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New '2-phenylnaphthalene'-mediated synthesis of benzo[*b*]naphtho[2,3-*d*]furan-6,11-diones and 6-oxa-benzo[*a*]anthracene-5,7,12-triones: first total synthesis of 6-oxa-benzo[*a*]anthracen-5-ones

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Abstract—We describe here a novel synthesis of benzo[*b*]naphtho[2,3-*d*]furan-6,11-diones based on the heteroannulation of 2-(2-bromophenyl)-3-hydroxy-1,4-naphthoquinones. The naphthoquinones were prepared from 3-(2-bromophenyl)naphthalen-2-ols, which were obtained by intramolecular aldol condensation of 2-[3-(2-bromophenyl)-2-oxo-propyl]benzaldehydes. Alternatively, benzo[*b*]naphtho[2,3-*d*]furan-6,11-diones were obtained more directly and efficiently by cyclization of 3-(2-bromophenyl)naphthalen-2-ols to benzo[*b*]-naphtho[2,3-*d*]furans and oxidation of the resulting compounds. Furthermore, the first 6-oxabenzo[*a*]anthracen-5-one described was similarly obtained from 2-[3-(2-formylphenyl)-2-oxopropyl]benzoic acid and oxidized to 6-oxa-benzo[*a*]anthracene-5,7,12-trione.

A tricyclic structural pattern, consisting of a either a phenyl ring attached to position 2 of a naphthalene nucleus or composed of various heterocyclic ring units with similar molecular structural arrangements, is present in a large number of biologically and pharmacologically active compounds.[1] Examples include benzo[*a*]pyrene and 7,12-dimethylbenz[*a*]anthracene (carcinogenic); coralyne and nitidine (antileukemic); chartreusin and rabelomycin (antibacterial, cytotoxic); camptothecin, streptonigrin, and ellipticine (antineoplastic); WS-5995A (anticoccidial); genistein (estrogenic); methaqualone (sedative, hypnotic, anticonvulsive); and gossypol (antioxidant, male contraceptive), among others.[1] The structural pattern per se may not be sufficient to provide biological activity. Nevertheless, by attachment of the appropriate groups or substituents to specific positions on both ring units, it is believed that compounds with the desired biological actions can be designed.

Among compounds possessing this structural pattern, it is evident that many antineoplastic agents assume a coplanar conformation. The coplanarity of the two ring systems can be achieved either by hydrogen-bond formation between the two ring units, as in streptonigrin, or through a condensed structure, such as camptothecin or ellipticine.[1]

On the basis of the concept outlined above, a search for suitable chemical structures to fulfil the requirements for drug design has been undertaken in recent years. For instance, it was found that 5*H*-benzo[*d*]naphtho[2,3-*b*]pyran-5,7,12-triones (**4**) include compounds like the antibiotic WS-5995 A,[2] which is produced by a new strain of Streptomyces designated *S. auranticolor*. In addition, two recently described synthetic analogues, *o*-quinone J1 and model *p*-quinone J7,[3] were shown to be antitumour agents that inhibit macromolecule synthesis, block nucleoside transport, induce DNA fragmentation, and decrease the growth and viability of L1210 leukemic cells more effectively than ellagic acid and genistein in vitro.

Closely related benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione **3** belongs to another family of compounds selected as suitable starting structures for drug design. These compounds also possess the characteristic '2-phenylnaphthalene-type' structural pattern, with the presence of the ether linkage connecting the rings making the structure planar. It was found that although this compound did not exhibit anticancer properties itself, compounds of type **3** bearing substituents at specific positions proved to be promising antitumoural agents.[4]

Keywords: Quinones; Heterocycles; Ketoacids; Ullman reaction.
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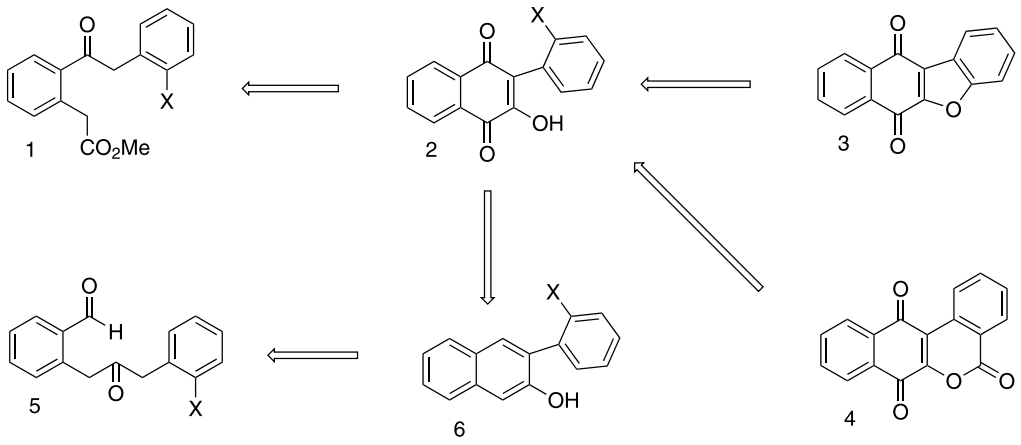
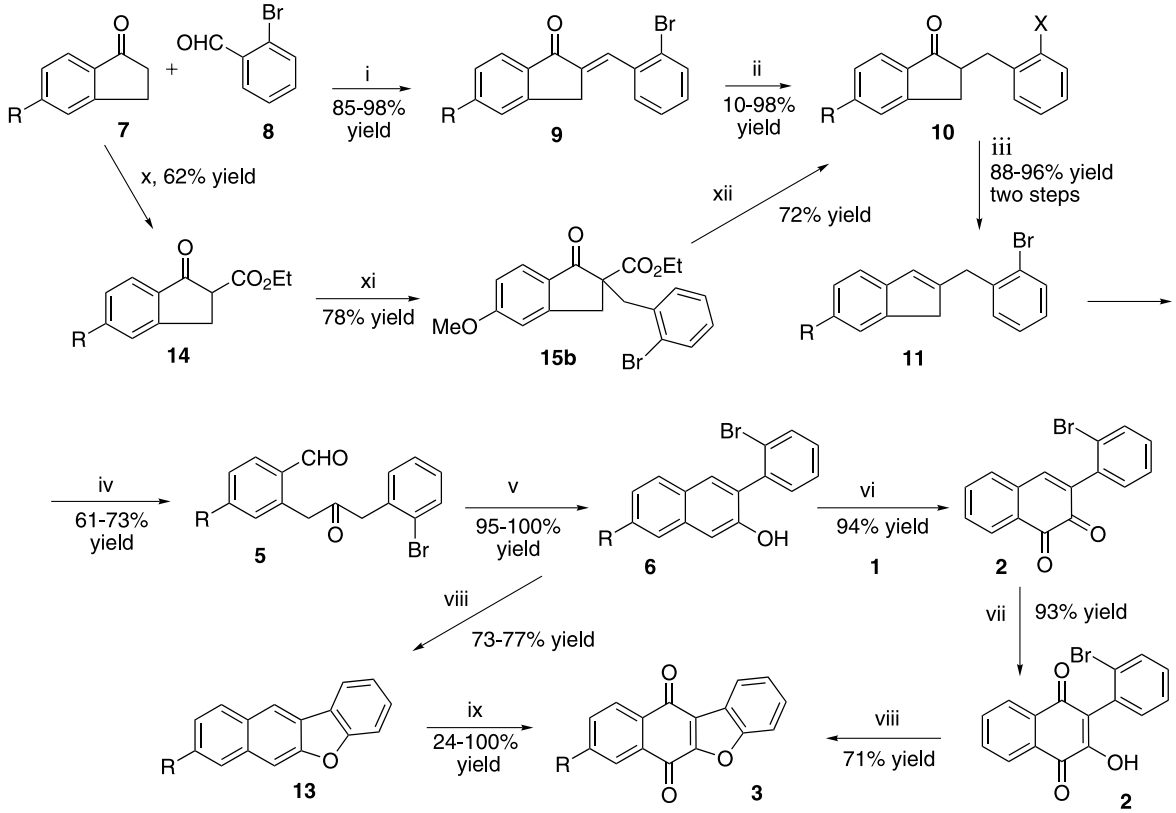


Scheme 1. X=Br, $CONEt_2$.

Previous syntheses of benzofuronaphthoquinones **3**,[5] benzopyronaphthoquinones **4**[6] and related compounds include a common 2-phenylnaphthalene-type strategy for the synthesis of these targets. This method is based on the heteroannulation of appropriate 2-phenyl-1,4-naphthoquinones **2** (Scheme 1) obtained by mixed intramolecular Claisen condensation of phenylacetylphenylacetic acids **1**.[5a,d,6h] However, this simple and efficient method is of limited scope due to the lack of availability of starting materials **1**.

We describe a novel, yet closely related, '2-phenylnaphthalene'-based synthesis of benzofuronaphthoquinones **3** and benzopyronaphthoquinones **4** that does not suffer from the limitations outlined above. This method also involves heteroannulation of 2-hydroxy-3-phenyl-1,4-naphthoquinones **2**, which can be obtained by intramolecular aldol cyclization of ketobenzaldehydes **5** followed by oxidation of the resulting 3-phenyl-2-naphthols **6**.[7]

This new route to naphthoquinones **2** was first applied to the synthesis of unsubstituted benzofuronaphthoquinone **3a**. The starting bromophenylketopropylbenzaldehyde **5a** was obtained as follows (Scheme 2): condensation of 1-indanone **7a** with *o*-bromobenzaldehyde (**8**) in basic conditions gave



Scheme 2. 3, **5**, **6**, **7**, **9**, **11**, **13**, **14**: (a) R=H; (b) R=OMe; **10**: (a) R=H, X=Br, (b) R=X=H; (c) R=OMe, X=Br; (d) R=OMe, X=H. Conditions. (i) NaMeO/MeOH, rt, 15–27 h. (ii) H_2, Pd/C, AcOEt, 1 atm, 75–210 min. (iii) (a) $NaBH_4$, MeOH, rt, 60–90 min; (b) H_2SO_4, reflux, 1–2 h. (iv) (a) O_3, −78 °C, 3–6 min; (b) Me_2S, −78 °C (4–7 h), rt (13 h). (v) NaOH aq, rt, 1.5–2 h. (vi) Fremy's salt, K_2HPO_4, acetone, rt, 1–4 h. (vii) H_2SO_4, MeOH, reflux, 29 h. (viii) CuO, K_2CO_3, pyr, reflux, 1.5–4 h. (ix) CrO_3, AcOH, reflux, 10 min. (x) NaH, $CO(OEt)_2$, benzene, reflux, 0.5 h. (xi) NaH, 2-bromobenzyl bromide, DMF, 60 °C, 44.5 h. (xii) 48% HBr. 96% AcOH, 120 °C, 1.5 h.

the bromobenzylideneindanone **9a** (98% yield),[8] which when subjected to controlled catalytic hydrogenation furnished the expected bromobenzylindanone **10a**[9] (98% yield) without the formation of compound **10b** through simultaneous hydrogenolysis of the C–Br bond. Subsequent reduction of indanone **10a** with $NaBH_4$ gave a mixture of indanols,[10] which was directly converted into bromobenzylindene **11a**[11] by refluxing with concentrated sulfuric acid for an hour. Finally, indene **11a** was transformed into the desired ketoaldehyde **5a** by ozonolysis.[12] This key intermediate was easily identified from spectroscopic and analytical data. The mass spectrum showed the molecular ion peaks at *m/z* 318 and *m/z* 316, with the typical isotope pattern expected for bromo compounds. The ^1H NMR spectrum contained a singlet at 10.01 ppm due to the aldehyde proton. Several representative signals in the ^{13}C NMR include a signal at 125.2 ppm, due to the carbon bearing the bromo- substituent, and two signals at 193.3 and 203.2 ppm, due to the ketone and aldehyde carbonyls, respectively.

Intramolecular aldol condensation of ketoaldehyde **5a** readily gave a quantitative yield of the expected bromophenylnaphthol **6a**.[13] Treatment of this compound with Fremy's salt yielded bromophenylnaphthoquinone **12a** in 94% yield[14] and this was reacted with sodium hydroxide in methanol at rt for 15 min to give bromophenylhydroxynaphthoquinone **2** in only 7% yield.[15] However, the yield of this reaction was improved to 93% when it was carried out under acidic conditions (H_2SO_4, MeOH, reflux).[16] Finally, when compound **2** was subjected to previously described Ullman reaction conditions,[15] the expected benzofuronaphthoquinone **3a** was obtained in 71% yield.

Alternatively, when 3-bromophenyl-2-naphthol **6a** was submitted to the Ullman reaction conditions,[15] 73% yield of the benzonaphthofuran **13a** was obtained. Oxidation of **13a** with CrO_3 in acetic acid[17] gave the target **3a** in quantitative yield. The molecular formula of compound **13a** ($C_{16}H_{10}O$) was confirmed by mass spectrometry. The ^1H NMR contained signals between 7.35 and 8.42 ppm due to the ten aromatic protons. Two characteristic signals in the ^{13}C NMR were observed at 154.8 and 157.6 ppm due to the carbons of the ethereal bridge.

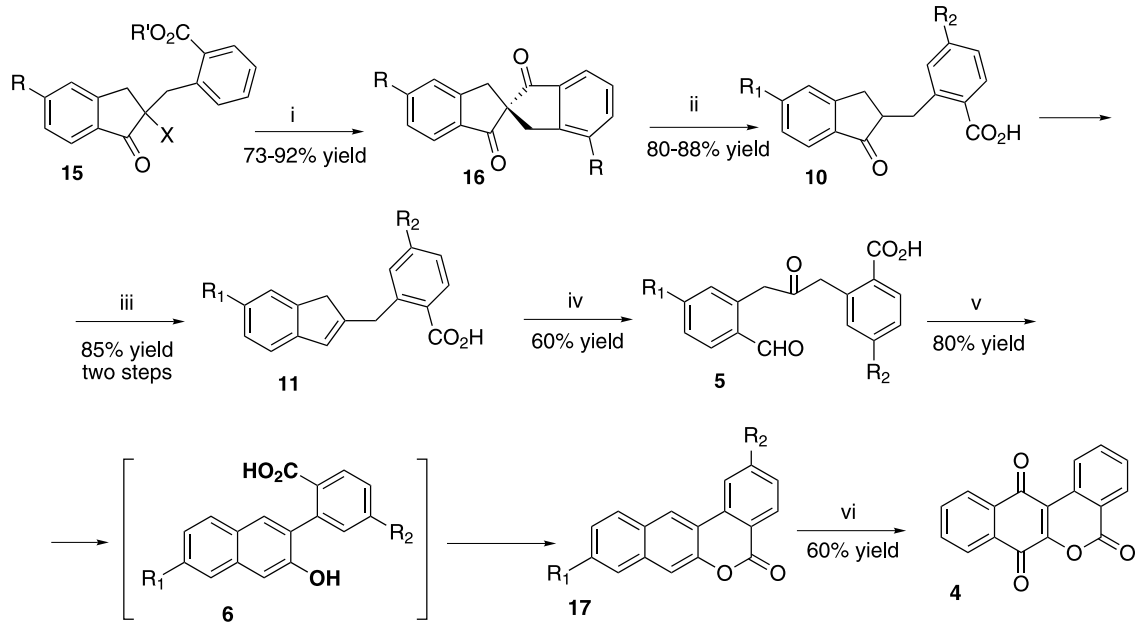
This alternative synthesis of **3a** is clearly more convenient than the route via hydroxyphenylnaphthoquinone **2a**, not only because it is both shorter and more efficient, but because it avoids experimental problems encountered with the former route due to the manipulation of quinone compounds in earlier stages of the synthesis. Moreover, this new route constitutes a novel synthetic approach to benzonaphthofurans **13**,[18] as illustrated by the preparation of benzonaphthofuran **13a** (brazan), which was originally isolated[2] from coal tar distillate.

The general interest of this novel route was immediately demonstrated by the similar transformation of methoxyindanone **7b** into benzonaphthofuran **13b** and its benzofuronaphthoquinone derivative **3b** via benzylideneindanone **9b**, benzylindanone **10b**, benzylindene **11b**, ketoaldehyde **5b** and bromophenylnaphthol **6b**. In this case, catalytic hydrogenation of benzylideneindanone **9b** was accompanied by the undesired hydrogenolysis of its C–Br bond. Indeed, an oil consisting of a mixture of the bromobenzylindanone **10c** (major component) and benzylindanone **10d** (minor component) was obtained and only a small portion the desired compound **10c** could be isolated from this. However, **10c** was efficiently obtained as follows: treatment of methoxyindanone **7b** with NaH and diethyl carbonate gave 2-ethoxycarbonyl-1-indanone **14b** in 62% yield. This compound was efficiently converted into 2-ethoxycarbonyl-1-indanone **15b** by reaction with NaH and *o*-bromobenzyl bromide.[19] Finally, a solution of **15b** and concentrated HBr was heated under reflux in acetic acid for 1.5 h. This reaction gave the desired *o*-bromobenzylindanone **10c** in 72% yield as a result of the hydrolysis of the ester functionality followed by decarboxylation of the resulting ketoacid.[20]

We next proceeded to apply this novel 2-phenylnaphthalene-based methodology for the synthesis of benzonaphthofurans **13** and benzofuronaphthoquinones **3** to the preparation of related benzonaphthopyranone **17a** and benzopyronaphthoquinone **4**.

2-Ethoxycarbonyl-1-indanone **14a** was quantitatively transformed into the corresponding 2-ethoxycarbonyl-2-benzyl-1-indanone **15a** by reaction[19] with 2-ethoxycarbonylbenzyl bromide, which was obtained[21] by reaction of *o*-ethoxycarbonyltoluene with NBS (Scheme 3). A solution of **15a** in acetic acid was reacted with HBr at 120 °C for 3.25 h in order to hydrolyse the two ester functions and to transform the resulting dicarboxylic acid **15c** into benzylindanone **10e** by decarboxylation.[20] Unexpectedly, the only compound formed was the spiro diindanone **16a**,[22] as deduced from spectroscopic and analytical data. The mass spectrum indicated a molecular formula $C_{17}H_{12}O_2$ for this compound. Moreover, the IR spectrum showed bands at 1720 and 1694 cm^{-1} due to the two carbonyl groups. The ^1H NMR spectrum showed two signals at 3.73 and 3.20 ppm, corresponding to the two methylene groups, together with signals for a total of eight aromatic protons. Characteristic signals in the ^{13}C NMR spectrum were observed at 153.8 ppm, due to the spiranic quaternary carbon, and 202.07 ppm, due to the carbonyl groups. Formation of spiro compound **16a** can be explained by assuming that indanone **15a** readily undergoes a highly regioselective hydrolysis of the ethoxycarbonyl group in the position α to the ketone. This is followed by decarboxylation and subsequent intramolecular mixed Claisen condensation of the resulting ethoxycarbonylbenzylindanone **15d** under the acidic reaction conditions.

As expected, reaction of **16a** with NaOH readily gave a retro-aldol process and led to the desired indanone ketoacid **10e**.[23] This compound was subjected to a reaction sequence similar to that used for the transformation of bromo compounds **6** into benzofuronaphthoquinones **3**. Thus, reduction of ketoacid **10e** with $NaBH_4$ gave a quantitative yield of a mixture of indanols, which were reacted with 10% HCl in dioxane to provide the desired indene **11c**. Subsequent ozonolysis of **11c** gave the key ketoaldehyde **5c**, which was reacted with NaOH directly to furnish the target compound **17a**. This process probably involves the initial formation of the expected 2-naphthol **6c** resulting



Scheme 3. 15: (a) R=H, R′=Et, X=CO_2Et; (c) R=H, R′=OH, X=CO_2H; (d) R=X=H, R′=Et; (e) R=OMe, R′=Et, X=CO_2Et; (f) R=OMe, R′=OH, X=CO_2H; (g) R=OMe, X=H, R′=Et. **10**: (e) R_1=R_2=H; (f) R_1=OMe, R_2=H; (g) R_1=H, R_2=OMe; **5**, **6**,**11**: (c) R_1=R_2=H; (d) R_1=OMe, R_2=H; (e) R_1=H, R_2=OMe. **16**, **17**: (a) R_1=R_2=H; (b) R_1=OMe, R_2=H; (c) R_1=H, R_2=OMe. Conditions. (i) HBr, AcOH, reflux, 3.25 h. (ii) 1.25 M aq NaOH, EtOH, reflux, 5 h. (iii) (a) $NaBH_4$, MeOH, 0–>5 °C, 8.25 h; (b) HCl, dioxan, reflux, 10.5 h. (iv) (a) O3, −78 °C, 3–6 min; (b) Me_2S, −78 °C (4–7 h), rt (13 h). (v) NaOH aq, rt, 1.5–2 h. (vi) CrO_3, AcOH, reflux, 10 min.

from the intramolecular aldol cyclization, followed by the spontaneous lactonization of this compound under the reaction conditions. Finally, as predicted, benzonaphthopyranone **17a** was easily oxidized to benzopyronaphthoquinone **4** when reacted with CrO_3.

The synthesis of **4** reported here is clearly more convenient than previous routes[6] via hydroxyphenylnaphthoquinones **2** and has the additional advantage that it allows the generation of the quinone moiety to be left until the final step of the synthesis. This aspect overcomes the problems associated with the manipulation of quinone compounds. Moreover, the new route constitutes the first total synthesis of 6-oxa-benzo[*a*]anthracen-5-one, as illustrated by the preparation of benzonaphthopyranone **17a**.

A predictable limitation of this route to benzonaphthopyranones **17** was confirmed in the attempt to obtain methoxybenzonaphthopyranone **17b** from 2-ethoxycarbonyl-2-benzyl-1-indanone **15e**, prepared by reaction of methoxyindanone **14b** with 2-ethoxycarbonylbenzyl bromide. As expected, treatment of **15e** with HBr, as described above, gave diindanone **16b** but reaction of this compound with NaOH gave a mixture of indanone ketoacids **10f** and **10g**. Since isolation of these compounds from the mixture was not very efficient, they could not be transformed into the corresponding benzonaphthopyranones **17b** and **17c**.

In conclusion, we describe here a divergent synthesis of benzofuronaphthoquinones **3** from phenylketopropylbenzaldehydes **5**. The route via 2-hydroxy-3-phenyl-1,4-naphthoquinones **2** constitutes a more generally applicable version of a previously described route. The alternative shorter and more efficient route includes a novel total synthesis of benzonaphthofurans **14** and the efficient oxidation of these materials to benzofuronaphthoquinones **3**. The extension of this novel synthetic methodology to benzopyronaphthoquinones **4** resulted in the first total synthesis of benzonaphthopyranone **17a**. This target compound was efficiently oxidized to unsubstituted benzopyronaphthoquinone **4**. This route does, however, seems to be limited to the preparation of benzonaphthopyranones **17** with a substitution pattern compatible with the opening of spiro compound **16** to a single indanone ketoacid **10**.

Work is now in progress to overcome this limitation and to extend the 2-phenylnaphthalene-based synthetic methodology reported here to the preparation of tetracyclic 2-phenylnaphtahlene derivatives other than benzonaphthofurans **14**, benzofuronaphthoquinones **3**, benzonaphthopyranones **17** and benzopyronaphthoquinones **4**. It is envisaged that the route will also include indolonaphthoquinones and ellipticines, which are known to show antitumour properties.

1. Experimental

1.1. General

Melting points were determined on a Kofler Thermogerate apparatus and are uncorrected. Infrared spectra were recorded on a MIDAC FTIR spectrophotometer. Nuclear magnetic resonance spectra were recorded, unless otherwise specified, on a Bruker WM-250 apparatus, using deuterochloroform solutions containing tetramethylsilane as internal standard. Mass spectra were obtained on a Kratos MS 50 TC mass spectrometer. Thin layer chromatography (tlc) was performed using Merck GF-254 type 60 silica gel and CH_2Cl_2/MeOH mixtures as eluants; the tlc spots were

visualized with ultraviolet light or iodine vapour. Column chromatography was carried out using Merck type 9385 silica gel. Solvents were purified as per Ref. 24. Solutions of extracts in organic solvents were dried with anhydrous sodium sulfate.

1.1.1. 2-(2-Bromobenzylidene)indan-1-one (9a). A solution of 1-indanone (1 g, 7.5 mmol) in dry MeOH (18 mL) was added dropwise under argon to a solution of 2-benzaldehyde (0.93 mL, 7.95 mmol) and sodium methoxide (120 mg, 2.35 mmol) in dry MeOH (22 mL). The mixture was stirred at rt for 15 h and poured into water (50 mL). The resulting suspension was acidified by the addition of 20% aq HCl and extracted with CH_2Cl_2 (3×100 mL). The combined organic extracts were dried and concentrated to dryness in vacuo. Crystallisation of the solid residue from MeOH yielded the title compound as white needless (2.2 g, 98%). Mp 134–136 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1695 (C=O), 1621 (C=C). ^1H NMR (δ, ppm): 3.94 (s, 2H, CH_2), 7.23 (m, 1H, Ar–H), 7.35–7.68 (m, 6H, 6×Ar–H), 7.91 (δ, 1H, J= 7.6 Hz, Ar–H), 7.97 (s, 1H, HC=C). ^{13}C NMR (δ, ppm): 31.7 (CH_2), 124.6 (CH), 126.2 (CH), 126.6 (C), 127.5 (CH), 127.8 (CH), 130.0 (CH), 130.5 (CH), 132.5 (CH), 133.6 (CH), 134.8 (CH), 135.4 (C), 137.1 (C), 138.0 (C), 149.8 (C), 193.8 (C=O). MS (*m/z*, %): 300 [$(M+2)^+$, 2], 298 (M^+, 1.7), 219 [$(M-79.9)^+$, 100], 189 (32). Anal. Calcd for $C_{16}H_{11}BrO$, C: 64.24; H: 3.71; Br: 26.71. Found C: 64.41; H: 3.68; Br: 27.03.

1.1.2. 2-(2-Bromobenzyl)indan-1-one (10a). 10% Pd–C (50 mg) was added to a deoxygenated solution of bromobenzylideneindanone **9a** (0.96 g, 3.21 mmol) in ethyl acetate (80 mL) and the mixture was stirred under a hydrogen atmosphere (1 atm) at rt for 1 h 15 min. After removal of the excess of hydrogen in vacuo, the reaction mixture was filtered though Celite, which was eluted with ethyl acetate. The filtrate was concentrated to dryness in vacuo to give the title compound as white crystals (0.947 g, 98% yield). Mp 67–69 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1710 (C=O). ^1H NMR (δ, ppm): 2.86 (m, 2H, $-CH_2$), 3.11–3.18 (m, 2H, CH_2, CH), 3.53 (dd, 1H, J=14.1 Hz, J'=4.0 Hz, CH_2), 7.10 (m, 1H, Ar–H), 7.23–7.34 (m, 2H, 2×Ar–H), 7.37–7.43 (m, 2H, 2×Ar–H), 7.55–7.61 (δ, 2H, J=7.5 Hz, 2×Ar–H), 7.79 (δ, 1H, J=7.5 Hz, Ar–H). ^{13}C NMR (δ, ppm): 32.1 (CH_2), 36.9 (CH_2), 47.5 (CH), 124.1 (CH), 124.9 (C), 126.7 (CH), 127.5 (CH), 127.6 (CH), 128.2 (CH), 131.0 (CH), 133.1 (CH), 134.9 (CH), 136.6 (C), 139.2 (C), 153.5 (C), 207.4 (C=O). MS (*m/z*, %): 301 [$(M+2)^+$, 0.15], 299 (M^+, 0.09), 221 [$(M-79.9)^+$, 100], 131 (26). Anal. Calcd for $C_{16}H_{13}BrO$, C: 63.81; H: 4.35; Br: 26.53. Found C: 64.09; H: 4.23; Br: 26.87.

1.1.3. 2-(2-Bromobenzyl)-1*H*-indene (11a). Small portions of $NaBH_4$ (540 mg, 1.43 mmol) were added every 15 min during 1 h to a solution of benzylindanone **10a** (700 mg, 0.23 mmol) in MeOH (60 mL) cooled to 0–5 °C using a water/ice bath. The mixture was stirred at rt for 30 min and poured into water (100 mL). The MeOH was evaporated in vacuo and the remaining suspension was extracted with CH_2Cl_2 (3×100 mL) and the combined organic extracts were washed with water (3×100 mL), dried and concentrated to dryness in vacuo. The remaining solid was immediately mixed with 9 M H_2SO_4 (75 mL) and the stirred suspension was refluxed in a dry atmosphere for 30 min. 20% aq NaOH was added until a basic pH was attained and the suspension was extracted with CH_2Cl_2 (3× 100 mL). The combined organic extracts were dried and concentrated to dryness in vacuo. The remaining solid was submitted to flash column chromatography (eluant: ethyl acetate/hexane, 0.3:9.7) to give the title compound in 96% yield (0.638 g) as a yellow oil. IR ($\bar{\nu}$, cm^{-1}, NaCl): 3071 (C=C). ^1H NMR (δ, ppm): 3.39 (s, 2H, $-CH_2$), 4.01 (s, 2H, $-CH_2$), 6.52 (s, 1H, HC=C), 7.13–7.34 (m, 6H, 6×Ar–H), 7.42 (δ, 1H, J=7.2 Hz, Ar–H), 7.63 (d, 1H, J=8.2 Hz, Ar–H). ^{13}C NMR (δ, ppm): 37.9 (CH_2), 41.1 (CH_2), 120.4 (CH), 123.6 (CH), 124.1 (CH), 124.8 (CBr), 126.4 (CH), 127.7 (CH), 128.1 (CH), 128.5 (CH), 131.1 (CH), 139.6 (C), 143.4 (C), 145.4 (C), 147.6 (C). HRMS: $C_{16}H_{13}Br$ (M^+), calcd 284.0201; found 284.0199.

1.1.4. 2-[3-(2-Bromophenyl)-2-oxopropyl]benzaldehyde (5a). N_2 and O_2 were bubbled consecutively for 10 min each through a solution of indene **11a** (400 mg, 1.39 mmol) in CH_2Cl_2 (60 mL) at −78 °C connected to an ozonizer. O_3 was then bubbled through the solution for 2 min until a blue colour appeared due to the presence of ozonide. O_2 was then bubbled through for 10 min to destroy the excess O_3 and finally N_2 was bubbled through for 5 min. Dimethyl sulfide (1.9 mL, 26.38 mmol) was added and the mixture was stirred at −78 °C under argon for 7 h and at rt for 13 h. The solvent was removed in vacuo and the solid residue was submitted to column chromatography (eluant: ethyl acetate/hexane, 0.5:9.5) to give the target compound (324 mg) in 73% yield as white crystals. Mp 68–69 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1719, 1693 (CHO, C=O). ^1H NMR (δ, ppm): 4.11 (s, 2H, CH_2), 4.20 (s, 2H, CH_2), 7.24–7.53 (m, 7H, 7×Ar–H), 7.56 (t, 1H, J=1.8 Hz, Ar–H), 10.01 (s, 1H, CHO). ^{13}C NMR (δ, ppm): 47.1 (CH_2), 50.0 (CH_2), 125.2 (C), 127.6 (CH), 127.8 (CH), 128.8 (CH), 132.2 (CH), 132.8 (2×CH), 133.7 (CH), 134.4 (C), 134.9 (C), 135.0 (CH), 135.8 (C), 193.3 (C=O), 203.2 (C=O). MS (*m/z*, %): 318 [$(M+2)^+$, 0.37], 316 (M^+, 0.34), 237 [$(M-79.9)^+$, 2], 171 (36.4), 169 (37.6), 147 (100), 119 (88), 91 (65). Anal. Calcd for $C_{16}H_{13}BrO_2$, C: 60.59; H: 4.13; Br: 25.19. Found C: 60.32; H: 4.19; Br: 24.96.

1.1.5. 3-(2-Bromophenyl)naphthalen-2-ol (6a). A solution of ketoaldehyde **5a** (200 mg, 0.63 mmol) in 5% aq NaOH (10 mL) was magnetically stirred in a dry atmosphere at rt for 1 h. The reaction mixture was acidified by adding 10% aq HCl and the resulting suspension was extracted with CH_2Cl_2 (3×25 mL). The combined organic extracts were washed with water (25 mL), dried and concentrated to dryness in vacuo to give a quantitative yield of the title compound (188 mg) as an oil. IR ($\bar{\nu}$, cm^{-1}, NaCl): 3535 (OH). ^1H NMR (δ, ppm): 7.18–7.42 (m, 6H, 6×Ar–H), 7.59 (s, 1H, Ar–H), 7.67–7.73 (m, 3H, 3×Ar–H). ^{13}C NMR (δ, ppm): 110.3 (CH), 124.0 (CH), 124.4 (C), 125.9 (C), 126.4 (CH), 126.7 (CH), 127.8 (2×CH), 128.6 (C), 130.0 (2× CH), 132.2 (CH), 133.2 (CH), 134.7 (C), 137.8 (C), 150.7 (C=O). MS (*m/z*, %): 300 [$(M+2)^+$, 66], 298 (M^+, 69), 219 (72), 218 (98), 191 880), 189 (100), 109 (42), 95 (63). HRMS: $C_{16}H_{11}BrO$ (M^+), calcd 297.9993; found 297.9994.

1.1.6. 3-(2-Bromophenyl)-1,2-naphthoquinone (12a). A solution of Fremy's salt (1.187 g, 4.42 mmol) and

potassium biphosphate (215 mg, 1.58 mmol) in water (30 mL) was added to a solution of naphthol **6a** (137 mg, 0.46 mmol) in acetone (13 mL). The suspension was stirred in a dry atmosphere at rt for 1 h and the acetone was evaporated in vacuo. The pink suspension was extracted with CH_2Cl_2 (3×25 mL) and the combined organic layers were washed with water (25 mL), dried and concentrated to dryness in vacuo. The solid residue was submitted to flash column chromatography (eluant: ethyl acetate/hexane, 1:9) and the title compound was isolated as red crystals (133 mg, 94% yield). Mp 164–166 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1675 (C=O). ^1H NMR (δ, ppm): 7.15–7.64 (m, 8H, 7× Ar–H, CH=C), 8.08 (d, 1H, J=7.6 Hz, Ar–H). ^{13}C NMR (δ, ppm): 123.4 (CBr), 127.4 (CH), 130.2 (2×CH), 130.3 (CH), 130.8 (CH), 131.1 (CH), 131.4 (C), 133.0 (CH), 134.7 (C), 135.5 (C), 135.9 (CH), 139.6 (C), 144.1 (CH), 178.8 (C=O), 178.9 (C=O). MS (*m*/*z*, %): 286 {[(M−28)+2]$^+$, 15.2}, 284 [(M−28)$^+$, 15.2}, 205 (100), 176 (43). Anal. Calcd for $C_{16}H_9BrO_2$, C: 61.37; H: 2.90; Br: 25.52. Found C: 61.72; H: 2.93; Br: 25.11.

1.1.7. 2-(2-Bromophenyl)-3-hydroxy-1,4-naphthoquinone (2a). 20% aq sulfuric acid (2 mL) was added to a suspension of quinone **12a** (31 mg, 0.09 mmol) in MeOH (2 mL) and the mixture was refluxed for 94 h. The MeOH was removed in vacuo and the resulting suspension was poured into water (25 mL) and extracted with CH_2Cl_2 (3× 25 mL). The combined organic extracts were washed with water (25 mL), dried and concentrated to dryness in vacuo. The solid residue was submitted to flash column chromatography (eluant: ethyl acetate/hexane, 1:1) and the title compound was obtained (30 mg, 93% yield) as red crystals. Mp 172–174 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 3425 (OH), 1635 (C=O). ^1H NMR (δ, ppm): 6.99–7.14 (m, 3H, 3× Ar–H), 7.46–7.55 (m, 2H, 2×Ar–H), 7.66 (t, 1H, J= 7.5 Hz, Ar–H), 7.94 (δ, 2H, J=7.6 Hz, 2×Ar–H). ^{13}C NMR (δ, ppm, $CDCl_3$/MeOD): 119.9 (C), 124.9 (C), 125.1 (2×CH), 125.7 (CH), 127.2 (CH), 129.9 (C), 130.4 (CH), 131.1 (CH), 132.2 (CH), 134.1 (CH), 134.4 (C), 136.0 (C), 167.5 (C), 181.1 (C=O), 189.1 (C=O). MS (*m*/*z*, %): 249 [(M−79.9)$^+$, 100], 165 (32). Anal. Calcd for $C_{16}H_9BrO_3$, C: 58.38; H: 2.76; Br: 24.28. Found C: 50.82; H: 2.83; Br: 24.62.

1.1.8. Benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione (3a). A mixture of naphthoquinone **2a** (30 mg, 0.09 mmol), CuO (23 mg, 0.28 mmol) and K_2CO_3 (64 mg, 5.1 mmol) in dry deoxygenated pyridine (3 mL) was refluxed under argon for 4 h. The mixture was then added to 20% aq HCl solution (40 mL) and the resulting suspension was extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were washed with 10% aq NaOH (3×25 mL), dried, filtered and concentrated in vacuo. The solid residue was submitted to flash column chromatography (eluant: ethyl acetate/hexane, 1:9) to give the title compound (16 mg, 71% yield) as yellow crystals. Mp 245–247 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1674 (C=O). ^1H NMR (δ, ppm): 7.48–7.81 (m, 5H, 5×Ar–H), 8.22–8.34 (m, 3H, 3×Ar–H). ^{13}C NMR (δ, ppm): 112.9 (CH), 122.7 (C), 124.0 (CH), 124.3 (C), 126.1 (CH), 126.8 (CH), 126.9 (CH), 129.6 (CH), 132.4 (C), 133.3 (C), 133.9 (CH), 134.2 (CH), 153.5 (C), 156.5 (C), 175.5 (C=O), 181.4 (C=O). MS (*m*/*z*, %): 248 (M$^+$, 100), 220 (46), 163 (51). Anal. Calcd for $C_{16}H_8O_3$, C: 77.42; H: 3.25. Found C: 77.29; H: 3.33.

1.1.9. Benzo[*b*]naphtho[2,3-*d*]furan (13a). Reaction of a suspension of bromonaphthol **6a** (30 mg, 0.10 mmol), CuO (0.31 mg, 3.1 mmol) and potassium carbonate (70 mg, 5.1 mmol) in dry deoxygenated pyridine was subjected to the same conditions as for the preparation of benzofuronaphthoquinone **3a**. The title compound was obtained as white crystals (16 mg, 73% yield). Mp 210–212 °C (MeOH). ^1H NMR (δ, ppm): 7.35–7.58 (m, 5H, 5× Ar–H), 7.93 (s, 1H, Ar–H), 7.96–8.07 (m, 3H, 3×Ar–H), 8.42 (s, 1H, Ar–H). ^{13}C NMR (δ, ppm): 106.9 (CH), 111.6 (CH), 119.1 (CH), 121.3 (CH), 122.7 (CH), 123.9 (C), 124.3 (CH), 125.4 (C), 125.9 (CH), 127.8 (CH), 128.3 (2×CH), 130.2 (C), 133.0 (C), 154.8 (CO), 157.6 (CO). MS (*m*/*z*, %): 218 (M$^+$, 100), 189 (24). Anal. Calcd for $C_{16}H_{10}O$, C: 88.05; H: 4.62. Anal. Calcd for $C_{16}H_{16}O$, C: 88.05; H: 4.62. Found C: 87.72; H: 4.67.

1.1.10. Benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione (3a). A solution of CrO_3 (75 mg, 0.76 mmol) in glacial acetic acid (6 mL) and water (1 mL) was added to a solution of benzonnaphthofuran **13a** (30 mg, 0.14 mmol) in glacial acetic acid and the mixture was refluxed during 10 min. The suspension was poured into CH_2Cl_2 (25 mL) and the organic phase was washed with water (3×25 mL), dried and concentrated in vacuo. The title compound was obtained as a yellow solid (34 mg, 100% yield).

1.1.11. 2-(2-Bromobenzylidene)-5-methoxyindan-1-one (9b). 1-Methoxyindanone **7b** (2 g, 12.33 mmol) and *o*-bromobenzaldehyde (1.526 mL, 13.07 mmol) were reacted under the same conditions as for the preparation of benzylideneindanone **9a** to give the title compound as white crystals (3.31 g, 85% yield). Mp 158–160 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1685 (C=O), 1628 (C=C). ^1H NMR (δ, ppm): 3.81 (s, 2H, CH_2), 3.86 (s, 3H, OCH_3), 6.88–6.91 (m, 2H, 2×Ar–H), 7.17 (m, 1H, Ar–H), 7.34 (t, J=7.5 Hz, 1H, Ar–H), 7.58–7.63 (m, 2H, 2×Ar–H), 7.77–7.85 (m, 2H, 2×Ar–H). ^{13}C NMR (δ, ppm): 31.7 (CH_2), 55.6 (CH_3), 109.5 (CH), 115.3 (CH), 126.1 (CH), 126.2 (C), 127.3 (CH), 129.7 (CH), 130.1 (CH), 131.0 (CH), 131.2 (C), 133.3 (CH), 135.3 (C), 137.5 (C), 152.5 (C), 165.2 (C=O), 191.9 (C=O). MS (*m*/*z*, %): 330 [(M+2)$^+$, 42], 328 (M$^+$, 43), 249 [(M−79.9)$^+$, 100], 243 (23). Anal. Calcd for $C_{17}H_{13}BrO_2$, C: 62.03; H: 3.98; Br: 24.27. Found C: 62.31; H: 4.05; Br: 23.96.

1.1.12. 2-(2-Bromobenzyl)-5-methoxyindan-1-one (10c). Catalytic hydrogenation of bromobenzylideneindanone **9b** (1 g, 2.94 mmol), under the same conditions as for analogue **10a**, resulted in a mixture of the title compound and benzylindanone **10d**. The mixture was purified by flash column chromatography (eluant: ethyl acetate/hexane, 1:9) to give the title compound (0.099 g, 9.8% yield) as a colourless oil. IR ($\bar{\nu}$, cm^{-1}, NaCl): 1701 (C=O). ^1H NMR (δ, ppm, $CDCl_3$): 2.81 (m, 2H, CH_2), 3.09 (m, 2H, CH_2), 3.50 (m, 1H, CH), 3.85 (s, 3H, OMe), 6.81–6.91 (m, 2H, ArH), 7.08 (m, 1H, ArH), 7.21–7.29 (m, 2H, ArH), 7.55 (m, 1H, ArH), 7.70 (dd, J=8.5 Hz, J'=2.8 Hz, 1H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 32.1 (CH_2), 36.9 (CH_2), 47.5 (CH), 55.5 (OMe), 109.6 (CH), 115.4 (CH), 124.7 (C), 125.6

(CH), 127.4 (CH), 128.0 (CH), 129.6 (C), 130.8 (CH), 132.9 (CH), 139.1 (C), 156.4 (C), 165.3 (C), 205.5 (C=O). HRMS: $C_{17}H_{15}BrO_2$ (M^+), calcd 330.0255; found 330.0258.

1.1.13. 5-Methoxy-1-oxoindan-2-carboxylic acid ethyl ester (14b). A solution of methoxyindanone **7b** (5.1 g, 32 mmol) in benzene (75 mL) was added dropwise under argon during 4.5 h to a mixture of 80% sodium hydride (1.66 g, 69 mmol), diethyl carbonate (7.5 mL, 62 mmol) and benzene (40 mL) under reflux. A further quantity of benzene (4.5 mL) was added and the mixture was heated for a further 0.5 h. Water (35 mL) and acetic acid (6 mL) were added to the reaction mixture and the organic layer was separated and the aqueous layer extracted with benzene (2× 75 mL) and diethyl ether (2×75 mL). The combined organic extracts were dried and concentrated in vacuo. The solid residue was submitted to flash column chromatography (eluant: CH_2Cl_2/hexane, 9:1) and the resulting solid was refluxed in hexane (500 mL) for 30 min and filtered immediately. The filtrate was concentrated to dryness in vacuo to give the title compound as white crystals (6.35 g, 62% yield). Mp 63–65 °C (ethyl acetate/hexane). IR ($\bar{\nu}$, cm^{-1}, KBr): 1262 (C–OMe), 1707 (CO_2Et), 1738 (C=O). ^1H NMR (δ, ppm): 1.25 (t, $J=7.2$ Hz, 3H, $-CH_3$), 3.21–3.29 (m, 1H, $-CH_2$), 3.41–3.48 (m, 1H, $-CH_2$), 3.62–3.66 (m, 1H, –CH), 3.83 (s, 3H, $-OCH_3$), 4.19 (q, $J=7.2$ Hz, 2H, $-CH_2O$), 6.84–6.87 (m, 2H, ArH), 7.61–7.64 (m, 1H, ArH). ^{13}C NMR (δ, ppm): 13.9 (CH_3), 30.0 (CH_2), 53.2 (CH), 55.4 (CH_3), 61.2 (CH_2), 109.2 (CH), 115.6 (CH), 125.8 (CH), 128.1 (C), 156.5 (C), 165.6 (C), 169.1 C=O), 197.3 (C=O). MS (*m/z*, %): 234 (M^+, 50), 188 (29), 160 (100).

1.1.14. 2-(2-Bromobenzyl)-5-methoxy-1-oxo-indan-2-carboxylic acid ethyl ester (15a). A mixture of 80% sodium hydroxide (24 mg, 1.13 mmol), indanone **14a** (237 mg, 1.10 mmol) and *N*,*N*-dimethylformamide (0.5 mL) was heated at 60 °C for 1 h. A solution of 98% 2-bromobenzyl bromide (290 mg, 1.16 mmol) in *N*,*N*-dimethylformamide (0.8 mL) was added and the mixture was heated at 60 °C for 44.5 h. A few drops of water were added and the suspension was extracted with diethyl ether (3×10 mL). The combined organic extracts were washed with saturated aq sodium chloride, dried and concentrated to dryness in vacuo. The solid residue was submitted to flash column chromatography (eluant: CH_2Cl_2/hexane, 3:1) and the title compound was isolated as a transparent oil (319 mg, 78% yield). IR ($\bar{\nu}$, cm^{-1}, KBr): 1263 (C–OMe), 1706 (CO_2Et), 1738 (C=O). ^1H NMR (δ, ppm, $CDCl_3$): 1.15 (t, $J=7.1$ Hz, 3H, $-CH_3$), 3.05 (δ, $J=17.5$ Hz, 1H, C*H*H), 3.43 (d, $J=14.7$ Hz, 1H, C*H*H), 3.58 (δ, $J=17.5$ Hz, 1H, C*H*H), 3.71 (s, 1H, C*H*H), 3.76 (s, 3H, OMe), 4.13 (q, $J=7.2$ Hz, 2H, $-OCH_2$), 6.74 (δ, $J=1.9$ Hz, 1H, ArH), 6.81 (m, 1H, ArH), 6.90–6.96 (m, 1H, ArH), 7.00–7.06 (m, 1H, ArH), 7.16 (m, 1H, ArH), m (m, 1H, ArH), 7.67 (m, 1H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 13.8 (CH_3), 34.9 (CH_2), 37.8 (CH_2), 55.4 (CH_3), 61.6 (CH_2), 109.0 (CH), 115.7 (CH), 125.9 (CH), 126.1 (CH), 127.2 (CH), 128.1 (CH), 130.9 (CH), 132.7 (CH), 136.4 (C), 156.6 (C), 165.6 (C), 170.6 (C=O), 199.9 (C=O). HRMS: $C_{20}H_{19}BrO_4$ (M^+), calcd 402.0467; found 402.0463.

1.1.15. 2-(2-Bromobenzyl)-5-methoxyindan-1-one (10c). A suspension of indanone **15a** (128 mg, 0.317 mmol), 48% HBr (0.7 mL) and 96% AcOH (0.6 mL) was stirred at 120 °C for 1.5 h. The mixture was cooled and diluted with water (5 mL). The organic material was extracted with diethyl ether (3×10 mL) and the combined organic extracts were dried and concentrated in vacuo. The solid residue was submitted to flash column chromatography (eluant: CH_2Cl_2/hexane, 5.5:4.5) and the title compound (76 mg, 72% yield) was isolated as an oil (76 mg, 72% yield). IR (NaCl, $\bar{\nu}$, cm^{-1}): 1701 (C=O). ^1H NMR (δ, ppm, $CDCl_3$): 2.81 (m, 2H, CH_2), 3.09 (m, 2H, CH_2), 3.50 (m, 1H, CH), 3.85 (s, 3H, –OMe), 6.81–6.91 (m, 2H, ArH), 7.08 (m, 1H, ArH), 7.21–7.29 (m, 2H, ArH), 7.55 (m, 1H, ArH), 7.70 (dd, $J=8.5$ Hz, $J'=2.8$ Hz, 1H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 32.1 (CH_2), 36.9 (CH_2), 47.5 (CH), 55.5 (CH_3), 109.6 (CH), 115.4 (CH), 124.7 (C), 125.6 (CH), 127.4 (CH), 128.0 (CH), 129.6 (C), 130.8 (CH), 132.9 (CH), 139.1 (C), 156.4 (C), 165.3 (C), 205.5 (C=O). HRMS: $C_{17}H_{15}BrO_2$ (M^+), calcd 330.0255; found 330.0251.

1.1.16. 2-(2-Bromobenzyl)-6-methoxy-1*H*-indene (11b). Following the procedure for the preparation of benzylindene **11a**, benzylindanone **10c** (780 mg, 2.35 mmol) was transformed into the title compound (3.71 mmol, 88% yield). Mp 62–64 °C (MeOH). ^1H NMR (δ, ppm): 3.29 (s, 2H, CH_2), 3.78 (s, 3H, $-OCH_3$), 3.90 (s, 2H, CH_2), 6.38 (s, 1H, HC=C), 6.76 (dd, 1H, $J=8.2$ Hz, $J'=2.4$ Hz, Ar–H), 6.96 (m, 1H, Ar–H), 7.13 (δ, 1H, $J=8.3$ Hz, Ar–H), 7.25–7.23 (m, 3H, 3×Ar–H), 7.55 (δ, 1H, $J=7.7$ Hz, Ar–H). ^{13}C NMR (δ, ppm): 37.9 (CH_2), 41.1 (CH_2), 55.5 (CH_3), 110.4 (CH), 111.7 (CH), 120.4 (CH). 124.7 (C), 126.1 (C), 127.5 (CH), 127.7 (CH), 127.9 (CH), 130.9 (CH), 132.9 (CH), 138.4 (C), 139.7 (C), 145.1 (C), 157.4 (CO). MS (*m/z*, %): 316 [$(M+2)^+$, 14.8], 316 (M^+, 15.0), 237 [$(M-79.9)^+$, 9], 145 (100). Anal. Calcd for $C_{17}H_{15}BrO$, C: 64.78; H: 4.80; Br: 25.25. Found C: 64.92; H: 4.79; Br: 24.87.

1.1.17. 2-[3-(2-Bromophenyl)-2-oxopropyl]-4-methoxybenzaldehyde (5b). Ozonolysis of benzylindene **11b** (195 mg, 0.62 mmol) under the same conditions as for analogue **11a** gave the title compound as a white solid (131 mg, 61% yield). Mp 87–88 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1723, 1684 (CHO, C=O). ^1H NMR (δ, ppm): 3.75 (s, 3H, OCH_3), 4.00 (s, 2H, CH_2), 4. 01 (s, 2H, CH_2), 6.62 (δ, 1H, $J=2.3$ Hz, Ar–H), 6.83 (dd, 1H, $J=8.5$ Hz, $J'=2.3$ Hz, Ar–H), 7.16–7.24 (m, 3H, 3×Ar–H), 7.47 (δ, 1H, $J=7.9$ Hz, Ar–H), 7.61 (δ, 1H, $J=8.5$ Hz, Ar–H), 9.76 (s, 1H, CHO). ^{13}C NMR (δ, ppm): 47.3 (CH_2), 49.9 (CH_2), 55.4 (CH_3), 112.2 (CH), 118.8 (CH), 125.0 (C), 127.5 (CH), 128.6 (C), 128.7 (CH), 132.1 (CH), 132.6 (CH), 134.8 (C), 137.8 (CH), 138.2 (C), 163.5 (C=O), 191.7 (C=O), 203.2 (C=O). MS (*m/z*, %): 348 [$(M+2)^+$, 0.52], 316 (M^+, 0.60), 267 [$(M-79.9)^+$, 2], 177 (92), 149 (100), 91 (33). Anal. Calcd for $C_{17}H_{15}BrO_3$, C: 58.81; H: 4.35; Br: 23.01. Found C: 59.12; H: 4.31; Br: 22.79.

1.1.18. 3-(2-Bromophenyl)-7-methoxynaphthalen-2-ol (6b). Reaction of ketoaldehyde **5b** with NaOH under the same conditions as for analogue **5a** provided the title compound as a colourless solid (344 mg, 95% yield). Mp 145–147 °C (EtOH/H_2O). IR ($\bar{\nu}$, cm^{-1}, NaCl): 3425 (OH). ^1H NMR (δ, ppm): 3.77 (s, 3H, $-OCH_3$), 6.87–6.92 (m, 2H,

2×Ar–H), 7.10–7.17 (m, 2H, 2×Ar–H), 7.26 (s, 1H, Ar–H), 7.27 (s, 1H, Ar–H), 7.44 (s, 1H, Ar–H), 7.51–7.60 (m, 2H, 2×Ar–H). ^{13}C NMR (δ, ppm): 55.2 (CH_3), 104.4 (CH), 109.4 (CH), 116.7 (CH), 124.0 (C), 124.5 (C), 127.6 (C), 127.7 (CH), 129.3 (CH), 127.3 (CH), 129.7 (CH), 132.2 (CH), 133.0 (CH), 136.0 (C), 138.0 (C), 151.3 (C), 158.3 (C). MS (*m*/*z*, %): 330 [$(M+2)^+$, 99.96], 316 (M^+, 100), 250 (37), 234 (60), 206 (59), 178 (46), 175 (36). Anal. Calcd for $C_{17}H_{13}BrO_2$, C: 62.03; H: 3.98; Br: 24.27. Found C: 59.69; H: 3.91; Br: 24.62.

1.1.19. 8-Methoxybenzo[*b*]naphtho[2,3-*d*]furan (13b). Reaction of naphthol **6b** (55 mg, 0.17 mmol) under the conditions used for analogue **6a** gave the title compound as a white solid (32 mg, 77% yield). Mp 208–210 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1222 (C–O–C). ^{1}H NMR (δ, ppm): 3.96 (s, 3H, $-OCH_3$), 7.14 (dd, 1H, $J=9.0$ Hz, $J'=2.4$ Hz, Ar–H), 7.24 (δ, 1H, $J=5.5$ Hz, Ar–H), 7.34 (t, 1H, $J=$ 7.3 Hz, Ar–H), 7.43–7.56 (m, 2H, 2×Ar–H), 7.79 (s, 1H, Ar–H), 7.90 (δ, 1H, $J=9.0$ Hz, Ar–H), 8.01 (δ, 1H, $J=$ 7.6 Hz, Ar–H), 8.30 (s, 1H, Ar–H). ^{13}C NMR (δ, ppm): 55.3 (CH_3), 105.4 (CH), 105.8 (CH), 111.4 (CH), 117.7 (CH), 119.1 (CH), 120.9 (CH), 122.7 (CH), 123.0 (C), 124.2 (C), 125.8 (C), 127.7 (CH), 129.8 (CH), 134.5 (C), 155.6 (C), 157.3 (C), 157.8 (C). MS (*m*/*z*, %): 248 (M^+, 93), 233 (18), 205 (100), 176 (22), 149 (29). Anal. Calcd for $C_{17}H_{12}O_2$, C: 82.24; H: 4.87. Found C: 81.89; H: 4.96.

1.1.20. 8-Methoxybenzo[*b*]naphtho[2,3-*d*]furan-6,11-dione (3b). Oxidation of benzonaphthofuran **13b** (15 mg, 0.06 mmol) under the same conditions as for analogue **13a** yielded the title compound as a yellow solid (4 mg, 24% yield). Mp 254–256 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, NaCl): 1679 (C=O). ^{1}H NMR (δ, ppm): 4.00 (s, 3H, OCH_3), 7.23 (m, 1H, Ar–H), 7.50–7.61 (m, 2H, 2×Ar–H), 7.68–7.71 (m, 2H, 2×Ar–H), 8.18 (d, 1H, $J=8.6$ Hz, Ar–H), 8.32 (d, 1H, $J=$ 7.5 Hz, Ar–H). ^{13}C NMR (δ, ppm): 56.0 (OCH_3), 111.0 (CH), 112.8 (CH), 119.9 (CH), 122.9 (C), 124.1 (CH), 124.4 (C), 126.0 (CH), 126.6 (C), 129.2 (CH), 129.6 (CH), 134.5 (C), 153.4 (C), 156.5 (C), 164.2 (C), 175.5 (C=O), 180.0 (C=O). MS (*m*/*z*, %): 278 (M^+, 13), 149 (56), 85 (37), 83 (38), 71 (50), 69 (37), 58 (100), 57 (70). Anal. Calcd for $C_{17}H_{10}O_4$, C: 73.38; H: 3.62. Found C: 73.51; H: 3.54.

1.1.21. 2-(2-Methoxycarbonylbenzyl)-1-oxoindan-2-carboxylic acid ethyl ester (15b). Treatment of indanone **14a** (4.602 g, 22.5 mmol) with *o*-methoxycarbonylbenzyl bromide under the same conditions as for analogue **14b** furnished the title compound as a white solid (650 mg, 52% yield). Mp 88–90 °C (MeOH). IR (,cm^{-1}, KBr): 1716 (3× C=O). ^{1}H NMR (δ, ppm, $CDCl_3$): 1.18 (t, $J=7$ Hz, 3H, CH_3), 3.05 (d, $J=17.5$ Hz, 1H, C*H*H), 3.58–3.70 (m, 2H, CH_2), 3.82 (s, 3H, OMe), 4.05 (d, $J=14$ Hz, 1H, C*H*H), 4.16 (q, $J=7$ Hz, 2H, CH_2O), 7.16–7.34 (m, 5H, ArH), 7.48–7.53 (m, 1H, ArH), 7.72–7.81 (m, 2H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 13.9 (CH_3), 35.6 (CH_2), 35.8 (CH_2), 52.0 (Me), 61.8 (C), 124.5 (CH), 126.1 (CH), 126.7 (CH), 127.4 (CH), 130.5 (CH), 131.1 (C), 131.4 (CH), 131.7 (CH), 135.1 (CH), 138.1 (C), 153.7 (C), 168.1 (C=O), 170.9 (C=O), 202.6 (C=O). MS (*m*/*z*, %, CI): 353 ($M^+ +1$, 48), 321 (100), 307 (58), 275 (69), 205 (68). Anal. Calcd for $C_{21}H_{20}O_5$, C: 71.58; H: 5.72. Found C: 71.96; H: 5.59.

1.1.22. 2,2′-Spirobiindanone (16a). A mixture of indanone **15b** (2.67 g, 7.58 mmol), 96% AcOH (5.5 mL) and 48% HBr (5 mL) was refluxed for 3.25 h. The cooled reaction mixture was diluted with water (40 mL) and the resulting suspension was extracted with diethyl ether (3×30 mL). The combined organic extracts were dried and concentrated in vacuo. Crystallisation of the solid residue from MeOH yielded the title compound as white crystals (1.731 g, 92% yield). Mp 171–173 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, KBr): 1694 (C=O), 1720 (C=O). ^{1}H NMR (δ, ppm, $CDCl_3$): 3.20 (d, $J=17$ Hz, 2H, $-CH_2$), 3.73 (d, $J=17$ Hz, 2H, $-CH_2$), 7.39–7.45 (m, 2H, ArH), 7.55–7.78 (m, 6H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 38.0 (CH_2), 65.3 (C), 124.9 (CH), 126.3 (CH), 127.8 (CH), 135.2 (CH), 135.4 (C), 153.8 (C), 202.7 (C=O). MS (*m*/*z*, %): 248 (M^+, 100), 220 (47), 191 (33). Anal. Calcd for $C_{17}H_{12}O_2$, C: 82.24; H: 4.87. Found C: 81.93; H: 4.79.

1.1.23. 2-(1-Oxoindan-2-ylmethyl)benzoic acid (10e). A stirred suspension of diindanone **16a** (1.731 mg, 6.97 mmol) and 1 M NaOH (1.25 mL) in EtOH (40 mL) was refluxed during 5 h. The ethanol was removed in vacuo and the remaining suspension was acidified by addition of 0.625 M HCl. The mixture was extracted with $CHCl_3$ (3× 75 mL) and the combined organic extracts were dried and concentrated in vacuo. Crystallisation of the solid residue from benzene provided the title compound as a white solid (1.632 mg, 88% yield). Mp 141–143 °C (benzene). IR ($\bar{\nu}$, cm^{-1}, KBr): 1688 (C=O), 1706 (C=O), 2906 (C–OH). ^{1}H NMR (δ, ppm, $CDCl_3$): 2.89 (d, $J=13.6$ Hz, 1H, C*H*H), 3.10–3.24 (m, 3H, C*H*H and CH_2), 3.77–3.87 (m, 1H, CH), 7.30–7.58 (m, 6H, Ar–H), 7.77 (d, 1H, Ar–H), 8.07–8.10 (m, 1H, ArH), 10.70 (br s, 1H, –OH). ^{13}C NMR (δ, ppm, $CDCl_3$): 32.3 (CH_2), 34.9 (CH_2), 48.6 (CH), 123.9 (CH), 126.4 (CH), 126.5 (CH), 127.3 (CH), 128.7 (C), 131.6 (CH), 131.8 (CH), 132.8 (CH), 134.7 (CH), 136.4 (C), 142.5 (C), 153.5 (C), 172.6 (C=O), 208.1 (C=O). MS (*m*/*z*, %): 266 (M^+, 46), 248 (100), 220 (49), 131 (63). Anal. Calcd for $C_{17}H_{14}O_3$, C: 76.68; H: 5.30. Found C: 77.03; H: 5.19.

1.1.24. 2-(1*H*-Inden-2-ylmethyl)benzoic acid (11c). Reaction of indanone **10e** (1.601 g, 6.01 mmol) under the same conditions as for analogue **10a** provided the title compound as a white solid (1.281 g, 85% yield). Mp 143–145 °C (ethyl acetate/hexane). IR ($\bar{\nu}$, cm^{-1}, KBr): 1687 (C=O), 2881 (C–OH). ^{1}H NMR (δ, ppm, $CDCl_3$): 3.34 (s, 2H, CH_2), 4.28 (s, 2H, CH_2), 6.37 (s, 1H, CH), 7.07–7.54 (m, 7H, ArH), 8.07–8.10 (m, 1H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 35.8 (CH_2), 41.2 (CH_2), 120.2 (CH), 123.4 (CH), 123.8 (CH), 126.2 (CH), 126.5 (CH), 127.7 (CH), 128.3 (C), 131.7 (CH), 131.8 (CH), 133.0 (CH), 142.6 (C), 143.3 (C), 145.3 (C), 149.4 (C), 172.7 (C=O). MS (*m*/*z*, %): 250 (M^+, 60), 232 (100), 202 (63), 115 (66). Anal. Calcd for $C_{17}H_{14}O_2$, C: 81.58; H: 5.64. Found C: 81.72; H: 5.57.

1.1.25. 2-[3-(2-Formylphenyl)-2-oxopropyl]benzoic acid (5c). Indene **10e** (100 mg, 0.40 mmol) was subjected to the ozonolysis conditions used for the transformation of analogue **10a** and the title compound was obtained as a white solid (50 mg, 44% yield). Mp 143–145 °C (ethyl acetate/hexane). IR ($\bar{\nu}$, cm^{-1}, KBr): ^{1}H NMR (δ, ppm, DMSO): 3.40 (s, 2H, CH_2), 3.47 (s, 2H, $-CH_2$), 6.27–6.78 (m, 7H, ArH), 6.94–7.05 (m, 1H, ArH), 9.13 (s, 1H, –CHO), 12.06 (br s, 1H, $-CO_2H$). ^{13}C NMR (δ, ppm, $CDCl_3$): 37.9

(CH_2), 38.5 (CH_2), 127.5 (CH), 127.8 (CH), 128.1 (CH), 128.7 (CH), 128.8 (CH), 129.2 (C), 129.4 (CH), 134.2 (CH), 134.8 (CH), 136.6 (C), 136.9 (C), 137.7 (C), 165.0 (C=O), 194.0 (C=O), 205.0 (C=O). HRMS: $C_{17}H_{14}O_4$, (M^{+}), calcd 282.0892; found 282.0888.

1.1.26. 6-Oxabenzo[*a*]anthracen-5-one (17a). Ketoaldehyde **5c** (88 mg, 0.31 mmol) was reacted with NaOH in the same way as analogue **5a** to give the title compound as a white solid (43 mg, 56% yield). Mp 190–192 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, KBr): 1725 (C=O). ^1H NMR (δ, ppm, $CDCl_3$): 7.42–7.89 (m, 7H, ArH), 8.20 (d, $J=8$ Hz, 1H, ArH), 8.33–8.42 (m, 2H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 113.5 (CH), 118.0 (C), 121.4 (C), 121.9 (CH), 122.4 (CH), 125.7 (CH), 127.2 (CH), 127.5 (CH), 128.2 (CH), 128.9 (CH), 130.1 (C), 130.6 (CH), 133.9 (C), 134.5 (C), 134.7 (CH), 148.7 (C), 160.9 (C=O). MS (*m*/*z*, %): 246 (M^{+}, 100), 218 (32), 189 (48). Anal. Calcd for $C_{17}H_{10}O_2$, C: 82.91; H: 4.09. Found C: 83.24; H: 3.97.

1.1.27. 6-Oxabenzo[*a*]anthracene-5,7,12-trione (4). Oxidation of dibenzochromanone **17a** (35 mg, 0.13 mmol) under the same conditions as for benzonaphthofuran **13a** gave the title compound as a yellow solid (16 mg, 41% yield). Mp 251–253 °C (MeOH/acetone/CH_2Cl_2). IR ($\bar{\nu}$, cm^{-1}, KBr): 1755 (C=O), 1679 (C=O). ^1H NMR (δ, ppm, TFA): 7.78–8.05 (m, 4H, ArH), 8.23 (t, $J=7.5$ Hz, 2H, ArH), 8.47 (d, $J=8$ Hz, 1H, ArH), 9.27 (d, $J=8.5$ Hz, 1H, ArH). ^{13}C NMR (δ, ppm, TFA): 118.0 (C), 121.3 (C), 126.7 (CH), 126.9 (CH), 128.3 (CH), 128.3 (C), 129.1 (C), 129.9 (CH), 131.1 (C), 131.8 (CH), 134.4 (CH), 135.8 (CH), 136.7 (CH), 149.5 (C), 161.7 (C=O), 178.8 (C=O), 184.1 (C=O). MS (*m*/*z*, %): 276 (M^{+}, 13), 248 (100), 220 (20), 163 (43). Anal. Calcd for $C_{17}H_8O_4$, C: 73.91; H: 2.82. Found C: 74.36; H: 2.77.

1.1.28. 5-Methoxy-2-(2-methoxycarbonylbenzyl)-1-oxoindan-2-carboxylic acid ethyl ester (15e). Reaction of 2-ethoxycarbonylindanone **14b** (1.159 g, 3.16 mmol) with *o*-methoxycarbonylbenzyl bromide under the same conditions as for analogue **14a** furnished the title compound as an oil (1.323 g, 73% yield). IR ($\bar{\nu}$, cm^{-1}, KBr): 1735 (C=O), 1717 (C=O). ^1H NMR (δ, ppm, $CDCl_3$): 1.19 (t, $J=7.0$ Hz, 3H, $-CH_3$), 3.56 (d, $J=17.5$ Hz, 1H, –C*H*H), 3.65 (d, $J=14.0$ Hz, 1H, –C*H*H), –), 3.81 (s, 3H, OMe), 3.83 (s, 3H, OMe), 3.87 (s, 1H, –C*H*H), 4.03 (d, $J=14.0$ Hz, 1H, –C*H*H), 4.16 (q, $J=7.0$ Hz, 2H, $-CH_2O$), 6.73 (d, $J=2.0$ Hz, 1H, ArH), 6.84 (m, 1H, ArH), 7.16–7.27 (m, 3H, ArH), 7.66 (d, $J=8.5$ Hz, 1H, ArH), 7.79 (m, 1H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 35.4 (CH_2), 35.7 (CH_2), 52.0 (CH_3), 55.5 (CH_3), 61.7 (CH_2), 61.9 (C), 109.0 (CH), 115.5 (CH), 126.0 (CH), 126.4 (CH), 128.1 (C), 130.3 (CH), 130.9 (CH), 131.2 (CH), 131.5 (C), 138.1 (C), 156.7 (C), 165.4 (C), 167.9 (C), 170.9 (C), 200.3 (C=O). HRMS: $C_{22}H_{22}O_6$ ($M^{+}+1$), calcd 383.1416; found 383.1419.

1.1.29. 5-Methoxy-2,2′-spirobiindanone (16b). A mixture of benzylindanone **15d** (1.393 g, 3.80 mmol) in 96% AcOH (5.5 mL) and 48% HBr (2.9 mL) was subjected to the same reaction conditions as for analogue **15b**. The title compound was obtained as a white solid (531 mg, 53% yield). Mp 176–78 °C (MeOH). IR ($\bar{\nu}$, cm^{-1}, KBr): 1709 (C=O), 1690 (C=O). ^1H NMR (δ, ppm, $CDCl_3$): 3.10–3.20 (m, 2H, CH_2), 3.63–3.75 (m, 2H, CH_2), 3.91 (s, 3H, OMe), 6.93–6.98 (m, 2H, ArH), 7.40 (t, $J=7.5$ Hz, 1H, ArH), 7.54–7.77 (m, 4H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 38.0 (CH_2), 38.1 (CH_2), 55.7 (CH_3), 65.4 (C), 109.4 (CH), 115.9 (CH), 124.7 (CH), 126.2 (CH), 126.4 (CH), 127.6 (CH), 128.4 (C), 135.1 (CH), 135.4 (C), 153.7 (C), 156.7 (C), 165.6 (C), 200.4 (C=O), 202.9 (C=O). MS (*m*/*z*, %): 278 (M^{+}, 100), 250 (52), 178 (28). Anal. Calcd for $C_{18}H_{14}O_3$, C: 77.68; H: 5.07. Found C: 77.84; H: 5.02.

1.1.30. 2-(5-Methoxy-1-oxoindan-2-ylmethyl)benzoic acid and 4-methoxy-2-(1-oxoindan-2-ylmethyl)benzoic acid (10f–10g). Reaction of spiroindanone **16b** (451 mg, 1.72 mmol) under the same conditions as for analogue **16a** provided a solid reaction mixture. Purification by flash column chromatography (eluant: CH_2Cl_2/MeOH, 98.5/1.5) led to the isolation of small fractions of ketoacid **10f** (71 mg, 30% yield) and ketoacid **10g** (29 mg, 12% yield) as white solids.

1.1.31. Ketoacid a. Mp 150–152 °C (benzene/CH_2Cl_2). IR ($\bar{\nu}$, cm^{-1}, KBr): 3434 (OH), 1709 (C=O), 1679 (C=O). ^1H NMR (δ, ppm, $CDCl_3$): 2.90 (d, $J=13.5$ Hz, 1H, C*H*H), 3.16–3.23 (m, 3H, C*H*H and CH_2), 3.77–3.85 (m, 4H, CH and OMe), 6.80–6.87 (m, 2H, ArH), 7.32–7.41 (m, 2H, ArH), 7.52–7.57 (m, 1H, ArH), 7.77 (d, $J=7.5$ Hz, 1H, ArH), 8.11 (d, $J=9.0$ Hz, 1H, ArH) ^{13}C NMR (δ, ppm, $CDCl_3$): 32.3 (CH_2), 35.1 (CH_2), 48.6 (CH), 55.4 (CH_3), 111.7 (CH), 117.1 (CH), 120.6 (C), 123.9 (CH), 126.5 (CH), 127, (CH), 134.5 (CH), 134.7 (CH), 136.6 (C), 139.3 (C), 145.7 (C), 153.6 (C), 163.1 (C=O), 207.9 (C=O). MS (*m*/*z*, %): 296 (M^{+}, 25), 278 (100), 250 (46). Anal. Calcd for $C_{18}H_{16}O$, C: 72.96; H: 5.44. Found C: 73.15; H: 5.37.

1.1.32. Ketoacid b. Mp 143–145 °C (benzene/CH_2Cl_2). IR ($\bar{\nu}$, cm^{-1}, KBr): 1257 (C–OMe), 1703 (C=O ketone and C=O acid); 3430 (C–OH). ^1H NMR (δ, ppm, $CDCl_3$): 2.84 (d, $J=14.5$ Hz, 1H, –C*H*H), 3.06–3.17 (m, 3H, C*H*H and CH_2), 3.77–3.84 (m, 4H, CH and OMe), 6.83–6.90 (m, 2H, ArH), 7.29–7.38 (m, 2H, ArH), 7.46–7.52 (m, 1H, ArH), 7.71 (d, $J=8.5$ Hz, 1H, ArH), 8.05–8.08 (m, 1H, ArH). ^{13}C NMR (δ, ppm, $CDCl_3$): 32.3 (CH_2), 35.0 (CH_2), 48.8 (CH), 55.6 (CH_3), 109.6 (CH), 115.4 (CH), 125.7 (CH), 126.5 (CH), 129.7 (C), 131.6 (CH), 131.8 (CH), 132.8 (CH), 140.5 (C), 142.5 (C), 148.0 (C), 156.5 (C), 165.4 (C=O), 206.3 (C=O). MS (*m*/*z*, %): 296 (M^{+}, 74), 278 (57), 250 (29), 161 (100). Anal. Calcd for $C_{18}H_{16}O$, C: 72.96; H: 5.44. Found C: 72.69; H: 5.48.

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