Synthetic Studies on Tricyclospirodienones; Model Chemistry for Novel Mimics of Steroid Substrates

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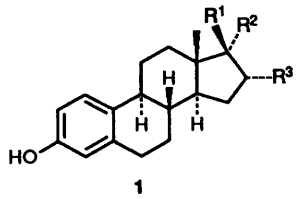
As part of a programme to synthesize aryltricyclospirodienones **3**, potential steroid antimetabolites, the formation of tricyclospirodienones **4** from substituted tetralins has been studied. 1-Allyl- and 1-(but-3-enyl)-tetralins **9** and **11** were synthesized from the 6-alkoxytetralols **8** and the corresponding pivaloates **10** using allytrimethylsilane/zinc iodide and 1-(but-3-enyl)magnesium bromide respectively, and were used to prepare the epoxides **20** and **21**, the iodides **13**, **16** and **19**, and the nitro compounds **14** and **17**. Phenol-*exo*-spirocyclisations of the iodides were shown to proceed smoothly in the 5- and 6-*exo-tet* senses; in contrast, the epoxides failed to cyclise in these formally allowed modes and only the 7-*endo* type, *i.e.* **21** (α-H) ⟶ **30** was viable. Cyclisation *via* phenylthiiranium and phenylselenonium ions followed a similar pattern. Under acid catalysis the epoxide **21** formed the 5-*exo* products **36** and **37**, which on further acid treatment gave the tetracycles **38** and **39** respectively. The α-oxocarbocation from the diazo ketones **41** provided the spirodienone **43**. The ω-nitropropyl and ω-nitrobutyl-6-hydroxytetralins **14c** and **17c** underwent stereospecific intramolecular coupling between phenolate and nitronate functions to afford tricyclospirodienones **46** and **47** respectively.

The biogenesis of mammalian sex hormones from cholesterol involves a cascade of oxidative processes culminating in the formation of estrogens **1** from androgens **2**.[1] This stage is conducted by the enzyme aromatase, which belongs to the cytochrome *P*-450 group. The mechanism of action of such enzymes has been the subject of intensive research in recent years, from which has emerged an understanding of the major features of the mode of operation of *P*-450-catalysed hydroxylation in general,[2] and the specific action of aromatase.[3] Estrogens have an important role in certain diseases including gynaecomastia, endometriosis and most importantly mammary carcinoma. About one third of breast cancers are hormone related, and hence considerable attention has been paid to the chemotherapeutic inhibition of estrogen biogenesis.[4] This is particularly important for post-menopausal women, for whom the main sourses of estrogen are extragonadal tissues – fat, liver, *etc.* Aromatase is a particularly suitable target since it catalyses the unique and final biosynthetic step, and blockage of its function appears unlikely to interfere with other essential steriod hormone levels. A number of aromatase inhibitors have been devised,[4,5] with differing modes of action, including reversible competitive inhibition, quasi-irreversible complexation to haem iron, irreversible binding, and suicide inhibition. Some of these compounds are in clinical use, but interest remains in producing new inhibitors with improved selectivity, which will not affect cytochrome *P*-450 enzymes involved in general steroid and other metabolic processes.

Our attention was drawn to the potential of 2-aryltetralin relatives as aromatase-substrate analogues.† Non-steroidal compounds generally metabolise at a slower rate than do steroid drugs, with clinical advantage.[6] Computer graphics indicate that the aryldecalin structure has similar geometry to the steroid ring system, and the estrogen-antagonist properties of aryltetralins supports this parallel.[7] We chose as our target the general structure **3**. This compound contains a spirodienone unit in which the steroid A/B angular methyl is replaced by a fused ring residue, which lacks the freedom of rotation of the methyl; repeated oxidation at steroid C-19 requires such rotation and would thus be prevented in analogue **3**. Further, the spiro ring would permit control over the stereochemistry of



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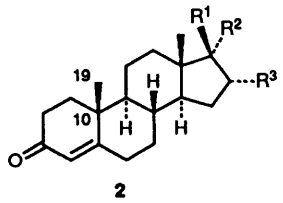

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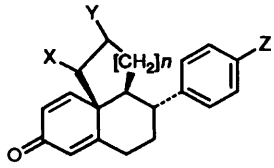
a; R^1R^2 = O, R^3 = H
b; R^1 = OH, R^2 = R^3 = H
c; R^1 = R^3 = OH, R^2 = H



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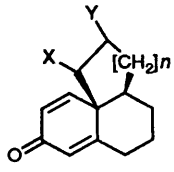

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substituents X, Y in the proximity of haem iron, with potential for enhancement of selectivity. The dienone moiety of model **3** mimics the androgen ring A, and the Δ^1 double bond promotes irreversible inhibition in certain steroid inhibitors.[8]

The major problem in the synthesis of compounds **3** was considered to be the requirement for methods for forming the tricyclospirodienone core **4**. Although some well known routes to spirodienones exist, their extension to tricyclo systems was expected to be limited by additional steric and other constraints. Our initial aim was, therefore, to devise a range of methods suitable for the structures of type **4** before proceeding to selected potential inhibitors. In this paper we report our results.[9]

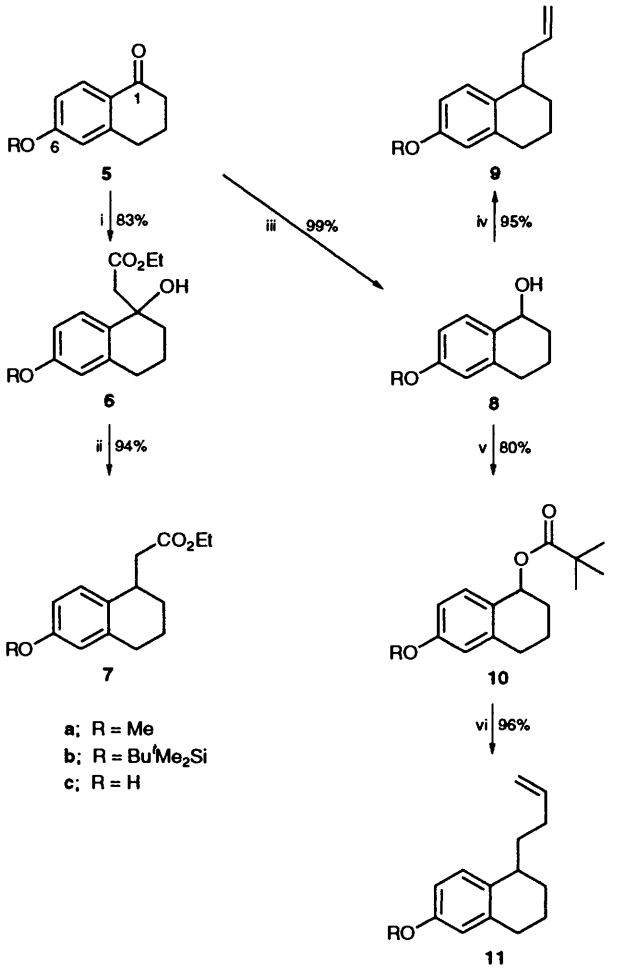
Results and Discussion‡

We decided to use 6-methoxytetralone **5a** as starting material,

† We are grateful to Dr. F. T. Boyle, Zeneca, for valuable discussions.

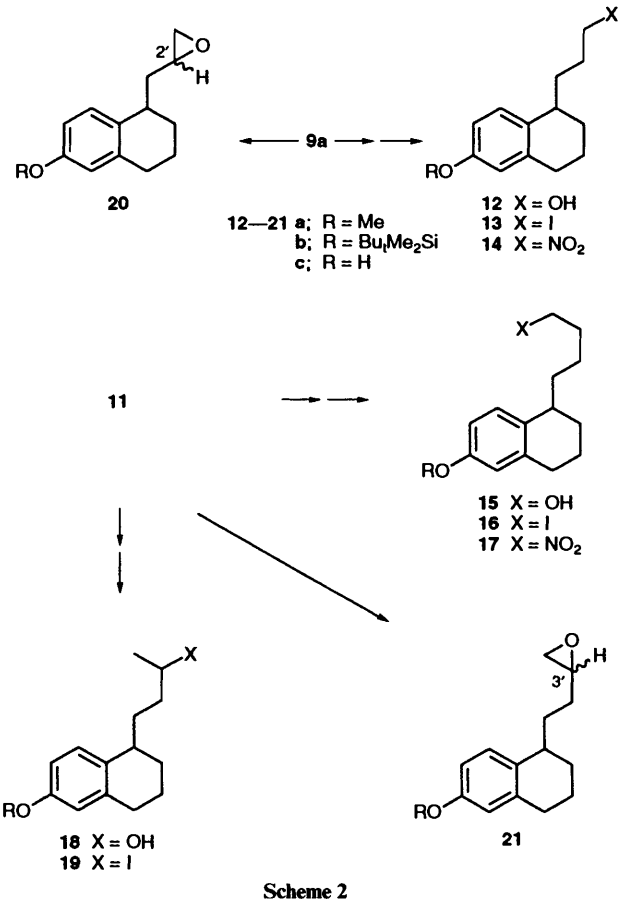
‡ Locants used in this section correspond to the numbering schemes displayed in the structures, and do not necessarily correspond to the numbering schemes used for the systematic nomenclature in the Experimental section.

and we needed to attach C_2, C_3 and C_4 side chains to tetralin C-1 to obtain the desired precursors to investigate various spirocyclisations. Despite the considerable industrial interest in tetralones and their relatives, very few methods for these operations have been reported and new approaches had to be investigated (Scheme 1).



Scheme 1 (Yields for R = Me). *Reagents and conditions:* i, $BrCH_2CO_2Et$, Zn–Hg; ii, H_2, Pt; iii, $NaBH_4$, MeOH; iv, $H_2C{=}CHCH_2SiMe_3$, ZnI_2, – 16 °C; v, Me_3CCOCl, pyridine; vi, $H_2C{=}CHCH_2CH_2Br$, Mg, Et_2O, 0 °C.

A C_2 side chain was added by employing a Reformatsky reaction as modified by Stork,[10] to yield the hydroxy ester **6a**; hydrogenolysis of the benzylic alcohol gave the desired ester **7a**. For the addition of a C_3 unit at C-1 it was found that reaction of 6-methoxytetralol **8a** with allyltrimethylsilane at −20 °C catalysed by zinc iodide[11] gave the allyltetralin **9a**. A C_4 side chain was introduced by preparation of the pivalate ester **10a** from 6-methoxytetralol **8a**, which was then displaced by but-3-enylmagnesium bromide[12] to provide the 1-butenyltetralin **11a** in high yield. The major complication of these preparations was the tendency for C-1 substitution to be superceded by elimination; thus, when attempts were made to replace the pivaloyloxy group using allyl-, rather than but-3-enylmagnesium bromide, the only product was 3,4-dihydro-6-methoxynaphthalene. Similarly trials with copper-promoted Grignard reagents led to elimination as a competing pathway, which became the major route in the case of 6-*tert*-butyldimethylsiloxy derivatives. In this last case, substitution may be favoured by the more electron-releasing 6-methoxy group, while the Gilman reagents may be poorer nucleophiles than the corresponding Grignards because of steric bulk.

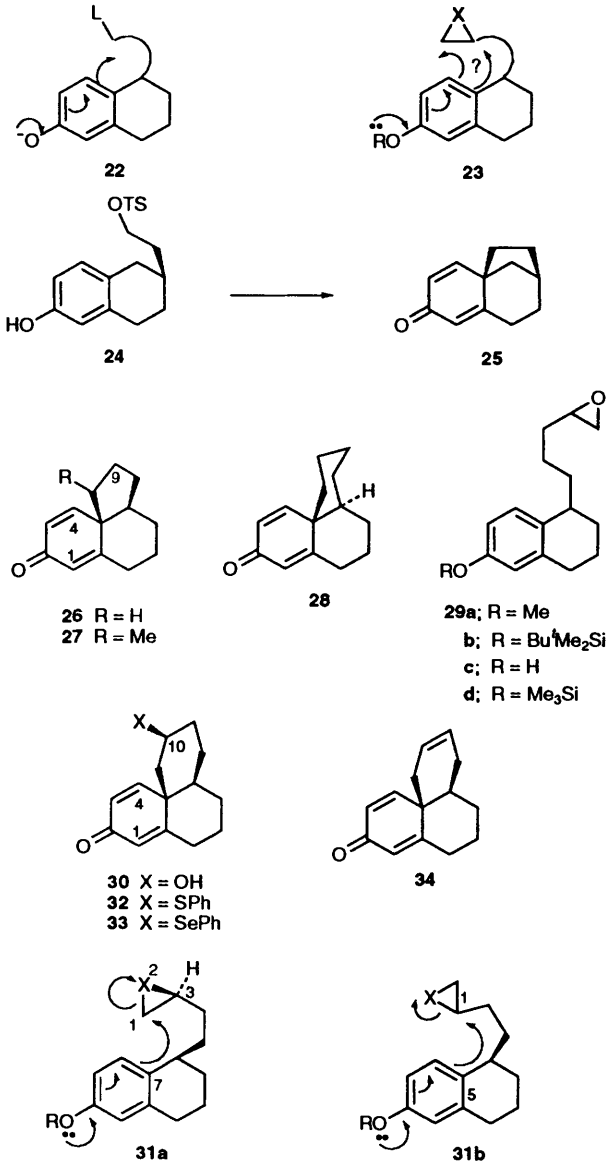


Scheme 2

Functional manipulation (Scheme 2) of the alkenyl units then provided the requisite substrates for investigation of spirocyclisation. Thus, *e.g.*, hydroboration–oxidation afforded the alcohols **12a** and **15a**, treatment of which with iodotrimethylsilane gave the corresponding iodides **13c** and **16c**, with concurrent demethylation. The secondary alcohol **18a** was obtained through acetoxymercuriation–demercuriation, and was converted into the corresponding phenolic iodide **19c**. The nitroalkanes **14c** and **17c** were prepared by reaction of the appropriate iodides with Amberlyst-supported nitrite. The epoxides **20c** and **21c** were accessed through epoxidation–desilylation of the alkenes **9b** and **11b**, obtained in turn from 6-*tert*-butyldimethylsiloxytetralone **5b**.

Our first attempts at spirocyclisation followed the best precedented route, that of anionic cyclisation as discovered by Winstein and Baird[13] and applied to both bicyclospiro and bicyclofused systems. However, we know of only one application to tricyclospirodienones, *i.e.* **24** ⟶ **25**.[14] Intramolecular phenolic alkylations can be classified into Ar_1^--*n* and Ar_2^--*n* types,[15] the subscripts denoting the position of ring closure. Ar_1^--3 and Ar_1^--5 types are favourable, whereas the Ar_1^--6 mode is relatively slow. Baldwin's generalisations, as applied to enolate anions,[16] may also be extended to cover such phenolate cyclisations.

We found in practice that spirocyclisations of type **22**, Ar_1^--5 or 6, are viable, but in cases **23** involving phenol-*exo*-ring closure with *endo*- or *exo-tet* ring opening, only one specific geometry is permitted. Thus, treatment of each iodide **13c**, **16c** and **19c** with potassium *tert*-butoxide–*tert*-butyl alcohol at reflux overnight gave the desired spiro compounds **26**–**28** in good yield; both diastereoisomers of iodide **19c** reacted, giving product **27** also as two diastereoisomers; inversion of configuration seems likely but is unproven. These cyclisations follow phenol-*exo* (*cf.* enol-*exo*)/5- or 6-*exo-tet* modes, both of



which are regarded as favourable within Baldwin's classification. The additional geometric constraints inherent in cyclisations from these bicyclic reactants clearly do not hinder cyclisation, in contrast to the cases below.

The epoxides **20c**, **21c** and **29c** (prepared in an analogous fashion to **21c** by using pent-1-enylmagnesium bromide) were prepared from the *tert*-butyldimethylsily derivatives of the corresponding phenolic alkenes by epoxidation [*m*-chloroperbenzoic acid (MCPBA)] and desilylation, and were treated with potassium *tert*-butoxide–*tert*-butyl alcohol at reflux over a period of 48 h. Phenolic epoxide **21c**, as a mixture of diastereoisomers, afforded dienone **30** as a single stereoisomer. The cyclohexanol structure, rather than the alternative hydroxymethyl cyclopentane, was shown *inter alia* by δ_C 67.08 (*C*HOH), and the stereochemistry was apparent from nuclear Overhauser enhancement (NOE) measurements (irradiation of 10-H, 4-H signal increases by 8.6%; irradiation of 4-H, 10-H signal increases by 8.3%). This structure can only be derived by cyclisation of diastereoisomer **21c** with 3'-H_α (60%), in an *endo* fashion. Thus, in these related cyclisations, a transition state resembling structure **31a** (X = O) was preferred over one like its rotamer **31b** (X = O); furthermore, only one stereochemistry is permitted. Thus, phenol-*exo*/7-*endo*-*tet* cyclisation was favoured over a phenol-*exo*/5-*exo*-*tet* reaction at a more substituted centre. This is in agreement with the seminal work of Stork *et al.*[17] on epoxy nitrile cyclisations; a preference for the 5-*exo*-*tet* mode was only observed with equal substitution at both competing centres. The phenolic epoxides **20c** and **29** both failed to cyclise on prolonged reflux in *tert*-butyl alcohol with potassium *tert*-butoxide, showing that neither 8- or 6-*endo* closure at a primary carbon, nor 4- or 6-*exo*-cyclisation at a secondary carbon, are kinetically viable. In contrast, Stork and Cohen[18] showed the 4-*exo*-*tet* route to be a good method for the preparation of cyclobutanes, and that 6-*endo* closure at a secondary centre was possible, although slow. Hence the cyclisations of epoxides investigated here are notably more constrained than in previous examples.

We then turned our attention to mechanistically related cationic processes. The butenyltetrahydronaphthol **11c** was treated at −16 °C with methyl benzenesulfenate boron trifluoride[19] to give rise to the sulfide **32** as the single stereoisomer shown, albeit in only 15% yield. The same naphthol was also treated with *N*-(phenylseleno)phthalimide[19,20] in dichloromethane at −70 °C to afford the phenyl selenide **33** in 28% yield, again as a single stereoisomer. The formation of a new six-, rather than five-, membered ring was shown by oxidation and thermal elimination of the sulfur function to provide the cyclohexene **34**, not the alternative methylenecyclopentane. It is clear from the epoxide example that only one phenylthiiranium stereoisomer and one phenylselenonium stereoisomer have the correct geometries for cyclisation, with yields 30 and 56% respectively.

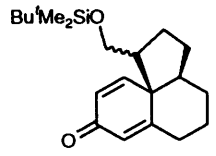
With the phenolic epoxides **20c** and **21c** in hand, it was of interest to examine their behaviour under acid catalysis. Epoxide **21c** was treated with boron trifluoride–diethyl ether in dichloromethane at −78 °C. The crude product exhibited the IR characteristics of a dienone, but on chromatography on silica underwent further reaction. Therefore, in a further experiment, the crude dienone was treated with *tert*-butylchlorodimethylsilane and imidazole before purification. Chromatography now gave the dienone **35** as a mixture (3 : 2) of diastereoisomers (43%). The formation of a five-, rather than a six-, membered ring was clearly shown by the presence of an hydroxymethylene group, δ_C 63.60 and 54.99. The formation of this 6.6.5 spiro ring system is in line with reaction through a secondary, not primary, carbocation with the kinetically preferred five-membered transition state.

The free primary alcohols **36** and **37** initially obtained isomerised to new products on silica gel G, or more efficiently in dichloromethane containing catalytic toluene-*p*-sulfonic acid (PTSA), to yield the separable tetracycles **38** and **39**, respectively, in which Michael addition of the hydroxy group to enone has occurred. The 9α-hydroxymethylene compound **36** is set up to form an O–C(4) bond, while the 9β-epimer **37** gives rise to an O–C(1) bond. Product **38** displays one olefinic hydrogen in the NMR spectrum, δ_H 5.90(s), while isomer **39** exhibits δ_H 5.92(d) and 6.69(d), each *J* 10.2.

Treatment of epoxide **29c** in dichloromethane at −78 °C with boron trifluoride–diethyletherate gave, after protection (BuᵗMe₂Si, TBDMS) of the hydroxy group in the crude product, the 6.6.6 spirodienone **40**, but only in trace quantities. Phenolic epoxide **20c** was recovered unchanged from a parallel reaction; this may indicate that participation of the aryl group is necessary for epoxide-ring opening under these conditions.

We also report that a cationic spirocyclisation (using boron trifluoride) of diazo ketone **41**, prepared from ester **7a** *via* acetoxy acid **42**, gave the spirodienedione **43** (62%), following the precedents set by Beames and Mander.[21]

Radical methods offered further scope for entry into the desired spiro tricyclo systems, with new functional assemblies. We were attracted by the unexploited possibilities offered by the intramolecular oxidative coupling of phenolate and nitronate functions. Three, closely related, examples of such reactions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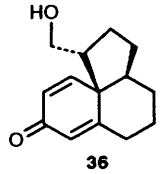
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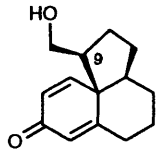
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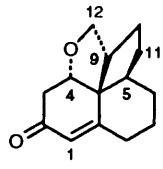
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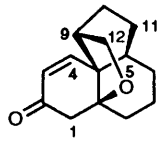
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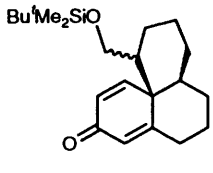
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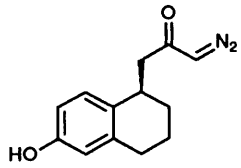
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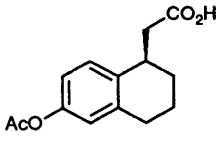
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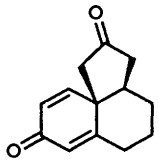
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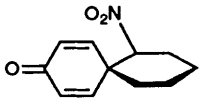
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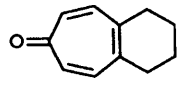
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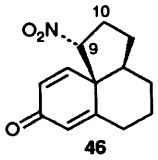
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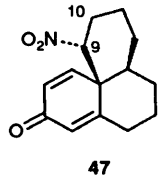
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have been reported;[22] *e.g.*, *p*-(5-nitropentyl)phenol was oxidised with iron(III) to the spirodienone **44**. This product was base labile, rearranging to the tropolone **45**. It appeared to us that this novel reaction would lead us to the desired ring systems, and that in a tricyclospirodienone the geometry would not allow rearrangement to tropolones.

Reaction of the nitro naphthol **14c** (see above) in a two-phase dichloromethane–aq. potassium ferricyanide*–potassium hydroxide system, with high reactant dilution, gave the desired product **46** as a single stereoisomer (70%). The stereochemistry was deduced from ^{1}H NMR data; models show the 9-H–C-9–C-10–10-H^a and 9-H–C-9–C-10–10-H^b dihedrals to be approximately 20°, 40° for α-NO_2, and approximately 20°, 100° for β-NO_2. The spectrum shows $J_{9,10a} = J_{9,10b} = 8.8$ Hz, supporting the 9α-nitro configuration.

For a 6.6.6-fused system, a C_4 side chain was needed; this was available in the nitrophenol **17c** (see above). This, under the reaction conditions above, gave the desired spirodienone **47** in 66% yield. The α-nitro stereochemistry is demonstrated by $J_{9ax,10ax}$ 12.3, $J_{9ax,10eq}$ 4.3 Hz. The stereospecificity of these couplings is not caused by thermodynamic factors, since no 1-deuteriation was observed under dichloromethane–potassium hydroxide–D_2O conditions similar to those of the coupling. Kinetic control through secondary orbital overlap may be implied.

With these results in hand the way is cleared to turn to the synthesis of aryltricyclospirodienones of biological interest, and this work is now in progress.

Experimental

Unless otherwise stated the following apply. M.p.s. were determined using a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded using Perkin-Elmer 1600 or 1720-X spectrometers, for solutions in chloroform. UV spectra were recorded using a Philips PU 8720 spectrophotometer. ^{1}H NMR spectra were obtained on Bruker WP80SY, WM250, AM400 and JEOL FX270 instruments at 80, 250, 400 and 270 MHz, respectively. All NMR measurements were obtained for dilute solutions in deuteriochloroform containing tetramethylsilane as internal standard. Chemical shifts (δ) are given in ppm; coupling constants (J) are given in Hz. ^{13}C NMR spectra were recorded on JEOL FX90Q, FX270 and Bruker WM250 and AM400 instruments at 22.5, 67.5, 62.5 and 100 MHz, respectively. Designations were determined by DEPT pulse sequences, in conjugation with broad-band decoupling. Mass spectra were recorded on AEI MS902 or on a VG 707OE instrument by electron impact. Analytical TLC was performed on Camlab silica gel HF_{254} plates, which were visualised with UV light (254 nm), or *p*-anisaldehyde spray reagent. Column chromatography was performed using silica gel 60. Evaporation refers to evaporation under reduced pressure. Light petroleum refers to the fraction boiling in the range 40–60 °C. Ether refers to diethyl ether.

1,2,3,4-*Tetrahydro*-6-*methoxy*-1-*naphthyl Pivalate* **10a**.—1,2,3,4-Tetrahydro-6-methoxy-1-naphthol **8a** (9.5 g, 0.053 mol) was dissolved in dry pyridine (10.5 g, 2.5 and equiv.) and the solution was stirred under nitrogen. Pivaloyl chloride (7.75 g, 0.064 mol, 1.2 mol equiv.) was slowly added (5 min) and the mixture was then stirred for 1.5 h. Ether (50 cm^3) was then added and the pyridine was removed by successive washes with aq. copper sulfate. The ethereal solution was then washed successively with aq. sodium hydrogen carbonate and brine, dried ($MgSO_4$), filtered and evaporated to give a brown oil. This was purified by column chromatography; elution with 25% ether–light petroleum gave the *title compound* **10a** as a clear oil (11.2 g, 80%). A small sample solidified in the fridge and was recrystallised from light petroleum to give crystals, m.p. 42.5–43.5 °C (Found: C, 73.4; H, 8.7%; M$^+$, 262.160. $C_{16}H_{22}O_3$ requires C, 73.24; H, 8.46%; M, 262.157); ν_{max}(KBr)/cm^{-1} 2967, 2940, 2875, 1709, 1611, 1504, 1038 and 867; δ_H(80 MHz) 1.19 (9

* Potassium hexacyanoferrate(III), $K_3[Fe(CN)_6]$.

H, s, CMe_3), 1.86 (4 H, m, 2-, 3-H_2), 2.75 (2 H, m, 4-H_2), 3.76 (3 H, s, OMe), 5.98 (1 H, br t, *J* 3.9, 1-H), 6.55–6.80 (2 H, m, 5-, 7-H) and 7.15 (1 H, d, *J* 9.1, 8-H); δ_C(67.5 MHz) 18.96 (C-3), 27.24 [CH_2]$_3$), 29.14 and 29.33 (C-2, -4), 38.67 (CMe_3), 55.01 (OMe), 69.29 (C-1), 112.29 and 113.14 (C-5, -7), 127.58 (C-8a), 130.55 (C-8), 139.26 (C-4a), 158.98 (C-6) and 178.06 (C=O).

1-(*But*-3-*enyl*)-1,2,3,4-*tetrahydro*-6-*methoxynaphthalene* **11a**.—The pivalate **10a** (2.50 g, 9.54 mmol) was dissolved in dry ether (10 cm^3) and the solution was stirred under nitrogen in an ice–salt-bath. An ethereal solution of but-3-enylmagnesium bromide [prepared from 4-bromobut-1-ene (2.70 g, 0.020 mol), magnesium (0.57 g, 0.023 mol) and dry ether (10 cm^3)] was slowly added. After the mixture had been stirred for 10 min, the ice–salt-bath was replaced by an ice-bath and the mixture was stirred overnight. The reaction was then quenched with cold, dil. hydrochloric acid and the aqueous layer was separated. The ethereal solution was washed with brine, dried ($MgSO_4$) and evaporated, and the residue was purified by column chromatography with 10% ether–light petroleum as eluent to yield the *title compound* **11a** as a clear oil (1.98 g, 96%) (Found: C, 83.5; H, 9.5%; M^+, 216.150. $C_{15}H_{20}O$ requires C, 83.27; H, 9.33%; *M*, 216.151); ν_{max}(film)/cm^{-1} 3074, 2995, 2931, 2857, 1639, 1608, 1500 and 909; λ_{max}(EtOH)/nm 218 (ε/dm^3 mol^{-1} cm^{-1} 10 070) and 280 (2800); δ_H(250 MHz) 1.55–1.90 (6 H, m, 2- and 3-H_2, CH_2=CHCH_2CH_2), 2.15 (2 H, m, CH_2=CHCH_2), 2.72 (3 H, m, 1- and 4-H_2). 3.75 (3 H, s, OMe), 4.96 (1 H, d, *J* 10.0, C*H*H=CH), 5.03 (1 H, dd, *J* 17.0 and 2.0, CH*H*=CH), 5.85 (1 H, m, CH_2=C*H*), 6.58 (1 H, m, 5-H), 6.69 (1 H, dd, *J* 8.5 and 2.7, 7-H) and 7.14 (1 H, d, *J* 8.5, 8-H); δ_C(22.5 MHz) 20.10, 27.85, 30.23, 31.64 and 36.35 (5 × CH_2), 36.51 (C-1), 55.21 (OMe), 112.03 and 113.77 (C-5 and -7), 114.53 (CH_2=CH), 129.53 (C-8), 133.54 (C-8a), 138.31 (C-4a), 139.07 (CH_2=*C*H) and 157.59 (C-6).

1-*Allyl*-1,2,3,4-*tetrahydro*-6-*methoxynaphthalene* **9a**.—The 6-methoxy-1-naphthol **8a** (2.40 g, 13.5 mmol) was dissolved in dry dichloromethane (50 cm^3) and the solution was cooled in a solid CO_2–tetrachloromethane-bath. Zinc iodide (4.73 g, 14.8 mmol) and allyltrimethylsilane (1.69 g, 14.8 mmol) were added and the resulting mixture was stirred under nitrogen for 15 min. The mixture was then filtered, washed with water (50 cm^3), dried ($MgSO_4$) and filtered. Evaporation yielded a brown oil, which was purified by column chromatography; elution with 10% ether–light petroleum afforded *title compound* **9a** as a clear oil (2.59 g, 95%) (Found: C, 83.3; H, 9.2%; M^+, 202.133. $C_{14}H_{18}O$ requires C, 83.11; H, 8.97%; M, 202.135); ν_{max}(film)/cm^{-1} 3074, 2931, 1640, 1608, 1501, 911 and 834; λ_{max}(EtOH)/nm 278 (ε 2880); δ_H(250 MHz) 1.75 (4 H, m, 2- and 3-H_2), 2.25–2.55 (2 H, m, CH_2=CHCH_2) 2.75 (2 H, m, 4-H_2), 2.79 (1 H, m, 1-H), 3.77 (3 H, s, OMe), 5.07 (2 H, m, CH_2=CH), 5.82 (1 H, m, CH_2=C*H*), 6.60 (1 H, d, *J* 2.8, 5-H), 6.70 (1 H, dd, *J* 8.5 and 2.8, 7-H) and 7.11 (1 H, d, *J* 8.5, 8-C); δ_C(22.5 MHz) 20.10, 27.85 and 30.29 (3 × CH_2), 36.89 (C-1), 41.55 (CH_2=CH*C*H_2), 55.21 (OMe), 112.09 and 113.77 (C-5 and -7), 116.04 (CH_2=CH), 128.48 (C-8), 132.83 (C-8a), 137.60 (CH_2=*C*H), 138.47 (C-4a) and 157.65 (C-6).

6-tert-*Butyldimethylsiloxy*-3,4-*dihydronaphthalen*-1(2H)-*one* **5b**.—3,4-Dihydro-6-hydroxynaphthalen-1(2*H*)-one **5c** (16.9 g, (0.104 mol) was dissolved in dry dimethylformamide (DMF) (100 cm^3). *tert*-Butylchlorodimethylsilane (17.2 g, 0.114 mol) and imidazole (15.6 g, 0.229 mol) were added, and the resulting solution was stirred under nitrogen at room temperature for 3 h. The solution was then poured into water (500 cm^3) and extracted with ether (200 cm^3). The organic layer was washed successively with water (3 × 100 cm^3) and brine (100 cm^3) and was then dried ($MgSO_4$) and filtered. Evaporation yielded a dark brown oil, which was purified by column chromatography; elution with 50% ether–light petroleum afforded 6-tert-*butyldimethylsiloxy*-3,4-*dihydronaphthalen*-1(2H)-*one* **5b** (15.5 g, 92%) as a light brown oil. A small sample crystallised in the fridge after several weeks, and was recrystallised from hexane to yield crystals, m.p. 35–35.5 °C (Found: C, 69.8; H, 9.1%; M^+, 276.153. $C_{16}H_{24}O_2Si$ requires C, 69.53; H, 8.76%; *M*, 276.155); ν_{max}(film)/cm^{-1} 3075, 3044, 2953, 2927, 2894, 2856, 1676, 1602, 899, 837 and 783; λ_{max}(EtOH)/nm 221 (ε 17 700) and 270 (23 200); δ_H(250 MHz) 0.24 (6 H, s, $SiMe_2$), 0.99 (9 H, s, $SiCMe_3$), 2.11 (2 H, m, 3-H_2), 2.60 (2 H, t, *J* 6.4, 2-H_2), 2.89 (2 H, t, *J* 6.0, 4-H_2), 6.67 (1 H, s, 5-H), 6.74 (1 H, d, *J* 9.0, 7-H) and 7.95 (1 H, d, *J* 9.0, 8-H); δ_C(22.5 MHz) −4.37 ($SiMe_2$), 18.16 (Si*C*Me_3), 23.36 (C-3), 25.58 ($SiCMe_3$), 29.91 and 38.91 (C-2 and -4), 118.65 and 119.09 (C-5 and -7), 126.89 (C-8a), 129.49 (C-8), 146.71 (C-4a), 160.20 (C-6) and 196.83 (C=O).

6-tert-*Butyldimethylsiloxy*-1,2,3,4-*tetrahydro*-1-*naphthol* **8b**.—The naphthone **5b** (7.94 g, 0.029 mol) was dissolved in methanol (80 cm^3), and sodium borohydride (0.60 g, 0.016 mol) was carefully added. The mixture was stirred for 3 h at room temperature and was then poured into water (150 cm^3) and extracted with ether (3 × 50 cm^3). The combined extracts were washed with water (2 × 50 cm^3), dried ($MgSO_4$), and filtered. Evaporation yielded a light brown oil, which was purified by column chromatography and elution with 50% ether–light petroleum to afford 6-tert-*butyldimethylsiloxy*-1,2,3,4-*tetrahydro*-1-*naphthol* **8b** (7.45 g, 93%) as a clear oil (Found: M^+, 278.169. $C_{16}H_{26}O_2Si$ requires *M*, 278.170); ν_{max}(film)/cm^{-1} 3343br, 2932, 2886, 2859, 1609, 1256, 873, 840 and 780; λ_{max}(EtOH)/nm 220 (ε 5050) and 274 (610); δ_H(250 MHz) 0.18 (6 H, s, $SiMe_2$), 0.98 (9 H, s, $SiCMe_3$), 1.60–2.05 (4 H, m, 2- and 3-H_2), 1.72 (1 H, br s, OH), 2.69 (2 H, m, 2-H_2), 4.71 (1 H, m, C*H*OH), 6.50–6.75 (2 H, m, 5- and 7-H) and 7.34 (1 H, d, *J* 8.2, 8-H); δ_C(22.5 MHz) −4.43 ($SiMe_2$), 18.16 (Si*C*Me_3). 18.70 (C-3), 25.69 ($SiCMe_3$), 29.43 and 32.41 (C-2 and -4), 67.51 (CHOH), 118.00 and 119.68 (C-5 and -7), 129.87 (C-8), 131.98 (C-8a), 138.37 (C-4a) and 154.79 (C-6).

1-*Allyl*-6-tert-*butyldimethylsiloxy*-1,2,3,4-*tetrahydronaphthalene* **9b**.—6-*tert*-Butyldimethylsiloxy-1,2,3,4-tetrahydro-1-naphthol (6.75 g, 0.024 mol) was dissolved in dry dichloromethane (100 cm^3) and the solution was cooled in a solid CO_2–tetrachloromethane-bath. Zinc iodide (8.52 g, 0.027 mol) and allyltrimethylsilane (3.04 g, 0.027 mol) were added and the resulting mixture was stirred under nitrogen for 15 min. The mixture was then filtered, washed with water (50 cm^3), dried ($MgSO_4$), and filtered. Evaporation yielded a brown oil, which was purified by column chromatography and elution with 5% ether–light petroleum to afford 1-*allyl*-6-tert-*butyldimethylsiloxytetrahydronaphthalene* **9b** as a clear oil (7.18 g, 98%) (Found: M^+, 302.205. $C_{19}H_{30}OSi$ requires *M*, 302.207); ν_{max}(film)/cm^{-1} 3075, 2930, 2858, 1640, 1608, 1477, 839 and 780; λ_{max}(EtOH)/nm 276 (ε 2190); δ_H(250 MHz) 0.19 (6 H, s, $SiMe_2$), 0.98 (9 H, s, $SiCMe_3$) 1.75 (4 H, m, 2- and 3-H_2), 2.25–2.55 (2 H, m, CH_2=CHCH_2), 2.67 (2 H, m, 4-H_2), 2.77 (1 H, m, 1-H), 5.04 (2 H, m, CH_2=CH), 5.82 (1 H, m, CH_2=C*H*), 6.53 (1 H, d, *J* 2.6, 5-H), 6.60 (1 H, dd, *J* 8.3 and 2.6, 7-H) and 7.03 (1 H, d, *J* 8.3, 8-H); δ_C(22.5 MHz) −4.11 ($SiMe_2$), 18.42 (Si*C*Me_3), 20.10 (CH_2), 25.85 (Si*C*Me_3), 27.80 and 30.14 (2 × CH_2), 37.09 (C-1), 41.61 (CH_2=CH*C*H_2), 116.09 (CH_2=CH), 117.67 and 120.05 (C-H and C-7), 129.42 (C-8), 133.43 (C-8a), 137.77 (CH_2=*C*H), 138.53 (C-4a) and 153.47 (C-6).

6-tert-*Butyldimethylsiloxy*-1,2,3,4-*tetrahydro*-1-*naphthyl Pivalate* **10b**.—The naphthol **8b** (7.30 g, 0.026 mol) was dissolved in dry pyridine (5.2 g, 2.5 mol equiv.) and the solution

was stirred under nitrogen. Pivaloyl chloride (3.76 g, 0.031 mol, 1.2 mol equiv.) was slowly added (5 min) and the mixture was then stirred for 1.5 h. Ether (50 cm^3) was then added and the pyridine was removed by successive washes with aq. copper sulfate. The ethereal solution was then washed successively with aq. sodium hydrogen carbonate and brine, dried ($MgSO_4$), filtered, and evaporated to give a brown oil. This was purified by column chromatography and elution with 10% ether–light petroleum to give the *title compound* **10b** as a light brown oil (7.22 g, 76%) (Found: C, 69.7; H, 9.2%; M^+, 362.227. $C_{21}H_{34}O_3Si$ requires C, 69.57; H, 9.46%; *M*, 362.228); ν_{max}(film)/cm^{-1} 2957, 2932, 2860, 1724, 1611, 872 and 841; λ_{max}(EtOH)/nm 222 (ε 8450) and 274 (820); δ_H(80 MHz) 0.24 (6 H, s, $SiMe_2$), 0.98 (9 H, s, $SiCMe_3$), 1.11 (9 H, s, CMe_3), 1.89 (4 H, m, 2- and 3-H_2), 2.73 (2 H, m, 4-H_2), 5.90 (1 H, br t, *J* 3.7, 1-H), 6.55–6.75 (2 H, m, 5- and 7-H) and 7.08 (1 H, d, *J* 8.3, 8-H); δ_C(22.5 MHz) −4.43 ($SiMe_2$), 18.05 ($SiCMe_3$), 18.92 (C-3), 25.63 ($SiCMe_3$), 27.04 (CMe_3), 29.21 (C-2 and -4), 38.64 (CMe_3), 69.35 (C-1), 117.89 and 119.63 (C-5 and -7), 127.92 (C-8a), 130.35 (C-8), 139.08 (C-4a), 155.11 (C-6) and 177.70 (C=O).

1-(*But*-3-*enyl*)-6-tert-*butyldimethylsiloxy*-1,2,3,4-*tetrahydronaphthalene* **11b**.—6-*tert*-Butyldimethylsiloxy-1,2,3,4-tetrahydronaphthyl pivalate **10b** (4.75 g, 0.013 mol) was dissolved in dry ether (25 cm^3) and the solution was stirred under nitrogen in an ice–salt-bath. An ethereal solution of but-3-enylmagnesium bromide [prepared from 4-bromobut-1-ene (3.51 g, 0.026 mol), magnesium (0.73 g, 0.03 mol) and dry ether (15 cm^3)] was slowly added. After the mixture had been stirred for 10 min, the ice–salt-bath was replaced by an ice-bath and the mixture was stirred overnight, during which time the temperature was not allowed to rise above 0 °C. The reaction was then quenched with cold, dil. hydrochloric acid and the aqueous layer was separated. The ethereal solution was washed with brine, dried ($MgSO_4$), and evaporated, and the residue purified by column chromatograhy, and elution with 5% ether–light petroleum yielded the *title compound* **11b** as a clear oil (3.80 g, 92%) (Found: C, 76.2; H, 10.1%; M^+, 316.220. $C_{20}H_{32}OSi$ requires C, 75.90; H, 10.20%; *M*, 316.222); ν_{max}(film)/cm^{-1} 3076, 2995, 2930, 2858, 1641, 1609, 1498, 959, 910 and 840; λ_{max}(EtOH)/nm 275 (ε 1500); δ_H(250 MHz) 0.20 (6 H, s, $SiMe_2$), 0.97 (9 H, s, $SiCMe_3$), 1.55–1.90 (6 H, m, 2- and 3-H_2, CH_2=CHCH_2CH_2), 2.15 (2 H, m, CH_2=CHCH_2), 2.72 (3 H, m, 1-H and 4-H_2), 4.95 (1 H, d, *J* 9.7, C*H*H=CH), 5.03 (1 H, d, *J* 17.3, b-CH*H*=CH), 5.83 (1 H, m, CH_2=C*H*), 6.53 (1 H, m, 5-H), 6.59 (1 H, d, *J* 8.3, 7-H) and 6.99 (1 H, d, *J* 8.3, 8-H); δ_C(22.5 MHz) −4.11 ($SiMe_3$), 18.41 ($SiCMe_3$), 20.15 (CH_2) 25.95 ($SiCMe_3$), 27.96, 30.12, 31.75 and 36.46 (4 × CH_2), 36.68 (C-1), 114.58 (CH_2=CH), 117.61 and 120.05 (C-5 and -7), 129.42 (C-6), 134.14 (C-8a), 138.36 (C-4a), 139.23 (CH_2=*C*H) and 153.42 (C-6).

6-tert-*Butyldimethylsiloxy*-1,2,3,4-*tetrahydro*-1-(*pent*-4-*enyl*)-*naphthalene*.—6-*tert*-Butyldimethylsiloxy-1,2,3,4-tetrahydronaphthyl pivalate **10b** (1.21 g, 3.34 mmol) was dissolved in dry ether (40 cm^3) and the solution was stirred under nitrogen in an ice–salt-bath. An ethereal solution of pent-4-enylmagnesium bromide [prepared from 5-bromopent-1-ene (1.05 g, 7 mmol), magnesium (0.24 g, 10 mmol) and dry ether (10 cm^3)] was slowly added. After the mixture had been stirred for 10 min, the ice–salt-bath was replaced by an ice-bath and the mixture was stirred overnight, while the temperature was not allowed to rise above 0 °C. The reaction was then quenched with cold, dil. hydrochloric acid and the aqueous layer was separated. The ethereal solution was washed with brine, dried ($MgSO_4$) and evaporated, and the residue was purified by column chromatography with 1% ether–light petroleum as eluent to yield the *title compound* as a clear oil (0.96 g, 87%) (Found: M^+, 330.239. $C_{21}H_{34}OSi$ requires M, 330.238); ν_{max}(film)/cm^{-1} 3077, 2930, 2858, 1641, 1609, 1498 and 910; λ_{max}(EtOH)/nm 277 (ε 4790); δ_H(250 MHz) 0.23 (6 H, s, $SiMe_2$), 1.01 (9 H, s, $SiCMe_3$), 1.40–1.95 (8 H, m, 2- and 3-H_2, CH_2=CHCH_2-CH_2CH_2), 2.15 (2 H, m, CH_2=CHCH_2), 2.73 (3 H, m, 1-H and 4-H_2), 5.03 (2 H, m, CH_2=CH), 5.88 (1 H, m, CH_2=C*H*), 6.57 (1 H, d, *J* 2.6, 5-H), 6.67 (1 H, dd, *J* 8.3 and 2.6, 7-H) and 7.04 (1 H, d, *J* 8.3, 8-H); δ_C(22.5 MHz) −4.17 ($SiMe_3$), 18.37 ($SiCMe_3$), 20.15 (CH_2), 25.90 ($SiCMe_3$), 26.87, 28.00, 30.12, 34.18 and 36.68 (5 × CH_2), 37.06 (C-1), 114.53 (CH_2=CH), 117.51 and 118.85 (C-5 and -7), 128.32 (C-8), 134.29 (C-8a), 138.25 (C-4a), 139.12 (CH_2=*C*H) and 153.26 (C-6).

3-(1,2,3,4-*Tetrahydro*-6-*methoxy*-1-*naphthyl*)*propan*-1-*ol* **12a**.—The alkene **9a** (2.88 g, 14.3 mmol) was dissolved in hexane (30 cm^3) and the solution was cooled to 0 °C under nitrogen. Hydroboration was achieved by dropwise addition of borane–methyl sulfide complex (2.5 cm^3; 2 mol dm^{-3} in toluene). Following the addition, the cooling bath was removed and the solution was stirred at room temperature for 3.5 h. The solution was then refluxed for 1.5 h, after which ethanol (30 cm^3) and 2 mol dm^{-3} aq. sodium hydroxide (10 cm^3) were added. The mixture was cooled to 0 °C and aq. 30% hydrogen peroxide (1.7 cm^3) was carefully added. The mixture was refluxed for 1 h and then poured into ice–water (100 cm^3) and extracted with ether (3 × 50 cm^3). The combined extracts were washed with brine, dried ($MgSO_4$) and filtered. Evaporation yielded an oily residue, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford 3-(1,2,3,4-tetrahydromethoxy-1-naphthyl)propan-1-ol[23] **12a** (2.50 g, 80%) as a clear oil (Found: C, 76.25; 9.4%; M^+, 220.147. Calc. for $C_{14}H_{20}O_2$ C, 76.31; H, 9.16%; M, 220.146); ν_{max}(film)/cm^{-1} 3352vbr, 2933, 2862, 1608, 1500, 1255, 1045, 910, 874 and 835; λ_{max}(EtOH)/nm 279 (ε 2980) and 286 (2700); δ_H(400 MHz) 1.50–1.95 (8 H, m, 4 × CH_2), 2.06 (1 H, s, OH), 2.72 (3 H, m, 1-H and 4-H_2), 3.63 (2 H, t, *J* 6.1, CH_2OH), 3.75 (3 H, s, OMe), 6.58 (1 H, d, *J* 2.5, 5-H), 6.68 (1 H, dd, *J* 8.5 and 2.5, 7-H) and 7.07 (1 H, d, *J* 8.5, 8-H); δ_C(22.5 MHz) 19.99, 27.90 30.01 and 30.44 (4 × CH_2), 32.94 (C-4), 36.76 (C-1), 55.10 (MeO), 62.90 (CH_2OH), 111.82, 113.61 (C-5 and -7), 129.26 (C-8), 133.32 (C-8a), 138.15 (C-4a) and 157.32 (C-6).

5,6,7,8-*Tetrahydro*-5-(3-*iodopropyl*)-2-*naphthol* **13c**.—A mixture of the alcohol **12a** (0.56 g, 2.58 mmol) sodium iodide (2.13 g, 14.3 mmol, 5.5 mol equiv.), chlorotrimethylsilane (1.40 g, 12.9 mmol, 5 mol equiv.) and dry acetonitrile (30 cm^3) was heated under reflux overnight under nitrogen and was then poured into ice–water (100 cm^3). The mixture was extracted with ether (3 × 50 cm^3) and the combined extracts were washed with brine, dried ($MgSO_4$), filtered and evaporated. The resulting dark brown residue was purified by column chromatography with 25% ether–light petroleum as eluent to yield the *title iodide* **13c** as a light red-brown oil (0.65 g, 81%) (Found: M^+, 316.032. $C_{13}H_{17}IO$ requires M, 316.032); ν_{max}(film)/cm^{-1} 3346vbr, 3018, 2929, 2858, 1611, 1498, 927 and 869; λ_{max}(EtOH)/nm 281 (ε 2300); δ_H(250 MHz) 1.60–1.90 (8 H, m, 4 × CH_2), 2.69 (3 H, m, 5-H and 8-H_2), 3.19 (2 H, m, CH_2I), 4.90 (1 H, br s, OH), 6.52 (1 H, d, *J* 2.7, 1-H), 6.61 (1 H, dd, *J* 8.3 and 2.7, 3-H) and 7.02 (1 H, d, *J* 8.3, 4-H); δ_C(22.5 MHz) 7.21 (CH_2I), 20.05, 27.96, 29.91 and 31.42 (4 × CH_2), 36.25 (C-5), 37.82 (C-8), 113.17 and 115.45 (C-1 and -3), 129.64 (C-4), 133.00 (C-4a), 138.63 (C-8a) and 153.37 (C-2).

4-(1,2,3,4-*Tetrahydro*-6-*methoxy*-1-*naphthyl*)*butan*-1-*ol* **15a**.—The alkene **11a** (0.60 g, 2.78 mmol) was dissolved in hexane (10 cm^3) and the solution was cooled to 0 °C under nitrogen. Hydroboration was achieved by dropwise addition of borane–

methyl sulfide complex (0.5 cm^3; 2 mol dm^{-3} in toluene). Following the addition, the cooling bath was removed and the solution was stirred at room temperature for 1 h before being refluxed for 1 h, after which ethanol (10 cm^3) and 2 mol dm^{-3} aq. sodium hydroxide (2 cm^3) were added. The mixture was cooled to 0 °C and aq. 30% hydrogen peroxide (0.35 cm^3) was carefully added. The mixture was refluxed for 1 h and then poured into ice–water (30 cm^3) and extracted with ether (3 × 15 cm^3). The combined extracts were washed with brine, dried ($MgSO_4$) and filtered. Evaporation yielded an oily residue, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford the *title compound* **15a** (0.57 g, 88%) as a clear oil (Found: C, 77.0; H, 9.65%; M^+, 234.162. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46%; *M*, 234.162); ν_{max}(film)/cm^{-1} 3355vbr, 2932, 2860, 1608, 1500, 1254, 1041, 870, 835 and 811; λ_{max}(EtOH)/nm 279 (ε 1500); δ_H(250 MHz) 1.40–1.90 (10 H, m, 5 × CH_2), 2.72 (3 H, m, 1-H and 4-H_2), 3.65 (2 H, t, *J* 6.4, CH_2OH), 3.76 (3 H, s, OMe), 6.59 (1 H, d, *J* 2.7, 5-H), 6.69 (1 H, dd, *J* 8.5 and 2.7, 7-H) and 7.07 (1 H, d, *J* 8.5, 8-H); δ_C(22.5 MHz) 20.05, 23.62, 27.84, 30.18 and 33.16 (5 × CH_2), 36.90 (1-H), 55.27 (MeO), 62.90 (CH_2OH), 111.98 and 113.66 (C-5 and -7), 129.42 (C-6), 133.65 (C-8a), 138.25 (C-4a) and 157.38 (C-6).

5,6,7,8-*Tetrahydro*-5-(4-*iodobutyl*)-2-*naphthol* **16c**.—A mixture of the alcohol **15a** (2.30 g, 9.83 mmol), sodium iodide (8.1 g, 0.054 mol, 5.5 mol equiv.), chlorotrimethylsilane (5.3 g, 0.048 mol, 5 mol equiv.) and dry acetonitrile (30 cm^3) were heated under reflux for 2 h under nitrogen and was then poured into ice–water (100 cm^3). The mixture was extracted with ether (3 × 50 cm^3) and the combined extracts were washed with brine, dried ($MgSO_4$), filtered and evaporated. The resulting dark brown residue was purified by column chromatography with 50% ether–light petroleum as eluent to yield the *title iodide* **16c** as a light red-brown oil (2.85 g, 88%) (Found: M^+, 330.054. $C_{14}H_{19}IO$ requires *M*, 330.048); ν_{max}(film)/cm^{-1} 3360, 3017, 2930, 2856, 1613, 1503, 927, 869, 838 and 813; λ_{max}(EtOH)/nm 282 (ε 2300); δ_H(250 MHz) 1.40–2.00 (10 H, m, 5 × CH_2), 2.86 (3 H, m, 5-H and 8-H_2), 3.19 (2 H, tt, *J* 8.5 and 2.5, CH_2I) 4.96 (1 H, br s, OH), 6.52 (1 H, d, *J* 2.6, 1-H), 6.61 (1 H, dd, *J* 8.4 and 2.6, 3-H) and 7.00 (1 H, d, *J* 8.4, 4-H); δ_C(22.5 MHz) 7.05 (CH_2I), 20.00, 27.85, 28.39, 29.96, 33.86 and 35.98 (6 × CH_2), 36.90 (C-5), 113.17 and 115.39 (C-1 and -3), 129.64 (C-4), 133.60 (C-4a), 138.69 (C-8a) and 153.21 (C-2).

4-(1,2,3,4-*Tetrahydro*-6-*methoxy*-1-*naphthyl*)*butan*-2-*ol* **18a**.—A solution of alkene **11a** (1.08 g, 5 mmol) in tetrahydrofuran (THF) (2.5 cm^3) was added to a mixture of mercury(II) acetate (1.60 g, 5 mmol), water (5 cm^3) and THF (2.5 cm^3) and the reaction mixture was stirred at room temperature for 2 h. A solution of sodium borohydride (0.38 g, 10 mmol) in 2 mol dm^{-3} aq. sodium hydroxide (12 cm^3) was then added, causing an almost instantaneous precipitation of mercury. The liquid mixture was decanted, poured into water (50 cm^3), and extracted with ether (3 × 30 cm^3). The combined extracts were washed with brine, dried and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford the *title compound* **18a** as a clear, oily 1:1 mixture of diastereoisomers (0.26 g, 26%) (Found: C, 76.7; H, 9.1%; M^+, 234.165. $C_{15}H_{22}O_2$ requires C, 76.87; H, 9.47%; *M*, 234.162); ν_{max}(film)/cm^{-1} 3369vbr, 2932, 2861, 1609, 1500, 1258, 1039, 958, 939 and 910; λ_{max}(EtOH)/nm 280 (ε 2340); δ_H(400 MHz) 1.18 (3 H, m, Me), 1.40–1.90 (8 H, m, 4 × CH_2), 2.70 (3 H, m, 1-H and 4-H_2), 3.74 (3 H, s, OMe), 3.77 (1 H, m, CHOH), 6.58 (1 H, d, *J* 2.4, 5-H), 6.68 (1 H, dd, *J* 8.8 and 2.4, 7-H) and 7.07 (1 H, d, *J* 8.8, 8-H); δ_C(100 MHz) 19.95 and 19.97 (CH_2), 23.52 and 23.75 (Me), 27.61, 30.15, 32.92 and 33.06 (3 × CH_2), 36.86 and 36.94 (C-1), 36.97 and 37.05 (C-H), 55.21 (MeO), 68.28 and 68.48 (CHOH), 111.98 and 113.66 (C-5 and -7), 129.42 and 129.53 (C-8), 133.40 (C-8a), 138.30 (C-4a) and 157.32 (C-6).

5,6,7,8-*Tetrahydro*-5-(3-*iodobutyl*)-2-*naphthol* **19c**.—A mixture of the alcohol **18a** (0.457 g, 0.010 mol, 5.2 mol equiv.) and dry acetonitrile (25 cm^3) was heated under reflux for 2 h under nitrogen and was then poured into ice–water (100 cm^3). The mixture was extracted with ether (3 × 50 cm^3) and the combined extracts were washed with brine, dried ($MgSO_4$), filtered and evaporated. The resulting dark brown residue was purified by column chromatography with gradient elution from 25% ether–light petroleum to 50% ether–light petroleum to yield the *title iodide* **19c** as a light red-brown, oily mixture of diastereoisomers (0.52 g, 80%) (Found: M^+, 330.044. $C_{14}H_{19}IO$ requires *M*, 330.048); ν_{max}(film)/cm^{-1} 333vbr, 3019, 2928, 2859, 1611, 1499, 929 and 872; λ_{max}(EtOH)/nm 282 (ε 1600); δ_H(250 MHz) 1.55–2.01 (11-H, m, Me, 4 × CH_2), 2.70 (3 H, m, 5-H and 8-H_2), 4.19 (1 H, m, CHI), 4.90 (1 H, br s, OH), 6.53 (1 H, m, 1-H), 6.62 (1 H, m, 3-H) and 7.00 (1 H, m, 4-H).

2,3,3a,4,5,6-*Hexahydrocyclopenta*[d]*naphthalen*-8(1H)-*one* **26**.—Phenolic iodide **13c** (0.095 g, 0.30 mmol) was dissolved in dry *tert*-butyl alcohol (30 cm^3) and potassium *tert*-butoxide (0.038 g, 0.34 mmol, 1.1 mol equiv.) was added. The solution was refluxed under nitrogen overnight and then poured into water (50 cm^3). The mixture was extracted with ether (3 × 30 cm^3). The combined extracts were washed with water, dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography with 50% ether–light petroleum as eluent to yield the *spirodienone* **26** as a light brown oil (52 mg, 92%) (Found: M^+, 188.119. $C_{13}H_{16}O$ requires M, 188.120); ν_{max}(film)/cm^{-1} 2932, 1660, 1622, 910 and 878; λ_{max}(EtOH)/nm 244 (ε 12 600); δ_H(250 MHz) 1.40–2.50 (13 H, m, 6 × CH_2 and 3a-H), 6.16 (1 H, m, 7-H), 6.19 (1 H, dd, *J* 10.5 and 2.0, 9-H), 6.98 (1 H, d, *J* 10.5, 10-H); δ_C(22.5 MHz) 21.89, 28.12, 29.96, 31.21, 33.21 and 35.27 (6 × CH_2), 48.87 (C-3a), 52.39 (C-10a), 126.39 and 126.71 (C-7 and -9), 153.86 (C-10), 165.76 (C-6a) and 186.85 (C=O).

5,6,7,7a,8,9,10,11-*Octahydrobenzo*[d]*naphthalen*-3-*one* **28**.—The phenolic iodide **16c** (0.140 g, 0.42 mmol) was dissolved in dry *tert*-butyl alcohol (40 cm^3) and potassium *tert*-butoxide (0.05 g, 0.445 mmol, 1.05 mol equiv.) was added. The solution was refluxed under nitrogen overnight and then poured into water (50 cm^3). The mixture was extracted with ether (3 × 30 cm^3). The combined extracts were washed with water, dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography, with 50% ether–light petroleum as eluent to yield the *spirodienone* **28** as a clear oil (39 mg, 46%) (Found: M^+, 202.136. $C_{14}H_{18}O$ requires *M*, 202.136); ν_{max}(film)/cm^{-1} 3074, 2995, 2931, 2857, 1659, 1608, 1500, 909 and 900; λ_{max}(EtOH)/nm 246 (ε 12 300); δ_H(80 MHz) 1.00–2.70 (15 H, m, 7 × CH_2, 7a-H), 6.14 (1 H, m, 4-H), 6.33 (1 H, dd, *J* 11.5 and 2.2, 2-H) and 7.65 (1 H, d, *J* 11.5, 1-H); δ_C(100 MHz) 19.82, 22.04, 26.79, 27.22, 28.10, 31.47 and 33.47 (7 × CH_2), 40.91 (C-7a), 44.12 (C-11a), 125.47 and 127.87 (C-2 and -4), 154.23 (C-1), 168.98 (C-4a) and 186.26 (C=O).

2,3,3a,4,5,6-*Hexahydro*-1-*methylcyclopenta*[d]*napthalen*-8(1H)-*one* **27**.—The phenolic iodide **19c** (0.220 g, 0.67 mmol) was dissolved in dry *tert*-butyl alcohol (60 cm^3) and potassium *tert*-butoxide (0.089 g, 0.73 mmol, 1.05 mol equiv.) was added. The solution was refluxed under nitrogen overnight and then poured into water (100 cm^3). The mixture was extracted with ether (3 × 50 cm^3). The combined extracts were washed with water, dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography with 50% ether–light petroleum as eluent to yield the *spirodienone* **27** as a clear, oily,

1:1 mixture of diastereoisomers (101 mg, 75%) (Found: M^+, 202.135. $C_{14}H_{18}O$ requires *M*, 202.136); ν_{max}(film)/cm^{-1} 2932, 1661, 1622, 899 and 874; λ_{max}(EtOH)/nm 249 (ε 10 300); δ_H(250 MHz) 0.69 (3 H, d, *J* 4.3, Me) and 0.89 (3 H, d, *J* 4.5, Me), 1.30–2.70 [2 × 12 H, m, 2 × (5 × CH_2), 2 × CH], 6.08 (1 H, dd, *J* 6.1 and 1.1, 9-H), 6.18 and 6.23 (each 1 H, br s, 7-H), 6.32 (1 H, dd, *J* 6.4 and 1.1, 9-H), 6.79 (1 H, d, *J* 6.1, 10-H) and 6.87 (1 H, d, *J* 6.4, 10-H).

3-(6-tert-*Butyldimethylsiloxy*-1,2,3,4-*tetrahydro*-1-*naphthyl*)-1,2-*epoxypropane* **20b**.—The alkene **9b** (1.51 g, 5.0 mmol) and MCPBA (1.12 g, 6.5 mmol) were dissolved in dichloromethane (30 cm^3) and the resulting solution was heated under reflux for 2 h and then allowed to cool. Saturated aq. sodium sulfite (30 cm^3) was added to the mixture which was then stirred vigorously for 15 min. The organic phase was separated off and washed successively with aq. sodium hydrogen carbonate and brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 10% ether–light petroleum as eluent to afford the *title compound* **20b** as a clear oil (0.75 g, 47%), isolated as a mixture of diastereoisomers (Found: M^+, 318.203. $C_{19}H_{30}O_2Si$ requires *M*, 318.202); ν_{max}(film)/cm^{-1} 2930, 2858, 1608, 1498, 1262, 877, 840 and 781; λ_{max}(EtOH)/nm 277 (ε 1630); δ_H(250 MHz) 0.19 (6H, s, $SiMe_2$), 0.98 (9 H, s, $SiBu^t$), 1.65–2.00 (6 H, m, 3 × CH_2), 2.47 [1 H, m, C*H*H(O)CH], 2.75 (3 H, m, 1-H and 4-H_2), 3.00 [1 H, m, CH*H*(O)CH], 3.00 [1 H, m, CH_2(O)C*H*], 6.54 (1 H, s, 5-C), 6.60 (1 H, d, *J* 8.3, 7-H) and 7.01 (1 H, d, *J* 8.3, 8-H); δ_C(22.5 MHz) −4.23 ($SiMe_2$), 18.31 (Si*C*Me_3), 18.82 +20.27 (CH_2), 25.89 (SiC*Me*$_3$), 28.45 + 29.04, and 29.85 +30.01 (2 × CH_2), 34.94 + 35.76 (C-1), 40.04 + 40.20 (CH_2), 47.13 + 47.83 [*C*H_2(O)CH], 50.83 + 51.58 [CH_2(O)*C*H], 117.61 + 117.78, and 120.10 + 120.21 (C-5 and -7), 129.15 +129.48 (C-8), 132.73 + 132.89 (C-8a), 138.31 + 138.42 (C-4a) and 153.64 (C-6).

4-(6-tert-*Butyldimethylsiloxy*-1,2,3,4-*tetrahydro*-1-*naphthyl*)-1,2-*epoxybutane* **21b**.—The alkene **11b** (1.00 g, 3.0 mmol) and MCPBA (0.62 g, 3.6 mmol) were dissolved in dichloromethane (25 cm^3) and the resulting solution was heated under reflux for 1 h and then allowed to cool. Saturated aq. sodium sulfite (20 cm^3) was added to the mixture which was then stirred vigorously for 15 min. The organic phase was separated off and washed successively with aq. sodium hydrogen carbonate and brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 10% ether–light petroleum as eluent to afford the *title compound* **21b** as a clear oil (0.50 g, 46%), isolated as a mixture of diastereoisomers (Found: M^+, 332.217. $C_{20}H_{32}O_2Si$ requires *M*, 332.217); ν_{max}(film)/cm^{-1} 2930, 2858, 1609, 1497, 1262, 960, 840 and 781; λ_{max}(EtOH)/nm 277 (ε 1260); δ_H(400 MHz) 0.18 (6 H, s, $SiMe_2$), 0.97 (9 H, s, $SiBu^t$), 1.55–1.90 (8 H, m, 4 × CH_2), 2.47 [1 H, m, C*H*H(O)CH], 2.73 [4 H, m, 1-H, 4-H_2, and CH*H*(O)CH], 2.92 [1 H, m, CH_2(O)C*H*], 6.53 (1 H, d, *J* 2.2, 5-H), 6.60 (1 H, dd, *J* 8.3 and 2.2, 7-H) and 7.00 (1 H, br d, *J* 8.3, 8-H); δ_C(22.5 MHz) −4.22 ($SiMe_2$), 18.37 (Si*C*Me_3), 20.21 (CH_2), 25.90 (SiC*Me*$_3$), 28.01, 30.01 + 30.34, and 32.94 + 33.10 (3 × CH_2), 36.90 (1-C), 47.08 + 47.19 [*C*H_2(O)CH], 52.44 + 52.66 [CH_2(O)*C*H], 117.61 and 120.05 (C-5 and -7), 129.26 + 129.37 (C-8), 133.54 (C-8a), 138.31 (C-4a) and 153.42 (C-6).

5-(6-tert-*Butyldimethylsiloxy*-1,2,3,4-*tetrahydro*-1-*naphthyl*)-1,2-*epoxypentane* **29b**.—6-*tert*-Butyldimethylsiloxy-1,2,3,4-*tetrahydro*-1-(*pent*-4-*enyl*)*naphthalene* (see above) (0.91 g, 2.77 mmol) and MCPBA (0.52 g, 3.0 mmol) were dissolved in dichloromethane (30 cm^3) and the resulting solution was heated under reflux for 1 h and then allowed to cool. Saturated aq. sodium sulfite (20 cm^3) was added to the mixture which was then stirred vigorously for 15 min. The organic phase was separated off and washed successfully with aq. sodium hydrogen carbonate and brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 10% ether–light petroleum as eluent to afford the *title compound* **29b** as a clear oil (036 g, 38%), isolated as a mixture of diastereoisomers (Found: M^+, 346.228. $C_{21}H_{34}O_2Si$ requires M, 346.233); ν_{max}(film)/cm^{-1} 2931, 2858, 1608, 1496, 1260, 841 and 780; λ_{max}(EtOH)/nm 277 (ε 3350); δ_H(250 MHz) 0.21 (6 H, s, $SiMe_2$), 1.01 (9 H, s, $SiBu^t$), 1.50–1.90 (10 H, m, 5 × CH_2), 2.51 [1 H, m, C*H*H(O)CH], 2.71 (3 H, m, 1-H and 4-H_2), 2.78 [1 H, m, CH*H*(O)CH], 2.95 [1 H, m, CH_2(O)C*H*], 6.55 (1 H, d, *J* 2.5, 5-H), 6.63 (1 H, dd, *J* 8.4 and 2.5, 7-H) and 7.02 (1 H, br d, *J* 8.4, 8-H); δ_C(22.5 MHz) −4.23 ($SiMe_2$), 18.31 (Si*C*Me_3), 20.10 and 23.89 (2 × CH_2), 25.89 (SiC*Me*$_3$), 27.86, 30.07 and 32.89 (3 × CH_2), 36.89 (C-4), 37.06 (C-1), 47.08 [*C*H_2(O)CH], 52.33 [CH_2(O)*C*H], 117.56 and 119.99 (C-5 and -7), 129.32 (C-8), 133.97 (C-8a), 138.25 (C-4a) and 153.32 (C-6).

5-(2,3-*Epoxypropyl*)-5,6,7,8-*tetrahydro*-2-*naphthol* **20c**.—Tetrabutylammonium fluoride (TBAF) (2.1 cm^3; 1 mol dm^{-3} solution in THF) was added to a stirred solution of the epoxide **20b** (0.62 g, 1.9 mmol) in dry THF (10 cm^3) at 0 °C under nitrogen. The solution was stirred for 10 min and then saturated aq. ammonium chloride (15 cm^3) was added. The mixture was extracted with ether (3 × 25 cm^3) and the combined extracts were washed with brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford the *title compound* **20c** as a clear oil (0.375 g, 94%), isolated as a mixture of diastereoisomers (Found: M^+, 204.114. $C_{13}H_{16}O_2$ requires *M*, 204.115); ν_{max}(film)/cm^{-1} 3381vbr, 2932, 1612, 1587, 1503, 1258, 966, 919 and 870; λ_{max}(EtOH)/nm 282 (ε 1810); δ_H(250 MHz) 1.65–2.00 (6 H, m, 3 × CH_2), 2.55 [1 H, m, C*H*H(O)CH], 2.67 (2 H, m, 8-H_2), 2.84 [1 H, m, CH*H*(O)CH], 2.97 (1 H, m, 5-H), 3.08 [1 H, m, CH_2(O)C*H*], 6.28 (1 H, br s, OH), 6.54 (1 H, d, *J* 2.4, 1-H), 6.61 (1 H, dd, *J* 8.3 and 2.4, 3-H) and 6.99 (1 H, d, *J* 8.3, 4-H); δ_C(22.5 MHz) 19.67 + 20.10, 28.34 + 28.83, and 29.69 + 29.91 (3 × CH_2), 34.78 + 35.49 (C-5), 39.82 + 39.83 (C-8), 47.45 + 48.11 [*C*H_2(O)CH], 51.52 + 52.12 [CH_2(O)*C*H], 113.17 + 113.39, and 115.44 + 115.56 (C-1 and -3), 129.42 + 129.70 (C-4), 131.75 + 131.92 (C-4a), 138.53 + 138.63 (C-8a) and 153.80 (C-2).

5-(3,4-*Epoxybutyl*)-5,6,7,8-*tetrahydro*-2-*naphthol* **21c**.—TBAF (1.39 cm^3; 1 mol dm^{-3} solution in THF) was added to a stirred solution of the epoxide **21b** (0.439 g, 1.32 mmol) in dry THF (15 cm^3) at 0 °C under nitrogen. The solution was stirred for 10 min and then saturated aq. ammonium chloride (15 cm^3) was added. The mixture was extracted with ether (3 × 25 cm^3) and the combined extracts were washed with brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford the *title compound* **21c** as a clear oil (0.277 g, 96%), isolated as a mixture of diastereoisomers (Found: C, 76.8; H, 8.6%; M^+, 218.130. $C_{14}H_{18}O_2$ requires C, 77.02; H, 8.32%; *M*, 218.131); ν_{max}(film)/cm^{-1} 3369vbr, 2931, 1612, 1500, 1455, 1261, 984, 916 and 835; λ_{max}(EtOH)/nm 282 (ε 1930); δ_H(250 MHz) 155–195 (8 H, m, 4 × CH_2), 2.54 [1 H, m, C*H*H(O)CH], 2.69 (3 H, m, 5-H and 8-H_2), 2.79 [1 H, m, CH*H*(O)CH], 2.97 [1 H, m, CH_2(O)C*H*], 5.01 (1 H, br s, OH), 6.53 (1 H, d, *J* 2.5, 1-H), 6.61 (1 H, dd, *J* 8.3 and 2.5, 3-H) and 7.00 (1 H, d, *J* 8.3, 4-H); δ (22.5 MHz) 19.99 + 20.10, 27.96, 29.96, and 30.12 + 30.29 (4 × CH_2), 32.89 + 33.10 (C-8), 36.79 (C-5), 47.59

[CH_2(O)CH], 52.98 + 53.20 [CH_2(O)CH], 113.28 and 115.45 (C-1 and -3), 129.53 (C-4), 132.67 (C-4a), 138.58 (C-8a) and 153.80 (C-2).

5-(4,5-*Epoxypentyl*)-5,6,7,8-*tetrahydro*-2-*naphthol* **29c**.—TBAF (1.15 cm^3; 1 mol dm^{-3} solution in THF) was added to a stirred solution of the epoxide **29b** (0.361 g, 1.04 mmol) in dry THF (10 cm^3) at 0 °C under nitrogen. The solution was stirred for 10 min and then saturated aq. ammonium chloride (15 cm^3) was added. The mixture was extracted with ether (3 × 25 cm^3) and the combined extracts were washed with brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford the *title compound* **29c** as a clear oil (0.233 g, 97%), isolated as a mixture of diastereoisomers (Found: M^+, 232.145. $C_{15}H_{20}O_2$ requires *M*, 232.146); ν_{max}(film)/cm^{-1} 3374vbr, 2932, 2860, 1611, 1585, 1499, 1260, 911, 837 and 816; λ_{max}(EtOH)/nm 285 (ε 1630); δ_H(250 MHz) 1.45–1.90 (10 H, m, 5 × CH_2), 2.55 [1 H, m, C*H*H(O)CH], 2.68 (3 H, m, 5-H and 8-H_2), 2.81 [1 H, t, *J* 4.5, CH*H*(O)CH], 2.98 [1 H, m, CH_2(O)C*H*], 5.90 (1 H, br s, OH), 6.53 (1 H, d, *J* 2.6, 1-H), 6.61 (1 H, dd, *J* 8.3 and 2.6, 3-H) and 6.99 (1 H, br d, *J* 8.3, 4-H); δ_C(22.5 MHz) 19.99, 23.84, 27.85, 29.96 and 32.72 (5 × CH_2), 36.84 (C-8), 36.95 (C-5), 47.46 [CH_2(O)CH], 52.88 [CH_2(O)CH], 113.17 and 115.34 (C-1 and -3), 129.53 (C-4), 133.16 (C-4a), 138.47 (C-8a) and 153.59 (C-2).

5,6,7,7a,8,9,10,11-*Octahydro*-10-*hydroxybenzo*[d]*naphthalen*-3-*one* **30**.—Phenolic epoxide **21c** (0.166 g, 0.76 mmol) was dissolved in dry *tert*-butyl alcohol (70 cm^3), and potassium *tert*-butoxide (0.094 g, 0.84 mmol, 1.1 mol equiv.) was added. The solution was refluxed under nitrogen for 40 h and was then poured into water (100 cm^3). The mixture was extracted with ether (3 × 40 cm^3). The combined extracts were washed with water, dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography with gradient elution from 50% ether–light petroleum to ethyl acetate to yield the *title spirodienone* **30** as a diastereoisomerically pure solid (49 mg, 60% for the one isomer). This was further purified by recrystallisation from ethyl acetate, to furnish crystals, m.p. 140–143 °C (Found: C, 76.7; H, 8.5%; M^+, 218.132. $C_{14}H_{18}O_2$ requires C, 77.02; H, 8.32%; *M*, 218.131); ν_{max}(film)/cm^{-1} 3357vbr, 2944, 2865, 1655, 1611, 1384, 935 and 890; λ_{max}(EtOH)/nm 245 (ε 21 700); δ_H(250 MHz) 1.30–2.70 (13 H, m, 6 × CH_2 and 7a-H), 4.05 (1 H, tt, *J* 11.2 and 4.8, C*H*OH), 6.12 (1 H, d, *J* 2.0, 4-H), 6.27 (1 H, dd, *J* 15.7 and 2.0, 2-H) and 7.31 (1 H, d, *J* 15.7, 1-H); δ_C(22.5 MHz) 26.44, 27.25, 27.96, 29.69 and 33.37 (5 × CH_2), 40.09 (C-7a), 40.42 (C-5), 46.05 (C-11a), 67.02 (CHOH), 125.52 and 128.12 (C-2 and -4), 153.48 (C-1), 167.73 (C-4a) and 186.14 (C=O).

Tricyclospirodienone **35**.—A solution of the phenolic epoxide **21c** (0.210 g, 0.963 mmol) in dry dichloromethane (3 cm^3) was added to a stirred solution of boron trifluoride–diethyl ether (0.304 g, 2.14 mmol) in dry dichloromethane (100 cm^3) at −78 °C under nitrogen. The mixture was stirred for 45 min and then the reaction was quenched with saturated aq. solution hydrogen carbonate (50 cm^3). After warming to room temperature, the organic phase was separated, washed with brine, dried ($MgSO_4$) and filtered, and the solvent was evaporated off.

The residue was dissolved in dry DMF (10 cm^3). Imidazole (0.24 g, 3.5 mmol) and *tert*-butylchlorodimethylsilane (0.26 g, 1.75 mmol) were added and the mixture was stirred overnight under nitrogen before being poured into water (50 cm^3) and extracted with ether (3 × 20 cm). The combined extracts were washed with water (2 × 50 cm^3), dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 30% ether–light petroleum as eluent to afford the *tricyclospirodienone* **35** as a clear, oily mixture of diastereoisomers in the approximate ratio 3:2 (0.139 g, 43%) (Found: MH^+, 333; *m/z*, 275.142. $C_{20}H_{32}O_2Si$ requires MH, 333; *M* − Bu^t, 275.147); ν_{max}(film)/cm^{-1} 2929, 2857, 1662, 1623, 907 and 837; λ_{max}(EtOH)/nm 249 (ε 16 600); δ_H(250 MHz) 0.06 (6 H, s, $SiMe_2$), 0.91 (min) (9 H, s, $SiBu^t$), 1.02 (maj) (9 H, s, $SiBu^t$), 1.40–2.85 (12 H, 5 × CH_2 and 2 × CH), 3.31 (min) (2 H, d, *J* 6.6, CH_2OSi), 3.50 (maj) (2 H, m, CH_2OSi), 6.11 (maj) (1 H, dd, *J* 9.9 and 2.0, ?-H_2), 6.18 (maj) (1 H, m, 7-H), 6.22 (min) (1 H, m, 7-H), 6.31 (min) (1 H, dd, *J* 10.2 and 2.0, 9-H), 6.87 (maj) (1 H, d, *J* 9.9, 10-H) and 6.94 (min) (1 H, d, *J* 10.2, 10-H).

Tricyclospirodienone **40**.—A solution of the phenolic epoxide **29c** (0.122 g, 0.526 mmol) in dry dichloromethane (3 cm^3) was added to a stirred solution of boron trifluoride–diethyl ether (0.164 g, 1.15 mmol) in dry dichloromethane (50 cm^3) at −78 °C under nitrogen. The mixture was stirred for 2 h and then the reaction was quenched with saturated aq. sodium hydrogen carbonate (50 cm^3). After warming to room temperature, the organic phase was separated, washed with brine, dried ($MgSO_4$) and filtered, and the solvent was evaporated off.

The residue was dissolved in dry DMF (5 cm^3). Imidazole (0.15 g, 2.2 mmol) and *tert*-butylchlorodimethylsilane (0.26 g, 1.1 mmol) were added and the mixture was stirred overnight under nitrogen before being poured into water (50 cm^3) and extracted with ether (3 × 20 cm^3). The combined extracts were washed with water (2 × 50 cm^3), dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue which consisted mainly of starting material. Purification by column chromatography with 30% ether–light petroleum as eluent afforded a trace of the *tricyclospirodienone* **40** (~0.001 g) as an oily, single diastereoisomer (Found: *m/z*, 289.174. $C_{21}H_{34}O_2Si$ requires *M* − Bu^t, 289.162); ν_{max}($CHCl_3$)/cm^{-1} 2929, 2856, 1657, 1614, 888, 866 and 839; δ_H(250 MHz) −0.04 (6 H, s, $SiMe_2$), 0.85 (9 H, s, $SiBu^t$), 1.40–2.60 (14 H, 6 × CH_2, 2 × CH), 3.02 (1 H, dd, *J* 8.5 and 6.9, C*H*HOSi), 3.24 (1 H, dd, *J* 8.5 and 4.3, CH*H*OSi), 6.19 (1 H, m, 4-H), 6.34 (1 H, dd, *J* 10.2 and 1.9, 2-H) and 7.48 (1 H, d, *J* 10.2, 1-H).

Cationic Double Cyclisation of Phenolic Epoxide **21c**.—A solution of phenolic epoxide **21c** (0.180 g, 0.833 mmol) in dry dichloromethane (3 cm^3) was added to a stirred solution of boron trifluoride–diethyl ether (0.260 g, 1.83 mmol) in dry dichloromethane (80 cm^3) at −78 °C under nitrogen. The mixture was stirred for 45 min and then quenched with saturated aq. sodium hydrogen carbonate (50 cm^3). After warming to room temperature, the organic phase was separated, washed with brine, dried ($MgSO_4$) and filtered, and the solvent was evaporated off.

The residue was dissolved in dichloromethane (10 cm^3) and a catalytic amount of PTSA was added. After 10 min, the organic phase was washed with saturated aq. sodium hydrogen carbonate, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded a solid which contained two tetracyclic compounds; these were separated by column chromatography with gradient elution from 50% ether–light petroleum to ether.

Tetracyclic compound **38** (37 mg, 21%) was isolated as a solid, which was recrystallised from hexane to give a powder, m.p. 88–91 °C (Found: M^+, 218.130. $C_{14}H_{18}O_2$ requires *M*, 218.131); ν_{max}(KBr)/cm^{-1} 2930, 2858, 1671, 1622, 1065 and 864; λ_{max}(EtOH)/nm 241 (ε 27 100); δ_H*(270 MHz) 1.20–2.40 (11 H, m, 5 × CH_2, 5-H), 2.53 (1 H, dd, *J* 16.5 and 5.0, 3-H^a), 2.76 (1 H, dd, *J* 16.5 and 2.8, 3-H^b), 2.82 (1 H, m, 9-H), 3.55 (1 H, dd, *J*

* NMR locants refer to the trivial numbering shown in the structure.

8.9 and 3.6, 12-H[a]), 4.00 (2 H, m, 12-H[b] and 4-H) and 5.90 (1 H, s, 1-H); δ_C(67.5 MHz) 27.69, 29.67, 30.14, 31.02, 33.06 and 40.11 (6 × CH_2),44.60 and 48.72 (C-5 and -9), 60.02 (C-4a), 74.11 (C-12), 79.89 (C-4), 124.01 (C-1), 164.02 (C-8a) and 197.21 (C=O).

The *tetracyclic compound* **39** (35 mg, 19%) was isolated as a solid, which was recrystallised from ethanol–water to afford crystals, m.p. 81.5 °C (Found: M^+, 218.131); ν_{max}(KBr)/cm^{-1} 2938, 2881, 1669, 1610, 1065, 900 and 868; λ_{max}(EtOH)/nm 234 (ε 11 400); δ_H*(270 MHz) 1.25–2.05 (11 H, m, 5 × CH_2, 5-H), 2.14 (1 H, d, *J* 14.9, 1-H[a]), 2.78 (1 H, m, 9-H), 2.86 (1 H, d, *J* 14.9, 1-H[b]), 3.61 (1 H, dd, *J* ~9.0 and 2.6, 12-H[a]), 4.20 (1 H, t, *J* ~9.0, 12-H[b]), 5.92 (1 H, d, *J* 10.2, 3-H) and 6.69 (1 H, d, *J* 10.2, 4-H); δ_C(67.5 MHz) 15.02, 25.39, 31.16, 33.34 and 34.05 (5 × CH_2), 47.15 (C-1), 47.48 (C-5), 53.08 (C-9), 54.56 (C-4a), 74.12 (C-12), 84.96 (C-8a), 126.85 (C-3), 156.33 (C-4) and 199.80 (C=O).

5-(*But*-3-*enyl*)-5,6,7,8-*tetrahydro*-2-*naphthol* **11c**.—TBAF (3.7 cm^3; 1 mol dm^{-3} solution in THF) was added to a stirred solution of 1-(but-3-enyl)-6-*tert*-butyldimethylsiloxy-1,2,3,4-tetrahydronaphthalene **11b** (1.128 g, 3.57 mmol) in dry THF (15 cm^3) at 0 °C under nitrogen. The solution was stirred for 10 min and then saturated aq. ammonium chloride (20 cm^3) was added. The mixture was extracted with ether (3 × 30 cm^3) and the combined extracts were washed with brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with 30% ether–light petroleum as eluent to afford the *title compound* **11c** (0.79 g), containing an impurity from the cleaved *tert*-butyldimethylsilyl group, as a mixture of diastereoisomers (Found: M^+, 202.138. $C_{14}H_{18}O$ requires *M*, 202.136); ν_{max}(film)/cm^{-1} 3346vbr, 2931, 2859, 1611, 911 and 839; δ_H(250 MHz) 0.07 (impurity, s, $SiMe_2$), 0.97 (impurity, s, $SiBu^t$), 1.45–2.29 (8 H, m, 4 × CH_2), 2.62 (3 H, m, 5-H and 8-H_2), 3.78 (1 H, br s, OH), 4.98 (1 H, m, CH_2=C*H*), 5.85 (2 H, m, CH_2=CH), 6.56 (2 H, m, 1- and 3-H) and 6.99 (1 H, d, *J* 8.7, 4-H); δ_C(22.5 MHz) −3.56 (impurity, $SiMe_2$), 19.89 (CH_2), 25.69 (impurity, $SiBu^t$), 27.75, 29.91, 31.54 and 36.25 (4 × CH_2), 36.42 (C-5), 114.43 (*C*H_2=CH), 115.29 and 120.05 (C-1 and -3), 129.60 (C-4), 133.44 (C-4a), 138.53 (C-8a), 139.02 (CH_2=*C*H) and 153.32 (C-2).

5,6,7,7a,8,9,10,11-*Octahydro*-10-*phenylthiobenzo*[d]*naphthalen*-3-*one* **32**.—Methyl benzensulfenate (0.31 g, 2.21 mol) was dissolved in dry dichloromethane (200 cm^3) and the solution was cooled in an ice-bath under nitrogen. Boron trifluoride–diethyl ether (0.63 g, 4.44 mmol) was added and this mixture was stirred for 10 min. A solution of alkene **11c** (0.407 g, 2.01 mmol) in dry dichloromethane (5 cm^3) was added and the mixture was stirred for 35 min, after which the reaction was quenched with saturated aq. sodium hydrogen carbonate (50 cm^3). The organic layer was separated, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded a yellow oil, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford the *title compound* **32** (93 mg, 15%) as a light yellow oil (Found: M^+, 310.133. $C_{20}H_{22}OS$ requires *M*, 310.139); ν_{max}(film)/cm^{-1} 3054, 2928, 2859, 1660, 1622, 1601, 942, 922 and 873; λ_{max}(EtOH)/nm 253 (ε 16 500); δ_H(250 MHz) 1.35–2.73 (14 H, m, 6 × CH_2, 7a-H, C*H*SPh), 6.28 (1 H, d, *J* 1.9, 4-H), 6.36 (1 H, dd, *J* 10.2 and 1.9, 2-H), 6.90 (1 H, d, *J* 10.2, 1-H) and 7.22 (5 H, m, Ph); δ_C(22.5 MHz) 28.01, 28.93, 29.53, 30.29, 32.78 and 35.70 (6 × CH_2), 45.67 (C-7a), 49.35 (PhS*C*H), 55.64, (C-11a), 126.34, 127.64, 129.04, 129.42 and 129.80 (Ar C-*o*, -*m*-*p*, C-2 and -4), 136.25 (Ar C-*ipso*), 150.44 (C-1), 164.58 (C-4a) and 186.58 (C=O).

* NMR locants refer to the trivial numbering shown in the structure.

5,6,7,7a,8,9,10,11-*Octahydro*-10-*phenylselenobenzo*[d]*naphthalen*-3-*one* **33**.—Boron trifluoride–diethyl ether (0.73 g, 5.14 mmol) was added to a stirred solution of *N*-(phenylseleno)-phthalimide (0.78 g, 2.58 mmol) in dry dichloromethane (110 cm^3) at −78 °C under nitrogen. The mixture was stirred for 10 min and then a solution of the alkene **11c** (0.407 g, 2.01 mmol) in dry dichloromethane (5 cm^3) was added and the mixture was stirred for 2 h, after which the reaction was quenched with saturated aq. sodium hydrogen carbonate (50 cm^3). After warming to room temperature, the organic layer was separated, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded a yellow oil, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford the *title compound* **33** (120 mg, 28%) as a light yellow oil (Found: M^+, 358.083. $C_{20}H_{22}OSe$ requires *M*, 358.084); ν_{max}(film)/cm^{-1} 3049, 2926, 2858, 1660, 1621, 1601, 938, 924 and 873; λ_{max}(EtOH)/nm 246 (ε 14 100); δ_H(250 MHz) 1.30–2.85 (14 H, m, 6 × CH_2, 7a-H and C*H*SePh), 6.25 (1 H, d, *J* 1.9, 4-H), 6.36 (1 H, dd, *J* 10.2 and 1.9, 2-H), 6.89 (1 H, d, *J* 10.2, 1-H), 7.22 (3 H, m, 3 × ArH) and 7.38 (2 H, m, 2 × ArH); δ_C(100 MHz) 27.62, 29.12, 29.17, 29.24, 30.19 and 32.60 (6 × CH_2), 46.64 (C-7a), 49.20 (PhSe*C*H), 55.97 (C-11a), 127.06, 127.54, 129.13, 129.95 and 132.61 (Ar C-*o*, -*m*, -*p*, C-4 and C-2), 129.74 (Ar C-*ipso*), 150.47 (C-1), 164.58 (C-4a) and 186.61 (C=O).

5,6,7,7a,8,11-*Hexahydrobenzo*[d]*naphthalen*-3-*one* **34**.—The phenyl sulfide **32** (41 mg, 0.132 mmol) was dissolved in a mixture of THF (5 cm^3) and water (1.5 cm^3), and sodium periodate (0.03 g, 0.140 mmol) was added. This mixture was stirred at room temperature for 24 h and then more sodium periodate (0.04 g, 0.187 mol) was added. The mixture was stirred for 4 days and was then poured into water (30 cm^3) and extracted with ether (3 × 20 cm^3). The combined extracts were dried ($MgSO_4$) and filtered, and the solvent was evaporated off.

The residue was dissolved in dry dichloromethane (5 cm^3) and potassium *tert*-butoxide (19 mg, 0.17 mmol) was added. The solution immediately changed colour to yellow. The solution was poured into water (30 cm^3) and extracted with ether (3 × 15 cm^3). The combined organic phase was washed with brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded an oily residue, which was purified by column chromatography with ether as eluent to afford the *title compound* **34** as an oil (16 mg, 60%) (Found: M^+, 200.119. $C_{14}H_{16}O$ requires M, 200.120); δ_H(250 MHz) 0.70–2.75 (11 H, 5 × CH_2 and 7a-H), 5.32 (1 H, m, C*H*=CH), 5.60 (1 H, m, CH=C*H*), 6.53 (1 H, d, *J* 1.9, 4-H), 6.62 (1 H, dd, *J* 10.3 and 1.9, 2-H) and 6.96 (1 H, d, *J* 10.3, 1-H).

2-(6-*Acetoxy*-1,2,3,4-*tetrahydro*-1-*naphthyl*)*acetic Acid* **42**.—A solution of 2-(1,2,3,4-tetrahydro-6-methoxy-1-naphthyl)acetic acid[24] (9.98 g) in acetonitrile (80 cm^3) under nitrogen was treated with chlorotrimethylsilane (25.9 cm^3) and sodium iodide (12.23 g). The mixture was refluxed for 2 h, after which it was poured into water. The product was extracted with ether, and the acidic fraction was isolated through washing with aq. sodium carbonate. The crude acid was dissolved in a mixture of pyridine (20 cm^3) and acetic anhydride (20 cm^3) and the solution was set aside overnight. The reagents were then evaporated off, and the residue was stirred with a mixture of methanol (50 cm^3) and water (50 cm^3) for 1 h. After evaporation with methanol the organic products were collected into ether and the acidic fraction was separated through aq. sodium carbonate, to yield a brown oil. This was purified by chromatograhy on Florisil [ethyl acetate–hexane (2:3)] to afford the *title acid* **42** (2.64 g, 26%) as a pale yellow oil (Found: M^+, 248.104. $C_{14}H_{16}O_4$ requires M, 248.104); ν_{max}(film)/cm^{-1} 3500–2700, 1760 and 1715; δ_H 1.82 (4 H, m, 2- and 3-H_2), 2.34 (3

H, s, Ac), 2.86 (4 H, m, 4-H_2 and CH_2CO), 2.94 (1 H, m, 1-H), 6.76 (1 H, br s, 5-H), 6.81 (1 H, dd, *J* 3 and 9, 7-H) and 7.15 (1 H, d, *J* 9, 8-H).

Diazomethyl (1,2,3,4-Tetrahydro-6-hydroxy-1-naphthyl)-methyl Ketone **41**.—A solution of the acid **42** (2.64 g) in dry dichloromethane (30 cm^3) with DMF (0.15 cm^3) was cooled to −20 °C and oxalyl dichloride (1.86 cm^3) was added. The mixture was stirred at −20 °C for 2 h, after which it was evaporated. The residual acid chloride was dissolved in toluene (10 cm^3) and the solution was added dropwise to an ethereal solution of diazomethane (1.05 g) at 0 °C. The solution was set aside overnight, then was flushed with argon, and evaporated. The product was chromatographed on Florisil [ethyl acetate–hexane (1:4)] to afford the acetoxy diazo ketone (0.383 g); this was dissolved in methanol (5 cm^3) and treated with aq. sodium carbonate (0.31 g)–sodium hydrogen carbonate (0.37 g) (4 cm^3). The mixture was stirred at room temperature for 2 h, poured into ice–water (50 cm^3), and the pH was adjusted to 7–8 using dil. aq. oxalic acid. The product was extracted with ether and the dried extracts were evaporated to afford the *title diazo ketone* **41** (293 mg, 13%) as a yellow solid [Found: $(M - N_2)^+$, 202.100. $C_{13}H_{14}O_2$ requires *m/z*, 202.100]; ν_{max}(KBr)/cm^{-1} 3400–3300, 2100 and 1620; δ_H 1.80 (4 H, m, 2- and 3-H_2), 2.70 (4 H, m, 4-H_2 and CH_2CO), 3.35 (1 H, m, 1-H), 4.87 (1 H, OH) ?.25 (1 H, C*H*N_2), 6.58 (1 H, br s, 5-H), 6.65 (1 H, dd, *J* 3 and 9, 7-H) and 7.08 (1 H, d, *J* 9, 8-H).

3a,4,5,6-*Tetrahydrocyclopenta*[d]*naphthalene*-2,8(1H,3H)-*dione* **43**.—Boron trifluoride–diethyl ether (25 cm^3) was added to a vigorously stirred solution of the above diazo ketone (100 mg) in dichloromethane (5 cm^3) under nitrogen at room temperature. The solution was stirred for 15 min, diluted with water (1 cm^3) and stirred for 5 min more before being diluted with brine and extracted with ethyl acetate. The extracts were dried and evaporated, and the residue was chromatographed on Florisil [ethyl acetate–hexane gradient (1:9 → 1:0)]. The fractions of lowest R_f yielded the *title spirodienone* **43** (59 mg, 62%) as a yellow solid, m.p. 118–120 °C (Found: M^+, 202.100. $C_{13}H_{14}O_2$ requires *M*, 202.100); ν_{max}(KBr)/cm^{-1} 1745, 1661 and 1620; δ_H 1.45 (2 H, m, 5-H_2), 1.94 (1 H, m, 4-H^a), 2.06 (1 H, m, 4-H^b), 2.10 (1 H, d, *J* 19, 1-H^a), 2.21 (1 H, d, *J* 19, 1-H^b), 2.36 (1 H, m, 3a-H), 2.44 (1 H, dd, *J* 4 and 12, 6-H^a), 2.52 (1 H, d, *J* 12, 6-H^b), 2.81 (2 H, m, 3-H_2), 6.26 (1 H, d, *J* 1.8, 7-H), 6.28 (1 H, dd, *J* 1.8 and 10.1, 9-H) and 7.08 (1 H, d, *J* 10.1, 10-H).

5,6,7,8-*Tetrahydro*-5-(3-*nitropropyl*)-2-*naphthol* **14c**.—Amberlyst-supported nitrite reagent (0.79 g) was added to a solution of 5,6,7,8-tetrahydro-5-(3-iodopropyl)-2-naphthol **13c** (0.50 g, 1.58 mmol) in dry benzene (30 cm^3). The mixture was stirred under nitrogen for 24 h and then another portion of the nitrite reagent was added. The mixture was stirred for 24 h and then the mixture was filtered. Evaporation of the solvent yielded a brown oily residue, which was purified by column chromatograhy with 50% ether–light petroleum as eluent to afford the *title compound* **14c** (0.175 g, 47%) as a yellow oil (Found: M^+, 235.119. $C_{13}H_{17}NO_3$ requires *M*, 235.121); ν_{max}(film)/cm^{-1} 3374vbr, 3019, 2932, 2863, 1611, 1551, 929, 870 and 840; λ_{max}(EtOH)/nm 281 (ε 1890); δ_H(250 MHz) 1.55–2.15 (8 H, m, 4 × CH_2), 2.68 (2 H, t, *J* 5.7, 8-H_2), 2.76 (1 H, m, 5-H), 4.39 (2 H, t, *J* 7.0, CH_2NO_2), 5.25 (1 H, br s, OH), 6.54 (1 H, d, *J* 2.6, 1-H), 6.62 (1 H, dd, *J* 7.8 and 2.6, 3-H) and 6.97 (1 H, d, *J* 7.8, 4-H); δ_C(22.5 MHz) 19.74, 25.19, 27.60, 29.73 and 33.23 (5 × CH_2), 36.29 (C-5), 75.92 (CH_2NO_2), 113.15 and 115.35 (C-1 and -3), 129.49 (C-4), 132.17 (C-4a), 138.67 (C-8a) and 153.43 (C-2).

5,6,7,8-*Tetrahydro*-5-(4-*nitrobutyl*)-2-*naphthol* **17c**.—Amberlyst-supported nitrite reagent (0.78 g) was added to a solution of 5,6,7,8-tetrahydro-5-(4-iodobutyl)-2-naphthol **16c** (0.50 g, 1.51 mmol) in dry benzene (30 cm^3). The mixture was stirred under nitrogen for 24 h and then another portion of the nitrite reagent was added. The mixture was stirred for 24 h and then the mixture was filtered. Evaporation of the solvent yielded a brown oily residue, which was purified by column chromatography with 50% ether–light petroleum as eluent to afford the *title compound* **17c** (0.185 g, 49%) as a yellow oil (Found: M^+, 249.137. $C_{14}H_{19}NO_3$ requires *M*, 249.137); ν_{max}(film)/cm^{-1} 3401vbr, 3019, 2931, 2861, 1612, 1551, 929 and 875; λ_{max}(EtOH)/nm 281 (ε 1830); δ_H(250 MHz) 1.40–2.10 (10 H, m, 5 × CH_2), 2.66 (3 H, m, 5-H and 8-H_2), 4.37 (2 H, t, *J* 7.0, CH_2NO_2), 5.10 (1 H, br s, OH), 6.53 (1 H, d, *J* 2.6, 1-H), 6.61 (1 H, dd, *J* 8.3 and 2.6, 3-H) and 6.97 (1 H, d, *J* 8.3, 4-H).

2,3,3a,4,5,6-*Hexahydro*-1-*nitrocyclopenta*[d]*naphthalen*-8-(1H)-*one* **46**.—5,6,7,8-Tetrahydro-5-(3-nitropropyl)-2-naphthol **14c** (88 mg, 0.374 mmol) was dissolved in a mixture of 1 mol dm^{-3} aq. potassium hydroxide (0.83 g, 2.1 base equiv.) and dichloromethane (1 cm^3). This solution was added dropwise over a period of 10 min to a vigorously stirred mixture of previously degassed deionised water (100 cm^3), dichloromethane (60 cm^3) and potassium ferricyanide [$K_3Fe(CN)_6$] (0.62, 1.88 mmol). The mixture was vigorously stirred for 1.75 h. The organic phase was then separated, washed with brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded a solid, which was purified by column chromatography with 50% ether–light petroleum as eluent to yield the *spirodienone* **46** as a solid (61 mg, 70%). Recrystallisation from ethyl acetate afforded crystals, m.p. 119–120 °C (Found: C, 66.8; H, 6.6; N, 5.6%; M^+, 233.105. $C_{13}H_{15}NO_3$ requires C, 66.92; H, 6.49; N, 6.01%; *M*, 233.105); ν_{max}(KBr)/cm^{-1} 2931, 2854, 1664, 1625, 1606 and 1545; λ_{max}(EtOH)/nm 241 (ε 22 200); δ_H(250 MHz) 1.40–3.00 (11 H, m, 5 × CH_2 and 3a-H), 5.41 (1 H, t, *J* 8.8, $CHNO_2$), 6.29 (2 H, m, 7- and 9-H) and 6.94 (1 H, d, *J* 10.6, 10-H); δ_C(22.5 MHz) 24.81, 27.68, 28.34, 29.80 and 32.35 (5 × CH_2), 49.25 (C-3a), 55.26 (C-10a), 90.15 ($CHNO_2$), 127.91 and 130.51 (C-7 and -9), 145.73 (C-10), 159.92 (C-6a) and 185.28 (C=O).

5,6,7,7a,8,9,10,11-*Octahydro*-11-*nitrobenzo*[d]*naphthalen*-3-*one* **47**.—5,6,7,8-Tetrahydro-5-(4-nitrobutyl)-2-naphthol **17c** (83.2 mg, 0.344 mmol) was dissolved in a mixture of 1 mol dm^{-3} aq. potassium hydroxide (0.74 g, 2.1 base equiv.) and dichloromethane (1 cm^3). This was added dropwise during 10 min to a vigorously stirred mixture of previously degassed deionised water (100 cm^3), dichloromethane (50 cm^3) and potassium ferricyanide (0.55, 1.67 mmol). The mixture was stirred vigorously for 2.5 h. The organic phase was then separated, washed with brine, dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded a solid, which was purified by column chromatography with 50% ether–light petroleum as eluent to yield the *spirodienone* **47** as a solid (54.5 mg, 66%). Recrystallisation from ethyl acetate afforded crystals, m.p. 145–148 °C (Found: M^+, 247.119. $C_{14}H_{17}NO_3$ requires M, 247.121); ν_{max}(KBr)/cm^{-1} 2942, 2869, 1664, 1625, 1606 and 1544; λ_{max}(EtOH)/nm 242 (ε 15 600); δ_H(250 MHz) 1.40–2.85 (13 H, m, 6 × CH_2 and 7a-H), 5.32 (1 H, dd, *J* 12.3 and 4.3, $CHNO_2$), 6.19 (1 H, d, *J* 2.0, 4-H), 6.36 (1 H, dd, *J* 10.4 and 2.0, 2-H) and 7.48 (1 H, d, *J* 10.4, 1-H); δ_C(22.5 MHz) 19.07, 25.73, 26.06, 27.14, 28.50 and 33.05 (6 × CH_2), 45.83 (C-7a), 47.57 (C-11a), 86.19 ($CHNO_2$), 127.96 and 131.00 (C-2 and -4), 146.81 (C-1), 162.52 (C-4a) and 184.79 (C=O).

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