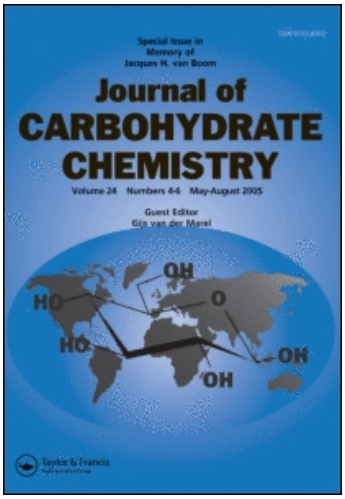

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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Reinaldo Molina Ruiz[ab]; Iran Otero Martinéz[b]; Manfred Michalik[c]; Helmut Reinke[a]; José Quincoces Suarez[d]; Klaus Peseke[a]
[a] Fachbereich Chemie, Universität Rostock, Rostock, Germany [b] Centro de Bioactivos Químicos, Universidad Central de Las Villas, Carretera a Camajuaní, Santa Clara, Cuba [c] Leibniz-Institut für Organische Katalyse, Rostock, Germany [d] Universidade Bandeirante de Sao Paulo, Sao Paulo, Brazil

Online publication date: 28 November 2004

To cite this Article Ruiz, Reinaldo Molina , Martinéz, Iran Otero , Michalik, Manfred , Reinke, Helmut , Suarez, José Quincoces and Peseke, Klaus(2004) 'Synthesis of Novel Anellated Pyranosides as Precursors of *C*-Nucleoside Analogues Using Isopropyl 6-*O*-Acetyl-3-deoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose', Journal of Carbohydrate Chemistry, 23: 5, 337 — 351
To link to this Article: DOI: 10.1081/CAR-200035744
URL: http://dx.doi.org/10.1081/CAR-200035744

JOURNAL OF CARBOHYDRATE CHEMISTRY
Vol. 23, No. 5, pp. 337–351, 2004

Synthesis of Novel Anellated Pyranosides as Precursors of *C*-Nucleoside Analogues Using Isopropyl 6-*O*-Acetyl-3-deoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose[#]

Reinaldo Molina Ruiz,[1,2] Iran Otero Martinéz,[2] Manfred Michalik,[3] Helmut Reinke,[1] José Quincoces Suarez,[4] and Klaus Peseke[1,*]

[1]Fachbereich Chemie, Universität Rostock, Rostock, Germany
[2]Centro de Bioactivos Químicos, Universidad Central de Las Villas, Carretera a Camajuaní, Santa Clara, Cuba
[3]Leibniz-Institut für Organische Katalyse, Rostock, Germany
[4]Universidade Bandeirante de Sao Paulo, Sao Paulo, Brazil

CONTENTS

[#]Dedicated to Professor Dr. Günther Oehme on the occasion of his 65th birthday.

*Correspondence: Klaus Peseke, Fachbereich Chemie, Universität Rostock, D-18051 Rostock, Germany; Fax: +49-381-498-6412; E-mail: klaus.peseke@chemie.uni-rostock.de.

DOI: 10.1081/CAR-200035744
0732-8303 (Print); 1532-2327 (Online)

ABSTRACT

Isopropyl 6-*O*-acetyl-3-deoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose (**3**) was converted to the corresponding 3-[bis(methylthio)methylene] derivative **4** with a push–pull activated C–C double bond. Treatment of **4** with hydrazine and methylhydrazine afforded the pyrano[3,4-*c*]pyrazol-5-ylmethyl acetates **5a** and **5b**, respectively. Desulfurization of compound **4** with sodium boron hydride yielded the 3-[(methylthio)methylene]hexopyranosid-2-ulose **7**. Compound **7** was reacted with amines to furnish 3-aminomethylene-hexopyranosid-2-uloses **8**, **9**. Reaction of **7** with hydrazine hydrate, hydrazines, hydroxylamine, and benzamidine afforded the pyrazolo, isoxazalo, and pyrimido anellated pyranosides (**10**–**13**).

Key Words: Deoxyuloses; Thiosugars; Branched sugars; Push–pull alkenes; Heteroanellated pyranosides.

INTRODUCTION

The development of new methods for the synthesis of anellated monosaccharide derivatives has attracted a current interest in organic chemistry[1–4] because of the biological importance showing some compounds in this class, for example, anti-inflammatory drugs, spruce budworm antifeedants, and herbicidin nucleoside antibiotics[5–7] or as inhibitors of different glycosidases.[8,9] Continuing our studies[2,10–15] concerning the preparation of biyclic and polycyclic compounds on the basis of pyranosides, we report here the preparations of pyrazolo, isoxazolo, and pyrimido anellated pyranosides on the basis of isopropyl 6-*O*-acetyl-3-deoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose.

RESULTS AND DISCUSSION

2-Hydroxyglycals are versatile reagents and offer a wide reaction spectrum such as the well-known Ferrier rearrangement of 2-hydroxyglycals with alcohols and Lewis acids to yield enones.[16–18] 2,3,4,6-Tetra-*O*-acetyl-2-hydroxy-D-galactal (**1**) was reacted with isopropanol and boron trifluoride etherate to furnish isopropyl 6-*O*-acetyl-3,4-dideoxy-α-D-*glycero*-hex-3-enopyranosid-2-ulose (**2**).[19–21] Uhrig and Varela reported the highly diastereoselective addition of ethanethiol to enone **2** in dichloromethane in the presence of triethylamine to yield isopropyl 6-*O*-acetyl-3-deoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose (**3**).[22] However, we used basic alumina

in toluene according to the Essig method[23] obtaining compound **3** in 78% yield. By this method, the workup is much easier in comparison with the methods described by Varela as well as the yield of the reaction is also slightly increased (Sch. 1).

Treatment of pyranosidulose **3** with carbon disulfide in the presence of an excess of methyl iodide in tetrahydrofuran at 0°C using sodium hydride as base yielded isopropyl-6-*O*-acetyl-3-[bis(methylthio)methylen]-3-deoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose (**4**). This push–pull activated branched-chain sugar showed an upfield shift for C-3 ($\delta = 133.0$) in the ^{13}C NMR spectrum, whereas the signal of C-3′ was shifted downfield ($\delta = 158.0$) typical for such polarized alkenes.[24] In the ^{1}H NMR spectrum the corresponding signals of the thiomethyl groups were found at $\delta = 2.42$ and 2.43.

Compound **4** may be regarded as α-oxoketen-*S*,*S*-acetal[25] and, therefore, should react easily with hydrazines to form pyrazoles. Treatment of **4** with hydrazine hydrate in tetrahydrofuran under reflux led to the displacement of one methylthio group and the cyclization occurred by attack of the hydrazino group on the carbonyl C-atom under elimination of water to furnish a crystalline compound. The isolated pyrano[3,4-*c*]pyrazole can exist in the two tautomeric forms (4*R*,5*R*,7*S*)-4-ethylsulfanyl-7-isopropoxy-3-methylsulfanyl-2,4,5,7-tetrahydro-pyrano[3,4-*c*]pyrazol-5-yl-methyl acetate (**5a**) and (4*R*,5*R*,7*S*)-4-ethylsulfanyl-7-isopropoxy-3-methylsulfanyl-1,4,5,7-tetrahydropyrano[3,4-*c*]pyrazol-5-ylmethyl acetate (**6**), but, a decision which tautomer is present could not be taken. Due to the fast NH-proton exchange, no signal for an NH-proton in the ^{1}H NMR spectrum was observed and the atoms C-3 and C-7a appear as broadened signals in the ^{13}C NMR spectrum.

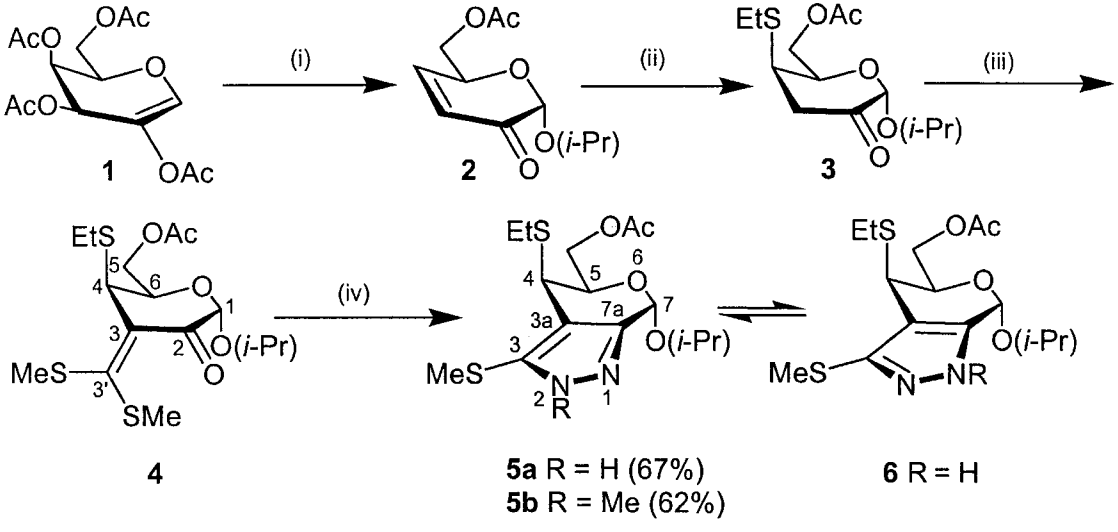
In order to prepare the corresponding *N*-methyl-substituted pyrano[3,4-*c*]pyrazol derivative, the ulose **4** was treated with methylhydrazine at r.t. The (4*R*,5*R*,7*S*)-7-isopropoxy-2-methyl-3-methylsulfanyl-2,4,5,7-tetrahydropyrano[3,4-*c*]pyrazol-5-ylmethyl-acetate (**5b**) was obtained in good yield. Lack of a signal for one of the methylthio groups in the NMR spectra of **5b** and only one carbonyl band in the IR spectra showed that a cyclization had taken place. In ^{1}H,^{1}H-NOESY spectrum cross-peaks were found between the protons of the methyl group and methylthio group confirming the position of the methyl group at N-2.

Compound **4** did not react with other nucleophiles under several reaction conditions. This behavior of **4** could be attributed to the relatively high stability of its push–pull system and also to the steric hindrance of the two methylthio groups.

According to the push–pull concept[26], the displacement of one of the methylthio groups through hydrodesulfurization should give a compound with increased electrophilic reactivity.

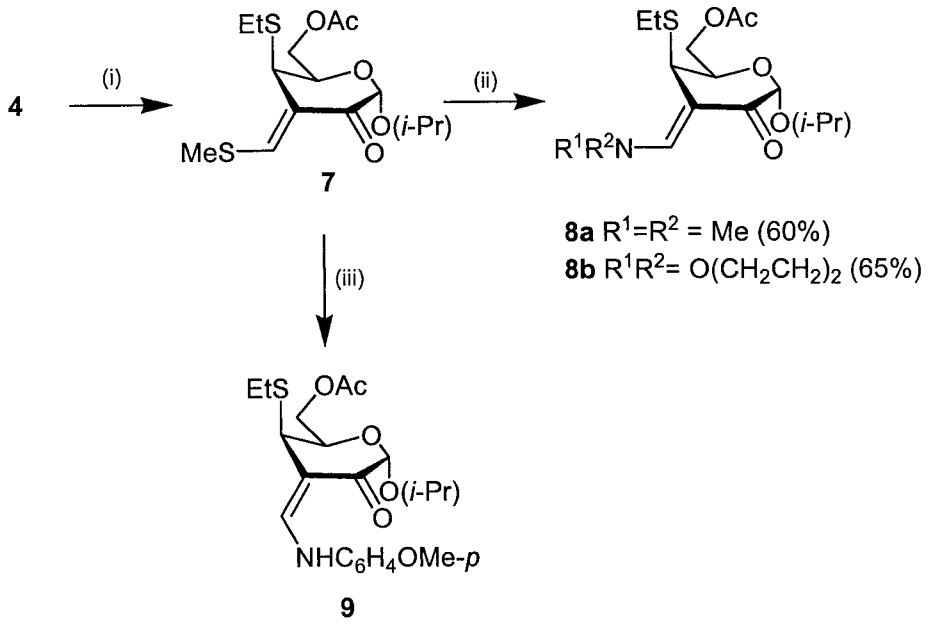
With sodium borohydride in acetic acid, the bis(methylthio)methylene ulose **4** reacted in only 10 min to furnish isopropyl (3*Z*)-6-*O*-acetyl-3-deoxy-4-*S*-ethyl-3-[(methylthio)-methylen]-4-thio-α-D-*threo*-hexopyranos-2-ulose (**7**) in 70% yield as a crystalline solid. The lack of one methylthio group and the appearance of an additional olefinic proton signal in the NMR spectrum showed that a hydrodesulfurization successfully took place. Furthermore, the NMR data showed the presence of only one isomer. NOE experiments confirmed the Z-configuration of compound **7** in chloroform solution (Sch. 2).

The ^{13}C NMR spectrum of compound **7** showed the expected upfield signals of C-3′ ($\delta = 150.3$) and C-3 ($\delta = 129.0$) in comparison with **4**. On the other hand, the mass spectrum displayed a peak for M^+ at m/z 348 which confirmed the structure for compound **7**.



Reagents and Reactions: (i) *i*-PrOH, $BF_3{\cdot}OEt_2$; (ii) EtSH, Al_2O_3, toluene; (iii) CS_2, NaH, MeI, THF (80%); (iv) H_2NNHR, MeOH (R = H, Me)

Scheme 1. Synthesis of push–pull activated branched-chain and pyrazolo anellated pyranosides.



Reagents and Reactions: (i) $NaBH_4$, AcOH (70%); (ii) R^1R^2NH, MeOH (R^1= R^2 = Me, R^1R^2= $O(CH_2CH_2)_2$; (iii) *p*-$MeOC_6H_4NH_2$, MeOH (90%)

Scheme 2. Synthesis of methylthio and aminomethylene uloses.

Furthermore, an x-ray structure analysis of compound **7** was performed. An ORTEP-drawing with the numbering scheme of the atoms is shown in Fig. 1. The central sugar ring adopts a conformation between a half-chair and a half-boat with puckering parameters[27] of $Q = 0.540(5)$ Å (puckering amplitude), $\Theta = 52.7(5)^\circ$, and $\Phi = 328.0(7)^\circ$.

As expected, compound **7** reacted with secondary amines at r.t. in methanol easily under substitution of the methylthio group to yield the corresponding aminomethylene uloses **8** as (Z)-isomers. The NMR spectra confirmed the substitution of the methylthio group and the presence of only one isomer. In the NOESY spectra of compounds **8**, cross-peaks between the signals for H-4 and the protons of the carbon atoms bonded to nitrogen was detected.

However, the treatment of ulose **7** with *p*-anisidine afforded the isopropyl (3*E*)-6-*O*-acetyl-3-[(*p*-anisidino)methylene]-3-deoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranos-2-ulose (**9**). The ^{1}H NMR spectrum of compound **9** indicated the existence of an NH-group which is included in an intramolecular hydrogen bound with the CO-group. The NH signal at $\delta = 12.6$ did not show any upfield shift in the spectra at higher temperature. These results proved the postulated (E)-configuration.

On the other hand, the compound **7** was treated with hydrazine hydrate in methanol at r.t. After column chromatography, the (4*R*,5*R*,7*S*)-4-ethylsulfanyl-7-isopropoxy-1,4,5,7-tetrahydropyrano[3,4-*c*]pyrazol-5-ylmethyl acetate (**10**) was isolated in 60% yield (Sch. 3). In the ^{1}H NMR spectrum appeared a singlet for an NH proton, therefore, the proton should

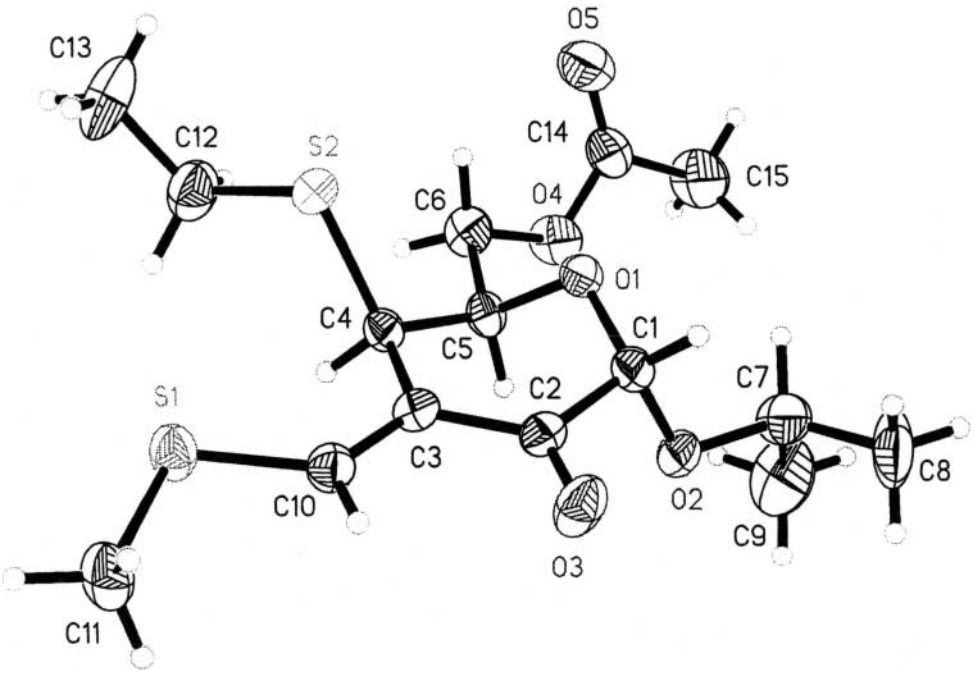
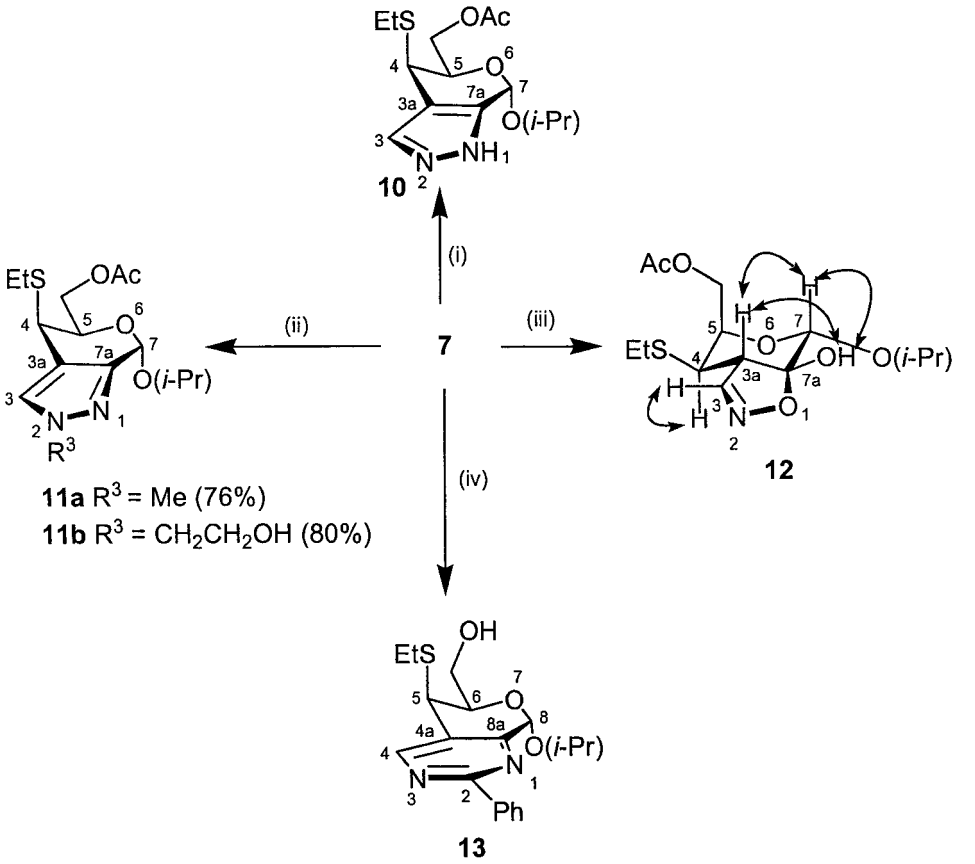


Figure 1. ORTEP-drawing of **7**, 30% probability of the thermal ellipsoids.

be bounded on N-1. Methylhydrazine and 2-hydrazino-ethanol, respectively, and compound **7** were reacted to furnish the 2-substituted (4*R*,5*R*,7*S*)-4-ethylsulfanyl-7-isopropoxy-2,4,5,7-tetrahydropyrano[3,4-*c*]pyrazol-5-ylmethyl acetates **11** in good yields. The cross-peaks between the H-3 and the protons of the methyl group and hydroxyethyl group, respectively, in the ^{1}H,^{1}H-NOESY spectra confirmed the position of these groups at N-2.

Treatment of thioenolether **7** with hydroxylamine in methanol at room temperature afforded the (3a*S*,4*R*,5*R*,4R,7*S*,7a*R*)-4-ethylsulfanyl-4,5,7,7-tetrahydro-7a-hydroxy-7-isopropoxy-3a*H*-pyrano[4,3-*d*]isoxazol-5-ylmethyl acetate (**12**) in 50% yield. In contrast to the formation of the pyrazolo anellated pyranosides **5**, **6**, **10**, and **11**, elimination of water in the case of **12** did not occur. Therefore, in the IR spectrum of **12** a band at 3402^{-1} and in the ^{1}H NMR spectrum an OH-signal at $\delta = 6.68$ were observed. Signals for the saturated carbon atoms C-3a and C-7a appeared in the expected area at $\delta = 57.1$ and 100.2, respectively. Furthermore, in the ^{1}H,^{1}H-NOESY spectra cross-peaks between the proton signals of H-3 and H-4; H-3a, OH-7a, and H-7 were found which confirm the postulated $^{1}C_4$-conformation.

Finally, the pyrimido anellated pyranoside **13** could be synthesized by cyclization reactions of compound **7** with benzamidines liberated from the corresponding nitrate using sodium methanolate. The IR spectrum and the ^{13}C NMR spectrum showed not any signals for a carbonyl group indicating that under these reaction conditions, the cleavage of the acetyl group occurred.



Reagents and Reactions: (i) NH_2NH_2, MeOH (60%); (ii) $RNHNH_2$, MeOH (R^3= Me, CH_2CH_2OH); (iii) NH_2OH, MeOH (50%); (iv) $PhC(NH_2)=NH_2^+NO_3^-$, NaOMe, MeOH (60%)

Scheme 3. Syntheses of pyrazolo, isoxazolo, and pyrimido anellated pyranosides.

EXPERIMENTAL

General Methods

Melting points were determined with a Boëtius melting point apparatus and are corrected. Optical rotations were measured with a Polar LμP (IBZ Meßtechnik) polarimeter. IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. ^1H and ^{13}C NMR spectra were recorded with a Bruker AC 250 (250.1 and 62.9 MHz, respectively) and a Bruker ARX 300 (300.1 and 75.5 MHz, respectively). The calibration of spectra was carried out by means of solvent peaks ($CDCl_3$: $\delta^1H = 7.25$; $\delta^{13}C = 77.0$; DMSO-d_6: $\delta^1H = 2.50$; $\delta^{13}C = 39.7$; dioxane: $\delta^1H = 3.71$; $\delta^{13}C = 67.6$ for recording in D_2O).

The ^{13}C NMR signals were assigned by DEPT and/or two-dimensional $^{1}H,^{13}C$ correlation spectra. Mass spectra were obtained with an AMD 402/3 spectrometer (AMD Intectra GmbH). Elemental analyses were performed with a Leco CHNS-932. Column chromatography was carried out on silica gel 60 (63–200 μm, Merck). Thin-layer chromatography (TLC) was performed on silica gel 60 GF_{254} foils (Merck) with detection by UV-light and by charring with 10% methanolic sulfuric acid. Solvents and liquid reagents were purified and dried according to the recommended procedures.

Isopropyl 6-*O*-acetyl-3-deoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose (3). Compound **3** was prepared according to Essig method[23] and the spectral data were in agreement with data reported previously by Uhrig and Varela.[22]

Isopropyl 6-*O*-acetyl-3-deoxy-4-*S*-ethyl-3-[bis(methylthio)methylene]-4-thio-α-D-*threo*-hexopyranosid-2-ulose (4). Sodium hydride (130 mg of 55–60% dispersion in oil, ~2.5 mmol), carbon disulfide (150 μL, 2.5 mmol), and methyl iodide (269 μL, 4 mmol) were added to a stirred solution of **3** (290 mg, 1.0 mmol) in anhydrous THF (45 mL) at 0°C. The mixture was stirred for 2 hr, then poured into ice-water (30 mL) and extracted with chloroform (3 × 20 mL). The combined extracts were washed with water (3 × 20 mL), and dried over Na_2SO_4. After evaporating the solvent, the syrup obtained was chromatographed on a column of silica gel (toluene/ethyl acetate, 6 : 1) to obtain a yellowish syrup. Yield: 315 mg (80%); $[\alpha]_D^{24.6}$ −30.9° (*c* 0.5, chloroform); IR (KBr): 1744 (C═O, Ac), 1697 (C═O, C-2), 1454 (C═C) cm^{-1}; ^{1}H NMR: δ 1.17, 1.21 [2 × d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 1.19 (t, 3H, $J = 7.6$, SCH_2CH_3), 2.07 (s, 3H, Ac), 2.42 (s, 3H, SMe), 2.43 (s, 3H, SMe), 2.52 (m, 2H, SCH_2CH_3), 3.98 [m, 1H, $CH(CH_3)_2$], 4.36 (d, 2H, H-6), 4.64 (m, 1H, $J < 1.0$ Hz, H-4), 4.65 (m, 1H, $J < 1.0$ Hz, H-5), 4.87 (s, 1H, H-1); ^{13}C NMR: δ 14.7 (SCH_2CH_3), 19.4, 18.5 (SMe), 20.8 ($COCH_3$), 23.2, 21.8 [$CH(CH_3)_2$], 24.4 (SCH_2CH_3), 44.5 (C-4), 64.5 (C-6), 70.6 (C-5), 71.2 [$CH(CH_3)_2$], 97.3 (C-1), 133.0 (C-3), 158.0 (C-3′), 170.8 ($COCH_3$), 192.0 (C-2); MS (EI, 70 eV), *m/z* (%): 395.4 (34, $M + 1^+$), 333.2 (100); MS, (CI, *iso*-butane), *m/z* (%): 394.3 (58, M^+).

Anal. Calcd for $C_{16}H_{26}O_5S_3$: C, 48.71; H, 6.64; S, 24.38. Found: C, 48.93; H, 6.59; S, 24.04.

(4*R*,5*R*,7*S*)-4-Ethylsulfanyl-7-isopropoxy-3-methylsulfanyl-2,4,5,7-tetrahydropyrano[3,4-*c*]pyrazol-5-ylmethyl acetate (5a). Hydrazine hydrate (80%, 200 mg, 3.2 mmol) was added to a stirred solution of **4** (394 mg, 1.0 mmol) in anhydrous THF (15 mL) at r.t. The mixture was stirred and heated under reflux for 2 hr. The solvent was evaporated under reduced pressure. The resulting syrup was purified on a column of silica gel (toluene/ethyl acetate, 1 : 1) to give white crystals. Yield: 241 mg (67%); mp 151–153°C; $[\alpha]_D^{23.3}$ −139.4° (*c* 1.0, chloroform); IR (KBr): 3455 (NH), 1744 (C═O), 1458 (C═C) cm^{-1}; ^{1}H NMR: δ 1.14 (t, 3H, $J = 7.6$ Hz, SCH_2CH_3), 1.25 [d, 6H, $J = 6.4$ Hz, $CH(CH_3)_2$], 2.08 (s, 3H, Ac), 2.47 (s, 3H, SMe), 2.58 (m, 2H, SCH_2CH_3), 3.80 (d, 1H, $J_{4,5} = 2.5$ Hz, H-4), 4.15 [m, 1H, $CH(CH_3)_2$], 4.45 (m, 2H, CH_2OAc), 4.48 (m, 1H, H-5), 5.79 (s, 1H, H-7); ^{13}C NMR: δ 14.6 (SCH_2CH_3), 17.6 (SMe), 20.9 ($COCH_3$), 21.8, 23.5 $CH(CH_3)_2$, 24.6 (SCH_2CH_3), 37.6 (C-4), 65.4 (CH_2OAc), 69.5 (C-5), 70.0 [$CH(CH_3)_2$], 91.8 (C-7), 118.0 (C-3a), 128.0 (C-3), 148.0 (C-7a), 170.8 (C═O); MS (EI, 70 eV), *m/z* (%): 360.0 (29, M^+), 239 (100).

Anal. Calcd for $C_{15}H_{24}N_2O_4S$: N, 7.77; S, 17.79. Found: N, 7.74; S, 17.63.

(4*R*,5*R*,7*S*)-7-Isopropoxy-2-methyl-3-methylsulfanyl-2,4,5,7-tetrahydropyrano[3,4-*c*]pyrazol-5-ylmethylacetate (5b). Methylhydrazine (50 μL, 1.5 mmol) was added to a stirred solution of **4** (394 mg, 1.0 mmol) in absolute methanol (15 mL) at r.t. The

mixture was stirred for 8 hr. The solvent was evaporated under reduced pressure. The resulting syrup was purified on a column of silica gel (toluene/ethyl acetate, 2 : 1) to give white crystals. Yield: 254 mg (62%); mp 142–144°C; $[\alpha]_D^{25.2}$ +63.2° (*c* 0.5, chloroform); IR (KBr): 1742 (C═O), 1457 (C═C) cm^{-1}; ^1H NMR: δ 1.18 [d, 6H, $J = 6.4$ Hz, $CH(CH_3)_2$], 1.18 (t, 3H, $J = 7.3$ Hz, SCH_2CH_3), 2.08 (s, 3H, Ac), 2.48 (s, 3H, SMe), 2.61 (m, 2H, SCH_2CH_3), 3.85 (d, 1H, $J_{4,5} = 2.5$ Hz, H-4), 3.96 (s, 3H, NMe), 4.15 [m, 1H, $CH(CH_3)_2$], 4.45 (m, 2H, CH_2OAc), 4.48 (m, 1H, H-5), 5.79 (s, 1H, H-7); ^{13}C NMR: δ 14.6 (SCH_2CH_3), 17.6 (SCH_3), 20.8 ($COCH_3$), 21.8, 23.5 [$CH(CH_3)_2$], 24.6 (SCH_2CH_3), 37.6 (C-4), 44.3 (NCH_3), 64.8 (CH_2OAc), 69.5 (C-5), 71.3 [$CH(CH_3)_2$], 93.4 (C-7), 121.1 (C-3a), 128.2 (C-3), 149.3 (C-7a), 170.3 (C═O); MS (EI, 70 eV), *m/z* (%): 374.0 (45, M^+), 239 (100).

Anal. Calcd for $C_{16}H_{26}N_2O_4S_2$: C, 51.31; H, 7.00; N, 7.48; S, 17.12. Found: C, 52.04; H, 6.79; N, 8.16; S, 17.23.

Isopropyl (3*Z*)-6-*O*-acetyl-3-deoxy-4-*S*-ethyl-3-[(methylthio)methylene]-4-thio-α-D-*threo*-hexopyranosid-2-ulose (7). Sodium boron hydride (110 mg, 3.0 mmol) was added carefully in small portions to a cooled and stirred solution of **4** (394 mg, 1.0 mmol) in glacial acetic acid (15 mL). The suspension was stirred at 0°C for 10 min. The mixture was diluted with chloroform (50 mL), washed with saturated sodium carbonate solution (2 × 50 mL), and then washed with water (100 mL). The aqueous layer was separated, extracted with chloroform (3 × 10 mL), and the organic layer was evaporated to dryness, the residue was crystallized from ethanol afforded white crystals. Yield: 240 mg (70%); mp 62–63°C; $[\alpha]_D^{25.9}$ +117.7° (*c* 0.5, chloroform); IR (KBr): 1731 (C═O, Ac), 1674 (C═O, C-2), 1521 (C═C) cm^{-1}; ^1H NMR: δ 1.16, 1.22 [2 × d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 1.21 (t, 3H, $J = 7.6$ Hz, SCH_2CH_3), 2.07 (s, 3H, Ac), 2.51 (s, 3H, SMe), 2.52 (m, 2H, SCH_2CH_3), 3.75 (d, 1H, $J_{4,5} = 2.8$ Hz, H-4), 4.01 [m, 1H, $CH(CH_3)_2$], 4.38 (m, 2H, H-6), 4.68 (m, 1H, H-5), 4.87 (s, 1H, H-1), 7.83 (s, 1H, H-3′); ^{13}C NMR: δ 14.5 (SCH_2CH_3), 18.2 (SMe), 20.8 ($OCOCH_3$), 23.2, 21.4 [$CH(CH_3)_2$], 25.4 (SCH_2CH_3), 44.5 (C-4), 64.9 (C-6), 68.4 (C-5), 71.0 [$CH(CH_3)_2$], 96.5 (C-1), 129.0 (C-3), 149.8 (C-3′), 170.6 ($COCH_3$), 186.9 (C-2); MS (EI, 70 eV), *m/z* (%): 348 (M^+): 43 (100).

Anal. Calcd for $C_{15}H_{24}O_5S_2$: C, 51.70; H, 6.94; S, 18.40. Found: C, 51.86; H, 6.84; S, 18.55.

X-ray Structure Determination of **7**

The data collection was performed on a Bruker P4 four circle diffractometer with MoK_α radiation ($\lambda = 0.71073$ Å) and a graphite monochromator in routine ω-scan after checking the crystal quality by a rotational photo and determining a reasonable reduced cell. Further data: crystal size $0.53 \times 0.18 \times 0.15\ mm^3$, yellowish, part of needle, $T = 293(2)$ K, $C_{15}H_{24}O_5S_2$, $M = 348.46$, monoclinic, space group (Hermann–Mauguin) $P2_1$, space group (Hall) $P2yb$, $a = 5.257(1)$, $b = 17.136(4)$, $c = 10.254(3)$ Å, $\alpha = \gamma = 90°$, $\beta = 94.88°(2)$, $V = 920.4(4)\ Å^3$, $Z = 2$, ρ_{calc} $1.257\ Mg\ m^{-3}$, $\mu = 0.307\ mm^{-1}$, $F(0\,0\,0) = 372$, data collection range: $1.99 \le \Theta \le 22.00°$, $-5 \le h \le 5$, $-18 \le k \le 18$, $-10 \le l \le 10$, 2644 reflections collected, 2263 independent reflections [R(int) = 0.0471], 1842 observed [$I > 2\sigma(I)$], completeness to $\Theta = 22.00°$: 100 %, $R_1 = 0.0518$(obs.), $wR_2 = 0.1164$(obs.), GOF (F^2) = 1.004, max./min. residual electron density: $+0.173/-0.143\ e\ Å^{-3}$. The weighting scheme was calculated

according to $w^{-1} = \sigma^2 \ (F_o^2) + (0.0531P)^2 + 0.000P$ with $P = (F_o^2 + 2F_c^2)/3$. The structure was solved by direct methods (Bruker SHELXTL) and refined by the full matrix least-squares method of the Bruker SHELXTL software package. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms introduced into theoretical positions and refined according to the riding model. CCDC 207583 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223-336033; E-mail: deposit@ccdc.cam.ac.uk).

General Method for the Reaction of **7** with Amines

To a stirred solution of **7** (50 mg, 0.14 mmol) in methanol (5 mL), the amine was added. The mixture was stirred at r.t. for 30 min. The solvent was evaporated in a rotary evaporator. The crude product was purified by column chromatography (chloroform/methanol, 20 : 1).

Isopropyl (3*Z*)-6-*O*-acetyl-3-deoxy-3-[(dimethylamino)methylene]-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose (8a). Compound **7** and an aqueous solution of dimethylamine (40%, 20 μL, 0.2 mmol) afforded according to the general method a colorless syrup. Yield: 30 mg (60%); $[\alpha]_D^{23.2}$ −85.2° (*c* 1.0, chloroform); IR (KBr): 1731 (C═O, Ac), 1674 (C═O, C-2), 1520 (C═C) cm^{-1}; ^1H NMR: δ 1.15 (t, 3H, $J = 7.6$ Hz, SCH_2CH_3), 1.20, 1.22 [2 × d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 2.06 (s, 3H, Ac), 2.59 (m, 2H, SCH_2CH_3), 3.27 (s, 6H, NMe_2), 3.90 (d, 1H, $J_{4,5} = 2.5$ Hz, H-4), 4.01 [m, 1H, $J = 6.1$ Hz, $CH(CH_3)_2$], 4.38 (m, 2H, H-6), 4.68 (m, 1H, H-5), 4.87 (s, 1H, H-1), 7.83 (s, 1H, H-3′); ^{13}C NMR: δ 14.6 (SCH_2CH_3), 20.9 ($COCH_3$), 23.3, 21.5 [$CH(CH_3)_2$], 23.4 (SCH_2CH_3), 40.1 [$N(CH_3)_2$], 41.8 (C-4), 66.1 (C-6), 69.6 (C-5), 70.3 [$CH(CH_3)_2$], 96.7 (C-1), 100.0 (C-3), 152.1 (C-3′), 170.8 ($COCH_3$), 188.1 (C-2); MS (EI, 70 eV), *m/z* (%): 345.0 (27, M^+) 224.0 (100).

Anal. Calcd for $C_{16}H_{27}NO_5S$: C, 55.63; H, 7.88; N, 4.05; S, 9.28. Found: C, 56.02; H, 7.64; N, 3.76; S, 9.45.

Isopropyl (3*Z*)-6-*O*-acetyl-3-desoxy-4-*S*-ethyl-3-[(morpholino)methylene]-4-thio-α-D-*threo*-hexopyranosid-2-ulose (8b). Compound **7** and morpholine (15 μL, 0.14 mmol) afforded according to the general method a colorless syrup. Yield: 35 mg (65%); $[\alpha]_D^{24.3}$ −129.2° (*c* 1.0, chloroform); IR (KBr) 1742 (C═O, Ac), 1681 (C═O, C-2), 1520 (C═C) cm^{-1}; ^1H NMR: δ 1.14 (t, 3H, $J = 7.6$ Hz, SCH_2CH_3), 1.21, 1.23 [2 × d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 2.04 (s, 3H, Ac), 2.57 (m, 2H, SCH_2CH_3), 3.51 (m, 1H, H-4), 3.73 m, 8H, $N[(CH_2)_2]_2O$, 4.00 [m, 1H, $J = 6.1$ Hz, $CH(CH_3)_2$], 4.33 (m, 2H, H-6), 4.63 (m, 1H, H-5), 4.80 (s, 1H, H-1), 7.58 (s, 1H, H-3′); ^{13}C NMR: δ 14.8 (SCH_2CH_3), 20.9 ($COCH_3$), 21.5, 23.4 [$CH(CH_3)_2$], 23.7 (SCH_2CH_3), 42.5 (C-4), 52.2, 52.0 [$N(CH_2)_2$], 65.9 (C-6), 66.9, 66.8 [$O(CH_2)_2$], 69.4 (C-5), 70.4 [$CH(CH_3)_2$], 96.6 (C-1), 99.9 (C-3), 149.8 (C-3′), 170.8 ($COCH_3$), 188.5 (C-2); MS (EI, 70 eV), *m/z* (%): 387.0 (12, M^+), 266.0 (100).

Anal. Calcd for $C_{18}H_{29}NO_6S$: C, 55.79; H, 7.54; N, 3.61; S, 8.27. Found: C, 55.62; H, 7.34; N, 3.79; S, 8.12.

Isopropyl (3*Z*)-6-*O*-acetyl-3-[(*p*-anisidino)methylene]-3-desoxy-4-*S*-ethyl-4-thio-α-D-*threo*-hexopyranosid-2-ulose (9). Compound **7** and *p*-anisidine (17 mg,

0.14 mmol) afforded according to the general method yellowish crystals. The eluent for column chromatography was toluene/ethyl acetate (5 : 1). Yield: 55 mg (90%); mp 125–127°C; $[\alpha]_D^{23.4}$ −105.7° (*c* 1.0, chloroform); IR (KBr): 3433 (NH), 1741 (C═O, Ac), 1645 (C═O, C-2); ^{1}H NMR: δ 1.17 (t, 3H, $J = 7.6$ Hz, SCH_2CH_3), 1.24 [d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 2.06 (s, 3H, Ac), 2.60 (m, 2H, SCH_2CH_3), 3.62 (d, 1H, $J_{4,5} = 2.8$ Hz, H-4), 3.77 (s, 3H, OMe), 4.04 [m, 1H, $J = 6.1$ Hz, $CH(CH_3)_2$], 4.36 (m, 2H, H-6), 4.61 (m, 1H, H-5), 4.89 (s, 1H, H-1), 6.87 (m, 2H, *m*-H, *p*-$MeOC_6H_4$), 7.03 (m, 2H, *o*-H, *p*-$MeOC_6H_4$), 7.57 (d, 1H, $J_{3',NH} = 12.5$ Hz, H-3′), 12.63 (d, 1H, $J_{3',NH} = 12.5$ Hz, NH); ^{13}C NMR: δ 14.6 (SCH_2CH_3), 20.8 ($COCH_3$), 23.3, 21.5 [$CH(CH_3)_2$], 23.6 (SCH_2CH_3), 43.9 (C-4), 55.6 (OCH3), 65.9 (C-6), 69.1 (C-5), 70.4 [$CH(CH_3)_2$], 95.8 (C-1), 102.4 (C-3), 115.1 (*m*-C, *p*-$MeOC_6H_4$), 118.7 (*o*-C, *p*-$MeOC_6H_4$), 132.6 (*p*-C, *p*-$MeOC_6H_4$), 149.6 (C-3′), 157.3 (*i*-C, *p*-$MeOC_6H_4$), 170.7 ($COCH_3$), 188.6 (C-2); MS (EI, 70 eV), *m*/*z* (%): 424.0 (57, M^+), 302.0 (100).

Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.56; H, 6.90; N, 3.31; S, 7.57. Found: C, 59.78; H, 6.84; N, 3.01; S, 7.69.

(4*R*,5*R*,7*S*)-4-Ethylsulfanyl-7-isopropoxy-1,4,5,7-tetrahydropyrano[3,4-*c*]pyrazol-5-ylmethyl acetate (10). Hydrazine hydrate (80%, 20 μL, 0.2 mmol) was added to a stirred solution of **7** (50 mg, 0.14 mmol) in absolute methanol (5 mL) at r.t. The mixture was stirred for 10 min. The solvent was evaporated under reduced pressure. The residue obtained was purified on a column of silica gel (toluene/ethyl acetate, 1 : 1) afforded white crystals. Yield: 26 mg (60%); mp 124–126°C; $[\alpha]_D^{23.4}$ −80.5° (*c* 1.0, chloroform); IR (KBr): 3450 (NH), 1745 (C═O), 1457 (C═C) cm^{-1}; ^{1}H NMR: δ 1.11 (t, 3H, $J = 7.3$ Hz, SCH_2CH_3), 1.26 [d, 6H, $J = 6.4$ Hz, $CH(CH_3)_2$], 2.07 (s, 3H, Ac), 2.38 (m, 2H, SCH_2CH_3), 3.85 (d, 1H, $J_{4,5} = 3.0$ Hz, H-4), 4.17 [m, 1H, $CH(CH_3)_2$], 4.41 (m, 2H, CH_2OAc), 4.55 (m, 1H, H-5), 5.84 (s, 1H, H-7), 7.46 (s, 1H, H-3); ^{13}C NMR: δ 14.5 (SCH_2CH_3), 20.9 ($COCH_3$), 21.8, 23.5 [$CH(CH_3)_2$], 24.0 (SCH_2CH_3), 37.4 (C-4), 65.6 (CH_2OAc), 69.1 (C-5), 69.8 [$CH(CH_3)_2$], 92.3 (C-7), 115.9 (C-3a), 127.5 (C-3), 145.0 (C-7a), 170.8 (C═O); MS (EI, 70 eV), *m*/*z* (%): 314.0 (51, M^+), 169.0 (100).

Anal. Calcd for $C_{14}H_{22}N_2O_4S$: C, 53.48; H, 7.05; N, 8.91; S, 10.20. Found: C, 53.49; H, 6.99; N, 9.40; S, 9.87.

(4*R*,5*R*,7*S*)-4-Ethylsulfanyl-2,4,5,7-tetrahydropyrano-7-isopropoxy-2-methyl[3,4-*c*]pyrazol-5-ylmethyl acetate (11a). The reaction of **7** (50 mg, 0.14 mmol) with methylhydrazine (0.2 mmol) was carried out as described above for **10** to give white crystals. Yield: 35 mg (76%); mp 53–55°C; $[\alpha]_D^{24.0}$ −72.7° (*c* 1.0, chloroform); IR (KBr); 1745 (C═O), 1457 (C═C) cm^{-1}; ^{1}H NMR: δ 1.17 (t, 3H, $J = 7.3$ Hz, SCH_2CH_3), 1.31 [d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 2.11 (s, 3H, Ac), 2.45 (m, 2H, SCH_2CH_3), 3.86 (d, 1H, $J_{4,5} = 3.0$ Hz, H-4), 3.93 (s, 3H, MeN), 4.21 [m, 1H, $J = 6.1$ Hz, $CH(CH_3)_2$], 4.44 (m, 2H, CH_2OAc), 4.61 (m, 1H, H-5), 5.83 (s, 1H, H-7), 7.31 (s, 1H, H-3); ^{13}C NMR: δ 14.5 (SCH_2CH_3), 20.8 ($COCH_3$), 21.7, 23.4 [$CH(CH_3)_2$], 24.1 (SCH_2CH_3), 37.4 (C-4), 39.3 (CH_3N), 65.6 (CH_2OAc), 68.8 (C-5), 69.5 [$CH(CH_3)_2$], 92.5 (C-7), 116.5 (C-3a), 127.3 (C-3), 146.5 (C-7a), 170.7 (C═O); MS (EI, 70 eV), *m*/*z* (%): 328.0 (14, M^+), 183.0 (100).

Anal. Calcd for $C_{15}H_{24}N_2O_4S$: C, 54.86; H, 7.37; N, 8.53; S, 9.76. Found: C, 54.69; H, 7.18; N, 8.71; S,10.03.

(4*R*,5*R*,7*S*)-4-Ethylsulfanyl-2-(2-hydrazino-ethyl)-2,4,5,7-tetrahydro-7-isopropoxy-pyrano[3,4-*c*]pyrazol-5-ylmethyl acetate (11b). The reaction of **7** (50 mg, 0.14 mmol) with 2-hydrazino-ethanol (0.2 mmol) was carried out as described above for

10. The reaction was completed after 1.5 hr. The residue was purified on a column of silica gel (chloroform/methanol, 25 : 1) to give white crystals. Yield: 40 mg (80%); mp 101–103°C; $[\alpha]_D^{24.0}$ −129.1° (*c* 1.0, chloroform); IR (KBr): 3320.3 (OH), 1743.8 (C═O) cm^{-1}; ^1H NMR δ 1.13 (t, 3H, $J = 7.3$ Hz, SCH_2CH_3), 1.26, 1.27 [d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 2.07 (s, 3H, Ac), 2.42 (m, 2H, SCH_2CH_3), 3.81 (d, 1H, $J_{4,5} = 3.0$ Hz, H-4), 3.95 (t, 2H, $J_{CH_2,CH_2} = 4.9$ Hz, CH_2N), 4.19 [m, 1H, $CH(CH_3)_2$], 4.22 (m, 2H, CH_2OH), 4.40 (m, 2H, CH_2OAc), 4.56 (m, 1H, H-5), 5.78 (s, 1H, H-7), 7.36 (s, 1H, H-3); ^{13}C NMR: δ 14.5 (SCH_2CH_3), 20.9 ($COCH_3$), 21.7, 23.4 [$CH(CH_3)_2$], 24.3 (SCH_2CH_3), 37.4 (C-4), 54.3 (CH_2N), 61.5 (CH_2OH), 65.6 (CH_2OAc), 68.8 (C-5), 69.7 [$CH(CH_3)_2$], 92.5 (C-7), 116.4 (C-3a), 127.6 (C-3), 146.7 (C-7a), 170.8 (C═O); MS (EI, 70 eV), m/z (%): 358.0 (36, M^+), 213.0 (100).

Anal. Calcd for $C_{16}H_{26}N_2O_5S$: C, 53.61; H, 7.31; N, 7.82; S, 8.94. Found, C: 53.72; H, 7.21; N, 8.04; S, 8.71.

(3a*S*,4*R*,5*R*,4*R*,7*S*,7a*R*)-4-Ethylsulfanyl-4,5,7,7-tetrahydro-7a-hydroxy-7-isopropoxy-3a*H*-pyrano[4,3-*d*]isoxazol-5-ylmethyl acetate (12). The reaction of **7** (50 mg, 0.14 mmol) with an aqueous solution of hydroxylamine (50%, 20 μL, 0.2 mmol) was carried out as described above for **10**. The reaction was completed after 1.5 hr. The residue was purified on a column of silica gel (chloroform/methanol, 1 : 1) to give white crystals. Yield: 31 mg (50%); mp 99–101°C; $[\alpha]_D^{24.0}$ −189.6° (*c* 1.0, chloroform); IR (KBr): 3402 (OH), 1741 (C═O) cm^{-1}; ^1H NMR: δ 1.22 (t, 3H, $J = 7.3$ Hz, SCH_2CH_3), 1.22, 1.27 [2 × d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 2.07 (s, 3H, Ac), 2.54 (m, 2H, SCH_2CH_3], 3.31 (dd, 1H, $J_{4,5} = 3.4$ Hz, $J_{3a,4} = 7.5$ Hz, H-4), 3.58 (dd, 1H, $J_{3a,4} = 7.5$ Hz, $J_{3a,3} = 1.8$ Hz, 3a), 4.09 [m, 1H, $J = 6.1$ Hz, $CH(CH_3)_2$], 4.24 (m, 2H, CH_2OAc), 4.33 (m, 1H, H-5), 5.04 (s, 1H, H-7), 6.68 (s, 1H, OH), 7.35 (d, 1H, $J_{3a,3} = 1.8$, H-3); ^{13}C NMR: δ 14.7 (SCH_2CH_3), 20.8 ($COCH_3$), 21.5, 23.2 [$CH(CH_3)_2$], 27.3 (SCH_2CH_3), 41.5 (C-4), 57.1 (C-3a), 64.7 (CH_2OAc), 68.9 (C-5), 71.4 [$CH(CH_3)_2$], 94.9 (C-7), 100.2 (C-7a), 148.6 (C-3), 170.7 (C═O); MS (EI, 70 eV), m/z (%): 334 (18, M^+), 157 (100).

Anal. Calcd for $C_{14}H_{23}NO_6S$: C, 50.44; H, 6.95; N, 4.20; S, 9.62. Found: C, 50.22; H, 7.11; N, 4.04; S, 9.55.

(5*R*,6*R*,8*S*)-5-Ethylsulfanyl-5,8-dihydro-8-isopropoxy-2-phenyl-6*H*-pyrano[3,4–*d*]pyrimidin-6-yl)methanol (13). Sodium (23 mg, 1 mmol) was dissolved in 10 mL anhydrous ethanol, and benzamidinium nitrate (156 mg, 1.0 mmol) was added. The mixture was stirred for approximately 30 min until the corresponding sodium salt precipitated and filtered. The filtrate (5 mL) was added to a solution of **7** (174 mg, 0.5 mmol) in methanol (10 mL). The mixture was stirred at r.t. until the reaction was completed (monitored by t.l.c.). The mixture was diluted with chloroform (10 mL) and neutralized with an aqueous solution of ammonium chloride. The aqueous layer was separated, extracted with chloroform (3 × 10 mL) and the organic layer was evaporated to dryness, the residue was purified by column chromatography (toluene/ethyl acetate, 1 : 1) to give a colorless syrup. Yield: 108 mg (60%); $[\alpha]_D^{24.0}$ −235.7° (*c* 1.0, chloroform); IR (KBr): 3457 (OH), 1406 (C═C) cm^{-1}; ^1H NMR: δ 1.13 (t, 3H, $J = 7.6$ Hz, SCH_2CH_3), 1.31, 1.38 [2 × d, 6H, $J = 6.1$ Hz, $CH(CH_3)_2$], 2.47 (m, 2H, SCH_2CH_3), 3.87 (dd, 1H, H-5), 4.08 (m, 2H, Ac), 4.22 [m, 1H, $CH(CH_3)_2$], 4.67 (m, 1H, $J_{5,6} = 2.8$ Hz, H-6), 5.67 (s, 1H, H-8), 7.48 (m, 3H, *m, p*-H, Ph), 8.44 (m, 2H, *o*-Ph), 8.86 (s, 1H, H-4); ^{13}C NMR: δ 13.4 (SCH_2CH_3), 21.9, 23.5 [$CH(CH_3)_2$], 24.3 (SCH_2CH_3), 39.6 (C-5), 63.8 (CH_2OH), 70.1 (C-6), 71.5 [$CH(CH_3)_2$], 95.5 (C-8), 130.9, 128.6, 128.31 (*o, m, p*-Ph), 164.2 (C-2),

126.0 (C-4a), 137.0 (*i*-Ph), 159.2 (C-4), 161.0 (C-8a); MS (EI, 70 eV), m/z (%): 361.0 (46, M^+), 197.0 (100).

Anal. Calcd for $C_{19}H_{24}N_2O_3S$: C, 63.31; H, 6.71; N, 7.77; S, 8.89. Found: C, 62.83; H, 6.58; N, 7.56; S, 8.75.

ACKNOWLEDGMENTS

J. Q. is grateful to the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, Brasil) and the Deutscher Akademischer Austauschdienst for financial support. R. M. would like to thank the Deutscher Akademischer Austauschdienst for a scholarship.

We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

REFERENCES

1. Ferrier, R.J.; Middleton, S. The conversion of carbohydrate derivatives into functionalized cyclohexanes and cyclopentanes. Chem. Rev. **1993**, *93*, 2779–2831.
2. Peseke, K.; Thiele, G.; Michalik, M.; Powell, D.R. Anellation reactions of pyranose derivatives. Liebigs Ann. **1997**, 1019–1022.
3. Dötz, K.H.; Ehlenz, R.; Paetsch, D. Carbene complex modified glycals: synthesis and reactivity. Angew. Chem. Int. Ed. Engl. **1997**, *36*, 2376–2378.
4. Piaoa, M.-Z.; Imafuku, K. Convenient synthesis of amino-substituted pyranopyranones. Tetrahedron Lett. **1997**, *38*, 5301–5302.
5. Takeda, Y.; Morimoto, Y.; Matsumoto, T.; Honda, G.; Tabata, M.; Fujita, T.; Otsuka, H.; Sezik, E.; Yesilada, E. Nepetanudoside, an iridoide glucoside with an unusual stereostructure from *Nepeta nuda* ssp. *Albiflora*. J. Nat. Prod. **1995**, *58*, 1217–1221.
6. Mohammad-Ali, A.K.; Chan, T.H.; Thomas, A.W.; Jewett, B.; Strunz, G.M. Spruce budworm (*Choristaneura fumiferana*) antifeedants 4. Synthesis of specionin and biological studies. Can. J. Chem. **1994**, *72*, 2137–2143.
7. Ichikawa, S.; Shuto, S.; Matsuda, A. The first synthesis of herbicidin B. Stereoselective construction of the tricyclic undecose moiety by a conformational restriction strategy using steric repulsion between adjacent bulky silyl protecting groups on a pyranose ring. J. Am. Chem. Soc. **1999**, *121*, 10270–10280.
8. Deloisy, S.; Thang, T.T.; Olesker, A.; Lukacs, G. Synthesis of α-azido aldehydes. Stereoselective formal access to the immunosuppressant myriocin. Tetrahedron Lett. **1994**, *35*, 4783–4786.
9. Kanno, K.I.; Hatanaka, K.; Nishimura, S.-I. New procedure for preparation of oxazoline derivative of 2-acetamido-2-deoxy-D-glucopyranose. Carbohydr. Lett. **1994**, *1*, 9–12.
10. Methling, K.; Aldinger, S.; Peseke, K.; Michalik, M. New anellation reactions of pyranose derivatives. J. Carbohydr. Chem. **1999**, *18*, 429–439.

11. Gómez, M.; Quincoces, J.; Peseke, K.; Michalik, M.; Reinke, H. Synthesis of anellated pyranose derivatives on the basis of levoglucosenone. J. Carbohydr. Chem. **1999**, *18*, 851–865.
12. Kuhla, B.; Peseke, K.; Thiele, G.; Michalik, M. An approach to C-branched and heterocyclic annelated pyranosides by reaction of α-D-erythro-hexopyranosid-2-ulose with orthoformic acid derivatives. J. Prakt. Chem. **2000**, *342*, 240–244.
13. Gómez Andreu, M.; Peseke, K.; Reinke, H.; Quincoces Suàrez, J.; Michalik, M. Synthesis and reactions of branched-chain anhydrouloses with push–pull functionality. J. Prakt. Chem. **2000**, *342*, 389–395.
14. Gómez, M.; Quincoces, J.; Feist, H.; Michalik, M.; Reinke, H.; Peseke, K. Synthesis of anellated anhydropyranoses on the basis of 1,6-anhydro-3-deoxy-4-methylsulfanyl-3-(methylsulfanyl)methylene-β-D-*erythro*-hexopyranos-2-ulose. J. Carbohydr. Chem. **2001**, *20*, 307–314.
15. Herrera, L.; Feist, H.; Michalik, M.; Quincoces, J.; Peseke, K. Synthesis of anellated carbasugars on the basis of (−)-quinic acid. Carbohydr. Res. **2003**, *338*, 293–298.
16. Varela, O.; De Fina, G.M.; Lederkremer, R.M. Stereoselective synthesis of deoxyhexopyranosides and deoxypyranosid 2-uloses from 2-hydroxyglycal-derived precursors. Carbohydr. Res. **1993**, *246*, 371–376.
17. Seeberger, P.H.; Eckhardt, M.; Gutteridge, C.A.; Danishefsky, S.J. Coupling of glycal derived thioethyl glycosyl donors with glycal acceptors. An advance in the scope of the glycal assembly. J. Am. Chem. Soc. **1997**, *119*, 10064–10072.
18. Toshima, K.; Nagai, H.; Ushiki, Y.; Matsumara, S. Novel glycosidations of glycals using BCl_3 or BBr_3 as a promoter for catalytic and stereoselective syntheses of 2-deoxy-α-glycosides. Synlett **1998**, 1007–1009.
19. Valera, O.; de Fina, G.M.; de Lederkremer, R.M. The reaction of 2-hydroxyglycal esters with alcohols in the presence of *N*-iodosuccinimide, stereoselective synthesis of α-anomers of alkyl 3-deoxyhex-2-enopyranosides and 3,4-dideoxyhex-3-enopyranosid-2-uloses. Carbohydr. Res. **1987**, *167*, 187–196.
20. de Fina, G.M.; Varela, O.; de Lederkremer, R.M. Convenient synthesis of chiral pyranones from carbohydrates. Synthesis **1988**, 891–893.
21. Hanessian, S.; Tyle, P.C.; Chapleur, Z. Reaction of lithium dimethylcuprate with conformationally biased β-acyloxy enol esters—regio and stereocontrolled access to functionalized six-carbon chiral synthons. Tetrahedron Lett. **1988**, *46*, 4583–4586.
22. Uhrig, M.L.; Varela, O. Michael addition of thiols to sugar enones. Synthesis of 3-deoxy-4-thiohexopyranosid-2-uloses as key precursors of 3-deoxy- and C-2 branches-chain 4-thiosugars. Aust. J. Chem. **2002**, *55*, 155–160.
23. Essig, M. Michael additions of thiols to levoglucosenone. Carbohydr. Res. **1986**, *156*, 225–231.
24. Michalik, M.; Peseke, K.; Radeglia, R. ^{13}C- und ^{15}N-NMR-spektroskopische untersuchungen an push–pull-butadienen. J. Prakt. Chem. **1985**, *327*, 103–108.
25. Dieter, R.K. α-Oxo ketene dithioacetals and related compounds: versatile three-carbon synthons. Tetrahedron **1986**, *42*, 3029–3095.
26. Peseke, K.; Thiele, G.; Michalik, M. A new approach to *C*-branched monosaccharides by stereoselective hydrodesulfurization of methyl 4,6-*O*-benzylidene-3-[*bis*(methylthio)-methylene]-3-deoxy-α-D-*erythro*-hexopyranosidulose. Liebigs Ann. **1995**, 1633–1636.

27. Cremer, D.; Pople, J.A. A general definition of ring puckering coordinates. J. Am. Chem. Soc. **1975**, *97*, 1354–1358.

Received June 12, 2003
Accepted October 13, 2003