Heteroatom Chemistry
Volume 6, Number 2, 1995

Synthesis of *C*-Nucleosides via Coupling of Ribosyl Fluoride with Typical Aromatic Heterocycles Bearing a TMS Group

Masataka Yokoyama,* Mitsuru Nomura, Takeshi Tanabe, and Hideo Togo

Department of Chemistry, Faculty of Science, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263, Japan

Received 20 September 1994

ABSTRACT

The direct coupling reaction of D-*ribosyl fluoride with typical π-excessive aromatic heterocycles such as furan, thiophene, pyrrole, benzofuran, benzothiophene, and indole and their trimethylsilyl derivatives was performed in the presence of boron trifluoride to afford the corresponding C-nucleosides in moderate to good yields.*

INTRODUCTION

As a part of our study directed toward *C*-nucleoside synthesis [1], we aimed to develop a straightforward preparation of *C*-nucleosides having typical π-excessive heterocycles as the base moiety. The direct coupling of a protected D-ribosyl bromide with lithium salts of aromatic heterocycles has been known to undergo many side reactions [1g]. However, our preliminary experiments showed that D-ribosyl fluoride was a good candidate for direct coupling with aromatic heterocycles and further the use of aromatic heterocycles substituted with a trimethylsilyl group could incease the yield. Herein, we wish to report a facile coupling reaction of D-ribosyl fluoride with π-excessive heterocycles.

Glucopyranosyl fluoride has been utilized exclusively for the *O*-glucosylation reaction in organic synthesis [2]. On its application to carbon–carbon bond formation [3], Suzuki and co-workers have reported only the glucosylation of aromatic compounds such as phenol and naphthol derivatives [3h].

RESULTS AND DISCUSSION

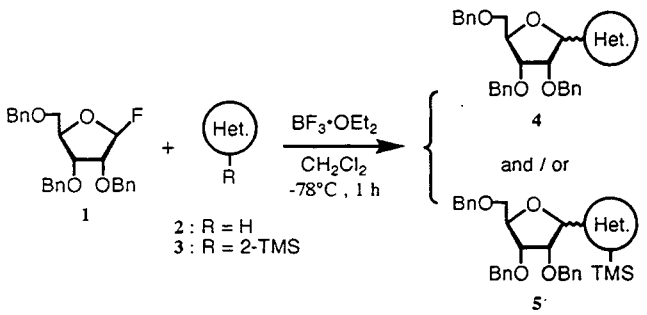
It was found that when aromatic heterocycles **2**, such as furan, thiophene, pyrrole, and their benzoderivatives, were allowed to react with 2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl fluoride **1** [4] in the presence of boron trifluoride etherate, the corresponding *C*-nucleosides **4** were obtained in moderate to good yields.

Then we attempted to increase the yield of **4** by utilizing aromatic heterocycles activated by a TMS group. In this case, the electrophilic substitution of the aromatic heterocycles occurred at their *ipso*- and/or 5(3)-positions and the expected increase of total yield (*ipso*-substituted products **4** and 5(3)-substituted products **5**) was observed, except in the cases of pyrrole, benzothiophene, and indole (Scheme 1). 1-Phenylsulfonyl-2-TMS-indole did not undergo a clean coupling reaction. The formation of **5** is not particularly surprising, because, in the reactions of 2-TMS-furan, 2-TMS-thiophene, and 1-methyl-2-TMS-pyrrole with several acylating reagents, the corresponding 5-substituted products were formed [5]. It is a general tendency that electrophilic substitutions of benzothiophenes and indole take place mainly at the 3-position, resulting in the formation of **4e**, **4f**, and **5e** [6]. The electron

Dedicated with gratitude to Prof. Shigeru Oae on the occasion of his seventy-fifth birthday.

*To whom correspondence should be addressed.

1042-7163/95/$5.00 + .25



SCHEME 1

densities of HOMOs in benzofuran, benzothiophene, and indole derivative were calculated by PM3 (CAChe™ MOPAC version 6.10, Stewart) and are shown in Figure 1. The computed results support the experimental facts.

Compounds **5** could easily be converted to **4** by protodesilylation [7]. Thus, each reaction mixture was subjected to the usual desilylation procedure (CF_3CO_2H or *p*-TsOH/H_2O/THF, rt or 70°C) to give only **4** [**4a**: 72% (α/β = 1/5); **4b**: 78% (α/β = 9/5)]. The results are summarized in Table 1.

The structures of **4a**, **4b**, **4d**, **4e**, and **4f** and their TMS derivatives were determined by comparison with the NMR data of their deprotected products [1g,1h] The structures of **4c** and **5c** were determined by the $J_{1',2'}$ values of their NMR data (α-forms of **4c** and **5c**: $J_{1',2'}$ = 2.0 and 2.2 Hz; β-forms of **4c** and **5c**: $J_{1',2'}$ = 4.6 and 3.1 Hz).

The phenylsulfonyl groups of **4c** and **5c** could be removed in 80–90% yields by a modified treatment employing potassium hydroxide in dioxane solution containing a suitable crown ether (see the Experimental section) [8]. When the α-form of **4b** was treated for 1 hour under these reaction conditions it changed to a mixture of α- and β-forms (α/β = 5/2). Therefore, 2-ribosyl aromatic heterocycles were found to undergo epimerization under the specified reaction conditions.

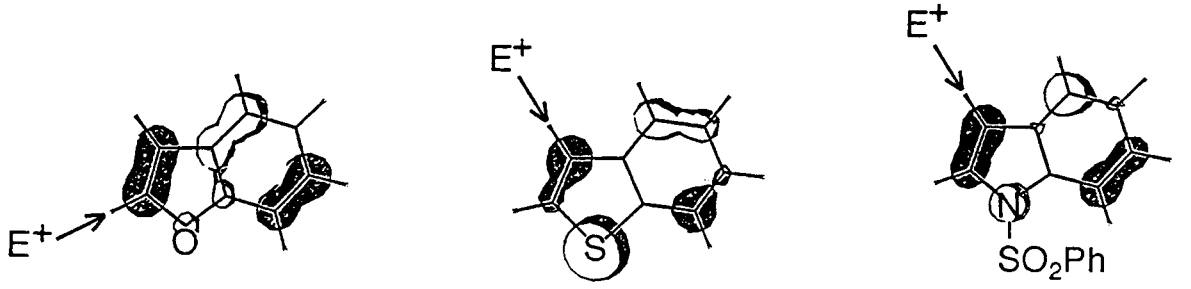
Next, compounds **4** were deprotected in the usual manner using boron trichloride, and the α- and β-epimers could be separated by recycling preparative HPLC. In order to examine the stereoselectivity of this reaction, the use of the α-epimer in place of β-D-ribofuranosyl fluoride produced no significant effect on the distribution of products. Therefore, the electrophilic substitution of the heterocycles is considered to proceed via an S_N cut 1 type of reaction.

In conclusion, the present reaction affords a simple method for the synthesis of *C*-nucleosides bearing several kinds of π-excessive heterocycles. Further, compounds **5** obtained by this method are synthetically useful because they can be converted to the corresponding iodo, acyl, and alcohol derivatives by iododesilylation [9], acylation [10], and butoxide-catalyzed addition reaction to an aldehyde [11] respectively.

EXPERIMENTAL

General

Microanalyses were performed with a Perkin-Elmer 2400 elemental analyzer at the Chemical Analysis Center of Chiba University. IR spectra were recorded on a Hitachi 215 spectrometer. Mass spectra were obtained on Hitachi M-60 and JEOL-JMS-HX110 mass spectrometers. ^{1}H NMR spectra were measured [$CDCl_3$ as a solvent (unless specified otherwise) using tetramethylsilane (TMS) as an internal reference] with JEOL-JNM-FX270, JNM-GSX400, and JNM-GSX500 spectrometers. Chemical shifts are expressed in δ values. 2D ^{1}H NMR (COSY and NOESY) data were measured with JNM-GSX-400 and JNM-GSX-500 spectrometers. Wakogel C-200 and C-300 were used for TLC and Wakogel B-5F for preparative TLC (pTLC). Recycling preparative high performance liquid chromatography (HPLC) was performed with a Japan Analytical Industry LC-908 instrument.



benzofuran benzothiophene 1-phenylsulfonylindole

FIGURE 1

TABLE 1 Synthesis of **4** and **5** via Coupling of **1** with **2** or **3**

Het–R (*Heterocycles*)	**2** *and* **3** (*R*)	*Isolated Yields* (%) **4** (α/β)	**5** (α/β)
Furan	**2** (H)	20 (2/11)	—
(**a**)	**3** (2-TMS)	28 (1/2)	44 (1/21)
Thiophene	**2** (H)	50 (2/7)	—
(**b**)	**3** (2-TMS)	58 (3/2)	20 (2/1)
Pyrrole[a]	**2** (H)	79 (13/3)	—
(**c**)	**3** (2-TMS)	3 (6/1)	66 (6/1)
Benzofuran	**2** (H)	10 (α)	—
(**d**)	**3** (2-TMS)	43 (9/2)	23 (α)
Benzothiophene	**2** (H)	51 (α)[b]	—
(**e**)	**3** (2-TMS)	0	33 (9/4)[c]
Indole[d] (**f**)	**2** (H)	88 (1/1)[e]	—

[a]1-Phenylsulfonylpyrrole.
[b]Benzyl-protected 3-benzothienyl-D-ribose.
[c]Benzyl-protected 3-[2-(trimethylsilyl)benzothienyl]-D-ribose.
[d]1-Phenylsulfonylindole.
[e]Benzyl-protected 3-indolyl-D-ribose.

Materials

2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl fluoride [4] 1-phenylsulfonylpyrrole [12], 1-phenylsulfonylindole [12], and TMS heterocycles [5] were prepared according to the literature.

Synthesis of C-Nucleosides; Typical Procedure

To a solution of 2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl fluoride (84 mg, 0.2 mmol) and each trimethylsilyl-substituted or nonsubstituted aromatic heterocycle (0.6 mmol) in dry CH_2Cl_2 (1 mL) was added $BF_3 \cdot OEt_2$ (0.17 mL, 1.4 mmol) at −78°C. After being stirred for 1 hour at the same temperature, the reaction mixture was treated with $NaHCO_3$ aq (3 mL), extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified in the usual way using pTLC on silica gel.

*2-(2,3,5-Tri-O-benzyl-*D*-ribofuranosyl)furan* (**4a**). Oil; IR (neat) 2840, 1095 cm^{-1}, HRMS (FAB) calcd for $C_{30}H_{30}O_5Na$ $(M + Na)^+$: 493.1991; found: 493.1994. Anal. calcd for $C_{30}H_{30}O_5$: C, 76.57; H, 6.43; found: C, 76.75; H, 6.29. ^1H NMR (500 MHz, $CDCl_3$): (α-form) δ 3.60 (dd, 1H, 5′-H, J_{gem} = 8.0, $J_{4',5'}$ = 3.0 Hz), 3.74 (dd, 1H, 5′-H, J_{gem} = 8.0, $J_{4',5'}$ = 2.8 Hz), 4.10–4.26 (m, 3H, 2′,3′,4′-H), 4.28–4.65 (m, 6H, benzyl-H), 5.12 (d, 1H, 1′-H, $J_{1',2'}$ = 3.6 Hz), 6.39 (dd, 1H, furan 4-H, J = 3.3, 1.9 Hz), 6.49 (m, 1H, furan 3-H), 7.12–7.42 (m, 16H, furan 5-H, Ph-H).

(β-form) δ 3.60 (d, 2H, 5′-H, $J_{4',5'}$ = 4.3 Hz), 4.04 (dd, 1H, 3′-H, $J_{2',3'}$ = 5.1, $J_{3',4'}$ = 4.7 Hz), 4.16 (dd, 1H, 2′-H, $J_{1',2'}$ = 6.0, $J_{2',3'}$ = 5.1 Hz), 4.28 (dd, 1H, 4′-H, $J_{3',4'}$ = 4.7, $J_{4',5'}$ = 4.3 Hz), 4.47–4.65 (m, 6H, benzyl-H), 5.03 (d, 1H, 1′-H, $J_{1',2'}$ = 6.0 Hz), 6.31–6.33 (m, 2H, furan 3,4-H), 7.16–7.37 (m, 16H, furan 5-H, Ph-H).

*2-(2, 3, 5-Tri-O-benzyl-*D*-ribofuranosyl)thiophene* (**4b**). Oil; IR (neat) 2830, 1080 cm^{-1}. HRMS (FAB) calcd for $C_{30}H_{30}O_4SNa$ $(M + Na)^+$: 509.1763; found: 509.1771. Anal. calcd for $C_{30}H_{30}O_4S$: C, 74.05; H, 6.21; found: C, 73.90; H, 6.07. ^1H NMR (500 MHz, $CDCl_3$): (α-form) δ 3.59–3.77 (m, 2H, 5′-H), 4.03 (dd, 1H, 2′-H, $J_{1',2'}$ = 3.3, $J_{2',3'}$ = 3.7 Hz), 4.24–4.28 (m, 2H, 3′,4′-H), 4.34–4.60 (m, 6H, benzyl-H), 5.33 (d, 1H, 1′-H, $J_{1',2'}$ = 3.3 Hz), 6.96–7.08 (m, 1H, thiophene 4-H), 7.16 (d, 1H, thiophene 3-H, $J_{3',4'}$ = 2.2 Hz), 7.18–7.20 (m, 1H, thiophene 5-H), 7.22–7.33 (m, 15H, Ph-H).

(β-form) δ 3.60 (d, 2H, 5′-H, $J_{4',5'}$ = 4.4 Hz), 3.91 (dd, 1H, 2′-H, $J_{1',2'}$ = 6.6, $J_{2',3'}$ = 5.0 Hz), 4.01 (dd, 1H, 3′-H, $J_{2',3'}$ = 5.0, $J_{3',4'}$ = 3.8 Hz), 4.31 (dd, 1H, 4′-H, $J_{3',4'}$ = 3.8, $J_{4',5'}$ = 4.4 Hz), 4.49–4.63 (m, 6H, benzyl-H), 5.26 (d, 1H, 1′-H, $J_{1',2'}$ = 6.6 Hz), 6.95 (dd, 1H, thiophene 4-H, J = 3.9, 4.9 Hz), 7.05 (m, 1H, thiophene 3-H), 7.21–7.34 (m, 16H, thiophene 5-H, Ph-H).

*2- (2, 3, 5- Tri -O-benzyl-*D*-ribofuranosyl)pyrrole.* A mixture of compound **4c** (121.8 mg, 0.2 mmol), 18-crown-6 (52.8 mg, 0.2 mmol), KOH (1.0 g, 17.9 mmol), CH_3OH (2 mL), and dioxane (2 mL) was stirred for 1 hour at room temperature. The resulting mixture was quenched with 1 M HCl (15 mL), extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under the reduced pressure. The residue was purified by pTLC on silica gel (eluent: ethyl acetate/hexane, 5:1, R_f = 0.4); yield; 85%, Oil; IR (neat) 3260, 2840, 1440, 1100 cm^{-1}. HRMS (FAB) calcd for $C_{30}H_{32}O_4N$ $(M + H)^+$: 470.2331; found: 470.2336. Anal. calcd for $C_{30}H_{31}O_4N$: C, 76.73; H, 6.65; N, 2.98; found: C, 76.69; H, 6.58; N, 3.19. ^1H NMR (500 MHz, $CDCl_3$): (α-form) δ 3.69 (dd, 1H, 5′-H, J_{gem} = 10.2, $J_{4',5'}$ = 1.7 Hz), 3.98 (dd, 1H, 5′-H, J_{gem} = 10.2, $J_{4',5'}$ = 2.1 Hz), 3.93–4.76 (m, 9H, 2′,3′,4′-H, benzyl-H), 5.22 (d, 1H, 1′-H, $J_{1',2'}$ = 2.0 Hz), 5.89–6.05 (m, 3H, pyrrole 3,4,5-H), 7.15–7.38 (m, 15H, Ph-H), 9.42 (brs, 1H, pyrrole 1-H).

(β-form) δ 3.51 (dd, 1H, 5′-H, J_{gem} = 10.1, $J_{4',5'}$ = 3.3 Hz), 3.60 (dd, 1H, 5′-H, J_{gem} = 10.1, $J_{4',5'}$ = 3.4 Hz), 3.93–4.76 (m, 9H, 2′,3′,4′-H, benzyl-H), 5.18 (d, 1H, 1′-H, $J_{1',2'}$ = 4.6 Hz), 6.05–6.19 (m, 3H, pyrrole 3,4,5-H), 7.15–7.38 (m, 15H, Ph-H), 9.29 (brs, 1H, pyrrole 1-H).

*2-(2, 3, 5-Tri-O -benzyl-*D*-ribofuranosyl)benzofuran* (**4d**). Oil; IR (neat) 2850, 1450, 1080 cm^{-1}. HRMS (FAB) calcd for $C_{34}H_{32}O_5$ $(M)^+$: 520.2250; found: 520.2261. Anal. calcd for $C_{34}H_{32}O_5$: C, 78.44; H, 6.20; found: C, 78.70; H, 6.07. ^1H NMR (500 MHz, $CDCl_3$): (α-form) δ 3.62 (dd, 1H, 5′-H, J_{gem} = 11.0, $J_{4',5'}$ = 3.5 Hz), 3.78 (dd, 1H, 5′-H, J_{gem} = 11.0, $J_{4',5'}$ = 2.8 Hz), 4.09–4.63 (m, 9H, 2′,3′,4′-H, benzyl-H), 5.23 (d, 1H, 1′-H, $J_{1',2'}$ = 3.5 Hz), 6.87 (s, 1H, benzofuran

3-H), 7.09–7.56 (m, 19H, benzofuran 4,5,6,7-H, Ph-H).

(β-form) δ 3.65 (dd, 1H, 5'-H, J_{gem} = 6.7, $J_{4',5'}$ = 4.1 Hz), 3.71 (dd, 1H, 5'-H, J_{gem} = 6.7, $J_{4',5'}$ = 3.9 Hz), 4.12 (dd, 1H, 3'-H, $J_{2',3'}$ = 5.2, $J_{3',4'}$ = 5.0 Hz), 4.26 (dd, 1H, 2'-H, $J_{1',2'}$ = 5.5, $J_{2',3'}$ = 5.2 Hz), 4.35 (ddd, 1H, 4'-H, $J_{3',4'}$ = 5.0, $J_{4',5'}$ = 4.1, $J_{4',5'}$ = 3.9 Hz), 4.53–4.65 (m, 6H, benzyl-H), 5.18 (d, 1H, 1'-H, $J_{1',2'}$ = 5.5 Hz), 6.70 (s, 1H, benzofuran 3-H), 7.07–7.49 (m, 19H, benzofuran 4,5,6,7-H, Ph-H).

3-(2,3,5-Tri-O-benzyl-D-ribofuranosyl)benzothiophene (**4e**). Oil; IR (neat) 2850, 1440, 1080 cm^{-1}. HRMS (FAB) calcd for $C_{34}H_{32}O_4S$ $(M)^+$: 536.2021; found: 536.2023. Anal. calcd for $C_{34}H_{32}O_4S$: C, 76.09; H, 6.01; found: C, 76.03; H, 6.02. ^1H NMR (500 MHz, $CDCl_3$): (α-form) δ 3.66 (dd, 1H, 5'-H, J_{gem} = 11.0, $J_{4',5'}$ = 3.3 Hz), 3.82 (dd, 1H, 5'-H, J_{gem} = 11.0, $J_{4',5'}$ = 2.5 Hz), 3.97, 4.04 (d × 2, 1H × 2, benzyl-H, J_{gem} = 11.8 Hz), 4.24 (t, 1H, 2'-H, $J_{1',2'}$ = 3.0 Hz), 4.35–4.63 (m, 6H, 3',4'-H, benzyl-H), 5.46 (dd, 1H, 1'-H, $J_{1',2'}$ = 3.0, $J_{1',2}$ = 0.8 Hz), 6.84–7.37 (m, 17H, benzothiophene 5,6-H, Ph-H), 7.65 (d, 1H, benzothiophene 2-H, $J_{1',2}$ = 0.8 Hz), 7.71 (m, 1H, benzothiophene 4-H), 7.88 (m, 1H, benzothiophene 7-H).

3-(2, 3, 5-Tri - O-benzyl-D-ribofuranosyl)indole. Desulfonylation of compound **4f** was carried out by the same method as described in 2-(2,3,5-tri-*O*-benzyl-D-ribofuranosyl) pyrrole. Oil; IR (neat) 3250, 2800, 1420, 1060 cm^{-1}. HRMS (FAB) calcd for $C_{34}H_{33}O_4N$ $(M)^+$: 519.2410; found: 519.2388. Anal. calcd for $C_{34}H_{33}O_4N$: C, 78.59; H, 6.40; N, 2.70; found: C, 78.89; H, 6.40; N, 3.00. ^1H NMR (500 MHz, $CDCl_3$): (α-form) δ 3.64–4.69 (m, 11H, 2',3',4',5'-H, benzyl-H), 5.45 (d, 1H, 1'-H, $J_{1',2'}$ = 3.4 Hz), 6.97–7.65 (m, 20H, indole 2,4,5,6,7-H, Ph-H), 8.16 (brs, 1H, indole 1-H).

(β-form) δ 3.66 (dd, 1H, 5'-H, J_{gem} = 10.5, $J_{4',5'}$ = 3.6 Hz), 3.75 (dd, 1H, 5'-H, J_{gem} = 10.5, $J_{4',5'}$ = 3.9 Hz), 4.11–4.35 (m, 3H, 2',3',4'-H), 4.53–4.69 (m, 6H, benzyl-H), 5.33 (d, 1H, 1'-H, $J_{1',2'}$ = 6.3 Hz), 6.99 (dd, 1H, indole 5-H, $J_{4,5}$ = 8.0, $J_{5,6}$ = 0.8 Hz), 7.15–7.36 (m, 18H, indole 2,6,7-H, Ph-H), 7.65 (d, 1H, indole 4-H, $J_{4,5}$ = 8.0 Hz), 8.02 (brs, 1H, indole 1-H).

2-(2, 3, 5-Tri-O-benzyl-D-ribofuranosyl)-5-(trimethylsilyl)furan (**5a**). Oil, IR (neat) 2890, 1720, 1120, 850 cm^{-1}. HRMS (FAB) calcd for $C_{33}H_{37}O_5Si$ $(M - H)^+$: 541.2410; found: 541.2415. ^1H NMR (270 MHz, $CDCl_3$): (α-form) δ 0.28 (s, 9H, TMS-H), 3.40–4.60 (m, 11H, 2',3',4',5'-H, benzyl-H), 5.28 (d, 1H, 1'-H, $J_{1',2'}$ = 3.8 Hz), 6.09–6.55 (m, 2H, furan 3, 4-H), 7.13–7.40 (m, 15H, Ph-H).

(β-form) δ 0.22 (s, 9H, TMS-H), 3.58–3.63 (m, 2H, 5'-H), 4.05 (dd, 1H, 2'-H, $J_{1',2'}$ = 5.6, $J_{2',3'}$ = 5.0 Hz), 4.15 (dd, 1H, 3'-H, $J_{2',3'}$ = 5.0, $J_{3',4'}$ = 4.7 Hz), 4.25–4.35 (m, 1H, 4'-H), 4.51–4.66 (m, 6H, benzyl-H), 5.08 (d, 1H, 1'-H, $J_{1',2'}$ = 5.6 Hz), 6.29 (d, 1H, furan 4-H, $J_{3,4}$ = 3.3 Hz), 6.53 (d, 1H, furan 3-H, $J_{3,4}$ = 3.3 Hz), 7.22–7.35 (m, 15H, Ph-H).

2-(2, 3, 5-Tri-O-benzyl-D-ribofuranosyl)-5-(trimethylsilyl)thiophene (**5b**). Oil; IR (neat) 2880, 1720, 850 cm^{-1}. HRMS (FAB) calcd for $C_{33}H_{37}O_4SSi$ $(M - H)^+$: 557.2182; found: 557.2176. ^1H NMR (270 MHz, $CDCl_3$): (α-form) δ 0.29 (s, 9H, TMS-H), 3.55–4.64 (m, 11H, 2',3',4',5'-H, benzyl-H), 5.37 (d, 1H, 1'-H, $J_{1',2'}$ = 3.2 Hz), 6.96–7.10 (m, 17H, thiophene 3,4-H, Ph-H).

(β-form) δ 0.30 (s, 9H, TMS-H), 3.65 (d, 2H, 5'-H, $J_{4',5'}$ = 4.3 Hz), 3.93 (dd, 1H, 2'-H, $J_{1',2'}$ = 6.3, $J_{2',3'}$ = 5.0 Hz), 4.02 (dd, 1H, 3'-H, $J_{2',3'}$ = 5.0, $J_{3',4'}$ = 3.9 Hz), 4.27–4.34 (m, 1H, 4'-H), 4.52–4.63 (m, 6H, benzyl-H), 5.29 (d, 1H, 1'-H, $J_{1',2'}$ = 6.3 Hz), 7.18 (s, 2H, thiophene 3,4-H), 7.39–7.75 (m, 15H, Ph-H).

1-Penylsulfonyl-2-(2, 3, 5-tri-O-benzyl-D-ribofuranosyl)-5-(trimethylsilyl)pyrrole (**5c**). Mp 116–124°C; IR (KBr) 2900, 1720, 1370, 1160, 850 cm^{-1}. HRMS (FAB) calcd for $C_{39}H_{43}O_6NSSi$ $(M)^+$: 681.2580; found: 681.2579. ^1H NMR (500 MHz, $CDCl_3$): (α-form) δ 0.31 (s, 9H, TMS-H), 3.47–4.71 (m, 11H, 2',3',4',5'-H, benzyl-H), 5.26 (d, 1H, 1'-H, $J_{1',2'}$ = 2.2 Hz), 6.49 (d, 1H, pyrrole 4-H, $J_{3,4}$ = 3.3 Hz), 6.62 (d, 1H, pyrrole 3-H, $J_{3,4}$ = 3.3 Hz), 7.21–7.51 (m, 20H, SO_2Ph-H, Ph-H).

(β-form) δ 0.31 (s, 9H, TMS-H), 3.47–4.71 (m, 11H, 2',3',4',5'-H, benzyl-H), 5.27 (d, 1H, 1'-H, $J_{1',2'}$ = 3.1 Hz), 6.66–6.68 (m, 2H, pyrrole 3,4-H), 7.21–7.51 (m, 20H, SO_2Ph-H, Ph-H).

3-(2, 3, 5-Tri-O-benzyl-D-ribofuranosyl)-2-(trimethylsilyl)benzofuran (**5d**). Oil; IR (neat) 2880, 1440, 1250, 1030, 850 cm^{-1}. HRMS (FAB) calcd for $C_{37}H_{40}O_5Si$ $(M)^+$: 592.2645; found: 592.2639. ^1H NMR (500 MHz, $CDCl_3$): (α-form) δ 0.33 (s, 9H, TMS-H), 3.68 (dd, 1H, 5'-H, J_{gem} = 11.0, $J_{4',5'}$ = 3.3 Hz), 3.81 (dd, 1H, 5'-H, J_{gem} = 11.0, $J_{4',5'}$ = 2.5 Hz), 4.04–4.63 (m, 9H, 2',3',4'-H, benzyl-H), 5.33 (d, 1H, 1'-H, $J_{1',2'}$ = 3.0 Hz), 6.82–7.36 (m, 17H, benzofuran 5,6-H, Ph-H), 7.46 (d, 1H, benzofuran 7-H, J = 8.3 Hz), 7.79 (d, 1H, benzofuran 4-H, J = 7.4 Hz).

3-(2, 3, 5-Tri-O-benzyl-D-ribofuranosyl)-2-(trimethylsilyl)benzothiophene (**5e**). Oil; IR (neat) 2870, 1440, 1250, 1100, 850 cm^{-1}. HRMS (FAB) calcd for $C_{37}H_{40}O_4SSi$ $(M)^+$: 608.2417; found: 608.2413. ^1H NMR (270 MHz, $CDCl_3$): (α-form) δ 0.36 (s, 9H, TMS-H), 3.65–4.89 (m, 11H, 2',3',4',5'-H, benzyl-H), 5.48 (d, 1H, 1'-H, $J_{1',2'}$ = 2.3 Hz), 6.72–8.11 (m, 19H, benzothiophene 4,5,6,7-H, Ph-H).

(β-form) δ 0.44 (s, 9H, TMS-H), 3.65–4.89 (m, 11H, 2',3',4',5'-H, benzyl-H), 5.34 (d, 1H, 1'-H, $J_{1',2'}$ = 8.6 Hz), 6.91–8.11 (m, 19H, benzothiophene 4,5,6,7-H, Ph-H).

2-(D-Ribofuranosyl)thiophene. To a solution of **4b** (80 mg, 0.17 mmol) in CH_2Cl_2 (20 mL) was added

dropwise a solution of 1 M BCl_3 in CH_2Cl_2 (0.8 mL, 0.8 mmol) at −78°C. After being stirred for 1 hour at the same temperature, the mixture was added to dry CH_3OH/CH_2Cl_2 (1:1, 8 mL) and then neutralized with powdered $NaHCO_3$ at room temperature. The resulting mixture was filtered and washed with dry CH_3OH. The combined filtrate and washings were condensed and purified by pTLC on silica gel (eluent: $CHCl_3/CH_3OH$, 9:1, R_f = 0.2); yield: 35%, ^1H NMR (270 MHz, $CDCl_3/CD_3OD$): (α-form) δ 3.67–4.37 (m, 8H, 2′,3′,4′,5′-H, 2′,3′,5′-OH), 5.32 (d, 1H, 1′-H, $J_{1',2'}$ = 3.0 Hz), 6.97–7.10 (m, 2H, thiophene 3,4-H), 7.27–7.34 (m, 1H, thiophene 5-H).

(β-form) δ 3.67–4.37 (m, 8H, 2′,3′,4′,5′-H, 2′,3′,5′-OH), 5.01 (d, 1H, 1′-H, $J_{1',2'}$ = 5.9 Hz), 6.97–7.10 (m, 2H, thiophene 3,4-H), 7.27–7.34 (m, 1H, thiophene 5-H). Each anomer was separated from a mixture of α- and β-forms by HPLC (column: JAIGEL GS-320A (8 mmϕ × 500 mm); eluent: CH_3OH/H_2O, 45:55).

3-(D-Ribofuranosyl)indole. ^1H NMR (270 MHz, $CDCl_3/CD_3OD$): (α-form) δ 3.25–4.28 (m, 8H, 2′,3′,4′,5′-H, 2′,3′,5′-OH), 5.05 (d, 1H, 1′-H, $J_{1',2'}$ = 6.0 Hz), 7.05–7.37 (m, 3H, indole 2,5,6,7-H), 7.68 (d, 1H, indole 4-H, J = 7.7 Hz), 9.46 (brs, 1H, indole 1-H).

(β-form) δ 3.25–4.28 (m, 8H, 2′,3′,4′,5′-H, 2′,3′,5′-OH), 4.80 (d, 1H, 1′-H, $J_{1',2'}$ = 9.0 Hz), 7.05–7.37 (m, 3H, indole 2,5,6,7-H), 7.61 (d, 1H, indole 4-H, J = 8.0 Hz), 9.54 (brs, 1H, indole 1-H). Each anomer was separated from a mixture of α- and β-forms by HPLC (column: JAIGEL GS-320 (20 mmϕ × 500 mm); eluent: CH_3OH; cycle: 12 times).

ACKNOWLEDGMENT

This work was supported by Grant-in-Aid No. 06453061 for Scientific Research from the Ministry of Education, Science and Culture, Japan.

REFERENCES

[1] (a) M. Yokoyama, N. Yamada, H. Togo, *Chem. Lett.*, 1990, 753; (b) H. Togo, N. Ogasawara, T. Kuramochi, M. Yokoyama, *Chem. Express, 6*, 1991, 595; (c) H. Togo, M. Aoki, M. Yokoyama, *Chem. Lett.*, 1991, 1691; (d) M. Yokoyama, K. Sujino, M. Irie, N. Yamazaki, T. Hiyama, N. Yamada, H. Togo, *J. Chem. Soc., Perkin Trans., 1*, 1991, 2801; (e) H. Togo, M. Aoki, M. Yokoyama, *Tetrahedron Lett., 32*, 1991, 6559; (f) H. Togo, S. Ishigami, M. Yokoyama, *Chem. Lett.*, 1992, 1673; (g) M. Yokoyama, T. Tanabe, A. Toyoshima, H. Togo, *Synthesis*, 1993, 517; (h) M. Yokoyama, A. Toyoshima, T. Akiba, H. Togo, *Chem. Lett.*, 1994, 265.

[2] T. Mukaiyama, M. Yoshiyuki, S. Shoda, *Chem. Lett.*, 1981, 431; S. Hashimoto, M. Hayashi, R. Noyori, *Tetrahedron Lett., 25*, 1984, 1379; (c) T. Matsumoto, M. Katsuki, H. Jona, K. Suzuki, *J. Am. Chem. Soc., 113*, 1991, 6982.

[3] (a) M. Chemielewski, J. N. BeMiller, D. P. Cerretti, *Carbohydr. Res., 97*, 1981, Cl; (b) G. Grynkiewicz and J. N. BeMiller, *Carbohydr. Res. 108*, 1982, 229; (c) F. G. DeLas Heras, A. San Felix, P. Fernandez-Resa, *Tetrahedron, 39*, 1983, 1617; (d) K. C. Nicolaou, R. E. Dolle, A. Chucholowski, J. L. Randall, *J. Chem. Soc. Chem. Commun.*, 1984, 1153; (e) K. C. Nicolaou, A. Chucholowski, R. E. Dolle, J. L. Randall, *J. Chem. Soc. Chem. Commun.*, 1984, 1155: (f) R. B. Meyers, Y. C. Lee, *Carbohydr. Res., 132*, 1984, 61; (g) Y. Araki, N. Kobayashi, Y. Ishido, J. Nagasawa, *Carbohydr. Res., 171*, 1987, 125; (h) M. Katsuki, K. Suzuki, *Tetrahedron Lett., 30*, 1989, 833; (i) G. N. Drew, P. H. Gross, *J. Org. Chem., 56*, 1991, 509.

[4] G. H. Posner, S. R. Haines, *Tetrahedron Lett., 26*, 1985, 5; T. Mukaiyama, Y. Hashimoto, S. Shoda, *Chem. Lett.*, 1983, 935.

[5] R. A. Benkeser, R. B. Currie, *J. Am. Chem. Soc., 70*, 1948, 1780; J. R. Pratt, F. H. Pinkerton, S. F. Thames, *J. Organometal. Chem., 38*, 1972, 29.

[6] R. M. Acheson: *An Introduction to the Chemistry of Heterocyclic Compounds*, John Wiley & Sons, Inc., New York, pp. 193 and 221 (1976).

[7] F. K. Kipping, L. L. Lloyd, *J. Chem. Soc.*, 1901, 449.

[8] J. Rokach, P. Hamel, M. Kakushima, G. M. Smith, *Tetrahedron Lett., 22*, 1981, 4901.

[9] S. R. Wilson, L. A. Jacob, *J. Org. Chem., 51*, 1986, 4833.

[10] K. Dey, C. Eaborn, D. R. M. Walton, *Organometallics in Chemical Synthesis, 1*, 1970–1971, 151.

[11] F. Effenberger, W. Spiegler, *Angew. Chem., Int. Ed. Engl., 20*, 1981, 265.

[12] E. P. Papadopoulos, N. F. Haidar, *Tetrahedron Lett, 14*, 1968, 1721.