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A ROUTE TO LONG-CHAIN AMINO SUGARS BY THREE SUBSTITUTED THIAZOLES AS AUXILIARIES: THIAZOLE-2-CARBONITRILE N-OXIDE, 2-TRIMETHYLSILYLTHIAZOLE, AND 2-THIAZOLYLMETHYLENETRIPHENYL-PHOSPHORANE≠

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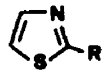
Summary: The nitrile oxide-furan cycloadduct thiazole furoisoxazoline **4a** is transformed into the 5-amino-5-deoxy dialdoidofuranose derivative **8** through selective elaboration of the three heterocyclic rings: i) bis-hydroxyalkylation of dihydrofuran carbon-carbon double bond; ii) reductive cleavage of the isoxazoline ring; iii) conversion of thiazole into formyl. One- and two-carbon chain extension of the resulting amino hexose by reaction with 2-trimethylsilylthiazole and 2-thiazolylmethylenetriphenyl-phosphorane respectively affords C_7 and C_8 homologues.

2-Substituted thiazoles **1** are convenient masked equivalents of aldehydes since the thiazole nucleus represents a remarkably stable system which survives a variety of reaction conditions and tolerates other functional group manipulations; nevertheless, it can be converted into the formyl group through a sequence of simple and high yield operations, *viz.* alkylation to the N-quaternary thiazolium salt, reduction to the thiazolidine, metal assisted hydrolysis.[1,2] Once this feature is combined with the reactivity of an appropriate functional group R attached to C-2 of the thiazole ring, one may design synthetic routes to complex molecular systems. In fact, we have extensively employed 2-trimethylsilylthiazole (**1a**) as a protected formyl trimethylsilane (**2a**) for the stereoselective homologation of chiral polyoxygenated aldehydes into long-chain carbohydrates *via* an iterative thiazole-addition and formyl-unmasking sequence.[2,3] Furthermore, 2-thiazolylmethylenetriphenylphosphorane (**1b**) has proven to be a new protected formyl phosphorane **2b** for the two-carbon-chain elongation of aldehydes *via* a Wittig-olefination and formyl-unmasking sequence.[4] Having decided to extend this concept to other functionally substituted thiazoles, we report here our previously described 2-thiazolecarbonitrile N-oxide (**1c**)[5] as a precursor to

≠ Dedicated to Professor Edward C. Taylor on the occasion of his 65th birthday.

amino sugars via a cycloaddition and formyl-unmasking sequence. Central to this methology is the nitrile oxide-furan addition, a highly regioselective 1,3-dipolar cycloaddition which has been originally described by Caramella, Grünanger, Houk and their coworkers[6a] and whose synthetic value as a key step towards amino sugars (Isoxazoline Route) has been substantially disclosed by Jäger and his students.[6b] We hoped that the use of nitrile oxide **1c** as a new masked formyl nitrile oxide (**2c**)[7] would provide additional efficiency to the isoxazoline route to amino sugars.



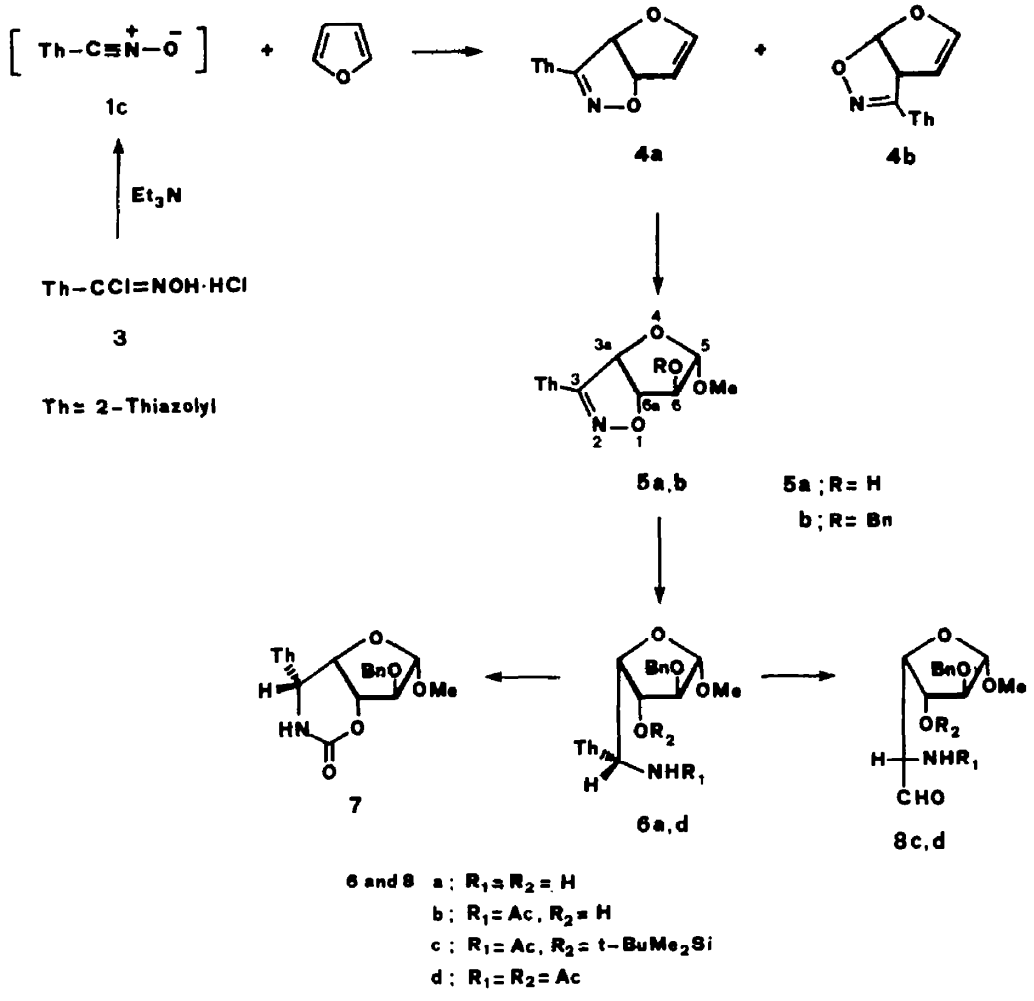
1 ≡ R-CHO **2**

a, R = $SiMe_3$
b, R = $\bar{C}H\text{-}\overset{+}{P}Ph_3$
c, R = CNO

The chlorooxime hydrochloride **3**, which can be readily obtained by chlorination of 2-formylthiazole oxime,[5] has already proven to be a convenient precursor to nitrile oxide **1c**. Thus, slow addition of a highly diluted solution of triethylamine in furan to a suspension of **3** in furan afforded the furoisoxazoline **4a** in excellent isolated yield (82%) (Scheme 1). Under these conditions, the formation of the regioisomer **4b** as well as the nitrile oxide dimer (furoxan)[5] was completely suppressed.[8] The stereochemistry (regio- and diastereo-) of cycloadduct **4a** was assigned from the nmr δ values of 3a-H (6.42 ppm) and 6a-H (6.07 ppm) (J = 8.8 Hz) which compare quite well with those of other nitrile oxide-furan cycloadducts.[6] It is worth pointing out that the high isolated yield of furoisoxazoline **4a** indicates that nitrile oxide **1c** is an effective 1,3-dipolar system. The high reactivity of **1c** may be attributed to the electron acceptor character of the 2-thiazolyl group,[9] since electron-attracting substituents are known to increase the 1,3-dipolar reactivity of nitrile oxides.[10]

The thiazole substituted furoisoxazoline **4a** proved to be easily transformed into the amino sugar **8** by selective elaboration of the three heterocyclic moieties. Reactions at the cis-fused bicyclic system were carried out by a sequence conceptually identical to that of Jäger.[6b] This involves bis-hydroxyalkylation of the carbon-carbon double bond of the furan part of **4a** by reaction with m-chloroperbenzoic acid in methanol and alkylation of the free hydroxy group with benzyl bromide to give the trans-dialkoxyfuranoside **5b** (70% isolated yield). The assigned trans-arrangement of the H atoms at C-4, C-5 and C-6a is supported by the ^1H nmr spectrum of **5a** showing two singlets for 4-H and 5-H and a doublet for 6a-H. Hence, since no other diastereoisomers were observed (nmr) in the crude **5a**, the sequential steps which may be reasonably invoked, viz. exo-epoxidation and selective epoxide opening by methanol, must have occurred with high stereoselectivity. Likewise, the isoxazoline ring cleavage by

Scheme I

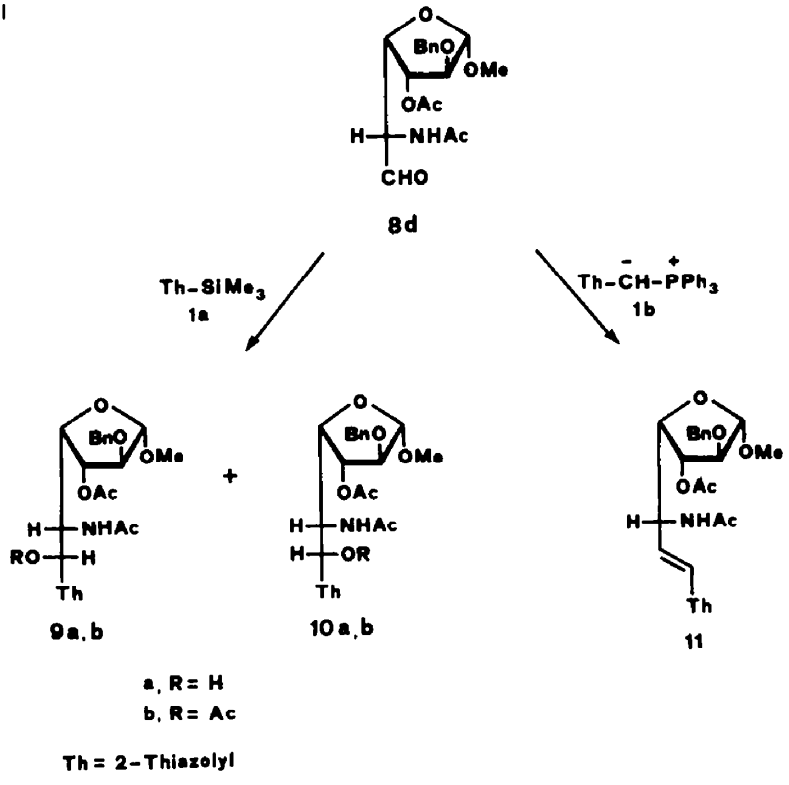


lithium aluminum hydride (LAH) proved to be highly stereoselective since from **5b** essentially a single diastereomer **6a** was obtained in fair yield (78% isolated). As for other furoisoxazolines cleavage by LAH,[6b] the stereochemistry of **6a** was assigned by assuming hydride delivery to the C=N bond from the exo face. Fortunately, the endo-thiazole group does not appear to create severe overcrowding in this process since, in contrast to that reported for the 3-phenyl substituted furoisoxazoline,[6b] products from cycloreversion of **5b** were not observed. The stereochemistry of **6a** (and by inference of its precursors **4a** and **5a**) was unequivocally established following conversion with carbonyldiimidazole to the furo-1,3-oxazinone **7**, which proved to be suitable for X-ray analysis.[11] Hence, the main steric course of the 1,3-dipolar cycloaddition of **1c** to furan, as well as of the hydroxyalkylation of **4a** and the reductive

cleavage of **5** by LAH have been unequivocally demonstrated. The subsequent elaboration involved the formyl deblocking from the thiazole ring[1,2] in protected forms of **6a**, *viz.* the O-*tert*-butyldimethylsilyl-N-acetyl **6c** (42%) and the O,N-diacetyl derivative **6d** (49%). Both **6c** and **6d**, upon sequential treatment with methyl iodide, sodium borohydride, and mercuric chloride in water, afforded the corresponding protected 5-amino-5-deoxy dialdoidofuranoses **8c** and **8d** in fair overall yields (78-84%). The above results indicate that the thiazole nucleus is relevant in the synthetic scheme to the amino sugar **8** (Thiazole-Isoxazoline Route) particularly with respect to the activation of nitrile oxide-furan cycloaddition and the efficiency as masked formyl group equivalent. Therefore, the thiazole nucleus is expected to be more widely applicable in this scheme than other formyl protecting groups employed so far[7].

One- and two-carbon chain elongation of the protected amino dialdohexose **8** was carried out by reaction with the substituted thiazoles **1a** and **1b** (Scheme 2). The N-acetylamino derivative **8d** reacted sluggishly with 2-trimethylsilythiazole (**1a**) in dichloromethane to give a mixture of diastereomers **9a** and **10a** in 50:50 ratio and 54% overall yield after 3 days at room temperature. Some degree of diastereoselectivity (70:30) for this reaction was achieved using tetrahydrofuran as a solvent although the overall yield was lower (30%). The identification of diastereomers **9a** and **10a** as well as of their O-acetyl derivatives **9b** and **10b** from their nmr spectra was ambiguous. However, by analogy with the main steric course of the addition of **1a** and Grignard reagents to

Scheme II



N-monoprotected α-amino aldehydes,[12] the threo (syn) configuration of the major diastereomer **9a** obtained in THF seems likely. Further to that, the Wittig-type reaction of **8d** with the phosphorane **1b** generated in toluene as previously described,[4] afforded exclusively the E-alkene sugar **11** in acceptable yield (38%).[13] By virtue of the thiazole-formyl equivalence, compounds **9**, **10** and **11** are thiazole masked precursors of aminoheptoses and aminooctoses respectively.

In conclusion, we have developed a route to long-chain amino sugars which exploits the reaction of three different functionally substituted thiazoles **1a-c**, viz. a nitrile oxide, a trimethylsilyl derivative, and a methylenephosphorane. The importance of amino sugars in natural products chemistry and their synthesis from non-sugar precursors are commonplace in organic chemistry.[6,14]

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra (in $CDCl_3$) were obtained on a 80 MHz WP-80 spectrometer. Chemical shifts are given in parts per million from tetramethylsilane as internal standard. Infrared spectra were recorded on a Perkin Elmer Model 297 grating spectrometer. Mass spectra were obtained at 70 eV on a Varian Mat CH-7 high resolution mass spectrometer. 2-(Trimethylsilyl)-thiazole (**1a**) was prepared as decribed.[3] 2-Thiazolylmethylenetriphenyl-phosphorane (**1b**) was generated in situ from the corresponding phosphonium chloride and potassium tert-butoxide.[4] 2-Thiazolylhydroxamoyl chloride hydrochloride (**3**), the precursor of nitrile oxide **1c** was prepared as described.[5]

Cycloaddition of Thiazole-2-carbonitrile N-oxide (1c) to Furan. A solution of triethylamine (2.78 mL, 20 mmol) in furan (100 mL) was added dropwise over a period of 48 h to a suspension of 2-thiazolylhydroxamoyl chloride hydrochloride (**3**) (2 g, 10 mmol) in furan (72 mL, 1 mol) at room temperature and under N_2. The solvent was removed under vacuum and diethyl ether (50 mL) was added to the residue. After washing the solution with saturated $NaHCO_3$, the organic layer was dried (Na_2SO_4), filtered and the solvent was removed in vacuo. Flash chromatography of the residue (silica gel, 7:3 petroleum ether-diethyl ether) gave 1.59 g (82%) of 3-(2-thiazolyl)-3a,6a-dihydrofuro[2,3-d]isoxazole (**4a**): mp 58-60° C (from diethyl ether-n-hexane); IR (CCl_4) 1605 cm^{-1}; ^{1}H NMR δ 5.42 (t, 1 H, J = 2.6 Hz), 6.07 (dm, 1 H, J = 8.8 Hz), 6.42 (d, 1 H, J = 8.8 Hz), 6.68 (m, 1 H), 7.48 (d, 1 H), 8.00 (d, 1 H, J = 3.2 Hz); mass spectrum m/e (relative intensity) 194 (M^+, 68, 164 (100), 136 (50). Anal. Calcd for $C_8H_6N_2O_2S$: C, 49.47; H, 3.12; N, 14.43. Found: C, 49.45; H, 3.09; N, 14.45.

6-Hydroxy-5-methoxy-3-(2-thiazolyl)-tetrahydrofuro[2,3-d]isoxazole (5a). A solution of the furoisoxazoline **4a** (2 g, 10.3 mmol) in dry methanol (80 mL) was added dropwise to a cooled (0° C) and stirred solution of m-chloroperbenzoic acid (3.56 g, 20.6 mmol) in the same solvent (80 mL). Stirring was continued for 20 h at room temperature, the solution was concentrated and then anhydrous Na_2CO_3 was added. The mixture was stirred for 20 min and then the solid filtered off. The solution was added to a stirred suspension of Al_2O_3 [Aluminum Oxide 90 active, neutral (I) Merck (70-230 mesh ASTM)] (90 g) in dry diethyl ether (70 mL) and methanol (40 mL) (the suspension was stirred for 30 min before adding the reaction mixture).[15] After 2 h, methanol (160 mL) was added and stirring was continued for 3 h to extract the product. The suspension was filtered through Celite and Al_2O_3 was washed several time with methanol. The solvent was removed under vacuum and the residue was chromatographed (silica gel, 7:3 dichloromethane-ethyl acetate) to give 2.36 g (95%) of the 6-hydroxy-5-methoxy derivative **5a**: sirup oil; ^{1}H NMR δ 3.1 (s, 3 H), 4.56 (s, 1 H), 5.09 (s, 1 H), 5.11 (d, 1 H, J = 7.6 Hz), 6.23 (d, 1 H, J = 7.6 Hz), 7.47 (d, 1 H, J = 4.2 Hz), 7.99 (d, 1 H, J = 3.2 Hz). Anal. Calcd for $C_9H_{10}N_2O_4S$: C, 44.63; H, 4.16; N,

11.57. Found: C, 44.60; H, 4.12; N, 11.62.

6-Benzyloxy-5-methoxy-3-(2-thiazolyl)-tetrahydrofuro[2,3-d]isoxazole (5b). To a solution of **5a** (0.4 g, 1.65 mmol) in dry tetrahydrofuran (30 mL) was added portionwise NaH 50% (90 mg, 1.98 mmol). The reaction mixture was stirred and gently refluxed for 20 min and then benzyl bromide (0.23 mL, 1.98 mmol) was added together with tetrabutylammonium iodide (0.1-0.2 g). After 2 h, the solvent was removed under vacuum and water was added. After extraction with diethyl ether and usual work up, the residue was chromatographed (silica gel, 7:3 petroleum ether-ethyl acetate) to give 0.4 g (73%) of 6-benzyloxy derivative **5b**: mp 88-90° C (from ethyl acetate-n-hexane); ^{1}H NMR δ 3.07 (s, 3 H), 4.27 (s, 1 H), 4.66 (S, 2 H), 5.0 (d, 1 H, J = 8 Hz), 5.1 (s, 1 H), 6.17 (d, 1 H, J = 8 Hz), 7.33 (s, 5 H), 7.41 (d, 1 H, J = 3.2 Hz), 7.97 (d, 1 H, J = 3.2 Hz); mass spectrum m/e (relative intensity) 332 (M^+, 10), 272 (72), 243 (100), 91 (80). Anal. Calcd for $C_{16}H_{16}N_2O_4S$: C, 57.83; H, 4.85; N, 8.43. Found: C, 57.87; H, 4.81; N, 8.41.

Methyl (5S)-5-Amino-2-O-benzyloxy-5-deoxy-5-(2-thiazolyl)-α-L-xylofuranoside (6a). To a stirred and cooled (0° C) suspension of lithium aluminum hydride (LAH) (0.51 g, 13.5 mmol) in diethyl ether (60 mL) was added dropwise a solution of the furoisoxazoline **5b** (1.49 g, 4.5 mmol) in the same solvent (60 mL). After 3 h stirring at room temperature, the reaction mixture was hydrolyzed (per gramme $LiAlH_4$: 1.0 mL of H_2O, 0.75 mL of 20% NaOH, 1-3.5 mL H_2O until the precipitate became colorless and granular[16]). The solvent was decanted and dichloromethane was added to the solid and stirred for 12 h. The solid was filtered off and washed throughly with dichloromethane. The combined solvents were evaporated in vacuo to give the crude product **6a** (1.18 g, 78%): mp 91-93° C; ^{1}H NMR δ 3.37 (br, 3 H), 3.45 (s, 3 H), 4.06 (s, 1 H), 4.35 (m, 2 H), 4.67 (m, 3 H), 4.98 (s, 1 H), 7.31 (s, 6 H), 7.75 (d, 1 H, J = 3.6 Hz). Anal. Calcd for $C_{16}H_{20}N_2O_4S$: C, 57.13; H, 5.99; N, 8.33. Found: C, 57.09; H, 6.01; N, 8.30.

N,O-Acetylation of 6a. To a stirred solution of the amino alcohol **6a** (0.34 g, 1 mmol) and triethylamine (0.17 mL, 1.3 mmol) in dichloromethane (10 mL) was added acetyl chloride (0.1 mL, 1.3 mmol). After 1 h at room temperature, the mixture was washed with saturated $NaHCO_3$ and dried (Na_2SO_4). The solvent was removed under vacuum and the residue was chromatographed (silica gel, 1:1 dichloromethane-ethyl acetate) to give 0.08 g (19%) of the N,O-diacetyl derivative **6d** and 0.25 g (66%) of the N-acetyl derivative **6b**.

The N,O-diacetyl derivative **6d** showed the following: mp 104-106° C (from ethyl acetate-petroleum ether); IR ($CHCl_3$) 1740, 1680 cm^{-1}; ^{1}H NMR δ 2.06 (s, 3 H), 3.45 (s, 3 H), 4.02 (m, 1 H), 4.67 (dd, 2 H), 4.96 (d, 1 H), 5.37 (m, 3 H), 6.90 (br, 1 H), 7.25 (d, 1 H, J = 3.2 Hz), 7.35 (s, 5 H), 7.75 (d, 1 H, J = 3.2 Hz); mass spectrum m/e (relative intensity) 420 (M^+, 30), 265 (100), 91 (80). Anal. Calcd for $C_{20}H_{24}N_2O_6S$: C, 57.13; H, 5.75; N, 6.66. Found: C, 57.09; H, 5.78; N, 6.60.

The N-acetyl derivative **6b**: mp 118-120° C (from ethyl acetate-petroleum ether); IR ($CHCl_3$) 1650 cm^{-1}; ^{1}H NMR δ 2.02 (s, 3 H), 3.35 (s, 3 H), 3.95 (m, 1 H), 4.95 (m, 1 H), 4.6 (s, 2 H), 4.7 (m, 1 H), 4.92 (s, 1 H), 5.75 (m, 1 H), 6.9 (br, 1 H), 7.3 (s, 6 H), 7.7 (d, 1 H, J = 3.2 Hz); mass spectrum m/e (relative intensity) 378 (M^+, 30), 265 (30), 91 (100). Anal. Calcd for $C_{18}H_{22}N_2O_5S$: C, 57.13; H, 5.86; N, 7.40. Found: C, 57.15; H, 5.81; N, 7.44.

The acetylation of **6a** (0.34 g, 1 mmol) with an excess (3 equiv) of acetyl chloride and triethylamine gave after 3 h at room temperature, usual work-up and chromatography 0.2 g (49%) of **6d** and and 0.041 g (11%) of **6b**.

O-Silylation of 6b. A solution of the N-acetyl derivative **6b** (0.22 g, 0.58 mmol), triethylamine (0.2 mL, 1.4 mmol) and tert-butyldimethylsilyl chloride (0.21 g, 1.4 mmol) in dimethylformamide (5 mL) was stirred for 48 h at room temperature. The solvent was removed under vacuum, the residue was diluted with ethyl acetate and washed with saturated NaCl. The organic layer was dried (Na_2SO_4) and the residue was chromatographed (silica gel, 1:1 ethyl acetate-petroleum ether) to give 0.2 g (70%) of **6c**: mp 91-93° C (from ethyl

acetate-petroleum ether); IR (CCl_4) 1700 cm^{-1}; ^1H NMR δ 0.087 (s, 6 H), 0.9 (s, 9 H), 2.0 (s, 3 H), 3.33 (s, 3 H), 4.17 (dd, 1 H), 4.57 (m, 3 H), 4.87 (d, 1 H), 5.02 (dd, 1 H), 5.5 (dd, 1 H), 7.17 (d, 1 H, J = 3.2 Hz), 7.32 (s, 5 H), 7.72 (s, 1 H, J = 3.2 Hz). Anal. Calcd for $C_{24}H_{36}N_2O_5SSi$: C, 58.50; H, 7.36; N, 5.69. Found: C, 58.55; H, 7.33; N, 5.72.

7-Benzyloxy-6-methoxy-4-(2-thiazolyl)-tetrahydrofuro[2,3-e]1,3-oxazin-2-one (7). A solution of the amino alcohol **6a** (0.49 g, 1.46 mmol) and 1,1'-carbonyldiimidazole (0.35 g, 2 mmol) in tetrahydrofuran (10 mL) was stirred for 2 h at room temperature. The solvent was removed under vacuum and the residue was chromatographed (silica gel, 1:1 dichloromethane-ethyl acetate) to give 0.44 g (83%) of the furo-1,3-oxazinone **7**: mp 189° C, dec.; IR (KBr) 1710 cm^{-1}; ^1H NMR δ 3.35 (s, 3 H), 4.19 (s, 1 H), 4.64 (s, 2 H), 4.87 (s, 2 H), 5.00 (s, 1 H), 5.10 (s, 1 H), 6.00 (br, 1 H), 7.35 (s, 5 H), 7.45 (d, 1H, J = 3.2 Hz), 7.80 (d, 1 H, J = 3.2 Hz); mass spectrum m/e (relative intensity) 362 (M^+, 35), 271 (10), 205 (45), 91 (100). Anal. Calcd for $C_{17}H_{18}N_2O_5S$: C, 56.35; H, 5.01; N, 7.73. Found: C, 56.39; H, 5.04; N, 7.70.

Formyl Group Unmasking in Xylofuranoside Derivatives 6c and 6d. General Procedure. A solution of the xylofuranoside **6** (4.6 mmol) and methyl iodide (6.5 g, 46 mmol) in acetonitrile (30 mL) was refluxed untill the total disappearance of **6** by t.l.c. (ca. 2 h). The solvent was evaporated under reduced pressure and the residue was dissolved in methanol (40 mL) To the solution was added portionwise $NaBH_4$ (0.34 g, 9.2 mmol) at 0° C and, after 30 min stirring, acetone (2 mL). The solvent was evaporated, the residue was treated with saturated NaCl and extracted with ethyl acetate. The solvent was removed in vacuo and the residue dissolved in acetonitrile (4 mL) was added to a solution of 1.2 equiv of $HgCl_2$ in acetonitrile/water 4/1 (20 mL). After stirring at room temperature for 15 min, the reaction mixture was filtered and the solvent was removed under vacuum. The residue was treated with saturated NaCl and extracted with dichloromethane. Distillation of the solvent gave the aldehyde **8**.

From **6c**, the aldehyde **8c** (1.68g, 84%): oil; IR (CCl_4) 1740, 1695 cm^{-1}; ^1H NMR δ 0.062 (s, 6 H), 0.87 (s, 9 H), 2.03 (s, 3 H), 3.40 (s, 3 H), 3.84 (dd, 1 H), 4.47 (m, 2 H), 4.56 s, 2 H), 4.81 (m, 2 H), 6.7 (br, 1 H), 7.3 (s, 5 H), 9.62 (s, 1 H). Anal. Calcd for $C_{22}H_{35}NO_6Si$: C, 60.38; H, 8.06; N, 3.20. Found: C, 60.33; H, 8.00; N, 3.22.

From **6d**, the aldehyde **8d** (1.3 g , 78%): oil; IR ($CHCl_3$) 1740, 1680 cm^{-1}; ^1H NMR δ 2.03 (s, 6 H), 3.40 (s, 3 H), 4.0 (m, 1 H), 4.62 (m, 3 H), 4.90 (d, 1 H), 5.18 (m, 2 H), 6.8 (br, 1 H), 7.31 (s, 5 H), 9.62 (s, 1 H). Anal. Calcd for $C_{18}H_{23}NO_7$: C, 59.18; H, 6.33; N, 3.83. Found: C, 59.15; H, 6.37; N, 3.80.

Reaction of Dialdose 8d with 2-Trimethylsilylthiazole (1a). A solution of dialdose **8d** (0.3 g, 0.82 mmol) and 2-trimethylsilylthiazole **1a** (0.19 g, 1.2 mmol) in dichloromethane (5 mL) was stirred for 3 days at room temperature. Tetrabutylammonium fluoride in tetrahydrofuran (1 mL) was added and stirring continued for 1 h. The mixture was washed with saturated NaCl and dried (Na_2SO_4). The solvent was removed under vacuum and the residue was chromatographed (silica gel, ethyl acetate) to give 0.1 g (27%) of **9a** and 0.1 g (27%) of **10a**.

The diastereomer **9a**: oil; IR ($CHCl_3$) 1745, 1680, 1610 cm^{-1}; ^1H NMR δ 1.94 (s, 3 H), 2.06 (s, 3 H), 3.42 (s, 3 H), 3.95 (dd, 1 H), 4.42 (m, 1 H), 4.62 (d, 2 H), 4.90 (d, 1 H), 5.00 (m, 1 H), 5.27 (m, 2 H), 6.50 (br, 1 H), 7.32 (s, 5 H), 7.75 (d, 1 H, J = 3.2 Hz). Anal. Calcd for $C_{21}H_{26}N_2O_7S$: C, 55.99; H, 5.82; N, 6.22. Found: C, 56.03; H, 5.80; N, 6.20.

The diastereoisomer **10a**: oil; IR ($CHCl_3$) 1735, 1680, 1610 cm^{-1}; ^1H NMR δ 1.95 (s, 3 H), 2.06 (s, 3 H), 3.42 (s, 3 H), 3.96 (dd, 1 H), 4.32 (m, 1 H), 4.62 (d, 2 H), 4.90 (m, 2 H), 5.20 (m, 2 H), 6.65 (br, 1 H), 7.32 (s, 6 H), 7.75 (d, 1 H, J = 3.2 Hz). Anal. Calcd for $C_{21}H_{26}N_2O_7S$: C, 55.99; H, 5.82; N, 6.22. Found: C, 55.94; H, 5.83; N, 6.25.

The reaction was also carried out in tetrahydrofuran (5 mL) starting from **7d**

(0.171 g, 0.46 mmol) and **1a** (0.5 g, 3.2 mmol) and stirred for 48 h. After usual work up, chromatography of the residue gave 0.018 g (8.7%) of **10a** and 0.043 g (21%) of **9a**.

Acetylation of the Diastereomers 9a and 10a. General Procedure. A solution of **9a** (or **10a**) (0.045 g, 0.1 mmol) and acetyl chloride (0.078 g, 1 mmol) in pyridine (2 mL) was stirred at room temperature for 30 min. The mixture was diluted with diethyl ether and washed with saturated $NaHCO_3$. The organic layer was dried (Na_2SO_4) and the residue was chromatographed (silica gel, ethyl acetate) to give the acetyl derivative **9b** (or **10b**).

From **9a**, the acetyl derivative **9b** (0.047 g, 93%): oil; IR ($CHCl_3$) 1785, 1695 cm^{-1}; ^1H NMR δ 1.84 (s, 3 H), 2.06 (s, 3 H), 2.13 (s, 3 H), 3.43 (s, 3 H), 3.97 (dd, 1 H), 4.46 (m, 1 H), 4.60 (s, 2 H), 4.72 (dd, 1 H), 4.87 (d, 1 H), 5.20 (dd, 1 H), 6.03 (d, 1 H, J = 7.1 Hz), 6.45 (br, 1 H), 7.30 (s, 6 H), 7.74 (d, 1 H, J = 3.2 Hz). Anal. Calcd for $C_{23}H_{28}N_2O_8S$: C, 56.09; H, 5.73; N, 5.69. Found: C, 56.12; H, 5.75; N, 5.65.

From **10a**, the acetyl derivative **10b** (0.045 g, 91%): oil; IR ($CHCl_3$) 1785, 1695 cm^{-1}; ^1H NMR δ 1.91 (s, 3 H), 2.06 (s, 3 H), 2.12 (s, 3 H), 3.46 (s, 3 H), 3.97 (dd, 1 H), 4.39 (m, 1 H), 4.58 (s, 2 H), 4.73 (dd, 1 H), 4.88 (d, 1 H), 5.17 (dd, 1 H), 6.26 (d, 1 H, J = 7.6 Hz), 6.58 (br, 1 H), 7.30 (s, 6 H), 7.79 (d, 1 H, J = 3.4 Hz). Anal. Calcd for $C_{23}H_{28}N_2O_8S$: C, 56.09; H, 5.73; N, 5.69. Found: C, 56.09; H, 5.70; N, 5.71.

Reaction of Dialdose 8d with 2-Thiazolylmethylenetriphenylphosphorane 1b. To a stirred suspension of 2-thiazolylmethyltriphenylphosphonium chloride[5] (0.4 g, 1 mmol) in toluene (20 mL) was added potassium tert-butoxide (0.11 g, 1 mmol). After 30 min, a solution of the aldehyde **8d** (0.18 g, 0.5 mmol) in toluene (5 mL) was added dropwise. After 12 h at room temperature, the mixture was filtered through Celite and the solvent was removed under vacuum. The residue was chromatographed (silica gel, 7:3 ethyl acetate-petroleum ether) to give 0.084 g (38%) of the alkene **11**: oil; IR (CCl_4) 1750, 1690 cm^{-1}; ^1H NMR δ 2.00 (s, 3 H), 2.07 (s, 3 H), 3.45 (s, 3 H), 4.05 (dd, 1 H), 6.5 (dd, 1 H, J = 4.2 Hz, J = 16 Hz), 6.78 (d, 1 H, J = 16 Hz), 7.17 (d, 1 H, J = 3.1 Hz), 7.30 (s, 6 H), 7.70 (d, 1 H, J = 3.1 Hz); mass spectrum m/e (relative intensity) 446 (M^+, 30), 265 (10), 200 (20), 84 (80), 57 (100). Anal. Calcd for $C_{22}H_{26}N_2O_6S$: C, 59.18; H, 5.87; N, 6.28. Found: C, 59.15; H, 5.83; N, 6.31.

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with Professor V. Jäger.

(8) In early experiments, the portionwise addition of the chlorooxime hydrochloride **3** as a solid or as a suspension in diethyl ether to a mixture of excess furan and triethylamine in furan afforded **4a** in lower yield (42%) together with the regioisomer **4b** (10%): oil; ^{1}H NMR δ 4.95 (m, 1 H), 5.37 (m, 1 H), 6.45 (m, 1 H), 6.62 (d, 1 H, J = 8 Hz), 7.4 (d, 1 H), 7.85 (d, 1 H). Anal. Calcd for $C_8H_6N_2O_2S$: C, 49.47; H, 3.12; N, 14.43. Found: C, 49.50; H, 3.14; N, 14.40.

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(11) We thank Professor V. Bertolasi (Department of Chemistry, University of Ferrara) for the X-ray structure determination of **7**. Full details of the crystallographic analysis will be published in a forthcoming report.

(12) The addition of vinylmagnesium bromide to Boc-L-phenylalaninal has been reported to give a mixture (56:44) of the threo and erythro allylic alcohols, see Hanson, G. J.; Lindberg, T. J. J. Org. Chem., **1985**, 50, 5399. Likewise, the addition of **1a** to the same aldehyde gives a mixture (80:20) of the threo and erythro adducts (unpublished data from this Laboratory).

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