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TETRAHEDRON

Manganese(III) Acetate Initiated Oxidative Free Radical Reaction Between 1,4-Naphthoquinones And Ethyl Nitroacetate

Che-Ping Chuang*, Yi-Lung Wu and Ming-Chyuan Jiang

Department of Chemistry, National Cheng Kung University, Tainan, Taiwan, 70101, R.O.C.

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Abstract: The manganese(III) initiated oxidative free radical reaction between 1,4-naphthoquinones and ethyl nitroacetate is described. Nitromethyl radical **1** can be generated effectively from the oxidation of ethyl nitroacetate by manganese(III) acetate. Naphtho[2,3-*d*]isoxazole-4,9-diones, benzo[*f*]indole-4,9-diones and benzo[*b*]acridine-6,11-diones were prepared effectively from readily available 1,4-naphthoquinones and ethyl nitroacetate.

INTRODUCTION

Free radical reactions have become increasingly important in organic synthesis in the last two decades.[1] Compounds containing the quinone group represent an important class of biologically active molecules that are widespread in nature.[2,3] Electrophilic radicals produced from the manganese(III) acetate oxidation of β-dicarbonyl compounds undergo efficient addition to a C-C double bond.[1d,1e,4,5] These reactions can be performed intermolecularly and intramolecularly. The free radical addition of a carbon center radical to quinones has been reported.[5c-5f,6] Nitromethyl radical can be generated from nitromethane and manganese(III) acetate.[7] We believe that radical **1** can be produced from the reaction between ethyl nitroacetate and manganese(III) acetate although this reaction has not been studied. This report described our results on the reaction between 1,4-naphthoquinone derivatives and ethyl nitroacetate *via* manganese(III) initiated oxidative free radical reaction.

RESULTS AND DISCUSSION

We began our studies with the reaction shown in equation 1. 1,4-Naphthoquinone was treated with ethyl nitroacetate (4 eq) and manganese(III) acetate (6 eq) in acetic acid at 70 °C. After heating for 15 h the dark brown color of manganese(III) acetate disappeared and another 4 equivalents of ethyl acetate and 6 equivalents of manganese(III) acetate were added. The reaction mixture was heated for another 15 h and **3a** was obtained in 55% yield (Table 1, entry a). A possible mechanism for this reaction is shown in Scheme 1. Initiation occurs with the manganese(III) acetate oxidation of ethyl nitroacetate to produce radical **1**. This radical intermediate undergoes intermolecular addition followed by elimination of hydrogen atom to give **5**, which undergoes further intramolecular nucleophilic addition followed by dehydration and oxidation to produce **3a**. We also performed this reaction in acetonitrile. In acetonitrile, the yield of **3a** is 45% (Table 1, entry b) and it proceeds in a much slower reaction rate (96 h). The generalities of this reaction are illustrated in Table 1. **3a**

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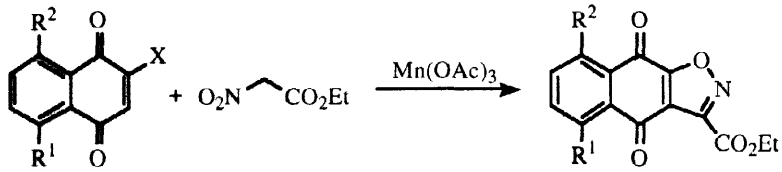


(Eq. 1)

2a: R^1 = H, R^2 = H, X = H
2b: R^1 = OMe, R^2 = H, X = H
2c: R^1 = H, R^2 = H, X = Br
2d: R^1 = H, R^2 = H, X = OMe
2e: R^1 = OMe, R^2 = OMe, X = H
2f: R^1 = OMe, R^2 = H, X = Br

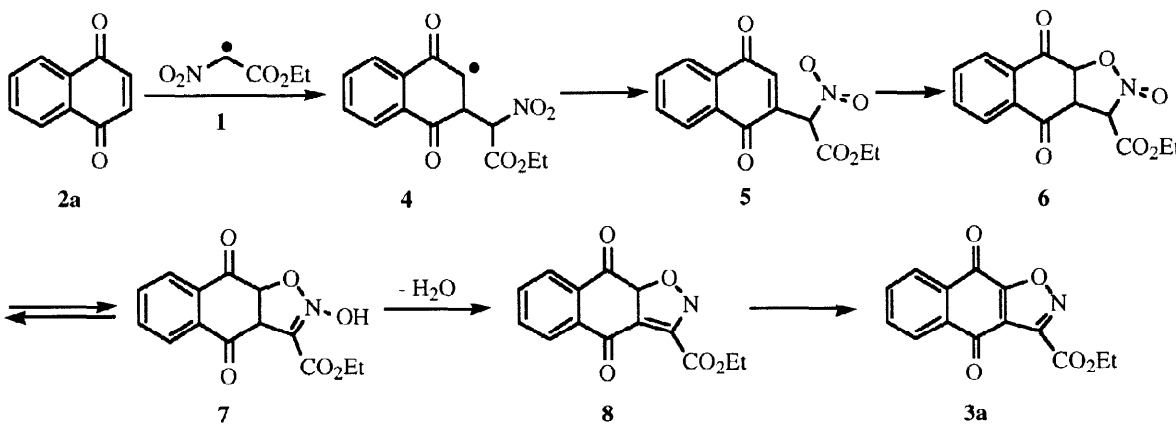
3a: R^1 = H, R^2 = H
3b: R^1 = OMe, R^2 = H
3c: R^1 = H, R^2 = OMe
3d: R^1 = OMe, R^2 = OMe

Table 1. The Free Radical Reaction Between 1,4-Naphthoquinone Derivatives And Ethyl Nitroacetate.

Entry	Quinones	Solvent	Product	Yield (Ratio)[a]
a	**2a**	HOAc	**3a**	55%
b	**2a**	CH_3CN	**3a**	45%
c	**2a**	HOAc	**3a**	58%[b]
d	**2b**	HOAc	**3b** + **3c**	62% (1:1.1)
e	**2b**	CH_3CN	**3b** + **3c**	48% (1:1.2)
f	**2c**	CH_3CN	**3a**	60%
g	**2d**	CH_3CN	**3a**	28%
h	**2e**	HOAc	**3d**	48%
i	**2e**	CH_3CN	**3d**	48%
j	**2f**	CH_3CN	**3b**	68%

a. The ratio refers to isomeric products and is determined from the ^1H NMR integration of methoxy groups in the inseparable mixture of regioisomers.

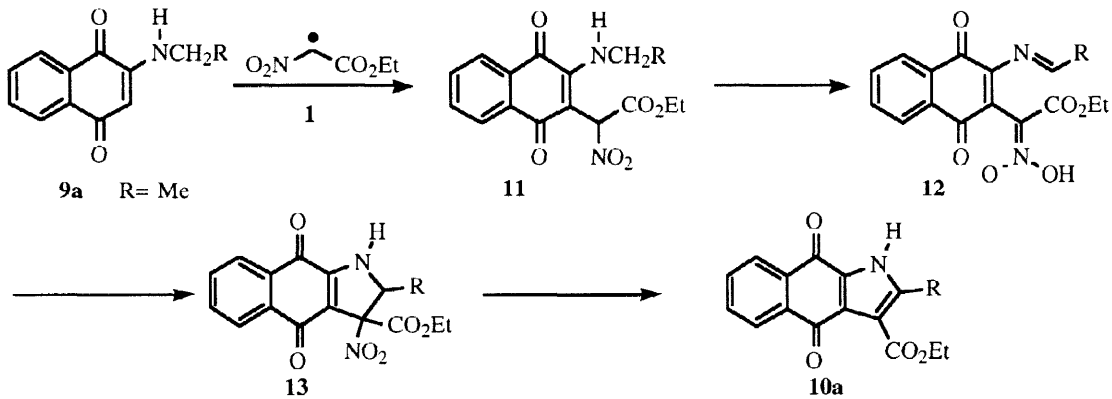
b. 1,4-Dihydroxynaphthalene was used as starting material.



Scheme 1

can also be obtained effectively by using 1,4-dihydroxynaphthalene as starting material (entry c). With **2b**, it led to the formation of an inseparable mixture of isomers, **3b** and **3c** (entries d and e). With 2-substituted naphthoquinones **2c** and **2d**, **3a** was obtained *via* a similar mechanism shown in Scheme 1 (entries f, g). **3b**

was produced regiospecifically from bromoquinone **2f** (entry j). This can be rationalized that the orientation of free radical addition to quinones was directed by quinonoidal bromine.[5c] We have recently shown that the use of acetonitrile as solvent in similar reaction is advantageous for acid sensitive naphthoquinones.[5d,5f] Due to the acid liability of methoxy- and amino- substituted naphthoquinones, they were only performed in acetonitrile. In contrast to **2c** and **2d**, when aminoquinone **9a** was treated with ethyl nitroacetate (4 eq) and manganese(III) acetate (6 eq) under similar conditions the only isolated product was benzo[*f*]indole **10a** and no **3a** could be found. A proposed mechanism for the formation of **10a** is outlined in Scheme 2. The addition of radical **1** to quinone ring followed by oxidation gives **11**, which is oxidized by manganese(III) acetate to produce imine **12**. This imine **12** undergoes further intramolecular nucleophilic addition followed by elimination of nitrous acid to produce **10a**. The scope for the formation of benzo[*f*]indole-4,9-dione **10** from 2-amino-1,4-naphthoquinone is illustrated in Table 2.

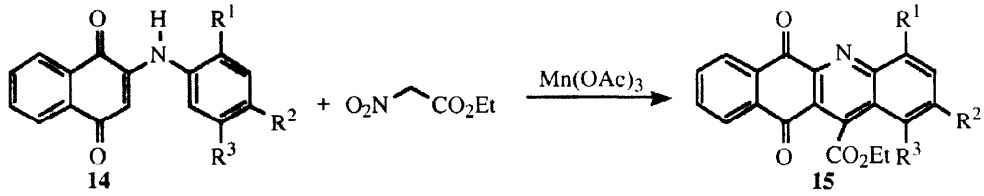


Scheme 2

Table 2. The Free Radical Reaction Between 2-Alkylamino-1,4-naphthoquinones And Ethyl Nitroacetate.

Entry	Quinones	Product	Yield
a	**9a:** R = Me	**10a**	21%
b	**9b:** R = Pr	**10b**	24%
c	**9c:** R = *p*-Tolyl	**10c**	48%
d	**9d:** R = Bn	**10d**	21%
e	**9e:** R = *i*-Pr	**10e**	31%
f	**9f:** R = *t*-Bu	**10f**	54%

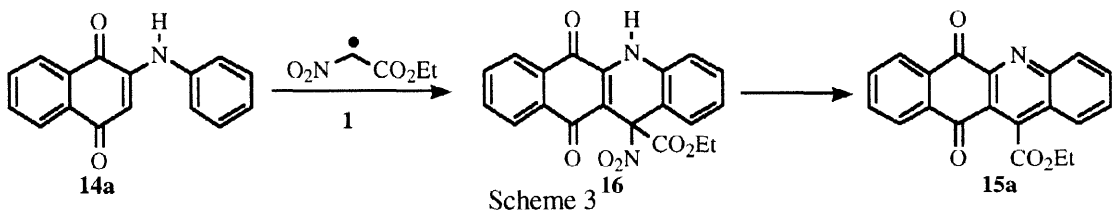
The oxidative free radical reaction between 2-anilino-1,4-naphthoquinones and malonates has been studied in this laboratory.[5d] We continue this manganese(III) acetate initiated free radical reaction of 2-anilino-1,4-naphthoquinones with ethyl nitroacetate. The reaction of **14a** and ethyl nitroacetate (4 eq) with manganese(III) acetate (6 eq) in acetonitrile gave **15a** in 27% yield (Eq. 2). This free radical reaction presumably occurs *via* the addition of radical **1** to quinone ring and anilino ring consecutively followed by oxidation to give **16**, which undergoes further elimination of nitrous acid to produce **15a** (Scheme 3). The generalities for the preparation of benzo[*b*]acridine-6,11-dione **15** from 2-anilino-1,4-naphthoquinone are shown in Table 3.



14 15 (Eq. 2)

Table 3. The Free Radical Reaction Between 2-Anilino-1,4-naphthoquinones And Ethyl Nitroacetate.

Entry	Quinones	Product	Yield
a	**14a:** R^1 = H, R^2 = H, R^3 = H	**15a**	27%
b	**14b:** R^1 = H, R^2 = OMe, R^3 = H	**15b**	24%
c	**14c:** R^1 = H, R^2 = Me, R^3 = H	**15c**	31%
d	**14d:** R^1 = H, R^2 = CO_2Et, R^3 = H	**15d**	31%
e	**14e:** R^1 = OMe, R^2 = H, R^3 = Cl	**15e**	32%
f	**14f:** R^1 = H, R^2 = Cl, R^3 = H	**15f**	43%



14a 16 15a

Scheme 3

In conclusion, nitromethyl radical **1** can be generated from ethyl nitroacetate and manganese(III) acetate and it undergoes efficient addition to C-C double bond of 1,4-naphthoquinone derivatives. This free radical reaction provides a novel method for the synthesis of naphtho[2,3-*d*]isoxazole-4,9-diones, benzo[*f*]indole-4,9-diones and benzo[*b*]acridine-6,11-diones from readily available 1,4-naphthoquinones and ethyl nitroacetate.

EXPERIMENTAL

Melting points are uncorrected. Nmr spectra were recorded on Bruker AMX-400 spectrometer. Elemental analyses were performed with a Heraeus CHN-Rapid Analyzer. Analytical thin layer chromatography was performed by precoated silica gel 60 F-254 plates (0.25 mm thick) of EM Laboratories and visualized either by uv or by spraying with 5% phosphomolybdic acid in ethanol following by heating. The reaction mixture was purified by column chromatography over EM Laboratories silica gel (70-230 Mesh).

Typical experimental procedure for the preparation of naphtho[2,3-*d*]isoxazole-4,9-dione 3 in acetic acid: A solution of 137 mg (0.87 mmol) of 1,4-naphthoquinone, 475 mg (3.57 mmol) of ethyl nitroacetate and 1.36 g (5.07 mmol) of manganese(III) acetate in 10 ml of acetic acid was heated in a 70 °C oil bath for 15 h (the dark brown color of manganese(III) acetate disappeared), followed by the addition of 470 mg (3.53 mmol) of ethyl nitroacetate and 1.36 g (5.07 mmol) of manganese(III) acetate. The reaction mixture was heated for another 15 h and then diluted with 100 ml of ethyl acetate, washed with 50 ml of saturated aqueous sodium bisulfite, three 50-ml portions of water, three 50-ml portions of aqueous saturated sodium bicarbonate, dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over 20 g of silica

gel (eluted with hexane-ethyl acetate, 8:1) followed by recrystallization (hexane-ethyl acetate) to give 130 mg (55%) of **3a**.

Typical experimental procedure for the preparation of naphtho[2,3-*d*]isoxazole-4,9-dione 3 in acetonitrile: A solution of 129 mg (0.82 mmol) of 1,4-naphthoquinone, 435 mg (3.27 mmol) of ethyl nitroacetate and 1.31 g (4.89 mmol) of manganese(III) acetate in 10 ml of acetonitrile was heated in an 80 °C oil bath for 48 h (the dark brown color of manganese(III) acetate disappeared), followed by the addition of 432 mg (3.25 mmol) of ethyl nitroacetate and 1.31 g (4.89 mmol) of manganese(III) acetate. The reaction mixture was heated for another 48 h and then diluted with 100 ml of ethyl acetate, washed with 50 ml of saturated aqueous sodium bisulfite, three 25-ml portions of water, dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over 20 g of silica gel (eluted with hexane-ethyl acetate, 8:1) followed by recrystallization (hexane-ethyl acetate) to give 100 mg (45%) of **3a**.

4,9-Dihydro-4,9-dioxo-3-ethoxycarbonylnaphtho[2,3-*d*]isoxazole 3a: yellow platelets; mp 109-110 °C; IR ($CHCl_3$) 3030, 2990, 1745, 1690, 1595, 1480, 1340, 1320, 1270, 1270, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (t, J=7.2 Hz, 3H, CH_3), 4.58 (q, J=7.2 Hz, 2H, OCH_2), 7.81-7.94 (m, 2H, ArH), 8.23-8.33 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$) δ 14.0(q), 63.4(t), 120.1(s), 127.5(d), 127.8(d), 131.7(s), 133.4(s), 134.5(d), 135.5(d), 153.5(s), 157.9(s), 165.7(s), 172.6(s), 176.4(s); Anal. Calcd for $C_{14}H_9NO_5$: N, 5.16; C, 62.00; H, 3.34. Found: N, 5.09; C, 61.71; H, 3.40.

4,9-Dihydro-4,9-dioxo-3-ethoxycarbonyl-5-methoxynaphtho[2,3-*d*]isoxazole 3b: yellow crystals; mp 186-187 °C; IR ($CHCl_3$) 3030, 2940, 1750, 1695, 1680, 1605, 1580, 1470, 1285, 1270 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (t, J=7.1 Hz, 3H, CH_3), 4.04 (s, 3H, OCH_3), 4.57 (q, J=7.1 Hz, 2H, OCH_2), 7.44 (d, J=8.0 Hz, 1H, ArH), 7.77 (t, J=8.0 Hz, 1H, ArH), 7.92 (d, J=8.0 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 14.0(q), 56.6(q), 63.4(t), 120.1(d), 120.25(d), 120.32(s), 121.3(s), 134.1(s), 135.5(d), 153.8(s), 158.2(s), 161.0(s), 163.8(s), 172.4(s), 175.9(s); Anal. Calcd for $C_{15}H_{11}NO_6$: N, 4.65; C, 59.80; H, 3.68. Found: N, 4.63; C, 59.69; H, 3.72.

4,9-Dihydro-4,9-dioxo-5,8-dimethoxy-3-ethoxycarbonylnaphtho[2,3-*d*]isoxazole 3d: red crystals; mp 195-196 °C; IR ($CHCl_3$) 3010, 2985, 2940, 2840, 1745, 1680, 1565, 1270, 1180, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (t, J=7.1 Hz, 3H, CH_3), 3.99 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 4.55 (q, J=7.1 Hz, 2H, OCH_2), 7.40 (d, J=9.5 Hz, 1H, ArH), 7.46 (d, J=9.5 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 14.0(q), 56.9(q), 57.1(q), 63.3(t), 119.7(s), 120.4(s), 120.9(d), 122.0(s), 123.1(d), 153.4(s), 155.0(s), 155.8(s), 158.3(s), 164.5(s), 171.7(s), 175.9(s); Anal. Calcd for $C_{16}H_{13}NO_7$: N, 4.23; C, 58.01; H, 3.96. Found: N, 4.18; C, 57.72; H, 4.03.

Typical experimental procedure for the preparation of benzo[*f*]indole-4,9-dione 10 and benzo[*b*]acridine-6,11-dione 15: A solution of 151 mg (0.75 mmol) of **8a**, 412 mg (3.10 mmol) of ethyl nitroacetate and 1.21 g (4.51 mmol) of manganese(III) acetate in 10 ml of acetonitrile was heated in an 80 °C oil bath for 36 h. The reaction mixture was diluted with 100 ml of ethyl acetate, washed with 50 ml of saturated aqueous sodium bisulfite, three 25-ml portions of water, dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over 20 g of silica gel (eluted with dichloromethane-ethyl acetate, 15:1) followed by recrystallization (hexane-ethyl acetate) to give 44 mg (21%) of **10a**.

4,9-Dihydro-4,9-dioxo-3-ethoxycarbonyl-2-methyl-1*H*-benzo[*f*]indole 10a: orange crystals; mp 244-245 °C; IR ($CHCl_3$) 3425, 3220, 3020, 1715, 1650, 1595, 1440, 1370, 1270 cm^{-1}; ^1H NMR ($CDCl_3$) δ

1.45 (t, J=7.1 Hz, 3H, CH_3), 2.67 (s, 3H, CH_3), 4.44 (q, J=7.1 Hz, 2H, OCH_2), 7.68 (t, J=7.0 Hz, 1H, ArH), 7.72 (t, J=7.0 Hz, 1H, ArH), 8.10 (d, J=7.0 Hz, 1H, ArH), 8.20 (d, J=7.0 Hz, 1H, ArH), 10.75 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 13.5(q), 14.3(q), 60.9(t), 114.0(s), 125.8(d), 126.0(s), 127.5(d), 131.7(s), 132.0(s), 132.8(d), 134.0(d), 134.8(s), 142.5(s), 163.9(s), 176.2(s), 178.9(s); Anal. Calcd for $C_{16}H_{13}NO_4$: N, 4.94; C, 67.84; H, 4.63. Found: N, 4.85; C, 67.74; H, 4.62.

4,9-Dihydro-4,9-dioxo-3-ethoxycarbonyl-2-propyl-1*H*-benzo[*f*]indole 10b : yellow platelets; mp 197-198 °C; IR ($CHCl_3$) 3425, 3230, 3120, 2970, 2930, 1715, 1650, 1595, 1565, 1500, 1385 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (t, J=7.5 Hz, 3H, CH_3), 1.45 (t, J=7.1 Hz, 3H, CH_3), 1.82 (sextet, J=7.5 Hz, 2H, CH_2), 3.05 (t, J=7.5 Hz, 2H, CH_2), 4.44 (q, J=7.1 Hz, 2H, OCH_2), 7.66(td, J=7.4, 1.2 Hz, 1H, ArH), 7.70 (td, J=7.4, 1.2 Hz, 1H, ArH), 8.05 (dd, J=7.4, 1.2 Hz, 1H, ArH), 8.18 (dd, J=7.4, 1.2 Hz, 1H, ArH), 11.55 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 13.8(q), 14.2(q), 22.9(t), 29.1(t), 60.8(t), 113.9(s), 125.6(d), 126.2(s), 127.4(d), 131.6(s), 132.1(s), 132.7(d), 133.9(d), 134.7(s), 147.0(s), 163.9(s), 176.4(s), 179.0(s); Anal. Calcd for $C_{18}H_{17}NO_4$: N, 4.50; C, 69.44; H, 5.50. Found: N, 4.45; C, 69.22; H, 5.57.

4,9-Dihydro-4,9-dioxo-3-ethoxycarbonyl-2-*p*-tolyl-1*H*-benzo[*f*]indole 10c : orange needles; mp 251-252 °C; IR ($CHCl_3$) 3425, 3225, 3010, 1725, 1660, 1595, 1530, 1370, 1280 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (t, J=7.1 Hz, 3H, CH_3), 2.34 (s, 3H, CH_3), 4.42 (q, J=7.1 Hz, 2H, OCH_2), 7.22 (d, J=7.7 Hz, 2H, ArH), 7.54 (d, J=7.7 Hz, 2H, ArH), 7.65 (t, J=7.4 Hz, 1H, ArH), 7.71 (t, J=7.4 Hz, 1H, ArH), 8.01 (d, J=7.4 Hz, 1H, ArH), 8.17 (d, J=7.4 Hz, 1H, ArH), 10.88 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 14.0(q), 21.3(q), 61.7(t), 114.3(s), 126.2(s), 126.3(d), 126.5(s), 127.2(d), 127.8(d), 129.6(d), 131.8(s), 132.7(s), 133.0(d), 133.8(d), 134.3(s), 140.0(s), 140.2(s), 164.8(s), 175.9(s), 179.4(s); Anal. Calcd for $C_{22}H_{17}NO_4$: N, 3.90; C, 73.53; H, 4.77. Found: N, 3.81; C, 73.54; H, 4.81.

2-Benzyl-4,9-dihydro-4,9-dioxo-3-ethoxycarbonyl-1*H*-benzo[*f*]indole 10d: orange crystals; mp 213-214 °C; IR ($CHCl_3$) 3410, 3230, 3070, 3130, 2940, 1715, 1660, 1595, 1565, 1425, 1385 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (t, J=7.1 Hz, 3H, CH_3), 4.39 (s, 2H, CH_2), 4.44 (q, J=7.1 Hz, 2H, OCH_2), 7.23-7.35 (m, 5H, ArH), 7.65 (td, J=7.5, 1.0 Hz, 1H, ArH), 7.71 (td, J=7.5, 1.0 Hz, 1H, ArH), 8.03 (dd, J=7.5, 1.0 Hz, 1H, ArH), 8.19 (dd, J=7.5, 1.0 Hz, 1H, ArH), 10.12 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 14.2(q), 33.2(t), 61.1(t), 114.0 (s), 125.88 (s), 125.91(d), 127.4(d), 127.5(d), 128.9(d), 129.1(d), 132.05(s), 132.08(s), 132.9(d), 133.9(d), 134.7(s), 136.3(s), 144.0(s), 163.8(s), 176.1(s), 179.0(s); Anal. Calcd for $C_{22}H_{17}NO_4$: N, 3.90; C, 73.55; H, 4.77. Found: N, 3.77; C, 73.40; H, 4.76.

4,9-Dihydro-4,9-dioxo-3-ethoxycarbonyl-2-isopropyl-1*H*-benzo[*f*]indole 10e: yellow platelets; mp 237-238 °C; IR ($CHCl_3$) 3430, 3255, 2980, 1715, 1655, 1475, 1445, 1385, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (d, J=7.0 Hz, 6H, CH_3), 1.45 (t, J=7.1 Hz, 3H, CH_3), 3.67 (septet, J=7.0 Hz, 1H, CH), 4.45 (q, J=7.1 Hz, 2H, OCH_2), 7.68 (td, J=7.4, 1.4 Hz, 1H, ArH), 7.71 (td, J=7.4, 1.4 Hz, 1H, ArH), 8.11 (dd, J=7.4, 1.4 Hz, 1H, ArH), 8.19 (dd, J=7.4, 1.4 Hz, 1H, ArH), 10.34 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 14.2(q), 21.8(q), 26.4(d), 61.1(t), 112.9(s), 125.8(s), 125.9(d), 127.4(d), 131.6(s), 132.3(s), 132.9(d), 133.8(d), 134.7(s), 150.6(s), 164.2(s), 176.1(s), 179.2(s); Anal. Calcd for $C_{18}H_{17}NO_4$: N, 4.46; C, 69.39; H, 5.53. Found: N, 4.50; C, 69.44; H, 5.50.

2-*tert*-Butyl-4,9-dihydro-4,9-dioxo-3-ethoxycarbonyl-1*H*-benzo[*f*]indole 10f: yellow platelets; mp 265-266 °C; IR ($CHCl_3$) 3440, 3275, 2980, 1730, 1660, 1595, 1505, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (t, J=7.1 Hz, 3H, CH_3), 1.47 (s, 9H, CH_3), 4.47 (q, J=7.1 Hz, 2H, OCH_2), 7.64-7.73 (m, 2H, ArH), 8.07-

8.18 (m, 2H, ArH), 9.87 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 14.0(q), 29.6(q), 33.4(s), 61.8(t), 113.8(s), 125.9(s), 126.2(d), 127.0(d), 129.7(s), 132.9(s), 133.1(d), 133.6(d), 134.1(s), 147.7(s), 166.2(s), 175.5(s), 179.7(s); Anal. Calcd for $C_{19}H_{19}NO_4$: N, 4.30; C, 70.14; H, 5.89. Found: N, 4.29; C, 70.03; H, 5.92.

6,11-Dihydro-6,11-dioxo-12-ethoxycarbonylbenzo[*b*]acridine 15a: yellow crystals; mp 210-211°C; IR ($CHCl_3$) 3000, 1730, 1690, 1595, 1375, 1335, 1260, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.54 (t, J=7.2 Hz, 3H, CH_3), 4.75 (q, J=7.2 Hz, 2H, OCH_2), 7.82 (t, J=7.6 Hz, 1H, ArH), 7.85-7.94 (m, 2H, ArH), 7.98 (d, J=8.4 Hz, 1H, ArH), 8.00 (t, J=7.6 Hz, 1H, ArH), 8.33-8.41 (m, 1H, ArH), 8.45-8.51 (m, 1H, ArH), 8.53 (d, J=8.4 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 14.1(q), 62.8(t), 122.6(s), 125.4(s), 126.2(d), 127.7(d), 128.2(d), 130.7(d), 131.8(d), 133.3(s), 133.4(d), 133.9(s), 134.86(d), 134.93(d), 142.7(s), 147.5(s), 149.9(s), 167.1(s), 181.0(s), 181.6(s); Anal. Calcd for $C_{20}H_{13}NO_4$: N, 4.23; C, 72.50; H, 3.95. Found: N, 4.19; C, 72.47; H, 4.00.

6,11-Dihydro-6,11-dioxo-12-ethoxycarbonyl-2-methoxybenzo[*b*]acridine 15b: yellow powder; mp 228-229 °C; IR ($CHCl_3$) 3015, 2400, 1730, 1680, 1620, 1595, 1260, 1245 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.54 (t, J=7.1 Hz, 3H, CH_3), 3.97 (s, 3H, OCH_3), 4.74 (q, J=7.1 Hz, 2H, OCH_2), 7.09 (s, 1H, ArH), 7.59 (d, J=8.2 Hz, 1H, ArH), 7.78-7.90 (m, 2H, ArH), 8.27-8.35 (m, 1H, ArH), 8.39 (d, J=8.2 Hz, 1H, ArH), 8.42-8.49 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 14.2(q), 55.8(q), 62.6(t), 102.8(d), 123.1(s), 127.0(d), 127.1(s), 127.6(d), 128.1(d), 133.3(s), 133.4(d), 133.9(s), 134.6(d), 134.9(d), 140.3(s), 145.2(s), 146.5(s), 161.0(s), 167.5(s), 181.0(s), 182.0(s); Anal. Calcd for $C_{21}H_{15}NO_5$: N, 3.88; C, 69.80; H, 4.18. Found: N, 3.87; C, 69.74; H 4.23.

6,11-Dihydro-6,11-dioxo-12-ethoxycarbonyl-2-methylbenzo[*b*]acridine 15c: yellow powder: mp 203-204 °C; IR ($CHCl_3$) 3000, 1730, 1685, 1625, 1600, 1550, 1500, 1270, 1255 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.54 (t, J=7.2 Hz, 3H, CH_3), 2.63 (s, 3H, CH_3), 4.76 (q, J=7.2 Hz, 2H, OCH_2), 7.70 (d, J=1.6 Hz, 1H, ArH), 7.82 (dd, J=8.7, 1.6 Hz, 1H, ArH), 7.85-7.93 (m, 2H, ArH), 8.32-8.39 (m, 1H, ArH), 8.42 (d, J=8.7 Hz, 1H, ArH), 8.46-8.55 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 14.1(q), 22.2(q), 62.8(t), 122.8(s), 124.8(d), 125.5(s), 127.7(d), 128.2(d), 131.5(d), 133.4(s), 134.0(s), 134.8(d), 134.9(d), 136.0(d), 141.7(s), 141.7(s), 146.8(s), 148.8(s), 167.4(s), 181.2(s), 181.8(s); Anal. Calcd for $C_{21}H_{15}NO_4$: N, 4.06; C, 73.02; H, 4.38. Found: N, 4.05; C, 73.07; H, 4.46.

6,11-Dihydro-6,11-dioxo-2,12-diethoxycarbonylbenzo[*b*]acridine 15d: yellow needles; mp 205-206 °C; IR ($CHCl_3$) 3180, 3000, 2940, 1725, 1690, 1595, 1555, 1405, 1390, 1280, 1255 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.47 (t, J=7.1 Hz, 3H, CH_3), 1.58 (t, J=7.1 Hz, 3H, CH_3), 4.49 (q, J=7.1 Hz, 2H, OCH_2), 4.79 (q, J=7.1 Hz, 2H, OCH_2), 7.84-7.95 (m, 2H, ArH), 8.32-8.39 (m, 1H, ArH), 8.43-8.50 (m, 1H, ArH), 8.50-8.59 (m, 2H, ArH), 8.67 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 14.1(q), 14.2(q), 61.9(t), 63.0(t), 123.0(s), 124.6(s), 127.7(d), 128.2(d), 128.8(d), 131.9(d), 132.6(d), 133.2(s), 133.7(s), 135.01(d), 135.04(d), 144.0(s), 148.9(s), 151.2(s), 164.8(s), 166.5(s), 180.6(s), 181.2(s); Anal. Calcd for $C_{23}H_{17}NO_6$: N, 3.47; C, 68.48; H, 4.25. Found: N, 3.36; C, 68.41; H, 4.26.

1-Chloro-6,11-dihydro-6,11-dioxo-12-ethoxycarbonyl-4-methoxybenzo[*b*]acridine 15e: orange powder; mp 243-244 °C; IR ($CHCl_3$) 3005, 2940, 1730, 1690, 1600, 1560, 1540, 1435, 1365, 1260, 1245 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.52 (t, J=7.2 Hz, 3H, CH_3), 4.15 (s, 3H, OCH_3), 4.61 (dq, J=10.7, 7.2 Hz, 1H, OCH), 4.80 (dq, J=10.7, 7.2 Hz, 1H, OCH), 7.19 (d, J=8.6 Hz, 1H, ArH), 7.79 (d, J=8.6 Hz, 1H, ArH), 7.84-7.92 (m, 2H, ArH), 8.32-8.39 (m, 1H, ArH), 8.42-8.49 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ

13.7(q), 56.7(q), 62.8(t), 110.8(d), 121.6(s), 123.9(s), 124.5(s), 127.9(d), 128.0(d), 133.2(d), 133.6(s), 133.8(s), 134.9(d), 135.0(d), 141.2(s), 143.0(s), 146.3(s), 156.3(s), 167.1(s), 180.1(s), 181.5(s); Anal. Calcd for $C_{21}H_{14}ClNO_5$: N, 3.54; C, 63.73; H, 3.57. Found: N, 3.53; C, 63.39; H, 3.60.

1-Chloro-6,11-dihydro-6,11-dioxo-12-ethoxycarbonylbenzo[*b*]acridine 15f: light yellow powder; mp 251-252°C; IR ($CHCl_3$) 3015, 2400, 1730, 1690, 1595, 1550, 1250, 1215 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.54 (t, J=7.1 Hz, 3H, CH_3), 4.75 (q, J=7.1 Hz, 2H, OCH_2), 7.86-7.96 (m, 4H, ArH), 8.32-8.38 (m, 1H, ArH), 8.43-8.51 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$) δ 14.1(q), 63.1(t), 123.3(s), 124.9(d), 126.0(s), 127.8(d), 128.3(d), 133.2(d), 133.3(s), 133.8(s), 134.5(d), 135.0(d), 135.1(d), 137.2(s), 141.7(s), 147.6(s), 148.3(s), 166.6(s), 180.7(s), 181.4(s); Anal. Calcd for $C_{20}H_{12}ClNO_4$: N, 3.82; C, 65.49; H, 3.57. Found: N, 3.78; C, 65.30; H, 3.34.

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