The enantioselective synthesis of elecanacin through an intramolecular naphthoquinone-vinyl ether photochemical cycloaddition

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Received 1st December 2005, Accepted 20th December 2005
First published as an Advance Article on the web 19th January 2006
DOI: 10.1039/b517008g

Elecanacin, an unusual cyclobuta-fused naphthalene-1,4-dione derivative isolated from the bulbs of *Eleutherine Americana* Merr. *et* Heyne (Iridaceae) has been obtained, together with its epimer isoelecanacin, by a 2 + 2 cycloaddition resulting from irradiation of 5-methoxy-2-(2-vinyloxypropyl)-naphthalene-1,4-dione. The synthesis of enantiopure elecanacin starting with (*R*)-propylene oxide has established the absolute configuration of the natural product and has revealed that the sample isolated from the bulbs possessed an enantiomeric excess of only 14%.

Introduction

During a search for bioactive constituents from plants of the Iridaceae family used in traditional medicine, Hara and coworkers isolated from the bulbs of *Eleutherine Americana* Merr. *et* Heyne (Iridaceae) a novel dione which they named elecanacin and whose structure (Fig. 1)was deduced as **1** by means of NMR spectroscopy.[1] The absolute stereochemistry was not determined and was arbitrarily depicted as shown in **1** [systematic name: (2*α*, 3*aα*, 4*a*β, 10*aR**)-6-methoxy-2-methyl-1,2,4,4*a*-tetrahydro-10*H*-naphtho[2′,3′:2,3]cyclobuta[1,2-*b*]furan-5,10(3*aH*)-dione]. Also isolated from the same plant were the isomeric and well-known[2–5] pyranonaphthoquinones eleutherin **2** and isoeleutherin **3**.

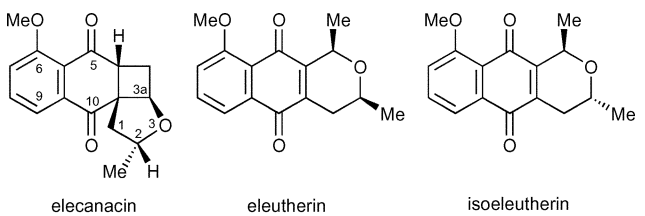
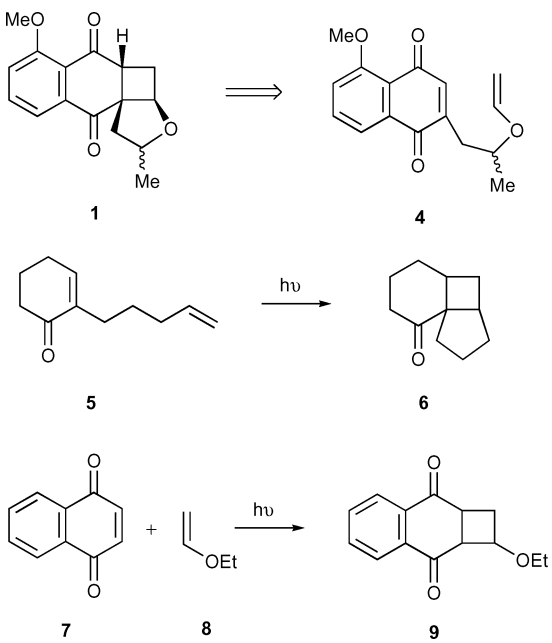


Fig. 1 Structures of elecanacin (absolute configuration is depicted arbitrarily), eleutherin and isoeleutherin.

The ring skeleton of **1** is somewhat unusual for a natural product and has not previously been reported; hence we felt that confirmation of the structure by synthesis was desirable. Leaving aside for the moment the question of the configuration of the methyl-substituted carbon of the tetrahydrofuran ring, simple retrosynthetic considerations suggest that **1** should be accessible through an intramolecular photochemical cycloaddition of the vinyl ether moiety to the double bond within the substituted naphthoquinone **4**. This is based on the premise that intramolecular photocycloadditions in cyclohexenones possessing tethered terminal alkene chains attached to the 2-position are well-known[6] (*e.g.* **5** → **6**)[7] and that the intermolecular photoaddition of ethyl vinyl ether **8** to 1,4-naphthoquinone **7** is reported to give **9**, albeit only in 8% yield.[8] However, intramolecular photoadditions within 2-alkenyl-substituted 1,4-naphthoquinones have, to our knowledge, not been reported. Here we describe the application of such a reaction to the syntheses of racemic and chiral elecanacin; the latter establishes the absolute configuration of the natural product.



Scheme 1 Retrosynthetic analysis for elecanacin and examples of enone and enedione photocycloadditions.

Results and discussion

The synthesis of racemic elecanacin was achieved as shown in Scheme 2.

Allylation of 5-methoxynaphthalen-1-ol **10** followed by Claisen rearrangement and *in situ* acetylation afforded acetate **12**. Careful ozonolysis provided aldehyde **13** which was immediately treated with an excess of methylmagnesium iodide to give the phenolic

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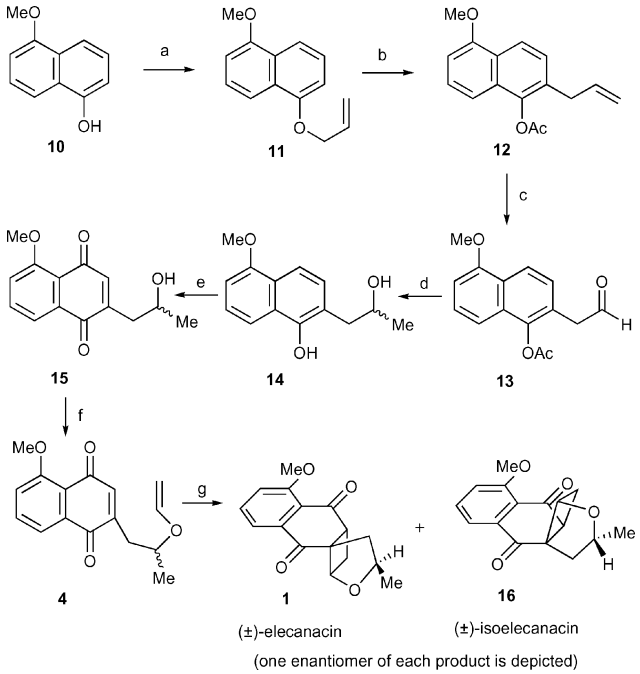


Scheme 2 (a) allyl bromide, K_2CO_3, Me_2CO, reflux, 97%; (b) Ac_2O, $PhNMe_2$, 170 °C, 95%; (c) O_3, CH_2Cl_2–MeOH, −78 °C, then $(NH_2)_2CS$; (d) MeMgI, THF; (e) Fremy's salt, 41% for steps c–e; (f) $EtOCH{=}CH_2$, $Hg(OAc)_2$, 57%; (g) hυ at 350 nm, CH_2Cl_2, 25% **1** and 38% **16**.

alcohol **14**. Oxidation with Fremy's salt yielded the hydroxyquinone **15** which was converted into the vinyl ether **4** in the usual fashion. Irradiation of **4** in dichloromethane at 350 nm cleanly gave two products. These were separated by careful chromatography, and the slightly more polar product, isolated in 25% yield, was (±)-elecanacin, whose ^1H and ^{13}C NMR spectra were identical with those of the naturally occurring (+)-enantiomer. The more mobile component, obtained in 38% yield, we have named isoelecanacin and is formulated as **16** on the basis of NMR (COSY, HMBC, HMQC and NOESY) evidence. The NMR spectral data for **1** and **16** are collected in Table 1 and the key NOESY correlations within the oxabicyclo[3.2.0]heptane framework are displayed in Fig. 2. The aromatic proton signals in both isomers display second order characteristics, even at 500 MHz, rather than the first order pattern implied[1] for elecanacin.

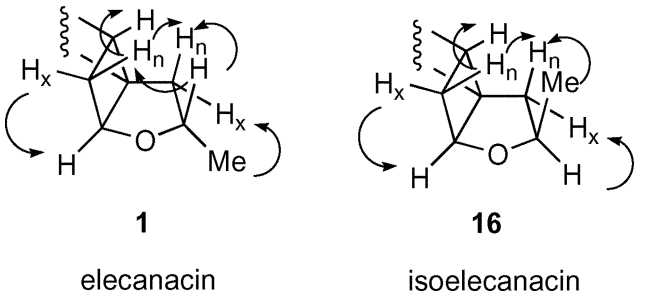


Fig. 2 Key NOESY correlations within the 2-oxabicyclo[3.2.0]heptyl framework of elecanacin (ref. 1) and isoelecanacin (this work).

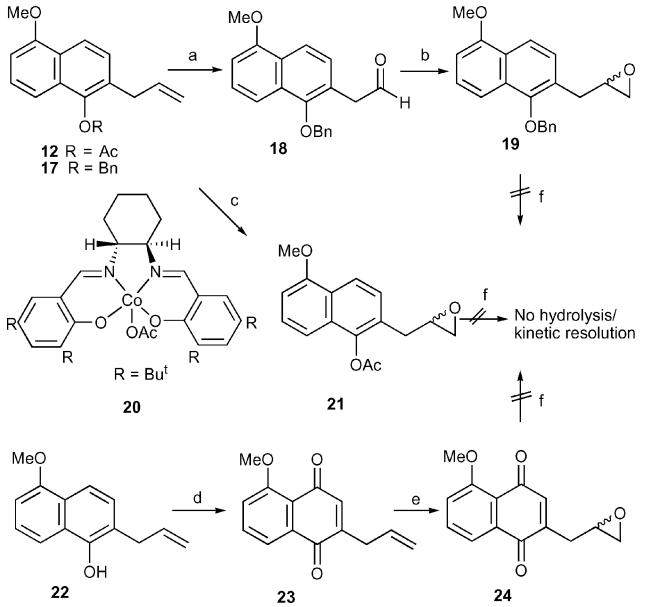
In the photochemical cycloaddition reaction, compounds **1** and **16** arise by addition of the vinyl ether moiety to the two diastereotopic faces of the carbon–carbon double bond of the naphthoquinone system of **4**. Monitoring of the reaction showed that both products were formed at early stages and control experiments established that **1** and **16** were photostable and not interconverted under the irradiation conditions.

Our first approach to enantiopure elecanacin (Scheme 3) was based on the assumption that hydrolytic kinetic resolution of a racemic epoxide such as **19** or **21** using Jacobsen's catalyst[9,10] **20** would provide a chiral epoxide, which on reductive opening with lithium aluminium hydride and removal of the protecting group could deliver one enantiomer of the phenolic alcohol **14** depicted in Scheme 2. In the event, epoxidation of the monosubstituted ethylene moiety of acetate **12** and benzyl ether **17** with *m*-chloroperoxybenzoic acid proceeded sluggishly and appeared to be accompanied by degradation of the electron-rich naphthalene ring system. The epoxy acetate **21** could be obtained in poor yield by treatment of **12** with dimethyldioxirane, while the epoxy benzyl ether **19** was obtained satisfactorily by reaction of aldehyde **18** with dimethylsulfoxonium methylide. Unfortunately both **19**

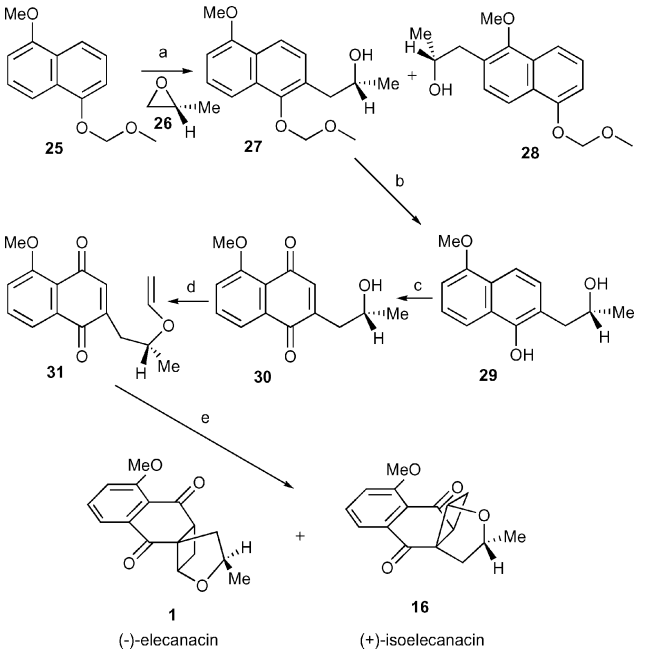
Table 1 ^{13}C; ^1H NMR data for elecanacin and isoelecanacin (300 MHz, $CDCl_3$)

	Position	Elecanacin	Isoelecanacin
	1	45.3; 2.29, dd, *J* 12.6, 10.0, H_x;[a] 2.20, dd, *J* 12.6, 4.7, H_n	45.5; 1.75, dd, *J* 12.6, 9.6, H_x; 2.86, dd, *J* 12.6, 5.5, H_n
	2	76.6; 4.60–4.48, m	81.5; 4.38–4.31, m
	3a	80.9; 4.62–4.58, m	81.6; 4.46–4.43, m
	4	31.0; 2.65–2.50, m	31.6; 2.52–2.49, m
	4a	45.3; 3.23–3.17, m	47.5; 3.30–3.29, m
	5	196.2[b]	196.1[b]
	5a	124.3	124.4
	6	159.2	159.3
	7	117.2; 7.29, X part of ABX	117.4; 7.29, X part of ABX
	8	134.9[c]; *c.* 7.64, B part of ABX	134.8; *c.* 7.66, B part of ABX
	9	119.3[c]; *c.* 7.68, A part of ABX	119.4; *c.* 7.66, A part of ABX
	9a	138.2	137.5
	10	195.8[b]	195.7[b]
	10a	61.2	59.7
	Me	19.2; 1.45, d, *J* 5.9	20.6; 1.42, d, *J* 6.1
	MeO	56.5; 3.96, s	56.5; 3.96, s

[a] H_x is *exo* within the oxabicyclo[3.2.0]heptane moiety, H_x is *endo*. [b] Values can be interchanged within each column. [c] As assigned in ref. 1 and consistent with incremental shift calculations.



Scheme 3 (a) O_3, CH_2Cl_2–MeOH, −78 °C, then $(NH_2)_2CS$, 65%; (b) trimethylsulfoxonium iodide, NaH, Me_2SO, 69%; (c) dimethyldioxirane, Me_2CO, 23%; (d) Fremy's salt, 91%; (e) *m*-Cl–C_6H_4–CO_3H, CH_2Cl_2, 67%; (f) **20**, H_2O.



Scheme 4 (a) BuLi, THF, −78 °C, HMPA, **26**, 53% **27** and 13% **28**; (b) CBr_4, 2-propanol, reflux, 73%; (c) Fremy's salt, 97%; (d) $EtOCH{=}CH_2$, $Hg(OAc)_2$, 51%; (e) hυ at 350 nm, CH_2Cl_2, 24% **1** and 40% **16**.

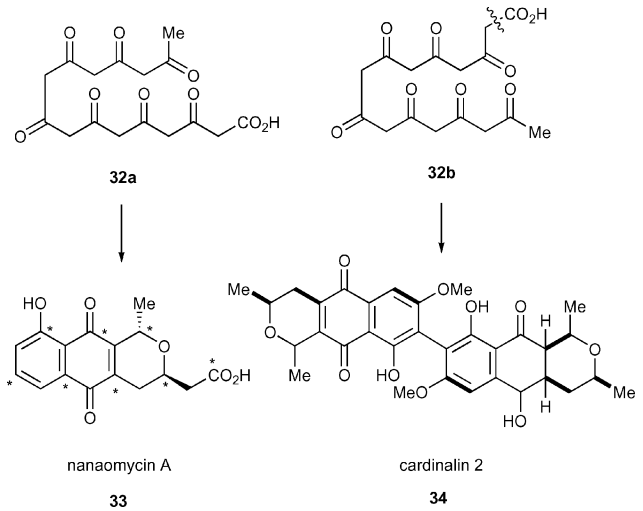
and **21** were recovered essentially unchanged when exposed to the usual conditions for hydrolytic kinetic resolution, even after long reaction times. Since we felt that the electron-rich naphthalene moieties of **19** and **21** could possibly interfere in the catalytic hydrolytic cycle, we prepared the quinonoid epoxide **24** by treatment of quinone **23** with *m*-chloroperoxybenzoic acid. However **24** also was recovered unchanged when subjected to the reaction conditions. Control reactions showed that, using the same batch of catalyst, simple epoxides such as epichlorohydrin and propylene oxide were resolved under these conditions, as described in the literature.[9,10] Although the hydrolytic kinetic resolution of the epoxides **19**, **21** and **24** may well be achievable with further experimentation, particularly in regard to variation of the organic solvent,[10] we adopted instead the approach outlined in Scheme 4.

Metallation of 1-methoxy-5-(methoxymethoxy)naphthalene[11] **25** with *n*-butyllithium followed by sequential addition of HMPA and (*R*)-(+)-propylene oxide **26** afforded the desired alcohol **27** (53%) together with alcohol **28** (13%) resulting from metallation and alkylation *ortho* to the methoxy group. Removal of the MOM protecting group of **27** was achieved by action of carbon tetrabromide in refluxing 2-propanol.[12] The enantiomeric ratio for the resulting alcohol **29** was estimated to be greater than 95 : 5 by examination of its ^{1}H NMR spectrum in the presence of the chiral shift reagent europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate], indicating that the enantiomeric excess (ee) within **29** was greater than 90%. Surprisingly the chiral shift reagent failed to induce significant chemical shift changes for protons near the stereocentre and the only significant induced shift was observed for the aromatic proton 8-H. A more precise upper limit for the ee could not be ascertained at this stage due to some line-broadening of this signal.

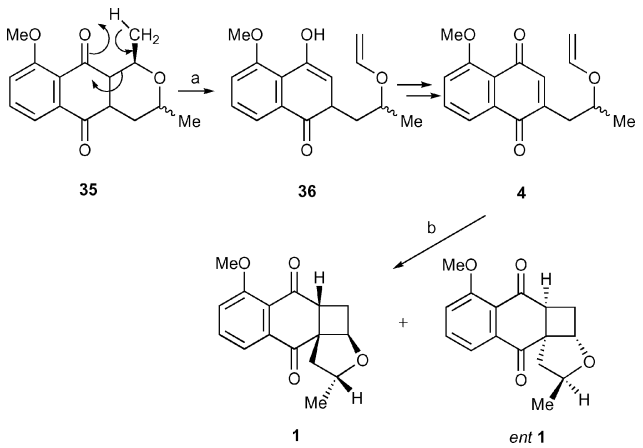
Oxidation of **29** with Fremy's salt provided the quinone **30**, which was converted into the vinyl ether **31** as in the racemic series. Irradiation followed by chromatographic separation gave (2*R*, *3aR*, *4aR*, *10aR*)-elecanacin **1** having $[\alpha]_D$ − 145° ($CHCl_3$) after recrystallisation and an ee of (99.5% as determined by HPLC using a chiral stationary phase. The optical rotation reported[1] for natural elecanacin is +20.7° and thus the major natural enantiomer is the mirror image of **1**, and the configuration is (*2S*, *3aS*, *4aS*, *10aS*) (see structure *ent*-**1** in Scheme 6 later). From the magnitude of the reported rotation, the enantiomeric excess is only 14% and thus elecanacin is another example of a natural product that does not occur in enantiopure form.[13]

Although the biosynthesis of eleutherin **2** and isoeleutherin **3** does not appear to have been investigated, it presumably involves a polyketide pathway, as has been established for other pyranonaphthoquinones.[14,15] For example, labelling experiments have revealed that the bacterial metabolite nanaomycin A **33** is assembled from an octaketide by a folding resulting from orientation **32a** (Scheme 5), whereas in the biosynthesis of cardinalin 2 **34** in the fruiting bodies of the toadstool *Dermocybe cardinalis* the alternative orientation **32b** for cyclisation of the octaketide has been established.[15] It has been suggested that this also may be the pathway for the synthesis of pyranonaphthoquinones in plants.[15]

Given that eleutherin and isoeleutherin are polyketide-derived, what is the biogenetic origin of elecanacin? We note that, *formally* the vinyl ether **4** can be derived from the Norrish type II cleavage of **35**, the dihydro-derivative of eleutherin and isoeleutherin, followed by oxidation (Scheme 6). Subsequent intramolecular 2 + 2 cycloaddition would then deliver elecanacin **1**. The enantiomeric ratio of the product **1** would be determined by the configurational ratio at 2-C inherent within **35**. Since both eleutherin and isoeleutherin co-occur in the plant, the involvement of a biosynthetic precursor such as **35** having both configurations at



Scheme 5 Incorporation of 1-^{13}C labelled acetate into nanaomycin and of 1,2-$^{13}C_2$ labelled acetate into cardinalin 2 (identified labelled units shown in bold).



Scheme 6 Formal derivation of vinyl ether **4** and elecanacin **1** from the dihydro derivative **35** of eleutherin and isoeleutherin.

the methyl-substituted carbon would explain the low ee observed for elecanacin.

Of the pericyclic reactions possibly involved in biological systems,[16] the Diels–Alder reaction has attracted considerable attention and evidence has been presented for the existence of Diels–Alderases.[17,18] Although the suggestion that elecanacin could possibly be generated *in vivo* by a sequence involving pericyclic reactions as shown in Scheme 6 must be regarded as highly speculative, we note that ethylene has been reported to arise from a Norrish type II fragmentation of enzymatically generated triplet butanal, providing an example of a photobiochemical reaction without light.[19] The cleavage step a in Scheme 6 therefore has some precedence. Furthermore, very recently evidence has been presented that the conversion of isochorismate to salicylate and pyruvate, catalysed by the enzyme isochorismate pyruvate lyase, involves a one-step pericyclic retro-ene process.[20] However, at this stage there appear to be no enzyme-mediated analogies for the 2 + 2 cycloaddition. We consider it unlikely that the vinyl ether **4** is in fact a natural product and that elecanacin then arises as an artifact through photochemical cyclisation during isolation and workup.

Although we find that in solution **4** undergoes ready cyclisation when exposed to ambient laboratory light, elecanacin is, as in the preparative reactions, accompanied by isoelecanacin **16**. In view of the close chromatographic R_f values of these products, we believe it to be unlikely that **16** would have been missed during the isolation of **1**.[1] Thus elecanacin is more likely to be a product of a diastereoselective enzyme-mediated reaction rather than an artifact arising from photochemical transformation of **4**.

Conclusion

In summary, we have confirmed the nature of the novel ring system of elecanacin **1** and the absolute configuration and low ee of the natural product through rational synthesis. The biochemical pathway that generates **1** in the plant remains to be elucidated.

Experimental

General details have been given previously.[21] Irradiations were carried out through Pyrex in an Oliphant photochemical chamber reactor equipped with Sylvania F 815/BLB tubes emitting at 350 nm. HPLC was performed using a Chiracel OD column (Daicel Chemical Industries) fitted to an ICI 1110 pump interfaced with a Hewlett Packard Series 1050 instrument using UV detection at 254 nm. The solvent was 2-propanol-hexane 1 : 5 with a flow rate of 0.5 mL min^{-1}.

5-Methoxy-1-(2-propenyloxy)naphthalene 11

The procedure was adapted from that described by Eisenhuth and Schmid.[4] 5-Methoxy-1-naphthol **10** (3.51 g, 20.2 mmol), allyl bromide (2.8 ml, 3.88 g, 32.1 mmol) and potassium carbonate (4.28 g, 31.0 mmol) in acetone (90 ml) were refluxed for 3 h under a nitrogen atmosphere. The reaction mixture was allowed to cool to room temperature, left to stand overnight and then poured into water (450 ml) and extracted with ether (3 × 60 ml). The combined organic extracts were washed successively with 10% sodium hydroxide solution (50 ml), water (50 ml) and brine (50 ml), then dried and evaporated to give 5-methoxy-1-(2-propenyloxy)naphthalene as a yellow crystalline solid (4.17 g, 97%), mp 96–98 °C (lit.,[21] 98 °C). δ_H (200 MHz, $CDCl_3$) 7.91 (1H, d, *J* 8.5, ArH), 7.85 (1H, d, *J* 8.5, ArH), 7.43–7.32 (2H, m, 2 × ArH), 6.86 (2H, d, *J* 7.7, 2 × ArH), 6.19 (1H, ddt, *J* 17.3, 10.5 and 5.1, CH, vinylic), 5.53 (1H, dtd, *J* 17.3, 1.5 and 1.5, CH, vinylic), 5.34 (1H, dtd, *J* 10.5, 1.5 and 1.5, CH, vinylic), 4.72 (2H, ddd, *J* 5.1, 1.5 and 1.5, CH_2), 4.00 (3H, s, OCH_3).

5-Methoxy-2-(2-propenyl)naphthalen-1-yl acetate 12

A stirred solution of 5-methoxy-1-(2-propenyloxy)naphthalene (4.17 g, 19.5 mmol) in acetic anhydride (31.0 ml, 33.5 g, 328 mmol) and *N*,*N*-diethylaniline (100 ml, 93.3 g, 625 mmol) was heated at 165–170 °C (bath) for 6 h under an argon atmosphere, then allowed to cool to room temperature and left to stir for 24 h. The solution was diluted with water (250 ml) and extracted with ether (3 × 60 ml). The combined ether extracts were washed with 2 M hydrochloric acid solution (3 × 100 ml), followed by saturated sodium carbonate solution (80 ml) and brine (80 ml), dried and evaporated to give 5-methoxy-2-(2-propenyl)naphthalen-1-yl acetate as a yellow-brown oil (4.74 g, 95%), which was pure by

^{1}H NMR. δ_H (200 MHz, $CDCl_3$) 8.11 (1H, d, *J* 8.8, ArH), 7.46–7.29 (3H, m, ArH), 6.80 (1H, d, *J* 7.4, ArH), 6.06–5.82 (1H, m, CH, vinylic), 5.18–5.04 (2H, m, 2 × CH, vinylic), 3.97 (3H, s, OCH_3), 3.43 (2H, ddd, *J* 6.6, 1.5 and 1.5, CH_2), 2.45 (3H, s, CH_3).

5-Methoxy-2-(2-formylmethyl)naphthalen-1-yl acetate 13

Ozone was bubbled through a solution of 5-methoxy-2-(2-propenyl)naphthalen-1-yl acetate (3.87 g, 15.1 mmol) in dichloromethane/methanol (4 : 1, 180 ml) at −78 °C until TLC indicated that all the starting material had been consumed (45 min). The solution did not turn blue. Oxygen, followed by nitrogen was bubbled through the solution in order to displace the ozone. The cold solution was added dropwise to a stirred suspension of thiourea (1.41 g, 18.5 mmol) and sodium bicarbonate (826 mg, 9.84 mmol) in dichloromethane (50 ml) at ice bath temperature and stirred for 1.5 h under a nitrogen atmosphere. The resulting reaction mixture was diluted with water (350 ml) and the organic layer was separated. The aqueous layer was extracted with dichloromethane (2 × 40 ml) and the combined organic extracts were washed with brine, dried and evaporated to give the aldehyde as a yellow oil (4.03 g), which was refrigerated overnight. δ_H (200 MHz, $CDCl_3$) 9.69 (1H, t, *J* 2.4, CHO), 8.20 (1H, d, *J* 8.8, ArH), 7.48–7.30 (3H, m, ArH), 6.85 (1H, d, *J* 7.5, ArH), 4.00 (3H, s, OCH_3), 3.70 (2H, d, *J* 2.4, CH_2), 2.46 (3H, s, CH_3). Due to its instability, the aldehyde was used directly in the next reaction without purification or further characterisation.

1-(1-Hydroxy-5-methoxynaphthalen-2-yl)propan-2-ol 14

A solution of methyl iodide (6.2 ml, 14.1 g, 99.7 mmol) in anhydrous tetrahydrofuran (35 ml) was added dropwise to magnesium turnings (2.28 g, 93.8 mmol) at room temperature under an argon atmosphere. The mixture was stirred and diluted by the dropwise addition of anhydrous tetrahydrofuran (70 ml). Upon completion of the reaction, the Grignard reagent was cooled in an ice bath and a solution of crude 5-methoxy-2-(2-formylmethyl)naphthalen-1-yl acetate (4.03 g, 15.6 mmol) in anhydrous tetrahydrofuran (100 ml) was added dropwise. Then the resulting mixture was allowed to warm to room temperature and stirring was continued for a further 2 h. The reaction mixture was carefully quenched with water (300 ml), acidified with concentrated hydrochloric acid, and extracted with ethyl acetate (3 × 70 ml). The combined organic extracts were washed with water (70 ml) followed by brine (70 ml), dried and evaporated to give *1-(1-hydroxy-5-methoxynaphthalen-2-yl)propan-2-ol* as an orange oil (3.55 g), which was used directly in the next reaction. A small sample was subjected to radial chromatography. Elution with 10% ethyl acetate-light petroleum gave a clear oil, which solidified upon refrigeration and recrystallised from dichloromethane-light petroleum as white plates, mp 83–84 °C (Found: C, 72.4; H, 7.0. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%). (Found M^+, 232.1103. $C_{14}H_{16}O_3$ requires 232.1099). Mass Spectrum *m/z*: 232 (M, 25%), 214 (100), 212 (28), 199 (47), 187 (18), 186 (29), 171 (28), 169 (21), 128 (21), 115 (43). δ_H (300 MHz, $CDCl_3$) 7.88 (1H, dt, *J* 8.5 and 0.8, ArH), 7.74 (1 H, dd, *J* 8.5 and 0.6, ArH), 7.37 (1 H, dd, *J* 8.5 and 7.7, ArH), 7.12 (1H, d, *J* 8.5, ArH), 6.80 (1H, d, *J* 7.7, ArH), 4.36–4.27 (1H, m, CH), 3.99 (3H, s, OCH_3) 3.01 (1H, dd, *J* 14.7 and 2.5, CH of methylene), 2.90 (1H, dd, *J* 14.7 and 7.1, CH of methylene), 1.27 (3H, d, *J* 6.2, CH_3). δ_C (75.5 MHz, $CDCl_3$) 155.1 (C), 150.9 (C), 129.0 (CH), 126.8 (C), 126.0 (C), 125.0 (CH), 118.9 (C), 114.6 (CH), 113.5 (CH), 103.8 (CH), 70.9 (CH), 55.5 (OCH_3), 40.5 (CH_2), 23.2 (CH_3).

2-(2-Hydroxypropyl)-5-methoxynaphthalene-1,4-dione 15

A solution of 1-(1-hydroxy-5-methoxynaphthalen-2-yl)propan-2-ol (3.48 g, 15.0 mmol) in ethyl acetate (80 ml) was added to a separating funnel containing Fremy's salt (8.25 g, 30.8 mmol) dissolved in an aqueous borax buffer solution (0.025 M sodium tetraborate, 250 ml; 0.1 M sodium hydroxide, 121 ml). The resulting mixture was shaken until TLC indicated that the starting material had been consumed (*ca* 40 min). The mixture was diluted with brine (50 ml) and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (4 × 60 ml). The combined organic extracts were washed with brine (80 ml), dried and evaporated to give a yellow oil, which was subjected to silica gel filtration. Elution with 30% ethyl acetate-light petroleum gave 2-(2-hydroxypropyl)-5-methoxynaphthalene-1,4-dione as a yellow oil (1.54 g, 41% over 3 steps) which solidified upon refrigeration. A small sample recrystallised from ethyl acetate-light petroleum as fine yellow needles, mp 95–96 °C (lit.,[4] 96–97 °C). (Found M^+, 246.0894. $C_{14}H_{14}O_4$ requires 246.0892). Mass Spectrum *m/z*: 246 (M, 23%), 230 (27), 204 (73), 203 (54), 202 (100), 187 (15), 175 (17), 174 (32), 173 (38), 159 (25), 144 (15), 131 (23), 115 (34). ($_H$ (300 MHz, $CDCl_3$) 7.75 (1H, dd, *J* 7.7 and 1.2, ArH), 7.66 (1H, dd, *J* 8.4 and 7.7, ArH), 7.29 (1 H, dd, *J* 8.4 and 1.1, ArH), 6.78 (1H, t, *J* 1.0, CH, vinylic), 4.15–4.03 (1H, m, CH), 4.00 (3H, s, OCH_3) 2.74 (1H, ddd, *J* 13.8, 4.1 and 1.0, CH of methylene), 2.59 (1H, ddd, *J* 13.8, 8.0 and 1.0, CH of methylene), 1.29 (3H, d, *J* 6.2, CH_3). δ_C (75.5 MHz, $CDCl_3$) 186.1 (C=O), 184.3 (C=O), 159.4 (C), 145.6 (C), 139.2 (CH), 134.7 (CH), 134.3 (C), 119.8 (C), 119.5 (CH), 117.8 (CH), 66.7 (CH), 56.4 (OCH_3), 39.1 (CH_2), 23.7 (CH_3). λ_{max} (CH_2Cl_2) (log ε) 247 (4.14), 268 (3.22), 354 (4.06), 396 (3.54). ν_{max}(CH_2Cl_2)/cm^{-1} 1658 (C=O).

5-Methoxy-2-(2-vinyloxypropyl)naphthalene-1,4-dione 4

A solution of 2-(2-hydroxypropyl)-5-methoxynaphthalene-1,4-dione (1.43 g, 5.80 mmol) and mercuric acetate (351 mg, 1.10 mmol) in ethyl vinyl ether (35 ml, 26.4 g, 366 mmol) and dichloromethane (10 ml) in a foil-covered flask was refluxed for 6 h under an argon atmosphere. The solution was kept at room temperature for 2 days, then poured into water and extracted with dichloromethane (3 × 40 ml). The combined organic extracts were washed with brine, dried and evaporated to give a yellow residue, which was subjected to silica gel filtration. Elution with 15% ethyl acetate-light petroleum gave *5-methoxy-2-(2-vinyloxypropyl)naphthalene-1,4-dione* (903 mg, 57%) as a yellow oil. (Found M^+, 272.1054. $C_{16}H_{16}O_4$ requires 272.1049). Mass Spectrum *m/z*: 273 (M(1, 17%), 272 (M, 97), 243 (16), 230 (34), 229 (100), 228 (36), 227 (18), 215 (15), 213 (31), 211 (19), 205 (19), 202 (27), 201 (19), 188 (27), 187 (36). δ_H (300 MHz, $CDCl_3$) 7.74 (1H, dd, *J* 7.7 and 1.2, ArH), 7.66 (1H, dd, *J* 8.3 and 7.7, ArH), 7.28 (1 H, dd, *J* 8.3 and 1.2, ArH), 6.75 (1H, t, *J* 1.0, CH, vinylic), 6.27 (1H, dd, *J* 6.7 and 14.2, CH, vinylic), 4.30 (1H, dd, *J* 14.2 and 1.7, CH, vinylic), 4.26–4.15 (1H, m, CH), 4.00–3.99 (1H, m, CH, vinylic), 3.99 (3H, s, OCH_3) 2.79 (1H, ddd, *J* 13.9, 7.4 and 1.1, CH of methylene), 2.67 (1H, ddd, *J* 13.9, 5.3 and

1.1, CH of methylene), 1.27 (3H, d, *J* 6.2, CH_3). δ_C (75.5 MHz, $CDCl_3$) 185.4 (C=O), 184.3 (C=O), 159.4 (C), 150.3 (CH), 144.7 (C), 139.3 (CH), 134.7 (CH), 134.2 (C), 119.4 (CH), 117.7 (CH), 88.8 (CH_2), 77.2 (C), 73.2 (CH), 56.4 (OCH_3), 36.1 (CH_2), 20.0 (CH_3). λ_{max} (CH_2Cl_2) (log ε) 230 (4.10), 238 (4.15), 262 (4.06), 333 (3.22), 249 (3.24), 393 (3.46). ν_{max} (CH_2Cl_2)/cm^{-1} 1658 (C=O).

(±)-Elecanacin 1 and and (±)-isoelecanacin 16

A deoxygenated solution of 5-methoxy-2-(2-vinyloxypropyl)-naphthalene-1,4-dione **4** (122 mg, 0.45 mmol) in anhydrous dichloromethane (50 ml) was irradiated at 350 nm through Pyrex for 65 min, when TLC indicated that all the starting material had been consumed. The solvent was evaporated and the yellow residue was subjected to careful radial chromatography. Elution with 20% ethyl acetate-light petroleum gave (±)-*isoelecanacin* **16** (46 mg, 38%) as a yellow oil, which solidified upon refrigeration and recrystallised from dichloromethane-light petroleum as white needles, mp 114–115 °C. (Found M^+, 272.1048. $C_{16}H_{16}O_4$ requires 272.1049). Mass Spectrum *m*/*z*: 273 (M + 1, 16%), 272 (M, 100), 270 (22), 244 (22), 243 (87), 242 (20), 241 (16), 229 (41), 228 (20), 227 (30), 217 (19), 211 (19), 201 (15), 189 (19), 187 (22), 153 (65), 136 (57), 135 (17), 128 (16), 115 (27), 108 (19), 107 (71), 106 (55), 105 (39), 104 (17), 90 (19), 89 (96). The ^{13}C and ^1H NMR spectral data are given in Table 1. ν_{max} (CH_2Cl_2)(cm^{-1} 1683 (C=O). Analysis on the Chiracel OD column showed two peaks in a ratio of 48 : 52 at retention times 19.2 and 22.6 min. Further elution with 30% ethyl acetate-light petroleum gave (±)-*elecanacin* **1** (31 mg, 25%) as a yellow oil which could not be induced to crystallise (lit.,[1] mp 198 °C for optically active material). (Found M^+, 272.1050. $C_{16}H_{16}O_4$ requires 272.1049). Mass Spectrum *m*/*z*: 273 (M + 1, 17%), 272 (M, 100), 244 (22), 243 (88), 229 (30), 228 (19), 227 (21), 217 (15), 215 (15), 211 (15), 202 (16), 201 (15), 189 (17), 187 (17), 135 (18), 128 (16), 115 (23). The ^{13}C and ^1H NMR spectral data are shown in Table 1 and are identical with those of natural elecanacin. ν_{max} (CH_2Cl_2)/cm^{-1} 1684 (C=O). Analysis on the Chiracel OD column showed two peaks in the ratio of 52 : 48 at retention times 26.5 and 39.2 min.

When the irradiation was repeated and the reaction was interrupted at low conversion of reactant, elecanacin and isoelecanacin were found to be present in the same ratio as at complete conversion (TLC and NMR analysis). Irradiation of pure samples of elecanacin and isoelecanacin in dichloromethane led to no change.

Conversion of the vinyl ether **4** into elecanacin and isoelecancin also was observed when a solution of **4** in dichloromethane was kept in ambient laboratory light.

2-(2,3-Epoxypropyl)-5-methoxynaphthalen-1-yl acetate 21

A cold solution of an excess of dimethyldioxirane in acetone (60 ml), prepared according to the procedure described by Murray and Singh,[22] was added to a solution of 5-methoxy-2-(2-propenyl)naphthalen-1-yl acetate (1.16 g, 453 mmol) in acetone (10 ml) and left to stir for 16 h at room temperature. The solution was diluted with water (350 ml) and extracted with ethyl acetate (3 × 70 ml). The extracts were washed with brine, dried and evaporated to give a brown oil, which was subjected to silica gel filtration. Elution with 5% ethyl acetate-light petroleum returned unreacted starting material as a yellow oil (89 mg). Further elution with 10% ethyl acetate-light petroleum gave a yellow oil (348 mg), which was subjected to radial chromatography. Elution with 5% ethyl acetate-light petroleum gave the *epoxide* as a colourless oil (279 mg, 23%). (Found: M^+, 272.1042. $C_{16}H_{16}O_4$ requires 272.1049). Mass spectrum (FAB) *m*/*z*: 273 (M (1, 74%), 272 (M, 100), 231 (32), 230 (88), 213 (64), 212 (32), 187 (35). δ_H (300 MHz, $CDCl_3$) 8.15 (1H, d, *J* 8.7, ArH), 7.44–7.39 (2H, m, ArH), 7.30 (1H, d, *J* 8.5, ArH), 6.82 (1H, d, *J* 7.1, ArH), 3.99 (3H, s, OCH_3), 3.22–3.18 (1H, m, CH, X of ABX), 3.01 (1H, dd, *J* 14.6 and 5.5, CH of methylene), 2.88–2.79 (2H, m, 2 × CH of methylene), 2.59 (1H, m, CH of methylene), 2.49 (3H, s, CH_3). δ_C (75.5 MHz, $CDCl_3$) 169.3 (C=O), 155.6 (C), 144.3 (C), 128.1 (C), 127.0 (CH), 126.8 (CH), 126.4 (C), 125.9 (C), 120.5 (CH), 113.2 (CH), 104.1 (CH), 55.6 (OCH_3), 51.4 (CH), 47.0 (CH_2), 33.5 (CH_2), 20.7 (CH_3).

1-Benzyloxy-5-methoxy-2-(2-propenyl)naphthalene 17

Benzyl bromide (6.13 g, 35.8 mmol) was added to a mechanically stirred suspension of 5-methoxy-2-(2-propenyl)naphthalen-1-ol (6.40 g, 29.9 mmol) and potassium carbonate (6.52 g, 47.2 mmol) in acetone (200 ml) and the mixture was refluxed for 3 h under an argon atmosphere. The mixture was diluted with water (400 ml) and extracted with ether (3 × 60 ml). The combined organic extracts were washed with 10% sodium hydroxide solution (60 ml) followed by brine (70 ml), dried and evaporated to give a yellow oil (9.70 g). Kugelrohr distillation under a vacuum gave *1-benzyloxy-5-methoxy-2-(2-propenyl)naphthalene* (7.63 g, 84%) as a pale yellow oil, which solidified upon refrigeration. A sample recrystallised from light petroleum as white plates, mp 46–47 °C. (Found: M^+, 304.1455. $C_{21}H_{20}O_2$ requires 304.1463). Mass spectrum *m*/*z*: 304 (M, 60%), 214 (18), 213 (100), 198 (20), 153 (20), 115 (18), 91 (90), 77 (23). δ_H (300 MHz, $CDCl_3$) 8.03 (1H, d, *J* 8.7, ArH), 7.73 (1H, d, *J* 8.5, ArH), 7.59–7.56 (2H, m, ArH), 7.48–7.32 (5H, m, ArH), 6.82 (1H, d, *J* 7.3, ArH), 6.10–5.96 (1H, m, CH, vinylic), 5.14–5.06 (2H, m, 2 × CH, vinylic), 5.02 (2H, s, OCH_2), 4.01 (3H, s, OCH_3), 3.61 (2H, ddd, *J* 5.0, 1.4 and 1.4, CH_2). δ_C (75.5 MHz, $CDCl_3$) 155.8 (C), 151.8 (C), 137.5 (C), 137.2 (CH), 129.4 (C), 129.1 (C), 128.6 (CH), 128.0 (CH), 127.7 (CH), 127.5 (CH), 126.0 (CH), 125.9 (C), 118.2 (CH), 115.9 (CH_2), 114.4 (CH), 103.6 (CH), 76.2 (CH_2), 55.5 (OCH_3), 34.0 (CH_2).

2-(1-Benzyloxy-5-methoxynaphthalen-2-yl)ethanal 18

Ozone was bubbled through a solution of 1-benzyloxy-5-methoxy-2-(2-propenyl)naphthalene **17** (2.31 g, 7.60 mmol) in dichloromethane(methanol (4 : 1, 180 ml) at −78 °C, until TLC indicated that the starting material had been consumed (*ca.* 20 min). The solution did not turn blue. Oxygen, followed by argon was bubbled through the solution in order to displace the ozone. The cold solution was added dropwise to a stirred suspension of thiourea (687 mg, 9.02 mmol) and sodium bicarbonate (457 mg, 5.44 mmol) in dichloromethane (60 ml) at ice bath temperature and stirred for 1.5 h under an argon atmosphere. The reaction mixture was then diluted with water (300 ml), the organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 60 ml). The combined organic extracts were washed with brine (80 ml), dried and evaporated to give a yellow oil, which was subjected to silica gel filtration. Elution with 5%

ethyl acetate-light petroleum gave the *aldehyde* as a faint yellow oil (1.51 g, 65%). (Found: M^+, 306.1251. $C_{20}H_{18}O_3$ requires 306.1256). Mass spectrum *m/z*: 306 (M, 24%), 288 (54), 215 (43), 198 (26), 187 (54), 155 (25), 149 (29), 127 (19), 115 (22), 91 (100), 84 (20), 83 (17), 77 (18), 71 (20), 69 (21), 57 (36). δ_H (300 MHz, $CDCl_3$) 9.70 (1H, t, *J* 2.2, CHO), 8.09 (1H, dd, *J* 8.6 and 0.4, ArH), 7.73 (1H, d, *J* 8.5, ArH), 7.50–7.36 (6H, m, ArH), 7.26 (1H, d, *J* 8.6, ArH), 6.86 (1H, d, *J* 7.3, ArH), 5.02 (2H, s, OCH_2), 4.02 (3H, s, OCH_3), 3.78 (2H, d, *J* 2.2, CH_2). δ_C (75.5 MHz, $CDCl_3$) 199.7 (C=O), 155.9 (C), 152.9 (C), 136.8 (C), 129.2 (C), 128.6 (CH), 128.3 (CH), 128.0 (CH), 127.4 (CH), 126.8 (C), 126.5 (CH), 122.1 (C), 118.9 (CH), 114.3 (CH), 104.2 (CH), 76.2 (CH_2), 55.6 (OCH_3), 45.3 (CH_2).

1-Benzyloxy-2-(2,3-epoxypropyl)-5-methoxynaphthalene 19

Trimethylsulfoxonium iodide (999 mg, 4.54 mmol) was added portionwise over 20 min to sodium hydride (60% oil dispersion, 186 mg, 4.65 mmol) in anhydrous dimethyl sulfoxide (4 ml) under an argon atmosphere and the resulting suspension was stirred for 30 min. 2-(1-Benzyloxy-5-methoxynaphthalen-2-yl)ethanal **18** (526 mg, 1.72 mmol) in anhydrous dimethyl sulfoxide (4 ml) was added dropwise and the resulting mixture was stirred at room temperature for 1 h 45 min. The mixture was quenched with ice, diluted with water (80 ml) and extracted with ether (4 × 40 ml). The combined organic extracts were washed with brine (50 ml), dried and evaporated to give a yellow oil, which was subjected to silica gel filtration. Elution with 5% ethyl acetate-light petroleum afforded the *epoxide* **21** as a colourless oil (383 mg, 69%). (Found: M^+, 320.1422. $C_{21}H_{20}O_3$ requires 320.1412). Mass spectrum *m/z*: 321 (M+1, 20%), (M, 89), 230 (23), 229 (28), 201 (15), 199 (57), 187 (22), 186 (24), 171 (37), 155 (20), 128 (20), 127 (22), 115 (23), 91 (100), 77 (24), 69 (17), 57 (23). δ_H (300 MHz, $CDCl_3$) 8.04 (1H, d, *J* 8.9, ArH), 7.72 (1H, d, *J* 8.5, ArH), 7.57–7.39 (7H, m, ArH), 6.83 (1H, d, *J* 7.3, ArH), 5.05 (2H, s, OCH_2), 4.01 (3H, s, OCH_3), 3.24–3.18 (1H, m, CH, X of ABX), 3.10 (1H, dd, *J* 14.3 and 5.3, CH of methylene), 3.00 (1H, dd, *J* 14.3 and 5.4, CH of methylene), 2.85 (1H, m, CH of methylene), 2.60 (1H, m, CH of methylene). δ_C (75.5 MHz, $CDCl_3$) 155.8 (C), 152.3 (C), 137.4 (C), 129.3 (C), 128.6 (CH), 128.1 (CH), 127.7 (CH), 127.4 (CH), 126.7 (C), 126.3 (C), 126.2 (CH), 118.5 (CH), 114.3 (CH), 103.8 (CH), 76.3 (CH_2), 55.6 (OCH_3), 52.1 (CH), 47.1 (CH_2), 32.9 (CH_2).

5-Methoxy-2-(2-propenyl)naphthalene-1,4-dione 23

The procedure was adapted from that of Eisenhuth and Schmid.[4] 5-Methoxy-1-naphthol (4.21 g, 24.2 mmol), allyl bromide (3.4 ml, 4.6 g, 38 mmol) and potassium carbonate (5.14 g, 37.2 mmol) in acetone (110 ml) were refluxed for 3 h under a nitrogen atmosphere. The reaction mixture was allowed to cool, then poured into water and extracted with ether (3 × 60 ml). The extracts were washed with 10% aqueous sodium hydroxide solution (40 ml) followed by brine, dried and evaporated to give 5-methoxy-1-(2-propenyloxy)naphthalene as a pale brown solid (4.89 g, 94%), which was pure by ^{1}H NMR. δ_H (200 MHz, $CDCl_3$) 7.91 (1H, d, *J* 8.5, ArH), 7.85 (1H, d, *J* 8.5, ArH), 7.43–7.32 (2H, m, 2 × ArH), 6.86 (2H, d, *J* 7.7, 2 × ArH), 6.19 (1H, ddt, *J* 17.3, 10.5, 5.1, CH, vinylic), 5.53 (1H, dtd, *J* 17.3, 1.5, 1.5, CH, vinylic), 5.34 (1H, dtd, *J* 10.5, 1.5, 1.5, CH, vinylic), 4.72 (2H, ddd, *J* 5.1, 1.5, 1.5, CH_2), 4.00 (3H, s, OCH_3). The foregoing ether (4.89 g, 22.9 mmol) was heated at 160–185 °C (oil bath) for 2 h 15 min under an argon atmosphere, affording almost pure 4-methoxy-2-(2-propenyl)naphthalen-1-ol **22** as a pale brown waxy solid (4.62 g). δ_H (200 MHz, $CDCl_3$) 7.80 (1H, d, *J* 8.5, ArH), 7.73 (1H, d, *J* 8.5, ArH), 7.38 (1H, dd, *J* 8.5, 7.7, ArH, 7.21 (1H, d, *J* 8.5, ArH), 6.81 (1H, d, *J* 7.7, ArH), 6.18–5.99 1H, (m, CH, vinylic), 5.50 (1H, s, br, OH), 5.30–5.20 (2H, m, 2 × CH, vinylic), 3.99 (3H, s, OCH_3), 3.58 (2H, ddd, *J* 6.2, 1.6, 1.6, CH_2). A solution of the phenol **22** (1.49 g, 6.96 mmol) in ether (30 ml) was added to a separating funnel containing Fremy's salt (5.23 g, 19.5 mmol) dissolved in an aqueous borax buffer solution (0.025 M sodium tetraborate, 148 ml; 0.1 M sodium hydroxide, 72 ml). The resulting mixture was shaken until TLC indicated that all the starting material had been consumed (*ca* 1.5 h). Argon was bubbled through the solution to evaporate most of the ether, during which time a yellow-brown precipitate separated. The solid was collected and dried over phosphorus pentoxide to give 5-methoxy-2-(2-propenyl)naphthalene-1,4-dione **23** (1.44 g, 91%), which was pure by ^{1}H NMR and used in the next reaction without further purification. A sample recrystallised from dichloromethane-light petroleum as yellow needles, mp 95–96 °C (lit.,[4] 96–97 °C). δ_H (200 MHz, $CDCl_3$) 7.76–7.57 (2H, m, ArH), 7.26 (1H, d, *J* 7.7, ArH), 6.68 (1H, s, 3-CH, vinylic), 5.96–5.76 (1H, m, CH, vinylic), 5.22–5.12 (2H, m, 2 × CH, vinylic), 3.98 (3H, s, OCH_3), 3.58 (2H, ddd, *J* 6.8, 1.9 and 1.3, CH_2).

2-(2,3-Epoxypropyl)-5-methoxynaphthalen-1,4-dione 24

m-Chloroperoxybenzoic acid (70%, 278 mg, 1.13 mmol) was added to a stirred solution of 5-methoxy-2-(2-propenyl)naphthalen-1,4-dione **23** (212 mg, 0.93 mmol) in dichloromethane (10 ml) at ice bath temperature under an argon atmosphere. After 3 h, the mixture was allowed to warm to room temperature and left to stir for a further 21 h. The mixture was diluted with dichloromethane (50 ml) and washed with 2.5% sodium bisulfite solution (20 ml), followed by saturated sodium bicarbonate solution (2 × 25 ml) and brine (30 ml), dried and evaporated to give a yellow-orange solid (257 mg), which was subjected to radial chromatography. Elution with 40% ethyl acetate-light petroleum returned unreacted starting material (21 mg). Further elution with 70% ethyl acetate-light petroleum gave the *epoxide* **24** as an orange crystalline solid (152 mg, 67%, 74% based on recovered starting material). A sample recrystallised from ethyl acetate-light petroleum as orange plates, mp 159–160 °C. (Found: C, 68.9; H, 5.0. $C_{14}H_{12}O_4$ requires C, 68.85; H, 4.95%). (Found: M^+, 244.0731. $C_{14}H_{12}O_4$ requires 244.0736). Mass spectrum *m/z*: 246 (M + 2, 35%), 245 (M (1, 16), 244 (M, 100), 228 (15), 227 (23), 216 (27), 215 (42), 214 (32), 213 (32), 202 (73), 201 (52), 200 (31), 199 (24), 198 (43), 197 (29), 187 (30), 186 (117), 185 (56), 184 (20), 183 (31), 174 (15), 173 (45), 171 (23), 169 (24), 168 (24), 159 (21), 157 (48), 156 (26), 155 (25), 145 (22), 144 (21), 143 (21), 141 (22), 133 (16), 131 (20), 129 (42), 128 (90), 127 (39), 116 (25), 115 (77), 105 (23), 104 (39), 102 (20), 91 (18), 89 (16), 77 (29), 76 (71), 75 (21), 64 (15), 63 (26). δ_H (300 MHz, $CDCl_3$) 7.75 (1H, dd, *J* 7.6 and 1.1, ArH), 7.67 (1H, dd, *J* 8.3 and 7.6, ArH), 7.30 (1H, dd, *J* 8.3 and 1.1, ArH), 6.84 (1H, t, *J* 1.2, 3-CH, vinylic), 4.00 (3H, s, OCH_3), 3.22–3.16 (1H, m, CH, X of ABX), 2.91–2.82 (2H, m, CH of methylene and CH of oxirane methylene), 2.66–2.57 (2H, m, CH of methylene and CH of oxirane methylene). δ_C (75.5 MHz, $CDCl_3$) 185.1 (C=O),

184.1 (C=O), 159.5 (C), 144.4 (C), 138.5 (CH), 134.8 (CH), 134.2 (C), 119.8 (C), 119.4 (CH), 117.9 (CH), 56.5 (OCH_3), 50 (CH), 47 (CH_2), 32.2 (CH_2). ν_{max} (CH_2Cl_2) 1660 cm^{-1} (C=O).

Attempted hydrolytic kinetic resolution of the epoxides **19**, **21** and **24** under standard conditions[9,10] in each case returned starting material exhibiting no significant optical rotation.

5-Methoxy-1-methoxymethoxynaphthalene 25

This was prepared as described[11] and obtained in 86% yield as colourless needles mp 74–75 °C (lit.,[11] 75–76 °C). δ_H (200 MHz, $CDCl_3$) 7.91 (2H, m, ArH), 7.45–7.35 (2H, m, ArH), 7.14 (1H, d, *J* 7.6, ArH), 6.86 (1H, d, *J* 7.6, ArH), 5.40 (3H, s, CH_2), 4.01 (3H, s, OCH_3), 3.56 (3H, s, CH_3).

(*R*)-Propylene oxide 26

The procedure described by Jacobsen and coworkers was followed.[9,10] The precatalyst, (*R*,*R*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicalidene)-1,2-cyclohexanediaminocobalt(II) (604 mg, 1.00 mmol) and glacial acetic acid (123 mg, 2.05 mmol) in toluene (5 ml) were stirred for 2 h at room temperature while exposed to the atmosphere. The solvent was evaporated under reduced pressure leaving the crude (*R*,*R*)-(salen)Co(III)(OAc) catalyst as a dark brown residue. Anhydrous propylene oxide (35 ml, 29.0 g, 499 mmol) was added and the resulting solution was cooled in an ice-water bath. Water (4.90 ml, 272 mmol) was added slowly to the stirring solution, ensuring the temperature stayed between 15–20 °C. After the addition was complete (*ca* 0.5 h), the solution was allowed to warm to room temperature and left to stir for 18 h. Distillation gave (*R*)-propylene oxide bp 35 °C, (12.0 g, 41%), $[\alpha]_D^{20}$ + 14.0 (neat) (lit.,[23] $[\alpha]_D^{31}$ + 13.8 (neat)), followed by 1,2-propanediol bp 46 °C(0.7 mm Hg (16.9 g, 45%). The remaining residue was diluted with methanol and the red precatalyst (563 mg) was recovered by filtration.

(2*R*)-1-(5-Methoxy-1-methoxymethoxynaphthalen-2-yl)propan-2-ol 27

n-Butyllithium in hexane (1.6 M, 5.4 ml, 8.6 mmol) was added dropwise to a stirred solution of 5-methoxy-1-methoxymethoxynaphthalene (1.43 g, 6.56 mmol) in anhydrous tetrahydrofuran (30 ml) cooled in an ice-water bath under an argon atmosphere. After 2 h the mixture was treated with hexamethylphosphoramide (3.54 ml, 20.3 mmol), followed by the immediate dropwise addition of (*R*)-propylene oxide (491 mg, 8.45 mmol) in anhydrous tetrahydrofuran (2 ml). The resulting yellow solution was allowed to warm to room temperature and left to stir for17 h. The solution was diluted with saturated ammonium chloride (70 ml) and extracted with ether (3 × 50 ml). The combined organic extracts were washed with water (40 ml), followed by brine (50 ml), dried and evaporated to give a yellow oil (2.18 g), which was subjected to silica gel filtration. Elution with 1% ethyl acetate-light petroleum returned unreacted starting material as a white crystalline solid (293 mg). Further elution with 10% ethyl acetate-light petroleum gave (*2R*)-*1*-(*1-methoxy-5-methoxymethoxynaphthalen-2-yl*)*propan-2-ol* **28** (66 mg) as a colourless oil, which became a white crystalline solid upon refrigeration and recrystallised from dichloromethane-light petroleum as white plates, mp 74–75 °C. $[\alpha]_D^{21}$ −26.9 (*c* 0.015 in CH_2Cl_2). (Found: M^+, 276.1366. $C_{16}H_{20}O_4$ requires 276.1362). Mass spectrum *m*/*z*: 276 (M, 41%), 258 (36), 226 (18), 214 (56), 212 (19), 201 (15), 200 (40), 199 (34), 198 (17), 187 (23), 185 (24), 171 (23), 169 (15), 157 (17), 155 (24), 153 (20), 149 (37), 141 (18), 139 (16), 129 (18), 128 (31), 127 (23), 121 (15), 115 (37), 109 (17), 107 (20), 105 (17), 98 (16), 97 (24), 96 (16), 95 (29), 93 (18), 91 (19), 86 (49), 85 (20), 84 (78), 83 (38), 82 (23), 81 (45), 79 (19), 78 (40), 77 (33), 71 (36), 70 (33), 69 (100), 68 (24), 67 (34), 63 (62), 61 (15), 60 (32), 57 (67), 56 (34). ($_H$ (300 MHz, $CDCl_3$) 8.03 (1H, dd, *J* 8.6 and 0.4, ArH), 7.73 (1H, dt, *J* 8.4 and 0.8, ArH), 7.44 (1H dd, *J* 8.4 and 7.7, ArH),7.33 (1H, d, *J* 8.6, ArH), 7.09 (1H, dd, *J* 7.7 and 0.8, ArH), 5.39 (2H, s, OCH_2O), 4.16 (1H, m, CH), 3.94 (3H, s, OCH_3), 3.54 (3H, s, OCH_3), 2.96 (2H, d, *J* 6.2, CH_2), 2.29 (1H, s, br, OH), 1.28 (3H, d, *J* 6.2, CH_3). δ_C (75.5 MHz, $CDCl_3$) 153.8 (C), 153.2 (C), 129.2 (C), 128.2 (CH), 127.5 (C), 126.5 (C), 126.1 (CH), 118.3 (CH), 115.4 (CH), 107.7 (CH), 94.6 (OCH_2O), 68.6 (CH), 61.8 (OCH_3), 56.2 (OCH_3), 39.9 (CH_2), 23.2 (CH_3). Further elution with 10% ethyl acetate-light petroleum gave a fraction containing a 15 : 85 mixture of (*2R*)-*1*-(*1-methoxy-5-methoxymethoxynaphthalen-2-yl*)*propan-2-ol* **28** and the title alcohol, (*2R*)-*1*-(*5-methoxy-1-methoxymethoxynaphthalen-2-yl*)*propan-2-ol* **27** as a pale yellow oil (1.13 g), which was used directly in the next reaction. The crude oil obtained from a second reaction was subjected to careful radial chromatography. Elution with 5% ethyl acetate-light petroleum allowed the isolation of a small analytical sample of (*2R*)-*1*-(*5-methoxy-1-methoxymethoxynaphthalen-2-yl*)*propan-2-ol* **27** as a colourless oil. $[\alpha]_D^{21}$ + 8.7 (*c* 0.078 in CH_2Cl_2). (Found: M^+, 276.1359. $C_{16}H_{20}O_4$ requires 276.1362). Mass spectrum *m*/*z*: 276 (M, 21%), 244 (24), 215 (30), 214 (100), 199 (41), 187 (49), 115 (20). δ_H (300 MHz, $CDCl_3$) 8.03 (1H, d, *J* 8.6, ArH), 7.59 (1H, d, *J* 8.6, ArH), 7.41 (1H, dd, *J* 8.6, 7.6, ArH), 7.33 (1H, d, *J* 8.6, ArH), 6.81 (1H, d, *J* 7.6, ArH), 5.18 (1H, d, *J* 5.9, CH), 5.16 (1H, d, *J* 5.9, CH), 4.23 (1H, m, CH), 3.99 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 3.10–2.94 (2H, m, CH_2), 2.32 (1H, d, *J* 4.6, OH), 1.30 (3H, d, *J* 6.2, CH_3). δ_C (75.5 MHz, $CDCl_3$) 155.7 (C), 151.6 (C), 129.4 (C), 128.3 (C), 127.7 (C), 126.3 (CH), 126.1 (CH), 118.8 (CH), 114.2 (CH), 103.8 (CH), 100.3 (CH_2), 68.6 (CH), 57.6 (OCH_3), 55.6 (OCH_3), 40.1 (CH_2), 23.6 (CH_3).

(2*R*)-1-(1-Hydroxy-5-methoxy-2-naphthalenyl)propan-2-ol 29

A 15 : 85 mixture of (2*R*)-1-(1-methoxy-5-methoxymethoxynaphthalen-2-yl)propan-2-ol and (2*R*)-1-(5-methoxy-1-methoxymethoxynaphthalen-2-yl)propan-2-ol (1.13 g) in anhydrous 2-propanol (20 ml) was treated with carbon tetrabromide (141 mg, 0.425 mmol) and refluxed for 1.5 h under an argon atmosphere. The solution was concentrated under reduced pressure and the resulting yellow oil was subjected to silica gel filtration. Elution with 5% ethyl acetate-light petroleum gave (*2R*)-*1*-(*1-hydroxy-5-methoxy-2-naphthalenyl*)*propan-2-ol* **29** as a white crystalline solid (696 mg, 73%), which recrystallised from ethyl acetate-light petroleum as white plates, mp 85–86 °C. $[\alpha]_D^{21}$ − 6.7 (*c* 0.009 in CH_2Cl_2). The NMR spectral properties of this material were identical with those of the (2*R*,*S*) compound prepared previously.

Treatment of a sample of the (2*R*,*S*)-alcohol with the chiral shift reagent europium tris[3-heptafluoropropylhydroxymethylene)-(+)-camphorate] (7.5 mol%) separated the 8-H proton doublet signal into two doublets in the ^{1}H NMR spectrum. The enantiomeric

excess within the (2*R*)-alcohol was estimated to be greater than 90% by examination of the H-8 signal in the ^{1}H NMR spectrum of a sample of **29** which had been treated with 7.5 mol% of the chiral shift reagent.

(2*R*)-2-(2-Hydroxypropyl)-5-methoxynaphthalene-1,4-dione 30

A solution of (*2R*)-1-(1-hydroxy-5-methoxy-2-naphthalenyl)-propan-2-ol **29** (696 mg, 3.00 mmol) in ether (15 ml) was added to a separating funnel containing Fremy's salt (1.718 g, 6.11 mmol) dissolved in an aqueous borax buffer solution (0.025 M sodium tetraborate, 84 ml; 0.1 M sodium hydroxide, 41 ml). The resulting mixture was shaken until TLC indicated that the starting material had been consumed (*ca* 30 min). The mixture was extracted with chloroform (4 × 50 ml) and the combined organic extracts were washed with brine (60 ml), dried and evaporated to give (*2R*)-*2-(2-hydroxypropyl)-5-methoxynaphthalene-1,4-dione* **30** as a yellow crystalline solid (717 mg, 97%), which was pure by ^{1}H NMR. A sample recrystallised from ethyl acetate-light petroleum as bright yellow needles, mp 116–117 °C. $[\alpha]_D^{20}$ − 25.3 (*c* 0.015 in CH_2Cl_2). The NMR spectral properties of this material were identical with those of the (2*R*,*S*) compound prepared previously.

(2*R*)-5-Methoxy-2-(2-vinyloxypropyl)naphthalene-1,4-dione 31

A solution of (2*R*)-2-(2-hydroxypropyl)-5-methoxynaphthalene-1,4-dione **30** (692 mg, 2.81 mmol) and mercuric acetate (212 mg, 0.66 mmol) in ethyl vinyl ether (17 ml, 12.8 g, 178 mmol) and dichloromethane (4.5 ml) in a foil-covered flask was heated under reflux for 5.5 h under an argon atmosphere. The solution was allowed to left to stand at room temperature overnight and was then diluted with dichloromethane (40 ml) and washed with water (80 ml). The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 × 40 ml). The combined organic extracts were washed with brine (50 ml), dried and evaporated to give a yellow oil, which was subjected to silica gel filtration. Elution with 15% ethyl acetate-light petroleum gave the *vinyl ether* **31** as a yellow oil (393 mg, 51%, 81% based on recovered starting material). $[\alpha]_D^{21}$ − 15.6 (*c* 0.010 in CH_2Cl_2). The NMR spectral properties of this material were identical with those of the (2*R*,*S*) compound prepared previously. Further elution with 40% ethyl acetate-light petroleum returned unreacted starting material as a yellow crystalline solid (255 mg).

(−)-Elecanacin 1 and (+)-isoelecanacin 16

A deoxygenated solution of (2*R*)-5-methoxy-2-(2-vinyloxy-propyl)naphthalene-1,4-dione **31** (131 mg, 0.482 mmol) in anhydrous dichloromethane (50 ml) was irradiated at 350 nm through Pyrex for 65 min, when TLC indicated that all the starting material had been consumed. The solvent was evaporated and the yellow residue was subjected to careful radial chromatography. Elution with 20% ethyl acetate-light petroleum gave (+)-*isoelecanacin* **16** (53 mg, 40%) as a yellow crystalline solid, which recrystallised from dichloromethane/light petroleum as pale yellow plates, mp 138–139 °C. $[\alpha]_D^{21}$ + 110.4 (*c* 0.010 in CH_2Cl_2). Analysis on the Chiracel OD column showed two peaks in the ratio of 1 : 99 at retention times 20.1 and 23.4 min, giving an ee of 98% for this material. The NMR spectral properties of this sample were identical with those of the (2*R*,*S*) compound prepared previously. Further elution with 30% ethyl acetate-light petroleum gave (−)-*elecanacin* **1** as a pale yellow crystalline solid (31 mg, 24%), which recrystallised from dichloromethane-light petroleum as faint yellow plates, mp 167–168 °C (lit.,[1] 198 °C for material of low ee). $[\alpha]_D^{21}$ − 145.2 (*c* 0.004 in $CHCl_3$) (lit.,[1] + 20.7 in $CHCl_3$). Analysis on the Chiracel OD column showed a single peak at retention time 26.1 min. Under these conditions <0.5% of the other enantiomer (expected retention time 39.2 min) could have been detected. The ee of this sample was thus >99%. The NMR spectral properties of this material were identical with those of (2*R*,*S*) compound prepared previously.

Acknowledgements

We thank Dr Lindsay Byrne for 2D NMR spectra and chiral shift reagent experiments. Dr Tony Reader recorded the mass spectra while Professor Robin Giles (Murdoch University) kindly provided the chiral HPLC column and Dr Gavin Flematti assisted with the HPLC analyses. Professor Y. Imakura (Naruto University, Takashima) supplied ^{13}C and ^{1}H NMR spectra of natural elecanacin.

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