Ring-D aromatic phytosteroids; a model for biogenesis by way of carbon radical rearrangement

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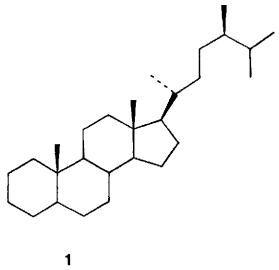
A mechanism is postulated for the biogenesis of the unique ring-D aromatic phytosteroids from *Nicandra physaloides*, which involves rearrangement, ring expansion, and aromatisation of a carbon radical generated by cytochrome P450 (Scheme 1). In support, model hydrindene acids 15b and 18b have been synthesized and subjected to homolytic decarboxylation; the latter acid yielded 6-methyltetralin 24, in biomimetic fashion. The isomeric acid afforded not only 6-methyltetralin 24 but also 5-methyltetralin 26; mechanisms for this unusual rearrangement are discussed.

The Solanaceae is an extensive plant family containing commercially important species, *e.g.* potatoes, tomatoes and peppers. A striking phytochemical characteristic of the family is the presence of a remarkable range of oxidised phytosteroids based on 24-methylcholesterol **1**, which make up a substantial group known as the withanolides.[1] Various interesting biological properties are displayed by these compounds.



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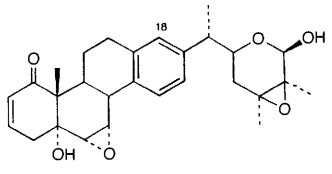
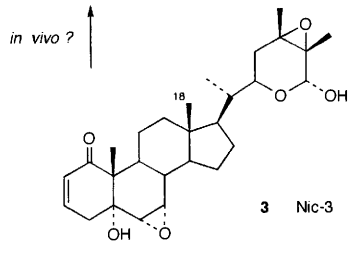


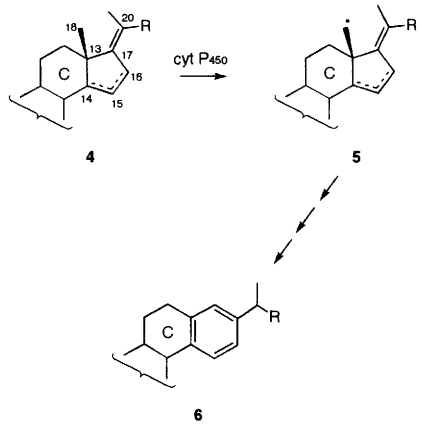
2 Nic - 1



3 Nic-3

A small but distinctive subset of this group, the nicandrenoids,[2] has been isolated from *Nicandra physaloides*, the Peruvian 'shoofly' plant. The main biologically active compound, Nic-1 **2**, exhibits both antifeedant and insecticidal properties,[2a] notably *versus* the tobacco hornworm, a specific feeder on solanaceous plants. Nic-1 and a few close relatives (Nic-1 lactone, Nic-17, Nic-12 and Nic-10)[2b,c] contain the unique structure feature of an aromatic ring-D, with the steroid side chain displaced from its common site adjacent to the C/D junction. Experiments have shown that the biogenesis involves ring expansion of ring-D with incorporation of the carbon originating from the C/D angular methyl, with subsequent aromatisation.[3] The natural product profile in *Nicandra physaloides* suggests that this step is likely to come late in the biosynthetic pathway and the more conventional phytosteroid Nic-3 **3** may be a precursor to Nic-1. Nic-1 would then lead on to Nic-10, -12 and -17 by side-chain modifications.

The course of the key expansion–aromatisation sequence could take various directions, but the pathway illustrated in Scheme 1 seemed to us to demand serious consideration. In this



4 **5** **6**

Scheme 1 Postulated biogenesis of Nic-1

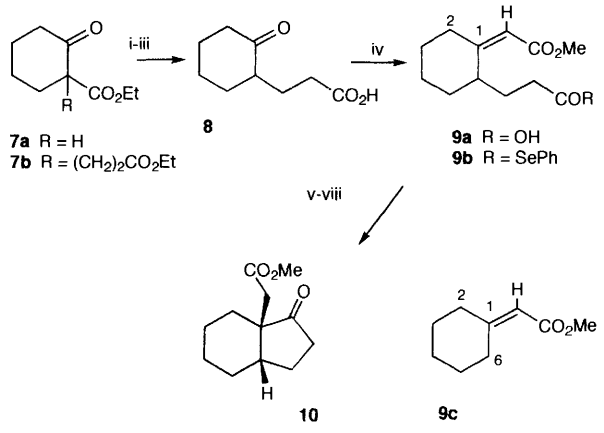
hypothesis, two double bonds are initially introduced into ring-D to form intermediate **4** Δ^{14} or Δ^{15}. The rearrangement is then triggered by cytochrome P-450 oxidation of C-18 to the corresponding radical **5**, an intermediate for hydroxylation. Although 'recoil' oxygenation is usually considered to be very fast,[4] it seems quite feasible that in secondary metabolism, relatively poor enzyme fit, associated with broad substrate acceptance, will result in a reduction of this rate. Rearrangement and ring expansion then ensue to the Nic-1 skeleton. The rate of rearrangement is postulated to be faster than that of recoil. This view is supported by results from investigations of biomimetic radical cyclisations to *O*-heterocycles.[5] After the ring expansion, aromatisation to **6** could result from either the oxidation of product radical to the corresponding carbocation followed by the loss of a proton, or by hydroxylation, *i.e.* the 'normal' P-450 reaction, and then dehydration.

To test this postulated mechanism, model compounds were needed so that biomimetic radical reactions could be carried out *in vitro*. The minimum requirements for these compounds included (i) the carbon skeleton of the C and D rings, with an alkyl group at the C/D ring junction and one adjacent to it on the D ring; (ii) the correct oxidation level, *i.e.* two double bonds in ring-D, one exocyclic; and (iii) a source for a methylene radical at the C/D ring junction, to be formed under non-

reducing conditions. Bearing these factors in mind we chose as our targets the hydrindenes **15b** and **18b** (Scheme 5), which are set up for radical generation by way of homolytic decarboxylation. In this paper we describe new syntheses of these compounds, and the fate of carbon radicals formed therefrom; preliminary accounts of these results have appeared.[6]

The literature offered few routes to such systems with angular substitutents other than methyl, but an apparently convenient method has been described involving alkylation of an hydrindanone enolate at the ring junction carbon with ethyl bromoacetate.[7] However, despite considerable efforts we were unable to obtain satisfactory yields using this chemistry, and thus we devised a new synthesis which we now describe.

The preparation of the diene acids **15b** and **18b**, were accomplished using a common hydrindenone intermediate **14** accessed by way of an acyl radical cyclisation strategy[8] (Scheme 2). Initially, ethyl 2-oxocyclohexanecarboxylate **7a**



7a R = H
7b R = $(CH_2)_2CO_2Et$

8

9a R = OH
9b R = SePh

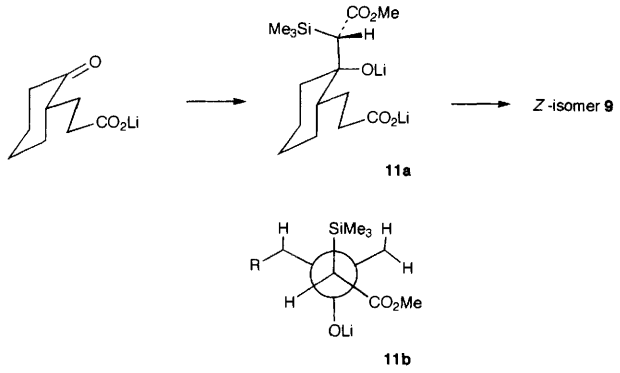
10 **9c**

Scheme 2 *Reagents:* i, KOBu^t, Bu^{t}OH; ii, $BrCH_2CH_2CO_2Et$; iii, aq.HCl; iv, LDA (3 equiv.), $TMSCH_2CO_2Me$ (3 equiv.); v, $(CO{\cdot}Cl)_2$; vi, PhSeNa; vii, PhH, reflux; viii, Bu_3SnH, AIBN, PhH

was alkylated with ethyl 3-bromopropionate in the presence of potassium *tert*-butoxide in *tert*-butyl alcohol to give the product diester **7b** in 85% yield. The ester functions were hydrolysed by dilute hydrochloric acid, and the resultant β keto acid decarboxylated, to give the keto acid **8**, purified by distillation to give a white solid, with mp 61.5–62 °C in agreement with the literature value.[9] The ketone moiety was converted into the α,β-unsaturated ester **9a**, by employing the Peterson olefination reaction,[10] using lithium diisopropylamide (LDA; 3 equiv.) and methyl trimethylsilyl acetate. Since distillation and column chromatography of the product both resulted in appreciable loss of material, it was subsequently used without further purification. However, the ^1H NMR spectrum of the crude product showed only one olefinic resonance, 5.53 (s) ppm, indicating that only one of the double bond isomers had been formed. This proved to be the *Z*-isomer, as demonstrated by comparison of the ^{13}C NMR spectra of phenyl seleneno ester **9b** and methyl cyclohexylideneacetate **9c**. The latter ester shows δ_C 29.8 and 37.9 ppm for C-2 and C-6, adjacent to the double bond. Allowance for γ-shielding[11] by an axial alkyl chain *ca.* 5 ppm in the *Z*-seleneno ester **9b** predicts δ_C *ca.* 32.9 for C-2, close to the observed value, 33.2 ppm. A conformation similar to **12** (Scheme 4) is envisaged.

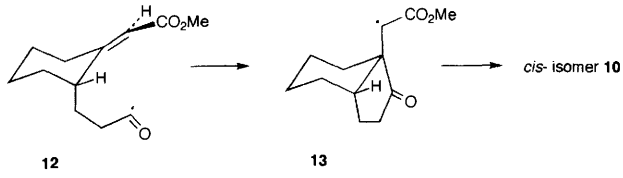
The formation of the *Z*-isomer is likely to be due to the stability of the intermediate alkoxy silane **11a**, whose preferred geometry is shown as **11b** in Scheme 3. The sterically large trimethylsilyl group occupies the least hindered site, with the methoxycarbonyl and the side chain moieties staggered. *syn*-Elimination of lithium trimethylsiloxide then generates the observed *Z*-stereochemistry.

The acid **9a** was then converted into the acid chloride, which



Scheme 3

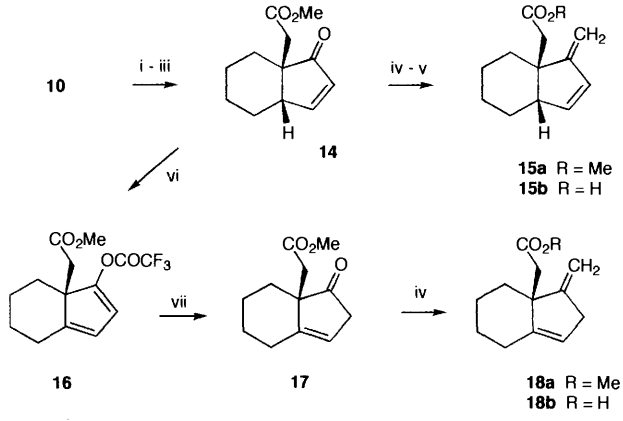
on treatment with sodium phenyl selenide[12] gave the corresponding phenyl seleneno ester **9b**. This was then treated with tributyltin hydride and azoisobutyronitrile (AIBN) in refluxing benzene to afford hydrindanone **10** (91%). A comparison with a small quantity of material prepared using the method of House[7] indicated that acyl radical cyclisation had exclusively given the *cis*-ring junction. This selectivity is believed to be a result of the conformation of the intermediate radical **12**. The *Z*-unsaturated ester forces the side chain into an axial orientation, so that the radical is ideally positioned to cyclise to the *cis*-product **13** (Scheme 4).



12 **13**

Scheme 4

Dehydrogenation of the cyclopentanone moiety was achieved by α-phenyl selenylation[13] (Scheme 5), followed by



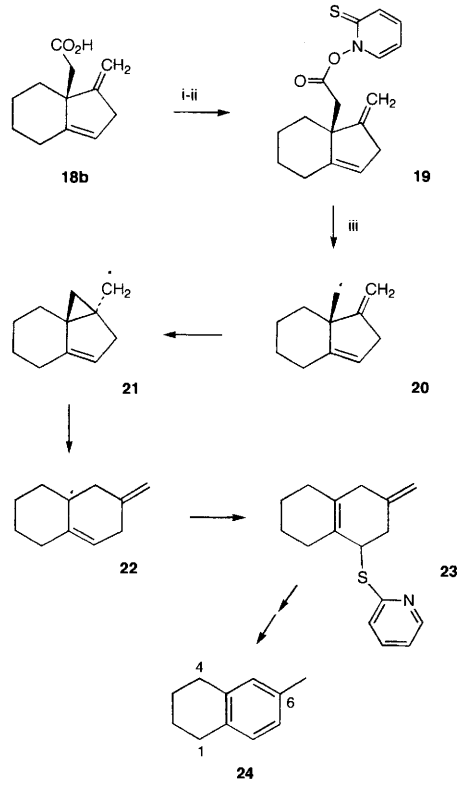
Scheme 5 *Reagents:* i, PhSeCl; ii, DMDO, −78°; iii, Et_3N; iv, CH_2I_2, Zn, $TiCl_4$; v, K_2CO_3, MeOH; vi, $(CF_3CO)_2O$; vii; MeOH

oxidative elimination using dimethyldioxirane to give the enone **14** (43%). This product was characterised from spectral results [ν_{max} 1736 and 1708 cm^{-1}, and δ_H 6.23 (dd) and 7.55 (dd) ppm] and was used to prepare both desired diene acids **15b** and **18b**. Thus, methylenation of the ketone **14** with the mild Nozaki[14] method, using methylene diiodide, zinc and titanium(IV) chloride afforded the conjugated diene ester **15a** [δ_H 4.64 (s), 4.97 (s), 5.97 (d) and 6.13 (d)] in 52% yield, and the corresponding diene acid **15b** was obtained by saponification with methanolic potassium carbonate.

The unconjugated diene acid was reached by deconjugation of the enone **14**. This was achieved by preparing the dienol trifluoroacetate **16** using trifluoroacetic anhydride[15] and then

treating this product with methanol, when kinetically favoured α-protonation gave the β,γ-unsaturated enone **17** (56%) together with some starting material (28%). Methylenation as before gave the unconjugated diene ester **18a** [δ_H 4.88 (dd), 5.00 (dd) and 5.35 (d)] which was surprisingly stable to double-bond migration under acid conditions. Saponification of the methyl ester gave the second diene acid **18b**.

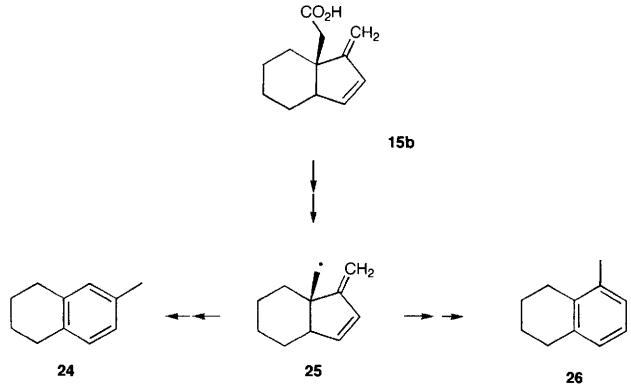
The two acids **15b** and **18b** were separately subjected to radical decarboxylation using the methodology of Barton and co-workers,[16] to generate the thiohydroxamate esters *in situ* from the acid chlorides. Following our earlier work on biomimetic radical cyclisations [5] we carried out the reactions in refluxing benzene with irradiation of the mixtures with a tungsten filament lamp. Under these conditions the unconjugated diene acid **18b** gave a product which, after chromatography to remove a trace of polar material, gave a hydrocarbon fraction. We were delighted when GLC analysis showed this material to be largely 6-methyltetralin **24**, the expected biomimetic product. This was confirmed by mass and ^{1}H NMR spectroscopy and GC comparison with authentic material.† The low yield (2–5%) may be ascribed to a combination of circumstances; the small reaction scale (22 mg of acid **18b**), the relative volatility of the tetralin, and the fact that the complete sequence requires at least five distinct steps (mean yield *ca.* 50% per step). The likely mechanism (Scheme 6) commences with



Scheme 6 Ring expansion and aromatisation. *Reagent:* i, $(COCl)_2$, DMF, CH_2Cl_2; ii, 2-sulfanylpyridine *N*-oxide sodium salt, DMAP, PhH, reflux, dark; iii, tungsten lamp, reflux, 1 h

generation of the primary radical **20** by homolysis of the hydroxamate **19**. 3-*exo-trig* Cyclisation of **20**, followed by fragmentation of the resultant strained bicyclo[3.1.0]hexene **21**, gives the more stable allylic radical **22**. This, in turn, can trap the pyridine-2-thiyl liberated from the Barton decarboxylation. Aromatisation results from the thermal *syn* elimination of 2-sulfanylpyridine followed by prototropic shifts to afford 6-methyltetralin **24**. This parallels the biogenetic transformation of Nic-3 **3** into Nic-1 **2** and offers circumstantial support for the hypothesis outlined above.

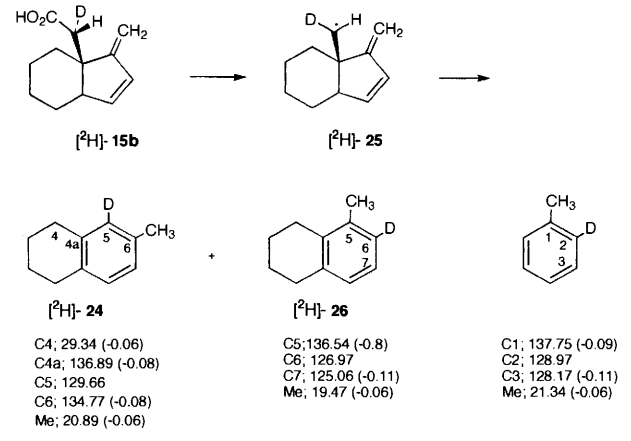
Radical generation of the conjugated diene acid **15b** (88 mg) was also investigated, with unexpected and curious results. Thus, the thiohydroxamate ester derived from the acid **15b**, was photolysed as before to generate the radical **25**. The hydrocarbon fraction contained a *ca.* 1 : 1 mixture of the hoped-for biomimetic product, 6-methyltetralin **24**, together with the isomeric 5-methyltetralin **26**, in an overall 23% yield (Scheme 7). The identity of each of these was again confirmed by



Scheme 7 Ring expansion, rearrangement and aromatisation

spectroscopic and chromatographic (GLC) comparisons with authentic samples.†

Various mechanistic interpretations for this surprising result have been considered.[6] The remote possibility of photochemical rearrangement of the tetralin products was ruled out experimentally. To eliminate some other hypotheses, an isotopic labelling experiment was carried out using the monodeuterio acid [^{2}H]-**15b** (Scheme 8). The required labelled acid was



Scheme 8 Deuterium labelling

accessed by acyl radical cyclisation of the phenyl seleneno ester **9b** using tributyltin deuteride as hydrogen donor to give the monodeuterio hydrindanone, which was further elaborated to acid [^{2}H]-**15b** using the synthetic sequence described above (Scheme 5). Homolytic decarboxylation *via* the thiohydroxamate ester generated the deuteriated radical [^{2}H]-**25** and hence the monodeuteriated 6- and 5- methyltetralins [^{2}H]-**24** and [^{2}H]-**26**, respectively, as well as the undeuteriated tetralins.

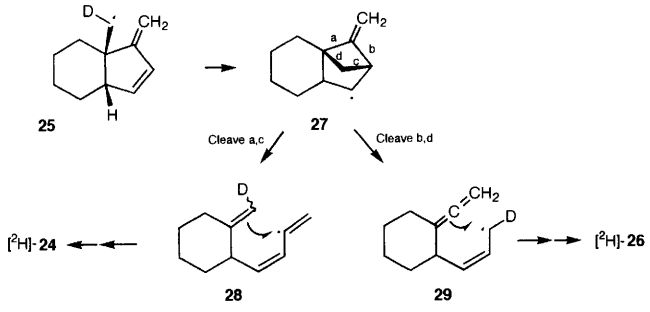
The sites of the deuterium labels were revealed unambiguously by examining the ^{13}C NMR spectra, which showed deuterium induced upfield β and γ shifts. These were accurately measured by separation of the ^{13}C lines of the deuteriated and non-deuteriated material. The relevant chemical shifts (δ, $CDCl_3$ are shown, along with those for [2-^{2}H]toluene for comparison. The

† We are grateful to Dr W. A. Smith and BP Research, Sunbury, for supplying authentic reference samples of 5-methyltetralin and 6-methyltetralin.

deuterium NMR spectrum was also scrutinised and showed only a multiplet in the range 6.9–7.5 ppm, giving no indication that any deuterium was present in the methyl groups.

Since a planar conformationally mobile monodeuterio radical [^{2}H]-**25** is an intermediate in these reactions any deuterium shift must have been partial, leaving residual deuterium to mark the starting site. Thus, it is clear from these results that no intramolecular deuterium transfers, 1,3 or other have occurred, and that the original angular carbon appears at C-5 in 6-methyltetralin and at C-6 in 5-methyltetralin.

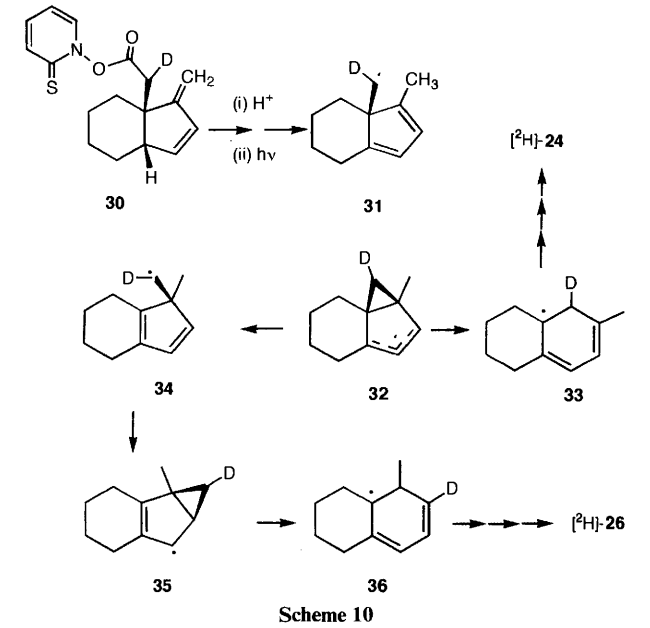
These experimental observations remain difficult to explain in a totally satisfactory manner. A simplistic mechanistic interpretation (Scheme 9), could involve the primary radical **25**



Scheme 9

cyclising to the endocyclic double bond of the diene. Intermediate **27** could then fragment by breaking bonds a and c to give the vinyl radical **28**, which is then set up to undergo 6-*endo-trig* cyclisation leading to 6-methyltetralin. Alternatively, cleavage of bonds b and d in radical **27** gives the allylic radical **29**, which could cyclise in a 6-*exo-dig* fashion leading to 5-methyltetralin. The degree of concertedness in such bond cleavages would remain an open question. Various difficulties are encountered in this scheme; *e.g.* it would have to be postulated that the two alternative cleavage pathways of radical **31** proceed at similar rates to produce products in an approximately 1 : 1 ratio, while the allylic radical **29** and the dienyl vinyl radical **28** would have to retain *cis* configurations long enough for cyclisation to proceed.

An ingenious alternative suggestion, (Scheme 10) has been proposed by a referee.‡ The key feature of this proposal is the



Scheme 10

‡ We thank a referee for constructive suggestions.

isomerisation of the starting exocyclic diene, at the acylthiohydroxamate stage **30**, to the endocyclic form, followed by decarboxylation to radical **31**. 3-*endo-trig* Cyclisation would afford the radical **32**, hypothesized either to open to the cyclohexadienyl radical **33**, or to undergo a 'cyclopropane walk' to the isomeric radical **35** *via* the cyclopentadienyl radical **34**, before cleaving to the new cyclohexadienyl radical **33**. This mechanism also presents various drawbacks, *e.g.* the σ-bond cleavages required in the ring-merging processes **32**→**33** and **35**→**36** are not favourable on stereoelectronic grounds.[17] Further, the initial isomerisation to an endocyclic diene must be postulated to occur only with the conjugated diene acid **15b**, and not with the unconjugated diene acid **18b**. Since such double-bond shifts must be presumed to be prototropic (intramolecular hydrogen migration being geometrically not feasible), such differentiation between the two systems would be hard to understand.

It appears that a fully satisfactory mechanistic rationalisation of this unexpected reaction is not on hand at present, and perhaps must await further investigation. However, the mechanistic uncertainties associated with the rearrangement in Scheme 7 do not affect our conclusion that, from a biogenetic point of view, these results give credence to the postulate of Scheme 1, where intermediate **4** has a Δ^{14} double bond. The Δ^{15} isomer cannot be completely excluded, since the direction of the rearrangement could be enzymically controlled.

Experimental

All melting points were determined on a Kofler hot-stage apparatus and are uncorrected. UV spectra were recorded on a Philips PU 8720 spectrophotometer as solutions in ethanol. IR spectra were obtained using a Perkin-Elmer 1720-X instrument. ^{1}H NMR spectra were variously recorded on Bruker WP 80 SY (80 MHz), Bruker WM 250 (250 MHz), JEOL EX 270 (270 MHz), and Bruker AM 400 (400 MHz) instruments; spectra were recorded as dilute solutions in deuteriochloroform unless otherwise stated. The chemical shifts were recorded relative to an internal tetramethylsilane standard and the multiplicity of a signal is designated with one of the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, br = broad and m = multiplet. Observed coupling constants (*J*) are reported in Hz. ^{13}C NMR were recorded on either a JEOL EX 270 (67.8 MHz) or a Bruker AM 400 (100.6 MHz) instrument; chemical shifts are reported relative to chloroform (77.0 ppm) on a broad band decoupled mode, and the multiplicities were obtained using a DEPT sequence. Mass spectra were recorded on an AEI MS-902 or an MM-701CF instrument, using electron impact ionisation at 70 eV unless otherwise stated. Microanalytical data were obtained on a Perkin-Elmer 240B elemental analyser. Gas liquid chromatography was performed on a Perkin-Elmer 8410 Gas Chromatograph, programmed for an injection temperature of 60 °C, with a heat-up rate of 8 °C min^{-1}. An SGE capillary column (25 m) packed with BP1 bonded phase fused silica (film thickness of 40 μm) was used. Column chromatography was performed using either Merck silica gel 60 or BDH alumina Brockmann grade 1 and the solvents were redistilled before use. All reactions and columns were monitored by TLC using Camlab silica gel F254 pre-coated plastic plates which were visualised with UV light and then with either acidic anisaldehyde or ethanolic phosphomolybdic acid dip. Routinely, dry organic solvents were stored under nitrogen. Benzene, diethyl ether and toluene were dried over sodium wire. Other organic solvents were dried by distillation from the following: THF (sodium, benzophenone), dichloromethane (calcium hydride), methanol/ethanol (sodium alkoxide) and acetonitrile (phosphorus pentoxide then potassium carbonate). Organic extracts were dried over either anhydrous magnesium sulfate or anhydrous sodium sulfate and the solvent was removed on a Buchi rotary evaporator. Where necessary, reactions requiring anhydrous

conditions were performed in a flame- or oven-dried apparatus under a nitrogen or argon atmosphere. A Buchi GKR-50 Kugelrohr was used for bulb-to-bulb distillations.

Ethyl 3-(1-ethoxycarbonyl-2-oxocyclohexyl)propanoate 7b

Ethyl 2-oxocyclohexanecarboxylate (29.40 g, 173 mmol) was added to a solution of potassium *tert*-butoxide (20.35 g, 181 mmol) in *tert*-butyl alcohol (800 cm^3) and the resulting mixture was heated under reflux under nitrogen for 30 min. A solution of ethyl 3-bromopropionate (31.26 g, 173 mmol) in *tert*-butyl alcohol (100 cm^3) and then added dropwise. Reflux of the resultant mixture was then continued for 2 h, after which it was cooled and evaporated and the residue was partitioned between ether and water. The separate and combined organic phases were washed with water and brine, dried ($MgSO_4$), concentrated and distilled *in vacuo* to give the title ester as a colourless oil (39.78 g, 85%), bp 195–200 °C/22 mmHg (lit.,[18] bp 146–148 °C/0.5 mmHg) (Found: C, 62.3; H, 8.4%; M^+ 270.147. Calc. for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20%; M^+, 270.147); ν_{max}(liquid film)/cm^{-1} 1734 (ester C=O) and 1713 (ketone C=O); δ_H(270 MHz, $CDCl_3$) 1.25 (3 H, t, *J* 7.3, 1-$O_2CH_2CH_3$), 1.27 (3 H, t, *J* 6.9, 1′-$CO_2CH_2CH_3$), 1.41–2.31 (8 H, m, 3,4′,5′,6′-H_2), 2.37–2.52 (4 H, m, 2,3′-H_2), 4.12 (2 H, q, *J* 7.3, -1-$O_2CH_2CH_3$), [4.21 (1 H, q, *J* 6.9) and 4.22 (1 H, q, *J* 6.9), (1′-$CO_2CH_2CH_3$)]; δ_C(67.8 MHz, $CDCl_3$) 13.9 (CH_3), 14.0 (CH_3), 22.3 (CH_2), 27.3 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 36.1 (CH_2), 40.8 (CH_2), 59.8 (C), 60.2 (CH_2), 61.2 (CH_2), 171.5 (C), 172.8 (C) and 207.3 (C); *m*/*z* 270 (M^+, 6%), 225 (100) and 197 (10).

3-(2-Oxocyclohexyl)propanoic acid 8

A mixture of the ester **7b** (30.55 g, 113 mmol) and hydrochloric acid (2 mol dm^{-3}; 600 cm^3) was heated under reflux for 48 h. On cooling, the mixture was extracted thoroughly into diethyl ether, and the combined extracts were then extracted into aqueous sodium hydrogen carbonate. The combined aqueous phases were acidified and extracted with diethyl ether after which the combined ether extracts were washed with brine, dried ($MgSO_4$) and concentrated. Distillation of the residue *in vacuo* gave the title acid as a colourless oil which solidified to give a white solid (13.85 g, 72%), mp 61.5–62 °C (lit.,[9] mp 62–63 °C), bp 138–140 °C/0.35 mmHg (Found: C, 63.25; H, 8.6%; M^+, 170.094. Calc. for $C_9H_{14}O_3$: C, 63.51; H, 8.29%; M^+, 170.094); ν_{max}(solid film)/cm^{-1} 3400–2600 (O–H) and 1697br (ketone C=O, acid C=O); δ_H(270 MHz, $CDCl_3$) 1.36–2.15 (8 H, m, 3,4′,5′,6′-H_2) and 2.25–2.53 (5 H, m, 2,3′-H_2, 1′-H); δ_C(67.8 MHz, $CDCl_3$) 24.4 (CH_2), 24.9 (CH_2), 27.9 (CH_2), 31.5 (CH_2), 34.0 (CH_2), 42.0 (CH_2), 49.5 (CH), 179.6 (C) and 212.9 (C); *m*/*z* 170 (M^+, 39%) and 98 (100).

Methyl (*Z*)-2-(carboxyethyl)cyclohexylideneacetate 9a

A solution of diisopropylamine (6.18 g, 61.2 mmol) in dry THF (150 cm^3) was cooled to −15 °C under nitrogen and then treated with butyllithium (1.6 mol dm^{-3} solution in hexane; 38 cm^3, 60.8 mmol). After 10 min the solution was cooled to −78 °C and then treated with methyl (trimethylsilyl)acetate (8.93 g, 61.2 mmol), added dropwise over 10 min. After a further 10 min a solution of 3-(2-oxocyclohexyl)propanoic acid (3.46 g, 20.4 mmol) in dry THF (20 cm^3) was subsequently added to the mixture which was then kept at −78 °C for an additional hour. The reaction mixture was then left to warm slowly to room temperature at which time it was acidified and extracted into diethyl ether. The organic phase was extracted with aqueous sodium hydrogen carbonate. The aqueous phase was carefully acidified and the free acid extracted into diethyl ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated to give the *title* ester as a pale yellow oil (4.23 g, 92%) [Found: $(M - H_2O)^+$, 208.107. $C_{12}H_{18}O_4$ requires $(M - H_2O)^+$, 208.110]; ν_{max}(liquid film)/cm^{-1} 3600–2600br (O–H), 1713 (acid C=O, ester C=O), 1643 (C=C); δ_H(270 MHz, $CDCl_3$) 1.36–1.93 (10 H, m, 3,3′,4′,5′,6′-H_2), 2.05–2.34 (2 H, m, 2-H_2), 3.51 (3 H, s, OMe), 3.79 (1 H, m, 1′-H) and 5.53 (1 H, s, C=CH); δ_C(67.8 MHz, $CDCl_3$) 20.2 (CH_2), 26.6 (CH_2), 28.1 (CH_2), 31.6 (CH_2, CH_2), 32.9 (CH_2), 35.1 (CH), 50.5 (CH_3), 114.5 (CH), 164.8 (C), 166.6 (C) and 179.4 (C); *m*/*z* 208 [$(M - H_2O)^+$, 15%], 166 (100) and 149 (95).

Methyl (*Z*)-2-(phenylselanylcarbonylethyl)cyclohexylideneacetate 9b

Oxalyl chloride (4.77 g, 37.6 mmol) and DMF (2 drops) were added to a solution of the acetate **9a** (6.02 g, 26.6 mmol) in dry benzene (80 cm^3) and the mixture was stirred at room temperature under nitrogen for 3 h. It was then evaporated under reduced pressure to give the crude acid chloride. This was then taken up in dry THF (100 cm^3) and the solution added to a solution of sodium phenyl selenide (26.6 mmol) in THF (prepared from sodium sand and diphenyl diselenide[12]) and stirred for 10 min. The reaction mixture was then diluted with diethyl ether and washed with aqueous sodium hydrogen carbonate (from which any starting material could be reclaimed), sodium hydroxide and brine and then dried ($MgSO_4$) and evaporated. Column chromatography [silica, light petroleum (bp 40–60 °C)–ethyl acetate] gave the *title compound* as a yellow oil (4.51 g, 46%) [Found: C, 59.1; H, 6.2%; $(M - SePh)^+$, 209.118. $C_{18}H_{22}O_3Se$ requires C, 59.18; H, 6.07%; $(M - SePh)^+$, 209.117]; ν_{max}(liquid film)/cm^{-1} 1714 (br, seleneno ester C=O, ester C=O), 1614 and 1579 (C=C, Ar); δ_H(400 MHz, $CDCl_3$) 1.37–1.45 (1 H, m, 4′a-H), 1.53–1.63 (3 H, m, 5′-H_2, 6′a-H), 1.71–1.73 (1 H, m, 6′b-H), 1.83–1.90 (2 H, m, 3a,4′b-H), 2.01–2.08 (2 H, m, 3b,3′a-H), 2.28–2.34 (1 H, m, 3′b-H), [2.62 (1 H, ddd, *J* 16.1, 5.5, 4.4), 2.79 (1 H, ddd, *J* 16.1, 5.8, 4.3), 2-H_2], 3.86 (3 H, s, OMe), 3.95 (1 H, m, 1′-H), 5.68 (1 H, s, C=CH), [7.34–7.38 (3 H, m), 7.48–7.51 (2 H, m), Ph]; δ_C(67.8 MHz, $CDCl_3$) 20.5 (CH_2), 27.4 (CH_2), 28.4 (CH_2), 31.9 (CH_2), 33.2 (CH_2), 35.3 (CH), 45.6 (CH_2), 50.9 (CH_3), 114.9 (CH), 126.5 (C), 128.7 (CH), 129.2 (CH), 135.8 (CH), 164.9 (C), 166.7 (C) and 200.2 (C); *m*/*z* 209 [$(M - SePh)^+$, 29%], 177 (19) and 149 (100).

7a-Methoxycarbonylmethyl-*cis*-perhydroindan-1-one 10

Method A. A solution of the ester **9b** (1.62 g, 4.44 mmol) in dry benzene (300 cm^3) was heated under reflux under nitrogen for 30 min. This solution was then treated with tributyltin hydride (1.55 g, 5.33 mmol) and AIBN (73 mg, 0.44 mmol) in dry benzene (20 cm^3) which was added by a syringe pump over 1 h. After a further 2 h under reflux under nitrogen the reaction mixture was cooled and evaporated under reduced pressure. Column chromatography [silica, light petroleum (bp 40–60 °C)–ethyl acetate] gave the *title ketone* as a pale yellow oil which solidified with time (846 mg, 91%), mp 40–41 °C (from pentane) (lit.,[7] mp 39.5–40 °C) (Found: M^+ 210.128. Calc. for $C_{12}H_{18}O_3$: M^+, 210.126); ν_{max}(liquid film)/cm^{-1} 1737 (ester C=O, ketone C=O) cm^{-1}; δ_H(270 MHz, $CDCl_3$) 1.17–1.65 (8 H, m, 4,5,6,7-H_2), 1.83–1.98 (2 H, m, 3-H_2), 2.39–2.47 (1 H, m, 3a-H), [2.70 (1 H, d, *J* 16.5), 2.71 (1 H, d, *J* 16.5), CH_2CO_2Me] and 3.63 (3 H, s, OMe); δ_C(67.8 MHz, $CDCl_3$) 20.6 (CH_2), 21.6 (CH_2), 22.8 (CH_2), 24.7 (CH_2), 28.3 (CH_2), 36.4 (CH_2), 37.2 (CH_2), 37.8 (CH), 48.7 (C), 51.6 (CH_3), 171.9 (C) and 220.8 (C); *m*/*z* 210 (M^+, 4%) and 137 (100).

Method B. Methyllithium (1.4 mol dm^{-3} in diethyl ether; 2.10 cm^3, 2.93 mmol) was added to a solution of 1,2,4,5,6,7-hexahydro-7a *H*-inden-3-yl acetate (241 mg, 1.33 mmol) in dry DME (6 cm^3) at 0 °C. After 5 min methyl bromoacetate (550 mg, 3.60 mmol) was added to the resultant enolate, and after 30 s the reaction mixture was quenched with hydrochloric acid (1 mol dm^{-3}; 5 cm^3) and diluted with diethyl ether. The organic phase was washed with aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated. Column chromatography [silica, light petroleum (bp 40–60 °C)–ethyl acetate] gave the title compound as a yellow oil (66 mg, 34%),

the spectroscopic data for which were identical with those described above.

7a-Methoxycarbonyldeuteriomethyl-*cis*-perhydroindan-1-one
The experiment described under Method A above was repeated but with replacement of the tributyltin hydride by tributyltin deuteride as hydrogen donor to give the *title ketone* (Found: M^+, 211.137. $C_{12}H_{17}O_3D$ requires: M^+, 211.132); NMR spectral data were identical with those of the non-deuteriated compound except: δ_H(270 MHz, $CDCl_3$) 2.70 (1 H, br, $CHDCO_2Me$); δ_C(67.8 MHz, $CDCl_3$) 36.72 (t, J 19.6, C).

7a-Methoxycarbonylmethyl-*cis*-3a,4,5,6,7,7a-hexahydro-1*H*-inden-1-one 14
A solution of the ketone **10** (738 mg, 3.52 mmol) and phenylselanyl chloride (922 mg, 4.81 mmol) in ethyl acetate (20 cm^3) was stirred at room temperature under nitrogen for 18 h after which it was evaporated under reduced pressure. The residue was subjected to flash chromatography [silica, light petroleum (bp 40–60 °C), light petroleum (bp 40–60 °C)–ethyl acetate]. The colourless selenide was dissolved in methylene dichloride (30 cm^3) and the solution cooled to −78 °C. Dimethyldioxirane was then added to the mixture until no more selenide could be seen on TLC. The reaction mixture was subsequently treated with triethylamine (2 cm^3) and then allowed to warm to room temperature for 18 h. After this it was diluted with methylene dichloride and washed with aqueous sodium hydroxide, hydrochloric acid, water and brine, dried ($MgSO_4$) and evaporated. Column chromatography [silica, light petroleum (bp 40–60 °C)–ethyl acetate] gave the *title compound* as a yellow oil (298 mg, 43%) (Found: M^+, 208.113. $C_{12}H_{16}O_3$ requires M^+, 208.110); ν_{max}(liquid film)/cm^{-1} 1736 (ester C=O), 1708 (enone C=O) and 1588 (C=C), δ_H(270 MHz, $CDCl_3$) [1.25–1.60 (6 H, m), 1.68–1.88 (2 H, m), 4,5,6,7-H_2], [2.64 (1 H, d, J 16.5), 2.68 (1 H, d, J 16.5), CH_2CO_2Me], 3.06 (1 H, m, 3a-H), 3.62 (3 H, s, OMe), 6.23 (1 H, dd, J 5.9, 2.3, 2-H) and 7.55 (1 H, dd, J 5.9, 2.3, 3-H); δ_C(67.8 MHz, $CDCl_3$) 19.1 (CH_2), 19.7 (CH_2), 24.7 (CH_2), 30.7 (CH_2), 39.1 (CH_2), 45.5 (CH), 47.8 (C), 51.6 (CH_3), 132.1 (CH), 166.9 (CH), 171.8 (C) and 213.2 (C); m/z 208 (M^+, 26%), 177 (19), 149 (23) and 135 (29).

7a-Methoxycarbonyldeuteriomethyl-*cis*-3a,4,5,6,7,7a-hexahydro-1*H*-inden-1-one
7a-Methoxycarbonyldeuteriomethyl-*cis*-perhydroindan-1-one was treated in an identical manner to that described in the above experiment to give the title compound. The ^1H NMR data were identical with those of the undeuteriated material except for the following resonance: δ_H(250 MHz, $CDCl_3$) 2.62 (1 H, br, $CHDCO_2Me$).

7a-Methoxycarbonylmethyl-1-methylene-*cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene 15a
Diiodomethane (3.02 g, 11.25 mmol) was added to a stirred suspension of zinc (1.35 g, 20.75 mmol) in dry THF (25 cm^3) at room temperature under argon. After 30 min titanium(IV) chloride (1 mol dm^{-3} in dichloromethane, 2.3 cm^3) was added to the mixture at 0 °C and the resultant suspension stirred at room temperature for 30 min, when a solution of the ketone **14** (359 mg, 1.73 mmol) in dry THF (5 cm^3) was added. After 15 min the reaction mixture was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether. The organic phase was separated, washed with aqueous sodium hydrogen carbonate and brine and then dried ($MgSO_4$) and evaporated. Column chromatography [silica, light petroleum (bp 40–60 °C)–ethyl acetate] gave the *title compound* as a colourless oil (185 mg, 52%) (Found: M^+, 206.133. $C_{13}H_{18}O_2$ requires: M^+, 206.131); ν_{max}(liquid film)/cm^{-1} 1737 (ester C=O), 1632 (C=C) and 869 (R_2C=CH_2), 736 (*cis*-RHC=CRH); δ_H(250 MHz, $CDCl_3$) [1.32–1.45 (5 H, m), 1.62–1.80 (3 H, m), 4,5,6,7-H_2], [2.40 (1 H, d, J 14.2), 2.48 (1 H, d, J 14.2), CH_2CO_2Me], 2.93 (1 H, m, 3a-H), 3.62 (3 H, s, OMe), [4.64 (1 H, s), 4.97 (1 H, s), C=CH_2], 5.97 (1 H, d, J 5.8, 3-H) and 6.13 (1 H, d, J 5.8, 2-H); δ_C(67.8 MHz, $CDCl_3$) 19.7 (CH_2), 19.7 (CH_2), 26.3 (CH_2), 32.7 (CH_2), 44.6 (CH_2), 45.5 (C), 49.1 (CH), 51.2 (CH_3), 103.2 (CH_2), 132.23 (CH_2), 141.7 (CH), 160.2 (C) and 172.3 (C); m/z 206 (M^+, 28%), 147 (38) and 132 (100); λ_{max}(EtOH)/nm 222 (5100).

7a-Methoxycarbonyldeuteriomethyl-1-methylene-*cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene
7a-Methoxycarbonyldeuteriomethyl-*cis*-3a,4,5,6,7,7a-hexahydro-1*H*-inden-1-one was treated in an identical manner to that described in the above experiment to give the title compound, ^1H NMR spectrum of which was identical with that of the undeuteriated compound except for the following resonance: δ_H(250 MHz, $CDCl_3$) 2.45 (1 H, br, $CDHCO_2Me$).

7a-Carboxymethyl-1-methylene-*cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene 15b
A solution of the ester **15a** (162 mg, 0.78 mmol) and potassium carbonate (400 mg, 2.90 mmol) in water (10 cm^3) and methanol (15 cm^3) was heated under reflux for 18 h. On cooling, the reaction mixture was washed with diethyl ether after which the aqueous phase was acidified and the free acid then extracted into diethyl ether. The extract was washed with brine, dried ($MgSO_4$) and evaporated to give the *title acid* as a pale yellow oil (133 mg, 88%) (Found: M^+, 192.115. $C_{12}H_{16}O_2$ requires: M^+, 192.115); ν_{max}(liquid film)/cm^{-1} 3500–2500 (br, OH), 1707 (acid C=O), 1632 (C=C), 868 (R_2C=CH_2), 735 (*cis*-RHC=CRH); δ_H(270 MHz, $CDCl_3$) [1.25–1.44 (5 H, m), 1.62–1.79 (3 H, m), 4,5,6,7-H_2], [2.42 (1 H, d, J 14.4), 2.50 (1 H, d, J 14.4), CH_2CO_2H], 2.94 (1 H, m, 3a-H), [4.68 (1 H, s), 4.99 (1 H, s), C=CH_2], 5.97 (1 H, d, J 5.7, 3-H) and 6.14 (1 H, d, J 5.7, 2-H); δ_C(100.6 MHz, $CDCl_3$) 19.7 (CH_2), 19.8 (CH_2), 26.4 (CH_2), 32.8 (CH_2), 44.5 (CH_2), 45.6 (C), 49.1 (CH), 103.5 (CH_2), 132.3 (CH), 141.7 (CH), 160.0 (C) and 178.0 (C); m/z 192 (M^+, 57%), 149 (32), 132 (100) and 117 (95); λ_{max}(EtOH)/nm 237 (9300).

7a-Carboxydeuteriomethyl-1-methylene-*cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene
7a-Methoxycarbonyldeuteriomethyl-1-methylene-*cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene was treated in an identical way to that described in the above experiment to give the *title acid* (Found: M^+, 193.122. $C_{12}H_{15}O_2D$ requires: M^+, 193.121); the ^1H NMR spectral data were identical with those of the undeuteriated compound except for the following resonance: δ_H(250 MHz, $CDCl_3$) 2.49 (1 H, br, $CHDCO_2Me$).

Barton decarboxylation: general method
The acid (0.5 mmol) was stirred, under nitrogen, with oxalyl chloride (0.25 cm^3) and dry DMF (50 cm^3) in dry methylene dichloride (5 cm^3) for 2 h. After evaporation of the mixture, the residue was dissolved in dry benzene (5 cm^3) and evaporated again to give the crude acid chloride. A solution of the crude acid chloride in benzene (5 cm^3) was added in one portion to a dried (Dean and Stark), refluxing suspension of 2-sulfanylpyridine *N*-oxide (sodium salt) (90 mg, 0.6 mmol) and DMAP (10 mg) in benzene (80 cm^3) in the dark (foil). After 30 min the foil was removed and the resulting bright yellow mixture irradiated with a 200W UV/vis lamp for 1 h. After cooling, the reaction mixture was washed with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography [silica, pentane or light petroleum–ethyl acetate] to give the product.

Biomimetic radical decarboxylation of compound 15b
Decarboxylation of compound **15b** (88 mg, 0.46 mmol) by the general method described above with 2-sulfanylpyridine *N*-oxide (sodium salt) (84 mg) and DMAP (9 mg) in benzene (80 cm^3) gave a 1:1 mixture of 5-methyltetralin **26** and 6-

methyltetralin **24** as a colourless oil (16 mg, 23%) which co-ran on GC with authentic samples[17] (Found: M^+, 146.111. Calc. for $C_{11}H_{14}$: *M*, 146.110); δ_H(250 MHz, $CDCl_3$) [1.76–1.89 (m), 2.61 (t, *J* 6.4), 2.70–2.85 (m), methylenes], [2.20, (s), 2.27, (s), Me], and 6.88–7.03 (m, Ar); *m/z* 146, (M^+, 84), 131 (100), 118 (71), 105 (39), 91 (24) and 77 (9); GC retention times 10.1 and 10.6 min.

Authentic 5-methyltetralin **26** had; δ_H(250 MHz, $CDCl_3$) 1.77–1.81 (4 H, m, 2,3-H_2), 2.20 (3 H, s, Me), 2.61 (2 H, t, *J* 6.4, 1-H_2), 2.76 (2 H, t, *J* 6.4, 4-H_2) and 6.91–7.03 (3 H, m, 6,7,8′-H); δ_C(100.6 MHz, $CDCl_3$) 19.4 (CH_3), 22.9 (CH_2), 23.4 (CH_2), 26.7 (CH_2), 30.1 (CH_2), 125.0 (CH), 126.9 (CH), 127.0 (CH), 135.5 (C), 136.5 (C) and 137.0 (C); *m/z* 146 (M^+, 87%), 131 (100), 118 (63), 105 (35), 91 (19) and 77 (11); GC retention time 10.6 min. Authentic 6-methyltetralin **24** displayed δ_H(250 MHz, $CDCl_3$) 1.75–1.80 (4 H, m, 2,3-H_2), 2.27 (3 H, s, Me), 2.72 (4 H, br s, 1,4-H_2) and 6.88–7.01 (3 H, m, 5,7,8-H); δ_C(100.6 MHz, $CDCl_3$) 20.9 (CH_3), 23.3 (CH_2), 23.4 (CH_2), 29.0 (CH_2), 29.3 (CH_2), 126.2 (CH), 129.0 (CH), 129.6 (CH), 134.0 (C), 134.7 (C) and 136.9 (C); *m/z* 146 (M^+, 93%), 131 (100), 118 (84), 105 (35), 91 (18) and 77 (8); GC retention time 10.1 min.

Biomimetic radical decarboxylation of compound [^{2}H]-15b

Decarboxylation of compound [^{2}H]-**15b** (170 mg, 0.88 mmol) by the general method described above with the 2-sulfanylpyridine *N*-oxide (sodium salt) (163 mg) and DMAP (17 mg) in benzene (150 cm^3) gave a 1 : 1 : 1 : 1 mixture of 5-methyltetralin, 5-methyl[6-^{2}H]tetralin, 6-methyltetralin and 6-methyl[5-^{2}H]-tetralin as a colourless oil (Found: M^+, 147.117, 146.106. Calc. for $C_{11}H_{13}D$: 147.116. Calc. for $C_{11}H_{14}$: *M*, 146.110); δ_H(250 MHz, $CDCl_3$) [1.76–1.89 (m), 2.61 (t, *J* 6.4), 2.70–2.85 (m), methylenes], [2.20, (s), 2.27, (s), Me] and 6.88–7.03 (m, Ar); δ_D(61.4 MHz, $CFCl_3$–CH_2Cl_2) 6.9–7.5 (m, ArD); δ_C(100.6 MHz, $CDCl_3$) 19.4 (CH_3), 19.5 (CH_3), 20.9 (CH_2), 20.9 (CH_3), 22.9 (CH_3), 23.3 (CH_2), 23.4 (CH_2), 23.4 (CH_2), 26.7 (CH_2), 29.0 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 30.1 (CH_2), 124.9 (CH), 125.1 (CH), 126.2 (CH), 126.8 (CH), 126.9 (CH), 127.0 (CH), 129.0 (CH), 129.7 (CH), 134.0 (C), 134.7 (C), 134.8 (C), 135.5 (C), 136.4 (C), 136.5 (C), 136.8 (C), 136.9 (C) and 137.1 (C); *m/z* 147, (M^+, 31), 146 (M^+, 13), 119 (9), 118 (6), 106 (99), 105 (23), 92 (17) and 91 (14).

7a-Methoxycarbonylmethyl-1,4,5,6,7,7a-hexahydro-2*H*-inden-1-one 17

A mixture of the ketone **14** (162 mg, 0.78 mmol) and trifluoroacetic anhydride (5 cm^3) was heated under reflux under nitrogen for 6 h. After the mixture had cooled, the excess of trifluoroacetic anhydride was removed under reduced pressure and the crude dienol trifluoroacetate treated with methanol (5 cm^3). The resultant solution was heated under reflux for 30 min and then concentrated. Column chromatography [silica, light petroleum (bp 40–60 °C)–ethyl acetate] gave unchanged starting material (46 mg) and the *title compound* as a colourless oil (90 mg, 56% (78% based on recovered starting material)) (Found: M^+, 208.108. $C_{12}H_{16}O_3$ requires M^+, 208.110); ν_{max}(liquid film)/cm^{-1} 1746 br (ester C=O, ketone C=O) and 1652 (C=C); δ_H(250 MHz, $CDCl_3$) [1.21–1.35 (2 H, m), 1.48–1.93 (4 H, m), 5,6,7-H_2], [2.12 (1 H, m), 2.35 (1 H, m), 4-H_2], [2.69 (1 H, d, *J* 15.3), 2.91 (1 H, d, *J* 15.3), CH_2CO_2Me], [2.84 (1 H, ddd, *J* 23.0, 2.3, 2.3), 3.06 (1 H, ddd, *J* 23.0, 4.0, 1.9), 2-H_2], 3.59 (3 H, s, OMe) and 5.72 (1 H, dd, *J* 2.0, 1.9, 3-H), δ_C(67.8 MHz, $CDCl_3$) 21.6 (CH_2), 27.5 (CH_2), 27.8 (CH_2), 33.9 (CH_2), 38.3 (CH_2), 42.0 (CH_2), 51.4 (CH_3), 52.5 (C), 117.7 (CH), 145.9 (C), 170.9 (C) and 221.2 (C); *m/z* 208 (M^+, 100%), 177 (28) and 148 (67).

7a-Methoxycarbonylmethyl-1-methylene-1,4,5,6,7,7a-hexahydro-2*H*-inden-1-one 18a

Diiodomethane (603 mg, 2.25 mmol) was added to a stirred suspension of zinc (270 mg, 4.13 mmol) in dry THF (5 cm^3) at room temperature under argon. After 30 min titanium(IV) chloride (1 mol dm^{-3} in CH_2Cl_2; 0.46 cm^3) was added at 0 °C to the mixture and the resultant suspension stirred at room temperature for 30 min, when a solution of the ketone **17** (100 mg, 0.48 mmol) in dry THF (1 cm^3) was also added. After 30 min the reaction mixture was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether. The organic phase was separated and washed with aqueous sodium hydrogen carbonate and brine and then dried ($MgSO_4$) and evaporated. Column chromatography [silica, light petroleum (bp 40–60 °C)–ethyl acetate] of the residue gave unchanged ketone **17a** (59 mg) and the *title compound* as a colourless oil [31 mg, 32% (75% based on recovered starting material)] (Found: M^+, 206.125. $C_{13}H_{18}O_2$ requires M^+, 206.131); ν_{max}(liquid film)/cm^{-1} 1738 (ester C=O), 1671 and 1646 (C=C); δ_H(250 MHz, $CDCl_3$) [1.15–1.39 (2 H, m), 1.50–2.16 (5 H, m), 2.33 (1 H, br, d, *J* 13.7), 4,5,6,7-H_2], [2.45 (1 H, d, *J* 13.4), 2.74 (1 H, d, *J* 13.4), CH_2CO_2Me], [2.94 (1 H, m, J_{gem} 20.7), 3.12 (1 H, m, J_{gem} 20.7), 2-H_2], 3.59 (3 H, s, OMe), [4.88 (1 H, dd, *J* 2.2, 2.0), 5.00 (1 H, dd, *J* 2.1, 2.0), C=CH_2] and 5.35 (1 H, d, *J* 1.8, 3-H); δ_C(67.8 MHz, $CDCl_3$) 22.4 (CH_2), 26.7 (CH_2), 27.3 (CH_2), 37.8 (CH_2), 38.5 (CH_2), 41.3 (CH_2), 50.7 (C), 51.2 (CH_3), 105.8 (CH_2), 119.3 (CH), 146.7 (C), 158.0 (C) and 172.1 (C); *m/z* 206 (M^+, 54%), 133 (100), 132 (100) and 117 (57).

7a-Carboxymethyl-1-methylene-1,4,5,6,7,7a-hexahydro-2*H*-indene 18b

A solution of compound **18a** (29.0 mg, 0.14 mmol) and potassium carbonate (100 mg, 0.73 mmol) in water (2 cm^3) and methanol (4 cm^3) was heated under reflux for 18 h. On cooling, the reaction mixture was washed with diethyl ether and the aqueous phase acidified. The free acid was then extracted into diethyl ether and the extract washed with brine, dried ($MgSO_4$) and evaporated to give the *title acid* as a colourless oil (23.5 mg, 87%) (Found: M^+, 192.116. $C_{12}H_{16}O_2$ requires M^+, 192.115); ν_{max}(liquid film)/cm^{-1} 3300–2400 (br, O–H), 1696 (acid C=O) and 1648 (C=C); δ_H(250 MHz, $CDCl_3$) [1.14–1.40 (2 H, m), 1.47–2.15 (5 H, m), 2.33 (1 H, br d, *J* 13.8), 4,5,6,7-H_2], [2.46 (1 H, d, *J* 13.4), 2.74 (1 H, d, *J* 13.4), CH_2CO_2Me], [2.94 (1 H, m, J_{gem} 20.7), 3.14 (1 H, m, J_{gem} 20.7), 2-H_2], [4.92 (1 H, dd, *J* 2.2, 2.0), 5.02 (1 H, dd, *J* 2.1, 2.0), C=CH_2] and 5.36 (1 H, d, *J* 1.7, 3-H); δ_C(67.8 MHz, $CDCl_3$) 22.4 (CH_2), 26.7 (CH_2), 27.3 (CH_2), 37.8 (CH_2), 38.5 (CH_2), 41.3 (CH_2), 50.8 (C), 106.2 (CH_2), 119.7 (CH), 146.3 (C), 157.7 (C) and 177.8 (C); *m/z* 192 (M^+, 48%), 147 (33) and 132 (100).

Biomimetic radical decarboxylation of 7a-carboxymethyl-1-methylene-1,4,5,6,7,7a-hexahydroindene 18b

Barton decarboxylation of compound **18a** (2.8 (22 mg, 0.11 mmol) by the general method described above with 2-sulfanylpyridine *N*-oxide (sodium salt) (21 mg) and DMAP (2 mg) in benzene (20 cm^3) gave a trace (*ca.* 1 mg, 5%) of 6-methyltetralin **24** as a colourless oil which co-ran on GC with an authentic sample† (Found: M^+, 146. Calc. for $C_{11}H_{14}$: M^+, 146); δ_H(250 MHz, $CDCl_3$) 2.27 (s, Me) and 6.88–6.99 (m, Ar); GC retention time 10.1 min.

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