A Novel Entry into Cyclopropanated Sugar Amino Acids

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Reaction of sugar triflates (**1**) and (**2**) with *tert*-butyl cyanoacetate in presence of sodium hydride affords the cyclopropanated sugars (**3**) and (**4**), followed by selective hydrolysis of the ester group to free acids (**5**) and (**6**), respectively. Couplings of (**5**) and (**6**) with protected glycine and L-alanine lead to cyclopropanated sugar amino acids (**7–10**). The coupling of **6** with benzyl 3,4-(“exo”-aminomethyl)methano-3,4-dideoxy- β -L-arabinopyranoside (**11**) furnished benzyl 3,4-[(C-cyano-amido)methano-(benzyl 3,4-(“exo”-methylene)methano-3,4-dideoxy- β -L-arabinopyranosido)]-3,4-dideoxy- β -L-arabinopyranoside (**12**), suggesting an “exo” orientation of the ester group in **3** and **4**.

Introduction

A recent report from this laboratory [1] described a simple sequence of reactions for converting the readily available L-arabinose and D-arabinose into 3,4-cyclopropanated sugars *via* 2,3-anhydropyranosides. The route has considerable potential for syntheses of structural variants of 3,4-cyclopropanated sugars by appropriate modification of steps from the key intermediates. The present work describes such a variation to afford high-yielding syntheses of a new type of cyclopropanated sugar amino acids of potential biochemical interest.

Results and Discussion

The benzyl 2,3-anhydro-4-O-trifluoromethanesulfonyl- β -L-ribosepyranoside (**1**) and its α -D-isomer (**2**) are prepared by previously published methods [2–4] from L- and D-arabinose, respectively, and both of these are treated with *tert*-butyl cyanoacetate in the presence of sodium hydride to obtain the cyclopropanated sugar derivatives (**3**) and (**4**). Apparently, the sodium enolate of *tert*-butyl cyanoacetate initially displaces, with inversion, the triflyl group which is followed by further alkylation by the *trans*-oriented oxirane ring. The two different conformers 1H_o and oH_1 can be safely assigned to the compounds **3** and **4**, based

on the chemical shifts of 1-H in their 1H NMR spectra [1]. Interestingly, we obtained a complete control on the newly formed chiral center, *i.e.* the bulky ester group is apparently in “exo” orientation in both the cases, as suggested by the proceeding reactions. The selective hydrolysis of the ester function with normal acidic and basic reagents caused considerable difficulties due, either to the hydrolysis of both the cyano and ester moieties, or formation of a complex mixture of products. However, saponification with 80% trifluoroacetic acid in dichloromethane cleanly affords the free acids (**5**) and (**6**) in almost theoretical yields. The compound **5** is reacted with hydrochlorides of carboxyl-protected naturally occurring amino acids including methyl- and benzyl-esters of glycine and the benzyl ester of L-alanine, respectively. The reactions are carried out in dimethylformamide in the presence of 4-methylmorpholine, affecting coupling with “Castro Reagent” ($BOP^+PF_6^-$) [5–6] to yield cyclopropanated sugar amino acids (**7–9**). The analogous reaction of **6** with the benzyl ester of glycine leads to compound **10**. The compounds **5**, **7**, **8** and **9** are shown to exist almost entirely in the 1H_o conformation by 1H NMR spectroscopy, while oH_1 can be assigned to **6** and **10**. Similar conformations are observed for **3** and **4** from which it can be inferred that hydrolysis of the ester group and subsequent amide bond formation does not change the conformational stability of the molecule (Scheme 1).

The bulky ester group in compounds **3** and **4** was expected to be in “exo” orientation according

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Scheme 1.

Scheme 2.

to earlier findings of Schöllkopf *et al.* [7–8] in analogous but simpler cyclopropane derivatives. Further indication to this effect is provided by coupling of **6** with benzyl 3,4-(“exo”-aminomethyl)methano-3,4-dideoxy-β-L-arabinopyranoside (**11**) [1] under the conditions described in the foregoing. The facile coupling and high yield of the resulting compound **12** suggest similar orientation of the carboxyl group in **5** (and hence the ester moiety in **3**) as that of the aminomethyl group in **11** for which “exo”-orientation has already been established [1]. The evidence, however, is not con-

clusive and further insight to the stereochemistry of the newly forming chiral centre in 6,6-disubstituted-3,4-cyclopropanated sugars would be provided later with the help of X-ray crystallography. The ¹H NMR spectrum shows that ^oH₁ conformations are retained by both the sugar molecules of product **12**, once again revealing that amide bond formation does not change the conformational stability of this type of compounds (Scheme 2).

Experimental

The melting points are recorded on a Büchi 510 apparatus and are uncorrected. The optical rotations are measured on a digital polarimeter OLD 5, Carl Zeiss. The elemental analyses are performed on a Carlo Erba elemental analyzer. The field desorption mass spectra are recorded on a Varian MAT 711 mass spectrometer and the NMR spectra on a Bruker WM-400 spectrometer. The assignments of the ¹³C NMR spectra are made through comparison with the corresponding ones of a similar series of compounds [1] as well as published data of various carbohydrate derivatives [9].

Benzyl 3,4-(C-cyano-tert-butyloxycarbonyl)methano-3,4-dideoxy-α-D-arabinopyranoside (3): A solution of 0.1 g (3.33 mmol) sodium hydride in 10 ml abs. tetrahydrofuran is cooled to 0 °C, then dropwise 0.5 ml (3.58 mmol) *tert*-butyl cyanoacetate are added and stirred for 10 min. A solution of 1 g (2.82 mmol) benzyl 2,3-anhydro-4-O-trifluoromethanesulfonyl-β-L-ribofuranoside (**1**) in 10 ml tetrahydrofuran is slowly added and stirred for further 20 min at 0 °C. Then the reaction mixture is kept at room temperature for 5 h, the solvent removed, 15 ml water added and extracted thrice with 20 ml dichloromethane. The organic phase is washed with 50 ml water, 30 ml saturated sodium chloride solution, dried over Na₂SO₄, freed of the solvent and crystallized from ether/*n*-hexane as colourless needles. Yield 0.82 g (84%), m.p. 156–157 °C, [*α*]_D = –25.5° (c=1, CHCl₃). – FAB-MS: *m/z* = 346 (M+1)⁺. – ¹H NMR (400 MHz, CDCl₃): δ = 7.36–7.27 (m, 5 H, Ar–H), 4.87 (d, 1 H, *J*_{gem} = 11.6 Hz, OCHPh), 4.51 (d, 1 H, *J*_{gem} = 11.6 Hz, OCHPh), 4.36 (d, 1 H, *J*_{5',5} = 12.9 Hz, 5'-H), 4.16 (d, 1 H, *J*_{1,2} = 7.5 Hz, 1-H), 4.14 (dd, 1 H, *J*_{5,4} = 3.5 Hz, *J*_{5,5'} = 13.1 Hz, 5-H), 3.84 (ddd, 1 H, *J*_{2,1} = 7.4 Hz, *J*_{2,OH} = 2.9 Hz, *J*_{2,3} = 1.2 Hz, 2-H), 2.38 (d, 1 H, *J*_{OH,2} = 2.9 Hz, OH), 2.17 (dd, 1 H, *J*_{3,4} = 9.5 Hz, *J*_{3,2} = 1.1 Hz, 3-H), 2.01 (dd, 1 H, *J*_{4,3} = 9.5 Hz, *J*_{4,5} = 3.4 Hz, 4-H), 1.48 (s, 9 H,

$C(CH_3)_3$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6 (C=O), 137.0–128.0 (Ar–C), 114.3 (CN), 101.7 (C-1), 84.3 ($C(CH_3)_3$), 70.3 (O– CH_2 Ph), 66.0 (C-2), 62.0 (C-5), 32.4 (C-3), 27.9 (CH_3), 27.3 (C-4), 23.1 (C-6).

$C_{19}H_{23}NO_5$ (345.39)

Calcd	C 66.07	H 6.71	N 4.05%,
Found	C 66.75	H 6.62	N 4.06%.

Benzyl 3,4-(C-(cyano-tert-butoxycarbonyl)methano-3,4-dideoxy- β -L-arabinopyranoside (4): Is prepared from **2** in exactly the same manner as described for **3**. Colourless needles from ether/*n*-hexane. Yield 0.85 g (87%), m.p. 111–112 °C, $[\alpha]_D = +131.2^\circ$ (c=1, $CHCl_3$). – FD-MS: m/z 346 (M+1)⁺. – 1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 5H, Ar–H), 4.85 (d, 1H, $J_{1,2} = 4.6$ Hz, 1-H), 4.77 (d, 1H, $J_{gem} = 11.6$ Hz, OCHPh), 4.54 (d, 1H, $J_{gem} = 11.6$ Hz, OCHPh), 4.07 (dd, 1H, $J_{5',4} = 3.7$ Hz, $J_{5',5} = 12.8$ Hz, 5'-H), 3.95 (d, 1H, $J_{5,5'} = 12.8$ Hz, 5-H), 3.86 (dd, 1H, $J_{2,1} = 4.6$ Hz, $J_{2,OH} = 11.0$ Hz, 2-H), 2.63 (d, 1H, $J_{OH,2} = 11.0$ Hz, OH), 2.15 (d, 1H, $J_{3,4} = 10.0$ Hz, 3-H), 2.08 (dd, 1H, $J_{4,3} = 9.9$ Hz, $J_{4,5'} = 3.7$ Hz, 4-H), 1.47 (s, 9H, $C(CH_3)_3$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.7 (CO), 136.3–128.2 (Ar–C), 114.4 (CN), 93.0 (C-1), 84.2 ($C(CH_3)_3$), 70.2 (OCH₂–Ph), 62.1 (C-2), 54.2 (C-5), 31.1 (C-3), 27.8 (CH_3), 26.8 (C-4), 23.1 (C-6).

$C_{19}H_{23}O_5N$ (345.39)

Calcd	C 66.07	H 6.71	N 4.05%,
Found	C 65.75	H 6.62	N 4.22%.

Benzyl 3,4-(C-(cyano-carboxy)methano-3,4-dideoxy- α -D-arabinopyranoside (5): 1 g (2.89 mmol) **3** is stirred with 30 ml of an 80% cooled solution of trifluoroacetic acid in dichloromethane for 30 min. The solvent removed *in vacuo* and the residue dried under high vacuum over phosphorous pentoxide. Yield 0.82 g (98%), m.p. 58–60 °C, $[\alpha]_D = -21.3^\circ$ (c=1, $CHCl_3$). – FD-MS: m/z 290 (M+1)⁺. The 1H and ^{13}C NMR spectra are similar to **3** except the disappearance of peaks due to the methyl resonances of the *tert*-butyl ester moiety.

$C_{15}H_{15}NO_5$ (289.28)

Calcd	C 62.28	H 5.22	N 4.84%,
Found	C 62.01	H 5.53	N 4.36%.

Benzyl 3,4-(C-(cyano-carboxy)methano-3,4-dideoxy- β -L-arabinopyranoside (6): Is obtained from **4** in the same manner as **5**. Yield 0.73 g (97%), m.p. 52–54 °C, $[\alpha]_D = 11.9^\circ$ (c=1, $CHCl_3$). – FD-MS: m/z 290 (M+1)⁺. The 1H and ^{13}C NMR spectra are

similar to **4** except the disappearance of the methyl peaks of the *tert*-butyl ester group.

$C_{15}H_{15}NO_5$ (289.28)

Calcd	C 62.28	H 5.23	N 4.84%,
Found	C 61.87	H 5.35	N 4.75%.

Benzyl 3,4-(C-(cyano-methyl glycinato)methano-3,4-dideoxy- α -D-arabinopyranoside (7): 0.35 g (1.20 mmol) of **5** and 0.17 g (1.35 mmol) of the hydrochloride of methyl glycinate are dissolved in 20 ml dimethylformamide and cooled at 0 °C for 20 min. Afterwards 0.3 ml (2.72 mmol) 4-methylmorpholine and 1.07 g (2.41 mmol) BOP are added. After 6 h the solvent is removed *in vacuo* and the residue taken up in 50 ml ethyl acetate. After washing 3 times with a 10% solution of sodium bicarbonate, water, 10% dil. hydrochloric acid, water, drying over anhydrous Na_2SO_4 and removal of the solvent, an oily residue is obtained which is column-chromatographed over silica gel using methanol-ethyl acetate (1:4) as eluent. The product crystallizes from ethyl acetate/petroleum ether as colourless needles. Yield 0.38 g (87%), m.p. 50 °C, $[\alpha]_D = -15.4^\circ$ (c=1, $CHCl_3$). – FD-MS: $m/z = 361$ (M+1)⁺. – 1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 5H, Ar–H), 7.09 (br.s, 1H, NH), 4.84 (d, 1H, $J_{gem} = 11.7$ Hz, 1-OCHPh), 4.50 (d, 1H, $J_{gem} = 11.7$ Hz, 1-OCHPh), 4.30 (d, 1H, $J_{5',5} = 12.9$ Hz, 5'-H), 4.16 (d, 1H, $J_{1,2} = 7.3$ Hz, 1-H), 4.09 (dd, 1H, $J_{5,5'} = 13.0$ Hz, $J_{5,4} = 3.2$ Hz, 5-H), 3.98 (t, 2H, $J_{NH-CH_2} = 5.3$ Hz, 6-H), 3.80 (d, 1H, $J_{2,1} = 7.2$ Hz, 2-H), 3.72 (s, 3H, OCH₃), 3.01 (br.s, 1H, OH), 2.24 (d, 1H, $J_{3,4} = 9.4$ Hz, 3-H), 2.11 (dd, 1H, $J_{4,3} = 9.4$ Hz, $J_{4,5} = 3.0$ z, 4-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4 ($COOCH_3$), 165.0 ($C=O$), 136.7–127.9 (Ar–C), 115.9 (CN), 101.9 (C-1), 70.3 (OCH₂Ph), 65.9 (C-2), 62.0 (C-5), 52.4 (OCH₃), 41.8 (CH_2NH), 32.3 (C-3), 27.4 (C-4), 22.5 (C-6).

$C_{18}H_{20}N_2O_6$ (360.36)

Calcd	C 59.99	H 5.59	N 7.77%,
Found	C 59.86	H 6.06	N 7.47%.

Benzyl 3,4-(C-(cyano-benzyl glycinato)methano-3,4-dideoxy- α -D-arabinopyranoside (8): 0.5 g (1.73 mmol) of **5** and 0.4 g (1.98 mmol) of the hydrochloride of benzyl glycinate are taken up in 20 ml DMF, cooled at 0 °C for 20 min and then 0.35 ml (3.18 mmol) 4-methylmorpholine and 1.52 g (3.43 mmol) BOP are added. The reaction is carried out and worked up in the same manner as described for **7**. The purification is done by column chromatography over silica gel using dichloromethane-acetone (9:1) as eluent. Crystallization from ethyl acetate/*n*-hexane provided white flakes of **8**. Yield

0.5 g (66%), m.p. 140–142 °C, $[\alpha]_D = +1.7^\circ$ ($c=1$, CHCl_3). – FD-MS: $m/z = 437$ ($M+1$)⁺. – ^1H NMR (400 MHz, CDCl_3): $\delta = 7.35\text{--}7.24$ (m, 10H, Ar-H), 7.07 (br.t, 1H, $J_{\text{NH-CH}_2} = 5.3$ Hz, CONH), 5.16 (s, 2H, COOCH_2Ph), 4.86 (d, 1H, $J_{\text{gem}} = 11.7$ Hz, 1-OCHPh), 4.51 (d, 1H, $J_{\text{gem}} = 11.7$ Hz, 1-OCHPh), 4.31 (d, 1H, $J_{5',5} = 12.9$ Hz, 5'-H), 4.17 (d, 1H, $J_{1,2} = 7.3$ Hz, 1-H), 4.12 (dd, 1H, $J_{5,5'} = 12.9$ Hz, $J_{5,4} = 3.2$ Hz, 5-H), 4.03 (dd, 2H, $J_{\text{gem}} = 7.9$ Hz, $J_{\text{CH}_2\text{-NH}} = 5.4$ Hz, NHCH_2), 3.82 (dd, 1H, $J_{2,1} = 7.3$ Hz, $J_{2,\text{OH}} = 2.4$ Hz, 2-H), 2.59 (d, 1H, $J_{\text{OH},2} = 3.3$ Hz, OH), 2.26 (dd, 1H, $J_{3,2} = 0.9$ Hz, $J_{3,4} = 9.4$ Hz, 3-H), 2.18 (dd, 1H, $J_{4,3} = 9.4$ Hz, $J_{4,5} = 3.0$ Hz, 4-H). – ^{13}C NMR (100 MHz, CDCl_3): $\delta = 168.7$ (COOCH_2Ph), 165.0 (CONH), 136.8–128.0 (Ar-C), 115.8 (CN), 101.9 (C-1), 70.4 (1-OCH₂Ph), 67.4 (PhCH_2O), 66.1 (C-2), 62.1 (C-5), 42.1 (CH_2NH), 32.2 (C-3), 27.4 (C-4), 22.6 (C-6).

$\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_6$ (436.45)

Calcd	C 66.04	H 5.54	N 6.42%
Found	C 65.49	H 5.85	N 6.14%

Benzyl 3,4-(C-cyano-benzyl alaninato)methano-3,4-dideoxy- α -D-arabinopyranoside (9): Is prepared from **5** by the same procedure as that applied for **8** using 0.4 g (1.85 mmol) of the hydrochloride of benzyl alaninate. The product, after purification through column chromatography, crystallized from ethyl acetate/*n*-hexane as colourless needles. Yield 0.55 g (71%), m.p. 118 °C, $[\alpha]_D = +1.7^\circ$ ($c=1$, CHCl_3). – FD-MS: $m/z = 451$ ($M+1$)⁺. – ^1H NMR (400 MHz, CDCl_3): $\delta = 7.37\text{--}7.31$ (m, 10H, Ar-H), 6.93 (d, 1H, $J_{\text{NH}} = 7.2$ Hz, NH), 5.19 (d, 1H, $J_{\text{gem}} = 12.2$ Hz, COOCHPh), 5.14 (d, 1H, $J_{\text{gem}} = 12.2$ Hz, COOCHPh), 4.87 (d, 1H, $J_{\text{gem}} = 11.6$ Hz, 1-OCHPh), 4.55 (q, 1H, $J_{\text{CH},\text{CH}_3} = 7.2$ Hz), 4.51 (d, 1H, $J_{\text{gem}} = 11.6$ Hz, 1-OCHPh), 4.31 (d, 1H, $J_{5',5} = 12.9$ Hz, 5'-H), 4.16 (d, 1H, $J_{1,2} = 7.3$ Hz, 1-H), 4.11 (dd, 1H, $J_{5,5'} = 12.9$ Hz, $J_{5,4} = 3.3$ Hz, 5-H), 3.83 (ddd, 1H, $J_{2,1} = 7.3$ Hz, $J_{2,3} = 1.0$ Hz, $J_{2,\text{OH}} = 3.0$ Hz, 2-H), 2.34 (d, 1H, $J_{\text{OH},2} = 3.0$ Hz, OH), 2.27 (dd, 1H, $J_{3,4} = 9.4$ Hz, $J_{3,2} = 1.0$ Hz, 3-H), 2.06 (dd, 1H, $J_{4,3} = 9.3$ Hz, $J_{4,5} = 3.0$ Hz, 4-H), 1.44 (d, 3H, $J_{\text{CH}_3,\text{CH}} = 7.2$ Hz, CH_3). – ^{13}C NMR (100 MHz, CDCl_3): $\delta = 171.7$ ($\text{CH}(\text{CH}_3)\text{COO}$), 164.1 (CONH), 136.5–128.1 (Ar-C), 115.8 (CN), 101.9 (C-1), 70.3 (1-OCH₂Ph), 67.3 (PhCH_2OCO), 66.1 (C-12), 62.1 (C-5), 49.2 ($\text{CH}(\text{CH}_3)$), 31.9 (C-3), 27.3 (C-4), 18.0 (C-6), 17.9 (CH_3).

$\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_6$ (450.47)

Calcd	C 66.65	H 5.82	N 6.22%
Found	C 66.72	H 5.68	N 6.35%

Benzyl 3,4-(C-cyano-benzyl glycinato)methano-3,4-dideoxy- β -L-arabinopyranoside (10): The synthesis of **10** is performed in an analogous manner as that of **8**. 0.65 g (2.18 mmol) **6** are treated with 0.5 g (2.47 mmol) benzyl glycinate hydrochloride in the presence of 0.5 ml (4.48 mmol) 4-methylmorpholine and 2 g (4.51 mmol) BOP. Yield 0.7 g (71%), m.p. 112 °C, $[\alpha]_D = +9.9^\circ$ ($c=1$, CHCl_3). – FD-MS: $m/z = 437$ ($M+1$)⁺. – ^1H NMR (400 MHz, CDCl_3): $\delta = 7.38\text{--}7.30$ (m, 10H, Ar-H), 6.98 (t, 1H, $J_{\text{NH}} = 5.3$ Hz, CONH), 5.17 (s, 2H, COOC_2Ph), 4.84 (d, 1H, $J_{1,2} = 4.6$ Hz, 1-H), 4.75 (d, 1H, $J_{\text{gem}} = 11.6$ Hz, 1-OCHPh), 4.53 (d, 1H, $J_{\text{gem}} = 11.6$ Hz, 1-OCHPh), 4.13–3.99 (overlapping multiplets, 3, $\text{NHCH}_2 + 5'$ -H), 3.86 (d, 1H, $J_{5,5'} = 12.9$ Hz, 5-H), 3.82 (dd, 1H, $J_{2,1} = 4.6$ Hz, $J_{2,3} = 1.2$ Hz, 2-H), 2.83 (d, 1H, $J_{\text{OH}} = 11.1$ Hz, OH), 2.23 (d, 1H, $J_{3,4} = 9.9$ Hz, 3-H), 2.18 (dd, 1H, $J_{4,3} = 9.9$ Hz, $J_{4,5'} = 3.5$ Hz, 4-H). – ^{13}C NMR (100 MHz, CDCl_3): $\delta = 168.7$ (COOC_2Ph), 165.0 (CONH), 136.33–128.1 (Ar-C), 93.17 (C-1), 70.24 (1-OCH₂Ph), 67.39 (PhCH_2OCO), 62.3 (C-2), 54.1 (C-5), 42.0 (NHCH_2CO), 30.9 (C-3), 26.8 (C-4), 22.8 (C-6).

$\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_6$ (436.45)

Calcd	C 66.04	H 5.54	N 6.42%
Found	C 65.27	H 5.68	N 6.19%

Benzyl 3,4-[(C-cyano-amido)methano-(benzyl-3,4-(“exo”-methylene)-methano-3,4-dideoxy- β -L-arabinopyranosido)]methano-3,4-dideoxy- β -L-arabinopyranoside (12): 0.60 g (2.07 mmol) **6** and 0.52 g (2.08 mmol) of **11** are dissolved in 20 ml dimethylformamide and then 0.45 ml (4.09 mmol) 4-methylmorpholine and 1.83 g (4.13 mmol) BOP are added. The reaction product is worked up and purified as described for **7** to furnish, after crystallization from ethyl acetate/*n*-hexane, colourless needles. Yield 0.75 g (69.5%), m.p. 67–70 °C, $[\alpha]_D = +178.7^\circ$ ($c=1$, CHCl_3). – FD-MS: $m/z = 406$ ($M\text{--CN--CH}_2\text{Ph}$)⁺. – ^1H NMR (400 MHz, CDCl_3): $\delta = 7.38\text{--}7.30$ (m, 10H, Ar-H), 6.54 (br.t, $J_{\text{NH-CH}_2} = 5.5$ Hz, NH), 4.85 (d, 1H, $J_{1,2} = 4.7$ Hz, 1-H), 4.77 (d, 1H, $J_{\text{gem}} = 11.7$ Hz, 1-OCHPh), 4.76 (d, 1H, $J_{\text{gem}} = 11.6$ Hz, 1-OCHPh), 4.55 (d, 1H, $J_{1',2'} = 3.4$ Hz, 1'-H), 4.54 (d, 1H, $J_{\text{gem}} = 11.8$ Hz, 1-OCHPh), 4.49 (d, 1H, $J_{\text{gem}} = 11.7$ Hz, 1-OCHPh), 4.09–4.05 (overlapping multiplets, 2H, 5"-H + 5'''-H), 3.90 (d, 1H, $J_{5,5''} = 12.7$ Hz, 5-H), 3.83 (ddd, 1H, $J_{2,1} = 4.7$ Hz, $J_{2,3} = 1.0$ Hz, $J_{2,\text{OH}} = 11.2$ Hz, 2-H), 3.78 (ddd, 1H, $J_{2',1'} = 4.5$ Hz, $J_{2',3'} = 1.1$ Hz, $J_{2',\text{OH}} = 9.0$ Hz, 2'-H), 3.73 (d, 1H, $J_{5',5} = 11.3$ Hz, 5'-H), 3.23 (m, 1H, $J_{\text{vic}} = 6.2$ Hz, 7-H), 3.13 (m, 1H, $J_{\text{vic}} = 5.8$ Hz, 7-H), 2.75 (d, 1H, $J_{\text{OH},2} = 11.2$ Hz, OH), 2.61 (d, 1H, $J_{\text{OH},2'} = 9.0$ Hz, OH), 2.22

(d, 1H, $J_{3,4}$ = 9.9 Hz, 3-H), 2.18 (dd, 1H, $J_{4,3}$ = 9.9 Hz, $J_{4,5}$ = 3.2 Hz, 4-H), 1.05–0.92 (overlapping multiplets, 3H, 3'-H, 4'-H+6'-H). – ^{13}C NMR (100 MHz, CDCl_3): δ = 164.5 (CONH), 136.9–127.8 (Ar-C), 116.1 (CN), 93.8 (C-1'), 93.2 (C-1), 70.2 (1'-OCH₂Ph), 69.7 (1-OCH₂Ph), 64.5 (C-2), 62.4 (C-2'), 58.0 (C-5), 54.2 (C-5'), 43.6 (C-7), 30.6 (C-3), 26.4 (C-3'), 22.8 (C-6), 20.5 (C-4), 20.3 (C-4'), 15.0 (C-6').

$\text{C}_{29}\text{H}_{32}\text{N}_2\text{O}_7$ (520.56)

Calcd C 66.91 H 6.20 N 5.38%,

Found C 66.88 H 6.51 N 4.64%.

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