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 Ag₂O.

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. A number of methods for the syntheses of bikaverin, a red pigment that reveals significant biological activity, using appropriately substituted benzo[b]xanthene-6,11,12-trione derivatives as precursors have been reported. In these papers several multi-step approaches to the construction of this benzoxyanthrenetrione 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 Ag₂O in THF according to the reported procedure to give 11H-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) to give the expected 2-benzoylated hydroquinone derivative (4e).
In conclusion, we demonstrated a two-step general synthesis of $11H$-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.

$11H$-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 Ag₂O [prepared from 0.49 g (3.1 mmol) of silver nitrate by the literature method] 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 ¹H NMR spectrum of this product was identical to that reported in the literature.⁷

2-Methyl-11H-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) (CHCl₃–hexane); νmax/cm⁻¹ 1684, 1636, 1616; δH 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 C₁₈H₁₀O₄: C, 74.48; H, 3.47. Found: C, 74.27; H, 3.60.

2-Chloro-11H-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) (CHCl₃–hexane); νmax/cm⁻¹ 1684, 1609; δH 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 C₁₇H₇O₄Cl: C, 65.72; H, 2.27. Found: C, 65.99; H, 2.37.

2-Bromo-11H-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); νmax/cm⁻¹ 1686 and 1606; δH 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); δC 116.99, 120.85, 121.04, 126.71, 127.42, 127.48, 129.35, 130.52, 134.02, 135.99, 138.37, 157.39, 173.53, 178.56, and 180.25; MS m/z 354 (M⁺, 100). Anal. Calcd for C₁₇H₇O₄Br: C, 57.49; H, 1.99. Found: C, 57.42; H, 1.97.

2-Methoxy-11H-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 NH₄Cl (20 mL) was added, and the mixture was extracted with CHCl₃ twice (10 mL each). The combined extracts were dried over anhydrous NaSO₄ and evaporated. The residue was separated and allowed to react with Ag₂O 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 ¹H NMR spectrum of this product was identical to that reported in the literature.⁷

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REFERENCES