Boron Trifluoride-Catalyzed Rearrangement of 2-Aryloxytetrahydropyrans: A New Entry to C-Arylglycosidation

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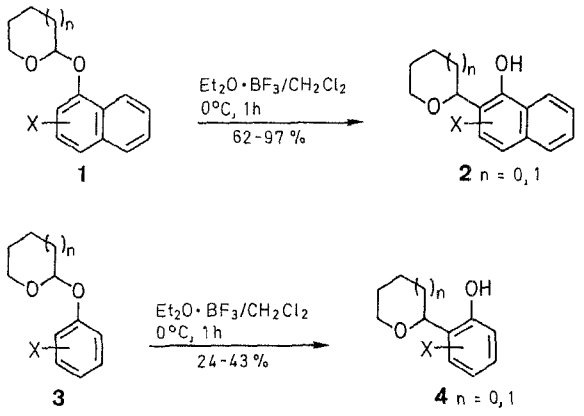
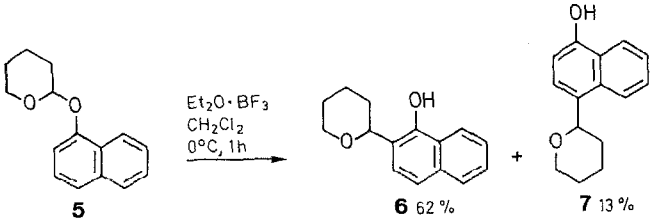
Treatment of 2-aryloxytetrahydropyrans with boron trifluoride afforded 2-aryltetrahydropyrans via rearrangement in good yield. Aryl *O*-glycopyranosides were converted into the corresponding *C*-glycopyranosides by the same procedure.

Introduction of a carbohydrate residue in an aromatic nucleus has become an important method for the synthesis of naturally occurring *C*-glycosides.[1,2] During the course of our studies on the total synthesis of lactoquinomycin,[3] we sought to develop new methodologies for *C*-arylglycosidation in which a *C*-glycosidic bond would be efficiently introduced at the *ortho*-position of 1-naphthol. We now wish to report that the 2-tetrahydropyranyl (THP) moiety of 2-aryloxytetrahydropyrans **1** and **3** (n = 1) rearranged in the desired sense on treatment with boron trifluoride and yielded the corresponding 2-aryltetrahydropyrans **2** and **4** (n = 1), respectively. Moreover, this methodology, which is reminiscent of the Fries rearrangement, is well suited for the conversion of *O*-arylglycopyranosides to the corresponding *C*-arylglycopyranosides.



1 **3**

2-(1-Naphthyloxy)tetrahydropyran (**5**),[4] prepared by the procedure of Grieco et al.[5] in quantitative yield, was treated with a catalytic amount of boron trifluoride etherate in dichloromethane at 0 °C to afford 2-(1-hydroxy-2-naphthyl)tetrahydropyran (**6**). The regioisomer **7** was also isolated as a minor product. ^{1}H-NMR spectroscopy was useful in distinguishing between the regioisomers; the phenolic proton for **6** was observed at lower field (δ = 9.08 as a sharp singlet) due to intramolecular hydrogen bonding, while that for **7** was observed at higher field (δ = 6.00 as a broad singlet).



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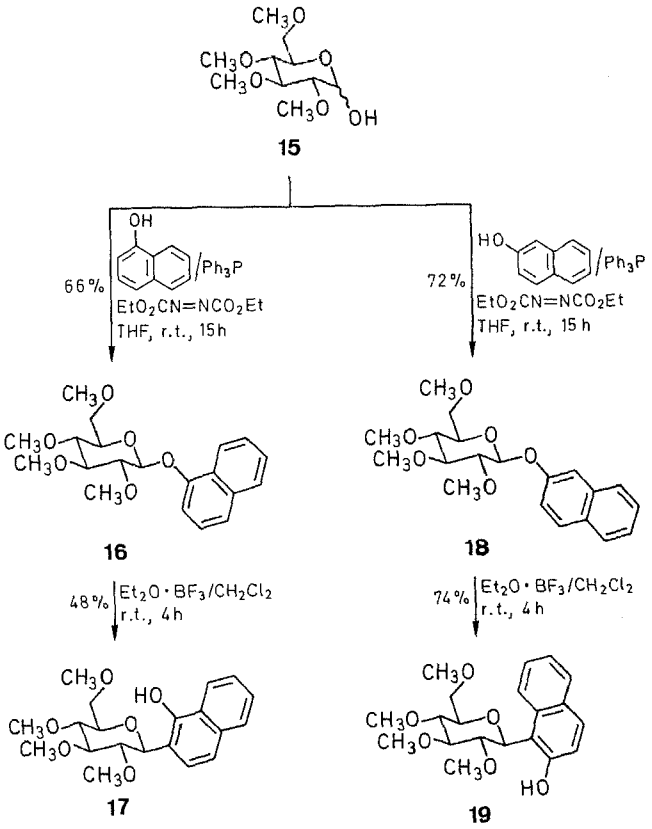
We investigated additional examples of this reaction including aryl 2-tetrahydrofuranyl (THF) ethers **1** and **3** (n = o),[6] and the products obtained, under the same reaction conditions, are listed in Table. Although THP and THF ethers of phenols did not undergo rearrangement, the ethers of phenols with an electron-donating group at the *meta*-position were converted into rearranged products **12–14** in modest yield. Thus, the reaction reported here is a simple and mild method for introduction of THP and THF groups *ortho* to the hydroxyl group of naphthols and activated phenols.

We applied this method to the transformation of *O*-glycopyranosides to *C*-glycopyranosides. *O*-Glycoside **16** was prepared from 2,3,4,6-tetra-*O*-methyl-D-glucose (**15**)[7] and 1-naphthol by Mitsunobu's method,[8] and was treated with an excess of boron trifluoride etherate[9] at room temperature to afford the corresponding *C*-glycoside **17**. The same procedure was applied to 2-naphthol to give the *C*-glycoside **19**.

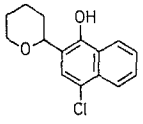
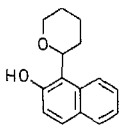
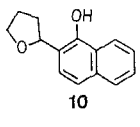
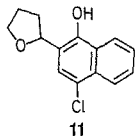
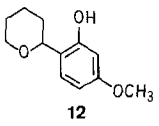
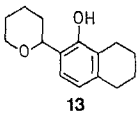
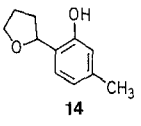


Although it is known that reactions of glycals,[10] *O*-glycosyl trichloroacetimidates,[1] and pyridyl thioglycosides[2] with alkoxy-substituted benzene derivatives, in the presence of Lewis acids, yield *C*-arylglycosides, the new method reported here provides an efficient and mild method for *C*-arylglycosidation.

2-Aryltetrahydropyrans 2 and 2-Aryltetrahydrofurans 4; General Procedure:

Preparation of Aryl 2-THP (or 2-THF) Ethers **1** *and* **3**: A solution of the naphthol or phenol, (1.4 mmol) and dihydropyran or dihydrofuran (2.8 mmol, 2 equiv) in CH_2Cl_2 (5 mL) containing pyridinium *p*-toluenesulfonate[5] (0.07 mmol, 0.05 equiv) is stirred for 1 h at room temperature. The solution is diluted with ether (15 mL), washed with water (2 × 10 mL), and dried ($MgSO_4$). After evaporation of the solvents, the crude product is purified by column chromatography [silica gel (5 g; 70–230 mesh), elution gradient: 1 → 5 % EtOAc in *n*-hexane] to give the aryl 2-THP (or 2-THF) ether in quantitative yield.

Table. 2-Aryltetrahydropyrans and 2-Aryltetrahydrofurans Prepared

Product	Yield[a]	mp (°C) bp (°C)/ mbar[b]	Molecular Formula[c]	IR[d] ν_{OH} (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[e] δ, J(Hz)	MS (20 eV)[f] m/z (%)
6	62	140–150/1.3	$C_{15}H_{16}O_2$ (228.3)	3320	1.60–2.05 (m, 6H); 3.60–3.75 (m, 1H); 4.20–4.30 (m, 1H); 3.68–4.75 (m, 1H); 7.03 (d, 1H, J = 8.55); 7.31 (d, 1H, J = 8.55); 7.40–7.50 (m, 2H); 7.70–7.77 (m, 1H); 8.20–8.30 (m, 1H); 9.10 (s, 1H)	228 (M^+, 100); 210 (24); 181 (36); 157 (35); 144 (42); 71 (38)
7	13	146–147	$C_{15}H_{16}O_2$ (228.3)	3190	1.40–2.10 (m, 6H); 3.60–3.90 (m, 1H); 4.10–4.35 (m, 1H); 4.85–5.05 (m, 1H); 6.39 (d, 1H, J = 7.0); 6.00 (br s, 1H); 7.24 (d, 1H, J = 7.0); 7.35–7.60 (m, 2H); 7.90–8.20 (m, 2H)	228 (M^+, 63); 172 (28); 171 (28); 144 (35); 61 (28); 43 (100)
 **8**	65	135–140/1.3	$C_{15}H_{15}ClO_2$ (262.7)	3300	1.40–1.95 (m, 6H); 3.35–3.70 (m, 1H); 4.00–4.25 (m, 1H); 4.40–4.60 (m, 1H); 7.07 (s, 1H); 7.40–7.60 (m, 2H); 8.00–8.35 (m, 2H); 9.10 (s, 1H)	264 (M^+ + 2, 35); 262 (M^+, 100); 244 (18); 215 (37); 178 (73); 115 (42)
 **9**	97	110–111	$C_{15}H_{16}O_2$ (228.3)	3230	1.50–2.05 (m, 6H); 3.55–3.85 (m, 1H); 4.20–4.40 (m, 1H); 5.20–5.40 (m, 1H); 7.10 (d, 1H, J = 8.8); 7.20–7.80 (m, 4H); 7.66 (d, 1H, J = 8.8); 9.22 (s, 1H)	228 (M^+, 74); 210 (23); 183 (40); 181 (71); 169 (100); 157 (66); 71 (50)
 **10**	83	46–48	$C_{14}H_{14}O_2$ (214.3)	3230	1.75–2.40 (m, 4H); 3.85–4.25 (m, 2H); 5.00–5.20 (m, 1H); 6.99 (d, 1H, J = 8.5); 7.20–7.55 (m, 3H); 7.60–7.80 (m, 1H); 8.20–8.40 (m, 1H); 9.50 (s, 1H)	214 (M^+, 100); 183 (85); 181 (30); 155 (20)
 **11**	76	120–125/1.3	$C_{14}H_{13}ClO_2$ (248.7)	3250	1.80–2.40 (m, 4H); 3.80–4.20 (m, 2H); 4.95–5.15 (m, 1H); 7.07 (s, 1H); 7.40–7.60 (m, 2H); 8.00–8.35 (m, 2H); 9.51 (s, 1H)	250 (M^+ + 2, 36); 248 (M^+, 100); 216 (54); 215 (57); 212 (50); 182 (46)
 **12**	24	76–77	$C_{12}H_{16}O_3$ (208.3)	3310	1.45–2.00 (m, 6H); 3.40–3.70 (m, 1H); 3.73 (s, 3H); 4.00–4.20 (m, 1H); 4.35–4.55 (m, 1H); 6.35 (dd, 1H, J = 7.9, 2.5); 6.40 (d, 1H, J = 2.5); 6.84 (d, 1H, J = 7.9); 8.30 (s, 1H)	208 (M^+, 100); 190 (18); 163 (53); 151 (34); 137 (81)
 **13**	43	180–185/1.3	$C_{15}H_{20}O_2$ (232.3)	3360	1.50–2.00 (m, 10H); 2.55–2.80 (m, 4H); 3.40–3.70 (m, 1H); 4.00–4.25 (m, 1H); 4.40–4.55 (m, 1H); 6.56 (d, 1H, J = 7.1); 6.71 (d, 1H, J = 7.1); 8.35 (s, 1H)	232 (M^+, 100); 214 (62); 187 (30); 185 (23); 161 (46)
 **14**	29	85–90/1.3	$C_{11}H_{14}O_2$ (178.2)	3300	1.70–2.20 (m, 4H); 2.28 (s, 3H); 3.75–4.05 (m, 2H); 5.65–5.75 (m, 1H); 6.65–7.10 (m, 4H)	178 (M^+, 18); 108 (100); 71 (68); 43 (24)

[a] Yield of isolated product based on starting naphthol or phenol.
[b] Microdistillation, bath temperature is given.
[c] Satisfactory microanalyses obtained: C ±0.28, H ±0.17.
[d] Recorded on a Hitachi 215 Infrared spectrophotometer. IR spectra of oil samples (**6**, **8**, **11**, **13**, and **14**) were recorded as film. Those of solid samples (**7**, **9**, **10**, and **12**) were recorded as KBr pellet.
[e] Obtained on a JEOL FX90A spectrometer.
[f] Recorded on a Hitachi RMU-6MG spectrometer.

Rearrangement of Aryl 2-THP (or 2-THF) Ethers **1** *and* **3** *to 2-Aryltetrahydropyrans* **2** *and 2-Aryltetrahydrofurans* **4**, *Respectively:* A solution of the ether **1** or **3** (0.5 mmol) in CH_2Cl_2 (0.5 mL) is added to a stirred solution of $Et_2O \cdot BF_3$ (6.2 µL, 0.05 mmol, 0.1 equiv) in CH_2Cl_2 (5 mL) at 0 °C over 3 min. After stirring at the same temperature for 1 h, the starting material has completely disappeared (monitored by TLC). Water (1 mL) is added, and the mixture is washed with brine (2 × 5 mL). The organic layer is dried ($MgSO_4$) and concentrated, and the crude product is purified by column chromatography [silica gel (10 g; 70–230 mesh), elution gradient: 1 → 5% EtOAc in *n*-hexane] to give the pure product. Typical examples are given in the Table.

β-1-(1-Naphthyloxy)-2,3,4,6-tetra-*O*-methyl-D-glucopyranose (16): To a stirred solution of 2,3,4,6-tetra-*O*-methyl-D-glucopyranose[7] (**15**; 492 mg, 2.08 mmol) and 1-naphthol (200 mg, 1.39 mmol) in THF (6 mL) at 0 °C are added Ph_3P (544 mg, 2.08 mmol) and a solution of diethyl azodicarboxylate (362 mg, 2.08 mmol) in THF (2 mL). The mixture is stirred at room temperature for 15 h. The solution is concentrated under reduced pressure, and the product is isolated by column chromatography [silica gel (60 g; 70–230 mesh), elution gradient: 1 → 10%, EtOAc in *n*-hexane] to afford **16**; yield: 239 mg (66%); mp 94–95 °C (CH_3OH); $[\alpha]_D^{20}$ – 101° (c = 1.25, $CHCl_3$).

$C_{20}H_{26}O_6$	calc.	C 66.28	H 7.23
(362.4)	found	66.35	7.24

MS (20 eV): m/z = 362 (M^+, 9); 218 (99); 187 (100).

^{1}H-NMR ($CDCl_3$)[11]: δ = 3.38 (s, 3 H); 3.58 (s, 3 H); 3.70 (s, 3 H); 3.76 (s, 3 H); 3.30–3.76 (m, 6 H); 5.05 (d, 1 H, J = 7.8 Hz); 7.05 (d, 1 H, J = 7.8 Hz); 7.37 (t, 1 H, J = 7.8 Hz); 7.40–7.55 (m, 3 H); 7.75–7.85 (m, 1 H); 8.25–8.30 (m, 1 H).

β-1-Deoxy-1-(1-hydroxy-2-naphthyl)-2,3,4,6-tetra-*O*-methyl-D-glucopyranose (17):

To a stirred solution of **16** (115 mg, 0.318 mmol) in CH_2Cl_2 (5 mL) at 0°C is added $Et_2O \cdot BF_3$ (122 µL, 0.954 mmol, 3 equiv) dropwise, and the solution is stirred at room temperature for 4 h. After the usual work-up (as described in the general procedure), *C*-glycoside **17** is obtained as a colorless oil; yield: 55 mg (48%); $[\alpha]_D^{20}$ – 9.5° (c = 1.05, $CHCl_3$).

HRMS (70 eV): calc. for $C_{20}H_{26}O_6$: m/z = 362.1730; found 362.1758.

MS (20 eV): m/z = 362 (M^+, 77) 228 (35); 200 (48); 187 (100).

IR (film): ν = 3350 cm^{-1} (OH).

^{1}H-NMR ($CDCl_3$): δ = 3.04 (s, 3 H); 3.45 (s, 3 H); 3.61 (s, 3 H); 3.68 (s, 3 H); 3.25–3.80 (m, 6 H); 4.46 (d, 1 H, J = 9.3 Hz); 7.55 (d, 1 H, J = 8.3 Hz); 7.37 (d, 1 H, J = 8.3 Hz); 7.40–7.55 (m, 2 H); 7.70–7.85 (m, 1 H); 8.20–8.30 (m, 1 H); 8.36 (s, 1 H).

β-1-Deoxy-1-(2-hydroxy-1-naphthyl)-2,3,4,6-tetra-*O*-methyl-D-glucopyranose (19):

The preparation of *O*-glycoside **18**, followed by the conversion into *C*-glycoside **19**, is achieved using the same procedure as described above in 72% and 74% yield, respectively. β-1-(2-Naphthyloxy)-2,3,4,6-tetra-*O*-methyl-D-glucopyranose **(18)**: mp 93–94°C (CH_3OH); $[\alpha]_D^{20}$ – 62° (c = 1.28, $CHCl_3$).

$C_{20}H_{26}O_6$	calc.	C 66.28	H 7.23
(362.4)	found	66.42	7.23

MS (20 eV): m/z = 362 (M^+, 12.5); 218 (100); 187 (75); 112 (75).

^{1}H-NMR ($CDCl_3$)[11]: δ = 3.40 (s, 3 H); 3.57 (s, 3 H); 3.68 (s, 3 H); 3.70 (s, 3 H); 3.25–3.75 (m, 6 H); 4.98 (d, 1 H, J = 7.3 Hz); 7.20–7.50 (m, 4 H); 7.70–7.80 (m, 3 H).

C-Glycoside **19**: $[\alpha]_D^{20}$ + 89.8° (c = 1.76, $CHCl_3$).

HRMS (70 eV): calc. for $C_{20}H_{26}O_6$: m/z = 362.1730; found 362.1765.

MS (20 eV): m/z = 362 (M^+, 100); 330 (11); 255 (26); 188 (30).

IR (film): ν = 3300 cm^{-1} (OH).

^{1}H-NMR ($CDCl_3$)[11]: δ = 2.71 (s, 3 H); 3.41 (s, 3 H); 3.62 (s, 3 H); 3.68 (s, 3 H); 3.35–3.70 (m, 6 H); 5.24 (d, 1 H, J = 9.5 Hz); 7.13 (d, 1 H, J = 8.8 Hz); 7.30 (t, 1 H, J = 8.8 Hz); 7.44 (t, 1 H, J = 8.8 Hz); 7.72 (d, 1 H, J = 8.8 Hz); 7.97 (d, 1 H, J = 8.8 Hz); 8.51 (s, 1 H).

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(1) Schmidt, R. R., Hoffmann, M. *Tetrahedron Lett.* **1982**, *23*, 409.
(2) Stewart, A. O., Williams, R. M. *J. Am. Chem. Soc.* **1985**, *107*, 4289.
(3) Okabe, T., Nomoto, K., Funabashi, H., Okuda, S., Suzuki, H., Tanaka, N. *J. Antibiot.* **1985**, *38*, 1327.
(4) Auterhoff, H., Egle, D. *Arch. Pharm. (Weinheim, Ger.)* **1970**, *303*, 688.
(5) Miyashita, M., Yoshikoshi, A., Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.
(6) There is a report of the synthesis of 2-aryltetrahydrofuran, which is produced by the reaction of *p*-hydroquinones and dihydrofuran in the presence of (1*R*)-camphor-10-sulfonic acid in toluene at 60°C:
Shiraishi, M., Terao, S. *J. Chem. Soc. Perkin Trans. 1* **1983**, 1591.
(7) West, E. S., Holden, R. S. *Org. Synth. Coll. Vol. III*, **1955**, 800.
(8) Mitsunobu, O. *Synthesis* **1981**, 1.
(9) When *O*-glycosides **16** and **18** were treated with 0.5–1 equivalent of $Et_2O \cdot BF_3$, the reaction proceeded very slowly.
(10) Grynkiewicz, G., Zamojski, A. *Z. Naturforsch.* **1980**, *35b*, 1024.
(11) The spectral data were obtained on a JEOL FX 270 spectrometer.