Convenient Synthesis of 1,4-Dihydroxy-2-(ω-Hydroxyalkoxy)Anthracene-9,10-Diones and their Conjugation with D-Glucal

Sebastian Budniok and Krzysztof Z. Walczak*

Department of Organic Chemistry, Bioorganic Chemistry and Biotechnology, Silesian University of Technology, Krzywoustego 4, 44-100 Gliwice, Poland

Received April 25, 2012: Revised June 14, 2012: Accepted June 28, 2012

Abstract: Purpurin, 1,2,4-trihydroxyanthraquinone, was regioselectively alkylated under basic conditions using bromoalcohol of varying chain length. As a base, potassium carbonate, tetrabutylammonium hydroxide or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was used. The reaction of alkylation proceeded exclusively on the 2-hydroxyl group of the purpurin molecule. Addition of the obtained 2-(ω-hydroxyalkoxy)purpurins to protected D-glucal catalysed by triphenylphosphine hydrobromide gave an access to new glycoconjugates with high enantioselectivity. In parallel experiments, the same substrates reacted in the presence of boron trifluoride etherate yielding the appropriate unsaturated adducts as a result of Ferrier rearrangement.

Keywords: Addition reaction, alkylation, bromoalcohols, D-glucal, glycoconjugates, purpurin.

INTRODUCTION

Purpurin belongs to anthraquinones present in the madder roots (*Rubia tinctorum*, *R. akane*, *R. cordifolia*) and possesses numerous valuable properties. It has been used mainly as a red cotton dye [1, 2]. Due to a lower energy level of the singlet excited state (π, π*), purpurin acts as a fluorescent molecule, as opposed to anthraquinone [3-6]. Purpurin forms complexes with metal ions like aluminium, iron or chromium, used as the mordant agents in textile dyeing [5, 7, 8]. Moreover, many anthraquinone derivatives are DNA-complexing or intercalating agents exhibitng activity against various types of tumours [9-12]. Due to these facts, also purpurin derivatives have been considered as potent bioactive compounds. Purpurin is a specific inhibitor of spermidine-induced autoactivation of pro-PHBP (Plasma hyaluronan-binding protein, factor VII activating protease), responsible for the activation of blood coagulating factor VII [13]. According to the reported data, purpurin is a competitive inhibitor of cytochrome P450 inhibiting the mutagenicity of a number of heterocyclic amines in the Ames mutagenicity test thus, decreasing the rate of their degradation [14-17]. The inhibitory effect of purpurin on nitrogen oxide production and suppression effects on induced nitrogen synthase expression were recently reported [18]. In addition, purpurin has been reported to exhibit various pharmacological and biological activities including anticancer [19], antiviral [20], antifungal [21] and enzyme regulatory function [22, 23].

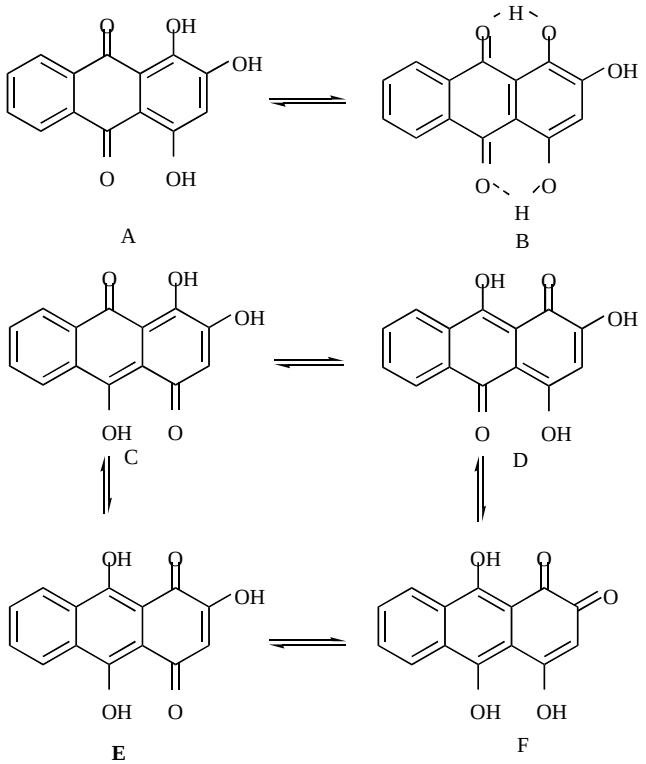
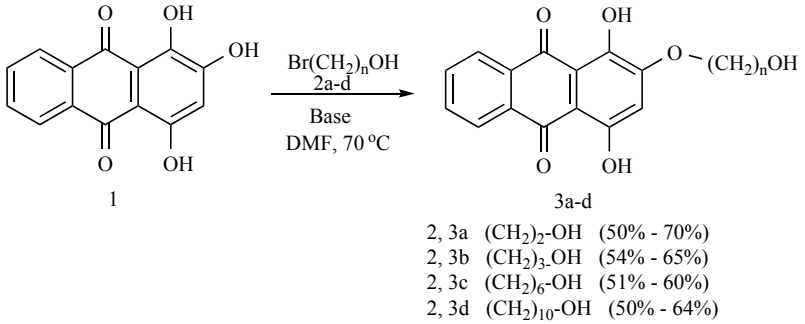


Fig. (1). The representation of hydrogen bonding and tautomers of 1,2,4-trihydroxyanthraquinone.

As a part of our research program, we were interested in purpurin O-alkylated derivatives as synthons for the synthesis of glycoconjugates. Regioselective O-alkylation of purpurin using ω-bromoalcohols of a different length in carbon chain as alkylating agents followed by the addition reaction to unsaturated sugars give rise to glycoconjugates. The latter

*Address correspondence to these authors at the Department of Organic Chemistry, Bioorganic Chemistry and Biotechnology, Silesian University of Technology, Krzywoustego 4, 44-100 Gliwice; Tel: +4832 2371083; Fax: +4832 2372094; E-mail: krzysztof.walczak@polsl.pl

1875-6255/12 $58.00+.00



Scheme 1. Alkylation of purpurin using ω-bromoalcohols.

Table 1. 2-(ω-Hydroxyalkoxy)purpurins 3a-d.

Entry	ω-Bromoalcohol	Base	Time [h]	Yield [%]	Mp. [°C]
1	2-bromoethanol	K_2CO_3	12	70	205-206
2	2-bromoethanol	$(Bu)_4NOH$	12	53	
3	2-bromoethanol	DBU	12	70*	
4	3-bromopropanol	K_2CO_3	7	60	168-169
5	3-bromopropanol	$(Bu)_4NOH$	7	54	
6	3-bromopropanol	DBU	7	65	
7	6-bromohexanol	K_2CO_3	6	57	164-165
8	6-bromohexanol	$(Bu)_4NOH$	6	51	
9	6-bromohexanol	DBU	6	60	
10	10-bromodecanol	K_2CO_3	6	61	118-120
11	10-bromodecanol	$(Bu)_4NOH$	6	50	
12	10-bromodecanol	DBU	6	64	

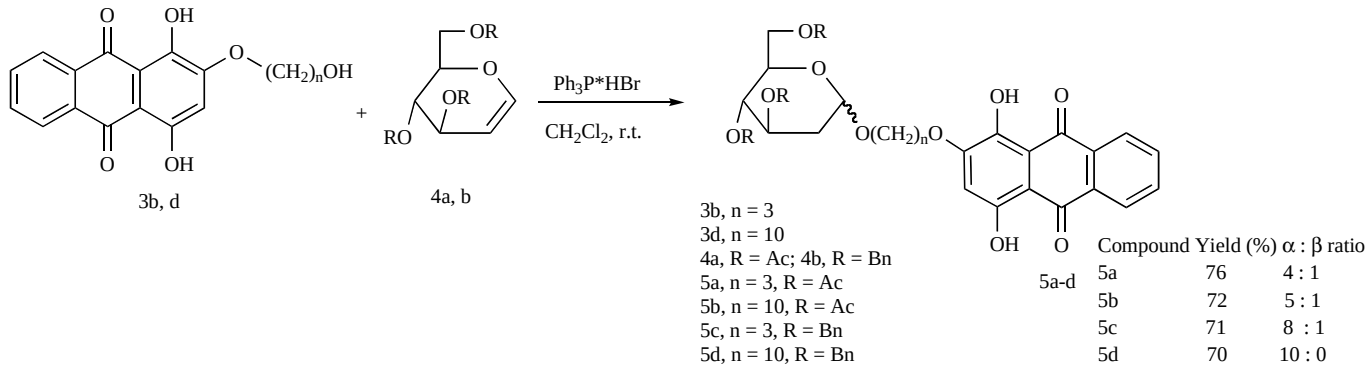
*69 % of yield was obtained when the reaction was carried out for 6 h

compounds revealed higher solubility in aqueous media as compared with the unsubstituted purpurin, being sparingly soluble in water. Solubility of anthraquinones in water being crucial for their bioavailability would be the matter of our further investigation.

Purpurin is formally the 1,2,4-trihydroxy-anthraquinone, where two hydroxyl groups, namely OH-1 and OH-4 are involved in the formation of hydrogen bonds with two carbonyl groups present in the molecule. It suggests that alkylation should mainly occur on 2-OH group (Fig. **1**, structures **A** and **B**). On the other hand, a possible tautomerism should be considered since protons can shift to the carbonyl groups and create new reactions centers (Fig. **1**, structures **C**-**F**). Similar effects can also be expected for anions formed under basic conditions where the stabilization by resonance operates [24]. Experimental results of purpurin acylation and alkylation confirmed the expectations about reactivity of the hydroxyl groups. Thus purpurin acylated with acetic anhydride in pyridine at low temperature gave 2-acetate in 50% yield [25]. Similar results were obtained with other acylating agent [6]. Purpurin treated with diazomethane at 0 °C in THF solution gave 2-*O*-methyl ether in 95% yield [25]. Alkylation using other alkyl halides usually gave a mixture of mono-, di- and triethers in moderate yields [2].

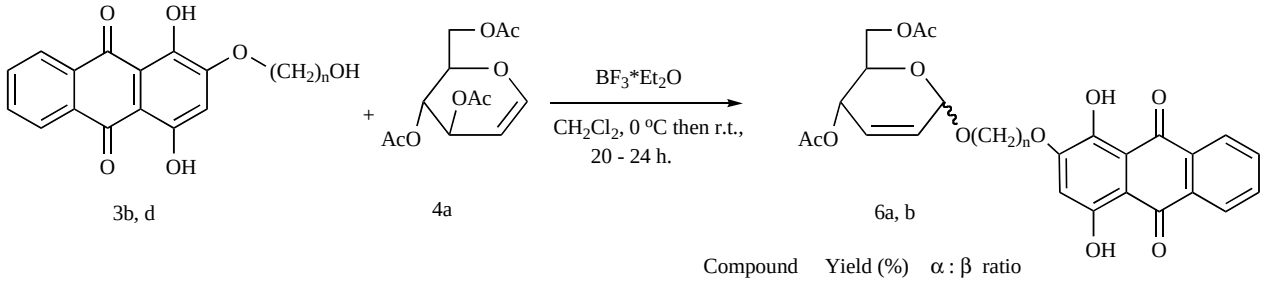
RESULTS AND DISCUSSION

Our primary synthetic targets, 2-(ω-hydroxyalkoxy) purpurins, bearing terminal hydroxyl group were obtained in reaction of purpurin with ω-bromoalcohols under basic conditions. Three different deprotonating agents, namely potassium carbonate, tetrabutylammonium hydroxide (TBAOH) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were used for generation of the purpurin anion. DBU and TBAOH were used in a molar ratio of base to purpurin as 0.95 to 1 equiv., whereas potassium carbonate as of 0.5. The alkylation reactions were carried out in DMF at 70 °C (Scheme **1**, Table **1**). In the primary trials (1, 2 and 3) the time of the reactions was 12 h. The next experiments were performed in shorter time of 7h to 6 h (entries 4-12), without significant decrease in the yield of the expected 2-(ω-hydroxyalkoxy) purpurin derivatives. In all the experiments performed, the best results were obtained when DBU was used as a depro-



Compound	Yield (%)	α : β ratio
5a	76	4 : 1
5b	72	5 : 1
5c	71	8 : 1
5d	70	10 : 0

Scheme 2. Addition of 2-(ω-hydroxyalkoxy)purpurins to protected D-glucal.



Compound	Yield (%)	α : β ratio
3b, 6a, n = 3;	53	9 : 1
3d, 6b, n = 10;	81	9 : 1

Scheme 3. Addition of 2-(ω-Hydroxyalkoxy)purpurins to D-glucal under conditions of Ferrier's rearrangement.

tonating agent. Even on reducing the time of reaction to 6 h, the yield of the appropriate 2-(ω-hydroxyalkoxy)purpurins **3a-d** isolated by column chromatography exceeded 60% and was better in comparison with reported data.

For the synthesis of glycoconjugates, we selected commercially available 3,4,6-tri-O-acetyl-D-glucal and its O-benzylated analogue. The D-glucal derivative 4a or 4b was treated at room temperature with a slight excess (0.1 equiv.) of the appropriate purpurin derivative (3b or 3d) in the presence of triphenylphosphine hydrobromide as the catalyst (Scheme **2**). Consumption of the starting sugar derivative was monitored by TLC (toluene : AcOEt, 1:1, v/v). Purification on silica gel packed column extracted the expected product (5a-d) as the anomeric mixture with the predominating α-anomer as calculated from the intensity of the H-1 proton (anomeric proton). The amounts of β-anomer varied between 20% in the case of 5a to the undetectable amount in NMR for 5d. In the case of 3,4,6-tri-O-benzyl-D-glucal, the amounts of α-anomer radically increased in comparison with acetylated derivatives. The ratio of α:β anomers varied from 4:1 to 8:1 when compared to propoxy derivatives (5a and 5c). The same proportion was observed for conjugates with dodecyloxy linker 5b and 5d – 5:1 to 10:0, respectively. The formation of α-anomer as a major product was observed early in addition reaction of simple alcohols to protected D-glucal [26, 27]. In order to compare the reaction, we decided to repeat the reactions of the 3b and 3d derivatives with D-glucal (4a) in the presence of boron trifluoride diethyletherate (Scheme **3**). This reaction is known as Ferrier reaction, proceeding *via* rearrangement [28, 29]. The appropriate products of Ferrier rearrangement, 4,6-di-O-acetyl-2,3-dideoxy-D-hexenopyr-anosides 6a and 6b were obtained in satisfactory yield. The NMR data indicated the formation of both anomers again with α-anomer as the major product (the roughly α:β ratio 9:1). At this stage of investigation, we are unable to predict the factors affecting stereochemistry of the addition reaction. Probably, introduction of the bulky protecting group on the available hydroxyl groups can turn stereochemistry of the addition towards exclusively α-anomer. Unfortunately, even numerous trials did not allow separating the anomeric mixture to the particular anomers.

CONCLUSION

In summary, we have developed an effective method for the regioselective alkylation of purpurin. Use of ω-bromoalcohols of a different length in carbon chain as alkylating agents in the presence of base provided exclusively 2-*O*-alkylated products in satisfactory yield. It should be mentioned that inspections of the post-reaction mixtures indicated only the presence of unreacted purpurin, while the products of substitution in other positions of purpurin ring were not detected by TLC. The obtained alkoxy derivatives of purpurin when reacted with protected D-glucal derivatives in the presence of Ph_3P*HBr or BF_3*Et_2O as the catalyst gave the α-anomers as a major or sole products. The formation of adducts proceeded with satisfactory yield.

EXPERIMENTAL

NMR spectra were recorded at 300 MHz for ^{1}H NMR and 75.5 MHz for ^{13}C NMR on a Varian Inova 300 MHz; (δ) values are in parts per million (ppm) relative to tetramethylsilane as an internal standard. Mass spectra were recorded at

ESI Mass Spectrometer ABSciex System 4000 QTRAP® at positive and negative modes of ionisation. Optical rotation measurements were performed at 25 °C on a JASCO p-2000 Series polarimeter at the D sodium line. Elemental analyses were obtained using a Perkin–Elmer 240C apparatus. The reagents were purchased from Lancaster. TLC $60F_{254}$ plates and silica gel 60 (0.040–0.063 mm) were purchased from Merck.

1,4-Dihydroxy-2-(ω-hydroxyalkoxy)anthracene-9,10-dione (**3a-d**)

To a solution of 1,3,4-trihydroxyanthraquinone (1; 256 mg, 1mmol) in DMF (5.0 mL) deprotonating agent (DBU;145 mg, 0.95 mmol; K_2CO_3; 66 mg, 0.5 mmol) was added and then the resulting mixture was stirred at 70 °C for 30 minutes. Next ω-bromoalcohol (**2a-d**) (1.5 mmol) was added and stirring at 70 °C was continued for the defined time (6 to 12 h). The progress of the reaction was monitored by TLC ($CHCl_3$/MeOH 95:5, v/v). The reaction mixture was evaporated to dryness and the residual oil was purified on a silica gel packed column using a mixture of $CHCl_3$/MeOH (95:5, v/v). The fractions containing product were collected, combined and then evaporated giving crystalline orange solids.

Procedure with a use of TBAOH as deprotonating agent

To a solution of tetrabutylammonium hydroxide (TBAOH) in methanol (259.5 mg, 1 mmol, 2.56 mL of 12.5 % solution) 1,3,4-trihydroxyanthraquinone (1; 256 mg, 1 mmol) was added and the mixture was stirred at room temperature for 20 minutes, followed by evaporation to dryness. The traces of methanol were removed by co-evaporation with toluene (20 mL). The dry tetrabutyloammonium salt of purpurin was dissolved in anhydrous DMF (5 mL) and ω-bromoalcohol **2a-d** (1.5 mmol) was added while stirring. The reaction mixture was stirred at 70 °C for fixed time (6 to 12 h). The progress of reaction was monitored by TLC ($CHCl_3$/MeOH 95:5, v/v). The work-up and isolation of product were performed as in the procedure described above.

1,4-Dihydroxy-2-(2-hydroxyethoxy)anthracene-9,10-dione (**3a**)

^{1}H NMR (DMSO-d_6), δ: 3.79 (dd, *J* = 4.5, 5.1 Hz, 2H, H-2'), 4.14 (t, *J* = 4.5 Hz, 2H, H-1'), 5.03 (t, *J* = 5.1 Hz, 1H, 2'-OH), 6.86 (s, 1 H, H-3), 7.85-7.93 (m, 2 H, H-5, H-6), 8.14-8.18 (m, 2H, H-7, H-8), 13.15 (s, 1H, 4-OH), 13.39 (s, 1H, 1-OH). ^{13}C NMR (DMSO-d_6), δ: 59.1 (C-2'), 71.4 (C-1'), 105.4 (C-1_a), 107.8 (C-3), 111.9 (C-4_a), 126.3 (C-6), 126.5 (C-7), 132.6 (C-5_a), 133.2 (C-8_a), 134.3 (C-5), 135.0 (C-8), 149.7 (C-2), 157.0 (C-4), 160.2 (C-1), 183.7 (C-10), 186.6 (C-9). Anal. Calcd for $C_{16}H_{12}O_6$: C, 64.00; H, 4,03. Found: C, 63.80; H, 4.35. MS m/z (%): 323.3 (100) $[M+Na]^+$, 299.4 (100) $[M]^-$

1,4-Dihydroxy-2-(3-hydroxypropoxy)anthracene-9,10-dione (**3b**)

^{1}H NMR (DMSO-d_6), δ: 1.94 (dd, *J* = 6.0, 6.3 Hz, 2H, H-2'), 3.59 (dd, *J* = 5.7, 6.0 Hz, 2H, H-3'), 4.23 (t, *J* = 6.3 Hz, 2H, H-1'), 4.64 (t, *J* = 5.7 Hz, 1H, 3'-OH), 6.96 (s, 1H, H-3), 7.92-7.99 (m, 2H, H-5, H-6), 8.23-8.28 (m, 2H, H-7, H-8), 13.20 (s, 1H, 4-OH), 13.48 (s, 1H, 1-OH). ^{13}C NMR (DMSO-d_6), δ: 31.5 (C-2'), 56.9 (C-3'), 66.5 (C-1'), 105.1 (C-4_a), 107.5 (C-3), 111.6 (C-1_a), 126.2 (C-5), 126.4 (C-8), 132.4 (C-6), 133.1 (C-7), 134.1 (C-5_a), 134.9 (C-8_a), 149.6 (C-1), 156.8 (C-2), 160.2 (C-4), 183.5 (C-10), 186.3 (C-9). Anal. Calcd for $C_{17}H_{14}O_6$: C, 64.97; H, 4.49. Found: C, 65.20; H, 4.70. MS m/z (%): 337.3 (100) $[M+Na]^+$, 313.5 (100) $[M]^-$

1,4-Dihydroxy-2-(6-hydroxyhexyloxy)anthracene-9,10-dione (**3c**)

^{1}H NMR ($CDCl_3$), δ : 1.45-1.68 (m, 7H, H-6', H-5', H-4', 6'-OH), 1.96 (dd, *J* = 6.6, 7.8 Hz, 2H, H-2'), 3.68 (brs, 2H, H-6'), 4.14 (t, *J* = 6.6 Hz, 2H, H-1'), 6.68 (s, 1H, H-3), 7.77-7.86 (m, 2H, H-5, H-6), 8.33-8.36 (m, 2H, H-7, H-8), 13.49 (s, 1H, 4-OH), 13.57 (s, 1H, 1-OH). ^{13}C NMR ($CDCl_3$), δ: 25.4 (C-4'), 25.7 (C-3'), 28.6 (C-5'), 32.5 (C-2'), 62.8 (C-6'), 69.6 (C-1'), 105.9 (C-1_a), 107.4 (C-3), 112.6 (C-4_a), 126.8 (C-6), 126.9 (C-7), 133.3 (C-5_a), 133.7 (C-8_a), 134.1 (C-5), 134.5 (C-8), 150.6 (C-2), 160.9 (C-4), 161.1 (C-1), 184.3 (C-10), 187.2 (C-9). Anal. Calcd for $C_{20}H_{20}O_6$: C, 67.41; H, 5.66. Found: C, 67.70; H, 5.91. MS m/z (%): 735.8 (100) $[2MNa]^+$, 379.5 (67) $[M+Na]^+$, 355.4 (100) $[M]^-$

1,4-Dihydroxy-2-(10-hydroxydecyloxy)anthracene-9,10-dione (**3d**)

^{1}H NMR ($CDCl_3$), δ: 1.25-1.33 (m, 12H, 6 x CH_2), 1.46-1.63 (m, 3H, CH_2, 10'-OH), 1.93 (dd, *J* = 6.9, 7.8 Hz, 2H, H-2'), 3.64 (t, *J* = 6.6 Hz, 2H, H-10'), 4.11 (t, *J* = 6.6 Hz, 2H, H-1'), 6.65 (s, 1H, H-3), 7.76-7.82 (m, 2H, H-5, H-6), 8.30-8.33 (m, 2H, H-7, H-8), 13.45 (s, 1H, 4-OH), 13.54 (s, 1H, 1-OH). ^{13}C NMR ($CDCl_3$), δ: 25.7 (C-6'), 25.8 (C-5'), 28.6 (C-7'), 29.2 (C-4'), 29.4 (C-8'), 29.4 (C-3'), 29.5 (C-9'), 32.8 (C-2'), 63.1 (C-10'), 69.8 (C-1'), 105.9 (C-1_a), 107.3 (C-3), 112.3 (C-4_a), 126.8 (C-6), 126.9 (C-7), 133.2 (C-5_a), 133.7 (C-8_a), 134.1 (C-5), 134.5 (C-8), 150.6 (C-2), 157.3 (C-4), 161.0 (C-1), 184.2 (C-10), 187.1 (C-9). Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.89; H, 6.84 Found: C, 69.71; H, 7.21. MS m/z (%): 435.7 (100) [M+Na]+, 411.8 (100) [M]-

Synthesis of conjugates in the presence of Ph_3P*HBr (general procedure)

To a solution of D-glucal **4a, b** (1 mmol) in anhydrous CH_2Cl_2 (5 mL), Ph_3P*HBr (0.15 mmol) was added and the resulting mixture was stirred at room temperature for 15 minutes. Next the purpurin derivative **3b** or **3d** (1.1 mmol) was added and the stirring at room temperature was continued for the defined time (20 to 24 h). The progress of reaction was monitored by TLC (toluene/ethyl acetate 1:1; to 4:1 v/v). The reaction mixture was evaporated to dryness and the residual oil was purified on a silica gel packed column using a mixture of toluene: ethyl acetate (1:1 to 4:1, v/v). The fraction, containing product was collected, combined and evaporated to give the desired product.

2-[(1,4-dihydroxy-anthracene-9,10-dione)]propoxy-3-yl 3,4,6-tri-*O*-acetyl-2-deoxy-D-arabinohexopyranoside (**5a**)

α Anomer: ^{1}H NMR ($CDCl_3$), δ: 1.83 (ddd, *J* = 3.6, 12.0, 13.2 Hz 1H, H-2_a), 2.01 (2s, 6H, $2CH_3CO$), 2.08 (s, 3H, CH_3CO), 2.20 - 2.24 (m, 2H, CH_2), 2.27 (ddd, *J* = 1.2, 5.0, 13.2 Hz 1H, H-2_b) 3.63 (dt, *J* = 6.0, 10.8 Hz, 1H, OCH_{2a}), 3.91 (dt, *J* = 5.4, 10.8 Hz, 1H, OCH_{2b}), 3.94-3.96 (m, 1H, H-5), 4.05 (dd, *J* = 2.4, 12.0 Hz, 1H, H-6_b), 4.24-4.28 (m, 3H, Pur-OCH_2, H-6_a), 4.95 (dd, *J* = 9.6, 10.2 Hz 1H, H-4), 5.00 (dd, *J* = 1.2, 3.6 Hz, 1H, H-1), 5.31 (ddd, *J* = 5.0, 9.6, 12.0

Hz, 1H, H-3), 6.72 (s, 1H, H-3'), 7.78-7.84 (m, 2H, H-5', H-6'), 8.33-8.35 (m, 2H, H-7', H-8'), 13.42 (s, 1H, 4'-OH), 13.51 (s, 1H, 1'-OH). β Anomer: δ: 1.62 - 1.79 (m, 1H, H-2_a), 2.21-2.25 (m, 1H, H-2_b), 4.61(dd, *J* = 1.8, 9.6 Hz, 1H, H-1) ^{13}C NMR ($CDCl_3$), δ: 20.82, 20.87, 21.09 ($3CH_3$), 28.88 (CH_2), 35.10 (C-2), 62.48 (OCH_2), 63.77 (OCH_2) 66.45 (C-6), 68.08 (C-3), 69.19 (C-4), 69.51 (C-5), 97.21 (C-1),106.34 (C-1'$_a$), 107.78 (C-3'), 112.67 (C-4'$_a$), 126.98 (C-6'), 127.14 (C-7'), 133.43 (C-5'$_a$), 133.96 (C-8'$_a$), 134.22 (C-5'), 134.70 (C-8'), 150.59 (C-2'), 157.08 (C-4'), 160.95 (C-1'), 170.02, 170.31, 170.84 (3C=O)184.59 (C-10'), 187.38 (C-9'). MS m/z (%): 609.2 (100) $[M+Na]^+$, 585.6 (100) $[M]^-$

2-[(1,4-dihydroxy-anthracene-9,10-dione)]decyloxy-10-yl 3,4,6-tri-O-acetyl-2-deoxy-D-arabinohexopyranoside (**5b**)

α Anomer: ^{1}H NMR ($CDCl_3$), δ: 1.15 – 1.32 (m, 12H, $6CH_2$), 1.49-1.58 (m, 2H, $OCH_2\underline{CH_2}$), 1.82 (ddd, *J* = 3.3, 11.7, 12.6 Hz, 1H, H-2_a), 1.93 (dt, *J* = 5.4, 7.5 Hz, $\underline{CH_2}CH_2O$), 2.01, 2.04, 2.10 (3s, 9H, CH_3CO), 2.23 (dt, *J* = 5.4, 12.6 Hz, 1H, H-2_b), 3.39 (dt, *J* = 6.6, 12.6 Hz, 1H, O-CH_{2a}), 3.60 (dt, *J* = 6.6, 9.3 Hz, 1H, OCH_{2b}), 3.94-3.99 (m, 1H, H-5), 4.05 (dd, *J* = 12.3, 2.1 Hz, 1H, H-6_b), 4.13 (t, *J* = 6.6, Hz, 2H, Pur-OCH_2), 4.31 (dd, *J* = 4.6, 12.3 Hz, 1H, H-6_a), 4.95 (d, *J* = 3.3 Hz, 1H, H-1), 5.00 (dd, *J* = 9.3, 8.4 Hz, 1H, H-4), 5.33 (ddd, *J* = 9.3, 11.7, 5.4 Hz, 1H, H-3), 6.67 (s, 1H, H-3'), 7.76-7.91 (m, 2H, H-5', H-6'), 8.31-8.36 (m, 2H, H-7', H-8'), 13.48 (s, 1H, 4'-OH), 13.57 (s, 1H, 1'-OH). β Anomer, δ: 1.49 – 1.66 (m, 1H, H-2_a), 4.55(d, *J* = 7.8 Hz, 1H, H-1) ^{13}C NMR ($CDCl_3$), δ: 20.74, 20.80, 20.97 ($3CH_3$), 25.85 (CH_2), 26.18 (CH_2), 28.61 (CH_2), 29.25 (CH_2), 29.39 ($2CH_2$), 29,42 ($2CH_2$), 35.09 (C-2), 62.43 (OCH_2), 67.71 (OCH_2) 67.87 (C-6), 69.19 (C-3), 69.51 (C-4), 69.78 (C-5), 96.89 (C-1), 105.96 (C-1'$_a$), 107.34 (C-3'), 112.65 (C-4'$_a$), 126.80 (C-6'), 126.96 (C-7'), 133.29 (C-5'$_a$), 133.74 (C-8'$_a$), 134.11 (C-5'), 134.49 (C-8'), 150.64 (C-2'), 157.32 (C-4'), 160.99 (C-1'), 169.92, 170.19, 170.72 (3C=O), 184.29 (C-10'), 187.19 (C-9'). MS m/z (%): 707.8 (100) $[M+Na]^+$, 683.9 (100) $[M]^-$

2-[(1,4-dihydroxy-anthracene-9,10-dione)]propoxy-3-yl 3,4,6-tri-O-benzyl-2-deoxy-α-D-arabinohexopyranoside (**5c**)

$[\alpha]_D^{26}$ +23.6° (c 1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$), δ: 1.72 (ddd, *J* = 3.6, 12.0, 13.2 Hz 1H, H-2_a), 2.10-2.17 (m, 2H, CH_2), 2.26-2.29 (m, 1H, H-2_b), 3.60-3.74 (m, 5H, OCH_{2a}, OCH_{2b}, H-5, H-6_a, H-6_b), 3.87 (ddd, *J* = 1.2, 5.0, 8.8 Hz, 1H, H-4), 3.96 (ddd, *J* = 5.0, 8.8, 11.5 Hz, 1H, H-3), 4.17-4.23 (m, 2H, Pur-OCH_2), 4.47-4.50 (m, 2H, CH_2Ar), 4.61-4.64 (m, 2H, CH_2Ar), 4.67 (d, *J* = 11.0 Hz, 1H, CH_2Ar), 4.85 (d, *J* = 11.0 Hz, 1H, CH_2Ar), 4.98 (d, *J* = 3.0 Hz, 1H, H-1), 6.70 (s, 1H, H-3'), 7.12-7.28 (m, 15H, HAr), 7.78-7.82 (m, 2H, H-5', H-6'), 8.30-8.32 (m, 2H, H-7', H-8'), 13.44 (s, 1H, 4'-OH), 13.54 (s, 1H, 1'-OH). ^{13}C NMR ($CDCl_3$), δ: 28.80 (CH_2), 35.39 (C-2), 63.13, 66.53, 68.83, 70.94, 71.77, 73.45 ($2OCH_2$, C-3, C-4, C-5, C-6), 74.87, 77.49, 78.14 ($3CH_2Ph$), 97.49 (C-1), 106.11 (C-1'$_a$), 107.56 (C-3'), 112.45 (C-4'$_a$), 126.82 (C-6'), 126.96 (C-7'), 127.50, 127.56, 127.62, 127.69, 127.81, 128.24, 128.28, 128.31, 128.34 (Ph), 133.29 (C-5'$_a$), 133.75 (C-8'$_a$), 134.11 (C-5'), 134.51 (C-8'), 138.09, 138.45, 138.64 (Ph), 150.52 (C-2'), 157.04 (C-4'), 160.84 (C-1'), 184.38 (C-10'), 187.21 (C-9'). MS m/z (%): 753.5 (60) $[M+Na]^+$, 729.7 (100) $[M]^-$

2-[(1,4-dihydroxy-anthracene-9,10-dione)]decyloxy-10-yl 3,4,6-tri-O-benzyl-2-deoxy-α-D-arabinohexopyranoside (**5d**)

$[\alpha]_D^{26}$ +16.5° (c 1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$), δ: 1.23-1.34 (m, 12H, $6CH_2$), 1.47-1.54 (m, 2H, OCH_2CH_2), 1.71 (ddd, *J* = 3.6, 11.4, 13.2 Hz, 1H, H-2_a), 1.92 (dt, *J* = 6.6, 13.5 Hz, $OCH_2\underline{CH_2}$), 2.28 (dd, *J* = 4.8, 13.2 Hz, 1H, H-2_b), 3.35 (dt, *J* = 6.9, 9.9 Hz, 1H, OCH_{2a}), 3.57-3.81 (m, 5H, OCH_{2b}, H-4, H-5, H-6_a, H-6_b), 3.99 (ddd, *J* = 4.8, 9.0, 11.4 Hz, 1H, H-3), 4.07-4.13 (m, 2H, Pur-OCH_2), 4.49-4.53 (m, 2H, CH_2Ar), 4.61-4.70 (m, 3H, CH_2Ar), 4.88 (d, *J* = 11.0 Hz, 1H, CH_2Ar), 4.94 (d, *J* = 3.6 Hz, 1H, H-1), 6.64 (s, 1H, H-3'), 7.14-7.34 (m, 15H, HAr), 7.74-7.84 (m, 2H, H-5', H-6'), 8.30-8.33 (m, 2H, H-7', H-8'), 13.46 (s, 1H, 4'-OH), 13.55 (s, 1H, 1'-OH). ^{13}C NMR ($CDCl_3$), δ: 25.86 (CH_2), 26.20 (CH_2), 28.62 (CH_2), 29.27 (CH_2), 29.43 ($2CH_2$), 29,52 ($2CH_2$), 35.57 (C-2), 67.37, 69.02, 69.76, 70.71, 71.73, 73.44 ($2OCH_2$, C-3, C-4, C-5, C-6), 74.94, 77.80, 78.38 ($3CH_2Ph$), 97.31 (C-1), 105.95 (C-1'$_a$), 107.34 (C-3'), 112.37 (C-4'$_a$), 126.77 (C-6'), 126.93 (C-7'), 127.45, 127.54, 127.81, 127.92, 128.28, 128.31 (Ph), 133.30 (C-5'$_a$), 133.68 (C-8'$_a$), 134.12 (C-5'), 134.44 (C-8'), 138.23, 138.57, 138.78 (Ph), 150.68 (C-2'), 157.32 (C-4'), 161.00 (C-1'), 184.22 (C-10'), 187.11 (C-9'). MS m/z (%): 851.7 (100) $[M+Na]^+$, 827.4 (100) $[M]^-$

Synthesis of glycoconjugates in the presence of boron-trifluoride (general procedure)

To a solution of glucal **4a** (1 mmol) in anhydrous CH_2Cl_2 (5 mL), BF_3*Et_2O (0.10 mmol) was added at 0 °C followed by the addition of purpurin derivative **3b** or **3d** (1.1 mmol) while stirring and then the reaction was continued at room temperature. The progress of reaction was monitored by TLC (toluene/ethyl acetate 2:1, or hexane/ethyl acetate 2:1 v/v). When TLC indicated the complete consumption of substrate (20 - 24 h), the reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$. The organic layer was separated, washed with brine, dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure to colourless oil. The residual oil was purified on a silica gel packed column using a mixture of toluene/ethyl acetate or hexane/ethyl acetate (1:2, v/v). The fraction containing product, was collected, combined together and evaporated, to give desired products.

2-[(1,4-dihydroxy-anthracene-9,10-dione)]propoxy-3-yl 4,6-di-*O*-acetyl-2,3-dideoxy-D-erythro-hex-2-enopyranoside (**6a**)

^{1}H NMR ($CDCl_3$), δ: 1.25 – 1.34 (m, 2H, CH_2), 2.09 (s, 6H, $2CH_3CO$), 2.23-2.34 (m, 2H, OCH_2), 3.75 (td, *J* = 6.3, 6.3, 9.9 Hz, 1H, OCH_{2a}), 3.99-4.27 (m, 4H, OCH_{2b}, H-6_a, H-6_b, H-5), 5.07 (bs, 1H, H-1), 5.29-5.34 (m, 1H, H-4), 5.80-5.96 (m, 2H, H-2, H-3), 6.70 (s, 1H, H-3'), 7.77-7.85 (m, 2H, H-5', H-6'), 8.31-8.34 (m, 2H, H-7', H-8'), 13.41 (s, 1H, 4'-OH), 13.51 (s, 1H, 1'-OH). ^{13}C NMR ($CDCl_3$), δ: 20.71, 20.91 ($2CH_3$), 29,68 (CH_2), 62.93, 63.00, 64.82, 65.34, 66.57 ($2OCH_2$, C-4, C-5, C-6), 94.56 (C-1), 106.01 (C-1'$_a$), 107.52 (C-'3), 112.48 (C-4'$_a$), 126.81 (C-6'), 126.97 (C-7'), 127.61 (C-2'), 129.27 (C-3'), 133.29 (C-5'$_a$), 133.74 (C-8'$_a$), 134.08 (C-5'), 134.48 (C-8'), 150.50 (C-2'), 157.04 (C-4'), 160.79 (C-1'), 170.11, 170.59 (2C=O), 184.33 (C-

10'), 187.13 (C-9'). MS m/z (%): 549.4 (100) $[M+Na]^+$, 525.7 (100) $[M]^-$

2-[(1,4-dihydroxy-anthracene-9,10-dione)]decyloxy-10-yl 4,6-di-O-acetyl-2,3-dideoxy-D-erythro-hex-2-enopyranoside (**6b**)

^{1}H NMR ($CDCl_3$), δ: 1.29 - 1.53 (m, 12H, $6CH_2$), 1.56 - 1.63 (m, 2H, OCH_2CH_2), 1.92 (q, *J* = 7.8 Hz, 2H, $O-CH_2CH_2$), 2.08, 2.10 (2s, 6H, $2CH_3CO$), 3.48-3.52 (m, 1H, OCH_{2a}), 3.74-3.79 (m, 1H, OCH_{2b}), 4.09-4.26 (m, 5H, $Pur-OCH_2$, H-6_a, H-6_b, H-5), 5.02 (bs, 1H, H-1), 5.30-5.32 (m, 1H, H-4), 5.82-5.84 (m, 1H, H-2), 5.87-5.88 (m, 1H, H-3), 6.66 (s, 1H, H-3'), 7.77-7.83 (m, 2H, H-5', H-6'), 8.32-8.34 (m, 2H, H-7', H-8'), 13.45 (s, 1H, 4'-OH), 13.54 (s, 1H, 1'-OH). ^{13}C NMR ($CDCl_3$), δ: 20.77, 20.95 ($2CH_3$), 25.89 (CH_2), 26.25 (CH_2), 28.65 (CH_2), 29.28 (CH_2), 29.40 (CH_2), 29.45 (CH_2), 29,50 (CH_2), 29,54 (CH_2), 63.06, 65.38, 66.92, 68.98, 69.78 ($2OCH_2$, C-4, C-5, C-6), 94.40 (C-1), 106.01 (C-1'$_a$), 107.38 (C-3'), 112.43 (C-4'$_a$), 126.82 (C-6'), 126.97 (C-7'), 128.00 (C-2'), 128.99 (C-3'), 133.34 (C-5'$_a$), 133.72 (C-8'$_a$), 134.16 (C-5'), 134.48 (C-8'), 150.72 (C-2'), 157.35 (C-4'), 161.02 (C-1'), 170.22, 170.69 (2C=O), 184.27 (C-10'), 187.17 (C-9'). MS m/z (%): 647.5 (100) $[M+Na]^+$, 623.6 (100) $[M]^-$

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflicts of interest.

ACKNOWLEDGEMENTS

Research study was partly financed by the European Union Structural Funds in Poland (UDA-POKL.04.01.01-00-114/09-01).

REFERENCES

[1] Singh, R.; Geetanjali; Chauhan, S.M.S. 9,10-Anthraquinones and other biologically active compounds from the genus *Rubia*. *Chem. Biodiv*., **2004**, *1*, 1241-1264.

[2] Drivas, I.; Blackburn, R.S.; Rayner, Ch. M. Natural anthraquinonoid colorants as platform chemicals in the synthesis of suitable disperse dyes for polyesters. *Dyes Pigm*., **2011**, *88*, 7-17.

[3] Miliani, C., Romani, A.; Favaro, G. Acidichromic effects in 1,2-di- and 1,2,4-tri-hydroxyanthraquinones. A spectrophotometric and fluorimetric study. *J. Phys. Org. Chem.*, **2000**, *13*, 141-150.

[4] Navas, D. A. Absorption and emission spectroscopy and photochemistry of 1,10-anthraquinone derivatives: a review. *J. Photochem. Photobiol. A: Chemistry*, **1990**, *53*, 141-167.

[5] Grazia, Ch.; Clementi, C.; Miliani, C.; Romani, A. Properties of alizarin and purpurin Al(III) complexes in solution and in solid state. *Photochem. Photobiol. Sci*., **2011**, *10*, 1249-1254.

[6] Shadi, I.D.; Chowdhry, B.Z.; Snowden, M.J.; Withnall, R. Semi-quantitative analysis of alizarin and purpurin by surface-enhanced resonance Raman spectroscopy (SERRS) using silver colloids. *J. Raman Spectrosc*., **2004**, *35*, 800-807.

[7] De Sousa, A.T.; Bessler, K.E.; Lemos, S.S.; Javier, E.; Gatto, C.C. Organotin complexes of alizarin and purpurin. *Z. Anorg. Algemm. Chem*., **2009**, *635*, 106-111.

[8] Idris, K.A.; Sedaira, H.; Ahmed, H.M. An insight into the solution equilibria of magnesium(II) with purpurin and spectrophotometric determination of magnesium. *Talanta*., **2001**, *54*, 369-375.

[9] Fukuda, I.; Kaneko, A.; Nishiumi, S.; Kawase, M.; Nishikiori, R.; Fujitake, N.; Ashida, H. Structure-activity relationship of anthraquinones on the suppression of DNA-binding activity of the aryl hydrocarbon receptor induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *J. Biosci. Bioengin*., **2009**, *107*, 296-300.

[10] Wang, Q.; Gao, F.; Yuan, X.; Li, W.; Liu A.; Jiao, K. Electrochemical studies on the binding of carcinogenic anthraquinone dye, purpurin (C.I. 58 205) with DNA. *Dyes Pigm*., **2010**, *84*, 213-217.

[11] Hollis Showalter, H.D.; Johnson, J.L.; Werbel, L.M.; Leopold, W.R.; Jackson, R.C.; Elslager, E.F. 5-[(Aminoalkyl)amino]-substituted anthra[1,9-cd]pyrazol-6(2*H*)-ones as novel anticancer agents. Synthesis and biological evaluation. *J. Med. Chem.*, **1984**, *27*, 253-255.

[12] Andreani, A.; Rambaldi, M.; Bonazzi, D.; Lelli, G.; Bossa, R.; Galatulas, I. Anthraquinone derivatives. *Arch. Pharm. (Weinheim)*, **1985**, *318*, 842-848.

[13] Nishimura, N.; Takai, M.; Yamamoto, E.; Hasumi, K. Purpurin as specific inhibitor of spermidine-induced autoactivation of the protease plasma hyaluronan-binding protein. *Biol. Pharm. Bull*., **2010**, *33*, 1430-1433.

[14] Marczylo, T.; Hayatsu, T.; Arimoto-Kabayashi, S.; Tada, M.; Fujita, K.; Kamataki, T.; Nakayama, K.; Hayatsu, H. Protection against the bacterial mutagenicity of heterocyclic amines by purpurin, a natural anthraquinone pigment. *Mutation Res.*, **1999**, *444*, 451-461.

[15] Marczylo, T.; Arimoto-Kobayashi, S.; Hayatsu, H. Protection against Trp-P-2 mutagenicity by purpurin: mechanism *in vitro* antimutagenesis. *Mutagenesis*, **2000**, *15*, 223-228.

[16] Takahashi, E.; Fujita, K.; Kamataki, T.; Arimoto-Kobayashi, S.; Okamoto, K.; Negishi, T. Inhibition of human cytochrome P450 1B1, 1A1 and 1A2 by antigenotoxic compounds, purpurin and alizarin. *Mutation Res.*, **2002**, *508*, 147-156.

[17] Takahashi, E.; Arimoto, S.; Okamoto, K.; Negishi, T. Enhancement of phase II enzyme activity by purpurin resulting in the suppresion of MeIQx-DNA-adduct formation in mice. *Mutation Res. Gen Toxic. Envir. Mut.*, **2007**, *626*, 128-134.

[18] Lee, Hoi-S. Suppression effect of purpurin derivatives on nitric oxide synthase. J. *Korean Soc. Appl. Biol. Chem*., **2011**, *54*, 302-307.

[19] Son, J.K.; Jung, S.J.; Jung, J.H.; Fang, Z.; Lee, C.S.; Seo, C.S.; Moon, D.C.; Min, B.S.; Kim, M. R.; Woo, M.H. Anticancer constituents from the roots of *Rubia cordifolia* L. *Chem. Pharm. Bull*., **2008**, *56*, 213-216.

[20] Brinkworth, R.I.; Fairlie, D.P. Hydroxyquinones are competitive non-peptide inhibitors of HIV-1 proteinase. *Biochem. Biophys. Acta*, **1995**, *1253*, 5-8.

[21] Kang, K.; Fong. W.P.; Tsang, P.W.K. Novel antifungal activity of purpurin against *Candida* species *in vitro*. *Med. Mycol.*, **2010**, *48*, 904-11.

[22] Hiipakka, R.A.; Zhang, H.Z.; Dai, W.; Dai, Q.; Liao, S. Structure-activity relationships for inhibition of human 5α-reductases by polyphenols. *Biochem. Pharm*., **2002**, *63*, 1165-1176.

[23] Hao, N.J.; Huang, M.P.; Lee, H. Structure-activy relationship of anthraquinones as inhibitors of 7-ethoxycoumarin *O*-deethylase and mutagenicity of 2-amino-3-methylimidazo[4,5-f]quinoline. *Mutation Res.*, **1995**, *328*, 183-191.

[24] Fain, V. Ya.; Zaistev, B.E.; Ryabov, M.A. Tautomerism of anthraquinones: I. Purpurin and anions derived therefrom. *Russ. J. Org. Chem*., **2005**, *41*, 38-46.

[25] Allevi, P.; Anastasia, M.; Fiecchi, A.; Sanvito, A. M.; Scala, A.; Simple synthesis of mono- and bismethyl ethers of purpurin (1,2,4-trihydroxyanthraquinone). *Synthesis*, **1991**, *6*, 438-440.

[26] Bolitt, V.; Mioskowski, Ch. Direct preparation of 2-deoxy-D-glucopyranosides from glucals without Ferrier rearrangement. *J. Org. Chem*., **1990**, *55*, 5812-5813.

[27] Rauter, A. P.; Almeida, T.; Vicente, A. I.; Ribeiro, V.; Bordado, J. C.; Marques, J. P.; Ribeiro, F. J.; Oliveira, C.; Guisnet, M. Reactions of *N*-, *S*- and *O*-nucleophiles with 3,4,6-tri-*O*-benzyl-D-glucal mediated by triphenylphosphane hydrobromide versus those with HY Zeolite. *Eur. J. Org. Chem.*, **2006**, *10*, 2429-2439.

[28] Ferrier, R. J.; Prasad, N. Unsaturated carbohydrates. Part X. Epoxidations and hydroxylations of 2,3-dideoxy-α-D-hex-2-enopyranosides. The four methyl 4,6-di-*O*-acetyl-2,3-anhydro-α-D- hexopyranosides. *J. Chem. Soc. (C)*, **1969**, *4*, 570-575.

[29] Pierwocha, A.W.; Walczak, K. The use of tri-*O*-acetyl-D-glucal and -D-galactal in the synthesis of ω-aminoalkyl 2-deoxy- and 2,3-dideoxy-D-hexopyranosides. *Carbohydr. Res.*, **2008**, *343*, 2680-2686.