMR (50.3 MHz, acetone-d_6) δ 131.1 (NCS), 100.0 (C-1), 73.7 (C-3), 72.1 (C-2), 71.2 (C-4), 70.2 (C-5), 55.0 (Me), 46.3 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.64; H, 5.42; N, 6.11; S, 13.50.

Methyl 6-deoxy-6-isothiocyanato-β-D-glucopyranoside (22): 89%; mp 108–110 °C (from ether); R_f 0.41 ($CHCl_3$–MeOH (4:1)); $[\alpha]_D$ −196° (*c* 0.9, MeOH); FABMS *m/z* 258 [(M + Na)$^+$]; IR (KBr) 3403, 2103 cm^{-1}; ^1H NMR (200 MHz, CD_3OD) supplementary material (Table IV); ^{13}C NMR (50.3 MHz, acetone-d_6) δ 131.8 (NCS), 103.6 (C-1), 76.0 (C-3), 73.5 (C-5), 73.4 (C-2), 71.0 (C-4), 56.2 (Me), 46.4 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.71; H, 5.42; N, 6.07; S, 13.59.

Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-glucopyranoside (23): mp 98–99 °C (ether–hexane); R_f 0.37 (hexanes–AcOEt (1:2)); $[\alpha]_D$ +129° (*c* 1, $CHCl_3$); EIMS *m/z* 361 ($M^{\bullet+}$); IR (KBr) 2128, 1744, 1242 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) supplementary material (Table IV); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 169.8, 169.7, 169.4 (3CO), 134.0 (NCS), 96.5 (C-1), 70.3 (C-2), 69.6 (C-3), 69.3 (C-4), 67.4 (C-5), 55.6 (OMe), 45.7 (C-6), 20.4, 20.3 (2C) (3 $COCH_3$). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.50; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.51; H, 5.36; N, 3.51; S, 8.71.

Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-isothiocyanato-β-D-glucopyranoside (24): syrup; R_f 0.38 (hexanes–AcOEt (1:2)); $[\alpha]_D$ −28° (*c* 1.1, $CHCl_3$); EIMS *m/z* 361 ($M^{\bullet+}$); IR (film) 2106, 1753, 1240 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) supplementary material (Table IV); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.0, 169.4, 169.2 (3CO), 135.4 (NCS), 101.4 (C-1), 72.2 (C-3), 72.1 (C-5), 71.0 (C-2), 69.8 (C-4), 57.1 (OMe), 46.2 (C-6), 20.5, 20.4 (2C) (3 $COCH_3$). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.50; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.42; H, 5.13; N, 3.71; S, 8.62.

Methyl 6-deoxy-6-isothiocyanato-α-D-mannopyranoside (25): syrup; 93%; R_f 0.53 ($CHCl_3$–MeOH (4:1)); $[\alpha]_D$ +71° (*c* 1.3, acetone); FABMS *m/z* 258 [(M + Na)$^+$]; IR (film) 3391, 2101 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) supplementary material (Table IV); ^{13}C NMR (50.3 MHz, acetone-d_6) δ 130.9 (NCS), 101.5 (C-1), 71.5 (C-3), 71.2 (C-2), 70.6 (C-5), 68.4 (C-4), 54.5 (Me), 46.5

(C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.84; H, 5.62; N, 6.02; S, 13.68.

Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-mannopyranoside (26): mp 114–115 °C (ether–hexane); R_f 0.48 (hexanes–AcOEt (1:2)); $[\alpha]_D$ +62° (*c* 1.1, $CHCl_3$); EIMS *m/z* 361 ($M^{\bullet+}$); IR (KBr) 2103, 1746, 1222 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) supplementary material (Table IV); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 169.9, 169.7, 169.6 (3CO), 134.1 (NCS), 98.4 (C-1), 69.9 (C-3), 69.1 (C-2), 68.4 (C-5), 67.1 (C-4), 55.6 (OMe), 46.0 (C-6), 20.7, 20.5 (2C) ($3COCH_3$). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.50; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.40; H, 5.13; N, 3.57; S, 8.55.

General Procedure for the Preparation of (5*R*)-(4-Deoxy-1-*O*-methyl-glycopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thiones. To a stirred solution of the respective deoxyisothiocyanato sugar (0.5 g, 2.12 mmol) in DMF (50 mL) was added Et_3N (0.1 mL, 0.7 mmol). The reaction mixture was heated at 80 °C for 30 min and then concentrated to dryness.

Peracetylated derivatives were obtained by conventional acetylation in virtually quantitative yields.

(5*R*)-(4-Deoxy-1-*O*-methyl-β-L-arabinopyranoso)[5,4-*e*]-tetrahydro-1,3-oxazine-2-thione (27): syrup; 87%; R_f 0.40 ($CHCl_3$–MeOH (3:1)); $[\alpha]_D$ +105° (*c* 1, MeOH); UV (MeOH) 249 nm (ϵ_{mM} 3.8); FABMS *m/z* 258 [(M + Na)$^+$]; IR (film) 3381, 1670, 1557, 1170, 1060 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) Table I and supplementary material (Table V); ^{13}C NMR (50.3 MHz, CD_3OD) δ 188.3 (C=S), 102.3 (C-1), 79.9 (C-4), 70.0, 69.9 (C-2,3), 60.4 (C-5), 56.5 (Me), 45.6 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.78; H, 5.49; N, 6.02; S, 13.74.

***N*-Acetyl-(5*R*)-(2,3-di-*O*-acetyl-4-deoxy-1-*O*-methyl-β-L-arabinopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thione (28)**: foam; R_f 0.55 (hexanes–AcOEt (2:3)); $[\alpha]_D$ +336° (*c* 1, $CHCl_3$); UV ($CHCl_3$) 281 nm (ϵ_{mM} 12.9); EIMS *m/z* 361 ($M^{\bullet+}$); IR (film) 1740, 1708, 1223 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) Table I and supplementary material (Table V); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 187.1 (C=S), 174.1 (CO amide), 170.3, 169.7 (2 CO ester), 97.2 (C-1), 75.9 (C-4), 67.6 (C-2), 67.1 (C-3), 60.8 (C-5), 55.8 (OMe), 48.0 (C-6), 26.6 ($NCOCH_3$) 20.6, 20.4 (2 $COCH_3$). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.50; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.42; H, 5.28; N, 3.50; S, 8.71.

(5*R*)-(4-Deoxy-1-*O*-methyl-α-D-xylopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thione (29): 93%; mp 173–174 °C (ether–EtOH); R_f 0.70 ($CHCl_3$–MeOH (4:1)); $[\alpha]_D$ +16° (*c* 1.2, MeOH); UV (MeOH) 251 nm (ϵ_{mM} 12.2); FABMS *m/z* 258 [(M + Na)$^+$]; IR (KBr) 3304, 1653, 1555, 1177, 1053 cm^{-1}; ^1H NMR (200 MHz, CD_3OD) Table I and supplementary material (Table V); ^{13}C NMR (50.3 MHz, CD_3OD) δ 188.1 (C=S), 102.1 (C-1), 81.9 (C-4), 73.5 (C-3), 71.5 (C-2), 61.4 (C-5), 56.4 (Me), 46.2 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.70; H, 5.44; N, 6.00; S, 13.62.

(5*R*)-(4-Deoxy-1-*O*-methyl-β-D-xylopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thione (30): 84%; mp 173–174 °C (MeOH); R_f 0.65 ($CHCl_3$–MeOH (4:1)); $[\alpha]_D$ −188° (*c* 0.6, MeOH); UV (MeOH) 252 nm (ϵ_{mM} 13.6); FABMS *m/z* 258 [(M + Na)$^+$]; IR (KBr) 3322, 1665, 1554, 1168, 1086 cm^{-1}; ^1H NMR (200 MHz, CD_3OD) Table I and supplementary material (Table V); ^{13}C NMR (75.5 MHz, CD_3OD) δ 187.8 (C=S), 105.6 (C-1), 81.2 (C-4), 75.0 (C-3), 74.0 (C-2), 64.6 (C-5), 57.6 (Me), 45.7 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.79; H, 5.58; N, 6.02; S, 13.60.

***N*-Acetyl-(5*R*)-(2,3-di-*O*-acetyl-4-deoxy-1-*O*-methyl-α-D-xylopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thione (31)**: mp 174–175 °C (EtOH); R_f 0.30 (hexanes–AcOEt (1:2)); $[\alpha]_D$ −84° (*c* 1.3, $CHCl_3$); UV (CH_2Cl_2) 281 nm (ϵ_{mM} 13.1); EIMS *m/z* 361 ($M^{\bullet+}$); IR (KBr) 1748, 1709, 1236 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) Table I and supplementary material (Table V); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 187.4 (C=S), 173.6 (CO amide), 170.0, 169.1 (2 CO ester), 97.5 (C-1), 77.3 (C-4), 70.5 (C-2), 67.4 (C-3), 61.8 (C-5), 55.7 (OMe), 47.8 (C-6), 26.0 ($NCOCH_3$) 20.6, 20.5 (2 $COCH_3$). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.50; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.51; H, 5.36; N, 3.51; S, 8.71.

***N*-Acetyl-(5*R*)-(2,3-di-*O*-acetyl-4-deoxy-1-*O*-methyl-β-D-xylopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thione (32)**: mp 141–142 °C (EtOH); R_f 0.48 (hexanes–AcOEt (2:3)); $[\alpha]_D$ −28.6° (*c* 1, $CHCl_3$); UV (CH_2Cl_2) 281 nm (ϵ_{mM} 10.5); EIMS *m/z* 361 ($M^{\bullet+}$); IR (KBr) 1755, 1696, 1223 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) Table I and supplementary material (Table V); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.4 (C=S), 173.6 (CO amide), 169.5, 169.4 (2 CO ester), 101.6 (C-1), 76.7 (C-4), 71.3 (C-3), 70.4 (C-2), 65.9 (C-5), 57.3 (OMe), 47.7 (C-6), 26.0 ($NCOCH_3$) 20.6, 20.5 (2 $COCH_3$). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.50; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.51; H, 5.37; N, 3.78; S, 8.71.

(5*R*)-(4-Deoxy-1-*O*-methyl-α-D-lyxopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thione (33): amorphous solid; 87%; R_f 0.61 ($CHCl_3$–MeOH (4:1)); $[\alpha]_D$ −37° (*c* 1.1, MeOH); UV (MeOH) 250 nm (ϵ_{mM} 13.3); FABMS *m/z* 258 [(M + Na)$^+$]; IR (KBr) 3330, 1673, 1557, 1170, 1072 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) Table I and supplementary material (Table V); ^{13}C NMR (125.7 MHz, CD_3OD) δ 188.5 (C=S), 103.6 (C-1), 80.0 (C-4), 72.0 (C-3), 68.8 (C-2), 62.0 (C-5), 55.7 (Me), 45.8 (C-6). Anal. Calcd for $C_8H_{13}NO_5S$: C, 40.84; H, 5.57; N, 5.95; S, 13.63. Found: C, 40.67; H, 5.30; N, 5.91; S, 13.45.

***N*-Acetyl-(5*R*)-(2,3-di-*O*-acetyl-4-deoxy-1-*O*-methyl-α-D-lyxopyranoso)[5,4-*e*]tetrahydro-1,3-oxazine-2-thione (34)**: mp 139–140 °C (EtOH); R_f 0.80 (hexanes–AcOEt (2:3)); $[\alpha]_D$ −148° (*c* 1, $CHCl_3$); UV (CH_2Cl_2) 281 nm (ϵ_{mM} 12.5); EIMS *m/z* 361 ($M^{\bullet+}$); IR (KBr) 1748, 1711, 1221 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) Table I and supplementary material (Table V); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1 (C=S), 173.6 (CO amide), 169.4, 169.3 (2 CO ester), 99.3 (C-1), 75.1 (C-4), 68.7 (C-2), 67.3 (C-3), 62.7 (C-5), 55.6 (OMe), 47.8 (C-6), 26.0 ($NCOCH_3$) 20.6, 20.5 (2 $COCH_3$). Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.50; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.41; H, 5.30; N, 3.91; S, 8.85.

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Supplementary Material Available: Tables of ^1H NMR data of 6, 8–15, and 17–34 (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.