Complete Stereoselective Synthesis of Quasi-Enantiomeric Pseudo Imino-*C*-disaccharides: Parallel Kinetic Resolution of a Racemic *cis*-Dihydroxypyrroline *N*-Oxide by 1,2-Glycals

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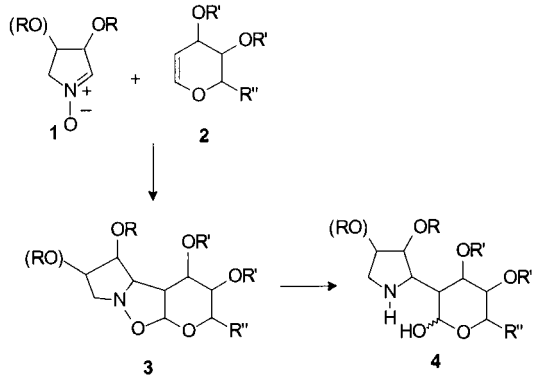
Cycloadditions of hydroxylated enantiopure pyrroline *N*-oxides to 1,2-glycals display high double-asymmetric induction. The selectivity is controlled by the stereochemistry at C-3 of the glycal. A parallel kinetic resolution experiment with a racemic *cis*-dihydroxypyrroline *N*-oxide allowed the synthesis of two different pseudo imino-*C*-disaccharides precursors in a completely enantiopure form, totally avoiding the formation of minor cycloadducts.

We have recently reported a novel intermolecular cycloaddition of enantiopure pyrroline *N*-oxides **1** to glycals **2** (Scheme 1)[1][2] aimed at the straightforward synthesis of a new class of (1→2)-linked pseudo imino-*C*-disaccharides **4**.[3] The interest of these compounds rests in their presumed selectivities in inhibition of glycosidases,[4] since incorporation of a common sugar by a non-hydrolizable carbon link might improve the enzyme-selectivity of simple iminosugars.[3d][5]



Scheme 1. Synthetic plan

Our studies on the cycloaddition reaction of several nitrones with glycals proved that the stereoselectivity is controlled by the pseudoequatorial group on C-3 of the latter compounds, according to other reported examples of cycloadditions to 1,2-glycals.[6] The single cycloaddition product isolated in each case is the result of a preferred approach of nitrone, in an *exo* fashion, *anti* to the substituent on C-3 of glycal,[1] which determines the approach of the nitrone to the *bottom* or *top* face of glycals placed according to Haworth convention. From an approach of this type, "matched" or "mismatched" interactions derive, depending on the enantiomorphic form of the nitrone employed (Scheme 2). This double asymmetric induction is responsible for the quite different reactivity of nitrone **5**[7] derived from D-tartaric acid with D-glucal **6** and with L-rhamnal **7**.[1] The "mismatched" interaction occurs when the *exo* approach, *anti* to the C-3 group of L-rhamnal **7**, forces the nitrone to react *syn* with respect to the vicinal *O*-*tert*-butyl group.[1c] Vice versa, the enantiomorphic nitrone **10**[7] derived from L-tartaric acid affords with L-rhamnal **7** the "matched" *top-anti* cycloadduct **11** in high yield,[1c] while the "mismatched" *bottom-syn* adduct **12** to D-glucal **6** is formed much more slowly and with definitely more moderate yield (Scheme 2).[1b]

The different reactivity of nitrones approaching *syn* or *anti* with respect to vicinal OR protecting groups, and the high selectivity of the *bottom* face of D-glucal **6** and the *top* face of L-rhamnal **7**, appears nicely suited for a kinetic resolution of racemic nitrones.[8] In fact, reaction of racemic nitrone **13** (synthesized in 5 steps from D- or L-arabinose)[9] with an excess of glucal **6** afforded a 3.3:1 mixture of the two *bottom-exo* adducts **14** and **15** with recovery of enantioenriched (3*S*,4*R*)-nitrone **13** (37% e.e., Scheme 3).

The stereochemistry of the adduct **14** (and consequently the absolute configuration of the enriched nitrone **13**) has been confirmed by ^{1}H-NMR coupling constants and by COSY and NOESY experiments. A partial kinetic resolution of the same racemic nitrone **13** with L-rhamnal **7** afforded, as expected, a 4.1:1 mixture of the adducts **16** and **17** with recovery of enantioenriched (3*R*,4*S*)-nitrone **13** (43% e.e., Scheme 3). The enantiomeric excess of the nitrone **13** was determined by ^{1}H-NMR experiments with Yb(hfc)$_3$ as a chiral shift reagent. Minor cycloadducts **15** and **17**, deriving from "mismatched" *exo-syn* approaches, were not fully characterized (minor impurities deriving from a third cycloadduct were detected in the ^{1}H-NMR spectra of the crude reaction mixture). Cycloadducts **14** and **16** can be considered quasi-enantiomers,[10] differing only at the C-6

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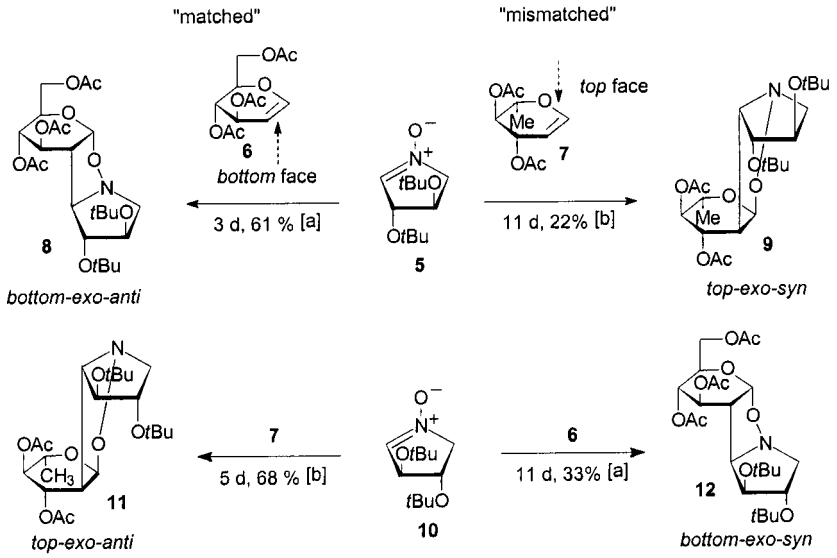
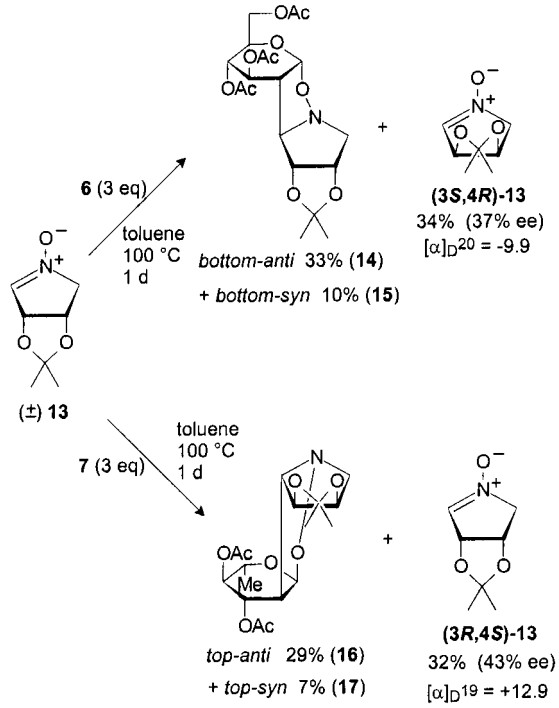


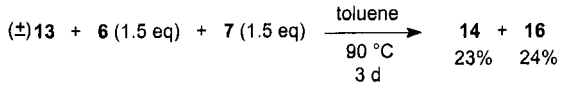
Scheme 2. Double asymmetric induction; reaction conditions: toluene, 100°C, 3 equiv. of glycal; [a] see ref.[1b]; [b] see ref.[1c]



Scheme 3. Kinetic resolutions of racemic nitrone **13**

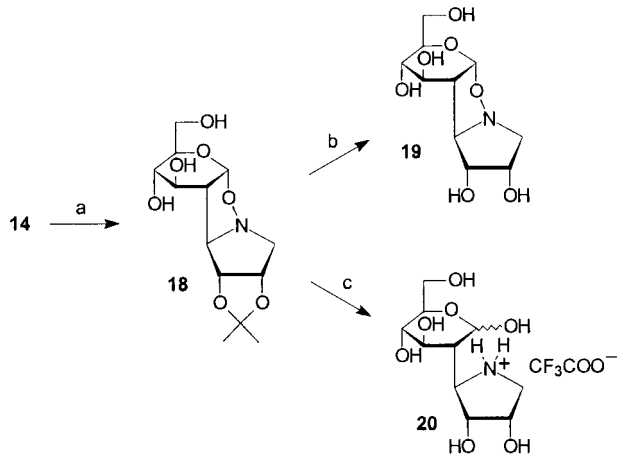
substituent of the sugar portion and possessing all the stereocenters with opposite configuration.

Albeit the shown kinetic resolutions did not afford nitrones with high ee values, they suggested that a good selectivity might be achieved in an experiment of parallel kinetic resolution (PKR), a concept recently introduced by Vedejs and Chen.[11] In a PKR experiment a racemate is treated with two reagents which display opposite reactivity and afford two distinct chiral products enantiomerically pure. If the two competing reactions have similar rates, a PKR experiment allows maintenance of the optimum 1:1 substrate ratio, and, therefore, the intrinsic maximum selectivity throughout. Adducts **14** and **16** were formed with comparable rates and they are distinct products (quasi enantiomers). The conditions for a PKR experiment were then satisfied.



Scheme 4. Parallel kinetic resolution (PKR)

Racemic nitrone **13** was treated with a slight excess of the two glycals **6** and **7** (Scheme 4). Only the *exo-anti* cycloadducts **14** and **16**, deriving from "matched" interactions, were obtained in a 1:1 ratio with exclusion of the disfavoured cycloadducts, indicating that nearly ideal relative rate conditions were achieved. Adducts **14** and **16** can be employed for the synthesis of pseudo imino-*C*-disaccharides having opposite configurations at all the stereogenic carbon atoms (quasi-enantiomeric pseudo imino-*C*-disaccharides).



Scheme 5. a) Na (20 mol-%), MeOH, room temp., 12 h, 92% of **18**; b) TFA/H_2O, 1:1, room temp., 3.5 h, 82% of **19**; c) H_2, Pd(5%/C), MeOH, room temp., 5 h, then TFA/H_2O, 1:1, 0−5°C, 2 d, 100% of **20**

Indeed, a simple sequence of deprotection reactions carried out on cycloadduct **14** gave the tricyclic isoxazolidine **19**, precursor of the pseudo iminodisaccharide **20**, obtained as the trifluoroacetate salt by reductive cleavage of the isoxazolidine N−O bond (Scheme 5).

Since symmetrically substituted enantiomerically pure nitrone **13** is not available,[12] this PKR experiment represents the optimal utilization of racemic nitrone **13** for the simultaneous combinatorial-like synthesis of two different chiral products in an enantiomerically pure form, in a completely stereoselective manner.

Experimental Section

General Procedure for the Cycloaddition Reactions: A 1 M toluene solution of nitrone (**5** or **10**, 0.5 mmol, 1 equiv.), containing a threefold excess of L-rhamnal **7** (1.5 mmol, 3 equiv.), was heated at 100°C until the nitrone was completely consumed (TLC control). The crude mixture was then purified by flash column chromatography on silica gel.

(2*S*,3*S*,4*S*,4a*S*,4b*S*,5*R*,6*R*,9a*S*)-3,4-Diacetoxy-5,6-bis(*tert*-butoxy)-2-methyloctahydro-2*H*-pyrano[3,2-*d*]pyrrolo[1,2-*b*]isoxazole (9): Reaction time: 11 d. − Yield: 22%. − R_f (AcOEt/petroleum ether, 1:4) = 0.26. − M.p. 190−192°C (diisopropyl ether); $[\alpha]_D^{22} = -42.0$ (c = 0.2 in $CHCl_3$). − IR ($CDCl_3$): $\tilde{\nu}$ = 2980 (CH) cm^{-1}, 2937 (CH), 1743 (C=O), 1365, 1242 (C−O). − ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.50 (d, J = 5.0 Hz, 1 H, 9a-H), 5.29 (t,[13] J = 8.5 Hz, 1 H, 4-H), 4.79 (dd, J = 9.5, 8.5 Hz, 1 H, 3-H), 4.17−4.02 (m, 2 H, 2-H, 6-H), 3.88 (dd, J = 8.5, 6.0 Hz, 1 H, 5-H), 3.75 (dd, J = 8.0, 1.0 Hz, 1 H, 4b-H), 3.42 (dd, J = 14.0, 6.0 Hz, 1 H, 7-H), 2.91 (ddd, J = 8.0, 5.0, 1.0 Hz, 1 H, 4a-H), 2.89 (dd, J = 14.0, 8.5 Hz, 1 H, 7-H^b), 2.07 (s, 3 H, acetoxy), 2.05 (s, 3 H, acetoxy), 1.22 (d, J = 6.0 Hz, 3 H, methyl), 1.20 (s, 9 H, *t*Bu), 1.17 (s, 9 H, *t*Bu). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.2 (s, acetoxy), 166.0 (s, acetoxy), 99.7 (d, C-9a), 77.3 (d), 76.9 (d), 74.5 (s, *t*Bu), 73.7 (s, *t*Bu), 73.6 (d), 72.5 (d), 69.1 (d), 66.9 (d), 60.5 (t), 47.4 (d, C-4a), 28.4 (q, 3 C, *t*Bu), 28.3 (q, 3 C, *t*Bu), 20.7 (q, 2 C, acetoxy), 17.4 (q, methyl). − MS (70 eV); *m*/*z* (%): 386 (3) [M^+ − 57], 326 (12), 314 (3), 266 (4), 230 (8), 210 (7), 112 (17), 84 (75), 57 (100). − $C_{22}H_{37}NO_8$ (443): calcd. C 59.58, H 8.41, N 3.16; found C 59.70, H 8.24, N 3.08.

(2*S*,3*S*,4*S*,4a*S*,4b*S*,5*S*,6*S*,9a*S*)-3,4-Diacetoxy-5,6-bis-(*tert*-butoxy)-2-methyloctahydro-2*H*-pyrano[3,2-*d*]pyrrolo[1,2-*b*]isoxazole (11): Reaction time: 5 d. − Yield: 68%. − R_f (AcOEt/petroleum ether, 1:4) = 0.37. − M.p. 108−110°C (diisopropyl ether); $[\alpha]_D^{22} = +16.8$ (c = 0.7 in $CHCl_3$). − IR ($CDCl_3$): $\tilde{\nu}$ = 2978 (CH) cm^{-1}, 2938 (CH), 1741 (C=O). − ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.79 (d, J = 5.2 Hz, 1 H, 9a-H), 5.24 (t,[13] J = 8.1 Hz, 1 H, 4-H), 4.74 (dd, J = 9.5, 8.1 Hz, 1 H, 3-H), 4.08 (dq, J = 9.5, 6.2 Hz, 1 H, 2-H), 3.84 (dt,[13] J = 5.2, 2.8 Hz, 1 H, 6-H), 3.76 (t,[13] J = 2.5 Hz, 1 H, 5-H), 3.53 (t, J = 2.5 Hz, 1 H, 4b-H), 3.43 (dd, J = 13.9, 5.2 Hz, 1 H, 7-H), 3.23 (dd, J = 13.9, 2.8 Hz, 1 H, 7-H^b), 2.73 (ddd, J = 7.9, 5.1, 2.5 Hz, 1 H, 4a-H), 2.05 (s, 3 H, acetoxy), 2.04 (s, 3 H, acetoxy), 1.21 (d, J = 6.2 Hz, 3 H, methyl), 1.17 (s, 9 H, *t*Bu), 1.16 (s, 9 H, *t*Bu). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.1 (s, acetoxy), 170.1 (s, acetoxy), 98.7 (d, C-9a), 82.9 (d), 78.4 (d), 75.8 (d), 74.1 (s, 2 C, *t*Bu), 73.5 (d), 72.8 (d), 67.0 (d), 64.0 (t), 49.6 (d, C-4a), 28.6 (q, 3 C, *t*Bu), 28.2 (q, 3 C, *t*Bu), 20.7 (q, 2 C, acetoxy), 17.4 (q, methyl). − MS (70 eV); *m*/*z* (%): 443 (7) [M^+], 386 (20) [M^+ − 57], 326 (66), 314 (17), 226 (32), 84 (100). − $C_{22}H_{37}NO_8$ (443): calcd. C 59.58, H 8.41, N 3.16; found C 60.04, H 8.37, N 2.84.

Kinetic Resolution of the Nitrone (±)-13 with D-Glucal 6: A 1 M toluene solution of nitrone **(±)-13** (160.2 mg, 1.02 mmol), containing a threefold excess of D-glucal **6** (833 mg, 3.06 mmol), was heated at 100°C for 24 h. Purification of the crude reaction mixture by flash chromatography with an eluent of increasing polarity afforded **14** (R_f = 0.22, eluent AcOEt/petroleum ether, 1:1, 144.5 mg, 0.334 mmol, 33%), **15** with traces of a third cycloadduct (R_f = 0.5, eluent AcOEt, 43.8 mg, 0.102 mmol, 10%), and the recovered nitrone **(−)-13** (R_f = 0.27, eluent AcOEt/MeOH, 8:1, 54.4 mg, 0.347 mmol, 34%).

(2*R*,3*R*,4*R*,4a*R*,4b*R*,5*R*,6*S*,9a*R*)-3,4-Diacetoxy-2-(acetoxymethyl)-5,6-(*O*-isopropylidene)octahydro-2*H*-pyrano[3,2-*d*]pyrrolo[1,2-*b*]-isoxazole (14): M.p. 36−38°C; $[\alpha]_D^{22} = +2.4$ (c = 0.5 in $CHCl_3$). − IR ($CDCl_3$): $\tilde{\nu}$ = 2993 (CH) cm^{-1}, 2940 (CH), 1739 (C=O), 1368, 1231 (C−O). − ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.54 (d, J = 5.9 Hz, 1 H, 9a-H), 5.28 (t, J = 6.6 Hz, 1 H, 4-H), 5.01 (dd, J = 9.4, 6.6 Hz, 1 H, 3-H), 4.98 (q,[13] J = 6.0 Hz, 1 H, 6-H), 4.53 (dd, J = 6.0, 3.1 Hz, 1 H, 5-H), 4.32 (dd, J = 12.2, 4.7 Hz, 1 H, 1′-H), 4.16 (ddd, J = 9.4, 4.7, 2.4 Hz, 1 H, 2-H), 4.11 (dd, J = 12.2, 2.4 Hz, 1 H, 1′-H), 3.77 (t, J = 3.1 Hz, 1 H, 4b-H), 3.61 (dd, J = 14.4, 6.0 Hz, 1 H, 7-H), 3.21 (dd, J = 14.4, 5.8 Hz, 1 H, 7-H^b), 2.82 (td,[13] J = 6.3, 3.1 Hz, 1 H, 4a-H), 2.08 (s, 3 H, acetoxy), 2.07 (s, 3 H, acetoxy), 2.05 (s, 3 H, acetoxy), 1.50 (s, 3 H, isopropylidene), 1.32 (s, 3 H, isopropylidene). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.7 (s, acetoxy), 170.2 (s, acetoxy), 169.7 (s, acetoxy), 114.2 (s, isopropylidene), 98.6 (d, C-9a), 84.4 (d), 81.5 (d), 74.9 (d), 72.0 (d), 68.7 (d), 68.0 (d), 62.3 (t, 2 C), 49.5 (d, C-4a), 27.0 (q, isopropylidene), 24.9 (q, isopropylidene), 20.9 (q, acetoxy), 20.7 (q, 2 C, acetoxy). − MS (70 eV); *m*/*z* (%): 430 (1) [M^+ + 1], 369 (1), 267 (11), 249 (3), 158 (7), 43 (100). − $C_{19}H_{27}NO_{10}$ (429): calcd. C 53.13, H 6.34, N 3.26; found C 53.12, H 6.31, N 2.97.

(2*R*,3*R*,4*R*,4a*R*,4b*R*,5*S*,6*R*,9a*R*)-3,4-Diacetoxy-2-(acetoxymethyl)-5,6-(*O*-isopropylidene)octahydro-2*H*-pyrano[3,2-*d*]pyrrolo[1,2-*b*]-isoxazole (15): ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.36 (d, J = 4.1 Hz, 1 H, 9a-H), 5.33−5.26 (m, 2 H, 3-H, 4-H) 4.88 (td, J = 5.8, 3.1 Hz, 1 H, 6-H), 4.42 (dd, J = 5.8, 1.0 Hz, 1 H, 5-H), 4.26 (dd, J = 12.0, 5.8 Hz, 1 H, 1′-H), 4.12 (dd, J = 12.0, 3.0 Hz, 1 H, 1′-H), 4.05 (br. d, J = 11.4 Hz, 1 H, 4b-H), 3.65 (ddd, J = 8.9, 5.8, 3.0 Hz, 1 H, 2-H), 3.58 (dd, J = 13.6, 3.1 Hz, 1 H, 7-H), 3.31 (dd, J = 13.6, 5.8 Hz, 1 H, 7-H^b), 3.03−2.98 (m, 1 H, 4a-H), 2.10 (s, 3 H, acetoxy), 2.06 (s, 3 H, acetoxy), 2.04 (s, 3 H, acetoxy), 1.51 (s, 3 H, isopropylidene), 1.29 (s, 3 H, isopropylidene).

(−)-(3*S*,4*R*)-(*O*-isopropylidene)-1-pyrroline *N*-Oxide [(−)-13]: 37% e.e. − $[\alpha]_D^{20} = -9.9$ (c = 0.3 in $CHCl_3$).

Kinetic Resolution of the Nitrone (±)-13 with L-Rhamnal 7: A 1 M toluene solution of nitrone **(±)-13** (157 mg, 1.0 mmol), containing a threefold excess of **L-rhamnal 7** (642 mg, 3.0 mmol), was heated at 100°C for 24 h. Purification of the crude reaction mixture by flash chromatography with an eluent of increasing polarity afforded **16** (R_f = 0.4, eluent AcOEt/petroleum ether 1:1, 108 mg, 0.29 mmol, 29%), the presumed *top-syn* cycloadduct **17** with traces of a third cycloadduct (R_f = 0.3, eluent AcOEt/petroleum ether, 1:1, 26 mg, 0.07 mmol, 7%), and the recovered nitrone **(+)-13** (R_f = 0.27, eluent AcOEt/MeOH, 8:1, 50 mg, 0.32 mmol, 32%).

(2*S*,3*S*,4*S*,4a*S*,4b*S*,5*S*,6*R*,9a*S*)-3,4-Diacetoxy-5,6-(*O*-isopropylidene)-2-methyloctahydro-2*H*-pyrano[3,2-*d*]pyrrolo[1,2-*b*]isoxazole (16): M.p. 111−112°C (diisopropyl ether); $[\alpha]_D^{20} = -15.8$ (c = 0.5 in $CHCl_3$). − IR ($CDCl_3$): $\tilde{\nu}$ = 3023 (CH) cm^{-1}, 2941 (CH), 1745 (C=O), 1578, 1545, 1421, 1366, 1220 (C−O). − ^1H NMR ($CDCl_3$,

200 MHz): δ = 5.46 (d, *J* = 5.8 Hz, 1 H, 9a-H), 5.21 (t, *J* = 6.8 Hz, 1 H, 4-H), 4.95 (q,[13] *J* = 5.8 Hz, 1 H, 6-H), 4.74 (dd, *J* = 9.6, 6.8 Hz, 1 H, 3-H), 4.50 (dd, *J* = 6.4, 3.2 Hz, 1 H, 5-H), 3.98 (dq, *J* = 9.6, 6.2 Hz, 1 H, 2-H), 3.75 (t, *J* = 3.2 Hz, 1 H, 4b-H), 3.56 (dd, *J* = 14.4, 5.8 Hz, 1 H, 7-H), 3.18 (dd, *J* = 14.4, 5.2 Hz, 1 H, 7-H^b), 2.72 (td,[13] *J* = 6.2, 3.2 Hz, 1 H, 4a-H), 2.05 (s, 3 H, acetoxy), 2.01 (s, 3 H, acetoxy), 1.18 (d, *J* = 6.2 Hz, 3 H, methyl), 1.49 (s, 3 H, isopropylidene), 1.30 (s, 3 H, isopropylidene). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.3 (s, acetoxy), 170.1 (s, acetoxy), 114.2 (s, isopropylidene) 98.7 (d, C-9a), 84.2 (d), 81.5 (d), 75.0 (d), 73.2 (d), 72.1 (d), 66.5 (d), 62.4 (t), 49.5 (d, C-4a), 27.0 (q, isopropylidene), 24.9 (q, isopropylidene), 21.0 (q, acetoxy), 20.8 (q, acetoxy), 17.6 (q, methyl). − MS (70 eV); *m/z* (%): 371 (0.6) [M$^+$], 251 (66), 165 (13), 158 (17), 111 (20), 86 (49), 84 (100). − $C_{17}H_{25}NO_8$ (371): calcd. C 54.98, H 6.78, N 3.77; found C 54.83, H 6.71, N 3.64.

(+)-(3*R*,4*S*)-(*O*-Isopropylidene)-1-pyrroline *N*-Oxide [(+)-13]: 43% e.e. − $[\alpha]_D^{19}$ = +12.9 (*c* = 0.2 in $CHCl_3$).

Parallel Kinetic Resolution of the Nitrone (±)-13 with D-Glucal 6 and L-Rhamnal 7: A solution of nitrone **(±)-13** (47.1 mg, 0.3 mmol), D-glucal **6** (122.8 mg, 0.45 mmol) and L-rhamnal **7** (96.7 mg, 0.45 mmol) in toluene (0.15 mL) was heated at 90°C for 3 d until the nitrone was completely consumed (TLC control). Purification of the crude reaction mixture by flash chromatography, eluent AcOEt/petroleum ether, 1:1, afforded **16** (R_f = 0.4, 26.7 mg, 0.072 mmol, 24%), and **14** (R_f = 0.22, 29.6 mg, 0.069 mmol, 23%).

(2*R*,3*R*,4*R*,4a*R*,4b*R*,5*R*,6*S*,9a*R*)-3,4-Dihydroxy-2-(hydroxymethyl)-5,6-(*O*-isopropylidene)octahydro-2*H*-pyrano[3,2-*d*]pyrrolo[1,2-*b*]-isoxazole (18). A lump of Na (20 mol-%) was added to a solution of **14** (273 mg, 0.636 mmol) in anhydrous MeOH (1.8 mL) and the mixture was stirred for 12 h at room temp. under N_2. After removal of the solvent, the crude reaction mixture was purified by flash chromatography, eluent CH_2Cl_2/MeOH, 8:1, to afford **18** (R_f = 0.26, 177.1 mg, 0.584 mmol, 92%) as a white solid. M.p. 165−166°C (AcOEt); $[\alpha]_D^{22}$ = +17.3 (*c* = 0.8 in MeOH). − ^{1}H NMR (200 MHz, CD_3OD): δ = 5.58 (d, *J* = 5.2 Hz, 1 H, 9a-H), 4.99 (q,[13] *J* = 6.0 Hz, 1 H, 6-H), 4.67 (dd, *J* = 6.0, 2.6 Hz, 1 H, 5-H), 3.92 (t, *J* = 2.6 Hz, 1 H, 4b-H), 3.86−3.59 (m, 4 H), 3.59 (dd, *J* = 14.3, 6.0 Hz, 1 H, 7-H), 3.43 (dd, *J* = 8.7, 8.1 Hz, 1 H), 3.20 (dd, *J* = 14.3, 5.6 Hz, 1 H, 7-H^b), 2.56 (ddd, *J* = 7.8, 5.2, 2.6 Hz, 1 H, 4a-H), 1.51 (s, 3 H, isopropylidene), 1.35 (s, 3 H, isopropylidene). − ^{13}C NMR (50 MHz, CD_3OD): δ = 114.6 (s, isopropylidene), 101.0 (d, C-9a), 85.5 (d), 82.1 (d), 76.0 (d), 75.6 (d), 74.0 (d), 70.6 (d), 63.6 (t), 62.5 (t), 52.8 (d, C-4a), 27.4 (q, isopropylidene), 25.1 (q, isopropylidene). − MS (70 eV); *m/z* (%): 304 (0.4) [M$^+$ + 1], 253 (7), 225 (3), 184 (6), 157 (30), 111 (58), 85 (64), 41 (100). − $C_{13}H_{21}NO_7$ (303): calcd. C 51.48, H 6.98, N 4.62; found C 51.35, H 7.12, N 4.27.

(2*R*,3*R*,4*R*,4a*R*,4b*R*,5*R*,6*S*,9a*R*)-3,4,5,6-Tetrahydroxy-2-(hydroxymethyl)octahydro-2*H*-pyrano[3,2-*d*]pyrrolo[1,2-*b*]isoxazole (19): The deacetylated cycloadduct **18** (55 mg, 0.181 mmol) was dissolved at 0°C in a 1:1 mixture of TFA/H_2O (1 mL) and stirred at room temp. for 3.5 h. The solvent was distilled off and the light brown residue was dissolved in MeOH (4 mL) and stirred with Amberlyst A26 for 2.5 h at room temp. The resin was filtered off and the solution concentrated to afford a yellow oil. Purification by flash chromatography, eluent CH_2Cl_2/MeOH/30% aq. NH_3, 5:5:1, afforded **19** (R_f = 0.33, 39.1 mg, 0.149 mmol, 82%) as a white solid. M.p. 171−173°C (dec.) (EtOH); $[\alpha]_D^{24}$ = +32.6 (*c* = 0.4 in MeOH). − ^{1}H NMR (500 MHz, D_2O): δ = 5.63 (d, *J* = 4.4 Hz, 1 H, 9a-H), 4.34 (q,[13] *J* = 4.6 Hz, 1 H, 6-H), 4.08 (dd, *J* = 6.7, 4.8 Hz, 1 H, 5-H), 3.83−3.73 (m, 3 H, 4b-H, 1′-H), 3.69 (ddd, *J* = 9.7, 4.4, 2.9 Hz, 1 H, 2-H), 3.58 (t, *J* = 9.4 Hz, 1 H), 3.47 (t, *J* = 9.6 Hz, 1 H), 3.39 (dd, *J* = 13.9, 4.9 Hz, 1 H, 7-H), 3.34 (dd, *J* = 13.9, 4.3 Hz, 1 H, 7-H^b), 2.52 (dd, *J* = 9.2, 4.4 Hz, 1 H, 4a-H). − ^{13}C NMR (50 MHz, D_2O): δ = 101.8 (d, C-9a), 77.1 (d), 76.8 (d), 75.1 (d), 74.8 (d), 73.8 (d), 71.0 (d), 64.1 (t), 62.8 (t), 52.7 (d, C-4a). − MS (70 eV); *m/z* (%): 245 (1) [M$^+$ − 18], 215 (3), 168 (4), 112 (42), 85 (43), 60 (67), 55 (100). − $C_{10}H_{17}NO_7$ (263): calcd. C 45.63, H 6.51, N 5.32; found C 45.23, H 6.45, N 4.92.

(2′*R*,3′*R*,4′*S*)-2-Deoxy-2-[2-(3,4-dihydroxy)pyrrolidinyl]-D-glucose (20): The deacetylated cycloadduct **18** (101.8 mg, 0.336 mmol) was dissolved in MeOH (3 mL) and stirred under hydrogen at room temp. for 5 h in presence of Pd (5%/C) (86 mg). The mixture was then filtered through Celite and concentrated, dissolved in a 1:1 mixture of TFA/H_2O (6 mL) at 0°C and kept at 0−5°C for 2 d. It was then concentrated, dissolved again in MeOH and stirred in the presence of Amberlyst A-26 for 1.5 h. It was then filtered through Celite, concentrated, and dissolved in a 10% aqueous mixture with TFA (4.4 mL). Concentration afforded quantitatively the salt **20** as a vitreous solid. − α/β = 36:64 (determined by ^{1}H NMR). − ^{1}H NMR (200 MHz, D_2O): δ = 5.30 (d, *J* = 3.0 Hz, α, 1 H), 4.90 (d, *J* = 9.0 Hz, β, 1 H), 4.72 (d, *J* = 8.8 Hz, β, 1 H), 4.35 (dd, *J* = 9.4, 4.4 Hz, β, 1 H), 4.24, 4.17 (α 3 H, β, 1 H), 3.78−3.55 (m, 4 H), 3.40−3.09 (m, 3 H), 2.04−1.97 (m, 1 H). − ^{13}C NMR (50 MHz, D_2O): δ = 163.8 [s, COO^-, (q, $^2J_{C\text{-}F}$ = 38 Hz)], 115.0 [s, CF_3,(q, $^1J_{C\text{-}F}$ = 302 Hz)] 96.0 (d, β, C-1), 92.9 (d, α, C-1), 77.9 (d, β), 74.1 (d, β), 73.7 (d, α), 73.4 (d, β), 73.2 (d, α), 72.9 (d, α), 72.8 (d, β), 71.6 (d, β), 71.3 (d, α) 71.1 (d, α), 63.0 (t, β), 62.8 (t, α), 60.8 (d, β, C-2′), 59.0 (d, α, C-2′), 51.7 (t, α, C-5′), 51.5 (t, β, C-5′), 48.5 (d, β, C-2), 44.1 (d, α, C-2).

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