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1,2-Acyl group migration in the oxidative free radical reaction of 2-substituted-1,4-quinones

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ABSTRACT

Oxidative free radical reactions of 2-substituted-1,4-quinone derivatives are described. Electrophilic carbon-centered radical produced by the manganese(III) acetate oxidation of α-chloro-β-ketoester undergoes efficient addition to the C–C double bond of 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone, and this reaction provides a novel method for the synthesis of spirolactam **3** and indole-2,4,7-trione **4**. It shows high chemoselectivity depending on the migratory aptitude of the substituent on α-chloro-β-ketoester. Imine radical can be generated from the oxidation of β-enamino carbonyl compound with Mn(III) or Ce(IV) salt. With 2-hydroxy-1,4-naphthoquinone, spirolactam **6** was prepared from β-enamino carbonyl compound effectively. TBACN/$CHCl_3$ is the most effective reaction condition for the formation of **6**.

1. Introduction

Carbon–carbon bond forming reactions mediated by radical have received considerable attention in organic synthesis during the last two decades.[1] Naturally occurring quinones such as mitosenes, kinamycins, murrayaquinones, etc. represent an important class of biologically significant natural products.[2] A common building block to these compounds is the indoloquinone unit. The development of new synthetic methodologies for the synthesis of indoloquinone ring system is therefore important.[3,4] The oxidative free radical reaction mediated by metal salts has been developed into a versatile protocol for the formation of highly functionalized products from simple precursors.[1d–f,5–8] Among these, manganese(III) acetate and cerium(IV) ammonium nitrate (CAN) have been used most efficiently. Previously, we found that oxidative free radical reactions of 2-(alkylamino)-1,4-naphthoquinones with β-ketoesters produced benzo[*f*]indole-4,9-diones and benzo[*f*]indole-2,4,9-triones effectively.[6f,j,k] In this report, we wish to describe our results on the formation of the unexpected spirolactam from 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone or 2-hydroxy-1,4-naphthoquinone via the 1,2-acyl group migration.

2. Results and discussion

We first tried the manganese(III)-mediated reaction of 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone (**1**) with α-chloro-β-ketoester **2** as shown in Eq. 1. When 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone (**1**) was treated with ethyl 2-chloroacetoacetate (**2a**) and manganese(III) acetate in acetic acid at room temperature, spirolactam **3a** was obtained in 39% yield (Table 1, entry 1). Contrary to the manganese(III)-mediated reactions of **1** with β-ketoesters, there are no indole-4,7-diones and indole-2,4,7-triones can be found in this reaction.[9] Although the mechanistic details of this reaction are unclear, **3a** may be formed by the reaction mechanism presented in Scheme 1. Initiation occurs with the manganese(III) oxidation of **2a** to produce radical **A-a** (R^1=Me, R^2=OEt). Intermolecular addition of this radical intermediate **A-a** to quinone ring followed by oxidation gives **C-a**, which is then oxidized by manganese(III) acetate followed by elimination of a chlorine atom to produce **E-a**. Imine **E-a** undergoes nucleophilic addition of acetate ion (Nu=OAc) followed by cyclization to generate **G-a**. Protonation of **G-a** followed by 1,2-acyl group migration and hydrolysis generates **3a** (path a). The generalities of this reaction were examined with other β-ketoesters **2b** and **2c**. Spirolactams **3b** and **3c** were also formed in poor yields (entries 2 and 3). According to the proposed mechanism shown above, we believed that **3a** could be obtained in a better reaction yield when additional metal salt was added. Indeed, when **1** was treated with

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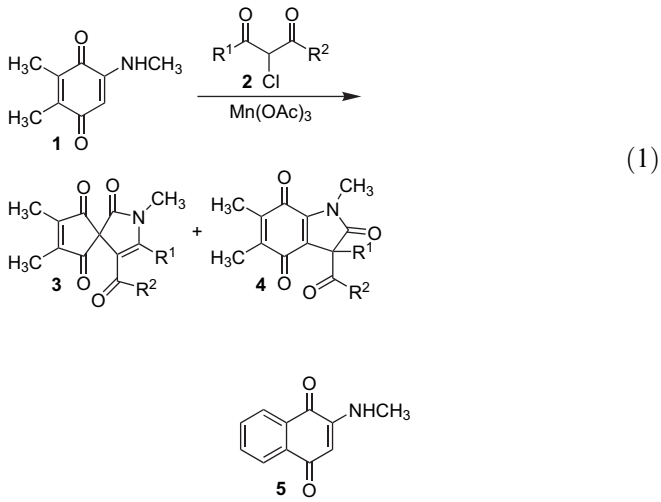
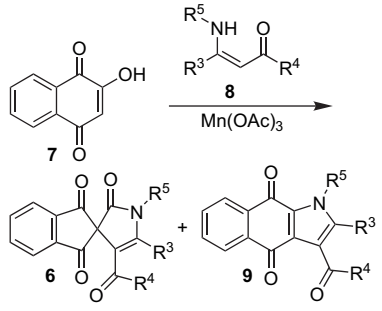


(1)

Table 1
Free radical reactions between 2-(methylamino)-1,4-quinones and α-chloro-β-ketoesters

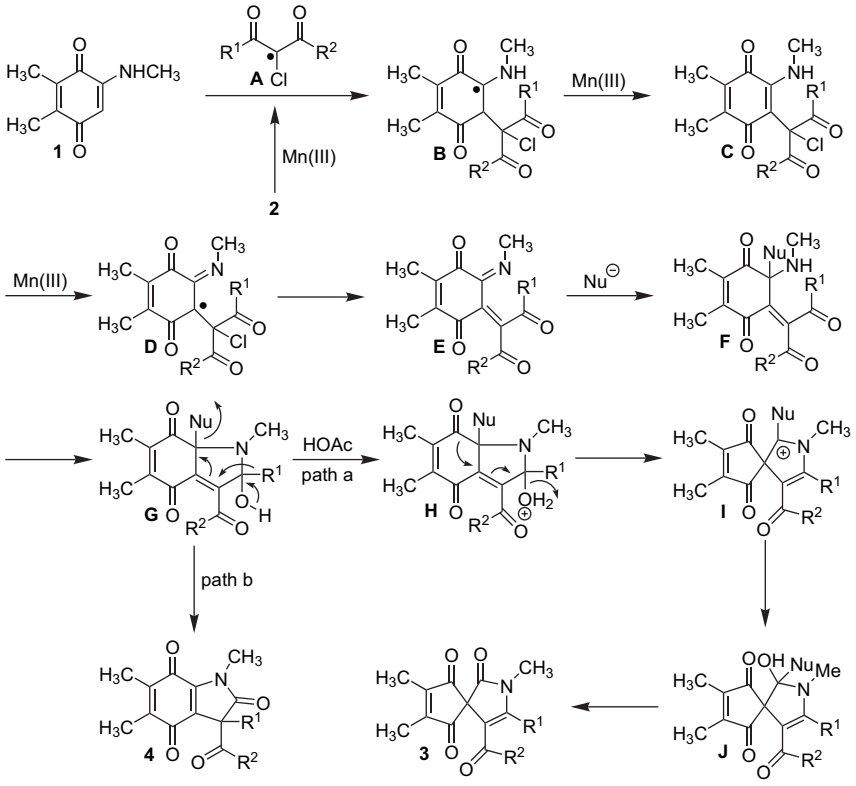
Entry	Quinone	Ketoester	Metal salt	Product (yield (%))
1	**1**	**2a**: R^1=Me, R^2=OEt	—	**3a** (39)
2	**1**	**2b**: R^1=Et, R^2=OEt	—	**3b** (28)
3	**1**	**2c**: R^1=^{n}Pr, R^2=OEt	—	**3c** (28)
4	**1**	**2a**: R^1=Me, R^2=OEt	KCN	**3a** (57)
5	**1**	**2a**: R^1=Me, R^2=OEt	NaCl	**3a** (68)
6	**1**	**2b**: R^1=Et, R^2=OEt	NaCl	**3b** (58)
7	**1**	**2c**: R^1=^{n}Pr, R^2=OEt	NaCl	**3c** (61)
8	**1**	**2d**: R^1=$(CH_2)_2$Ph, R^2=OEt	NaCl	**3d** (66)
9	**5**	**2a**: R^1=Me, R^2=OEt	NaCl	**6f** (40)
10	**1**	**2e**: R^1=^{i}Pr, R^2=OMe	—	**4a** (30)
11	**1**	**2f**: R^1=CH_2OMe, R^2=OMe	—	**4b** (48)

2a, manganese(III) acetate, and potassium cyanide in acetic acid, the reaction yield of **3a** rose to 57% (entry 4). In the presence of sodium chloride, **3a** can be obtained in an even better reaction yield (68%, entry 5). Other examples are also shown in Table 1 (entries 6–8). In all cases, spirolactams **3** were produced in much better reaction yields than those performed without sodium chloride. The structure of **3a** was revealed by ^{1}H NMR and ^{13}C NMR analyses. In addition, the NMR-based structure was confirmed by single crystal X-ray analysis (Fig. 1).[10] Reaction of **1** in acetic acid with methyl 2-chloro-isobutyrylacetate (**2e**, R^1=^{i}Pr, R^2=O Me) and manganese(III) acetate, instead of the expected spirolactam **3e**, afforded indole-2,4,7-trione **4a** exclusively in 30% yield (entry 10). Indole-2,4,7-trione **4a** was formed presumably via the alkyl group migration of **G-e** (R^1=^{i}Pr) (path b, Scheme 1). The different behavior of **G-e** can be ascribed to the higher migratory aptitude of the isopropyl group. Analogous result was obtained with **2f** (entry 11).[11]



(2)

This manganese(III)-mediated oxidative free radical reaction was next performed with corresponding 1,4-naphthoquinone derivative. In contrast to 2-(methylamino)-1,4-benzoquinone **1**, reaction of 2-(methylamino)-1,4-naphthoquinone (**5**) with ethyl



Scheme 1.

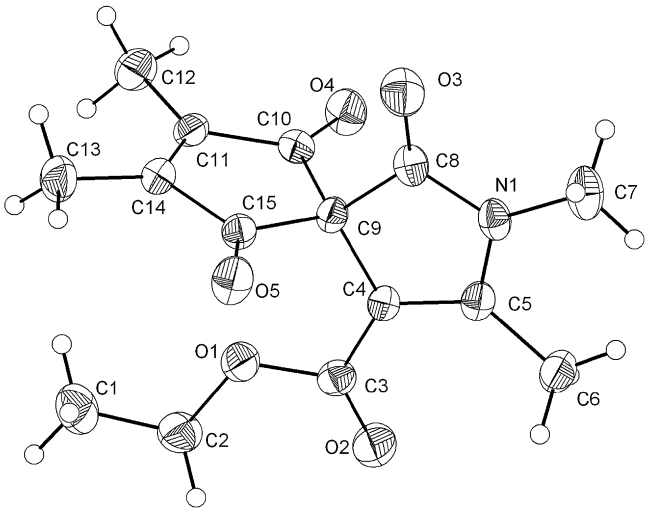


Figure 1. The molecular structure of compound **3a**.

2-chloroacetoacetate (**2a**) produced spirolactam **6f** in a much lower yield (40%, Table 1, entry 9). Earlier, we have reported that the analogues of **6f** can be formed from the manganese(III)-mediated reaction of 2-hydroxy-1,4-naphthoquinone (**7**) with β-enamino carbonyl compound **8** (Eq. 2).[12] A possible mechanism for this reaction is outlined in Scheme 2. Initiation occurs with the manganese(III) oxidation of **8** to produce imine radical **K**. Imine radical **K** undergoes intermolecular addition to quinone ring followed by oxidation to give **M**, which subsequently undergoes either condensation reaction to produce **9** (path a) or manganese(III) oxidation to generate radical **N** (path b). 1,2-Acyl group migration[13] of radical **N** followed by oxidation and intramolecular nucleophilic addition generates **6**. As shown in Table 2, spirolactams **6a–d** were prepared effectively from β-enamino ketones **8a–d** (44–56% yield, entries 1–4). On the contrary, with β-enamino ester **8e**, the yield of **6e** is rather poor (27% yield, entry 5). This fair to poor reaction yield of **6** is presumably due to the liability of **8** in acetic acid. To improve the reaction yield of **6**, we next attempted to study this reaction in non-acidic condition with cerium(IV) salt. Treatment of **7** and **8a** with CAN in methanol led to the deterioration of **7** and no desired product

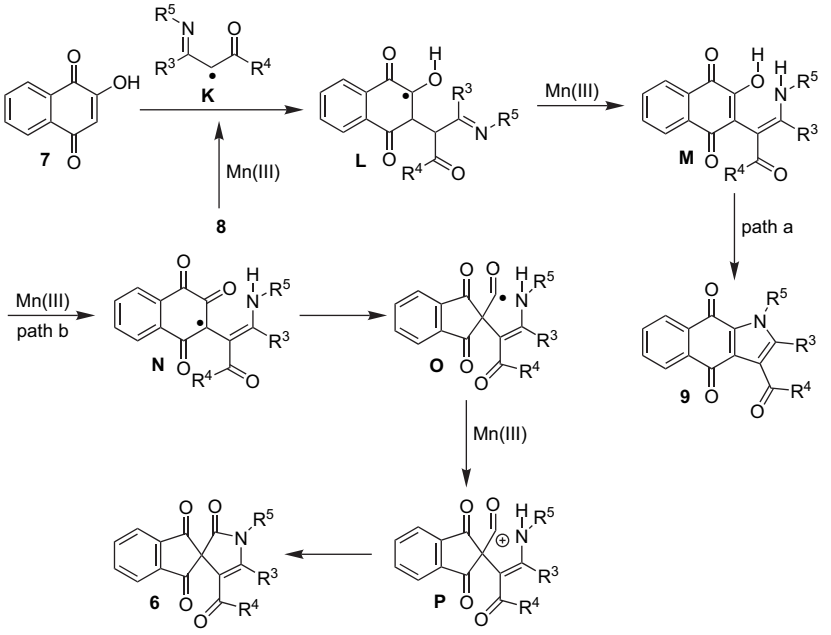
Table 2
Free radical reactions between 2-hydroxy-1,4-naphthoquinone and β-enamino carbonyl compounds

Entry	β-Enamino carbonyl compound	Metal salt	Solvent	Product (yield (%))
1	**8a**: R^3=Me, R^4=Me, R^5=Me	$Mn(OAc)_3$	HOAc	**6a** (51), **9a** (5)
2	**8b**: R^3=Me, R^4=Ph, R^5=Me	$Mn(OAc)_3$	HOAc	**6b** (49), **9b** (10)
3	**8c**: R^3=Et, R^4=Et, R^5=Me	$Mn(OAc)_3$	HOAc	**6c** (44), **9c** (trace)[a]
4	**8d**: R^3=^{i}Pr, R^4=^{i}Pr, R^5=Me	$Mn(OAc)_3$	HOAc	**6d** (52)
5	**8e**: R^3=^{n}Pr, R^4=OEt, R^5=Me	$Mn(OAc)_3$	HOAc	**6e** (27)
6	**8a**: R^3=Me, R^4=Me, R^5=Me	CAN	MeOH	**6a** (0)
7	**8a**: R^3=Me, R^4=Me, R^5=Me	TBACN	CH_3CN	**6a** (66)
8	**8a**: R^3=Me, R^4=Me, R^5=Me	TBACN	MeOH	**6a** (83)
9	**8a**: R^3=Me, R^4=Me, R^5=Me	TBACN	$CHCl_3$	**6a** (91)
10	**8b**: R^3=Me, R^4=Ph, R^5=Me	TBACN	$CHCl_3$	**6b** (77)
11	**8c**: R^3=Et, R^4=Et, R^5=Me	TBACN	$CHCl_3$	**6c** (88)
12	**8d**: R^3=^{i}Pr, R^4=^{i}Pr, R^5=Me	TBACN	$CHCl_3$	**6d** (91)
13	**8e**: R^3=^{n}Pr, R^4=OEt, R^5=Me	TBACN	$CHCl_3$	**6e** (72)
14	**8f**: R^3=Me, R^4=OEt, R^5=Me	TBACN	$CHCl_3$	**6f** (85)
15	**8g**: R^3=Ph, R^4=OEt, R^5=Et	TBACN	$CHCl_3$	**6g** (83)

[a] Compound **9c** cannot be isolated from the reaction mixture; however, it can be detected by thin-layer chromatography.

6a could be isolated (entry 6). It has been reported that tetra-*n*-butylammonium cerium(IV) nitrate (TBACN) oxidized 1,3-dicarbonyl compounds more slowly than CAN.[14] We expected that **6a** could be generated in a better yield by using TBACN. Indeed, with TBACN, the reaction between 2-hydroxy-1,4-naphthoquinone (**7**) and **8a** in acetonitrile at room temperature afforded **6a** exclusively in a better reaction yield (66%, entry 7). In attempt to investigate the range of solvents compatible with this reaction, reaction between **7** and **8a** was next performed in other solvents. The change of solvent to methanol and chloroform gave **6a** as the only product in 83 and 91% yields, respectively (entries 8 and 9). Since TBACN/$CHCl_3$ is the most effective reaction condition for the formation of **6a**, so the scope of this reaction was explored with a variety of β-enamino carbonyl compound **8** under this optimized reaction condition. All of these results are listed in Table 2 (entries 9–15). Spirolactams **6** were prepared effectively from both β-enamino ketones **8a–d** and β-enamino esters **8e–g** in good to excellent yields.

In conclusion, radical **A** generated from the manganese(III) acetate oxidation of α-chloro-β-ketoester undergoes efficient addition to the C–C double bond of 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone. This free radical reaction provides a novel



Scheme 2.

method for the synthesis of spirolactam **3** and indole-2,4,7-trione **4**, and it shows high chemoselectivity depending on the migratory aptitude of the substituent (R^1) on α-chloro-β-ketoester. With 2-(methylamino)-1,4-naphthoquinone, the corresponding spirolactam **6f** was also obtained but in a lower yield. Imine radical **K** can be generated from the oxidation of β-enamino carbonyl compound by Mn(III) or Ce(IV) salt. By the reaction of 2-hydroxy-1,4-naphthoquinone and β-enamino carbonyl compound with TBACN, this spirolactam **6** can be produced in good yield. TBACN/$CHCl_3$ is the most effective reaction condition for the formation of **6**.

3. Experimental

3.1. General

Melting points are uncorrected. Infrared spectra were taken with a Hitachi 260-30 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 or AVANCE 300 spectrometer. Chemical shifts are reported in parts per million relative to TMS as internal reference. Elemental analyses were performed with Heraeus CHN-Rapid Analyzer. X-ray diffraction structure analyses were performed with a Nonius Kappa CCD diffractometer. Structure analysis was made by using SHELXTL program on a personal computer. Analytical thin-layer chromatography was performed with precoated silica gel 60 F-254 plates (0.25 mm thick) and visualized by UV. The reaction mixture was purified by column chromatography over silica gel (70–230 mesh). The starting 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone (**1**),[15] 2-(methylamino)-1,4-naphthoquinone (**5**),[16] and α-chloro-β-ketoesters **2** were synthesized according to literature procedures.[17] The spectral data of **4a** and **4b** have been reported.[9]

3.2. Typical experimental procedure for the reaction between 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone (1) and α-chloro-β-ketoester 2

A mixture of 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone (**1**, 126 mg, 0.76 mmol), ethyl 2-chloroacetoacetate (**2a**, 503 mg, 3.07 mmol), and $Mn(OAc)_3$ (1.23 g, 4.57 mmol) in acetic acid (10 mL) was stirred at room temperature for 1 h. The reaction mixture was diluted with ethyl acetate (100 mL), washed with saturated aqueous sodium bisulfite (50 mL), water (2×50 mL), saturated aqueous sodium bicarbonate (50 mL), and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography on silica (20 g) using ethyl acetate/hexane (1:4) as eluent, followed by crystallization (ethyl acetate/hexane) to give **3a** (88 mg, 39%).

*3.2.1. Ethyl 2,3,7,8-tetramethyl-1,6,9-trioxo-2-aza-spiro[4,4]nona-3,7-diene-4-carboxylate **3a***

Yellow crystals; mp 132–133 °C; IR (KBr) 1695, 1385, 1325, 1290, 1165 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, *J*=7.1 Hz, 3H, CH_3), 2.13 (s, 6H, 2×CH_3), 2.54 (s, 3H, CH_3), 3.07 (s, 3H, NCH_3), 4.03 (q, *J*=7.1 Hz, 2H, OCH_2); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 9.8 (2×q), 12.5 (q), 13.8 (q), 26.8 (q), 59.9 (t), 66.5 (s), 105.0 (s), 157.8 (2×s), 158.5 (s), 162.1 (s), 169.9 (s), 195.4 (2×s). Anal. Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.86; H, 5.88; N, 4.81.

*3.2.2. Ethyl 3-ethyl-2,7,8-trimethyl-1,6,9-trioxo-2-aza-spiro[4,4]-nona-3,7-diene-4-carboxylate **3b***

Yellow crystals; mp 132–133 °C; IR (KBr) 2980, 1695, 1290, 1165, 1095 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, *J*=7.1 Hz, 3H, CH_3), 1.29 (t, *J*=7.6 Hz, 3H, CH_3), 2.13 (s, 6H, 2×CH_3), 2.96 (q, *J*=7.6 Hz, 2H, CH_2), 3.09 (s, 3H, NCH_3), 4.03 (q, *J*=7.1 Hz, 2H, OCH_2); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 9.8 (2×q), 12.3 (q), 13.8 (q), 19.4 (t), 26.7 (q), 59.9 (t), 66.5 (s), 104.3 (s), 157.8 (2×s), 161.9 (s), 164.0 (s), 170.3 (s), 195.4 (2×s). Anal. Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.94; H, 6.32; N, 4.53.

*3.2.3. Ethyl 2,7,8-trimethyl-3-propyl-1,6,9-trioxo-2-aza-spiro[4,4]nona-3,7-diene-4-carboxylate **3c***

Yellow crystals; mp 114–115 °C; IR (KBr) 2965, 1695, 1290, 1165, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.08 (t, *J*=7.5 Hz, 3H, CH_3), 1.11 (t, *J*=7.1 Hz, 3H, CH_3), 1.69 (sextet, *J*=7.5 Hz, 2H, CH_2), 2.13 (s, 6H, 2×CH_3), 2.93 (t, *J*=7.5 Hz, 2H, CH_2), 3.08 (s, 3H, NCH_3), 4.03 (q, *J*=7.1 Hz, 2H, OCH_2); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 9.8 (2×q), 13.5 (q), 13.8 (q), 21.4 (t), 26.9 (q), 27.6 (t), 59.9 (t), 66.6 (s), 105.0 (s), 157.8 (2×s), 162.0 (s), 162.3 (s), 170.3 (s), 195.4 (2×s). Anal. Calcd for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39. Found: C, 63.95; H, 6.60; N, 4.34.

*3.2.4. Ethyl 2,7,8-trimethyl-3-(2-phenylethyl)-1,6,9-trioxo-2-aza-spiro[4,4]nona-3,7-diene-4-carboxylate **3d***

Yellow crystals; mp 140–141 °C; IR (KBr) 1695, 1625, 1290, 1200, 1145 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, *J*=7.1 Hz, 3H, CH_3), 2.14 (s, 6H, 2×CH_3), 2.73 (s, 3H, NCH_3), 2.99 (t, *J*=7.5 Hz, 2H, CH_2), 3.18 (t, *J*=7.5 Hz, 2H, CH_2), 4.04 (q, *J*=7.1 Hz, 2H, OCH_2), 7.21–7.26 (m, 1H, ArH), 7.28–7.35 (m, 4H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 9.8 (2×q), 13.8 (q), 26.6 (q), 28.4 (t), 34.5 (t), 60.0 (t), 66.5 (s), 105.1 (s), 126.6 (d), 128.52 (2×d), 128.59 (2×d), 139.5 (s), 157.8 (2×s), 161.8 (s), 162.1 (s), 170.2 (s), 195.3 (2×s). Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.28; H, 6.08; N, 3.67. Found: C, 69.16; H, 6.06; N, 3.60.

3.3. Typical experimental procedure for the reaction between 2-hydroxy-1,4-naphthoquinone (7) and β-enamino carbonyl compound 8

A solution of 2-hydroxy-1,4-naphthoquinone (**7**, 150 mg, 0.86 mmol), 4-methylamino-3-penten-2-one (**8a**) [prepared from the reaction of 2,4-pentanedione (259 mg, 2.59 mmol) and 40% aqueous methylamine (240 g, 3.1 mmol)], and TBACN (3.43 g, 3.44 mmol) in chloroform (10 mL) was stirred at room temperature for 30 min. After workup as described above, the crude product was purified by column chromatography on silica (20 g) using ethyl acetate/hexane (1:2) as eluent, followed by crystallization (ethyl acetate/hexane) to give **6a** (222 mg, 91%).

*3.3.1. 4′-Acetyl-1′,5′-dimethyl-spiro[indene-2,3′-pyrrole]-1,2′,3(1′H)-trione **6a***

White crystals; mp 277–278 °C; IR ($CHCl_3$) 3010, 1760, 1715, 1615, 1425 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 3.12 (s, 3H, NCH_3), 7.84–7.90 (m, 2H, ArH), 8.01–8.08 (m, 2H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.8 (q), 27.2 (q), 28.9 (q), 71.0 (s), 119.0 (s), 124.4 (2×d), 135.7 (2×d), 143.3 (2×s), 156.1 (s), 170.0 (s), 189.6 (s), 193.2 (2×s). Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.87; H, 4.70; N, 4.95.

*3.3.2. 4′-Benzoyl-1′,5′-dimethyl-spiro[indene-2,3′-pyrrole]-1,2′,3(1′H)-trione **6b***

White crystals; mp 232–233 °C; IR ($CHCl_3$) 3010, 2955, 1715, 1605, 1580 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.03 (s, 3H, CH_3), 3.11 (s, 3H, NCH_3), 7.34–7.45 (m, 2H, ArH), 7.45–7.62 (m, 3H, ArH), 7.81–7.91 (m, 2H, ArH), 8.01–8.11 (m, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.6 (q), 27.1 (q), 71.3 (s), 117.8 (s), 124.4 (2×d), 128.1 (2×d), 128.4 (2×d), 131.8 (d), 135.8 (2×d), 139.2 (s), 143.5 (2×s), 156.9 (s), 170.4 (s), 189.2 (s), 193.1 (2×s). Anal. Calcd for $C_{21}H_{15}NO_4$: C, 73.04; H, 4.38; N, 4.06. Found: C, 72.80; H, 4.49; N, 4.12.

*3.3.3. 5′-Ethyl-1′-methyl-4-propanoyl-spiro[indene-2,3′-pyrrole]-1,2′,3(1′H)-trione **6c***

White crystals; mp 187–188 °C; IR ($CHCl_3$) 2985, 1715, 1635, 1605, 1460 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.02 (t, *J*=7.1 Hz, 3H, CH_3), 1.41 (t, *J*=7.6 Hz, 3H, CH_3), 2.63 (q, *J*=7.1 Hz, 2H, CH_2), 2.93 (q,

J=7.6 Hz, 2H, CH_2), 3.14 (s, 3H, NCH_3), 7.82–7.92 (m, 2H, ArH), 8.01–8.09 (m, 2H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 7.6 (q), 12.8 (q), 20.5 (t), 27.0 (q), 33.4 (t), 71.1 (s), 117.9 (s), 124.4 (2×d), 135.7 (2×d), 143.3 (2×s), 160.8 (s), 170.4 (s), 192.7 (s), 193.3 (2×s). Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.44; H, 5.50; N, 4.53.

3.3.4. 4′-Isobutanoyl-5′-isopropyl-1′-methyl-spiro[indene-2,3′-pyrrole]-1,2′,3(1′H)-trione **6d**

White crystals; mp 165–166 °C; IR ($CHCl_3$) 2980, 1760, 1715, 1630, 1590 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, J=6.8 Hz, 6H, 2×CH_3), 1.52 (d, J=7.3 Hz, 6H, 2×CH_3), 2.94 (septet, J=6.8 Hz, 1H, CH), 3.26 (s, 3H, NCH_3), 3.91 (septet, J=7.3 Hz, 1H, CH), 7.80–7.91 (m, 2H, ArH), 8.01–8.10 (m, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 19.1 (2×q), 19.7 (2×q), 27.1 (q), 29.7 (d), 38.0 (d), 71.5 (s), 117.2 (2×d), 124.4 (2×d), 135.5 (s), 143.2 (2×s), 163.1 (s), 170.9 (s), 193.2 (s), 197.8 (2×s). Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.74; H, 6.25; N, 4.10.

3.3.5. Ethyl 1′-methyl-5′-propyl-1,1′,2′,3-tetrahydro-1,2′,3-trioxo-spiro[indene-2,3′-pyrrole]-4′-carboxylate **6e**

White crystals; mp 146–147 °C; IR ($CHCl_3$) 2975, 1705, 1630, 1430, 1345 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (t, J=7.1 Hz, 3H, CH_3), 1.11 (t, J=7.5 Hz, 3H, CH_3), 1.74 (sextet, J=7.5 Hz, 2H, CH_2), 2.99 (t, J=7.5 Hz, 2H, CH_2), 3.12 (s, 3H, NCH_3), 3.91 (q, J=7.1 Hz, 2H, OCH_2), 7.85–7.91 (m, 2H, ArH), 8.08–8.10 (m, 2H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.4 (q), 13.7 (q), 21.5 (t), 27.1 (q), 27.7 (t), 60.1 (t), 70.4 (s), 105.9 (s), 124.3 (2×d), 135.8 (2×d), 143.5 (2×s), 162.0 (s), 162.9 (s), 170.5 (s), 193.3 (2×s). Anal. Calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.71; H, 5.63; N, 4.08.

3.3.6. Ethyl 1′,5′-dimethyl-1,1′,2′,3-tetrahydro-1,2′,3-trioxo-spiro[indene-2,3′-pyrrole]-4′-carboxylate **6f**

White crystals; mp 123–124 °C; IR (KBr) 2980, 1710, 1290, 1170, 1065 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (t, J=7.1 Hz, 3H, CH_3), 2.59 (s, 3H, CH_3), 3.11 (s, 3H, NCH_3), 3.92 (q, J=7.1 Hz, 2H, OCH_2), 7.86–7.88 (m, 2H, ArH), 8.04–8.10 (m, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.5 (q), 13.3 (q), 26.8 (q), 60.0 (t), 70.2 (s), 105.8 (s), 124.2 (2×d), 135.8 (2×d), 143.3 (2×s), 158.9 (s), 162.0 (s), 170.0 (s), 193.2 (2×s). Anal. Calcd for $C_{17}H_{15}NO_5$: C, 65.17; H, 4.83; N, 4.47. Found: C, 65.08; H, 4.81; N, 4.43.

3.3.7. Ethyl 1′-ethyl-5′-phenyl-1,1′,2′,3-tetrahydro-1,2′,3-trioxo-spiro[indene-2,3′-pyrrole]-4′-carboxylate **6g**

White crystals; mp 185–186 °C; IR (KBr) 2990, 1715, 1380, 1270, 1075 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.65 (t, J=7.1 Hz, 3H, CH_3), 1.02 (t, J=7.1 Hz, 3H, CH_3), 3.42 (q, J=7.1 Hz, 2H, NCH_2), 3.76 (q, J=7.1 Hz, 2H, OCH_2), 7.53 (br s, 5H, ArH), 7.87–7.93 (m, 2H, ArH), 8.08–8.14 (m, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.9 (q), 13.8 (q), 36.4 (t), 59.9 (t), 70.7 (s), 107.6 (s), 124.1 (2×d), 128.2 (2×d), 128.4 (s), 128.7 (2×d), 130.0 (d), 135.7 (2×d), 143.3 (2×s), 159.3 (s), 161.1 (s), 170.0 (s), 192.7 (2×s). Anal. Calcd for $C_{23}H_{19}NO_5$: C, 70.94; H, 4.92; N, 3.60. Found: C, 70.81; H, 4.97; N, 3.53.

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References and notes

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9. Manganese(III)-mediated reactions of **1** with β-ketoesters generate indole-4,7-diones and indole-2,4,7-triones. See: Chuang, C.-P.; Tsai, A.-I. *Tetrahedron* **2007**, *63*, 11911.
10. Crystal data for **3a**: $C_{15}H_{17}NO_5$, M=291.30, T=200(2) K, λ=0.71073 Å, monoclinic, space group *Pn*, a=7.4869(2) Å, b=7.8791(2) Å, c=12.3767(4) Å, α=90°, β=96.7830(10)°, γ=90°, V=724.99(4) Å^3, Z=2, D_c=1.334 mg/m^3, μ=0.101 mm^{-1}, F(000)=308, crystal size 0.75×0.7×0.6 mm^3, reflections collected 5027, independent reflections 2518 [R (int)=0.0442], refinement method, full-matrix least-squares on F^2, goodness-of-fit on F^2 1.076, final R indices [$I>2\sigma(I)$] R_1=0.0552, wR_2=0.1465, R indices (all data) R_1=0.0580, wR_2=0.1507, largest diff. peak and hole 0.454 and −0.304 e Å^{-3}. Crystallographic data for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 672265. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
11. Indole-2,4,7-triones **4a** and **4b** can be produced in much better reaction yields by the manganese(III)-mediated reaction of **1** with β-ketoesters in CF_3CH_2OH. See: Ref. 9.
12. Preliminary communication has been reported. See: Ref. 6i.
13. Similar 1,2-acyl group migration has been reported. See: Chuang, C.-P.; Tsai, A.-I. *Tetrahedron* **2007**, *63*, 9712.
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