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Study of 1-deoxy-1-(indol-3-yl)-L-sorbose, 1-deoxy-1-(indol-3-yl)-L-tagatose, and their analogs

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Abstract

Alkaline degradation of the ascorbigen 2-*C*-[(indol-3-yl)methyl]-α-*L*-*xylo*-hex-3-ulofuranosono-1,4-lactone (**1a**) led to a mixture of 1-deoxy-1-(indol-3-yl)-L-sorbose (**2a**) and 1-deoxy-1-(indol-3-yl)-L-tagatose (**3a**). The mixture of diastereomeric ketoses underwent acetylation and pyranose ring opening under the action of acetic anhydride in pyridine in the presence of 4-dimethylaminopyridine (DMAP) with the formation of a mixture of (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(indol-3-yl)-L-*xylo*-hex-1-enitol (**4a**) and (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(indol-3-yl)-L-*lyxo*-hex-1-enitol (**5a**), which were separated chromatographically. Deacetylation of **4a** or **5a** afforded cyclised tetrols, tosylation of which in admixture resulted in 1-deoxy-1-(indol-3-yl)-3,5-di-*O*-tosyl-α-L-sorbopyranose (**12a**) and 1-deoxy-1-(indol-3-yl)-4,5-di-*O*-tosyl-α-L-tagatopyranose (**13a**). Under alkaline conditions **13a** readily formed 2-hydroxy-4-hydroxymethyl-3-(indol-3-yl)cyclopenten-2-one (**15a**) in 90% yield. Similar transformations were performed for *N*-methyl- and *N*-methoxyindole derivatives.

Keywords: Ascorbigen; Indolylketoses; Sorbose; Tagatose; Polyols

1. Introduction

1-Heteroaryl-containing 1-deoxyketopyranoses occur as subunits in a number of cytotoxic polyketide natural compounds. Synthetic access to such subunits is based on laborious multistep syntheses.[1–3] In contrast, the diastereomeric 1-deoxy-1-(indol-3-yl)-α-L-sorbopyranose (**2a**) and 1-deoxy-1-(indol-3-yl)-α-L-tagatopyranose (**3a**) are readily obtainable by degradation of the ascorbigen 2-*C*-[(indol-3-yl)methyl]-α-L-xylo-*hex*-3-ulofuranosono-1,4-lactone (**1a**) through a sequential domino reaction including hydrolysis, decarboxylation, and isomerization.[4] These ketoses are also of interest as they are formed in the blood and tissues of animals which obtained ascorbigen orally.[5] As ascorbigen is the most abundant indole-derived ingredient of cruciferous vegetables, which human and animals obtain with food, the study of the products of ascorbigen transformation *in vivo* is important. Neoascorbigen, namely 2-*C*-[(1-methoxyindol-3-yl)methyl]-α-L-*xylo*-hex-3-ulofuranosono-1,4-lactone[6] (**1c**) is also a component of human and animal diet,[6] and the study of products of neascorbigen degradation is important. However, the individual products of alkaline degradation of ascorbigens have not until now been investigated.

2. Results and discussion

The goal of this project was the investigation of acylated derivatives of 1-deoxy-1-indolyl ketoses and the elaboration of methods for obtaining the individual 1-deoxy-1-(indol-3-yl)-L-sorbose (**2a**) and -L-tagatose (**3a**). These compounds and their *N*-methyl analogs **2b** and **3b** were obtained from ascorbigen (**1a**) or *N*-methylascorbigen (**1b**) as mixtures of diastereomers.[4] Alkaline degradation of neoascorbigen (**1c**) under the conditions described for ascorbigen (Et_3N, MeOH,

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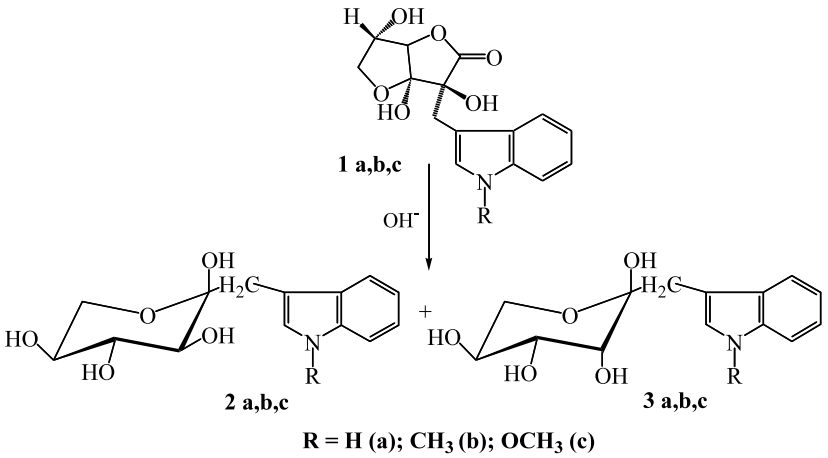
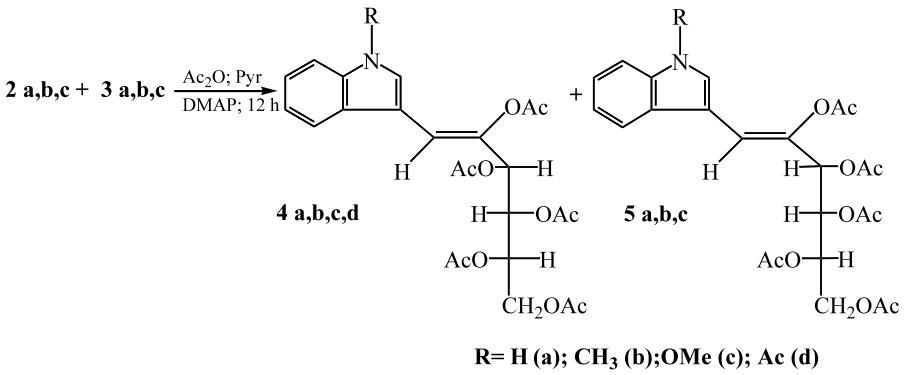
60 °C) failed.[6] We obtained in 56% net yield a mixture of 1-deoxy-1-(1-methoxyindol-3-yl)-α-L-sorbopyranose (**2c**) and 1-deoxy-1-(1-methoxyindol-3-yl)-α-L-tagatopyranose (**3c**) under milder conditions by the degradation of **1c** in potassium phosphate buffer at pH 7.4 (Scheme 1). HPLC analysis of the crude reaction mixture demonstrated the presence of two compounds. The ^{1}H NMR spectrum also showed the presence of two components having parameters close to those of a **2a** + **3a** mixture. [4] The mixture was characterized by mass spectroscopy and used for further investigation without additional purification.

Reaction of the **2b** and **3b** mixture with Ac_2O in pyridine in the presence of DMAP at room temperature for 12 h resulted in per-*O*-acetylation, opening of the pyranose ring, and formation of a mixture of (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(1-methylindol-3-yl)-L-*xylo*-hex-1-enitol (**4b**) and (*E*)-penta-*O*-acetyl-1-deoxy-1-(1-methylindol-3-yl)-2,3,4,5,6-L-*lyxo*-hex-1-enitol (**5b**) in 58% net yield (Scheme 2). The compounds were separated by column chromatography followed by crystallization to give the individual **4b** (40%) and **5b** (18%). Similarly, a mixture of the products of neoascorbigen degradation **2c** and **3c** produced, after peracetylation and chromatographic separation, the individual 1-methoxyindolyl derivatives (**4c**) (30%) and (**5c**) (20%). Acetylation of the *N*-unsubstituted indolylketoses **2a** + **3a** led to a more-complex mixture of *N*-unsubstituted penta-*O*-acetyl and hexa-*N*,*O*-acetyl derivatives. The individual (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(indol-3-yl)-L-*xylo*-hex-1-enitol (**4b**) (10%), (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(indol-3-yl)-L-*lyxo*-hex-1-enitol (**5b**) (13%), and the *N*-acetyl derivative **4d** (4%) were isolated by column chromatography followed by crystallization. In the ^{1}H NMR spectra of compounds **4** and **5** the H-1 singlet at 6.5–6.8 ppm and the H-3 doublet at the 5.5–5.8 ppm are diagnostic (Table 1). The *E*-geometry of the double bond was shown by NOE difference experiments. In compounds **4a**,**b**,**c**,**d** and **5a**,**b**,**c** irradiation of the H-3 doublet led to the enhancement of the H-1 singlet by 12–14%, it demonstrating the *trans*-orientation of the indole ring and the acetylated polyol moiety. The structures of compounds **4a**,**b**,**c**,**d** and **5a**,**b**,**c** were also supported by HRMS spectra.

Acetylation of the **2b** + **3b** mixture by the same reagents for 1 h produced another complex mixture of compounds, which were separated by column chro-



Scheme 1.

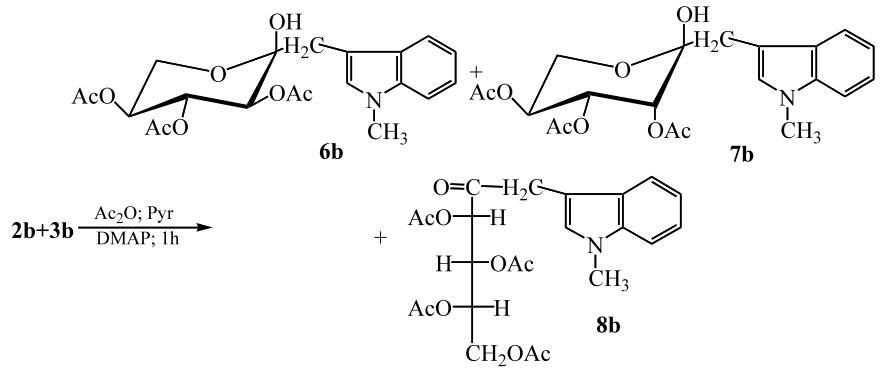


Scheme 2.

Table 1
Chemical shifts (ppm) and coupling constants values J (Hz) of the carbohydrate moiety in ^{1}H NMR spectra of the compounds

Compd./ Solvent	Signals of hydrogen atoms							
	H-1a	H-1b	H-3 ($J_{3,4}$)	H-4 ($J_{4,3}$) [$J_{4,5}$]	H-5	H-6a ($J_{6a,6b}$) [$J_{6a,5}$]	H-6b ($J_{6b,6a}$) [$J_{6b,5}$]	Other
4a $CDCl_3$	6.55 s		5.71 d (8.1)	5.62 dd (8.1) [3.2]	5.48 m	4.06 dd (11.7) [6.6]	4.33 dd (11.7) [5.3]	Ac, 5s, 2.05; 2.07 2.12; 2.14 2.23
4b Acetone-d_6	6.71 s		5.74 d (7.9)	5.60 dd (7.9) [3.5]	5.42 m	4.03 dd (11.7) [6.6]	4.28 dd (11.7) [5.1]	Ac, 5s, 1.98; 2.00 2.09; 2.12 2.31
4c $CDCl_3$	6.54 s		5.66 d (8.0)	5.57 dd (8.0) [3.2]	5.42 m	4.03 dd (11.7) [6.5]	4.28 dd (11.7) [5.1]	Ac, 5s, 2.02; 2.03 2.09; 2.10 2.26
5a Acetone-d_6	6.75 s		5.63 d (8.9)	5.59 dd (8.9) [2.4]	5.52 m	4.02 dd (11.7) [7.5]	4.31 dd (11.7) [4.7]	Ac, 5s, 1.98; 1.99 2.26; 2.72 2.85
5b Acetone-d_6	6.71 s		5.60 d (9.1)	5.56 dd (9.1) [2.2]	5.50 m	4.00 dd (11.7) [7.6]	4.31 dd (11.7) [4.6]	Ac, 5s, 1.95; 1.98 1.99; 2.09 2.26
5c $CDCl_3$	6.61 s		5.55 m 2H	5.50 m	3.94 dd (11.7) [7.5]	4.32 dd (11.7) [4.9]	Ac, 5s, 1.98; 1.99 2.04; 2.11 2.23	
6b $CDCl_3$	2.88 d (14.5)	3.02 d (14.5)	5.11 dd (9.9) $J_{3,3OH}$ 1.5	5.49 t (9.9)	5.01 m	3.62 t (10.9)	3.76 dd (10.9) [6.0]	Ac, 3s, 1.99; 2.01; 2.14; OH-group, d, 2.78 $J_{3OH,3}$ 1.5
7b $CDCl_3$	2.83 d J_{ab} 14.5	3.18 d J_{ab} 14.5	5.43 d (3.4)	5.45 dd (3.4) [10.4]	5.24 m	3.60 t (10.8)	3.86 dd (10.8) [5.3]	Ac, 3s, 1.99; 2.01 2.21 OH-group, s, 2.78
8b $CDCl_3$	3.88 d (17.5)	3.89 d (17.5)	5.39 d (2.9)	5.60 dd (2.9) [6.4]	5.20 m	3.86 dd (12.3) [5.7]	4.19 dd (12.3) [4.2]	Ac, 4s, 1.88; 1.92 2.02; 2.14
12a $CDCl_3$	3.04 d (14.6)	3.26 d (14.6)	4.60 dd ($J_{3,4}$ 9.3) [$J_{3,3OH}$ 1.5]	4.08 td ($J_{4,3}$ 9.3) [$J_{4,4OH}$ 3.7]	4.46 m	3.70 m	Me of Tos, s, 6H, 2.47; 2 OH groups 2.66, m, 2H	
12b Pyridine-d_5	3.61 d (14.4)	3.80 d (14.4)	5.38 d (9.5)	4.68 t (9.1)	5.00 m	4.29 t (10.7)	4.20 dd (10.8) [6.3]	Me of Ts, s, 6H, 2.09
13a $CDCl_3$	3.00 d (14.7)	3.40 d (14.7)	4.26 d (3.0)	4.87 dd (3.0) [9.6]	4.78 m	3.63 t (11.1)	3.80 dd (11.1) [6.0]	Me of Ts, 2s, 6H, 2.42; 2.46
13b Pyridine-d_5	3.64 d (14.7)	3.76 d (14.7)	4.72 d (2.9)	5.68 dd (2.9) [9.7]	5.60 m	4.32 m	Me of Ts, 2s, 6H, 2.10; 2.16	
16b $CDCl_3$	2.90 dd J_{ab} 14.4 $J_{1b,2}$ 7.6	3.09 dd J_{ab} 14.4 $J_{1a,2}$ 5.1	5.27 [a] m 2H	5.38 dd (6.8) [4.1]	5.18 m	3.88 dd (11.7) [6.2]	4.16 dd (11.7) [4.9]	Ac, 5s, 1.55; 1.91 2.05; 2.11 2.15

[a] Corresponds to H-2 and H-3.



Scheme 3.

matography to give partially *O*-acetylated ketopyranoses 3,4,5-tri-*O*-acetyl-1-deoxy-1-(1-methylindol-3-yl)-α-L-sorbopyranose (**6b**) (14%), 3,4,5-tri-*O*-acetyl-1-deoxy-1-(1-methylindol-3-yl)-α-L-tagatopyranose (**7b**) (12%), and also an open-chain keto derivative, 3,4,5,6-tetra-*O*-acetyl-1-deoxy-1-(1-methylindol-3-yl)-L-sorbose (**8b**) (21%). An individual open-chain tagatose derivative failed to be isolated (Scheme 3).

It is note worthy that tetra-*O*-acetates of ketopyranose forms were not isolated. The structures of compounds **6b**, **7b**, and **8b** were supported by ^{1}H NMR data. In the ^{1}H NMR spectrum of compound **6b** the values of $J_{3,4}$ and $J_{4,5}$ correspond to *trans*-diaxially disposed H-3 and H-4, showing the L-sorbopyranose configuration and the $_5C^2$ conformation. The value of $J_{3,4}$ (3.4 Hz) in the spectrum of **7b** demonstrates the axial-equatorial disposition of these atoms and the L-tagatopyranose configuration. The acyclic structure of **8b** was assigned on the basis of its ^{13}C NMR spectrum, in which the signal of the 2-CO group at 200.96 ppm is present (Table 2). Deacetylation of this compound led to **2b**, supporting the L-sorbose stereochemistry.

Various deacetylation reagents for the individual per-*O*-acetyl ketoses **4** and **5** were studied. Deacetylation of **4b** or **5b** with the use of MeONa or K_2CO_3 in methanol was accompanied by the epimerization at C-3 leading to a mixture of diastereomers **2b** and **3b**; in the mixture obtained from **4b** the sorbose derivative **2b** predominated, and in the mixture obtained from **5b** the tagatose structure **3b** was predominant. The structures of the products of deacetylation were studied by HPLC and NMR methods. Use of milder agents such as Na_2CO_3 or Et_3N in methanol afforded the individual ketose **2b** from **4b**. The ^{1}H NMR parameters of the isolated **2b** were identical to those described for **2b** when it was earlier[4] studied in admixture with **3b**. Under these conditions compound **5b**, produced a mixture of tautomeric (**3b**) forms. The ^{1}H NMR spectrum showed the presence of the α-L-pyranose (~ 70%), and ~ 30% of other isomers, which were not identified. The ratio between the α-L-pyranose and the other isomers was very sensitive to the solvent and temperature, for example in the presence of CF_3CO_2D at 37 °C the content of α-L-pyranose form was about 50%. These deacetylated compounds showed one peak in HPLC; the acetylation quantitatively produced the individual **5b**. Deacetylation of **4a** or **5a** led to the individual components **2a** and **3a**; the latter was also in equilibrium with other tautomers (Scheme 5). These results demonstrate that 1-deoxy-(1-indol-3-yl)-α-L-tagatopyranose is conformationally unstable due to the presence of two neighboring axial hydroxyl groups, resulting in an equilibrium between the α-L-pyranose and some other isomeric form (open or cyclic or both) in solution.

Persilylation of **2b** led to a tetra-trimethylsilyl compound, whereas **3b** under the same conditions gave a penta–trimethylsilyl derivative; similarly **2a** gave penta- and **3a** hexa-trimethylsilyl derivatives, allowing attribution of the structure **9a**,**b** to the sorbose and **10a**,**b** to the tagatose persilylated derivatives respectively (MS-data) (Scheme 4). This demonstrates facile opening of the tagatopyranose ring or the presence of open-chain forms in compounds **3a** and **3b**, in contrast to sorbopyranose derivatives **2a** and **2b**.

Deacetylation of compounds **4** and **5** was always accompanied by the formation of 3-formylindoles (**11**), which were the predominant reaction products at temperatures above over 40 °C. The formation of 3-formylindoles can be explained by oxidative radical degradation at the double bond[7] (Scheme 5).

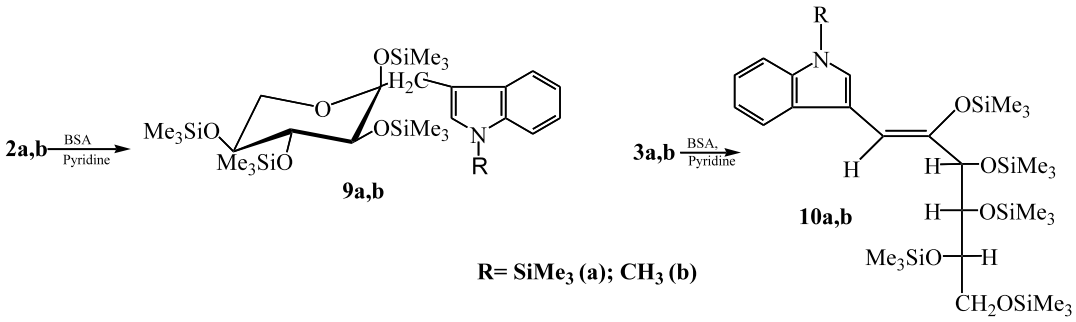
Tosylation of the **2b** + **3b** mixture by tosyl chloride in pyridine under argon produced a complex mixture from which mixtures of 1-deoxy-1-(1-methylindol-3-yl)-(3,5-di-*O*-tosyl)-α-L-sorbopyranose (**12b**) and 1-deoxy-1-(1-methylindol-3-yl)-4,5-di-*O*-tosyl-α-L-tagatopyranose (**13b**) were isolated in 35–40% net yield by column chromatography. These compounds were then separated by preparative HPLC. Similar tosylation of the **2a** + **3a** mixture followed by column chromatography and then by preparative HPLC gave the individual **12a** and **13a**. Chemical shifts of carbohydrate hydrogen atoms of compounds **12b** and **13b** were compared with those of the corresponding starting ketoses **2b** and **3b**

Table 2
^{13}C NMR spectra of compounds **4b**, **6b** and **8b**

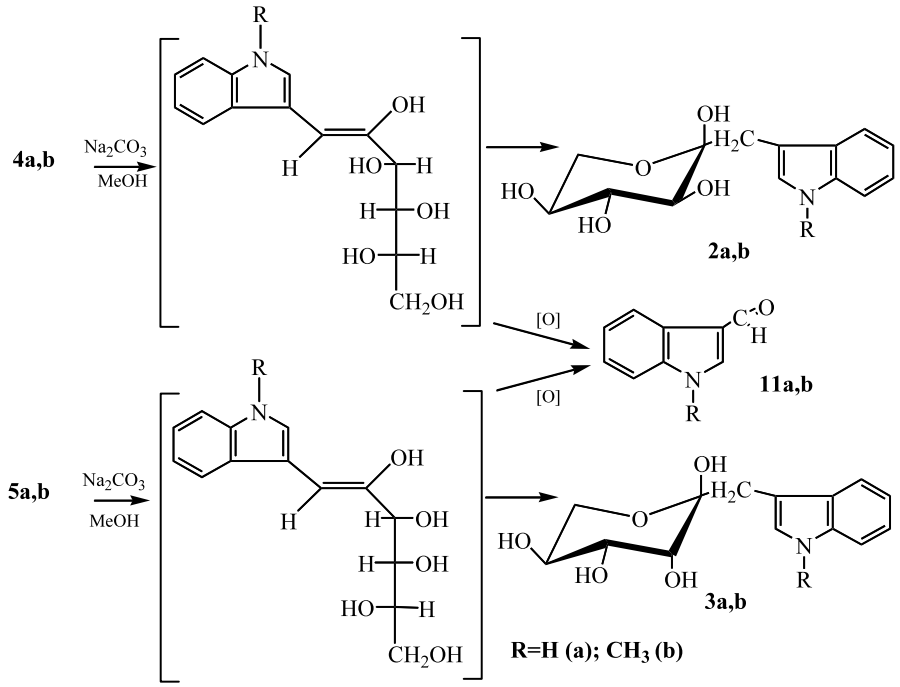
Compd/Solvent	Indole ring		NMe	Carbohydrate moiety		Other (acetyl groups)	
	CH	*quart*.C		CH	CH_2 or *quart*.C or CO	CH_3	CO
4b $CDCl_3$	109.30; 118.97; 120.03; 122.25; 128.61	107.38; 136.35; 136.66	33.02	68.94; 69.81; 72.99; 115.29	61.81; 126.97	20.54; 20.57; 20.62; 20.78; 20.98	167.97; 169.62; 169.68; 169.80; 170.33
6b $CDCl_3$	109.19; 119.41; 119.99; 121.97; 129.55	105.05 128.67; 137.08	32.76	69.68; 71.28; 72.57	33.25; 58.98; 96.56	20.66; 20.71; 20.82	169.99; 170.11; 170.15
8b $CDCl_3$	109.25; 118.59; 119.36; 121.86; 128.34	104.88; 127.56 136.77	32.65	68.80; 69.27; 74.63	36.34; 61.62; 200.96	18.72; 20.33; 20.54; 20.60	169.48; 169.58; 169.61; 170.12

(Table 1). The signals of hydrogen atoms connected with the same carbon atom as the *O*-sulfonyl group are shifted downfield ($\Delta \sim 1$ ppm) in comparison with the corresponding nonsulfonylated compound. This comparison allowed the conclusion that, in the sorbopyranose derivatives **12b**, the hydroxyl groups at the positions 3 and 5 are tosylated, whereas in the tagatopyranose derivatives **13b** the tosyl moieties are in positions 4 and 5. The structures of **12a** and **13a** were ascribed by analogy. The difference in reactivities between hydroxyl groups can be correlated with the difference in the orientation of 3-OH group in these two series (*eq*.OH in **12** and *ax*.OH in **13**). In methanolic NaOH solution, compound **13a** underwent decomposition with the formation of 2-hydroxy-4-hydroxymethyl-3-(indol-3-yl)cyclopent-2-enone (**15a**) in 90% yield, identical with the compound previously obtained by the acidic degradation of ascorbigen[8]. Similarly **13b** produces **15b** in 95% yield. Earlier we have demonstrated that the transformation of ascorbigen into **15a** proceeds via the dienone **14** with the *cis*-orientation of the indole and hydroxyl groups.[8] A similar transformation is described for the 4,5-ditosylate of 1-deoxy-1-propylamino-β-D-fructopyranose which forms under neutral or basic conditions 2-hydroxy-4-hydroxymethyl-3-propylamino-cyclopent-2-enone, a compound having a framework similar to that of **15**.[9] The formation of the intermediate dienone **14** from 3,5-ditosylate **12** is not possible and, in contrast to the ditosyl tagatose derivatives **13**, the ditosyl derivatives of sorbopyranose **12** form intractable mixtures of unidentified compounds, among which cyclopentenone derivatives **15** were not identified (Scheme 6). This is in accordance with the mechanism proposed.

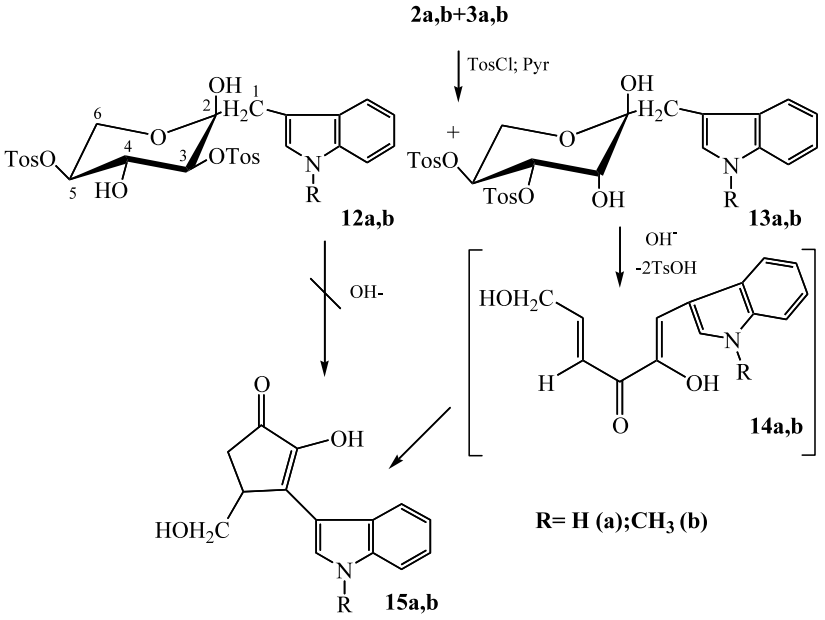
Catalytic hydrogenation of **4b** over 5% Pd/C at 1 atm yielded in 90% yield an individual penta-*O*-acetyl-1-de-



Scheme 4.



Scheme 5.



Scheme 6.

oxy-1-(1-methylindol-3-yl)-hexitol, with either the L-*ido*- or L-*gulo*-configuration (**16**) (Scheme 7). The configuration of the C-2 asymmetric center of **16** remains to be elucidated. Compound **16** is an acetylated analog of 4-(indol-3-yl)butane-1,2,3-triol, a toxic indole alkaloids, produced by a fungus *Balancia epichloë (*Weese) which parasitizes pasture grasses and is involved with ergot-type syndromes observed in cattle grazed on infected pastures.[10]

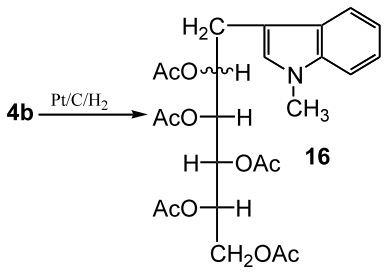
3. Experimental

3.1. General methods

NMR spectra were recorded on a Varian VXR-400 instrument operated at 400 MHz (^{1}H NMR) or at 100.6 MHz (^{13}C NMR), using solvents as internal standards. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. High resolution mass spectra were registered on a MAT 8430 Finnigan instrument (USA) with data operating system SS-300 (EI, 70eV, direct introduction, temperature of ion source 250 °C). Electron impact (EI) and FAB spectra were registered on a SSQ 710 Finnigan MAT instrument (USA), (EI: 70eV, direct introduction, FAB: reactant gas xenon, glycerol matrix). Analytical TLC was performed on Kieselgel F_{254} plates (E.Merck), preparative TLC chromatography on plates (20 × 20 cm, 0.5 mm) with Kieselgel 60 F_{254} (E.Merck), and column chromatography on Kieselgel 60 (E.Merck), using the following systems of solvents: A (3:2 petroleum ether–EtOAc), B (2:1 petroleum ether–EtOAc), C (5:1 $CHCl_3$–CH_3OH), D (1:1 petroleum ether–EtOAc), E (10:1 $CHCl_3$–CH_3OH). Analytical HPLC analyses were performed on a Millichrom 5 instrument (Russia), on a Diasorb C 16 column (2 × 120 mm and particle size 7 μm), injection volume 5 μL at 280 nm, by isocratic elution, using systems of solvents: no. 1 (80:20 0.01 M H_3PO_4–CH_3CN) and no. 2 (30:70 H_2O–CH_3CN). Preparative HPLC was performed on a Shimadzu HPLC series LC 10 instrument on a Diasorb C 16 column (15 × 250 mm and particle size 7 μm), with injection volume 50 μL, at 280 nm, using systems of solvents: no. 3 (40:60 H_2O–CH_3CN) and no. 4 (30:70 H_2O–CH_3CN). Melting points were determined on a Büchi SMP-20 apparatus and are uncorrected. Silylation of compounds **2a**,**b** and **3a**,**d** was performed using solution of BSA in pyridine (Pierce). Neoascorbigen [6] and mixtures of **2a** + **3a**[4] and **2b** + **3b** [4] were obtained as earlier described.

3.2. 1-Deoxy-1-(1-methoxyindol-3-yl)-α-L-sorbopyranose (2c) and 1-deoxy-1-(1-methoxyindol-3-yl)-α-L-tagatopyranose (3c)

A solution of neoascorbigen **1c** (2.3 g, 6.9 mmol) in potassium phosphate buffer (100 mL, pH 7.4) was



Scheme 7.

incubated at 40 °C for 4 h, then the solution was saturated with NaCl, extracted with EtOAc (3 × 50 mL), dried (Na_2SO_4) and evaporated in vacuo to give the mixture of **2c** and **3c** (1.2 g, 56%) as AN amorphous powder, R_f 0.48 (C); R_t: 25.02 min (**2c**) and 22.35 min (**3c**) (system no. 1); HR-MS, m/z: Found 309.1218, Calcd for $C_{15}H_{19}NO_6$ 309.1212.

3.3. (*E*)-2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-(1-methylindol-3-yl)-L-*xylo*-hex-1-enitol (4b) and (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(1-methylindol-3-yl)-L-*lyxo*-hex-1-enitol (5b)

A solution of mixed **2b** and **3b** (1.3 g, 4.44 mmol) and DMAP (60 mg) in dry pyridine (20 mL) was cooled to −10 °C, and then Ac_2O (2.52 mL, 26.64 mmol) was added. The mixture was kept at rt. for 12 h and then it was dissolved in 1N HCl (300 mL), and extracted with diethyl ether (3 × 50 mL). The extract was washed with brine, dried (Na_2SO_4), and evaporated in vacuo to give a mixture (1.8 g, 81%) of **4b** and **5b** as light-brown crystals. It was chromatographed on silica gel (A), the fractions were evaporated, and after crystallizing from diethyl ether gave the individual **4b** (0.9 g, 40%) and **5b** (0.4 g, 18%).

Compound **4b**: White crystals, mp 161–163 °C (Et_2O); $[\alpha]_D^{20}$ −111° (*c* 0.5, $CHCl_3$); R_f 0.40 (D); Anal. Calcd for $C_{25}H_{29}NO_{10}$: C, 59.62; H, 5.81; N, 2.78. Found: C, 59.56; H, 5.78; N, 2.74.

Compound **5b**: White crystals, mp 133–135 °C (Et_2O); $[\alpha]_D^{20}$ +24.6° (*c* 0.5, $CHCl_3$); R_f 0.46 (D); Anal. Calcd for $C_{25}H_{29}NO_{10}$: C, 59.62; H, 5.81; N, 2.78. Found: C, 59.61; H, 5.89; N, 2.66.

3.4. (*E*)-2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-(1-methoxyindol-3-yl)-L-*xylo*-hex-1-enitol (4c) and (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(1-methoxylindol-3-yl)-L-*lyxo*-hex-1-enitol (5c)

(*E*)-2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-(1-methoxyindol-3-yl)-L-*xylo*-hex-1-enitol (**4c**) and (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(1-methoxylindol-3-yl)-L-*lyxo*-hex-1-enitol (**5c**) were obtained by the same procedure as **4b** and **5b**, starting from the mixture of **2c** and **3c** (150 mg, 0.49 mmol), DMAP (5 mg), pyridine (6 mL) and Ac_2O (0.3 mL). After extraction, and evaporation a mixture of **4c** and **5c** (200 mg, 79%) was obtained, which gave after column chromatography (A) followed by crystallization from diethyl ether the individual **4c** (60 mg, 30%) and **5c** (40 mg, 20%).

Compound **4c**: White crystals; mp 129–131 °C (Et_2O); $[\alpha]_D^{20}$ −95° (*c* 0.5, $CHCl_3$); R_f 0.26 (B); HR-MS, m/z: Found 519.1735, Calcd for $C_{25}H_{29}NO_{11}$ 519.1740.

Compound **5c**: White crystals; mp 133–135 °C (Et_2O); $[\alpha]_D^{20}$ +20° (*c* 0.5, $CHCl_3$); R_f 0.33 (B); HR-MS, m/z: Found 519.1736, Calcd for $C_{25}H_{29}NO_{11}$ 519.1740.

3.5. (*E*)-2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-(indol-3-yl)-L-*xylo*-hex-1-enitol (4a), (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(indol-3-yl)-L-*lyxo*-hex-1-enitol (5a), and (*E*)-1-(1-acetylindol-3-yl)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-L-*xylo*-hex-1-enitol (4d)

(*E*)-2,3,4,5,6-Penta-*O*-acetyl-1-deoxy-1-(indol-3-yl)-L-*xylo*-hex-1-enitol (**4a**), (*E*)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-1-(indol-3-yl)-L-*lyxo*-hex-1-enitol (**5a**), and (*E*)-1-(1-acetylindol-3-yl)-2,3,4,5,6-penta-*O*-acetyl-1-deoxy-L-*xylo*-hex-1-enitol (**4d**) were obtained by the same procedure as **4b** and **5b**, using a mixture of **2a** and **3a** (1.3 g, 4.66 mmol), DMAP (60 mg), pyridine (20 mL) and Ac_2O (2.64 mL, 27.96 mmol). After extraction and evaporation, a mixture of **4a**, **4d**, **5a** (1.8 g) was obtained, which gave after column chromatography (A) followed by crystallization from diethyl ether the individual **4a** (225 mg, 10%), **5a** (300 mg, 13%,) and **4d** (250 mg, 11%).

Compound **4a**: White crystals, mp 164–166 °C (Et_2O); $[\alpha]_D^{20}$ −101° (*c* 0.5, $CHCl_3$); R_f 0.26 (D); HR-MS, m/z: Found 489.1630, Calcd for $C_{24}H_{27}NO_{10}$ 489.1634.

Compound **5a**: White crystals, mp 125–127 °C (Et_2O); $[\alpha]_D^{20}$ +23° (*c* 0.5, $CHCl_3$); R_f 0.39 (D) Anal. Calcd for $C_{24}H_{27}NO_{10}$: C, 58.88; H, 5.56; N, 2.86. Found: C, 58.85; H, 5.48; N, 2.76.

Compound **4d**: Yellow syrup; $[\alpha]_D^{20}$ −60° (*c* 0.5, $CHCl_3$); R_f 0.33 (D); HR-MS, m/z: Found 531.1737, Calcd for $C_{26}H_{29}NO_{11}$ 531.1741.

3.6. (3,4,5-Tri-*O*-acetyl)-1-deoxy-1-(1-methylindol-3-yl)-α-L-sorbopyranose (6b), (3,4,5-tri-*O*-acetyl)-1-deoxy-1-(1-methylindol-3-yl)-α-L-tagatopyranose (7b) and (3,4,5,6-tetra-*O*-acetyl)-1-deoxy-1-(1-methylindol-3-yl)-L-sorbose (8b)

A solution of **2b** and **3b** mixture (300 mg, 1.02 mmol) and DMAP (10 mg) in dry pyridine (8 mL) was cooled to −20 °C, and then Ac_2O (0.58 mL, 6.12 mmol) was added, and the mixture was incubated at −20 °C for 20 min, stirred at rt. for 40 min, dissolved in 1 M HCl (100 mL), and extracted with EtOAc (3 × 25 mL). The extract was washed with brine, dried (Na_2SO_4) and evaporated in vacuo to give a mixture of **6b**, **7b** and **8b** as a light brown oil. It was chromatographed on silica gel (A), the fractions were evaporated to give the individual products:

Compound **6b**: 50 mg, 12%; white crystals, mp 134–136 °C (Et_2O); R_f 0.38 (B); $[\alpha]_D^{20}$ +33.6° (*c* 0.5, $CHCl_3$); Anal. Calcd for $C_{21}H_{25}NO_8$: C, 60.14; H, 6.01; N, 3.34. Found: C, 60.02; H, 6.02; N, 3.09.

Compound **7b**: 60 mg, 14%; white crystals, mp 176–178 °C ($CHCl_3$); R_f 0.30 (B); $[\alpha]_D^{20}$ −12.8° (*c* 0.5, $CHCl_3$); Anal. Calcd for $C_{21}H_{25}NO_8$: C, 60.14; H, 6.01; N, 3.34. Found: C, 59.95; H, 5.96; N, 3.21.

Compound **8b**: 100 mg, 21%; yellow syrup, R_f 0.34 (B). HR-MS, m/z: Found 461.1683, Calcd for $C_{23}H_{27}NO_9$ 461.1686.

3.7. 1-Deoxy-1-(1-methylindol-3-yl)-α-L-sorbopyranose (2b)

To a solution of **4b** (100 mg, 0.2 mmol) in MeOH (5 mL) was added dry Na_2CO_3 (20 mg), and the mixture was incubated at rt. for 3 h. The Na_2CO_3 was filtered off, and the filtrate was evaporated in vacuo. The residue was chromatographed by preparative TLC (C) to give **2b** a as white amorphous powder (40 mg, 70%); $[\alpha]_D^{20}$ −18° (*c* 0.5 MeOH); R_f 0.42 (C); R_t 22.49 min (system 1); FAB-MS of per-silylated **2b**, m/z: 581 (90%) $[C_{27}H_{51}NO_5Si_4\ (M)]^+$; 437 (21%) $[M-(SiMe_3)_2]^+$; 365 (14%) $[M-(SiMe_3)_3]^+$; 73 (100%) $[SiMe_3]^+$.

Anal. Calcd for $C_{15}H_{19}NO_5$: C, 61.42; H, 6.53; N, 4.78. Found: C, 61.29; H, 6.52; N, 4.75.

1-Methyl-3-formylindole (**11b**, 6 mg, 4%), R_f 0.80 (*E*) identical with the authentic sample was also isolated.

3.8. 1-Deoxy-1-(1-methylindol-3-yl)-L-tagatose (3b)

1-Deoxy-1-(1-methylindol-3-yl)-L-tagatose (**3b**) was obtained similarly from **5b** (100 mg, 0.2 mmol) as a white amorphous powder (37 mg, 65%); $[\alpha]_D^{20}$ +7.9° (*c* 0.7 MeOH); R_f 0.42 (C); R_t 17.78 min (system 1); FAB-MS of per-silylated **3b**, m/z: 653 (80%) $[C_{30}H_{59}NO_5Si_5\ (M)]^+$; 581 (47%) $[M-SiMe_3)]^+$; 437 (5%) $[M-(SiMe_3)_3]^+$; 73 (100%) $[SiMe_3]^+$; HR-MS, m/z: Found 293.1260, Calcd for $C_{15}H_{19}NO_5$ 293.1263.

1-Methyl-3-formylindole (**11b**, (4.5 mg, 3%) was also isolated.

3.9. 1-Deoxy-1-(indol-3-yl)-α-L-sorbopyranose (2a)

1-Deoxy-1-(indol-3-yl)-α-L-sorbopyranose (**2a**) was obtained similarly from **4a** in 67% yield as white amorphous powder, $[\alpha]_D^{20}$ −7.5° (*c* 0.8 MeOH); R_f 0.29 (C); R_t 9.02 min (system 1); FAB-MS of silylated **2a**, m/z: 639 (58%) $[C_{29}H_{57}NO_5Si_5\ (M)]^+$; 567 (12%) $[M-(SiMe_3)]^+$; 495 (2%) $[M-(SiMe_3)_2]^+$; 73 (100%) $[SiMe_3]^+$

Anal. Calcd for $C_{14}H_{17}NO_5$: C, 60.20; H, 6.13; N, 5.06. Found C, 60.10; H, 6.05; N, 4.90.

3-Formylindole (**11a**, 4%) identical with an authentic sample, was also isolated, R_f 0.44 (E).

3.10. 1-Deoxy-1-(indol-3-yl)-L-tagatose (3a)

1-Deoxy-1-(indol-3-yl)-L-tagatose (**3a**) was obtained similarly from **5a** as a white amorphous powder (61%), $[\alpha]_D^{20}$ +8° (*c* 0.5 MeOH); R_f 0.29 (C); R_t 7.95 min (system 1); FAB-MS of silylated **3a**, m/z: 711 (62%) $[C_{32}H_{65}NO_5Si_6\ (M)]^+$; 639 (63%) $[M-(SiMe_3)]^+$; 73 (100%) $[SiMe_3]^+$

HR-MS, m/z: Found 279.1096, Calcd for $C_{14}H_{17}NO_5$ 279.1107.

3-Formylindole (**11a**) also was isolated (3%).

3.11. 1-Deoxy-1-(1-methylindol-3-yl)-(3,5-di-*O*-tosyl)-α-L-sorbopyranose (12b) and 1-deoxy-1-(1-methylindol-3-yl)-(4,5-di-*O*-tosyl)-α-L-tagatopyranose (13b)

To a solution of **2b** and **3b** mixture (500 mg, 1.7 mmol) under argon in dry pyridine (30 mL),with 3Å molecular sieves added, was added dropwise a solution of TsCl (1.13 g, 5.95 mmol) in dry pyridine (5 mL) and the mixture was stirred at rt for 7 h. The mixture was diluted with diethyl ether (70 mL), washed with 3% aq. $NaHSO_4$ several times, then by brine, dried (Na_2SO_4), and evaporated in vacuo. After column chromatography (A), an inseparable mixture of **12b** and **13b** was obtained (410 mg, 40%) as a yellow syrup, R_f 0.43 (A). Individual components **12b** and **13b** were isolated by preparative HPLC (the sample concentration was 200 mg/mL in CH_3CN, system 4, flow rate 3.0 μL/min, R_t 33.88 and 26.07 min respectively).

Compound **12b**: $[\alpha]_D^{20}$ −42° (*c* 0.42, $CHCl_3$; R_t 12.55 min (anal. HPLC, system no. 2); FAB-MS m/z: 602 (44%) $[M+H]^+$; 584 (100%) $[M-H_2O]^+$; 430 (52%) $[M-TosOH]^+$. Anal. Calcd for $C_{29}H_{31}NO_9S_2$: C, 57.89; H, 5.19; N, 2.33. Found: C, 57.78; H, 5.25; N, 2.20.

Compound **13b**: $[\alpha]_D^{20}$ +24.1° (*c* 0.6, $CHCl_3$); R_t 9.70 min (anal. HPLC, system no. 2); FAB-MS m/z: 602 (70%) $[M+H]^+$; 584 (100%) $[M-H_2O]^+$; 430 (17%) $[M-TosOH]^+$. Anal. Calcd for $C_{29}H_{31}NO_9S_2$: C, 57.89; H, 5.19; N, 2.33. Found: C, 57.81; H, 5.28; N, 2.29.

3.12. 1-Deoxy-1-(indol-3-yl)-(3,5-di-*O*-tosyl)-α-L-sorbopyranose (12a) and 1-deoxy-1-(indol-3-yl)-(4,5-di-*O*-tosyl)-α-L-tagatopyranose (13a)

1-Deoxy-1-(indol-3-yl)-(3,5-di-*O*-tosyl)-α-L-sorbopyranose (**12a**) and 1-deoxy-1-(indol-3-yl)-(4,5-di-*O*-tosyl)-α-L-tagatopyranose (**13a**) were obtained from a mixture of **2a** and **3a** (500 mg) and separated similarly, the inseparable mixture of **12a** and **13a** (370 mg, 35%) was obtained by the column chromatography as a yellow syrup R_f 0.21 (A). The individual **12a** and **13a** were separated by preparative HPLC (the sample concentration was 300 mg/mL in CH_3CN, system no. 3, flow rate 2.0 μL/min, R_t 45.91 and 37.52 min respectively).

Compound **12a**: White amorphous powder. $[\alpha]_D^{20}$ −57.5° (*c* 0.2, $CHCl_3$); R_t 7.62 min (anal. HPLC, system no. 2); FAB-MS, m/z: 588 (20%) $[MH]^+$; 570 (100%) $[M-OH]^+$; 416 (68%) $[M-TosOH]^+$. Anal. Calcd for $C_{28}H_{29}NO_9S_2$: C, 57.23; H, 4.97; N, 2.38. Found: C, 57.15; H, 4.99; N, 2.24.

Compound **13a**: White amorphous powder. $[\alpha]_D^{20}$ + 15.3° (*c* 0.5, $CHCl_3$); R_t 6.16 min (anal. HPLC, system no. 2); FAB-MS, *m*/*z*: 588 (20%) $[MH]^+$; 570 (100%) $[M-OH]^+$; 416 (60%) $[M-TosOH]^+$. Anal. Calcd for $C_{28}H_{29}NO_9S_2$: C, 57.23; H, 4.97; N, 2.38. Found: C, 57.19; H, 5.03; N, 2.29.

3.13. 2-Hydroxy-4-hydroxymethyl-3-(indol-3-yl)cyclopenten-2-on (15a)

To a solution of **13a** (20 mg, 0.034 mmol) in MeOH (5 mL) was added under argon degassed 10% aq. NaOH (1 mL), and then the mixture was stirred at rt for 0.5 h, diluted with brine (30 mL), extracted by EtOAc (2 × 10 mL), and the extract was evaporated in vacuo to give, after TLC (E) **15a** (7.5 mg, 90%) as a yellow amorphous powder identical with the authentic sample by HPLC and ^{1}H NMR data.[8] R_f 0.28 (E).

3.14. 2-Hydroxy-4-hydroxymethyl-3-(1-methylindol-3-yl)cyclopenten-2-one (15b)

2-Hydroxy-4-hydroxymethyl-3-(1-methylindol-3-yl)

× cyclopenten-2-one (**15b**) was obtained and purified similarly from **13b** (20 mg, 0.033 mmol)to give **15b** as yellow crystals in 95% yield. All chromatography and NMR parameters were the same as those of the compound earlier described.[8] R_f 0.38 (E), mp 221–224 °C ($CHCl_3$).

3.15. Penta-*O*-acetyl-1-deoxy-1-(1-methylindol-3-yl)-hexitol (16b)

To a solution of **4b** (100 mg, 0.2 mmol) in EtOAc (20 mL) was added 5% Pt/C (100 mg) and the mixture was hydrogenated at 1.2 atm, then filtered, and the filtrate was evaporated in vacuo. Preparative TLC (B) led to **16b** (90 mg, 90%) as white crystals, mp 96–99 °C (from $CHCl_3$); $[\alpha]_D^{20}$ −9.2° (*c* 0.5, $CHCl_3$); R_f 0.53 (D); HR-MS, *m*/*z*: Found 505.1941, Calcd for $C_{25}H_{31}NO_{10}$ 505.1948.

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