Monosaccharidic Push-pull Butadienes: Versatile Synthetic Intermediates

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Monosaccharidic push-pull butadienes are interesting building blocks for the synthesis of various heterocyclic and natural products due to their biological prevalence and significant π-electron interactions between donor and acceptor groups. A series of 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-formyl-D-*arabino*-hex-1-enitol (**2**) and 1,5-anhydro-3,4-di-*O*-benzyl-2-deoxy-2-formyl-L-*erythro*-hex-1-enitol (**4**) derived push-pull branched chain sugars have been synthesized by condensation with active methylene compounds using basic aluminum oxide (Al_2O_3) or anhydrous sodium acetate (NaOAc) at room temperature. The compounds have been fully characterized by spectroscopic techniques and elemental analyses.

Key words: Push-pull Butadiene, Nucleoside Analogs, Active Methylene Compounds, Condensation, Formyl Glycal

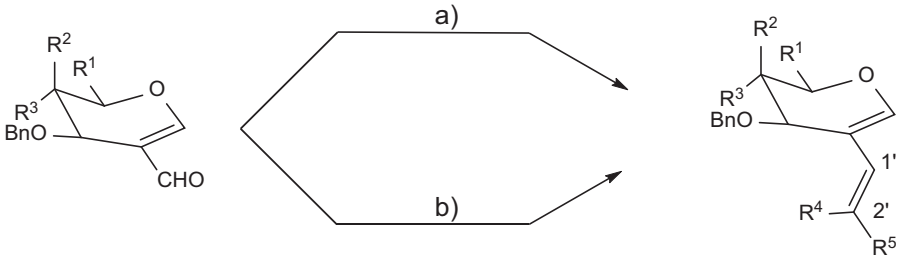
Introduction

Carbohydrates are involved in a wide variety of biological functions and consequently show enormous potential as therapeutic agents for a number of cases ranging from infectious diseases to cancer therapies [1 – 4]. Push-pull butadienes are the class of compounds in which the electron-releasing and electron-withdrawing groups are attached on either end of the butadiene chain that enhances the conjugation in the system [5, 6]. In these types of systems, the C=C double bonds usually become more polarized due to π-electron delocalization [7 – 9]. Several branched chain sugars have been reported starting from hexose and pentose glycals which were used as synthetic intermediates to synthesize a variety of nucleoside analogs [10]. All these sugars are suitable precursors for cyclization reactions with various *N*-nucleophiles leading to different types of heterocyclic and carbocyclic anellated monosaccharides [11].

Results and Discussion

Our earlier studies [12 – 14] have shown that formyl glycals when reacted with an active methylene compound under Knoevenagel–Cope conditions afford push-pull butadienes. Because of the biological potential [15] of this family of compounds and in accord with our efforts on exploring new synthetic methods, now the transformations of benzyl-protected 2-formylglucal and 2-formylarabinal [16] using Al_2O_3 and in another method anhydrous NaOAc, to obtain C-2(3) branched-chain glycals with an integrated push-pull butadiene structural unit are described (Scheme 1).

Sodium acetate and aluminum oxide were selected because of their basic character and because they give better yields than similar compounds [17]. 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-formyl-D-*arabino*-hex-1-enitol (**2**) and 1,5-Anhydro-3,4-di-*O*-benzyl-2-deoxy-2-formyl-L-*erythro*-hex-1-enitol (**4**) were treated with various active methylene compounds (Table 1) to give the monosaccharidic butadienes **3a**–**e** and **5a**–**e** as yellow syrups. For compounds **3a**–**e** a longer reaction time was required due to the lower basicity when aluminum oxide was applied, but no side products were observed in dichloromethane at room temperature. Heating of the mixture at higher temperature resulted in the formation of various side products and lower yields.



2 : $R^1 = CH_2OBn$, $R^2 = H$, $R^3 = OBn$
4 : $R^1 = H$, $R^2 = OBn$, $R^3 = H$

3a–e, 5a–e

Scheme 1. Reagents and conditions: a) CH_2Cl_2, $CH_2R^4R^5$, Al_2O_3, r. t.; b) ethanol, $CH_2R^4R^5$, anhydrous NaOAc, r. t.

Table 1. Monosaccharidic push-pull butadienes **3a–e** and **5a–e** (Bn = benzyl).

Compound	R^1	R^2	R^3	R^4	R^5
3a	CH_2OBn	H	OBn	CN	$CONH_2$
3b	CH_2OBn	H	OBn	$COCH_3$	$CONH_2$
3c	CH_2OBn	H	OBn	$COOCH_3$	$COOCH_3$
3d	CH_2OBn	H	OBn	$COCH_3$	CONHPh
3e	CH_2OBn	H	OBn	$COCH_3$	*p*-ClCONHPh
5a	H	OBn	H	CN	$CONH_2$
5b	H	OBn	H	$COCH_3$	$CONH_2$
5c	H	OBn	H	$COOCH_3$	$COOCH_3$
5d	H	OBn	H	$COCH_3$	CONHPh
5e	H	OBn	H	$COCH_3$	*p*-ClCONHPh

Table 2. Yields of compounds **3a–e** and **5a–e** using Al_2O_3 (method A; see Scheme 1) and NaOAc (method B).

Compound	Yield (%)	
	method A	method B
3a	46	47
3b	44	54
3c	51	60
3d	46	59
3e	51	59
5a	46	55
5b	43	53
5c	40	55
5d	49	57
5e	45	58

The IR and NMR spectra of compounds **3a–e** showed the absence of signals for the formyl group and the formation of a butadiene unit. The comparison with the spectra of similar compounds [18] whose structures were analyzed by means of 2D experiments allowed the assignment of all ^{13}C NMR signals. The intense color of the compounds could be due to the 'push-pull' property of the *C*-branched butadiene moiety which causes characteristic alternating chemical shifts of sp^2 carbon atoms of C-1, C-2 and C-1′ and C-2′.

Moreover, similar results were obtained when anhydrous sodium acetate was used as a base to prepare compounds **5a–e**. It is noteworthy that the yields were better when anhydrous sodium acetate was used (Table 2). The IR and NMR spectra of compounds **5a–e** showed the absence of signals for the formyl group. According to the ^{13}C NMR spectra, a CN group is present in compound **5a**, while a strong absorption in the IR spectrum also confirms the presence of a nitrile group. In the ^1H NMR spectrum of compounds **3a**, **3b**, **5a**, and **5b**, two NH signals were found, one of which is significantly downfield ($\delta = 8$ ppm) due to an intramolecular hydrogen bond N–H···O, while the other appears at around $\delta = 6$ ppm.

The NMR spectra of **3a–e** and **5a–e** showed the existence of only the *E*-isomers which was proved by gated decoupling (GD) spectra in which a large coupling constant ($J = 13$ Hz) was found for the CN substituent and H-1′ at the exocyclic butadiene unit of **3a**. On the other hand there is a smaller value ($J = 6.6$ Hz) for the coupling between H-1′ and the attached carbonyl group, in accordance with the configuration reported by Peseke *et al.* for similar compounds [19].

Experimental Section

Organic solvents used were dried by standard methods. Tri-*O*-benzyl-D-glucal, L-arabinose, anhydrous sodium acetate, active methylene compounds, and basic aluminum oxide were purchased from Aldrich and were used as obtained. IR spectra were recorded with a Perkin Elmer BX FT-IR spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker instrument at 500.133 and 125.76 MHz, respectively, at 293 K in $CDCl_3$. The mass spectra were obtained on a Micromass LCT mass spectrometer. The elemen-

tal analyses for C, H and N were done on a Perkin-Elmer CHN-2440 analyzer (C, H, N) and were in full agreement with the proposed compositions. Thin-layer chromatography (TLC) was performed with fluorescent silica gel HF_{254} plates (Merck) viewed under UV 254 and 265 nm light and charring with 10 % sulfuric acid in ethanol. Merck silica gel 60 (230 – 400 mesh) was used for column chromatography separations.

*General procedure for the preparation of compounds **3a–e** and **5a–e***

Method A

To a vigorously stirred solution of formyl glucal (**2**) or arabinal (**4**) (1.0 mmol) in CH_2Cl_2 (10 mL) was added the active methylene compound (1.1 mmol) followed by Al_2O_3 (3 equiv. by wt). The resulting mixture was then stirred for 5 h for completion of the reaction, the progress of the reaction being monitored by TLC. The solid was filtered off, and the filtrate was evaporated to afford the crude product which was purified by column chromatography to give the desired compound.

Method B

To a vigorously stirred solution of formyl glucal (**2**) or arabinal (**4**) (1.0 mmol) in ethanol (10 mL) was added an active methylene compound (1.1 mmol) followed by anhydrous sodium acetate (1.2 mmol). The resulting mixture was then stirred for 3 h for completion of the reaction, the progress of the reaction being monitored by TLC. The solvent was evaporated to afford the crude product which was purified by column chromatography to give the desired compound.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2-cyano-2-amino-carbonyl-vinyl]-2-deoxy-D-arabino-hex-1-enitol (**3a**)*

$R_f = 0.58$ (toluene-ethyl acetate, 8 : 2), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 3.40$ (dd, 1H, $J_{6a,6b} = 10.8$, $J_{5,6a} = 5.5$ Hz, H-6a), 3.59 (dd, 1H, $J_{5,6b} = 7.5$ Hz, H-6b), 3.89 (t, 1H, H-4), 4.30 (d, 1H, $J = 10.9$ Hz, C*H*HPh), 4.32 (m, 2H, CH_2Ph), 4.50 (q, 2H, $J = 11.9$ Hz, CH_2Ph), 4.55 (d, 1H, $J_{3,4} = 2.4$ Hz, H-3), 4.67 (m, 1H, H-5), 4.67 (d, 1H, $J = 10.9$ Hz, C*H*HPh), 6.05 (br, 1H, NH), (6.95 (s, 1H, H-1), 7.02 – 7.35 (m, 16H, Ph, H-1′), 8.24 (br, 1H, NH). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 67.5$, 67.9, 70.1, 70.3, 71.5, 73.1, 74.4, 78.1, 90.7, 111.9, 113.5, 127 – 128.5 (*o*-, *m*-, *p*-Ph), 136.2, 136.9, 137.1, 157.6, 157.8 (C-1′), 160.6 (C-1), 166.3 (C=O). – IR (film): $\nu = 3319$, 3187 (NH_2), 2224 (CN), 1710 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) = 511$ (27) $[M+H]^+$, 403 (30) $[M–OCH_2Ph]^+$, 297 (19). – $C_{31}H_{30}N_2O_5$ (510.22): calcd. C 72.92, H 5.92, N 5.49; found C 72.87, H 5.90, N 5.45.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2-acetyl-2-amino-carbonyl-vinyl]-2-deoxy-D-arabino-hex-1-enitol (**3b**)*

$R_f = 0.62$ (toluene-ethyl acetate, 8 : 2), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 2.05$ (s, 3H, CH_3), 3.45 (dd, 1H, $J_{6a,6b} = 10.5$ Hz, $J_{5,6a} = 5.5$, H-6a), 3.57 (dd, 1H, $J_{5,6b} = 7.4$ Hz, H-6b), 3.87 (t, 1H, H-4), 4.32 (d, 1H, $J = 10.7$ Hz, C*H*HPh), 4.30 (m, 2H, CH_2Ph), 4.51 (q, 2H, $J = 12.1$ Hz, CH_2Ph), 4.52 (d, 1H, $J_{3,4} = 2.4$ Hz, H-3), 4.66 (m, 1H, H-5), 4.67 (d, 1H, $J = 10.7$ Hz, C*H*HPh), 5.95 (br, 1H, NH), 6.92 (s, 1H, H-1), 7.02 – 7.32 (m, 16H, Ph, H-1′), 8.28 (br, 1H, NH). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 30.1$, 67.6, 67.9, 70.3, 70.5, 71.3, 73.3, 74.6, 78.4, 111.7, 113.6, 126.5 – 128.5 (*o*-, *m*-, *p*-Ph), 132.5, 136.1, 137.1, 137.2, 155.2 (C-1′), 157.9, 160.3 (C-1), 166.1 (C=O), 163.6 (C=O). – IR (film): $\nu = 3310$, 3180 (NH_2), 1680, 1700 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) = 528$ (21) $[M+H]^+$, 420 (43) $[M–OCH_2Ph]^+$, 313 (17). – $C_{32}H_{33}NO_6$ (527.23): calcd. C 72.85, H 6.30, N 2.65; found C 72.82, H 6.27, N 2.63.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2,2-methoxy-carbonyl-vinyl]-2-deoxy-D-arabino-hex-1-enitol (**3c**)*

$R_f = 0.57$ (toluene-ethyl acetate, 8 : 2), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 2.03$ (s, 6H, 2 × CH_3), 3.41 (dd, 1H, $J_{6a,6b} = 10.7$, $J_{5,6a} = 5.5$ Hz, H-6a), 3.55 (dd, 1H, $J_{5,6b} = 7.4$ Hz, H-6b), 3.85 (t, 1H, H-4), 4.30 (d, 1H, $J = 10.4$ Hz, C*H*HPh), 4.33 (m, 2H, CH_2Ph), 4.53 (q, 2H, $J = 12.2$ Hz, CH_2Ph), 4.50 (d, 1H, $J_{3,4} = 2.4$ Hz, H-3), 4.64 (ddd, 1H, H-5), 4.65 (d, 1H, $J = 10.4$ Hz, C*H*HPh), 6.90 (s, 1H, H-1), 7.05 – 7.30 (m, 16H, Ph, H-1′). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 14.1$, 14.3, 67.4, 67.8, 70.5, 70.6, 71.1, 73.2, 74.4, 78.5, 94.7, 111.5, 113.2, 126.4 – 128.7 (*o*-, *m*-, *p*-Ph), 136.1, 137.2, 137.4, 154.2 (C-1′), 157.7, 160.3 (C-1), 163.7 (C=O), 163.8 (C=O). – IR (film): $\nu = 1722$, 1725 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) = 559$ (17) $[M+H]^+$, 451 (23) $[M–OCH_2Ph]^+$, 343 (10). – $C_{33}H_{34}O_8$ (558.23): calcd. C 70.95, H 6.13; found C 70.92, H 6.17.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2-acetyl-2-N-(phenylamino)carbonyl-vinyl]-2-deoxy-D-arabino-hex-1-enitol (**3d**)*

$R_f = 0.52$ (toluene-ethyl acetate, 7 : 3, yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 2.06$ (s, 3H, CH_3), 3.42 (dd, 1H, $J_{6a,6b} = 10.9$, $J_{5,6a} = 5.5$ Hz, H-6a), 3.60 (dd, 1H, $J_{5,6b} = 7.4$ Hz, H-6b), 3.87 (t, 1H, H-4), 4.31 (d, 1H, $J = 11.2$ Hz, C*H*HPh), 4.31 (m, 2H, CH_2Ph), 4.49 (q, 2H, $J = 12.1$ Hz, CH_2Ph), 4.53 (d, 1H, $J_{3,4} = 2.4$ Hz, H-3), 4.65 (ddd, 1H, $J_{4,5} = 5.5$ Hz, H-5), 4.66 (d, 1H, $J = 11.2$ Hz, C*H*HPh), 6.93 (s, 1H, H-1), 7.05 – 7.31 (m, 17H, Ph, H-1′), 7.40 (m, 3H, Ph), 10.2 (br, 1H, NH). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 29.4$, 67.4, 67.8, 70.3, 70.5, 71.6,

73.3, 74.6, 78.3, 82.2, 111.7, 113.7, 127.2 – 129.5 (*o*-, *m*-, *p*-Ph), 136.3, 136.7, 137.3, 152.7 (C-1′), 157.7, 160.4 (C-1), 167.3 (C=O), 198.1 (C=O). – IR (film): $\nu = 3315$, (NH), 1690, 1698 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) =$ 604 (17) $[M+H]^+$, 390 (41) $[M–2 \times OCH_2Ph]^+$, 299 (29). – $C_{38}H_{37}NO_6$ (603.26): calcd. C 75.60, H 6.18, N 2.32; found C 75.63, H 6.16, N 2.35.

*1,5-Anhydro-3,4,6-tri-O-benzyl-2-[(E)-2-acetyl-2-N-(p-chlorophenyl)-carboxamide-vinyl]-2-deoxy-D-arabino-hex-1-enitol (**3e**)*

$R_f = 0.52$ (toluene-ethyl acetate, 8:2), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 2.09$ (s, 3H, CH_3), 3.41 (dd, 1H, $J_{6a,6b} = 10.8$, $J_{5,6a} = 5.4$ Hz, H-6a), 3.57 (dd, 1H, $J_{5,6b} = 7.5$ Hz, H-6b), 3.90 (t, 1H, H-4), 4.33 (d, 1H, $J =$ 11.2 Hz, C*H*HPh), 4.33 (m, 2H, CH_2Ph), 4.50 (q, 2H, $J =$ 11.9 Hz, CH_2Ph), 4.53 (d, 1H, $J_{3,4} = 2.5$ Hz, H-3), 4.67 (ddd, 1H, H-5), 4.66 (d, 1H, $J = 11.2$ Hz, C*H*HPh), 6.97 (s, 1H, H-1), 7.07 – 7.33 (m, 18H, Ph, H-1′), 7.39 (m, 2H, Ph), 10.5 (br, 1H, NH). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 29.5$, 67.5, 67.7, 70.1, 70.4, 71.3, 73.6, 74.5, 78.4, 81.1, 111.5, 112.9, 127.2 – 129.2 (*o*-, *m*-, *p*-Ph), 136.2, 136.6, 137.5, 152.9 (C-1′), 157.6, 160.1 (C-1), 167.4 (C=O), 198.5 (C=O). – IR (film): $\nu = 3238$, 3365 (NH), 1692, 1705 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) = 638$ (21) $[M+H]^+$, 425 (15) $[M–2 \times OCH_2Ph]^+$, 271 (42). – $C_{38}H_{36}ClNO_6$ (637.22): calcd. C 71.52, H 5.69, N 2.19; found C 71.56, H 5.71, N 2.18.

*1,5-Anhydro-3,4-di-O-benzyl-2-[(E)-2-cyano-2-amino-carbonyl-vinyl]-2-deoxy-L-erythro-hex-1-enitol (**5a**)*

$R_f = 0.52$ (toluene-ethyl acetate, 7:3), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 3.81$ (quintet (AB), 1H, H-4), 4.15 (dddd, 1H, $J_{5a,5b} = 10.6$ Hz, H-5a), 4.32 (dd, 1H, H-5b), 4.66 (dd, 2H, $J = 11.9$ Hz, CH_2Ph), 5.02 (dd, 2H, $J = 10.5$ Hz, CH_2Ph), 5.16 (m, 1H, $J_{3,4} = 3.8$ Hz, H-3), 6.08 (br, 1H, NH), 7.10 (s, 1H, H-1), 7.15 – 7.30 (m, 10 H, Ph), 7.58 (s, 1H, H-1′), 8.35 (br, 1H, NH). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 64.2$, 66.5, 71.9, 72.3, 74.1, 92.5, 113.1, 116.6, 127.6, 127.7, 128.2, 128.3, 128.4, 128.7 (Ph), 137.2, 138.5 (*i*-Ph), 157.4 (C-1′), 162.3 (C-1), 167.5 (C=O), 198.3 (C=O). – IR (film): $\nu = 3319$ (NH), 2225 (CN), 1700 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) =$ 391 (11) $[M+H]^+$, 284 (15) $[M–OCH_2Ph]^+$, 177 (40). – $C_{23}H_{22}N_2O_4$ (390.16): calcd. C 70.75, H 5.68, N 7.17; found C 70.72, H 5.71, N 7.19.

*1,5-Anhydro-3,4-di-O-benzyl-2-[(E)-2-acetyl-2-amino-carbonyl-vinyl]-2-deoxy-L-erythro-hex-1-enitol (**5b**)*

$R_f = 0.52$ (toluene-ethyl acetate, 8:2), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 2.08$ (s, 3H, CH_3), 3.80 (quintet (AB), 1H, H-4), 4.13 (dddd, 1H, $J_{5a,5b} =$ 10.4 Hz, H-5a), 4.30 (dd, 1H, H-5b), 4.66 (dd, 2H, $J =$ 11.9 Hz, CH_2Ph), 5.0 (dd, 2H, $J = 10.7$ Hz, CH_2Ph), 5.15 (m, 1H, $J_{3,4} = 4.2$ Hz, H-3), 6.01 (br, 1H, NH), 7.12 (s, 1H, H-1), 7.13 – 7.27 (m, 10 H, Ph), 7.55 (s, 1H, H-1′), 8.24 (br, 1H, NH). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 64.2$, 66.5, 71.9, 72.3, 74.1, 92.5, 116.6, 127.6, 127.7, 128.2, 128.3, 128.4, 128.7 (Ph), 137.2, 138.5 (*i*-Ph), 155.3 (C-1′), 162.3 (C-1), 164.1 (C=O), 166.3 (C=O). – IR (film): $\nu = 3334$ (NH), 1690, 1705 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) = 408$ (19) $[M+H]^+$, 300 (23) $[M–OCH_2Ph]^+$, 193 (36). – $C_{24}H_{25}NO_5$ (407.17): calcd. C 70.74, H 6.18, N 3.44; found C 70.73, H 6.16, N 3.45.

*1,5-Anhydro-3,4-di-O-benzyl-2-[(E)-2,2-methoxycarbonyl-vinyl]-2-deoxy-L-erythro-hex-1-enitol (**5c**)*

$R_f = 0.52$ (toluene-ethyl acetate, 8:2), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 3.80$ (quintet (AB), 1H, H-4), 4.13 (dddd, 1H, $J_{5a,5b} = 10.7$ Hz, H-5a), 4.31 (dd, 1H, H-5b), 4.66 (dd, 2H, $J = 11.9$ Hz, CH_2Ph), 5.05 (dd, 2H, $J = 10.5$ Hz, CH_2Ph), 5.14 (dd, 1H, $J_{3,4} = 4.0$ Hz, H-3), 7.12 (s, 1H, H-1), 7.15 – 7.28 (m, 10 H, Ph), 7.57 (s, 1H, H-1′). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 14.1$, 14.2, 66.5, 71.9, 72.3, 74.1, 92.5, 113.1, 116.4, 127.5, 127.4, 128.6, 128.3, 128.4, 128.5 (Ph), 137.2, 138.3 (*i*-Ph), 153.6 (C-1′), 162.4 (C-1), 163.2 (C=O), 163.4 (C=O). – IR (film): $\nu =$ 1725, 1728 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) =$ 439 (18) $[M+H]^+$, 224 (15) $[M–2 \times OCH_2Ph]^+$. – $C_{25}H_{26}O_7$ (438.17): calcd. C 68.48, H 5.98; found C 68.47, H 5.96.

*1,5-Anhydro-3,4-di-O-benzyl-2-[(E)-2-acetyl-2-N-(phenylamino)carbonyl-vinyl]-2-deoxy-L-erythro-hex-1-enitol (**5d**)*

$R_f = 0.55$ (toluene-ethyl acetate, 8:2), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 3.78$ (quintet (AB), 1H, H-4), 4.12 (dddd, 1H, $J_{5a,5b} = 10.5$ Hz, H-5a), 4.33 (dd, 1H, H-5b), 4.65 (dd, 2H, $J = 12.2$ Hz, CH_2Ph), 5.02 (dd, 2H, $J = 10.5$ Hz, CH_2Ph), 5.15 (m, 1H, $J_{3,4} = 3.7$ Hz, H-3), 7.13 (s, 1H, H-1), 7.15 – 7.27 (m, 12 H, Ph), 7.35 (m, 3H, Ph), 7.57 (s, 1H, H-1′), 10.3 (br, 1H, NH). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 29.6$, 64.4, 66.3, 71.5, 72.1, 74.3, 94.7, 112.8, 116.3, 127.6, 127.8, 127.9, 128.1, 128.4, 128.5, 128.7, 128.9, 129.1, 129.5 (*o*-, *m*-, *p*-Ph), 137.3, 138.5 (*i*-Ph), 152.4 (C-1′), 162.5 (C-1), 167.2 (C=O), 197.7 (C=O). – IR (film): $\nu =$ 3340 (NH), 1694, 1698 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) = 484$ (31) $[M+H]^+$, 376 (19) $[M–OCH_2Ph]^+$, 257 (53). – $C_{30}H_{29}NO_5$ (483.20): calcd. C 70.75, H 5.68, N 7.17; found C 70.72, H 5.71, N 7.19.

*1,5-Anhydro-3,4-di-O-benzyl-2-[(E)-2-acetyl-2-N-(p-chlorophenyl)-carboxamide-vinyl]-2-deoxy-L-erythro-hex-1-enitol (**5e**)*

$R_f = 0.57$ (toluene-ethyl acetate, 7:3), yellowish syrup. – ^{1}H NMR (500.133 MHz, $CDCl_3$): $\delta = 3.76$ (quintet (AB),

1H, H-4), 4.11 (dddd, 1H, $J_{5a,5b} = 10.5$ Hz, H-5a), 4.30 (dd, 1H, H-5b), 4.63 (dd, 2H, $J = 12.0$ Hz, CH_2Ph), 5.04 (dd, 2H, $J = 10.4$ Hz, CH_2Ph), 5.15 (m, 1H, $J_{3,4} = 4.2$ Hz, H-3), 7.15 (s, 1H, H-1), 7.12 – 7.29 (m, 10 H, Ph), 7.37 (m, 3H, Ph), 7.53 (s, 1H, H-1′), 10.41 (br, 1H, NH). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 29.5$, 64.2, 66.1, 71.3, 71.9, 74.1, 94.5, 112.7, 116.5, 127.4, 127.7, 127.8, 128.1, 128.3, 128.5, 128.6, 128.9, 129.5 (*o*-, *m*-, *p*-Ph), 137.1, 138.3 (*i*-Ph), 152.8 (C-1′), 162.3 (C-1), 167.3 (C=O), 197.8 (C=O). – IR (film): $\nu = 3210$, 3340 (NH), 1690, 1705 (C=O) cm^{-1}. – MS (CI, isobutane): $m/z(\%) = 482$ (37) $[M–Cl]^+$, 410 (13) $[M–OCH_2Ph]^+$, 376 (45). – $C_{30}H_{28}ClNO_5$ (517.17): calcd. C 69.56, H 5.45, N 2.70; found C 69.56, H 5.42, N 2.73.

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