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A NEW ROUTE TO BENZO[*b*]XANTHENE-6,11,12-TRIONE DERIVATIVES BASED ON THE PHOTOINDUCED *o*-HYDROXYBEZOYLATION OF 1,4-NAPHTHOQUINONE

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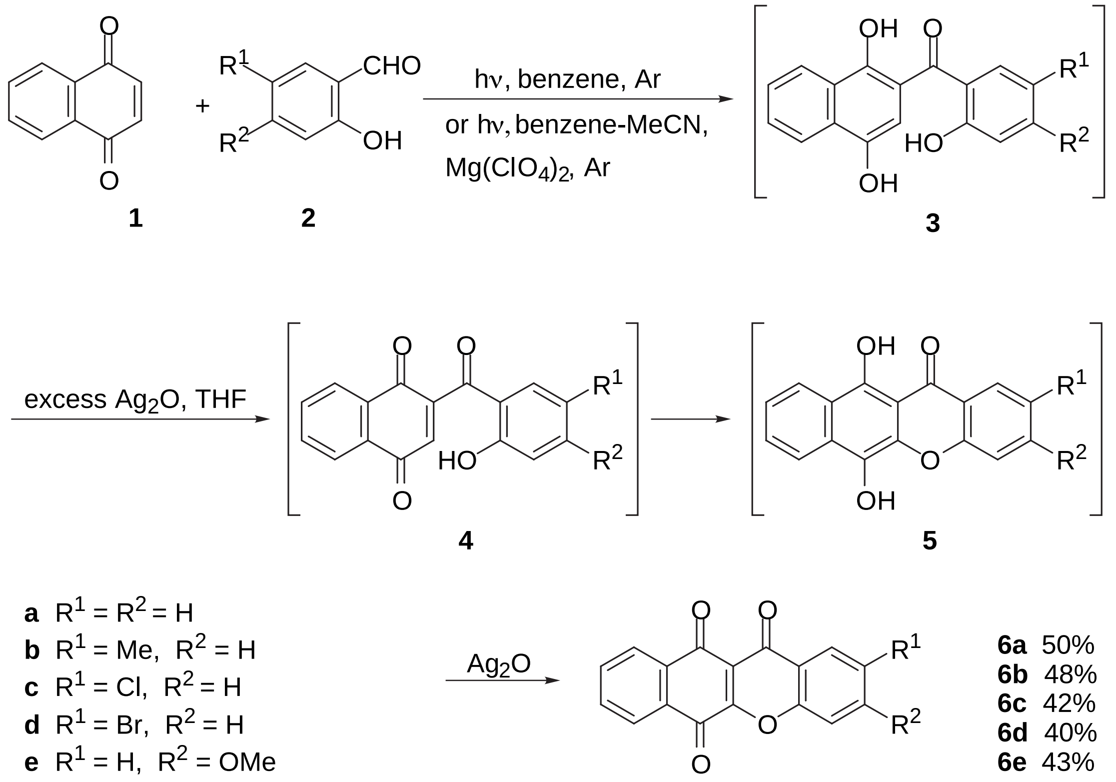
Abstract- A two-step procedure for the synthesis of the title xanthenequinone derivatives is described. The procedure involves the photoinduced acylation of 1,4-naphthoquinone with 2-hydroxybenzaldehydes, followed by treatment with Ag_2O.

We report herein a convenient preparation of benzo[*b*]xanthene-6,11,12-trione derivatives based on the photoinduced acylation of 1,4-naphthoquinone with 2-hydroxybenzaldehydes, which is an application of the photochemically mediated reaction of 1,4-quinone with simple aldehydes.1 A number of methods for the syntheses of bikaverin, a red pigment[2] that reveals significant biological activity,[2,3] using appropriately substituted benzo[*b*]xanthene-6,11,12-trione derivatives as precursors have been reported.[4] In these papers several multi-step approaches to the construction of this benzoxanthenetrione skeleton have been described. Photoreaction of 1,4-naphthoquinone (**1**) with 2-hydroxybenzaldehydes (**2**) for several days afforded 2-(2-hydroxybenzoyl)naphthalene-1,4-diols (**3**). These hydroquinone derivatives were treated with an excess amount of Ag_2O in THF according to the reported procedure[5] to give 11*H*-benzo[*b*]xanthene-6,11,12-triones (**6**) in moderate-to-fair yields based on **1**, *via* 2-(2-hydroxybenzoyl)-1,4-naphthoquinones (**4**) and 5,11-dihydroxybenzo[*b*]xanthen-12-one intermediates (**5**), as shown in the Scheme. Each of the *o*-hydroxybenzoylated hydroquinone derivatives (**3**) could not be isolated in a pure form, because it was contaminated probably by the corresponding intermediates (**4**) and (**5**). The photoreactions were conducted in benzene under an argon atmosphere, except for using 2-hydroxy-4-methoxybenzaldehyde (**2e**). No desired product was formed in the photoreaction of **1** with **2e** under the above-mentioned conditions. The reaction of **1** with **2e** was carried out in benzene-acetonitrile (7 : 3) containing an equimolar amount of magnesium perchlorate to **1** (Takuwa's conditions)[6] to give the expected 2-benzoylated hydroquinone derivative (**4e**).



In conclusion, we demonstrated a two-step general synthesis of 11*H*-benzo[*b*]xanthene-6,11,12-triones (**6**) from 1,4-naphthoquinone and *o*-hydroxybenzaldehydes. The simple operation and the readily availability of the starting materials make this method attractive.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Perkin-Elmer 1600 Series FT IR spectrophotometer as KBr disk. The ^{1}H NMR spectra were determined in $CDCl_3$ using TMS as an internal reference with a JEOL JNM-GX270 FT NMR spectrometer operating at 270 MHz. *J* values are given in Hz. The ^{13}C NMR spectrum was determined in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. Low-resolution MS analyses were performed on a JEOL AUTOMASS 20 spectrometer (Center for Joint Research and Development, this University). TLC was carried out on a Merck Kieselgel 60 PF_{254}. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use. All chemicals used in this study were commercially available.

11*H*-Benzo[*b*]xanthene-6,11,12-trione (6a). Typical Procedure. A solution of 1,4-naphthoquinone (**1**) (0.15 g, 0.96 mmol) and *o*-hydroxybenzaldehyde (**2a**) (0.23 g, 1.9 mmol) in benzene (10 mL) in a pyrex test tube was irradiated with a 500W high pressure mercury arc lamp under argon for 4 days at rt. After evaporation of the solvent, the residue was subjected to column chromatography on silica gel (1:3 AcOEt–hexane) to remove the unreacted starting materials and the remainder was eluted with

AcOEt. The AcOEt eluent was concentrated to give a residual solid, which was dissolved in THF (5 mL) and was added to a stirring suspension of Ag_2O [prepared from 0.49 g (3.1 mmol) of silver nitrate by the literature method[5]] in THF (5 mL) in the presence of anhydrous sodium sulfate (3 g). After stirring for 2 h, the solid was filtered off and the filtrate was concentrated. The residual solid was recrystallized from AcOEt–hexane to give pure **6a** (0.13 g, 50%): mp 279 ˚C (decomp) [lit.,[7] 276–278 ˚C (decomp)]. The ^{1}H NMR spectrum of this product was identical to that reported in the literature.[7]

2-Methyl-11*H*-benzo[*b*]xanthene-6,11,12-trione (6b): Prepared from **1** and 2-hydroxy-5-methylbenzaldehyde (**1b**) in a similar way as described above for the preparation of **6a**; mp 244 ˚C (decomp) ($CHCl_3$–hexane); ν_{max}/cm^{-1} 1684, 1636, 1616; δ_H 2.51 (3H, s), 7.6–7.7 (2H, s), 7.75–7.95 (2H, s), 8.11 (1H, s), 8.22 (1H, dd, *J* = 7.6, 2.3), 8.27 (1H, d, *J* = 7.6); MS *m/z* 290 (M^+, 100). Anal. Calcd for $C_{18}H_{10}O_4$: C, 74.48; H, 3.47. Found: C, 74.27; H, 3.60.

2-Chloro-11*H*-benzo[*b*]xanthene-6,11,12-trione (6c): Prepared from **1** and 5-chloro-2-hydroxybenzaldehyde (**1c**) in a similar way as described above for the preparation of **6a**; mp 231 ˚C (decomp) ($CHCl_3$–hexane); ν_{max}/cm^{-1} 1684, 1609; δ_H 7.71 (1H, dd, *J* = 8.9, 0.6), 7.75 (1H, dd, *J* = 8.9, 2.3), 7.83 (1H, td, *J* = 7.6, 1.7), 7.90 (1H, td, *J* = 7.6, 1.7), 8.2–8.3 (3H, m); MS *m/z* 310 (M^+, 100). Anal. Calcd for $C_{17}H_7O_4Cl$: C, 65.72; H, 2.27. Found: C, 65.99; H, 2.37.

2-Bromo-11*H*-benzo[*b*]xanthene-6,11,12-trione (6d): Prepared from **1** and 5-bromo-2-hydroxybenzaldehyde (**1d**) in a similar way as described above for the preparation of **6a**; mp 242 ˚C (decomp) (AcOEt–hexane); ν_{max}/cm^{-1} 1686 and 1606; δ_H 7.64 (1H, d, *J* = 8.9), 7.75–7.95 (3H, m), 8.2–8.3 (2H, m), and 8.44 (1H, d, *J* = 2.6); δ_C 116.99, 120.85, 121.04, 126.71, 127.42, 127.48, 129.35, 130.52, 134.02, 135.99, 138.37, 153.35, 157.39, 173.53, 178.56, and 180.25; MS *m/z* 354 (M^+, 100). Anal. Calcd for $C_{17}H_7O_4Br$: C, 57.49; H, 1.99. Found: C, 57.42; H, 1.97.

2-Methoxy-11*H*-benzo[*b*]xanthene-6,11,12-trione (6e). A solution of **1** (0.20 g, 1.3 mmol) and 2-hydroxy-4-methoxybenzaldehyde (**2e**) (0.40 g, 2.6 mmol) in acetonitrile-benzene (3 : 7, 20 mL) containing magnesium perchlorate (0.29 g, 1.3 mmol) in a pyrex test tube was irradiated with a 500 W high pressure mercury arc under argon for 4 days at rt. After evaporation of the solvent, 10% aqueous NH_4Cl (20 mL) was added, and the mixture was extracted with $CHCl_3$ twice (10 mL each). The combined extracts were dried over anhydrous $NaSO_4$ and evaporated. The residue was separated and allowed to react with Ag_2O in a similar manner as described for the preparation of **6a** to give **6e** (0.17 g, 43%); mp 287 ˚C (decomp) (AcOEt–hexane) [lit.,[7] 285–287 ˚C (decomp)]. The ^{1}H NMR spectrum of this product was identical to that reported in the literature.[7]

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