Generation of Alkoxycarbenium Ion Pools from Thioacetals and Applications to Glycosylation Chemistry

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Materials. Dichloromethane was washed with water, distilled from P₂O₅, redistilled from dried K₂CO₃ to remove a trace amount of acid, and stored over molecular sieves 4A. α -Phenylthio ethers **1**,¹ **5**,² and **6**² were prepared according to the procedures in the literatures. Thioglycosides **9**^{3,14,15} and **10**^{14,16} were prepared according to the literature. Glycosyl acceptors **19**³, **22**⁴ were prepared as reported. Compounds **4**,¹³ **7**,¹³ and **8**,¹³ glycosides **11**,⁷ **12**,⁵ **13**,¹⁰ **14**,¹⁰ **15**,⁸ **16**,⁶ **17**,⁹ **18**,⁶ and **20**^{9,11} obtained by the present method were characterized by comparison of their ¹H NMR spectra with those of authentic samples reported in the literature.

Generation of Alkoxycarbenium Ions. Typical Procedure. The anodic oxidation was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7, ca. 320 mg, dried at 250 °C/1 mmHg for 1 h before use) and a platinum plate cathode (40 mm x 20 mm). In the anodic chamber was placed a solution of α -phenylthioether (0.4 mmol) in 0.3 M Bu₄NBF₄/CH₂Cl₂ (8.0 mL). In the cathodic chamber were placed 0.3 M Bu₄NBF₄/CH₂Cl₂ (8.0 mL) and trifluoromethanesulfonic acid (150.1 mg, 0.4 mmol). The constant current electrolysis (8 mA) was carried out at -78 °C with magnetic stirring until 2.5 F/mol of electricity was consumed.

NMR Analysis of Alkoxycarbenium Ion (2). ¹H and ¹³C NMR spectra were recorded in CD₂Cl₂ on a JEOL A-500 spectrometer. Chemical shifts are reported using methylene signals at δ 5.32 (¹H NMR) and δ 53.80 (¹³C NMR) as standards. The anodic oxidation was carried out in a divided cell equipped with a carbon felt anode and a platinum plate cathode. In the anodic chamber were placed a solution of 1-methoxy-1-phenylthiononane (**1**) (40.3 mg, 0.175 mmol) in 3.5 mL of 0.3 M Bu₄NBF₄/CD₂Cl₂. In the cathodic chamber were placed trifluoromethanesulfonic acid (29.7 mg, 0.198 mmol) and 0.3 M Bu₄NBF₄/CD₂Cl₂ (3.5 mL). The constant current electrolysis (3.5 mA) was carried out at -78 °C with magnetic stirring. After 1.4 F/mol of electricity was consumed, the reaction mixture of the anodic chamber was transferred to a 5 mm ϕ NMR tube with a septum cap under Ar atmosphere at -78 °C. The NMR measurement was carried out at -80 °C: ¹H NMR (500 MHz, CD₂Cl₂, selected) δ 4.95 (s, 3H), 9.55 (s, 1H); ¹³C NMR (125.65 MHz, CD₂Cl₂, selected) δ 40.7 (CH₃OCH₂), 76.1 (CH₃OCH), 230.9 (CH₃OCH). In the NMR spectra the other signals could not be assigned because of overlap of the signals of Bu₄NBF₄ used as electrolyte.

The signals due to the thiophenyl group leaving from **1** were also observed: ¹H NMR δ 7.2-8.0 (m); ¹³C NMR δ 116.5, 119.0, 124.1, 130.3.

4-Methoxy-dodec-1-ene (4). A Typical Procedure of Reaction between Alkoxycarbenium Ion and Carbon Nucleophile. The electrolysis of **1** (91.6 mg, 0.397 mmol) was carried out as described above. To the “cation pool” thus generated in the anodic chamber, was added allyltrimethylsilane (93.9 mg, 0.822 mmol) at -78 °C and the reaction mixture was stirred for 10 min. The solvent was removed under reduced pressure and the residue was quickly filtered

through a short column (2 x 3 cm) of silica gel to remove Bu₄NBF₄. The silica gel was washed with ether (150 mL). The GC analysis of the combined filtrate indicated that **4** was formed in 80% yield (GC *t*_R 6.3 min, column, OV-1; 0.25 mm x 25 m; initial oven temperature, 100 °C; rate of temperature increase, 10 °C/min): TLC *R*_f 0.38 (hexane/EtOAc 10:1); ¹H NMR (300 MHz, CDCl₃) δ 0.88 (t, *J* = 6.6 Hz, 3H), 1.16-1.40 (m, 12H), 1.40-1.53 (m, 2H), 2.24-2.28 (m, 2H), 3.16-3.24 (m, 2H), 3.34 (s, 3H), 5.03-5.19 (m, 2H), 5.75-5.89 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 14.0, 22.6, 25.2, 29.2, 29.5, 29.7, 31.8, 33.3, 37.7, 56.5, 80.5, 116.7, 135.1; IR (neat) 2928, 1100, 912 cm⁻¹; LRMS (EI) *m/e* 197 (M⁺-H), 157 (M⁺-CH₂CH=CH₂); HRMS (EI) calcd for C₁₃H₂₅O (M⁺-H): 197.1905, found: 197.1915; Anal. Calcd for C₁₃H₂₆O: C, 78.72; H, 13.21. Found: C, 78.79; H, 13.13.

Glycosylation by Low-Temperature Electrolysis in the Absence of Glycosyl Acceptors (One-Pot Procedure). The anodic oxidation was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7, ca. 320 mg, dried at 250 °C/1 mmHg for 1 h before use) and a platinum plate cathode (40 mm x 20 mm). In the anodic chamber was placed a solution of **10** (65.7 mg, 0.2 mmol) in 0.1 M Bu₄NClO₄/CH₂Cl₂ (12.0 mL). In the cathodic chamber were placed 0.1 M Bu₄NClO₄/CH₂Cl₂ (12.0 mL) and trifluoromethanesulfonic acid (150.1 mg, 0.4 mmol). The constant current electrolysis (4 mA) was carried out at -78 °C with magnetic stirring until 1.25 F/mol of electricity was consumed. To the solution thus obtained in the anodic chamber, was added methanol (32.0 mg, 1.0 mmol). The reaction mixture was stirred for 1-2 min at -78 °C. After triethylamine (40.5 mg, 0.4 mmol) was added, the reaction mixture was warmed to room temperature. The solvent was removed under reduced pressure and the residue was quickly filtered through a short column (2 x 10 cm) of silica gel to remove Bu₄NClO₄. The silica gel was washed with ether (150 mL). The combined filtrate was purified with flash chromatography (hexane/EtOAc 3:1 to 1:1) to give **12α** and **12β** (total 33.7 mg, 67%, diastereomer ratio was α/β = 15:85).

Glycosylation by Low-Temperature Electrolysis in the Presence of Glycosyl Acceptors: (In-Situ Procedure). The anodic oxidation was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7, ca. 320 mg, dried at 250 °C/1 mmHg for 1 h before use) and a platinum plate cathode (40 mm x 20 mm). In the anodic chamber was placed a solution of **10** (65.9 mg, 0.201 mmol) and methanol (63.8 mg, 1.991 mmol) in 0.1 M Bu₄NTEPB/CH₂Cl₂ (12.0 mL). In the cathodic chamber were placed 0.1 M Bu₄TEPB/CH₂Cl₂ (12.0 mL) and trifluoromethanesulfonic acid (80.8 mg, 0.538 mmol). The constant current electrolysis (4 mA) was carried out at -78 °C with magnetic stirring until 1.25 F/mol of electricity was consumed. After addition of triethylamine (48.2 mg, 0.476 mmol), the reaction mixture was warmed to room temperature. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc (1 mL), and then hexane (10 mL) was added. Bu₄TEPB precipitated. After the solution phase was separated by decantation, the solid materials were dissolved in EtOAc (1 mL) and hexane (10 mL) was added. Bu₄TEPB precipitated. After the solution phase was separated by decantation, the solid materials were dissolved in EtOAc (1 mL) and hexane (10 mL) was added. Bu₄TEPB precipitated (three times in total). The solution phase was separated by decantation. The solution phase was combined and the solvent was removed with a rotary evaporator under reduced pressure to give the crude product. Purified with flash chromatography (hexane/EtOAc 3:1 to 1:1) to give **12α** and **12β** (total 45.3 mg, 90%, diastereomer ratio was α/β = 63:37).

Methyl-6-*O*-(2,3,4,6-tetra-*O*-methyl- α -D-glucopyranosyl)-2,3,4-tri-*O*-benzyl- α -D-glucopyranoside (21 α).¹² Prepared from **10** (65.7 mg, 0.200 mmol) and **19** (914.8 mg, 1.969 mmol) in the in-situ procedure, and purified with flash chromatography (hexane/EtOAc 5:3 to 1:1) (111.3 mg, 82%, α : β = 67:33). TLC R_f 0.34 (hexane/EtOAc 1:1); ¹H NMR (400 MHz, CDCl₃) δ 3.16 (dd, J = 3.6, 9.6 Hz, 1H), 3.19 (dd, J = 8.8, 10.0 Hz, 1H), 3.37 (s, 3H), 3.38 (s, 3H), 3.38 (s, 3H), 3.44-3.66 (m, 6H), 3.52 (s, 3H), 3.61 (s, 3H), 3.72-3.81 (m, 3H), 4.00 (dd, J = 9.2, 9.2 Hz, 1H), 4.20 (d, J = 7.6 Hz, 1H), 4.62 (d, J = 11.2 Hz, 1H), 4.66 (d, J = 12.0 Hz, 1H), 4.80 (d, J = 12.0 Hz, 1H), 4.81 (d, J = 10.8 Hz, 1H), 4.91 (d, J = 11.2 Hz, 1H), 4.98 (d, J = 11.2 Hz, 1H), 4.99 (d, J = 3.2 Hz, 1H), 7.27-7.37 (m, 15H); ¹³C NMR (100 MHz, CDCl₃) δ 55.2, 58.2, 59.2, 60.4, 60.8, 66.1, 69.9, 70.1, 71.0, 73.3, 74.9, 75.8, 77.8, 79.4, 79.7, 81.5, 82.1, 83.0, 96.5, 97.8, 127.5, 127.5, 127.6, 127.8, 127.9, 128.0, 128.2, 128.2, 128.3, 137.9, 138.2, 138.5; IR (KBr) 2909, 1069, 740, 698 cm⁻¹; LRMS (FAB) m/e 681 (M⁺-H), 543 (M⁺-OMe-BnOH); HRMS (FAB) calcd for C₃₈H₄₉O₁₁ (M⁺-H): 681.3275, found: 681.3275.

Methyl-6-*O*-(2,3,4,6-tetra-*O*-methyl- β -D-glucopyranosyl)-2,3,4-tri-*O*-benzyl- α -D-glucopyranoside (21 β).¹² Prepared from **10** (65.3 mg, 0.199 mmol) and **19** (464.7 mg, 1.000 mmol) in the one-pot procedure, and purified with flash chromatography (hexane/EtOAc 5:3 to 1:1) and GPC (64.1 mg, 47%, β only). TLC R_f 0.34 (hexane/EtOAc 1:1); ¹H NMR (400 MHz, CDCl₃) δ 3.00-3.15 (m, 3H), 3.24 (ddd, J = 2.0, 5.2, 9.6 Hz, 1H), 3.36 (s, 3H), 3.37 (s, 3H), 3.48-3.59 (m, 4H), 3.50 (s, 3H), 3.56 (s, 3H), 3.60 (s, 3H), 3.66 (dd, J = 4.4, 10.8, 1H), 3.77, (ddd, J = 1.6, 4.4, 10.0, 1H), 3.98 (dd, J = 9.2, 9.6 Hz, 1H), 4.12 (dd, J = 2.0, 10.8 Hz, 1H), 4.20 (d, 3.6 Hz, 1H), 4.59 (d, J = 3.6 Hz, 1H), 4.63 (d, J = 10.8 Hz, 1H), 4.64 (d, J = 12.4 Hz, 1H), 4.78 (d, J = 12.4 Hz, 1H), 4.81 (d, J = 10.8 Hz, 1H), 4.88 (d, J = 10.8 Hz, 1H), 4.96 (d, J = 10.8 Hz, 1H), 7.26-7.35 (m, 15H); ¹³C NMR (75 MHz, CDCl₃) δ 55.1, 59.4, 60.4, 60.7, 60.8, 68.3, 69.8, 71.5, 73.4, 74.8, 74.9, 75.8, 78.0, 79.6, 79.8, 82.1, 83.5, 86.6, 98.0, 103.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.1, 128.4, 128.4, 138.1, 138.4, 138.7; IR (KBr) 2905, 1067, 739, 696 cm⁻¹; LRMS (FAB) m/e 681 (M⁺-H), 543 (M⁺-OMe-BnOH); HRMS (FAB) calcd for C₃₈H₄₉O₁₁ (M⁺-H): 681.3275, found: 681.3276.

Phenylthio-6-*O*-(2,3,4,6-tetra-*O*-methyl- β -D-glucopyranosyl)-2,3,4-tri-*O*-benzyl- β -D-glucopyranoside (23). Prepared from **10** (65.9 mg, 0.201 mmol) and **22** (540.2 mg 0.995 mmol) in the one-pot procedure, and purified with flash chromatography (hexane/EtOAc 3:1 to 2:1) and GPC (116.4 mg, 76%). This compound was characterized as a mixture of two diastereomers (α : β = ca. 1:4 by ¹H NMR): spectrum data of the major diastereomer was presented below. TLC R_f 0.18 (hexane/EtOAc 3:1); ¹H NMR (400 MHz, CDCl₃) δ 3.02 (dd, J = 8.0, 8.0 Hz, 1H), 3.10-3.26 (m, 3H), 3.36 (s, 3H), 3.42-3.90 (m, 7H), 3.51 (s, 3H), 3.51 (s, 3H), 3.61 (s, 3H), 4.17 (d, J = 10.8 Hz, 1H), 4.24 (d, J = 7.6 Hz, 1H), 4.60-4.93 (m, 7H), 7.20-7.55 (m, 20 H); ¹³C NMR (100 MHz, CDCl₃) δ 59.3, 60.3, 60.5, 60.7, 68.4, 71.2, 74.5, 74.8, 75.3, 75.8, 77.9, 78.6, 79.3, 80.7, 83.5, 86.2, 86.6, 87.3, 103.3, 127.0, 127.5, 127.6, 127.6, 127.6, 127.9, 128.2, 128.2, 128.2, 128.6, 128.8, 131.3, 132.1, 133.7, 137.8, 138.0; IR (neat) 2900, 1063, 745, 694 cm⁻¹; LRMS (FAB) m/e 761 (MH⁺), 651 (M⁺-SPh), 543 (M⁺-SPh-BnOH); HRMS (FAB) calcd for C₄₃H₅₃O₁₀S (MH⁺): 761.3359, found: 761.3355.

¹H and ¹³C NMR spectra of **21 α** , **21 β** , and **23** (mixture of α and β) are as follows:

^1H NMR spectrum of **21 α** .

^{13}C NMR spectrum of **21a**.

¹H NMR spectrum of **21β**.

¹³C NMR spectrum of **21β**.

¹H NMR spectrum of **23**.

¹³C NMR spectrum of **23**.

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