Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 63 (2007) 9712–9717
Tetrahedron

A novel oxidative free radical reaction between 2-amino-1,4-benzoquinones and benzoylacetonitriles

Che-Ping Chuang* and An-I. Tsai

Department of Chemistry, National Cheng Kung University, Tainan 70101, Taiwan

Received 15 May 2007; revised 4 July 2007; accepted 6 July 2007
Available online 6 August 2007

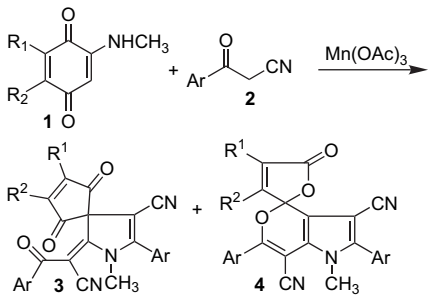
Abstract—The manganese(III) initiated oxidative free radical reaction between 2-amino-1,4-benzoquinones and benzoylacetonitriles is described. This free radical reaction provides a novel method for the synthesis of spirodione **3** and spirolactone **4**. With 5,6-dimethyl-2-methylamino-1,4-benzoquinone, spirodione **3** was obtained exclusively. On the contrary, with 5-methyl-2-methylamino-1,4-benzoquinone, spirolactone **4** was produced in high chemo- and regioselectivity. By heating with sodium acetate, spirodione **3** can be converted to **4** effectively.

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 indolequinone unit. The development of new synthetic methodologies for the synthesis of indolequinone ring system is therefore important.[3,4] The oxidative free radical reaction initiated 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 have been used most efficiently. Previously, we reported that oxidative free radical reactions of 2-amino-1,4-naphthoquinones with malonate, nitroacetate, and β-dicarbonyl compounds produced benzo[*f*]indole-4,9-diones, benzo[*f*]indole-2,4,9-triones, benzo[*b*]carbazole-6,11-diones, and benzo[*b*]acridine-6,11-diones effectively.[6] In this report, we wish to describe our results on the manganese(III) acetate initiated oxidative free radical reaction between 2-amino-1,4-benzoquinones and benzoylacetonitriles.

2. Results and discussion

We began our studies with the reaction shown in Eq. 1. When 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone (**1a**, R^1=R^2=Me) was treated with *p*-toluoylacetonitrile **2a** and manganese(III) acetate in acetic acid at room temperature, a yellow product spirodione **3a** was obtained in 55% yield (Table 1, entry 1). Contrary to the manganese(III) initiated reactions of **1a** with β-dicarbonyl compounds, no indole-4,7-diones and indole-2,4,7-triones can be found in this reaction.[6f,j,k,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) acetate oxidation of **2a** to produce radical **5a**. This radical intermediate **5a** undergoes intermolecular addition to quinone ring followed by oxidation to generate **6a**, which was then oxidized by manganese(III) acetate to produce radical **7a**. Radical **7a** undergoes 1,2-carbonyl group migration[10] followed by oxidation and intermolecular nucleophilic addition of another **2a** to give **10**, which then undergoes a further intramolecular condensation reaction to produce **3a**. The solvent effects play an important role in the manganese(III) acetate initiated oxidative free radical



(1)

Keywords: Manganese(III) acetate; Free radical; 2-Amino-1,4-benzoquinones; Benzoylacetonitriles; Regioselectivity.
* Corresponding author. Fax: +886 6 2740552; e-mail: cpchuang@mail.ncku.edu.tw

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.07.008

Table 1. Free radical reactions between 2-methylamino-1,4-benzoquinone **1** and benzoylacetonitrile **2**

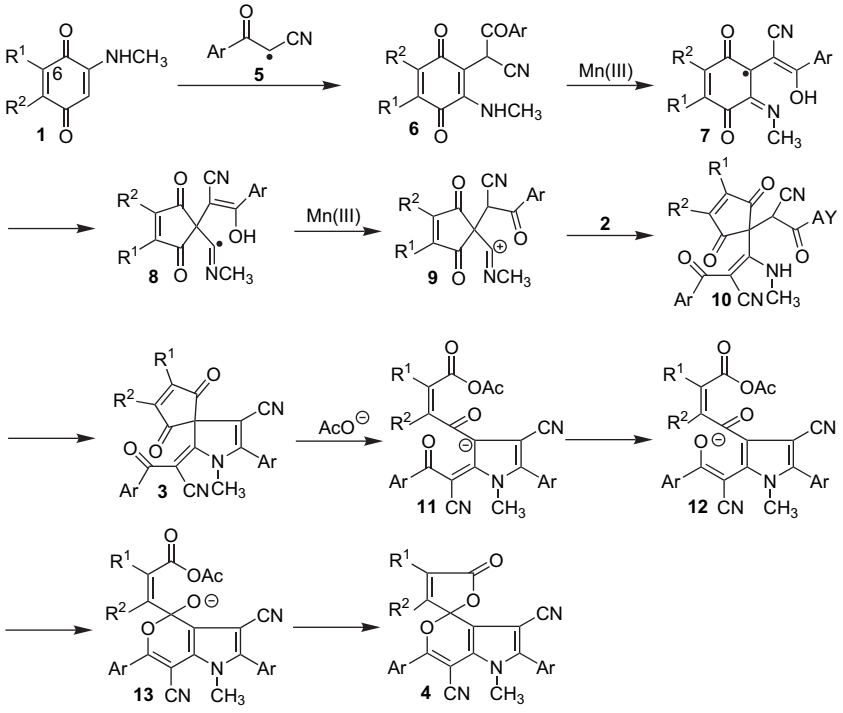
Entry	Quinone	Benzoylacetonitrile	Solvent	Reaction time	Product [yield (%)]
1	**1a**	**2a**: Ar=*p*-MePh	HOAc[a]	4 h	**3a** (55)
2	**1a**	**2a**: Ar=*p*-MePh	C_6H_6[b]	45 min	**3a** (31)
3	**1a**	**2a**: Ar=*p*-MePh	CF_3CH_2OH[b]	45 min	**3a** (40)
4	**1a**	**2a**: Ar=*p*-MePh	CH_3CN[b]	45 min	**3a** (69)
5	**1a**	**2b**: Ar=Ph	CH_3CN[b]	45 min	**3b** (66)
6	**1a**	**2c**: Ar=*p*-ClPh	CH_3CN[b]	45 min	**3c** (70)
7	**1a**	**2d**: Ar=*p*-MeOPh	CH_3CN[b]	45 min	**3d** (69)
8	**1b**	**2a**: Ar=*p*-MePh	CH_3CN[b]	2 h	**4d** (48)
9	**1b**	**2b**: Ar=Ph	CH_3CN[b]	2 h	**4e** (48)
10	**1b**	**2c**: Ar=*p*-ClPh	CH_3CN[b]	2 h	**4f** (53)
11	**1a**	**2a**: Ar=*p*-MePh	CH_3CN[b,c]	8 h	**4a** (75)
12	**1a**	**2b**: Ar=Ph	CH_3CN[b,c]	8 h	**4b** (74)
13	**1a**	**2c**: Ar=*p*-ClPh	CH_3CN[b,c]	8 h	**4c** (76)
14	**1b**	**2a**: Ar=*p*-MePh	CH_3CN[b,c]	2 h	**4d** (53)
15	**1b**	**2b**: Ar=Ph	CH_3CN[b,c]	2 h	**4e** (51)
16	**1b**	**2c**: Ar=*p*-ClPh	CH_3CN[b,c]	2 h	**4f** (60)

[a] Reaction temperature: RT.
[b] Reaction temperature: 80 °C.
[c] The reaction was performed with additional 5 equiv of sodium acetate.

reaction.[11] Reaction between **1a** and **2a** was next performed in other solvents. The change of solvent to benzene, 2,2,2-trifluoroethanol, and acetonitrile gave **3a** as the only product. It gave best result (69% yield) when acetonitrile was used as the solvent (entry 4). The generalities of this reaction were examined with other benzoylacetonitriles (entries 5–7). This reaction worked well and **3b–3d** were formed in 66–70% yields with dominant (*E*)-selectivity. These high stereoselectivities are presumably due to the steric effect between the benzoyl group and methyl group of the *Z* isomer. The structure of **3b** 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).[12]

To test the regioselectivity of this reaction, the reaction between 5-methyl-2-methylamino-1,4-benzoquinone (**1b**, R^1=H, R^2=Me) and benzoylacetonitrile **2** was next studied. Reaction of **1b** in acetonitrile with *p*-toluoylacetonitrile (**2a**) and manganese(III) acetate, instead of the expected product **3e** (R^1=H, R^2=Me, Ar=*p*-MePh), afforded a pale yellow product spirolactone **4d** exclusively in 48% yield (entry 8). No product derived from the addition of radical **5a** to the C_6 of **1b** can be found. This can be ascribed to the electron deficiency of radical intermediate **5a**, and this makes the rate of intermolecular addition to the C–C double bond bearing an electron-donating amino group much faster. Analogous results were obtained with other benzoylacetonitriles and the results are also summarized in Table 1 (entries 8–10). In all cases, spirolactone **4** was obtained as the only product. The structure of **4e** was confirmed by the ^{1}H NMR, ^{13}C NMR, and X-ray analyses (Fig. 2).[13] Spirolactone **4** was formed presumably from **3** via the reaction routes outlined in Scheme 1. Retro Claisen condensation of **3**, initiated by the addition of acetate ion to the carbonyl group of **3**, generates **11**. This anionic intermediate **11** undergoes intramolecular addition (via enolate **12**) followed by lactonization to produce **4**. The different behaviors between **1a** and **1b** in this reaction can be rationalized that the steric effect of R^1 group makes the nucleophilic addition of acetate ion to the carbonyl group of **3a** (R^1=Me) much slower than that of **3b** (R^1=H).

According to the proposed reaction mechanism shown above, we believe that **4a** can be obtained by the reaction of **3a** with sodium acetate (Eq. 2). Indeed, when **3a** was heated with sodium acetate in acetonitrile, **4a** was obtained in 99% yield (Table 2, entry 1). Other examples are also summarized in Table 2. In all cases, spirodione **3** was converted to the corresponding spirolactone **4** effectively. On



Scheme 1.

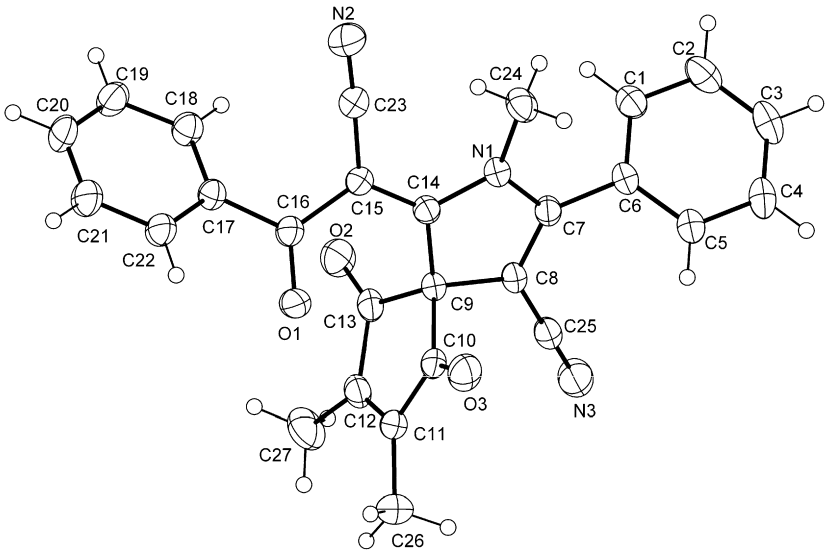


Figure 1. The molecular structure of compound **3b**.

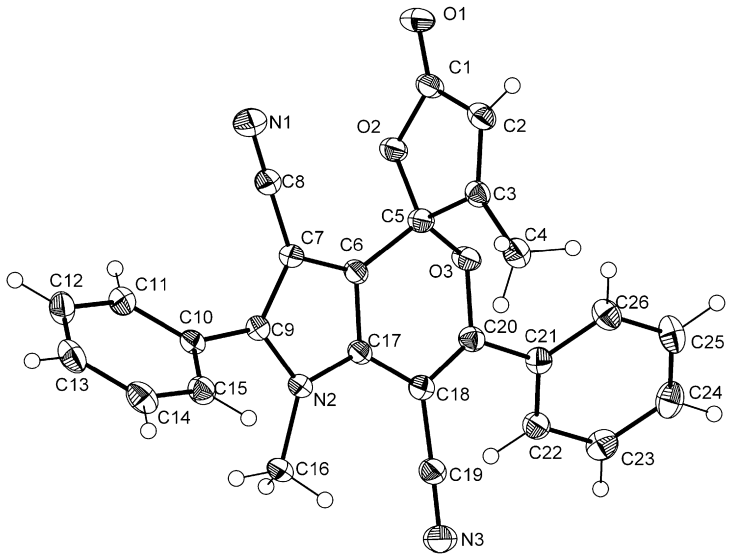
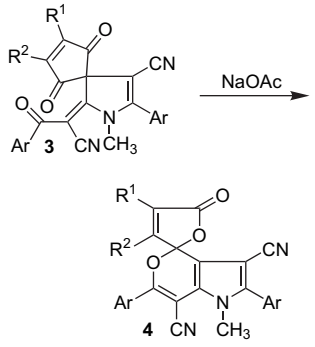


Figure 2. The molecular structure of compound **4e**.

the basis of this finding, we have continued to study this oxidative free radical reaction of **1** with manganese(III) acetate and sodium acetate. Treatment of **1a** with **2a**, manganese(III) acetate, and sodium acetate in acetonitrile gave **4a** in 76% yield (entry 11). The generalities of this reaction are also shown in Table 1 (entries 11–16). Spirolactones **4a**–**4c** were obtained directly from **1a** (entries 11–13). With **1b**, **4d**–**4f** were produced in a better reaction yields (entries 14–16) than those performed without sodium acetate (entries 8–10).



(2)

Table 2. Reactions between spiro-1,3-dione **3** and sodium acetate

Entry	Spirodiones	Reaction time (h)	Product [yield (%)]
1	**3a**: Ar=*p*-MePh	4	**4a** (99)
2	**3b**: Ar=Ph	4	**4b** (97)
3	**3c**: Ar=*p*-ClPh	4	**4c** (99)

In conclusion, carbon radical can be generated from the manganese(III) acetate oxidation of benzoylacetonitrile and it undergoes efficient addition to the C–C double bond of 2-amino-1,4-benzoquinones. This free radical reaction provides a novel method for the synthesis of spirodione **3**

and spirolactone **4**. These reactions gave best results in acetonitrile. With 5,6-dimethyl-2-methylamino-1,4-benzoquinone (**1a**), spirodione **3** was obtained exclusively. On the contrary, with 5-methyl-2-methylamino-1,4-benzoquinone (**1b**), spirolactone **4** was produced in high chemo- and regioselectivity. By heating with sodium acetate, spirodione **3** can be converted to **4** effectively.

3. Experimental

3.1. General

Melting points are uncorrected. Infrared spectra were obtained with a Hitachi 260-30 spectrometer. ^{1}H 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 an internal reference. Elemental analyses were performed with Heraeus CHN-Rapid Analyzer. X-ray diffraction structure analysis was 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) from EM Laboratories and visualized by UV. The reaction mixture was purified by column chromatography over EM Laboratories silica gel (70–230 mesh). The starting 2-amino-1,4-benzoquinone **1** was synthesized according to the literature procedure.[14]

3.2. Typical experimental procedure for the reaction between 2-(methylamino)-1,4-benzoquinone 1 and benzoylacetonitrile 2

A mixture of 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone (**1a**, 121 mg, 0.73 mmol), *p*-toluoylacetonitrile (**2a**, 466 mg, 2.93 mmol), and $Mn(OAc)_3$ (1.18 g, 4.4 mmol) in acetonitrile (10 mL) was stirred at 80 °C for 45 min. The reaction mixture was diluted with ethyl acetate (100 mL), washed with saturated aqueous sodium bisulfite (50 mL), water (2×50 mL), and 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 dichloromethane–hexane (2:1) as an eluent, followed by crystallization (ethyl acetate–hexane) to give **3a** (224 mg, 69%).

3.2.1. 1-[1-Cyano-2-oxo-2-(*p*-tolyl)-eth-(*E*)-ylidene]-2,7,8-trimethyl-6,9-dioxo-3-(*p*-tolyl)-2-aza-spiro-[4,4]nona-3,7-diene-4-carbonitrile 3a. Yellow crystals; mp 189–190 °C; IR (KBr) 2950, 2210, 1710, 1510, 1080 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17 (s, 6H, 2×CH_3), 2.39 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.68 (s, 3H, NCH_3), 7.22 (d, J=8.0 Hz, 2H, ArH), 7.33–7.41 (m, 4H, ArH), 7.63 (d, J=8.0 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 9.5 (2×q), 21.26 (q), 21.33 (q), 37.1 (q), 71.8 (s), 87.0 (s), 91.1 (s), 112.7 (s), 117.9 (s), 122.2 (s), 128.4 (2×d), 128.6 (2×d), 128.7 (2×d), 129.9 (2×d), 134.1 (s), 142.5 (s), 143.1 (s), 153.5 (2×s), 159.7 (s), 165.1 (s), 188.7 (s), 192.3 (2×s); Anal. Calcd for $C_{29}H_{23}N_3O_3$: C, 75.47; H, 5.02; N, 9.10. Found: C, 75.50; H, 5.06; N, 9.10.

3.2.2. 1-[1-Cyano-2-oxo-2-phenyl-eth-(*E*)-ylidene]-2,7,8-trimethyl-6,9-dioxo-3-phenyl-2-aza-spiro-[4,4]nona-3,7-diene-4-carbonitrile 3b. Yellow crystals; mp 202–203 °C; IR (KBr) 2925, 2210, 1710, 1520, 1010 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18 (s, 6H, 2×CH_3), 3.69 (s, 3H, NCH_3), 7.43 (t, J=7.6 Hz, 2H, ArH), 7.47–7.65 (m, 6H, ArH), 7.71 (d, J=7.1 Hz, 2H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 9.8 (2×q), 37.3 (q), 72.3 (s), 87.3 (s), 92.1 (s), 112.6 (s), 117.9 (s), 125.3 (s), 128.1 (2×d), 128.4 (2×d), 129.0 (2×d), 129.5 (2×d), 132.1 (d), 132.5 (d), 137.1 (s), 153.8 (2×s), 159.6 (s), 165.4 (s), 189.4 (s), 192.3 (2×s); Anal. Calcd for $C_{27}H_{19}N_3O_3$: C, 74.81; H, 4.42; N, 9.69. Found: C, 74.87; H, 4.41; N, 9.72.

3.2.3. 3-(*p*-Chlorophenyl)-1-[2-(*p*-chlorophenyl)-1-cyano-2-oxo-eth-(*E*)-ylidene]-2,7,8-trimethyl-6,9-dioxo-2-aza-spiro-[4,4]nona-3,7-diene-4-carbonitrile 3c. Yellow crystals; mp 183–184 °C; IR (KBr) 2210, 1710, 1520, 1295, 1255 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18 (s, 6H, 2×CH_3), 3.68 (s, 3H, NCH_3), 7.41 (d, J=8.5 Hz, 2H, ArH), 7.46 (d, J=8.5 Hz, 2H, ArH), 7.58 (d, J=8.5 Hz, 2H, ArH), 7.66 (d, J=8.5 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 9.7 (2×q), 37.3 (q), 72.4 (s), 87.0 (s), 92.5 (s), 112.3 (s), 117.6 (s), 123.5 (s), 128.4 (2×d), 129.85 (2×d), 129.92 (2×d), 130.3 (2×d), 135.1 (s), 138.7 (s), 138.9 (s), 153.8 (2×s), 158.3 (s), 165.4 (s), 188.0 (s), 192.0 (2×s); Anal. Calcd for $C_{27}H_{17}Cl_2N_3O_3$: C, 64.55; H, 3.41; N, 8.36. Found: C, 64.39; H, 3.51; N, 8.32.

3.2.4. 1-[1-Cyano-2-(*p*-methoxyphenyl)-2-oxo-eth-(*E*)-ylidene]-3-(*p*-methoxyphenyl)-2,7,8-trimethyl-6,9-dioxo-2-aza-spiro-[4,4]nona-3,7-diene-4-carbonitrile 3d. Yellow crystals; mp 186–187 °C; IR (KBr) 2205, 1705, 1600, 1520, 1255 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (s, 6H, 2×CH_3), 3.69 (s, 3H, NCH_3), 3.85 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 6.90 (d, J=8.8 Hz, 2H, ArH), 7.06 (d, J=8.7 Hz, 2H, ArH), 7.45 (d, J=8.7 Hz, 2H, ArH), 7.76 (d, J=8.8 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 9.8 (2×q), 37.5 (q), 55.4 (q), 55.5 (q), 71.6 (s), 87.3 (s), 90.6 (s), 113.2 (s), 113.5 (2×d), 115.0 (2×d), 117.3 (s), 118.3 (s), 129.5 (s), 130.8 (2×d), 131.1 (2×d), 153.9 (2×s), 159.9 (s), 162.5 (s), 163.3 (s), 165.4 (s), 187.6 (s), 192.7 (2×s); Anal. Calcd for $C_{29}H_{23}N_3O_5$: C, 70.58; H, 4.70; N, 8.51. Found: C, 70.34; H, 4.70; N, 8.46.

3.3. Typical experimental procedure for the reaction of spirodione 3 with sodium acetate

A mixture of spirodione **3a** (105 mg, 0.24 mmol) and NaOAc (126 g, 1.54 mmol) in acetonitrile (10 mL) was heated at 80 °C for 4 h. After workup as described above, the residue was chromatographed over silica gel (20 g, eluted with 2:1 dichloromethane–hexane) followed by crystallization (ethyl acetate–hexane) to give **4a** (104 mg, 99%).

3.4. Typical experimental procedure for sodium acetate-assisted reaction between 2-(methylamino)-1,4-benzoquinone 1 and benzoylacetonitrile 2

A mixture of 5,6-dimethyl-2-(methylamino)-1,4-benzoquinone (**1a**, 81 mg, 0.49 mmol), *p*-toluoylacetonitrile (**2a**, 308 mg, 1.94 mmol), $Mn(OAc)_3$ (780 g, 2.91 mmol), and NaOAc (205 g, 2.47 mmol) in acetonitrile (10 mL) was

heated at 80 °C for 8 h. After workup as described above, the crude product was purified by column chromatography on silica (20 g) using dichloromethane–hexane (2:1) as an eluent, followed by crystallization (ethyl acetate–hexane) to give **4a** (159 mg, 75%).

3.4.1. 1,3′,4′-Trimethyl-2,6-di-(*p*-tolyl)-1,2′,4,5′-tetrahydro-5′-oxo-spiro{furan-2′,4-pyrano[4,3-*b*]pyrrole}-3,7-dicarbonitrile 4a. Pale yellow crystals; mp 210–211 °C; IR (KBr) 2220, 1780, 1590, 1270, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.04 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 3.90 (s, 3H, NCH_3), 7.30 (d, J=8.2 Hz, 2H, ArH), 7.31–7.37 (m, 4H, ArH), 7.75 (d, J=8.2 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 8.6 (q), 11.6 (q), 21.2 (q), 21.5 (q), 33.4 (q), 80.5 (s), 87.3 (s), 105.3 (s), 108.8 (s), 113.6 (s), 115.9 (s), 124.4 (s), 125.2 (s), 127.9 (s), 128.7 (2×d), 129.2 (2×d), 129.5 (2×d), 129.7 (2×d), 140.2 (s), 142.7 (s), 145.3 (s), 152.4 (s), 162.9 (s), 169.4 (s); Anal. Calcd for $C_{29}H_{23}N_3O_3$: C, 75.47; H, 5.02; N, 9.10. Found: C, 75.42; H, 5.03; N, 9.08.

3.4.2. 1,3′,4′-Trimethyl-2,6-diphenyl-1,2′,4,5′-tetrahydro-5′-oxo-spiro{furan-2′,4-pyrano[4,3-*b*]pyrrole}-3,7-dicarbonitrile 4b. Pale yellow crystals; mp 172–173 °C; IR (KBr) 2220, 1780, 1590, 1270, 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.04 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 3.92 (s, 3H, NCH_3), 7.42–7.47 (m, 2H, ArH), 7.47–7.59 (m, 6H, ArH), 7.86 (d, J=7.5 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 8.6 (q), 11.6 (q), 33.5 (q), 81.1 (s), 87.6 (s), 105.3 (s), 109.0 (s), 113.4 (s), 115.7 (s), 125.2 (s), 127.3 (s), 128.5 (2×d), 128.7 (2×d), 129.1 (2×d), 129.3 (s), 129.7 (2×d), 130.0 (d), 130.6 (s), 131.9 (d), 145.2 (s), 152.4 (s), 162.8 (s), 169.3 (s); Anal. Calcd for $C_{27}H_{19}N_3O_3$: C, 74.81; H, 4.42; N, 9.69. Found: C, 74.85; H, 4.46; N, 9.67.

3.4.3. 2,6-Di-(*p*-chlorophenyl)-1,3′,4′-trimethyl-1,2′,4,5′-tetrahydro-5′-oxo-spiro{furan-2′,4-pyrano[4,3-*b*]pyrrole}-3,7-dicarbonitrile 4c. Pale yellow needles; mp 178–179 °C; IR (KBr) 2225, 1785, 1590, 1270, 1095 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.05 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 3.91 (s, 3H, NCH_3), 7.39 (d, J=8.4 Hz, 2H, ArH), 7.48 (d, J=8.7 Hz, 2H, ArH), 7.54 (d, J=8.4 Hz, 2H, ArH), 7.80 (d, J=8.7 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 8.7 (q), 11.6 (q), 33.6 (q), 81.3 (s), 88.1 (s), 105.2 (s), 109.5 (s), 113.1 (s), 115.4 (s), 125.3 (s), 125.7 (s), 129.0 (2×d), 129.6 (2×d), 129.7 (s), 130.1 (2×d), 131.0 (2×d), 136.5 (s), 138.3 (s), 144.0 (s), 152.2 (s), 161.7 (s), 169.2 (s); Anal. Calcd for $C_{27}H_{17}Cl_2N_3O_3$: C, 64.55; H, 3.41; N, 8.36. Found: C, 64.23; H, 3.58; N, 8.22.

3.4.4. 1,3′-Dimethyl-2,6-di-(*p*-tolyl)-1,2′,4,5′-tetrahydro-5′-oxo-spiro{furan-2′,4-pyrano[4,3-*b*]pyrrole}-3,7-dicarbonitrile 4d. Pale yellow needles; mp 255–256 °C; IR (KBr) 2915, 2220, 1785, 1600, 1155 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H, CH_3), 2.44 (s, 6H, 2×CH_3), 3.91 (s, 3H, NCH_3), 6.26 (s, 1H, CH), 7.31 (d, J=8.1 Hz, 2H, ArH), 7.33–7.38 (m, 4H, ArH), 7.76 (d, J=8.1 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.2 (q), 21.0 (q), 21.3 (q), 33.3 (q), 80.4 (s), 87.0 (s), 106.0 (s), 107.5 (s), 113.3 (s), 115.6 (s), 120.8 (d), 124.2 (s), 125.0 (s), 127.5 (s), 128.5 (2×d), 129.1 (2×d), 129.3 (2×d), 129.5 (2×d), 140.1 (s), 142.6 (s), 145.4 (s), 161.3 (s), 162.4 (s), 167.4 (s); Anal. Calcd for $C_{28}H_{21}N_3O_3$: C, 75.15; H, 4.73; N, 9.39. Found: C, 75.05; H, 4.77; N, 9.36.

3.4.5. 1,3′-Dimethyl-2,6-diphenyl-1,2′,4,5′-tetrahydro-5′-oxo-spiro{furan-2′,4-pyrano[4,3-*b*]pyrrole}-3,7-dicarbonitrile 4e. Pale yellow crystals; mp 220–221 °C; IR (KBr) 3060, 2225, 1790, 1590, 1215 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H, CH_3), 3.93 (s, 3H, NCH_3), 6.28 (s, 1H, CH), 7.43–7.48 (m, 2H, ArH), 7.49–7.60 (m, 6H, ArH), 7.87 (d, J=7.8 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.5 (q), 33.6 (q), 81.3 (s), 87.7 (s), 106.2 (s), 108.1 (s), 113.3 (s), 115.6 (s), 121.2 (d), 125.2 (s), 127.3 (s), 128.7 (2×d), 128.8 (2×d), 129.2 (2×d), 129.7 (2×d), 130.1 (d), 130.5 (s), 132.1 (d), 145.5 (s), 161.3 (s), 162.6 (s), 167.5 (s); Anal. Calcd for $C_{26}H_{17}N_3O_3$: C, 74.45; H, 4.09; N, 10.02. Found: C, 74.18; H, 4.16; N, 9.96.

3.4.6. 2,6-Di-(*p*-chlorophenyl)-1,3′-dimethyl-1,2′,4,5′-tetrahydro-5′-oxo-spiro{furan-2′,4-pyrano[4,3-*b*]pyrrole}-3,7-dicarbonitrile 4f. Pale yellow crystals; mp 277–278 °C; IR (KBr) 2225, 1805, 1780, 1590, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.20 (d, J=1.6 Hz, 3H, CH_3), 3.92 (s, 3H, NCH_3), 6.29 (q, J=1.6 Hz, 1H, CH), 7.40 (d, J=8.4 Hz, 2H, ArH), 7.49 (d, J=8.6 Hz, 2H, ArH), 7.55 (d, J=8.4 Hz, 2H, ArH), 7.81 (d, J=8.6 Hz, 2H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.5 (q), 33.7 (q), 81.5 (q), 88.1 (s), 106.0 (s), 108.5 (s), 113.0 (s), 115.3 (s), 121.4 (d), 125.3 (s), 125.6 (s), 128.8 (s), 129.1 (2×d), 129.6 (2×d), 130.1 (2×d), 131.0 (2×d), 136.7 (s), 138.5 (s), 144.2 (s), 161.1 (s), 161.5 (s), 167.3 (s); Anal. Calcd for $C_{26}H_{15}Cl_2N_3O_3$: C, 63.95; H, 3.10; N, 8.61. Found: C, 63.89; H, 3.12; N, 8.59.

Acknowledgements

We are grateful to the National Science Council of the ROC for financial support (Grant no. NSC-92-2113-M-006-008).

References and notes

1. (a) Hart, D. J. *Science* **1984**, *223*, 883; (b) Neumann, W. P. *Synthesis* **1987**, 665; (c) Curran, D. P. *Synthesis* **1988**, 417 and 489; (d) Melikyan, G. G. *Synthesis* **1993**, 833; (e) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519; (f) Snider, B. B. *Chem. Rev.* **1996**, *96*, 339.
2. (a) *The Chemistry of Functional Groups: The Chemistry of the Quinoid Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, NY, 1988; (b) Thomson, R. H. *Naturally Occurring Quinones IV: Recent Advances*; Chapman and Hall: London, 1997.
3. (a) Shaw, K. J.; Luly, J. R.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 4515; (b) Murphy, W. S.; O'Sullivan, P. J. *Tetrahedron Lett.* **1992**, *33*, 531; (c) O'Sullivan, P. J.; Moreno, R.; Murphy, W. S. *Tetrahedron Lett.* **1992**, *33*, 535.
4. (a) Yogo, M.; Ito, C.; Furukawa, H. *Chem. Pharm. Bull.* **1991**, *39*, 328; (b) Bittner, S.; Krief, P.; Massil, T. *Synthesis* **1991**, 215; (c) Knölker, H.-J.; O'Sullivan, N. *Tetrahedron* **1994**, *50*, 10893; (d) Åkermark, B.; Oslob, J. D.; Heuschert, U. *Tetrahedron Lett.* **1995**, *36*, 1325; (e) Echavarran, A. M.; Tamayo, N.; De Frutos, O.; Garcia, A. *Tetrahedron* **1997**, *50*, 16835.

5. (a) Oumar-Mahamat, H.; Moustrou, C.; Surzur, J.-M.; Berstrand, M. P. *J. Org. Chem.* **1989**, *54*, 5684; (b) Snider, B. B.; Wan, B. Y. F.; Buckman, B. O.; Foxman, B. M. *J. Org. Chem.* **1991**, *56*, 5328; (c) Citterio, A.; Sebastiano, R.; Carvayal, M. C. *J. Org. Chem.* **1991**, *56*, 5335; (d) Citterio, A.; Sebastiano, R.; Nicolini, M. *Tetrahedron* **1993**, *49*, 7743.
6. (a) Chuang, C.-P.; Wang, S.-F. *Tetrahedron Lett.* **1994**, *35*, 4365; (b) Chuang, C.-P.; Wang, S.-F. *J. Chin. Chem. Soc.* **1997**, *44*, 271; (c) Chuang, C.-P.; Wang, S.-F. *Tetrahedron* **1998**, *54*, 10043; (d) Chuang, C.-P.; Wang, S.-F. *Heterocycles* **1999**, *50*, 489; (e) Chuang, C.-P.; Wu, Y.-L.; Jiang, M.-C. *Tetrahedron* **1999**, *55*, 11229; (f) Jiang, M.-C.; Chuang, C.-P. *J. Org. Chem.* **2000**, *65*, 5409; (g) Wu, Y.-L.; Chuang, C.-P.; Lin, P.-Y. *Tetrahedron* **2001**, *57*, 5543; (h) Tsai, A.-I.; Wu, Y.-L.; Chuang, C.-P. *Tetrahedron* **2001**, *57*, 7829; (i) Chuang, C.-P.; Wu, Y.-L. *Tetrahedron Lett.* **2001**, *42*, 1719; (j) Tseng, C.-C.; Wu, Y.-L.; Chuang, C.-P. *Tetrahedron* **2002**, *58*, 7625; (k) Tseng, C.-M.; Wu, Y.-L.; Chuang, C.-P. *Tetrahedron* **2004**, *60*, 12249; (l) Chen, H.-L.; Lin, C.-Y.; Cheng, Y.-C.; Tsai, A.-I.; Chuang, C.-P. *Synthesis* **2005**, 977; (m) Lin, C.-Y.; Cheng, Y.-C.; Tsai, A.-I.; Chuang, C.-P. *Org. Biomol. Chem.* **2006**, 1097.
7. (a) Liao, Y.-J.; Wu, Y.-L.; Chuang, C.-P. *Tetrahedron* **2003**, *59*, 3511; (b) Chuang, C.-P.; Wu, Y.-L. *Tetrahedron* **2004**, *60*, 1841; (c) Tsai, A.-I.; Lin, C.-H.; Chuang, C.-P. *Heterocycles* **2005**, *65*, 2381; (d) Tsai, A.-I.; Chuang, C.-P. *Tetrahedron* **2006**, *62*, 2235.
8. (a) Jacobsen, N.; Torsell, K. *Acta Chem. Scand.* **1973**, *27*, 3211; (b) Brown, P. M.; Thomson, R. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 997; (c) Citterio, A.; Arnoldi, A.; Minisci, F. *J. Org. Chem.* **1979**, *44*, 2674; (d) Citterio, A.; Vismara, E.; Bernardi, R. *J. Chem. Res., Synop.* **1983**, 88; (e) Citterio, A.; Vismara, E.; Bernardi, R. *J. Chem. Res., Miniprint* **1983**, 876; (f) Williams, D. R.; Clark, M. P. *Tetrahedron Lett.* **1998**, *39*, 7629.
9. Reaction of **1a** with β-dicarbonyl compounds produced indole-4,7-diones and indole-2,4,7-triones.
10. Similar 1,2-carbonyl group migration has been reported. See: Ref. 6i.
11. (a) Snider, B. B.; Merritt, J. E.; Dombroski, M. A.; Buckman, B. O. *J. Org. Chem.* **1991**, *56*, 5544; (b) Snider, B. B.; McCarthy, B. A. *J. Org. Chem.* **1993**, *58*, 6217; (c) Ishibashi, H.; Toyao, A.; Takeda, Y. *Synlett* **1999**, 1468. Also see: Ref. 6k.
12. Crystal data for **3b**: $C_{27}H_{19}N_3O_3$, M=433.45, T=273 (2) K, λ=0.71073 Å, monoclinic, space group $P2(1)/n$, a=12.7814(3) Å, b=12.0618(3) Å, c=14.8407(4) Å, α=90°, β=98.168(1)°, γ=90°, V=2264.73(10) Å^3, Z=4, D_c=1.271 mg/m^3, μ=0.085 mm^{-1}, $F(000)$=904, crystal size 0.3×0.2×0.2 mm^3, reflections collected 53,317, independent reflections 7179 [R(int)=0.0540], refinement method, full-matrix least-squares on F^2, goodness-of-fit on F^2 0.949, final R indices [$I>2\sigma(I)$] R_1=0.0522, wR_2=0.1645, R indices (all data) R_1=0.0947, wR_2=0.1901, largest diff. peak and hole 0.363 and −0.408 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 646869. 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).
13. Crystal data for **4e**: $C_{26}H_{17}N_3O_3$, M=419.43, T=200 (2) K, λ=0.71073 Å, monoclinic, space group $P21/a$, a=11.7787(6) Å, b=15.2636(8) Å, c=11.8375(7) Å, α=90°, β=106.294(2)°, γ=90°, V=2042.73(19) Å^3, Z=4, D_c=1.364 mg/m^3, μ=0.091 mm^{-1}, $F(000)$=872, crystal size 0.38×0.32×0.18 mm^3, reflections collected 11,271, independent reflections 3646 [R(int)=0.0523], refinement method, full-matrix least-squares on F^2, goodness-of-fit on F^2 1.088, final R indices [$I>2\sigma(I)$] R_1=0.0605, wR_2=0.1586, R indices (all data) R_1=0.0908, wR_2=0.1889, largest diff. peak and hole 0.568 and −0.654 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 646872. 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).
14. (a) Kallmeyer, H.-J.; Tappe, C. *Arch. Pharmacol.* **1986**, *319*, 421; (b) Kallmeyer, H.-J.; Tappe, C. *Arch. Pharmacol.* **1986**, *41*, 29.