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Pyranoside-*into*-furanoside rearrangement of D-glucuronopyranoside derivatives

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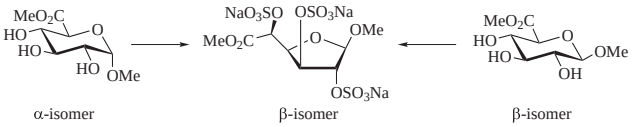
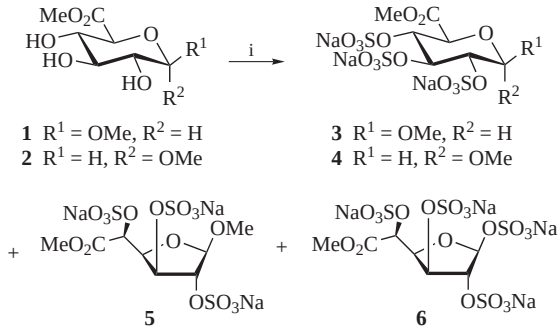
The pyranoside-*into*-furanoside (PIF) rearrangement of α- and β-D-glucuronopyranosides under acid-promoted sulfation proceeded significantly faster than similar isomerization of β-D-glucopyranosides.



Recently discovered[1–5] pyranoside-*into*-furanoside (PIF) rearrangement is a new reaction in carbohydrate chemistry, which represents the contraction of 6-membered pyranoside ring into 5-membered furanoside one under acid-promoted sulfation conditions.[6–8] This reaction followed by solvolytic de-O-sulfation opens the synthetic way towards a variety of selectively protected furanoside blocks suitable in the assembling of higher oligosaccharides. To date PIF rearrangement was successfully applied in the synthesis of oligosaccharides which are structurally related to those of bacteria *Klebsiella pneumoniae*[1] and *Enterococcus faecalis*,[2] fungi *Aspergillus fumigatus*[3] and the brown seaweed *Chordaria flagelliformis*.[4]

However, the influence of structural characteristics of parent pyranosides on the outcome of PIF rearrangement remains to be studied in more detail. In particular, there is no information on similar rearrangement of uronic acid derivatives. To fill this gap, we have studied the PIF rearrangement of isomeric methyl α- and β-D-glucuronopyranosides **1** and **2** under typical[8] conditions for PIF rearrangement and assessed the structures of formed products.

The treatment† of β-methyl glucuronopyranoside **1**[9] (Scheme 1, Table 1, entry 1) produced in 45 min per-O-sulfated derivative **3**‡ together with the corresponding product of PIF rearrangement, β-D-glucuronofuranoside **5**§ in the ratio 7 : 3. Further prolongation of the reaction to 24 h caused complete rearrangement to give β-furanoside **5** in 65% yield (entry 2), which was contaminated with minor product **6**¶ where anomeric methyl group was replaced with sulfo one. Under the same conditions β-D-glucopyranoside gave only 30% yield of the corresponding β-glucofuranoside.[8] This observation shows that PIF rearrangement of β-glucuronopyranosides proceedes significantly faster than in the case of corresponding β-glucopyranosides.



Scheme 1 *Reagents and conditions*: i, Py·SO_3, HSO_3Cl, DMF, then $NaHCO_3$.

The structure of furanoside **5** and in particular its β-anomeric configuration were confirmed by NMR data (Figure 1). Thus, ^{13}C NMR spectrum contained characteristic chemical shifts for

Table 1 The results of PIF rearrangement of pyranosides **1** and **2**.

Entry	Parent pyranoside	Reaction time/h	Reaction products and their ratios[a]	Yield of furanoside **5**[a]
1	**1**	0.75	**3** + **5** (7 : 3)	30%
2	**1**	24	**5** + **6** (2 : 1)[b]	65%
3	**2**	0.75	**4** + **5** (50 : 1)	2%
4	**2**	24	**4** + **5** (5 : 1)	17%

[a] The ratio and yields were determined by integration of non-overlapping signals for pyranoside (**3** or **4**), furanoside **5** and product **6** in ^1H NMR spectra. [b] Pyranoside product was not observed in NMR spectrum.

† *Protocol for PIF rearrangement.* The reagents Py·SO_3 (102 mg, 0.64 mmol) and HSO_3Cl (17 μl, 0.26 mmol) were added to a stirred solution of methyl pyranoside (0.058 mmol) in DMF (0.7 ml). The mixture was stirred at 25 °C for the required period of time and the solution was neutralized with aq. $NaHCO_3$, then concentrated *in vacuo* and co-evaporated with H_2O and D_2O. The residue was dissolved in D_2O and studied by NMR spectroscopy.

‡ *Selected NMR data for* **3**. ^1H NMR (600 MHz, D_2O) δ: 5.00–4.97 (m, 1H, H-4), 4.85 (d, 1H, H-1, $J_{1,2}$ 5.9 Hz), 4.79 (dd, 1H, H-3, $J_{3,4}$ 5.4 Hz, $J_{3,2}$ 4.2 Hz), 4.70 (d, 1H, H-5, $J_{5,4}$ 4.7 Hz), 4.37 (dd, 1H, H-2, $J_{2,1}$ 5.8 Hz, $J_{2,3}$ 4.2 Hz), 3.81 (s, 3H, CO_2Me), 3.55 (s, 3H, OMe). ^{13}C NMR (125 MHz, D_2O) δ: 101.7 (C-1), 77.3 (C-2), 76.0 (C-3), 75.0 (C-5), 74.2 (C-4), 58.7 (OMe), 54.5 (CO_2Me).

§ *Selected NMR data for* **5**. ^1H NMR (600 MHz, D_2O) δ: 5.19 (s, 1H, H-1), 5.07–5.05 (m, 1H, H-3), 5.06 (s, 1H, H-2), 4.97 (d, 1H, H-5, $J_{5,4}$ 8.0 Hz), 4.70 (dd, 1H, $J_{4,5}$ 8.0 Hz, $J_{4,3}$ 5.5 Hz), 3.84 (s, 3H, CO_2Me), 3.42 (s, 3H, OMe). ^{13}C NMR (125 MHz, D_2O) δ: 108.0 (C-1), 82.8 (C-2), 80.1 (C-4), 78.3 (C-3), 73.9 (C-5), 56.4 (OMe), 53.9 (CO_2Me).

¶ *Selected NMR data for* **6**. ^1H NMR (600 MHz, D_2O) δ: 5.95 (s, 1H, H-1), 5.24 (s, 1H, H-2), 5.10 (d, 1H, H-3, $J_{3,4}$ 5.0 Hz), 5.03 (d, 1H, H-5, $J_{5,4}$ 8.2 Hz), 4.72 (dd, 1H, H-4, $J_{4,5}$ 8.2 Hz, $J_{4,3}$ 5.0 Hz). ^{13}C NMR (125 MHz, D_2O) δ: 103.6 (C-1), 83.0 (C-2), 81.6 (C-4), 77.5 (C-3), 73.7 (C-5).

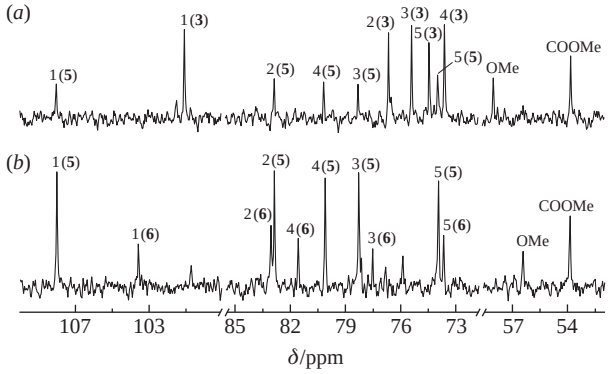


Figure 1 ^{13}C NMR spectra of β-glucuronopyranoside **1** per-O-sulfation products formed in (*a*) 45 min and (*b*) 24 h.

sulfated β-furanosides[8] (*e.g.*, C-1, 108.0 ppm; C-2, 82.8 ppm; C-4, 80.1 ppm) and ^{1}H NMR spectrum contained the right coupling constants. Moreover, the HMBC spectrum of product **5** exhibited a correlation peak between C-4/H-1 clearly evidencing the presence of the furanoside ring. The strong NOE between H-3 and H-4 also confirmed the structure of product **5** (see Figure 2). β-Configuration and the presence of anomeric sulfate in **6** was confirmed by singlet forms of H-1 and H-2 signals in ^{1}H NMR spectrum and down-field shift of H-1 signal (5.19 → 5.95 ppm) if compared with the spectrum of methyl glycoside **5**.

Surprisingly, the treatment of α-methyl pyranoside **2**[9] (entry 3) produced in 45 min the mixture of the product of its per-O-sulfation **4**†† together with traces of β-D-glucuronofuranoside **5** but not of its expected α-isomer. The prolongation of the reaction to 24 h favored to further conversion **4** → **5**, however, it proceeded slowly to give only 17% of β-furanoside **5**.

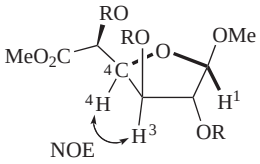


Figure 2 NMR data confirming β-glucuronofuranoside structure of product **5** (R = SO_3^-).

†† *Selected NMR data for* **4**. ^{1}H NMR (600 MHz, D_2O) δ: 5.23 (d, 1H, H-1, $J_{1,2}$ 3.3 Hz), 4.73 (dd, 1H, $J_{3,2}$ 8.6 Hz, $J_{3,4}$ 6.9 Hz), 4.58–4.54 (m, 2H, H-4, H-5), 4.46 (dd, 1H, H-2, $J_{2,3}$ 8.6 Hz, $J_{2,1}$ 3.3 Hz), 3.80 (s, 3H, CO_2Me), 3.50 (s, 3H, OMe). ^{13}C NMR (125 MHz, D_2O) δ: 97.5 (C-1), 75.1 (C-3), 74.6 (C-4), 74.4 (C-2), 71.2 (C-5), 56.9 (OMe), 54.0 (CO_2*Me*).

In conclusion, the study of capability of glucuronopyranosides to undergo PIF rearrangement under acid-promoted O-sulfation conditions showed that their reactivity was higher than that of glucopyranosides.[8] Moreover, formation of β-furanoside **5** from α-glucuronopyranoside **4** was observed, while the corresponding α-glucopyranoside did not rearrange at all under used conditions.[8] The side process of aglycon cleavage resulting in formation of glycosyl sulfate **6** also occurred intensively along with PIF rearrangement in the case of glucuronide **1**. We assume that the observed higher reactivity of glucuronides can be related to the presence of a COOMe group at C-5. The results of quantum calculations of reaction pathways in above described processes will be published elsewhere.

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References

1 V. B. Krylov, D. A. Argunov, D. Z. Vinnitskiy, S. A. Verkhnyatskaya, A. G. Gerbst, N. E. Ustyuzhanina, A. S. Dmitrenok, J. Huebner, O. Holst, H.-C. Siebert and N. E. Nifantiev, *Chem. Eur. J.*, 2014, **20**, 16516.
2 V. B. Krylov, A. G. Gerbst, D. A. Argunov, A. S. Dmitrenok, A. S. Shashkov, Z. Kaczynski, J. Huebner, O. Holst and N. E. Nifantiev, *Chem. Eur. J.*, 2015, **21**, 1749.
3 D. A. Argunov, V. B. Krylov and N. E. Nifantiev, *Org. Biomol. Chem.*, 2015, **13**, 3255.
4 D. Z. Vinnitskiy, V. B. Krylov, N. E. Ustyuzhanina, A. S. Dmitrenok and N. E. Nifantiev, *Org. Biomol. Chem*., 2016, **14**, 598.
5 V. B. Krylov, D. A. Argunov and N. E. Nifantiev, *Mendeleev Commun.*, 2014, **24**, 336.
6 V. B. Krylov, Z. M. Kaskova, D. Z. Vinnitskiy, N. E. Ustyuzhanina, A. A. Grachev, A. O. Chizhov and N. E. Nifantiev, *Carbohydr. Res*., 2011, **346**, 540.
7 V. B. Krylov, N. E. Ustyuzhanina, A. A. Grachev and N. E. Nifantiev, *Tetrahedron Lett.*, 2008, **49**, 5877.
8 V. B. Krylov, D. A. Argunov, D. Z. Vinnitskiy, A. G. Gerbst, N. E. Ustyuzhanina, A. S. Dmitrenok and N. E. Nifantiev, *Synlett*., 2016, **27**, 1659.
9 F. C. Baines, P. M. Collins and F. Farnia, *Carbohydr. Res*., 1985, **136**, 27.

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