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Note

Novobiocin-related compounds: synthesis of 3-benzoylamino-2-oxo-2*H*-1-benzopyran-7-yl D-glycopyranosides by the trichloroacetimidate methodology

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Abstract

A general stereoselective method for the synthesis of 4-deoxynovobiocin-related glycosides is described. 3-Benzoylamino-2*H*-1-benzopyran-7-yl 2,3,4,6-tetra-*O*-acetyl-D-glycopyranosides of glucose, galactose and mannose were synthesised from appropriate *O*-glycosyltrichloroacetimidates and *N*-(7-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)benzamides in boiling methylene chloride in the presence of boron trifluoride etherate. Heating of these products in a mixture of triethylamine and methanol gave the corresponding deprotected 3-benzoylamino-2-oxo-2*H*-1-benzopyran-7-yl β-D-glycopyranosides.

Keywords: Stereoselective synthesis; Coumarins; Mannosides; Galactosides; Glucosides

Glycosides containing the 2*H*-1-benzopyran-2-one moiety are important biologically active compounds [1]. Some decades ago, novobiocin, an antibiotic substance produced by the cultures *Streptomices spheroides* and *niveus*, and other 2*H*-1-benzopyran antibiotics were used clinically [2–4]. Due to the development of resistance and their toxicity they are now very rarely employed [2]. Recently, some drug-receptor binding models were introduced and enabled a systematic and rational design of novel inhibitors of various enzymes, such as DNA girase or topoisomerase [3]. These results, obtained from investigations involving novobiocin, launched further studies of this compound [5a,b] and related derivatives [5c]. It has also been shown that the 4-hydroxy group in novobiocin is not indispensable for the molecule to be bound in the enzyme [3b,c]; similar results were also observed with some related derivatives [5c].

Since noviosyl derivatives are neither easily available nor cheap substrates, we became interested in the preparation of model compounds possessing the 4-deoxynovobiocin-like pattern, i.e., compounds containing a benzoylamino moiety at C-3 of the 2*H*-1-benzopyran-2-one system and a sugar moiety at C-7, bound by the O-glycosidic linkage. We wanted

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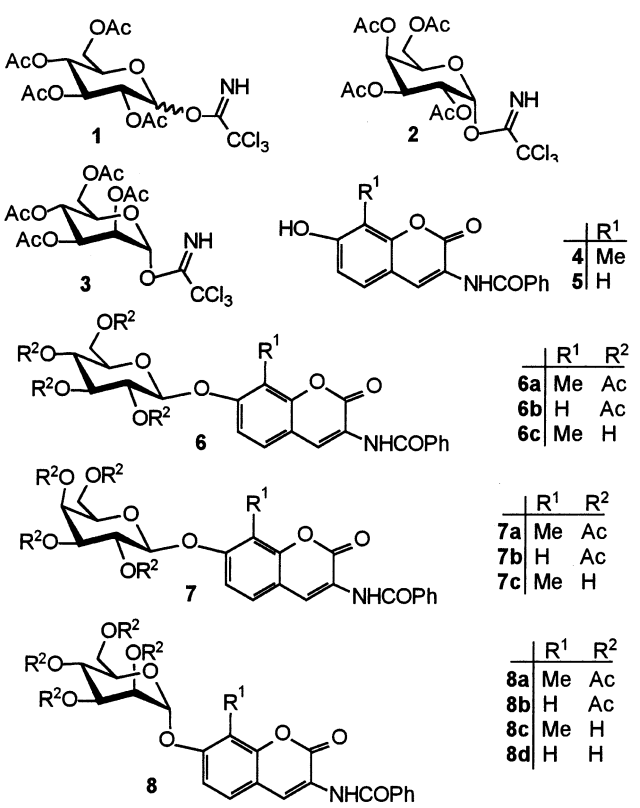
to prepare them in both forms, α and β. A critical point in the synthesis of such compounds is the formation of the glycosidic bond. In the past it was formed with variable success by glycosylation of 7-hydroxy-2*H*-1-benzopyran-2-one (umbelliferone) derivatives with glycosyl halides [4,6,7], under Mitsunobu's conditions [5c], by trichloroacetimidate methodology [8], etc. For the formation of the glycosidic linkage we have chosen trichloroacetimidate methodology, which was known to be a powerful tool for the formation of the glycosides with less reactive compounds like phenols [9]. The α/β selectivity in glycosylation can be to some extent controlled by an appropriate selection of protecting group, a catalyst and a solvent.

Here we report a highly efficient and stereoselective preparation of a series of 3-benzoylamino-2*H*-1-benzopyran-7-yl D-glycopyranosides **6**–**8** starting from various *O*-glycosyltrichloroacetimidates **1**–**3** [9c,10] and *N*-(7-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)benzamides **4** and **5** [11] in methylene chloride and in the presence of boron trifluoride etherate as an acidic catalyst. Starting from anomerically-pure α- and β-2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl trichloroacetimidates (**1**-α [10a] and **1**-β [9c]) we prepared the corresponding β-glycosides **6a**,**b**. Due to the low solubility of the benzopyran derivatives **4** and **5** in methylene chloride, the reactions were carried out in boiling methylene chloride in the presence of $BF_3{\cdot}Et_2O$. Although the trichloroacetimidates slowly decompose under the applied conditions, they can still be detected in the reaction mixture after 4 h of heating (as examined in separate experiments for **1**-β and **2**). They were used in quantities of 1.46–2.1 mmol (in the case of **1**-α 5 mmol) per mmol of the benzopyran derivatives **4** and **5**; they were added in two portions to the reaction mixtures. No formation of α-products was detected in these particular cases (Scheme 1, Table 1). Glycosidation of compounds **4** and **5** with related α-galactopyranosyl trichloroacetimidate (**2**), which was obtained by the separation of the mixture of anomers [10a] by column chromatography, gave products **7a**,**b** in 89 and 77% yields. Finally, the reactions between α-mannopyranosyl trichloroimidate (**3**) [10b] and compounds **4** or **5** resulted in the formation of the corresponding thermodynamically more stable α-mannosides **8a**,**b**, which we obtained in good yields (73 and 81%).

The acetylated products **6a**,**b**–**8a**,**b** can be deprotected as shown by the preparation of products **6c**, **7c** and **8c**,**d**. Deprotection was carried out by heating mixtures of acetylated derivatives in a 0.5 M solution of triethylamine in methanol. The corresponding products were obtained in 73–98% yields.

The structural integrity and the configuration at the anomeric centre in **6a**–**c**, **7a**–**c** and **8a**–**d** was determined with the use of NMR spectroscopy. Products **6a**,**b** and **7a**,**b** exhibit typical doublet signals for anomeric protons between δ 5.55 and 5.73 ppm with the coupling constants $J_{1,2}$ of 7.7–7.9 Hz. Similarly, the deacetylated compounds **6c** and **7c** show doublets at 4.96 and 4.91 ppm with the coupling constants $J_{1,2}$ of 7.2 and 7.5 Hz. The trans-diaxial orientation of 1′-H and 2′-H protons, and therefore the β configuration at C-1′ in **6a**–**c** and **7a**–**c**, was further established with the observation of strong NOE interactions between 1′-H and the axial protons 3′-H



Scheme 1.

Table 1
Reaction conditions and yields of the products **6a**,**b**–**8a**,**b**

Starting benzopyran (mmol)	Trichloroacetimidate (basic + additional amount) (mmol)	Reaction time and additional reaction time (h)	mL of solvent; mmol of catalyst	Product (yield, %) [a]
4 (0.57)	**1**-β (0.69 + 0.34)	1.5; 1.0	5; 0.24	**6a** (65)
4 (0.19)	**1**-α (0.23 + 0.72)	3; 0.5	3 [b]; 0.16	**6a** (57)
5 (0.76)	**1**-β (0.98 + 0.39)	4; 2	4; 0.24	**6b** (62)
5 (0.48)	**1**-α (0.62 + 0.40)	1; 0.5	4 [b]; 0.24	**6b** (51)
4 (0.57)	**2** (0.69 + 0.23)	1; 0.5	4; 0.24	**7a** (89)
5 (0.92)	**2** (1.11 + 0.23)	1; 0.5	8; 0.16	**7b** (77)
4 (0.57)	**3** (0.69 + 0.46)	1.5; 0.5	4 [b]; 0.24	**8a** (73)
5 (0.71)	**3** (1.06 + 0.35)	4; 1	4 [b]; 0.24	**8b** (81)

[a] Yields of TLC-pure products.
[b] Starting volume of CH_2Cl_2 was 1 mL smaller; an additional amount of trichloroimidate was added in 1 mL of CH_2Cl_2.

and 5′-H. The anomeric configuration of mannosides **8a**–**d** was elucidated on the basis of diagnostic [12] heteronuclear one-bond ^{13}C–^{1}H coupling constants of anomeric carbon atoms. In the case of compounds **8a** and **8c**, the $J_{C\text{-}1',H\text{-}1'}$ coupling constants were 174.6 and 170.9 Hz, which are typical for an equatorial hydrogen and thus α-anomeric glycosidic linkage. The absence of NOESY cross-peaks between the anomeric proton and the axial protons at C-3 and C-5 in **8c** is consistent with the equatorial position of the anomeric proton and therefore the α-anomeric linkage. An inspection of the proton–proton coupling constants along the pyranose seven-spin system indicates that sugar moieties in **6a**–**c**, **7a**–**c** and **8a**–**d** adopt conformations that are close to $^{4}C_1$ chair canonical forms.

In conclusion, we prepared some compounds related to novobiocin, which might be of interest for further investigations towards biologically active compounds. Our results have shown that trichloroacetimidates can also be successfully used at temperatures above room temperature. This seems to be especially useful when applying substrates, which are poorly soluble in the solvent used.

1. Experimental

Melting points were determined on a Kofler micro hot stage, and are uncorrected. ^{1}H and ^{13}C NMR (75 MHz) spectra were recorded with Varian VXR-300, Unity + 300 and Bruker Advance DPX 300 spectrometers, using TMS as an internal standard. The coupling constants (J) are given in Hz. IR spectra were obtained with a Perkin–Elmer Spectrum 1000 spectrophotometer. Mass spectra were recorded with a VG-Analytical AutoSpec Q instrument. Elemental analyses (C, H, N) were performed with a Perkin–Elmer 2400 CHN Analyzer. Optical rotations were measured in a 1 dm path-length cell on a Perkin–Elmer 241 MC Polarimeter and the concentrations are given in g/100 mL. Column chromatography was performed with Silica Gel 60 (E. Merck, 60–63 μm). Thin-layer chromatography was carried out on Fluka silica gel TLC cards. The starting compounds **1**–**5** [9c,10,11] were prepared as described in the literature. Compound **2** was obtained as an anomerically-pure α product from the mixture of anomers [10a] by a column chromatography, using a mixture of EtOAc and light petroleum (1:5) as an eluant. Methylene chloride was dried over P_4O_{10} and distilled before use. All other reagents were used as received from commercial suppliers.

General procedure for the synthesis of glycosides **6a**,**b**–**8a**,**b**.—To a suspension of a benzopyran derivative (**4** or **5**) in dry CH_2Cl_2 under an atmosphere of dry nitrogen (dried over a drierite column) a basic amount of an appropriate trichloroimidate (**1**, **2** or **3**) was added. After stirring for 10 min at ambient temperature $BF_3{\cdot}OEt_2$ was added, and the

mixture was heated under reflux for a certain period of time. An additional amount of trichloroimidate was then added and heating was continued for a period of time. The solvent was removed under reduced pressure and further isolation was carried out, as specified for each case.

For the isolation of **6a**,**b**, **7a** and **8b**, the solids were dissolved in ~20 mL of warm EtOAc, the remaining solid (benzopyran derivative **4** or **5**) was filtered off and the filtrate was purified by column chromatography. The eluant for **6a** was first a mixture of EtOAc/light petroleum 1:3 followed by a mixture 1:2; for **6b** EtOAc/light petroleum 1:3; for **7a** EtOAc/light petroleum 1:2; and for **8a** EtOAc/light petroleum 1:2. For the isolation of **7b**, the solid was suspended in a minimal amount of a mixture of $CHCl_3$/light petroleum 1:1, the crystalline product was filtered off and the filtrate was purified by column chromatography (eluant EtOAc/light petroleum 1:3). Product **8b** was isolated with purification by column chromatography with the eluant EtOAc/light petroleum 1:2. In all cases, the products obtained by column chromatography were suspended in a small amount of abs EtOH and filtered off. Details and yields are given in Table 1.

General procedure for deprotection of acetylated derivatives **6**–**8**.—A mixture of 1 mmol of acetylated compound in a 0.5 M Et_3N soln in MeOH (10 mL) was heated under reflux for 4 h. The starting materials dissolved within 1 h of heating and later the product began to precipitate. The reaction mixture was left overnight at 5 °C, the separated product was filtered, washed with a small amount of cold MeOH and crystallised. Yields of TLC-pure products: **6c** (from **6a**) 73%, **7c** (from **7a**) 98%, **8c** (from **8a**) 77%, **8d** (from **8b**) 96%.

Analytical and spectroscopic data of products **6**–**8**

*3-Benzoylamino-8-methyl-2-oxo-2*H-*1-benzopyran-7-yl 2,3,4,6-tetra*-O-*acetyl-β*-D-*glucopyranoside* (**6a**). White solid, mp 188–190 °C (from EtOAc/light petroleum); $[\alpha]_D$ −40.3° (*c* 0.8, DMSO); IR ν_{max}/cm^{-1} 1753, 1715, 1670, 1608, 1527; ^{1}H NMR (DMSO-d_6): δ 1.99, 2.02, 2.03 and 2.06 (12 H, 4 s, 4 Ac), 2.16 (3 H, s, Me), 4.12 (1 H, dd, J_1 2.1, J_2 12.5, 6′-H_a), 4.23 (1 H, dd, J_1 5.0, J_2 12.5, 6′-H_b), 4.32 (1 H, m, 5′-H), 5.04 (1 H, dd, $J_1 = J_2$ 9.4, 4′-H), 5.17 (1 H, dd, J_1 7.9, J_2 9.4, 2′-H), 5.45 (1 H, dd, $J_1 = J_2$ 9.4, 3′-H), 5.63 (1 H, d, *J* 7.9, 1′-H), 7.13 (1 H, d, *J* 9, 6-H), 7.61 (4 H, m, 5-H, 3 H of Ph), 7.96 (2 H, m, Ph), 8.57 (1 H, s, 4-H), 9.63 (1 H, br s, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.39, 170.09, 169.30, 169.08, 165.97, 158.96, 155.89, 148.93, 133.53, 132.44, 128.87, 127.06, 125.60, 123.69, 122.44, 115.97, 115.31, 112.28, 99.17, 72.42, 72.13, 70.86, 68.17, 61.80, 20.61, 20.55, 20.52, 20.50, 8.12; *m*/*z* (FABMS): 626 (MH^+, 24%), 331 (43), 169 (82), 105 (100). Anal. Calcd for $C_{31}H_{31}NO_{13}$: C, 59.52; H, 4.99; N, 2.24. Found: C, 59.36; H, 4.93; N, 2.21.

*3-Benzoylamino-2-oxo-2*H-*1-benzopyran-7-yl 2,3,4,6-tetra*-O-*acetyl-β*-D-*glucopyranoside* (**6b**). White solid, mp 116.5–119 °C (EtOAc/light petroleum); $[\alpha]_D$ −11.0° (*c* 0.5, DMSO); IR ν_{max}/cm^{-1} 1755 br, 1675, 1614, 1528; ^{1}H NMR (DMSO-d_6): δ 1.98 (3 H, s), 2.03 (3 H, s), 2.04 (6 H, br s) (4 Ac), 4.12 (1 H, dd, J_1 2.3, J_2 12, 6′-H_a), 4.21 (1 H, dd, J_1 5.6, J_2 12, 6′-H_b), 4.33 (1 H, deg ddd, 5′-H), 5.03 (1 H, dd, $J_1 = J_2$ 9.8, 4′-H), 5.11 (1 H, dd, J_1 7.9, J_2 9.8, 2′-H), 5.41 (1 H, dd, $J_1 = J_2$ ca. 9.8, 3′-H), 5.73 (1 H, d, *J* 7.9, 1′-H), 7.03 (1 H, dd, J_1 9, J_2 2.3, 6-H), 7.12 (1 H, d, *J* 2.3, 8-H), 7.59 (3 H, m, Ph), 7.76 (1 H, d, *J* 9, 5-H), 7.96 (2 H, m, Ph), 8.57 (1 H, s, 4-H), 9.63 (1 H, s, NH); ^{13}C NMR (DMSO-d_6): δ 169.95, 169.60, 169.32, 169.11, 165.80, 157.86, 157.61, 151.45, 133.50, 132.20, 129.20, 129.34, 128.63, 127.88, 127.57, 122.36, 114.42, 114.08, 103.24, 96.65, 91.34, 71.92, 71.02, 70.50, 67.93, 61.62, 20.39, 20.33; *m*/*z* (FABMS): 612 (MH^+, 21%), 331 (44), 169 (83), 105 (100). Anal. Calcd for $C_{30}H_{29}NO_{13}$: C, 58.92; H, 4.78; N, 2.29. Found: C, 59.20; H, 4.96; N, 2.18.

*3-Benzoylamino-8-methyl-2-oxo-2*H-*1-benzopyran-7-yl β*-D-*glucopyranoside* (**6c**). White solid, mp 237–239 °C (dec, MeOH); $[\alpha]_D$ +33.4° (*c* 0.5, DMSO); IR ν_{max}/cm^{-1} 1703, 1660, 1608, 1534; ^{1}H NMR (DMSO-d_6): δ 2.29 (3 H, s, Me), 3.15–3.42 (4 H, m, 2′-H, 3′-H, 4′-H, 5′-H, covered with water), 3.48 (1 H, deg ddd, 6′-H_a), 3.71 (1 H, deg ddd, 6′-H_b), 4.56 (1 H, t, $J_1 = J_2$ ca. 6, 6′-OH), 4.96 (1 H, d, *J* 7.2, 1′-H), 5.03 (1 H, d, *J* 4.9, OH), 5.09 (1 H, d, *J* 4.5, OH), 5.39 (1 H, d, *J* 4.9, OH), 7.18 (1 H, d, *J* 9, 6-H), 7.58 (4 H, m, 5-H, 3 H

of Ph), 7.97 (2 H, m, Ph), 8.54 (1 H, s, 4-H), 9.61 (1 H, br s, NH); ^{13}C NMR (DMSO-d_6): δ 165.74, 158.11, 156.98, 149.33, 133.56, 132.11, 128.64, 128.59, 127.52, 126.03, 121.52, 113.72, 113.52, 112.06, 100.81, 77.11, 76.51, 73.27, 69.64, 60.66, 8.10; *m/z* (FABMS): 458 (MH^+), 295, 107, 71. Anal. Calcd for $C_{23}H_{23}NO_9 \cdot H_2O$: C, 58.10; H, 5.30; N, 2.95. Found: C, 58.02; H, 5.30; N, 2.83.

*3-Benzoylamino-8-methyl-2-oxo-2*H-*1-benzopyran-7-yl 2,3,4,6-tetra*-O-*acetyl-β*-D-*galactopyranoside* (**7a**). White solid, mp 178–179 °C (EtOAc/light petroleum); $[\alpha]_D$ −14.0° (*c* 0.7, DMSO); IR ν_{max}/cm^{-1} 1752, 1717, 1674, 1609, 1529; ^{1}H NMR (DMSO-d_6): δ 1.97, 2.04 and 2.07 (9 H, 3 s, 3 Ac), 2.16 (6 H, br s, Me, Ac), 4.14 (2 H, m, 6′-H_a, 6′-H_b), 4.51 (1 H, pseudo t, *J* ca. 6.5, 5′-H), 5.32 (2 H, m, 2′-H, 3′-H), 5.38 (1 H, m, 4′-H), 5.55 (1 H, d, *J* 7.7, 1′-H), 7.13 (1 H, d, *J* 8.8, 6-H), 7.61 (4 H, m, 5-H, 3 H of Ph), 7.97 (2 H, m, Ph), 8.56 (1 H, s, 4-H), 9.63 (1 H, s, NH); ^{13}C NMR (DMSO-d_6): δ 169.93, 169.80, 169.49, 169.33, 165.80, 157.91, 155.75, 149.27, 133.51, 132.14, 128.59, 128.05, 127.54, 126.18, 122.03, 114.34, 113.73, 111.62, 97.91, 70.54, 69.87, 68.17, 67.15, 61.25, 20.46, 20.42, 20.35, 20.29, 7.72; *m/z* (FABMS): 626 (MH^+, 46%), 331 (88), 169 (31), 105 (100). Anal. Calcd for $C_{31}H_{31}NO_{13}$: C, 59.52; H, 4.99; N, 2.24. Found: C, 59.28; H, 5.03; N, 2.14.

*3-Benzoylamino-2-oxo-2*H-*1-benzopyran-7-yl 2,3,4,6-tetra*-O-*acetyl-β*-D-*galactopyranoside* (**7b**). White solid, 103–104.5 °C (EtOH); $[\alpha]_D$ +16.7° (*c* 0.6, DMSO); IR ν_{max}/cm^{-1} 1752, 1675, 1614, 1527; ^{1}H NMR (DMSO-d_6): δ 1.96, 2.03, 2.06 and 2.16 (12 H, 4 s, 4 Ac), 4.12 (2 H, d, *J* 6.4, 6′-CH_2), 4.52 (1 H, deg dt, *J* ca. 6.4, 5′-H), 5.27 (2 H, m, 2′-H, 3′-H), 5.38 (1 H, deg dd, 4′-H), 5.64 (1 H, d, *J* 7.9, 1′-H), 7.02 (1 H, dd, J_1 2.3, J_2 8.7, 6-H), 7.12 (1 H, d, *J* 2.3, 8-H), 7.59 (3 H, m, Ph), 7.77 (1 H, d, *J* 8.7, 5-H), 7.96 (2 H, m, Ph), 8.57 (1 H, s, 4-H), 9.63 (1 H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 170.38, 170.14, 170.04, 169.29, 166.06, 158.89, 157.87, 150.89, 133.53, 132.55, 128.96, 128.81, 127.10, 123.41, 122.78, 115.25, 114.93, 104.24, 99.21, 71.45, 70.69, 68.36, 66.78, 61.42, 20.70, 20.64, 20.63, 20.55; *m/z* (FABMS): 612 (MH^+, 28%), 154 (100). Anal. Calcd for $C_{30}H_{29}NO_{13}$: C, 58.92; H, 4.78; N, 2.29. Found: C, 59.06; H, 4.78; N, 2.30.

*3-Benzoylamino-8-methyl-2-oxo-2*H-*1-benzopyran-7-yl β*-D-*galactopyranoside* (**7c**). White solid, mp 216–219 °C (dec, MeOH/water); $[\alpha]_D$ −12.3° (*c* 0.5, DMSO); IR ν_{max}/cm^{-1} 1714, 1662, 1609, 1532; ^{1}H NMR (DMSO-d_6): δ 2.29 (3 H, s, Me), 3.41–3.75 (6 H, m, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H_a, 6′-H_b), 4.53 (1 H, d, *J* 4.5, OH), 4.65 (1 H, t, *J* 5.5, 6′-OH), 4.87 (1 H, d, *J* 6.0, OH), 4.91 (1 H, d, *J* 7.5, 1′-H), 5.23 (1 H, d, *J* 5.7, OH), 7.18 (1 H, d, *J* 8.7, 6-H), 7.58 (4 H, m, 5-H, 3 H of Ph), 7.96 (2 H, m, Ph), 8.54 (1 H, s, 4-H), 9.61 (1 H, br s, NH); ^{13}C NMR (DMSO-d_6): δ 165.73, 158.11, 157.10, 149.36, 133.57, 132.10, 128.72, 128.58, 127.52, 125.99, 121.47, 113.72, 113.44, 112.06, 101.46, 75.64, 73.18, 70.29, 68.10, 60.36, 8.11; *m/z* (FABMS): 458 (MH^+), 295, 105, 71. Anal. Calcd for $C_{23}H_{23}NO_9$: C, 60.39; H, 5.07; N, 3.06. Found: C, 60.58; H, 5.14; N, 3.07.

*3-Benzoylamino-8-methyl-2-oxo-2*H-*1-benzopyran-7-yl 2,3,4,6-tetra*-O-*acetyl-α*-D-*mannopyranoside* (**8a**). White solid, mp 162–164 °C (EtOAc/light petroleum); $[\alpha]_D$ +49.3° (*c* 0.3, DMSO); IR ν_{max}/cm^{-1} 1752, 1673, 1604, 1525; ^{1}H NMR (DMSO-d_6): δ 1.94, 2.00, 2.05 and 2.17 (12 H, 4 s, 4 Ac), 2.32 (3 H, s, Me), 3.99 (2 H, dd, J_1 2.3, J_2 12, 6′-H_a), 4.05 (1 H, m, 5′-H), 4.19 (1 H, dd, J_1 5.2, J_2 12, 6′-H_b), 5.23 (1 H, m, 4′-H), 5.42 (2 H, m, 2′-H, 3′-H), 5.90 (1 H, d, *J* 1.6, 1′-H), 7.24 (1 H, d, *J* 8.7, 6-H), 7.59 (4 H, m, 5-H, 3 H of Ph), 7.97 (2 H, m, Ph), 8.56 (1 H, s, 4-H), 9.62 (1 H, s, NH); ^{13}C NMR ($CDCl_3$): δ 170.37, 169.92, 169.86, 169.60, 166.00, 159.03, 154.82, 149.02, 133.55, 132.43, 128.88, 127.08, 125.67, 123.78, 122.40, 115.39, 115.10, 111.59, 96.05, 69.65, 69.22, 68.77, 65.62, 62.03, 20.79 (2 × C), 20.62 (2 × C), 8.41; *m/z* (FABMS): 626 (MH^+, 13), 331 (26), 169 (48), 105 (100). Anal. Calcd for $C_{31}H_{31}NO_{13}$: C, 59.52; H, 4.99; N, 2.24. Found: C, 59.71; H, 5.08; N, 2.24.

*3-Benzoylamino-2-oxo-2*H-*1-benzopyran-7-yl 2,3,4,6-tetra*-O-*acetyl-α*-D-*mannopyranoside* (**8b**). White solid, mp 146–148.5 °C (EtOAc/light petroleum); $[\alpha]_D$ +76.3° (*c* 0.5, DMSO); IR ν_{max}/cm^{-1} 1756 br, 1673, 1611, 1528; ^{1}H NMR (DMSO-d_6): δ 1.92, 1.99, 2.05 and 2.17

(12 H, 4 s, 4 Ac), 3.99 (1 H, dd, J_1 2, J_2 12, 6′-H_a), 4.09 (1 H, deg ddd, 5′-H), 4.18 (1 H, dd, J_1 5.6, J_2 12, 6′-H_b), 5.21 (1 H, dd, $J_1 = J_2$ 9.6, 4′-H), 5.38 (2 H, m, 2′-H, 3′-H), 5.93 (1 H, d, J ca. 0.8, 1′-H), 7.21 (1 H, dd, J_1 2.3, J_2 8.7, 6-H), 7.28 (1 H, d, J 2.3, 8-H), 7.58 (3 H, m, Ph), 7.77 (1 H, d, J 8.7, 5-H), 7.96 (2 H, m, Ph), 8.57 (1 H, s, 4-H), 9.63 (1 H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 170.39, 169.87, 169.85, 169.59, 165.97, 158.82, 156.70, 150.87, 133.47, 132.47, 128.88, 128.81, 127.06, 123.33, 122.72, 115.10, 114.50, 104.16, 95.97, 69.48, 69.01, 68.60, 65.70, 61.99, 20.78, 20.60, 20.59, 20.57; m/z (FABMS): 612 (MH^+, 24), 331 (49), 169 (60), 105 (100). Anal. Calcd for $C_{30}H_{29}NO_{13}$: C, 58.92; H, 4.78; N, 2.29. Found: C, 59.15; H, 4.76; N, 2.31.

*3-Benzoylamino-8-methyl-2-oxo-2*H*-1-benzopyran-7-yl-α-*D*-mannopyranoside* (**8c**). White solid, mp 215–218 °C (dec, MeOH); $[\alpha]_D$ −15.6° (c 0.5, DMSO); IR ν_{max}/cm^{-1} 1708, 1669, 1607, 1544; ^{1}H NMR (DMSO-d_6): δ 2.26 (3 H, s, Me), 3.38 (1 H, m, 5′-H), 3.43–3.63 (3 H, m, 4′-H, 6′-H_a, 6′-H_b), 3.76 (1 H, ddd, J_1 ca. 3.4, J_2 ca. 6.0, J_3 ca. 9.4, 3′-H), 3.93 (1 H, m, 2′-H), 4.44 (1 H, dd, $J_1 = J_2$ 6, 6′-OH), 4.79 (1 H, d, J 6.0, 3′-OH), 4.86 (1 H, d, J 5.6, 4′-OH), 5.10 (1 H, d, J 4.5, 2′-OH), 5.55 (1 H, d, J 1.9, 1′-H), 7.27 (1 H, d, J 8.7, 6-H), 7.58 (4 H, m, 5-H, 3 H of Ph), 7.96 (2 H, m, Ph), 8.53 (1 H, s, 4-H), 9.60 (1 H, br s, NH); ^{13}C NMR (DMSO-d_6): δ 165.73, 158.07, 155.79, 149.41, 133.54, 132.12, 128.73, 128.60, 127.53, 126.06, 121.53, 113.61, 113.50, 112.05, 98.78, 75.37, 70.81, 69.99, 66.65, 60.99, 8.06; m/z (FABMS): 458 (MH^+), 295, 105. Anal. Calcd for $C_{23}H_{23}NO_9 \cdot H_2O$: C, 58.10; H, 5.30; N, 2.95. Found: C, 57.84; H, 5.43; N, 2.94.

*3-Benzoylamino-2-oxo-2*H*-1-benzopyran-7-yl α-*D*-mannopyranoside* (**8d**). White solid mp 216–218 °C (dec, MeOH); $[\alpha]_D$ +127.3° (c 0.5, DMSO); IR ν_{max}/cm^{-1} 1712, 1672, 1612, 1533; ^{1}H NMR (DMSO-d_6): δ 3.28–3.55 (3 H, m, 4′-H, 6′-H_a, 6′-H_b), 3.62 (1 H, ddd, J_1 1.8, J_2 5.7, J_3 11.7, 5′-H), 3.70 (1 H, ddd, J_1 3.3, J_2 ca. 5.9, J_3 ca. 11.7, 3′-H), 3.87 (1 H, m, 2′-H), 4.52 (1 H, dd, $J_1 = J_2$ ca. 5.9, 6′-OH), 4.81 (1 H, d, J 6.0, 3′-OH), 4.87 (1 H, d, J 5.6, 4′-OH), 5.11 (1 H, d, J 4.5, 2′-OH), 5.53 (1 H, d, J 1.7, 1′-H), 7.11 (1 H, dd, J_1 2.3, J_2 8.7, 6-H), 7.24 (1 H, d, J 2.3, 8-H), 7.60 (3 H, m, Ph), 7.71 (1 H, d, J 8.7, 5-H), 7.97 (2 H, m, Ph), 8.55 (1 H, s, 4-H), 9.63 (1 H, br s, NH); ^{13}C NMR (DMSO-d_6): δ 165.74, 158.07, 158.04, 151.60, 133.53, 132.16, 129.06, 128.62, 128.49, 127.57, 121.84, 114.63, 113.57, 103.62, 98.96, 75.33, 70.56, 69.82, 66.62, 61.00; m/z (FABMS): 444 (MH^+), 281, 105, 71. Anal. Calcd for $C_{22}H_{21}NO_9 \cdot 0.5H_2O$: C, 58.41; H, 4.90; N, 3.10. Found: C, 58.34; H, 4.90; N, 3.08.

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