# Dehydroxy Substitution Reactions of the Anomeric Hydroxy Groups in Some Protected Sugars Initiated by Anodic Oxidation of Triphenylphosphine

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**The anodic transformation of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (4) and 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (5) to the corresponding alkoxy phosphonium ions induces dehydroxy substitution of the sugars at the anomeric positions. Their dehydroxy fluorination and chlorination has been achieved by constant-current electrolysis with $CH_2Cl_2$–1,2-dimethoxyethane/$Ph_3P$/$Ph_3PH\cdot BF_4$ and with $CH_2Cl_2$/$Ph_3P$/$Et_4N\cdot Cl$, respectively. The electrolysis in the presence of $Ph_3P$ has proved to serve *O*-glycosylation with 4 or 5 as a glycosyl donor, provided that an aliphatic alcohol as a glycosyl acceptor is a weaker nucleophile, such as $(CF_3)_2CHOH$, $CF_3CH_2OH$, and *tert*-BuOH, than the protected sugar toward $Ph_3P^{+\cdot}$ generated anodically from $Ph_3P$. The present electrochemical reactions for 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose were unsuccessful, except for the dehydroxy chlorination.**

**Key words** anodic oxidation; dehydroxy substitution; anomeric hydroxy group; glycosyl halide; glycosylation; triphenylphosphine

We recently reported that alkoxy triphenylphosphonium ions ($Ph_3P^+$-OR·$X^-$; X=$ClO_4$ or $BF_4$) are effectively prepared by the reaction of $Ph_3P^{+\cdot}$, anodically generated from $Ph_3P$, with primary or secondary aliphatic alcohols.[1] The isolated phosphonium ions have proved to function as alkylating reagents for soft nucleophiles such as $Br^-$, $Cl^-$, $SCN^-$, and PhSH.[1] In addition, it was of great interest to find that the thermal decomposition of electrochemically formed $Ph_3P^+$-OR·$BF_4^-$ in tetrahydrofuran (THF) or dioxane affords the corresponding alkyl fluorides (R-F), where a fluorine atom from the tetrafluoroborate anion attacks the carbon α to the oxygen atom in the salt from the side opposite the oxy phosphonium moiety *via* an *SN*2 mechanism.[2]

In our continued efforts to develop synthetically useful reactions initiated by anodic oxidation of phosphorus compounds, we turned our attention to the electrochemical reaction of $Ph_3P$ in the presence of a lactol **1** in place of a simple aliphatic alcohol (Chart 1). This is because a phosphonium ion **2**, anodically generated from **1**, will undergo *in situ* decomposition into an oxonium ion **3**, which is expected to behave as a much more reactive electrophile than **2** itself. Thus, we have examined the possibility of anodic oxidation of $Ph_3P$ as a tool to replace anomeric hydroxy groups in protected sugars with nucleophiles not stepwise but in a single stage. In this paper, we describe the dehydroxy substitution reactions of some protected sugars at their anomeric positions, initiated by anodic formation of the corresponding alkoxy triphenylphosphonium ions.

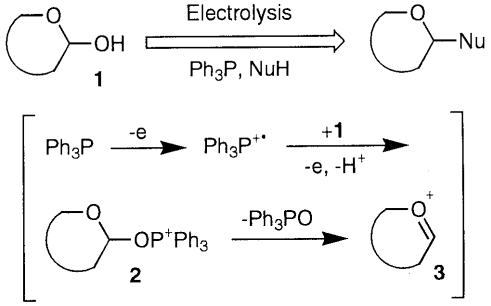
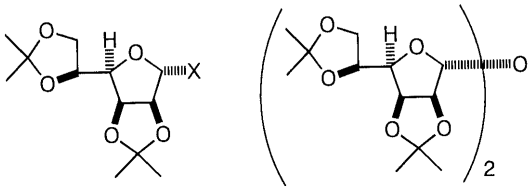



Chart 1

## Results and Discussion

To examine whether or not dehydroxy substitution reactions of anomeric hydroxy groups in protected sugars can be induced by anodic oxidation of $Ph_3P$, 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**4**), 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**5**), and 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (**6α**, **6β**) (Chart 2) were utilized as model substrates. The electrochemical reactions of the sugars were carried out by constant-current electrolysis (CCE) at room temperature under $N_2$ atmosphere. An undivided cell, equipped with a graphite plate anode and a Pt foil cathode, was used for the CCE throughout. Table 1 summarizes the results of dehydroxy fluorination and chlorination of **4**—**6** by the electrolysis in the presence of $Ph_3P$.

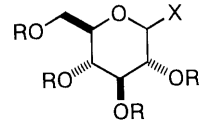
When a mixture of $Ph_3P$, **4**, and $Ph_3PH\cdot BF_4$ in $CH_2Cl_2$



**4**: X = OH
**7**: X = F
**8**: X = Cl



**9**



**5**: R = Bn, X = OH (α : β=82:18)
**6α**: R = Ac, X = α-OH
**6β**: R = Ac, X = β-OH
**10α**: R = Bn, X = α-F
**11α**: R = Bn, X = α-Cl
**12**: R = Ac, X = F
**13α**: R = Ac, X = α-Cl

Chart 2

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Table 1. Dehydroxy Halogenation of **4**—**6** by Constant-Current Electrolysis in the Presence of $Ph_3P$[a]

| Run | Substrate | Electrolysis conditions: Solvent/electrolyte/current (mA) | Products (%) | Recovered substrate (%) |
|---|---|---|---|---|
| 1 | **4** | $CH_2Cl_2/Ph_3PH\cdot BF_4$/40 | **7** (56) **9** (25) | **4** (4) |
| 2 | **4** | $CH_2Cl_2$–DME (5:1)/$Ph_3PH\cdot BF_4$/40 | **7** (72) **9** (12) | — |
| 3 | **4** | $CH_2Cl_2/Bu_4N\cdot ClO_4$/40 | **8** (68) **9** (8) | **4** (9) |
| 4 | **4** | $CH_2Cl_2/Et_4N\cdot Cl$/80 | **8** (94) | — |
| 5 | **5** | $CH_2Cl_2$–DME (5:1)/$Ph_3PH\cdot BF_4$/40 | **10α** (16) | **5** (36) |
| 6 | **5** | $CH_2Cl_2/Et_4N\cdot Cl$/80 | **11a** (88) | — |
| 7 | **6α** | $CH_2Cl_2$–DME (5:1)/$Ph_3PH\cdot BF_4$/40 | **12** (0) | **6** (89)[b] |
| 8 | **6α** | $CH_2Cl_2/Et_4N\cdot Cl$/80 | **13α** (25) | **6** (42)[b] |
| 9 | **6β** | $CH_2Cl_2$–DME (5:1)/$Ph_3PH\cdot BF_4$/40 | **12** (0) | **6** (100)[b] |
| 10 | **6β** | $CH_2Cl_2/Et_4N\cdot Cl$/80 | **13α** (29) | **6** (50)[b] |

a) The electrolysis was carried out in an undivided cell, where 3 F/mol of electricity on a substrate had been allowed to be consumed. b) The configuration at C-1 was not determined.

was subjected to CCE, a glycosyl fluoride **7** was obtained in moderate yield, along with a dimer **9** (Table 1, run 1). The result was quite encouraging, indicating that an alkoxy triphenylphosphonium ion **2**, generated anodically from a lactol such as **4**, smoothly enters the reaction course depicted in Chart 1 even at room temperature. This finding is a fine contrast with the previous observation that similar decomposition of the alkoxy phosphonium ions derived from simple primary and secondary aliphatic alcohols requires heating under reflux in dioxane and THF, respectively.[2] No formation of its β-anomer suggested that the dehydroxy fluorination proceeds not *via* an *S*N2 but an *S*N1 process, where a fluorine atom arising from tetrafluoroborate attacks an oxonium ion such as **3** from a sterically less hindered α-side. When the electrolysis for a mixture of $Ph_3P$, **4**, and $Ph_3PH\cdot BF_4$ was conducted in $CH_2Cl_2$ containing 1,2-dimethoxyethane (DME) as a co-solvent, the formation of **7** was improved, the yield being 72% (run 2). It was reported that **4** was converted into **7** in 57% yield probably *via* the same alkoxy triphenylphosphonium tetrafluoroborate, which was chemically formed by a modified Mitsunobu reaction with $Ph_3P$, diethyl azodicarboxylate, and triethyloxonium tetrafluoroborate.[3] However, the present electrochemical method seems more useful as an effective and simple tool for the preparation of **7** from **4** than the chemical method.

The dehydroxy chlorination of **4** initiated by anodic oxidation of $Ph_3P$ was realized just by changing a supporting electrolyte from $Ph_3PH\cdot BF_4$ to $Bu_4N\cdot ClO_4$. Thus, CCE for a mixture of **4**, $Ph_3P$, and the ammonium salt in $CH_2Cl_2$ afforded **8** in 68% (run 3). From the observed stereochemical outcome, it was suggested that the reaction involves an *S*N1 mechanism similar to the case for the formation of **7**. As for the source of the chlorine atom incorporated into **8** in the electrolysis, cathodic reduction of $CH_2Cl_2$ seems to play an important role. When CCE was carried out in $CH_2Cl_2$ containing $Ph_3PH\cdot BF_4$, the cathodic reaction consisted of an evolution of $H_2$ gas as well as liberation of free $Ph_3P$. However, it seems likely that replacing $Ph_3PH\cdot BF_4$ with $Bu_4N\cdot ClO_4$ forces $CH_2Cl_2$ to undergo reductive cleavage of C–Cl bond, generating chloride anion. Since the presence of thus generated chloride anion seemed to cause no problem in the anodic formation of an alkoxy phosphonium ion from $Ph_3P$ and **4**, it was expected that the deliberate addition of the nucleophilic ion would improve the yield for the electrochemical dehydroxy chlorination of **4**. This was the case. When $Et_4N\cdot Cl$ was used as a supporting electrolyte instead of $Bu_4N\cdot ClO_4$, the formation of **8** took place almost quantitatively (run 4).

The dehydroxy fluorination and chlorination of **5**, **6α**, and **6β** were attempted by CCE under the conditions used in runs 2 and 4, respectively. The results are also included in Table 1. The stereoselective transformation of **5** into a glycosyl fluoride **10α** was brought about by anodic oxidation of $Ph_3P$ as in the case of **4**, although the yield was not satisfactory (run 5). The electrolysis under the same conditions proved unsuccessful for the dehydroxy fluorination of **6α** or **6β**, and merely resulted in recovering the protected sugar in a large amount (runs 7, 9). Substitution of the anomeric hydroxy group in **5** with chloride ion was effectively performed by CCE using $Et_4N\cdot Cl$ as a supporting electrolyte (run 6). Both anomers of **6** also underwent the electrochemical dehydroxy chlorination in contrast to the case of the fluorination, giving the same product **13α** in around 25% yields (runs 8, 10).

Based on the results described so far, the reactivity of anomeric hydroxy groups in **4**—**6** seems to be a determinant of how successfully the dehydroxy substitution reactions at the anomeric positions are induced by anodic oxidation of $Ph_3P$. In general, etherified sugars show much higher anomeric reactivities as glycosyl acceptors as well as glycosyl donors than their esterified counterparts.[4] These well-known phenomena are responsible for the changes in the effectiveness for the electrochemical transformation of **4**, **5**, and **6**. Namely, the formation of the corresponding alkoxy triphenylphosphonium ion such as **2** depicted in Chart 1 will be favored in the following order: **4**>**5**>**6**, which must be reflected in the results of the present dehydroxy halogenations. In addition, it is likely that a protic supporting electrolyte $Ph_3PH\cdot BF_4$ decreases the nucleophilic reactivities of the sugars more than those in the presence of an aprotic salt $Bu_4N\cdot ClO_4$ or $Et_4N\cdot Cl$. This is probably because to a certain extent, the protonation by the protic salt prevents the anomeric hydroxy group from attacking $Ph_3P^{+\cdot}$, to form the corresponding phosphonium ion. Thus, the present dehydroxy halogenation, especially for **5** and **6** with weaker anomeric reactivities, seemed to proceed more effectively in the electrolysis with the ammonium salts rather than $Ph_3PH\cdot BF_4$. In the electrolysis with $Et_4N\cdot Cl$ as a supporting electrolyte, a reaction sequence in which $Ph_3PCl_2$ is initially formed at the anode and then reacts with the sugars cannot be ruled out, although our previous work[1,5,6] suggests that $Ph_3P^{+\cdot}$ reacts with the anomeric hydroxy groups in the electrolysis with $Ph_3PH\cdot BF_4$ or $Bu_4N\cdot ClO_4$ as a supporting electrolyte.

The possibility of the dehydroxy substitution of **4**—**6** initiated by anodic oxidation of $Ph_3P$ as a tool for *O*-glycosylation was also examined. The study seemed intriguing for the following reasons: (i) the electrochemical method might provide a novel methodology for *O*-glycosylation, which is crucial for the synthesis of glycoconju-

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gates of biological importance[7]; (ii) the electrophilic reactivity of $Ph_3P^{+\cdot}$ against various alcohols will be elucidated, which will be helpful for further development of synthetically useful reactions with the electrochemically formed alkoxy phosphonium ions. In order to achieve a desired *O*-glycosylation, the electrolysis of $Ph_3P$ must be carried out in the presence of both the protected sugar and $R^1OH$. Two routes affording a glycoside from the two components can be envisaged as shown in Chart 3: route A *via* the formation of **2** (*cf.* Chart 1) from the protected sugar; route B including the transformation of $R^1OH$ into the corresponding phosphonium ion ($Ph_3P^+$-$OR^1$) (**14**). However, it has been found that **14** with $ClO_4^-$ or $BF_4^-$ as a counter anion is unable to work as an alkylating reagent for aliphatic alcohols, or even for their alkoxides.[8] Accordingly, it is conceivable that a glycoside is afforded through the present electrochemical reaction only when $Ph_3P^{+\cdot}$ initially reacts with the protected sugar, leading to the formation of an alkylating reagent such as **3** (*cf.* Chart 1), which is active enough for $R^1OH$ to react with. Thus, analysis of the electrolysis products will compare the reactivities of the protected sugar and $R^1OH$ toward $Ph_3P^{+\cdot}$: the sugar $>R^1OH$ by the formation of a desired glycoside, the sugar $<R^1OH$ through no formation of a desired glycoside or the formation of **14**.

To establish the scope and limitation of the present electrolysis in the presence of the protected sugar as a tool for *O*-glycosylation, the reactivity of **4** with $Ph_3P^{+\cdot}$ was first compared with those of various aliphatic alcohols ($R^1OH$) based on the above argument. Taking electronic and steric effects into consideration, $(CF_3)_2CHOH$ (**15**), $CF_3CH_2OH$ (**16**), *tert*-BuOH, iso-PrOH, and EtOH were used as $R^1OH$ (Chart 3). A mixture of $Ph_3P$, **4**, and $R^1OH$ was subjected to CCE in $CH_2Cl_2$ containing $Ph_3PH \cdot ClO_4$ (method A) or $Bu_4N \cdot ClO_4$ (method B) as a supporting electrolyte using an undivided cell. The electrolysis was carried out at room temperature under $N_2$ atmosphere. The results are summarized in Table 2.

When the perfluorinated alcohols and *tert*-BuOH were utilized as $R^1OH$, the electrochemical condensation of **4** with $R^1OH$ was successfully achieved, giving the corresponding glycosides **17a—c** in fair to good yields (runs 2—4). Accordingly, the protected sugar seemed to have a higher nucleophilicity than these alcohols in the reaction with $Ph_3P^{+\cdot}$, allowing route A in Chart 3 to prevail. The lack of formation of their $\beta$-isomers in these electrolyses

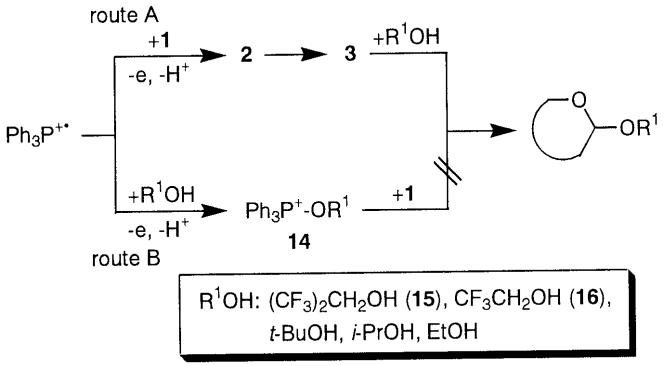


Chart 3

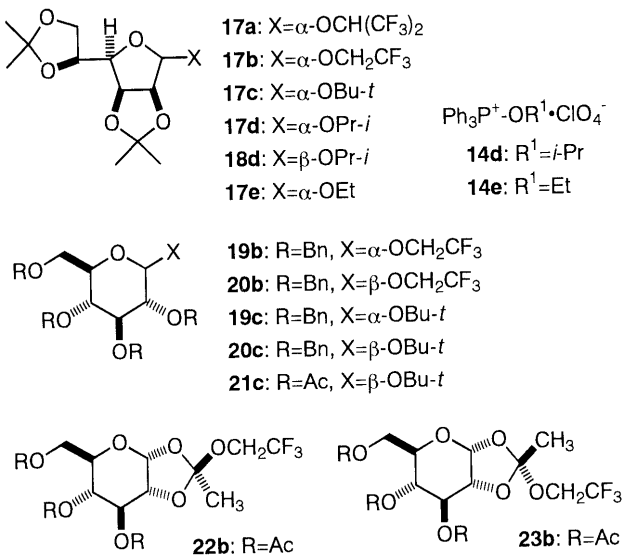


Chart 4

Table 2. Condensation of **4—6** with $R^1OH$ by Constant-Current Electrolysis in the Presence of $Ph_3P$[a]

| Run | Substrate | $R^1OH$ (ml) | Electrolysis method[b] | Products (%) | Recovered substrate (%) |
|---|---|---|---|---|---|
| 1 | **4** | **15** (3) | A | **17a** (6) **9** (6) | **4** (73) |
| 2 | **4** | **15** (3) | B | **17a** (57) **9** (25) | **4** (4) |
| 3 | **4** | **16** (2) | B | **17b** (92) | — |
| 4 | **4** | *tert*-BuOH (1) | A | **17c** (79) | — |
| 5 | **4** | *tert*-BuOH (1) | B | **17c** (20) **8** (42) | — |
| 6 | **4** | iso-PrOH (2) | A | **17d** (6) **18d** (4) **14d** (67) | **4** (25) |
| 7[c] | **4** | iso-PrOH (2) | B | — | **4** (56) |
| 8 | **4** | EtOH (2) | A | **17e** (2) **14e** (75) | **4** (53) |
| 9[c] | **4** | EtOH (2) | B | **17e** (9) | **4** (82) |
| 10 | **5** | **16** (2) | B | **19b**+**20b** (82, 70 : 30)[d,e] | — |
| 11 | **5** | *tert*-BuOH (1) | A | **19c**+**20c** (62, 46 : 54)[d,f] | **5** (17) |
| 12 | **6α** | **16** (2) | B | **22b**+**23b** (57, 94 : 6)[d,g] | **6** (32)[h] |
| 13 | **6α** | *tert*-BuOH (1) | A | **21c** (7) | **6** (80)[h] |
| 14 | **6β** | **16** (2) | B | **22b**+**23b** (87, 92 : 8)[d,g] | — |

*a*) The electrolysis was carried out in $CH_2Cl_2$ using an undivided cell, where 3 F/mol of electricity on a substrate had been allowed to be consumed. *b*) Method A: $Ph_3PH \cdot ClO_4$/40 mA; method B: $Bu_4N \cdot ClO_4$/20 mA. *c*) $^{31}P$-NMR spectra indicated that no **14** existed in crude products. *d*) Obtained as a mixture of both isomers. *e—g*) The ratio between the two isomers was determined with $^1H$-, $^{13}C$-, and $^{19}F$-NMR spectra, respectively. *h*) The configuration at C-1 was not determined.

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demonstrates that the glycosylation initiated by anodic oxidation of $Ph_3P$ proceeds not *via* an *SN*2 but an *SN*1 mechanism, where an oxonium ion **3** is probably a crucial intermediate as in the case of the dehydroxy halogenation described above. The electrochemical glycosylation of iso-PrOH and EtOH with **4** was unsuccessful (runs 6—9). In CCE by method A, phosphonium ions **14d** and **14e** from iso-PrOH and EtOH, respectively, were obtained in good yields (runs 6, 8). In each of the electrolyses in the presence of iso-PrOH or EtOH, **4** was always recovered. The observations indicate that route B predominates over route A when iso-PrOH and EtOH are used as $R^1OH$. Further quantitative studies are needed for strict estimation of the reactivities of alcohols examined here toward $Ph_3P^{+\cdot}$. The reactivities do, however, appear to roughly follow the order EtOH and iso-PrOH > **4** > **15**, **16**, and *tert*-BuOH, based on the results.

It should be mentioned here that the stereoselectivity in the electrochemical glycosylation with **4** was disturbed when iso-PrOH was used as a glycosyl acceptor, leading to the formation of a mixture of α- and β-anomers (3 : 2) (run 6). Although the exact origin of the observed stereochemical outcome is not clear, the nucleophilicity and molecular size of iso-PrOH might be responsible for inducing an *SN*2 process. The anomeric configurations for all of the products **17a—e** and **18d** were easily established from the splitting patterns for the anomeric protons on $^1$H-NMR spectra: **17** exhibits an H-1 signal as a singlet, whereas the H-1 of **18d** is observed as a doublet.

Electrochemical glycosylation of **16** and *tert*-BuOH was also effectively performed when **5** was used as a glycosyl donor. In each case, glycosides **19** and **20** were obtained as a mixture in a good yield, although the stereoselectivity was not satisfactory (runs 10, 11). The structures for both **19** and **20** were determined by comparing the chemical shifts for the signals due to C-1 carbons on the $^{13}$C-NMR spectra, based on the argument that a β-D-glucopyranoside exhibits the corresponding signal at around 100 ppm, which is shifted to a lower magnetic field than that for its α-anomer.[9]

The ability of **6** as a glycosyl donor in the present electrochemical reaction was quite poor, as expected. When the electrolysis was carried out for **6α** or **6β** in the presence of **16**, no formation of a desired glycoside was observed. The isolated products were 1,2-orthoacetates **22b** and **23b**, suggesting that an oxonium **3** anodically generated from **6** is transformed into a more stable cyclic acetoxonium ion through well-known neighboring-group participation.[4c,10] The structures of **22b** and **23b** were determined by the recognized characteristic of the methyl group in the orthoacetate moiety on $^1$H-NMR spectra.[11,12] Utilizing *tert*-BuOH as a glycosyl acceptor in CCE for **6α** resulted in the formation of the corresponding glycoside **21c** in poor yield. The anomeric configuration was confirmed by the coupling constant between H-1 and H-2 on its $^1$H-NMR spectrum.

In conclusion, it was demonstrated that the anodic oxidation of $Ph_3P$ in the presence of lactols such as protected sugars leads to the formation of the corresponding alkoxy phosphonium ions, similar to the case of the electrolysis of primary and secondary aliphatic alcohols, as long as steric and/or stereoelectronic effects do not attenuate the nucleophilicities of the anomeric hydroxy groups. Further, the phosphonium ions proved to decompose *in situ* to oxonium ions, which work as glycosyl donors for nucleophiles like $BF_4^-$, $Cl^-$, and aliphatic alcohols. Although a limitation was observed for aliphatic alcohols as a glycosyl acceptor in *O*-glycosylation by the present electrochemical reaction, this study has provided a criterion for the reactivities of various alcohols including protected sugars **4—6** toward $Ph_3P^{+\cdot}$, which will further contribute to the design of the anodic oxidation of $Ph_3P$ as a unique synthetic tool.

## Experimental

Infrared (IR) spectra were taken on a JASCO VALOR-III spectrometer. $^1$H-, $^{13}$C-, and $^{19}$F-NMR spectra were obtained in $CDCl_3$ at 200, 67.8, and 188.3 MHz on Varian VXR-200 and JEOL EX-270 spectrometers. Chemical sifts were expressed in parts per million (δ), where tetramethylsilane (TMS) was used as an internal standard for $^1$H- and $^{13}$C-NMR spectra, and hexafluorobenzene for $^{19}$F-NMR spectra. Mass spectra (MS) were recorded at 70 eV with a direct inlet system on a JEOL JMS-HX100 spectrometer. For column chromatography, $SiO_2$ (Wakogel C-200) was used. CCE was carried out with a Hokuto Denko HA301, HA104, or HA105 potentiostat/galvanostat connected with a Hokuto Denko HF201 coulomb/amperehour meter.

**Materials** Protected sugars **6α** and **6β** were prepared by treatment of 1,2,3,4,6-penta-*O*-acetyl-α-D-glucose and 1,2,3,4,6-penta-*O*-acetyl-β-D-glucose with piperidine in THF,[13] respectively. $CH_2Cl_2$ for the electrolysis was distilled from $P_2O_5$. All other chemicals were of reagent grade and were used without further purification.

**General Procedure for the Electrolysis** A solution (30 ml) of a protected sugar (3 mmol), $Ph_3P$ (4, 5 or 6 mmol), and a supporting electrolyte (4, 5 or 6 mmol) in an undivided cell equipped with a graphite plate anode (12.5 $cm^2$) and a Pt foil cathode (4.0 $cm^2$) was subjected to CCE (20, 40 or 80 mA) at room temperature under an $N_2$ atmosphere. After 3.0 F/mol (*vs.* a protected sugar) had been passed, the electrolyte was washed with water, and the aqueous layer was extracted with $CH_2Cl_2$ (50 ml × 2). The combined organic layer was washed with brine, dried over $MgSO_4$, and then concentrated under reduced pressure, and the residue was subjected to silica gel column chromatography (*n*-hexane–ethyl acetate) to give the products. The products **7**,[3] **8**,[12] **10α**,[14] **11α**,[12] and **13α**,[15] were identified by comparison of their spectroscopic data with those described in the cited references. Other products gave satisfactory physical data as shown below.

2,3 : 5,6-Di-*O*-isopropylidene-α-D-mannofuranosyl 2,3 : 5,6-Di-*O*-isopropylidene-α-D-mannofuranoside (**9**): White powder, mp 185—186 °C. $^1$H-NMR δ: 5.23 (1H, s, H-1), 4.79 (1H, dd, $J$ = 6.0, 3.8 Hz), 4.57 (1H, d, $J$ = 6.0 Hz), 4.44—4.35 (1H, m), 4.15—3.98 (2H, m), 3.91 (1H, dd, $J$ = 8.0, 3.8 Hz), 1.48 (3H, s), 1.45 (3H, s), 1.38 (3H, s), 1.34 (3H, s). $^{13}$C-NMR δ: 112.49 (s), 108.97 (s), 101.29 (d), 97.43 (d), 84.80 (d), 80.70 (d), 79.25 (d), 72.74 (d), 66.65 (t), 26.65 (q), 25.61 (q), 24.93 (q), 24.26 (q). *Anal.* Calcd for $C_{24}H_{38}O_{11}$: C, 57.36; H, 7.62. Found: C, 57.09; H, 7.39.

1,1,1,3,3,3-Hexafluoroisopropyl 2,3 : 5,6-Di-*O*-isopropylidene-α-D-mannofuranoside (**17a**): Pale yellow oil. $^1$H-NMR δ: 5.24 (1H, s, H-1), 4.86 (1H, dd, $J$ = 5.9, 3.5 Hz), 4.78 (1H, d, $J$ = 5.9 Hz), 4.49—4.37 (2H, m), 4.15—3.93 (3H, m), 1.47 (3H, s), 1.44 (3H, s), 1.39 (3H, s), 1.34 (3H, s). $^{13}$C-NMR δ: 121.67 (sq, $J_{CF}$ = 283.2 Hz), 121.15 (sq, $J_{CF}$ = 282.0 Hz), 113.28 (s), 109.54 (s), 107.65 (d), 84.74 (d), 82.07 (d), 79.26 (d), 72.70 (d), 71.23 (d of quintet, $J_{CF}$ = 32.9 Hz), 66.79 (t), 26.79 (q), 25.88 (q), 25.21 (q), 24.49 (q). $^{19}$F-NMR δ: −74.79 (s, $CF_3$). *Anal.* Calcd for $C_{15}H_{20}F_6O_6$: C, 43.91; H, 4.91. Found: C, 44.13; H, 4.87.

2,2,2-Trifluoroethyl 2,3 : 5,6-Di-*O*-isopropylidene-α-D-mannofuranoside (**17b**): Colorless oil. $^1$H-NMR δ: 5.08 (1H, s, H-1), 4.82 (1H, dd, $J$ = 6.0, 3.6 Hz), 4.69 (1H, d, $J$ = 6.0 Hz), 4.46—4.37 (1H, m) 4.16—3.81 (5H, m), 1.47 (3H, s), 1.46 (3H, s), 1.38 (3H, s), 1.33 (3H, s). $^{13}$C-NMR δ: 123.79 (sq, $J_{CF}$ = 277.8), 112.97 (s), 109.34 (s), 106.65 (d), 84.87 (d), 81.13 (d), 79.37 (d), 72.99 (d), 66.81 (t), 64.02 (tq, $J_{CF}$ = 34.9 Hz), 26.85 (q), 25.88 (q), 25.19 (q), 24.49 (q). $^{19}$F-NMR δ: −75.30 (t, $J$ = 8.4 Hz, $CF_3$). *Anal.* Calcd for $C_{14}H_{21}F_3O_6$: C, 49.12; H, 6.18. Found: C, 49.11; H, 6.03.

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*tert*-Butyl 2,3 : 5,6-Di-*O*-isopropylidene-α-D-mannofuranoside (**17c**): Colorless oil. $^1$H-NMR $\delta$: 5.27 (1H, s, H-1), 4.79 (1H, dd, $J$=5.8, 3.6 Hz), 4.53 (1H, d, $J$=6.0 Hz), 4.42—4.33 (1H, m) 4.13—3.96 (3H, m), 1.47 (3H, s) 1.45 (3H, s), 1.38 (3H, s), 1.31 (3H, s), 1.23 (9H, s). $^{13}$C-NMR $\delta$: 112.27 (s), 109.18 (s), 101.80 (d), 86.32 (d), 79.80 (d), 79.75 (d), 75.02 (s), 73.28 (d), 66.99 (t), 28.70 (3C, q), 26.90 (q), 25.88 (q), 25.28 (q), 24.65 (q). *Anal.* Calcd for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.58; H, 8.76.

Isopropyl 2,3 : 5,6-Di-*O*-isopropylidene-α-D-mannofuranoside (**17d**): Colorless oil. $^1$H-NMR $\delta$: 5.10 (1H, s, H-1), 4.79 (1H, dd, $J$=6.0, 3.6 Hz), 4.56 (1H, d, $J$=5.9 Hz), 4.44—4.35 (1H, m) 4.15—3.80 (4H, m), 1.47 (3H, s) 1.45 (3H, s), 1.38 (3H, s), 1.32 (3H, s), 1.16 (3H, t, $J$=6.6 Hz), 1.14 (3H, d, $J$=6.5 Hz). $^{13}$C-NMR $\delta$: 112.42 (s), 109.20 (s), 104.63 (d), 85.43 (d), 80.18 (d), 79.64 (d), 73.22 (d), 69.25 (d), 67.01 (t), 26.88 (q), 25.88 (q), 25.21 (q), 24.49 (q), 23.41 (q), 21.49 (q). *Anal.* Calcd for $C_{15}H_{26}O_6$: C, 59.58; H, 8.67. Found: C, 59.40; H, 8.40.

Isopropyl 2,3 : 5,6-Di-*O*-isopropylidene-β-D-mannofuranoside (**18d**): Colorless oil. $^1$H-NMR $\delta$: 4.79 (1H, d, $J$=3.5 Hz, H-1), 4.69 (1H, dd, $J$=6.0, 3.8 Hz), 4.57 (1H, dd, $J$=6.0, 3.5 Hz), 4.46 (1H, dt, $J$=7.8, 5.3 Hz), 4.09 (2H, d, $J$=5.3 Hz), 3.97 (1H, quint, $J$=6.2 Hz), 3.54 (1H, dd, $J$=7.8, 3.8 Hz), 1.55 (3H, s), 1.45 (3H, s), 1.38 (3H, s), 1.36 (3H, s), 1.27 (3H, d, $J$=6.2 Hz), 1.22 (3H, d, $J$=6.2 Hz). $^{13}$C-NMR $\delta$: 113.53 (s), 109.18 (s), 101.26 (d), 79.95 (d), 79.01 (d), 76.80 (d), 73.37 (d), 72.43 (d), 66.92 (t), 27.03 (q), 25.71 (q), 25.32 (q), 25.16 (q), 23.14 (q), 21.85 (q). *Anal.* Calcd for $C_{15}H_{26}O_6$: C, 59.58; H, 8.67. Found: C, 59.29; H, 8.48.

Ethyl 2,3 : 5,6-Di-*O*-isopropylidene-α-D-mannofuranoside (**17e**): Colorless oil. $^1$H-NMR $\delta$: 4.99 (1H, s, H-1), 4.78 (1H, dd, $J$=6.0, 3.7 Hz), 4.58 (1H, d, $J$=5.9 Hz), 4.45—4.36 (1H, m) 4.15—4.00 (2H, m), 3.93 (1H, dd, $J$=7.6, 3.6 Hz), 3.76—3.61 (1H, m), 3.53—3.37 (1H, m), 1.47 (3H, s), 1.46 (3H, s) 1.38 (3H, s), 1.32 (3H, s), 1.19 (3H, t, $J$=7.0 Hz). $^{13}$C-NMR $\delta$: 112.52 (s), 109.20 (s), 106.09 (d), 85.17 (d), 80.21 (d), 79.59 (d), 73.22 (d), 66.97 (t), 62.84 (t), 26.92 (q), 25.91 (q), 25.19 (q), 24.54 (q), 14.97 (q). *Anal.* Calcd for $C_{14}H_{24}O_6$: C, 58.31; H, 8.39. Found: C, 58.50; H, 8.18.

2,2,2-Trifluoroethyl 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranoside Obtained as a Mixture of α- and β-Isomers (**19b** and **20b**, Respectively) (70 : 30): White powder. $^{13}$C-NMR (α-anomer) $\delta$: 97.75 (d, C-1). $^{13}$C-NMR (β-anomer) $\delta$: 103.59 (d, C-1). $^{19}$F-NMR (α-anomer) $\delta$: −74.68 (t, $J$=9.2 Hz, $\underline{CF}_3$). $^{19}$F-NMR (β-anomer) $\delta$: −75.25 (t, $J$=8.5 Hz, $\underline{CF}_3$). *Anal.* Calcd for $C_{36}H_{37}F_3O_6$: C, 69.44; H, 5.99. Found: C, 69.24; H, 5.93.

*tert*-Butyl 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranoside Obtained as a Mixture of α- and β-Anomers (46 : 54): Colorless oil. $^1$H-NMR (α-anomer) $\delta$: 5.14 (1H, d, $J$=3.8 Hz, H-1). $^{13}$C-NMR (α-anomer) $\delta$: 91.45 (d, C-1). $^{13}$C-NMR (β-anomer) $\delta$: 97.81 (d, C-1). *Anal.* Calcd for $C_{38}H_{44}O_6$: C, 76.48; H, 7.43. Found: C, 76.37; H, 7.43.

3,4,6-Tri-*O*-acetyl-1,2-*O*-[1-(2,2,2-trifluoroethoxy)-ethylidene)-α-D-glucopyranoside Obtained as a Mixture of Exo and Endo Diastereoisomers (**22b** and **23b**, Respectively): White powder. $^1$H-NMR (**22b**) $\delta$: 5.75 (1H, d, $J$=5.4 Hz, H-1), 2.13 (3H, s), 2.11 (6H, s), 1.74 (3H, s). $^1$H-NMR (**23b**) $\delta$: 5.68 (1H, d, $J$=5.1 Hz, H-1). $^{13}$C-NMR (**22b**) $\delta$: 170.71 (s), 169.63 (s), 169.14 (s), 123.57 (sq, $J_{CF}$=277.0), 121.13 (s), 97.11 (d, C-1), 73.04 (d), 69.74 (d), 68.09 (d), 67.17 (d), 63.05 (t), 61.51 (tq, $J_{CF}$=35.3 Hz), 20.77 (3C, q), 20.29 (q). $^{13}$C-NMR (**23b**) $\delta$: 122.17 (s), 97.20 (d, C-1). $^{19}$F-NMR (**22b**) $\delta$: −75.49 (t, $J$=9.1 Hz, $\underline{CF}_3$). $^{19}$F-NMR (**23b**) $\delta$: −74.98 (t, $J$=8.5 Hz, $\underline{CF}_3$). *Anal.* Calcd for $C_{16}H_{21}F_3O_{10}$: C, 44.65; H, 4.92. Found: C, 44.72; H, 4.79.

*tert*-Butyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranoside (**21c**): White powder. $^1$H-NMR $\delta$: 5.25 (1H, t, $J$=9.5 Hz), 5.08—4.89 (2H, m), 4.64 (1H, d, $J$=7.9 Hz, H-1), 4.22 (1H, dd, $J$=12.1, 5.7 Hz), 4.09 (1H, dd, $J$=12.1, 2.6 Hz), 3.73—3.64 (1H, m), 2.06 (3H, s) 2.03 (3H, s), 2.02 (3H, s), 2.00 (3H, s), 1.23 (9H, s). $^{13}$C-NMR $\delta$: 170.65 (s), 170.38 (s), 169.47 (s), 169.16 (s), 95.52 (d), 76.55 (s), 73.12 (d), 71.64 (d), 71.59 (d), 68.88 (d), 62.44 (t), 28.42 (3C, q), 20.72 (2C, q), 20.65 (2C, q). *Anal.* Calcd for $C_{18}H_{28}O_{10}$: C, 53.46; H, 6.98. Found: C, 53.23; H, 6.75.

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