CSIRO PUBLISHING

www.publish.csiro.au/journals/ajc *Aust. J. Chem.* **2003**, *56*, 585–595

A Total Synthesis of the Styryllactone (+)-Goniodiol from Naphthalene*

Martin G. Banwell,[A,B] *Mark J. Coster*,[A] *Alison J. Edwards*,[A] *Ochitha P. Karunaratne*,[A] *Jason A. Smith*,[A] *Lee L. Welling*[A] *and Anthony C. Willis*[A]

[A]Research School of Chemistry, Institute of Advanced Studies, The Australian National University, Canberra 0200, Australia.

[B]Author to whom correspondence should be addressed (e-mail: mgb@rsc.anu.edu.au).

The cytotoxic natural product (+)-goniodiol (1) has been prepared in twelve steps from the enantiomerically pure *cis*-dihydrocatechol (2), which is readily obtained by microbial oxidation of naphthalene. Elaboration of compound (2) involves an initial oxidative cleavage to dialdehyde (7) followed by reduction to give diol (12). Conversion of compound (12) into acetal (17) required, inter alia, selective oxidation of the benzylic alcohol moiety followed by a metal-catalyzed decarbonylation of the resulting aldehyde. Allylation of compound (17) with allyltributylstannane in the presence of lithium perchlorate gave a ca. 2.7 : 1 mixture of alcohols (18) and (19), each of which was converted into the corresponding acrylate under standard conditions. Subjection of these ester derivatives to a ring-closing metathesis (RCM) reaction with Grubbs' first-generation catalyst gave the anticipated lactones (22) and (23). Acid-catalyzed removal of the acetonide protecting group within compound (22) then afforded (+)-goniodiol (1), while analogous deprotection of congener (23) afforded 6-*epi*-(+)-goniodiol (24).

Manuscript received: 21 November 2002.
Final version: 21 February 2003.

Introduction

The styryllactone (+)-goniodiol (1) (Diagram 1) was first isolated by Talapatra and coworkers[1] in 1985 from the leaves and twigs of the Asian tree *Goniothalamus sesquipedalis*, and again in 1991 by McLaughlin et al.[2] from ethanol extracts of the stem bark of *Goniothalamus giganteus* Hook f. & Thomas (Annonaceae). The latter group also established that the compound exhibits significant cytotoxicity (IC_{50} $1.22 \times 10^{-1}\,\mu g\,mL^{-1}$) against the A-549 human lung tumour cell line whilst being essentially completely non-toxic ($LC_{50} > 500\,\mu g\ mL^{-1}$) in a brine shrimp assay. The naturally occurring diacetate derivative of (+)-goniodiol also shows some toxicity towards *Aedes aegypti* larvae.[3] Such properties of this and other styryllactones have prompted considerable effort directed towards the synthesis of members of the class. The most popular target has been (+)-goniodiol, at least in part because a number of its natural congeners can be obtained by simple manipulations of this 'parent system'.[4] The first synthesis of the title compound was reported in 1992 by Honda et al.,[5] who used readily available 2,3-*O*-isopropylidene-D-glyceraldehyde as starting material. Two years later, Zhou[6] described a synthesis starting with the Sharpless asymmetric epoxidation of (*E*)-cinnamyl alcohol. The first of Vatele's three syntheses[7–9] was detailed in 1996 and employed a monosaccharide-derived auxiliary to establish chirality

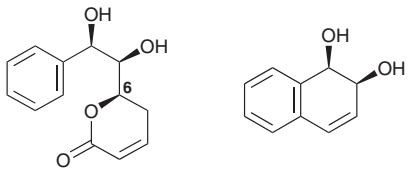


Diagram 1.

in the target molecule, whilst two related syntheses from the same group used (*R*)-mandelic acid as starting material. In 1997 Mukai and Hanaoka reported[10] the preparation of compound (1) from the metal complex (+)-tricarbonyl[η^6-*o*-(trimethylsilyl)benzaldehyde] chromium(0), whilst in the following year, Ley and Dixon[11] described a synthesis from commercially available (*S*)-glycidol which involved an anomeric oxygen-to-carbon rearrangement as the pivotal step. Very recently, Lin et al.[12] described an enantioselective synthesis of (+)-goniodiol starting with asymmetric dihydroxylation (AD) of 1-phenylbuta-1,3-diene, whilst a US group exploited an asymmetric alkoxyallylboration–ring-closing metathesis sequence to achieve the same target.[13] Herein we report that (+)-goniodiol (1) can be prepared from the enantiomerically pure 'naphthalene diol' (2),[14] a compound available in multi-gram quantities by means of microbial dihydroxylation of naphthalene. The present work

*Aspects of this work have been reported previously in communication form: M. G. Banwell, M. J. Coster, O. P. Karunaratne, J. A. Smith, *J. Chem. Soc., Perkin Trans. 1* **2002**, 1622.

 10.1071/CH02242 0004-9425/03/060585

thus provides the first application of this abundant metabolite to the synthesis of natural products and serves to highlight the extraordinary utility of such enzymatically derived dihydrocatechols.[14,15]

Results and Discussion

Retrosynthetic analysis of target (1) (Fig. 1) suggests that the lactone ring could be generated by ring-closing methathesis of the acrylate (3) which should, in turn, be accessible by a reaction sequence involving allylation of the aliphatic aldehyde within dialdehyde (4) and acrylation of the resulting homoallylic alcohol as well as decarbonylation of the aromatic aldehyde moiety. The latter operation, which is not often utilized in natural products synthesis, would serve to excise the single superfluous carbon associated with the starting material. Dialdehyde (4) could, in turn, be generated by oxidative cleavage of a suitably protected form of the starting diol (2).

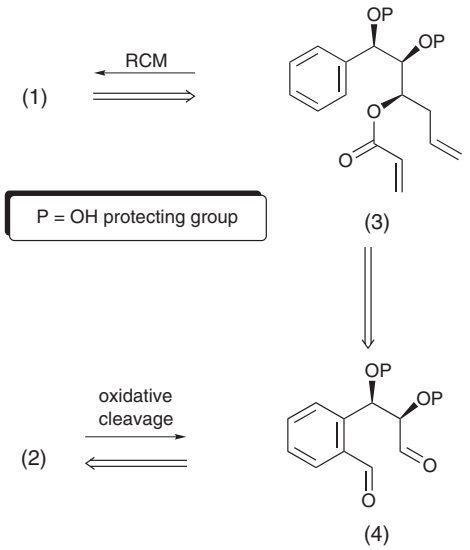
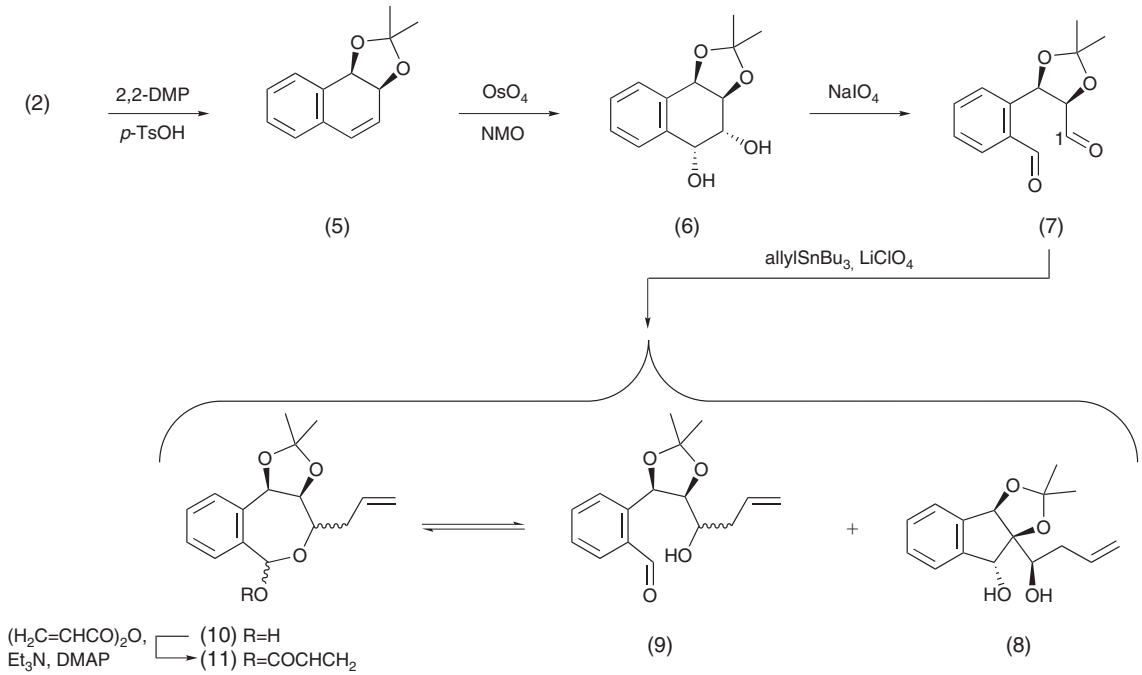


Fig. 1. Retrosynthetic analysis of (+)-goniodiol.

In initial attempts (Scheme 1) to implement the ideas delineated in the retrosynthetic analysis, compound (2) was converted into the previously reported[16] acetonide (5), which was then subjected to *cis*-1,2-dihydroxylation under the UpJohn conditions[17] to give a diastereoisomerically pure and crystalline diol (6) (73%). Whilst the stereochemical outcome of this reaction has not been rigorously proven, the assignment of the illustrated configurations to the newly introduced hydroxy groups within (6) follows by analogy to related conversions observed in these and other laboratories,[14,15] and involves *cis*-dihydroxylation from the sterically less-hindered face of the alkene in precursor (5). Oxidative cleavage of compound (6) could be effected with sodium periodate in aqueous methanol at pH 7, and the dialdehyde (7) thereby obtained in quantitative yield. Direct oxidative cleavage of alkene (5) with $OsO_4/NaIO_4$ was less efficient, giving product (7) in 69% yield. On the basis that the aliphatic aldehyde moiety within compound (7) would be more electrophilic than its aromatic counterpart, attempts were made to selectively allylate the former. When a combination of allyltributylstannane and lithium perchlorate[18] was employed for this purpose, and calcium hydride added in an effort to convert any hydrated form of compound (7) into the aldehyde itself, the crystalline allylation product (8) (43%) was obtained as the only isolable product of reaction. The structure of compound (8) was established by single-crystal X-ray analysis (Fig. 2, Tables 1 and 2) and most likely arises via a base-catalyzed intramolecular Claisen–Schmidt reaction of dialdehyde (7) followed by allylation of the resulting aldol at the carbonyl residue. In the absence of added calcium



Scheme 1.

hydride, the allylation of compound (7) proceeded in the expected manner and the homoallylic alcohol (9) was obtained as the predominant reaction product (50%). Due to the complexities of the NMR data, the lack of crystalline material, and the lack of synthetic utility (see below) of compound (9), the configuration at the new stereogenic centre within this product has not been determined. In an effort to exploit hydroxyaldehyde (9) in the synthesis of target (1) the acrylate derivative was sought. However, reaction of compound (9) with acrylic anhydride in the presence of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) as an acylation catalyst and using triethylamine as base afforded ester (11) (22%; derived from lactol (10) which must be in equilibrium with hydroxyaldehyde (9)) as the only isolable product. In a similar vein, attempts to decarbonylate compound (9) using conditions successfully employed for the analogous conversion of a related substrate (see below) were unsuccessful, with acetonide group migration appearing to be one of several processes taking place under the conditions employed. Attempts to selectively mono-decarbonylate what should be the more reactive aromatic aldehyde moiety within dicarbonyl compound (7) were also unsuccessful.

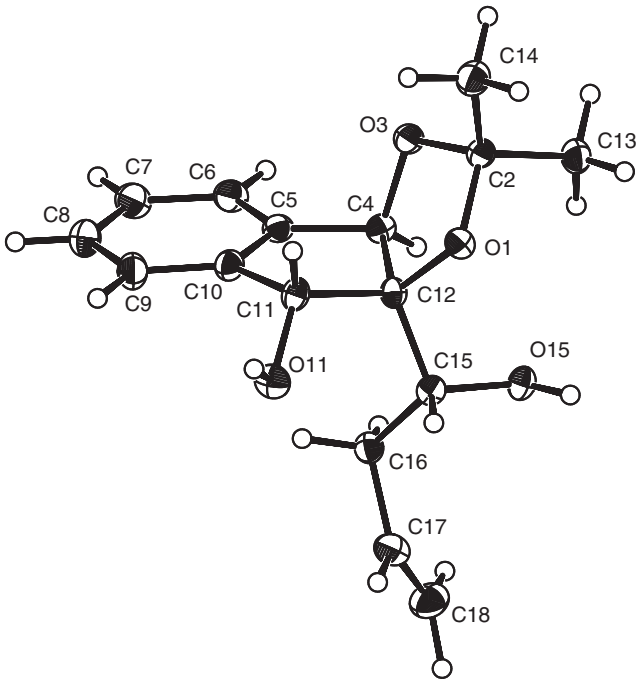


Fig. 2. Anisotropic displacement ellipsoid plot of $C_{16}H_{20}O_4$ (8) with labelling of non-hydrogen atoms. Ellipsoids show 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

Table 1. Selected bond lengths (Å) for $C_{16}H_{20}O_4$(8)

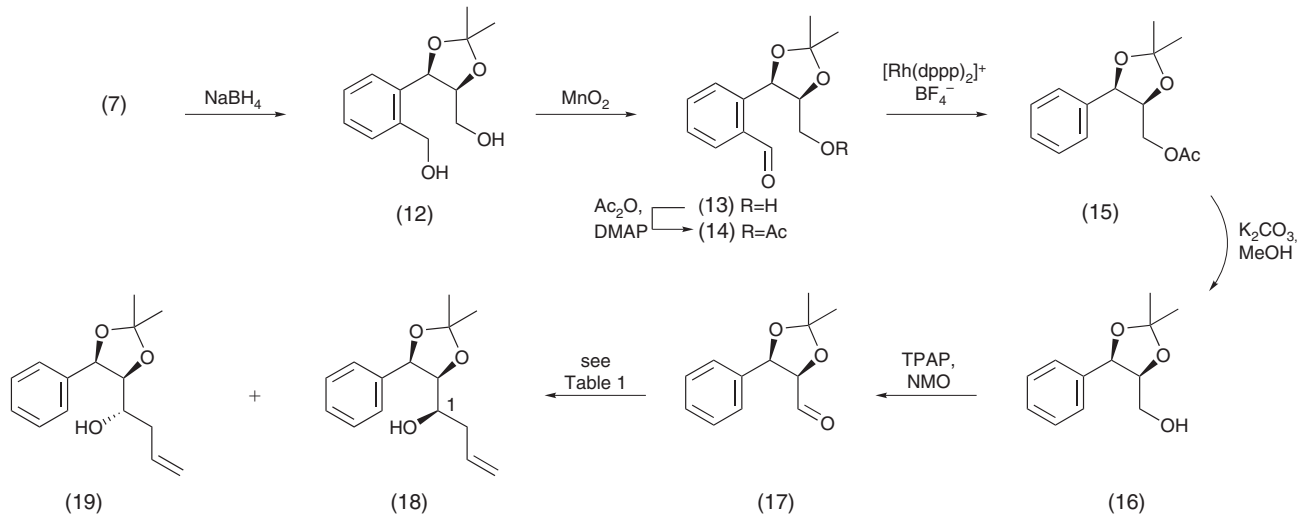
Atoms	Distance	Atoms	Distance
O(1)–C(2)	1.452(3)	C(5)–C(10)	1.386(4)
O(1)–C(12)	1.441(2)	C(6)–C(7)	1.400(4)
O(3)–C(2)	1.429(2)	C(7)–C(8)	1.383(4)
O(3)–C(4)	1.431(3)	C(8)–C(9)	1.391(4)
O(11)–C(11)	1.416(3)	C(9)–C(10)	1.390(3)
O(15)–C(15)	1.447(3)	C(10)–C(11)	1.518(3)
C(2)–C(13)	1.510(3)	C(11)–C(12)	1.558(3)
C(2)–C(14)	1.502(3)	C(12)–C(15)	1.525(3)
C(4)–C(5)	1.501(3)	C(15)–C(16)	1.531(3)
C(4)–C(12)	1.542(3)	C(16)–C(17)	1.496(3)
C(5)–C(6)	1.392(3)	C(17)–C(18)	1.321(4)

The early stages of the ultimately successful route to (+)-goniodiol (1) are shown in Scheme 2 and began with the reduction of dialdehyde (7) to the corresponding and previously reported[19] diol (12) (64% from (7)). The benzylic alcohol moiety within this last compound was selectively oxidized to the corresponding benzaldehyde (13) (70%) using 'precipitated active' manganese dioxide as supplied by Merck–Schuchardt. In order to prevent acetonide group migration during the subsequent decarbonylation step the hydroxy group within compound (13) was protected as the corresponding acetate (14) (55%).

Several reagents were examined in connection with efforts to effect decarbonylation of compound (14). Whilst readily available Wilkinson's complex $[RhCl(PPh_3)_3]$ did affect the desired reaction in refluxing xylene, stoichiometric quantities of this 'catalyst' are required because the resulting carbonyl–metal complex is stable and does not, therefore, 'turn-over'.[20] Although such problems can sometimes be overcome by adding diphenyl phosphorazidate,[20] this proved ineffective in the present case. In principle, such difficulties could be avoided by using the cationic rhodium complex bis[1, 3-bis(diphenylphosphino) propane]rhodium tetrafluoroborate, $[Rh(dppp)_2]^+ BF_4^-$.[21] In order to examine such possibilities, this complex was prepared by reaction of commercially available $[Rh_2Cl_2(1,5\text{-cod})_2]$

Table 2. Selected bond angles (degrees) for $C_{16}H_{20}O_4$(8)

Atoms	Angle	Atoms	Angle	Atoms	Angle
C(2)–O(1)–C(12)	109.70(14)	C(4)–C(5)–C(10)	110.25(18)	O(1)–C(12)–C(4)	103.91(16)
C(2)–O(3)–C(4)	107.58(14)	C(6)–C(5)–C(10)	120.8(2)	O(1)–C(12)–C(11)	110.54(18)
O(1)–C(2)–O(3)	104.76(15)	C(5)–C(6)–C(7)	118.1(3)	C(4)–C(12)–C(11)	104.55(17)
O(1)–C(2)–C(13)	109.72(18)	C(6)–C(7)–C(8)	120.9(2)	O(1)–C(12)–C(15)	108.86(16)
O(3)–C(2)–C(13)	111.27(19)	C(7)–C(8)–C(9)	120.9(3)	C(4)–C(12)–C(15)	115.86(18)
O(1)–C(2)–C(14)	109.55(19)	C(8)–C(9)–C(10)	118.3(3)	C(11)–C(12)–C(15)	112.72(18)
O(3)–C(2)–C(14)	108.31(17)	C(5)–C(10)–C(9)	121.0(2)	O(15)–C(15)–C(12)	109.47(18)
C(13)–C(2)–C(14)	112.9(2)	C(5)–C(10)–C(11)	111.08(19)	O(15)–C(15)–C(16)	106.94(18)
O(3)–C(4)–C(5)	109.49(17)	C(9)–C(10)–C(11)	127.9(2)	C(12)–C(15)–C(16)	113.69(18)
O(3)–C(4)–C(12)	103.21(16)	O(11)–C(11)–C(10)	113.28(18)	C(15)–C(16)–C(17)	111.31(19)
C(5)–C(4)–C(12)	105.35(18)	O(11)–C(11)–C(12)	113.81(18)	C(16)–C(17)–C(18)	126.1(3)
C(4)–C(5)–C(6)	128.9(2)	C(10)–C(11)–C(12)	103.76(18)		



Scheme 2.

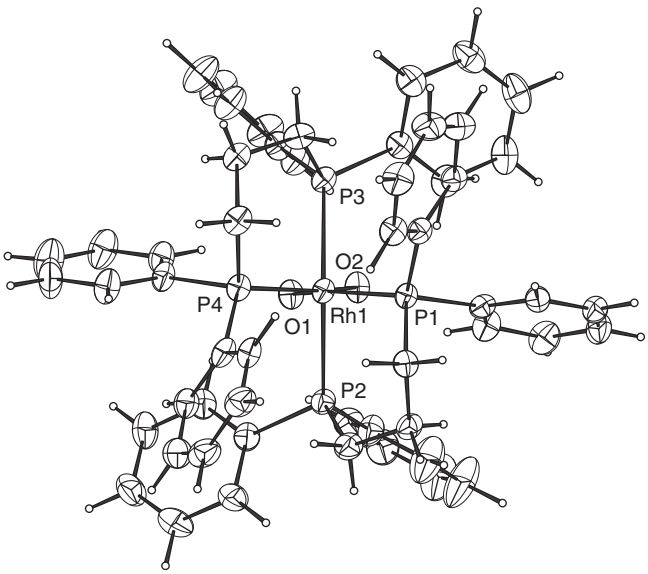


Fig. 3. Anisotropic displacement ellipsoid plot of the cation of $[Rh(dppp)_2O_2]^+BF_4^-\cdot 2CH_3COCH_3$ (50% probability level) derived from X-ray crystallographic data.

Table 3. Selected bond lengths (Å) for $[Rh(dppp)_2O_2]^+BF_4^-\cdot 2CH_3COCH_3$

Atoms	Distance	Atoms	Distance
Rh(1)–P(1)	2.3445(15)	P(2)–C(16)	1.841(6)
Rh(1)–P(2)	2.3763(16)	P(2)–C(22)	1.834(6)
Rh(1)–P(3)	2.3873(17)	P(3)–C(28)	1.840(5)
Rh(1)–P(4)	2.3360(15)	P(3)–C(31)	1.820(6)
Rh(1)–O(1)	2.034(4)	P(3)–C(37)	1.826(6)
Rh(1)–O(2)	2.047(4)	P(4)–C(30)	1.836(6)
P(1)–C(1)	1.841(6)	P(4)–C(43)	1.828(6)
P(1)–C(4)	1.839(6)	P(4)–C(49)	1.832(6)
P(1)–C(10)	1.825(6)	O(1)–O(2)	1.426(5)
P(2)–C(3)	1.831(7)		

Table 4. Selected bond angles (degrees) for $[Rh(dppp)_2O_2]^+ BF_4^-\cdot 2CH_3COCH_3$

Atoms	Angle	Atoms	Angle
P(1)–Rh(1)–P(2)	90.93(6)	P(3)–Rh(1)–O(1)	88.28(12)
P(1)–Rh(1)–P(3)	95.04(5)	P(4)–Rh(1)–O(1)	109.54(12)
P(2)–Rh(1)–P(3)	170.52(5)	P(1)–Rh(1)–O(2)	110.11(11)
P(1)–Rh(1)–P(4)	99.84(5)	P(2)–Rh(1)–O(2)	87.12(12)
P(2)–Rh(1)–P(4)	95.11(5)	P(3)–Rh(1)–O(2)	83.93(12)
P(3)–Rh(1)–P(4)	91.12(5)	P(4)–Rh(1)–O(2)	149.95(11)
P(1)–Rh(1)–O(1)	150.38(12)	O(1)–Rh(1)–O(2)	40.90(15)
P(2)–Rh(1)–O(1)	82.91(13)		

(cod = cyclooctadiene) with silver tetrafluoroborate in the presence of 1,3-bis(diphenylphosphino)propane (dppp). However, this yellow-red compound readily incorporates dioxygen into the coordination sphere to give the tan-coloured complex $[Rh(dppp)_2O_2]^+BF_4^-$,[22] in a process that most likely takes place during attempts to effect recrystallization from solvents which are not fully deoxygenated. The structure of the latter complex, which has previously been characterized by NMR spectroscopic methods, was confirmed by single-crystal X-ray analysis (Fig. 3, Tables 3 and 4). In keeping with the behaviour of related complexes,[23] heating a solution of $[Rh(dppp)_2O_2]^+BF_4^-$ in acetone under a nitrogen atmosphere overnight resulted in regeneration of its deoxygenated counterpart, which readily affects the desired conversion (14)→(15) (92% at 93% conversion) in xylene at 140°C. With due care, this decarbonylation reaction can be carried out on a 500 mg scale.

Hydrolysis of acetate (15) was accomplished with potassium carbonate in methanol, and the resulting and previously reported[6] alcohol (16)† (96%) was oxidized to aldehyde (17)[6]† (62%) using the Ley–Griffith reagent.[26] The allylation of compound (17) proved to be rather difficult to

† Whilst the triol corresponding to compound (16) has been prepared by asymmetric dihydroxylation (AD) of (*Z*)-cinnamyl alcohol, the enantiomeric excesses observed are rather modest (ca. 70%).[24,25] The analogous dihydroxylation of (*Z*)-cinnamaldehyde does not appear to have been examined but AD of ethyl (*Z*)-cinnamate gives the corresponding diol in 63% *e.e.* This material has been carried forward, using standard protection and reduction steps, to give *ent*-(17) of the same enantiomeric purity.[25]

Table 5. Allylating agents employed in attempts to effect diastereoselective conversion of aldehyde (17) into homoallylic alcohol (18)

Entry	Allylating agent	Literature reference	Solvent	Temperature (°C)	Yield (%)	Ratio of (18)/(19)[A]
1	Allylmagnesium chloride	[27]	THF	0	52	3 : 4
2	Allylmagnesium bromide	[27]	ether	0	47	2 : 3
3	Allyltrimethylsilane with $BF_3{\cdot}OEt_2$	[28]	DCM	−78	13	1 : 1
4	Allyltrimethylsilane with $SnCl_4$	[29]	DCM	−78	ca. 85	1 : 2
5	(−)-*B*-allyldiisopinocampheylborane	[30]	ether	18	ca. 50	1 : 1
6	Diisopropyl (*S*,*S*)-tartrate allylboronate	[31]	ether	−78	89	3 : 11
7	Allyltributylstannane at 19 kbar	[32]	DCM	18	76	1 : 3
8	Allyltributylstannane with $SnCl_4$	[33]	DCM	−78	64	2 : 3
9	Allyltributylstannane with $MgBr_2{\cdot}OEt_2$	[34]	DCM	−78	60	4 : 3
10	Allyltributylstannane with $LiClO_4$	[18]	ether	18	70	8 : 3

[A] Ratio determined by ^{1}H NMR analysis.

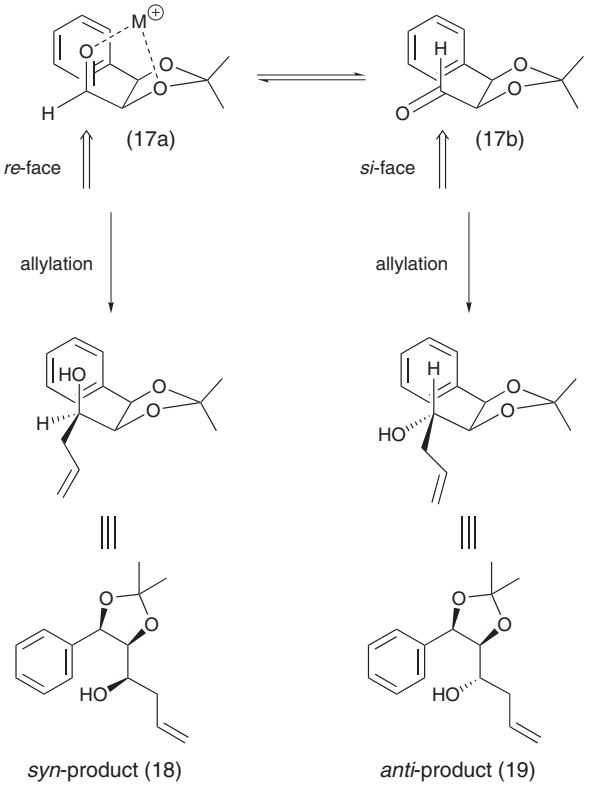


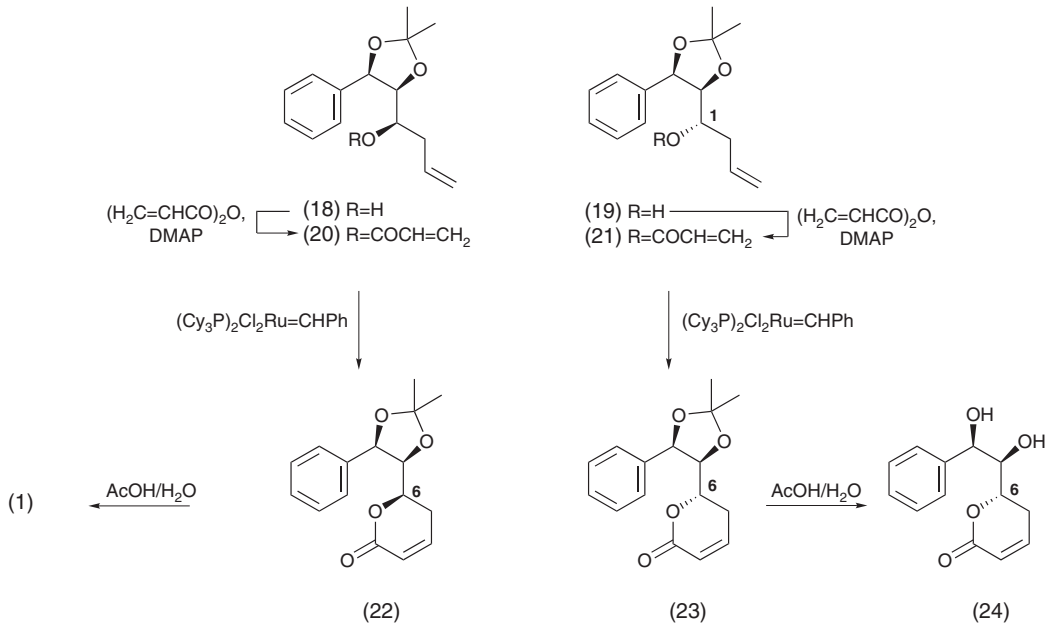
Fig. 4. Chelation and non-chelation controlled allylation of aldehyde (17).

achieve with appropriate levels of diastereoselection. Indeed, a wide range of reagents and conditions[18,27–35] were examined (Table 5) in an effort to obtain high yields of the required *syn*-product (18), but in most instances (Entries 1–8) the *anti*-isomer (19) predominated. On the basis that the required *re*-face attack of the nucleophile at the aldehyde carbonyl moiety within substrate (17) could be best effected under conditions of chelation control[36] (Fig. 4), the combination of allyltributylstannane and magnesium bromide diethyl etherate was examined and, in this case, a 4 : 3 mixture of compounds (18) and (19) were obtained (Entry 9). This ratio could be improved slightly by using lithium perchlorate as the Lewis acid catalyst (Entry 10), and under such conditions a ca. 8 : 3 mixture of products (18) and (19) was obtained (70% combined yield). These products could be separated from one another by semi-preparative reverse-phase HPLC techniques and the assignment of stereochemistry within each of them follows from their conversions into (+)-goniodiol (1) and its C6-epimer (24), respectively.

Details associated with completion of the synthesis of target (1) from precursor (18) are shown in Scheme 3. Formation of the required acrylate esters of compounds (18) and (19) proved surprisingly difficult and the only useful conditions for effecting reaction involved using acrylic anhydride in the presence of DMAP. Replacing DMAP with the much-touted scandium triflate[37] as an acylation catalyst failed to deliver any esterified products. The esters (20) (47%) and (21) (52%) were each subjected to reaction with $(Cy_3P)_2Cl_2Ru{=}CHPh$ (Grubbs' 'first generation' catalyst).[38] In keeping with the behaviour of many other acrylates derived from homoallylic alcohols,[39] compounds (20) and (21) readily engaged in the anticipated RCM reaction thus affording the expected pyranones (22) and (23) (79% and 73%), respectively. The spectroscopic and physical data derived from product (22) matched those obtained on authentic material,[11] which was kindly provided by Professor S. V. Ley (Cambridge University). The acetonide moieties associated with each of compounds (22) and (23) could be removed by brief treatment with aqueous acetic acid at 80°C and, in this manner (+)-goniodiol (1) (98%) and its C6-epimer (24) (85%) were obtained. The NMR spectral data derived from compound (1), prepared as described above, matched those of authentic material.[6*a*,11] Furthermore, the specific rotation of the natural and synthetic materials were in good agreement (see Experimental section). The spectral data derived from isomer (24) were also in full accord with the assigned structure. Interestingly, the specific rotation of the C6-epimer of (+)-goniodiol was negative $\{[\alpha]_D$ –47.4° (*c* 0.27)$\}$.

Conclusion

The work described here should serve to highlight the utility of enantiomerically pure metabolite (2) as a starting material for chemical synthesis. Since various heterocyclic and other analogues of this compound are also available in optically pure form[14,19] the reaction sequences detailed above could be used to assemble analogues of (+)-goniodiol (1) which



Scheme 3.

vary, inter alia, in the nature and substitution patterns on the aromatic ring. In addition, the manner in which the pyranone moiety of target (1) is assembled should enable rapid construction of analogues varying in the nature of substituents on this ring. Overall, then, the route to (+)-goniodiol described here should be amenable to the assembly of a range of analogues, including other naturally occurring congeners, that would be useful in developing a comprehensive structure–activity relationship (SAR) profile of this interesting class of cytotoxic agent.

Experimental

General

Melting points were recorded with a Kofler hot-stage apparatus and are uncorrected. Unless otherwise indicated, proton (δ_H) and carbon (δ_C) NMR spectra were recorded with a Varian Unity 300 or Varian Gemini 300 spectrometer operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C. All such spectra were recorded, unless indicated to the contrary, in deuterochloroform ($CDCl_3$) solution at 22°C. The protonicities of the carbon atoms observed in ^{13}C NMR spectra were determined by attached proton test (APT) experiments. Infrared spectra (ν_{max}) were recorded with either a Perkin-Elmer 983G infrared spectrophotometer or a Perkin-Elmer 1800 Series FTIR instrument. Samples were analyzed either as thin films on NaCl plates (for liquids) or as KBr disks (for solids). Low-resolution electron-impact mass spectra (m/z) were recorded at 70 eV on either a VG Micromass 7070F mass spectrometer or a JEOL AX-505H mass spectrometer. High-resolution mass spectra were recorded with a VG Micromass 7070F instrument. HPLC separations were performed with an HP1090 HPLC instrument incorporating a diode-array detector interfaced with HP ChemStation software and on-board autosampler. An Alltech Apollo 5 μm C18 250 × 4.6 mm analytical column operating at 40°C was employed. Peak detection was by UV at 230 nm and 1 : 1 v/v MeCN/H_2O was used as the eluting solvent at a flow rate of 1 mL min^{-1}. Optical rotations were determined on a Perkin-Elmer 241 polarimeter at the sodium D line (589 nm) using spectroscopic grade chloroform (unless otherwise specified) at 20°C and at the concentrations (c) (g/100 mL) indicated. Measurements were carried out in a cell with a path length of 1 dm. Elemental analyses were performed by the Australian National University Microanalytical Services Unit located within the Research School of Chemistry. Tetrahydrofuran (THF) was distilled, under nitrogen, from sodium benzophenone ketyl, dichloromethane from calcium hydride, and methanol from magnesium methoxide. pH 7 Buffer solution was prepared by dissolving potassium dihydrogenphosphate (85 g) and sodium hydroxide (14.5 g) in water (950 mL).

Synthetic Studies

*(3a*S*,4*R*,5*R*,9b*R*)-3a,4,5,9b-Tetrahydro-2,2-dimethylnaphtho[1,2-*d*]-1,3-dioxole-4,5-diol (6)*

A magnetically stirred solution of alkene (5)[16] (4.00 g, 16.9 mmol) in acetone/water (150 mL of 2 : 1 v/v mixture) was treated with *N*-methylmorpholine *N*-oxide (NMO) (3.96 g, 33.8 mmol, 2 mole equiv.) followed by OsO_4 (1.7 mL of a 2.5 wt% solution in *t*-butanol, 0.17 mmol, 1 mol%). The resulting mixture was stirred at 18°C for 16 h then treated with $Na_2S_2O_3$ (300 mL of a 10% w/v aqueous solution). After 0.25 h the reaction mixture was extracted with diethyl ether (2 × 200 mL) and then ethyl acetate (2 × 200 mL). The combined organic phases were dried (Na_2SO_4), filtered through a 5 cm pad of TLC-grade silica gel (ethyl acetate elution), and the filtrate concentrated under reduced pressure to give a brown solid. Recrystallization (ethyl acetate/hexane) of this material then gave the *title diol* (6) (3.41 g, 73%) as off-white needles, mp 145–146°C, $[\alpha]_D$ +19.7° (*c* 1.0) (Found: C, 65.9; H, 6.8%. $C_{13}H_{16}O_4$ requires C, 66.1; H, 6.8%). ν_{max} (KBr)/cm^{-1} 3480, 3178, 2988, 2891, 2868, 1454, 1376, 1242, 1221, 1091, 1064, 868, 771. δ_H 7.50–7.36 (4 H, complex m), 5.28 (1 H, d, *J* 6.7), 4.87 (1 H, dd, *J* 4.9 and 2.9), 4.53 (1 H, app. t, *J* 6.3), 4.04 (1 H, m), 2.93 (1 H, d, *J* 4.9), 2.78 (1 H, d, *J* 4.4), 1.48 (3 H, s), 1.44 (3 H, s). δ_C 136.2, 132.2, 129.7, 129.1, 128.8, 127.9, 109.3, 76.6, 74.6, 73.1, 69.8, 27.5, 25.2. Mass spectrum (70 eV; EI) m/z 235 (1%, $[M-H^{\bullet}]^+$), 221 (44, $[M-CH_3^{\bullet}]^+$), 178 (24), 161 (100), 133 (57), 131 (50), 115 (15), 103 (19), 91 (25), 77 (20).

*(4*R-cis*)-5-(2′-Formylphenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxaldehyde (7)*

Method A. A magnetically stirred solution of diol (6) (1.18 g, 5.00 mmol) in methanol/1 M pH 7 buffer (180 mL of 5 : 1 v/v mixture) was treated with water (ca. 10 mL) until homogeneous. The resulting solution was cooled on an ice bath and $NaIO_4$ (1.60 g, 7.5 mmol, 1.5 mole equiv.) was added in portions over 5 min. The resulting mixture

was removed from the ice bath and allowed to stir at 18°C for 1 h and was then diluted with water (200 mL) and extracted with diethyl ether (4 × 100 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give *compound* (7) (1.18 g, 100%) as a clear, colourless oil. δ_H 10.04 (1 H, s), 9.02 (1 H, d, *J* 2.8), 7.83 (2 H, m), 7.64 (1 H, m), 7.54 (1 H, m), 6.21 (1 H, d, *J* 7.9), 5.06 (1 H, dd, *J* 7.9 and 2.8), 1.77 (3 H, s), 1.58 (3 H, s). This material was used, without purification, in the next step of the reaction sequence.

Method B. A magnetically stirred solution of alkene (5) (2.05 g, 10.1 mmol) in 1,2-dimethoxyethane (DME)/water (160 mL of 3 : 1 v/v mixture) was treated with OsO_4 (53 mL of a 2.5 wt% solution in *t*-butanol, 1.02 mmol, 10 mol%). After 0.5 h, the reaction mixture was treated, in portions over 5 min, with $NaIO_4$ (6.55 g, 30.6 mmol, 3 mole equiv.). The resulting mixture was stirred at 18°C for 20 h then treated with $Na_2S_2O_3$ (30 mL of a 20% w/v aqueous solution). After 0.33 h the reaction mixture was diluted with water (200 mL) and extracted with diethyl ether (6 × 50 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give compound (7) (1.64 g, 69%) as a light-yellow and unstable oil. This material was identical, as judged by ^{1}H NMR analysis, with the material obtained by Method A.

*(1′*R*,3a*R*,8*R*,8a*S*)-8-Hydroxy-8a-(1′-hydroxybut-3′-en-1′-yl)-2,2-dimethyl-8,8a-dihydro-8*H*-indeno[1,2-*d*]-1,3-dioxol-8-ol (8)*

A magnetically stirred solution of dialdehyde (7) (47 mg, 0.20 mmol) in diethyl ether (1 mL) was treated with calcium hydride (ca. 20 mg) for 30 min. The solvent was removed under reduced pressure and replaced with lithium perchlorate (2 mL of a 5 M solution in ether) and the resultant mixture was treated with allyltributylstannane (68 μL, 0.22 mmol). After 4 h at 18°C the reaction mixture was quenched with pH 7 buffer solution (5 mL), diluted with water (20 mL), and extracted with dichloromethane (3 × 5 mL). The combined organic phases were washed with water (1 × 5 mL) and brine (1 × 5 mL) before being dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a colourless oil. Subjection of this material to flash chromatography (silica, 5 : 95 → 2 : 3 v/v ethyl acetate/hexane gradient elution) provided, after concentration of the appropriate fractions (R_f 0.2 in 3 : 7 v/v ethyl acetate/hexane), *compound* (8) (24 mg, 43%) as white needles, mp 104–106°C, $[\alpha]_D$ +86.5° (*c* 0.5) (Found: $[M-CH_3^{\bullet}]^+$, 261.1126. $C_{16}H_{20}O_4$ requires $[M-CH_3^{\bullet}]^+$, 261.1127). ν_{max} (KBr)/cm^{-1} 3401, 2988, 2934, 1641, 1381, 1370, 1243, 1212, 1027, 755. δ_H 7.50–7.37 (4 H, complex m), 5.97 (1 H, m), 5.59 (1 H, s), 5.35 (1 H, d, *J* 4.0), 5.27–5.18 (2 H, complex m), 4.08 (1 H, ddd, *J* 9.8, 6.3 and 2.5), 3.34 (1 H, d, *J* 4.0), 2.66 (1 H, d, *J* 6.3), 2.62 (1 H, m), 2.47 (1 H, m), 1.47 (3 H, s), 0.87 (3 H, s). δ_C 142.5, 141.8, 135.2, 129.9(9), 129.9(6), 125.8(5), 125.7(7), 118.3, 112.7, 94.0, 85.4, 81.8, 72.8, 36.6, 28.7, 28.5. Mass spectrum (70 eV; EI) *m*/*z* 261 (4%, $[M-CH_3^{\bullet}]^+$), 218 (30), 177 (49), 177 (49), 159 (100), 147 (43), 131 (75), 119 (34), 103 (35), 91 (43), 77 (25), 65 (19).

*(4*S-cis*)-5-(2′-Formylphenyl)-2,2-dimethyl-(1′-hydroxybut-3′-en-1′-yl)-1,3-dioxolane (9)*

A magnetically stirred solution of dialdehyde (7) (234 mg, 1.00 mmol) in lithium perchlorate (10 mL of a 5 M solution in ether) was treated with allyltributylstannane (340 μL, 1.1 mmol) for 4 h at 18°C. The reaction mixture was then quenched with pH 7 buffer solution (50 mL), diluted with water (200 mL), and extracted with dichloromethane (3 × 50 mL). The combined organic phases were washed with water (1 × 20 mL) and brine (1 × 20 mL) before being dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a colourless oil. Subjection of this material to flash chromatography (silica, 5 : 95 → 2 : 3 v/v ethyl acetate/hexane elution) provided, after concentration of the appropriate fractions (R_f 0.1 in 1 : 4 v/v ethyl acetate/hexane), the *title aldehyde* (9) (139 mg, 50%) as a clear, light-yellow oil containing ca. 10% starting dialdehyde (7) as impurity. This material could be purified by further flash chromatography (silica, 15 : 30 : 55 v/v/v diethyl ether/dichloromethane/hexane elution) to provide an essentially pure sample of the *title aldehyde* (9) (R_f 0.3) as a clear, colourless oil and approximately a 10 : 1 mixture of epimers (as judged by ^{13}C NMR analysis), $[\alpha]_D$ –184.0° (*c* 2.4) (Found: $[M-CH_3^{\bullet}]^+$, 261.1126. $C_{16}H_{20}O_4$ requires $[M-CH_3^{\bullet}]^+$, 261.1127). ν_{max} (NaCl)/cm^{-1} 3468, 2984, 1696, 1575, 1380, 1213, 1057, 881, 757. δ_H (major epimer) 10.03 (1 H, s), 7.93 (1 H, d, *J* 7.8), 7.80 (1 H, dd, *J* 7.5 and 1.3), 7.64 (1 H, dt, *J* 7.8 and 1.3), 7.52 (1 H, dt, *J* 7.5 and 0.9), 5.94 (1 H, d, *J* 7.3), 5.64 (1 H, m), 4.95 (1 H, m), 4.88 (1 H, m), 4.68 (1 H, dd, *J* 7.3 and 2.9), 3.02 (1 H, m), 2.06–1.85 (3 H, complex m), 1.68 (3 H, s), 1.53 (3 H, s). δ_C (major epimer) 193.4 (CH), 138.8 (C), 135.3 (CH), 134.6 (CH), 134.0 (CH), 132.9 (C), 128.0 (2 × CH), 117.1 (CH_2), 108.0 (C), 79.3 (CH), 76.4 (CH), 68.8 (CH), 39.6 (CH_2), 27.0 (CH_3), 24.7 (CH_3). Mass spectrum (70 eV; EI) *m*/*z* 261 (6%, $[M-CH_3^{\bullet}]^+$), 235 (6), 201 (17), 177 (99), 159 (39), 148 (55), 147 (73), 133 (74), 131 (72), 119 (90), 118 (100), 91 (68), 77 (39).

*[3a*S*-(3aα,10bα)]-2,2-Dimethyl-4-(prop-2′-enyl)-3a,4,6,10b-tetrahydro-1,3-dioxolo[4,5-*d*][2]benzoxepin-4(3a*H*)-one (11)*

A magnetically stirred solution of alcohol (9) (37.4 mg, 0.135 mmol) and DMAP (132 mg, 1.08 mmol) in anhydrous THF (0.5 mL) maintained at −20°C under a nitrogen atmosphere was treated with acrylic anhydride (5.2 mL of a 0.26 M solution in THF, 1.35 mmol, ca. 10 mole equiv.). The resulting solution was left at −20°C for 16 h before being quenched by the addition of water (10 mL) and was then extracted with dichloromethane (3 × 5 mL). The combined organic portions were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (silica, 5 : 95 → 3 : 7 v/v ethyl acetate/hexane gradient elution) provided, after concentration of the appropriate fractions (R_f 0.5 in 3 : 7 v/v ethyl acetate/hexane), the *title compound* (11) (9.8 mg, 22%) as a clear, colourless oil. δ_H 7.46–7.35 (4 H, complex m), 7.37 (1 H, s), 6.53 (1 H, dd, *J* 17.3 and 1.5), 6.23 (1 H, dd, *J* 17.3 and 10.5), 5.94 (1 H, dd, *J* 10.5 and 1.5), 5.70 (1 H, m), 5.14 (1 H, d, *J* 6.5), 5.06 (1 H, m), 4.96 (1 H, m), 4.26 (1 H, dd, *J* 6.5 and 1.0), 3.87 (1 H, ddd, *J* 8.8, 4.9 and 1.0), 2.47 (1 H, m), 2.23 (1 H, m), 1.67 (3 H, s), 1.50 (3 H, s).

*(4*R-cis*)-5-[2′-(Hydroxymethyl)phenyl]-2,2-dimethyl-1,3-dioxolane-4-methanol (12)*

A magnetically stirred and chilled (ice-bath) solution of dialdehyde (7) (1.64 g, 7.00 mmol) in methanol (100 mL) was treated, in portions over 0.25 h, with sodium borohydride (1.10 g, 29.1 mmol, ca. 4 mole equiv.). After 2 h the reaction mixture was quenched with brine (200 mL) and the resulting mixture extracted with ethyl acetate (4 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a brown oil. Subjection of this material to flash chromatography (silica gel, ethyl acetate elution) gave, after concentration of the appropriate fractions (R_f 0.4), the title diol (12)[19] [1.06 g, 64% from (7)] as a viscous, light-brown oil, $[\alpha]_D$ –80.3° (*c* 3.0) (Found: $[M-CH_3^{\bullet}]^+$, 223.0969. $C_{13}H_{18}O_4$ requires $[M-CH_3^{\bullet}]^+$, 223.0970). ν_{max} (NaCl)/cm^{-1} 3385, 2934, 1380, 1214, 1164, 1108, 1041, 752. δ_H 7.54 (1 H, br d, *J* 7.2), 7.33 (1 H, m), 7.26–7.21 (2 H, complex m), 5.54 (1 H, d, *J* 7.0), 4.66 (1 H, br dd, *J* 12.0 and 4.3), 4.50–4.41 (2 H, complex m), 3.74 (1 H, br s), 3.24 (1 H, m), 3.00 (1 H, m), 2.83 (1 H, br s), 1.61 (3 H, s), 1.47 (3 H, s). δ_C 137.5, 135.2, 129.4, 128.5, 128.2, 127.2, 108.6, 78.6, 75.3, 63.7, 62.5, 27.5, 24.9. Mass spectrum (70 eV; EI) *m*/*z* 223 (2%, $[M-CH_3^{\bullet}]^+$), 220 (12), 178 (8), 163 (6), 149 (14), 133 (21), 120 (100), 91 (31), 77 (13), 59 (65).

*(4*S-cis*)-5-[2′-(Formyl)phenyl]-2,2-dimethyl-1,3-dioxolane-4-methanol (13)*

A solution of diol (12) (1.06 g, 4.47 mmol) in DME (45 mL) was treated with 'precipitated active' manganese dioxide (7.78 g, 89.5 mmol, from MERCK-Schuchardt), and the resulting mixture was stirred at 18°C for 16 h then filtered through a pad of Celite. The solids thus retained were washed with DME (45 mL) and the combined filtrates concentrated under reduced pressure to give an orange-red solid. Subjection of this material to flash chromatography (silica, 3 : 7 ethyl acetate/hexane elution) gave, after concentration of the appropriate fractions (R_f 0.3 in 1 : 1 v/v ethyl acetate/hexane), the *title hydroxyaldehyde* (13) (746 mg, 70%) as a pale-yellow oil, $[\alpha]_D$ –237.0° (*c* 6.5) (Found: $[M-CH_3^{\bullet}]^+$, 221.0813. $C_{13}H_{16}O_4$ requires $[M-CH_3^{\bullet}]^+$,

221.0814). ν_{max} (KBr)/cm^{-1} 3467, 2987, 2936, 2744, 1694, 1600, 1575, 1381, 1213, 1166, 1044, 907, 868, 756. δ_H 10.04 (1 H, br s), 7.89 (1 H, d, *J* 7.6), 7.81 (1 H, dd, *J* 7.5 and 1.5), 7.64 (1 H, br dt, *J* 7.6 and 1.5), 7.53 (1 H, br dt, *J* 7.5 and 1.1), 6.00 (1 H, br d, *J* 7.3), 4.84 (1 H, m), 3.02 (2 H, dd, *J* 6.5 and 5.3), 1.67 (3 H, s), 1.57 (1 H, t, *J* 6.5), 1.53 (3 H, s). δ_C 193.2, 138.2, 135.1, 133.8, 132.8, 127.9, 127.1, 108.3, 77.9, 75.2, 62.7, 27.4, 24.7. Mass spectrum (ESI+) *m*/*z* 259 (100%, $[M+Na]^+$), 235 (18, $[M-H^{\bullet}]^+$), 219 (23).

*(4*S-cis*)-5-[2′-(Formyl)phenyl]-2,2-dimethyl-1,3-dioxolane-4-methanol Acetate (14)*

A magnetically stirred solution of alcohol (13) (2.26 g, 9.6 mmol) in anhydrous dichloromethane (40 mL) maintained under a nitrogen atmosphere was treated with acetic anhydride (5.5 mL, 57.31 mmol, 6 mole equiv.), pyridine (4.7 mL, 57.31 mmol) and then DMAP (100 mg). The resulting mixture was stirred at 18°C for 16 h then treated with acetic anhydride (1.83 mL, 19.1 mmol, 2 mole equiv.) and pyridine (1.56 mL, 19.1 mmol). After 1 h, $NaHCO_3$ (100 mL of a saturated aqueous solution) was added and stirring continued for 0.5 h. The separated organic layer was washed with NH_4Cl (3 × 20 mL of a saturated aqueous solution) and brine (1 × 20 mL) then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a yellow oil (2.34 g). Subjection of this material to flash chromatography (silica, 3 : 7 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions (R_f 0.5) gave the title *acetate* (14) (1.47 g, 55%) as a clear, colourless oil, $[\alpha]_D$ −235.8° (*c* 5.7) (Found: $[M-CH_3^{\bullet}]^+$, 263.0918. $C_{15}H_{18}O_5$ requires $[M-CH_3^{\bullet}]^+$, 263.0919). ν_{max} (KBr)/cm^{-1} 2988, 2938, 2743, 1743, 1698, 1600, 1576, 1373, 1239, 1214, 1167, 1045, 873, 757. δ_H 10.03 (1 H, s), 7.88 (1 H, d, *J* 7.8), 7.79 (1 H, d, *J* 6.5), 7.63 (1 H, dd, *J* 7.8 and 7.5), 7.51 (1 H, dd, *J* 7.5 and 6.5), 6.01 (1 H, d, *J* 7.0), 4.95 (1 H, dt, *J* 7.0 and 5.8), 3.51 (2 H, d, *J* 5.8), 1.85 (3 H, s), 1.65 (3 H, s), 1.52 (3 H, s). δ_C 193.4, 170.6, 138.0, 135.5, 134.4, 133.2, 128.4, 127.4, 108.9, 75.6, 75.5, 64.4, 27.7, 25.2, 21.0. Mass spectrum (70 eV; EI) *m*/*z* 263 (3%, $[M-CH_3^{\bullet}]^+$), 220 (2), 203 (13), 178 (10), 160 (100), 147 (28), 118 (98), 105 (17), 91 (21), 77 (15).

Bis[1,3-bis(diphenylphosphino)propane]rhodium Tetrafluoroborate and Bis[1,3-bis(diphenylphosphino)propane]dioxorhodium Tetrafluoroborate

The yellow-red coloured bis[1,3-bis(diphenylphosphino)propane]-rhodium tetrafluoroborate was prepared according to the method of James and Mahajan[22] but was observed to turn to a tan-coloured and crystalline solid on attempted dissolution in various solvents. ^{31}P NMR and single-crystal X-ray analyses (see Crystallography section, Fig. 3, Tables 4 and 5) of the latter established it to be bis[1,3-bis(diphenylphosphino)propane]dioxorhodium tetrafluoroborate. Heating an acetone solution of this tan-coloured complex under a nitrogen atmosphere for 16 h followed by concentration of the cooled solution under reduced pressure, dissolution of the residue in deoxygenated dichloromethane, and layering this with degassed diethyl ether resulted in the formation of yellow-red crystals of $[Rh(dppp)_2]^+BF_4^-\cdot 2CH_3COCH_3$, which could be employed in the decarbonylation of compound (14) as described below.

*(4*S-cis*)-5-Phenyl-2,2-dimethyl-1,3-dioxolane-4-methanol Acetate (15)*

A degassed solution of aldehyde (14) (660 mg, 2.37 mmol) in xylene (8 mL) was added, by cannula, to bis[1,3-bis(diphenylphosphino) propane]rhodium tetrafluoroborate[21,22] (120 mg, 0.12 mmol, 5 mol%). The resulting mixture was heated at reflux with stirring for 16 h then another portion (5 mol%) of catalyst was added and heating was continued for a further 6 h. The cooled reaction mixture was then diluted with diethyl ether (20 mL) and filtered through a pad of Celite which was washed with diethyl ether (20 mL). The combined filtrates were concentrated under reduced pressure and the resulting brown oil subjected to flash chromatography (silica gel, 10–30% v/v ethyl acetate in hexane, gradient elution), thereby yielding two fractions, A and B.

Concentration of fraction A (R_f 0.25 in 1 : 4 v/v ethyl acetate/hexane) gave the starting aldehyde (14) (48.6 mg, 7% recovery), which was identical in all respects with an authentic sample.

Concentration of fraction B (R_f 0.4 in 1 : 4 v/v ethyl acetate/hexane) gave the title acetate (15)[6] (509 mg, 92% at 93% conversion) as a white crystalline solid, mp 65–68°C, $[\alpha]_D$ −109° (*c* 1.1) (Found: $M^{+\bullet}$, 250.1205; C, 67.1; H, 7.2%. $C_{14}H_{18}O_4$ requires $M^{+\bullet}$, 250.1205; C, 67.2; H, 7.3%). ν_{max} (KBr)/cm^{-1} 1735, 1376, 1237, 1212, 1087, 1033, 983, 752, 704. δ_H 7.38–7.30 (5 H, complex m), 5.32 (1 H, d, *J* 6.9), 4.56 (1 H, ddd, *J* 8.0, 6.9 and 4.4), 3.71 (1 H, dd, *J* 11.7 and 4.4), 3.61 (1 H, dd, *J* 11.7 and 8.0), 1.92 (3 H, s), 1.65 (3 H, s), 1.49 (3 H, s). δ_C 170.8, 136.3, 128.7, 128.5, 126.7, 109.5, 78.7, 76.5, 64.5, 27.6, 25.2, 20.9. Mass spectrum (70 eV; EI) *m*/*z* 250 (0.4%, $M^{+\bullet}$), 235 (25), 192 (19), 148 (100), 133 (82), 119 (61), 101 (78), 91 (68).

*(4*S-cis*)-5-Phenyl-2,2-dimethyl-1,3-dioxolane-4-methanol (16)*

A magnetically stirred solution of acetate (15) (42 mg, 0.17 mmol) in MeOH (10 mL) was treated with solid potassium carbonate (232 mg, 1.68 mmol, 10 mole equiv.). After 0.5 h the reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic phases were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the title alcohol (16)[6] (33.4 mg, 96%) as an off-white solid, mp 57–58°C (lit.[6] mp 57–58°C) $[\alpha]_D$ −84° (*c* 3.7 in MeOH) [lit.[6] $[\alpha]_D$ −112° (*c* 1.2 in $CHCl_3$)], (Found: $[M-CH_3^{\bullet}]^+$, 193.0869. $C_{12}H_{16}O_3$ requires $[M-CH_3^{\bullet}]^+$, 193.0865). ν_{max} (KBr)/cm^{-1} 3436, 2989, 2935, 1494, 1455, 1374, 1265, 1213, 1162, 1048, 902, 859, 742, 701. δ_H 7.37–7.27 (5 H, complex m), 5.30 (1 H, d, *J* 7.0), 4.45 (1 H, ddd, *J* 8.2, 7.0 and 4.4), 3.22 (1 H, dd, *J* 11.6 and 8.2), 3.08 (1 H, dd, *J* 11.6 and 4.4), 1.72 (1 H, br s), 1.64 (3 H, s), 1.49 (3 H, s). δ_C 136.4, 128.6, 128.3, 126.5, 109.2, 79.1, 78.5, 63.2, 28.0, 25.5. Mass spectrum (70 eV; EI) *m*/*z* 208 (<1%, $M^{+\bullet}$), 193 (26, $[M-CH_3^{\bullet}]^+$), 177 (14), 165 (22), 148 (86), 133 (60), 119 (67), 91 (99), 77 (45), 59 (100).

*(4*R-cis*)-2,2-Dimethyl-5-phenyl-1,3-dioxolane-4-carboxaldehyde (17)*

A magnetically stirred mixture of alcohol (16) (35.9 mg, 0.172 mmol), NMO (61 mg, 0.521 mmol, ca. 3 mole equiv.), and activated powdered molecular sieves (4 Å, ca. 150 mg) in anhydrous dichloromethane (5 mL), maintained under a nitrogen atmosphere at 0°C, was treated with tetrapropylammonium perruthenate(VII) (10.4 mg, 0.03 mmol, ca. 17 mol%). After 1 h the reaction mixture was filtered through a pad of Celite covering an equivalent pad of TLC-grade silica gel. The 'column' comprising these two adsorbents was eluted with additional dichloromethane (30 mL) and the combined filtrates were concentrated under reduced pressure to give the title aldehyde (17)[6] (21.9 mg, 62%) as a clear, light-yellow oil, $[\alpha]_D$ −33° (*c* 2.9 in MeOH) (Found: $[M-CH_3^{\bullet}]^+$, 191.0707. $C_{12}H_{14}O_3$ requires $[M-CH_3^{\bullet}]^+$, 191.0708). ν_{max} (KBr)/cm^{-1} 2989, 2917, 1734, 1455, 1381, 1263, 1217, 1158, 1062, 909, 740. δ_H (CD_2Cl_2) 9.13 (1 H, d, *J* 3.1), 7.37–7.31 (5 H, complex m), 5.48 (1 H, d, *J* 7.8), 4.59 (1 H, dd, *J* 7.8 and 3.1), 1.74 (3 H, s), 1.53 (3 H, s). δ_C (CD_2Cl_2) 199.7, 134.9, 128.9, 128.7, 126.7, 111.5, 83.1, 79.9, 27.2, 25.2. Mass spectrum (70 eV; EI) *m*/*z* 191 (10%, $[M-CH_3^{\bullet}]^+$), 177 (40), 148 (43), 119 (68), 100 (52), 91 (100), 85 (70), 77 (36), 65 (30).

(αR,4S,5R)-2,2-Dimethyl-5-phenyl-α-propenyl-1,3-dioxolane-4-methanol (18) and (αS,4S,5R)-2,2-Dimethyl-5-phenyl-α-propenyl-1,3-dioxolane-4-methanol (19)

Allyltributylstannane (200 μL, 0.645 mmol) was added to a magnetically stirred solution of compound (17) (44.7 mg, 0.217 mmol) in lithium perchlorate (2 mL of a 5 M solution in diethyl ether). The resultant solution was stirred under an atmosphere of nitrogen at 18°C for 4 h then cooled to 0°C and quenched by the addition of pH 7 buffer solution (5 mL). The ensuing mixture was diluted with water (20 mL) and then extracted with dichloromethane (3 × 5 mL). The combined organic portions were washed with water (1 × 5 mL) and brine (1 × 5 mL) before being dried (Na_2SO_4), filtered, and concentrated under reduced pressure

to afford a colourless oil. Subjection of this material to flash chromatography (silica, 5 : 95 → 2 : 3 v/v ethyl acetate/hexane gradient elution) provided, after concentration of the appropriate fractions (R_f 0.26 in 3 : 7 v/v ethyl acetate/hexane), a ca. 8 : 3 mixture of compounds (18) and (19) (37.8 mg, 70%) as a clear, colourless oil. Subjection of this material to semi-preparative reverse-phase HPLC afforded two fractions, A and B.

Concentration of fraction A (R_t 23.1 min) afforded *compound* (18) as a clear, colourless oil, $[\alpha]_D$ –31.7° (*c* 1.4) (Found: $M^{+\bullet}$, 248.1423. $C_{15}H_{20}O_3$ requires $M^{+\bullet}$, 248.1412). ν_{max} (NaCl)/cm^{-1} 3501, 2985, 2916, 1640, 1495, 1455, 1380, 1213, 1161, 1054, 915, 876, 700. δ_H 7.39–7.26 (5 H, complex m), 5.64 (1 H, m), 5.27 (1 H, d, *J* 6.9), 4.95 (1 H, m), 4.83 (1 H, m), 4.19 (1 H, t, *J* 6.7), 3.36 (1 H, m), 2.19 (1 H, d, *J* 3.4), 1.79 (2 H, m), 1.67 (3 H, s), 1.50 (3 H, s). δ_C 136.4 (C), 134.4 (CH), 128.5 (CH), 128.3 (CH), 127.1 (CH), 117.3 (CH_2), 108.7 (C), 80.7 (CH), 79.1 (CH), 69.5 (CH), 37.8 (CH_2), 27.4 (CH_3), 25.2 (CH_3). Mass spectrum *m*/*z* 248 (4%, $M^{+\bullet}$), 233 (36, $[M-CH_3^{\bullet}]^+$), 207 (10), 177 (6), 148 (100), 119 (52), 91 (51), 59 (26).

Concentration of fraction B (R_t 25.4 min) afforded *compound* (19) as a clear, colourless oil, $[\alpha]_D$ –55.9° (*c* 0.5) (Found: $M^{+\bullet}$, 248.1419. $C_{15}H_{20}O_3$ requires $M^{+\bullet}$, 248.1412). ν_{max} (NaCl)/cm^{-1} 3585, 3470, 3073, 2988, 2916, 2849, 1640, 1495, 1455, 1381, 1259, 1214, 1161, 1054, 875, 752, 700. δ_H 7.44–7.26 (5 H, complex m), 5.75 (1 H, m), 5.33 (1 H, d, *J* 6.6), 5.08 (1 H, m), 5.04 (1 H, m), 4.17 (1 H, dd, *J* 8.8 and 6.6), 3.40 (1 H, m), 2.46 (1 H, m), 2.15 (1 H, m), 1.62 (3 H, s), 1.48 (3 H, s), 0.96 (1 H, d, *J* 4.1). δ_C 137.1 (C), 134.5 (CH), 128.6 (CH), 128.3 (CH), 127.3 (CH), 118.0 (CH_2), 108.7 (C), 81.0 (CH), 79.4 (CH), 69.2 (CH), 38.2 (CH_2), 27.4 (CH_3), 25.0 (CH_3). Mass spectrum *m*/*z* 248 (21%, $M^{+\bullet}$), 233 (60, $[M-CH_3^{\bullet}]^+$), 207 (5), 177 (5), 148 (100), 119 (41), 91 (38).

*(α*R*,4*S*,5*R*)-2,2-Dimethyl-5-phenyl-α-propenyl-1,3-dioxolane-4-methanol Acrylate (20)*

A magnetically stirred solution of alcohol (18) (27.4 mg, 0.11 mmol) and DMAP (108 mg, 0.88 mmol, ca. 8 mole equiv.) in anhydrous THF (1 mL) maintained at −20°C under a nitrogen atmosphere was treated, dropwise, with acrylic anhydride (1.7 mL of a 0.26 M solution in THF, 0.44 mmol, ca. 20 mole equiv.). After completion of the addition the solution was warmed to 18°C, stirred for 3 h, and the reaction mixture was then diluted with NH_4Cl (20 mL of a saturated aqueous solution). The separated aqueous phase was extracted with ethyl acetate (3 × 10 mL) and the combined organic phases dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a bright-yellow oil. Subjection of this material to flash chromatography (silica gel, 1 : 9 v/v ethyl acetate/hexane elution) afforded, after concentration of the appropriate fractions (R_f 0.2), *compound* (20) (15.6 mg, 47%) as a white crystalline solid, mp 42–43°C, $[\alpha]_D$ −94.5° (*c* 1.1) (Found: $M^{+\bullet}$, 302.1529. $C_{18}H_{22}O_4$ requires $M^{+\bullet}$, 302.1518). ν_{max} (NaCl)/cm^{-1} 3078, 2985, 2936, 1727, 1638, 1405, 1296, 1269, 1249, 1216, 1191, 1059, 985, 879, 805, 736, 701. δ_H 7.36–7.24 (5 H, complex m), 6.32 (1 H, dd, *J* 17.4 and 1.4), 6.04 (1 H, dd, *J* 17.4 and 10.4), 5.80 (1 H, dd, *J* 10.4 and 1.4), 5.62 (1 H, m), 5.34 (1 H, d, *J* 7.2), 5.01 (1 H, m), 4.96 (1 H, m), 4.65 (1 H, dt, *J* 6.3 and 4.6), 4.44 (1 H, dd, *J* 7.2 and 4.6), 2.09 (2 H, m), 1.67 (3 H, s), 1.50 (3 H, s). δ_C 165.1 (C), 136.3 (C), 133.2 (CH), 130.5 (CH_2), 128.9 (CH), 128.5 (CH), 128.2 (CH), 126.7 (CH), 118.3 (CH_2), 109.1 (C), 78.6 (CH), 78.5 (CH), 71.4 (CH), 35.8 (CH_2), 26.9 (CH_3), 25.4 (CH_3). Mass spectrum *m*/*z* 302 (3%, $M^{+\bullet}$), 287 (43, $[M-CH_3^{\bullet}]^+$), 244 (20), 148 (100), 138 (22), 119 (21), 91 (21), 55 (74).

*(α*S*,4*S*,5*R*)-2,2-Dimethyl-5-phenyl-α-propenyl-1,3-dioxolane-4-methanol Acrylate (21)*

Acrylation of alcohol (19) (19.1 mg, 0.77 mmol) in the same manner as used for congener (18) (see immediately above) afforded a light-yellow oil on workup. Subjection of this material to flash chromatography (silica gel, 1 : 9 v/v ethyl acetate/hexane elution) gave, after concentration of the appropriate fractions (R_f 0.2), *compound* (21) (12.2 mg, 52%) as a white crystalline solid, mp 36–38°C, $[\alpha]_D$ –11.1° (*c* 0.6) (Found: $M^{+\bullet}$, 302.1518. $C_{18}H_{22}O_4$ requires $M^{+\bullet}$, 302.1518). ν_{max} (NaCl)/cm^{-1} 2986, 1727, 1639, 1405, 1381, 1263, 1188, 1057, 984, 917, 879, 806, 699. δ_H 7.32–7.17 (5 H, complex m), 6.10 (1 H, dd, *J* 17.1 and 1.5), 5.80–5.56 (3 H, complex m), 5.31 (1 H, d, *J* 6.7), 4.96 (1 H, br d, *J* ca. 9.5), 4.95 (1 H, br d, *J* ca. 18.2), 4.66 (1 H, ddd, *J* 8.3, 6.1 and 4.2), 4.47 (1 H, dd, *J* 8.3 and 6.7), 2.42–2.34 (2 H, complex m), 1.65 (3 H, s), 1.48 (3 H, s). δ_C 164.3 (C), 136.2 (C), 133.1 (CH), 130.2 (CH_2), 128.3 (CH), 128.1 (CH), 128.0 (CH), 126.9 (CH), 118.0 (CH_2), 108.8 (C), 79.2 (CH), 78.1 (CH), 71.3 (CH), 35.2 (CH_2), 27.3 (CH_3), 25.0 (CH_3). Mass spectrum *m*/*z* 302 (19%, $M^{+\bullet}$), 287 (85, $[M-CH_3^{\bullet}]^+$), 244 (56), 230 (8), 203 (6), 148 (100), 138 (27), 91 (22), 55 (70).

*(6*R*)-6-[(4*S*,5*R*)-2,2-Dimethyl-5-phenyl-1,3-dioxolan-4-yl]-5,6-dihydro-2*H*-pyran-2-one (22)*

$(Cy_3P)_2Cl_2Ru{=}CHPh$ (4 mL of a 2.5 mM solution in degassed dichloromethane, 10.0 μmol) was added, in four portions over a 6 h period, to a magnetically stirred solution of compound (20) (12.6 mg, 41.7 μmol) in degassed dichloromethane (20 mL) maintained under nitrogen. The resulting solution was stirred at 18°C for 4 h, treated with dimethyl sulfoxide (DMSO) (71 μL, 1.0 mmol), left stirring at 18°C for 16 h, and then concentrated under reduced pressure to afford a yellow oil. Subjection of this material to flash chromatography (silica, 1 : 4→3 : 2 v/v ethyl acetate/hexane gradient elution) provided, after concentration of the appropriate fractions (R_f 0.2 in 2 : 3 v/v ethyl acetate/hexane), compound (22)[11] (9.0 mg, 79%) as colourless needles, mp 137–138°C, $[\alpha]_D$ –95.1° (*c* 0.45 in EtOH) (Found: $[M-CH_3^{\bullet}]^+$, 259.0970. $C_{16}H_{18}O_4$ requires $[M-CH_3^{\bullet}]^+$, 259.0970). ν_{max} (NaCl)/cm^{-1} 2984, 2932, 1716, 1494, 1455, 1379, 1246, 1216, 1152, 1074, 1062, 1029, 915, 872, 815, 744, 700. δ_H 7.48–7.44 (2 H, complex m), 7.39–7.27 (3 H, complex m), 6.67 (1 H, ddd, *J* 9.7, 6.2 and 2.5), 5.86 (1 H, ddd, *J* 9.7, 2.5 and 0.9), 5.33 (1 H, d, *J* 6.9), 4.34 (1 H, dd, *J* 6.9 and 4.0), 4.00 (1 H, dt, *J* 12.2 and 4.0), 2.40 (1 H, ddt, *J* 18.2, 12.2 and 2.5), 1.85 (1 H, dddd, *J* 18.2, 6.2, 4.0 and 0.9), 1.69 (3 H, s), 1.51 (3 H, s). δ_C 163.1 (C), 144.3 (CH), 135.7 (C), 128.4 (CH), 128.3 (CH), 127.3 (CH), 121.1 (CH), 109.9 (C), 79.4 (CH), 79.1 (CH), 75.6 (CH), 26.6 (CH_3), 25.9 (CH_2), 25.3 (CH_3). Mass spectrum *m*/*z* 259 (33%, $[M-CH_3^{\bullet}]^+$), 216 (29), 148 (56), 119 (41), 111 (43), 97 (62), 82 (64), 71 (72), 57 (100).

*(6*S*)-6-[(4*S*,5*R*)-2,2-Dimethyl-5-phenyl-1,3-dioxolan-4-yl]-5,6-dihydro-2*H*-pyran-2-one (23)*

Subjection of diene (21) (12.0 mg, 0.040 mmol) to ring-closing metathesis in the same manner as described immediately above and used for congener (20) afforded a light-yellow oil on workup. This material was subjected to flash chromatography (silica, 1 : 4 → 1 : 1 v/v ethyl acetate/hexane gradient elution) providing, after concentration of the appropriate fractions (R_f 0.2 in 3 : 7 v/v ethyl acetate/hexane), *compound* (23) (7.9 mg, 73%) as colourless needles, mp 97–98°C, $[\alpha]_D$ –27.3° (*c* 0.4) (Found: $M^{+\bullet}$, 274.1212. $C_{16}H_{18}O_4$ requires $M^{+\bullet}$, 274.1205). ν_{max} (NaCl)/cm^{-1} 2988, 2920, 1734, 1494, 1455, 1382, 1246, 1213, 1162, 1065, 1034, 984, 864, 815, 745, 700. δ_H 7.40–7.27 (5 H, complex m), 6.74 (1 H, ddd, *J* 9.8, 6.3 and 2.4), 5.83 (1 H, dd, *J* 9.8 and 2.4), 5.43 (1 H, d, *J* 7.1), 4.54 (1 H, t, *J* ca. 7.1), 3.98 (1 H, ddd, *J* 11.2, 7.1 and 3.9), 2.43 (1 H, ddt, *J* 18.6, 11.2 and 2.4), 2.23 (1 H, ddd, *J* 18.6, 6.3 and 3.9), 1.65 (3 H, s), 1.49 (3 H, s). δ_C 162.9 (C), 145.1 (CH), 136.7 (C), 128.4 (CH), 128.3 (CH), 127.1 (CH), 121.1 (CH), 109.3 (C), 79.1 (CH), 78.8 (CH), 75.9 (CH), 26.8 (CH_3), 26.0 (CH_2), 24.6 (CH_3). Mass spectrum *m*/*z* 274 (2%, $M^{+\bullet}$), 259 (32, $[M-CH_3^{\bullet}]^+$), 216 (47), 177 (10), 148 (95), 133 (13), 119 (38), 100 (50), 97 (68), 82 (100).

*(+)-Goniodiol {(6*R*)-6-[(1*R*,2*R*)-1,2-Dihydroxy-2-phenylethyl]-5,6-dihydro-2*H*-pyran-2-one} (1)*

A magnetically stirred solution of acetonide (22) (4.4 mg, 16.0 μmol) in acetic acid/water (4 mL of a 1 : 1 v/v mixture) was heated at 80°C for 0.5 h then cooled to 0°C and pH 7 buffer solution (20 mL) was added. The resulting mixture was diluted with brine (10 mL) then extracted with ethyl acetate (4 × 10 mL). The combined organic portions were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give a colourless oil. Subjection of this material to flash chromatography (silica, 1 : 4 → 4 : 1 v/v ethyl acetate/dichloromethane gradient elution) provided, after concentration of the appropriate fractions

(R_f 0.25 in 3 : 2 v/v ethyl acetate/dichloromethane), (+)-goniodiol (1)[1,2] (3.7 mg, 98%) as a clear, colourless oil, $[\alpha]_D$ +72.1° (*c* 0.3 in $CHCl_3$) [lit.[2] $[\alpha]_D$ +74.4° (*c* 0.3 in $CDCl_3$)] (Found: $[M+Na]^+$, 257.0782. $C_{13}H_{14}O_4$ requires $[M+Na]^+$, 257.0784). ν_{max} (NaCl)/cm^{-1} 3409, 2923, 1704, 1389, 1259, 1029, 817, 701. δ_H (500 MHz) 7.44–7.32 (5 H, complex m), 6.93 (1 H, ddd, *J* 9.0, 6.5 and 2.0), 6.00 (1 H, dd, *J* 9.0 and 2.5), 4.95 (1 H, dd, *J* 7.5 and 5.5), 4.80 (1 H, m), 3.73 (1 H, m), 2.80 (1 H, m), 2.65 (1 H, d, *J* 5.5), 2.32 (1 H, d, *J* 8.5), 2.18 (1 H, ddd, *J* 18.5, 6.0 and 3.5). δ_C (125 MHz) 163.6, 146.1, 140.7, 128.8, 128.4, 126.5, 120.6, 75.0, 73.7, 26.1 (one signal obscured by resonances due to $CDCl_3$). Mass spectrum (ESI) *m*/*z* 491 (18%, $[2M+Na]^+$), 257 (100, $[M+Na]^+$).

6-epi-*(+)-Goniodiol {(6*S*)-6-[(1*R*,2*R*)-1,2-Dihydroxy-2-phenylethyl]-5,6-dihydro-2*H*-pyran-2-one} (24)*

Hydrolysis of acetonide (23) (7.4 mg, 27.0 μmol) in the same manner as described immediately above for congener (22) afforded a clear, colourless oil on workup. Subjection of this material to flash chromatography (silica, 1 : 4 → 4 : 1 v/v ethyl acetate/dichloromethane gradient elution) provided, after concentration of the appropriate fractions (R_f 0.3 in 1 : 1 v/v ethyl acetate/dichloromethane), *6*-epi-(+)-*goniodiol* (24) (5.4 mg, 85%) as a clear, colourless oil, $[\alpha]_D$ –47.4° (*c* 0.27) (Found: $M^{+\bullet}$, 234.0895. $C_{13}H_{14}O_4$ requires $M^{+\bullet}$, 234.0892). ν_{max} (NaCl)/cm^{-1} 3405, 2913, 1701, 1389, 1261, 1075, 1038. δ_H 7.44–7.32 (5 H, complex m), 6.92 (1 H, ddd, *J* 9.8, 6.3 and 2.2), 5.98 (1 H, dd, *J* 9.8 and 2.2), 4.92 (1 H, d, *J* 5.4), 4.37 (1 H, dt, *J* ca. 12.6 and 5.4), 4.17 (1 H, br t, *J* 5.4), 2.68 (1 H, ddt, *J* 18.4, 12.6 and 2.2), 2.54–2.47 (3 H, complex m). δ_C 164.0 (C), 146.1 (CH), 139.7 (C), 128.8 (CH), 128.6 (CH), 126.9 (CH), 120.9 (CH), 78.1 (CH), 74.9 (CH), 73.9 (CH), 24.6 (CH_2). Mass spectrum *m*/*z* 234 (35%, $M^{+\bullet}$), 216 (3, $[M-H_2O]^{+\bullet}$), 188 (3), 177 (5), 144 (5), 128 (37), 107 (100), 69 (56).

Crystallography

Crystal Data

Compound (8). $C_{16}H_{20}O_4$, *M* 276.33, *T* 200 K, monoclinic, space group $P2_1$, *a* 9.4227(3), *b* 6.4126(2), *c* 12.1884(5) Å, *β* 100.8003(14)°, *V* 723.43(4) $Å^3$, *Z* 2, D_c 1.269 g cm^{-3}, *μ* 0.90 cm^{-1}, λ($Mo_{K\alpha}$) 0.71073 Å, 1799 unique data ($2\theta_{max}$ 54.86°), 1223 with $I > 2\sigma(I)$, *R* 0.031, *wR* 0.029, *S* 1.069. See Tables 1 and 2 for selected bond lengths and angles.

$[Rh(dppp)_2O_2]^+BF_4^- \cdot 2CH_3COCH_3$. $C_{60}H_{64}BF_4O_4P_4Rh$, *M* 1162.772, *T* 200 K, monoclinic, space group $P2_1/n$, *a* 11.70970(10), *b* 14.65970(10), *c* 32.0154(3) Å, β 98.8272(3)°, *V* 5430.69(8) $Å^3$, *Z* 4, D_c 1.422 g cm^{-3}, *μ* 4.9 cm^{-1}, λ($Mo_{K\alpha}$) 0.71073 Å, 12805 unique data ($2\theta_{max}$ 55.8°), 4765 with $I > 3\sigma(I)$, *R* 0.045, *wR* 0.051, *S* 1.041. See Tables 3 and 4 for selected bond lengths and angles.

Structure Determination

Intensity data were collected on a Nonius Kappa CCD diffractometer and extracted from diffraction images using the DENZO[40] package. Analytical absorption corrections were applied.[41] Both structures were solved by direct methods[42] and expanded using Fourier techniques.[43] Full-matrix least-squares refinement[43] was on *F*, non-hydrogen atoms were refined anisotropically while hydrogen atoms were included at geometrically determined positions and ride on the carbon of attachment. For structure (8) hydrogen atoms attached to oxygen were refined. Significant but readily modelled disorder was observed for both the BF_4^- anion and solvating acetone molecules (see CIF for detailed description).

Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited with the Cambridge Crystallographic Data Centre (CCDC Nos 198403 and 198404 for compound (8) and the ruthenium complex, respectively).

Acknowledgments

Dr Gregg Whited (Genencor International, Palo Alto) is thanked for providing substantial quantities of the diol (2). Generous financial support from the Institute of Advanced Studies and the Australian Research Council is warmly acknowledged. Professors S. V. Ley (University of Cambridge) and W.-S. Zhou (Shanghai Institute of Organic Chemistry) are thanked for providing spectral data derived from synthetic samples of compounds (1) and (22). Technical assistance from Dr Eric Wenger (Research School of Chemistry) and Dr Carl Braybrook (CSIRO Molecular Science, Melbourne) is gratefully acknowledged.

References

[1] S. K. Talapatra, D. Basu, T. Deb, S. Goswami, B. Talapatra, *Indian J. Chem., Sect. B* **1985**, *24*, 29.
[2] X.-P. Fang, J. E. Anderson, C.-J. Chang, J. L. McLaughlin, *J. Nat. Prod*. **1991**, *54*, 1034.
[3] G. C. L. Ee, H. L. Lee, S. H. Goh, *Nat. Prod. Lett*. **1999**, *13*, 137.
[4] J.-P. Surivet, J.-M. Vatele, *Tetrahedron* **1999**, *55*, 13 011.
[5] (*a*) M. Tsubuki, K. Kanai, T. Honda, *J. Chem. Soc., Chem. Commun.* **1992**, 1640. (*b*) M. Tsubuki, K. Kanai, H. Nagase, T. Honda, *Tetrahedron* **1999**, *55*, 2493.
[6] (*a*) Z.-C. Yang, W.-S. Zhou, *J. Chem. Soc., Chem. Commun*. **1995**, 743. (*b*) Z.-C. Yang, W.-S. Zhou, *Heterocycles* **1997**, *45*, 367.
[7] (*a*) J.-P. Surivet, J. Goré, J.-M. Vatele, *Tetrahedron Lett*. **1996**, *37*, 371. (*b*) J.-P. Surivet, J. Goré, J.-M. Vatele, *Tetrahedron* **1996**, *52*, 14 877.
[8] J.-P. Surivet, J.-N. Volle, J.-M. Vatele, *Tetrahedron: Asymmetry* **1996**, *7*, 3305.
[9] J.-P. Surivet, J.-M. Vatele, *Tetrahedron Lett*. **1998**, *39*, 7299.
[10] C. Muka, S. Hirai, M. Hanaoka, *J. Org. Chem*. **1997**, *62*, 6619.
[11] D. J. Dixon, S. V. Ley, E. W. Tate, *J. Chem. Soc., Perkin Trans. 1* **1998**, 3125.
[12] J. Chen, G.-Q. Lin, Z.-M. Wang, H.-Q. Liu, *Synlett* **2002**, 1265.
[13] P. V. Ramachandran, J. S. Chandra, M. V. R. Reddy, *J. Org. Chem*. **2002**, *67*, 7547.
[14] For an excellent review on the production and general synthetic utility of these types of compounds see T. Hudlicky, D. Gonzalez, D. T. Gibson, *Aldrichimica Acta* **1999**, *32*, 35.
[15] M. G. Banwell, A. J. Edwards, G. J. Harfoot, K. A. Jolliffe, M. D. McLeod, K. J. McRae, S. G. Stewart, M. Vögtle, *Pure Appl. Chem*. **2003**, *75*, 219.
[16] M. G. Banwell, V. S. Bridges, J. R. Dupuche, S. L. Richards, J. M. Walter, *J. Org. Chem*. **1994**, *59*, 6338.
[17] V. VanRheenen, R. C. Kelly, D. Y. Cha, *Tetrahedron Lett*. **1976**, 1973.
[18] K. J. Henry, P. A. Grieco, C. T. Jagoe, *Tetrahedron Lett*. **1992**, *33*, 1817.
[19] G. M. Whited, J. C. Downie, T. Hudlicky, S. P. Fearnley, T. C. Dudding, H. F. Olivo, D. Parker, *Bioorg. Med. Chem*. **1994**, *2*, 727.
[20] M. A. Andrews, G. L. Gould, S. A. Klaeren, *J. Org. Chem*. **1989**, *54*, 5257.
[21] M. A. Aubart, L. H. Pignolet, 'Bis[1,3-bis(diphenylphosphino) propane]rhodium tetrafluoroborate', in *Encyclopedia of Reagents for Organic Synthesis* (Ed. L. A. Paquette) **1995** (John Wiley and Sons: Chichester).
[22] B. R. James, D. Mahajan, *Can. J. Chem*. **1980**, *58*, 996.
[23] J. A. McGinnety, N. C. Payne, J. A. Ibers, *J. Am. Chem. Soc*. **1969**, *91*, 6301.
[24] M. S. VanNieuwenhze, K. B. Sharpless, *Tetrahedron Lett*. **1994**, *35*, 843.
[25] D. Xu, K. B. Sharpless, *Tetrahedron Lett*. **1994**, *35*, 4685.
[26] W. P. Griffth, S. V. Ley, *Aldrichimica Acta* **1990**, *23*, 13.
[27] S. Florio, V. Capriati, 'Allylmagnesium Bromide', in *Encyclopedia of Reagents for Organic Synthesis* (Ed. L. A. Paquette) **1995** (John Wiley and Sons: Chichester).

[28] M. T. Reetz, K. Kesseler, A. Jung, *Tetrahedron Lett*. **1984**, *25*, 729.
[29] C. H. Heathcock, S. Kiyooka, T. A. Blumenkopf, *J. Org. Chem*. **1984**, *49*, 4214.
[30] H. C. Brown, K. S. Bhat, R. S. Randad, *J. Org. Chem*. **1989**, *54*, 1570.
[31] B. W. Gung, X. Xue, W. R. Roush, *J. Am. Chem. Soc*. **2002**, *124*, 10 692, and references therein.
[32] Y. Yamamoto, K. Maruyama, K. Matsumoto, *J. Chem. Soc., Chem. Commun*. **1983**, 489.
[33] M. Shimagaki, H. Takubo, T. Oishi, *Tetrahedron Lett*. **1985**, *26*, 6235.
[34] G. E. Keck, K. A. Savin, E. N. K. Cressman, D. E. Abbott, *J. Org. Chem*. **1994**, *59*, 7889.
[35] For a useful discussion of the allylation of related systems see M. Carda, E. Castillo, S. Rodriguez, F. Gonzalez, J. A. Marco, *Tetrahedron: Asymmetry* **2001**, *12*, 1417, and references therein.
[36] For useful reviews dealing with chelation-controlled processes see (*a*) A. Mengel, O. Reiser, *Chem. Rev*. **1999**, *99*, 1191. (*b*) M. T. Reetz, *Acc. Chem. Res*. **1993**, *26*, 462.
[37] D. Longbottom, *Synlett* **1999**, 2023.
[38] T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res*. **2001**, *34*, 18.
[39] (*a*) Y. Du, D. F. Wiemer, *Tetrahedron Lett*. **2001**, *42*, 6069, and references therein. (*b*) B. M. Trost, V. S. C. Yeh, *Org. Lett*. **2002**, *4*, 3513.
[40] Z. Otwinoski, W. Minor, *Methods Enzymol*. **1997**, *276*, 307.
[41] P. Coppens, in *Crystallographic Computing* (Eds F. R. Ahmed, S. R. Hall, C. P. Huber) **1970**, pp. 255–270 (Munksgaard: Copenhagen).
[42] A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori, R. Spagna, *J. Appl. Crystallogr*. **1999**, *32*, 115.
[43] D. J. Watkin, C. Prout, J. R. Carruthers, P. W. Betteridge, R. I. Cooper, *CRYSTALS Issue 11* **2001** (Chemical Crystallography Laboratory: Oxford).