A Facile Synthesis of Anomeric Methyl DL-Tolyposaminides, Methyl DL-Forosaminides, and Related Substances[1)]

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The reaction of β-nitro alcohols (2-nitroethanol, 1-nitro-2-propanol, and 1-nitro-2-butanol) with acrylaldehyde in the presence of diethylamine–formic acid gave anomeric mixture of 4-nitro-DL-pento-, hexo-, and heptopyranoses (**5**) in reasonable yields. **5** were converted to the corresponding methyl 4-amino-DL-pento-, hexo-, and heptopyranosides (**8**) by *O*-methylation followed by reduction. Anomeric methyl DL-tolyposaminides and DL-forosaminides were synthesized in a good yield from anomeric methyl 4-nitro-2,3,4,6-tetradeoxy-DL-*erythro*-hexopyranosides (**6b**$_1$ and **6b**$_2$). The configuration of methyl 4-nitro-DL-hexo-, and heptopyranosides (**6b** and **6c**) and methyl 4-acetamido-DL-hexo- and heptopyranosides (**8b** and **8c**) was established on the basis of PMR data.

As a part of the investigation on the exploration of newer synthetic reactions for aliphatic nitro compounds, we had been interested in a facile route to some nitropyranose derivatives, which are potentially useful as substrates for versatile syntheses of amino sugars, especially in the syntheses of amino-polydeoxy sugars contained in several antibiotics, *e.g.*, tolyposamine[2)] and forosamine.[3)] Recently several synthetic routes to these amino-polydeoxy sugars starting from carbohydrate[4)] or non-carbohydrate[5)] precursors have been reported. In this paper we describe a facile synthesis of 4-amino-polydeoxy sugars (**7**) *via* the respective 4-nitro derivatives (**5**) which were obtained by one-step cyclization reaction of β-nitro alcohols with acrylaldehyde using diethylamine–formic acid.[6)]

The reaction of excess nitro alcohols: 2-nitroethanol (**1a**), 1-nitro-2-propanol (**1b**), or 1-nitro-2-butanol (**1c**) with acrylaldehyde in the presence of a catalytic amount of diethylamine–formic acid (1: 1.75 mol) at 60±5 °C for about 20 h gave anomeric mixtures of 4-nitro-DL-pento-, hexo-, and heptopyranoses (**5a**—**5c**) in a reasonable yield (Table 1). In the case of **5b**, optimum reaction conditions were examined and **5b** was obtained in a 52% yield by equimolar reaction of **1b** with acrylaldehyde at reflux temperature in benzene for 20 h. **5c** was separated into two diastereomers (**5c**$_1$ and **5c**$_2$)

Table 1. 4-Nitro-DL-pento-, hexo-, and heptopyranoses (**5**)

Compound No.	R	Mp (°C)	Yield (%)	α:β[a)]	Formula	Found (%) C	Found (%) H	Found (%) N	Calcd (%) C	Calcd (%) H	Calcd (%) N	IR (KBr) ν_{max} cm^{-1}		
5a	H	81.5—84	39	b)	$C_5H_9NO_4$	41.17	6.04	9.73	40.81	6.17	9.52	3350,	1550,	1380
5b	CH_3	64.5—68.5	52	4:3	$C_6H_{11}NO_4$	44.96	6.93	8.91	44.72	6.83	8.69	3360,	1550,	1350
5c$_1$[c)]	C_2H_5	126.5—128[d)]	66	1:1	$C_{14}H_{16}N_2O_7$[d)]	52.13	5.00	8.77	51.85	4.97	8.64	3400,	1550,	1380[e)]
5c$_2$[c)]	C_2H_5	113.5—116.5[d)]	22	1:1		51.66	4.99	8.60				3400,	1550,	1380[e)]

a) Anomeric composition was determined from signal intensity of anomeric protons in PMR spectra. b) Anomeric composition could not be determined because of overlapping with another signals. c) A diastereomer of **5c**. d) Melting points and analytical data were of *p*-nitrobenzoyl derivatives of **5c**. e) Measured in NaCl for liquid film.

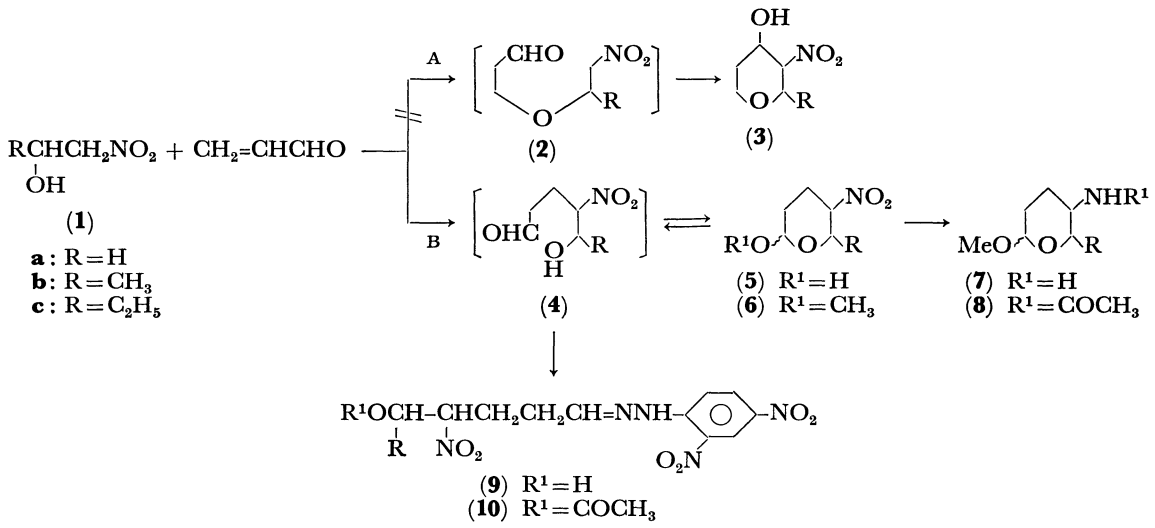

Fig. 1.

Table 2. δ-Hydroxy-γ-nitroaldehyde 2,4-dinitrophenylhydrazones (**9**)

Compound No.	R	Mp (°C)	Yield (%)	Formula	Found (%)			Calcd (%)		
					C	H	N	C	H	N
9a	H	126.5—127.5	79	$C_{11}H_{13}N_5O_7$	40.49	3.98	21.41	40.37	4.00	21.40
9b	CH_3	138—140	6	$C_{12}H_{15}N_5O_7$	41.95	4.37	20.29	42.23	4.43	20.52
9c$_1$[a]	C_2H_5	86—90	5	$C_{13}H_{17}N_5O_7$	43.92	4.98	19.47	43.94	4.82	19.71
9c$_2$[a]	C_2H_5	115—117	34		43.88	4.87	19.43			

a) A diastereomer of **9c**.

Table 3. Methyl 4-nitro-DL-pento-, hexo-, and heptopyranosides (**6**)

Compound No.	Bp°C/Torr (Mp °C)	n_D^{20}	Yield (%)	Formula	Found (%)			Calcd (%)			IR (film) ν_{max} cm^{-1}	
					C	H	N	C	H	N		
6a	40—45[a]/0.05	1.4600	84	$C_6H_{11}NO_4$	44.34	6.73	8.98	44.71	6.88	8.69	1550,	1370
6b$_1$	33—35/0.02	1.4520	55	$C_7H_{13}NO_4$	48.12	7.54	7.61	47.99	7.48	8.00	1550,	1375
6b$_2$	39—41/0.02[b]	1.4562	20		47.89	7.52	7.83				1550,	1345
6c$_1$	49—51/0.04	1.4532	41		51.19	8.16	7.00				1550,	1375
6c$_2$	58—60/0.03	1.4540	20	$C_8H_{15}NO_4$	51.03	8.06	6.99	50.78	7.99	7.40	1550,	1390
6c$_3$	(36.5—37)[c]	—	37		50.52	8.09	7.24				1550,	1370[e]
6c$_4$	(44—45)[d]	—	13		51.08	8.16	7.30				1550,	1370[e]

a) Bath temperature. b) Mp 31.5—32°C recrystallized from ethanol–water. c) Recrystallized from ethanol–water. d) Recrystallized from hexane. e) Measured in KBr disk.

through column chromatography on silica gel.

We attempted an alternative route (path A) for cyclization, where 2-substituted 4-hydroxy-3-nitrotetrahydropyran (**3**) is formed *via* initial ether formation[7] followed by intramolecular condensation[8] as shown in Fig. 1. However, the formation of **3** could not be detected on TLC analysis and column chromatographic purification.

The main structure of **5** was deduced from the following experimental data: (i) The formation of 2,4-dinitrophenylhydrazone (**9**) of δ-hydroxy-γ-nitroaldehyde (**4**), as well as its acetate (**10a**). (ii) Treatment of **5b** with hydrochloric acid in methanol gave α- and β-anomers of methyl hexopyranosides (**6b**$_1$ and **6b**$_2$) which were separated by silica gel column chromatography with benzene as eluant. Analogous methylation of **5c**$_1$ gave anomeric methyl heptopyranosides (**6c**$_1$ and **6c**$_2$). **5c**$_2$ was also methylated to give **6c**$_3$ and **6c**$_4$. Ordinary methylation[9] of **5** using methyl iodide and silver oxide also gave the same **6**. On the other hand, methylation of **5a** under above conditions gave only α-anomer of **6a**. These results are shown in Table 3.

The assignment of configuration of **6** was based on its PMR spectral data. The chemical shifts and coupling constants were assigned as shown in Table 4 with the aid of double resonance method. The anomeric configuration of **6** was readily deduced from the first-order analysis of its spectrum. In the spectrum of **6a**, **6b**$_1$, **6c**$_1$, and **6c**$_3$ a relatively low-field signal (δ 4.65—4.87) of a methine proton exhibits a singlet with fine splitting ($J_{1,2}$<5 Hz), which is assigned to the equatorial hydrogen of C-1. Hence the anomeric configuration is α. On the other hand, in **6b**$_2$ and **6c**$_2$, the anomeric proton exhibits a pair of doublet ($J_{1,2a}$=9 Hz, and $J_{1,2e}$<3 Hz), which is deduced to be the axial hydrogen of the β-anomers. The methoxyl group of α-anomers appeared at higher field (δ 3.40—3.43) in comparison with that of β-anomers (δ 3.52—3.53) as shown in Table 4.

The orientation of C-3 and C-4 positions was established by spin decoupling studies. In the PMR spectrum of **6b**$_1$, irradiation of C-6 methyl protons (δ 1.25) collapsed C-5 methin proton (δ 4.28, multiplet) to a doublet ($J_{4,5}$=9 Hz). Reasonably assuming that **6** has chair conformation, a relatively large H-4, H-5 coupling

Table 4. PMR data of methyl 4-nitro-DL-pento-, hexo-, and heptopyranosides (**6**)

Compound No.	Chemical shift (δ in $CDCl_3$)[a]								Coupling Constant (Hz)				Configuration
	H-1	H-2	H-3	H-4	H-5	H-6	H-7	OCH_3	$J_{1,2a}$	$J_{1,2e}$	$J_{4,5}$	$J_{5,6}$	
6a	4.65	2.3	1.8	4.10	4.3	—	—	3.43	5.0	3.0	b)	—	α
6b$_1$	4.70	2.2	1.9	4.2	4.28	1.25	—	3.42	3.5	2.0	9.0	6.0	α-*erythro*
6b$_2$	4.47	2.3	1.9	4.1	3.94	1.32	—	3.52	9.0	3.0	9.0	6.0	β-*erythro*
6c$_1$	4.72	1.7—2.7		4.40	3.99	1.58	1.00	3.40	3.0	3.0	9.8	5.0	α-*erythro*
6c$_2$	4.46	1.7—2.5		4.18	3.75	1.53	1.02	3.53	9.0	2.5	9.5	6.0	β-*erythro*
6c$_3$	4.87	1.8—2.6		4.57	3.90	1.53	1.05	3.40	3.0	3.0	2.8	7.0	α-*threo*
6c$_4$	4.5	1.9—2.6		4.5	3.61	1.69	1.06	3.53	b)	b)	2.5	6.5	β-*threo*

a) Chemical shifts are in δ scale from TMS as internal standard at 100 MHz. b) Could not be observed from the spectrum by overlapping with another signals.

6b$_1$: R=CH_3, R^1=NO_2 **6b$_2$**: R=CH_3, R^1=NO_2 **6c$_3$**: R=C_2H_5, R^1=NO_2 **6c$_4$**: R=C_2H_5, R^1=NO_2
6c$_1$: R=C_2H_5, R^1=NO_2 **6c$_2$**: R=C_2H_5, R^1=NO_2
8b$_1$: R=CH_3, R^1=NHAc **8b$_2$**: R=CH_3, R^1=NHAc Ac: $COCH_3$, Bz: COC_6H_5
8c$_1$: R=C_2H_5, R^1=NHAc **8c$_2$**: R=C_2H_5, R^1=NHAc
11: R=CH_3, R^1=NHBz **12**: R=CH_3, R^1=NHBz
13: R=CH_3, R^1=NMe_2 **14**: R=CH_3, R^1=NMe_2

Fig. 2. Only the formulae for D-compounds are given.

constant (9 Hz) could be taken as an indication of 4,5-diaxial arrangement of protons.[2] From the above data, **6b$_1$** was concluded to be a methyl 4-nitro-2,3,4,6-tetradeoxy-α-DL-*erythro*-hexopyranoside, and **6c$_1$** was analogously assigned to α-*erythro* configuration. Accordingly **6b$_2$** and **6c$_2$** (anomer of **6b$_1$** and **6c$_1$**) were deduced to have a β-*erythro* configuration. In the spectrum of **6c$_3$**, irradiation of H-6 (δ 1.53) changed the H-5 signal (δ 3.90) into a doublet which has a relatively small coupling constant ($J_{4,5}$=2.8 Hz). Moreover, irradiation of H-5 collapsed the H-4 signal (δ 4.57) to a singlet with fine splitting ($J_{3a,4}$ and $J_{3e,4}$<3 Hz), indicating the equatorial orientation of C-4 hydrogen. Hence, we ascribed it to α-*threo* configuration. Alternatively, β-*threo* configuration was assigned to the minor product (**6c$_4$**), corroborated by $J_{4,5}$ (2.5 Hz) and the chemical shift of the methoxyl group (δ 3.53). This deduction is supported by the fact that **6c$_1$** and **6c$_3$** gave the same PMR spectrum in the presence of NaOD in D_2O in which they would be converted to the same aci-nitro type compound. It should be noted that stereoselectivity of this cyclization reaction depends on the kind of nitro alcohols. The reaction of acrylaldehyde with 1-nitro-2-propanol gave only the anomeric *erythro* isomers, whereas that with 1-nitro-2-butanol gave all the possible isomers.

The reduction of **6a**, **6b$_1$**, **6b$_2$**, **6c$_1$**, and **6c$_2$** over Raney nickel catalyst afforded the corresponding methyl 4-aminopyranosides, which were subsequently acetylated in the usual manner giving methyl 4-acetamido-DL-pento-, hexo-, and heptopyranosides (**8a**, **8b$_1$**, **8b$_2$**, **8c$_1$**, and **8c$_2$**) in reasonable yields (Table 5). However the yield of **8a** remained rather low under the same reaction condition. The structure of **8** was established by its PMR spectra (Table 6) as described above for compound **6**. The large coupling constants between H-4 and H-5 ($J_{4,5}$=9.5—10.0 Hz) strongly suggest that **8b$_1$**, **8b$_2$**, **8c$_1$**, and **8c$_2$** have *erythro* configuration as well as their corresponding nitropyranosides (**6**). Another evidence was provided by a correlation of reference compounds **11** and **12**. The configuration of **8a** was not deduced except anomeric configuration (see Table 6) because the spectrum was rather complicated.

The anomeric methyl *N*-benzoyl-DL-tolyposaminides (methyl 4-benzamido-2,3,4,6-tetradeoxy-α- and β-DL-*erythro*-hexopyranoside (**11** and **12**) were synthesized respectively from the corresponding methyl 4-nitro-DL-*erythro*-hexopyranosides (**6b$_1$** and **6b$_2$**) by hydrogenation followed by benzoylation in a good yield. **11** and **12** were identical with the authentic samples[10] by the

Table 5. Methyl 4-acetamido-DL-pento-, hexo-, and heptopyranosides (**8**)

Compound No.	Mp °C	Yield[a] (%)	Formula	Found (%) C	H	N	Calcd (%) C	H	N	IR (KBr) ν_{max} cm^{-1}			
8a	viscous oil	31	$C_8H_{15}NO_3$	55.09	8.46	7.72	55.47	8.73	8.09	3300,	1650,	1550,	1280[d]
8b$_1$	87.5—90[b]	86	$C_9H_{17}NO_3$	57.61	9.04	7.65	57.73	9.15	7.48	3290,	1635,	1550,	1275
8b$_2$	149.5—150.5[c]	73		57.44	9.07	7.27				3270,	1635,	1560,	1270
8c$_1$	101.5—102.5[b]	91	$C_{10}H_{19}NO_3$	59.70	9.56	6.72	59.67	9.52	6.96	3220,	1640,	1570,	1280
8c$_2$	134—135.5	73		59.60	9.44	6.80				3240,	1630,	1550,	1290

a) Based on methyl 4-aminopyranosides (**7**). b) Recrystallized from petroleum ether. c) Recrystallized from ligroin. d) Measured in NaCl for liquid film.

Table 6. PMR data of methyl 4-acetamido-DL-pento-, hexo-, and heptopyranosides (**8**)

Compound No.	Chemical shift (δ in $CDCl_3$) H-1	H-2	H-3	H-4	H-5	H-6	H-7	OCH_3	NAc	Coupling constant (Hz) $J_{1,2a}$	$J_{1,2e}$	$J_{4,5}$	Configuration
8a	4.58	1.3—2.2		3.57	4.0	—	—	3.43	2.02	3.5	2.0	a)	α
8b$_1$	4.63	1.6—2.2		*ca.* 3.6	3.52	1.18	—	3.33	1.99	3.0	3.0	10.0	α-*erythro*
8b$_2$	4.35	1.4—2.3		*ca.* 3.6	3.33	1.27	—	3.50	1.99	8.0	3.0	9.5	β-*erythro*
8c$_1$	4.70	1.6—2.2		*ca.* 3.8	3.32	1.5	0.97	3.35	1.98	3.0	3.0	9.5	α-*erythro*
8c$_2$	4.33	1.6—2.3		*ca.* 3.7	3.06	1.45	0.98	3.50	1.98	9.0	2.5	9.5	β-*erythro*

a) Could not be obtained because of covering by OMe protons signal.

mixed melting point determination, and IR and PMR spectra.

The reductive dimethylation of **6b**$_1$ and **6b**$_2$ over Raney nickel in the presence of formaldehyde led to methyl 2,3,4,6-tetradeoxy-4-dimethylamino-α-DL-*erythro*-hexopyranoside (methyl α-DL-forosaminide, **13**) and its β-anomer (**14**), respectively. The IR and PMR spectra of these compounds were in good agreement with those of the reported data.[4b]

Experimental

All boiling and melting points are uncorrected. TLC was carried out on Kiesel gel G (Merck), and spots were detected with iodine vapor or 10% sulfuric acid on hot plate. Kanto Kagaku silica gel (up to 100 mesh) was used for column chromatography. PMR spectra were recorded with a 60 MHz Varian T-60 spectrometer and a 100 MHz JEOL PS-100 spectrometer with a spin decoupler. Chemical shifts are given in δ value. IR spectra were measured for either liquid films or potassium bromide disks with a JASCO Model IRA-1 spectrometer.

*Typical Procedure for the Cyclization: 4-Nitro-2,3,4,6-tetradeoxy-*DL*-hexopyranose (5b).* A mixture of 3 g (53.6 mmol) of acrylaldehyde and 5.61 g (53.6 mmol) of 1-nitro-2-propanol[11] was refluxed in 30 ml of benzene for about 20 h in the presence of diethylamine and formic acid (1: 1.75 mol; employed 0.5 wt % of total reagent). After removal of the solvent *in vacuo*, the oily product was chromatographed on silica gel using di-isopropyl ether–hexane (2: 1) as eluant. 4.5 g of anomeric mixture (α: β=4: 3 by PMR signal intensity) of **5b** was thus obtained in 52% yield. In the case of **5a** and **5c**, excess nitro alcohols (4 equivalent to acrylaldehyde) were employed. **5c** was separated into two diastereomers (**5c**$_1$ and **5c**$_2$) through the column on silica gel with ethyl acetate–chloroform (1: 2) as eluant. Yields, physical constants and elemental analyses of **5a**—**5c** were summarized in Table 1.

Typical Procedure of Hydrazone Formation: 5-Hydroxy-4-nitropentanal 2,4-Dinitrophenylhydrazone (9a). To a solution of 0.6 g (4.1 mmol) of **5a** in 6 ml of methanol, 0.81 g (4.1 mmol) of 2,4-dinitrophenylhydrazine–hydrochloric acid (0.5 ml) in methanol (40 ml) was added and the solution was heated to boiling for 2 min. The reaction mixture was allowed to stand overnight at room temperature. The precipitated yellow crystals were collected and recrystallized from ethanol to give 1.05 g of **9a** in 79% yield; mp 126.5—127.5 °C, IR (KBr): 3480 (OH), 3280 (NH), 1610 (C=N), 1550, 1515, and 1330 cm^{-1} (C–NO$_2$). In the case of **9b** and **9c**, 2,4-dinitrophenylhydrazine–phosphoric acid reagent[12] was employed. The results are summarized in Table 2.

5-Acetoxy-4-nitropentanal 2,4-dinitrophenylhydrazone (10a). Trifluoroacetic anhydride (1.9 ml) was added to a solution of 190 mg (0.58 mmol) of **9a** in 0.8 ml of acetic acid. The mixture was heated at 55—60 °C for 15 min. After cooling to room temperature aqueous sodium hydrogencarbonate was added to the solution and it was extracted with chloroform. The extracts were dried over anhydrous sodium sulfate and the solvent was evaporated. The red-brownish residue was crystallized with ethyl acetate–hexane (1: 1) mixture and recrystallized from methanol to give 17 mg (3%) of **10a**, mp. 129—130 °C, IR (KBr): 3280 (NH), 1740 (acetyl C=O), 1620 (C=N), 1550, 1515, and 1330 cm^{-1} (C–NO$_2$). Found: C, 42.41; H, 4.22; N, 18.98%. Calcd for $C_{13}H_{15}N_5O_8$: C, 42.28; H, 4.09; N, 18.97%.

Typical Procedure of O*-Methylation of 5: Methyl 4-Nitro-2,3,4,6-tetradeoxy-α- and β-*DL*-*erythro*-Hexopyranosides (6b$_1$ and 6b$_2$).* i) Hydrochloric acid (0.03 ml) in 3 ml of methanol was added to 300 mg (1.86 mmol) of **5b** and the solution was heated at 50 °C for 0.5 h to give two products, α and β anomer of methyl hexopyranoside (**6b**$_1$ and **6b**$_2$), which were separated by silica gel column chromatography with benzene as developer. The first moving isomer was collected and distilled to give 180 mg of α-anomer (**6b**$_1$) in 55% yield; bp 33—35 °C/0.02 Torr, IR (liq. film): 1550 and 1375 cm^{-1} (C–NO$_2$). The second moving isomer was also collected and recrystallized from ethanol–water to give 65 mg of β-anomer (**6b**$_2$), 20% yield, mp 31.5—32 °C, IR (KBr): 1550 and 1345 cm^{-1} (C–NO$_2$). ii) A mixture of **5b**, excess methyl iodide, and silver oxide was stirred for 2.5 h at room temperature. Insoluble salts were filtered off and the filtrate was evaporated to give also an anomeric mixture of methyl hexopyranosides (**6b**) in analogous yield as above i). **6a**, **6c**$_1$, **6c**$_2$, **6c**$_3$, and **6c**$_4$ were also obtained from corresponding **5a** and diastereomeric **5c** in analogous way.

*Typical Procedure of Reduction and Acetylation of 6: 4-Acetamido-2,3,4,6-tetradeoxy-α-*DL*-erythro-hexopyranoside (8b$_1$).* To a suspension of Raney nickel T1 catalyst[13] (5 ml) in 50 ml of methanol was added 500 mg (2.86 mmol) of **6b**$_1$. The mixture was hydrogenated under 3.5 kg/cm^2 of hydrogen (initial) for 2 h at room temperature. The catalyst was filtered off and the solvent was evaporated to yield 250 mg of **7b**$_1$ as light yellow oil in 61% yield. Without further purification **7b**$_1$ was acetylated with 2.5 ml of pyridine and 4 ml of acetic anhydride under stirring for 1 h at room temperature. After removal of the solvent the residue was chromatographed on silica gel to give 277 mg of **8b**$_1$ as colorless crystals in 86% yield based on **7b**$_1$; mp 87.5—90 °C (from petroleum ether). **8a**, **8b**$_2$, **8c**$_1$, and **8c**$_2$ were also obtained in a similar procedure. The results are shown in Table 5.

Methyl N*-Benzoyl-α-*DL*-tolyposaminide (11).* **7b**$_1$ obtained by the reduction of 450 mg (2.57 mmol) of **6b**$_1$ described as above, was subsequently benzoylated with 580 mg of benzoic anhydride in methanol for 0.5 h at room temperature. The reaction mixture was poured into 20 ml of aqueous sodium hydrogencarbonate and extracted with chloroform (3×40 ml). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give 505 mg (79% based on **6b**$_1$) of **11** as colorless crystals. Recrystallization from ethyl acetate–petroleum ether gave analytically pure sample; mp 148—149 °C (Reported[10] mp 148—149 °C), mixed mp 148—149 °C, IR and PMR spectra were identical with those of the authentic sample.[10] IR (KBr): 3220 (NH), 1625 (amide I), 1560 (amide II), 1275 cm^{-1} (amide III), PMR (CDCl$_3$ at 100 MHz): δ 1.25 (3H, d, H-6 $J_{5,6}$=6 Hz), 1.7—2.0 (4H, m, H-2,3), 3.35 (3H, s, OCH$_3$), 3.70 (1H, d-d, H-5, $J_{4,5}$=9 Hz, $J_{5,6}$=6 Hz), 3.6—4.1 (1H, m, H-4), 4.68 (1H, s with fine splitting, H-1, $J_{1,2a}$ and $J_{1,2e}$<3 Hz), 6.05 (1H, d, NH), 7.4 and 7.75 (5H, m, C$_6$H$_5$). Found: C, 67.52; H, 7.74; N, 5.51%. Calcd for $C_{14}H_{19}NO_3$: C, 67.44; H, 7.68; N, 5.62%.

Methyl N*-Benzoyl-β-*DL*-tolyposaminide (12).* Reduction and benzoylation of **6b**$_2$, carried out according to the procedure described above, gave **12** in 84% yield; mp 171.5—172.5 °C (from ethyl acetate–petroleum ether) (Reported[10] mp 169—171 °C). No depression was observed on mixed melting point. IR and PMR spectra were identical with those of the authentic sample.[10] IR (KBr): 3210 (NH), 1630 (amide I), 1570 (amide II), 1275 cm^{-1} (amide III). PMR (CDCl$_3$ at 100 MHz): δ 1.31 (3H, d, H-6, $J_{5,6}$=6 Hz), 1.5—2.3 (4H, m, H-2,3), 3.48 (3H, s, OCH$_3$), 3.47 (1H, d-d, H-5, $J_{4,5}$=9 Hz, $J_{5,6}$=6 Hz), 3.7—4.0 (1H, m, H-4), 4.37 (1H, d-d, H-1, $J_{1,2a}$=8 Hz, $J_{1,2e}$=3 Hz), 6.20 (1H, d, NH), 7.4 and 7.75 (5H, m, C$_6$H$_5$). Found: C, 67.78; H, 7.66; N, 5.91%.

Calcd for $C_{11}H_{19}NO_3$: C, 67.44; H, 7.68; N, 5.62%.

Methyl α-DL-Forosaminide (13). To a solution of 520 mg (2.97 mmol) of **6b**$_1$ in 80 ml of ethanol, was added 1 ml of aqueous formaldehyde (*ca.* 40%), 70 mg of sodium acetate, and Raney nickel T1 catalyst (3 ml of ethanolic slurry). The mixture was hydrogenated under 3.5 kg/cm^2 of hydrogen (initial) for 4 h at room temperature. After removal of the catalyst, the solvent was evaporated and the residue was dissolved with 50 ml of 2.5% aqueous ammonia. The solution was extracted with chloroform (3×15 ml), dried over anhydrous sodium sulfate and evaporated. The residual oil was distilled to give 255 mg of **13** as colorless oil in 49% yield; bp 57—59 °C/2.5 Torr (Reported[4b] bp 30—35 °C (bath)/0.5 Torr for D-isomer) n_D^{20} 1.4458. The PMR spectrum was identical with that reported data[4b] for D-isomer. IR (liq. film): 2820 and 2780 cm^{-1} (NMe_2), PMR ($CDCl_3$ at 100 MHz): δ 1.22 (3H, d, H-6, $J_{5,6}$=6.5 Hz), 1.5—2.0 (4H, m, H-2,3), 2.23 (6H, s, NMe_2), *ca.* 2.3 (1H, m, H-4), 3.33 (3H, s, OMe), 3.77 (1H, q, H-5, $J_{4,5}$=10 Hz, $J_{5,6}$=6.5 Hz), 4.59 (1H, s with fine splitting, H-1, $J_{1,2a}$ and $J_{1,2e}$<3 Hz).

Methyl β-DL-forosaminide (14). Reductive dimethylation of **6b**$_2$ as described above for **13**, gave **14** in 57% yield; bp 60—65 °C (bath)/2.5 Torr, n_D^{20} 1.4477. IR (liq. film): 2820 and 2770 cm^{-1} (NMe_2), PMR ($CDCl_3$ at 100 MHz): δ 1.33 (3H, d, H-6, $J_{5,6}$=6 Hz), 1.5—2.1 (4H, m, H-2,3), 2.28 (6H, s, NMe_2), *ca.* 2.3 (1H, m, H-4), 3.50 (3H, s, OMe), 3.35—3.6 (1H, m, H-5), 4.30 (1H, m, H-1).

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