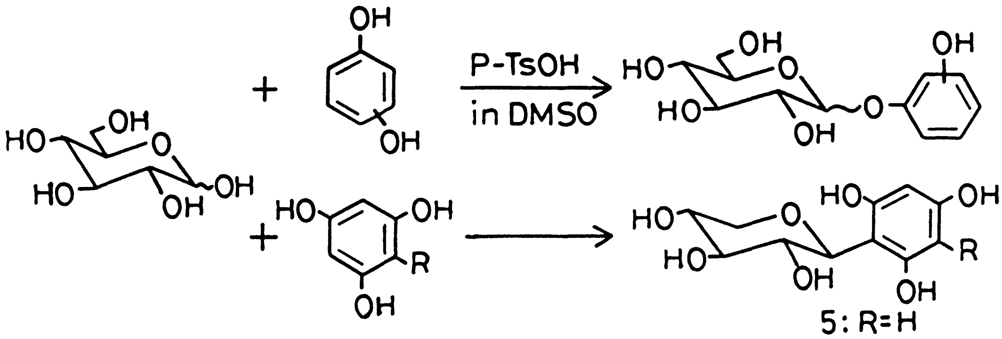
CHEMISTRY LETTERS, pp. 1487-1488, 1983.

# DIRECT CONDENSATION OF POLYHYDRIC PHENOLS WITH GLUCOSE

Jun-ichi ONODERA,* Mitsuru TAKANO, Yuji KISHI,
Noriko YOKOYAMA, and Ryosuke ISHIDA
Department of Applied Chemistry, Faculty of Engineering,
Yamagata University, Yonezawa 992

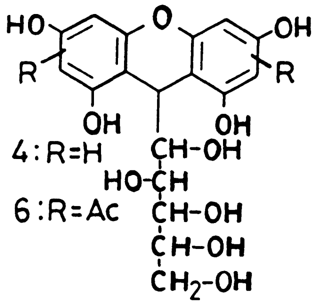
Acid-catalyzed direct condensation reaction of polyhydric phenols with free glucose in DMSO gave O-α-D-glucopyranoside in preference to its β-anomer; however, phloroglucinol and phloroacetophenone gave C-β-D-glucopyranoside instead.

Recently, various glucosidation methods have been reported. In these reactions, glucose which had some or all of its hydroxyl groups protected with acetyl or benzyl groups was used as a glucosidating agent. Few reports are available on the direct condensation of glucose with phenols; therefore, we investigated the direct condensation of glucose with phenols, specially with hydroquinone (1), phloroglucinol (2) and phloroacetophenone (3).



5: R=H

7: R=Ac



4:R=H

6:R=Ac

Glucose, p-toluenesulfonic acid and 1 were stirred in DMSO at 100°C for 10 h. The reaction mixture was poured into diethyl ether-benzene and the resulting viscous oil was chromatographed on a column of silica gel with ethyl acetate-ethanol (10:1-5:2) as the eluent. Hydroquinone-O-α-D-G (α-arbutin, G expresses glucopyranosyl group) and hydroquinone-O-β-D-G (β-arbutin) were obtained in 11 and 4% yield, respectively. This condensation also proceeded with the strongly acidic cation exchange resin or methanesulfonic acid and the addition of $ZnCl_2$ slightly enhanced the formation of the α-anomer. Other dihydric phenols also gave O-α-D-G in preference to its β-anomer (Table 1).

The condensation of trihydric phenols was as follows. Pyrogallol gave a mixture of 1- and 2-O-glucosides with a formation ratio of 6:4, both of which were composed of 70% of the α-isomer and 30% of β-isomer. Phloroglucinol under the

Table 1. Condensation of polyhydric phenols with glucose

| Run | Phenols | Reaction conditions[a)] | | | Yield/% | Isomer distribution[b)] | | |
|---|---|---|---|---|---|---|---|---|
| | | Solvent | Temp/ C | Time/h | | α | β | C[c)] |
| 1 | **1** | DMSO | 100 | 10 | 15 | 75 | 25 | - |
| 2 | Catechol | DMSO | 100 | 10 | 11 | 95 | 5 | - |
| 3 | Resorcinol | DMSO | 100 | 8 | 11 | 65 | 25 | 10 |
| 4 | Pyrogallol | DMSO | 100 | 8 | 10 | 70 | 30 | - |
| 5 | **2** | DMSO | 75 | 10 | 11 | - | - | 100 |
| 6 | **3** | DMF | 120 | 10 | 10 | - | - | 100 |

a) Solvent 5 ml, phenols 5 g and glucose 2 g were used in each reactions.
b) Calculated from the amount of acetates which were isolated after acetylation and chromatography.
c) C-glucosidation.

same reaction conditions gave **4**[1)] as the main product but at a reaction temperature of below 80°C, phloroglucinol-C-β-D-G (**5**), mp 158-160°C (heptaacetate mp 147-149°C), was produced in 11% yield. On the other hand, **3** under the same reaction conditions as above gave an yellow powder whose structure was considered to be **6** from $^1$H-NMR and mass spectra of its acetate. This undesired reaction could be suppressed when the condensation was carried out with DMF instead of DMSO as the solvent at 120°C; phloroacetophenone-C-β-D-G (**7**), mp 167-169°C (heptaacetate mp 193-194°C), was obtained in about 10% yield. Since phloroacetophenone-2-O-α-D-G (**8**) and its β-anomer (**9**) prepared through the known route[2)] immediately formed unidentified condensation products by treatment under the above reaction conditions, O-glucosides of **3** would not be obtained because of their instability. C-α-D-G of **3** could not be formed because of its steric hindrance.

Furthermore, this condensation reaction of **3** with D-xylose and L-arabinose was investigated and the corresponding C-β-D-xylopyranoside, mp 185-187°C, and C-α-L-arabinopyranoside, mp 138-141°C, were obtained.

In view of ready separation of the glucosides from the reaction mixture, the direct condensation reaction would provide a convenient mean for its preparation albeit the low yield and may be applicable also for the synthesis of C-glucosyl flavonoids.

The authors are sincerely grateful to Dr. Yutaka Fujise of Tohoku University for his helpful discussions and measurment of NMR spectra.

References

1) The structure of this compound was considered to be 4 by the comparison of the $^1$H-NMR spectrum of its acetate with that of 1,1-diphenyl-1-desoxy-D-glucitol ( C. D. Hurd and W. A. Bonner, J. Am. Chem. Soc., 67, 1664 (1945) ).
2) T. Kariyone, M. Takahashi, and K. Takahashi, J. Pharm. Soc. Jpn., 72, 13 (1952); R. B. Conrow and S. Bernstein, J. Org. Chem., 36, 863 (1971).

( Received July 5, 1983 )