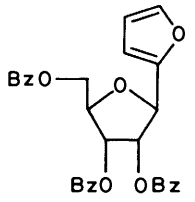
C-Nucleosides. Part 9.† Synthesis of Carbazole and Pyrrole *C*-Nucleosides from 2-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)furan

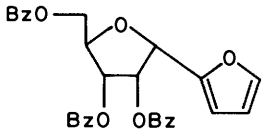
Isamu Maeba,* Tomohiko Takeuchi, Takashi Iijima, Kazuhiro Kitaori, and Hiroko Muramatsu
Faculty of Pharmacy, Meijo University, Tempaku-ku, Nagoya 468, Japan

The synthesis of carbazole and pyrrole *C*-nucleosides from 2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-furan (**1**) is described. The key synthetic intermediate γ-keto aldehyde (**7**) can be obtained from the tetrahydrofuran (**5**), which was prepared by hydrogenation of the dihydrofuran (**3**) using 10% palladium–carbon. Treatment of compound (**7**) with indole in dichloromethane under acidic conditions afforded the protected carbazole (**9**). Deprotection of compound (**9**) with methanolic sodium hydroxide afforded compound (**11**) in 55% yield. Treatment of the furan (**5**) with ethyl carbamate in the presence of 50% trifluoroacetic acid in acetone afforded, in 26% yield, ethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrole-1-carboxylate (**15**) and its α isomer (**16**) in a 7:1 ratio. Deprotection of compounds (**15**) and (**16**) with methanolic sodium hydroxide afforded compounds (**19**) and (**20**).

The biological activity shown by various *C*-nucleosides has provided the impetus for considerable synthetic effort.[1] Recently, 2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)furan (**1**) has been shown to be a useful intermediate for the synthesis of various *C*-nucleosides.[2] The carbazole group of naturally occurring compounds has aroused considerable interest in the past twenty years due to its biological activity.[3] Whereas



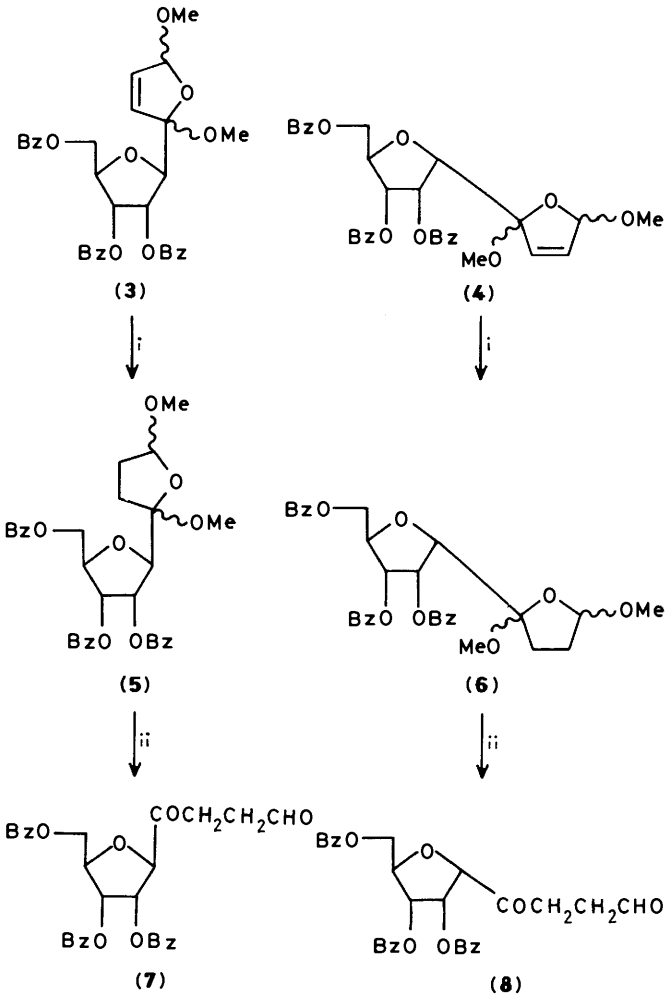
(**1**)



(**2**)

Kozikowski and Cheng[4] have prepared *N*-phenylsulphonyl-4-(β-D-ribofuranosyl)-9*H*-carbazole, to our knowledge no carbazole *C*-nucleosides have been prepared with a glycosyl moiety at C-1. It therefore seemed desirable to synthesize some carbazole *C*(1)-nucleosides, which may show interesting and/or improved biological effects. We now report the synthesis of 1-(β-D-ribofuranosyl)-9*H*-carbazoles from compound (**1**), employing the key synthetic intermediate γ-keto aldehyde (**7**) obtained from 2,5-dimethoxy-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)tetrahydrofuran (**5**) by tetrahydrofuran ring opening (Scheme 1).

The starting tetrahydrofuran derivative (**5**) was prepared by hydrogenation of 2,5-dimethoxy-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2,5-dihydrofuran (**3**) with 10% palladium–carbon in methanol. The crude tetrahydrofuran derivative (**5**) was treated with 50% aqueous trifluoroacetic acid (TFA) in acetone at room temperature for 4 h to afford the ring-opened product (**7**). It is reasonable to assume that compound (**7**) has the β configuration, since complete inversion to the other isomer (*i.e.*, from β to α) under the reaction conditions would be highly unlikely. To confirm this, we also attempted to prepare the corresponding α isomer from compound (**2**) by procedures analogous to those for the preparation of the β isomer. The α isomer can be distinguished from its β counterpart on the basis of its ^{1}H n.m.r. data. The chemical



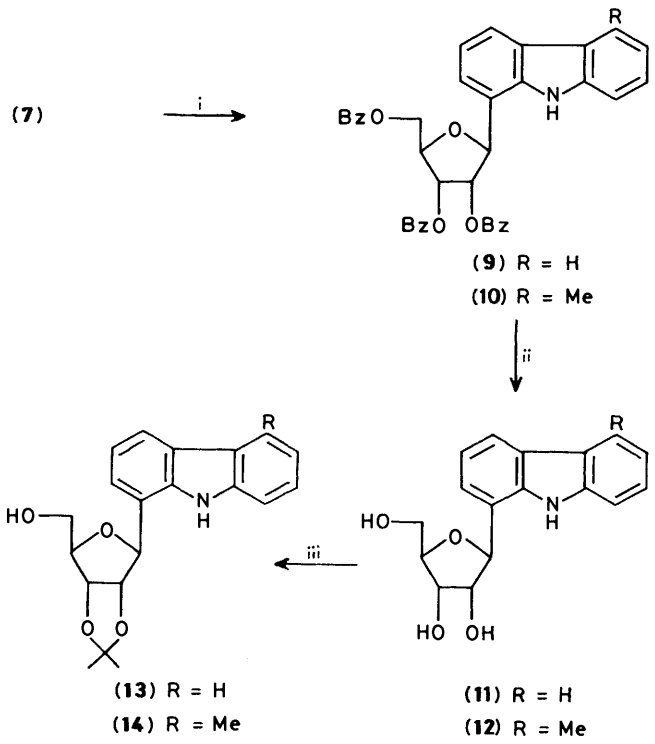
Scheme 1. *Reagents:* i, 10% Pd–C/MeOH; ii, 50% TFA, acetone

shift of the anomeric proton in compound (**8**) (δ 5.01) appears downfield from that of compound (**7**) (δ 4.82) since the β face location of this anomeric proton placed it out of the shielding influence of the 2′-oxygen. This is in agreement with the general trend seen for most nucleoside anomeric pairs.[5]

The procedure for conversion of the furan ring of compound

† Part 8 is I. Maeba, M. Suzuki, N. Takahashi, T. Iijima, and H. Furukawa, *J. Heterocycl. Chem.*, 1988, **25**, 503.

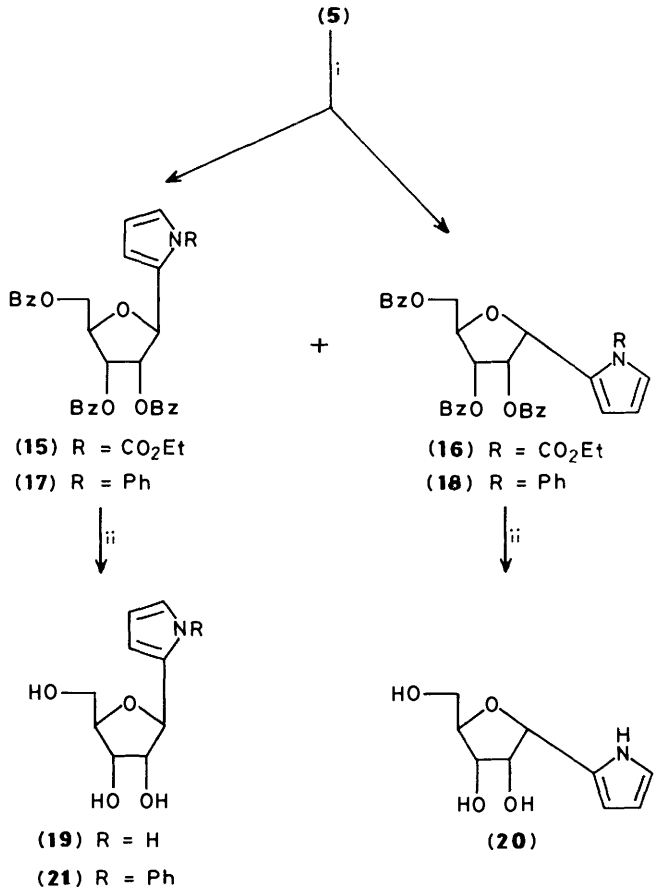
(1) into a carbazole ring utilized the Lewis acid-catalysed double condensation of the γ-keto aldehyde (7) with 2,3-unsubstituted indoles.[6] Treatment of compound (7) with indole in dichloromethane under acidic condition at room temperature afforded 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-9*H*-carbazole (9) in 10% yield. Deprotection of compound (9) with methanolic sodium hydroxide afforded 1-(β-D-ribofuranosyl)-9*H*-carbazole (11) in 55% yield. By the same procedure, the 5-methylcarbazole (10) and its deprotected compound (12) were prepared from 4-methylindole (Scheme 2). Structural assign-



Scheme 2. *Reagents:* i, indoles, BF_3·Et_2O, CH_2Cl_2; ii, 1M-NaOH–MeOH; iii, PTSA, acetone

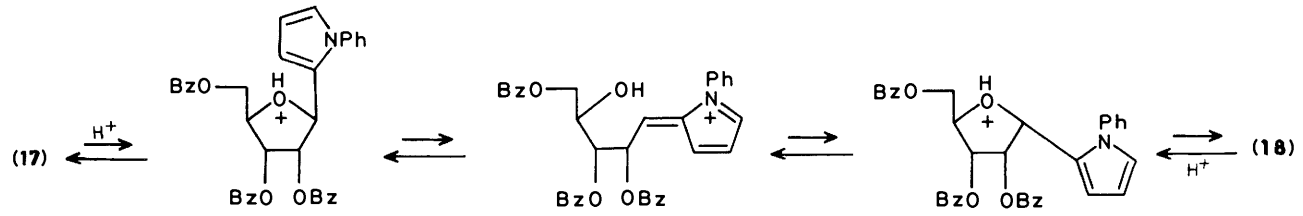
ments of compounds (11) and (12) were based on u.v., ^1H, ^{13}C n.m.r., and high-resolution mass spectra (see Experimental section). The u.v. spectra of compounds (11) and (12) exhibited similar patterns to that of the parent carbazole.[7] On the other hand, none of the corresponding α carbazole was obtained from compound (8) under a variety of experimental conditions using acidic condensing agents. In order to determine the anomeric configuration, the isopropylidene acetal (13) was synthesized from compound (11) by using ethyl orthoformate and acetone in the presence of toluene-*p*-sulphonic acid (PTSA). Its ^1H n.m.r. spectrum showed two singlets at δ 1.37 and 1.70 (Δδ 0.33 p.p.m.: a value of less than 0.10 p.p.m. would be expected in the case of an α anomer[8]). The proton of C-4′ showed a quartet, and the absorption of 3′-H was well resolved, the coupling of 3′-H and 4′-H being ~4.0 Hz. In α anomers this coupling constant should be zero, resulting in an apparent triplet for 4′-H.[9] These results thus showed that the β ribofuranoside configuration had been preserved during the reaction sequence.

A convenient route for the synthesis of pyrroles from furans is through the acid-catalysed reaction of amines with 2,5-dialkoxytetrahydrofurans which may in turn be prepared by the reaction of furan with alcohols and bromine or by electrolytic alkoxylation of furan, and subsequent hydrogenation of the dihydrofurans.[10] Attempted ring transformation of compound (5) into the corresponding pyrrole with ammonia or ammonium acetate under a variety of conditions led to decomposition of the starting material. Treatment of (5) with ethyl carbamate in the presence of 50% TFA in acetone at reflux temperature afforded two major products. These were separable by preparative t.l.c. (p.l.c.) and identified as ethyl 2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrole-1-carboxylate (15) and its α isomer (16) in a combined yield of 26% and in a 7:1 ratio, respectively. The assignments of the anomeric configuration at C-1′ to products (15) and (16) were based on comparison of their ^1H n.m.r. spectra. The chemical shift of the anomeric proton in compound (16) (δ 6.16) appeared downfield from that of compound (15) (δ 5.91) since the β face location of this anomeric proton placed it out of the shielding influence of the 2′-oxygen. The removal of the sugar protecting groups and *N*-ethoxycarbonyl group in compounds (15) and (16) was readily accomplished in methanolic sodium hydroxide at room temperature, resulting in 2-(β-D-ribofuranosyl)pyrrole (19) and α isomer (20) in 48 and 36% yield, respectively (Scheme 3).



Scheme 3. *Reagents:* i, RNH_2, H^+; ii, 5% NaOH–MeOH

Treatment of compound (5) with aniline in the presence of PTSA in benzene at room temperature afforded the 1-phenyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrole (17) and α isomer (18) in a combined yield of 51% and a 7:1 ratio, based on the intensities of the signals for the anomeric and the pyrrole ring protons. The separation of the pure β anomer from the mixture was carried out by p.l.c. The spectrum of compound (18) exhibited a signal for 1′-H appearing further downfield than that for compound (17). This indicated that compounds (17) and (18) are the β and α glycoside, respectively. On the other hand, treatment of the α tetrahydrofuran derivative (4) with aniline in the presence of 50% TFA in benzene at room



Scheme 4.

temperature afforded compound (**17**) and α isomer (**18**) in a combined yield of 41% and a 7:1 ratio, respectively. Even if a single isomer (configuration only at C-1′) of the THF derivative was used, a mixture of β and α anomers (**17**) and (**18**) was obtained due to anomerization during the reaction, which is consistent with our previous observation. Owing to the electron-donor properties of the pyrrole heterocycle, protonation of the ribofuranose ring oxygen atom, subsequent ring opening, and cyclization yields predominantly the thermodynamically more stable isomer (**17**) (Scheme 4). Deprotection of compound (**17**) with methanolic sodium hydroxide afforded 1-phenyl-2-(β-D-ribofuranosyl)pyrrole (**21**) in 79% yield. Studies to evaluate the biological activity of these pyrrole *C*-nucleosides will be reported elsewhere.

Experimental

M.p.s were determined on a Yanagimoto apparatus and are uncorrected. I.r. spectra were measured with a JASCO IRA-1 spectrometer. ^{1}H N.m.r. spectra were measured with a JNM-GX-270 spectrometer, with tetramethylsilane as internal standard. ^{13}C N.m.r. spectra were recorded on a JEOL JNM-FX-100 Fourier transform spectrometer operating at 25.00 MHz, with tetramethylsilane as internal standard. U.v. spectra were obtained on a JASCO UVIDEC-610 spectrophotometer. Elemental analyses were determined in the analytical centre of this faculty. Analytical t.l.c. was performed on glass plates coated with a 0.5 mm layer of silica gel GF_{254} (Merck). The compounds were detected with u.v. light (254 nm). Column chromatography was performed on silica gel C-200 (74—149 μm, Wakogel).

2,5-*Dimethoxy*-2-(2′,3′,5′-*tri*-O-*benzoyl*-β- *and* -α-D-*ribofuranosyl*)*tetrahydrofuran* (**5**) *and* (**6**).—To a suspension of 10% palladium–carbon (300 mg) in methanol (15 ml) was added a solution of the dihydrofuran (**3**)[11] (736.4 mg, 1.28 mmol) in methanol (15 ml) and the mixture was stirred under hydrogen at atmospheric pressure and 40 °C for 4 h. After the catalyst was removed by filtration, the solvent was evaporated off under reduced pressure. The residue was chromatographed over a column of silica gel with chloroform as eluant, to give the β *isomeric mixture* (**5**) (679.1 mg, 91.1%) as a syrup which was chromatographically inseparable (Found: C, 66.3; H, 5.6. $C_{32}H_{32}O_{10}$ requires C, 66.66; H, 5.59%).

In the same manner the α *isomeric mixture* (**6**) (288 mg, 97%) was obtained as a syrup from the α dihydrofuran (**4**)[11] (296 mg, 0.51 mmol) (Found: C, 66.4; H, 5.21%).

4-*Oxo*-4-(2′,3′,5′-*tri*-O-*benzoyl*-β- *and* -α-D-*ribofuranosyl*)*butanal* (**7**) *and* (**8**).—To a solution of the β tetrahydrofuran derivative (**5**) (373.7 mg, 0.65 mmol) in acetone (10 ml) at 0 °C was added 50% TFA (2.9 ml), and the resulting solution was stirred at room temperature for 4 h. The reaction mixture was neutralized with saturated aqueous sodium hydrogen carbonate and then extracted with chloroform (3 × 30 ml). The extracts were combined, washed with water, dried ($MgSO_4$) and evaporated under reduced pressure to afford a syrup, which was chromatographed over a column of silica gel with chloroform–benzene (9:1) as eluant, to give the *product* (**7**) (290.1 mg, 84.4%) as a syrup (Found: C, 67.0; H, 5.0. $C_{30}H_{26}O_9 \cdot \frac{1}{2}H_2O$ requires C, 66.78; H, 5.05%); $\delta_H(CDCl_3)$ 2.78 (2 H, t, *J* 6.1 Hz, 2- or 3-H_2), 2.95 (2 H, t, *J* 6.1 Hz, 3- or 2-H_2), 4.62 (3 H, m, 4′-H and 5′-H_2), 4.82 (1 H, d *J* 4.0 Hz, 1′-H) 5.65 (1 H, t, *J* 4.0 Hz, 3′-H), 5.82 (1 H, t, *J* 4.0 Hz, 2′-H), 7.18—8.20 (15 H, m, Ph), and 9.77 (1 H, s, CHO); $\delta_C(CDCl_3)$ 31.12, 37.20 (C-2 and -3), 63.94 (C-5′), 72.37, 73.30, 80.32, 85.47 (C-1′, -2′, -3′, and -4′), 128.47—133.27 (Ar-C), 165.27, 166.21 (ArC=O), 199.79 (C-4), and 205.34 (C-1).

In the same manner the α *isomer* (**8**) (73.2 mg, 83%) was obtained as a syrup from the α tetrahydrofuran derivative (**6**) (96 mg, 0.15 mmol) (Found: C, 67.0; H, 5.0. $C_{30}H_{26}O_9 \cdot \frac{1}{2}H_2O$ requires C, 66.78; H, 5.05%); $\delta_H(CDCl_3)$ 2.75 (2 H, t, *J* 6.4 Hz, 2- or 3-H_2), 3.03 (2 H, t, *J* 6.4 Hz, 3- or 2-H_2), 4.57 (1 H, dd, *J* 12.1 and 4.0 Hz, 5′-H_a), 4.74 (1 H, dd, *J* 12.1 and 3.7 Hz, 5′-H_b), 4.80—4.85 (1 H, m, 4′-H), 5.01 (1 H, d, *J* 4.7 Hz, 1′-H) 5.82 (1 H, dd, *J* 7.4 and 4.7 Hz, 3′-H), 6.23 (1 H, t, *J* 4.7 Hz, 2′-H), 7.25—8.10 (15 H, m, Ph), 9.74 (1 H, s, CHO); $\delta_C(CDCl_3)$ 32.41, 36.80 (C-2 and C-3), 63.89 (C-5′), 72.84, 73.25, 79.10, 83.72 (C-1′, -2′, -3′, and -4′), 128.36—133.62 (Ar-C), 164.92, 165.21, 166.09 (ArC=O), 199.67 (C-4), and 204.88 (C-1).

1-(2′,3′,5′-*Tri*-O-*benzoyl*-β-D-*ribofuranosyl*)-9H-*carbazole* (**9**).—A solution of keto aldehyde (**7**) (141.9 mg, 0.26 mmol) and indole (32.5 mg, 0.28 mmol) in dichloromethane (10 ml) containing $BF_3 \cdot Et_2O$ (19 mg) was heated at 40 °C for 3 h. The reaction mixture was neutralized with saturated aqueous sodium hydrogen carbonate solution and then extracted with chloroform (3 × 50 ml). The extracts were combined, washed with water, dried ($MgSO_4$), and evaporated under reduced pressure to give a syrup. The mixture was chromatographed over a column of silica gel with chloroform–benzene (1:1) as eluant, to give the *product* (**9**) (16.7 mg, 10.2%) as a syrup (Found: C, 74.3; H, 5.0; N, 2.3. $C_{38}H_{29}NO_7$ requires C, 74.61; H, 4.78; N, 2.29%); $\delta_H[(CD_3)_2CO]$ 4.94—5.07 (3 H, m, 4′-H and 5′-H_2), 5.84—5.98 (3 H, m, 1′-, 2′-, and 3′-H), 7.13—8.18 (22 H, m, ArH), and 10.23 (1 H, s, NH); $\delta_C(CDCl_3)$ 64.00 (C-5′), 71.72, 76.35, 80.44, 82.37 (C-1′, -2′, -3′, and -4′), 111.16 (C-8), 118.88—125.84 (carbazole-C), 128.47—133.68 (Ar-C), 136.66, 139.88 (C-8a and -9a), and 165.50, 166.21 (C=O).

5-*Methyl*-1-(2′,3′,5′-*tri*-O-*benzoyl*-β-D-*ribofuranosyl*)-9H-*carbazole* (**10**).—A solution of keto aldehyde (**7**) (140.7 mg, 0.26 mmol) and 4-methylindole (39.3 mg, 0.3 mmol) in dichloromethane (10 ml) containing $BF_3 \cdot Et_2O$ (19 mg) was heated at 40 °C for 3 h. Work-up as above gave *compound* (**10**) (36 mg, 21.7%) as a syrup (Found: C, 70.3; H, 5.0; N, 2.1. $C_{39}H_{31}NO_7 \cdot 2H_2O$ requires C, 70.79; H, 5.33; N, 2.12%); $\delta_H(CDCl_3)$ 2.87 (3 H, s, Me), 4.86 (1 H, m, 4′-H), 4.98 (2 H, m, 5′-H_2), 5.75 (3 H, apparent s, 1′-, 2′-, and 3′-H), 6.95—8.15 (21 H, m, ArH), and 9.92 (1 H, s, NH); $\delta_C(CDCl_3)$ 20.83 (Me), 64.00 (C-5′), 71.78, 76.35, 80.38, 82.43 (C-1′, -2′, -3′, and -4′), 108.76 (C-8), 118.82—133.74 (carbazole-C and Ar-C), 136.66, 139.94 (C-8a and 9a), and 165.50, 166.27 (C=O).

1-(β-D-*Ribofuranosyl*)-9H-*carbazole* (**11**).—To a solution of the carbazole (**9**) (20.1 mg, 0.033 mmol) in methanol–THF (2:1;

1 ml) at 0 °C was added 5% aqueous NaOH (0.2 ml) during 35 min; the mixture was rendered neutral with acetic acid and evaporated. The residue was purified by p.l.c. with chloroform–methanol (9:1) as developer, to give the *product* (**11**) (5.4 mg, 55.0%) as a syrup (Found: M^+, 299.1158. $C_{17}H_{17}NO_4$ requires M, 299.1157); $\lambda_{max.}$(MeOH) 236 (ε 19 000), 260 (10 900), 293 (7 900), 325 (2 200), and 338 nm (2 200); $\delta_H(CD_3OD)$, 3.97 (2 H, m, 5′-H_2), 4.15 (1 H, m, 4′-H), 4.30—4.35 (2 H, m, 2′- and 3′-H), 5.02 (1 H, d, *J* 7.6 Hz, 1′-H), 7.15 (2 H, apparent t, 3- and 6-H), 7.32—7.36 (2 H, m, 7- and 8-H), 7.42 (1 H, d, *J* 8.1 Hz, 2-H), 8.01 (1 H, dd, *J* 7.8 and 1.0 Hz, 5-H), and 8.03 (1 H, d, *J* 8.1 Hz, 4-H); $\delta_C(CD_3OD)$ 62.99 (C-5′), 73.69, 76.64, 86.40, 87.27 (C-1′, -2′, -3′, and -4′), 111.74 (C-8), 119.35, 119.67, 120.83, 120.86 (C-3, -4, -5, and -6), 123.45, 123.99, 125.04 (C-4a, -4b, and -1), 125.86, 126.56 (C-2 and -7), and 138.63, 141.38 (C-8a and -9a).

5-*Methyl*-1-(β-D-*ribofuranosyl*)-9H-*carbazole* (**12**).—To a solution of the carbazole (**10**) (45.7 mg, 0.07 mmol) in methanol–THF (2:1; 1 ml) at 0 °C was added 5% aqueous NaOH (0.2 ml) during 35 min; the mixture was rendered neutral with acetic acid and evaporated. Work-up as above gave *compound* (**12**) (15.8 mg, 69%) as a syrup (Found: M^+, 313.1307. $C_{18}H_{19}NO_4$ requires M, 313.1312); $\lambda_{max.}$(MeOH) 239 (45 800), 263 (21 00), 290 (13 100), 324 (3 600), and 338 nm (3 900); $\delta_H(CD_3OD)$ 2.83 (3 H, s, Me), 3.97 (2 H, apparent s, 5′-H_2), 4.17 (1 H, m, 4′-H), 4.29—4.38 (2 H, m, 2′- and 3′-H), 5.03 (1 H, d, *J* 7.4 Hz, 1′-H), 6.91 (1 H, d, *J* 5.7 Hz, 6-H), 7.14 (1 H, t, *J* 8.1 Hz, 3-H), 7.21—7.36 (3 H, m, 2-, 7-, and 8-H), and 8.10 (1 H, dd, *J* 8.1 and 1.0 Hz, 4-H); $\delta_C(CD_3OD)$ 21.00 (Me), 62.95 (C-5′), 73.66, 76.52, 86.47, 87.17 (C-1′, -2′, -3′, and -4′), 109.34 (C-8), 119.23, 121.10 (C-3 and -6), 122.33, 122.97, 125.54 (C-4a, -4b, and -1), 123.21 (C-4), 125.25, 126.37 (C-2 and -7), 133.80 (C-5), 138.53, 141.34 (C-8a and -9a).

1-(2′,3′-O-*Isopropylidene*-β-D-*ribofuranosyl*)-9H-*carbazole* (**13**).—Ethyl orthoformate (0.1 ml, 0.6 mmol) was added to a well stirred suspension of the carbazole (**11**) (4.6 mg, 0.016 mmol) in acetone (1 ml) containing PTSA monohydrate (12 mg) and the mixture was kept at room temperature for 18 h. The reaction mixture was neutralized with sodium hydrogen carbonate and stirred for 15 min. The solid was collected by filtration and thoroughly washed with acetone. The filtrate and washings were combined, and evaporated under reduced pressure to give a syrup, which was purified by p.l.c. with chloroform–methanol (9:1) as developer, to give the acetonide (**13**) (4.3 mg, 82.3%) as a syrup; $\delta_H(CDCl_3)$ 1.37 and 1.70 (6 H, each s, isopropylidene Me) 4.01 (1 H, dd, *J* 11.4 and 2.0 Hz, 5′-H_a), 4.14 (1 H, dd, *J* 11.4 and 2.7 Hz, 5′-H_b), 4.35 (1 H, q, 4′-H), 4.76 (1 H, t, *J* 5.7 Hz, 2′-H), 5.00 (1 H, dd, *J* 5.7 and 4.0 Hz, 3′-H), 5.20 (1 H, d, *J* 5.7 Hz, 1′-H), 7.16—7.41 (5 H, m, 2-, 3-, 6-, 7-, and 8-H), 8.02 (2 H, apparent t, 4- and 5-H), 9.75 (1 H, s, NH).

1-(2′,3′-O-*Isopropylidene*-β-D-*ribofuranosyl*)-5-*methyl*-9H-*carbazole* (**14**).—Ethyl orthoformate (0.1 ml, 0.6 mmol) was added to a well stirred suspension of the carbazole (**12**) (5.9 mg, 0.02 mmol) in acetone (1 ml) containing PTSA monohydrate (10 mg) and the mixture was kept at room temperature for 18 h. Work-up as above gave compound (**14**) (5.0 mg, 75%) as a syrup; $\delta_H(CDCl_3)$ 1.38, 1.70 (6 H, each s, isopropylidene Me), 2.87 (3 H, s, Me), 4.02 (1 H, dd, *J* 11.4 and 2.4 Hz, 5′-H_a), 4.15 (1 H, dd, *J* 11.4 and 2.7 Hz, 5′-H_b), 4.36 (1 H, q, 4′-H), 4.77 (1 H, t, *J* 5.4 Hz, 2′-H), 4.99 (1 H, dd, *J* 5.4 and 4.0 Hz, 3′-H), 5.22 (1 H, d, *J* 5.4 Hz, 1′-H), 6.99 (1 H, d, *J* 6.3 Hz, 6-H), 7.18—7.40 (4 H, m, 2-, 3-, 7-, and 8-H), 8.14 (1 H, dd, *J* 7.7 and 1.0 Hz, 4-H), and 9.75 (1 H, s, NH).

Ethyl 2-(2′,3′,5′-*Tri*-O-*benzoyl*-β- *and* -α-D-*ribofuranosyl*)-*pyrrole*-1-*carboxylate* (**15**) *and* (**16**).—To a solution of compound (**5**) (207 mg, 0.36 mmol) and ethyl carbamate (160 mg, 1.8 mmol) in acetone (1.2 ml) at 0 °C was slowly added 50% TFA (0.25 ml) during 10 min. The mixture was stirred for 12 h at room temperature and then was heated at 65 °C for 21 h. Water was added, and then the mixture was extracted with chloroform (3 × 30 ml). The dried extracts, on evaporation, afforded a syrup. T.l.c. ($CHCl_3$) showed that the light yellow syrup contained two major components (R_F 0.29 and 0.19). The mixture was separated by p.l.c. with chloroform as developer (× 3).

Compound (**15**) (48.5 mg, 23%); R_F 0.29; a foam (Found: C, 67.8; H, 5.0; N, 2.3. $C_{33}H_{29}NO_9$ requires C, 67.91; H, 5.01; N, 2.40%); $\delta_H(CDCl_3)$ 1.34 (3 H, t, CH_2*Me*), 4.35 (2 H, q, CH_2Me), 4.59 (1 H, dd, J 11.4 and 3.7 Hz, 5′-H_a), 4.69 (1 H, m, 4′-H), 4.75 (1 H, dd, *J* 11.4 and 3.0 Hz, 5′-H_b), 5.80 (1 H, dd, *J* 7.4 and 4.7 Hz, 3′-H), 5.91 (1 H, d, *J* 3.7 Hz, 1′-H), 5.96 (1 H, dd, *J* 4.7 and 3.7 Hz, 2′-H), 6.14 (1 H, t, *J* 3.4 Hz, 4-H), 6.50 (1 H, m, 3-H), 7.27 (1 H, d, *J* 3.4 Hz, 5-H), and 7.29—8.08 (15 H, m, Ph); $\delta_C(CDCl_3)$ 14.16 (Me), 63.59, 63.89 (CH_2), 71.78, 75.76, 77.05, 77.87 (C-1′, -2′, -3′, and -4′), 110.92, 113.14 (C-3 and -4), 122.56 (C-5), 128.36—133.21 (C-2 and Ar-C), and 150.24, 165.33, 166.21 (C=O).

Compound (**16**) (6.3 mg, 3%); R_F 0.19; syrup (Found: C, 68.1; H, 5.0; N, 2.4%); $\delta_H(CDCl_3)$ 1.31 (3 H, t, CH_2*Me*), 4.30 (2 H, q, CH_2Me), 4.61 (1 H, dd, *J* 11.8 and 4.4 Hz, 5′-H_a), 4.73 (1 H, dd, *J* 11.8 and 3.7 Hz, 5′-H_b), 4.80 (1 H, m, 4′-H), 5.90 (dd, 1, *J* 7.1 and 5.0 Hz, 3′-H), 6.16 (2 H, apparent s, 1′- and 2′-H), 6.23 (1 H, t, *J* 4.4. Hz, 4-H), 6.54 (1 H, m, 3-H), 7.21 (1 H, dd, *J* 4.4 and 1.7 Hz, 5-H), and 7.26—8.09 (15 H, m, Ph); $\delta_C(CDCl_3)$ 14.10 (Me), 63.53, 64.59 (CH_2), 72.95, 73.06, 77.40, 77.98 (C-1′, -2′, -3′, and - 4′), 111.04, 113.26 (C-3 and -4), 121.39 (C-5), 128.24—133.21 (C-2 and Ar-C), and 150.41, 164.86, 165.33, 166.27 (C=O).

1-*Phenyl*-2-(2′,3′,5′-*tri*-O-*benzoyl*-β- *and* -α-D-*ribofuranosyl*)-*pyrrole* (**17**) *and* (**18**).—Aniline (8 mg, 0.1 mmol) was added to a well stirred suspension of compound (**5**) (51 mg, 0.09 mmol) in benzene (2 ml) containing PTSA monohydrate (16 mg) and the mixture was kept at room temperature for 18 h, then neutralized with sodium hydrogen carbonate, and the mixture was stirred for 15 min. The solid was collected by filtration and thoroughly washed with acetone. The filtrate and washings were combined, and evaporated under reduced pressure to give a syrup, which was purified by silica gel column chromatography with chloroform as eluant to give a syrup (31 mg, 59.6%; β:α *ca.* 7:1). A small sample of the syrup was separated by p.l.c. and each of the two bands (visible under u.v. light) was eluted with chloroform. The slower moving component contained a β,α mixture (β:α *ca.* 5:2), but the faster moving component gave the pure 2-(β-D-*ribofuranosyl*)*pyrrole* (**17**) as a syrup (Found: C, 72.3; H, 4.85; N, 2.3. $C_{36}H_{29}NO_7 \cdot \frac{1}{2}H_2O$ requires C, 72.47; H, 5.05; N, 2.35%); $\delta_H(CDCl_3)$ 4.50—4.75 (3 H, m, 4′-H and 5′-H_2), 5.14 (1 H, d, *J* 6.7 Hz, 1′-H), 5.79 (1 H, t, *J* 6.7 Hz, 3′-H), 5.95 (1 H, t, *J* 6.7 Hz, 2′-H), 6.25 (1 H, t, *J* 3.3 Hz, 4-H), 6.48 (1 H, dd, *J* 3.3 and 1.7 Hz, 3-H), 6.85 (1 H, dd, *J* 3.3 and 1.7 Hz, 5-H), and 7.30—8.20 (20 H, m, Ph); $\delta_C(CDCl_3)$ 64.23 (C-5′), 72.60, 74.71, 74.94, 79.62 (C-1′, -2′, -3′, and -4′), 108.81, 109.34 (C-3 and -4), 124.20 (C-5), 126.30—133.21 (Ar-C), 139.58 (C-2), and 165.09, 165.32, 166.14 (C=O).

Mixture of β isomer (**17**) and α isomer (**18**) (*ca.* 5:2): $\delta_H(CDCl_3)$ 4.50—4.80 (3 H, m, 4′-H and 5′-H_2), 5.14 ($\frac{5}{7}$ H, d, *J* 6.7 Hz, 1′-H, β anomer), 5.34 ($\frac{2}{7}$ H, d, *J* 3.7 Hz, 1′-H, α anomer), 5.75—5.81 (1 H, m, 3′-H), 5.85 ($\frac{2}{7}$ H, dd, *J* 4.7 and 3.7 Hz, 2′-H, α anomer), 5.95 ($\frac{5}{7}$ H, t, *J* 6.7 Hz, 2′-H, β anomer), 6.19 ($\frac{2}{7}$ H, dd, *J* 3.7 and 2.7 Hz, 4-H, α anomer), 6.25 ($\frac{5}{7}$ H, t, *J* 3.3 Hz, 4-H, β anomer), 6.48 ($\frac{5}{7}$ H, dd, *J* 3.3 and 1.7 Hz, 3-H, β anomer), 6.58 ($\frac{2}{7}$ H, dd, *J* 3.7 and 1.7 Hz, 3-H, α anomer), 6.78 ($\frac{2}{7}$ H, dd, *J* 2.7 and 1.7 Hz, 5-H, α anomer), 6.85 ($\frac{5}{7}$ H, dd, *J* 3.3 and 1.7 Hz, 5-H, β anomer), and 7.27—8.20 (20 H, m, Ph).

Reaction of 2,5-*Dimethoxy*-2-(2′,3′,5′-*tri*-O-*benzoyl*-α-D-*ribofuranosyl*)*tetrahydrofuran* (**6**) *with Aniline*.—To a solution of compound (**6**) (50.7 mg, 0.09 mmol) and aniline (8 mg, 0.9 mmol) in benzene (2 ml) at 0 °C was slowly added 50% TPA (0.25 ml) during 10 min. The mixture was stirred for 1 h at room temperature. Water was added, and then the mixture was extracted with chloroform (3 × 30 ml). The dried extracts, on evaporation, afforded a syrup, which was chromatographed over a column of silica gel with chloroform as eluant, to give the products (**17**) and (**18**) (21.3 mg, 41%; *ca.* 7:1), as confirmed by comparison of ^{1}H n.m.r. spectra.

2-(β-D-*Ribofuranosyl*)*pyrrole* (**19**).—To a solution of compound (**15**) (22.3 mg, 0.038 mmol) in methanol (1.5 ml) at 0 °C was added 5% aqueous NaOH (0.5 ml) during 2 h; the mixture was rendered neutral with acetic acid, and evaporated. The residue was chromatographed over a column of silica gel with chloroform–methanol (85:15) as eluant, to give the *product* (**19**) (3.6 mg, 47.6%) as a syrup (Found: M^+, 199.0849. $C_9H_{13}NO_4$ requires M, 199.0843); $\delta_H(CD_3OD)$ 3.67 (1 H, dd, J 11.9 and 4.2 Hz, 5′-H_a), 3.78 (1 H, dd, J 11.9 and 3.4 Hz, 5′-H_b), 3.90 (1 H, q, 4′-H), 4.03 (1 H, t, J 6.4 Hz, 2′-H), 4.10 (1 H, dd, J 6.4 and 4.5 Hz, 3′-H), 4.75 (d, 1, J 6.4 Hz, 1′-H), 6.02 (1 H, t, J 3.4 Hz, 4-H), 6.09 (1 H, dd, J 3.4 and 1.5 Hz, 3-H), and 6.71 (1 H, dd, J 3.4 and 1.5 Hz, 5-H).

2-(α-D-*Ribofuranosyl*)*pyrrole* (**20**).—To a solution of compound (**16**) (14 mg, 0.024 mmol) in methanol (1.5 ml) at 0 °C was added 5% aqueous NaOH (0.5 ml) during 2 h; the mixture was rendered neutral with acetic acid, and evaporated. Work-up as above gave *compound* (**20**) (1.7 mg, 36%) as a syrup (Found: M^+, 199.0825); $\delta_H(CD_3OD)$ 3.63 (1 H, dd, J 11.9 and 4.4 Hz, 5′-H_a), 3.78 (1 H, dd, J 11.9 and 2.7 Hz, 5′-H_b), 3.97 (1 H, q, 4′-H), 4.10 (1 H, t, J 3.4 Hz, 2′-H), 4.28 (1 H, dd, J 7.4 and 3.4 Hz, 3′-H), 5.01 (1 H, d, J 3.4 Hz, 1′-H), 6.02 (1 H, t, J 3.4 Hz, 4-H), 6.10 (1 H, dd, J 3.4 and 1.5 Hz, 3-H), and 6.76 (1 H, dd, J 3.4 and 1.5 Hz, 5-H).

1-*Phenyl*-2-(β-D-*ribofuranosyl*)*pyrrole* (**21**).—To a solution of compound (**17**) (40.8 mg, 0.07 mmol) in methanol (1.5 ml) at 0 °C was added 5% aqueous NaOH (0.5 ml) during 2 h; the mixture was rendered neutral with acetic acid, and evaporated. Work-up as above gave *compound* (**21**) (15.1 mg, 79%) as a syrup (Found: M^+, 275.1148. $C_{15}H_{17}NO_4$ requires M, 275.1156); $\delta_H(CD_3OD)$ 3.60 (1 H, dd, J 12.0 and 5.1 Hz, 5′-H_a), 3.67 (1 H, dd, J 12.0 and 4.2 Hz, 5′-H_b), 3.80 (1 H, q, 4′-H), 4.00 (1 H, dd, J 5.9 and 4.2 Hz, 3′-H), 4.24 (1 H, dd, J 7.3 and 5.9 Hz, 2′-H), 4.58 (1 H, d, J 7.3 Hz, 1′-H), 6.24 (1 H, t, J 2.9 Hz, 4-H), 6.41 (1 H, dd, J 2.9 and 1.7 Hz, 3-H), 6.87 (1 H, dd, J 2.9 and 1.7 Hz, 5-H), and 7.45—7.47 (5 H, m, Ph).

References

1 For recent reviews, see: U. Hacksell and G. D. Daves, *Prog. Med. Chem.*, 1985, **22**, 1; J. G. Buchanan, *Prog. Chem. Org. Nat. Prod.*, 1983, **44**, 243; S. R. James, *J. Carbohydr. Nucleosides Nucleotides*, 1979, **6**, 415; S. Hanessian and A. G. Pernet, *Adv. Carbohydr. Chem. Biochem.*, 1976, **33**, 111.

2 I. Maeba, F. Usami, and H. Furukawa, *J. Org. Chem.*, 1984, **49**, 1534; I. Maeba, T. Ishikawa, and H. Furukawa, *Carbohydr. Res.*, 1985, **140**, 332; I. Maeba, O. Hara, M. Suzuki, and H. Furukawa, *J. Org. Chem.*, 1987, **52**, 2368; I. Maeba, M. Suzuki, O. Hara, T. Takeuchi, T. Iijima, and H. Furukawa, *ibid.*, p. 4521; I. Maeba, T. Takeuchi, T. Iijima, and H. Furukawa, *ibid.*, 1988, **53**, 1401.

3 B. Burtner and G. Lehman, *J. Am. Chem. Soc.*, 1940, **62**, 527; R. Knoefel, *J. Pharmacol. Exp. Ther.*, 1933, **47**, 69; J. Maisin, P. Desmedt, and L. Jacqmin, *Compt. Rend. Soc. Biol.*, 1927, **96**, 1056; W. Freudenberg in 'Elderfield's Heterocyclic Compounds,' Wiley, New York, 1952, vol. 3; D. P. Chakraborty, *Fortschr. Chem. Org. Naturst.*, 1977, **34**, 299; J. A. Joule, *Adv. Heterocycl. Chem.*, 1984, **35**, 83.

4 A. P. Kozikowski and X-H Cheng, *J. Chem. Soc., Chem. Commun.*, 1987, 680.

5 C. K. Chu, F. M. El-Kabbani, and B. B. Thompson, *Nucleosides, Nucleotides*, 1984, **3**, 1.

6 R. W. Guthrie, A. Brossi, F. A. Mennona, J. G. Mullin, and R. W. Kierstead, *J. Med. Chem.*, 1975, **18**, 755.

7 G. R. Clemo and D. G. I. Felton, *J. Chem. Soc.*, 1952, 1658.

8 J-L. Imbach and B. L. Kam, *J. Carbohydr., Nucleosides, Nucleotides*, 1974, **1**, 271.

9 H. Ohrui, G. H. Jones, J. G. Moffatt, M. L. Maddox, A. T. Christensen, and S. K. Byram, *J. Am. Chem. Soc.*, 1975, **97**, 4602.

10 H. C. van der Plas, 'Ring Transformation of Heterocycles,' Academic Press, New York, 1973, vol. 1, p. 154.

11 I. Maeba, K. Iwata, F. Usami, and H. Furukawa, *J. Org. Chem.*, 1983, **48**, 2998.

Received 1*st August* 1988; *Paper* 8/03126F