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Regioselective Synthesis and Photooxygenations of Furonaphthopyrones Starting from 2,7-Naphthalenediol

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Abstract: Three angular furonaphthopyrones **4**, **9**, **12** were regioselectively synthesized starting from 2,7-naphthalenediol in three steps, respectively. An easy separation of Pechmann condensation products **1** and **2** of 2, 7-naphthalenediol with ethyl acetoacetate was described. The photooxygenations of **4**, **12** were investigated and a hydroperoxide **18** was isolated and fully characterized.

INTRODUCTION

Owing to their ability to intercalate into nucleic acids and photoreact with pyrimidines,[1] furocoumarins such as psoralens have very strong photobiological effects. For this reason, they are widely used in the photochemotherapy (PUVA-therapy) of hyperproliferatives skin diseases,[2] as photochemical reagents for the investigation of nucleic acid structure and function,[3] and as light-activated pesticides.[4] More recently, they are also utilized in the treatment of human immunodeficiency disease (AIDS).[5] Although PUVA-therapy proves to be very effective, some undiserable side effects are present such as a persistant erythema,[6] genotoxicity,[7] phototoxicity and a possible risk of skin cancer,[8] which may be attributed to furocoumarin interstrand crosslinks with DNA rather than to monofunctional adducts.[9] To enhance the photobinding properties and reduce side effects, a wide range of structural modifications of psoralens have been attempted.[10]

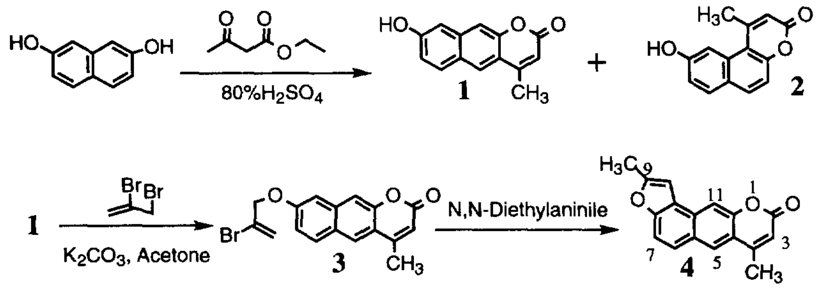
In the course of our work concerning access to new monofunctional analogous of psoralens, we recently described the synthesis, crystal structure and DNA intercalation of furonaphthopyrones and their sulfur analogous, which were expected to decrease the toxicity, and have photophysical and photobiological properties superior to furocoumarins by incorporating an additional benzene ring between active double bonds of the α-pyrone and the furan moities.[11] The differences of photobiological and mutagenic activities between psoralens and angelicins[12] indicate that the geometries of active double bonds of α-pyrone and the furan moieties play crucial role in their properties. We report here the synthesis of several furonaphthopyrones with new skeleton structure and potentially interesting photobiological features. Since it has been reported that furocomarins serve as photosensitizers for molecular oxygen[13] and themselves react with the *in situ* generated singlet oxygen$(^1O_2)$ to give biologically active products,[14] we have also investigated the photooxygenations of the novel furonaphthopyrones **4** and **12**.

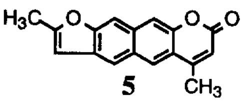
RESULTS AND DISCUSSION

The Pechmann condensation[15] of 2,7-naphthalenediol with ethyl acetoacetate in 80% H_2SO_4 afforded the regioselective isomers **1** and **2** with a ratio of 3:2 and in 71% total yield. Although this reaction has been investigated,[16] the separation of these two isomers failed because of their poor solubilities in general solvents and extreme similarity of polarity. We have sucessfully separated these two isomers by means of adjusting the pH value of their aq solution and recrystallisation from acetic acid. The ratio of two isomers was slightly dependent on the reaction temperature. This successful separation will be valuable to extend the studies on naphthopyrones.[17]

Hydroxynaphthopyrone **1** or **2** readily reacted with 2,3-dibromopropene in the presence of K_2CO_3 to give the corresponding ether intermediates **3** and **6**. Naphthopyrone **3** was refluxed in N,N-diethylaniline to give **4** exclusively in moderate yield without its regioisomer **5** (Scheme 1), which was in line with the fact that the Claisen rearrangement of (β-allyloxy)naphthalenes occurred exclusively to the adjacent α position.[18] In contrast, **6** was refluxed in N,N-diethylaniline to yield very complex products without the expected furonaphthopyrone **7**. This is probably because **7** was unstable.[19]

Scheme 1





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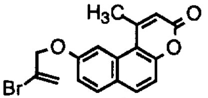

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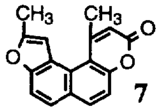

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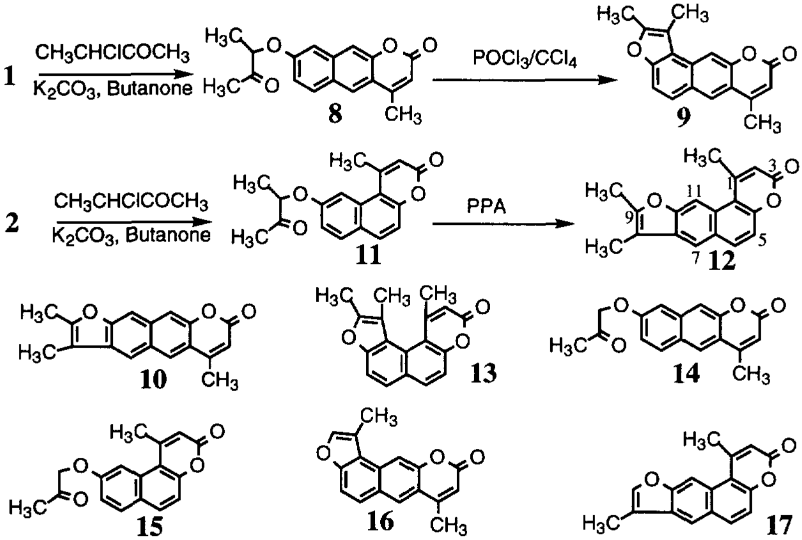
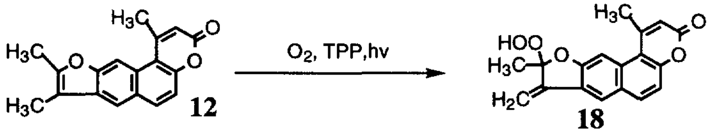
Reaction of **1** and **2** with 3-chloro-2-butanone in the presence of K_2CO_3 gave compounds **8** and **11**. The dehydration and cyclization of **8** in presence of $POCl_3$ produced **9** as the major product in high yield; another product was detected by TLC and could be the regioisomer **10** but this material was not characterised(Scheme 2). A mixture of **11** and polyphosphoric acid was refluxed to give furonaphthopyrone **12** in high yield. Another isomer was detected by TLC, which could be isomer **13**. However, **13** was unstable to isolation and purification. On the other hand, naphthopyrone **14** or **15**, prepared from the reaction of **1** and **2** with chloroacetone, was converted into corresponding furonaphthopyrone **16** or **17** in the presence of $POCl_3$/or PPA in very low yield .

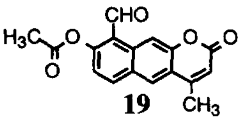
Scheme 2



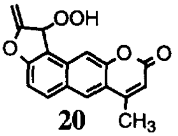
The photooxygenations of two new furonaphthopyrones were investigated (Scheme 3). The photooxygenation of **12** in methylene chloride and tetraphenyl-porphine (TPP) as sensitizer at -30 to -10°C gave the stable allyl hydroperoxide **18** whose structure was fully characterized. However, the photooxygenation of **4** using the same conditions yielded complicated products. The ^1H NMR and MS spectra showed that **19** was the major product and **20** was not formed.

Scheme 3





19



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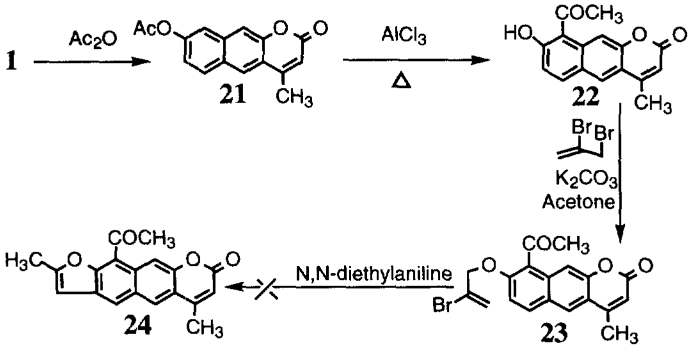
Our efforts have also focused on the synthesis of linear furonaphthopyrones by the route shown in Scheme 4. Unfortunately, we were unsuccessful. **1** was refluxed in acetic anhydride to give ester **21**. The Fries rearrangement of **21** catalyzed by $AlCl_3$ afforded **22**. Compound **23**, easily obtained through the etherification of **22**, was refluxed to give a complex mixture of products and the desirable Claisen rearrangement product **24** was not obtained.

Scheme 4



In conclusion, a practical and well thought out experimental procedure has been developed for production of biologically useful naphthopyrones from commercially available 2,7-naphthalenediol. The process has afforded efficient synthesis of angular furonaphthopyrones **4**, **9** and **12**, which may serve as novel monofunctional analogs of furocoumarins. Furthermore, the photooxygenations of compounds **4** and **12** has been investigated.

EXPERIMENTAL SECTION

General. Melting points were taken on a digital melting point apparatus WRS-1 made in Shanghai and uncorrected. Infrared spectra were recorded on a Nicolet FT IR-20sx or Spectrometor 7650 made in Shanghai, mass spectra on a Hitachi M 80 or HP5989A, ^{1}H NMR on a Bruker AM-300 or Brucker DRX-400 using $CDCl_3$ or TMS as internal standard. Combustion analysis for elemental composition was carried out on an Italy MOD.1106 analyzer run by the analysis center of the East China University of Science and Technology. Absorption spectra were measured in absolute ethanol on a Shimadlu UV-265, fluorescence spectra on a Perkin Elmer LS 50. Commercial reagents and solvents were purchased from standard chemical suppliers and used without further purification, 2,3-dibromopropene was prepared according to the literature procedure.[20]

4-Methyl-8-hydroxylnaphtho[2,3-b]pyran-2-one (1) and 1-methyl-9-hydroxylnaphtho[2,1-b]pyran-3-one (2). To a mixture of 16g of 2,7-naphthalenediol and 32 mL of ethyl acetoacetate was added 120 mL of 80% H_2SO_4 dropwise at 0°C. The mixture was stirred for 24h at room temperature and after the addition of 400 mL ice/water filtered, washed with water and dried to give a crude mixture of **1** and **2**. The filter cake was dissolved in aq 10% NaOH and the insoluble material was filtered. To the filtrate was added conc. HCl until pH value was 1 to 2. The solid was collected by filtration, washed with water, dried and recrytallized from acetic acid to give 9.7g of **1**. Crude **2** was obtained from the filtrate after standing overnight. After filtration and recrystallization from acetic acid, 6.5g of **2** was obtained. The total yield of two isomers was 71.5%. **1**: ^{1}H NMR(DMSO-d_6, 300MHz) δ 2.48(d, J=1.1Hz, 3H, 4-CH_3 overlapped by DMSO-d_6), 6.34(d, J=1.1Hz, 1H, 3-H), 7.12(dd, J_{AX}=8.9Hz, J_{AB}=2.2Hz, 1H, 7-H), 7.17(s, 1H, 9-H), 7.61(s, 1H, 10-H), 7.95(d, J_{AX}=8.9Hz, 1H, 6-H), 8.27(s, 1H, 5-H), 10.17(s, 1H, OH). MS(EI, 70ev), m/z(%): 227(19.3)[M+1], 226(100)[M], 198(52.5), 197(48.2). IR(KBr): 3400~3100(OH), 1690, 1625, 1571, 1485, 1454, 1442, 1340, 1240, 1188, 1146, 1068, 900, 872cm^{-1}. UV(ethanol) $\lambda_{max,nm}$(logε) 232(4.534), 280(4.112), 289(4.136), 356(4.059); Fl(ethanol) λ_{max}=477nm. **2**: ^{1}H NMR (DMSO-d_6, 300MHz) δ 2.86(s, 3H, 1-CH_3), 6.41(s, 1H, 2-H), 7.14(dd, J_{AX}= 8.7Hz, J_{AB}=2.0Hz, 1H, 8-H), 7.27(d, J=8.9Hz, 1H, 5-H), 7.90(d, J=8.7Hz, 1H, 7-H), 8.01(s, 1H, 10-H), 8.03(d, J=8.9Hz, 1H, 6-H), 10.11(s, 1H, OH). MS (EI, 70eV), m/z(%): 227(15.9)[M+1], 226(96.4)[M], 225(12.2), 209(14.6), 199(100), 197(50.4). UV(ethanol) $\lambda_{max,nm}$(logε) 236(4.617), 357(3.985); Fl(ethanol) λ_{max}=456nm.

4-Methyl-8-(2'-bromoallyloxy)-naphtho[2,3-b]pyran-2-one (3). also as a general procedure for synthesis of ether intermediates. A mixture of 0.693g (3.07mmol) of **1**, 1.280g of anhydrous K_2CO_3 and 1.530g of 2,3-dibromopropene in 50mL of dry acetone was refluxed for 9h. Inorganic salts was filtered and the filtrate was concentrated to *ca* 15mL. After the addition of 100 mL water, the solid was collected by filtration and recrystallized from methanol to give 0.568g of **3** as white solid in 53.7% yield. m.p.170.4 ~ 170.5°C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.54(d, J=1.0Hz, 3H, 4-CH_3), 4.80(d, J=1.4Hz, 2H, 2'-CH_2-), 5.75(dd, J=1.0Hz, J=2.0Hz, 1H, =CH_2), 6.07(d, J=1.8Hz, 1H, =CH_2), 6.31(d, J=1.0Hz, 1H, 3-H), 7.13(d, J_{AB}=2.5Hz, 1H, 9-H), 7.21(dd, J_{AX}=9.0Hz, J_{AX}=2.5Hz, 1H, 7-H), 7.60(s, 1H, 10-H), 7.86(d, J_{AX}=9.0Hz, 1H, 6-H), 8.02(s, 1H, 5-H). MS, m/z(%): 347(1.6) [M+2], 345(1.8)[M], 346(5.7), 344(5.7), 266(100)[M-Br], 197(36.6), 169(32.9). UV(ethanol) $\lambda_{max,nm}$(logε) 235 (5.023), 274(4.661), 285(4.665), 342(4.498); Fl(ethanol) λ_{max}=459nm. Anal. Calcd for $C_{17}H_{13}BrO_3$: C,59.15; H,3.80. Found: C,59.10; H,3.80.

2H-4,9-Dimethylfuro[2',3':7,8]naphtho[2,3-b]pyran-2-one (4). A mixture of 0.300g (0.87mmol) of **3** and 7mL N,N-diethylaniline was refluxed for 29h and cooled. The solid was collected, washed with10% HCl and water, and dried. The crude product was subject to TLC using a mixture of ethyl acetate and petroleum ether as eluent, and a yellow band was collected to give 94mg of **4** in 37.6% yield. m.p.245.7 ~ 245.9°C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.57(d, J=0.9Hz, 3H, 4-CH_3), 2.58(s, 3H, 9-CH_3), 6.33(d, J= 0.9 Hz, 1H, 3-H), 6.86(s, 1H, 10-H), 7.61(d, J=8.9Hz, 1H, 7-H), 7.72(d, J=8.9Hz, 1H, 6-H), 7.88(s, 1H, 11-H), 8.15 (s, 1H, 5-H). ^{13}C NMR($CDCl_3$, 100MHz) δ 14.24, 18.77, 102.00, 109.12, 112.57, 115.00, 118.34, 123.71, 124.46, 125.73, 126.93, 129.23, 150.64, 152.19, 152.96, 155.40, 160.92. MS, m/z(%), 264(100) [M], 236(22.4) [M-CO]. UV(ethanol) $\lambda_{max,nm}$(logε) 230(4.348), 287(4.458) (sh), 293(4.552), 329(3.872)(sh), 338(3.907); Fl(ethanol) λ_{max}=503nm. Anal. Calcd. for $C_{17}H_{12}O_3$: C,77.26; H,4.58. Found: C,77.16; H,4.44.

1-Methyl-9-(2'-bromoallyloxy)-naphtho[2,1-b]pyran-3-one(6). m.p.115.7 ~ 116.6°C. ^{1}H NMR($CDCl_3$, 300MHz) δ 2.92(s, 3H, 1-CH_3), 4.81(t, J=1.2Hz and 1.5Hz, 2H, 2'-CH_2-), 5.74(d, J=1.0Hz and 1.1Hz, 1H, =CH_2), 6.03(d, J=2.0Hz, 1H, = CH_2), 6.36(d, J=0.8Hz, 1H, 2-H), 7.24(dd, J_{AX}=9.0Hz, J_{AB}=2.3Hz, 1H, 8-H), 7.35(d, J=8.8Hz, 1H, 5-H), 7.85(d, J_{XA}=9.0Hz, 1H, 7-H), 7.90(d, J=8.8Hz, 1H, 6-H), 7.98(d, J_{AB}=2.3Hz, 1H, 10-H). MS(EI, 70eV) m/z: 347(5.7)[M+2], 345(6.4)[M], 346(26.8), 344(27.0), 266(19.4), 265(100), 237(25.1), 225(12.8), 197(80.5). UV(ethanol) $\lambda_{max,nm}$ (logε) 242(4.812), 275(4.078), 345(4.249); Fl(ethanol) λ_{max}=432nm. Anal. Cacld. for $C_{17}H_{13}BrO_3$: C,59.15; H,3.80. Found: C,59.14; H,3.81.

4-methyl-8-[(2'-oxobutan-3'-yl)oxy]naphtho[2,3-b]pyran-2-one (8). mp 167.2 ~ 167.4°C. ^{1}H NMR($CDCl_3$, 300MHz) δ 1.52(d, J=6.9Hz, 3H, 2'-CH_3), 2.14(s, 3H, $COCH_3$), 2.44(d, J=0.9Hz, 3H, 4-CH_3), 4.73(q, J=6.9Hz, 1H, 2'-H), 6.21(s, 1H, 3-H), 6.90(d, J_{BA}=2.4Hz, 1H, 9-H), 7.11(dd, J_{AX}=9.0Hz, J_{AB}=2.4Hz, 1H, 7-H), 7.46(s, 1H, 10-H), 7.78(d, J_{XA}=9.0Hz, 1H, 6-H), 7.92(s, 1H, 5-H). MS (EI, 70eV) m/z(%): 297 (28)[M+1], 296(100)[M], 253(90.0). IR(KBr): 3080, 3002, 2920, 1720, 1646, 1490, 1388, 1372, 1240, 1195, 1112, 892, 810cm^{-1}. UV(ethanol) $\lambda_{max,nm}$(logε) 275(4.303), 315(4.322), 342(4.216); Fl(ethanol) λ_{max}=464nm. Anal. Calcd for $C_{18}H_{16}O_4$: C,72.96; 5.44. Found: C,72.87; H,5.45.

2H-4,9,10-Trimethylfuro[2',3':7,8]naphtho[2,3-b]pyran-2-one (9). To a solution of 0.75g (2.53mmol) of **8** in 20mL of CCl_4 was added 15mL $POCl_3$ dropwise at room temperature. The mixture was refluxed for 5h and cooled to room temperature, and after the addition of 200mL of ice/water, the solid material was collected by filtration. After purification by column chromatography using petroleum/ethyl acetate (3:1) as eluent, 0.359g of **9** as yellow solid was obtained in 50.9% yield. R_f=0.421, m.p.287.6 ~ 288.1°C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.42(s, 3H, 10-CH_3), 2.48(s, 3H, 9-CH_3), 2.50(d, J=0.9Hz, 3H, 4-CH_3), 6.27(d, J=0.9Hz, 1H, 3-H), 7.51(d, J=8.9Hz, 1H, 7-H), 7.64(d, J=8.9Hz, 1H, 6-H), 8.09(s, 1H, 11-H), 8.16(s, 1H, 5-H). MS(EI, 70eV) m/z: 279(20.0)[M+1], 278(100)[M]. IR(KBr): 1710, 1628, 1472, 1440, 1406, 1390, 1280, 1210, 890cm^{-1}. Anal. Calcd. for $C_{18}H_{14}O_3$: C,77.68; H,5.07. Found: C,77.52; H,5.06.

1-Methyl-9-[(2'-oxobutan-3'-yl)oxy]naphtho[2,3-b]pyran-2-one(11). mp 189.3 ~ 189.4°C. ^{1}H NMR(CDCl$_3$, 300MHz) δ 1.61(d, J=6.8Hz, 3H, 2'-CH$_3$), 2.18(s, 3H, COCH$_3$), 2.84(s, 3H, 1-CH$_3$), 4.75(q, J=6.8Hz, 1H, 2'-H), 6.34(s, 1H, 2-H), 7.20(dd, J_{AX}=8.9Hz, J_{AB}=2.3Hz, 1H, 8-H), 7.34(d, J=8.8Hz, H, 5-H), 7.80(d, J_{BA}=2.3Hz, 1H, 10-H), 7.84(d, J_{XA}=8.9Hz, 1H, 7-H), 7.89(d, J= 8.8Hz, 1H, 6-H). MS(EI, 70eV): 297(14.4)[M+1], 296(65.0)[M], 253(100), 225(12.4). IR(KBr): 1720(br), 1630, 1556, 1520, 1434, 1370, 1230, 1220, 854, 842cm^{-1}. UV(ethanol) $\lambda_{max,nm}$(logε) 235(4.625), 269(3.952)(sh), 344(4.121); Fl(ethanol) λ_{max}=441nm. Anal. Calcd. for $C_{18}H_{16}O_4$: C,72.96; H,5.44. Found: C,72.90; H,5.40.

3H-1,8,9-Trimethylfuro[3',2':6,7]naphtho[2,1-b]pyran-3-one (12). A mixture of 0.523g (1.77mmol) of **11** and 20 mL of polyphosphuric acid was stirred for 4h at 140°C and cooled to room temperature. To the reaction mixture was added 150 mL of ice/water and stirred for 5 min. The solid material was collected by filtration, washed, dried, and purified by column chromatography using petroleum/ethyl acetate (3:1) to give 0.371g of crude product. After further purification by TLC, 0.226g of **12** as yellow in 46% was obtained. m.p. 228.4 ~ 228.5°C. ^{1}H NMR(CDCl$_3$, 300MHz) δ 2.26(s, 3H, 8-CH$_3$), 2.47(s, 3H, 9-CH$_3$), 2.98(s, 3H, 1-CH$_3$), 6.37(s, 1H, 2-H), 7.39(d, J=9.1Hz, 1H, 5-H), 7.88(s, 1H, 11-H), 8.05(d, J=9.1Hz, 1H, 6-H), 8.54(s, 1H, 7-H)ppm. ^{13}C NMR(CDCl$_3$, 100MHz) δ 7.95, 12.13, 26.47, 104.76, 109.19, 114.36, 115.82, 115.86, 118.07, 118.11, 127.02, 127.92, 130.57, 133.96, 153.75, 154.30, 160.60, 175.58. MS(EI, 70eV) m/z(%): 279(21.2)[M+1], 278(100)[M], 250(67.4). IR(KBr): 2930, 2860, 1720, 1650, 1525, 1456, 1432, 1382, 1364, 1276, 1202, 1176, 1060, 924, 875, 850cm^{-1}. UV(ethanol) $\lambda_{max,nm}$(logε) 202(4.132), 240(4.515), 301(4.356), 340(3.958), 368(3.884); Fl(ethanol) λ_{max}=462nm. Anal. Calcd. for $C_{18}H_{14}O_3$: C,77.68; H,5.07. Found: C,77.78; H,5.08.

4-Methyl-8-[(2'-oxopropan-3'-yl)oxy]naphtho[2,3-b]pyran-2-one(14). m.p. 195.2 ~ 197.2°C. ^{1}H NMR (CDCl$_3$, 300MHz) δ 2.35(s, 3H, COCH$_3$), 2.54(d, J=1.0Hz, 3H, 4-CH$_3$), 4.72(s, 2H, 2'-H), 6.31(d, J=1.0Hz, 1H, 3-H), 7.02(d, J_{BA}=2.4Hz, 1H, 9-H), 7.25(dd, J_{AX}=9.1Hz, J_{AB}= 2.4Hz, 1H, 7-H), 7.58(s, 1H, 10-H), 7.88(d, J_{XA}=9.1Hz, 1H, 6-H), 8.03(s, 1H, 5-H). MS(EI, 70eV) m/e: 283(26.6)[M+1], 282(100)[M], 239(61.5), 211(39.5), 209(39.4). UV(ethanol) $\lambda_{max,nm}$(logε) 233(4.775), 276(4.345), 285(4.375), 342(4.244); Fl(ethanol) λ_{max}=463nm. Anal. Calcd. for $C_{17}H_{14}O_4$: C,72.33; H,5.00. Found: C,72.10; H,4.98.

1-Methyl-9-[(2'-oxopropan-3'-yl)oxy]naphtho[2,1-b]pyran-2-one(15). m.p. 175.6 ~ 176.2°C. ^{1}H NMR (CDCl$_3$, 300MHz) δ 2.34(s, 3H, COCH$_3$), 2.88(s, 3H, 1-CH$_3$), 4.70(s, 2H, 2'-CH$_2$-), 6.35(s, 1H, 2-H), 7.23(dd, J_{AX}=8.8Hz, J_{AB}=2.2Hz, 1H, 8-H), 7.35(d, JXA=8.8Hz, 1H, 7-H), 7.86(d, J=9.1Hz, 1H, 5-H), 7.88(d, J_{BA}=2.2Hz, 1H, 10-H), 7.90(d, J=9.1Hz, 1H, 6-H). MS(EI, 70eV), m/z(%): 283(27.9)[M+1], 282 (100)[M], 254(16.1), 239(17.9). UV(ethanol) $\lambda_{max,nm}$(logε) 246(4.852), 268(3.922)(sh), 346(4.112); Fl(ethanol) λ_{max}=431nm. Anal. Calcd for $C_{17}H_{14}O_4$:

C,72.33; H,5.00. Found: C,72.40; H,5.01.

3H-8,9-Dihydro-9-hydroperoxy-9-methyl-8-methylenefuro[3',2':6,7]naphtho[2,1-b] pyran-3-one (18). A solution of 50mg (0.18mmol) of **12** and 5mg tetraphenylporphine(TPP) in 40ml of CH_2Cl_2 was irradiated externally by means of a sodium lamp (100W) at -10 to -20°C for 90min while passing a continuous slow stream of dry oxygen gas through the solution. After the removal of the solvent and recrystallization from a mixture of $CHCl_3$ and petroleum ether, 11mg of **18** was obtained in 19.7% yield. m.p.145~146°C. ^{1}H NMR($CDCl_3$, 300MHz) δ 1.79(s, 3H, 10-CH_3), 2.89(s, 3H, 1-CH_3), 5.56(s, 1H, =CH), 6.01(s, 1H, =CH), 6.33(s, 1H, 2-H), 7.31(d, J=8.8Hz, 1H, 5-H), 7.89(d, J=8.8Hz, 1H, 6-H), 7.93(s, 1H, 11-H), 7.99(s, 1H, OOH), 8.57(s, 1H, 7-H). MS (EI, 70eV), m/z(%): 310(6.2)[M], 292(24.5) [M-H_2O], 268(100), 225(45.0). IR(Nujol): 3388 (OOH), 1722(sh), 1703(sh), 1639, 1554, 1164, 1078, 958, 891cm^{-1}. HRMS, Calcd. for $C_{18}H_{14}O_5$: 310.08412, Found: 310.0841.

8-Acetyloxy-4-methylnaphtho[2,3-b]pyran-2-one (21). A solution of 2.001g (8.85mmol) of **1** in 50ml of acetic anhydride was refluxed for 3h, cooled and poured into 400ml of water. After filtration, washing with water, drying and recrystalization from acetic acid, 1.672g of **21** as pale needles was obtained in 70.5% yield. m.p. 208.7 ~ 209.5°C. ^{1}H NMR($CDCl_3$, 300MHz) δ2.37(s, 3H, $COCH_3$), 2.54(s, 3H, 4-CH_3), 6.35(s, 1H, 3-H), 7.26(dd, J_{AX}=9.0Hz, J_{AB}=1.6Hz, 1H, 7-H), 7.60(d, J_{BA}=1.6Hz, 1H, 9-H), 7.66(s, 1H, 10-H), 7.90(d, J_{XA}= 9.0Hz, 1H, 6-H), 8.08(s, 1H, 5-H). MS(EI, 70eV), m/z(%): 268(86.1)[M], 226(48.3)[M-$H_2C=C=O$], 199(100). IR(KBr): 1758, 1722, 1649, 1636(sh), 1492, 1431, 1389, 1370, 1236, 1145, 1076, 1020, 946, 920, 885cm^{-1}. UV(ethanol) $\lambda_{max,nm}$(logε) 231(4.575), 266(4.456), 275(4.457), 323(4.243); Fl(ethanol) λ_{max}=458nm. Anal. Calcd. for $C_{16}H_{12}O_4$: C,71.64; H,4.51. Found: C,71.69; H,4.54.

9-Acetyl-4-methyl-8-hydroxylnaphtho[2,3-b]pyran-2-one (22). A mixture of 0.33g (1.23mmol) of **21** and 0.68g of dry $AlCl_3$ was rapidly heated to 120°C, then slowly to 170°C kept warm for 2h at this temperature, and cooled. After addition of some crushed ice and 10ml of 1:1 hydrochloric acid in ice bath, the reaction mixture was stirred for 2min at 100°C, cooled, and filtered to give pale solid, which was subject to column chromatograph using a mixture of methylene chloride and petroleum ether (1:1) as eluent, 100mg of **22** was obtained as orange solid in 30.4% yield. R_f =0.125, m.p.279.8 ~ 280.1°C. ^{1}H NMR (DMSO-d_6, 300MHz): δ2.52(s, 3H, 4-CH_3 , overlapped by the peak of DMSO-d_6), 2.63(s, 1H, 3H, $COCH_3$), 6.39(s, 1H, 3-H), 7.27(d, J=9.0Hz, 1H, 7-H), 7.64(s, 1H, 10-H), 8.09(d, J=9.0Hz, 1H, 6-H), 8.35(s, 1H, 5-H), 11.04(s, 1H, 8-OH). MS(EI, 70eV) m/z(%): 268(51.5)[M], 253(100)[M-CH_3]. IR(KBr): 3010-3400(OH), 1720, 1680, 1632, 1570, 1476,1442,1350, 1250, 1205, 1080, 1040, 898, 860cm^{-1}. UV(ethanol) $\lambda_{max,nm}$(logε) 228(4.390), 257(4.157)(sh), 292(4.104), 348(4.018). Anal. Calcd. for

$C_{16}H_{12}O_4$: C,71.64; H,4.51. Found: C,71.94; H,4.56.

4-Methyl-8-(2'-bromoallyloxyl)-9-acetylnaphtho[2,3-b]pyran-2-one(23). m.p. 207.5 ~ 207.9°C. ^{1}H NMR($CDCl_3$, 400MHz) δ 2.52(d, J=1.2Hz, 3H, 4-CH_3), 2.71(s, 3H, $COCH_3$), 4.85(t, J=1.3Hz, 2H, 2'-CH_2-), 5.75(m, 1H, =CH), 6.02(m, 1H, =CH), 6.31(d, J=1.2Hz, 1H, 3-H), 7.21(d, J=9.1Hz, 1H, 7-H), 7.66(s, 1H, 10-H), 7.97(d, J=9.1Hz, 1H, 6-H), 8.03(s, 1H, 5-H). MS(EI, 70eV), m/z(%): 388(16.1)[M], 386(15.8), [M], 307(17.9)[M-Br], 266 (100). IR(KBr): 1758, 1722, 1649, 1636(sh), 1492, 1431, 1389, 1370, 1236, 1145, 1076, 1020, 946, 920, 885cm^{-1}. Anal. Cald. for $C_{19}H_{15}BrO_4$: C,58.93; H,3.90. Found: C,58.70; H,3.78.

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