A CHEMICAL EVIDENCE OF REGIOCHEMISTRY IN THE DIELS-ALDER REACTION OF 4-OXYGENATED QUINOLINE-QUINONES WITH 1-METHOXY-3-TRIMETHYLSILYLOXY-1,3-BUTADIENES

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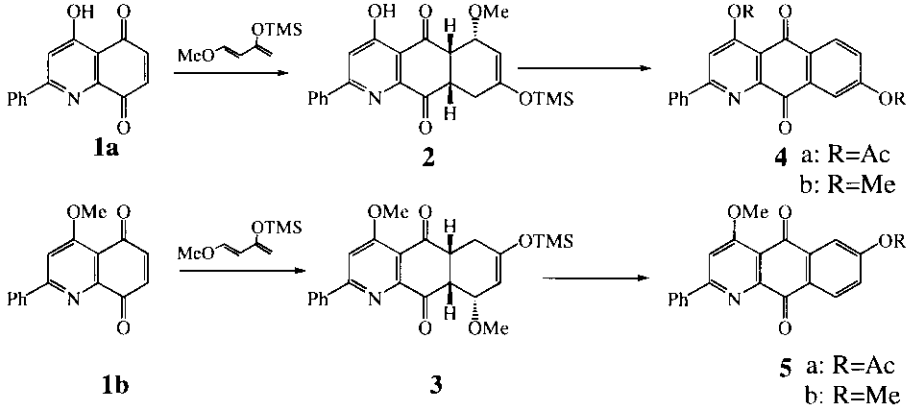
Abstract – The synthesis of four regioisomeric azaanthraquinones (**4a**, **b** and **5a**, **b**) was achieved in a regioselective manner by the Diels-Alder reaction of 4-oxygenated 6-bromo- and 7-bromoquinolinequinones (**11** and **15**) with 1-methoxy-3-trimethylsilyloxy-1,3-butadiene. The results gave a chemical evidence of the regiochemistry observed in the Diels-Alder reactions of non-halogenated 4-oxyquinolinequinones (**1a** and **1b**) which showed an inverse regioselectivity.

In our investigation about the synthesis of polycyclic nitrogen heterocycles we have discovered that the regioselectivity in the Diels-Alder (D-A) reaction of 4-oxyquinoline–5,8-dione (4-oxyquinolinequinone, **1**) with 1-methoxy-3-trimethylsilyloxy-1,3-butadiene varied depending on the structure of 4-oxy-substituents; that is, the 4-hydroxy derivative (**1a**) gave the D-A adduct (**2**), while the 4-methoxy derivative (**1b**) gave the regioisomeric adduct (**3**) in a regiospecific manner, respectively. The D-A adducts (**2**) and (**3**) were readily aromatized to give regioisomeric 4,8-dioxyganated 1-azaanthraquinone (**4**) and 4,7-dioxyganated derivative (**5**), respectively. Although their structures were well established by spectroscopic evidence

including the 2D nuclear Overhauser and exchange spectroscopy (NOESY) and the high resolution heteronuclear multiple bond correlation (HMBC) techniques, the chemical evidence about the structures was lacked. [1]



Scheme 1

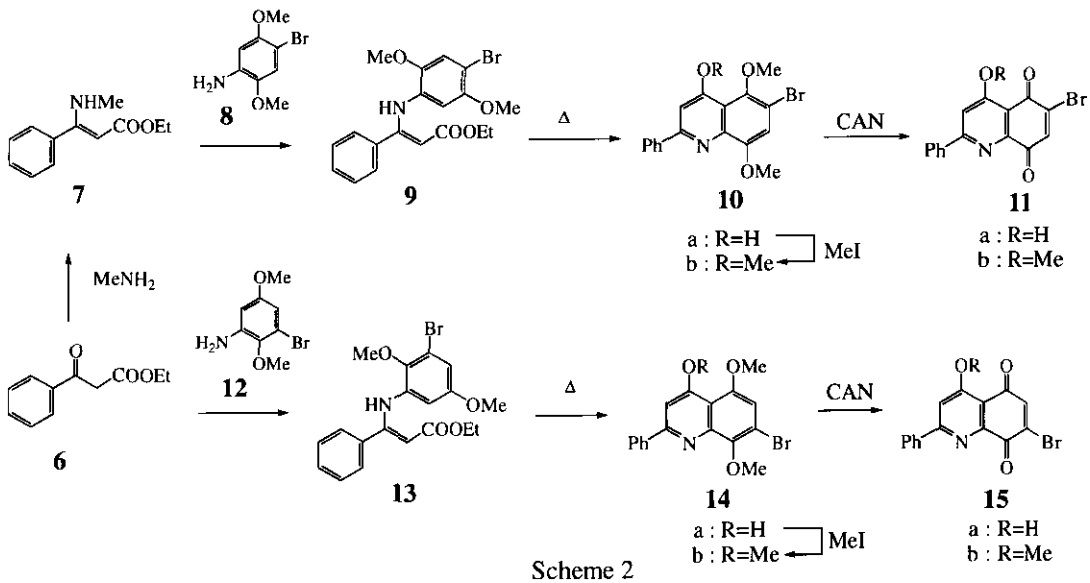
In this paper we describe the D-A reactions of 4-oxygenated 6-bromo- and 7-bromoquinolinequinones (**11** and **15**) with 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene) which should give the confirmatory evidence about the regiochemistries observed in the D-A reactions of **1a** and **1b** since the regiochemistry in the D-A reactions of halogenated quinones was well established to be determined by the position of halogen in the quinone moiety.[2] For example, P. Brassard *et al.* demonstrated by the D-A reactions of 2- and 3-chloronaphtoquinones having hydroxy and methoxy groups at the 5-position that the regiochemistry of the addition is determined by the sole position of the halogen atom and is independent of any other electronic effect including intramolecular hydrogen bonding.[3] The facts suggest that the reactions of **11** and **15** will produce the 1-azaanthraquinones (**4** and **5**) in a regioselective manner, respectively.

Preparation of Bromo-4-oxyquinolinequinones

The preparation of azadienophiles, 6-bromo-4-hydroxyquinolinequinone (**11a**) and 6-bromo-4-methoxy derivative (**11b**) was carried out as follow. The anilinoenamine (**9**) was synthesized by applying *N-N* exchange reaction which was highly effective in the amination of ketone by

aromatic amines with weak basicity.[4] The reaction of *N*-methylenamine (**7**) with 4-bromo-2,5-dimethoxyaniline (**8**)[5] in the presence of pyridinium *p*-toluenesulfonate (PPTS) under boiling $CHCl_3$ gave **9** in 93% yield. The enamine was then pyrolyzed in xylene at 300°C in a sealed tube to give the 6-bromo-4-hydroxy-5,8-dimethoxyquinoline (**10a**) in 89% yield. Methylation of **10a** with methyl iodide in the presence of a phase transfer catalyst gave the *O*-methyl derivative (**10b**) in 86% yield. Oxidation of **10a** and **10b** with cerium ammonium nitrate (CAN) gave the quinolinequinones (**11a** and **11b**) in 52% and 99% yields, respectively.

7-Bromo-4-oxyquinolinequinones (**15a** and **15b**) were synthesized by CAN oxidation of 7-bromo-4-hydroxy-5,8-dimethoxyquinoline (**14a**) and 7-bromo-4,5,8-trimethoxyquinoline (**14b**) which were also prepared in good overall yields in a similar way *via* the anilinoenamine (**13**). Although the *N*-*N* exchange reaction of **7** with 3-bromo-2,5-dimethoxyaniline (**12**)[6] gave **13** in only about 10% yield, the aniline (**12**) on reaction with ethyl benzoylacetate (**6**) in the presence of PPTS underwent the desired amination to give **13** in 82% yield.



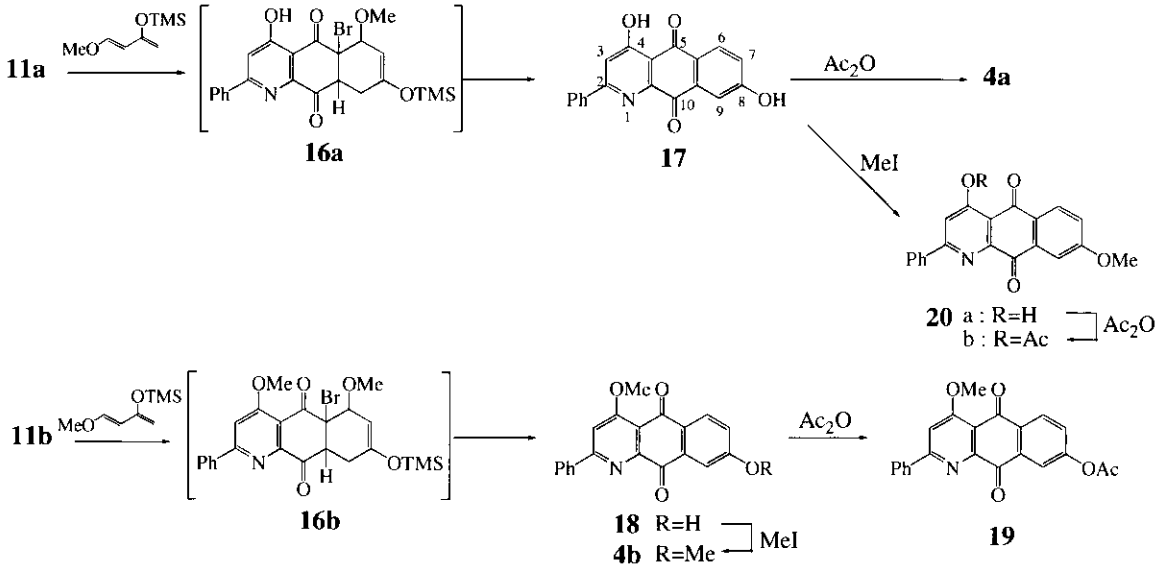
Scheme 2

Diels-Alder Reaction of 6-Bromo-4-oxyquinolinequinones (11)

D-A reaction of 6-bromo-4-hydroxyquinolinequinone (**11a**) with Danishefsky's diene was carried out on heating in benzene at 80°C for 5 min. The isolation of D-A adduct (**16a**) in a pure

form was failed because of its instability. However, the crude adduct was heated in toluene at 110°C for 1 h and purified with column chromatography to give 4,8-dihydroxy-1-azaanthraquinone (**17**), a C ring aromatized product, in 90% yield. The adduct (**17**) on acetylation with acetic anhydride in pyridine gave a 4,8-diacetoxy derivative (**4a**) in 90% yield. The diacetate (**4a**) was identical with the compound previously derived from the D-A adduct (**2**).[1] Thus, the regiochemistry of the D-A reaction of 4-hydroxyquinolinequinone (**1a**) was found to be identical with that of 6-bromo-4-hydroxyquinolinequinone (**11a**).

The D-A reaction of 6-bromo-4-methoxy derivative (**11b**) with the diene under similar conditions gave the D-A adduct (**16b**) as a crude product. The adduct could not be isolated in a pure form. Acetylation of crude **16b** caused concomitant aromatization of the C ring to give 8-acetoxy-4-methoxy-1-azaanthraquinone (**19**) in 87% yield. Treatment of **16b** with methyl iodide also caused the concomitant C ring aromatization to give the 4,8-dimethoxy-1-azaanthraquinone (**4b**) in 33% yield. This was proved to be identical with the compound derived from the D-A adduct (**2**).[1] Thus, the regiochemistry of the D-A reaction of **1a** was proved to be identical with that of 6-bromo-4-methoxy derivative (**11b**).



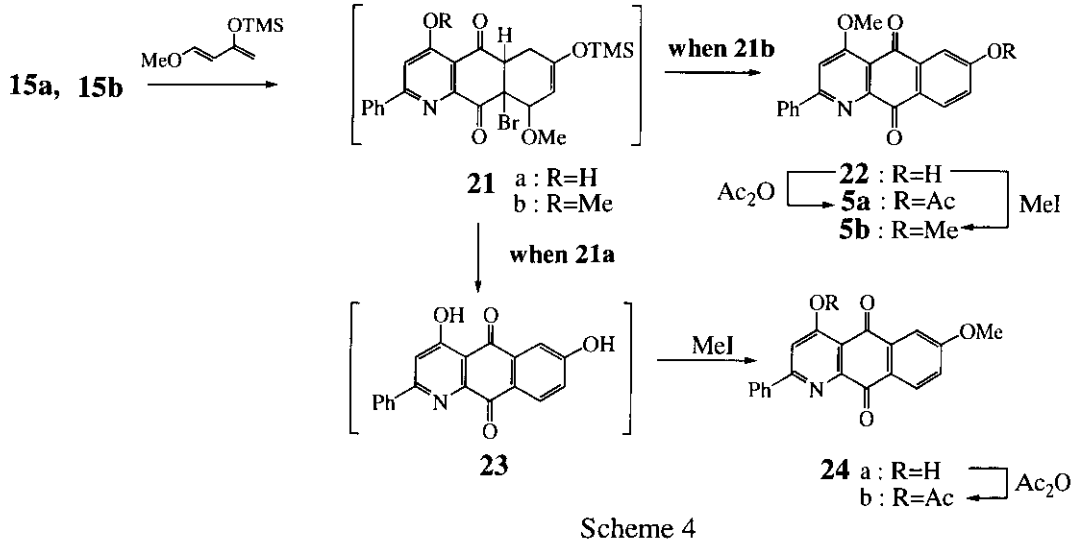
Sheme 3

Chemical correlation between D-A adducts (**16a**) and (**16b**) was obtained as follows. Treatment of **17** with methyl iodide in THF in the presence of a phase transfer catalyst gave 4-hydroxy-8-methoxy-1-azaanthraquinone (**20a**) in 85% yield, selectively. Acetylation of **20a** gave the 4-acetoxy-8-methoxy derivative (**20b**) in 94% yield. This compound was proved to be isomeric with 4-methoxy-8-acetoxy derivative (**19**) formed by acetylation of **18**. Further methylation of **20a** with methyl iodide under a more forced condition gave the 4,8-dimethoxy derivative (**4b**) in 75% yield. This transformation proved that the D-A reactions of **11a**, **11b** and **1a** with the diene proceeded with a same regiochemistry as depicted in Scheme 3.

Diels-Alder Reaction of 7-Bromo-4-oxyquinolinequinones (15)

The D-A reaction of 7-bromo-4-methoxyquinolinequinone (**15b**) with the diene was also carried out on heating in benzene at 80°C for 5 min. The adduct (**21b**) was also readily aromatized at the C ring to give **22** as a crude material. Acetylation of **22** gave 7-acetoxy-4-methoxy-1-azaanthraquinone (**5a**) in 87% yield and methylation of **22** gave 4,7-dimethoxy-1-azaanthraquinone (**5b**) in 45 % yields. The 1-azaanthraquinones (**5a** and **5b**) were identical with the compounds derived from the D-A adduct (3).

The D-A reaction of 7-bromo-4-hydroxy derivative (**15a**) with the diene under similar conditions followed by methylation of the crude D-A adduct (**21a**) gave 4-hydroxy-7-methoxy-



Scheme 4

1-azaanthraquinone (**24a**) in 81% yield. Further methylation of **24a** at 4-OH group did not proceed and the starting material was recovered. Thus, the chemical correlation between **24a** and **5b** was failed. However, acetylation of **24a** gave 4-acetoxy-7-methoxy derivative (**24b**) in 87% yield. The spectral data of **24b** were definitely different with those of other isomeric 1-azaanthraquinones, 4-OAc-8-OMe- (**20b**), 4-OMe-8-OAc- (**19**), and 4-OMe-7-OAc- (**5a**) derivatives. This fact indicated that the product is 4-OAc-7-OMe-1-azaanthraquinone (**24b**). Thus, the D-A reactions of **15a**, **15b** and **1b** were proved to proceed with a same regiochemistry.

In conclusion D-A reactions of 6-bromo- (**11a** and **11b**) and 7-bromo-4-oxyquinolinequinones (**15a** and **15b**) regioselectively proceeded with an inverse regiochemistry each other, as generally established in the D-A reactions of halogenated quinones. The results at the same time confirmed the regiochemistry observed in the D-A reaction of non-halogenated quinolinequinones (**1a** and **1b**) with the diene in a chemical mean.

EXPERIMENTAL

Unless otherwise stated, the following procedures were adopted. All melting points were measured on a Yanagimoto micro hot-stage melting point apparatus (Yanagimoto MP type) and are uncorrected. IR spectra were measured with a JASCO FT/IR-5000 as KBr disks and values are given in cm^{-1}. UV spectra were measured with a Hitachi U-3200 spectrophotometer in dioxane and values are given in λ_{max} nm (ε). NMR spectra were recorded on a JEOL JNM-α500 (^1H, 500 MHz; ^{13}C, 125 MHz) or a JNM-AL300 (^1H, 300 MHz; ^{13}C, 75 MHz) NMR spectrometer in $CDCl_3$ solution using tetramethylsilane (TMS) as an internal standard. The chemical shifts are given in δ values. Low-resolution mass spectra (LRMS) and high-resolution mass spectra (HRMS) were determined on a JEOL JMS-HX110A spectrometer at 30 eV with a direct inlet system. Elemental analyses were recorded on a Yanaco CHN-corder MT-3. For column chromatography, silica gel (Mallinkroft type 150A or Wako-gel C-200) was used. Thin layer chromatography (TLC) was performed on Merck precoated Silica-Gel 60 F254 plates. All organic extracts were washed with 5% HCl, 5% $NaHCO_3$, and water and dried over Na_2SO_4 before concentration *in vacuo*.

Preparatin of Ethyl 3-(4-bromo-2,5-dimethoxyphenylamino)-3-phenyl-2-propenoate (9)

A solution of **8** (935 mg, 4.03 mmol), **7** (1 g, 4.88 mmol.) and PPTS (1.2 g, 4.78 mmol) in $CHCl_3$ (20 mL) was refluxed for 18 h. After removal of precipitates by filtration, the filtrate was chromatographed with hexane-AcOEt (5:1) to give **9** (1.5 g, 93%) as colorless prisms from Et_2O-hexane, mp 96-98°C. IR: 3260, 1660, 1600. UV: 266 (13300), 348 (17300). ^{1}H-NMR: 1.31 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 3.20 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 4.22 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 5.03 (1H, s, 2-H), 5.77 (1H, s, 6'-H), 6.98 (1H, s, 3'-H), 7.4-7.9 (5H, m, Ph), 10.29 (1H, br s, NH). *Anal.* Calcd for $C_{19}H_{20}NO_4Br$: C, 56.17; H, 4.96; N, 3.45. Found: C, 55.94; H, 4.99; N, 3.22

Preparation of Ethyl 3-(3-bromo-2,5-dimethoxyphenylamino)-3-phenyl-2-propenoate (13)

A solution of **12** (3.3 g, 14.2 mmol), **6** (2.7 g, 14.1 mmol) and PPTS (0.7 g, 2.79 mmol) in benzene (120 mL) was refluxed for 5 h under using Dean-Stark water separator. After removal of the solvent in *vacuo*, the residue was purified by column chromatography with benzene to give **13** (4.7g, 83%) as colorless needles from Et_2O-hexane, mp 81-83°C. IR: 2836, 1595. UV: 215 (21700), 251 (13700), 329 (1700). ^{1}H-NMR: 1.31 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$), 3.30 (3H, s, 5'-OCH_3), 3.95 (3H, s, 2'-OCH_3), 4.23 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$), 5.08 (1H, s, 2-H), 5.64 (1H, d, J=3 Hz, 6'-H), 6.58 (1H, d, J=3 Hz, 4'-H), 7.37 (5H, s, Ph), 10.42 (1H, br s, NH). ^{13}C-NMR: 14.5 ($COOCH_2\underline{C}H_3$), 55.2 (5'-OCH_3), 60.0 ($COO\underline{C}H_2CH_3$), 60.8 (2'-OCH_3), 94.1 (C2), 106.0 (C6'), 111.7 (C4'), 117.0 (C3'), 127.9 (C3" and C5"), 128.8 (C2" and C6"), 130.0 (C4"), 135.6 (C1'), 135.9 (C1"), 141.7 (C2'), 155.4 (C4'), 157.1 (C3), 169.4 ($\underline{C}OOCH_2CH_3$). LRMS *m/z*: 405, 407 (M^+). *Anal.* Calcd for $C_{19}H_{20}NO_4Br$: C, 56.17; H, 4.96; N, 3.45. Found: C, 55.96; H, 5.10; N, 3.15.

Preparation of 6-Bromo-4-hydroxy-5,8-dimethoxy-2-phenylquinoline (10a)

A solution of **9** (2 g) in xylene (25 mL) was heated at 300°C for 11 h in a sealed tube under an Ar atmosphere. After removal of the solvent in *vacuo*, the residue was purified by column chromatography with benzene to give **10a** (1.6 g, 89%) as colorless prisms from $CHCl_3$-Et_2O, mp 167-169°C. IR: 1620, 1590, 1580. UV: 258 (32600), 335 (9500). ^{1}H-NMR: 3.92 (3H, s, OCH_3), 4.00 (3H, s, OCH_3), 6.48 (1H, d, J=2 Hz, 3-H), 7.15 (1H, s, 7-H), 7.5-7.6 (5H, m, Ph), 8.72 (1H, br s, NH). ^{13}C-NMR: 56.4 (OCH_3), 61.6 (OCH_3), 110.9 (C3), 114.7 (C7), 120.2 (C8a), 126.2 (C2' and C6'), 128.2 (C3' and C5'), 129.3 (C4'), 131.9 (C1'), 133.7 (C6), 143.9 (C5), 147.0 (C8), 149.4 (C2), 177.1 (C4). LRMS *m/z*: 359, 361 (M^+). *Anal.* Calcd for $C_{17}H_{14}NO_3Br$: C, 56.69; H, 3.92; N, 3.89. Found: C, 57.01; H, 4.01; N, 3.66.

Preparation of 7-Bromo-4-hydroxy-5,8-dimethoxy-2-phenylquinoline (14a)

A solution of **13** (2 g) in xylene (25 mL) was heated at 250°C for 17 h in a sealed tube under an Ar atmosphere. After removal of the solvent in *vacuo*, the residue was crystallized from $CHCl_3$-Et_2O to give 7-bromo-4-hydroxy-5,8-dimethoxy-2-phenylquinoline (**14a**) (1.54g, 86%) as

colorless needles. mp 153-155 °C. IR: 1626, 1595. UV: 270 (51200). LRMS *m/z*: 359, 361 (M^+). *Anal.* Calcd for $C_{17}H_{14}NO_3Br$: C, 56.69; H, 3.92; N, 3.89. Found: C, 56.68; H, 3.95; N, 3.75.

Methylation of 10a and 14a

A suspension of **10a** and **14a** (500 mg. 1.39 mmol), KOH (311 mg, 5.56 mmol), tetra-*n*-butylammonium bromide (TBAB) (896 mg, 2.78 mmol) and CH_3I (1.6 g, 11.27 mmol) in THF (20 mL) was stirred at rt for 16 h. The reaction mixture was filtered, and the filtrate was extracted with $CHCl_3$. The residue was purified by column chromatography with hexane-AcOEt (4:1) to give 4-methoxy derivatives (**10b**) and (**14b**), respectively.

6-Bormo-4,5,8-trimethoxy-2-phenylquinoline (10b) (447 mg, 86%). Colorless needles from $CHCl_3$-Et_2O, mp 153-154 °C. IR: 1589, 1562. UV: 270 (30800), 323 (5300). ^{1}H-NMR: 3.87 (3H, s, 4-OCH_3), 4.05 (3H, s, 8-OCH_3), 4.14 (3H, s, 5-OCH_3), 7.18 (1H, s, 3-H), 7.29 (1H, s, 7-H), 7.5-8.0 (5H, m, Ph). ^{13}C-NMR: 56.0 (8-OCH_3), 56.5 (5-OCH_3), 61.7 (4-OCH_3), 100.1 (C3), 112.7 (C7), 113.9 (C4a), 116.5 (C6), 127.5 (C2' and C6'), 128.7 (C3' and C5'), 129.4 (C4'), 139.6 (C1'), 142.1 (C5), 145.9 (C8), 152.4 (C8a), 157.7 (C2), 163.1 (C4). LRMS *m/z*: 373, 375 (M^+). HRMS *m/z* (M^+): Calcd for $C_{18}H_{16}NO_3Br$: 373.0313, 375.0292. Found: 373.0345, 375.0318.

7-Bromo-4,5,8-trimethoxy-2-phenylquinoline (14b) (454 mg, 87%). Colorless needles from $CHCl_3$-Et_2O, mp 151-152°C. IR: 1591, 1562. UV: 272 (50000). ^{1}H-NMR: 3.94 (3H, s, 4-OCH_3), 4.09 (3H, s, 5-OCH_3), 4.18 (3H, s, 8-OCH_3), 6.94 (1H, s, 3-H), 7.24 (1H, s, 6-H), 7.4-7.5 (3H, m, Ph), 8.1-8.3 (2H, m, Ph). ^{13}C-NMR: 55.8 (5-OCH_3), 56.5 (8-OCH_3), 61.6 (4-OCH_3), 98.4 (C3), 109.2 (C6), 112.5 (C7), 116.5 (C4a), 127.2 (C2' and C6'), 128.5 (C3' and C5'), 129.4 (C4'), 139.2 (C1'), 145.5 (C8a), 147.2 (C5), 152.7 (C8), 165.0 (C2), 177.1 (C4). LRMS *m/z*: 373, 375 (M^+). *Anal.* Calcd for $C_{18}H_{16}NO_3Br$: C, 57.77; H, 4.31; N, 3.74. Found: C, 57.69; H, 4.37; N, 3.55.

Preparation of 4-Hydroxy- and 4-Methoxyquinoline-5,8-diones----General procedure

CAN (3-4 mmol) in CH_3CN-H_2O (2:1) (30 mL) was added to a suspension of **10a**, **b** and **14a**, **b** (1 mmol) in CH_3CN-H_2O (2:1, 30 mL) with stirring at 0°C for 30 min. The reaction mixture was extracted with $CHCl_3$. The residue was purified by column chromatography with $CHCl_3$ to give **11a,b** and **15a,b** respectively.

6-Bromo-4-hydroxy-2-phenylquinoline-5,8-dione (11a) (52%). Yellow needles from Et_2O, mp 199-201°C. IR: 1678, 1651. UV: 281 (30000), 381 (3000). ^{1}H-NMR: 7.34-7.53 (3H, m, Ph), 7.57 (1H, s, 3-H), 7.63 (1H, s, 7-H), 8.1-8.2 (2H, m, Ph), 11.64 (1H, s, OH). ^{13}C-NMR: 112.3 (C3), 112.9 (C4a), 127.8 (C3' and C5'), 129.0 (C2' and C6'), 131.2 (C4'), 136.9 (C1'), 138.5 (C6), 140.9 (C7), 148.4 (C2), 163.9 (C8a), 167.5 (C4), 180.2 (C8), 183.1 (C5). LRMS *m/z*: 329, 331 (M^+). HRMS *m/z* (M^+): Calcd for $C_{15}H_8NO_3Br$: 328.9684, 330.9664. Found: 328.9674, 330.9647.

6-Bromo-4-methoxy-2-phenylquinoline-5,8-dione (11b) (99%). Yellow needles from $CHCl_3$-

Et_2O, mp 218-220°C. IR: 1673, 1576. UV: 277 (27000), 358 (1500). ^{1}H-NMR: 4.16 (3H, s, 4-OCH_3), 7.52 (1H, s, 3-H), 7.58 (1H, s, 7-H), 7.5-8.2 (5H, m, Ph). ^{13}C-NMR: 56.7 (4-OCH_3), 106.9 (C3), 116.2 (C4a), 127.6 (C2' and C6'), 129.0 (C3' and C5'), 131.0 (C4'), 137.3 (C6), 138.3 (C7), 141.6 (C1'), 149.3 (C2), 163.2 (C8a), 166.6 (C4), 175.8 (C8), 180.8 (C5). LRMS *m/z*: 343, 345 (M^+). HRMS *m/z* (M^+): Calcd for $C_{16}H_{12}NO_3Br$: 343

7-Bromo-4-hydroxy-2-phenylquinoline-5,8-dione (15a) (66%). Yellow needles from $CHCl_3$-Et_2O, mp 165-167°C (decomp). IR: 1686, 1638. UV: 277 (23300), 369 (4300). ^{1}H-NMR: 7.54 (1H, s, 3-H), 7.57 (1H, s, 6-H), 7.5-8.2 (5H, m, Ph). LRMS *m/z*: 329, 331 (M^+). HRMS *m/z* (M^+): Calcd for $C_{15}H_8NO_3Br$: 328.9684, 330.9666. Found: 328.9659, 330.9379.

7-Bromo-4-methoxy-2-phenylquinoline-5,8-dione (15b) (99%). Yellow needles from $CHCl_3$-Et_2O, mp 218-220°C. IR: 1688, 1659. UV: 276 (23300), 364 (1500). ^{1}H-NMR: 4.15 (3H, s, 4-OCH_3), 7.43 (1H, s, 3-H), 7.48 (1H, s, 6-H), 7.5-8.1 (5H, m, Ph). LRMS *m/z*: 343, 345 (M^+). *Anal.* Calcd for $C_{18}H_{16}NO_3Br$: C, 55.84; H, 2.93; N, 4.07. Found: C, 55.55; H, 3.03; N, 4.26.

Diels-Alder Reaction of 11a with 1-Methoxy-3-trimethylsilyoxy-1,3-butadiene

A solution of **11a** (150 mg, 0.45 mmol) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (313 mg, 1.82 mmol) in benzene (10 mL) was heated at 80°C for 30 min in a sealed tube under an Ar atmosphere. After removal of the solvent *in vacuo*, the product was washed with Et_2O. The residue was suspended in toluene (20 mL) and heated at 110°C in the presence of small amount of silica gel in a sealed tube for 2 h. After removal of the solvent *in vcauo*, the residue was purified by column chromatography with benzene-$CHCl_3$ (1:1) to give 4,8-dihydroxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**17**) (130 mg, 90%) as yellow needles from $CHCl_3$-Et_2O, mp 295-298°C. IR: 1673, 1638, 1591, 1562. UV: 288 (45400), 389 (5200). ^{1}H-NMR: 7.25 (1H, dd, *J*=9, 3 Hz, 7-H), 7.43 (1H, s, 3-H), 7.5-7.6 (3H, m, Ph-H), 7.69 (1H, d, *J*=3 Hz, 9-H), 8.1-8.2 (2H, m, Ph), 8.21 (1H, d, *J*=9 Hz, 6-H). LRMS *m/z*: 317 (M^+). HRMS *m/z* (M^+): Calcd for $C_{19}H_{11}NO_4$: 317.0686. Found: 317.0686

Acetylation of 17

17 (130 mg. 0.41 mmol) was treated with acetic anhydride-pyridine (1:2, 3 mL) at rt for 16 h. The reaction mixture was extracted with $CHCl_3$. The residue was purified by column chromatography with AcOEt:hexane (1:2) to give 4,8-diacetoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**4a**) (135 mg, 90%) as yellow needles from $CHCl_3$-Et_2O, mp 226-228 °C.[1]

Methylation of 17

17 (100 mg, 0.315 mmol) in THF (20 mL) was treated with CH_3I (386 mg, 2.65 mmol), KOH (90 mg, 1.61 mmol) and TBAB (203 mg, 0.63 mmol) at rt for 16 h. After removal of insoluble precipitates by filtration, the filtrate was extracted with $CHCl_3$. The residue was crystallized

from $CHCl_3$-Et_2O to give 4-hydroxy-8-methoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**20a**) (89 mg, 85%) as yellow needles, mp 229-231°C. IR: 1688, 1640, 1593. UV: 221 (25500), 287 (49800), 389 (5800). ^{1}H-NMR: 4.02 (3H, s, 8-OCH_3), 7.3-7.5 (3H, m, Ph-H), 7.49 (1H, dd, *J*=7, 3 Hz, 7-H), 7.56 (1H, s, 3-H), 7.80 (1H, d, *J*=3 Hz, 9-H), 8.1-8.2 (2H, m, Ph-H), 8.26 (1H, d, *J*=7 Hz, 6-H). LRMS *m/z*: 331 (M^+). HRMS *m/z* (M^+): Calcd for $C_{20}H_{13}NO_4$: 331.0845. Found: 331.0866.

Methylation of 20a

20a (85 mg, 0.26 mmol mg) in THF (20 mL) was treated with CH_3I (excess), KOH (120 mg, 2.14 mmol) and TBAB (167 mg, 0.52 mmol) at rt for 48 h. After removal of insoluble precipitates by filtration, the filtrate was extracted with $CHCl_3$. The residue was crystallized from $CHCl_3$-Et_2O to give 4,8-dimethoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**4b**) (66 mg, 75%) as yellow needles from $CHCl_3$-Et_2O, mp 274-275°C.[1]

Acetylation of 20a

20a (20 mg, 0.06 mmol) was treated with acetic anhydride-pyridine (1:2, 3 mL) at rt for 17 h. The reaction mixture was extracted with $CHCl_3$. The residue was crystallized from $CHCl_3$-Et_2O to give 4-acetoxy-8-methoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**20b**) (21 mg, 94%) as yellow prisms, mp 218-220°C. IR: 1773, 1690, 1659. UV: 224 (25000), 279 (32800). ^{1}H-NMR: 2.54 (3H, s, 4-$OCOCH_3$), 4.00 (3H, s, 8-OCH_3), 7.29 (1H, dd, *J*=8, 3 Hz, 7-H), 7.5-7.6 (3H, m, Ph), 7.75 (1H, s, 3-H), 7.76 (1H, d, *J*=3 Hz, 9-H), 8.1-8.2 (2H, m, Ph), 8.18 (1H, d, *J*=8 Hz, 6-H). LRMS *m/z*: 373 (M^+). HRMS *m/z* (M^+): Calcd for $C_{22}H_{15}NO_5$: 373.0950. Found: 373.0971.

Diels-Alder Reaction of 11b with 1-Methoxy-3-trimethylsilyoxy-1,3-butadiene

i) A solution of **11b** (200 mg, 0.58 mmol) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (400 mg, 2.32 mmol) in benzene (20 mL) was heated at 80°C for 30 min in a sealed tube under Ar atmosphere. After removal of the solvent *in vacuo*, the product was washed with Et_2O and treated with acetic anhydride-pyridine (1:2, 3 mL) at rt for 16 h. The reaction mixture was extracted with $CHCl_3$. The residue was crystallized from $CHCl_3$-Et_2O to give 8-acetoxy-4-methoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**19**) (153 mg, 87%) as yellow needles, mp 235-238°C. IR: 1752, 1717, 1692. UV: 216 (13200), 233 (31200), 239 (20600), 278 (43000). ^{1}H-NMR: 2.38 (3H, s, 8-$OCOCH_3$), 4.19 (3H, s, 4-OCH_3), 7.51-7.53 (3H, m, Ph-H), 7.54 (1H, dd, *J*=8, 2 Hz, 7-H), 7.57 (1H, s, 3-H), 8.01 (1H, d, *J*=2 Hz, 9-H), 8.16-8.17 (2H, m, Ph-H), 8.31 (1H, d, *J*=8 Hz, 6-H). ^{13}C-NMR: 21.1 (8-$OCOCH_3$), 56.8 (4-OCH_3), 107.3 (C3), 118.6 (C4a), 120.0 (C9), 127.8 (C2' and C6'), 128.0 (C7), 129.0 (C3' and C5'), 129.3 (C4'), 130.8 (C6), 131.7 (C9a), 134.0 (C5a), 137.8 (C1'), 151.3 (C8), 154.9 (C10a), 163.2 (C2), 167.3 (C8-$OCOCH_3$), 168.6 (C4), 181.08 (C5), 181.14 (C10). LRMS *m/z*: 373 (M^+). *Anal.* Calcd for $C_{22}H_{15}NO_5$: C, 70.77; H, 4.05; N, 3.75. Found: C, 70.51; H, 4.23; N, 3.50.

ii) The product obtained from D-A reaction of **11b** (100 mg, 0.29 mmol) was treated with CH_3I (165 mg, 1.16 mmol) and K_2CO_3 (160 mg, 1.16 mmol) in DMF (3 mL) at rt for 40 h. The reaction mixture was extracted with $CHCl_3$. The residue was purified by column chromatography with AcOEt-hexane (1:3) to give 4,8-dimethoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**4b**) (37 mg, 33%).

Diels-Alder Reaction of 15b with 1-Methoxy-3-trimethylsilyoxy-1,3-butadiene

i) A solution of **15b** (40 mg, 0.12 mmol) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (80 mg, 0.47 mmol) in benzene (2 mL) was heated at 80°C for 5 min in a sealed tube under an Ar atmosphere. After removal of the solvent *in vacuo*, the product was washed with Et_2O and treated with acetic anhydride-pyridine (1:2, 3 mL) at rt for 16 h. The reaction mixture was extracted with $CHCl_3$. The residue was crystallized from $CHCl_3$-Et_2O to give 7-acetoxy-4-methoxy-2-phenylbenzo[*g*]quinoline- 5,10-dione (**5a**) (35 mg, 87%) as yellow needles, mp 233-234 °C.[1]

ii) The product obtained from D-A reaction of **15b** (90 mg, 0.26 mmol) was treated with CH_3I (165 mg, 1.16 mmol) and K_2CO_3 (160 mg, 1.16 mmol) in DMF (3 mL) at rt for 17 h. The reaction mixture was extracted with $CHCl_3$. The residue was purified by column chromatography with AcOEt-hexane (1:3) to give 4,7-dimethoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**5b**) 42 mg (45%) as yellow needles from $CHCl_3$-Et_2O, mp 245-248 °C.[1]

Diels-Alder Reaction 15a with 1-Methoxy-3-trimethylsilyoxy-1,3-butadiene

A solution of **15a** (100 mg, 0.3 mmol) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (209 mg, 1.21 mmol) in benzene (5 mL) was heated at 80°C for 5 min in a sealed tube under an Ar atmosphere. After removal of the solvent *in vacuo*, the product was washed with Et_2O. The product in THF (60 mL) was treated with CH_3I (344 mg, 2.24 mmol), KOH (80 mg, 1.42 mmol) and TBAB (195 mg, 0.6 mmol) at rt for 17 h. The reaction mixture was extracted with $CHCl_3$. The residue was purified by column chromatography with AcOEt-hexane (1:3) to give 4-hydoxy-7-methoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**24a**) (81 mg, 81%) as yellow needles from $CHCl_3$-MeOH, mp 243-246°C. IR: 1676, 1638. UV: 285 (38700), 346 (11200). ^{1}H-NMR: 4.01 (3H, s, 7-OCH_3), 7.32 (1H, dd, J=9, 3 Hz, 8-H), 7.3-7.6 (3H, m, Ph), 7.56 (1H, s, 3-H), 7.72 (1H, d, J=3 Hz, 6-H), 8.1-8.2 (2H, m, Ph), 8.34 (1H, d, J=9 Hz, 9-H). ^{13}C-NMR: 56.1 (7-OCH_3), 110.1 (C3), 112.5 (C6), 115.7 (C4a), 121.6 (C8), 127.6 (C9a), 128.28 (C2' and C6'), 128.34 (C5a), 129.2 (C1'), 129.3 (C3' and C5'), 130.6 (C4'), 131.1 (C9), 135.1 (C10a), 138.1 (C2), 151.0 (C7), 164.8 (C4), 180.0 (C5), 180.2 (C10). LRMS *m/z*: 331 (M^+). HRMS *m/z* (M^+): Calcd for $C_{20}H_{13}NO_4$: 331.0845. Found: 331.0891.

Acethylation of 24a

24a (30 mg, 0.09 mmol) was treated with acetic anhydride-pyridine (1:2, 3 mL) at rt for 16 h. The reaction mixture was extracted with $CHCl_3$. The residue was crystallized from $CHCl_3$-Et_2O to give 4-acetoxy-7-methoxy-2-phenylbenzo[*g*]quinoline-5,10-dione (**24b**) (26 mg, 87%) as yellow needles, mp 188-193°C. IR: 1773, 1684, 1671. UV: 277 (29600), 309 (31000). ^{1}H-NMR: 2.55 (3H, s, 4-OCOCH_3), 3.99 (3H, s, 7-OCH_3), 7.29 (1H, dd, *J*=8, 3 Hz, 8-H), 7.65 (1H, d, *J*=3 Hz, 6-H), 7.74 (1H, s, 3-H), 8.32 (1H, d, *J*=8 Hz, 9-H), 7.5-7.6 (3H, m, Ph), 8.2-8.3 (2H, m, Ph). ^{13}C-NMR: 21.3 (4-OCO$\underline{C}H_3$), 56.0 (7-OCH_3), 109.8 (C6), 118.9 (C3), 121.3 (C4a), 121.6 (C8), 126.5 (C9a), 127.8 (C2' and C6'), 129.1 (C3' and C5'), 130.2 (C9), 131.2 (C4'), 135.6 (C5a), 136.8 (C1'), 151.2 (C10a), 158.5 (C2), 163.6 (C4), 164.8 (C7), 168.5 (4-O$\underline{C}OCH_3$), 179.8 (C5), 181.6 (C10). LRMS *m/z*: 373 (M^+). HRMS *m/z* (M^+): Calcd for $C_{22}H_{15}NO_5$: 373.0948. Found: 373.0941.

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