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Elimination Reaction of *Aldehydo*-D-glucurono-6,3-lactone Derivatives

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(Received July 31, 1984)

Synopsis. D-Glucurono-6,3-lactone derivatives are converted to butenolide or dihydro-2*H*-pyran derivatives by treatment with triethylamine.

Because of the effect of the carbonyl group, uronic acid and aldonolactone derivatives readily underwent β-elimination reactions to yield unsaturated compounds.[1,2,3] D-Glucurono-6,3-lactone (**1**) derivatives were also susceptible to elimination reaction to give unsaturated compounds.[4,5] We wish to report herein the formation of butenolide or dihydro-2*H*-pyran derivatives by elimination reactions of 2,4,5-tri-*O*-acetyl-*aldehydo*-D-glucurono-6,3-lactone diacetyl acylal (**2**), *aldehydo*-D-glucurono-6,3-lactone ethylene dithioacetal (**3**),[6] or 2,4,5-tri-*O*-acetyl-*aldehydo*-D-glucurono-6,3-lactone ethylene dithioacetal (**4**) by treatment with triethylamine.

Acetolysis of methyl β-D-glucofuranosidurono-6,3-lactone with $BF_3 \cdot OEt_2$ in acetic anhydride afforded crystalline **2** in 55% yield. The compound **2** was also obtained from **1** or 1,2,5-tri-*O*-acetyl-β-D-glucurono-6,3-lactone in lower yields, 39% and 27%, respectively. The compound **2** was isolated from the mixture of **2** and 1,2,5-tri-*O*-acetyl-D-glucurono-6,3-lactone by crystallization from ethyl acetate–petroleum ether (1:4). Other acidic catalysts such as H_2SO_4, $AlCl_3$, H_3PO_4, and CF_3COOH did not afford **2**. Treatment of **2** with triethylamine afforded 3-acetoxy-5-(2,2-diacetoxyethylidene)-2(5*H*)-furanone (**5**). The results obtained with various solvents are summerized in Table 1, acetic anhydride was found to be the most suitable solvent and **5** was obtained in 91% yield.

Upon treatment of **4** with acetic anhydride-triethylamine, 3-acetoxy-5-[1-acetoxy-2-(1,3-dithiolan-2-yl) ethyl]-2(5*H*)-furanone (**6**) was obtained as a main product, together with 3-acetoxy-5-[2-(1,3-dithiolan-2-yl) ethylidene]-2(5*H*)-furanone (**7**), in 69% and 11% yields, respectively. This reaction also occurred smoothly in ethyl acetate, and **6** and **7** were also obtained in 74% and 16% yields, respectively.

On the other hand, when **3** was treated with acetic anhydride-triethylamine, the 6,3-lactone linkage rearranged to a 6,2-lactone linkage along with acetylation and elimination reactions. In this reaction, 3,5-diacetoxy-6-(1,3-dithiolan-2-yl)-5,6-dihydro-2*H*-pyran-2-one (**8**) was obtained in 83% yield, but the butenolide derivatives, **6** and **7**, and α-pyrone derivative were not obtained.

Table 1. Conversion of **2** into **5** by treatment with triethylamine

Solvent	Temp/°C	Time/h	Yield/%
CH_3CN	0	4	3
CH_3CN-Ac_2O	0	2	76
DMF	0	22	0
DMF-Ac_2O	0	3	65
EtOAc	60	2	0
EtOAc-Ac_2O	60	1	50
Ac_2O	0	24	91

The dithioacetal derivatives, **3** and **4**, tend mainly to give monounsaturated product, while **2** gave the conjugated unsaturated compound.

The product **5** and **7** were a mixture of *E* and *Z* isomers. The structures of the two isomers were easily determined by ^{1}H-NMR studies, since the olefinic hydrogen in the *E* isomer is considerably deshielded by virtue of its *cis* relationship to the butenolide oxygene.[7] In the ^{1}H-NMR spectrum of **8**, the value for $J_{5,6}$ (2.4 Hz) indicated the *cis* relationship for the two protons, H-5 and H-6,[8] and the other physical data are consistent with the proposed structure for **8**. Moreover, in the pharmacological screening tests of **5**, antihypertension and bradycardia activities were observed.

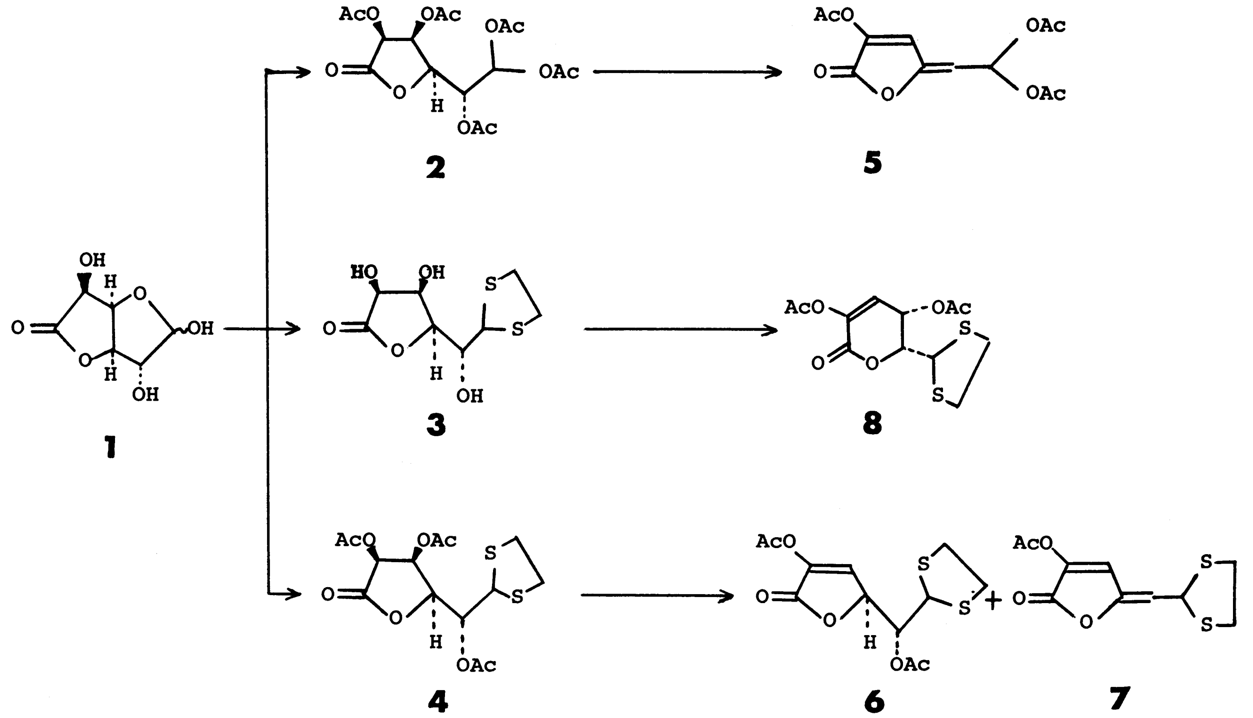
Experimental

Melting points are uncorrected. The infrared spectra and ^{1}H-NMR spectra were recorded on a JASCO A-102 spectrometer and a JNM PMX-60 spectrometer, respectively, under standard conditions.

*2,4,5-Tri-O-acetyl-*aldehydo*-D-glucurono-6,3-lactone Diacetyl Acylal (2).* To a mixture of acetic anhydride (12 ml) and $BF_3 \cdot OEt_2$ (2 ml) was added methyl β-D-glucofuranosidurono-6,3-lactone[9] (0.3 g). After heating the mixture at 60 °C for 16 h, the reagents were distilled off under reduced pressure. The residue was extracted with ethyl acetate-water and the organic layer was washed with 5% $NaHCO_3$ aq and water, dried and evaporated under reduced pressure. The residue was extracted with 15 ml of ethyl acetate-petroleum ether (1:4) and the insoluble material was **2** (0.25 g, 55%). It was recrystallized from acetone-petroleum ether: mp 202—203 °C. ^{1}H-NMR (DMSO-d_6) δ=2.10 (6H, s), 2.30 (9H, s), 5.00 (1H, dd, J=3.0, 7.8 Hz), 5.44 (1H, dd, J=3.2, 7.8 Hz), 5.63 (1H, dd, J=3.0, 4.9 Hz), 5.95 (1H, d, J=4.9 Hz), 6.63 (1H, d, J=3.2 Hz). IR 1805, 1770, 1750 cm^{-1}. Found: C, 47.51; H, 5.11%. Calcd for $C_{16}H_{20}O_{12}$: C, 47.52; H, 5.00%.

3-Acetoxy-5-(2,2-diacetoxyethylidene)-2(5H)-furanone (5). To a solution of **2** (0.3 g) in acetic anhydride (15 ml) triethylamine (0.5 ml) was added at 0 °C. After stirring for 24 h at 0 °C, the mixture was extracted with benzene-water. The benzene layer was washed with HCl aq and water, dried and evaporated under reduced pressure. The products were separated by column chromatography on silica gel (Wako gel C-200) with ethyl acetate-petroleum ether (2:3). The first moving compound was (*E*)-**5** (0.073 g, 34%) which was recrystallized from carbon tetrachloride-petroleum ether: mp 68 °C. The second moving compound was (*Z*)-**5** (0.12 g, 57%) as oil. (*E*)-**5**; ^{1}H-NMR ($CDCl_3$) δ= 2.13 (6H, s), 2.35 (3H, s), 5.75 (1H, d, J=7.6 Hz), 7.43 (1H, d), 7.77 (1H, s). IR 1780, 1760, 1740, 1680, 1615 cm^{-1}. Found: C, 50.64; H, 4.06%. Calcd for $C_{12}H_{12}O_8$: C, 50.71; H, 4.26%. (*Z*)-**5**; ^{1}H-NMR ($CDCl_3$) δ=2.13 (6H, s), 2.37 (3H, s), 5.47 (1H, d, J=8.0 Hz), 7.40 (1H, s), 7.65 (1H, d). IR 1790, 1760, 1680, 1615 cm^{-1}.

3-Acetoxy-5-[1-acetoxy-2-(1,3-dithiolan-2-yl)ethyl]-2(5H)-furanone (6) and 3-Acetoxy-5-[2-(1,3-dithiolan-2-yl)ethylidene]-2(5H)-



furanone (7). To a solution of **4** (0.150 g) in ethyl acetate (4 ml) triethylamine (0.4 ml) was added. After stirring for 19 h at room temperature, the solution was extracted with ethyl acetate–water. The organic layer was washed with HCl aq and water, dried and evaporated under reduced pressure. The products were separated by column chromatography on silica gel with benzene–ethanol (40:1.5). The first moving compound was **7** (0.016 g, 16%). The second moving compound was **6** (0.093 g, 74%) which was recrystallized from carbon tetrachloride–petroleum ether: mp 168—170 °C. **6**; ^{1}H-NMR ($CDCl_3$) δ=2.05 (3H, s), 2.28 (3H, s), 3.24 (4H, s), 4.83—5.00 (2H, m), 5.50—5.60 (1H, m), 7.00 (1H, d, J=2.0 Hz). IR 1775, 1750, 1650 cm^{-1}. Found: C, 44.97; H, 4.53%. Calcd for $C_{12}H_{14}O_6S_2$: C, 45.27; H, 4.43%. (E)-**7**; ^{1}H-NMR ($CDCl_3$) δ=2.33 (3H, s), 3.35 (4H, s), 5.30 (1H, d, J=11.0 Hz), 5.84 (1H, d), 7.69 (1H, s). (Z)-**7**; ^{1}H-NMR ($CDCl_3$) δ=2.33 (3H, s), 3.35 (4H, s), 5.37 (1H, d, J=10.4 Hz), 5.71 (1H, d), 7.28 (1H, s).

*3,5-Diacetoxy-6-(1,3-dithiolan-2-yl)-5,6-dihydro-2*H*-pyran-2-one (8).* To a solution of **3** (0.200 g) in acetic anhydride (3 ml) triethylamine (0.3 ml) was added. After stirring for 1 h at room temperature, the reagent were distilled off under reduced pressure. The residue was extracted with benzene–water and the organic layer washed with 5% $NaHCO_3$ aq and water, dried and evaporated under reduced pressure. The product was separated by column chromatography on silica gel with benzene–ethanol (40:1.5). Obtained **8** was recrystallized from carbon tetrachloride–petroleum ether (0.210 g, 83%): mp 91—92 °C. ^{1}H-NMR ($CDCl_3$) δ= 2.11 (3H, s), 2.35 (3H, s), 3.23 (4H, s), 4.42 (1H, dd, J=2.4, 10.0 Hz), 4.77 (1H, d, J=10.0 Hz), 5.58 (1H, dd, J=2.4, 6.4 Hz), 6.63 (1H, d, J= 6.4 Hz). IR 1770, 1660 cm^{-1}. Found: C, 45.10; H, 4.62%. Calcd for $C_{12}H_{14}O_6S_2$: C, 45.27; H, 4.43%.

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