Preparation and Route of Asterriquinone Monoalkyl Ether from Asterriquinone Diacetate by Treatment with a Mixture of Alcohol and Alkali, Followed by Acidification[1)]

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3-Alkoxy-6-hydroxy-*p*-benzoquinones were prepared by the treatment of 3,6-diacetoxy-*p*-benzoquinones with a mixture of alcohol and alkali, followed by acidification. The key intermediate acetoxy-alkoxy-*p*-benzoquinones were formed by the base-catalyzed addition of an alkoxy anion to the conjugated double bonds in the diacetoxy-*p*-benzoquinone ring, followed by an acetoxy anion elimination. This method was applied for preparing a novel *o*-quinone derivative of asterriquinone (ARQ) by the addition of 2-haloethanol and intramolecular *O*-alkylation.

Key words asterriquinone monoalkyl ether; hydroxy-*p*-benzoquinone; alkoxy anion addition; conjugated double bond; *o*-quinone derivative; cytotoxicity

Asterriquinone (ARQ); 2,5-bis[1-(1,1-dimethyl-2-propenyl)-1*H*-indol-3-yl]-3,6-dihydroxy-2,5-cyclohexadiene-1,4-dione (**1**) is a metabolic product of *Aspergillus terreus* IFO 6123.[2)] ARQ and its analogues, *e.g.* de-bis-1,1-dimethylallyl ARQ, have been shown to have antitumor activity against transplantable animal tumors,[3)] as well as an inhibitory effect on human immunodeficiency virus type 1 (HIV-1) reverse transcriptase[4)] and protease.[5)] As it was indicated that hydroxy-*p*-benzoquinone compounds will hopefully be derived to act as potent anti-HIV drugs,[6)] ARQ might be a useful lead compound for developing the new drugs of cancer or AIDS therapy by chemical modification of its dihydroxy-*p*-benzoquinone moiety.

Recently, we showed that **1** formed DNA-interstrand cross-links, caused cellular apoptosis, and accumulated at the G_1 phase of the cell cycle toward mouse leukemia P388 cells (P388)[7)]; these biological actions depended on its bis-indolyl-hydroxy-*p*-benzoquinone structure.[8,9)] Moreover, we obtained ARQ monohexyl ether (**2f**)[1)] which has an IC_{50} value (0.07 μM) against P388 of about 18-fold more than that of **1** (1.28 μM).[10)] This suggested that the transformation of ARQ diacetate (**3**) to ARQ monoalkyl ether (**2**) by treatment with a mixture of alcohol and solid alkali, followed by acidification,[1)] is useful for preparing more effective derivatives involving hydroxy-*p*-benzoquinone compounds. In this paper, we propose the route from **3** to **2**, and apply this route to prepare novel ARQ monoalkyl ethers (**2g**—**i**) and a novel *o*-quinone derivative of ARQ (**11**).

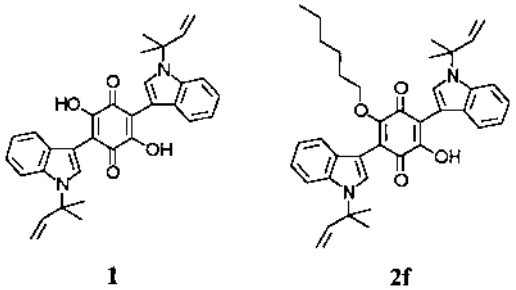
Results and Discussion

We initiated the preparation of ARQ monoalkyl ether (**2**) with the alkylation of ARQ monoacetate (**6**) which is a metabolic product of *Aspergillus terreus* IFO 6123,[11)] then hydrolyzed the resulting ARQ monoalkyl ether acetate (**4**) (Chart 1, route A). However, since the amounts of **6** available from a natural source were insufficient as a starting material, we converted **3** into **6**.[12)] During some attempts at preparing **6** from **3**, ARQ monoalkyl ethers (**2a**, **b**) were obtained in 93 and 63% yield from **3** by a 1-step reaction (Chart 1, route B). This result is sufficient for our purpose, because of the short step reactions from **1** in comparison with the preparation of **2a** from **1** *via* **3**, **6** and **4** (Chart 1).

A closely related reaction has been reported by Horii *et al.*; thus, treatment of 1,6,11-triacetoxy-8-(1-acetoxyethyl)-naphthacenequinone with a mixture of KOH and aq. EtOH gave 6-ethoxy-1,11-dihydroxy-8-(1-hydroxyethyl)naphthacenequinone in 47% yield.[13)] However, its mechanism has not been investigated. Thus, we propose the condition and the route for this transformation from **3** to **2a**. First, **3** was treated with a mixture of MeOH and 5% aq. Na_2CO_3, K_2CO_3, NaOH, or KOH to give **1** and trace amounts of **2a**. In contrast, treatment of **3** with a mixture of MeOH and solid alkali, followed by acidification, gave **2a** in good yield (Table 1).

Based upon the above results, we obtained ARQ monobutyl (**2d**), monopentyl (**2e**), monohexyl (**2f**), mono-trifloroethyl (**2g**), mono-trichloroethyl (**2h**), and monophenyl (**2i**) ethers (Table 2, Chart 2).

During the transformation of **3** to **2a**, the color tone of the reaction mixture turned from purple to yellow before acidification. Then, the UV spectrophotometric course of the reaction mixture was measured. Figure 2 showed that the peak at 292 nm increased until 60 min, then decreased, and after 150 min the quinoid n–π^* transition at 450—550 nm disappeared. However, the yellow color tone of the reaction mixture hardly changed by the elongation of the reaction time, but immediately changed to reddish-brown by acidification. The spectral change suggested at least one intermediate exists in this transformation, and it will be converted into **2a** by



1 **2f**

Fig. 1. Chemical Structures of Asterriquinone (**1**) and Asterriquinone Monohexyl Ether (**2f**)

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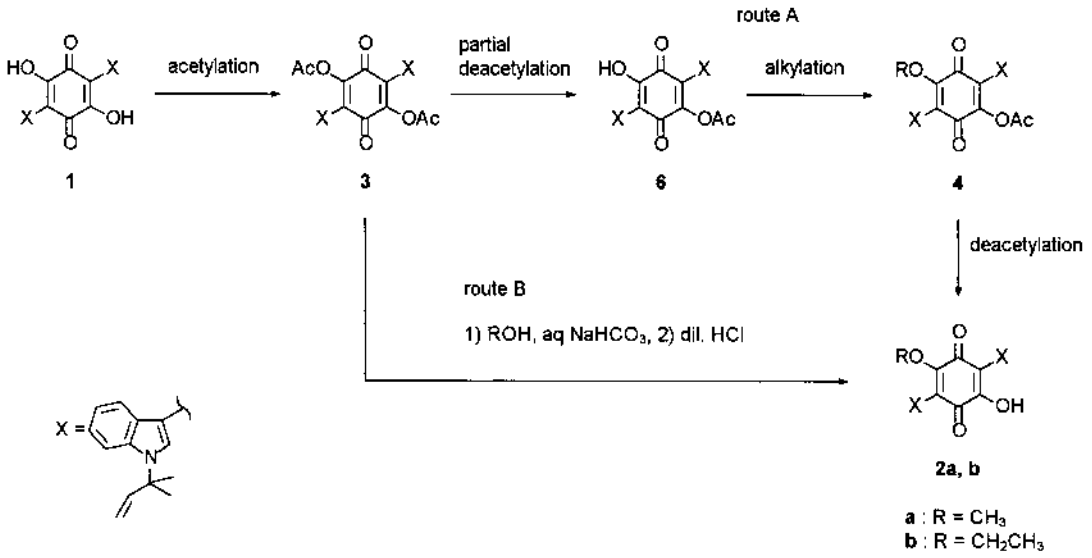


Chart 1

Table 1. Reaction of **3** with a Mixture of MeOH and Solid Alkali

Entry	Alkali (mol eq)	React. temp.	React. time	**2a** (yield %)
1	$NaHCO_3$ (1)	Reflux	3 h	96
2	$NaHCO_3$ (20)	Reflux	15 min	94
3	Na_2CO_3 (1)	Reflux	2 h	95
4	Na_2CO_3 (20)	Reflux	10 min	91
5	K_2CO_3 (1)	Reflux	30 min	98
6	K_2CO_3 (20)	Reflux	10 min	91
7	NaOH (1)	r.t.	30 s	92
8	KOH (1)	r.t.	30 s	88

Table 2. Preparation of **2** from **3**

Solvent	React. temp. (°C)	React. time	**2** (yield %)
MeOH	Reflux	10 min	**2a** (98)
EtOH	Reflux	15 min	**2b** (93)
PrOH	85	30 min	**2c** (87)
BuOH[a)]	85	1 h	**2d** (63)
PenOH[a)]	85	1 h	**2e** (61)
HexOH[a)]	85	1 h	**2f** (55)
2,2,2-Trifluoroethanol[a)]	85	20 min	**2g** (72)
2,2,2-Trichloroethanol[a)]	85	20 min	**2h** (76)
Phenol[a)]	85	15 min	**2i** (56)

a) Compound **3** was dissolved in DMF then mixed with solvent.

acidification. We attempted to isolate the intermediate from the mechanistic interest.

Next, the yellow colored reaction mixture was filtered, the filtrate was extracted with hexane, the organic layer was dried over anhydrous Na_2SO_4 and was then evaporated *in vacuo*. The residue was purified by column chromatography (SiO_2) to give yellow prisms (**5a**) of mp 165—166 °C (dec.) (hexane). Its formula, $C_{35}H_{38}N_2O_5$, was established by elemental analysis. The IR spectrum (KBr) showed hydroxy group absorption at 3248 cm^{-1}, a carbonyl group at 1638 cm^{-1} and an acetal group at 1062 cm^{-1}. The ^{1}H-NMR spectrum ($CDCl_3$) indicated the presence of three methoxy groups, two equivalent ones [δ 3.33 (6H, s)] and the other one [δ 3.59 (3H, s)], and one hydroxy group [δ 6.36 (1H, s)].

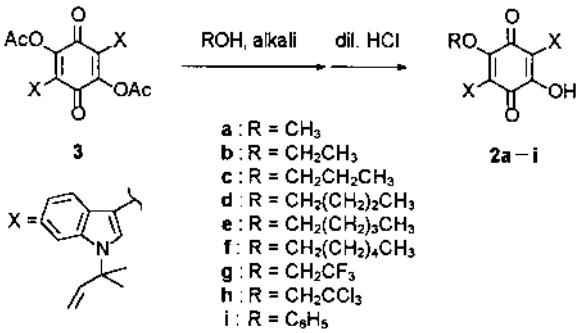


Chart 2

These results suggest that **5a** is a mono-dimethyl acetal of **2a**. The position of the acetal group in **5a** was confirmed by observation of the differential nuclear Overhauser effect experiments, and the structure of **5a** was determined as 2,5-bis-[1-(1,1-dimethyl-2-propenyl)-1*H*-indol-3-yl]-3-hydroxy-1,1,6-trimethoxy-2,5-cyclohexadien-4-one. It was shown that **5a** is the intermediate of this transformation, because **5a** was converted into **2a** in quantitative yield by treating **5a** with a mixture of 1 N HCl and MeOH.

Treatment of **3** (0.017 mmol) with a mixture of MeOH and solid $NaHCO_3$ (1 mol eq) under reflux for 60 min gave ARQ monomethyl ether acetate (**4a**)[12] in 98% yield. Also, **5a** was obtained from **4a** by similar treatment. Similarly, ARQ monoethyl ether acetate (**4b**) and ARQ monopropyl ether acetate (**4c**) were also transformed into ARQ monoethyl ether mono-diethyl acetal (**5b**) and ARQ monopropyl ether mono-dipropyl acetal (**5c**) by treatment with a mixture of a corresponding alcohol [EtOH or propanol (PrOH)] and solid K_2CO_3, then the acid-catalyzed hydrolysis of **5b** and **5c** gave **2b** and ARQ monopropyl ether (**2c**), respectively, in quantitative yields. Furthermore, treatment of **3** with a mixture of EtOH or PrOH and solid K_2CO_3 gave **4b** (yield, 10%) and **5b** (yield, 86%), or **4c** (yield, 21%) and **5c** (yield, 75%), respectively. These results indicated that **2** was transformed from **3** *via* **4** and **5**. Additionally, **4a** and **5a** were never obtained from **2a** or **6** by treatment with a mixture of MeOH and

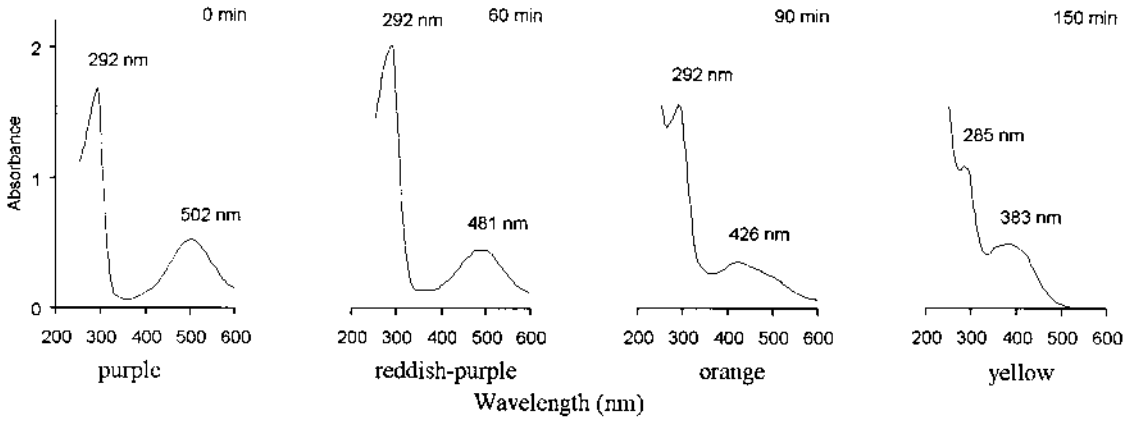
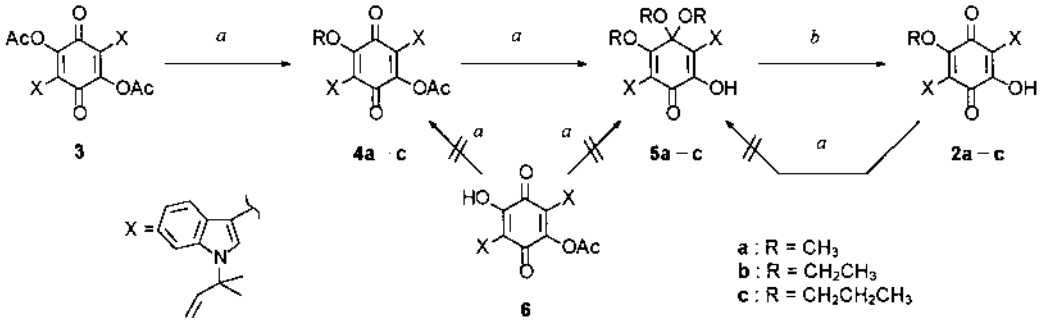


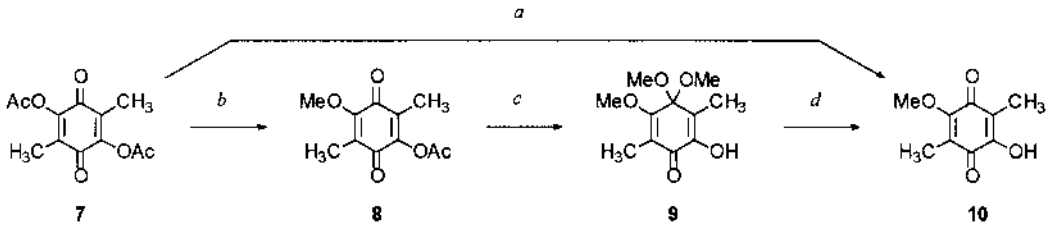
Fig. 2. The UV Spectrophotometric Course of the Reaction Mixture

Compound **3** (0.018 mmol) was treated with a mixture of MeOH (20 ml) and $NaHCO_3$ (1 mol eq) under reflux. After the indicated time, 0.3 ml of reaction mixture was sampled, added to 2.7 ml of MeOH, then measured. Spectra obtained at specific times are shown on the curve.



Reagent: *a*) ROH, alkali; *b*) dil. HCl, MeOH.

Chart 3



a) Treatment with a mixture of MeOH and $NaHCO_3$ (1 mol eq) under reflux for 15 min, then acidification with 0.1 N HCl, yield 92%; *b*) treatment with a mixture of MeOH and $NaHCO_3$ (1 mol eq) at room temperature for 10 min, then acidification with 0.1 N HCl, yield 57%; *c*) treatment with a mixture of MeOH and 5% aq. $NaHCO_3$ at room temperature for 10 min, then slight acidification with 0.1 N HCl, 85%; *d*) treatment with a mixture of MeOH and 0.1N HCl at room temperature for 15 min, quantitative yield. These compounds were purified by column chromatography on oxalic acid - impregnated SiO_2 (oxalic-SiO_2).

Chart 4

K_2CO_3 (Chart 3).

As examples of the preparation of quinone acetals, anodic oxidation of 1,4-dialkoxyaromatic compounds and chemical oxidation of phenols have been known.[14] However, no direct acetal formation from *p*-benzoquinones by alcohol and alkali has as yet been reported.

Similarly, 2,5-diacetoxy-*p*-xyloquinone (**7**) was treated with a mixture of MeOH and $NaHCO_3$ to give 2-hydroxy-5-methoxy-*p*-xyloquinone (**10**)[12] *via* 2-acetoxy-5-methoxy-*p*-xyloquinone (**8**)[12] and the mono-dimethyl acetal of **10** (**9**) (Chart 4).

From the above results, the proposed route of the transformation of **3** to **2** *via* **4** and **5** is depicted in Chart 5. Diacetoxy-*p*-benzoquinones (**3**, **7**) are transformed to acetoxy-alkoxy-*p*-benzoquinones (**4**, **8**) by a Michael addition of an alkoxy anion to the conjugated double bonds in the quinone ring, followed by an acetoxy anion elimination. Alkoxy-hydroxy-quinone mono-dialkyl acetals (**5**, **9**) are formed *via* hemiacetal (A) by alkoxy anion addition to the quinone carbonyl, and by the ester bond cleavage by alkoxy anion attack to acetyl carbonyl. Finally, alkoxy-hydroxy-*p*-benzoquinones (**2**, **10**) are formed *via* hemiacetal (B) by acid-catalyzed hy-

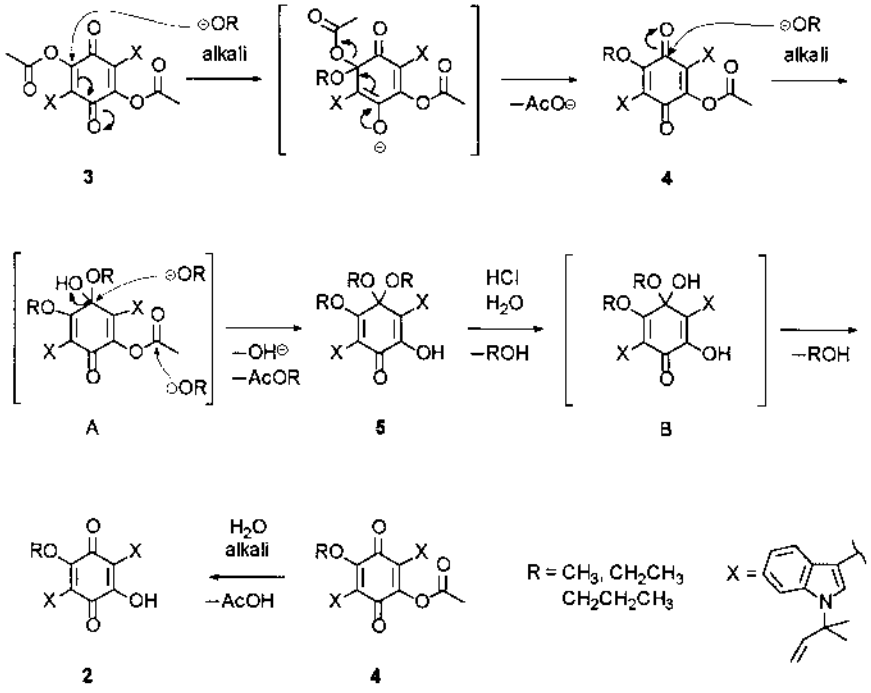
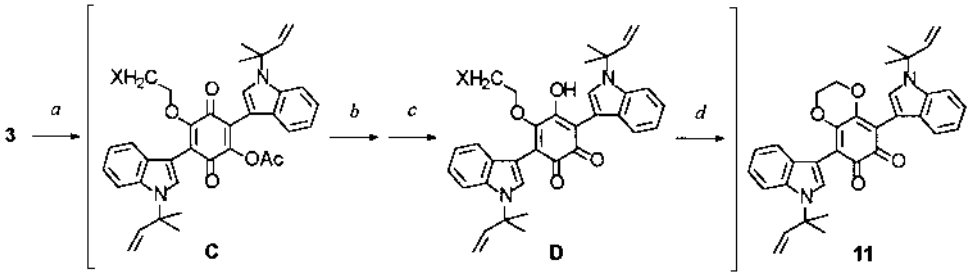


Chart 5



a) Halo-alkoxy anion addition and acetoxy anion elimination; *b*) ester bond cleavage by hydroxyl anion; *c*) tautomerization; *d*) intermolecular *O*-alkylation.

Chart 6

drolysis. In addition, it was thought that **2** was also obtained from **4** with the simple hydrolysis of the acetoxy group by the presence of H_2O.

Additionally, the novel *o*-quinone derivative of ARQ: 3,6-bis[1-(1,1-dimethyl-2-propenyl)-1*H*-indol-3-yl]-4,5-ethylenedioxy-3,5-cyclohexadiene-1,2-dione (**11**) was prepared from **3** in 67% yield by treatment with a mixture of 2-bromoethanol or 2-chloroethanol and 5% aq. $NaHCO_3$ in *N*,*N*-dimethylformamide (DMF) at 80 °C for 30 min. The proposed mechanism of this transformation is depicted in Chart 6.

Among novel derivatives (**2g**—**h** and **11**) and acetals (**5a**—**c**), acetal (**5a**) showed a weak cytotoxic effect against P388 (IC_{50}, 22.4 μM), while ARQ monoalkyl ethers (**2g**—**h**) and *o*-quinone derivative (**11**) showed potent cytotoxicity, similar to **1**. More detailed biological activities of these derivatives are now under investigation.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus MP-S3 and are uncorrected. Electron impact (EI)-, high resolution EI- (HR-EI-), FAB- and HR-FAB-MS were recorded on a JEOL JMS-700. Elemental analysis was carried out using a Perkin-Elmer 240C elemental analyzer. UV spectra were recorded on a Shimadzu UV-3000 spectrophotometer. IR spectra were recorded on a Hitachi 270-30 IR spectrometer. ^{1}H-NMR spectra were recorded on a JEOL GSX-400 (399.5 MHz). Each sample was dissolved in $CDCl_3$, chemical shifts are shown in δ values with reference to $CDCl_3$ as 7.26 ppm, and coupling constants (*J*) are expressed in hertz (Hz). Signal multiplicities are represented by s (singlet), d (doublet), t (triplet), dd (double doublet), and m (multiplet).

Materials ARQ (**1**) and ARQ monoacetate (**6**) were isolated from *Aspergillus terreus* IFO 6123.[2,11] 2,5-Diacetoxy-*p*-xyloquinone (**7**) was prepared by the method described in our previous paper.[12]

Chromatography Silica gel (SiO_2) (Wakogel C-200: Wako Pure Chemical Industries, Ltd.) or oxalic acid-impregnated silica gel (oxalic-SiO_2)[9] column chromatography was carried out with hexane–dichloromethane (CH_2Cl_2) (1 : 1→0 : 1, v/v).

Synthesis of 2,5-Bis[1-(1,1-dimethyl-2-propenyl)-1*H*-indol-3-yl]-3-alkoxy-6-hydroxy-2,5-cyclohexadiene-1,4-diones (2). General Procedure for 2a—h A mixture of **3** (0.34 mmol) and K_2CO_3 (50 mol eq) in alcohol (MeOH, EtOH, and PrOH) (20 ml) or alcohol [butanol (BuOH), pentanol (PenOH), hexanol (HexOH), 2,2,2-trifluoroethanol, and 2,2,2-trichloroethanol] (10 ml) plus DMF (1 ml) was refluxed. The reaction mixture was filtered, then the filtrate was poured into chilled 1 N HCl, the resulting precipitate was filtered off, washed with water, and dried *in vacuo*. The crude crys-

talline compound was purified by column chromatography (SiO_2). The reaction condition and yield are summarized in Table 2.

2b: Dark red needles (hexane) of mp 156—158 °C (dec.). *Anal*. Calcd for $C_{34}H_{34}N_2O_4$: C, 76.37; H, 6.41; N, 5.24, Found: C, 75.93; H, 6.50; N, 5.15. EI-MS *m/z*: 534 (M^+). HR-EI-MS *m/z*: 534.2517 (Calcd for 534.2519). IR (KBr) cm^{-1}: 3376 (OH), 1648 (C=O). UV λ_{max} (EtOH) nm (log ε): 225 (4.69), 288 (4.46), 293 (4.47), 480 (3.69). ^{1}H-NMR ($CDCl_3$) δ: 1.18 (3H, t, J=7.2), 1.83 (6H, s), 1.84 (6H, s), 4.09 (2H, q, J=7.2), 5.23 (1H, d, J=17.6), 5.26 (1H, d, J=17.6), 5.27 (1H, d, J=10.4), 5.28 (1H, d, J=10.4), 6.22 (2H, dd, J=10.4, 17.6), 7.13—7.16 (4H, m), 7.56—7.59 (3H, m), 7.60—7.63 (1H, m), 7.66 (1H, s, OH), 7.70 (1H, s), 7.77 (1H, s).

2c: Dark red needles (hexane) of mp 168—170 °C (dec.). *Anal*. Calcd for $C_{35}H_{36}N_2O_4$: C, 76.60; H, 6.62; N, 5.11. Found: C, 76.54; H, 6.70; N, 5.05. EI-MS *m/z*: 548 (M^+). HR-EI-MS *m/z*: 548.2670 (Calcd for 548.2675). IR (KBr) cm^{-1}: 3336 (OH), 1640 (C=O). UV λ_{max} (EtOH) nm (log ε): 227 (4.69), 288 (4.46), 294 (4.47), 480 (3.67). ^{1}H-NMR ($CDCl_3$) δ: 0.75 (3H, t, J=7.2), 1.51—1.58 (2H, m), 1.83 (12H, s), 3.99 (2H, t, J=7.2), 5.22 (1H, d, J=17.6), 5.26 (1H, d, J=17.6), 5.27 (1H, d, J=10.6), 5.28 (1H, d, J=10.8), 6.21 (1H, dd, J=10.6, 17.6), 6.22 (1H, dd, J=10.8, 17.6), 7.12—7.16 (4H, m), 7.57—7.59 (3H, m), 7.60—7.63 (1H, m), 7.66 (1H, s, OH), 7.68 (1H, s), 7.76 (1H, s).

2d: Dark red needles (hexane) of mp 158—160 °C (dec.). *Anal*. Calcd for $C_{36}H_{38}N_2O_4$: C, 76.83; H, 6.81; N, 4.98. Found: C, 77.00; H, 7.04; N, 4.93. EI-MS *m/z*: 562 (M^+). HR-EI-MS *m/z*: 562.2830 (Calcd for 562.2832). IR (KBr) cm^{-1}: 3352 (OH), 1648 (C=O). UV λ_{max} (EtOH) nm (log ε): 227 (4.69), 288 (4.46), 294 (4.46), 480 (3.68). ^{1}H-NMR ($CDCl_3$) δ: 0.72 (3H, t, J=7.4), 1.16—1.22 (2H, m), 1.49—1.53 (2H, m), 1.83 (12H, s), 4.02 (2H, t, J=6.4), 5.22 (1H, d, J=17.6), 5.26 (1H, d, J=17.6), 5.27 (1H, d, J=10.6), 5.28 (1H, d, J=10.6), 6.205 (1H, dd, v10.6, 17.6), 6.214 (1H, dd, J=10.6, 17.6), 7.12—7.16 (4H, m), 7.56—7.57 (3H, m), 7.61—7.63 (1H, m), 7.65 (1H, s, OH), 7.67 (1H, s), 7.77 (1H, s).

2e: Dark red needles (hexane) of mp 131—133 °C (dec.). *Anal*. Calcd for $C_{37}H_{40}N_2O_4$: C, 77.04; H, 7.00; N, 4.86. Found: C, 77.21; H, 7.06; N, 4.81. EI-MS *m/z*: 576 (M^+). HR-EI-MS *m/z*: 576.2988 (Calcd for 576.2988). IR (KBr) cm^{-1}: 3376 (OH), 1646 (C=O). UV λ_{max} (EtOH) nm (log ε): 225 (4.70), 286 (4.48), 292 (4.48), 476 (3.69). ^{1}H-NMR ($CDCl_3$) δ: 0.70—0.74 (3H, m), 1.10—1.12 (4H, m), 1.50—1.52 (2H, m), 1.83 (12H, s), 4.02 (2H, t, J=6.4), 5.22 (1H, d, J=17.6), 5.26 (1H, d, J=17.6), 5.27 (1H, d, J=10.6), 5.28 (1H, d, J=10.6), 6.206 (1H, dd, J=10.6, 17.6), 6.214 (1H, dd, J=10.6, 17.6), 7.11—7.19 (4H, m), 7.55—7.58 (3H, m), 7.61—7.63 (1H, m), 7.66 (1H, s, OH), 7.67 (1H, s), 7.76 (1H, s).

2f: Dark red needles (hexane) of mp 126—128 °C (dec.). *Anal*. Calcd for $C_{38}H_{42}N_2O_4$: C, 77.25; H, 7.17; N, 4.74. Found: C, 77.33; H, 7.36; N, 4.71. EI-MS *m/z*: 590 (M^+). HR-EI-MS *m/z*: 590.3149 (Calcd for 590.3145). IR (KBr) cm^{-1}: 3376 (OH), 1646 (C=O). UV λ_{max} (EtOH) nm (log ε): 225 (4.72), 287 (4.49), 293 (4.49), 480 (3.70). ^{1}H-NMR ($CDCl_3$) δ: 0.77 (3H, t, J=6.8), 1.04—1.16 (6H, m), 1.48—1.54 (2H, m), 1.83 (12H, s), 4.02 (2H, t, J=6.8), 5.22 (1H, d, J=17.6), 5.26 (1H, d, J=17.6), 5.27 (1H, d, J=10.6), 5.28 (1H, d, J=10.8), 6.205 (1H, dd, J=10.8, 17.6), 6.214 (1H, dd, J=10.6, 17.6), 7.13—7.15 (4H, m), 7.56—7.58 (3H, m), 7.60—7.63 (1H, m), 7.66 (1H, s, OH), 7.67 (1H, s), 7.76 (1H, s).

2g: Dark purple prisms (hexane) of mp 171—172 °C (dec.). EI-MS *m/z*: 588 (M^+). HR-EI-MS *m/z*: Calcd for $C_{34}H_{31}F_3N_2O_4$, 588.2236. Found: 588.2236. IR (KBr) cm^{-1}: 3356 (OH), 1648 (C=O). UV λ_{max} (EtOH) nm (log ε): 226 (4.67), 290 (4.48), 484 (3.67). ^{1}H-NMR ($CDCl_3$) δ: 1.82 (6H, s), 1.84 (6H, s), 4.50 (2H, q, J=8.4), 5.22 (1H, d, J=17.6), 5.26 (1H, d, J=17.6), 5.278 (1H, d, J=10.6), 5.284 (1H, d, J=11.0), 6.18 (1H, dd, J=10.6, 17.6), 6.21 (1H, dd, J=11.0, 17.6), 7.15—7.19 (4H, m), 7.55—7.59 (2H, m), 7.59 (1H, s, OH), 7.61—7.62 (2H, m), 7.75 (1H, s), 7.79 (1H, s).

2h: Dark purple prisms (hexane) of mp 195 °C (dec.). EI-MS *m/z*: 638 (M^+). HR-EI-MS *m/z*: Calcd for $C_{34}H_{31}C_{l3}N_2O_4$, 636.1349. Found: 636.1353. IR (KBr) cm^{-1}: 3364 (OH), 1646 (C=O), 782 (C-Cl). UV λ_{max} (EtOH) nm (log ε): 226 (4.63), 290 (4.37), 484 (3.48). ^{1}H-NMR ($CDCl_3$) δ: 1.82 (6H, s), 1.84 (6H, s), 4.75 (2H, s), 5.20 (1H, d, J=17.6), 5.265 (1H, d, J=17.6), 5.269 (1H, d, J=11.4), 5.28 (1H, d, J=10.6), 6.17 (1H, dd, J=10.6, 17.6), 6.22 (1H, dd, J=11.4, 17.6), 7.13—7.18 (4H, m), 7.54—7.56 (2H, m), 7.57—7.59 (1H, m), 7.61—7.63 (1H, m), 7.65 (1H, s, OH), 7.75 (1H, s), 7.79 (1H, s).

2,5-Bis[1-(1,1-dimethyl-2-propenyl)-1*H*-indol-3-yl]-3-hydroxy-6-phenoxy-2,5-cyclohexa-diene-1,4-dione (2i) Compound **3** (0.34 mmol) was treated with 5% $NaHCO_3$ (1 ml) in phenol (1 ml, at 45 °C) and DMF (1 ml) at 85 °C for 15 min. The reaction mixture was poured into chilled 1 N HCl, then the resulting precipitate was filtered off, washed with water, and dried *in vacuo*. The crude crystalline compound was purified by column chromatography (SiO_2) to give **2i** (0.19 mmol) in 56% yield. Dark purple needles (hexane) of mp 80—82 °C (dec.). *Anal*. Calcd for $C_{38}H_{34}N_2O_4$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.42; H, 5.81; N, 4.85. EI-MS *m/z*: 582 (M^+). HR-EI-MS *m/z*: 582.2519 (Calcd for 582.2523). IR (KBr) cm^{-1}: 3384 (OH), 2984, 1652 (C=O). UV λ_{max} (EtOH) nm (log ε): 276 (4.35), 293 (4.38), 490 (3.66). ^{1}H-NMR ($CDCl_3$) δ: 1.73 (6H, s), 1.79 (6H, s), 5.11 (1H, d, J=17.6), 5.22 (1H, d, J=10.6), 5.23 (1H, d, J=17.6), 5.24 (1H, d, J=10.8), 6.10 (1H, dd, J=10.6, 17.6), 6.17 (1H, dd, J=10.8, 17.6), 6.81—6.93 (5H, m), 7.13—7.17 (4H, m), 7.48—7.50 (1H, m), 7.54—7.56 (1H, m), 7.60—7.62 (1H, m), 7.62 (1H, s, OH), 7.65 (1H, s), 7.69—7.71 (1H, m), 7.76 (1H, s).

Preparation of 2,5-Bis[1-(1,1-dimethyl-2-propenyl)-1*H*-indol-3-yl]-3-acetoxy-6-alkoxy-2,5-cyclohexadiene-1,4-diones (4). **Method A, General Procedure** Compound **2** (0.05 mmol) was treated with Ac_2O–pyridine for 30 min. The reaction mixture was poured into ice water, then the resulting precipitate was filtered off, washed with water, and dried *in vacuo*. The crude crystalline compound was purified by column chromatography (SiO_2). Corresponding **4a**—**c** were obtained in quantitative yield, respectively.

Method B, General Procedure Compound **3** (0.034 mmol) was refluxed with K_2CO_3 (1 mol eq) in alcohol (MeOH, EtOH and PrOH) (30 ml). The reaction mixture was filtered, then the filtrate was poured into H_2O and extracted with hexane, the organic layer was dried over anhydrous Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography (SiO_2). The yields are described in Text.

4b: Dark red needles (hexane) of mp 167—169 °C (dec.). EI-MS *m/z*: 576 (M^+). HR-EI-MS *m/z*: 576.2619 (Calcd for $C_{36}H_{36}N_2O_5$: 576.2624). IR (KBr) cm^{-1}: 1778 ($OCOCH_3$), 1664 (C=O). UV λ_{max} (EtOH) nm (log ε): 222 (4.70), 291 (4.46), 497 (3.92). ^{1}H-NMR ($CDCl_3$) δ: 1.15 (3H, t, J=7.1), 1.825 (6H, s), 1.833 (6H, s), 2.13 (3H, s), 3.93 (2H, q, J=7.1), 5.21 (1H, d, J=17.6), 5.25 (1H, d, J=17.6), 5.27 (1H, d, J=10.6), 5.29 (1H, d, J=10.6), 6.20 (2H, dd, J=10.6, 17.6), 7.13—7.18 (4H, m), 7.54—7.60 (2H, m), 7.61—7.65 (2H, m), 7.759 (1H, s), 7.764 (1H, s).

4c: Dark red needles (hexane) of mp 134—136 °C (dec.). EI-MS *m/z*: 590 (M^+). HR-EI-MS *m/z*: 590.2781 (Calcd for $C_{37}H_{38}N_2O_5$: 590.2781). IR (KBr) cm^{-1}: 1770 ($OCOCH_3$), 1662 (C=O). UV λ_{max} (EtOH) nm (log ε): 222 (4.70), 291 (4.46), 497 (3.92). ^{1}H-NMR ($CDCl_3$) δ: 0.75 (3H, t, J=7.3), 1.51—1.54 (2H, m), 1.81(6H, s), 1.83 (6H, s), 2.13 (3H, s), 3.85 (2H, t, J=6.6), 5.20 (1H, d, J=17.6), 5.23 (1H, d, J=17.6), 5.25 (1H, d, J=10.6), 5.29 (1H, d, J=10.6), 6.19 (1H, dd, J=10.6, 17.6), 6.20 (1H, dd, J=10.6, 17.6), 7.13—7.18 (4H, m), 7.53—7.55 (1H, m), 7.57—7.64 (3H, m), 7.74 (1H, s), 7.75 (1H, s).

Preparation of 2,5-Bis[1-(1,1-dimethyl-2-propenyl)-1*H*-indol-3-yl]-3-hydroxy-1,1,6-trialkoxy-2,5-cyclohexadien-4-ones (5). General Procedure A mixture of **3** (0.034 mmol) or **4** (0.036 mmol) and K_2CO_3 (1 mol eq) in alcohol (MeOH, EtOH, PrOH) (30 ml) was refluxed. The reaction mixture was filtered, the filtrate was poured into H_2O and extracted with hexane, the organic layer was dried over anhydrous Na_2SO_4, and evaporated *in vacuo*. The residue was purified by column chromatography (SiO_2).

5a: Yellow prisms (hexane) of mp 165—166 °C (dec.). *Anal*. Calcd for $C_{35}H_{38}N_2O_5$: C, 74.18; H, 6.76; N, 4.94. Found: C, 74.17; H, 6.82; N, 4.87. EI-MS *m/z*: 566 (M^+). HR-EI-MS *m/z*: 566.2784 (Calcd for 566.2781). IR (KBr) cm^{-1}: 3248 (OH), 1638 (C=O), 1062 (acetal). UV λ_{max} (EtOH) nm (log ε): 226 (4.68), 284 (4.19), 366 (3.91). ^{1}H-NMR ($CDCl_3$) δ: 1.82 (6H, s), 1.83 (6H, s), 3.33 (6H, s), 3.59 (3H, s), 5.21 (1H, d, J=17.6), 5.264 (1H, d, J=10.6), 5.267 (1H, d, J=17.6), 5.272 (1H, d, J=10.6), 6.20 (1H, dd, J=10.6, 17.6), 6.23 (1H, dd, J=10.6, 17.6), 6.36 (1H, s, OH), 7.12—7.19 (4H, m), 7.49—7.51 (1H, m), 7.57—7.60 (2H, m), 7.66 (1H, s), 7.83—7.85 (1H, m), 7.93 (1H, s).

5b: Orange prisms (hexane) of mp 143—145 °C. FAB-MS (pos.) *m/z*: 608 (M^+). HR-FAB-MS *m/z*: Calcd for $C_{38}H_{44}N_2O_5$, 608.3250. Found: 608.3251. IR (KBr) cm^{-1}: 3272 (OH), 1644 (C=O), 1048 (acetal). UV λ_{max} (EtOH) nm (log ε): 225 (4.67), 284 (4.21), 368 (3.92). ^{1}H-NMR ($CDCl_3$) δ: 1.05 (3H, t, J=7.0), 1.15 (6H, t, J=7.0), 1.82 (6H, s), 1.84 (6H, s), 3.45—3.53 (2H, m), 3.55—3.62 (2H, m), 3.77 (2H, q, J=7.0), 5.20 (1H, d, J=17.6), 5.22 (1H, d, J=17.6), 5.27 (1H, d, J=10.6), 5.28 (1H, d, J=10.6), 6.20 (1H, dd, J=10.6, 17.6), 6.22 (1H, dd, J=10.6, 17.6), 6.45 (1H, s, OH), 7.10—7.20 (4H, m), 7.47—7.49 (1H, m), 7.56—7.58 (2H, m), 7.64 (1H, s), 7.91—7.93 (1H, m), 8.05 (1H, s).

5c: Yellow prisms (hexane) of mp 119—121 °C. FAB-MS (pos.) *m/z*: 650 (M^+). HR-FAB-MS *m/z*: Calcd for $C_{41}H_{50}N_2O_5$, 650.3720. Found: 650.3726. IR (KBr) cm^{-1}: 3416 (OH), 1646 (C=O), 1050 (acetal). UV λ_{max} (EtOH) nm (log ε): 226 (4.70), 285 (4.16), 378 (3.86). ^{1}H-NMR ($CDCl_3$) δ: 0.66 (3H, t, J=7.3), 0.73 (6H, t, J=7.3), 1.44—1.49 (2H, m), 1.51—1.56 (4H, m), 1.819 (6H, s), 1.821 (6H, s), 3.34—3.40 (2H, m), 3.47—3.52 (2H, m), 3.66 (2H, t, J=6.6), 5.19 (1H, d, J=17.2), 5.24 (1H, d, J=10.6), 5.25 (1H, d,

J=17.2), 5.29 (1H, d, J=10.6), 6.18 (1H, dd, J=10.6, 17.2), 6.22 (1H, dd, J=10.6, 17.2), 6.40 (1H, s, OH), 7.11—7.16 (4H, m), 7.48—7.50 (1H, m), 7.53—7.58 (2H, m), 7.64 (1H, s), 7.89—7.92 (1H, m), 8.03 (1H, s).

3-Hydroxy-1,1,6-trimethoxy-2,5-dimethyl-2,5-cyclohexadien-4-one (9) Compound **7** (0.060 mmol) was treated with 5% aq. $NaHCO_3$ (1 ml) in MeOH (3 ml) at room temperature for 15 min. The reaction mixture was poured into chilled water, 0.1 N HCl (4 ml) was added, then the mixture was extracted with diethyl ether. The organic layer was washed with water, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography (oxalic–SiO_2), and **9** (0.048 mmol) was obtained in 80% yield. Colorless prisms (hexane) of mp 132—134 °C (dec.). *Anal*. Calcd for $C_{11}H_{16}O_5$: C, 57.87; H, 7.07. Found : C, 57.94; H, 7.14. EI-MS *m/z*: 228 (M^+). HR-EI-MS *m/z*: 228.0996 (Calcd for 228.0998). IR (KBr) cm^{-1}: 3282 (OH), 1642 (C=O), 1020 (acetal). UV λ_{max} (EtOH) nm (log ε): 244 (4.02), 322 (3.38), 370 (3.18). ^{1}H-NMR ($CDCl_3$) δ: 1.83 (3H, s), 1.87 (3H, s), 3.10 (6H, s), 3.81 (3H, s), 6.09 (1H, s, OH).

Acid Hydrolysis of Acetal. General Procedure Compounds **5** or **9** were treated with a mixture of MeOH and 1 N HCl at room temperature for 15 min. The reaction mixture was extracted with diethyl ether. The organic layer was washed with water, dried over anhydrous Na_2SO_4 and evaporated. The residue was recrystallized from hexane, and corresponding **2** or **10** were obtained.

Preparation of 4,5-Ethylenedioxy-3,6-bis[1-(1,1-dimethyl-2-propenyl)-1*H*-indol-3-yl]-3,5-cyclohexadiene-1,2-dione (11) Compound **3** (0.059 mmol) was treated with a mixture of 2-bromoethanol (5 ml) or 2-chloroethanol (5 ml) and 5% aq. $NaHCO_3$ (5 ml) in DMF (1 ml) at 80 °C for 30 min. The reaction mixture was poured into 1 N HCl, then extracted with benzene. The organic layer was dried with anhydrous Na_2SO_4, then evaporated *in vacuo*. The residue was purified by oxalic acid-impregnated SiO_2 column chromatography. Compound **11** (0.040 mmol) was obtained in 67% yield. Dark blue needles (hexane) of mp 221—224 °C (dec.). EI-MS *m/z*: 532 (M^+). HR-EI-MS *m/z*: Calcd for $C_{34}H_{32}N_2O_4$, 532.2362. Found: 532.2359. IR (KBr) cm^{-1}: 2988, 1652 (C=O). UV λ_{max} (EtOH) nm (log ε): 226 (4.66), 298 (4.45), 680 (3.55). ^{1}H-NMR (CDCl3) δ: 1.81 (12H, s), 4.52 (4H, s), 5.26 (2H, d, J=17.2), 5.26 (2H, d, J=10.6), 6.21 (2H, dd, J=10.6, 17.2), 7.11—7.15 (4H, m), 7.43—7.45 (2H, m), 7.57—7.59 (2H, m), 7.65 (2H, s).

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