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Short Note

1-Hydroxy-3-(3-methylbut-2-enyloxy)anthracene-9,10-dione

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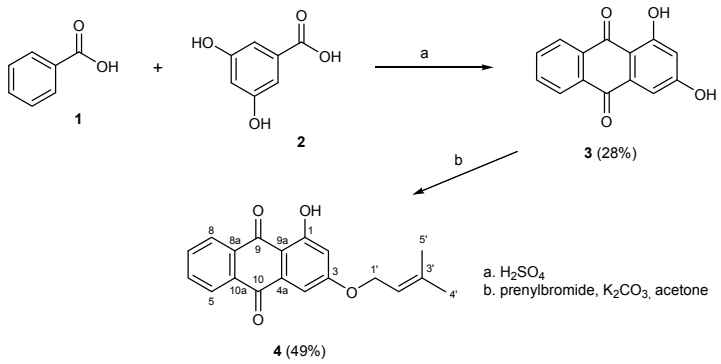
Abstract: An anthraquinone derivative, 1-hydroxy-3-(3-methylbut-2-enyloxy)anthracene-9,10-dione (**4**), has been synthesized in two steps from benzoic acid, 3,5-dihydroxybenzoic acid, and prenylbromide.

Keywords: anthraquinone; 1-hydroxy-3-(3-methylbut-2-enyloxy)anthracene-9,10-dione

1. Introduction

9,10-Antraquinones are a class of secondary metabolites that have been found in plants, bacteria, fungi, and lichens [1]. These compounds are characterized by a core structure of anthracene-9,10-dione and are diversified further by the presence of oxygenated functionalities which differ in number, types, and position. In addition, many 9,10-anthraquinones are also *C*-methylated, *C*-formylated, and *C*-carboxylated. However, 9,10-anthraquinones bearing prenylated or geranylated are very limited [2]. In search of bioactive compounds for antibaterial agents we had synthesized a number of 9,10-antraquinone derivatives, including a new *O*-prenylated anthraquinone 1-hydroxy-3-(3-methylbut-2-enyloxy)anthracene-9,10-dione (**4**). This compound was synthesized in two steps, starting from a condensation of benzoic acid (**1**) and 3,5-dihydroxybenzoic acid (**2**) to 1,3-dihydroxyanthracene-9,10-dione (**3**), and followed by a reaction of compound **3** with prenylbromide to give compound **4** (Scheme 1). Similar reaction of compound **3** with prenylbromide in the presence of sodium methoxide was reported to give a *C*-prenylation product, 1,3-dihydroxy-4-(methylbut-2-enyl)anthracene-9,10-dione [3,4].



Scheme 1. Synthesis of 1-hydroxy-3-(3-methylbut-2-enyloxy)anthracene-9,10-dione (**4**).

2. Experimental Section

2.1. Synthesis of 1,3-Dihydroxyanthracene-9,10-dione (**3**)

1,3-Dihydroxyanthracene-9,10-dione (**3**) was prepared from compounds **1** and **2** according to method described in [5] with some modifications. A mixture of compounds **1** (4.17 g, 34.1 mmol), **2** (1.5 g, 9.73 mmol) and concentrated sulphuric acid (39 mL) was refluxed at 120 °C for 2 h. The reaction mixture was then cooled to room temperature and was poured into ice-water (50 mL). The precipitated formed was filtered to give a greenish brown residue. The residue was fractionated using vacuum liquid chromatography (silica gel, *n*-hexane–EtOAc = 9:1) to afford 1,3,5,7-tetrahydroxyantracene-9,10-dione (0.63 g, 48%) and a fraction, which on further purification using centrifugal planar chromatography (silica gel, *n*-hexane–EtOAc = 9:1), gave compound **3** (0.66 g, 28%).

Orange solids. M.p. 270–271 °C; IR (KBr) $\nu_{max.}$, cm^{-1}: 3373, 3072, 1671, 1637, 1589, 1453, 1415, 1340, 1160, 1007, 861, 779, 712, 659, 601; ^{1}H-NMR (Agilent DD2, 500 MHz, DMSO-d_6) δ, ppm: 12.71 (s, 1-OH), 11.31 (br s, 3-OH), 6.59 (d, *J* = 2.1 Hz, H-2), 7.12 (d, *J* = 2.1 Hz, H-4), 8.13 (br d, *J* = 7.0 Hz, H-5), 7.87 (m, H-6), 7.89 (m, H-7), 8.17 (br d, *J* = 7.0 Hz, H-8); ^{13}C-NMR (Agilent DD2, 125 MHz, DMSO-d_6) δ, ppm: 165.3 (C-1), 108.3 (C-2), 164.7 (C-3), 107.7 (C-4), 135.0 (C-4a), 127.5 (C-5), 134.7 (C-6), 134.5 (C-7), 126.8 (C-8), 132.9 (C-8a), 185.9 (C-9), 109.4 (C-9a), 181.8 (C-10), 133.0 (C-10a); HRESIMS (Waters LCT Premier XE) *m*/*z*: found $[M - H]^-$ 239.0349; calcd. $[M - H]^-$ for $C_{14}H_8O_4$ 239.0344. The ^{1}H- and ^{13}C-NMR paramerers of **3** were assigned by the analysis of its HSQC and HMBC spectra, see Supplementary Materials.

2.2. Synthesis of 1-Hydroxy-3-(3-methylbut-2-enyloxy)anthracene-9,10-dione (**4**)

To a solution of compound **3** (0.1 g, 0.42 mmol) in acetone (10 mL), K_2CO_3 (0.29 g, 2.08 mmol) was added and was refluxed for 3 h. Prenylbromide (97 μL, 0.83 mL) was then added to the reaction mixture and the reflux was continued for another 21 h. After being cooled to room temperature, water (10 mL) was added and the products were extracted with dichloromethane (3 × 15 mL). The organic phase was washed with aqueous saturated NaCl solution (2 × 15 mL), dried with anhydrous Na_2SO_4, and was evaporated under reduce pressure to give a yellowish residue. The residue was purified by centrifugal planar chromatography (silica gel, *n*-hexane–EtOAc = 9:1) to give compound **4** (63 mg, 49%).

Yellow solids. M.p. 172–173 °C; IR (KBr) $\nu_{max.}$, cm^{-1}: 3445, 3085, 2921, 2862, 1678, 1636, 1592, 1484, 1448, 1374, 1288, 1208, 1154, 972, 794, 635; ^{1}H-NMR (Agilent DD2, 500 MHz, $CDCl_3$) δ, ppm: 12.87 (s, 1-OH), 6.71 (d, *J* = 2.3 Hz, H-2), 7.38 (d, *J* = 2.3 Hz, H-4), 8.26 (dd, *J* = 1.8, 7.1 Hz, H-5), 7.76 (m, H-6), 7.80 (m, H-7), 8.29 (dd, *J* = 1.7, 7.2 Hz, H-8), 4.65 (d, *J* = 6.7 Hz, H_2-1′), 5.49 (t, *J* = 6.7 Hz, H-2′), 1.82 (3H, s, H_3-4′), 1.79 (s, H_3-5′); ^{13}C-NMR (Agilent DD2, 125 MHz, $CDCl_3$) δ, ppm: 165.5 (C-1), 107.5 (C-2), 165.8 (C-3), 108.5 (C-4), 135.1 (C-4a), 127.5 (C-5), 134.2 (C-6), 134.4 (C-7), 126.9 (C-8), 133.7 (C-8a), 186.9 (C-9), 110.8 (C-9a), 182.6 (C-10), 133.7 (C-10a), 65.9 (C-1′), 118.4 (C-2′), 139.9 (C-3′), 26.0 (C-4′), 18.5 (C-5′). HRESIMS (Waters LCT Premier XE) *m*/*z*: found $[M - H]^-$ 307.0977; calcd. $[M - H]^-$ for $C_{19}H_{16}O_4$ 307.0970. These ^{1}H- and ^{13}C-NMR paramerers were assigned by the analysis of HSQC and HMBC spectra of **4**, see Supplementary Materials.

Supplementary Materials: The IR, NMR, and mass spectra of compounds **3** and **4** are available online at http://www.mdpi.com/1422-8599/2016/1/M888.

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Conflicts of Interest: The authors declare no conflict of interest.

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