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Synthesis of diastereomerically pure indolizidine and pyrrolizidine analogues from D-pentoses

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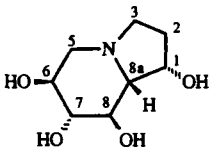
Abstract: Partially protected D-pentoses were stereoselectively transformed into the corresponding thiazolidines by the action of cysteamine. Then, a cyclisation with n-BuLi/TsCl or n-Bu_3P/DIAD led to indolizidine or pyrrolizidine analogues. Alternatively, a one-pot preparation of diastereomerically pure indolizidine analogues was realized from 5-*O*-tosyl-D-pentose derivatives and cysteamine. © 1997 Elsevier Science Ltd

Introduction

The naturally occurring hydroxylated indolizidine (castanospermine **1**) and pyrrolizidine (australine **2** or alexine **3**) have aroused much interest as a result of their potent inhibitory action against glycosidases. Several syntheses of these molecules from carbohydrates or other starting materials containing multiple stereogenic centres have been proposed.[1]



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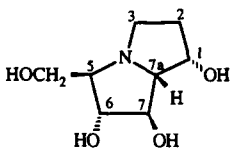

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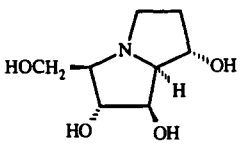

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In a preceding paper,[2] we reported a two-step synthesis of diastereomerically pure analogues of castanospermine and australine in which the C-1 carbon atom is replaced by a S atom. These analogues have been synthesized from 2,3-*O*-isopropylidene-D-ribofuranose **4** treated with 2-aminoethanethiol (cysteamine). The corresponding thiazolidine derivative **5** was obtained stereoselectively (2*R*:2*S*=8:92) and its cyclisation provided a mixture of compounds **6** (castanospermine analogue) and **7** (australine analogue). We describe herein an extension of these preliminary results applied to the pentose series in order to improve both the role of the protecting group on the stereoselective formation of thiazolidine and the synthesis of other analogues of castanospermine and australine.

Results and discussion

Condensation of unprotected D-ribose, D-lyxose, D-xylose or D-arabinose with cysteamine gave highly hydrophilic thiazolidines derivatives, but without any stereoselectivity (2*R*:2*S*=1:1). So, by analogy with our previous results,[2] we have synthesized their benzylidene[3] or isopropylidene[4] derivatives. In Scheme 1, are reported the structure of the thiazolidines obtained and the result of their cyclisation leading to indolizidine and/or pyrrolizidine derivatives.

The reaction of 2,3-*O*-benzylidene-D-ribofuranose **8**[5] with cysteamine (1.5 eq.) in methanol heated to reflux gave the thiazolidine derivative **9** in a C2 epimeric mixture 2*R*:2*S*=7:93, with the same stereoselectivity observed for the thiazolidine **5**, derived from the 2,3-*O*-isopropylidene-D-ribofuranose.[2,5] For this reaction, the imine intermediate was not isolable. The two privileged *cis* and

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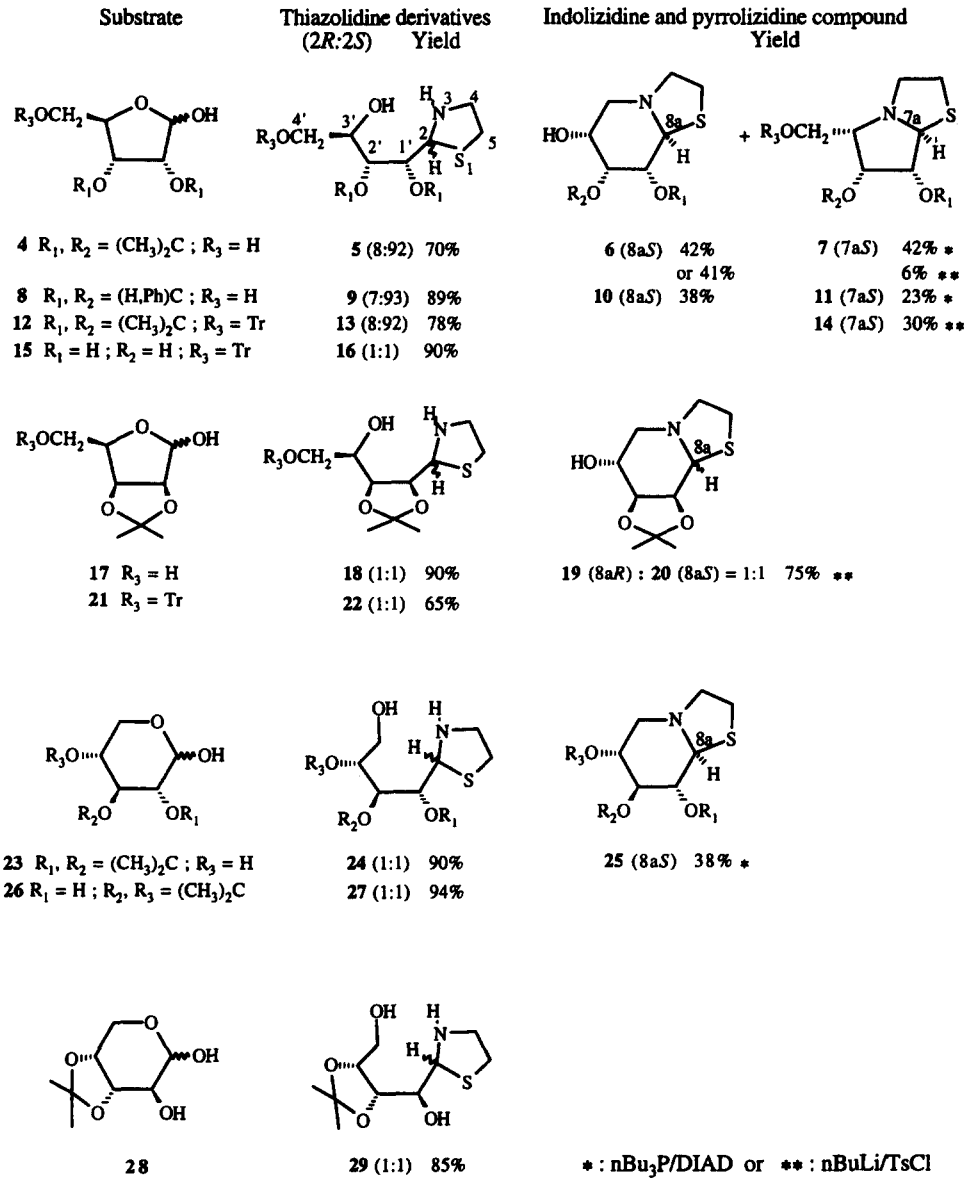
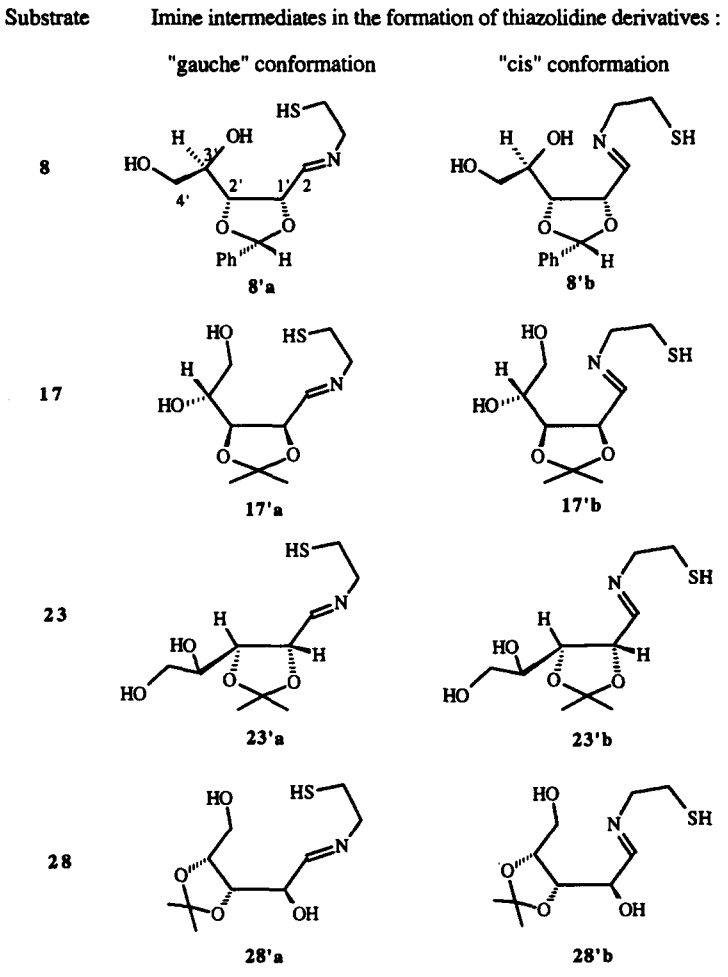


Scheme 1.

gauche conformations[6] of its more probable *E* isomer are represented in Scheme 2. According to the Cram–Felkin–Anh model,[7] the cyclisation must proceed by a nucleophilic attack of the S atom *anti* to the C1′-O1′ linkage. For the *gauche* conformation **8′a**, a steric and electrostatic repulsion between the S and O3′ atoms prevented the cyclisation. So, the formation of thiazolidine **9** (2*S*:2*R*=93:7) occurred *via* the *cis* conformation **8′b**. For this heterocyclisation, the benzylidene group inhibited the rotation around the C1′-C2′ linkage and was responsible for this stereoselectivity.

The introduction of a trityl group at the C5 hydroxyl group[8] in compound **12** did not enhance the formation of the 2*S* epimer, and the corresponding thiazolidine **13** was formed in the same ratio (2*S*:2*R*=92:8). Thus, the terminal position of a bulky group did not disturb the equilibrium between the two *cis* and *gauche* conformations. On the other hand, treatment with cysteamine of the 5-*O*-



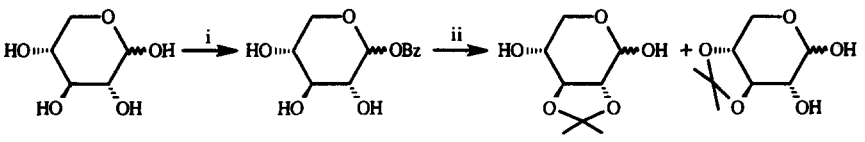
Scheme 2.

trityl-D-ribofuranose **15** in which the free C1′-C2′ rotation was recovered, was instantaneous at room temperature as well as at −20°C and led to thiazolidine derivative **16** as a 1:1 mixture of C2 epimers.

Surprisingly, in the case of the 2,3-*O*-isopropylidene-D-lyxose **17**,[5] the isopropylidene group did not exert the same stereocontrol. For the *gauche* and *cis* conformations of the imine derived from D-lyxose (**17′a** and **17′b** respectively), any steric and electrostatic effect was observed, the two epimers of the corresponding thiazolidine **18** being obtained in the 1:1 ratio. As observed with the 5-*O*-trityl-2,3-isopropylidene-D-ribose **12**, the introduction of a bulky group at the terminal position in compound **21** did not change the epimeric ratio.

From D-xylose, the 2,3- and 3,4-*O*-isopropylidene-D-xylose monotrans-acetonated **23** and **26** were first synthesized in a three-step process (Scheme 3).[9,12,13] Unfortunately, the formation of thiazolidines **24** and **27** derived respectively from **23** and **26** were obtained without any stereoselectivity. The *S* configuration of C3 in compound **23** allowed the cyclisation from the two imine conformations which were in equilibrium (**23′a** and **23′b**) (Scheme 2). This fact explained the formation of the thiazolidine **24** as a C2 epimeric mixture 1:1 (Scheme 1).

Likewise, the extension of the above methodology to the 3,4-*O*-isopropylidene-D-arabinose **28**[5] led



xylose 23 26

i : PPh_3/NCS/PhCOO$^-Na^+$ 60%

ii : 2-methoxypropene (2.5 eq.)/TsOH (cat.)/THF; MeONa/MeOH **23** (40%) and **26** (10 %)

Scheme 3.

to a mixture of epimeric thiazolidine **29** (Scheme 1; 2*R*: 2*S*=1:1). For this arabinose derivative, the C1′-C2′ free rotation allowed the cyclisation *via* the two rotamers **28′a** and **28′b** (Scheme 2).

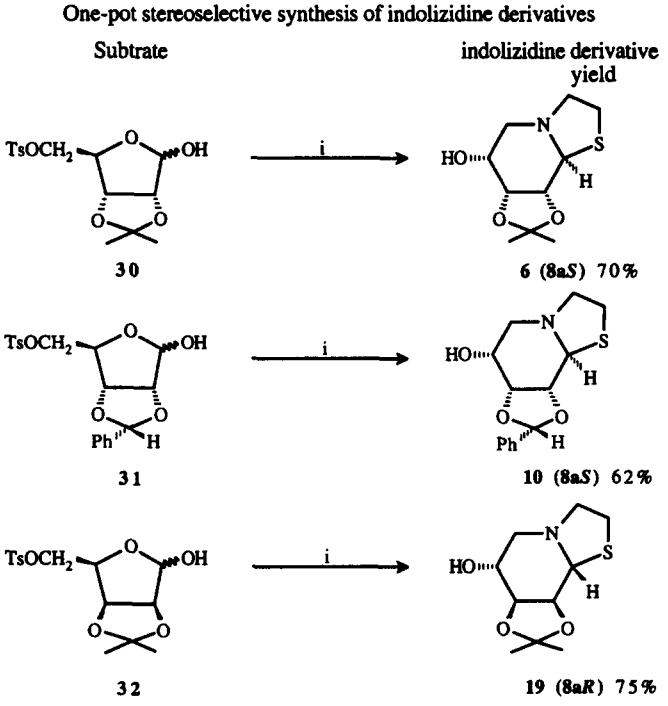
To obtain bicyclic analogues of castanospermine and australine, some thiazolidines were cyclised using two different activating reagents. With the system n-BuLi/TsCl,[10] the C2 epimeric mixture of lyxose thiazolidine **18** led to the same epimeric mixture of indolizidine **19**. From the thiazolidine **13**, a chemoselective sulfonylation and a subsequent cyclisation by nucleophilic attack of the amino function afforded only the 7a*S* pyrrolizidine compound **14** in 30% yield.

As previously observed for the cyclisation of thiazolidine derivative **5**,[2] compound **9** reacted with n-Bu_3P/DIAD[11] to afford the two bicyclic compounds: indolizidine and pyrrolizidine derivatives **10** and **11** in 38% and 23% yield respectively. The cyclisation of the C2 epimeric mixture of thiazolidine derivative of D-xylose **24**, in the same reaction conditions, was stereospecific and only furnished the indolizidine **25** in 38% yield with a pure C8a*S* configuration. The structure and configuration of compound **25** were established from its ^1H NMR spectrum obtained in deuterated chloroform. The doublet signal at 3.63 ppm with a $J_{8,8a}$ of 8.2 Hz indicated a *trans* configuration for H-8 and H-8a. This stereospecificity is different from the one observed with the epimeric mixture of lyxose thiazolidine **18**. The molecular representation of **24** showed that the sole 2*S* epimer can be cyclised into indolizidine **25** (Scheme 1). In the case of the 2*R* epimer, the same cyclisation will lead to a boat conformation, which is unfavourable.

In this work, an efficient and stereospecific synthesis of pure C8a epimer indolizidine derivative was targeted and a convenient one step synthesis was also researched (Scheme 4). Thus, treatment of the 5-*O*-tosyl-2,3-*O*-isopropylidene-D-ribofuranose **30** with cysteamine hydrochloride and sodium methoxide in methanol, gave the compound **6** in 70% yield. Likewise, the 8a*S* indolizidine **10** was obtained with the same stereospecificity from the 5-*O*-tosyl-2,3-*O*-benzylidene-D-ribofuranose **31**. This "one-pot" reaction was stereospecific and led to the only castanospermine analogue when the cyclisation *via* the thiazolidine derivatives (**5** or **9**) led to a mixture of castanospermine and australine analogues. More interesting was the application of this synthetic approach to the 5-*O*-tosyl-2,3-*O*-isopropylidene-D-lyxofuranose **32** which afforded the 8a*R* pure indolizidine **19** only in 75% yield. The configuration of this C8a epimer was determined by RX spectroscopy. This cyclisation was an example of kinetic control. The indolizidine formation occurred *via* the *cis* conformation **17′b** in which the nitrogen atom was near the C4′ carbon atom (Scheme 2).

In summary, we described two routes for the synthesis of diastereomerically pure indolizidine or pyrrolizidine analogues from D-pentoses.

The first route was realized *via* a thiazolidine intermediate which has been isolated. For substituted ribofuranose, the thiazolidine derivative was stereoselectively obtained from the sole "*cis*" conformation of the imine intermediate. Subsequent cyclisation led to diastereomerically pure indolizidine and pyrrolizidine analogues. For others substituted D-pentoses, the formation of thiazolidine occured via the "*gauche*" and "*cis*" conformations of the imine intermediate and was not stereoselective. Only the epimeric mixture derived from 2,3-*O*-isopropylidene-D-xylofuranose led to diastereomerically pure indolizidine analogues.



Scheme 4.

The second route was a "one-pot" procedure in which 5-*O*-tosyl derivatives reacted with cysteamine. This way only led to diastereomerically pure indolizidine analogues and was effective for D-ribose and D-lyxose derivatives. These strategies are now extended to hexose derivatives.

Experimental

Melting points were determined with a Buchi 535 apparatus and are uncorrected. TLC was performed on silica gel Merck 60 F_{254} plates with visualisation by UV light (254 nm) and/or by charring with a vanillin–H_2SO_4 or phosphomolybdic–H_2SO_4 reagents. Preparative column chromatography was performed using 230–400 mesh Merck silica gel. Optical rotations were measured with a Jasco-DIP-370 electronic micropolarimeter. NMR spectra were recorded on a Bruker 300WB spectrometer and chemical shifts are reported as δ values (ppm) relative to Me_4Si. Elemental analyses were performed by the Service Central de Microanalyse du CNRS of Vernaison (69-Rhône-France). All solvents were distilled before use. 2-Aminoethanethiol hydrochloride was purchased from Aldrich.

*2S-(1′,2′-O-Benzylidene-*D*-ribotetrahydroxybutyl)thiazolidine* **9**

Sodium methoxide (153 mg, 2.83 mmol) was added to 2-aminoethanethiol hydrochloride (450 mg, 2.83 mmol) in anhydrous methanol (10 mL). The mixture was stirred at room temperature under nitrogen for 30 min. Salts were removed by filtration, then 2,3-*O*-benzylidene-β-D-ribofuranose **8** (450 mg, 1.89 mmol) was added and the mixture was refluxed for 2.5 h. The solvent was removed under reduced pressure to give crude product which was purified on silica gel column eluting with ethyl acetate resulting in compound **9** as a C2 epimeric mixture *R:S*=7:93 (500 mg, 89%); 2*S* epimer: ^{1}H NMR ($CDCl_3$): δ 4.75 (d, 1H, $J_{1',2}$ 9.6 Hz, H-2), 4.18–4.09 (m, 2H, H-2′, H-1′), 3.94 (m, 1H, $J_{3',4'b}$ 5.8 Hz, H-3′), 3.85 (dd, 1H, $J_{4a',4b'}$ 11.5 Hz, H-4′), 3.67 (dd, 1H, $J_{3',4a'}$ 2.7 Hz, H-4a′), 3.31 (m, 1H, H-4b), 2.98–2.88 (m, 2H, H-5, H-4a), 2.68 (m, 1H, H-5); ^{13}C NMR: δ 135.8 (Cipso), 128.7, 127.5,

125.7 (Ph), 102.8 (CHPh), 78.9, 78.6 (C-1′, C-2′), 67.8 (C-3′), 67.7 (C-2), 63.4 (C-4′), 50.1 (C-4), 33.4 (C-5). Anal. calcd. for $C_{14}H_{19}O_4NS$: C,56.56; H, 6.39; N, 4.71; S, 10.77. Found: C, 56.12; H, 6.30; N, 4.65; S, 10.70.

(6R,7R,8R,8aS)-6,7,8-Trihydroxy-7,8-O-benzylideneperhydro[1,3]thiazolo[3,2a]pyridine ***10*** *and (5S,6R,7R, 7aS)-6,7-dihydroxy-6,7-O-benzylidene-5-hydroxymethylperhydro[1,3]thiazolo[3, 2a]pyrrole* ***11***

n-Bu_3P (785 μL, 3.15 mmol) and DIAD (620 μL, 3.15 mmol) were added to a solution of compound **9** (624 mg, 2.1 mmol) in dichloromethane (10 mL). The reaction mixture was refluxed for 2 h. The solvent was removed under reduced pressure and the crude residue was chromatographed on silica gel (hexane–ethyl acetate 8:2, then 7:3, 6:4 and 5:5) to give the compound **10** (225 mg, 38%) and compound **11** (130 mg, 23%) as syrup.

Compound **10**: $[\alpha]_D^{19}$ −57.4 (c 0.97, EtOAc); ^{1}H NMR ($CDCl_3$): δ 7.55–7.23 (m, 5H, Ph), 5.87 (s, 1H, CHPh), 4.42–4.30 (m, 3H, $J_{8,8a}$ 5.7 Hz, $J_{7,8}$ 4.5 Hz, H-8a, H-8, H-7), 4.02 (m, 1H, $J_{6,7}$ 3.9 Hz, $J_{5,6}$ 4.4 Hz, H-6), 3.34 (dd, 1H, $J_{3,3'}$ 10.4 Hz, H-3′), 2.99–2.73 (m, 4H, $J_{2,3}$ 5.6 Hz, H-5, H-3, H-2, H-2′), 2.52 (dd, 1H, H-5); ^{13}C NMR: δ 135.5 (Cipso), 128.6, 127.5, 125.8 (Ph), 103.1 (CHPh), 76.3 (C-8), 73.7 (C-7), 69.6 (C-8a), 64.9 (C-6), 57.6 (C-3), 49.9 (C-5), 28.8 (C-2). Anal. calcd. for $C_{14}H_{19}O_3NS$: C, 60.21; H, 6.09; N, 5.01; S, 11.46. Found: C, 61.53; H, 5.93; N, 5.13; S, 10.97.

Compound **11**: $[\alpha]_D^{29}$+1.68 (c 0.75, EtOAc); ^{1}H NMR ($CDCl_3$): δ 7.51–7.32 (m, 5H, Ph), 5.70 (s, 1H, CHPh), 4.97 (s, 1H, $J_{7,7a}$ 0 Hz, H-7a), 4.90–4.80 (m, 2H, H-7, H-6), 3.90 (dd, 1H, $J_{8,8'}$ 11.3 Hz, $J_{5,8'}$ 4.4 Hz, H-8′), 3.80 (dd, 1H, $J_{5,8}$ 6.7 Hz, H-8), 3.58 (m, 1H, H-3′), 3.03–2.84 (m, 3H, H-2, H-2′, H-3), 2.78 (m, 1H, H-5); ^{13}C NMR: δ 135.0 (Cipso), 128.9, 127.5, 126.1 (Ph), 104.4 (CHPh), 82.5–81.3 (C-6, C-7) 79.0 (C-7a), 62.5 (C-5), 60.0 (C-8), 54.0 (C-3), 29.7 (C-2). Anal. calcd. for $C_{14}H_{19}O_3NS$: C,60.21; H, 6.09; N, 5.01; S, 11.46. Found: C, 60.17; H, 6.17; N, 4.88; S, 10.89.

*2S-(1′,2′-O-Isopropylidene-4′-O-trityl-*D*-ribotetrahydroxybutyl)thiazolidine* ***13***

2,3-*O*-Isopropylidene-5-*O*-trityl-β-D-ribofuranose **12** (2g, 4.63 mmol) was converted to a thiazolidine as described above for **5** using 4 eq. of 2-aminoethanethiol hydrochloride and 4 eq. of sodium methoxide in methanol (25 mL), and heated to reflux for 4 h. Concentration under reduced pressure and purification by column chromatography on silica gel (hexane–ethyl acetate 7:3) afforded to crystalline thiazolidine **13** (1.8 g, 78%) as a C2 epimeric mixture *R:S*=2:98. C2*S* epimer: ^{1}H NMR ($CDCl_3$): δ 7.52 −7.16 (m, 15H, Ph), 5.24 (d, 1H, $J_{2,1'}$ 8.8 Hz, H−2), 4.91 (dd, 1H, $J_{2',3'}$ 8.4 Hz, H-2′), 4.62 (dd, 1H, $J_{1',2'}$ 4.6 Hz, H1′), 4.55 (m, 1H, H-3′), 4.09–4.01 (m, 3H, H-4b, H-4′a, H-4′b), 3.73–3.67 (m, 2H, H-4a, H-5b), 3.48 (m, 1H, H-5a), 2.31–2.26 (2s, 6H, CH_3); ^{13}C NMR: δ 143.2 (Cipso), 127.9, 126.7, 125.9 (Ph), 107.8 (CHPh), 85.5 ($C(Ph)_3$), 78.8 (C-1′), 76.7 (C-2′), 67.9 (C-2), 67.4 (C-3′), 64.5 (C-4′), 50.0 (C-4), 33.3 (C-5), 27.2–24.5 ($2CH_3$). Anal. calcd. for $C_{29}H_{33}O_4NS$: C, 70.80; H, 6.70; N, 2.80; S, 6.50. Found: C, 70.79; H, 6.79; N, 2.31; S, 5.34.

*(5S,6R,7R, 7aS)-6,7-Dihydroxy-6,7-*O*-isopropylidene-5-trityloxymethylperhydro[1,3]thiazolo[3, 2a]pyrrole* ***14***

To a solution of thiazolidine **13** (715 mg, 1.41 mmol) in 10 mL of THF, cooled at 0°C, was added n-BuLi 2.5 M in THF (570 μL, 1 eq.). After stirring at 0°C under nitrogen for 15 min, tosyl chloride (322 mg, 1.7 mmol) was added and the reaction mixture was stirred for 30 min at this temperature, then was heated at 70°C for 6 h. The mixture was concentrated and the residue was chromatographed on silica gel (hexane–ethyl acetate 95:5 and 9:1) to give the pure compound **14** as syrup (200 mg, 30%). $[\alpha]_D^{23}$ −12 (c 1.1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 7.51–7.16 (m, 15H, Ph), 4.83–4.76 (m, 3H, H-6, H-7, H-7a), 3.78 (dd, 1H, H-8′), 3.69 (dd, 1H, H-8), 3.32 (dd, 1H, H-3′), 2.96–2.78 (m, 3H, H-2, H-2′, H-3), 2.73 (m, 1H, H-5), 1.29–1.39 (2s, 6H, CH_3); ^{13}C NMR: δ 143.2 (Cipso), 127.9, 126.9, 126.1 (Ph), 110.6 (CHPh), 86.4 ($C(Ph)_3$) 82.0–80.4–80.0 (C-6, C-7, C-7a), 62.4 (C-5), 61.8 (C-8), 54.7 (C-3), 29.8 (C-2), 25.4–24.4 ($2CH_3$). Anal. calcd. for $C_{29}H_{31}O_3NS$: C,73.57; H, 6.55; N, 2.96; S, 6.76. Found: C, 73.78; H, 6.39; N, 3.06; S, 6.58.

(6R,7S,8R,8aS)-6,7,8-Trihydroxy-7,8-O-isopropylideneperhydro[1,3]thiazolo[3,2a]pyridine **25**

Thiazolidine **24** (425 mg, 1.7 mmol) was treated as described as above for thiazolidine **9**, using n-Bu_3P (640 µL, 2.55 mmol) and DIAD (500 µL, 2.55 mmol) for 24 h in refluxed THF (10 mL). After purification on silica gel column (hexane–ethyl acetate 7:3, 5:5, 3:7 and pure ethyl acetate), the only C-8a*S* indolizidine **25** was isolated in 38% yield (150 mg). mp 121–123°C; $[\alpha]_D^{22}$ −67 (c 1, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 3.97 (m, 1H, $J_{6,5}$ 8.5 Hz, H-6), 3.63 (d, 1H, $J_{8a,8}$ 8.2 Hz, H-8a), 3.39–3.32 (m, 2H, H-8, H-7), 3.30–3.23 (m, 2H, $J_{5,5'}$ 11.5 Hz, H-5′, H-3′), 2.99–2.92 (m, 2H, H-2, H-2′), 2.64 (m, 1H, H-3), 2.25 (dd, 1H, H-5), 1.38–1.37 (2s, 6H, $2CH_3$); ^{13}C NMR: δ 111.5 ($C(CH_3)_2$), 83.9–79.7 (C-8, C-7), 67.8 (C-6), 67.2 (C-8a), 54.6 (C-3, C-5), 30.0 (C-2), 26.7–26.5 ($2CH_3$). Anal. calcd. for $C_{10}H_{17}O_3NS$: C, 51.9; H, 7.30; N, 6.06; S, 13.80. Found: C, 51.66; H, 7.41; N, 5.84; S, 13.95.

General procedure for the one-pot preparation of indolizidine derivatives from 5-O-tosyl-pentose

To a solution of 2-aminoethanethiol hydrochloride (1 eq.) in anhydrous methanol was added sodium methoxide (1 eq.). The mixture was stirred under nitrogen at room temperature for 30 min, then salts were removed by filtration and the 5-*O*-tosyl-pentose derivative[14] (0.5 eq.) was added to the filtrate. The mixture was heated to reflux for 4 h. The methanol was removed under reduced pressure to give a crude product which was purified on silica gel column eluting with hexane–ethyl acetate (1:1 then 3:7).

(6R,7R,8R,8aS)-6,7,8-Trihydroxy-7,8-O-isopropylideneperhydro[1,3]thiazolo[3,2a]pyridine **6**

Yield: 70%. mp 120–121°C; $[\alpha]_D^{26}$ −81.8 (c 0.82, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 4.23–4.19 (m, 2H, $J_{8,8a}$ 4.2 Hz, H-8, H-7), 4.11 (d, 1H, H-8a), 3.89 (m, 1H, $J_{5,6}$ 7.7 Hz, H-6), 3.28 (dd, 1H, $J_{3,3'}$ 10.3 Hz, H-3′), 2.85–2.77 (m, 3H, H-2, H-2′, H-5′), 2.68 (m, 1H, $J_{2,3}$ 5.6 Hz, H-3), 2.40 (dd, 1H, $J_{5,5'}$ 11.2 Hz, H-5), 1.47–1.28 (2s, 6H, $2CH_3$); ^{13}C NMR: δ 108.7 ($C(CH_3)_2$), 75.5 (C-8), 72.8 (C-7), 69.6 (C-8a), 65.1 (C-6), 57.5 (C-3), 50.2 (C-5), 28.7 (C-2), 26.1–24.8 ($2CH_3$). Anal. calcd. for $C_{10}H_{17}O_3NS$: C,51.9; H, 7.30; N, 6.06; S, 13.80. Found: C, 51.61; H, 7.39; N, 5.89; S, 13.75.

(6R,7S,8S,8aR)-6,7,8-Trihydroxy-7,8-O-isopropylideneperhydro[1,3]thiazolo[3,2a]pyridine **19**

Yield: 75%. mp 107–108°C; $[\alpha]_D^{26}$+71.77 (c 1, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 4.43 (d, 1H, $J_{8,8a}$ 2.9 Hz, H-8a), 4.34 (dd, 1H, $J_{7,8}$ 5.3 Hz, H-8), 4.01 (t, 1H, $J_{6,7}$ 5.7 Hz, H-7), 3.88 (m, 1H, H-6), 3.32 (dd, 1H, H-3′), 2.93–2.78 (m, 3H, H-2, H-2′, H-5), 2.55–2.50 (m, 2H, H-3, H-5), 1.43–1.28 (2s, 6H, $2CH_3$); ^{13}C NMR: δ 108.4 ($C(CH_3)_2$), 76.8 (C-7), 74.4 (C-8), 70.6 (C-8a), 67.9 (C-6), 58.2 (C-3), 49.7 (C-5), 28.6 (C-2), 25.3–25.3 ($2CH_3$). Anal. calcd. for $C_{10}H_{17}O_3NS$: C, 51.9; H, 7.30; N, 6.06; S, 13.80. Found: C, 51.68; H, 7.47; N, 5.75; S, 13.92.

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9. The first step was an original benzoylation of the anomeric hydroxyl group with PPh_3:N-chlorosuccinimide and sodium benzoate. Previously, the same system was applied to D-glucose and led to 6-*O*-benzoyl-D-glucopyranose.[12] Then the treatment of the D-xylopyranosyl benzoate with 2-methoxypropene in the presence of a catalytic amount of *p*-toluenesulfonic acid[13] afforded two regioisomers: the 2,3-*O*-isopropylidene- and the 3,4-*O*-isopropylidene-D-xylopyranosyl benzoate

isolated in 40% and 10% yield respectively. Deprotection of the anomeric hydroxyl group was realized by treatment with sodium methoxide to give quantitatively **23** and **26**.

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