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Efficient Synthesis of Dihydrofuroquinolinones and Furoquinolinones by Silver(I)/Celite Promoted Oxidative Cycloaddition

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Abstract—A new synthesis of dihydrofuroquinolinones and furoquinolinones is achieved from 4-hydroxy-2-quinolones and a variety of olefins in the presence of Ag_2CO_3/Celite in moderate yields. The new method has been applied to the synthesis of the pseudoisodictamnine.

The dihydrofuroquinolinone and furoquinolinone alkaloids are widely distributed in nature.[1] They are primarily isolated from Rutaceae species as an angularly and linearly fused structure (Fig. 1). They are reported to have various biological activities such as antimicrobial, antimalarial, insecticidal, antineoplastic, antidiuretic, antiarrhythmic and sedative,[2] and members are also used as traditional medicines in China.[3] This wide range of biological properties has stimulated interest in the synthesis of dihydrofuroquinolinone and furoquinolinone derivatives. A number of synthetic approaches to dihydrofuroquinolinones and furoquinolinones have been well reported.[4] However, the previous work with many steps and low yields, as well as the difficulty in controlling regiochemistry of the linear and angular adduct, has prompted our research for better synthesis.

We have recently reported that Ag_2CO_3/Celite (Fétizon reagent) is a simple and convenient reagent for synthesis of dihydrofuran formation.[5] This reagent also seemed

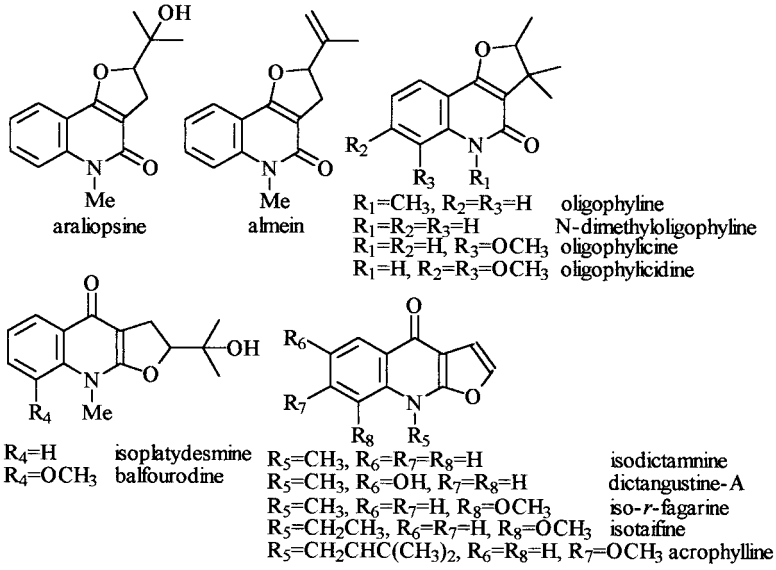

Figure 1.

Keywords: dihydrofuroquinolinones; furoquinolinones; pseudoisodictamnine.
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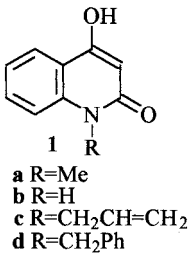
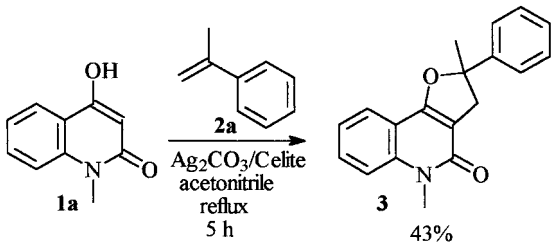


Figure 2.



Scheme 1.

ideal for the preparation of biologically interesting dihydrofuroquinolinone and furoquinolinone derivatives. We describe here the efficient synthesis of dihydrofuroquinolinone and furoquinolinone derivatives starting from 4-hydroxy-2-quinolones and a variety of olefins in the presence of Ag_2CO_3/Celite.

Two equivalents of Ag_2CO_3/Celite are used for the completion of these reactions. The starting material, 4-hydroxy-2-quinolone (**1a**), is commercially available. Materials **1b**–**1d** were readily prepared from isatoic anhydride by the Coppola method in 50, 70 and 77% yields, respectively (Fig. 2).[6]

Table 1. Reaction of 4-hydroxy-2-quinolones and olefins

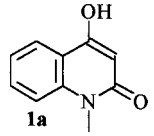
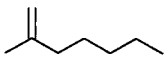
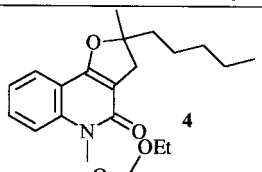
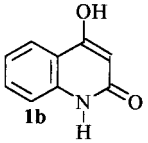
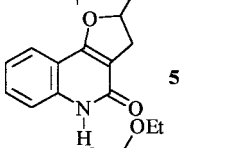
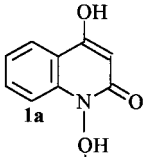
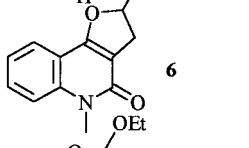
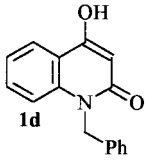
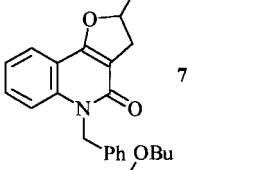
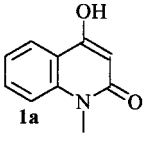
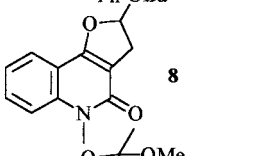
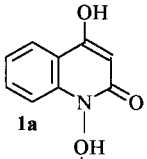
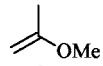
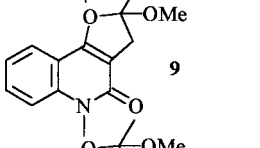
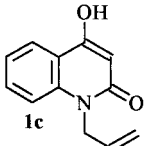
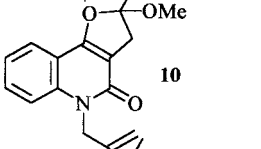
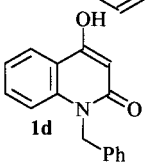
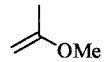
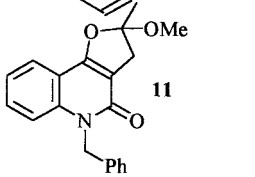
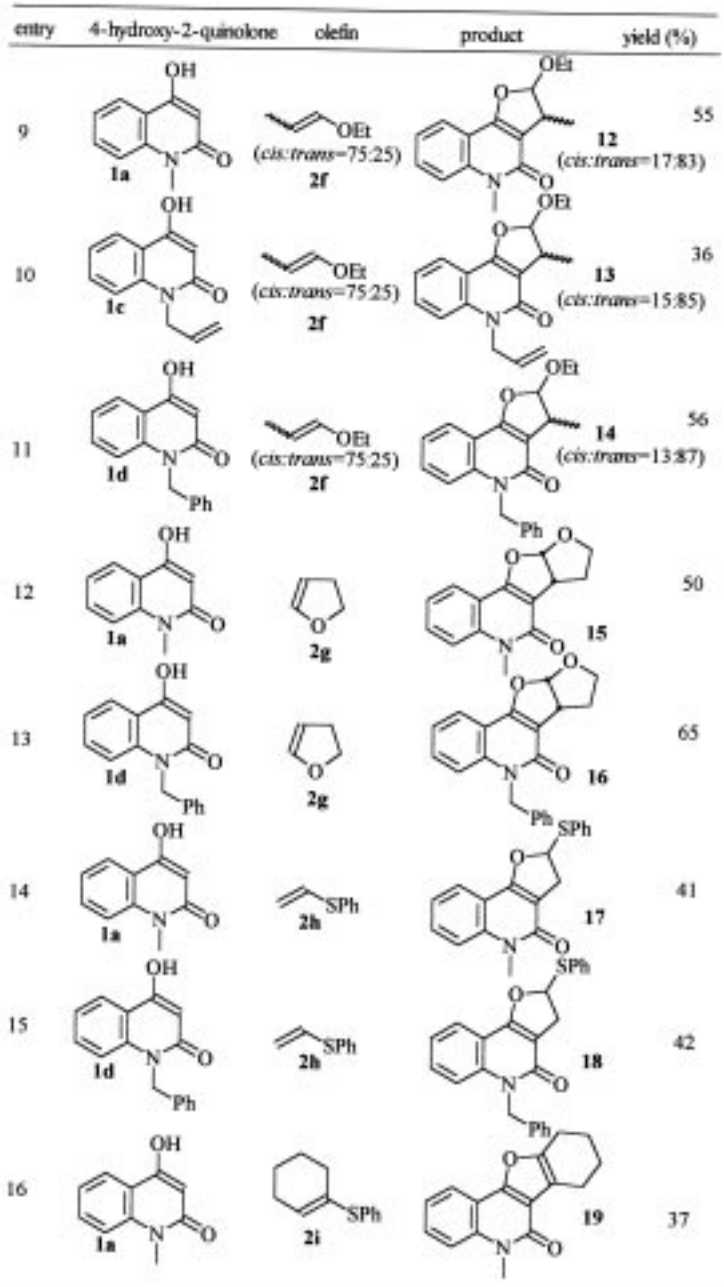
entry	4-hydroxy-2-quinolone	olefin	product	yield (%)
1	 **1a**	 **2b**	 **4**	41
2	 **1b**	 **2c**	 **5**	30
3	 **1a**	 **2c**	 **6**	40
4	 **1d**	 **2c**	 **7**	49
5	 **1a**	 **2d**	 **8**	45
6	 **1a**	 **2e**	 **9**	64
7	 **1c**	 **2e**	 **10**	54
8	 **1d**	 **2e**	 **11**	78

Table 1 (*continued*)

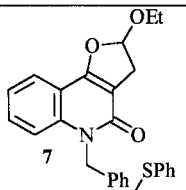
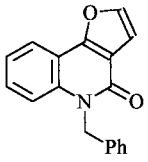
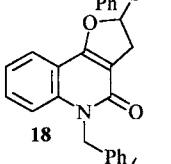
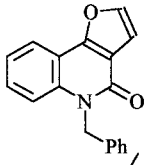
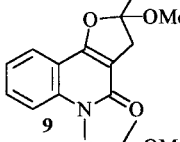
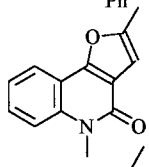
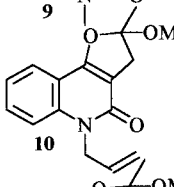
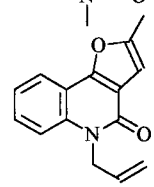
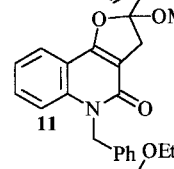
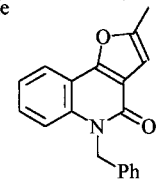
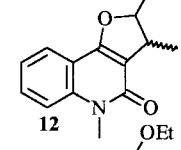
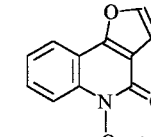
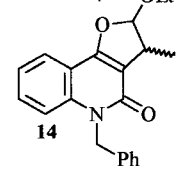
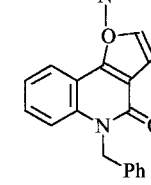


Treatment of **1a** with α-methylstyrene in refluxing acetonitrile for 5 h afforded dihydrofuroquinolinone **3** in 43% yield (Scheme 1). The assignment of **3** is confirmed by ^{1}H NMR analysis of the expected chemical shifts and geminal coupling constants associated with the methylene group of the dihydrofuran ring. In this reaction, only a single product was seen and no angular regioisomer was found.

Similarly, other results are summarized in Table 1. Reaction of **1a** with 2-methyl-1-heptene (**2b**) afforded the expected dihydrofuroquinolinone **4** in 41% yield. When ethyl vinyl ether (**2c**), butyl vinyl ether (**2d**) and 2-methoxypropene (**2e**) were used, dihydrofuroquinolinones **5**–**11** were produced in 30–78% yields (Table 1, entries 2–8). By employing ethyl-1-propenyl ether (**2f**) in a 3:1 mixture of the *cis* and *trans*-isomer, both *cis* and *trans* products **12**–**14** were obtained as inseparable mixtures (Table 1, entries 9–11). The assignment of the *cis* and *trans* stereochemistry was easily defined by observation of chemical shifts and the coupling constants; the acetal methine proton of the *cis*-isomer **12** appeared at δ 5.90 (7.3 Hz) and that of the *trans*-isomer **12** at δ 5.52 (2.2 Hz). The ratio is also calculated from ^{1}H NMR spectrum.

Additionally, these reactions provide a rapid synthetic route toward interesing polyheterocyclic compounds. For example, reactions of **1a** and **1d** with dihydrofuran (**2g**) afforded the polycyclic adducts **15** and **16** in 50 and 65% yields, respectively (Table 1, entries 12–13). The structures of **15** and **16** are also assigned as *cis*-compounds by analysis of the vicinal coupling constant and by the analogy with the earlier reported paper.[7] The acetal methine proton of **15**

Table 2. Synthesis of furoquinolinones

entry	dihydrofuroquinolinone	furoquinolinone	method	yield (%)
1		 **25**	a	40
2		 **25**	b	67
3		 **26**	a	92
4		 **27**	a	98
5		 **28**	a	97
6		 **29**	a	80
7		 **30**	a	50

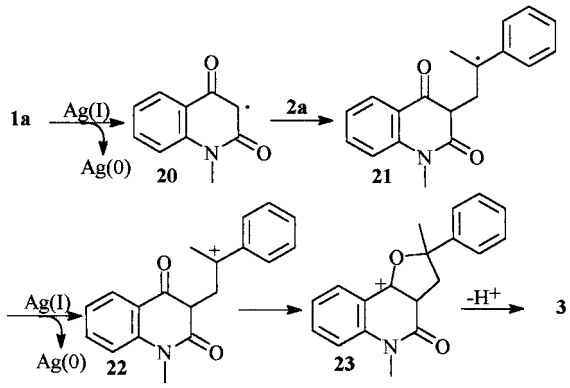
appeared as a doublet at δ 6.52 (5.8 Hz) and that of **16** as a doublet at δ 6.54 (5.8 Hz).

In order to extend the utility of this methodology, reactions of **1a** and **1d** were tested with vinyl sulfides. Reaction of **1a** and **1d** with vinyl sulfide **2h** gave the expected dihydrofuroquinolinone **17**and **18** in 41 and 42% yields, respectively. However, treatment of **1a** with cyclic vinyl sulfide **2i** afforded an unexpected product, **19** (37%), as a single compound without any trace of the expected dihydrofuran formation. The structure of **19** is confirmed by analysis of the expected chemical shifts associated with the two methylene group of allylic position and by HRMS. This result provides a concise synthetic entry into furoquinolinone as a one-step reaction.

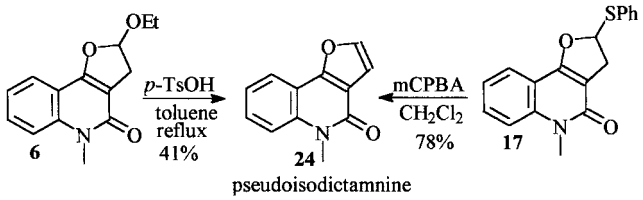
Although the exact mechanism of the reaction is still not clear, it is best described as shown in Scheme 2. The starting material **1a** is first oxidized by 1 equiv. of Ag(I) to generate the α-oxoalkyl radical **20**, which then attacks olefin **2a** to give the radical adduct **21**. The adduct **21** now undergoes fast oxidation by another 1 equiv. of Ag(I) to a carbocation **22**. Cyclization of the carbocation **22** furnishes intermediate **23**, which finally undergoes elimination to give **3**. However, the formation of **19** probably seems to proceed via cycloaddition and followed by elimination of the sulfide.

Next, conversion of dihydrofuroquinolinones to furoquinolinones was investigated. The conversions were carried out both by acid-catalyzed reaction (method A) and by mCPBA oxidation (method B) as shown in Scheme 3. Treatment of dihydrofuroquinolinone **6** with *p*-toluenesulfonic acid in toluene at reflux for 2 h afforded pseudoisodictamnine **24** in 41% yield. Although thermal equilibration of linear isodictamnine and angular pseudoisodictamnine has been reported, in this case, no linear natural isodictamnine was detected.[8] As another method for synthesis of furoquinolinone derivatives, dihydrofuroquinolinones were treated with mCPBA. For example, reaction of **17** with mCPBA at room temperature for 24 h in methylene chloride also afforded pseudoisodictamnine **24** in 78% yield as a one step reaction without any isolation of the intermediate sulfoxide. The other similar results are collected in Table 2. In entries 3–5, furoquinolinone derivatives **26**–**28** were obtained in high yields. Interestingly, both stereoisomer of *cis* and *trans* of entries 6 and 7 were readily transformed into furoquinolinones **29** and **30** in 80 and 50% yields, respectively.

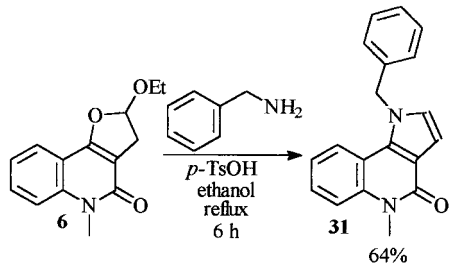
Finally, we turned our attention into the synthesis of biologically interesting systems. When **6** was treated with benzyl amine in the presence of *p*-TsOH at reflux in ethanol for 6 h, pyrroloquinolinone **31** was obtained in 64% yield (Scheme 4). Importantly, these types of pyrroloquinolinone derivatives are widely used as a key intermediate to



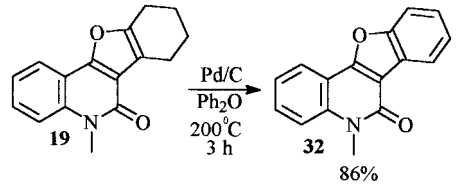
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

synthesize potassium-competitive inhibitors of the gastric (H^+/K^+)-ATPase.[9] On the other hand, when **19** was treated with Pd/C in phenyl ether at 200°C for 3 h, biologically interesting benzofuroquinolinone **32** was also produced in 86% yield (Scheme 5).

In summary, silver(I)/Celite mediated oxidative cycloaddition of 1,3-dicarbonyl compound to olefins is described. The method provides a convenient and efficient synthesis of biologically interesting dihydrofuroquinolinones, furoquinolinones and pyrroloquinolinone. The new method has been also applied to the synthesis of pseudoisodictamine.

Experimental

All experiments were carried out under a nitrogen atmosphere. Merck precoated silica gel plates (Art. 5554) with fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). Melting points were determined with microcover glasses on a Fisher–Johns apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Model ARX (300 MHz) spectrometer. IR spectra were recorded on a JASCO FTIR 5300 spectrophotometer. High resolution mass (HRMS) spectra were obtained on JEOL JMS-700 spectrometer at Korea Basic Science Institute. Combustion analysis was carried out at Scientific Instrument Center, Yeungnam University, Korea.

General procedure for synthesis of the dihydrofuroquinolinones

To a heterogeneous solution of silver(I) carbonate (2.2 mmol, 50 wt% on Celite) in acetonitrile (20 mL) was added 4-hydroxy-2-quinolone (1 mmol) and olefin (2–5 mmol) at room temperature. The reaction mixture was refluxed for 3 h and then cooled to room temperature. The suspension was filtered off and the inorganic material was washed with ethyl acetate (50 mL). The solvent was evaporated under reduced pressure to give the residue. The residue was purified by flash column chromatography on silica gel to give the dihydrofuroquinolinone.

2,5-Dimethyl-2-phenyl-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (3). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolone (**1a**) (175 mg, 1 mmol) with α-methylstyrene (**2a**) (354 mg, 3 mmol) in acetonitrile (20 mL) afforded **3** (125 mg, 43%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.91 (1H, d, J=7.8 Hz), 7.60 (1H, t, J=7.8 Hz), 7.48 (2H, d, J=7.5 Hz), 7.41–7.34 (3H, m), 7.30–7.25 (2H, m), 3.71 (3H, s), 3.49 (1H, d, J=15.4 Hz), 3.41 (1H, d, J=15.4 Hz), 1.86 (3H, s); IR (neat) 2973, 1661, 1640, 1597, 1570, 1507, 1462, 1422, 1356, 1292, 1254, 1190, 1094, 1057, 870, 756 cm^{-1}; HRMS m/z (M^+) calcd for $C_{19}H_{17}NO_2$, 291.1260. Found 291.1263.

2,5-Dimethyl-2-pentyl-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (4). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolone (**1a**) (175 mg, 1 mmol) with 2-methyl-1-heptene (**2b**) (337 mg, 3 mmol) in acetonitrile (20 mL) afforded **4** (117 mg, 41%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.76 (1H, d, J=7.6 Hz), 7.56 (1H, t, J=7.6 Hz), 7.36 (1H, d, J=8.5 Hz), 7.23 (1H, m), 3.70 (3H, s), 3.10 (1H, d, J=15.4 Hz), 2.93 (1H, d, J=15.4 Hz), 1.85–1.76 (3H, s), 1.42–1.30 (8H, m), 0.87 (3H, s); IR (neat) 2934, 2863, 1657, 1597, 1570, 1508, 1462, 1422, 1290, 1103, 1040, 864, 754 cm^{-1}; HRMS m/z (M^+) calcd for $C_{18}H_{23}NO_2$, 285.1730. Found 285.1729.

2-Ethoxy-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (5). Reaction of 4-hydroxy-1*H*-quinolinone (**1b**) (161 mg, 1 mmol) with ethyl vinyl ether (**2c**) (361 mg, 5 mmol) in acetonitrile (20 mL) afforded **5** (69 mg, 30%) as a solid: mp 199–201°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 11.28 (1H, s), 7.70 (1H, d, J=7.9 Hz), 7.47 (1H, t, J=7.6 Hz), 7.34 (1H, d, J=7.9 Hz), 7.18 (1H, t, J=7.6 Hz), 6.02 (1H, dd, J=7.0, 3.0 Hz), 4.04 (1H, m), 3.74 (1H, m), 3.37 (1H, dd, J=16.6, 7.0 Hz), 3.10 (1H, dd, J=16.6, 3.0 Hz), 1.27 (3H, t, J=7.1 Hz); IR (KBr) 2965, 1663, 1634, 1580, 1510, 1485, 1445, 1406, 1373, 1339, 1262, 1204, 1117, 1080, 978, 909, 874, 748 cm^{-1}; HRMS m/z (M^+) calcd for $C_{13}H_{13}NO_3$, 231.0896. Found 231.0895.

2-Ethoxy-5-methyl-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (6). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolone (**1a**) (175 mg, 1 mmol) with ethyl vinyl ether (**2c**) (361 mg, 5 mmol) in acetonitrile (20 mL) afforded **6** (98 mg, 40%) as a solid: mp 87–88°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.79 (1H, d, J=7.8 Hz), 7.59 (1H, t, J=8.6 Hz), 7.38 (1H, d, J=8.6 Hz), 7.23 (1H, m), 6.01 (1H, dd, J=7.1, 3.0 Hz), 4.03 (1H, m), 3.74 (1H, m), 3.71 (3H, s), 3.37 (1H, dd, J=16.7, 7.1 Hz), 3.10 (1H, dd, J=16.7, 3.0 Hz), 1.28 (3H, t, J=7.1 Hz); IR (KBr) 2977, 1661, 1597, 1571, 1508, 1458, 1425, 1359, 1289, 1255, 1197, 1095, 1041, 1000, 880, 753 cm^{-1}; HRMS m/z (M^+) calcd for $C_{14}H_{15}NO_3$, 245.1053. Found 245.1055; Anal. Calcd for $C_{14}H_{15}O_3N$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.48; H, 6.41; N, 5.68.

5-Benzyl-2-ethoxy-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (7). Reaction of 1-benzyl-4-hydroxy-1*H*-quinolinone

(**1d**) (251 mg, 1 mmol) with ethyl vinyl ether (**2c**) (361 mg, 5 mmol) in acetonitrile (20 mL) afforded **7** (157 mg, 49%) as a solid: mp 114–115°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.77 (1H, d, J=7.7 Hz), 7.40 (1H, t, J=7.9 Hz), 7.29–7.14 (7H, m), 6.03 (1H, dd, J=7.0, 3.1 Hz), 5.53 (2H, m), 4.03 (1H, m), 3.75 (1H, m), 3.41 (1H, dd, J=16.7, 7.1 Hz), 3.15 (1H, dd, J=16.7, 3.0 Hz), 1.26 (3H, t, J=6.6 Hz); IR (KBr) 3063, 2978, 1657, 1597, 1566, 1505, 1454, 1420, 1352, 1260, 1198, 1080, 995, 880, 754 cm^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{19}NO_3$, 321.1366. Found 321.1368.

2-Butoxy-5-methyl-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (8). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolone (**1a**) (175 mg, 1 mmol) with butyl vinyl ether (**2d**) (300 mg, 3 mmol) in acetonitrile (20 mL) afforded **8** (123 mg, 45%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.78 (1H, d, J=7.7 Hz), 7.57 (1H, t, J=7.7 Hz), 7.36 (1H, d, J=8.6 Hz), 7.24 (1H, m), 5.99 (1H, dd, J=7.0, 3.0 Hz), 3.96 (1H, m), 3.69 (3H, s), 3.66 (1H, m), 3.35 (1H, dd, J=16.7, 7.0 Hz), 3.09 (1H, dd, J=16.7, 2.9 Hz), 1.62 (2H, m), 1.38 (2H, m), 0.92 (3H, t, J=7.3 Hz); IR (neat) 2959, 2874, 1659, 1636, 1597, 1572, 1508, 1462, 1426, 1358, 1289, 1254, 1192, 1094, 1001, 880, 754 cm^{-1}; HRMS m/z (M^+) calcd for $C_{16}H_{19}NO_3$, 273.1366. Found 273.1367.

2-Methoxy-2,5-dimethyl-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (9). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolone (**1a**) (175 mg, 1 mmol) with 2-methoxypropene (**2e**) (361 mg, 5 mmol) in acetonitrile (20 mL) afforded **9** (157 mg, 64%) as a solid: mp 93–94°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.79 (1H, d, J=7.8 Hz), 7.57 (1H, t, J=7.8 Hz), 7.37 (1H, d, J=8.6 Hz), 7.23 (1H, m), 3.69 (3H, s), 3.33 (3H, s), 3.30 (1H, d, J=17.0 Hz), 3.08 (1H, d, J=17.0 Hz), 1.74 (3H, s); IR (KBr) 2982, 1663, 1599, 1570, 1507, 1462, 1422, 1356, 1290, 1240, 1103, 1044, 1001, 939, 907, 833, 762 cm^{-1}; HRMS m/z (M^+) calcd for $C_{14}H_{15}NO_3$, 245.1053. Found 245.1051.

5-Allyl-2-methoxy-2-methyl-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (10). Reaction of 1-allyl-4-hydroxy-1*H*-quinolinone (**1c**) (201 mg, 1 mmol) with 2-methoxypropene (**2e**) (361 mg, 5 mmol) in acetonitrile (20 mL) afforded **10** (147 mg, 54%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.79 (1H, d, J=7.8 Hz), 7.53 (1H, t, J=7.8 Hz), 7.53 (1H, d, J=8.7 Hz), 7.21 (1H, m), 5.89 (1H, m), 5.18 (1H, d, J=10.4 Hz), 5.07 (1H, d, J=17.2 Hz), 4.93 (2H, m), 3.35 (3H, s), 3.32 (1H, d, J=16.9 Hz), 3.10 (1H, d, J=16.9 Hz), 1.75 (3H, s); IR (neat) 2942, 1659, 1597, 1568, 1505, 1456, 1416, 1383, 1352, 1292, 1236, 1179, 1111, 1047, 924, 831, 756 cm^{-1}; HRMS m/z(M^+) calcd for $C_{16}H_{17}NO_3$, 271.1209. Found 271.1208.

5-Benzyl-2-methoxy-2-methyl-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (11). Reaction of 1-benzyl-4-hydroxy-1*H*-quinolinone (**1d**) (251 mg, 1 mmol) with 2-methoxypropene (**2e**) (361 mg, 5 mmol) in acetonitrile (20 mL) afforded **11** (251 mg, 78%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.78 (1H, d, J=7.8 Hz), 7.43–7.14 (8H, m), 5.52 (2H, m), 3.38 (3H, s), 3.37 (1H, d, J=16.9 Hz), 3.15 (1H, d, J=16.9 Hz), 1.77 (3H, s); IR (neat) 3032, 2940, 1659, 1597, 1568, 1503, 1454, 1416, 1383, 1352, 1290, 1175, 1109, 1047, 997, 901, 831, 754 cm^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{19}NO_3$, 321.1366. Found 321.1367.

2-Ethoxy-3,5-dimethyl-3,5-dihydro-2*H*-furo[3,2-*c*]quinolin-4-one (12). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolone (**1a**) (175 mg, 1 mmol) with ethyl 1-propenyl ether (**2f**) (431 mg, 5 mmol) in acetonitrile (20 mL) afforded **12** (143 mg, 55%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.79 (1H, d, J=7.6 Hz), 7.57 (1H, d, J=8.5 Hz), 7.36 (1H, d, J=8.5 Hz), 7.25 (1H, d, J=7.6 Hz), 5.90 (*cis*, 0.17H, d, J=7.3 Hz) and 5.52 (*trans*, 0.83H, d, J=2.2 Hz), 4,02 (1H, m), 3.75 (1H, m), 3.69 (3H, s), 3.68 (*cis*, 0.17H, m) and 3,42 (*trans*, 0.83H, m), 1.39 (3H, d, J=7.2 Hz), 1.29 (3H, m); IR (neat) 2978, 2934, 1659, 1595, 1570, 1508, 1460, 1422, 1354, 1290, 1244, 1096, 1047, 922 cm^{-1}; HRMS m/z (M^+) calcd for $C_{15}H_{17}NO_3$, 259.1209. Found 259.1207.

5-Allyl-2-ethoxy-3-methyl-3,5-dihydro-2*H*-furo[3,2-*c*]-quinolin-4-one (13). Reaction of 1-allyl-4-hydroxy-1*H*-quinolinone (**1c**) (201 mg, 1 mmol) with ethyl 1-propenyl ether (**2f**) (431 mg, 5 mmol) in acetonitrile (20 mL) afforded **13** (103 mg, 36%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.77 (1H, d, J=7.7 Hz), 7.50 (1H, t, J=8.7 Hz), 7.30 (1H, d, J=8.7 Hz), 7.19 (1H, t, J=7.7 Hz), 5.91 (1H, m), 5.89 (*cis*, 0.15H, m) and 5.50 (*trans*, 0.85H, d, J=2.5 Hz), 5.17 (1H, d, J=10.4 Hz), 5.06 (1H, d, J=17.2 Hz), 4.91 (2H, m), 3.98 (1H, m), 3.71 (1H, m), 3.40 (1H, m), 1.38 (3H, d, J=7.2 Hz), 1.25 (3H, t, J=7.1 Hz); IR (neat) 2978, 1661, 1597, 1568, 1504, 1454, 1416, 1350, 1292, 1254, 1111, 1057, 922, 870, 758 cm^{-1}; HRMS m/z (M^+) calcd for $C_{17}H_{19}NO_3$, 285.1366. Found 285.1367.

5-Benzyl-2-ethoxy-3-methyl-3,5-dihydro-2*H*-furo[3,2-*c*]-quinolin-4-one (14). Reaction of 1-benzyl-4-hydroxy-1*H*-quinolinone (**1d**) (251 mg, 1 mmol) with ethyl 1-propenyl ether (**2f**) (431 mg, 5 mmol) in acetonitrile (20 mL) afforded **14** (188 mg, 56%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.78 (1H, d, J=7.9 Hz), 7.39 (1H, t, J=8.6 Hz), 7.32–7.13 (7H, m), 5.92 (*cis*, 0.13H, d, J=7.3 Hz) and 5.54 (*trans*, 0.87H, J=2.5 Hz), 5.62 (1H, d, J=8.2 Hz), 5.42 (1H, d, J=8.1 Hz), 4.04 (1H, m), 3.74 (1H, m), 3.47 (1H, m), 1.43 (3H, d, J=7.2 Hz), 1.28 (3H, t, J=7.1 Hz); IR (neat) 3065, 2978, 1661, 1597, 1568, 1505, 1454, 1373, 1350, 1289, 1109, 961, 924, 868, 754 cm^{-1}; HRMS m/z (M^+) calcd for $C_{21}H_{21}NO_3$, 335.1522. Found 335.1519.

5-Methyl-5,6*b*,7,8-tetrahydro-9*aH*-9,10-dioxa-5-aza-pentaleno[2,1-*a*]naphthalen-6-one (15). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolone (**1a**) (175 mg, 1 mmol) with 2,3-dihydrofuran (**2g**) (350 mg, 5 mmol) in acetonitrile (20 mL) afforded **15** (122 mg, 50%) as a solid: mp 220°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.83 (1H, dd, J=7.9, 1.2 Hz), 7.61 (1H, t, J=8.6 Hz), 7.39 (1H, d, J=8.6 Hz), 7.26 (1H, m), 6.52 (1H, d, J=5.8 Hz), 4.15 (2H, m), 3.71 (3H, s), 3.69 (1H, m), 2.37 (1H, m), 2.21 (1H, m); IR (KBr) 3083, 2994, 1657, 1634, 1595, 1510, 1458, 1431, 1365, 1337, 1258, 1217, 1181, 1111, 1084, 947, 901, 868, 810, 760 cm^{-1}; HRMS m/z (M^+) calcd for $C_{14}H_{13}NO_3$, 243.0896. Found 243.0892.

5-Benzyl-5,6*b*,7,8-tetrahydro-9*aH*-9,10-dioxa-5-aza-pentaleno[2,1-*a*]naphthalen-6-one (16). Reaction of 1-benzyl-4-hydroxy-1*H*-quinolinone (**1d**) (251 mg, 1 mmol) with 2,3-dihydrofuran (**2g**) (350 mg, 5 mmol) in acetonitrile (20 mL) afforded **16** (208 mg, 65%) as a solid:

mp 164–165°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.80 (1H, d, J=7.9 Hz), 7.43 (1H, t, J=8.6 Hz), 7.30–7.15 (7H, m), 6.54 (1H, d, J=5.8 Hz), 5.64 (1H, d, J=16.2 Hz), 5.41 (1H, d, J=16.2 Hz), 4.18 (2H, dd, J=8.5, 3.1 Hz), 3.74 (1H, m), 2.41 (1H, dd, J=12.6, 4.9 Hz), 2.25 (1H, m); IR (KBr) 2994, 1657, 1640, 1595, 1568, 1503, 1454, 1420, 1327, 1289, 1258, 1169, 1138, 1076, 1038, 934, 914, 878, 756 cm^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{17}NO_3$, 319.1209. Found 319.1210.

5-Methyl-2-phenylsulfanyl-3,5-dihydro-2*H*-furo[3,2-*c*]-quinolin-4-one (17). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolinone (**1a**) (175 mg, 1 mmol) with phenyl vinyl sulfide (**2h**) (272 mg, 2 mmol) in acetonitrile (20 mL) afforded **17** (127 mg, 41%) as a solid: mp 127–128°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.71 (1H, dd, J=7.9, 1.4 Hz), 7.61–7.50 (3H, m), 7.33–7.25 (4H, m), 7.14 (1H, t, J=7.8 Hz), 6.29 (1H, dd, J=9.6, 5.8 Hz), 3.64 (1H, m), 3.63 (3H, s), 3.16 (1H, dd, J=16.7, 5.8 Hz); IR (KBr) 3059, 2942, 1661, 1638, 1597, 1508, 1462, 1441, 1290, 1248, 1152, 1100, 882, 858, 752 cm^{-1}; HRMS m/z (M^+) calcd for $C_{18}H_{15}NO_2S$, 309.0825. Found 309.0820.

5-Benzyl-2-phenylsulfanyl-3,5-dihydro-2*H*-furo[3,2-*c*]-quinolin-4-one (18). Reaction of 1-benzyl-4-hydroxy-1*H*-quinolinone (**1d**) (251 mg, 1 mmol) with phenyl vinyl sulfide (**2h**) (272 mg, 2 mmol) in acetonitrile (20 mL) afforded **18** (162 mg, 42%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.77 (1H, d, J=7.6 Hz), 7.60 (2H, m), 7.42 (2H, t, J=7.6 Hz), 7.34-7.15 (9H, m), 6.38 (1H, dd, J=9.7, 5.7 Hz), 5.52 (2H, s), 3.74 (1H, dd, J=16.7, 9.7 Hz), 3.29 (1H, dd, J=16.7, 5.7 Hz); IR (neat) 3063, 2932, 1661, 1599, 1568, 1503, 1470, 1454, 1414, 1373, 1300, 1258, 1134, 1086, 1026, 992, 909, 883, 733 cm^{-1}; HRMS m/z (M^+) calcd for $C_{24}H_{19}NO_2S$, 385.1138. Found 385.1136.

5-Methyl-7,8,9,10-tetrahydro-5*H*-11-oxa-5-aza-benzo[*a*]-fluoren-6-one (19). Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolinone (**1a**) (175 mg, 1 mmol) with (cyclohex-1-enylsulfanyl)-benzene (**2i**) (381 mg, 2 mmol) in acetonitrile (20 mL) afforded **19** (94 mg, 37%) as a solid: mp 140–143°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.92 (1H, d, J=7.9 Hz), 7.47 (1H, t, J=8.5 Hz), 7.38 (1H, d, J=7.9 Hz), 7.25 (1H, m), 3.73 (3H, s), 2.86 (2H, t, J=7.8 Hz), 2.74 (2H, t, J=7.9 Hz), 1.90 (2H, m), 1.80 (2H, m); IR (KBr) 2936, 1653, 1580, 1445, 1383, 1331, 1242, 1181, 1103, 1042, 972, 926, 747 cm^{-1}; HRMS m/z (M^+) calcd for $C_{16}H_{15}NO_2$, 253.1104. Found 253.1103.

General procedure for synthesis of the furoquinolinones

Method A. To a stirred solution of dihydrofuroquinolinone (0.5 mmol) in dry toluene (20 mL) was added 50 mg of *p*-toluenesulfonic acid. The mixture was stirred at reflux for 2 h and then cooled to room temperature, and added to saturated sodium bicarbonate solution (20 mL). The reaction mixture was extracted with ethyl acetate (3×25 mL), washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of solvent gave an oil which was purified by silica gel chromatography to give the furoquinolinone.

Method B. To a solution of dihydrofuroquinolinone (0.5 mmol) in dichloromethane (10 mL) was added mCPBA (1.2 mmol, 80% purity) at 0°C. The reaction mixture was stirred for 24 h at room temperature, and then poured into saturated aqueous sodium carbonate. The mixture was extracted with dichloromethane (3×25 mL), washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of solvent gave an oil which was purified by silica gel chromatography to give the furoquinolinone.

Pseudoisodictamnine (24).[4a] *Method A:* Reaction of **6** (123 mg, 0.5 mmol) with *p*-TsOH in toluene afforded **24** (41 mg, 41%) as a solid: mp 134–135°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.02 (1H, dd, J=7.9, 1.5 Hz), 7.63 (1H, d, J=2.0 Hz), 7.56 (1H, m), 7.48 (1H, m), 7.32 (1H, m), 7.08 (1H, d, J=2.0 Hz), 3.80 (3H, s); IR (KBr) 3121, 2937, 1660, 1583, 1502, 1439, 1358, 1317, 1228, 1122, 1084, 1020, 962, 742, 667 cm^{-1}.

Method B: Reaction of **17** (155 mg, 0.5 mmol) with mCPBA (259 mg, 1.2 mmol, 80% purity) in dichloromethane afforded **24** (78 mg, 78%).

5-Benzyl-5*H*-furo[3,2-*c*]quinolin-4-one (25). *Method A:* Reaction of **7** (161 mg, 0.5 mmol) with *p*-TsOH in toluene afforded **25** (55 mg, 40%) as a solid: mp 110–111°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.01 (1H, d, J=7.8 Hz), 7.65 (1H, d, J=1.9 Hz), 7.42–7.19 (8H, m), 7.12 (1H, d, J=1.9 Hz), 5.63 (2H, s); IR (KBr) 3030, 2928, 1663, 1609, 1584, 1564, 1454, 1375, 1308, 1238, 1154, 1080, 1026., 951, 889, 802, 752 cm^{-1}; HRMS m/z (M^+) calcd for $C_{18}H_{13}NO_2$, 275.0947. Found 275.0946.

Method B: Reaction of **18** (161 mg, 0.5 mmol) with mCPBA (259 mg, 1.2 mmol, 80% purity) in dichloromethane afforded **25** (92 mg, 67%).

2,5-Dimethyl-5*H*-furo[3,2-*c*]quinolin-4-one (26). Reaction of dihydrofuroquinolinone **9** (123 mg, 0.5 mmol) with *p*-TsOH in toluene afforded **26** (98 mg, 92%) as a solid: mp 100–101°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.95 (1H, d, J=7.5 Hz), 7.51 (1H, t, J=8.3 Hz), 7.42 (1H, d, J=8.3 Hz), 7.28 (1H, t, J=7.5 Hz), 6.63 (1H, s), 3.78 (3H, s), 2.49 (3H, s); IR (KBr) 3069, 1663, 1582, 1510, 1451, 1358, 1312, 1250, 1157, 1105, 1042, 970, 928, 824, 747 cm^{-1}; HRMS m/z (M^+) calcd for $C_{13}H_{11}NO_2$, 213.0790. Found 213.0794.

5-Allyl-2-methyl-5*H*-furo[3,2-*c*]quinolin-4-one (27) Reaction of dihydrofuroquinolinone **10** (136 mg, 0.5 mmol) with *p*-TsOH in toluene afforded **27** (117 mg, 98%) as a solid: mp 64–65°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.96 (1H, d, J=7.8 Hz), 7.46 (1H, t, J=7.8 Hz), 7.38 (1H, d, J=8.5 Hz), 7.23 (1H, m), 6.65 (1H, s), 5.97 (1H, m), 5.19 (1H, d, J=5.2 Hz), 5.09–5.01 (3H, m), 2.49 (3H, s); IR (KBr) 3084, 2940, 1669, 1580, 1505, 1433, 1360, 1335, 1298, 1254, 1188, 1132, 1103, 993, 955, 916, 814, 775 cm^{-1}; HRMS m/z (M^+) calcd for $C_{15}H_{13}NO_2$, 239.0947. Found 239.0947.

5-Benzyl-2-methyl-5*H*-furo[3,2-*c*]quinolin-4-one (28). Reaction of **11** (161 mg, 0.5 mmol) with *p*-TsOH in toluene afforded **28** (140 mg, 97%) as a solid: mp 152–153°C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.95 (1H, d, J=7.7 Hz), 7.38–

7.14 (8H, m), 6.69 (1H, s), 5.62 (2H, s), 2.51 (3H, s); IR (KBr) 3098, 1653, 1580, 1499, 1453, 1358, 1296, 1254, 1186, 1165, 1128, 1080, 1015, 955, 928, 841, 810, 775 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{19}H_{15}NO_2$, 289.1104. Found 289.1106.

3,5-Dimethyl-5*H*-furo[3,2-*c*]quinolin-4-one (29). Reaction of dihydrofuroquinolinone **12** (130 mg, 0.5 mmol) with *p*-TsOH in toluene afforded **29** (85 mg, 80%) as a solid: mp 155–156°C; ^1H NMR (300 MHz, $CDCl_3$), δ 7.98 (1H, d, *J*=7.9 Hz), 7.56 (1H, t, *J*=8.6 Hz), 7.43 (1H, d, *J*=8.6 Hz), 7.38 (1H, d, *J*=2.0 Hz), 7.30 (1H, t, *J*=7.9 Hz), 3.76 (3H, s), 2.43 (3H, s); IR (KBr) 2970, 1651, 1507, 1456, 1418, 1354, 1292, 1244, 1098, 1047, 974, 922, 870, 754 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{13}H_{11}NO_2$, 213.0790. Found 213.0789.

5-Benzyl-3-methyl-5*H*-furo[3,2-*c*]quinolin-4-one (30). Reaction of dihydrofuroquinolinone **14** (168 mg, 0.5 mmol) with *p*-TsOH in toluene afforded **30** (72 mg, 50%) as a solid: mp 119–120°C; ^1H NMR (300 MHz, $CDCl_3$), δ 7.97 (1H, d, *J*=7.8 Hz), 7.40 (1H, s), 7.37–7.12 (8H, m), 5.59 (2H, s), 2.45 (3H, s); IR (KBr) 3063, 2928, 1663, 1609, 1578, 1555, 1497, 1447, 1362, 1308, 1246, 1208, 1171, 1138, 1503, 968, 853, 752 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{19}H_{15}NO_2$, 289.1104. Found 289.1104.

1-Benzyl-5-methyl-1,5-dihydro-pyrrolo[3,2-*c*]quinolin-4-one (31). To a stirred solution of **6** (245 mg, 1 mmol) in ethanol (30 mL) was added benzyl amine (129 mg, 1.2 mmol) and *p*-toluenesulfonic acid (50 mg). The mixture was stirred at reflux for 6 h and then cooled to room temperature. After removing solvent, saturated ammonium chloride (30 mL) was added. The mixture was extracted with ethyl acetate (3×25 mL), washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of solvent gave an oil that was purified by silica gel chromatography to give **31** (185 mg, 64%) as a solid: mp 160–161°C; ^1H NMR (300 MHz, $CDCl_3$), δ 7.72 (1H, d, *J*=8.0 Hz), 7.44–7.27 (5H, m), 7.08–7.03 (3H, m), 6.99 (1H, d, *J*=3.0 Hz), 6.96 (1H, d, *J*=3.0 Hz), 5.65 (2H, s), 3.78 (3H, s); IR (KBr) 3104, 2928, 1644, 1574, 1497, 1454, 1402, 1264, 1329, 1260, 1109, 1009, 963, 858, 737 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{19}H_{16}N_2O$, 288.1264. Found 288. 1266.

5-Methyl-5*H*-11-oxa-5-aza-benzo[*a*]fluoren-6-one (32). To a stirred solution of **19** (127 mg, 0.5 mmol) in phenyl ether (5 mL) was added 10% Pd/C (0. 2 g). The mixture was heated at 200°C for 3 h and cooled to room temperature. The suspension was filtered off and the inorganic material was washed with ethyl acetate (50 mL). The solvent was evaporated under reduced pressure to give the residue. The residue was purified by flash column chromatography on silica gel to give **32** (107 mg, 86%) as a solid: mp 202–204°C; ^1H NMR (300 MHz, $CDCl_3$), δ 8.28 (1H, m), 8.17 (1H, d, *J*=7.8 Hz), 7.65–7.60 (2H, m), 7.50 (1H, d, *J*=8.6 Hz), 7.48–7.32 (3H, m), 3.84 (3H, s); IR (KBr) 3065, 1659, 1584, 1562, 1508, 1453, 1372, 1323, 1246, 1194, 1154, 1105, 1042, 970, 864, 814, 745 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{16}H_{11}NO_2$, 249.0790. Found 249.0787.

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