MODIFIED COUMARINS. 12. SYNTHESIS OF 3,4-CYCLOANNELATED COUMARIN β-D-GLUCOPYRANOSIDES

Ya. L. Garazd,[1] M. M. Garazd,[2] and V. P. Khilya[1]

UDC 547.814.5

O-β-*D*-*Glucopyranosides were synthesized using 3,4-cycloannelated hydroxycoumarins as aglycons. Phenolic hydroxyls were O-glycosylated via condensation of coumarin potassium salts with acetobromoglucose in homogeneous medium and in a liquid—liquid system using a phase-transfer catalyst.*

Key words: coumarins, glucosides, glucosylation, phase-transfer catalyst, synthesis.

Coumarins with bound sugars are widely distributed in nature. The most common of these compounds are O-glycosides with the sugar in various positions on the benzopyran ring [1]. Compared with the aglycons, they are more soluble in water and blood plasma. Their acetates and methyl ethers are highly soluble in lipids and other slightly polar media. Therefore, introducing carbohydrates into the coumarin structure can significantly change the hydrophilic-lipophilic balance and, consequently, affect its transport in biological systems. The biological activity of coumarin O-glycosides is of great interest owing to the high and varied pharmacological activity of coumarins. The synthesis of glycosides provides an additional capability to introduce into the coumarin core a variety of substituents that are promising from the viewpoint of biological activity. Therefore, we synthesized β-D-glucopyranosides of 5- and 7-hydroxy-3,4-cycloannelated coumarins.

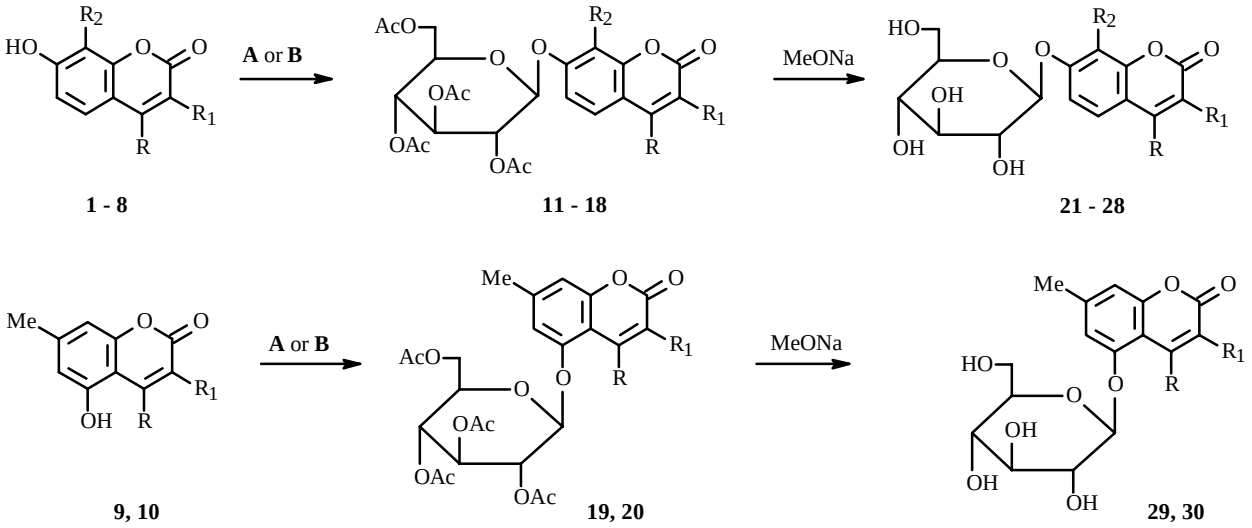
Hydroxycoumarins **1**-**6** and **9** and **10**, which were necessary for further transformations, were prepared by Pechmann condensation of polyphenols (resorcinol, 2-methylresorcinol, orcine) and ethyl-2-oxocyclopentanecarboxylate, ethyl-2-oxocyclohexanecarboxylate, or methyl-2-oxo-1-cycloheptanecarboxylate in the presence of conc. H_2SO_4 [2, 3]. 3-Hydroxybenzo[*c*]chromen-6-one (**7**) and 3-hydroxy-4-methylbenzo[*c*]chromen-6-one (**8**) were synthesized by the Hurtley method via condensation in NaOH solution of 2-bromobenzoic acid with resorcinol or 2-methylresorcinol, respectively, using copper sulfate solution (10%) as a catalyst [4].

The glycosylation methods used in the chemistry of benzopyrans are primarily modifications of the Koenigs—Knorr method [5]. The first method is based on glycosylation of phenol hydroxyls with acetobromosugars in the presence of silver carbonate or oxide [6, 7]. The second method consists of glycosylation of sodium or potassium salts of phenols with acetobromosugars in aqueous acetone [8, 9] or aqueous DMF [10]. Methods for synthesizing glycosides of benzopyrans under phase-transfer catalytic conditions in liquid—liquid or liquid—solid systems using phase-transfer crown ethers or quaternary ammonium salts as catalysts have been developed [11-14].

3,4-Annelated coumarins were glucosylated by two methods. The first was based on condensation of a glucosyl donor, acetobromoglucose (Ac_4Glu*p*Br) with potassium salts of hydroxycoumarins in aqueous acetone with cooling (0°C) by a modified Michael method [15]. Solutions of these salts were prepared using equivalent amounts of KOH solution (10%) and twice (relative to the base volume) the amount of acetone. Under such conditions the target per-O-acetylglucopyranosides **11**-**20** that contain the carbohydrate in the 5- or 7-position of the coumarin were prepared in yields of 24-56%.

1) Taras Shevchenko Kiev National University, 01033, Ukraine, Kiev, ul. Vladimirskaya, 64; 2) Institute of Bioorganic and Petroleum Chemistry, National Academy of Sciences of Ukraine, 02094, Ulraine, Kiev, ul. Murmanskaya, 1, e-mail: gmm@i.com.ua. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 7-12, January-February, 2004. Original article submitted December 12, 2003.

 0009-3130/04/4001-0006



A: Ac_4Glu*p*Br, KOH, H_2O-CH_3COCH_3
B: Ac_4Glu*p*Br, KOH, TBAB, H_2O-CH_2Cl_2

1, 11, 21: $RR_1 = (CH_2)_3$, $R_2 = H$; **2, 12, 22:** $RR_1 = (CH_2)_3$, $R_2 = CH_3$; **3, 13, 23:** $RR_1 = (CH_2)_4$, $R_2 = H$;
4, 14, 24: $RR_1 = (CH_2)_4$, $R_2 = CH_3$; **5, 15, 25:** $RR_1 = (CH_2)_5$, $R_2 = H$; **6, 16, 26:** $RR_1 = (CH_2)_5$, $R_2 = CH_3$;
7, 17, 27: RR_1 = -CH=CH-CH=CH-, $R_2 = H$; **8, 18, 28:** RR_1 = -CH=CH-CH=CH-, $R_2 = CH_3$;
9, 19, 29: $RR_1 = (CH_2)_3$; **10, 20, 30:** $RR_1 = (CH_2)_4$

The low glucosylation yields are explained by the fact that a side reaction occurs during the reaction, i.e., elimination of HBr from the acetobromoglucose to form 2-acetoxyglucal [15]. In our opinion, the second important hindrance during the synthesis is the poor solubility of the phenol salts in the aqueous acetone mixture. This creates heterogeneous reaction conditions. The potassium salts of hydroxycoumarins **1**, **2**, **7**, and **8** are poorly soluble in aqueous acetone. Therefore, the yields of glucosides **11**, **12**, **17**, and **18** under these conditions are low (24-30%).

The second method of glycosylating coumarins **1**, **2**, **7**, and **8** was effective. It is based on phase-transfer catalysis in a two-phase liquid—liquid system. Dichloromethane was used as the organic solvent; KOH solution (10%), as the base. The reaction between equivalent amounts of hydroxycoumarin, base, and acetobromoglucose was performed at room temperature in the presence of an equivalent amount of tetrabutylammonium bromide (TBAB) as phase-transfer catalyst [12]. Using this method, tetraacetylglucopyranosides **11**, **12**, **17**, and **18** were prepared in the highest yields (46-51%). In our opinion, this is explained by performing the reaction under homogeneous conditions. It should be noted that the yields of the glucosides did not increase substantially compared with the modified Michael method if this method was used for glucosylation of hydroxycoumarins **3**, **4**, **9**, and **10**, the potassium salts of which are sufficiently soluble in aqueous acetone.

Signals for protons of the coumarin aglycons and carbohydrates were unambiguously identified in the PMR spectra of the synthesized tetra-O-acetylglucopyranosides **11**-**20**. The configuration of the anomeric center was determined using PMR data. The presence of a doublet for the anomeric proton H-1 at 5.09-5.27 ppm with SSCC 7.6 Hz is consistent with formation of a 1,2-*trans*-glycoside bond (β-configuration) [16]. The IR spectra of **11**-**20** contain two bands at 1748-1758 and 1700-1732 cm^{-1} that are typical of stretching vibrations of the C=O bond of acetyls and coumarin rings, respectively.

Deacetylation of O-acetylglucopyranosides **11**-**20** by a modified Zemplen method (sodium methoxide in methanol) produced β-D-glucopyranosides **21**-**30** in high yields (83-97%). The PMR spectra of the synthesized glucosides contain signals for carbohydrate and aglycon fragments and, in contrast with the starting peracetates, lack signals for acetyls. Retention of the β-configuration was confirmed by the presence in the PMR spectra of a doublet for the anomeric proton H-1′ at 4.87-5.03 ppm with SSCC 7.6 Hz. The signal for the primary alcohol proton OH-6 resonates as a triplet at 4.45-4.62 ppm with SSCC 5.6 Hz; the secondary alcohol protons OH-2, OH-3, and OH-4, as doublets with SSCC 3.2-5.6 Hz at 5.05-5.42 ppm. The IR spectra of glucosides **21**-**30** exhibit two bands at 3384-3468 and 1692-1722 cm^{-1} that are typical of stretching vibrations of alcohol hydroxyls and coumarin C=O bonds, respectively.

EXPERIMENTAL

The course of reactions and purity of products were monitored using TLC on Merck 60 F254 plates with elution by $CHCl_3$:CH_3OH (9:1). Melting points were determined on a Kofler block. IR and UV spectra were measured on a Nicolet Nexus 475 FTIR spectrometer and a Specord M40 spectrophotometer, respectively. PMR spectra were recorded on Varian VXR-300 and Mercury-400 spectrometers at 300 and 400 MHz working frequencies, respectively, relative to TMS (internal standard). Elemental analyses of all compounds agreed with those calculated.

The syntheses of **1-4** and **7-10** have been described [2, 3, 17]. 2,3,4,6-Tetraacetyl-α-D-glucopyranosylbromide was prepared as before [18].

3-Hydroxy-6,7,8,9,10,11-hexahydrocyclohepta[*c*]chromen-6-one (5). A cooled (0°C) solution of resorcinol (11.0 g, 100 mmol) and methyl-2-oxo-1-cycloheptanecarboxylate (15.6 mL, 100 mmol) in absolute CH_3OH (20 mL) was vigorously stirred, cooled, treated dropwise with conc. H_2SO_4 (10 mL), stirred until thickened, left overnight at room temperature, and transferred into icewater (200 mL). The resulting precipitate was filtered off and crystallized from propan-2-ol (60%). Yield 59%, $C_{14}H_{14}O_3$, mp 198-199°C (lit. 188.5-189.5°C [19], 189-190°C [20]).

IR spectrum (KBr, cm^{-1}): 3219, 2929, 1679, 1614, 1568, 1514, 1385, 1324, 1311, 1236, 1150, 1097, 1075, 867, 779. UV spectrum (CH_3CN, λ_{max}, nm, log ε): 219 (4.20), 324 (4.20).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.52 (2H, m, CH_2-9), 1.61 (2H, m, CH_2-10), 1.86 (2H, m, CH_2-8), 2.74 (2H, m, CH_2-11), 2.90 (2H, m, CH_2-7), 6.65 (1H, d, J = 2.4, H-4), 6.73 (1H, dd, J = 2.4, J = 8.7, H-2), 7.60 (1H, d, J = 8.7, H-1), 10.23 (1H, s, OH-3).

3-Hydroxy-4-methyl-6,7,8,9,10,11-hexahydrocyclohepta[*c*]chromen-6-one (6) was prepared analogously to **5** from 2-methylresorcinol (12.4 g, 100 mmol) and methyl-2-oxo-1-cycloheptanecarboxylate (15.6 mL, 100 mmol). Yield 64%, $C_{15}H_{16}O_3$, mp 224-225°C.

IR spectrum (KBr, cm^{-1}): 3221, 2912, 1675, 1604, 1569, 1508, 1457, 1376, 1321, 1271, 1248, 1102, 1086, 808, 778. UV spectrum (EtOH, λ_{max}, nm, log ε): 206 (4.81), 223 (4.41), 331 (4.32).

PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.51 (2H, m, CH_2-9), 1.59 (2H, m, CH_2-10), 1.86 (2H, m, CH_2-8), 2.17 (3H, s, CH_3-4), 2.74 (2H, m, CH_2-11), 2.90 (2H, m, CH_2-7), 6.81 (1H, d, J = 8.7, H-2), 7.45 (1H, d, J = 8.7, H-1), 10.15 (1H, s, OH-3).

General Method for Glucosylation by Method A. A solution of hydroxycoumarin (**1-10**, 10 mmol) in acetone (10 mL) and KOH solution (5.6 mL, 10%, 10 mmol) was vigorously stirred, cooled (0°C) for 30 min, and treated in portions over 1 h with acetobromoglucose (4.11 g, 10 mmol). The resulting solution or suspension was stirred for 4 h with cooling (0°C), left overnight at room temperature, treated with $CHCl_3$ (50 mL), transferred to a separatory funnel, and treated successively with KOH solution (1 N, 2 × 50 mL) and water (50 mL). Acidification of the combined alkaline extracts regenerated unreacted hydroxycoumarin. The organic phase was dried over anhydrous $MgSO_4$. The solvent was removed in vacuum in a rotary evaporator. The oily product was crystallized from propan-2-ol.

General Method for Glucosylation by Method B. A mixture of hydroxycoumarin (**1-10**, 10 mmol), KOH solution (5.6 mL, 10%, 10 mmol), CH_2Cl_2 (10 mL), acetobromoglucose (4.11 g, 10 mmol), and TBAB (3.22 g) was held at room temperature, stirred vigorously for 1 h, and treated with $CHCl_3$ (50 mL), transferred to separatory funnel, and treated successively with NaCl saturated solution (50 mL), KOH solution (1 N, 2 × 50 mL), and water (50 mL). Acidification of the alkaline solution regenerated unreacted hydroxycoumarin. The organic phase was dried over anhydrous $MgSO_4$. Solvent was removed in vacuum in a rotary evaporator. The oily product was crystallized from propan-2-ol.

7-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-2,3-dihydrocyclopenta[*c*]chromen-4-one (11). Yield 26% (by method A), 51% (by method B), $C_{26}H_{28}O_{12}$, mp 172-173.5°C.

IR spectrum (KBr, cm^{-1}): 2928, 1758, 1700, 1630, 1618, 1438, 1372, 1244, 1172, 1088. UV spectrum (EtOH, λ_{max}, nm, log ε): 204 (4.65), 218 (4.22), 319 (4.13).

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.04, 2.06, 2.07, 2.12 (12H, four s, four CH_3COO), 2.21 (2H, m, CH_2-2), 2.91 (2H, m, CH_2-1), 3.06 (2H, m, CH_2-3), 3.91 (1H, ddd, J = 10.0, J = 5.6, J = 2.4, H-5′), 4.19 (1H, dd, J = 12.0, J = 2.4, H-6′α), 4.31 (1H, dd, J = 12.0, J = 5.6, H-6′β), 5.13 (1H, d, J = 7.6, H-1′), 5.17 (1H, dd, J = 10.0, J = 9.6, H-4′), 5.28-5.35 (2H, m, H-2′, H-3′), 6.92 (1H, dd, J = 2.4, J = 8.8, H-8), 7.00 (1H, d, J = 2.4, H-6), 7.37 (1H, d, J = 8.8, H-9).

7-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-6-methyl-2,3-dihydrocyclopenta[*c*]chromen-4-one (12). Yield 24% (by method A), 46% (by method B), $C_{27}H_{30}O_{12}$, mp 173.5-175°C.

IR spectrum (KBr, cm^{-1}): 2960, 1756, 1705, 1612, 1428, 1374, 1242, 1132, 1076, 1046. UV spectrum (EtOH, λ_{max}, nm, log ε): 206 (4.67), 220 (4.22), 318 (4.12).

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.05, 2.06, 2.07, 2.12 (12H, four s, four CH_3COO), 2.21 (2H, m, CH_2-2), 2.26 (3H, s, CH_3-6), 2.92 (2H, m, CH_2-1), 3.05 (2H, m, CH_2-3), 3.89 (1H, ddd, J = 10.0, J = 5.6, J = 2.4, H-5′), 4.20 (1H, dd, J = 12.0, J = 2.4, H-6′α), 4.30 (1H, dd, J = 12.0, J = 5.6, H-6′β), 5.11 (1H, d, J = 7.6, H-1′), 5.20 (1H, dd, J = 10.0, J = 9.6, H-4′), 5.27-5.36 (2H, m, H-2′, H-3′), 6.98 (1H, d, J = 8.8, H-8), 7.24 (1H, d, J = 8.8, H-9).

3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one (13). Yield 48% (by method A), 51% (by method B), $C_{27}H_{30}O_{12}$, mp 135.5-137°C.

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.76-1.90 (4H, m, CH_2-8, CH_2-9), 2.05, 2.06, 2.07, 2.12 (12H, four s, four CH_3COO), 2.53-2.59 (2H, m, CH_2-7), 2.72-2.79 (2H, m, CH_2-10), 3.92 (1H, ddd, J = 10.0, J = 5.6, J = 2.4, H-5′), 4.19 (1H, dd, J = 12.0, J = 2.4, H-6′α), 4.30 (1H, dd, J = 12.0, J = 5.6, H-6′β), 5.14 (1H, d, J = 7.6, H-1′), 5.17 (1H, dd, J = 10.0, J = 9.6, H-4′), 5.28-5.35 (2H, m, H-2′, H-3′), 6.91 (1H, dd, J = 8.8, J = 2.4, H-2), 6.94 (1H, d, J = 2.4, H-4), 7.48 (1H, d, J = 8.8, H-1).

3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-4-methyl-7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one (14). Yield 52% (by method A), 49% (by method B), $C_{28}H_{32}O_{12}$, mp 210-211.5°C.

IR spectrum (KBr, cm^{-1}): 2940, 1758, 1710, 1608, 1378, 1242, 1072, 1060, 1048. UV spectrum (EtOH, λ_{max}, nm, log ε): 207 (4.65), 222 (4.13), 318 (4.15).

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.75-1.91 (4H, m, CH_2-8, CH_2-9), 2.05, 2.06, 2.08, 2.09 (12H, four s, four CH_3COO), 2.26 (3H, s, CH_3-4), 2.54-2.60 (2H, m, CH_2-7), 2.72-2.78 (2H, m, CH_2-10), 3.89 (1H, ddd, J = 10.0, J = 5.6, J = 2.4, H-5′), 4.20 (1H, dd, J = 12.0, J = 2.4, H-6′α), 4.31 (1H, dd, J = 12.0, J = 5.6, H-6′β), 5.09 (1H, d, J = 7.6, H-1′), 5.20 (1H, dd, J = 10.0, J = 9.2, H-4′), 5.32 (1H, dd, J = 9.6, J = 8.8, H-3′), 5.37 (1H, dd, J = 9.6, J = 7.2, H-2′), 6.96 (1H, d, J = 8.8, H-2), 7.36 (1H, d, J = 8.8, H-1).

3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-6,7,8,9,10,11-hexahydrocyclohepta[*c*]chromen-6-one (15). Yield 56% (by method A), $C_{28}H_{32}O_{12}$, mp 188-189°C.

IR spectrum (KBr, cm^{-1}): 2932, 1756, 1710, 1608, 1380, 1224, 1076, 1060, 1044. UV spectrum (EtOH, λ_{max}, nm, log ε): 205 (4.55), 218 (4.13), 321 (4.12).

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.56-1.72 (4H, m, CH_2-8, CH_2-10), 1.83-1.97 (2H, m, CH_2-9), 2.05, 2.07, 2.13 (12H, three s, four CH_3COO), 2.86-2.96 (4H, m, CH_2-7, CH_2-11), 3.90 (1H, ddd, J = 10.0, J = 5.6, J = 2.4, H-5′), 4.18 (1H, dd, J = 12.4, J = 2.4, H-6′α), 4.31 (1H, dd, J = 12.4, J = 6.0, H-6′β), 5.15 (1H, d, J = 7.6, H-1′), 5.17 (1H, dd, J = 10.0, J = 9.6, H-4′), 5.27-5.36 (2H, m, H-2′, H-3′), 6.91 (1H, dd, J = 8.8, J = 2.4, H-2), 6.95 (1H, d, J = 2.4, H-4), 7.59 (1H, d, J = 8.8, H-1).

3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-4-methyl-6,7,8,9,10,11-hexahydrocyclohepta[*c*]chromen-6-one (16). Yield 51% (by method A), $C_{29}H_{34}O_{12}$, mp 192.5-194°C.

IR spectrum (KBr, cm^{-1}): 2924, 1758, 1708, 1602, 1444, 1370, 1224, 1134, 1046. UV spectrum (EtOH, λ_{max}, nm, log ε): 206 (4.76), 220 (4.31), 326 (4.19).

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.56-1.71 (4H, m, CH_2-8, CH_2-10), 1.86-1.95 (2H, m, CH_2-9), 2.05, 2.06, 2.08, 2.10 (12H, four s, four CH_3COO), 2.27 (3H, s, CH_3-4), 2.84-2.96 (4H, m, CH_2-7, CH_2-11), 3.89 (1H, ddd, J = 10.0, J = 5.2, J = 2.4, H-5′), 4.20 (1H, dd, J = 12.4, J = 2.4, H-6′α), 4.31 (1H, dd, J = 12.4, J = 6.0, H-6′β), 5.10 (1H, d, J = 7.6, H-1′), 5.20 (1H, dd, J = 10.0, J = 9.2, H-4′), 5.32 (1H, dd, J = 9.6, J = 8.8, H-3′), 5.37 (1H, dd, J = 9.6, J = 7.6, H-2′), 6.97 (1H, d, J = 8.8, H-2), 7.47 (1H, d, J = 8.8, H-1).

3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)benzo[*c*]chromen-6-one (17). Yield 30% (by method A), 46% (by method B), $C_{27}H_{26}O_{12}$, mp 173-174.5°C.

IR spectrum (KBr, cm^{-1}): 1748, 1722, 1620, 1460, 1380, 1248, 1240, 1236, 1178, 1100, 1066. UV spectrum (EtOH, λ_{max}, nm, log ε): 208 (4.51), 215 (4.52), 224 (4.50), 232 (4.49), 265 (4.18), 275 (4.26), 291 (4.01), 301 (4.07), 322 (3.94).

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.05, 2.07, 2.09, 2.14 (12H, four s, four CH_3COO), 3.92 (1H, ddd, J = 9.6, J = 6.0, J = 2.0, H-5′), 4.21 (1H, dd, J = 12.0, J = 2.4, H-6′α), 4.32 (1H, dd, J = 12.0, J = 5.6, H-6′β), 5.17 (1H, d, J = 7.6, H-1′), 5.19 (1H, dd, J = 10.0, J = 9.6, H-4′), 5.30-5.37 (2H, m, H-2′, H-3′), 6.99 (1H, dd, J = 8.8, J = 2.4, H-2), 7.02 (1H, d, J = 2.4, H-4), 7.56 (1H, t, J = 8.0, H-8), 7.82 (1H, t, J = 8.0, H-9), 7.98 (1H, d, J = 8.8, H-1), 8.04 (1H, d, J = 8.0, H-10), 8.38 (1H, d, J = 8.0, H-7).

3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-4-methylbenzo[*c*]chromen-6-one (18). Yield 25% (by method A), 49% (by method B), $C_{28}H_{28}O_{12}$, mp 220.5-222°C.

IR spectrum (KBr, cm^{-1}): 1758, 1740, 1732, 1612, 1468, 1382, 1276, 1242, 1230, 1216, 1116, 1072. UV spectrum (EtOH, λ_{max}, nm, log ε): 210 (4.49), 222 (4.59), 248 (4.21), 272 (4.23), 278 (4.26), 301 (3.95), 324 (3.93).

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.06, 2.07, 2.10, 2.11 (12H, four s, four CH_3COO), 2.31 (3H, s, CH_3-4), 3.92 (1H, ddd, J = 10.0, J = 5.6, J = 2.4, H-5′), 4.22 (1H, dd, J = 12.0, J = 2.4, H-6′α), 4.32 (1H, dd, J = 12.0, J = 5.6, H-6′β), 5.13 (1H, d, J = 7.6, H-1′), 5.22 (1H, dd, J = 10.0, J = 9.6, H-4′), 5.34 (1H, dd, J = 9.6, J = 8.8, H-3′), 5.39 (1H, dd, J = 9.6, J = 7.6, H-2′), 7.04 (1H, d, J = 8.8, H-2), 7.55 (1H, t, J = 8.0, H-8), 7.81 (1H, t, J = 8.0, H-9), 7.86 (1H, d, J = 8.8, H-1), 8.04 (1H, d, J = 8.0, H-10), 8.38 (1H, d, J = 8.0, H-7).

9-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-7-methyl-2,3-dihydrocyclopenta[*c*]chromen-4-one (19). Yield 46% (by method A), 49% (by method B), $C_{27}H_{30}O_{12}$, mp 186.5-188°C.

IR spectrum (KBr, cm^{-1}): 1760, 1710, 1620, 1370, 1238, 1076. UV spectrum (EtOH, λ_{max}, nm, log ε): 207 (4.63), 242 (3.84), 304 (4.21).

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.05, 2.06, 2.07 (12H, three s, four CH_3COO), 2.10 (2H, m, CH_2-2), 2.42 (3H, s, CH_3-7), 2.82 (2H, m, CH_2-3), 3.00-3.11 (1H, m, H-1α), 3.28-3.38 (1H, m, H-1β), 3.93 (1H, ddd, J = 9.6, J = 6.0, J = 2.0, H-5′), 4.17 (1H, dd, J = 12.0, J = 2.4, H-6′α), 4.26 (1H, dd, J = 12.0, J = 5.6, H-6′β), 5.17-5.35 (4H, m, H-1′, H-2′, H-3′, H-4′), 6.65 (1H, s, H-8), 6.91 (1H, s, H-6).

1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyloxy)-3-methyl-7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one (20). Yield 48% (by method A), 44% (by method B), $C_{28}H_{32}O_{12}$, mp 183.5-184.5°C.

PMR spectrum (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.66-1.77 (4H, m, CH_2-8, CH_2-9), 2.04, 2.05, 2.06, 2.07 (12H, four s, four CH_3COO), 2.39 (3H, s, CH_3-3), 2.50-2.59 (2H, m, CH_2-7), 2.72-2.82 (1H, m, H-10α), 3.00-3.12 (1H, m, H-10β), 3.92 (1H, ddd, J = 10.0, J = 5.6, J = 2.4, H-5′), 4.18 (1H, dd, J = 12.0, J = 2.4, H-6′α), 4.25 (1H, dd, J = 12.0, J = 6.0, H-6′β), 5.18 (1H, dd, J = 10.0, J = 8.8, H-4′), 5.27 (1H, d, J = 7.6, H-1′), 5.32 (1H, dd, J = 9.6, J = 8.8, H-3′), 5.36 (1H, dd, J = 9.6, J = 7.6, H-2′), 6.66 (1H, s, H-2), 6.85 (1H, s, H-4).

General Method for Deacetylation of 2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosides 11-20. A solution of peracetate (**11**-**20**, 5 mmol) in absolute CH_3OH (20 mL) was treated with sodium methoxide (50 mg) and boiled for 10-30 min (completion of the reaction determined by TLC). The precipitate that formed on cooling (0°C) was filtered off and washed with cold CH_3OH. The mother liquor was concentrated in vacuum in a rotary evaporator. An additional portion of glucopyranoside (**21**-**30**) formed upon cooling.

7-(β-D-Glucopyranosyloxy)-2,3-dihydrocyclopenta[*c*]chromen-4-one (21). Yield 85%, $C_{18}H_{20}O_8$, mp 252.5-253.5°C.

IR spectrum (KBr, cm^{-1}): 3440, 2932, 1704, 1626, 1392, 1298, 1256, 1168, 1088, 1074, 1036. UV spectrum (EtOH, λ_{max}, nm, log ε): 205 (4.77), 218 (4.33), 321 (4.28).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.10 (2H, m, CH_2-2), 2.74 (2H, m, CH_2-1), 3.06 (2H, m, CH_2-3), 3.16 (1H, m, H-4′), 3.28 (2H, m, H-2′, H-3′), 3.44 (2H, m, H-5′, H-6′α), 3.70 (1H, dd, J = 11.6, J = 4.8, H-6′β), 4.60 (1H, t, J = 5.6, OH-6), 5.01 (1H, d, J = 7.6, H-1′), 5.06 (1H, d, J = 4.4, OH), 5.13 (1H, d, J = 4.0, OH), 5.40 (1H, d, J = 4.4, OH), 7.02 (1H, d, J = 2.4, H-6), 7.08 (1H, dd, J = 2.4, J = 8.8, H-8), 7.54 (1H, d, J = 8.8, H-9).

7-(β-D-Glucopyranosyloxy)-6-methyl-2,3-dihydrocyclopenta[*c*]chromen-4-one (22). Yield 97%, $C_{19}H_{22}O_8$, mp 172-173.5°C.

IR spectrum (KBr, cm^{-1}): 3436, 2932, 1702, 1608, 1378, 1286, 1248, 1172, 1074. UV spectrum (EtOH, λ_{max}, nm, log ε): 206 (4.56), 219 (4.10), 321 (4.13).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.14 (2H, m, CH_2-2), 2.29 (3H, s, CH_3-4), 2.79 (2H, m, CH_2-1), 3.05 (2H, m, CH_2-3), 3.15-3.30 (4H, m, H-2′, H-3′, H-4′, H-5′), 3.48 (1H, m, H-6′α), 3.69 (1H, dd, J = 11.6, J = 4.8, H-6′β), 4.45 (1H, t, J = 5.6, OH-6), 4.87 (1H, d, J = 7.6, H-1′), 4.95 (1H, d, J = 4.4, OH), 5.05 (1H, d, J = 4.0, OH), 5.29 (1H, d, J = 4.4, OH), 7.11 (1H, d, J = 8.8, H-8), 7.34 (1H, d, J = 8.8, H-9).

3-(β-D-Glucopyranosyloxy)-7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one (23). Yield 88%, $C_{19}H_{22}O_8$, mp 214-215°C.

IR spectrum (KBr, cm^{-1}): 3412, 2940, 1692, 1610, 1392, 1284, 1262, 1176, 1080, 1052, 1042. UV spectrum (EtOH, λ_{max}, nm, log ε): 204 (4.66), 216 (4.23), 316 (4.21).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.67-1.82 (4H, m, CH_2-8, CH_2-9), 2.40 (2H, m, CH_2-7), 2.78 (2H, m, CH_2-10), 3.17 (1H, m, H-4′), 3.27 (2H, m, H-2′, H-3′), 3.39-3.48 (2H, m, H-5′, H-6′α), 3.70 (1H, dd, J = 11.6, J = 4.8, H-6′β), 4.59 (1H, t, J = 5.6, OH-6), 5.00 (1H, d, J = 7.6, H-1′), 5.06 (1H, d, J = 4.4, OH), 5.13 (1H, d, J = 4.0, OH), 5.38 (1H, d, J = 4.0, OH), 7.00 (1H, dd, J = 8.8, J = 2.0, H-2), 7.02 (1H, d, J = 2.0, H-4), 7.64 (1H, d, J = 8.8, H-1).

3-(β-D-Glucopyranosyloxy)-4-methyl-7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one (24). Yield 92%, $C_{20}H_{24}O_8$, mp 233-234.5°C.

IR spectrum (KBr, cm^{-1}): 3388, 2932, 1704, 1608, 1382, 1282, 1266, 1132, 1104, 1084, 1040. UV spectrum (EtOH, λ_{max}, nm, log ε): 205 (4.72), 221 (4.24), 318 (4.20).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.66-1.83 (4H, m, CH_2-8, CH_2-9), 2.24 (3H, s, CH_3-4), 2.41 (2H, m, CH_2-7), 2.77 (2H, m, CH_2-10), 3.20 (1H, m, H-4′), 3.29 (2H, m, H-2′, H-3′), 3.46 (2H, m, H-5′, H-6′α), 3.69 (1H, dd, J = 11.6, J = 4.8, H-6′β), 4.57 (1H, t, J = 5.6, OH-6), 4.93 (1H, d, J = 7.6, H-1′), 5.05 (1H, d, J = 4.4, OH), 5.12 (1H, d, J = 4.0, OH), 5.41 (1H, m, OH), 7.12 (1H, d, J = 8.8, H-2), 7.51 (1H, d, J = 8.8, H-1).

3-(β-D-Glucopyranosyloxy)-6,7,8,9,10,11-hexahydrocyclohepta[*c*]chromen-6-one (25). Yield 83%, $C_{20}H_{24}O_8$, mp 219-220.5°C.

IR spectrum (KBr, cm^{-1}): 3468, 2928, 1686, 1618, 1608, 1388, 1286, 1262, 1238, 1180, 1100, 1080, 1012. UV spectrum (EtOH, λ_{max}, nm, log ε): 205 (4.75), 219 (4.30), 324 (4.24).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.42-1.64 (4H, m, CH_2-8, CH_2-10), 1.78-1.89 (2H, m, CH_2-9), 2.75-2.81 (2H, m, CH_2-7), 2.94-3.00 (2H, m, CH_2-11), 3.16-3.48 (5H, m, H-2′, H-3′, H-4′, H-5′, H-6′α), 3.70 (1H, dd, J = 11.2, J = 5.2, H-6′β), 4.59 (1H, t, J = 5.6, OH-6), 5.01 (1H, d, J = 7.6, H-1′), 5.06 (1H, d, J = 5.6, OH), 5.13 (1H, d, J = 4.4, OH), 5.39 (1H, d, J = 4.4, OH), 7.00 (1H, dd, J = 8.8, J = 2.4, H-2), 7.03 (1H, d, J = 2.4, H-4), 7.82 (1H, d, J = 8.8, H-1).

3-(β-D-Glucopyranosyloxy)-4-methyl-6,7,8,9,10,11-hexahydrocyclohepta[*c*]chromen-6-one (26). Yield 89%, $C_{21}H_{26}O_8$, mp 136.5-138°C.

IR spectrum (KBr, cm^{-1}): 3348, 2924, 1700, 1602, 1370, 1268, 1074. UV spectrum (EtOH, λ_{max}, nm, log ε): 207 (4.69), 221 (4.19), 328 (4.16).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.39-1.68 (4H, m, CH_2-8, CH_2-10), 1.77-1.90 (2H, m, CH_2-9), 2.24 (3H, s, CH_3-4), 2.73-2.84 (2H, m, CH_2-7), 2.91-3.02 (2H, m, CH_2-11), 3.15-3.26 (2H, m, H-2′, H-3′, H-4′), 3.41 (1H, m, H-5′), 3.46 (1H, m, H-6′α), 3.69 (1H, dd, J = 11.2, J = 5.6, H-6′β), 4.58 (1H, t, J = 5.6, OH-6), 4.95 (1H, d, J = 7.6, H-1′), 5.06 (1H, d, J = 4.4, OH), 5.13 (1H, d, J = 4.0, OH), 5.41 (1H, d, J = 4.4, OH), 7.12 (1H, d, J = 8.8, H-2), 7.70 (1H, d, J = 8.8, H-1).

3-(β-D-Glucopyranosyloxy)benzo[*c*]chromen-6-one (27). Yield 92%, $C_{19}H_{18}O_8$, mp 258-259.5°C.

IR spectrum (KBr, cm^{-1}): 3388, 1722, 1620, 1458, 1396, 1280, 1184, 1090, 1040. UV spectrum (EtOH, λ_{max}, nm, log ε): 210 (4.59), 217 (4.59), 225 (4.56), 232 (4.56), 267 (4.25), 275 (4.32), 292 (4.11), 302 (4.17), 328 (4.03).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.16 (1H, m, H-4′), 3.29 (2H, m, H-2′, H-3′), 3.39-3.51 (2H, m, H-5′, H-6′α), 3.71 (1H, dd, J = 11.6, J = 4.8, H-6′β), 4.62 (1H, t, J = 5.6, OH-6), 5.03 (1H, d, J = 7.6, H-1′), 5.07 (1H, d, J = 5.2, OH), 5.14 (1H, d, J = 4.4, OH), 5.40 (1H, d, J = 4.4, OH), 7.08 (2H, m, H-2, H-4), 7.62 (1H, t, J = 8.0, H-8), 7.93 (1H, t, J = 8.0, H-9), 8.22 (1H, d, J = 8.8, H-1), 8.29 (1H, d, J = 8.0, H-10), 8.36 (1H, d, J = 8.0, H-7).

3-(β-D-Glucopyranosyloxy)-4-methylbenzo[*c*]chromen-6-one (28). Yield 87%, $C_{20}H_{20}O_8$, mp 303-304.5°C.

IR spectrum (KBr, cm^{-1}): 3384, 1716, 1606, 1468, 1404, 1280, 1196, 1168, 1076. UV spectrum (EtOH, λ_{max}, nm, log ε): 210 (4.41), 222 (4.49), 249 (4.09), 280 (4.15), 302 (3.85), 329 (3.78).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.30 (3H, s, CH_3-4), 3.20 (1H, m, H-4′), 3.29 (2H, m, H-2′, H-3′), 3.38 (1H, m, H-5′), 3.48 (1H, m, H-6′α), 3.71 (1H, dd, J = 11.6, J = 4.8, H-6′β), 4.61 (1H, t, J = 5.6, OH-6), 4.98 (1H, d, J = 7.6, H-1′), 5.06 (1H, d, J = 4.8, OH), 5.13 (1H, d, J = 4.0, OH), 5.42 (1H, d, J = 4.0, OH), 7.20 (1H, d, J = 8.8, H-2), 7.61 (1H, t, J = 8.0, H-8), 7.91 (1H, t, J = 8.0, H-9), 8.17 (1H, d, J = 8.8, H-1), 8.23 (1H, d, J = 8.0, H-10), 8.37 (1H, d, J = 8.0, H-7).

9-(β-D-Glucopyranosyloxy)-7-methyl-2,3-dihydrocyclopenta[*c*]chromen-4-one (29). Yield 83%, $C_{19}H_{22}O_8$, mp 200-201.5°C.

IR spectrum (KBr, cm^{-1}): 3408, 2920, 1706, 1680, 1620, 1556, 1498, 1460, 1384, 1260, 1148, 1080. UV spectrum (EtOH, λ_{max}, nm, log ε): 207 (4.50), 243 (3.72), 308 (4.10).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.02 (2H, m, CH_2-2), 2.36 (3H, s, CH_3-7), 2.67 (2H, m, CH_2-3), 3.15-3.59 (7H, m, CH_2-1, H-2′, H-3′, H-4′, H-5′, H-6′α), 3.69 (1H, dd, J = 10.8, J = 5.2, H-6′β), 4.60 (1H, t, J = 5.6, OH-6), 5.00 (1H, d, J = 7.6, H-1′), 5.06 (1H, d, J = 4.8, OH), 5.14 (1H, d, J = 4.4, OH), 5.34 (1H, d, J = 5.6, OH), 6.88 (1H, s, H-8), 6.89 (1H, s, H-6).

1-(*β*-D-Glucopyranosyloxy)-3-methyl-7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one (30). Yield 89%, $C_{20}H_{24}O_8$, mp 210-211.5°C.

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.59-1.74 (4H, m, CH_2-8, CH_2-9), 2.34 (3H, s, CH_3-3), 2.41 (2H, m, CH_2-7), 2.96-3.01 (1H, m, H-10*α*), 3.14-3.52 (6H, m, H-10*β*, H-2′, H-3′, H-4′, H-5′, H-6′*α*), 3.70 (1H, dd, J = 11.2, J = 5.2, H-6′*β*), 4.60 (1H, t, J = 5.6, OH-6), 5.00 (1H, d, J = 7.6, H-1′), 5.06 (1H, d, J = 4.4, OH), 5.14 (1H, d, J = 3.2, OH), 5.36 (1H, d, J = 5.2, OH), 6.82 (1H, s, H-2), 6.90 (1H, s, H-4).

ACKNOWLEDGMENT

We thank OAO "Eximed" (Kiev, Ukraine) for help in performing the work.

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