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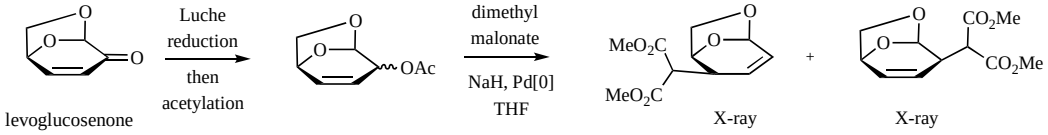
Graphical Abstract



levoglucosenone

X-ray

X-ray

Manipulating the Enone Moiety of Levoglucosenone:

1,3-Transposition Reactions Including Ones Leading to Isolevoglucosenone†

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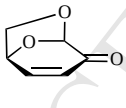
The manipulation of the enone moiety associated with the biomass-derived, homochiral and now abundant compound levoglucosenone (**1**) is described. While the trichloroacetimidates derived from the allylic alcohols **3** and **4** failed to engage in Overman-type rearrangements, certain ester derivatives reacted in the presence of Pd[0]-catalysts to give regio-isomeric mixtures of β,γ-unsaturated malonates or ketones, the structures of which were confirmed by single-crystal X-ray analyses. In other sequences involving 1,3-transposition reactions, an operationally simple means for converting compound **1** into isolevoglucosenone (**2**) is described.



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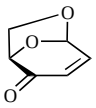

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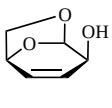

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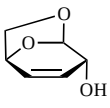

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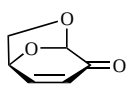
† Dedicated to the memory of Professor Sir Derek Barton and in recognition of his seminal contributions to so many aspects of organic chemistry.

INTRODUCTION

Levoglucosenone (**1**) can be generated through the acid-catalysed depolymerisation of cellulose and recent refinements of this process have allowed for the production of this homochiral material on the tonne scale from various forms of biomass including waste paper and sawdust.[1] As testimony to the scale and utility of this process, the ketone, Cyrene™, arising from the hydrogenation of the carbon-carbon double bond within compound **1**, is now being employed in a number of countries as a replacement for the soon-to-be banned polar aprotic solvent *N*-methylpyrrolidinone (NMP).[2] Given both the sustainable nature and the scale of its production, levoglucosenone is likely to become an increasingly important starting material in chemical synthesis, and all the more so if new means for manipulating it in useful ways can be developed.[3] The most obvious site for manipulation is the enone moiety and a range of methods for doing so has been reported in the literature,[1,4] including by us.[5] In particular, and like others,[3] we have sought to convert compound **1** into its quasi-enantiomer isolevoglucosenone (**2**). In our work[5] this was achieved using Wharton rearrangement chemistry and these studies prompted us to consider other means by which the required and related 1,3-transposition processes could be implemented within the 6,8-dioxabicyclo[3.2.1]octane framework associated with levoglucosenone. The work detailed in the following sections reveals new means for doing so.



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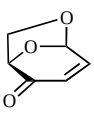

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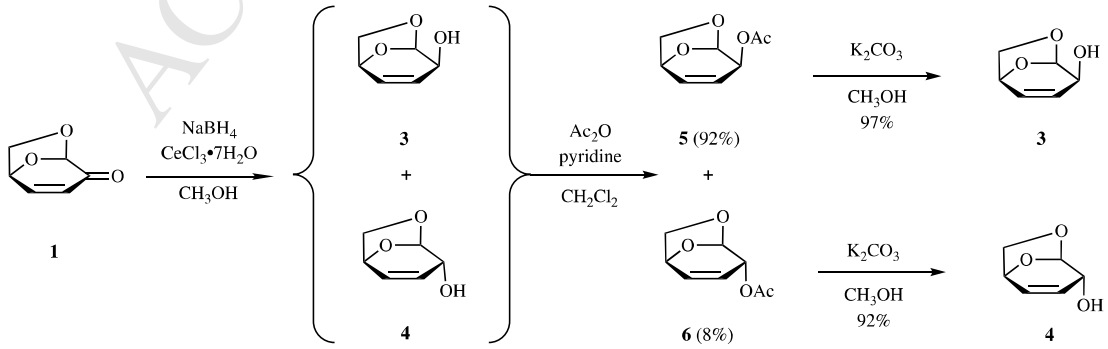
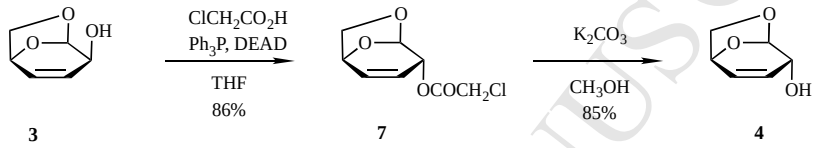
RESULTS AND DISCUSSION

The [3,3]-sigmatropic rearrangement of derivatives of the epimeric allylic alcohols arising from the 1,2-reduction of levoglucosenone became the focal point of our initial studies and efficient means for obtaining the first of these substrates are shown in Scheme 1. Specifically, then, enone **1** was subjected to 1,2-reduction in methanol at 0 °C using sodium borohydride in the presence of cerium trichloride and in this way a *ca*. 11:1 mixture of the anticipated and epimeric allylic alcohols **3** and **4** was obtained in 91% combined yield.[6] These could not be separated by conventional means and so the mixture was acetylated under standard conditions and the product esters **5**[6] (92%) and **6**[6] (8%) were each isolated in pure form using flash chromatographic techniques and then fully characterized. Each was treated with potassium carbonate in methanol and thus regenerating the corresponding and now epimerically pure allylic alcohols **3** (97%) and **4** (92%), respectively. The spectral data acquired on these were in agreement with those reported in the literature.[6] The preferential formation of epimer **3** in the initial reduction step is entirely consistent with previous observations and necessarily arises through selective delivery of hydride from the sterically less congested α-face of the enone moiety in substrate **1** (the corresponding β-face being shielded by the presence of the sterically demanding 1,6-anhydro-bridge).



Scheme 1

In order to secure workable quantities of the minor epimeric alcohol **4** for further study, the straightforward reaction sequence shown in Scheme 2 was developed. Specifically, then, the more abundant allylic alcohol **3** was subjected to a Mitsunobu reaction using triphenylphosphine/diethyl azodicarboxylate (DEAD) for activation and α-chloroacetic acid as the nucleophile.[6,7] By such means the inverted allylic α-chloroacetate **7** was obtained in 86% yield and when this was saponified using potassium carbonate in methanol then the target alcohol **4** was obtained in 85% yield.

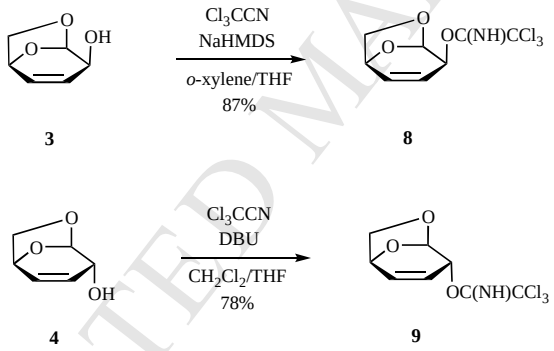


Scheme 2

The structures of all of the products of the reactions shown in Schemes 1 and 2 were confirmed by single-crystal X-ray analyses of derivatives of compounds **3** and **4**. Details of these analyses are presented below, including in the Experimental Section as well as in the Supplementary Information.

With allylic alcohols **3** and **4** now each available in useful quantities, an investigation into the participation of certain derivatives in [3,3]-sigmatropic rearrangement reactions began. Given our successes[8] in applying the Eschenmoser-Claisen rearrangement to various 2-cyclohexen-1-ols, each of compounds **3** and **4** was treated with *N*,*N*-dimethylacetamide dimethyl acetal in refluxing toluene but to no avail. Similarly, all attempts to effect Ireland-Claisen-type rearrangements[9] of acetates **5** and **6** under standard conditions also failed. In each instance either the relevant starting material (*viz*. **3**-**6**) was returned or, under more forcing conditions (involving higher

reaction temperatures), decomposition was observed. In an effort to engage allylic alcohols **3** and **4** in Overman rearrangement reactions,[10] an *o*-xylene/THF or dichloromethane/THF solution of each was treated (Scheme 3) with trichloroacetonitrile in the presence of either sodium hexamethyldisilazide (NaHMDS) or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and thereby affording the anticipated and crystalline trichloroacetimidates **8** (87%) and **9** (78%), respectively. The structure of each of products **8** and **9** was confirmed by single-crystal X-ray analysis, details of which are reported in the Experimental Section. Of course, these analyses also serve to confirm the structures of precursors **3** and **4** as well as the corresponding acetates.

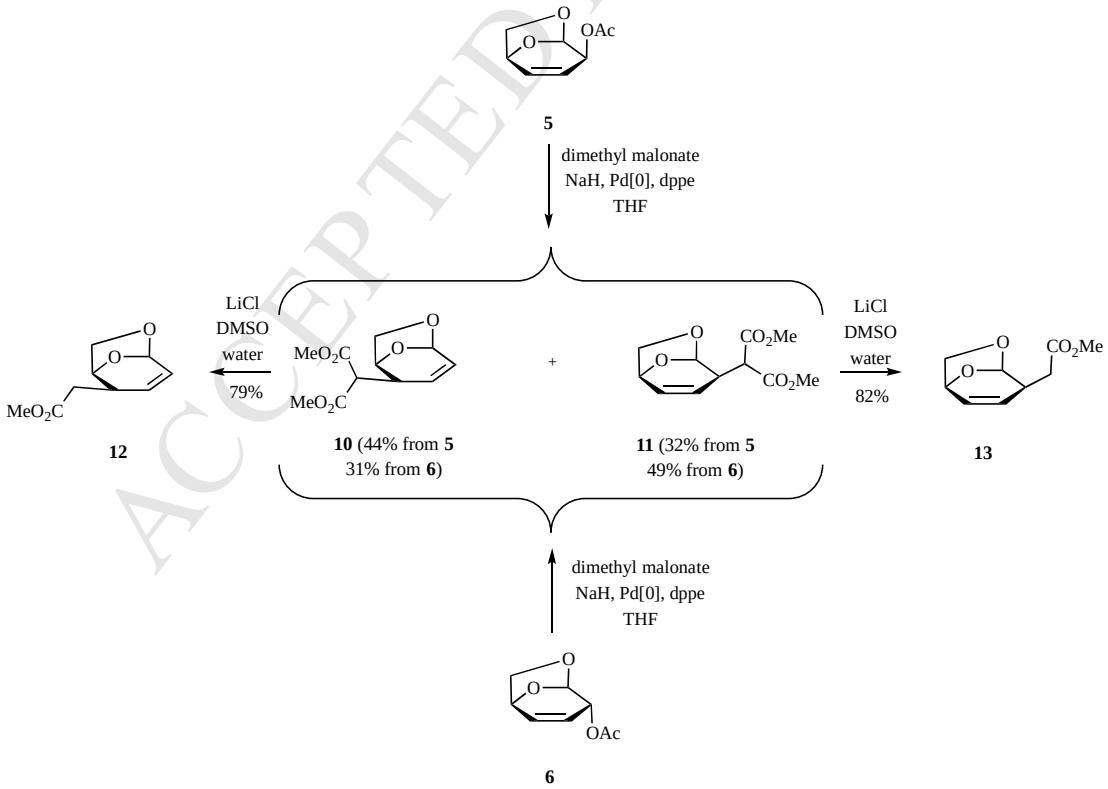


Scheme 3

Unfortunately, all attempts thus far to induce the Overman rearrangement of compounds **8** and **9** under a variety of conventional conditions failed. Once again, either the starting material was returned or, under more forcing conditions, decomposition was observed.

In light of our failures to effect [3,3]-sigmatropic rearrangements of compounds **3**-**6**, **8** and **9**, the Tsuji-Trost reactions of the allylic acetates were examined using $(Ph_3P)_4Pd$

as the catalyst, the sodium salt of dimethyl malonate as the nucleophile and 1,2-bis(diphenylphosphino)ethane (dppe) as an added ligand (Scheme 4)[11,12] – in the absence of dppe the illustrated transformations did not proceed very effectively at all. Under such conditions compound **5** reacted to give a chromatographically separable mixture of the regio-isomeric diesters **10** (44%) and **11** (32%), each of which was crystalline and the structures of which could, therefore, be confirmed by single-crystal X-ray analysis (see Experimental Section for details). Similar treatment of the epimeric allylic acetate **6** also gave a mixture of compounds **10** (31%) and **11** (49%). When reacted with LiCl in DMSO at 140 °C each of the product malonates was converted, *via* a demethylation/decarboxylation process (Krapcho decarboxylation),[13] into the corresponding methyl acetate derivatives, namely compounds **12** (79%) and **13** (82%).

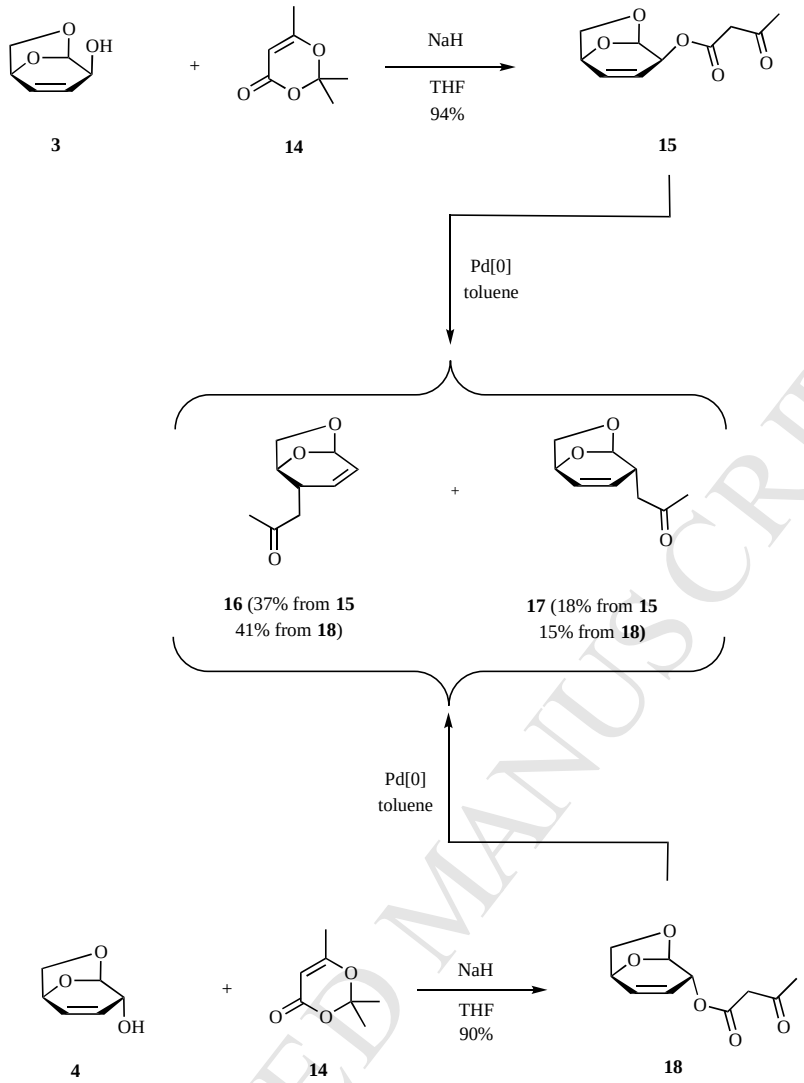


Scheme 4

The origins of the selectivities observed in the processes leading to malonates **10** and **11** remain to be established but the similarities of the outcomes are suggestive of the involvement of a common intermediate. This is most likely to be the π-allyl palladium complex in which the transition metal is co-ordinated to that face of the π-system opposite the 1,6-anhydro-bridge. The formation of this intermediate from precursor **5** would presumably follow a conventional (inversion) pathway but precisely how this same species is formed from epimer **6** is less obvious. It could be that interconversion of the two possible (π-allyl)palladium complexes is taking place or that *syn*-displacement of the acetate leaving group by Pd[0] is occurring.[14] Regardless, of the precise pathway involved, these results seem at odds with those of Matsumoto *et al* who reported[12] that the allylic and α-configured chloride corresponding to compound **6** reacts under essentially the same conditions to give a mixture of the epimeric forms of compounds **10** and **11**. Unfortunately, no spectral data were reported for Matsumoto's products and so relevant comparisons with our own (which are presented in the Experimental Section) cannot be made.

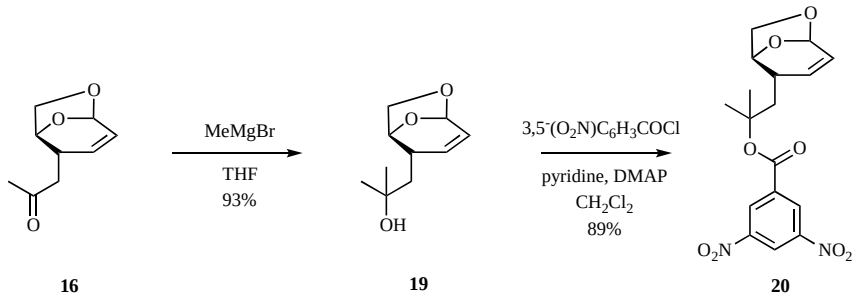
A stereo-complementary outcome to the one just described was observed when the palladium-catalysed Carroll-type rearrangement[15] was applied to the β-keto-esters derived from the epimeric alcohols **3** and **4** (Scheme 5). So, for example, treatment of the anion derived from alcohol **3** with readily available 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**14**)[16] afforded the β-keto-ester **15** (94%) that upon treatment with $(Ph_3P)_4Pd$ in refluxing toluene afforded a *ca*. 2:1 and chromatographically separable mixture of the regio-isomeric γ,δ-unsaturated methyl ketones **16** and **17** (55% combined yield). When the epimeric β-keto-ester **18**, readily obtained in 90% by treating the oxyanion derived from alcohol **4** with electrophile **14**, was exposed to $(Ph_3P)_4Pd$ in refluxing toluene then a *ca*. 3:1 mixture of compounds **16** and **17** was

obtained in 56% combined yield. Once again, the outcomes of this pair of reactions suggest the involvement of a common intermediate, probably the π-allyl palladium complex in which the metal is co-ordinated to that face of the π-system opposite the 1,6-anhydro-bridge and carrying, at the metal center, a carboxylate- or enolate-based ligand. This intermediate is presumably generated from substrate **15** in a conventional manner while its production from precursor **18** could involve pre-complexation of the palladium by the α-oriented and bidentate β-keto-ester residue. Regardless of the precise details of the Tsuji-Trost-type chemistries shown in Schemes 4 and 5, it seems that the intermediate π-allyl complexes invariably involve α-face selective co-ordination of the palladium.



Scheme 5

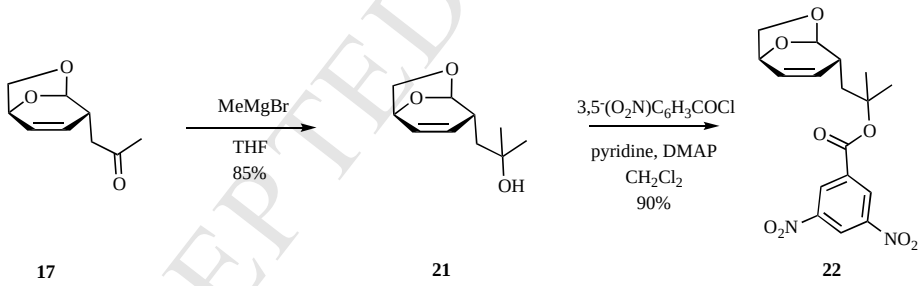
Given the pivotal nature of these conclusions, it was crucial to unambiguously establish the structure of each of products **16** and **17**. In the case of the former compound, this was done by the means outlined in Scheme 6. Specifically, compound **16** was treated with methylmagnesium bromide and the ensuing 3°-alcohol **19** (93%) then converted, under standard conditions, into the corresponding 3,5-dinitrobenzoate **20** (89%). This proved to be a crystalline compound and its structure could thus be determined by single-crystal X-ray analysis, details of which are provided in the Experimental Section.



16 **19** **20**

Scheme 6

In an analogous manner, ketone **17** was converted into the 3°-alcohol **21** (85%) (Scheme 7) on treatment with methylmagnesium bromide and this was, in turn, transformed into the corresponding 3,5-dinitrobenzoate **22** (90%) on exposure to 3,5-dinitrobenzoyl chloride in the presence of pyridine and DMAP. Compound **22** also proved to be a crystalline material and so its structure, too, was confirmed by single-crystal X-ray analysis.

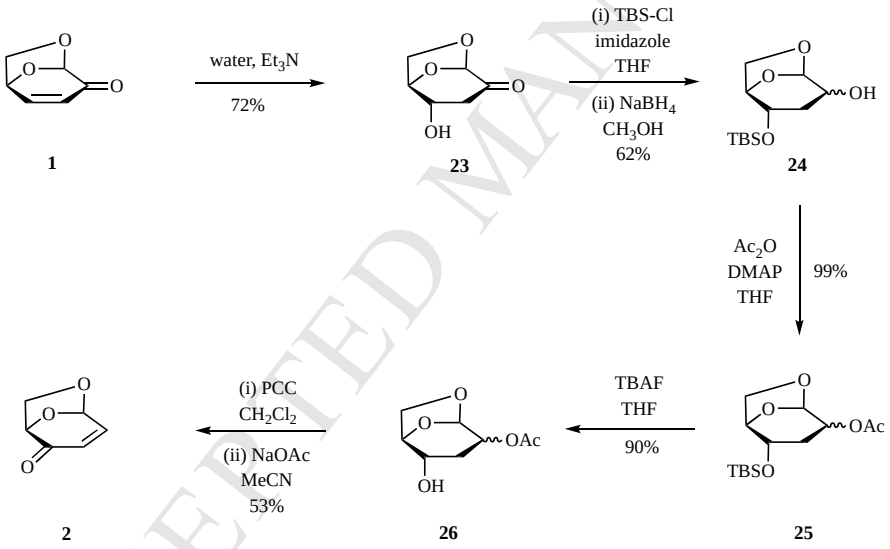


17 **21** **22**

Scheme 7

Another 1,3-transposition process, and one that allows for the ready formation of isolevoglucosenone (**2**) from congener **1**, is shown in Scheme 8. Thus, water readily adds to levoglucosenone (**1**) when it is dissolved in triethylamine and so forming the previously reported[17] β-hydroxyketone **23** (72%) that could be protected as the corresponding TBS-ether under conventional conditions. Reduction of this ether with

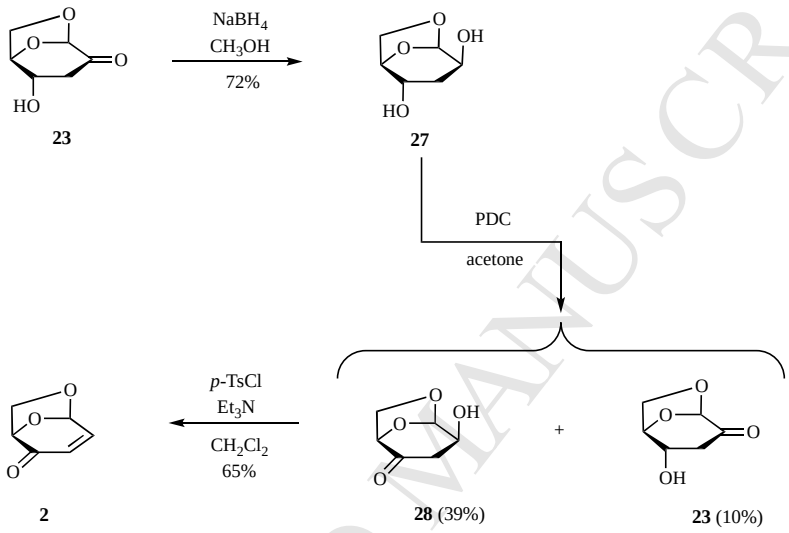
sodium borohydride in methanol then gave a *ca*. 4:3 mixture of the epimeric forms of alcohol **24** (62% combined yield), the structure of the α-configured one being confirmed by single crystal X-ray analysis. Acetylation of each of these alcohols using acetic anhydride in the presence of DMAP gave the corresponding and epimeric acetates **25** (99%). On exposure of these to tetra-*n*-butylammonium fluoride (TBAF) the anticipated epimeric forms of alcohol **26**[18] (90%) were obtained and when these were subjected to sequential treatment with pyridinium chlorochromate (PCC) and sodium acetate then isolevoglucosenone (**2**) was obtained in 53% yield. This material was identical, in all respects, to an authentic sample prepared by our earlier route.[5]



Scheme 8

Since the reaction sequence shown in Scheme 8 represents a rather minor variation on the route (from **1** → **2**) developed sometime ago by Furneaux and co-workers,[17] attempts were made to establish a more concise pathway to target **2**. To such ends, compound **23** (Scheme 9) was stereoselectively reduced to the *trans*-1,3-diol **27**[17] (70%) and on oxidation of this with a slight excess of pyridinium dichromate (PDC) a

chromatographically separable mixture of the mono-oxidation products **23** (10%) and **28**[19] (39%) was obtained. Treatment of the latter compound with *p*-toluenesulfonyl chloride (*p*-TsCl) and triethylamine in acetonitrile then gave, presumably *via* an E1cb elimination reaction involving the intermediate tosylate, isolevoglucosenone (**2**) in 65% yield.

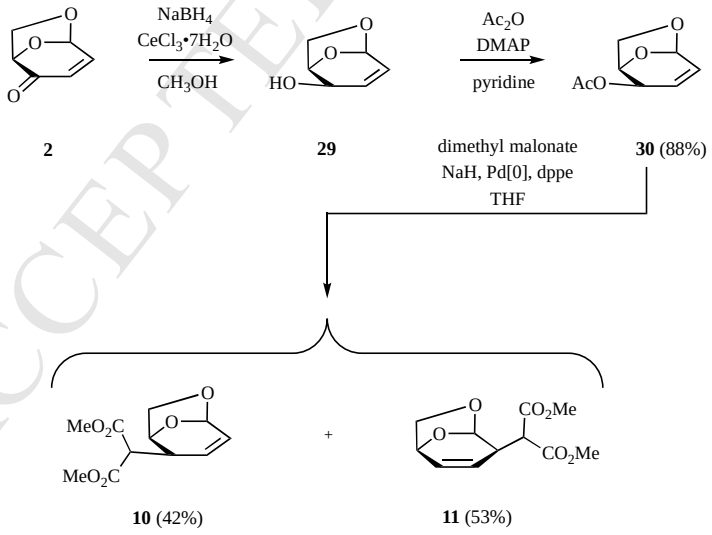


Scheme 9

In an effort to improve the efficiency of this three-step reaction sequence, various attempts were made to increase the selectivity and yield of the oxidation process leading to compound **28** but, thus far, to no avail. As such, the longer route (Scheme 8) remains the slightly higher yielding one (21% vs 18%) despite the additional steps involved. That said, further refinements of the shorter pathway seem warranted and are now being investigated. The outcomes of our efforts in this area will be reported in due course.

The ready acquisition of isolevolglucosenone by the route detailed immediately above allowed for a further exploration of the Tsuji-Trost chemistry of these systems. In

particular, and as shown in Scheme 10, compound **2** could be reduced in a completely stereoselective manner under Luche-type conditions to give the known allylic alcohol **29**. The illustrated β-configuration at the newly established stereogenic center is assigned on the basis that the steric demands of the 1,6-anhydrobridge in substrate **2** should direct hydride deliver to the α-face of the enone moiety. Acetylation of compound **29** was effected under standard conditions and the resulting and previously reported ester **30** (88% over two steps) was then subjected to reaction with the sodium salt of dimethyl malonate in the presence of $(Ph_3P)_4Pd$ and dppe to afford a mixture of the regio-isomeric di-esters **10** (42%) and **11** (53%). Thus, a similar product distribution is seen here as was observed when the regio-isomeric allylic acetate **5** (Scheme 4) was subjected to these same Tsuji-Trost reaction conditions. Of course, such outcomes suggest that both reactions are proceeding, as would be expected, through a common π-allyl palladium complex.



Scheme 10

CONCLUSIONS

We have described a series of palladium-catalysed and stereocontrolled (but non-regio-selective) 1,3-transpostion reactions of various esters of the alcohols **3** and **4** derived from levoglucosenone (**1**). In each case a π-allyl palladium complex wherein the transition metal is co-ordinated to the less hindered α-face of the bicyclic framework is likely to be involved. While the [3,3]-sigmatropic rearrangement of various derivatives of compounds **3** and **4** could not be implemented, the facile conjugate addition of water to enone **1** allowed for the development of simple synthetic routes to its quasi-enantiomer isolevoglucosenone (**2**) and a capacity, therefore, to study the chemistry of this less-explored isomer.

Taken together, the processes described above add to the repertoire of chemical transformations that can be applied to levoglucosenone (**1**), a homochiral and increasingly readily available building block that can be produced in a sustainable fashion and that is, therefore, likely to continue to assume increasing importance as a starting material in chemical synthesis.

EXPERIMENTAL SECTION

General Experimental Procedures

Unless otherwise specified, proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded at 18 °C in base-filtered $CDCl_3$ on a spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei. ^{1}H NMR data are recorded as follows: chemical shift (δ) [multiplicity, coupling constant(s) *J* (Hz), relative integral] where multiplicity is defined as s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet or combinations of the above. In relevant cases, the signal due to residual $CHCl_3$

appearing at δ_H 7.26 and the central resonance of the $CDCl_3$ "triplet" appearing at δ_C 77.0 were used to reference ^1H and ^{13}C NMR spectra, respectively. Samples were analyzed by infrared spectroscopy (ν_{max}) as thin films on KBr plates. Optical rotations were recorded using the sodium D-line (589 nm) in a cell with a path length of 1 dm, at the concentrations indicated and in the specified solvent at 22 °C. Specific rotations were then calculated in the usual manner. Low- and high-resolution electron impact (EI) mass spectra were recorded on a double focusing, triple sector machine. Low- and high-resolution ESI mass spectra were recorded on a triple-quadrupole mass spectrometer operating in positive ion mode. Melting points are uncorrected. Analytical thin layer chromatography (TLC) was performed on aluminum-backed 0.2 mm thick silica gel 60 F_{254} plates. Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating. These dips included phosphomolybdic acid/ceric sulfate/sulfuric acid (conc.)/water (37.5 g : 7.5 g : 37.5 g : 720 mL), potassium permanganate/potassium carbonate/5% sodium hydroxide aqueous solution/water (3 g : 20 g : 5 mL : 300 mL), and *p*-anisaldehyde or vanillin/sulfuric acid (conc.)/ethanol (15 g : 2.5 mL : 250 mL). Flash chromatographic separations were carried out following protocols defined by Still *et al*.[20] with silica gel 60 (40-63 μm) as the stationary phase and using the AR- or HPLC-grade solvents indicated. The melting points of solids purified by such means were recorded directly (ie after they had crystallized from the concentrated chromatographic fractions). Starting materials, reagents, drying agents, and other inorganic salts were generally commercially available and were used as supplied. Tetrahydrofuran (THF), methanol and dichloromethane were dried using a solvent purification system that is based upon a technology originally described by Grubbs *et al*.[21] Where necessary, reactions were performed under a nitrogen atmosphere.

Specific Chemical Transformations

Compounds 5 and 6. *Step i*: A magnetically stirred solution of compound **1** (1.00 g, 7.93 mmol) in methanol (25 mL) maintained at 0 °C was treated with $CeCl_3 \bullet 7H_2O$ (3.00 g, 8.05 mmol) then, in portions, with $NaBH_4$ (300 mg, 7.93 mmol). The ensuing mixture was stirred at 0 °C for 1 h before being concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 2:1 v/v ethyl acetate/hexane elution) to give, after concentration of the appropriate fractions (R_f = 0.5 in 5:4:1 v/v/v ethyl acetate/hexane/methanol), an inseparable mixture of compounds **3** and **4** (922 mg, 91%) as a white, crystalline solid.

Step ii: A magnetically stirred solution of compounds **3** and **4** (658 mg, 5.14 mmol) in pyridine (10 mL) was treated with acetic anhydride (2.00 mL, 21.16 mmol) then DMAP (14 mg, 0.11 mmol). After stirring the ensuing mixture at 22 °C for 2 h, the reaction mixture was concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica, gradient elution from 1:25 → 1:4 v/v ethyl acetate/petroleum benzene elution) to deliver two fractions, A and B.

Concentration of fraction A (R_f = 0.3 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane /hexane) gave compound **5** (802 mg, 92%) as a clear, colorless oil, $[\alpha]_D$ = −38 (*c* = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (m, 1H), 5.58 (m, 2H), 5.51 (m, 1H), 4.69 (t, *J* = 4.2 Hz, 1H), 3.98 (d, *J* = 6.6 Hz, 1H), 3.80 (m, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8 (C), 132.6 (CH), 124.9 (CH), 99.3 (CH), 71.8 (CH), 71.6 (CH_2), 71.5 (CH), 21.2 (CH_3); IR ν_{max} 2963, 2891, 1729, 1371, 1230, 1124, 1038, 981, 883, 802 cm^{-1}; MS (ESI, +ve) *m/z* 193 [$(M+Na)^+$, 100%]; HRMS $(M+H)^+$ calcd for $C_8H_{11}O_4$ 171.0652, found 171.0649.

Concentration of fraction B (R_f = 0.4 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane /hexane) gave compound **6** (70 mg, 8%) as a clear, colorless oil, $[\alpha]_D$ = −265 (*c* = 0.1,

$CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (ddd, *J* = 9.8, 4.7 and 1.5 Hz, 1H), 5.74 (m, 1H), 5.53 (t, *J* = 1.5 Hz, 1H), 4.76 (m, 2H), 3.71 (m, 2H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2 (C), 132.7 (CH), 122.9 (CH), 100.4 (CH), 70.5 (CH), 69.3 (CH_2), 66.5 (CH), 21.1 (CH_3); IR ν_{max} 3051, 2965, 2894, 1735, 1475, 1372, 1235, 1126, 1023, 885, 867, 800, 712 cm^{-1}; MS (ESI, +ve) *m/z* 193 [$(M+Na)^+$, 100%]; HRMS $(M+Na)^+$ calcd for $C_8H_{10}O_4Na$ 193.0477, found 193.0476.

Compound 3. A magnetically stirred solution of compound **5** (343 mg, 2.016 mmol) in methanol (5 mL) maintained at 22 °C was treated with K_2CO_3 (557 mg, 4.03 mmol). The resulting mixture was stirred for 2 h then concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica, 1.5:1 v/v ethyl acetate/petroleum spirit elution) to afford, after concentration of the appropriate fractions (R_f = 0.5 in 5:4:1 v/v/v ethyl acetate/hexane/methanol), compound **3** (249 mg, 97%) as a white, crystalline solid, m.p. = 58-60 °C, $[\alpha]_D$ = +190 (*c* = 0.2, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (m, 1H), 5.85 (m, 1H), 5.52 (m, 1H), 4.67 (m, 1H), 3.95 (m, 1H), 3.65 (m, 1H), 3.47 (m, 1H), 2.32 (broad s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.3 (CH), 126.4 (CH), 95.7 (CH), 77.0 (CH), 67.3 (CH), 62.7 (CH_2); IR ν_{max} 3401, 2976, 2891, 1385, 1170, 1096, 1053, 1010, 897, 709 cm^{-1}; MS (ESI, +ve) *m/z* 151 [$(M+Na)^+$, 100%], 129 [$(M+H)^+$, <1]; HRMS $(M+H)^+$ calcd for $C_6H_9O_3$ 129.0546, found 129.0544.

Compound 7. A magnetically stirred a solution of compound **3** (180 mg, 1.41 mmol) in THF (20 mL) maintained at 22 °C was treated with α-chloroacetic acid (266 mg, 2.82 mmol), triphenylphosphine (737 mg, 2.81 mmol) then diethyl azodicarboxylate (440 μL, 2.79 mmol). The ensuing mixture was stirred at 22 °C for 18 h then concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 2:25 v/v ethyl acetate/petroleum ether elution) afforded, after

concentration of the appropriate fractions (R_f = 0.4 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **7** (246 mg, 86%) as a white, crystalline solid, m.p. = 61-63 °C, $[\alpha]_D$ = −214 (*c* = 0.2, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (ddd, *J* = 9.9, 4.7 and 1.1 Hz, 1H), 5.79 (ddd, *J* = 9.9, 3.9 and 2.0 Hz, 1H), 5.55 (m, 1H), 4.81 (m, 1H), 4.77 (m, 1H), 4.10 (d, *J* = 0.9 Hz, 2H), 3.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6 (C), 133.4 (CH), 122.0 (CH), 100.0 (CH), 70.5 (CH), 69.2 (CH_2), 67.9 (CH), 40.9 (CH_2); IR ν_{max} 2961, 2895, 1758, 1326, 1295, 1260, 1169, 1126, 1020, 1000, 969, 911, 892, 804 cm^{-1}; MS (ESI, +ve) *m/z* 229 and 227 [$(M+Na)^+$, 30 and 100%]; HRMS $(M+Na)^+$ calcd for $C_8H_9{}^{35}ClO_4Na$ 227.0087, found 227.0086.

Compound 4 (from compound **6**). A magnetically stirred solution of compound **6** (70 mg, 0.41 mmol) in methanol (2.0 mL) maintained at 22 °C was treated with K_2CO_3 (170 mg, 1.22 mmol). The resulting mixture was stirred for 2 h then concentrated under reduced pressure. Subjection of the residue thus obtained to flash chromatography (silica, 1.5:1 v/v ethyl acetate/petroleum ether elution) afforded, after concentration of the appropriate fractions (R_f = 0.5 in 5:4:1 v/v/v ethyl acetate/hexane/methanol), compound **4** (49 mg, 92%) as a white, crystalline solid, m.p. = 57-59 °C, $[\alpha]_D$ = −242 (*c* = 0.2, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.18 (ddd, *J* = 9.8, 4.7 and 1.0 Hz, 1H), 5.81 (ddd, *J* = 9.8, 4.0 and 2.0 Hz, 1H), 5.52 (m, 1H), 4.68 (m, 1H), 3.68 (m, 2H), 3.63 (d, *J* = 3.9 Hz, 1H), 1.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.0 (CH), 126.6 (CH), 102.8 (CH), 70.8 (CH), 69.1 (CH_2), 66.0 (CH); IR ν_{max} 3400, 2959, 2892, 1403, 1123, 1052, 1029, 921, 892, 862, 851, 796, 727 cm^{-1}; MS (ESI, +ve) *m/z* 151 [$(M+Na)^+$, 100%], 129 [$(M+H)^+$, <1]; HRMS $(M+H)^+$ calcd for $C_6H_9O_3$ 129.0546, found 129.0544.

Compound 4 (from compound **7**). Following a procedure similar to that described immediately above, ester **7** (355 mg, 1.74 mmol) was converted into alcohol **4** (189 mg, 85%). This product was identical, in all respects, with an authentic sample.

Compound 8. A magnetically stirred solution of compound **3** (500 mg, 3.90 mmol) and trichloroacetontrile (470 μL, 4.69 mmol) in *o*-xylene (30 mL) maintained under a nitrogen atmosphere at 0 °C was treated with NaHMDS (780 μL of a 1.0 M solution in THF, 0.78 mmol). The ensuing mixture was stirred at 0 °C for 1 h then warmed to 22 °C before being concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:1 v/v diethyl ether/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4 in 1:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **8** (929 mg, 87%) as a white, crystalline solid, m.p. = 88-90 °C, $[\alpha]_D$ = −29 (*c* = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 6.26 (m, 1H), 5.86 (m, 1H), 5.77 (dt, *J* = 9.9 and 2.2 Hz, 1H), 5.65 (m, 1H), 4.71 (t, *J* = 4.2 Hz, 1H), 4.02 (d, *J* = 6.6 Hz, 1H), 3.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (C), 133.1 (CH), 124.3 (CH), 98.6 (CH), 76.1 (CH), 71.6 (CH_2), 71.5 (CH) (signal due to one carbon obscured/overlapping); IR ν_{max} 3341, 2981, 2891, 1664, 1358, 1334, 1275, 1124, 1077, 1032, 796 cm^{-1}; MS (EI, 70 eV) *m/z* 275, 273 and 271 ($M^{+\bullet}$, 1, 3 and 3%), 240, 238 and 236 (12, 48 and 75), 208 (59), 206 (45), 119 (95), 117 (100), 97 (37); HRMS $M^{+\bullet}$ calcd for $C_8H_8{}^{35}Cl_3NO_3$ 270.9570, found 270.9562.

Compound 9. DBU (82 μL, 0.55 mmol) was added to a magnetically stirred solution of compound **4** (351 mg, 2.74 mmol) and trichloroacetontrile (330 μL, 3.29 mmol) in dichloromethane (25 mL) maintained under a nitrogen atmosphere at 0 °C. The ensuing solution was stirred at 0 °C for 0.5 h then warmed to 22 °C before being concentrated under reduced pressure. The residue thus obtained was subjected to flash

chromatography (silica, 1:1 v/v diethyl ether/hexane elution) to afford, after concentration of the appropriate fractions (R_f = 0.4 in 1:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **9** (557 mg, 78%) as a white, crystalline solid, m.p. = 89-91 °C, $[\alpha]_D$ = −146 (*c* = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (broad s, 1H), 6.39 (m, 1H), 5.93 (ddd, *J* = 9.8, 3.8 and 1.9 Hz, 1H), 5.70 (m, 1H), 4.90 (m, 1H), 4.80 (m, 1H), 3.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9 (C), 133.3 (CH), 122.1 (CH), 99.7 (CH), 70.6 (CH), 70.4 (CH), 69.1 (CH_2) (signal due to one carbon obscured/overlapping); IR ν_{max} 3339, 2964, 2894, 1662, 1352, 1329, 1272, 1126, 1060, 1020, 997, 871, 831, 792, 645 cm^{-1}; MS (EI, 70 eV) *m/z* 275, 273 and 271 ($M^{+\bullet}$, 0.5, 1 and 1%), 240, 238 and 236 (9, 29 and 45), 208 (60), 206 (65), 119 (95), 117 (100), 97 (34); HRMS $M^{+\bullet}$ calcd for $C_8H_8{}^{35}Cl_3NO_3$ 270.9570, found 270.9567.

Compounds 10 and 11 (from compound **5**). Sodium hydride (76 mg of a 60% dispersion in mineral oil, 1.90 mmol) was added, in portions, to a magnetically stirred solution of dimethyl malonate (225 μL, 1.97 mmol) in THF (18 mL) maintained under a nitrogen atmosphere at 0 °C. The ensuing mixture was stirred for 1 h at 0 °C then added to a magnetically stirred solution of compound **5** (104 mg, 0.61 mmol), $Pd(Ph_3P)_4$ (35 mg, 0.03 mmol) and ethylenebis(diphenylphosphine) (24 mg, 0.06 mmol) in THF (7 mL) maintained under a nitrogen atmosphere at 22 °C. The ensuing mixture was heated under reflux for 18 h then cooled and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:20 → 1:10 v/v ethyl acetate/hexane gradient elution) and so affording two fractions, A and B.

Concentration of fraction A (R_f = 0.4 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) gave compound **10** (66 mg, 44%) as a white,

crystalline solid, m.p. = 84-86 °C, $[\alpha]_D$ = +18 (*c* = 0.5, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 5.90 (m, 1H), 5.55 (d, *J* = 9.8 Hz, 1H), 5.50 (m, 1H), 4.56 (broad s, 1H), 3.88 (m, 2H), 3.79 (s, 3H), 3.77 (s, 3H), 3.65 (m, 1H), 3.30 (d, *J* = 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9 (C), 167.8 (C), 128.5 (CH), 126.5 (CH), 96.0 (CH), 73.9 (CH), 63.8 (CH_2), 53.1 (CH_3), 53.0 (CH_3), 51.8 (CH), 40.7 (CH); IR ν_{max} 2956, 2898, 1752, 1735, 1436, 1256, 1152, 1126, 1072, 1036, 981, 906, 712 cm^{-1}; MS (EI, 70 eV) *m/z* 242 ($M^{+\bullet}$, 8%), 211 (30), 183 (30), 178 (31), 150 (27), 132 (50), 111 (57), 81 (100), 59 (43); HRMS $M^{+\bullet}$ calcd for $C_{11}H_{14}O_6$ 242.0790, found 242.0790.

Concentration of fraction B (R_f = 0.4 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) gave compound **11** (48 mg, 32%) as a white, crystalline solid, m.p. = 36-38 °C, $[\alpha]_D$ = −7 (*c* = 0.5, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 6.11 (m, 1H), 5.69 (s, 1H), 5.50 (m, 1H), 4.63 (m, 1H), 3.89 (d, *J* = 6.5 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.71 (m, 1H), 3.53 (d, *J* = 10.5 Hz, 1H), 3.31 (broadened d, *J* = 10.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7 (C), 168.2 (C), 130.6 (CH), 125.7 (CH), 101.4 (CH), 73.0 (CH_2), 70.8 (CH), 52.9 (CH_3), 52.8 (CH_3), 52.1 (CH), 43.0 (CH); IR ν_{max} 2955, 2890, 1751, 1735, 1436, 1261, 1151, 1122, 1072, 1053, 1019, 988, 885 cm^{-1}; MS (EI, 70 eV) *m/z* 242 ($M^{+\bullet}$, 1%), 211 (56), 153 (47), 137 (72), 132 (80), 81 (100), 79 (60), 59 (58); HRMS $M^{+\bullet}$ calcd for $C_{11}H_{14}O_6$ 242.0790, found 242.0786.

Compounds 10 and 11 (from compound **6**). Following the same procedure as described immediately above, compound **6** (104 mg, 0.61 mmol) was converted into a mixture of compounds **10** (46 mg, 31%) and **11** (73 mg, 49%). Each of these products was identical with an authentic sample.

Compound 12. A magnetically stirred solution of compound **10** (62 mg, 0.26 mmol) in DMSO (7 mL) was treated with LiCl (54 mg, 1.27 mmol) and water (5 drops). The

resulting mixture was heated at 140 °C for 2 h then cooled to 22 °C and subjected to flash chromatography (silica, 2:5 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions (R_f = 0.3 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) afforded compound **12** (37 mg, 79%) as a clear, colorless oil, $[\alpha]_D$ = −35 (*c* = 1.0, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (m, 1H), 5.58 (m, 1H), 5.49 (m, 1H), 4.58 (m, 1H), 3.85 (m, 2H), 3.70 (s, 3H), 3.37 (m, 1H), 2.36 (m, 1H), 2.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8 (C), 128.8 (CH), 127.5 (CH), 96.0 (CH), 75.0 (CH), 63.3 (CH_2), 52.0 (CH_3), 37.6 (CH), 34.2 (CH_2); IR ν_{max} 2956, 2899, 1735, 1436, 1262, 1198, 1168, 1121, 1071, 1035, 969, 903 cm^{-1}; MS (EI, 70 eV) *m/z* 184 ($M^{+\bullet}$, 4%), 153 (19), 124 (24), 95 (21), 81 (61), 32 (100); HRMS $M^{+\bullet}$ calcd for $C_9H_{12}O_4$ 184.0736, found 184.0741.

Compound 13. A magnetically stirred solution of compound **11** (110 mg, 0.45 mmol) in DMSO (7 mL) was treated with LiCl (96 mg, 2.26 mmol) then water (6 drops). The resulting mixture was heated at 140 °C for 18 h then cooled to 22 °C and subjected to flash chromatography (silica, 2:5 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions (R_f = 0.3 in 2:2.5:5.5 v/v/v ethyl acetate/ dichloromethane/hexane) afforded compound **13** (69 mg, 82%) as a clear, colorless oil, $[\alpha]_D$ = −46 (*c* = 1.0, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (m, 1H), 5.59 (m, 1H), 5.53 (m, 1H), 4.62 (t, *J* = 4.4 Hz, 1H), 3.88 (d, *J* = 6.3 Hz, 1H), 3.72 (m, 1H), 3.70 (s, 3H), 3.02 (m, 1H), 2.53 (dd, *J* = 16.4 and 8.0 Hz, 1H), 2.34 (dd, *J* = 16.4 and 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6 (C), 129.2 (CH), 128.1 (CH), 102.0 (CH), 73.0 (CH_2), 70.8 (CH), 51.8 (CH_3), 39.8 (CH), 34.3 (CH_2); IR ν_{max} 2953, 2887, 1734, 1437, 1348, 1264, 1166, 1122, 1071, 1051, 1018, 985, 880, 802 cm^{-1}; MS (EI, 70 eV) *m/z* 184 ($M^{+\bullet}$, 3%), 153 (65), 124 (73), 96 (87), 81 (100), 79 (95), 59 (57); HRMS $M^{+\bullet}$ calcd for $C_9H_{12}O_4$ 184.0736, found 184.0730.

Compound 15. Sodium hydride (200 mg, 60% dispersion in mineral oil, 5.0 mmol) was cautiously added to a magnetically stirred solution compound **3** (325 mg, 2.54 mmol) and 2,2,6-trimethyl-1,3-dioxin-4-one (**14**)[16] (0.5 mL, 3.80 mmol) in THF (15 mL) maintained under a nitrogen atmosphere at 0 °C. After a further 1 h the reaction mixture was quenched with a small amount of ice then concentrated under reduced pressure. The residue thus formed was subjected to flash chromatography (silica, 1:2 v/v ethyl acetate/petroleum ether elution) to afford, after concentration of the appropriate fractions (R_f = 0.4 in 4:2.5:5.5 v/v/v ethyl acetate/ dichloromethane/hexane), compound **15** and *ca*. 10% of a mono-enolic tautomer (506 mg, 94%) as a clear, colorless oil, $[\alpha]_D = -27$ (*c* = 0.2, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ (major tautomer) 6.21 (m, 1H), 5.69 (m, 2H), 5.64 (m, 1H), 4.69 (t, *J* = 4.2 Hz, 1H), 3.95 (d, *J* = 6.6 Hz, 1H), 3.79 (m, 1H), 3.53 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major tautomer) 200.2 (C), 167.1 (C), 133.0 (CH), 124.4 (CH), 99.0 (CH), 71.6 (CH), 71.5(2) (CH_2), 71.4(6) (CH), 50.1 (CH_2), 30.3 (CH_3); IR ν_{max} 2965, 2894, 1742, 1715, 1647, 1411, 1359, 1261, 1149, 1124, 1038, 983, 884 cm^{-1}; MS (ESI, +ve) *m/z* 235 [$(M+Na)^+$, 100%]; HRMS [$(M+Na)^+$ calcd for $C_{10}H_{12}O_5Na$ 235.0582, found 235.0583.

Compounds 16 and 17 (from compound **15**). A magnetically stirred solution of compound **15** (177 mg, 0.83 mmol) in dry, degassed toluene (15 mL) maintained under nitrogen was treated with $(Ph_3P)_4Pd$ (96 mg, 0.08 mmol). The ensuing mixture was heated under reflux for 18 h then cooled to 22 °C and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:10 → 1:5 v/v ethyl acetate/hexane elution gradient elution) to deliver two fractions, A and B.

Concentration of fraction A (R_f = 0.4 in 4:2.5:5.5 v/v/v ethyl acetate/ dichloromethane/hexane) gave compound **16** (52 mg, 37%) as a clear, colorless oil, $[\alpha]_D$ = +157 (*c* = 0.2, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 (m, 1H), 5.62 (m, 1H), 5.44 (d, *J* = 3.3 Hz, 1H), 4.40 (m, 1H), 3.98 (m, 1H), 3.68 (m, 1H), 2.87 (dd, *J* = 18.4 and 8.9 Hz, 1H), 2.59 (dd, *J* = 18.4 and 4.9 Hz, 1H), 2.43 (m, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.1 (C), 128.5 (CH), 128.1 (CH), 96.1 (CH), 74.8 (CH), 67.5 (CH_2), 45.2 (CH_2), 37.8 (CH), 30.5 (CH_3); IR ν_{max} 2971, 2894, 1713, 1638, 1477, 1362, 1155, 977, 902 cm^{-1}; MS (ESI, +ve) *m/z* 191 [$(M+Na)^+$, 100%]; HRMS [$(M+H)^+$ calcd for $C_9H_{13}O_3$ 169.0859, found 169.0856.

Concentration of fraction B (R_f = 0.5 in 2:2.5:5.5 v/v/v ethyl acetate/ dichloromethane/hexane) gave compound **17** (25 mg, 18%) as a clear, colorless oil, $[\alpha]_D$ = −206 (*c* = 0.2, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (m, 1H), 5.57 (m, 1H), 5.38 (broad s, 1H), 4.59 (t, *J* = 4.3 Hz, 1H), 3.92 (d, *J* = 6.3 Hz, 1H), 3.71 (m, 1H), 2.75-2.42 (complex m, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4 (C), 128.5 (CH), 127.9 (CH), 103.0 (CH), 72.7 (CH_2), 71.2 (CH), 45.3 (CH_2), 38.7 (CH), 30.4 (CH_3); IR ν_{max} 2956, 2887, 1714, 1638, 1408, 1359, 1247, 1120, 1019, 919, 870, 713 cm^{-1}; MS (ESI, +ve) *m/z* 191 [$(M+Na)^+$, 100%], 169 [$(M+H)^+$, <1]; HRMS [$(M+H)^+$ calcd for $C_9H_{13}O_3$ 169.0859, found 169.0855.

Compound 18. Sodium hydride (76 mg, 60% dispersion in mineral oil, 1.9 mmol) was added, with caution, to a magnetically stirred solution of compound **4** (122 mg, 0.95 mmol) and 2,2,6-trimethyl-1,3-dioxin-4-one (**14**)[16] (180 μL, 1.37 mmol) in THF (10 mL) maintained under a nitrogen atmosphere at 0 °C. After stirring for 1 h the reaction mixture was quenched with a small amount of ice then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:2 ethyl acetate/petroleum ether elution) to afford, after concentration of the

relevant fractions (R_f = 0.3 in 4:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane), compound **18** and *ca*. 15% of a mono-enolic tautomer (181 mg, 90%) as a clear, colorless oil, $[\alpha]_D$ = −261 (*c* = 0.2, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ (major tautomer) 6.33 (dd, *J* = 9.8 and 4.7 Hz, 1H), 5.78 (m, 1H), 5.55 (s, 1H), 4.82 (m, 1H), 4.75 (t, *J* = 4.4 Hz, 1H), 3.71 (m, 2H), 3.50 (s, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major tautomer) 200.2 (C), 166.3 (C), 133.1 (CH), 122.3 (CH), 100.1 (CH), 70.5 (CH), 69.2 (CH_2), 67.1 (CH), 50.0 (CH_2), 30.3 (CH_3); IR ν_{max} 2969, 2896, 1743, 1717, 1647, 1411, 1362, 1259, 1150, 1126, 1020, 871 cm^{-1}; MS (ESI, +ve) *m/z* 235 [$(M+Na)^+$, 100%]; HRMS [$(M+Na)^+$ calcd for $C_{10}H_{12}O_5Na$ 235.0582, found 235.0583.

Compounds 16 and 17 (from compound **18**). Following the same procedure as described above, compound **18** (34 mg, 0.16 mmol) was converted into a mixture of compounds **16** (11 mg, 41%) and **17** (4 mg, 15%). Each of these products was identical with an authentic sample.

Compound 19. A magnetically stirred solution of compound **16** (69 mg, 0.410 mmol) in THF (10 mL) maintained under a nitrogen atmosphere at 0 °C was treated methylmagnesium bromide (280 μL of a 3.0 M solution in THF, 0.84 mmol). After 0.5 h the reaction mixture was quenched with a small amount of ice then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 2:1 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions (R_f = 0.3 in 8:2.5:5.5 v/v/v ethyl acetate/dichloro-methane/hexane) gave compound **19** (71 mg, 93%) as a clear, colorless oil, $[\alpha]_D$ = +203 (*c* = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (m, 1H), 5.73 (m, 1H), 5.45 (d, *J* = 3.2 Hz, 1H), 4.68 (m, 1H), 3.97 (m, 1H), 3.64 (dd, *J* = 7.4 and 2.2 Hz, 1H), 2.13 (m, 1H), 1.94 (dd, *J* = 14.7 and 6.8 Hz, 1H), 1.62 (dd, *J* = 14.7 and 5.1 Hz,

1H), 1.41 (s, 1H), 1.28 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.7 (CH), 126.6 (CH), 96.0 (CH), 76.3 (CH), 71.2 (C), 67.6 (CH_2), 45.2 (CH_2), 39.7 (CH), 30.7 (CH_3), 29.9 (CH_3); IR ν_{max} 3447, 2959, 2895, 1638, 1472, 1380, 1171, 1141, 1107, 965, 903 cm^{-1}; MS (EI, 70 eV) *m/z* 184 ($M^{+\bullet}$, 5%), 169 (79), 109 (40), 95 (51), 81 (100), 59 (73), 43 (60); HRMS $M^{+\bullet}$ calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1104.

Compound 20. A magnetically stirred solution of compound **19** (70 mg, 0.38 mmol) in dichloromethane (20 mL) maintained under a nitrogen atmosphere at 0 °C was treated with pyridine (615 μL, 7.60 mmol), 3,5-dinitrobenzoyl chloride (175 mg, 0.76 mmol) and DMAP (95 mg, 0.78 mmol). The ensuing mixture warmed to 22 °C and stirred at this temperature for 18 h then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:5 v/v ethyl acetate/petroleum ether elution) and concentration of the appropriate fractions (R_f = 0.4 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) gave compound **20** (128 mg, 89%) as a white, crystalline solid, m.p. = 131-133 °C, $[\alpha]_D$ = +94 (*c* = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (t, *J* = 2.2 Hz, 1H), 9.10 (d, *J* = 2.2 Hz, 2H), 5.88 (m, 1H), 5.75 (m, 1H), 5.51 (d, *J* = 3.2 Hz, 1H), 4.52 (m, 1H), 4.00 (m, 1H), 3.65 (dd, *J* = 7.5 and 2.2 Hz, 1H), 2.30 (d, *J* = 6.6 Hz, 2H), 2.14 (m, 1H), 1.72 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (C), 148.8 (C), 135.5 (C), 129.4 (CH), 129.0 (CH), 127.3 (CH), 122.3 (CH), 96.2 (CH), 86.0 (C), 76.3 (CH), 67.3 (CH_2), 43.7 (CH_2), 39.1 (CH), 26.6 (CH_3), 26.2 (CH_3); IR ν_{max} 3101, 2980, 2895, 1725, 1628, 1544, 1344, 1292, 1266, 1172, 1126, 904, 730, 722 cm^{-1}; MS (ESI, +ve) *m/z* 401 [$(M+Na)^+$, 100%]; HRMS [$(M+Na)^+$ calcd for $C_{17}H_{18}N_2O_8Na$ 401.0955, found 401.0952.

Compound 21. A magnetically stirred solution of compound **17** (30 mg, 0.178 mmol) in THF (5 mL) maintained under a nitrogen atmosphere at 0 °C was treated with methylmagnesium bromide (120 μL of a 3.0 M solution in THF, 0.36 mmol). After stirring for 0.5 h the reaction mixture was quenched with a small amount of ice then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 2:1 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions (R_f = 0.3 in 8:2.5:5.5 v/v/v ethyl acetate/dichloro-methane/hexane) gave compound **21** (28 mg, 85%) as a clear, colorless oil, $[\alpha]_D$ = −192 (*c* = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (m, 1H), 5.68 (m, 1H), 5.60 (s, 1H), 4.58 (t, *J* = 4.3 Hz, 1H), 3.90 (d, *J* = 6.2 Hz, 1H), 3.71 (m, 1H), 2.24 (m, 1H), 1.73 (dd, *J* = 14.7 and 6.2 Hz, 1H), 1.49 (dd, *J* = 14.7 and 5.5 Hz, 1H), 1.41 (s, 1H), 1.26 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.1 (CH), 127.0 (CH), 104.4 (CH), 72.8 (CH_2), 71.1 (C), 71.0 (CH), 44.9 (CH_2), 40.3 (CH), 30.2 (CH_3), 30.0 (CH_3); IR ν_{max} 3448, 2969, 2885, 1638, 1471, 1364, 1115, 1018, 905, 874 cm^{-1}; MS (ESI, +ve) *m/z* 207 [$(M+Na)^+$, 100%]; HRMS [$(M+Na)^+$ calcd for $C_{10}H_{16}O_3Na$ 207.0997, found 207.0996.

Compound 22. A magnetically stirred solution of compound **21** (30 mg, 0.16 mmol) in dichloromethane (10 mL) maintained under a nitrogen atmosphere at 0 °C was treated with pyridine (265 μL, 3.28 mmol), 3,5-dinitrobenzoyl chloride (75 mg, 0.33 mmol) and DMAP (40 mg, 0.33 mmol). The resulting mixture was allowed to warm to 22 °C and stirred at this temperature for 18 h then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:5 v/v ethyl acetate/petroleum ether elution) and concentration of the appropriate fractions (R_f = 0.5 in 2:2.5:5.5 v/v/v ethyl acetate/dichloromethane/hexane) afforded compound **22** (56 mg, 90%) as a white, crystalline solid, m.p. = 162-165 °C, $[\alpha]_D$ =

−97 (*c* = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (t, *J* = 2.1 Hz, 1H), 9.10 (d, *J* = 2.1 Hz, 2H), 6.02 (m, 1H), 5.67 (m, 1H), 5.51 (d, *J* = 1.9 Hz, 1H), 4.65 (t, *J* = 4.3 Hz, 1H), 3.91 (d, *J* = 6.4 Hz, 1H), 3.73 (m, 1H), 2.26 (m, 1H), 2.20-2.05 (complex m, 2H), 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (C), 148.8 (C), 135.5 (C), 129.5 (CH), 128.7 (CH), 127.9 (CH), 122.3 (CH), 104.0 (CH), 86.1 (C), 72.8 (CH_2), 71.2 (CH), 43.0 (CH_2), 39.7 (CH), 26.6 (CH_3), 26.1 (CH_3); IR ν_{max} 3099, 2935, 2895, 1722, 1631, 1544, 1346, 1130, 1116, 1023, 921, 873, 723 cm^{-1}; MS (ESI, +ve) *m/z* 401 [$(M+Na)^+$, 100%]; HRMS [$(M+Na)^+$ calcd for $C_{17}H_{18}N_2O_8Na$ 401.0961, found 401.0952.

Compound 23. A magnetically stirred mixture of levoglucosenone (**1**) (3.78 g, 30.0 mmol) and water (300 mL) maintained at 22 °C was treated with triethylamine (3.0 ml, 2.37 mmol). After 1 h the reaction mixture was concentrated under reduced pressure and the ensuing residue subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/ petroleum ether elution). Concentration of the relevant fractions (R_f = 0.2) gave compound **23**[17] (3.11g, 72%) as a clear, yellow oil, $[\alpha]_D$ = –203.9 (*c* = 0.1, CH_3OH) {lit.[17] $[\alpha]_D$ = –143 (water) and –255 ($CHCl_3$)}: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07 (d, *J* = 1.2 Hz, 1H), 4.61 (dd, *J* = 5.0 and 2.2 Hz, 1H), 4.16 (d, *J* = 5.7 Hz, 1H), 4.04-3.74 (complex m, 2H), 3.37 (broad s, 1H), 2.83 (dd, *J* = 12.0 and 4.0 Hz, 1H), 2.46 (d, *J* = 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 101.3, 77.4, 70.3, 65.2, 40.8; IR ν_{max} 3446, 2971, 2912, 1734, 1114, 1008, 961, 907, 867 cm^{-1}; MS (ESI, +ve) *m/z* 199 [$(M+Na+MeOH)^+$, 100%] 167 [$(M+Na)^+$, 10]; HRMS [$(M+Na)^+$ calcd for $C_6H_8O_4Na$ 167.0315, found 167.0314.

TBS Ether of Compound 23. A magnetically stirred solution of compound **23** (432 mg, 3.00 mmol) and imidazole (408 mg, 6.00 mmol, 2 mole equiv.) in THF (30 mL) maintained under nitrogen at 22 °C was treated with TBS-Cl (904 mg, 6.00 mmol, 2

mole equiv.). The ensuing solution was heated under reflux for 24 h then cooled to 22 °C before being diluted with ethyl acetate (100 mL) then washed with $NaHCO_3$ (1 x 50 mL of a saturated aqueous solution), water (1 x 50 mL) and brine (1 x 50 mL). The separated organic layer was then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:20 v/v ethyl acetate/ petroleum ether elution) and concentration of the relevant fractions (R_f = 0.2) gave the title ether (563 mg, 73%) as a white, crystalline solid, m.p. = 55-58 °C, $[\alpha]_D$ = –163.6 (*c* = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (s, 1H), 4.53 (m, 1H), 4.22 (m, 1H), 4.05-3.74 (complex m, 2H), 2.79 (dd, *J* = 16.7 and 5.6 Hz, 1H), 2.35 (dm, *J* = 16.7 Hz, 1H), 0.90 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 101.3, 77.9, 71.0, 65.0, 41.1, 25.7, 18.1, –4.7, –4.8; IR ν_{max} 2956, 2931, 2901, 2858, 1740, 1257, 1119, 1086, 884, 839, 779 cm^{-1}; MS (ESI, +ve) *m/z* 313 [(M+Na+MeOH)$^+$, 100%] 281 [(M+Na)$^+$, 2]; HRMS [(M+Na)$^+$ calcd for $C_{12}H_{22}O_4SiNa$ 281.1180, found 281.1174.

Compound 24. A magnetically stirred solution of the above-mentioned TBS ether (720 mg, 2.78 mmol) in methanol (27 mL) maintained at 0 °C under a nitrogen atmosphere was treated, in portions, with $NaBH_4$ (105 mg, 2.78 mmol, 1 mole equiv.). The ensuing mixture was stirred at 0 °C for 0.5 h then warmed to 22 °C before being concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:5 v/v ethyl acetate/ petroleum ether elution) and so affording two fractions, A and B.

Concentration of fraction A (R_f = 0.4) gave the α-epimeric form of compound **24** (365 mg, 49%) as a white, crystalline solid, m.p. = 57-60 °C, $[\alpha]_D$ = –64.4 (*c* = 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (t, *J* = 1.9 Hz, 1H), 4.36 (m, 1H), 4.00-3.67 (complex m, 3H), 3.52 (m, 1H), 3.09 (d, *J* = 12.0 Hz, 1H), 2.02 (m, 1H), 1.74 (m,

1H), 0.93 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 102.4, 77.3, 68.2, 67.5, 65.4, 31.1, 25.7, 18.0, –4.8(9), –4.9(4); IR ν_{max} 3547, 2955, 2931, 2895, 2858, 1257, 1136, 1091, 1017, 921, 877, 838, 778 cm^{-1}; MS (ESI, +ve) *m/z* 283 [$(M+Na)^+$, 100%]; HRMS [$(M+Na)^+$ calcd for $C_{12}H_{24}O_4SiNa$ 283.1336, found 283.1330.

Concentration of fraction B (R_f = 0.2) gave the β-epimeric form of compound **24** (272 mg, 36%) as a white, crystalline solid, m.p. = 77-79 °C, $[\alpha]_D$ = –99.1 (*c* = 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (s, 1H), 4.30 (m, 1H), 3.87 (m, 1H), 3.80-3.70 (complex m, 2H), 3.69 (dd, *J* = 7.7 and 1.0 Hz, 1H), 2.01 (m, 1H), 1.75-1.50 (complex m, 2H), 0.91 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 102.7, 77.2, 68.7, 66.9, 66.3, 35.0, 25.8, 18.1, –4.7(5), –4.8(2); IR ν_{max} 3446, 3283, 2960, 2957, 2927, 2891, 2857, 1463, 1252, 1096, 1075, 899, 836, 775 cm^{-1}; MS (ESI, +ve) *m/z* 283 [$(M+Na)^+$, 100%]; HRMS [$(M+Na)^+$ calcd for $C_{12}H_{24}O_4SiNa$ 283.1336, found 283.1332.

Compound 25. A magnetically stirred solution of a *ca*. 1:1 mixture of the epimeric forms of compound **24** (357 mg, 1.37 mmol) and DMAP (170 mg, 1.37 mmol, 1 mole equiv.) in THF (7 mL) maintained at 22 °C under a nitrogen atmosphere was treated with acetic anhydride (280 mg, 2.75 mmol, 2 mole equiv.). The ensuing mixture was stirred for 18 h then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:20 v/v ethyl acetate/ petroleum ether elution) to afford two fractions, A and B.

Concentration of fraction A [R_f = 0.2(5)] gave the α-epimeric form of compound **25** (414 mg, 99% based on the relevant epimeric form of the precursor) as clear, colorless oil, $[\alpha]_D$ = –58.2 (*c* = 0.2, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 (t, *J* = 1.7 Hz, 1H), 4.59 (m, 1H), 4.42 (m, 1H), 3.87-3.70 (complex m, 2H), 3.66 (m, 1H),

2.11 (m, 1H), 2.09 (s, 3H), 1.76 (dm, J = 15.9 Hz, 1H), 0.92 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 99.6, 67.4, 66.3, 65.5, 29.0, 25.8, 21.2, 18.1, –4.7, –4.8 (one signal obscured or overlapping); IR ν_{max} 2955, 2930, 2895, 2857, 1728, 1372, 1245, 1143, 1106, 1021, 1001, 893, 835, 774 cm^{-1}; MS (ESI, +ve) *m/z* 325 [$(M+Na)^+$, 100%], 303 [$(M+H)^+$, 8]; HRMS [$(M+H)^+$ calcd for $C_{14}H_{27}O_5Si$ 303.1622, found 303.1632.

Concentration of fraction B (R_f = 0.2) gave the β-epimeric form of compound **25** (414 mg, 99% based on the relevant epimeric form of the precursor) as a clear, colorless oil, $[\alpha]_D$ = –103.9 (c = 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (t, J = 1.5 Hz, 1H), 4.95 (m, 1H), 4.33 (m, 1H), 3.85-3.65 (complex m, 3H), 2.03 (s, 3H), 1.95 (m, 1H), 1.79 (m, 1H), 0.88 (s, 9H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 100.2, 77.5, 69.5, 68.6, 66.4, 30.8, 25.7, 21.0, 18.1, –4.7(9), –4.8(6); IR ν_{max} 2955, 2930, 2895, 2857, 1734, 1366, 1238, 1146, 1123, 1100, 1045, 1031, 840, 775 cm^{-1}; MS (ESI, +ve) *m/z* 325 [$(M+Na)^+$, 100%], 303 [$(M+H)^+$, 3]; HRMS [$(M+H)^+$ calcd for $C_{14}H_{27}O_5Si$ 303.1622, found 303.1632.

Compound 26. A magnetically stirred solution of compound **25** (421 mg, 1.39 mmol) in THF (7 mL) maintained at 22 °C was treated with TBAF in THF (1.67 ml of an 1 M solution in THF, 1.67 mmol, 1.2 mole equiv.) The ensuing mixture was stirred at 22 °C for 5 h then concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica, diethyl ether elution) and so affording two fractions, A and B.

Concentration of fraction A [R_f = 0.2(5)] gave the α-epimeric form of compound **26** (238 mg, 91%) as a yellow, crystalline solid, m.p. = 56-62 °, $[\alpha]_D$ = –51.4 (c = 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.42 (s, 1H), 4.65 (m, 1H), 4.54 (m, 1H), 3.80-3.72 (complex m, 2H), 3.59 (m, 1H), 2.78 (broad s, 1H), 2.17 (m, 1H), 2.11 (s,

3H), 1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 99.4, 77.4, 68.2, 66.2, 65.6, 28.6, 21.1; IR ν_{max} 3483, 2971, 2901, 1727, 1373, 1243, 1139, 1078, 1002, 973, 921, 889 cm^{-1}; MS (ESI, +ve) *m/z* 211 [$(M+Na)^+$, 100%], 189 [$(M+H)^+$, <1]; HRMS [$(M+H)^+$ calcd for $C_8H_{13}O_5$ 189.0757, found 189.0754.

Concentration of fraction A (R_f = 0.2) gave the β-epimeric form of compound **26** (236 mg, 90%) as a clear, colorless oil, $[\alpha]_D$ = –144.9 (*c* = 0.14, CH_3OH): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (s, 1H), 4.96 (m, 1H), 4.50 (m, 1H), 3.95-3.80 (complex m, 3H), 2.14 (m, 1H), 2.08 (s, 3H), 1.85 (m, 1H) (signal due to hydroxyl group proton not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 100.3, 68.8, 68.1, 66.6, 30.2, 21.0 (one resonance obscured or overlapping); IR ν_{max} 3450, 2971, 2901, 1730, 1370, 1235, 1144, 1042, 980, 896 cm^{-1}; MS (ESI, +ve) *m/z* 211 [$(M+Na)^+$, 100%], 189 [$(M+H)^+$, <1]; HRMS [$(M+H)^+$ calcd for $C_8H_{13}O_5$ 189.0757, found 189.0754.

Compound 2. A magnetically stirred solution of compound **26** (261 mg, 1.39 mmol) in dichloromethane (7 mL) maintained at 22 °C was treated, in one portion, with PCC (900 mg, 4.16 mmol, 3 mole equiv.). The ensuing mixture was stirred for 24 h then treated with Celite™ (1.0 g) before being filtered through a sintered glass funnel. The filtrate was concentrated under reduced pressure and the residue thus obtained was subjected to flash chromatography (silica, 1:2 v/v ethyl acetate/petroleum ether elution). Concentration of the relevant fractions (R_f = 0.4) gave a light-yellow oil. This oil was dissolved in acetonitrile (7.0 ml) and while being maintained at 22 °C with magnetic stirring the resulting solution was treated, in one portion, with sodium acetate (341 mg, 3 mole equiv.). The ensuing mixture was heated under reflux for 8 h then cooled and concentrated under reduced pressure. The dark oil thus obtained was subjected to column chromatography (silica, 1:9 v/v ethyl acetate/petroleum ether elution) to give, after concentration of the relevant fractions (R_f = 0.2), compound **2**

(278 mg, 53%) as a clear, colorless oil. This material was identical, in all respects, with an authentic sample.[5]

Compound 27. A magnetically stirred solution of compound **23** (1.56 g, 10.83 mmol) in methanol (36 mL) maintained at 0 °C was treated, in one portion, with $NaBH_4$ (410 mg, 10.83 mmol, 1 mole equiv.). The ensuing mixture was stirred for 0.5 h at 0 °C then warmed to 22 °C before being concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:20 v/v methanol/ethyl acetate elution) and concentration of the relevant fractions (R_f = 0.2) gave compound **27**[17] (1.12 g, 72%) as a clear, colorless oil, $[\alpha]_D$ = –155.0 (*c* = 0.1, CH_3OH): ^{1}H NMR (400 MHz, CD_3OD) δ 5.22 (s, 1H), 4.38 (m, 1H), 3.88-3.68 (complex m, 4H), 1.92 (m, 1H), 1.71 (m, 1H) (signals due to hydroxyl group protons not observed); ^{13}C NMR (100 MHz, CD_3OD) δ 102.9, 76.7, 67.5, 66.1, 66.0, 33.0; IR ν_{max} 3368, 2957, 2900, 1138, 1049, 968, 900, 864 cm^{-1}; MS (ESI, +ve) *m/z* 169 [$(M+Na)^+$, 100%]; HRMS [$(M+Na)^+$ calcd for $C_6H_{10}O_4Na$ 169.0471, found 169.0476.

Compound 28. A magnetically stirred solution of compound **27** (146 mg, 1.0 mmol) in acetone (10 mL) maintained at 22 °C was treated with PDC (1.13 g, 3.0 mmol, 3 mole equiv.) and the ensuing mixture heated at 40 °C for 12 h before being cooled the treated with Celite (1.0 g). The ensuing mixture was filtered through a sintered glass funnel and the filtrate concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:4 v/v diethyl ether/petroleum ether elution) afforded two fractions, A and B.

Concentration of fraction A (R_f = 0.2) gave compound **23**[17] (14 mg, 10%) as a clear, yellow oil that was identical in all respects with an authentic sample.

Concentration of fraction B (R_f = 0.1) gave compound **28**[19] (56 mg, 39%) as a clear, colorless oil, $[\alpha]_D$ = –96.1 (*c* = 0.1, CH_3OH): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.58 (s,

1H), 4.50 (m, 1H), 4.15 (m, 1H), 4.04-3.85 (complex m, 2H), 2.94 (dd, *J* = 17.2 and 7.7 Hz, 1H), 2.31 (dd, *J* = 17.2 and 7.0 Hz, 1H), 2.10 (broad s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 101.3, 78.0, 69.6, 66.9, 43.0; IR ν_{max} 3441, 2980, 2901, 1733, 1720, 1133, 1120, 1066, 1020, 966, 834, 875 cm^{-1}; MS (ESI, +ve) *m/z* 199 [$(M+Na+MeOH)^+$, 100%] 167 [$(M+Na)^+$, 5]; HRMS [$(M+Na)^+$ calcd for $C_6H_8O_4Na$ 167.0322, found 167.0320.

Compound 2. A magnetically stirred solution of compound **28** (290 mg, 2.0 mmol) and trimethylamine (577 μL, 4.0 mmol, 2 mole equiv.) in dichloromethane (20 mL) maintained at 0 °C was treated with *p*-TsCl (572 mg, 3.0 mmol, 1.5 mole equiv.) After 0.5 h the reaction mixture was warmed to 22 °C, stirred at this temperature for 24 h then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:9v/v ethyl acetate/ petroleum ether elution) and concentration of the relevant fractions (R_f = 0.2) gave compound **2** (163 mg, 65%) as a clear, colorless oil.

Compound 30. *Step i*: A magnetically stirred solution of compound **2** (188 mg, 1.49 mmol) in methanol (8 mL) maintained at 0 °C was treated with $CeCl_3$•$7H_2O$ (555 mg, 1.49 mmol) then, in portions, with $NaBH_4$ (56 mg, 1.48 mmol). The ensuing mixture was stirred at 0 °C for 1 h before being filtered through a short pad of TLC grade silica gel that was washed with ethyl acetate (100 mL). The combined filtrates were concentrated under reduced pressure to give a white solid presumed to contain allylic alcohol **29**.[5,22]

Step ii: The crude product from step i was dissolved in pyridine (10 mL) and the resulting solution, while being stirred magnetically at 22 °C, was treated with acetic anhydride (700 μL, 7.40 mmol) then DMAP (12 mg). The resulting solution was stirred for 4 h then concentrated under reduced pressure. The ensuing residue was

subjected to flash chromatography (silica, 4:1 v/v hexane/ethyl acetate elution) and concentration of the appropriate fractions (R_f = 0.4) gave compound **30** (224 mg, 88%) as a clear, colorless oil, $[\alpha]_D$ = –52.5 (*c* = 0.2, $CHCl_3$). The ^1H and ^{13}C NMR spectral data obtained on this compound matched those reported[22] previously.

Compounds 10 and 11 (from compound **30**). Following the same procedure as described above for effecting the Tsuji-Trost reactions of allylic acetates **5** and **6**, compound **30** was converted into a chromatographically separable mixture of compounds **10** (42%) and **11** (53%). Each of these products was identical with an authentic sample.

X-ray Crystallographic Studies

Crystallographic Data.

Compound **8**. $C_8H_8Cl_3NO_3$, *M* = 272.51, *T* = 150 K, orthorhombic, space group $P2_12_12_1$, *Z* = 4, *a* = 6.0047(1) Å, *b* = 9.2700(2) Å, *c* = 18.8140(4) Å; *V* = 1047.25(4) Å^3, D_x = 1.728 g cm^{-3}, 2077 unique data ($2\theta_{max}$ = 145.4°), *R* = 0.023 [for 2043 reflections with $I > 2.0\sigma(I)$]; *Rw* = 0.060 (all data), *S* = 1.01.

Compound **9**. $C_8H_8Cl_3NO_3$, *M* = 272.51, *T* = 150 K, monoclinic, space group $P2_1$, *Z* = 2, *a* = 6.2433(2) Å, *b* = 9.1470(2) Å, *c* = 9.6606(2) Å; β = 90.256(2)°; *V* = 551.69(2) Å^3, D_x = 1.640 g cm^{-3}, 2026 unique data ($2\theta_{max}$ = 144.8°), *R* = 0.019 [for 2012 reflections with $I > 2.0\sigma(I)$]; *Rw* = 0.047 (all data), *S* = 1.00.

Compound **10**. $C_{11}H_{14}O_6$, *M* = 242.23, *T* = 150 K, monoclinic, space group $P2_1$, *Z* = 2, *a* = 8.1650(2) Å, *b* = 8.49383(13) Å, *c* = 8.7258(2) Å; β = 107.831(2)°; *V* = 576.08(2) Å^3, D_x = 1.396 g cm^{-3}, 1828 unique data ($2\theta_{max}$ = 144.4°), *R* = 0.024 [for 1795 reflections with $I > 2.0\sigma(I)$]; *Rw* = 0.057 (all data), *S* = 1.00.

Compound **11**. $C_{11}H_{14}O_6$, M = 242.23, T = 150 K, monoclinic, space group $P2_1$, Z = 2, a = 5.80882(5) Å, b = 7.49449(6) Å, c = 13.20425(12) Å; β = 91.2938(8)°; V = 574.69(1) Å^3, D_x = 1.400 g cm^{-3}, 2124 unique data ($2\theta_{max}$ = 144.4°), R = 0.022 [for 2111 reflections with $I > 2.0\sigma(I)$]; Rw = 0.057 (all data), S = 1.00.

Compound **20**. $C_{17}H_{18}N_2O_8$, M = 378.34, T = 150 K, monoclinic, space group $P2_1$, Z = 2, a = 9.7352(6) Å, b = 5.8003(4) Å, c = 15.9527(15) Å; β = 106.367(8)°; V = 864.30(8) Å^3, D_x = 1.454 g cm^{-3}, 2884 unique data ($2\theta_{max}$ = 147.4°), R = 0.058 [for 2522 reflections with $I > 2.0\sigma(I)$]; Rw = 0.171 (all data), S = 1.01.

Compound **22**. $C_{17}H_{18}N_2O_8$, M = 378.34, T = 150 K, orthorhombic, space group $P2_12_12_1$, Z = 4, a = 5.6020(1) Å, b = 10.3437(1) Å, c = 29.2615(4) Å; V = 1695.57(2) Å^3, D_x = 1.482 g cm^{-3}, 3312 unique data ($2\theta_{max}$ = 147.2°), R = 0.029 [for 3312 reflections with $I > 2.0\sigma(I)$]; Rw = 0.076 (all data), S = 1.00.

Compound **24** (α-epimer). $C_{12}H_{24}O_4Si$, M = 260.40, T = 150 K, orthorhombic, space group $P2_12_12_1$, Z = 4, a = 6.45626(7) Å, b = 11.44113(15) Å, c = 19.3950(2) Å; V = 1432.65(3) Å^3, D_x = 1.208 g cm^{-3}, 2893 unique data ($2\theta_{max}$ = 147.8°), R = 0.029 [for 2858 reflections with $I > 2.0\sigma(I)$]; Rw = 0.079 (all data), S = 1.00.

Structure Determination. Images for compounds **8**, **9**, **10**, **11**, **20**, **22** and **24** (α-epimer) were measured on a diffractometer (Cu Kα, mirror monochromator, λ = 1.54184 Å) fitted with an area detector and the data extracted using the CrysAlis package.[23] The structure solutions for all seven compounds were solved by direct methods (SIR92)[24] then refined using the CRYSTALS program package.[25] Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC nos., 1587832, 1587833, 1587834, 1587835, 1587836, 1587837 and 1587838). These data can be

obtained free-of-charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

ASSOCIATED CONTENT

Supporting Information

Cifs and Anisotropic Displacement Ellipsoid Plots from the Single-crystal X-ray Analyses of Compounds **8**, **9**, **10**, **11**, **20**, **22** and **24** (α-epimer). ^{1}H and ^{13}C NMR spectra of compounds **3-13** and **15-28**. This material is available free-of-charge via the Internet at http://pubs.acs.org.

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