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SILYL NITRONATES AND NITRILE OXIDES IN ORGANIC SYNTHESIS. A NOVEL ROUTE TO D,L-DEOXYSUGARS. USE OF ALUMINUM OXIDE AS SOLID PHASE BASE FOR GENERATION OF NITRILE OXIDES FROM HYDROXIMIC ACID CHLORIDES

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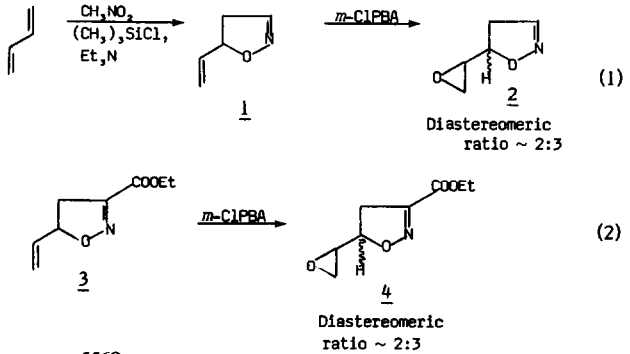
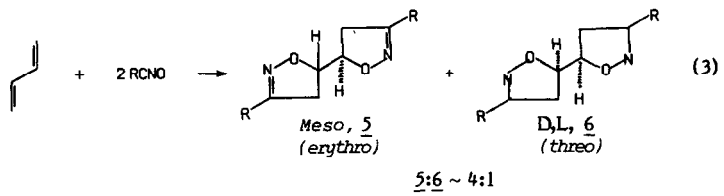
Abstract - Novel methodology is developed for a three step synthesis of deoxyaldoses and deoxyketoses: 1. Regioselective addition of silyl nitronate or nitrile oxide to a diene. 2. Stereospecific hydroxylation of the double bond. 3. Unmasking of the aldol moiety by catalytic reduction of the 2-isoxazoline. The syntheses of D,L-deoxyribose, D,L-oleose, D,L-digitoxose, D,L-2-deoxygalactose, 1,3-dideoxyfructose, 3-deoxyfructose etc. are described. Basic aluminum oxide is introduced as a solid phase base for the one step synthesis of 2-isoxazolines from aldoximes and olefins. An X-ray diffraction study of compound 13c verifies the stereochemical assignments.

In continuation of our studies of the application of silyl nitronates and nitrile oxides in organic synthesis[1,2] we have investigated the isoxazoline route to carbohydrates. It was reported in an earlier contribution that the 1,3-dipolar addition of the trimethylsilylester of *aci*-nitromethane to butadiene and subsequent epoxidation gave the masked 2-deoxypentose derivative 2, reaction (1).[3] The stereospecificity of the epoxidation was disappointingly low; the diastereomeric ratio was *ca.* 2:3. This was also the case, when 3-carboethoxy-5-vinyl-isoxazoline 3 was epoxidized to 4, eqn.(2). Moreover, regioselective opening of the epoxide may present problems and therefore this oxidation was abandoned. However, it was established that the nitrile oxide addition to the 5-vinyl group in 1 or 3 proceeded with considerable stereospecificity.[3] The *meso* (*erythro*) isomer 5 was the major product, *erythro/threo*, 5/6, ~ 4/1, eqn.(3). Nitrile oxide addition to some vinyl dioxolanes proceeded with a similar stereospecificity.[4] If we suppose that the attack takes place from the sterically least hindered side, the addition should proceed preferentially in the conformation A (Fig.1.), where the electronic repulsion between the two approaching oxygens is smaller than in conformation B. Calculations show that the oxygen atom in allylic ethers tends to adapt the "inside" position and the alkyl group the "anti" position in the transition state, as in A, thus favouring the formation of the *erythro* product.[5] It was observed that allylic hydroxy and ether functions tend to direct the osmium tetroxide catalyzed *cis*-hydroxylation in a similar fashion to give predominantly the *erythro* isomer[6a,b] and most recently it was independently demonstrated that osmylation of 5-vinyl-2-isoxalines gives the anticipitated *erythro* isomer as the major product.[6c] The suggested preferred conformation 7 of the osmium tetroxide oxidation of 5-vinyl isoxazoline is illustrated in Fig.2. The *erythro* derivative 8 was obtained as major product. Fig.3 shows the ^{13}C NMR spectrum of the crude mixture of 8 and 9, 4:1, produced in the oxidation step.The diastereomers 8 and 9 could be separ-



ated by preparative TLC and 8 gave by catalytic hydrogenation in aqueous methanol over $Pd/BaSO_4$ D,L-deoxyribose 10 in good yield as proved by ^{13}C NMR spectroscopy, TLC on silica and by comparison with an authentic sample. One equivalent of hydrogen was absorbed per mole of 2-isoxazoline.



(3)

This reaction represents a short and simple synthesis of deoxysugars from inexpensive starting materials, which can be generalized by the use of Z or E substituted dienes and other nitrile oxide precursors, reaction (4). The addition takes place regioselectively at the unsubstituted end of the diene. Thus, from nitromethane and 1-substituted butadienes 11a-d, 5-alkenyl-2-isoxazolines 12a-d are obtained which give rise to aldoses. Ketoses are obtained from butadienes and nitrile oxides *via* 2-isoxazolines 12e-h. The diastereomeric ratio in the *cis*-hydroxylation step was determined by ^{13}C NMR and the results are collected in Table 1. The ^{13}C shifts for compounds 12-14 are given in the experimental part. The anticipated major product 13d from E-3,5-hexadienoate 11d, and the intermediate isoxazoline 12d was not isolated but had lactonized during the work up to give compound 15. The major isomers 8, 13a-c crystallized slowly from the crude oily isomeric mixture. The isomers 13a-c,i give on reduction D,L-2,6-dideoxy-*lyxo*-hexose = oliose,[25] D,L-2-deoxy-*lyxo*-hexose = 2-deoxygalactose, methyl D,L-2-deoxy-*lyxo*-hexuronoate and D,L-digitoxose. The preferred catalyst was $Pd/BaSO_4$ treated with a trace of quinoline. Raney-Ni was also used but gave rise to overreduction with 3-unsubstituted isoxazolines. The highest diastereomeric ratio was obtained

Fig 1 Preferred conformation and direction of addition of a nitrile oxide to 5-vinyl-2-isoxazoline

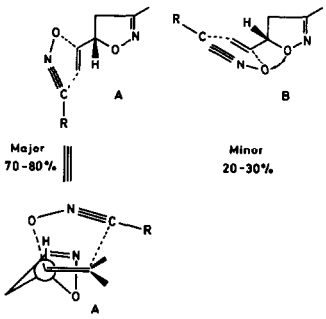


Fig 2 Preferred conformation for the osmium tetroxide oxidation of 5-vinyl-2-isoxazoline
Synthesis of 2-deoxyribose

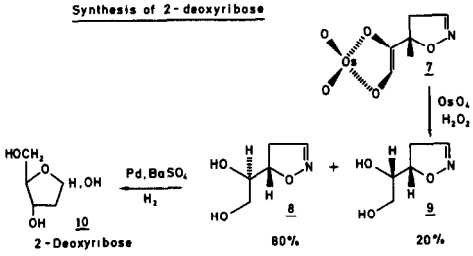


Fig 3

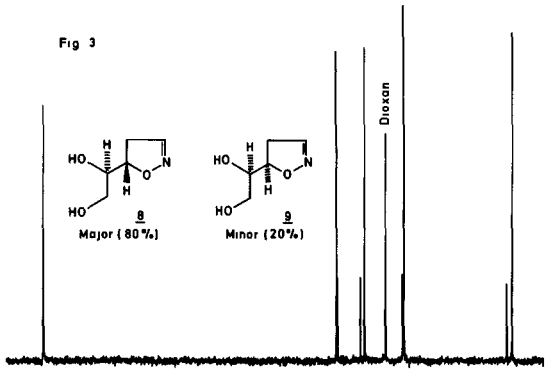


TABLE 1. Diastereomeric ratio and yields of osmium tetroxide oxidation of 5-alkenyl-2-isoxazolines, eqn.(4)

5-alkenyl-2-isoxazoline Compound	13:14[a]	Yield[d] % 13 + 14	Mp °C (*erythro*) 13	Derived carbohydrate (major isomer)
1	(8:9) 4.0:1	39	77-79	2-Deoxyribose[g]
12a	4.1:1	65	91-93	Oliose[h]
12b	3.3:1	91	110-113	2-Deoxygalactose[i]
12c	5.0:1	43	131-133	Methyl 2-Deoxygalacturonoate
12d	b	42[e]	96-98[f]	
12e	2.7:1[c]	38		
12f	2.7:1	57		
12g	3.1:1	60		2-Deoxy-*erythro*-hexulose[j]
12h	2.5:1	39		1,3-Dideoxy-*erythro*-hexulose[k]
12i	6.7:1	34		Digitoxose[l]

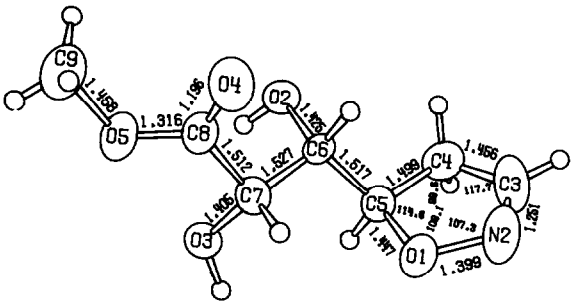
a) The diastereomeric ratio was determined by ^{13}C NMR unless otherwise stated. b) Only the lactone 15 was isolated as one single isomer. c) The ratio was determined by preparative TLC. d) Purified by preparative TLC, combined diol fraction. e) Yield of 15. f) Mp of lactone 15. g) Minor isomer, 2-deoxy-*threo*-pentose. h) Minor isomer, boivinose. i) Minor isomer, 2-deoxy-*xylo*-hexose. j) Minor isomer, 2-deoxy-*threo*-hexulose. k) Minor isomer, 1,3-Dideoxy-*threo*-hexulose. l) Minor isomer, Olivose.

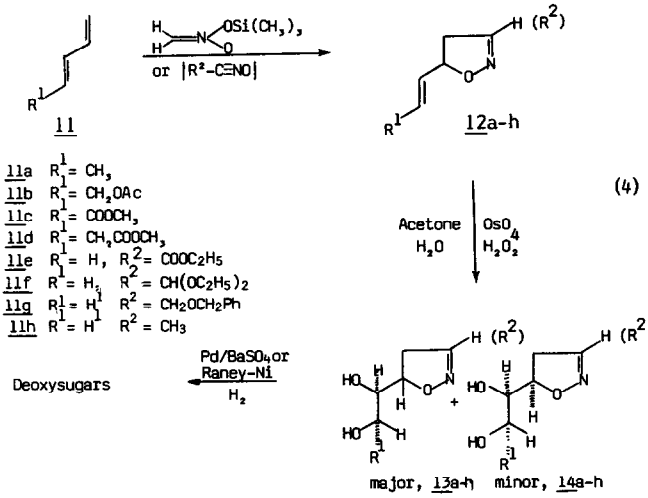
for isoxazoline 12i from Z-pentadiene. 13g and 13h are the precursors for 3-deoxy-*erythro*-hexulose and 1,3-dideoxy-*erythro*-hexulose, respectively. The ketoses obtained were not compared with authentic samples.

Crystal structures of 13c. The major product 13c from the osmium oxide catalyzed oxidation of isoxazoline 12c gives well shaped crystals, and to support our stereostructural assignments an X-ray determination was carried out.

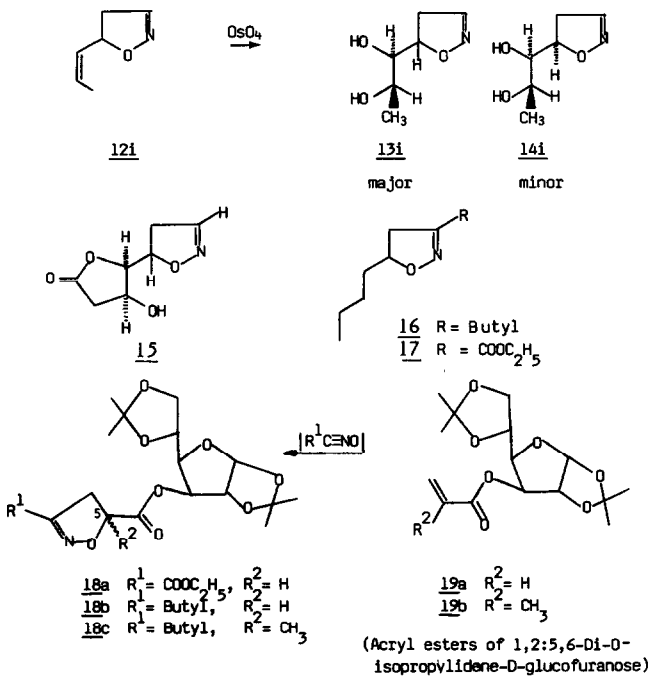
The molecule (Fig.4) consists of three almost planar moities; the isoxazoline ring, carbon atoms C4 to C8, and O3,C7,C8,O4,O5, C9. The plane defined by atoms C4 to C8 is almost parallel to {210}, the molecules are linked to their neighbours in the c-direction by hydrogen bonds, O3-H...O2' = 2.725Å. The isoxazoline ring is not completely planar, C5 being 0.150(5) Å out of the plane of the remaining 4 atoms with C6 in the axial position. Isoxazoline derivatives[10-14] show varying degrees of non-planarity; whilst the O-N-C-C fragment is planar within experimental error, the fifth carbon can be as much as 0.445 Å or as little as 0.002 Å out of the plane. Bond distances are normal, although the bond lengths within the isoxazoline ring are somewhat shorter than those in the highly substituted isoxazolines.[10-14] The very small C3-C4-C5 angle, 99.6(5)°, would seem to be typical for these rings.

Fig. 4. Perspective drawing of 13c showing bond distances (e.s.d.'s 0.005-0.009 Å) and the angles of the isoxazoline ring (e.s.d.'s 0.4-0.6





Synthesis of 2-isoxazolines. The preparative procedure was improved earlier by the use of N-chlorosuccinimide (NCS) in chloroform as chlorinating agent[15] for aldoximes and triethyl amine[16] was used as a base for the generation of the nitrile oxides. It was found that basic Al_2O_3 or Florisil could be used with advantage as a solid phase base which simplified the procedure further and the whole sequence of reactions can be performed in one step. The olefin, oxime, Al_2O_3 (basic) and NCS are all reacted together at the desired temperature in chloroform. When the hydroximoyl chloride is formed, it is immediately converted into the nitrile oxide by the base and subsequently trapped by the olefin. The yields of 2-isoxazolines are comparable to those of the earlier procedures.[15] Compounds 16-18 were prepared according to this procedure.



It was argued that absorption of the chiral acrylic ester precursor 19a on the alumina at -10 °C might improve the asymmetric induction from the glucose moiety at the C^5-centre of the 2-isoxazoline ring. However, it turned out that there was practically no difference between the induction obtained in this experiment and the induction obtained in experiments carried out in homogenous solution with triethyl amine as base at room temperature. The diastereomeric ratio was *ca.* 1.5-2:1. When the methacrylate was used, the diastereomeric ratio decreased to 1.2:1.

EXPERIMENTAL

Starting material. Butadiene, E- and Z-pentadiene, acryloyl chloride, chlorotrimethylsilane, and 1.2:5.6-di-O-isopropylidene-D-glucofuranose are commercial products.

Ethyl chloroximinoacetate,[17] *methyl E-pentadienenoate* 11c,[18] E-1-*pentadienol*[19] (the crude ester[18] was reduced instead of the acid), *methyl*-E-3,5-*hexadienoate* 11d,[20] were prepared according to the literature methods.

E-1-*Pentadienyl acetate* 11b, bp 47-49 °C/10 mmHg, was obtained by acetylation of E-1-*pentadienol* with 1.15 eqv of acetyl chloride in pyridine: CCl_4, 1:1, at 0 °C. ^{1}H NMR (CCl_4): δ 1.98 (3H,s), 4.43 (2H,d, *J* 5.6 Hz), 4.9-6.3 (5H,m).

19a was prepared by stirring 1.2:5,6-di-O-isopropylidene-D-glucofuranose, 1 eqv, with the triethylamine: acryloyl chloride complex, 1 eqv, in dry ether for 2 hrs. Filtration, washing the filtrate with water, and evaporation of the solvent gave the ester 19a admixed with unreacted starting material. They were separated by prep. TLC (SiO_2, $CHCl_3$). The yield of 19a was *ca.* 20%.

19b was prepared by acylation of 1,2:5,6-di-O-isopropylidene-D-glucofuranose with methacryloyl chloride in pyridine:chloroform, 1:2, at room temp. The yield of 19b was 64%. MS: 428 (M+1).

The preparation of 2-*isoxazolines* 1, 12a, and 12e[21] have been described in an earlier paper.

Synthesis of 2-isoxazolines from nitromethane and dienes. Preparation of 12b,c,d,i. The method described for 2-isoxazoline 1 was used with the exception that 30% excess of the nitromethane:triethylamine:chlorotrimethylsilane (1:1:1) reagent was used. The treatment with trifluoroacetic acid was reduced to 4 hrs. The isoxazolines were purified by distillation or by prep. TLC. The yields were *ca.* 30-45%. 12b, prepared from 1.0 g of 11b was purified by prep. TLC (SiO_2,$CHCl_3$, 0.5%,CH_3OH). The boiling point for 12c was 95 °C/0.2 mmHg and for 12d 115-118 °C/0.5 mmHg. 12i was purified by prep. TLC.

NMR *data for the 2-isoxazolines* 12a-d. 12a, ^{1}H NMR (CCl_4): δ 1.71 (3H,d, *J* 5.2 Hz), 2.58 (1H,ddd, *J* 17, 9, 2 Hz), 2.94 (1H,ddd, *J* 17, 10, 2 Hz), 4.67 (1H,dt, *J* 9.5, 6.5 Hz), 5.1-5.9 (2H,m), 6.81 (1H,br.s); ^{13}C NMR ($CDCl_3$): δ 17.67 (CH_3), 40.99 (CH_2), 79.62 (CH-O), 129.03, 130.26 (C=C), 146.06 (C=N).

12b, ^{1}H NMR (CCl_4): δ 1.98 (3H,s),2.61 (1H,ddd, *J* 18, 8, 2 Hz), 3.01 (1H,ddd, *J* 18, 10, 2 Hz), 4.44 (2H,d, *J* 4 Hz), 4.7 (1H,m), 5.66 (2H,m), 6.87 (1H,t, *J* 2 Hz); ^{13}C NMR ($CDCl_3$): δ 20.11 (CH_3), 41.14 (CH_2), 63.65 (CH_2-O), 78.15 (CH-O), 127.50, 131.51 (C=C), 145.81 (C=N), 170.53 (C=O).

12c, ^{1}H NMR ($CDCl_3$): δ 2.83 (1H,ddd, *J* 17, 18, 2 Hz), 3.22 (1H,ddd, *J* 17, 10, 2 Hz), 3.67 (3H,s), 5.00 (H,m), 5.99 (H,dd, *J* 16, 1 Hz), 6.71 (1H,dd, *J* 16, 5.5 Hz), 7.10 (1H,t, *J* 2 Hz); ^{13}C NMR ($CDCl_3$): δ 41.13 (CH_2), 51.78 (CH_3), 76.56 (CH-O), 122.15, 144.47 (C=C), 145.46 (C=N), 166.29 (C=O).

12d, ^{1}H NMR (CCl_4): δ 2.63 (1H,ddd, *J* 17, 8, 2 Hz), 2.97 (1H,ddd, *J* 17, 10, 2 Hz), 2.97 (2H,d, *J* 5.6 Hz), 3.60 (3H,s), 4.72 (1H,dt, *J* 5.6, 9.5 Hz), 5.2-6.0 (2H,m), 6.83 (1H,t, *J* 2 Hz).

Synthesis of 12f. To butadiene (8.6 g), nitroacetaldehyde diethylacetal[22] (10.7 g), trimethylchlorosilane (8.6 g) in 36 ml of benzene/acetonitrile (1:1), triethylamine (8.0 g) were added at -10 - 0 °C during 3 hrs with stirring. The temperature was slowly raised to room temp. The flask was stoppered and the mixture was stirred for 4 days. Trifluoroacetic acid (1 g) was added drop by drop with cooling and the product worked up as usual. 5.3 g of the isoxazoline 12f was obtained by distillation at 90-94 °C/0.3 mmHg. ^{1}H NMR ($CDCl_3$): δ 1.22 (6H,t, *J* 7 Hz), 2.83 (1H,dd, *J* 18, 9 Hz), 3.16 (1H,dd, *J* 18, 10 Hz), 3.3-3.9 (4H,m), 4.7-6.2 (4H,m), 5.09 (1H,s). ^{13}C NMR ($CDCl_3$): δ 15.04 (CH_3), 38.19 (C^4), 63.19 (CH_2O), 81.45 (C^5), 97.54 (CH<), 117.64 ($\underline{C}H_2$=C), 135.99 ($\underline{C}$H=C), 157.09 (C^3).

12g was prepared by the method of Larsen and Torssell[15] from the oxime of benzyloxyacetaldehyde[23] in a yield of *ca.* 50%, purified by prep. TLC (SiO_2, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 2.74 (1H,dd, *J* 17, 9 Hz), 3.08 (1H,dd, *J* 17, 10 Hz), 4.20 (2H,s), 4.42 (2H,s), 4.7-6.2 (3H,m), 7.24 (5H,s). ^{13}C NMR ($CDCl_3$): δ 40.82 (C^4), 64.57 (CH_2Ph), 72.70 (CH_2O), 81.53 (C^5), 117.70 ($\underline{C}H_2$=C), 127.97, 128.52 (C^2-C^6, Ar), 136.07 ($\underline{C}$H=C), 137.33 (C^1, Ar), 156.45 (C^3).

Benzyloxyacetaldoxime is prepared by stirring benzyloxyacetaldehyde diethylacetal[23] and hydroxylamine hydrochloride in THF:H_2O,2:1, for *ca.* 1 week.

12h, bp 69 °C/9 mmHg, was prepared from butadiene and nitroethane by the method of Das and Torssell.[3] ^{1}H NMR ($CDCl_3$): δ 1.90 (3H,s), 2.65 (1H,dd, *J* 17, 9 Hz), 3.02 (H,dd, *J* 17, 10 Hz)., 4.7-6.2 (4H,m).

12i. ^{13}C NMR ($CDCl_3$): δ 13.27 (CH_3), 41.49 (CH_2), 74.30 (CH-O), 128.83, 129.77 (C=C), 146.09 (C=N). ^{1}H NMR ($CDCl_3$): δ 1.69 (3H,d, *J* 6 Hz), 2.66 (1H,ddd, *J* 17, 9, 2 Hz), 3.07 (1H,ddd, *J* 17, 10, 2 Hz), 4.9-6.0 (3H,m), 7.1

(1H,br.s).

Osmium tetroxide oxidation of 5-alkenyl-2-isoxazolines. General procedure. To 10 mmol of 5-alkenyl-2-isoxazoline in 10 ml of acetone:water (4:1) were added 0.15 ml of a 10% solution of osmium tetroxide in *t*-butanol and then with stirring at 0 °C, drop by drop, 14 mmol of hydrogen peroxide (35%). The mixture was kept overnight in the refrigerator, reduced with 1 ml of 20% aqueous sodium sulfite solution, filtered, and most of the acetone was evaporated *in vacuo*. The remainder was repeatedly extracted with ethyl acetate: methanol (10:1). The collected organic phases were dried over sodium sulfate and evaporated *in vacuo* giving a crude mixture of hydroxylated 2-isoxazolines, 13 + 14, which was purified by prep. TLC (SiO_2, $CHCl_3$, 10% MeOH). The combined diastereomeric fraction was analyzed by ^{13}C NMR. In several cases it was possible to separate the isomers. The major isomer crystallized slowly out of the mixture.

8 and 9 are very water soluble and it is advisable to evaporate most of the water before the extraction with ethyl acetate:methanol (10:1). The crude product became slowly crystalline. The *erythro*-form 8 was separated from the *threo*-form 9 by prep. TLC (SiO_2, ether:methanol (10:1)), mp 77-79 °C. It can be recrystallized from a mixture of ether:methanol (6:1). The C^3-H proton of 2-isoxazolines is characteristically located as a broad singlet at δ 7.05 in $CDCl_3$ and 6.85 in CCl_4. 8: ^{13}C NMR (D_2O/H_2O): δ 37.03 (C^4), 63.02 (CH_2O), 72.41 (CH-O), 79.25 (C^5), 150.19 (C^3), 67.40 (dioxan). 9: δ 38.35 (C^4), 63.38 (CH_2-O), 73.41 (CH-O), 78.96 (C^5), 150.19 (C^3).

13a. ^{13}C NMR ($CDCl_3$): δ 19.42 (CH_3), 36.42 (C^4), 67.16 (CH-O), 74.82 (CH-O), 78.85 (C^5), 147.04 (C^3); ^{13}C NMR (D_2O/H_2O): δ 19.20 (CH_3), 37.14 (C^4), 67.40 (dioxan), 68.14 (CH-O), 75.20 (CH-O), 79.22 (C^5), 150.41 (C^3).

14a. ^{13}C NMR ($CHCl_3$): δ 19.56 (CH_3), 37.99 (C^4), 68.47 (CH-O), 75.82 (CH-O), 79.39 (C^5), 147.04 (C^3).

13b. ^{13}C NMR (D_2O/H_2O): δ 21.13 (CH_3), 37.95 (C^4), 66.60 (CH_2O, 67.40 (dioxan), 69.48 (CH-O), 71.45 (CH-O), 78.61 (C^5), 150.35 (C^3), 174.94 (C=O).

14b. ^{13}C NMR (D_2O/H_2O): δ 21.13 (CH_3), 38.56 (C^4), 66.60 (CH_2-O), 70.33 (CH-O), 72.95 (CH-O), 79.21 (C^5), 150.18 (C^3), 174.95 (C=O).

13c. ^{13}C NMR ($CDCl_3$): δ 37.90 (C^4), 52.95 (CH_3), 70.66 (CH-O), 71.92 (CH-O), 77.47 (C^5), 146.70 (C^3), 173.56 (C=O).

14c. ^{13}C NMR ($CDCl_3$): δ 37.90 (C^4), 52.95 (CH_3), 71.12 (CH-O), 73.11 (CH-O), 78.20 (C^5), 146.70 (C^3), 173.56 (C=O).

13e. ^{13}C NMR ($CDCl_3$): δ 14.10 (CH_3), 34.45 (C^4), 62.25 (CH_2CH_3), 62.96 (CH_2-O), 71.57 (CH-O), 83.80 (C^5), 152.30 (C^3), 160.52 (C=O).

14e. ^{13}C NMR ($CDCl_3$): δ 14.10 (CH_3), 35.84 (C^4), 62.26 (CH_2CH_3), 63.42 (CH_2O), 72.61 (CH-O), 84.00 (C^5), 152.31 (C^3), 160.29 (C=O).

13f. ^{13}C NMR ($CDCl_3$): δ 15.03 (CH_3), 34.14 (C^4), 63.11 (CH_2OH), 63.20 (CH_2CH_3), 71.98 (CHOH), 80.82 (C^5), 97.29 (CH<O>), 157.93 (C^3).

14f. ^{13}C NMR ($CDCl_3$): δ 35.00 (C^4), 63.55 (CH_2OH), 72.99 (CHOH).

13g. ^{13}C NMR ($CDCl_3$): δ 36.48 (C^4), 63.22 (CH_2OH), 64.46 (CH_2Ph), 71.93 (CHOH), 72.80 (C^3-CH_2O), 80.88 (C^5), 127.98, 128.52 (C^2-C^6, Ar), 137.26 (C^1, Ar), 157.29 (C^3).

14g. ^{13}C NMR ($CDCl_3$): δ 37.56 (C^4), 63.63 (CH_2OH), 72.80 (CHOH).

13h. ^{13}C NMR ($CDCl_3$): δ 23.01 (CH_3), 39.99 (C^4), 63.33 (CH_2OH), 72.08 (CHOH), 80.34 (C^5), 156.33 (C^3).

14h. ^{13}C NMR ($CDCl_3$): δ 40.89 (C^4), 63.74 (CH_2OH), 73.01 (CHOH).

13i. ^{13}C NMR ($CDCl_3$): δ 18.45 (CH_3), 36.41 (C^4), 68.48 (CHOH), 74.37 (CHOH), 78.91 (C^5), 147.19 (C^3).

14i. ^{13}C NMR ($CDCl_3$): δ 19.65 (CH_3), 38.14 (C^4), 69.00 (CHOH), 77.83 (C^5).

13a crystallized slowly from the diastereomeric mixture. It could be separated from 14a by addition of ethyl acetate and rapid filtration. The oily 14a went into solution. 13a was recrystallized from ether:methanol (8:1) mp 96-98 °C.

13b crystallized by addition of chloroform to the combined 13b + 14b fraction obtained from the prep. TLC, mp 110-113 °C.

13c, mp 131-133 °C, was crystallized in chloroform. 14c remained in the filtrate.

13e-h,i, 14e-h,i could not be brought to crystallization.

The lactone 15 was isolated as only product from the prep. TLC purification of the product from the osmium tetroxide oxidation of 12d. 15 crystallized slowly on standing, mp 96-98 °C from ethyl acetate.

15. $IR_{(film)}$: 3400(br.s) OH, 1770(s) C=O, 1615(m) C=N. ^{13}C NMR (D_2O/H_2O): δ 38.33 (C^4), 39.42 (CH_2), 67.40 (dioxan), 68.35 (CH-O), 75.99 (CH-O), 84.88 (C^5), 150.60 (C^3), 179.78 (C=O).

The reduction of 8 to D,L-2-deoxyribose, 10, was performed in methanol:water (5:1) over $Pd/BaSO_4$ treated with a drop of quinoline. Exactly one equivalent of hydrogen was absorbed in less than 2 hrs. The catalyst was filtered off and the filtrate evaporated to dryness giving 10 as an oily product in good yield. Ammonia is formed during the reduction and makes the solution slightly basic. Only one spot is visible on TLC. It has the same rf value as authentic 2-deoxyribose (SiO_2 or Al_2O_3, ethyl acetate:isopropanol:acetic acid:water (70:20:5:5)). The spots were developed by the anisaldehyde-sulfuric acid reagent.[24]

Reductions of 13a,b,c,i were performed as for 8. The formation of 2-deoxygalactose and digitoxose was proved by TLC and ^{13}C NMR and comparison with authentic specimens.

Simplified synthesis of 2-isoxazolines from olefins and aldoximes. Preparation of 3,5-dibutyl-2-isoxazoline 16. To pentanal oxime (0.50g, 5 mmol), 1-hexene (0.50 g, 5.6 mmol) and one drop of pyridine in chloroform (10ml) N-chlorosuccinimide (NCS, 0.67 g, 5 mmol) and aluminum oxide, basic, (3 g) were added. The mixture was stir-

red at room temp. overnight, filtered, and the solvent evaporated *in vacuo*. The oily 3,5-dibutyl-2-isoxazoline 16 was separated from the succinimide by dissolution in carbon tetrachloride and filtration. Evaporation of the solvent gave 16 in a yield of *ca.* 60%. ^{1}H NMR ($CDCl_3$): δ 0.92 (6H,br.t), 1.1-2.0 (10 H,m), 2.1-2.5 (2H,m), 2.57 (1H,dd, *J* 8.4, 16.4 Hz), 2.89 (1H,dd, *J* 9.8, 16.4 Hz), 4.4 (1H,m). In another run the hydroximic acid chloride was first generated from pentanal oxime, NCS and one drop of pyridine in chloroform.[15] The reaction was completed within 40 min. 1-Hexene and then Al_3O_3, basic, were added and the suspension was stirred for 20 hrs at 20 °C. Work up as above gave 16 in a yield of *ca.* 60%.

3-Ethoxycarbonyl-5-butyl-2-isoxazoline, 17, was obtained in a yield of 79%, when ethyl chloroximinoacetate[17] (0.88 g, 6 mmol) and hexene (0.50 g, 6 mmol) in chloroform (15 ml) was stirred with Florisil (3 g) for 20 hrs at 20 °C. ^{1}H NMR ($CDCl_3$): δ 0.91 (3H,br.t), 1.33 (3H,t, *J* 7 Hz), 1.1-1.9 (6H,m), 2.81 (1H,dd, *J* 17, 9 Hz). 3.20 (1H,dd, *J* 17, 10 Hz), 4.25 (2H,q, *J* 7 Hz), 4.7 (1H,m).

The 1.2:5.6-*Di-O-isopropylidine-D-glucofuranose isoxazolidines,* 18a-c, were prepared both according to the earlier described method[15] and the simplified procedure above from the corresponding acrylic esters, 19a,b. The crude product was purified by prep. TLC (SiO_2, $CHCl_3$) and a ^{13}C NMR spectrum was recorded from which the diastereomeric ratio was determined. The yields of 18a-c were *ca.* 60-70%.

Crystal structure of 13c. Crystal data $C_9H_{11}NO_4$, M = 197.2. Monoclinic, $P2_1/n$, a = 22.552(9), b = 9.026(5), c = 4.708(2) Å, β = 93.11(3)°, V = 956.9(8) Å^3, Z = 4, D_c = 1.369(1) cm^{-3}, F(000) = 416; crystal dimensions: 0.04 x 0.07 x 0.80 mm. Nb-filtered MoKα radiation. λ = 0.71069 Å, T = 297 K. 1364 independent reflections, $2\theta_{max}$ = 48°, were measured with a Huber 4-circle diffraktometer using the ω-2θ technique. There were 664 reflections with I > 3σ(I). The scan width (3.0 + 0.692tan θ)° was divided into 50 steps, each of which was measured for 2 s. No correction was made for absorption.

Solution and refinement. The structure was solved by direct methods using the MULTAN 80[7] programme system and refined by a full-matrix least-squares procedure using a modification of ORFLS,[8] hydrogen atoms were located from a difference synthesis. Positional parameters were refined for all atoms, anisotropic thermal parameters were refined for the non-hydrogen atoms, isotropic thermal parameters for the hydrogen atoms. No correction was necessary for extinction. Refinement converged to R(F) = 0.046, Rw(F) = 0.052, S =1.106 for 162 parameters and 644 reflections with $I > 3\sigma_c(I)$. The maximum shift in the final cycle was 0.09σ. The weighting scheme was $w = 1/\sigma^2$, where $\sigma = (\sigma_c(F^2) + 1.03F^2)^{1/2} - |F|$, $\sigma_c(F^2)$ is the standard deviation from counter statistics.

Atomic scattering factors were taken from International Tables for X-ray crystallography.[9] Atomic coordinates and bond distances and angles have been deposited at the Cambridge Crystallographic Data Centre.

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