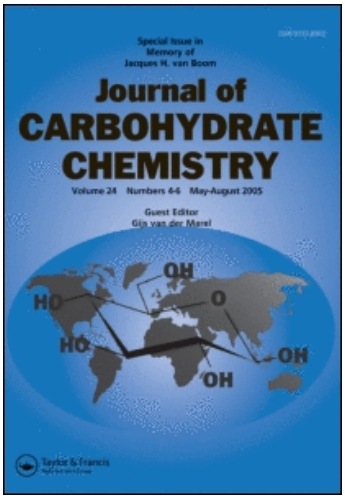

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SYNTHESIS OF α-METHYLENE-γ-LACTONES IN FURANOSIDIC SYSTEMS

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ABSTRACT

Synthesis of stereoisomeric α-methylene-γ-lactones in furanose- and furanuronoamide derivatives was easily accomplished by Reformatsky Reaction with ethyl bromomethylacrylic ester and zinc. Pyridinium chlorochromate/3Å molecular sieve powder showed to be an excellent reagent for the oxidation of secondary hydroxyl groups of a furanose system and of α-hydroxy amides.

INTRODUCTION

The α-methylene-γ-butyrolactone unit is a structural feature common to a large number of naturally occuring sesquiterpenes which exhibit a diversity of biological activities, namely antimicrobial,[1] antitumor,[2] allergenic,[2] and plant growth regulatory[3] activities. The cytotoxic action of plant sesquiterpenes and their ability to inactivate sulfydryl enzimes have been attributed to the presence of the α-methylene-γ-butyrolactone moiety.[4,5,6] Nevertheless, the

activity of the known plant-derived compounds is overshadowed by their high toxicity which precludes their clinical use. The search for new compounds bearing this unit in its structure, and for new synthetic methods[7,8] to obtain α-methylene-γ-lactones has been the aim of the investigations of many organic chemists during the past twenty years. Carbohydrates which are known to have the α-methylene--γ-lactone group in their structure include a monocyclic system derived from D-xylose,[9] a 2-deoxy-2-C-methylene-D-erythro-pentono--1,4-lactone,[10] a bicyclic system derived from D-galactose,[11] and a tricyclic compound with the structure of a 5-deoxy-5-C-methylene--α-D-xylo-hexofuranurono-6,3-lactone.[12]

RESULTS AND DISCUSSION

In the search for drugs for cancer chemoterapy which would exert a more selective action, we introduced the α-methylene-γ-lactone group into furanosidic derivatives via a Reformatsky reaction with ethyl bromomethylacrylic ester[13] and activated zinc[14] in anhydrous tetrahydrofuran at 50 °C under a nitrogen atmosphere.[15] These reaction conditions lead to the formation of the stereoisomeric lactones 2 and 3, 6 and 7, as well as 9 and 10, obtained respectively in 24% and 35% , 50% and 46%, 16% and 35% yields by reaction with the substrates 1,2;5,6-di-O-isopropylidene- α -D-ribo-hexofuranos-3-ulose (1),[16] 3-O-benzyl-1,2-O-isopropylidene- α -D-xylo-pentodialdo-1,4--furanose (5),[17] and 3-O-benzyl-1,2-O-isopropylidene-α-D-xylo-5-hexulo-furanuronoamide (8). The low yields obtained for the spirolactones 2 and 3 are due, in part, to the formation of the open chain form 4 in 41% yield, which is an α,β-unsaturated ester, a unit that is also responsible for biological activity.[4, 18] Also, compounds 9 and 10 are isolated in low yield because they contain the amide group in their structure, a feature which confers upon them a high solubility in water and a low solubility in the most common organic solvents used for extraction. The nature of the functional groups present in these molecules is responsible for varying degrees of lipophilicity that are observed. The diversity of their structures turns them into an interesting set of compounds to study the effects of structure on biological activity in carbohydrate models.

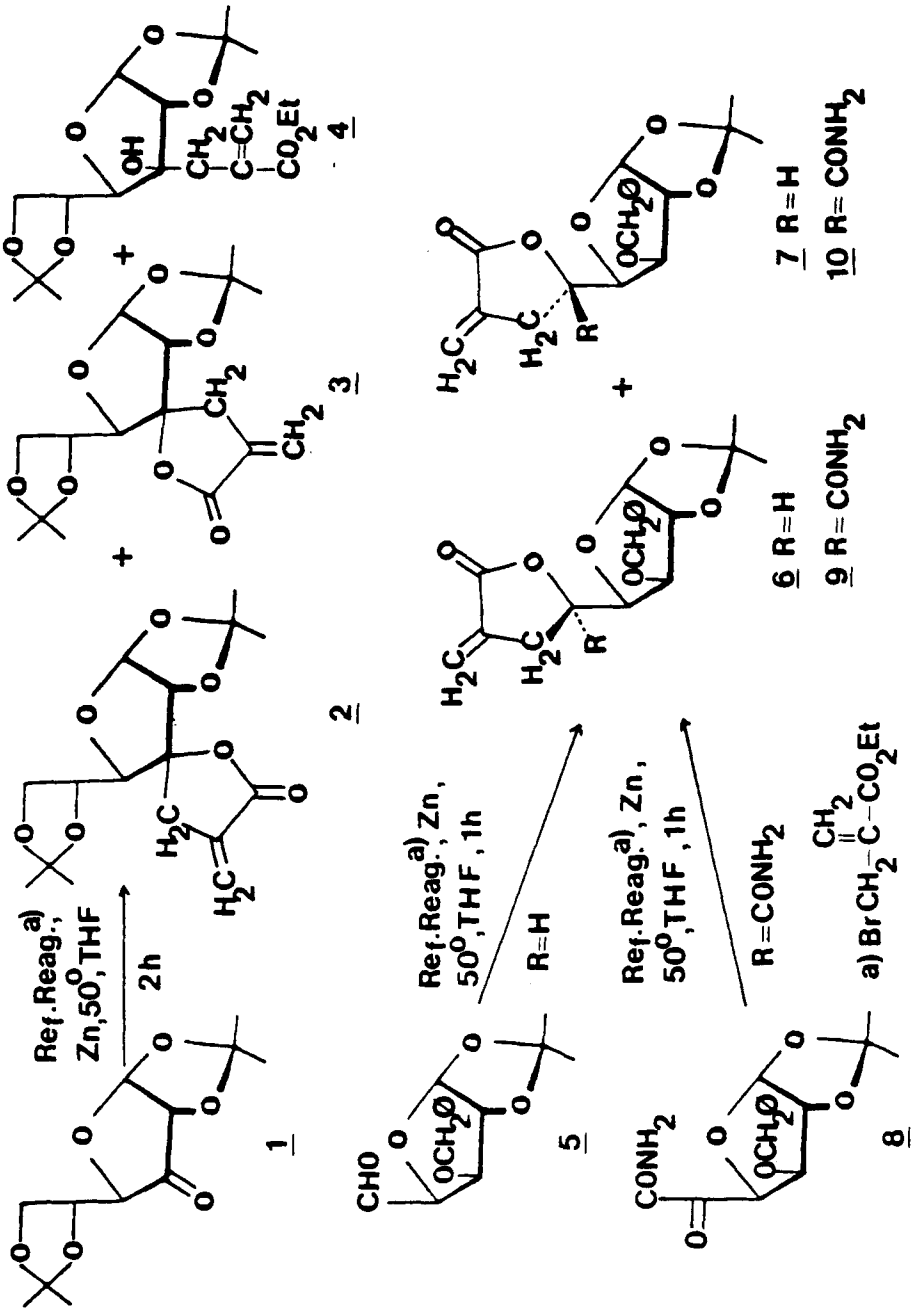


FIG.1

The formation of both stereoisomeric lactone forms leads to the synthesis of two diastereomers, which are in all cases easily separated by column chromatography on silica gel with mixtures of toluene and ethyl acetate. The fact that both isomers are obtained is very important because the biological activity may depend on the stereochemistry of the molecules, a phenomenon known for α,β-unsaturated lactone sesquiterpenes.[4]

Stereochemical assignment of the new chiral center created by the Reformatsky reaction was possible after examination of the ^{1}H NMR spectra. The hydrogen atoms of the methylene group from the lactone ring with sp_3 hybridization would be predicted to be diastereotopic in compounds 3, 4, 7, and 10 and equivalent in compounds 2, 6, and 9, facts which are confirmed by their proton spectra (see TABLE 3). The four peaks typical for an AB system are found at values between δ 2.43 and 3.35, presenting geminal coupling constants between 14.5 and 17.4 Hz in compounds 3, 4, 7 and 10. In compound 3 each of these peaks is split into a triplet due to the allylic coupling with the olefinic protons, with a $^4J_{cis}$ = 2.5 Hz and a $^4J_{trans}$ = 2.9 Hz. The spectrum of compound 7 also shows the same long-range coupling with the same values for the coupling constants $^4J_{cis}$ and $^4J_{trans}$ shown by compound 3, but the peaks of the AB system corresponding to these protons are split into a multiplet due to the additional coupling with the proton bonded to the C-5 carbon. In compounds 4 and 10, no allylic coupling is detected.

For compounds 2, 6, and 9, no AB system is found. Instead, each spectrum shows a multiplet corresponding to two almost equivalent protons at values respectively from δ 3.10 to 3.15, 2.94 to 3.00 and 3.09 to 3.13 ppm.

All these compounds show the molecular peak M^+ and the well known $[M-CH_3]^+$ fragment that is characteristic of the acetonide derivatives.[19] The base peak for the benzylated products (except 8) is at m/z = 91 corresponding to the tropylium ion, $C_7H_7^+$. The lactone fragments corresponding to the scission of the C-C bond between the lactone ring and the furanosidic portion of the molecule appear at m/z = 97 for 6 and 7 and at m/z = 140 for 9 and 10 with a relative intensity of 16.7, 20.0, 14.28, and 10.03, respectively. The mass spectra of compounds 9 and 10 show more intense peaks for the fragments

corresponding to m/z = 141 (respectively, 20.77 and 15.37). The peak at m/z = 249 corresponding to the furanosidic fragment appears in low relative intensities, respectively, of 1.98, 2.74, 9.29 and 3.36 for compounds 6, 7, 9, and 10. This is probably due to the instability of this fragment leading to a great number of other different fragments.[19,20,21] The fragments known to arise from isopropylidene groups are also present. The peak corresponding to m/z = 43 is intense in compounds 2 and 3, and it is the base peak for compounds 1, 4, and 8.

The uloses 1 and 8 were obtained respectively by oxidation of 1,2;5,6-di-O-isopropylidene-α-D-glucofuranose,[22] and of 3-O-benzyl--1,2-O-isopropylidene-α-D-glucofuranuronoamide (11) or 3-O-benzyl--1,2-O-isopropylidene-β-L-idofuranuronoamide (12), with pyridinium chlorochromate (PCC)/3Å molecular sieve powder in methylene chloride,[23] (1 under reflux during one hour in 95% yield, and 8 at room temperature also during one hour in 98% yield from either 11 or 12). The system PCC/3Å molecular sieve powder allowed the synthesis of the ulose 1 in yield and purity superior to the already known method with acetic anhydride/DMSO.[16] Whereas the hydroxy amides 11 and 12 could not be oxidized using common oxidation methods such as chromic oxide in acetic acid, acetic anhydride/DMSO and DMSO/dicyclohexylcarbodiimide,[24] pyridinium chlorochromate/3Å molecular sieve powder was shown to be a very effective method for the oxidation of these compounds. They were easily obtained from the aldehyde 5 in a one-pot reaction by treatment of its dioxane solution with an aqueous solution of sodium cyanide/potassium carbonate to synthesize the cyanhydrins, followed immediatly by addition of hydrogen peroxide to obtain the epimeric hydroxy amides 11 and 12. The mixture could be readily separated on a column of silica gel with 1:5 toluene–ethyl acetate giving the pure, less polar ido derivative and the more polar gluco isomer in yields of 55% and 43%, respectively.

The mass spectra of 1, 8, 11, and 12 show the molecular peaks M^+ and the fragments $[M-15]^+$. The base peak of the mass spectra appears at m/z = 91 for compounds 11 and 12 and at m/z = 43 for compounds 1 and 8.

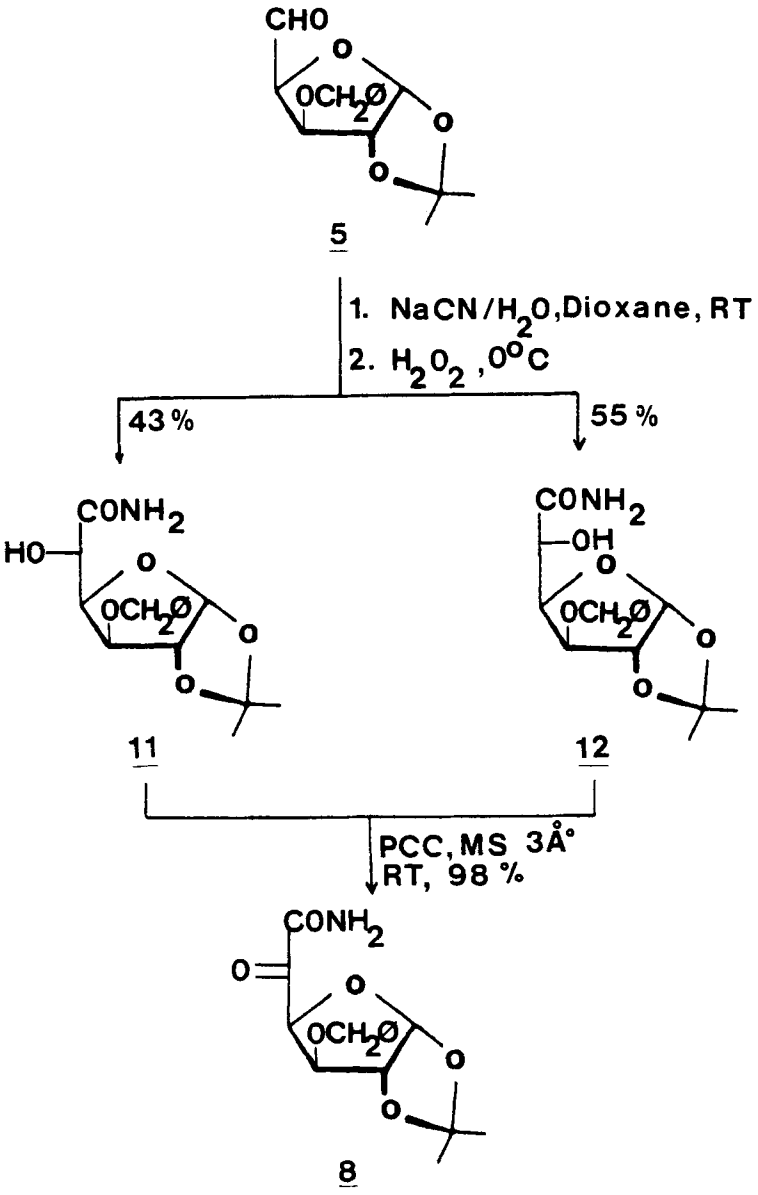


FIG. 2

EXPERIMENTAL

General Procedures. Melting points were determined on a melting point apparatus (Tottoli) and are uncorrected. ^{1}H and ^{13}C magnetic resonance spectra were recorded at 200 MHz with a Bruker WP-200 SY spectrometer using tetramethylsilane as internal standard. Mass spectra were recorded on an updated AEI MS9 of conventional geometry under the following conditions: ionizing energy 70 eV; accelerating voltage 8000 V; I. Rep. +1V; trap. cur. 0.2 mA; emission 0.5 mA; Fil. cur. 4A; source temp. 200 °C. Optical rotations were determined with a Perkin Elmer 141 polarimeter, and IR spectra were recorded on a Perkin Elmer 577 spectrometer. Analytical thin layer chromatography was performed on aluminium sheets coated with a 0.2 mm layer of silica gel 60 F_{254} (Merck). Column chromatography was performed on glass columns filled with silica gel 230–400 mesh (Merck). Compounds were detected with UV light (254 nm) and/or by spraying the sheets with a 3% vanillin–sulfuric acid solution.

Reformatsky Reaction. A solution of 0.97 g (5 mmol) ethyl bromomethylacrylic ester[13] [1.33 g (6.9 mmol) when reacting with 1] in 2.5 mL of anhydrous tetrahydrofuran was added dropwise with stirring under nitrogen at room temperature to a mixture of 0.35 g (5.35 mmol, 20 mesh) of granulated zinc (previously activated with 5% hydrochloric acid, washed with distilled water, ether, and dried carefully), and 3.6 mmol of carbonyl compound in 2 mL of anhydrous tetrahydrofuran. The mixture was stirred for 1 h (2 h in case of compound 1) at 50 °C, and then cooled to room temperature. After addition to the reaction mixture of 10 mL of dilute hydrochloric solution that had been cooled to 0 °C, and extraction with methylene chloride, the organic phase was washed with dilute sodium hydrogen carbonate solution and water. The organic phase was dried over anhydrous magnesium sulfate and finally evaporated to give a residue. Isolation of the stereoisomeric α-methylene-γ-lactones formed was achieved by column chromatography of the residue with 1:5 ethyl acetate–toluene.

Oxidation with PCC/3Å Molecular Sieve Powder. 3.2 g (15 mmol) of pyridinium chlorochromate[25] and 5 g of 3Å molecular sieve powder were suspended in 25 mL of methylene chloride previously dried over

TABLE 1. Yield, Physical Properties, and IR Spectra for Compounds 1–4 and 6–12

Comp. Nr.	Yield %	R_f [a]	$[\alpha]_D^{20}$ [b]	mp(°C)	IR (C=O) [c]	IR (C=C) [c]
1	95	0.43 [d]	+49.6° [e]	Syrup	1775	—
2	24	o.83	-7.5°	Syrup	1775	1630
3	35	0.62	+31.8°	88 [f]	1765	1670
4	41	0.73	+18.0°	44 [f]	1700	1625 [g]
6	50	0.85	-77.0°	Syrup	1760	1660
7	46	0.75	-46.2°	153 [f]	1750	1655 [h]
8	98	0.75 [d]	+4.2° [e]	Syrup	1775(ulose) [i] 1700(amide)	—
9	16	0.28 [j]	-32.0°	218 [f]	1770(lact.) 1650(amide)	1610 [h] [k]
10	35	0.33 [j]	+29.3°	Syrup	1770(lact.) 1675(amide)	1600 [i]
11	43	0.37 [d]	-27.8° [e]	110–112	1680(amide) [l]	—
12	55	0.52 [d]	-15.7° [e]	78–81	1680(amide) [l]	

a) 1:1 Ethyl acetate–toluene; b) c = 1, $CHCl_3$; c) cm^{-1}, film on NaCl, C=O strong absorption, C=C weak absorption; d) 5:1 ethyl acetate–toluene; e) 25 °C; f) decomposition beginning at; g) 3480, strong absorption, –OH; h) KBr; i) 3330, 3450 – 2 bands, strong absorption, $-NH_2$; j) 10:1 toluene –methanol; k) 3200, 3500 – 2 bands, strong absorption, $-NH_2$; l) 3400, 3480 – 2 bands, strong absorption, $-NH_2$ and –OH.

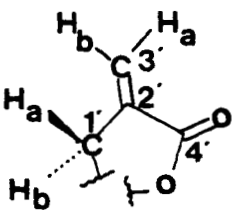
TABLE 2. Mass Spectra Data and Elemental Analysis for Compounds 1–4 and 6–12

Comp. Nr.	m/z (relative intensity)		Calcd.	Found
1	43 (100); 243, M^+–15(1.43); 258, M^+(0.03)	$C_{12}H_{18}O_6$(258.27)	C 55.81 H 7.02	C 55.93 H 7.06
2	43 (52.18); 61 (100); 311, M^+–15(13.05); 326, M^+(0.08)	$C_{16}H_{22}O_7$(326.34)	C 58.89 H 6.79	C 59.10 H 6.88
3	43 (71.43); 311, M^+–15(100); 326, M^+(0.28)	$C_{16}H_{22}O_7$(326.34)	C 58.89 H 6.79	C 58.96 H 7.14
4	43 (100); 357, M^+–15(0.40); 372, M^+(0.06)	$C_{18}H_{28}O_8$(372.41)	C 58.05 H 7.58	C 58.29 H 7.35
6	43 (5.57); 91 (100); 97 (16.7); 249 (1.98); 331, M^+–15(5.57); 346, M^+(0.25)	$C_{19}H_{22}O_6$(346.38)	C 65.88 H 6.40	C 65.60 H 6.36
7	43 (10.17); 91 (100); 97 (20.0); 249 (2.74); 331, M^+–15(5.87); 346, M^+(0.39)	$C_{19}H_{22}O_6$(346.38)	C 65.88 H 6.40	C 66.01 H 6.42
8	43 (100); 91 (61.54); 306, M^+–15(0.38); 321, M^+(0.08)	$C_{16}H_{19}O_6N$(321.33)	C 59.81 H 5.96 N 4.36	C 59.62 H 5.93 N 4.57
9	43 (14.50); 91 (100); 140 (14.28); 141 (20.77); 249 (9.29); 374, M^+–15(2.40); 389, M^+(0.48)	$C_{20}H_{23}O_7N$(389.40)	C 61.69 H 5.95 N 3.60	C 61.90 H 6.04 N 3.31
10	43 (12.03); 91 (100); 140 (10.03); 141 (15.37); 249 (3.36); 374, M^+–15(1.53); 389, M^+(0.13)	$C_{20}H_{23}O_7N$(389.40)	C 61.69 H 5.95 N 3.60	C 61.83 H 6.02 N 3.42
11	43 (22.55); 91 (100); 308, M^+–15(0.98); 323, M^+(0.10)	$C_{16}H_{21}O_6N$(323.35)	C 59.43 H 6.55 N 4.33	C 59.75 H 6.50 N 4.45
12	43 (25.00); 91 (100); 308, M^+–15(1.89); 323, M^+(1.00)	$C_{16}H_{21}O_6N$(323.35)	C 59.43 H 6.55 N 4.33	C 59.63 H 6.42 N 4.40

TABLE 3. ^{1}H NMR Spectroscopic Data (in $CDCl_3$, δ in ppm, J in Hz) for Compounds 2–4 and 6–12

Comp. Nr.

2 6.21(t,1H,H-3a'); $^4J_{3'a,1'a}$= $^4J_{3'a,1'b}$=1.5; 5.84(d,1H,H-1); $^3J_{1,2}$=3.6; 5.79(t,1H,H-3'b); $^4J_{3'b,1'a}$= $^4J_{3'b,1'b}$=1.5; 4.48(d,1H,H-2); 4.25–3.84(m,4H,H-4,H-5,H-6,H-6'); 3.15–3.10 (m,2H,H-1'a,H-1'b); 1.44(s,3H,CH_3-isop.); 1.36(s,3H,CH_3-isop.); 1.24(s,3H,CH_3-isop.); 1.20(s,3H,CH_3-isop.).



3 6.18(t,1H,H-3'a); $^4J_{3'a,1'a}$=$^4J_{3'a,1'b}$=2.9; 5.67(d,1H,H-1); $^3J_{1,2}$= =3.4; 5.59(t,1H,H-3'b); $^4J_{3'b,1'a}$=$^4J_{3'b,1'b}$=2.5; 4.11–3.87(m,4H, H-4,H-5,H-6,H-6'); 3.20,3.12,2.59 and 2.51(each t,2H,H-1'a,H-1'b) $^2J_{1'a,1'b}$=17.4; 1.54(s,3H,CH_3-isop.); 1.32(s,3H,CH_3-isop.); 1.28 (s,3H,CH_3-isop.); 1.18(s,3H,CH_3-isop.).

4 6.36(s,1H,H-3'a); 5.85(s,1H,H-3'b); 5.68(d,1H,H-1); $^3J_{1,2}$=3.7; 4.21–4.02(m,5H,H-2,H-4,H-5,CH_2(Et)); 3.87–3.78(m,2H,H-6,H-6'); 2.88(s,1H,-OH); 2.76.2.69,2.50 and 2.43(each s,2H,H-1'a,H-1'b); $^2J_{1'a,1'b}$=14.5; 1.50(s,3H,CH_3-isop.); 1.39(s,3H,CH_3-isop.);1.30 (s,3H,CH_3-isop.); 1.24(s,3H,CH_3-isop;t,3H,CH_3(Et)).

6 7.28–7.25(m,5H,aromat.); 6.16(t,1H,H-3'a);$^4J_{3'a,1'a}$=$^4J_{3'a,1'b}$= =2.9; 5.83(d,1H,H-1);$^3J_{1,2}$=3.6; 5.57(t,1H,H-3'b);$^4J_{3'b,1'a}$= = $^4J_{3'b,1'b}$=2.5; 4.80–4.69(q,1H,H-5); 4.63–4.49(m,3H,H-2,CH_2 (benzyl)); 4.10–4.04(m,1H,H-4); 4.01(d,1H,H-3);$^3J_{3,4}$=3.2; $^3J_{4,5}$=7.8; 3.00–2.94(m,2H,H-1'a,H-1'b); 1.38(s,3H,CH_3-isop.(endo)) 1.22(s,3H,CH_3-isop.(exo)).

7 7.31–7.22(m,5H,aromat.); 6.12(t,1H,H-3'a); $^4J_{3'a,1'a}$= $^4J_{3'a,1'b}$= =2.9; 5.93(d,1H,H-1), $^3J_{1,2}$=3.8; 5.46(t,1H,H-3'b); $^4J_{3'b,1'a}$=$^4J_{3'b,1'a}$=2.5; 4.77–4.66(m,1H,H-5); 4.66, 4.60, 4.39

(cont.)
and 4.33(2H,CH_2(benzyl),AB system); $^2J_{AB}$=11.7; 4.59(d,1H,H-2); 4.19-4.13(m,1H,H-4); 3.96(d,1H,H-3); $^3J_{3,4}$=3.8; $^3J_{4,5}$=6.4; 2.84, 2.77,2.52 and 2.45(each m,2H,H-1'a,H-1'b); $^2J_{1'a,1'b}$=15.2; $^3J_{5,1'a}$= =9.5; $^3J_{5,1'b}$=6.5; 1.41(s,3H,CH_3-isop.(endo)); 1.26(s,3H,CH_3-isop. (exo)).

8 7.31-7.12(m,5H,aromat.,1H,NH_2); 6.83(s,1H,NH_2); 5.98(d,1H,H-1); $^3J_{1,2}$=3.6; 5.48(d,1H,H-4); $^3J_{3,4}$=4.2; 4.73(d,1H,H-3); 4.52(d,1H, H-2); 4.52,4.46,4.40 and 4.34(2H, CH_2(benzyl), AB system); $^2J_{AB}$= =11.6; 1.38(s,3H,CH_3-isop.(endo)); 1.24(s,3H,CH_3-isop.(exo)).

9 7.22(s,5H,aromat.);6.47(s,1H,NH_2); 6.04(t,1H,H-3'a); $^4J_{3'a,1'a}$= = $^4J_{3'a,1'b}$=2.9; 5.90(d,1H,H-1); $^3J_{1,2}$=3.8; 5.62(s,1H,NH_2); 5.47 (t,1H,H-3'b); $^4J_{3'b,1'a}$= $^4J_{3'b,1'b}$=2.5; 4.51-4.46(m,4H,H-2,H-4, CH_2(benzyl)); 4.10(d,1H,H-3); $^3J_{3,4}$=4.1; 3.09-3.13(m,2H,H-1'a, H-1'b); 1.40(s,3H,CH_3-isop.(endo)); 1.24(s,3H,CH_3-isop.(exo)).

10 7.22(s,5H,aromat.); 6.28(s,1H,NH_2); 6.10(s,1H,H-3'a); 5.80(d,1H, H-1); $^3J_{1,2}$=3.9; 5.59(s,1H,NH_2); 5.49(s,1H,H-3'b); 4.68(d,1H,H-4); $^3J_{3,4}$=5.1; 4.56(d,1H,H-2); 4.56,4.50,4.39 and 4.33(2H,CH_2(benzyl), AB system); $^2J_{AB}$=11.4; 4.13(d,1H,H-3); 3.35,3.27,2.99 and 2.91 (each s,2H,H-1'a,H-1'b); $^2J_{1'a,1'b}$=15.6; 1.38(s,3H,CH_3-isop.(endo); 1.23(s,3H,CH_3-isop.(exo)).

11[a] 7.40-7.28(m,5H,aromat.); 7.00(s,1H,NH_2); 6.70(s,1H,NH_2); 5.92(d, 1H,H-1); $^3J_{1,2}$=2.9; 4.75(d,1H,H-2); 4.76,4.72,4.66 and 4.62(2H, CH_2(benzyl),AB system); $^2J_{AB}$=12.0; 4.51(d,1H,H-5); $^3J_{4,5}$=2.9; 4.44 and 4.40(dd,1H,H-4), 4.23(d,1H,H-3); $^3J_{3,4}$=2.9; 3.00(s,1H,-OH); 1.42(s,3H,CH_3-isop.(endo)); 1.29(s,3H,CH_3-isop.(exo)).

12[a] 7.42-7.27(m,5H,aromat.); 6.93(s,1H,NH_2); 6.89(s,1H,NH_2); 5.93(d, 1H,H-1); $^3J_{1,2}$=4.5; 4.75-4.63(m,3H,H-2 and CH_2(benzyl),AB system); $^2J_{AB}$=11.7; 4.27(s,1H,H-5); 4.21(d,1H,H-4); $^3J_{3,4}$=2.7; 4.12(d,1H,H-3) 3.05(s,1H,-OH); 1.42(s,3H,CH_3-isop.(endo)); 1.28(s,3H,CH_3-isop(exo)).

a) BRUKER CXP 300

TABLE 4. ^{13}C NMR Spectroscopic Data (δ in ppm, in $CDCl_3$) for Compounds 2–4 and 6–10

	2	3	4	6	7	8	9	10
CH_3(Et)	—	—	14.19	—	—	—	—	—
CH_3 (isop.)	24.26 25.10 25.65 25.70	25.11 26.37 26.42 26.80	25.40 26.49 26.76 26.83	26.18 26.81	26.42 26.89	26.29 26.98	25.42 26.07	25.68 26.79
C-1'	30.22	31.47	32.77	30.43	29.46	—	35.20	33.05
CH_2(Et)	—	—	61.16	—	—	—	—	—
C-6	67.68	68.22	68.07	—	—	b	—	—
CH_2 (benzyl)	—	—	—	72.54	71.95	66.83	71.36	72.00
C-2,C-3[a]	73.37	73.68	73.43[a]	73.29	75.67	82.35	81.13	81.47
C-4,C-5[c,d]	80.22 81.78[a] 84.11[a]	78.04 84.04[a] 85.17[a]	79.42[a] 81.02 82.28	81.39 81.68 82.55	81.92 82.17 82.23	83.38 84.44 c	81.72 82.10[d] 83.33[d]	82.79 83.05[d] 83.58[d]
C-1	104.56	103.17	103.78	105.24	105.74	105.37	104.43	105.16
C-isop.	107.92 110.64	110.11 114.14	109.72 112.68	111.99	112.25	112.41	111.22	112.26
C-3'	123.45	121.83	130.17	122.36	122.05	—	120.54	122.00
CH (arom.)	— — — — —	— — — — —	— — — — —	127.65 127.71 127.94 128.45 128.57	127.97 128.13 128.33 128.50 128.81	127.57 127.81 128.16 128.22 128.43	126.29 126.83 127.07 127.39 127.65	127.56 127.79 128.31 128.58 128.84
C-2'	133.28	133.47	135.26	133.93	133.86	—	132.89	132.79
C-arom.	—	—	—	137.30	136.91	136.72	136.71	137.00
C=O (amide)	—	—	—	—	—	161.41[b]	172.10	172.84
C-4'	164.53	168.13	168.08	169.71	169.65	—	168.09	168.84
C=O[c]	—	—	—	—	—	191.00[c]	—	—

4Å molecular sieve pellets. Five mmol of substrate were added to this suspension, and the reaction mixture was stirred for 1 h at room temperature (at 40 °C for compound 1). After filtration and evaporation of the solvent, the residue was purified by column chromatography with Florisil using 1:1 toluene–ethyl acetate.

3-O-benzyl-1,2-O-isopropylidene-α-D-gluco- and -β-L-ido-furanuronoamide (11 and 12). A solution of 1.5 g (30 mmol) of sodium cyanide and 1.5 g (10.9 mmol) of potassium carbonate in 25 mL of water was added to a solution of 0.56 g (2 mmol) of 3-O-benzyl-1,2-O-isopropylidene- α -D-xylo-pentodialdo-1,4-furanose (5) in 30 mL of dioxane, previously cooled to 10 °C. The reaction mixture was stirred at room temperature for 30 min and then cooled in an ice bath and stirred, while 5.5 mL of 30% hydrogen peroxide was added. After 1 h the mixture was added to 50 mL of ice water and the precipitate was collected and washed with cold water. The aqueous phase was extracted with chloroform, washed with water, and dried over anhydrous magnesium sulfate. After filtration and evaporation of the solvent, the residue and the previously precipitated compound mixture were purified by chromatography with a column of silica gel using 1:5 ethyl acetate-toluene.

Yields, physical properties, elemental analysis, and spectroscopic data for all the compounds synthesized by these methods are given in TABLES 1–4.

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REFERENCES

1. S. M. Tharib, S. O. Gnan, and G. B. Veitch, J. Food Protection, 46, 185 (1983).

2. P. Barbetti, and C. G. Casinovi, Ann. Ist. Super. Sanita, 17, 255 (1981).

3. A. D. Kagarlitskii, and S. M. Adekenov, Vestn. Akad. Nauk Kaz. SSR, 10, 9 (1984).

4. S. M. Kupchan, M. A. Eakin, and A. M. Thomas, J. Med. Chem., 14, 1147 (1971).

5. S. M. Kupchan, Fed. Proc., Fed. Am. Soc. Exp. Biol., 33, 2288 (1974).

6. J. H. Hall, K.- H. Lee, and S. A. Eigebaly, J. Pharm. Sci., 67, 1232 (1978).

7. P. A. Grieco, Synthesis, 67 (1975).

8. R. B. Gammill, C. A. Wilson, and T. A. Bryson, Synth. Commun., 5, 245 (1975).

9. V. Nair, and A. K. Sinhababu, J. Org. Chem., 45, 1893 (1980).

10. C. Papageorgiou, and C. Benezra, J. Org. Chem., 50, 157 (1985).

11. S. Hanessian, T. J. Liak, and D. M. Dixit, Carbohydr. Res., 88, C14 - C19 (1981).

12. A. P. Rauter, and H. Weidmann, Liebigs Ann. Chem., 2231 (1982).

13. A. F. Ferris, J. Org. Chem., 20, 780 (1955).

14. M. S. Newman, and F. J. Evans, Jr., J. Am. Chem. Soc., 77, 946 (1955).

15. E. Öhler, K. Reininger, and U. Schmidt, Angew. Chem. Internat. Edit., 9(6), 457 (1970).

16. J. D. Stevens, "Methods in Carbohydrate Chemistry", 7, 123 (1976).

17. M. L. Wolfrom, and S. Hanessian, J. Org. Chem., 27, 1800 (1962).

18. S. Kano, S. Shibuya, and T. Ebata, Heterocycles, 14, 661 (1980).

19. A. Glangetas, A. Buchs, and J. M. J. Tronchet, Biomed. Mass Spectrom. 3, 278 (1976).

20. A. Klemer, U. Hofmeister, and R. Lemmes, Carbohydr. Res., 68, 391 (1979).

21. H. Parolis, Carbohydr. Res., 114, 21 (1983).

22. O. Th. Schmidt, "Methods in Carbohydrate Chemistry", 2, 318 (1963).

23. J. Herscovici, and K. Antonakis, J. Chem. Soc. Chem. Commun., 561 (1980).

24. G. Trummlitz, and J. G. Moffatt, J. Org. Chem., 38, 1841 (1973).

25. E. J. Corey, and J. W. Suggs, Tetrahedron Lett., 2647 (1975).