Synthetic Studies on the C/D Ring Segment of Limonoids

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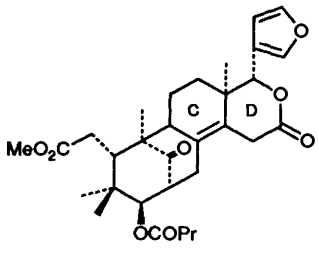
The diketone **3** has been synthesized from 4,7a-dimethyl-2,3,6,7-tetrahydroindene-1,5-dione **4**. The furyl alcohol **7** has been dehydrated to give the cyclopentene **9** and the resulting epoxide **10** and the diol **11** have been converted into the diketone **3**. Attempted Baeyer–Villiger oxidation of the dione **3** failed to give the expected lactone **2**.

In recent years, much effort has been devoted to finding new pest-control agents which are powerful, selective and biodegradable. Of particular importance in this connection, are natural substances, *e.g.* limonoids (tetranortriterpenoids) which have emerged as being promising insecticides.[1] In our studies we have focused attention on the active principles contained in the seeds of the African mahogany *Khaya ivorensis* (Meliaceae), which have been shown to be insect resistant. Thus, we recently isolated the novel limonoid **1**, which exhibited interesting antifeedant activity against Lepidopteran species.[2] Despite their growing biological interest, there are few approaches to the total synthesis of limonoids.[3] We were, therefore, interested in developing a new synthetic strategy towards the bicyclic model molecule **2**, which contained the CD furan moiety of the limonoid **1**, known to be of importance for insecticide activity.[4] It seemed likely that this compound would be useful in probing structure–activity relationships, while also having the required functionalities to provide further access to natural limonoids such as **1**.



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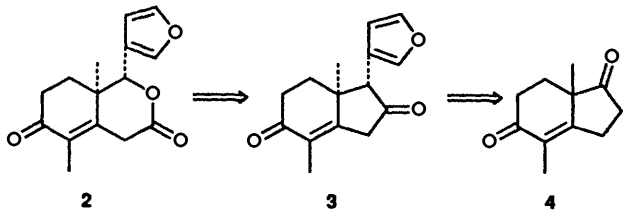
A synthesis of the target molecule needed to: (i) construct the bicyclic skeleton, (ii) introduce the β-furyl substituent and (iii) form the β-lactone moiety. Our strategy, see Scheme 1, was



2 **3** **4**

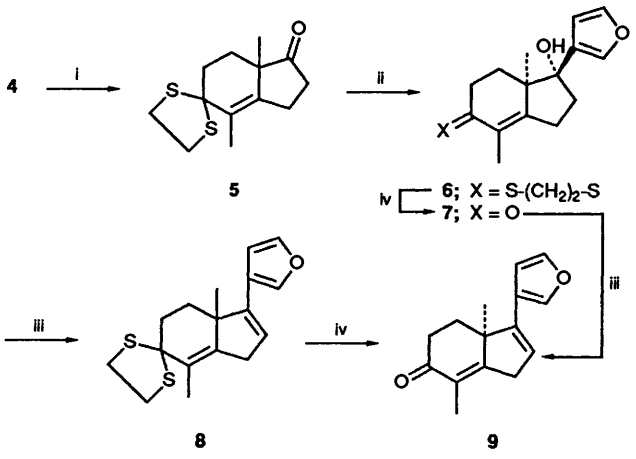
Scheme 1

based on Baeyer–Villiger oxidation of the key β-furyl cyclopentanone **3** which, in turn, derived from the bicyclic enedione **4**. An advantage of this approach was the availability of the dione **4** in optically pure form,[5] thus paving the way to a subsequent asymmetric synthesis.

For the racemic synthesis, the starting tetrahydroindenedione **4** was obtained (85%) by a Robinson annelation between 1-chloropentan-3-one and 2-methylcyclopentane-1,3-dione in water as previously described.[6] Initial reaction of the diketone **4** in the presence of 3-furyllithium gave a complex mixture containing a predominance of unchanged starting material. Transmetallation of the reagent (with magnesium or titanium) resulted only in poorer reactivity, little reaction being observed. Thus, since efficient introduction of the furyl group required selective protection of the unsaturated ketone, it was treated with a slight excess of ethane-1,2-dithiol in the presence of boron trifluoride–diethyl ether to give the thioacetal **5** (90%). Subsequent reaction of the latter with 3-furyllithium in THF at −78 °C gave the alcohol **6** as a single isomer (60%). Since *ca.* 20% of unchanged starting material was recovered after chromatography, we substituted the organolithium reagent for a dichlorocerate but without any noticeable improvement. The stereochemistry of the furyl alcohol **6** was assigned on the basis of nuclear Overhauser effect (NOE) experiments: the absence of a NOE on the furyl protons upon irradiation of the angular methyl group (and reciprocally), was in favour of a *trans* relationship between these two substituents. Selective formation of this diastereoisomer occurs, presumably, because of preferential attack of the organometallic reagent from the sterically less hindered β-face of the starting ketone, as previously observed in steroids.[9]

Several paths to the cyclopentanone **3**, *via* a common cyclopentene intermediate **8**, were considered, the first being a hydroboration–oxidation process. The alcohol **6** dehydrated in the presence of toluene-*p*-sulfonic acid in benzene gave only a complex mixture but with mesyl chloride in the presence of an excess of triethylamine[10] provided a mesylate which underwent *in situ* elimination to afford directly the alkene **8** (75%). Since attempted hydroboration of the latter in the presence of 9-BBN, thexylborane and borane was ineffective, starting material being recovered unchanged, we adopted a second approach involving rearrangement of an epoxide under acidic conditions. At this stage, the regioselective epoxidation of the cyclopentene moiety required the deprotection of the unsaturated oxo group of compound **8**. Conventional methods for the hydrolysis of thioacetals led to disappointing results: CAN,[11] Meerwein salt,[12] and SiO_2–$CuSO_3$[13] gave no reaction. Use of MeI–$CaCO_3$ in acetonitrile,[14] $PhI(CF_3CO_2)_2$,[15] and CuO–$CuCl_2$[16] gave complex mixtures whilst $HgO{\cdot}BF_3$,[17] $NCS{\cdot}AgNO_3$[18] and $Tl(NO_3)_3$, $3H_2O$[19] afforded only poor yields of the expected product. Since the poor stability of the resulting alkene in the reaction conditions (in particular in acidic medium) was thought to be responsible for these results, we carried out the deprotection step on the alcohol **6**. Upon treatment with thallium(III) nitrate, the latter compound gave the ketone **7** (91%) and this upon subsequent dehydration under conditions similar to those used for the alcohol **6** afforded the alkene **9** (86%) (Scheme 2).

The cyclopentene **9** was next epoxidized stereoselectively



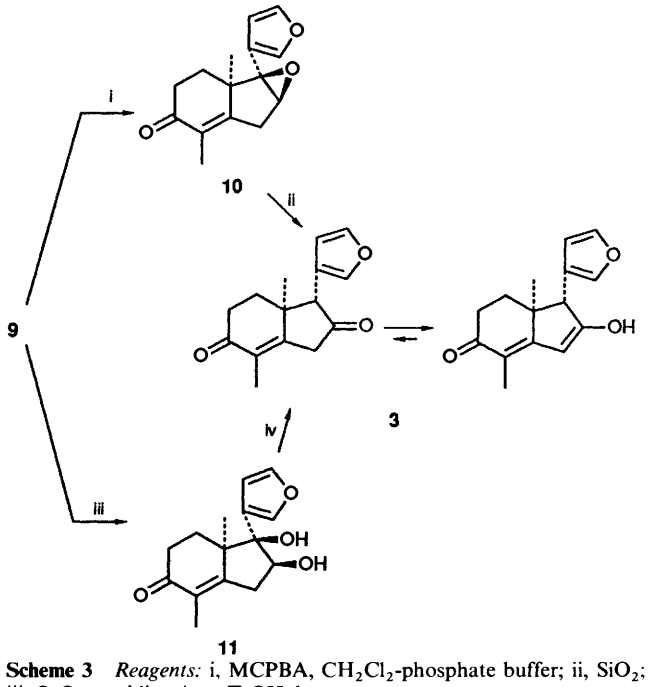
Scheme 2 *Reagents:* i, $HS(CH_2)_2SH$, $BF_3{\cdot}Et_2O$, MeOH; ii, 3-furyl lithium, THF; iii, MsCl, NEt_3, CH_2Cl_2; iv, $Tl(NO_3)_3{\cdot}3H_2O$, MeOH.

with *m*-chloroperbenzoic acid in a buffered two-phase system[20] to give the epoxide **10** quantitatively according to gas chromatography. A β configuration was tentatively assigned to the epoxy group on the basis of steric considerations, attack of the reagent from the α-side being hindered by the angular methyl group. This compound was particularly acid sensitive, chromatography on silica gel usually affording the expected product (40%). Moreover, in one instance, only the rearranged cyclopentanone **3** was isolated (15%). On the other hand, treatment of the epoxide **10** in the presence of Lewis acids such as $BF_3{\cdot}Et_2O$,[21] gave rise to an inseparable mixture of rearranged diones **3** together with, probably, its epimer (30% overall yield). According to gas chromatography, these compounds were obtained in variable ratios depending upon the reaction conditions.

We then considered preparation of the cyclopentanone **3** by a pinacolic rearrangement of the diol **11**. The latter was obtained by oxidation of the alkene **9** with OsO_4 in pyridine[22] as a single diastereoisomer (56%). Oxidation with OsO_4–NMO[23] resulted in a lower yield of product (44%), coupling of the starting alkene at the C-3 position, giving a mixture of diastereoisomeric dimers. Once again, we assumed that the attack of the reagent occurred from the β less hindered face of the starting molecule.

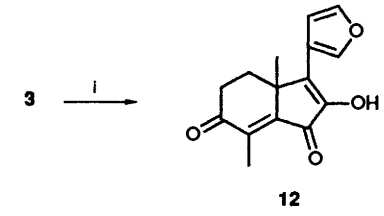
Consistent with this assignment were the observed ^1H chemical shifts at δ 1.3 and 1.0 for the angular 7a-methyl groups for compounds **7** and **11** respectively. These figures reflected the different relative disposition of the furan ring and the methyl group in each compound, a diamagnetic shielding effect arising from a *cis* configuration for the two substituents as previously observed in a similar series.[24] The diol **11** was then treated with toluene-*p*-sulfonic acid in refluxing benzene to induce a pinacolic rearrangement,[25] and give the desired diketone **3** (60%) (Scheme 3). This compound, poorly soluble in common solvents, was mostly enolised (as revealed by its NMR spectra in deuteriated DMSO) as a result of an extended conjugated system being formed with the α,β-unsaturated carbonyl group. Its *cis* stereochemistry was deduced from NOE experiments in $CDCl_3$ on a non-enolised soluble part, irradiation of the angular methyl group of dione **3** resulting in a NOE of the β′-H and α-H signals of the furan ring.

Having the requisite key cyclopentanone available, we then turned our attention to the final Baeyer–Villiger oxidation. Treatment of cyclopentanone **3** with anhydrous MCPBA in the presence of sodium hydrogen carbonate[24] in dichloromethane was ineffective, several days of reaction resulting only in slow degradation of the starting material. In order to overcome this problem, which is ascribable to a total enolisation of the system, we attempted to epoxidise the central double bond with



Scheme 3 *Reagents:* i, MCPBA, CH_2Cl_2-phosphate buffer; ii, SiO_2; iii, OsO_4, pyridine; iv, *p*-TsOH, benzene.

hydrogen peroxide in a basic medium. Under these conditions, we obtained none of the expected product, isolating instead the enolised triketone **12** (28%) resulting from the oxidation of the C-3 activated methylene of the cyclopentanone; such behaviour has been observed for α,β-unsaturated ketosteroids upon treatment with sodium peroxide[26] (Scheme 4).



Scheme 4 *Reagents:* H_2O_2, NaOH.

The last step of our strategy failed to give the target bicyclic lactone **2**, the presence of the α,β-unsaturated ketone, although essential for the subsequent extension to the total synthesis of limonoids such as **1**, inhibiting the expected reactivity of diketone **3**. However, our approach which is relatively short, stereocontrolled and amenable to an asymmetric synthesis, is still promising and its application to other limonoid models is under progress in our laboratory.

Experimental

M.p.s were determined with a Buchi 535 apparatus and are uncorrected. IR spectra were recorded with a Philips PU 9706 apparatus. ^1H and ^{13}C NMR spectra were obtained from Bruker AC 200 and WM 500 spectrometers. *J*-Values are given in Hz. Mass spectral data were determined on a ZAB HSQ VG spectrometer. Microanalyses were performed at the microanalysis laboratory, Université P. et M. Curie. Column chromatography was performed on Merck Kieselgel silica gel (230–400 mesh). THF was distilled from sodium–benzophenone before use. Dichloromethane was distilled over phosphorus pentaoxide. Reactions requiring anhydrous conditions were carried out under an atmosphere of nitrogen in an oven-dried flask. Extracts were dried over sodium sulfate prior to

evaporation of solvents under reduced pressure using a rotary evaporator.

4,7a-*Dimethyl*-2,3,6,7-*tetrahydroindene*-1,5-*dione* **4**.—This compound was prepared from 2-methylcyclopentane-1,3-dione and 1-chloropentan-3-one as previously described[6] (85%); b.p. 125 °C at 1 mmHg; δ_C(50 MHz, $CDCl_3$) 10.7 (q), 21.9 (q), 24.4 (t), 28.7 (t), 32.7 (t), 35.4 (t), 48.8 (s), 129.7 (s), 162.3 (s), 198.8 (s) and 217.6(s).

5,5-(1,2-*Ethylenedithio*)-4,7a-*dimethyl*-2,3,6,7-*tetrahydroinden*-1-*one* **5**.—To an ice-cooled solution of the diketone **4** (5 g, 28 mmol) in absolute methanol (125 cm^3) were successively added ethane-1,2-dithiol (2.6 cm^3, 31 mmol) and BF_3·Et_2O (3.8 cm^3, 31 mmol). The reaction mixture was stirred at room temperature for 3 days after which the solvent was evaporated and the solid residue dissolved in ethyl acetate (200 cm^3). The organic layer was washed with 5% aqueous sodium hydrogen carbonate (50 cm^3) and water (50 cm^3) and evaporated to leave a yellow solid, which was recrystallized from methanol to afford compound **5** (6.5 g, 90%), m.p. 96.5–97.5 °C (Found: C, 61.3; H, 7.2. $C_{13}H_{18}S_2O$ requires C, 61.4; H, 7.15%); ν_{max}/cm^{-1} 1745 (CO); δ_H(200 MHz, $CDCl_3$) 1.15 (3 H, s, 9-Me), 1.93 (3 H, s, 8-Me), 1.58–1.68 (2 H, m), 2.15–2.40 (3 H, m), 2.45–2.80 (3 H, m) and 3.10–3.52 (4 H, m, CH_2S); δ_C(50 MHz, $CDCl_3$) 15.4 (q), 22.5 (q), 24.2 (t), 28.8 (t), 39.5 (t), 40.0 (t), 40.4 (t), 41.7 (t), 48.2 (s), 70.6(s), 128.6(s), 139.7(s) and 219.3(s).

(1R*,7aR*)-5,5-(1,2-*Ethylenedithio*)-1-(3-*furyl*)-4,7a-*dimethyl*-2,3,6,7-*tetrahydroinden*-1-*ol* **6**.—A solution of 3-bromofuran (3.5 cm^3, 38.9 mmol) in anhydrous THF (30 cm^3) was added dropwise to a 2.5 mol dm^{-3} solution of BuLi in hexanes (17.2 cm^3, 43 mmol) at −78 °C and the mixture stirred at this temperature for 1 h. The ketone **5** (8 g, 31.5 mmol) dissolved in THF (30 cm^3) was then added dropwise over 30 min and the resulting mixture was kept at −78 °C for a further 30 min and finally overnight at room temperature. The solution was poured in water (100 cm^3) and then extracted with chloroform. The combined organic layers were washed with water and concentrated to leave a brown oil. Chromatography on silica gel [ethyl acetate–hexane (15:85)] gave the unchanged ketone **5** (1.8 g, 22%) and the expected alcohol **6** (6.1 g, 60%), m.p. 103 °C (from ethyl acetate–hexane); ν_{max}/cm^{-1} 3240 (OH); δ_H(500 MHz, $CDCl_3$) 1.20 (3 H, s, 9-Me), 1.38 (1 H, dt, *J* d, 14 and *J* t, 3.5), 1.51 (1 H, td, *J* t, 3.5 and *J* d, 14), 1.80 (1 H, br s, OH), 1.86 (3 H, s, 8-Me), 2.05 (1 H, m), 2.16–2.25 (2 H, m), 2.30–2.39 (2 H, m), 2.45–2.54 (1 H, m), 3.08–3.15 (1 H, m), 3.25–3.34 (2 H, m), 3.37–3.42 (1 H, m), 6.07 (1 H, dd, *J* 0.8 and 1.7, β′-H), 7.23 (1 H, dd, *J* 0.8 and 1.65, α-H) and 7.35 (1 H, t, *J* 1.75, α′-H); δ_C(50 MHz, $CDCl_3$), 15.5 (q), 20.8 (q), 26.0 (t), 29.6 (t), 37.7 (t), 39.8 (t), 40.8 (t), 41.3 (t), 47.5 (s), 70.8 (s), 82.3 (s), 109.1 (d), 127.6 (s), 131.3 (s), 138.1 (d), 142.7 (d) and 143.1 (s); *m/z* (EI) 322 (M^+, 10%) and 28 (100%) (Found: M^+, 322.0969. $C_{17}H_{22}O_2S_2$ requires *M*, 322.0977).

(1R*,7aR*)-1-(3-*Furyl*)-1-*hydroxy*-4,7a-*dimethyl*-2,3,6,7-*tetrahydroinden*-5-*one* **7**.—To an ice-cooled solution of the alcohol **6** (10 g, 31 mmol) in anhydrous THF (55 cm^3) was rapidly added a solution of $Tl(NO_3)_3$·$3H_2O$ (15.2 g, 34 mmol) in methanol (250 cm^3). After being stirred at 0 °C for 30 min, the reaction mixture was filtered off on a Celite pad and the filtrate was evaporated under reduced pressure. The residue was dissolved in water and extracted with chloroform. The combined extracts were washed with water and evaporated to leave a solid residue. Chromatography of this on silica gel [ethyl acetate–cyclohexane (1:1)] afforded compound **7** (6.72 g, 91%), m.p. 151.5 °C (from ethyl acetate) (Found: C, 72.75; H, 7.5. $C_{15}H_{18}O_3$ requires C, 73.15; H, 7.4); ν_{max}/cm^{-1} 1660 (conj. CO) and 3420 (OH); δ_H(200 MHz, $CDCl_3$) 1.3 (3 H, s, 9-Me), 1.65 (3 H, s, 8-Me), 1.60–1.80 (2 H, m), 2–2.90 (7 H, m), 6.10 (1 H, m, β′-H), 7.25 (1 H, m), 7.30 (1 H, m); δ_C(50 MHz, $CDCl_3$) 10.8 (q), 19.2 (q), 27.1 (t), 29.7 (t), 33.0 (t), 37.6 (t), 49.1 (s), 82.1 (s), 109.0 (d), 129.4 (s), 130.8 (s), 138.4 (d), 143.2 (d), 167.8 (s) and 198.5 (s).

1-(3-*Furyl*)-4,7a-*dimethyl*-6,7-*dihydro*-3H-*inden*-5-*one* **9**.—To an ice-cooled mixture of the alcohol **7** (5 g, 20.3 mmol) and triethylamine (10 cm^3, 71.7 mmol) in anhydrous dichloromethane (100 cm^3), was added dropwise mesyl chloride (4.25 cm^3, 54.9 mmol). The reaction mixture was stirred for 2 h at 0 °C and then for an additional 2 h at room temperature. The reddish solution was then diluted with further dichloromethane and washed successively with water (100 cm^3), 10% hydrochloric acid solution (100 cm^3), saturated aqueous sodium hydrogen carbonate (100 cm^3) and water (100 cm^3). Evaporation of the solvent left a brown oil which was chromatographed on silica gel [ethyl acetate–hexane (1:3)] to yield the expected alkene **9** as a light yellow oil (4 g, 86%); ν_{max}/cm^{-1} 1660 (conj. CO); δ_H(200 MHz, $CDCl_3$) 1.34 (3 H, s, Me), 1.70 (3 H, s, Me), 1.80–2.14 (1 H, m), 2.14–2.77 (3 H, m), 3.10–3.40 (2 H, m), 5.83 (1 H, t, *J* 2.2), 6.50 (1 H, m, β′-H), 7.38 (1 H, m) and 7.46 (1 H, m); δ_C(50 MHz, $CDCl_3$) 11.4 (q), 22.6 (q), 32.9 (t), 33.6 (t), 35.4 (t), 46.4 (s), 109.4 (d), 120 (s), 121.5 (d), 126.8 (s), 136.1 (d), 142.4 (s), 142.9 (d), 166.6 (s) and 197.9 (s); *m/z* (EI) 228 (M^+, 100%) and 213 (98%) (Found: M^+, 228.1151. $C_{15}H_{16}O_2$ requires *M*, 228.1150).

1,2-*Epoxy*-1-(3-*furyl*)-4,7a-*dimethyl*-2,3,6,7-*tetrahydroinden*-5-*one* **10**.—To a stirred solution of the alkene **9** (1.4 g, 6.14 mmol) in dichloromethane–phosphate buffer (100 cm^3; 1:1) [the buffer (pH 8.2) was prepared by adding 3.7 cm^3 of aqueous 0.1 mol dm^{-3} NaH_2PO_4 to 96.3 cm^3 of 0.1 mol dm^{-3} Na_2HPO_4], was added MCPBA (70–75% purity; 1.5 g) in small portions at 0 °C. After the mixture had been stirred for 2 h at 0 °C, a second portion of MCPBA (1.5 g) was added to it. The solution was stirred for an additional 2 h after which the organic layer was separated, washed with saturated aqueous sodium thiosulfate, 5% aqueous sodium hydrogen carbonate and water and evaporated to give the crude epoxide as an orange oil (1.6 g) in quantitative yield. This was pure enough to allow further reaction. Chromatography on silica gel [ethyl acetate–cyclohexane (4:6)] afforded the pure epoxide (0.6 g, 40%); ν_{max}/cm^{-1} 1660 (conj. CO); δ_H(200 MHz, $CDCl_3$) 1.20 (3 H, s, 9-Me), 1.70 (3 H, d, *J* 1.3, 8-Me), 1.90–2.10 (1 H, m), 2.10–2.40 (1 H, m), 2.40–2.60 (2 H, m), 2.60–2.80 (1 H, m), 2.90–3.10 (1 H, m), 3.80 (1 H, m), 6.40 (1 H, m, β′-H), 7.40 (1 H, m) and 7.50 (1 H, m); δ_C(50 MHz, $CDCl_3$) 11.6 (q), 20.8 (q), 29 (t), 32.4 (t), 32.7 (t), 45.4 (s), 60.4 (d), 65.7 (s), 11.2 (d), 118.7 (s), 131.4 (s), 141.4 (d), 143.2 (d), 162.6 (s) and 197.8 (s); *m/z* (EI) 244 (M^+, 90%) and 95 (100%) (Found: M^+, 244.1102. $C_{15}H_{16}O_3$ requires, *M*, 244.1099).

1-(3-*Furyl*)-1,2-*dihydroxy*-4,7a-*dimethyl*-2,3,6,7-*tetrahydroinden*-5-*one* **11**.—To a solution of the alkene **9** (0.45 g, 1.95 mmol) in pyridine (8 cm^3) was rapidly added crystalline osmium tetraoxide (0.5 g, 1.97 mmol). The reaction mixture was stirred at room temperature for 2 days after which a solution of sodium bisulfite (0.9 g) in water (15 cm^3) and pyridine (10 cm^3) was added to it and stirring continued for 30 min. The solution was subsequently extracted with dichloromethane and the combined extracts were washed with 20% hydrochloric acid and 3% aqueous sodium hydrogen carbonate and then evaporated to leave a black oily residue. This was chromatographed on silica gel [ethyl acetate–hexane (1:1)] to give the diol **11** as a white solid (0.29 g, 56%), m.p. 188 °C (from ethyl acetate–hexane); ν_{max}/cm^{-1} 3460, 3360 and 1620; δ_H(200

MHz, $CDCl_3$) 0.98 (3 H, s, Me), 1.51–1.62 (1 H, m), 1.7 (3 H, t, *J* 1.1, Me), 2.2 (2 H, br s, OH), 2.3–2.7 (4 H, m), 3 (1 H, m), 4.81 (1 H, dd, *J* 5.1 and 7.4), 6.41 (1 H, dd, *J* 0.9 and 1.4), 7.42 (1 H, t, *J* 1.6) and 7.47 (1 H, m); δ_C(50 MHz, $CDCl_3$) 11.4 (q), 20.9 (q), 26.7 (t), 33 (t), 35.4 (t), 49.3 (s), 74.2 (d), 81 (s), 109.6 (d), 125.3 (s), 129 (s), 140.6 (d), 143.5 (d), 166.6 (s) and 198.3 (s); *m/z* (EI) 262 ($[M]^+$, 15%), 149 (65%) and 45 (100%) (Found: M^+, 262.0931. $C_{15}H_{18}O_4$ requires *M*, 262.1205).

(1R*,7aR*)-1-(3-*Furyl*)-4,7a-*dimethyl*-1,6,7,7a-*tetrahydro-inden*-2,5-*dione* **3**.—A solution of the diol **11** (0.5 g, 1.9 mmol) in benzene (40 cm^3) was refluxed for 1.5 h in the presence of toluene-*p*-sulfonic acid (0.05 g, 0.26 mmol). Water was azeotropically removed using a Dean–Stark trap. After cooling to room temperature, the solution was washed with 5% aqueous sodium hydrogen carbonate (10 cm^3) and water (10 cm^3) and then evaporated to yield a solid residue. This was rapidly chromatographed [ethyl acetate–hexane (1:1)] to yield compound **3** (0.24 g, 52%), m.p. 189.5 °C; ν_{max}/cm^{-1} 3050, 1650, 1605 and 1530; δ_H(500 MHz, $CDCl_3$) 1.02 (3 H, s, 9-Me), 1.75 (3 H, t, *J* 1.5, 8-Me), 2–2.2 (2 H, m), 2.5–2.65 (2 H, m), 3.20–3.40 (2 H, J_{AB} 22.8), 3.52 (1 H, s), 6.3 (1 H, d, *J* 2, β′-H), 7.45 (1 H, t, *J* 2, α′-H) and 7.46 (1 H, m, α-H); δ_C(50 MHz, $CDCl_3$) 11.9 (q), 19.3 (q), 33.9 (t), 35.1 (t), 40.4 (t), 44.9 (s), 60.6 (d), 110.9 (d), 116.1 (d), 130.2 (s), 141.6 (d), 142.0 (d), 158.5 (s), 197.3 (s) and 210.2 (s); enol form δ_H(200 MHz, [$^2H_6$]DMSO) 0.8 (3 H, s, Me), 1.75 (3 H, s, Me), 1.8–2.0 (2 H, m), 2.3–2.5 (2 H, m), 3.45 (1 H, s), 5.6 (1 H, s), 6.35 (1 H, s, β′-H), 7.03 (1 H, m), 7.15 (1 H, m) and 10.1 (1 H, br s, OH); δ_C(50 MHz, [$^2H_6$]DMSO) 10.3 (q), 23.6 (q), 26.7 (t), 32.1 (t), 43.8 (t), 56.2 (d), 102.7 (s), 111.8 (d), 115.1 (d), 119.5 (s), 141.1 (d), 142.5 (d), 160.4 (s), 180.6 (s) and 203.3 (s); *m/z* (EI) 244 (M^+, 100%), 109 (75%) (Found: M^+, 244.1099. $C_{15}H_{16}O_3$ requires *M*, 244.1099).

1-(3-*Furyl*)-4,7a-*dimethyl*-1,6,7,7a-*tetrahydroindene*-2,3,5-*trione* **12**.—To an ice-cooled suspension of the enone **3** (0.1 g, 0.41 mmol) in methanol (4 cm^3) were successively added 30% hydrogen peroxide (0.5 cm^3) and then slowly 6 mol dm^{-3} aqueous NaOH (0.1 cm^3). The reddish reaction mixture was stirred at room temperature for 3 h and then diluted with water (10 cm^3) and extracted with methylene dichloride. Evaporation of the extract left a bright yellow solid residue which was chromatographed on silica gel [ethyl acetate–hexane (1:1)] to give compound **12** as the major product (0.03 g, 28%); m.p. 189 °C (from methanol); ν_{max}/cm^{-1} 3300, 1665, 1660, 1640 and 1600; δ_H(200 MHz, $CDCl_3$) 1.54 (3 H, s, 9-Me), 1.94–2.10 (1 H, td, *J* 27.7 and 6.1), 2.22 (3 H, s, Me), 2.44–2.94 (3 H, m), 6.86 (1 H, br s), 6.92 (1 H, dd, *J* 0.8 and 1.9, β′-H), 7.54 (1 H, t, *J* 1.7, α′-H) and 8.08 (1 H, br s, α-H); δ_C(50 MHz, $CDCl_3$), 10.5 (q), 24.3 (q), 31.5 (t), 34.4 (t) 40.9 (t), 109.6 (d), 117.4 (s), 134.5 (s), 135.9 (s), 143.8 (d), 144.9 (d), 149.9 (s), 150 (s), 188.6 (s) and 199.8 (s); *m/z* (NH_3, PICI) 276 ($M + NH_4^+$, 100%) and 259 (MH^+, 20%) [Found: M^+ (EI), 258.0893. $C_{15}H_{14}O_4$ requires *M*, 258.0892].

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