Lactol-regulated Silyloxy-Cope Rearrangement and Its Application to the Total Synthesis of Dictymal, an Aldehyde Possessing an Iridoid Dimeric Structure†

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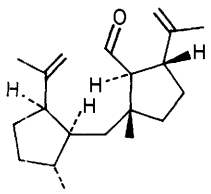
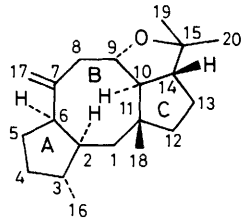
Dictymal, a congener of epoxydictymene isolated from a brown alga, *Dictyota dichotoma* has been totally synthesized *via* a lactol-regulated oxy-Cope rearrangement of an appropriately designed dimer obtained from two C_{10}-synthons (iridoids).

Several di- and sester-terpenoids possess a 5-8-5-membered tricyclic carbon skeleton, represented by fusicoccins[1] and ophiobolins.[2] Further members of this family are still being reported and their origin is now spread over a wide variety of organisms.[3] Because of their novel carbon framework and wide-ranging biological activities, attempts to synthesize these tricyclic metabolites have continued to appear in the literature.[4] Although success in the total synthesis of these tricyclic natural products is rare, to date, we have prepared cycloaraneosene,[5] hydroxycycloaraneosene,[6] albolic acid,[7] and ceroplastol II.[7]



(1)



(2)

It was thought that the synthesis of dictymal, (1*R*,2*S*,3*R*)-1-[(1*S*,2*R*,5*R*)-2-isopropenyl-5-methylcyclopentyl]methyl-2-formyl-3-isopropenyl-1-methylcyclopentane (**1**),‡ a congener of epoxydictymene (**2**) isolated from a brown alga, *Dictyota dichotoma* Lamouroux, by Matsumoto *et al.*,[8,9] was a worthwhile synthetic target since its carbon skeleton was identical with those of intermediates in our synthetic strategy for the preparation of 5-8-5-tricyclic compounds. Further, since (**1**) is thought to be biosynthesized by cleavage of the central B-ring of (**2**), synthesis of the former might provide a path to the latter. An unprecedented stereochemical feature noted in (**2**), and thus in (**1**), was a *trans-cis* relationship for 6-H, 11-Me, and 14-H.‡ According to our synthetic scheme, two of the three above-mentioned stereogenic centres, *i.e.*, C-6 and C-14, are inherited from the starting iridoids, and use of two molecules of (3*S*)-iridoid synthons appears appropriate to give an epimeric pair of condensates (**A**) and (**B**). From these, the desired configuration at C-11 could then be generated *via* a chair-formed transition Cope rearrangement. However, the silyloxy-Cope rearrangement of (**A**) is known to proceed stereoselectively *via* a boat-formed transition state to give an unwanted product (**C**).[10] While the epimer (**B**) rearranged unselectively to give the desired rearranged product (**D**) *via* a chair-formed transition state as a minor product, the major product (**E**) was an unwanted compound.[10]

Therefore, the 'lactol-regulated rearrangement' used in the ceroplastane synthesis[7] was again employed. Since a six-membered lactol ring fused to a 1,5-diene system regulates the enol of the rearranged product to be *E*-geometry, the transition state from an iridoid dimer having a same stereochemical arrangement with (**B**) must be a chair form and the configuration of C-11 must be a desired one as depicted in Scheme 1. It is therefore crucial to obtain a (**B**)-type compound as the major product in the chromium(II) chloride condensation.

Results and Discussion

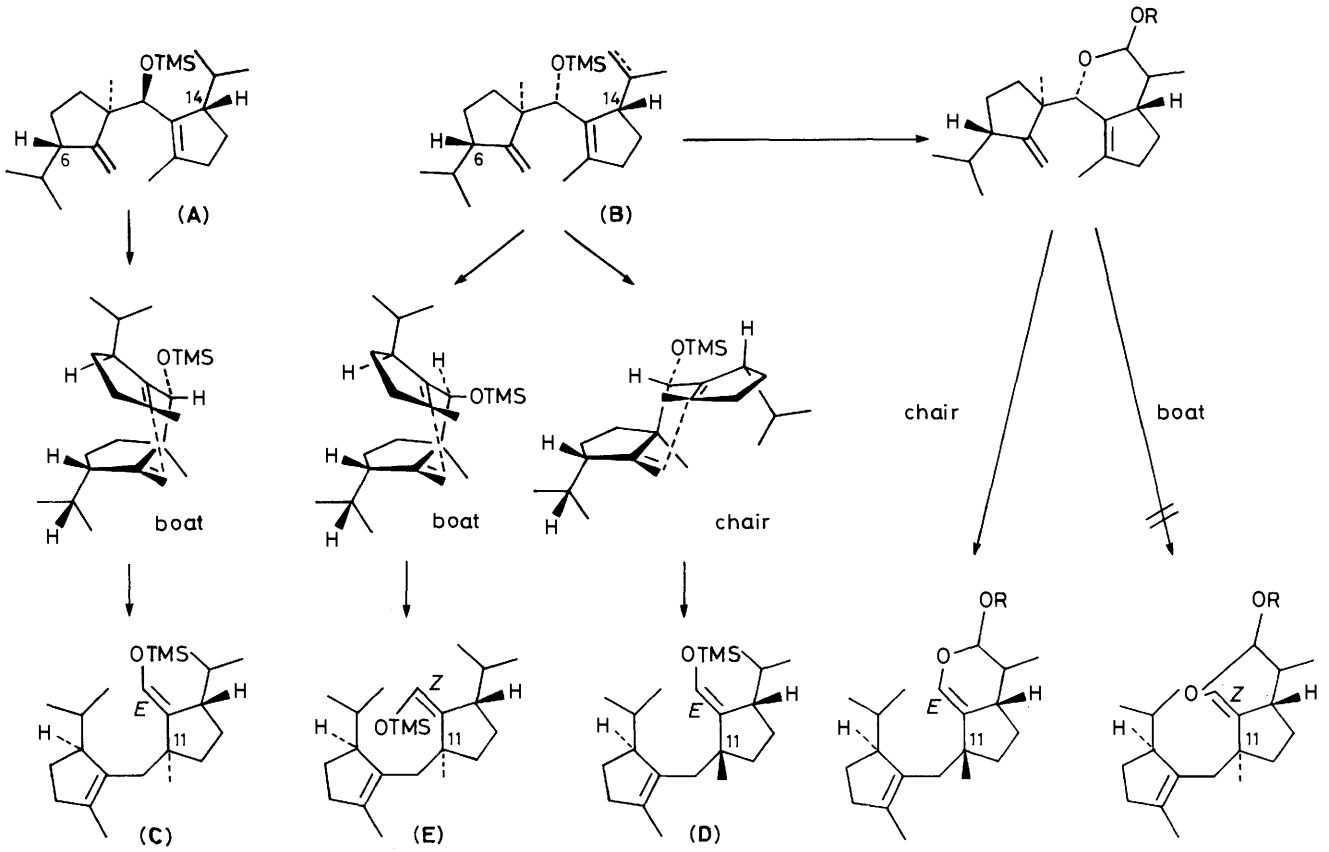
Chromium(II) *Chloride-mediated Coupling of Two* (3S)-*Iridoids.*—From previous experiments of chromium(II) chloride mediated[11] dimerizations with various combinations of iridoid synthons,[10,12] we recognized that the ratio of the epimeric products from two iridoid synthons having the same chirality at C-3, *e.g.*, (**A**) *vs.* (**B**), varied in each experiment. However, we found that the addition of propan-2-ol in the reaction medium causes, reproducibly, highly selective formation of an (**A**)-type product.[7] In contrast, the complete exclusion of air and moisture in this coupling reaction results in predominant formation of a (**B**)-type product with moderate selectivity. Although the mechanistic ambiguity remains to be clarified, we employed the latter conditions with (3*S*,8*R*)-9-benzyloxy-7-chloroirid-1-ene, (3*S*)-2-chloromethyl-3-[(1*R*)-2-benzyloxy-1-methylethyl]-1-methylcyclopent-1-ene (**3**), and (3*S*)-irida-1,8-dien-7-al, (5*S*)-2-formyl-5-isopropenyl-1-methylcyclopent-1-ene (**4**), to obtain the desired iridoid dimer (**5**).[10] Thus, (**3**) was coupled with (**4**) by means of chromium(II) chloride in a completely anhydrous medium under an argon atmosphere. The major product, in 62% yield, was the desired compound (**5**) having an α-hydroxy group;§ the hydroxy epimer (**6**) was obtained in a 17% yield.

Lactol-regulated Silyloxy-Cope Rearrangement.—To make a fused lactol ring, (**5**) was first converted into a silyloxy ether (**7**),

† Contents of this paper were preliminarily reported in *Chem Lett.*, 1987, 2295.

‡ Regardless of the numberings based on the systematic nomenclature for these complex compounds, the positional numbers and the ring letters shown in compound (**2**) are used throughout in this paper. To make correlations clear, these are also adopted for (**1**) and its synthetic intermediates although different numberings are used in the original paper, see ref. 9.

§ The stereochemistry of the hydroxy group can be unambiguously deduced from the ^{1}H n.m.r. chemical shifts of 3- and 11-methyl groups. For detailed discussions, see ref. 12.

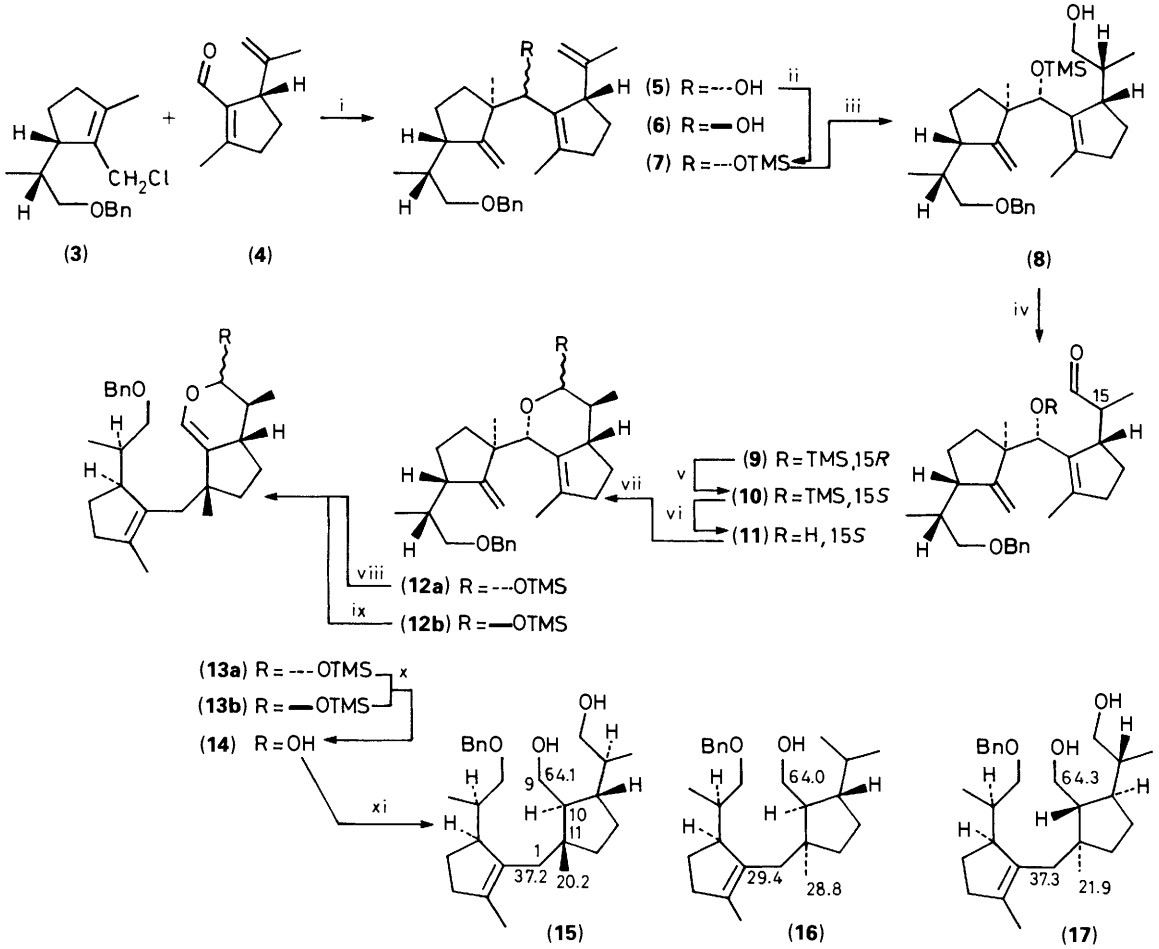


Scheme 1. Cope-rearrangements of iridoid dimers

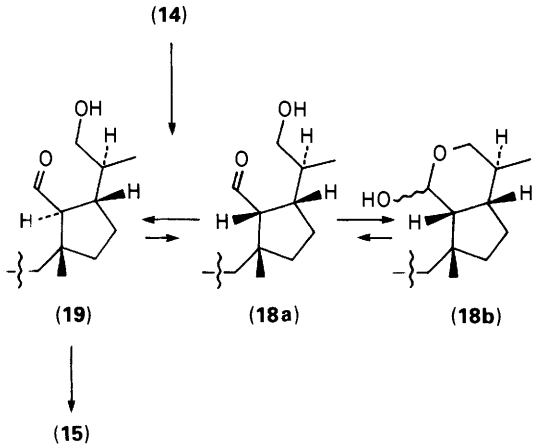
which was hydroborated with bis(3-methylbutan-2-yl)borane (disiamylborane). The hydroboration occurred diastereoselectively to afford a single product (**8**) in a 96% yield. Since hydroboration of irida-1,8-diene derivatives always occurs stereoselectively to give (3*S**,8*R**)-irid-1-en-9-ols without exceptions,[13] compound (**8**) should have a (15*R*)-configuration as depicted. Oxidation of compound (**8**) with pyridinium chlorochromate (PCC) gave the silyloxy aldehyde (**9**) the silylation of which was unsuccessful owing to a facile reversion under the reaction conditions. An unfavourable axial orientation of 15-Me in an expected cyclic acetal might be responsible for the occurrence of the silylation on the opened form of the hydroxy aldehyde. However, its epimer (**10**), produced by a potassium fluoride-on-Florisil treatment, was desilylated by pyridinium toluene-*p*-sulphonate (PPTS) treatment to give an hydroxy aldehyde (**11**), and further to a mixture of cyclic acetals (**12a**) and (**12b**) in a good yield. In addition to the different behaviour in the acetal formation, the ^{13}C n.m.r. chemical shifts of the methyl carbons adjacent to the α-carbon of the aldehyde in (**9**) and (**10**) were consistent with the above assignments of the stereochemistry at C-15. Thus, the values of the corresponding methyl shifts in (**9**) (δ 13.1) and (**10**) (δ 7.8) parallel those of dehydroiridodial (δ 10.7) and chrysomelidial (δ 7.8).[14]

The structures of the cyclic acetals (**12a**) and (**12b**) were deduced from the vicinal coupling constants of hydrogen at an anomeric position; these are 8 Hz for (**12a**) and 3 Hz for (**12b**). Both of (**12a**) and (**12b**) rearranged smoothly when heated at 180 °C. Although partial epimerization at an anomeric position took place to give a mixture of rearranged products (**13a**) and (**13b**) in both cases, the cyclic acetal structures were retained as expected. Therefore, it can be concluded that the rearrangements occurred *via* the chair-formed transition states and the configuration of C-11 in (**13a**) and (**13b**) was controlled in the desired fashion. Furthermore, spectral evidence for this conclusion was obtained as follows. A mixture of (**13a**) and (**13b**) was hydrolysed with PPTS in aqueous tetrahydrofuran (THF) to afford an enol-lactol (**14**). This anomeric mixture was reduced with sodium borohydride. A single diol (**15**) formed in good yield showed characteristic ^{13}C n.m.r. chemical shifts as listed in Scheme 2 together with those of our synthetic intermediates (**16**) and (**17**) in the syntheses of cycloaraneosene[5] and ceroplastol II.[7] An upfield shift of the methyl carbon at C-11 and a downfield shift of the methylene carbon of C-1 in (**15**) compared with those in (**16**) showed that the relationship of C-10 and C-11 in (**15**) is the reverse of that in (**16**). Further, that the *trans*-relationship between C-10 and C-14 is a feature common to (**15**) and (**16**), since the C-9 signals have similar values.[15] These conclusions were further supported by comparison of (**15**) with (**17**); from the fact that chemical shifts of these three positions are quite similar, we assume the configuration of the C-ring in (**15**) is pseudo-enantiomeric with that in (**17**). The Cope rearrangements of (**12a**) and (**12b**) thus certainly proceed *via* the desired chair-formed transition states. It transpired that the configurations of C-10 in (**15**) was the same as that of (**1**). The selective formation of this configuration during the reduction of the enol-lactol can be explained by a mixture of kinetic and thermodynamic factors (see Scheme 3).

The first step in the reduction of (**14**), after a ring-opening to a dialdehyde, should occur at the sterically less-hindered position to give a mixture of isomeric hydroxy aldehydes (**18a**) and (**19**), in which the former should predominate over the latter as the kinetically favoured product of protonation of the enol ether function. However, the subsequent step of the reduction (to the diols) will be more rapid in the case of the latter (**19**). Isomerization of (**18a**) to the more thermodynamically stable



Scheme 2. *Reagents and conditions:* i, $CrCl_3$–1/2LAH, THF–DMF (argon) [(**5**), 62%; (**6**), 17%]; ii, TMSCl, Py (85%); iii, bis(3-methylbutan-2-yl)borane, 3M NaOH, H_2O_2 (96%); iv, PCC, CH_2Cl_2 (84%); v, KF-Florisil, MeOH (84%); vi, PPTS, aq. THF (94%); vii, = reagent ii [(**12a**), 54%; (**12b**), 27%]; viii, 180 °C (toluene) [(**13a**):(**13b**) = 2:1, 81%]; ix, = conditions viii [(**13a**):(**13b**) = 1:4, 73%]; x, reagent vi (95%); xi, $NaBH_4$, aq. $NaHCO_3$–MeOH (93%)



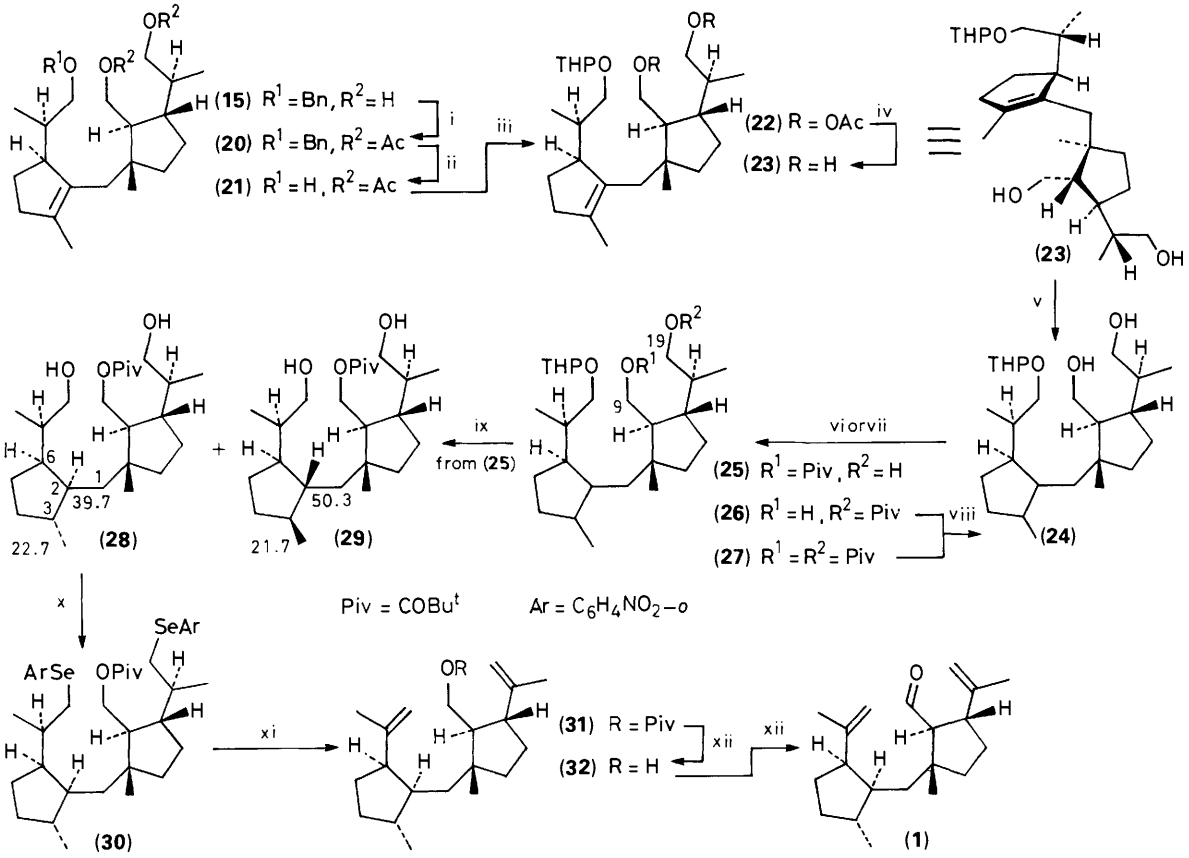
Scheme 3. Stereoselective reduction of the enol-lactol

(**19**) will be quite rapid under slightly basic reaction conditions;* (**18a**) will also tend to exist as a masked tautomeric lactol form (**18b**).

Formation of Saturated A-*Ring.*—A saturated A-ring, particularly having a *cis-trans* relationship at C-6, C-2, and C-3, is a further characteristic feature in the stereochemical arrangement of (**1**). It is, therefore, obvious that the isolated tetrasubstituted double bond must be reduced effectively with the desired stereoselectivity. For this we applied our previous method, a stereocontrolled dissolving metal reduction with an internal hydroxy group as a proton source.† Consequently, (**15**) was converted into (**23**) in four steps; acetylation to the diacetate (**20**), hydrogenolysis of the benzyl group to (**21**), tetrahydropyranyl (THP) etherification to (**22**), and reductive deacetylation. From the molecular model inspections and our previous results,[5] it was expected that the hydroxy group, which must be on the α-face of the A-ring as depicted, would deliver a proton to C-2 from the desired α-face in the reduction of (**23**). Hence, (**23**) was submitted to the sodium metal reduction in hexamethylphosphoric triamide (HMPA) with t-butyl alcohol. The reduction product (**24**) was obtained in 83% yield as a stereoisomeric mixture, the separation of which was not attempted at this stage, since the THP group in the molecule causes additional diastereoisomerism for each product. Prior to the hydrolysis of THP group, the selective protection of one of the hydroxy group was necessary for further transformations. Treatment of (**24**) with an equimolar amount of pivaloyl chloride and pyridine in dichloromethane gave the monoesters

* The reduction of similar compound in a aprotic medium, *i.e.*, LAH/THF, actually afforded a (**18a**)-type product which exists completely in a (**18b**)-type lactol form.

† For similar examples of stereocontrolled dissolving metal reduction, see J. K. Whitesell and M. A. Minton, *J. Am. Chem. Soc.*, 1987, **109**, 6403.



Scheme 4. *Reagents and conditions:* i, Ac_2O, Py (99%); ii, H_2–Pd/C (98%); iii, DHP, PPTS, CH_2Cl_2 (96%); iv, LAH (100%); v, Na, Bu^{t}OH, HMPA (83%); vi, BuLi, pivaloyl chloride [(**25**), 46%; (**26**), 16%; (**27**), 29%]; vii, pivaloyl chloride, Py [(**25**), 23%; (**26**), 55%; (**27**), (22%]; viii, = reagent iv (98%); ix, *p*-TsOH, MeOH [(**28**), 52%; (**29**), 37%]; x, *o*-$NO_2C_6H_4SeCN$, Bu_3P, THF (97%); xi, H_2O_2, THF (86%); xii, = reagent iv (95%); xiii, $(COCl)_2$, DMSO, Et_3N (95%)

(**25**) and (**26**) (1:2.4), together with diester (**27**). Acylation by quenching the monoanionic species of (**24**) with pivaloyl chloride also occurred with moderate selectivity but with a reversed ratio (2.9:1). The former result is reasonable, since the acylation occurred predominantly on the less hindered 19-hydroxy group. The latter result might be explained in terms of chelation of the lithium cation by the alkoxide and the remaining hydroxy group. In such a chelated form, the 19-hydroxy group is forced to be located in a concave area surrounded by both of A and C ring moieties. The undesired compounds (**26**) and (**27**) were reduced with LAH to (**24**) and the procedures were repeated to obtain a sufficient amount of the desired (**25**). A stereoisomeric mixture of (**25**) was then hydrolysed to diols and the isomers were chromatographically separated. Two isomers, thus obtained, were assigned to be the desired compound (**28**) and its diastereoisomer (**29**) by analyses of their ^{13}C n.m.r. spectra; the chemical shifts of the 3-methyl groups showed unequivocally a *trans*-relationship between C-2 and C-3 in both compounds; δ 22.7 for (**28**) and δ 21.7 (**29**).[5,15] Since 1-methylene carbon of (**28**) (δ 39.7) appeared at higher field than that of (**29**) (δ 50.3), it is clear that the relationship of C-2 and C-6 is *cis* in (**28**) and *trans* in (**29**).[5,15] Although the stereoselectivity of the dissolving metal reduction was only moderate [ratio (**28**):(**29**) = 52 : 37], it should be emphasized that kinetic protonation should have played an important role in the formation of desired (**28**), in which two bulky substituents on the A-ring are oriented *cis* to each other; there would be no chance to obtain such a crowded compound under normal conditions of dissolving metal reduction in which thermodynamic factors mainly control the product distributions.

Synthesis of Dictymal (**1**).—Only a few simple functional group transformations remained for the synthesis of (**1**). The hydroxy groups of (**28**) were first dehydrated[16] *via* the bis-selenide (**30**) to the diene (**31**) in a good yield. Then, the pivaloyl protecting group was removed by a reductive treatment to give an alcohol (**32**) which was, finally, converted into (**1**) by a Swern oxidation.[17] Synthetic (**1**), thus obtained, was identical with the natural (+)-dictymal in all respects. The structure of (**1**) was proposed[9] to have same absolute configuration as its congener (**2**), that of which has been confirmed by an *X*-ray crystallographic study.[8] The same sign for the optical rotations of synthetic and natural (**1**), +24° and +16.4°, respectively, proved the absolute configuration of (**1**) as proposed.[9]

Conclusion.—The total synthesis of the unique metabolite (**1**) has now been accomplished for the first time. Since the stereogenic centres in (**1**) all exist in (**2**), the total synthesis of (**2**) might be accomplished by appropriate transformations from a synthetic intermediate such as the monopivaloate (**26**).

Experimental

Elemental analyses were carried out by Miss S. Hirashima, Institute of Advanced Material Study, Kyushu University. The m.p.s were measured with a Yanagimoto Micro m.p. apparatus and are not corrected. N.m.r. spectra were measured by JEOL FX 100 spectrometer in $CDCl_3$ solution, unless otherwise specified, and the chemical shifts expressed were in δ units. Mass spectra were measured with a JEOL O1SG-2 spectrometer. I.r. spectra were taken as KBr disks for crystalline compounds or as liquid films inserted between NaCl plates for oily materials

using a JASCO IR-A 102 spectrometer. The optical rotations were measured with a Union Model PM-101 apparatus. The solvents for the reactions were carefully purified by distillation under the existence of appropriate dehydrating agents and an N_2 atmosphere immediately prior to use; therefore, those were anhydrous unless otherwise stated. The stationary phase for the column chromatography was Wakogel C-300 and the elution solvents were mixtures of hexane and ethyl acetate, unless otherwise stated.

$CrCl_2$-Mediated Condensation Reaction of Compounds (**3**) *and* (**4**).—A suspension of $CrCl_3$ (14.83 g) in THF (100 ml) was reduced with LAH (1.78 g) at 0 °C in a three-necked flask which was carefully dried and flushed with argon for complete exclusion of air and moisture. The resultant black suspension was diluted with *N*,*N*-dimethylformamide (DMF) (300 ml) and then into the mixture, were added, consecutively, a THF solution (5 ml) of (**4**) (8.59 g) and a THF soluton (5 ml) of (**3**) (10.87 g). After being stirred for 15 h at room temperature, the mixture was diluted with water and extracted with EtOAc. The extract was concentrated and the residue treated with $NaBH_4$ (680 mg) in MeOH (200 ml) to reduce the excess of (**4**) for easy purification of the products. The mixture obtained upon work-up was separated by Prep-500 system (PrepPAK-500 silica gel cartridge column, hexane–EtOAc 40:1), Nippon Waters & Co., to give (**6**) as an oil (2.68 g, 17%) (Found: C, 82.2; H, 9.95%. $C_{27}H_{38}O_2$ requires C, 82.18; H, 9.71%); $[\alpha]_D^{18}$ −48.2° (*c* 2.28 in $CHCl_3$); δ_H 1.08 (3 H, d, *J* 7 Hz), 1.09 (3 H, s), 1.70 (3 H, br s), 1.74 (3 H, br s), 3.19 (1 H, t, *J* 8.5 Hz), 3.44 (1 H, br m), 3.47 (1 H, dd, *J* 8.5, 4 Hz), 4.36 (1 H, br s), 4.42 (1 H, d, *J* 12 Hz), 4.47 (1 H, d, *J* 12 Hz), 4.67 (1 H, m), 4.75 (1 H, m), 4.88 (1 H, d, *J* 2.5 Hz), 5.02 (1 H, d, *J* 3 Hz), and 7.26 (5 H, br s); δ_C 15.3 (q), 17.2 (q), 20.5 (q), 23.6 (t), 25.1 (t), 29.4 (t), 34.9 (t), 35.3 (d), 37.1 (t), 48.4 (d), 52.0 (s), 54.0 (d), 72.8 (2 C, t), 75.0 (d), 106.2 (t), 109.1 (t), 127.2 (3 C, d), 128.1 (2 C, d), 136.1 (s), 138.3 (s), 138.7 (s), 151.7 (s), and 160.3 (s); $\nu_{max.}$ 3 590, 2 955, 2 945, 2 875, 1 640, 1 453, 1 370, 1 100, 892, 732, and 695 cm^{-1}; and (**5**) as an oil (9.48 g, 62%) (Found: C, 82.3; H, 9.9%); $[\alpha]_D^{20}$ −28.5° (*c* 2.00 in $CHCl_3$); δ_H 0.92 (3 H, s), 1.11 (3 H, d, *J* 7 Hz), 1.66 (3 H, br s), 1.92 (3 H, br s), 3.22 (1 H, t, *J* 8.5 Hz), 3.24 (1 H, br m), 3.48 (1 H, dd, *J* 8.5, 4 Hz), 4.13 (1 H, br s), 4.42 (1 H, d, *J* 12 Hz), 4.47 (1 H, d, *J* 12 Hz), 4.71 (2 H, br s), 4.90 (1 H, d, *J* 2.5 Hz), 4.95 (1 H, d, *J* 3 Hz), and 7.27 (5 H, br s); δ_C 16.5 (q), 17.1 (q), 19.4 (q), 25.0 (q), 25.1 (t), 28.4 (t), 32.7 (t), 34.7 (d), 39.1 (t), 49.7 (d), 53.8 (s), 59.1 (d), 72.7 (t), 73.0 (t), 75.2 (d), 104.5 (t), 110.8 (t), 127.4 (3 C, d), 128.2 (2 C, d), 135.5 (s), 138.2 (s), 138.8 (s), 148.4 (s), and 160.4 (s); $\nu_{max.}$ 3 590, 2 960, 2 875, 1 642, 1 455, 1 374, 1 100, 885, and 692 cm^{-1}.

TMS-Etherification of (**5**) *to give* (**7**).—A pyridine solution (100 ml) of (**5**) (9.48 g) was treated with TMSCl (3.7 ml) at room temperature for 12 h. The mixture was then diluted with aqueous $NaHCO_3$ and extracted with hexane–EtOAc (2:1). Silica-gel column chromatography of the extract gave (**7**) as an oil (9.84 g, 85%) (Found: C, 77.1; H, 10.0%. $C_{30}H_{46}O_2Si$ requires C, 77.20; H, 9.93%); $[\alpha]_D^{18}$ −38.8° (*c* 1.70 in $CHCl_3$); *m*/*z* 466 (M^+); δ_H 0.01 (9 H, s), 0.90 (3 H, s), 1.10 (3 H, d, *J* 6.5 Hz), 1.64 (3 H, br s), 1.85 (3 H, br s), 3.19 (1 H, t, *J* 9 Hz), 3.24 (1 H, br m), 3.49 (1 H, dd, *J* 9, 4 Hz), 4.16 (1 H, br s), 4.43 (1 H, d, *J* 12 Hz), 4.49 (1 H, d, *J* 12 Hz), 4.68 (2 H, m), 4.79 (1 H, d, *J* 3 Hz), 4.83 (1 H, d, *J* 2.5 Hz), and 7.28 (5 H, br s); δ_C 0.4 (3 C, q), 16.2 (q), 17.4 (q), 19.5 (q), 24.8 (q), 25.2 (t), 28.5 (t), 33.2 (t), 34.6 (d), 39.1 (t), 49.7 (d), 53.6 (s), 58.0 (d), 73.1 (2 C, t), 76.7 (d), 103.8 (t), 111.1 (t), 127.5 (d), 127.6 (2 C, d), 128.4 (2 C, d), 137.1 (s), 137.5 (s), 139.2 (s), 148.8 (s), and 161.5 (s); $\nu_{max.}$ 2 950, 1 640, 1 450, 1 368, 1 248, 1 080, 880, 838, 733, and 696 cm^{-1}.

Hydroboration of (**7**) *to give* (**8**).—A THF solution (5 ml) of (**7**) (4.90 g) was added to a THF solution (50 ml) of disiamylborane [prepared from 2-methylbut-2-ene (6.9 ml), BF_3·OEt_2 (3.8 ml), and $NaBH_4$ (980 mg)] at 0 °C and stirred at room temperature for 3 h. The mixture was then treated with 3M NaOH (10 ml) and H_2O_2 (35%; 10 ml) to give, after work-up and chromatographic purification, (**8**) as an oil (4.72 g, 96%) (Found: C, 74.1; H, 10.1%. $C_{30}H_{48}O_3Si$ requires C, 74.33; H, 9.98%); $[\alpha]_D^{18}$ −119.5° (*c* 1.97 in $CHCl_3$); δ_H 0.05 (9 H, s), 0.89 (3 H, s), 0.99 (3 H, d, *J* 7 Hz), 1.10 (3 H, d, *J* 7 Hz), 1.83 (3 H, br s), 2.59 (1 H, br m), 3.19 (1 H, t, *J* 9 Hz), 3.32 (1 H, br dd, *J* 10.5, 8.5 Hz), 3.48 (1 H, dd, *J* 9, 4 Hz), 3.61 (1 H, br dd, *J* 10.5, 5 Hz), 4.29 (1 H, br s), 4.42 (1 H, d, *J* 12 Hz), 4.48 (1 H, d, *J* 12 Hz), 4.83 (2 H, m), and 7.28 (5 H, br s); δ_C 0.5 (3 C q), 16.6 (q), 17.5 (2 C, q), 23.5 (t), 25.0 (q), 25.3 (t), 33.3 (t), 34.6 (d), 37.9 (d), 39.4 (t), 49.8 (d), 54.1 (s), 54.7 (d), 64.9 (t), 73.2 (2 C, t), 77.1 (d), 104.2 (t), 127.6 (d), 127.7 (2 C, d), 128.5 (2 C, d), 137.5 (s), 138.0 (s), 139.2 (s), and 161.4 (s); $\nu_{max.}$ 3 420, 2 955, 1 640, 1 450, 1 366, 1 246, 1 072, 878, and 840 cm^{-1}.

PCC-Oxidation of (**8**) *to give* (**9**).—A stirred CH_2Cl_2 solution (45 ml) of (**8**) (1.85 g) was treated with PCC (1.3 g), Celite (940 mg), and NaOAc (630 mg) under an N_2 atmosphere for 15 h at room temperature. The mixture was then diluted with ether and passed through a short Florisil column. Further chromatographic purification on a silica-gel column gave (**9**) as an oil (1.54 g, 84%) (Found: C, 74.4; H, 9.8%. $C_{30}H_{46}O_3Si$ requires: C, 74.64; H, 9.60%); $[\alpha]_D^{19}$ −160.4° (*c* 1.87 in $CHCl_3$); δ_H 0.03 (9 H, s), 0.92 (3 H, s), 1.04 (3 H, d, *J* 7 Hz), 1.10 (3 H, d, *J* 7 Hz), 1.82 (3 H, br s), 2.75 (2 H, br m), 3.19 (1 H, t, *J* 9 Hz), 3.47 (1 H, dd, *J* 9, 4 Hz), 4.32 (1 H, br s), 4.42 (1 H, d, *J* 12 Hz), 4.48 (1 H, d, *J* 12 Hz), 4.85 (2 H, br d, *J* 3 Hz), 7.27 (5 H, br s), and 9.67 (1 H, d, *J* 1 Hz); δ_C 0.5 (3 C, q), 13.1 (q), 16.4 (q), 17.4 (q), 25.0 (q), 25.0 (t), 25.4 (t), 33.5 (t), 34.7 (d), 38.9 (t), 48.2 (d), 49.7 (d), 53.4 (d), 53.9 (s), 73.1 (2 C, t), 77.1 (d), 104.4 (t), 127.7 (3 C, d), 128.5 (2 C, d), 136.8 (s), 139.1 (2 C, s), 161.4 (s), and 206.0 (d); $\nu_{max.}$ 2 955, 2 870, 2 720, 1 722, 1642, 1 454, 1 367, 1 248, 1 074, 874, 839, 746, and 697 cm^{-1}.

KF-*Catalysed Epimerization of* (**9**) *to give* (**10**).—An MeOH solution (40 ml) of (**9**) (1.54 g) was treated with KF (4 g) and Florisil (4 g) at room temperature for 15 h. The mixture was then diluted with water and extracted with ether, and the extract dried (K_2CO_3). The residue obtained by evaporation of the solvent under reduced pressure was chromatographed on a silica-gel column to give (**10**) as an oil {1.31 g, 85% [90% based on the consumed (**9**)]} (Found: C, 74.7; H, 9.8%. $C_{30}H_{46}O_3Si$ requires C, 74.64; H, 9.60%); $[\alpha]_D^{15}$ −94.5° (*c* 2.53 in $CHCl_3$); δ_H 0.03 (9 H, s), 0.94 (3 H, s), 0.98 (3 H, d, *J* 7 Hz), 1.10 (3 H, d, *J* 7 Hz), 1.86 (3 H, br s), 3.20 (1 H, t, *J* 9 Hz), 3.24 (1 H, br m), 3.48 (1 H, dd, *J* 9, 4 Hz), 4.20 (1 H, br s), 4.42 (1 H, d, *J* 12 Hz), 4.48 (1 H, d, *J* 12 Hz), 4.86 (1 H, br d, *J* 2.5 Hz), 7.27 (5 H, br s), and 9.65 (1 H, s); δ_C 0.4 (3 C, q), 7.8 (q), 16.5 (q), 17.5 (q), 24.0 (t), 25.1 (q), 25.4 (t), 33.4 (t), 34.6 (d), 39.8 (t), 49.5 (d), 49.9 (d), 53.0 (br s), 53.0 (br d), 73.1 (2 C, t), 78.6 (d), 104.2 (t), 127.6 (d), 127.7 (2 C, d), 128.5 (2 C, d), 136.0 (br s), 139.2 (2 C, s), 157.5 (br s), and 205.3 (d); $\nu_{max.}$ 2 955, 2 870, 2 700, 1 724, 1 642, 1 455, 1 368, 1 250, 1 097, 1 072, 877, 837, 734, and 697 cm^{-1}.

Formation of the Lactol TMS Ethers (**12a**) *and* (**12b**) *via* (**11**) *from* (**10**).—A mixture of (**10**) (2.27 g) and PPTS (2.2 g) in aqueous THF (80%; 110 ml) was stirred at room temperature for 2 d. After dilution with aqueous $NaHCO_3$, the mixture was extracted with EtOAc and chromatographed on a silica-gel column to give (**11**) as an oil (1.80 g, 94%); $[\alpha]_D^{15}$ −102.5° (*c* 2.96 in $CHCl_3$); $\nu_{max.}$ 3 450, 2 950, 1 720, 1 640, 1 450, 1 365, 875, 730, and 695 cm^{-1}; owing to its tautomeric nature the n.m.r. spectra of this compound were too complicated to be analysed. Subsequently, (**11**) (862 mg) was treated with TMSCl (0.55 ml) in pyridine (10 ml). After being stirred for 2 h at room

temperature, the mixture was diluted with aqueous $NaHCO_3$, and extracted with ether; work-up of the extract followed by chromatography on a silica-gel column gave the TMS ethers (**12a**) as an oil (551 mg, 54%) (Found: C, 74.7; H, 9.8%. $C_{30}H_{46}O_3Si$ requires C, 74.64; H, 9.60%); $[\alpha]_D^{15}$ −176.4° (*c* 1.48 in $CHCl_3$); δ_H 0.09 (9 H, s), 0.83 (3 H, d, *J* 7 Hz), 1.09 (3 H, d, *J* 7 Hz), 1.13 (3 H, s), 1.73 (3 H, br s), 3.19 (1 H, t, *J* 9 Hz), 3.52 (1 H, dd, *J* 9, 4 Hz), 3.74 (1 H, br s), 4.25 (1 H, d, *J* 8 Hz), 4.43 (1 H, d, *J* 12 Hz), 4.50 (1 H, d, *J* 12 Hz), 4.81 (1 H, d, *J* 2 Hz), 4.90 (1 H, d, *J* 2.5 Hz), and 7.28 (5 H, br s); δ_C 0.1 (3 C, q), 14.8 (q), 17.4 (q), 17.7 (q), 25.6 (q), 26.2 (t), 26.6 (t), 34.0 (t), 34.6 (d), 41.4 (t), 48.1 (s), 48.5 (d), 49.5 (d), 56.1 (d), 73.2 (t), 73.6 (t), 83.9 (d), 102.4 (d), 103.4 (t), 127.6 (d), 127.7 (2 C, d), 127.7 (s), 128.5 (2 C, d), 131.9 (s), 139.2 (s), and 163.9 (s); $\nu_{max.}$ 2 955, 2 870, 1 640, 1 454, 1 384, 1 367, 1 250, 1 122, 1 096, 1 041, 880, 842, 748, 732, and 696 cm^{-1}; and (**12b**) as an oil (273 mg, 27%) (Found: C, 74.6; H, 9.85%); $[\alpha]_D^{15}$ −176.4° (*c* 1.48 in $CHCl_3$); δ_H 0.08 (9 H, s), 0.77 (3 H, d, *J* 7 Hz), 1.10 (3 H, d, *J* 7 Hz), 1.15 (3 H, s), 1.74 (3 H, br s), 3.19 (1 H, t, *J* 9 Hz), 3.52 (1 H, dd, *J* 9, 4 Hz), 4.33 (1 H, br s), 4.43 (1 H, d, *J* 12 Hz), 4.50 (1 H, d, *J* 12 Hz), 4.81 (1 H, d, *J* 2 Hz), 4.86 (1 H, d, *J* 3 Hz), 4.92 (1 H, d, *J* 2.5 Hz), and 7.28 (5 H, br s); δ_C 0.1 (3 C, q), 14.9 (q), 17.5 (q), 17.9 (q), 25.5 (q), 25.6 (t), 26.7 (t), 34.5 (t), 35.4 (d), 40.8 (t), 46.3 (d), 48.0 (s), 49.3 (d), 51.1 (d), 73.2 (t), 73.7 (t), 77.1 (d), 95.4 (d), 104.5 (t), 126.5 (s), 127.6 (d), 127.8 (2 C, d), 128.5 (2 C, d), 132.9 (s), 139.2 (s), and 163.2 (s); $\nu_{max.}$ 2 955, 2 870, 1 642, 1 453, 1 366, 1 248, 1 094, 997, 896, 839, 745, and 697 cm^{-1}.

Cope Rearrangement of (**12a**) *and* (**12b**) *to give* (**13a**) *and* (**13b**).—(a) A toluene solution (5 ml) of (**12a**) (101 mg) was heated in a sealed tube at 180 °C for 24 h. Silica-gel column chromatography gave a mixture of a 2:1 mixture of (**13a**) and (**13b**) as an oil (82 mg, 81%) [Found: C, 74.7; H, 9.7% (analysed as a mixture). $C_{30}H_{46}O_3Si$ requires C, 74.64; H, 9.60%]; δ_H for (**13a**) 0.18 (9 H, s), 1.00 (3 H, s), 1.01 (6 H, d, *J* 7 Hz), 1.59 (3 H, br s), 2.75 (1 H, br m), 3.08 (1 H, t, *J* 9 Hz), 3.25 (1 H, dd, *J* 9, 4 Hz), 4.38 (1 H, d, *J* 12 Hz), 4.41 (1 H, d, *J* 12 Hz), 4.77 (1 H, d, *J* 8 Hz), 6.13 (1 H, d, *J* 3 Hz), and 7.26 (5 H, br s); δ_H for (**13b**) 0.12 (9 H, s), 0.93 (3 H, d, *J* 7 Hz), 1.00 (3 H, d, *J* 7 Hz), 1.03 (3 H, s), 1.59 (3 H, br s), 2.73 (1 H, br m), 3.08 (1 H, t, *J* 9 Hz), 3.25 (1 H, dd, *J* 9, 4 Hz), 4.38 (1 H, d, *J* 12 Hz), 4.41 (1 H, d, *J* 12 Hz), 5.04 (1 H, d, *J* 2.5 Hz), 5.98 (1 H, d, *J* 3 Hz), and 7.26 (5 H, br s); $\nu_{max.}$ 2 955, 2 870, 1 676, 1 454, 1 372, 1 252, 1 078, 1 014, 840, 750, 732, and 697 cm^{-1}.

(b) Similarly, a toluene solution (5 ml) of (**12b**) (105 mg) was heated in a sealed tube at 180 °C for 24 h to give a 1:4 mixture of (**13a**) and (**13b**) as an oil (77 mg, 73%).

Hydrolysis of a Mixture of (**13a**) *and* (**13b**) *to give* (**14**) *and Its Reduction to* (**15**).—A mixture of (**13a**) and (**13b**) (542 mg) was hydrolysed in aqueous THF (80%; 15 ml) with PPTS (300 mg) at room temperature for 15 h. The mixture was diluted with aqueous $NaHCO_3$, extracted with EtOAc, and chromatographed on a silica-gel column to give an anomeric mixture of the enol-lactol (**14**) as an oil [437 mg, 95% (α-anomer: β-anomer = 3:7)]; *m/z* 410 (M^+); δ_H 0.98—1.08 (6 H), 1.04 (3 H, s), 1.79 (3 H, br s), 2.72 (1 H, br m), 3.09 (1 H, t, *J* 9 Hz), 3.25 (1 H, dd, *J* 9, 4 Hz), 4.39 (1 H, d, *J* 12 Hz), 4.42 (1 H, d, *J* 12 Hz), 4.77 (0.3 H, br dd, *J* 8, 6 Hz), 5.09 (0.7 H, br t, *J* 2.5 Hz), 6.07 (0.7 H, d, *J* 2.5 Hz), 6.13 (0.3 H, d, *J* 3 Hz), and 7.26 (5 H, br s); $\nu_{max.}$ 3 415, 2 900, 2 850, 1 685, 1 454, 1 370, 1 100, 998, 734, and 698 cm^{-1}. Then, (**14**) (1.30 g) was treated with $NaBH_4$ (360 mg) in a mixture of MeOH (12 ml) and aqueous $NaHCO_3$ (3 ml) at 0—5 °C for 3 h. The mixture was then diluted with water, extracted with EtOAc, and the extract dried ($MgSO_4$). Silica-gel column chromatography of the extract gave (**15**) as an oil (1.22 g, 93%) (Found: M^+, 414.3135. $C_{27}H_{42}O_3$ requires *M*, 414.3132); $[\alpha]_D^{13}$ −6.9° (*c* 1.74 in $CHCl_3$); δ_H 0.73 (3 H, s), 0.89 (3 H, d, *J* 7 Hz), 1.02 (3 H, d, *J* 7 Hz), 1.59 (3 H, br s), 2.34 (1 H, d, *J* 14 Hz), 2.70 (1 H, br m), 3.09 (1 H, t, *J* 9 Hz), 3.27 (1 H, dd, *J* 9, 4 Hz), 3.29 (1 H, dd, *J* 11, 8.5 Hz), 3.42 (1 H, dd, *J* 10.5, 5 Hz), 3.61 (1 H, dd, *J* H, 4.5 Hz), 3.71 (1 H, dd, *J* 10.5, 5 Hz), 4.38 (1 H, d, *J* 12 Hz), 4.43 (1 H, d, *J* 12 Hz), and 7.27 (5 H, br s); δ_C 13.4 (q), 15.0 (q), 17.1 (q), 20.2 (q), 23.4 (t), 25.2 (t), 34.7 (d), 37.2 (t), 37.4 (t), 39.1 (d), 39.9 (t), 42.4 (d), 46.4 (s), 52.7 (2 C, d), 64.1 (t), 66.5 (t), 72 4 (t), 73.2 (t), 127.6 (3 C, d), 128.4 (2 C, d), 134.8 (s), 135.4 (s), and 138.9 (s); $\nu_{max.}$ 3 350, 2 955, 2 870, 1 454, 1 373, 1 238, 1 100, 1 090, 1 044, 733, and 696 cm^{-1}.

Acetylation of (**15**) *to give the Diacetate* (**20**).—A pyridine solution (12 ml) of (**15**) (1.20 g) was treated with Ac_2O (0.8 ml) and a catalytic amount of 4-dimethylaminopyridine (DMAP) at room temperature for 15 h. The mixture was diluted with aqueous $NaHCO_3$ and extracted with ether. The extract was chromatographed on a silica-gel column to give (**20**) as an oil (1.43 g, 99%) (Found: C, 74.9; H, 9.5%. $C_{31}H_{46}O_5$ requires C, 74.66; H, 9.30%); *m/z* 498 (M^+); $[\alpha]_D^{14}$ −23.2° (*c* 2.63 in $CHCl_3$); δ_H 0.74 (3 H, s), 0.86 (3 H, d, *J* 7 Hz), 1.02 (3 H, d, *J* 7 Hz), 1.59 (3 H, br s), 2.02 (6 H, s), 2.44 (1 H, d, *J* 14 Hz), 2.68 (1 H, br m), 3.09 (1 H, t, *J* 9 Hz), 3.27 (1 H, dd, *J* 9, 4 Hz), 3.88 (2 H, d, *J* 7 Hz), 4.06 (2 H, m), 4.39 (1 H, d, *J* 12 Hz), 4.44 (1 H, d, *J* 12 Hz), and 7.27 (5 H, br s); δ_C 11.5 (q), 14.9 (q), 17.1 (q), 20.1 (q), 20.8 (2 C, q), 23.3 (2 C, t), 34.5 (d), 34.6 (d), 37.1 (2 C, t), 40.1 (t), 42.4 (d), 46.0 (s), 49.4 (d), 52.7 (d), 65.7 (t), 68.7 (t), 72.2 (t), 73.1 (t), 127.5 (3 C, d), 128.4 (2 C, d), 134.6 (s), 135.6 (s), 139.1 (s), and 170.9 (2 C, s); $\nu_{max.}$ 2 950, 1 740, 1 453, 1 366, 1 230, 1 095, 1 031, 734, and 698 cm^{-1}.

Catalytic Hydrogenolysis of (**20**) *to give* (**21**).—An EtOH solution (15 ml) of (**20**) (1.43 g) was hydrogenolysed with Pd/C (5%; 130 mg) at room temperature for 15 h under an H_2 atmosphere. After removal of the catalyst by filtration, the solvent was removed and the residue was chromatographed on a silica-gel column to give (**21**) as an oil (1.14 g, 98%) (Found: M^+, 408.2828. $C_{24}H_{40}O_5$ requires *M*, 408.2874); $[\alpha]_D^{13}$ −14.4° (*c* 2.02 in $CHCl_3$); δ_H 0.76 (3 H, s), 0.88 (3 H, d, *J* 7 Hz), 0.95 (3 H, d, *J* 7 Hz), 1.62 (3 H, br s), 2.03 (3 H, s), 2.04 (3 H, s), 2.50 (1 H, d, *J* 14 Hz), 2.70 (1 H, br m), 3.15 (1 H, br dd, *J* 10.5, 9 Hz), 3.51 (1 H, dd, *J* 10.5, 6 Hz), 3.89 (1 H, d, *J* 7 Hz), and 4.07 (2 H, m); δ_C 11.4 (q), 14.9, 14.9 (q), 16.6 (q), 20.2 (q), 20.9 (2 C, q), 22.9 (t), 23.3 (t), 34.5 (d), 36.8 (d), 37.2 (2 C, t), 40.1 (t), 42.4 (d), 46.1 (s), 49.3 (d), 52.7 (d), 64.7 (t), 65.9 (t), 68.9 (t), 135.1 (s), 136.1 (s), 171.3 (2 C, s); $\nu_{max.}$ 3 440, 2 915, 1 730, 1 450, 1 365, 1 230, and 1 025 cm^{-1}.

THP-Etherification of (**21**) *to give* (**22**).—A CH_2Cl_2 solution (10 ml) of (**21**) (1.14 g), dihydropyran (0.45 ml), and PPTS (25 mg) was stirred at room temperature for 15 h. The mixture was diluted with aqueous $NaHCO_3$, extracted with ether, and the extract dried ($MgSO_4$). The extract was chromatographed on a silica-gel column to give (**22**) as an oil (1.32 g, 96%) (Found: M^+, 492.3435. $C_{29}H_{48}O_6$ requires: *M*, 492.3448); δ_H 0.76 (3 H, s), 0.88 (3 H, d, *J* 7 Hz), 1.00 (1.5 H, d, *J* 7 Hz), 1.02 (1.5 H, d, *J* 7 Hz), 1.60 (3 H, br s), 2.04 (6 H, s), 2.47 (1 H, d, *J* 14 Hz), 2.70 (1 H, br m), 3.0—4.0 (4 H, m), 3.89 (2 H, d, *J* 7 Hz), 4.07 (2 H, m), and 4.48 (1 H, br m); $\nu_{max.}$ 2 930, 1 738, 1 448, 1 362, 1 227, and 1 025 cm^{-1}.

Deacetylation of (**22**) *to give the Diol* (**23**).—A THF solution (10 ml) of (**22**) (1.32 g) was treated with LAH (200 mg) at 0—5 °C for 2 h. The mixture was diluted with ether and treated with a small amount of saturated aqueous NH_4Cl. The resultant supernatant was dried ($MgSO_4$) and evaporated and the residue was chromatographed on a silica-gel column to give (**23**) as an oil (1.10 g, 100%) (Found: M^+, 408.3226. $C_{25}H_{44}O_4$ requires: *M*, 408.3237); δ_H 0.74 (3 H, s), 0.89 (6 H, d, *J* 7 Hz), 1.00

(1.5 H, d, *J* 7 Hz), 1.02 (1.5 H, d, *J* 7 Hz), 1.60 (3 H, br s), 2.39 (1 H, d, *J* 14 Hz), 2.72 (1 H, br m), 3.0—4.0 (8 H, m), and 4.48 (1 H, br m); $\nu_{max.}$ 3 330, 2 930, 2 875, 1 452, 1 377, 1 117, and 1 023 cm^{-1}.

Dissolving Metal Reduction of (**23**) *to give an Isomeric Mixture of* (**24**).—Metallic Na (400 mg) was added with stirring to HMPA (20 ml) under an N_2 atmosphere. Bu^{t}OH (0.6 ml) was added to the blue solution formed. Compound (**23**) (1.10 g) in HMPA (5 ml) was then added at room temperature and stirring continued for 15 h. The mixture was then diluted with water and extracted with ether. Silica-gel column chromatography of the organic material gave an isomeric mixture of (**24**) as an oil (919 mg, 83%) (Found: M^+, 410.3400. $C_{25}H_{46}O_4$ requires: *M*, 410.3394); $\nu_{max.}$ 3 320, 2 950, 2 870, 1 454, 1 375, 1 240, 1 120, and 1 025 cm^{-1}.

Esterification of (**24**) *to give* (**25**), (**26**), *and* (**27**).—(a) Into a THF solution (10 ml) of BuLi (1.6M hexane solution; 1.38 ml) was added a THF solution (2 ml) of a stereoisomeric mixture of (**24**) (910 mg) at −78 °C under an N_2 atmosphere. The mixture was stirred to 10 min, after which pivaloyl chloride (0.3 ml) was added; the reaction mixture was then quenched with aqueous $NaHCO_3$ and extracted with EtOAc. Evaporation of the extract gave a residue which was chromatographed on a silica-gel column to give the dipivaloate (**27**) as an oily stereoisomeric mixture (334 mg, 29%), the 19-pivaloyl derivative (**26**) as an oily stereoisomeric mixture (158 mg, 16%), and the 9-pivaloyl derivative (**25**) as an oily stereoisomeric mixture (453 mg, 46%) (Found: M^+, 494.3966. $C_{30}H_{54}O_5$ requires *M*, 494.3968); $\nu_{max.}$ 3 430, 2 940, 2 870, 1 732, 1 460, 1 375, 1 282, 1 156, and 1 028 cm^{-1}; together with the recovered diol (**24**) (89 mg).

(b) Into a CH_2Cl_2 solution (2 ml) of (**24**) (193 mg) and pyridine (0.038 ml), pivaloyl chloride (0.058 ml) was added at −78 °C under an N_2 atmosphere. The mixture was warmed to −20 °C during 20 min after which it was diluted with aqueous $NaHCO_3$ and extracted with EtOAc; the extract was dried ($MgSO_4$) and evaporated and the residue subjected to chromatographic purification to give (**27**) (50 mg, 22%), (**26**) (107 mg, 55%), (**25**) (45 mg, 23%), and recovered (**24**) (33 mg).

LAH-Reduction of (**26**) *and* (**27**) *to give* (**24**).—A mixture of (**27**) (334 mg) and (**26**) (158 mg) in THF (5 ml) was treated with LAH (40 mg) at 0 °C for 30 min. The mixture was then diluted with ether and treated with a small portion of aqueous NH_4Cl. The supernatant was dried ($MgSO_4$) and the solvent evaporated; the residue was chromatographed on a silica-gel column to give (**24**) (368 mg, 100%).

Hydrolysis of the THP Group of (**25**) *and the Separation of the Stereoisomers* (**28**) *and* (**29**).—A MeOH solution (2 ml) of a stereoisomeric mixture of (**25**) (143 mg) was treated with *p*-TsOH (20 mg) at room temperature for 22 h. The mixture was diluted with aqueous $NaHCO_3$ and extracted with EtOAc. The extract was evaporated and the residue was chromatographed on a silica-gel column to give a stereoisomeric mixture of the diols (**28**) and (**29**). The separation of the isomers was performed by h.p.l.c. (Microporasil; $CHCl_3$–EtOAc = 5:1) to give compound (**28**) as an oil (62 mg, 52%) (Found: C, 73.1; H, 11.4. $C_{25}H_{46}O_4$ requires C, 73.12; H, 11.29%); $[\alpha]_D^{26}$ −3.2° (*c* 1.55 in $CHCl_3$); *m/z* 410 (M^+); δ_H 0.87 (3 H, d, *J* 7 Hz), 0.92 (3 H, s), 0.95 (3 H, d, *J* 7 Hz), 0.96 (3 H, d, *J* 6 Hz), 1.20 (9 H, s), 3.41 (1 H, dd, *J* 10.5, 7 Hz), 3.48 (2 H, d, *J* 7 Hz), 3.70 (1 H, dd, *J* 10.5, 3 Hz), 4.03 (1 H, dd, *J* 11.5, 5.5 Hz), and 4.10 (1 H, dd, *J* 11.5, 7 Hz); δ_C 11.5 (q), 16.4 (q), 21.2 (q), 22.7 (q), 23.0 (t), 27.3 (3 C, q), 28.2 (t), 31.0 (t), 36.0 (d), 37.8 (d), 38.8 (s), 39.2 (d), 39.4 (t), 39.7 (t), 41.9 (d), 44.8 (d), 44.8 (s), 45.3 (d), 50.3 (d), 65.7 (t), 67.6 (t), 67.7 (t), and 178.8 (s); $\nu_{max.}$ 3 360, 2 955, 2 870, 1 730, 1 710, 1 480, 1 462, 1 284, 1 154, and 1 032 cm^{-1}; and (**29**) as a powder (44 mg, 37%), m.p. 84—86 °C (Found: C, 73.1; H, 11.5%); $[\alpha]_D^{25}$ −28.6° (*c* 0.77 in $CHCl_3$); *m/z* 410 (M^+); δ_H 0.87 (3 H, d, *J* 6.5 Hz), 0.91 (3 H, s), 0.93 (3 H, d, *J* 7.5 Hz), 1.03 (3 H, d, *J* 6.5 Hz), 1.20 (9 H, s), 3.39 (1 H, dd, *J* 10.5, 7.5 Hz), 3.48 (2 H, d, *J* 6.5 Hz), 3.68 (1 H, dd, *J* 10.5, 4 Hz), 4.00 (1 H, dd, *J* 11.5, 6 Hz), and 4.14 (1 H, dd, *J* 11.5, 6 Hz); δ_C 11.6 (q), 16.7 (q), 21.1 (q), 21.7 (q), 23.3 (t), 27.3 (3 C, q), 27.6 (t), 33.1 (t), 37.9 (d), 38.8 (s), 39.4 (t), 39.9 (d), 40.1 (d), 42.0 (d), 45.0 (s), 45.9 (d), 50.1 (d), 50.3 (t), 52.4 (d), 65.8 (t), 66.5 (t), 67.6 (t), and 178.9 (s); $\nu_{max.}$ 3 345, 2 955, 2 870, 1 722, 1 448, 1 285, 1 154, and 1 025 cm^{-1}.

Formation of the Bis-selenide (**30**) *from* (**28**).—Bu_3P (0.066 ml) was added dropwise to a THF solution (2 ml) of the diol (**28**) (45.1 mg) and *o*-nitrophenyl selenocyanate (60 ml). After being stirred for 30 min at room temperature, the mixture was diluted with water and extracted with EtOAc. Silica-gel column chromatography of the extract afforded (**30**) as yellow needles (83.2 mg, 87%), m.p. 105—107 °C (Found: C, 57.0; H, 6.8; N, 3.6. $C_{37}H_{52}N_2O_6Se_2$ requires C, 57.07; H, 6.73; N, 3.60%); *m/z* 776, 778, and 780 (3:4:5; M^+); δ_H 0.93 (3 H, s), 0.98 (3 H, d, *J* 6.5 Hz), 1.06 (3 H, d, *J* 6.5 Hz), 1.10 (3 H, d, *J* 6 Hz), 1.13 (9 H, s), 2.71 (1 H, dd, *J* 11, 9 Hz), 2.82 (1 H, dd, *J* 11.5, 8.5 Hz), 2.90 (1 H, dd, *J* 11, 6.5 Hz), 4.10 (1 H, dd, *J* 11.5, 6 Hz), 7.30 (2 H, m), 7.51 (4 H, m), and 8.27 (2 H, dm, *J* 7.5 Hz); $\nu_{max.}$ 2 955, 2 870, 1 727, 1 510, 1 329, 1 301, 1 150, and 736 cm^{-1}.

Oxidative Treatment of (**30**) *to give* (**31**).—A THF solution (2 ml) of of the bis-selenide (**30**) (74.6 mg) was treated with H_2O_2 (35%, 0.05 ml) at room temperature for 6 h. The mixture was then diluted with water and extracted with hexane–EtOAc (3:1). Silica-gel column chromatography of the extract gave the diene (**31**) as an oil (30.8 mg, 86%) (Found: C, 80.0; H, 11.5. $C_{25}H_{42}O_2$ requires: C, 80.16; H, 11.30%); $[\alpha]_D^{27}$ +8° (*c* 0.99 in $CHCl_3$); *m/z* 374 (M^+); δ_H 0.90 (3 H, s), 1.00 (3 H, d, *J* 6.5 Hz), 1.17 (9 H, s), 1.68 (3 H, br s), 1.70 (3 H, br s), 2.46 (1 H, td, *J* 9.5, 7 Hz), 2.57 (1 H, br q, *J* 8 Hz), 3.98 (1 H, dd, *J* 11.5, 7 Hz), 4.00 (1 H, dd, *J* 11.5, 6 Hz), 4.65 (1 H, m), 4.66 (1 H, m), 4.71 (1 H, m), and 4.82 (1 H, br s); δ_C 19.0 (q), 21.4 (q), 22.1 (q), 22.9 (q), 27.2 (3 C, q), 28.5 (t), 28.7 (t), 31.8 (t), 38.7 (s), 38.8 (t), 40.3 (d), 40.9 (t), 44.5 (s), 45.9 (d), 49.7 (d), 50.1 (d), 50.5 (d), 65.1 (t), 110.6 (t), 111.6 (t), 146.9 (s), 147.3 (s), and 178.6 (s); $\nu_{max.}$ 3 080, 2 955, 2 870, 1 731, 1 644, 1 482, 1 460, 1 283, 1 157, and 886 cm^{-1}.

The LAH-Reduction of (**31**) *to give* (**32**).—A THF solution (2 ml) of (**31**) (29.5 mg) was treated with LAH (6 mg) at 0—25 °C for 1 h. The mixture was then diluted with aqueous NH_4Cl and extracted with EtOAc. The extract was evaporated under reduced pressure and the residue was purified by a silica-gel column chromatography to give (**32**) as an oil (21.8 mg, 95%) (Found: C, 82.9; H, 11.9. $C_{20}H_{34}O$ requires C, 82.70; H, 11.80%); $[\alpha]_D^{25}$ +22° (*c* 0.69 in $CHCl_3$); *m/z* 290 (M^+); δ_H 0.85 (3 H, s), 1.00 (3 H, d, *J* 6.5 Hz), 1.70 (3 H, m), 1.75 (3 H, m), 2.54 (1 H, td, *J* 9.5, 7 Hz), 2.59 (1 H, br q, *J* 8 Hz), 3.59 (1 H, dd, *J* 11, 7.5 Hz), 3.66 (1 H, br d, *J* 11 Hz), 4.66 (1 H, m), 4.70 (1 H, m), 4.82 (1 H, m), and 4.85 (1 H, m); δ_C 18.7 (q), 21.5 (q), 22.0 (q), 22.9 (q), 28.47 (t), 28.51 (t), 31.8 (t), 38.9 (t), 40.4 (d), 40.5 (t), 44.4 (s), 45.8 (d), 50.2 (d), 51.3 (d), 53.6 (d), 65.0 (t), 110.4 (t), 11.6 (t), 147.1 (s), and 150.1 (s); $\nu_{max.}$ 3 460, 3 075, 2 950, 2 865, 1 642, 1 452, 1 374, 1 030, 1 003, and 884 cm^{-1}.

Swern Oxidation of (**32**) *to give Dictymal* (**1**).—A CH_2Cl_2 solution (0.5 ml) of DMSO (0.1 ml) was added at −78 °C to a CH_2Cl_2 solution (2 ml) of ($COCl_2$) (0.063 ml) and the mixture was stirred at this temperature for 15 min under an N_2 atmosphere. A CH_2Cl_2 solution (1 ml) of (**32**) (140 mg) was then added and the mixture stirred for a further 30 min; after the addition of Et_3N (0.67 ml), the temperature was gradually

raised to −10 °C, and treated with aqueous $NaHCO_3$. The mixture was then extracted with EtOAc and the extract was dried ($MgSO_4$), the solvent evaporated, and the residue chromatographed on a silica-gel column to give (**1**) as an oil (*131* mg, *95%*); $[\alpha]_D^{29}$ +24° (*c* 0.46 in $CHCl_3$) (lit.,[9] +16.8°); δ_H 1.00 (3 H, d, *J* 7 Hz), 1.03 (3 H, s), 1.69 (6 H, br s), 2.35 (1 H, dd, *J* 9.5, 3.5 Hz), 2.60 (1 H, br q, *J* 8 Hz), 3.12 (1 H, td, *J* 9.5, 3.5 Hz), 4.66 (1 H, m), 4.69 (2 H, m), 4.83 (1 H, m), and 9.67 (1 H, d, *J* 3.5 Hz); $\delta_H(C_6D_6)$ 0.87 (3 H, s), 0.94 (3 H, d, *J* 6.8 Hz), 1.57 (3 H, m), 1.63 (3 H, m), 2.35 (1 H, dd, *J* 10, 3 Hz), 2.51 (1 H, m), 3.00 (1 H, m), 4.68 (1 H, m), 4.76 (2 H, m), 4.87 (1 H, m), and 9.56 (1 H, d, *J* 3 Hz); δ_C 20.5 (q), 21.9 (q), 22.5 (q), 22.9 (q), 28.5 (t), 28.9 (t), 31.8 (t), 39.8 (t), 40.4 (d), 41.2 (t), 45.9 (2 C, d), 47.8 (s), 50.2 (d), 64.8 (d), 110.2 (t), 112.1 (t), 146.7 (s), 147.0 (s), and 205.5 (d); $\nu_{max.}$ 3 080 2 955, 2 870, 2 715, 1 722, 1 644, 1 450, 1 373, and 886 cm^{-1}.

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