Preliminary communication

Acetalation and esterification of D-glucuronolactone

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Recently, new uronic acid derivatives have received increasing attention[1]. In the course of preparing alkali-stable derivatives of uronic acids, leaving the carboxyl group available for further synthetic operations, we have found that treatment of α-D-glucofuranurono-6,3-lactone with 2,2-dimethoxypropane in the presence of an acid catalyst yields derivatives in which all of the functional groups of the carbohydrate have participated in the reaction.

Methyl 1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranuronate (**1a**) was isolated in 15–20% yield after reaction of α-D-glucofuranurono-6,3-lactone with 2,2-dimethoxypropane and acetone in the presence of *p*-toluenesulfonic acid; sulfuric acid, trifluoroacetic acid, or concentrated hydrochloric acid were also satisfactory catalysts. Reaction conditions involved either boiling for 2 h under reflux, or keeping for 48 h at room temperature. Compound **1a** was obtained as a chromatographically (t.l.c. and g.l.c.) homogeneous syrup. Its n.m.r. spectrum in chloroform-*d* showed singlets at τ 8.49 (3 H), 8.58 (6 H), and 8.65 (3 H), indicating that **1a** was a di-*O*-isopropylidene derivative. A three-proton singlet at τ 6.14 suggested that **1a** was a methyl ester (rather than a methyl glycoside). A one-proton doublet at τ 3.87 was evidence for presence of an anomeric proton in a 1,2-*O*-isopropylidene-furanose structure[2]; upon irradiation at τ 5.35, this doublet became a singlet.

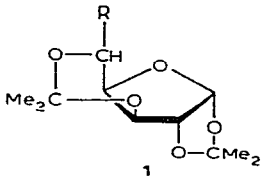
The mass spectrum of compound **1a** gave the highest *m/e* ratio at 273.0957 ($C_{12}H_{17}O_7$ requires 273.0974), consistent with loss of a methyl radical from the molecular ion. Subsequent loss of CO_2, or the loss of CO_2CH_3 radical from M^+ then gave rise to *m/e* 229.

For further study of the structure of **1a**, it was reduced with sodium bis(2-methoxyethoxy)aluminum hydride in benzene, affording alcohol **1b** in 85% yield. Compound **1b** had a mass spectrum (see Table I) strikingly similar to that of 6-deoxy-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose[3] (**1c**). Compound **1b** had previously been synthesized by a three-step procedure starting with 1,2-*O*-isopropylidene-α-D-glucofuranose[4].

TABLE I

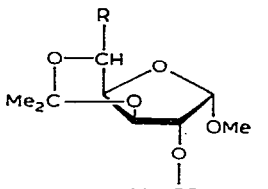
MASS-SPECTRAL DATA FOR COMPOUND **1b**

m/e	245	229	200	187	171	142	129	127
%	18	3	7	3	7	23	23	9
m/e	114	113	109	100	85	59	55	43
%	22	100	5	15	22	60	10	60



1

a, R = COOMe
b, R = CH_2OH
c, R = CH_3
d, R = CH_2OAc
e, R = CH_2Br



2

a, R = COOMe
b, R = CH_2OH

Compound **1b** was acetylated, to give **1d** (M^+-CH_3 · *m/e* 287, M^+–HOAc *m/e* 242). The n.m.r. spectrum of **1d** in chloroform-*d* showed one-proton doublets at τ 4.04 and 5.45, in addition to acetyl and isopropylidene absorptions at τ 7.92 (3 H), 8.51 (3 H), 8.62 (6 H), and 8.68 (3 H). The same acetate was obtained from the bromo derivative[5] (**1e**) by solvolysis with sodium acetate in refluxing *N,N*-dimethylformamide. The two products had identical i.r., n.m.r., and mass spectra, and identical mobility in t.l.c. and g.l.c.

When the reaction between 2,2-dimethoxypropane and α-D-glucofuranurono-6,3-lactone was prolonged, or conducted in the absence of acetone, a product formerly minor became important; it was isolated, in ~ 30% yield, as a chromatographically homogeneous syrup. Based on elemental analysis and on its i.r., n.m.r., and mass spectra, its structure was presumed to be **2a**. The n.m.r. and i.r. spectra showed it to be a methyl ester (three-proton singlet at τ 6.27; i.r. band at 1750 cm^{-1}) and a diisopropylidene acetal (three- and nine-proton singlets at τ 8.40 and 8.63, respectively; i.r. doublet at ~ 1375 cm^{-1}). A six-proton singlet at τ 6.47 corresponded to an overlap of a glycosidic methoxyl and an acetalic methoxyl group. Its mass spectrum gave the highest peak at *m/e* 319 (M^+-CH_3; $C_{14}H_{23}O_8$), the next prominent ion being at *m/e* 245, corresponding to the subsequent loss of the elements of 2-methoxypropane (H_3C–CHOMe–CH_3). On reduction of **2a** with sodium bis(2-methoxyethoxy)aluminum hydride, the product had a mass spectrum with the highest peak at *m/e* 291, consistent with the loss of CH_3 from the molecular ion of **2b**.

ACKNOWLEDGMENTS

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