Free radical reaction between 2-benzoyl-1,4-benzoquinones and 1,3-dicarbonyl compounds†

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A manganese(III)-mediated reaction between 2-benzoyl-1,4-benzoquinones and 1,3-dicarbonyl compounds that produces benzo[*c*]furan-4,7-diones and anthracene-1,4-diones with high chemoselectivity is described. With ethyl butyrylacetate, by changing the solvent, benzo[*c*]furan-4,7-diones and anthracene-1,4-diones can be generated in high chemoselectivities. With ethyl benzoylacetate, *N*,*N*-dimethyl acetoacetamide and 1,3-diones, benzo[*c*]furan-4,7-diones were produced effectively with high selectivity. With 2-alkyl-5-benzoyl-1,4-benzoquinones, the regioselectivity of this reaction was also studied and the corresponding benzo[*c*]furan-4,7-dione and anthracene-1,4-dione derivatives were obtained in high regioselectivity.

Introduction

Free radical reactions have received considerable attention during the last two decades and there is now a wealth of new radical reactions designed for organic synthesis.[1,2] The oxidative addition of carbon-centered radicals to alkenes mediated by metal salts has received considerable attention in organic synthesis for the construction of carbon–carbon bonds. Among these, manganese(III) acetate and cerium(IV) ammonium nitrate have been used most efficiently,[2–5] and the free radical reaction of 1,4-quinones has been reported.[5,6]

Compounds containing the quinone group represent an important class of biologically active molecules that are widespread in nature[7] such as viocristin (**1**),[8a] XR651 (**2**)[8b] and bhimamycin B (**3**)[8c] (Fig. 1). Previously, we found that the manganese(III) acetate mediated oxidative free radical reaction of 2-benzyl-(3-ethoxycarbonylmethyl)-1,4-naphthoquinones **4a** produced naphthacene-5,12-diones **6a** effectively. In contrast, with 2-benzoyl-(3-ethoxycarbonylmethyl)-1,4-naphthoquinones **4b**, in addition to the expected 6-hydroxy-naphthacene-5,12-diones **6b**, the novel naphtho[2,3-*c*]furan-4,9-diones **5** were also produced as the major products (Scheme 1) This is presumably due to the electron deficiency of the benzoyl group on **4b** which disfavours the intramolecular cyclization of electrophilic radical intermediate onto the C–C double bond of the benzoyl group.[5g] These naphthacene-5,12-diones and naphtho[2,3-*c*]furan-4,9-diones can also be generated directly from the intermolecular oxidative free radical reaction of 2-benzyl-1,4-naphthoquinones and 2-benzoyl-1,4-naphthoquinones with 1,3-dicarbonyl compounds.[5d,h] This report describes our results on manganese(III) acetate mediated reactions between 2-benzoyl-1,4-benzoquinones and 1,3-dicarbonyl compounds.

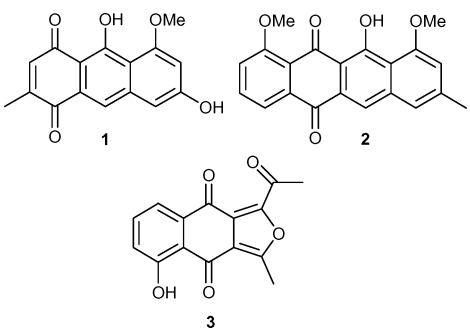
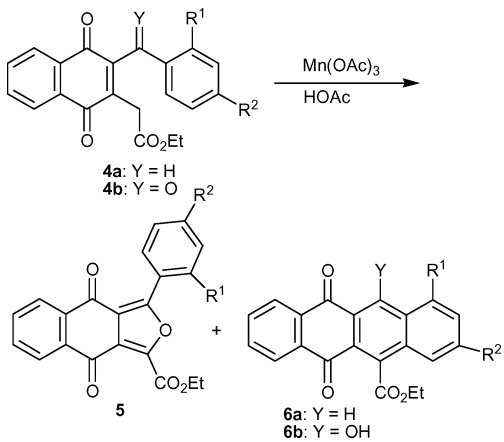


Fig. 1



Scheme 1 Intramolecular free radical reaction of 1,4-naphthoquinones.

Results and discussion

We began our studies of this manganese(III)-mediated reaction with 2-benzoyl-5,6-dimethyl-1,4-benzoquinones **7** and ethyl butyrylacetate (**8a**, R^3 = ^{n}PrCO) (Table 1). When 5-(4-methylbenzoyl)-2,3-dimethyl-1,4-benzoquinone (**7a**, $R^1 = H$, $R^2 =$ Me) was treated with **8a** and manganese(III) acetate in acetic

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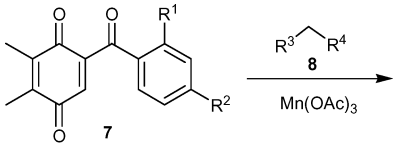
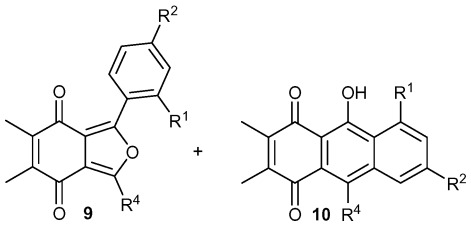
Table 1 Reaction with ethyl butyroylacetate (**8a**)[a]



8a: R^3 = ^{n}PrCO, R^4 = CO_2Et **8e**: R^3 = MeCO, R^4 = MeCO
8b: R^3 = ^{i}PrCO, R^4 = CO_2Et **8f**: R^3 = PhCO, R^4 = PhCO
8c: R^3 = PhCO, R^4 = CO_2Et
8d: R^3 = MeCO, R^4 = $CONMe_2$



Entry	Quinone	Solvent	Reaction time (h)	Product (yield (%))
1	**7a**: R^1 = H, R^2 = Me	HOAc	0.5	**9a** (36), **10a** (29)
2	**7b**: R^1 = H, R^2 = H	HOAc	0.5	**9b** (35), **10b** (29)
3	**7c**: R^1 = H, R^2 = Cl	HOAc	0.5	**9c** (41), **10c** (4)
4	**7d**: R^1 = H, R^2 = Br	HOAc	0.5	**9d** (45), **10d** (5)
5	**7e**: R^1 = Me, R^2 = H	HOAc	0.5	**9e** (56), **10e** (10)
6	**7f**: R^1 = Me, R^2 = Me	HOAc	0.5	**9f** (53), **10f** (15)
7	**7a**: R^1 = H, R^2 = Me	CH_3CN	3	**9a** (50), **10a** (5)
8	**7b**: R^1 = H, R^2 = H	CH_3CN	3	**9b** (41), **10b** (6)
9	**7c**: R^1 = H, R^2 = Cl	CH_3CN	3	**9c** (28), **10c** (0)
10	**7e**: R^1 = Me, R^2 = H	CH_3CN	3	**9e** (54), **10e** (8)
11	**7f**: R^1 = Me, R^2 = Me	CH_3CN	3	**9f** (59), **10f** (5)
12	**7a**: R^1 = H, R^2 = Me	$CHCl_3$	4	**9a** (50), **10a** (0)
13	**7b**: R^1 = H, R^2 = H	$CHCl_3$	4	**9b** (45), **10b** (0)
14	**7e** R^1 = Me, R^2 = H:	$CHCl_3$	4	**9e** (62), **10e** (trace)
15	**7f**: R^1 = Me, R^2 = Me	$CHCl_3$	4	**9f** (64), **10f** (0)
16	**7a**: R^1 = H, R^2 = Me	C_6H_6	4	**9a** (26), **10a** (0)
17	**7a**: R^1 = H, R^2 = Me	HCO_2H	0.5	**9a** (0), **10a** (25)
18	**7b**: R^1 = H, R^2 = H	HCO_2H	0.5	**9a** (0), **10a** (22)

[a] All reactions were carried with **7** (0.60 mmol), **8** (2.47 mmol) and manganese(III) acetate (2.50 mmol) at 70 °C.

acid at 70 °C, benzo[*c*]furan-4,7-dione **9a** and anthracene-1,4-dione **10a** were obtained in 36% and 29% yields, respectively (Table 1, entry 1). Although the mechanistic details of this reaction are unclear, **9a** and **10a** may be formed *via* the reaction route presented in Scheme 2. Manganese(III) acetate oxidation of **8a** produces radical **11a**. This radical intermediate **11a** undergoes intermolecular addition to the quinone ring followed by oxidation to give **12a**,[9] which is then oxidized by manganese(III) acetate to generate **13a**. Radical **13a** undergoes either (path a) a six-membered-ring free radical cyclization *via* **14a-B** and subsequent aromatization to give **15a**, which undergoes a further retro-Claisen condensation to produce **10a**,[10] or (path b) oxidation to give **16a**. This cationic intermediate **16a** undergoes a five-membered-ring cyclization followed by retro-Claisen condensation to generate **9a**.

The generalities of this reaction were examined with other 5-benzoyl-2,3-dimethyl-1,4-benzoquinones **7** (see Table 1, entries 1–6). In all cases, benzo[*c*]furan-4,7-diones **9** and anthracene-1,4-diones **10** were obtained in fair yields. In contrast to the reactions of 2-benzyl-1,4-naphthoquinones with β-ketoesters, **9** is the major product.[5d] This indicates that the electron deficiency of the benzoyl group disfavours the intramolecular cyclization of electrophilic radical **13** onto the C–C double bond of benzoyl group (path a). Interestingly, reaction of **7** bearing an additional electron-withdrawing halogen group gave the corresponding products **9** and **10** in excellent **9**/**10** ratio (entries 3 and 4). These results can be rationalized by considering that the electron deficiency of radical intermediate **7** makes the rate of six-membered-ring cyclization to the benzene ring bearing an electron-withdrawing halogen group (path a) much slower, meaning that the competitive oxidation of **7** (path b) becomes the major route.

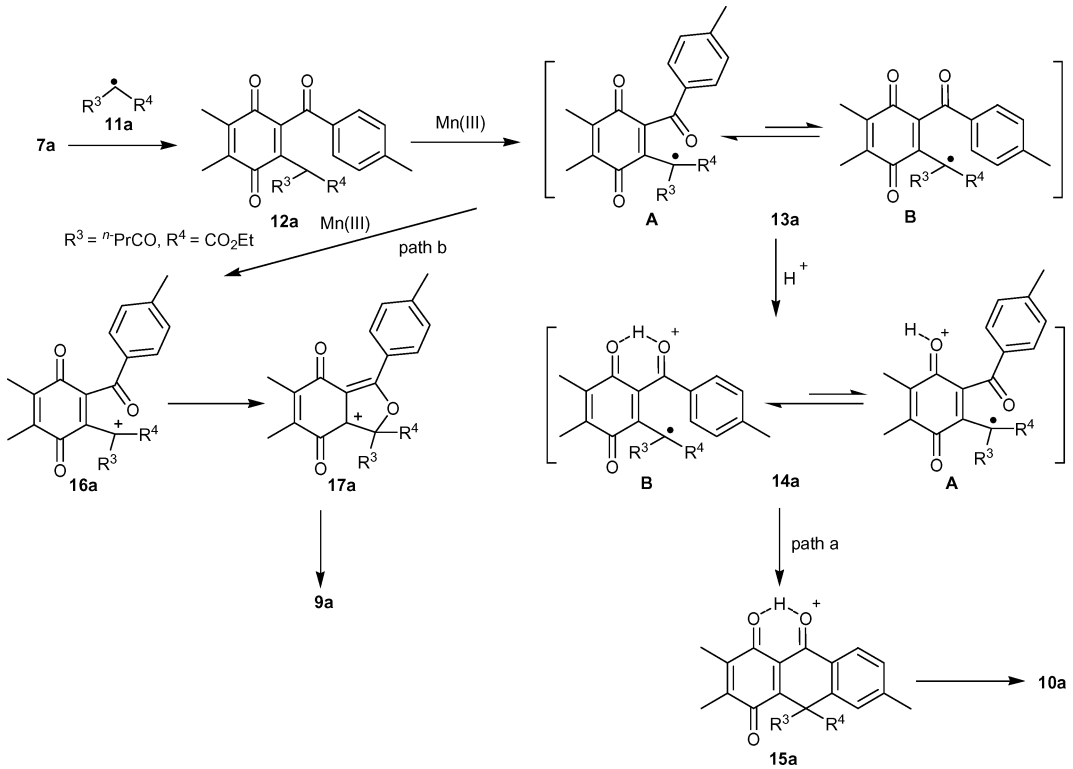
Solvent effects play an important role in the manganese(III) acetate mediated oxidative free radical reaction.[11] Reaction between **7a** and **8a** was next conducted in neutral solvents. The change of solvent to acetonitrile, chloroform and benzene gave **9a** and **10a** with a much higher **9a**/**10a** ratio than that performed in acetic acid (entries 7, 12 and 16), and gave best results when acetonitrile and chloroform were used. Analogous results were obtained with other 5-benzoyl-2,3-dimethyl-1,4-benzoquinones **7**, and are also summarized in Table 1 (entries 7–16). In all cases, benzo[*c*]furan-4,7-diones **9** were dominant. These results can be accounted for by the steric effect of the benzoyl group; **13-B** is the minor conformer in neutral solvents, and therefore the cyclization of **13** (path a) is slower and the oxidation of **13** (path b) becomes the major route.

This reaction was next performed in formic acid. Treatment of **7a** and **8a** with manganese(III) acetate in formic acid at 70 °C for 30 min resulted in the formation of **10a** exclusively in 25% yield (entry 17). This selective formation of **10a**, in contrast to those performed in neutral solvent, is presumably due to the coordination of proton with the carbonyl groups, leading to **14a-B** being the major conformer. The cyclization of radical **13a** (path a) *via* **14a-B** becomes the major route. It may also result from the coordination of proton with R^3 and R^4, which decreases the electron density and retards the oxidation of radical **13a** (path b).

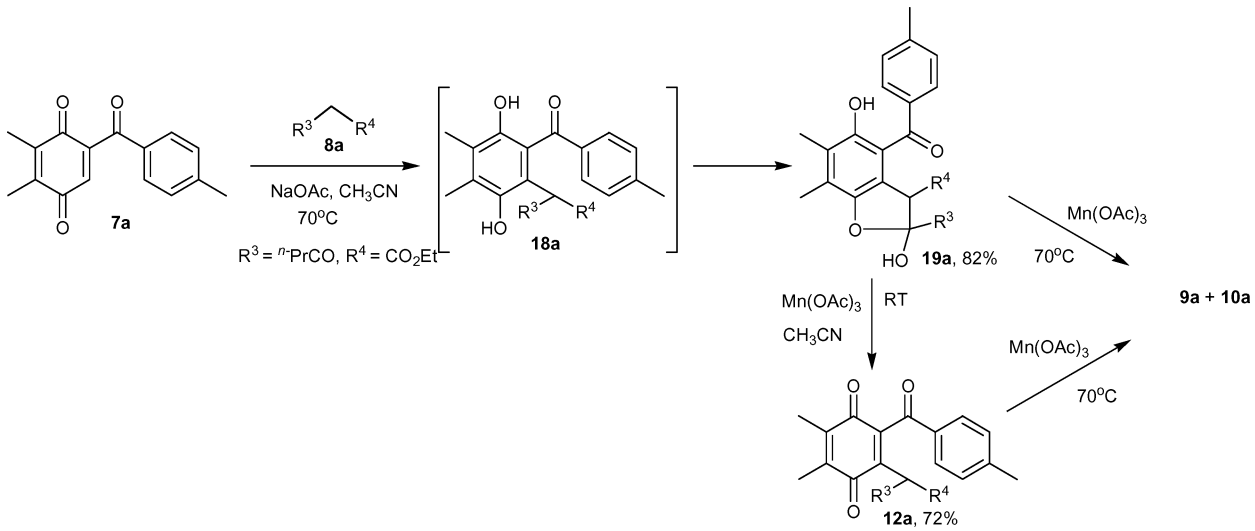
Considering the electron-withdrawing effect of the benzoyl group, it is likely that **12a** is produced *via* the nucleophilic addition of **8a** to the C–C double bond of **7a** followed by manganese(III) acetate oxidation. To test this hypothesis, we next performed the reaction between 5-(4-methylbenzoyl)-2,3-dimethyl-1,4-benzoquinone (**7a**) and ethyl butyrylacetate (**8a**) in the absence of manganese(III) acetate (Scheme 3). Treatment of **7a** and **8a** with sodium acetate in acetonitrile at 70 °C gave **18a**, which was converted to **19a** during purification as a stereoisomeric mixture in 82% yield. This nucleophilic adduct **19a** was then oxidized by manganese(III) acetate in acetonitrile at room temperature to give **12a** in 72% yield.

With **12a** and **19a** in hand, the radical reaction of **12a** and **19a** was next examined. When **12a** was treated with manganese(III) acetate in acetic acid at 70 °C, **9a** and **10a** were obtained in 39% and 30% yields, respectively (Table 2, entry 1). Reaction of **19a** with manganese(III) acetate in acetic acid at 70 °C also gave **9a** and **10a** in 43% and 32% yields, respectively (Table 2, entry 2). Other examples with acetonitrile and formic acid as solvents are also shown in Table 2. The results are similar to those in Table 1, except that **10a** was produced in a much better reaction yield in formic acid, and in all cases, **9a** and **10a** were obtained with high selectivity depending on the solvent used (entries 3–6). Based on these results, we believe that **12a** is formed mainly *via* the nucleophilic addition of **8a** to **7a** followed by manganese(III) oxidation.

The formation of benzo[2,3-*c*]furan-4,7-diones **9** is interesting. The corresponding isofuran derivatives have served as



Scheme 2 Probable mechanism.



Scheme 3 Nucleophilic reaction between **7a** and **8a**.

quinodimethane synthetic analogues in Diels–Alder reaction and are widely used in the preparation of complex molecules.[12] To improve the chemoselectivity for the formation of benzo[2,3-*c*]furan-4,7-diones **9**, this manganese(III)-mediated reaction of 5-benzoyl-2,3-dimethyl-1,4-benzoquinones **7** with other β-ketoesters **8b-c** was next investigated. Reaction of 5-benzoyl-2,3-dimethyl-1,4-benzoquinone (**7b**) with ethyl isobutyrylacetate (**8b**, $R^3 = {}^{i}PrCO$) and manganese(III) acetate in acetic acid afforded **9b** and **10b** in 42% and 12% yields, respectively (Table 3, entry 2). The **9b**/**10b** ratio rose to 42/6 when ethyl benzoylacetate (**8c**, $R^3 = PhCO$) was employed (Table 3, entry 4). The chemoselectivity of this reaction increases as the size of substituents (R^3) increases. This can be attributed to the steric effect exerted by R^3 group – the cyclization rate of **13** (path a) is retarded by the larger R^3 group and the oxidation of **13** (path b) becomes the major route. On the basis of this finding, by choosing ethyl benzoylacetate (**8c**) as the nucleophilic precursor, the generalities of this reaction were also examined with a variety of 5-benzoyl-2,3-dimethyl-1,4-benzoquinones **7**. The results are summarized in Table 3 (entries 3–8). In all cases, 5-benzoyl-2,3-dimethyl-1,4-benzoquinone **7** was converted to the corresponding benzo[*c*]furan-4,7-dione **9** with high chemoselectivity. This reaction was also conducted

Table 2 Radical reaction of nucleophilic adduct (see right-hand side of Scheme 3)

Entry	Nucleophilic adduct	Solvent	Reaction time (h)	Product (yield (%))
1	**12a**	HOAc	0.5	**9a** (39), **10a** (30)[a]
2	**19a**	HOAc	0.5	**9a** (43), **10a** (32)[b]
3	**12a**	CH_3CN	4	**9a** (45), **10a** (0)[a]
4	**19a**	CH_3CN	4	**9a** (48), **10a** (0)[b]
5	**12a**	HCO_2H	0.5	**9a** (6), **10a** (67)[a]
6	**19a**	HCO_2H	0.5	**9a** (3), **10a** (73)[b]

[a] These reactions were carried with **12a** (0.43 mmol) and manganese(III) acetate (1.08 mmol) at 70 °C. [b] These reactions were carried with **19a** (0.37 mmol) and manganese(III) acetate (1.81 mmol) at 70 °C.

Table 3 Reaction with β-ketoester and β-ketoamide[a]

Results	Quinone	β-Ketoester or β-ketoamide	Product (yield (%))
1	**7a**: R^1 = H, R^2 = Me	**8b**	**9a** (45), **10a** (2)
2	**7b**: R^1 = H, R^2 = H	**8b**	**9b** (42), **10b** (12)
3	**7a**: R^1 = H, R^2 = Me	**8c**	**9a** (44), **10a** (7)
4	**7b**: R^1 = H, R^2 = H	**8c**	**9b** (42), **10b** (6)
5	**7c**: R^1 = H, R^2 = Cl	**8c**	**9c** (27), **10c** (0)
6	**7d**: R^1 = H, R^2 = Br	**8c**	**9d** (31), **10d** (0)
7	**7e**: R^1 = Me, R^2 = H	**8c**	**9e** (66), **10e** (0)
8	**7f**: R^1 = Me, R^2 = Me	**8c**	**9f** (69), **10f** (4)
9	**7a**: R^1 = H, R^2 = Me	**8d**	**9g** (69), **10g** (0)
10	**7b**: R^1 = H, R^2 = H	**8d**	**9h** (62), **10h** (0)
11	**7c**: R^1 = H, R^2 = Cl	**8d**	**9i** (48), **10i** (0)
12	**7f**: R^1 = Me, R^2 = Me	**8d**	**9j** (75), **10j** (0)

[a] All reactions were carried with **7** (0.60 mmol), **8** (2.47 mmol) and manganese(III) acetate (2.50 mmol) at 70 °C in acetic acid (10 cm^3) for 30 min.

with *N*,*N*-dimethyl acetoacetamide (**8d**). Reaction of **7a** and **8d** with manganese(III) acetate under above conditions led to the formation of **9g** in 69% yield, and no **10g** was found (Table 3, entry 9). The results of the reaction between other 5-benzoyl-2,3-dimethyl-1,4-benzoquinones **7** and **8d** are also summarized in Table 3 (entries 10–12). In all cases, **9** is the only product. Again, this high chemoselectivity can be ascribed to the steric effect exerted by the larger R^4 (= $CONMe_2$) group of **8d** (compared to that of **8a**, $R^4 = CO_2Et$), resulting in the oxidation of **13** being the major route (path b).

Next, we investigated this manganese(III)-mediated reaction with 1,3-diketones **8e** and **8f**. When **7a** was treated with pentandione (**8e**) and manganese(III) acetate in acetic acid, **9k** and **10k** were obtained in 36% and 7% yields, respectively (Table 4, entry 1). The scope of this reaction is shown in Table 4 (entries 1–6). In all cases, 5-benzoyl-2,3-dimethyl-1,4-benzoquinone **7** was converted to the corresponding isofuran product **9** with high chemoselectivity. It can be rationalized that the radical intermediate **13e** bearing a stronger electron-withdrawing R^4 (= COMe) group is more electron-deficient and this makes the intramolecular cyclization of **13e** to the benzoyl group (path a) slower than that of **13a** ($R^4 = CO_2Et$). With dibenzoylmethane (**8f**), bearing a larger benzoyl group, isofuran products **9** were obtained exclusively (Table 4, entries 7–12).

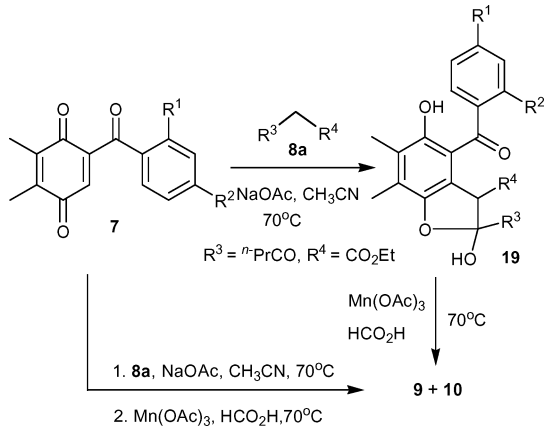
As shown in Table 2, with formic acid as solvent, anthracene-1,4-dione **10a** was produced from the radical reaction between **19a** and manganese(III) acetate in 73% yield with high chemoselectivity (entry 6). Compounds containing the anthracene-1,4-dione subunit are an important class of biologically active molecules that are widespread in nature.[7,8a,b] We therefore continued to study this manganese(III)-mediated reaction with other nucleophilic adducts **19** in formic acid, and the results are listed in Table 5 (entries 1–3). In all cases, anthracene-1,4-diones **10** were obtained selectively from nucleophilic adducts **19**. In attempt to enhance the efficiency of this reaction, we investigated the development of a one-pot process, in which **19** was generated *in situ* from **7** and **8**. Reaction

Table 4 Reaction with 1,3-diketones[a]

Entry	Quinone	1,3-Diketone	Product (yield (%))
1	**7a**: R^1 = H, R^2 = Me	**8e**	**9k** (36), **10k** (7)
2	**7b**: R^1 = H, R^2 = H	**8e**	**9l** (31), **10l** (5)
3	**7c**: R^1 = H, R^2 = Cl	**8e**	**9m** (35), **10m** (0)
4	**7d**: R^1 = H, R^2 = Br	**8e**	**9n** (39), **10n** (0)
5	**7e**: R^1 = Me, R^2 = H	**8e**	**9o** (42), **10o** (0)
6	**7f**: R^1 = Me, R^2 = Me	**8e**	**9p** (43), **10p** (0)
7	**7a**: R^1 = H, R^2 = Me	**8f**	**9q** (81), **10q** (0)
8	**7b**: R^1 = H, R^2 = H	**8f**	**9r** (81), **10r** (0)
9	**7c**: R^1 = H, R^2 = Cl	**8f**	**9s** (54), **10s** (0)
10	**7d**: R^1 = H, R^2 = Br	**8f**	**9t** (55), **10t** (0)
11	**7e**: R^1 = Me, R^2 = H	**8f**	**9u** (74), **10u** (0)
12	**7f**: R^1 = Me, R^2 = Me	**8f**	**9v** (79), **10v** (0)

[a] All reactions were carried with **7** (0.60 mmol), **8** (2.47 mmol) and manganese(III) acetate (2.50 mmol) at 70 °C in acetic acid (10 cm^3) for 30 min.

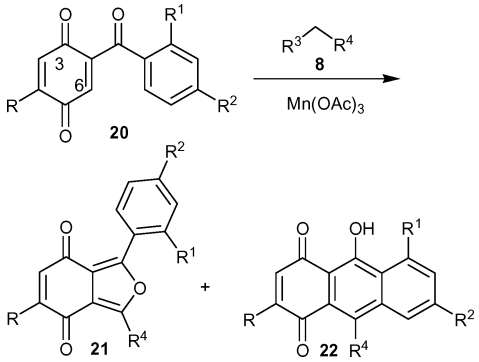
Table 5 Chemoselective formation of anthracene-1,4-dione **10**



Entry	Quinone	Nucleophilic adduct (yield (%), ratio)	Product (yield (%))
1	**7a**: R^1 = H, R^2 = Me	**19a** (82, 11:1)[a,b]	**9a** (3), **10a** (73)[c]
2	**7b**: R^1 = H, R^2 = H	**19b** (82, 11:1)[a,b]	**9b** (5), **10b** (75)[c]
3	**7f**: R^1 = H, R^2 = Me	**19c** (82, 11:1)[a,b]	**9f** (trace), **10f** (75)[c]
4	**7a**: R^1 = H, R^2 = Me	—	**9a** (0), **10a** (58)[d]
5	**7b**: R^1 = H, R^2 = H	—	**9b** (trace), **10b** (52)[d]
6	**7f**: R^1 = H, R^2 = Me	—	**9f** (trace), **10f** (55)[d]

[a] These reactions were carried with **7** (0.69 mmol), **8a** (1.40 mmol) and sodium acetate (2.09 mmol) in acetonitrile (10 cm^3) at 70 °C for 1 h. [b] The stereoisomeric ratio was determined by NMR integration. [c] These reactions were carried with **19** (0.37 mmol) and manganese(III) acetate (1.81 mmol) in formic acid (10 cm^3) at 70 °C for 30 min. [d] These one-pot reactions were carried by heating **7** (0.59 mmol), **8** (1.18 mmol) and sodium acetate (1.17 mmol) in acetonitrile (5 cm^3) at 70 °C for 1 h, and then manganese(III) acetate (2.95 mmol) and formic acid (15 cm^3) were added. This reaction mixture was then heated at 70 °C for 30 min.

Table 6 Regioselectivity of 2-alkyl-5-benzoyl-1,4-benzoquinones **20**[a]



Entry	Quinone	β-Ketoester or β-ketoamide	Product (yield(%))
1	**20a**: R = Me, R^1 = H, R^2 = Me	**8a**	**21a** (34), **22a** (20)
2	**20b**: R = Me, R^1 = H, R^2 = H	**8a**	**21b** (36), **22b** (22)
3	**20c**: R = Me, R^1 = H, R^2 = Cl	**8a**	**21c** (56), **22c** (4)
4	**20d**: R = Et, R^1 = H, R^2 = Me	**8a**	**21d** (37), **22d** (28)
5	**20e**: R = ^{t}Bu, R^1 = H, R^2 = Me	**8a**	**21e** (37), **22e** (24)
6	**20f**: R = Bn, R^1 = H, R^2 = Me	**8a**	**21f** (37), **22f** (26)
7	**20a**: R = Me, R^1 = H, R^2 = Me	**8d**	**21g** (54), **22g** (0)
8	**20b**: R = Me, R^1 = H, R^2 = H	**8d**	**21h** (47), **22h** (0)
9	**20c**: R = Me, R^1 = H, R^2 = Cl	**8d**	**21i** (43), **22i** (0)
10	**20d**: R = Et, R^1 = H, R^2 = Me	**8d**	**21j** (64), **22j** (0)
11	**20e**: R = ^{t}Bu, R^1 = H, R^2 = Me	**8d**	**21k** (62), **22k** (0)
12	**20f**: R = Bn, R^1 = H, R^2 = Me	**8d**	**21l** (66), **22l** (0)

[a] All reactions were carried with **20** (0.64 mmol), **8** (2.61 mmol) and manganese(III) acetate (2.66 mmol) in acetic acid (10 cm^3) at 70 °C for 30 min.

of **7a** and **8a** with sodium acetate in acetonitrile at 70 °C for 1 h was followed by the addition of manganese(III) acetate and formic acid without the isolation of **19a**. This reaction mixture was heated further at 70 °C for 30 min to give **10a** in 58% yield (entry 4). Other examples are also shown in Table 5 (entries 5 and 6). In all cases, 5-benzoyl-2,3-dimethyl-1,4-benzoquinone **7** was converted to the corresponding anthracene-1,4-dione **10** effectively by this one-pot process.

We then continued to examine the regioselectivity of this oxidative free radical reaction with 2-alkyl-5-benzoyl-1,4-benzoquinones (**20**). We first tried the reaction between 2-methyl-5-(4-methylbenzoyl)-1,4-benzoquinone (**20a**, R = Me) and ethyl butyrylacetate (**8a**, R^3 = ^{n}PrCO) (Table 6). When **20a** was treated with **8a** and manganese(III) acetate in acetic acid at 70 °C, benzo[*c*]furan-4,7-dione **21a** (34%) and anthracene-1,4-dione **22a** (20%) were obtained (Table 6, entry 1). No product derived from the addition of **8a** to the C3 of **20a** was found. This is presumably due to the rate of nucleophilic addition of **8a** to the C–C double bond of the quinone ring (bearing an electron-withdrawing benzoyl group) being much faster. Analogous results were obtained with other 2-alkyl-5-benzoyl-1,4-benzoquinones **20**, and are listed in Table 6 (entries 1–6). In all cases, **21** and **22** were obtained regioselectively. *N*,*N*-Dimethyl acetoacetamide (**8d**) behaved similarly, giving only **21** derived from the addition of **8d** to the C6 of **20** (entries 7–12).

Conclusions

1,4-Benzoquinone **12**, generated *via* the nucleophilic addition of 1,3-dicarbonyl compounds **8** to the C–C double bond of the quinone ring, undergoes efficient manganese(III)-mediated cyclization reactions. This reaction provides a method for the synthesis of benzo[*c*]furan-4,7-diones and anthracene-1,4-diones from readily available 2-benzoyl-1,4-benzoquinones and 1,3-dicarbonyl compounds. With ethyl butyrylacetate, by changing the solvent, benzo[*c*]furan-4,7-diones **9** and anthracene-1,4-diones **10** can be generated in high chemoselectivities. With ethyl benzoylacetate, *N*,*N*-dimethyl acetoacetamide and 1,3-diones, benzo[*c*]furan-4,7-dione **9** was produced effectively in high selectivity. We also studied this reaction with 2-alkyl-5-benzoyl-1,4-benzoquinones **20**, and found that benzo[*c*]furan-4,7-diones **21** and anthracene-1,4-diones **22** derived from the nucleophilic addition of **8** to C6 of **20** were obtained in high regioselectivity.

Experimental

General considerations

Melting points are uncorrected. Infrared spectra were taken with a Hitachi 260-30 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE-300 or AMX-400 spectrometer. Chemical shifts are reported in ppm relative to TMS as internal reference. Elemental analyses were performed with Heraeus CHN-Rapid Analyzer. Mass spectra were recorded on a Jeol JMS-SX 102A mass spectrometer. 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-benzoyl-1,4-benzoquinones **7** and **20** were synthesized by the CAN oxidative demethylation[13] of corresponding 2-benzoyl-1,4-dimethoxybenzenes.[14]

Typical experimental procedure for the manganese(III)-mediated reaction of 2-benzoyl-1,4-benzoquinones with β-ketoesters, β-ketoamide and 1,3-diketones

A mixture of 5-benzoyl-2,3-dimethyl-1,4-benzoquinone (**7b**) (143 mg, 0.60 mmol), ethyl butyrylacetate (**8a**) (391 mg, 2.47 mmol) and manganese(III) acetate (671 mg, 2.50 mmol) in acetic acid (10 cm^3) was heated at 70 °C for 30 min. The reaction mixture was diluted with ethyl acetate (100 cm^3), washed with saturated aqueous sodium bisulfite (50 cm^3), water (3 × 50 cm^3), aqueous saturated sodium bicarbonate (3 × 50 cm^3), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by column chromatography over silica gel (20 g) (eluting with 2:1 dichloromethane–hexane) followed by recrystallization ($CHCl_3$–hexane) to give **9b** (68 mg, 35%) and **10b** (56 mg, 29%).

4,7-Dihydro-5,6-dimethyl-4,7-dioxo-3-phenybenzo[*c*]furan-1-carboxylic acid ethyl ester 9b. Yellow crystals; mp 161–162 °C (from $CHCl_3$–hexane); (Found: C, 70.27; H, 4.93. $C_{19}H_{16}O_5$ requires C, 70.36; H, 4.97%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3015, 1730, 1665, 1400, 1375 and 1280; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.48 (3 H, t, *J* 7.1, CH_3), 2.17 (6 H, s, 2 × CH_3), 4.51 (2 H, q, *J* 7.1, OCH_2), 7.49–7.56 (3 H, m, ArH) and 8.39–8.46 (2 H, m, ArH); δ_C(75.4 MHz; $CDCl_3$; Me_4Si) 13.18 (q), 13.25 (q), 14.2 (q), 62.3 (t), 117.3 (s), 124.9 (s), 127.6 (s), 128.52 (2 × d), 128.55 (2 × d), 131.7 (d), 141.8 (s), 145.3 (s), 145.5 (s), 157.4 (s), 157.5 (s), 179.4 (s) and 180.3 (s).

1,4-Dihydro-9-hydroxy-2,3-dimethyl-1,4-dioxoanthracene-10-carboxylic acid ethyl ester 10b. Red crystals; mp 169–170 °C (from $CHCl_3$–hexane); (Found: C, 70.26; H, 4.96. $C_{19}H_{16}O_5$ requires C, 70.36; H, 4.97%); $\nu_{max}(CHCl_3)/cm^{-1}$ 2990, 1660, 1605, 1300 and 1270; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.47 (3 H, t, *J* 7.2, CH_3), 2.20 (3 H, s, CH_3), 2.22 (3 H, s, CH_3), 4.63 (2 H, q, *J* 7.2, OCH_2), 7.66–7.80 (2 H, m, ArH), 7.83 (1 H, d, *J* 8.0, ArH), 8.52 (1 H, d, *J* 8.0, ArH) and 14.35 (1 H, s, OH); δ_C(75.4 MHz; $CDCl_3$; Me_4Si) 12.5 (q), 13.3 (q), 14.1 (q), 62.1 (t), 107.6 (s), 123.9 (s), 124.9 (d), 126.9 (s), 127.0 (d), 127.3 (s), 129.1 (d), 131.7 (d), 132.8 (s), 144.4 (s), 146.1 (s), 162.6 (s), 169.1 (s), 183.1 (s) and 189.1 (s).

Typical experimental procedure for the nucleophilic reaction between 2-benzoyl-1,4-benzoquinones and ethyl butyrylacetate

A solution of 5-(4-methylbenzoyl)-2,3-dimethyl-1,4-benzoquinone (**7a**) (174 mg, 0.69 mmol), ethyl butyrylacetate (**8a**) (221 mg, 1.40 mmol) and sodium acetate (171 mg, 2.09 mmol) in acetonitrile (10 cm^3) was heated at 70 °C for 1 h. The reaction mixture was diluted with ethyl acetate (100 cm^3), washed with water (3 × 50 cm^3), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by column chromatography over silica gel (20 g) (eluting with 1:15 ethyl acetate–hexane) to give **19a** (225 mg, 82%) as a mixture of isomeric products in 11:1 ratio. The major isomer can be obtained in pure form by recrystallization (ethyl acetate–hexane)

(2*S,3*R**)-2,3-Dihydro-2,5-dihydroxy-6,7-dimethyl-4-(4-methylbenzoyl)-2-propylbenzo[*b*]furan-3-carboxylic acid ethyl ester 19a.** Yellow crystals; mp 88–89 °C; ν_{max}(KBr)/cm^{-1} 3445, 2965, 1730, 1615 and 1335; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.00 (3 H, t, *J* 7.5, CH_3), 1.08 (3 H, t, *J* 7.1, CH_3), 1.53 (2 H, sextet, *J* 7.5, CH_2), 1.85–1.95 (2 H, m, CH_2), 2.22 (6 H, s, 2 × CH_3), 2.44 (3 H, s, CH_3), 3.73–3.97 (2 H, m, OCH_2), 3.88 (1 H, s, CH), 7.25 (2 H, d, *J* 7.6, ArH), 7.49 (2 H, d, *J* 7.6, ArH) and 10.42 (1 H, s, OH); δ_C(75.4 MHz; $CDCl_3$; Me_4Si) 11.7 (q), 13.1 (q), 13.6 (q), 14.1 (q), 16.6 (t), 21.7 (q), 40.9 (t), 57.2 (d), 61.5 (t), 109.4 (s), 115.6 (s), 118.0 (s), 127.1 (s), 127.8 (s), 129.12 (2 × d), 129.20 (2 × d), 136.5 (s), 143.3 (s), 149.8 (s), 153.8 (s), 169.8 (s) and 199.6 (s); *m*/*z* (EI) 412.1896 (M^+. $C_{24}H_{28}O_6$ requires 412.1885), 394 (13%), 348 (19), 324 (35), 296 (100) and 283 (39).

Manganese(III)-mediated oxidation reaction of nucleophilic adduct 19a

A mixture of **19a** (150 mg, 0.36 mmol) and manganese(III) acetate (195 mg, 0.73 mmol) in acetonitrile (10 cm^3) was stirred at RT for 3 h. The reaction mixture was diluted with ethyl acetate (100 cm^3), washed with saturated aqueous sodium bisulfite (50 cm^3), water (3 × 50 cm^3), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by column chromatography over silica gel (20 g) (eluting with 1:15 ethyl acetate–hexane) to give **12a** (108 mg, 72%).

2-[1,4-Dihydro-3-(4-methylbenzoyl)-1,4-dioxo-naphthalen-2-yl]-3-oxo-hexanoic acid ethyl ester 12a. Yellow oil; ν_{max}(KBr)/cm^{-1} 3270, 1650, 1605, 1455, 1285, 825; δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.86 (3 H, t, *J* 7.3, CH_3), 1.19 (3 H, t, *J* 7.1, CH_3), 1.42–1.57 (2 H, m, CH_2), 2.00–2.21 (2 H, m, CH_2), 2.09 (3 H, s, CH_3), 2.13 (3 H, s, CH_3), 2.39 (3 H, s, CH_3), 3.93–4.22 (2 H, m, OCH_2), 7.19 (2 H, d, *J* 8.0, ArH), 7.70 (2 H, d, *J* 8.0, ArH), 12.96 (1 H, s, OH); δ_C(75.4 MHz; $CDCl_3$; Me_4Si) 12.2 (q), 12.7 (q), 13.7 (q), 14.1 (q), 19.1 (t), 21.7 (q), 35.4 (t), 60.8 (t), 94.1 (s), 129.1 (2 × d), 129.2 (2 × d), 133.0 (s), 137.6 (s), 140.9 (s), 141.7 (s), 143.4 (s), 145.3 (s), 170.3 (s), 178.9 (s), 185.8 (s), 185.9 (s), 191.6 (s); *m*/*z* (EI) 410.1734 (M^+. $C_{24}H_{26}O_6$ requires 410.1739), 393 (58%), 347 (66) and 321 (100).

Typical experimental procedure for the manganese(III)-mediated radical reaction of 12a

A mixture of **12a** (178 mg, 0.43 mmol) and manganese(III) acetate (290 mg, 1.08 mmol) in acetic acid (10 cm^3) was heated at 70 °C for 30 min. The reaction mixture was diluted with ethyl acetate (100 cm^3), washed with saturated aqueous sodium bisulfite (50 cm^3), water (3 × 50 cm^3), aqueous saturated sodium bicarbonate (3 × 50 cm^3), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by column chromatography over silica gel (20 g) (eluting with 2:1 dichloromethane–hexane) followed by recrystallization ($CHCl_3$–hexane) to give **9a** (57 mg, 39%) and **10a** (44 mg, 30%).

4,7-Dihydro-5,6-dimethyl-3-(4-methylphenyl)-4,7-dioxobenzo-[*c*]furan-1-carboxylic acid ethyl ester 9a. Yellow crystals; mp 161–162 °C (from $CHCl_3$–hexane); (Found: C, 70.89; H, 5.42. $C_{20}H_{18}O_5$ requires C, 70.99; H, 5.36%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3010, 1730, 1665, 1610 and 1280; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.47 (3 H, t, *J* 7.1, CH_3), 2.14 (6 H, s, 2 × CH_3), 2.42 (3 H, s, CH_3), 4.50 (2 H, q, *J* 7.1, OCH_2), 7.30 (2 H, d, *J* 8.2, ArH) and 8.32 (2 H, d, *J* 8.2, ArH); δ_C(75.4 MHz; $CDCl_3$; Me_4Si) 13.0 (q), 13.2 (q), 14.1 (q), 21.6 (q), 62.1 (t), 116.7 (s), 124.75 (s), 124.81 (s), 128.4 (2 × d), 129.2 (2 × d), 141.4 (s), 142.3 (s), 145.0 (s), 145.4 (s), 157.4 (s), 157.6 (s), 179.3 (s) and 180.1 (s).

1,4-Dihydro-9-hydroxy-2,3,6-trimethyl-1,4-dioxoanthracene-10-carboxylic acid ethyl ester 10a. Red needles; mp 168–169 °C

(from $CHCl_3$–hexane); (Found: C, 70.91; H, 5.36. $C_{20}H_{18}O_5$ requires C, 70.99; H, 5.36%); $\nu_{max}(CHCl_3)/cm^{-1}$ 2925, 1720, 1655, 1500 and 1265; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.47 (3 H, t, *J* 7.1, CH_3), 2.17 (3 H, s, CH_3), 2.19 (3 H, s, CH_3), 2.54 (3 H, s, CH_3), 4.63 (2 H, q, *J* 7.1, OCH_2), 7.50 (1 H, d, *J* 8.4, ArH), 7.57 (1 H, s, ArH), 8.37 (1 H, d, *J* 8.4, ArH) and 14.31 (1 H, s, OH); δ_C(75.4 MHz; $CDCl_3$; Me_4Si) 12.4 (q), 13.2 (q), 14.1 (q), 22.1 (q), 62.0 (t), 107.1 (s), 124.1 (s), 124.7 (d), 125.2 (s), 126.2 (d), 126.4 (s), 131.1 (d), 133.0 (s), 142.5 (s), 144.3 (s), 145.9 (s), 162.6 (s), 169.2 (s), 183.1 (s) and 188.8 (s).

Typical experimental procedure for the manganese(III)-mediated radical reaction of nucleophilic adduct 19

A mixture of **19a** (151 mg, 0.37 mmol) and manganese(III) acetate (486 mg, 1.81 mmol) in acetonitrile (10 cm^3) was heated at 70 °C for 4 h. The reaction mixture was diluted with ethyl acetate (100 cm^3), washed with saturated aqueous sodium bisulfite (50 cm^3), water (3 × 50 cm^3), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by column chromatography over silica gel (20 g) (eluting with 2:1 dichloromethane–hexane) followed by recrystallization ($CHCl_3$–hexane) to give **9a** (60 mg, 48%).

Typical experimental procedure for the one-pot reaction

A solution of 5-(4-methylbenzoyl)-2,3-dimethyl-1,4-benzoquinone (**7a**) (150 mg, 0.59 mmol), ethyl butyrylacetate (**8a**) (186 mg, 1.18 mmol) and sodium acetate (145 mg, 1.77 mmol) in acetonitrile (5 cm^3) was heated at 70 °C for 1 h. To the reaction mixture manganese(III) acetate (791 mg, 2.95 mmol) and formic acid (15 cm^3) were then added. After being heated at 70 °C for another 30 min, the reaction mixture was diluted with ethyl acetate (100 cm^3), washed with saturated aqueous sodium bisulfite (50 cm^3), water (3 × 50 cm^3), aqueous saturated sodium bicarbonate (3 × 50 cm^3), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by column chromatography over silica gel (20 g) (eluting with 2:1 dichloromethane–hexane) followed by recrystallization ($CHCl_3$–hexane) to give **10a** (115 mg, 58%).

Typical experimental procedure for the manganese(III)-mediated reaction of 2-alkyl-5-benzoyl-1,4-benzoquinones

A mixture of 2-benzoyl-5-methyl-1,4-benzoquinone (**20b**) (144 mg, 0.64 mmol), ethyl butyrylacetate (**8a**) (412 mg, 2.61 mmol) and manganese(III) acetate (712 mg, 2.66 mmol) in acetic acid (10 cm^3) was heated at 70 °C for 30 min. The reaction mixture was diluted with ethyl acetate (100 cm^3), washed with saturated aqueous sodium bisulfite (50 cm^3), water (3 × 50 cm^3), aqueous saturated sodium bicarbonate (3 × 50 cm^3), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by column chromatography over silica gel (20 g) (eluting with 2:1 dichloromethane–hexane) followed by recrystallization ($CHCl_3$–hexane) to give **21b** (70 mg, 36%) and **22b** (44 mg, 22%).

4,7-Dihydro-6-methyl-4,7-dioxo-3-phenylbenzo[*c*]furan-1-carboxylic acid ethyl ester 21b. Yellow crystals; mp 115–116 °C (from $CHCl_3$–hexane); (Found: C, 69.62; H, 4.56. $C_{18}H_{14}O_5$ requires C, 69.67; H, 4.55%); ν_{max}(KBr)/cm^{-1} 2985, 1715, 1675, 1535 and 1215; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.48 (3 H, t, *J* 7.1, CH_3), 2.17 (3 H, d, *J* 1.4, CH_3), 4.51 (2 H, q, *J* 7.1, OCH_2), 6.78 (1 H, q, *J* 1.4, CH), 7.32–7.59 (3 H, m, ArH) and 8.38–8.49 (2 H, m, ArH); δ_C(75.4 MHz; $CDCl_3$; Me_4Si) 14.1 (q), 16.2 (q), 62.3 (t), 117.6 (s), 124.7 (s), 127.3 (s), 128.4 (2 × d), 128.6 (2 × d), 131.9 (d), 138.0 (d), 142.3 (s), 149.6 (s), 157.2 (s), 157.3 (s), 179.9 (s) and 180.2 (s).

1,4-Dihydro-9-hydroxy-3-methyl-1,4-dioxoanthracene-10-carboxylic acid ethyl ester 22b. Red crystals; mp 143–144 °C (from $CHCl_3$–hexane); (Found: C, 69.65; H, 4.56. $C_{18}H_{14}O_5$ requires C, 69.67; H, 4.55%); ν_{max}(KBr)/cm^{-1} 2990, 1730, 1645, 1600 and 1225; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.47 (3 H, t, *J* 7.2, CH_3), 2.21 (3 H, d, *J* 1.4, CH_3), 4.63 (2 H, q, *J* 7.2, OCH_2), 6.91 (1 H, q, *J* 1.4, CH), 7.66–7.81 (2 H, m, ArH), 7.84 (1 H, d, *J* 7.8, ArH), 8.52 (1 H, d, *J* 7.8, ArH) and 14.13 (1 H, s, OH); δ_C(100.6 MHz; $CDCl_3$; Me_4Si) 14.1 (q), 16.8 (q), 62.2 (t), 107.9 (s), 123.6 (s), 124.9 (d), 127.1 (d), 127.3 (s), 127.4 (s), 129.3 (d), 131.8 (d), 132.7 (s), 136.4 (d), 150.6 (s), 162.5 (s), 168.8 (s), 183.8 (s) and 189.1 (s).

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