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AN ENOLATE CLAISEN ROUTE TO C-PYRANOSIDES

DEVELOPMENT AND APPLICATION TO AN IONOPHORE SYNTHON

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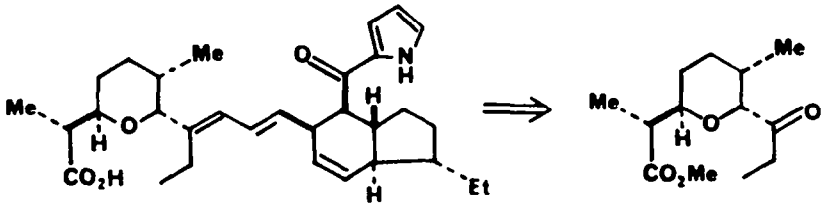
Abstract—A new method for the stereoselective synthesis of dihydropyrans of various substitution patterns is described, involving the Ireland ester enolate Claisen rearrangements of 6-alkenyl-1,4-dioxan-2-ones. The method has been applied to an enantioselective synthesis of the "left-wing" tetrahydropyran portion **2** of the ionophore antibiotic indanomycin (**1**). The synthetic sequence employed for the production of **2** proceeded in greater than 29% overall yield in 12 steps from the allylic alcohol **26**, thus underscoring the utility of the heterocycle synthesis described.

The C-pyranoside moiety is an important structural component in a variety of natural products of emerging chemical and biological significance. Such polysubstituted hydropyran units, wherein the ring carbons flanking the heterocycle oxygen have carbon side-chain substituents, are found in the ionophore antibiotics indanomycin (X-14547A) (**1**)[1] and salinomycin,[2] the antifungal agent ambruticin,[3] and the marine natural product palytoxin,[4] *inter alia*.

This presence has resulted in a number of reports describing synthetic approaches to C-pyranosides.[5,6] These efforts can be divided into two classifications: those involving modification of a carbohydrate by the introduction of a carbon nucleophile at the anomeric site of a pyranoside derivative, and those in which the hydropyran heterocycle is synthetically derived. In general, the first approach enjoys the advantage of ready access to highly functionalized, homochiral carbohydrate starting materials. The second approach has the potential for greater flexibility based upon its independence from carbohydrate structure, wherein excessive or inappropriate functionality can cause problems. In this paper we describe an example of a non-carbohydrate approach to structurally diverse C-pyranosides in racemic and optically pure forms, including an enantioselective synthesis of the "left-wing" tetrahydropyran subunit **2** of indanomycin (**1**).[7]



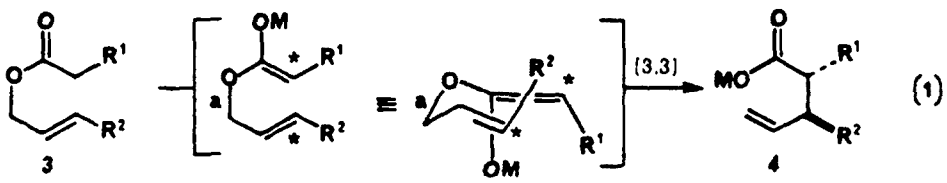
X-14547A
1

2

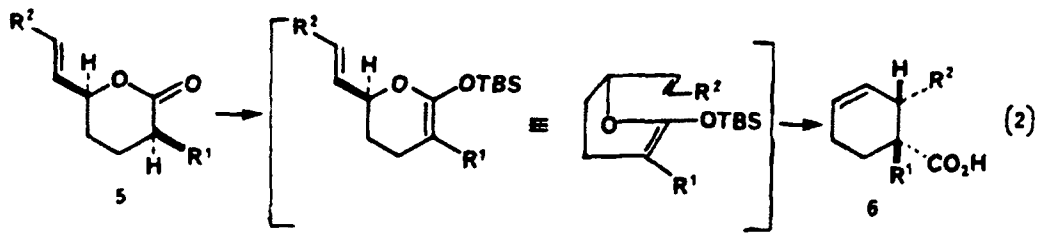
The Ireland ester enolate Claisen rearrangement[8] has been widely employed in our laboratories[9] and others[10] in a variety of modifications for the stereocontrolled synthesis of acyclic and cyclic carbon assemblages. In Eq. (1) this reaction is exemplified for an acyclic case, wherein the enolate (M = Li) or the trialkylsilyl ketene acetal (M = —SiR_3) of an allylic alcohol ester **3** undergoes a [3,3]-sigmatropic rearrangement to give a γ,δ-unsaturated acid derivative **4**. The power inherent in this synthetic procedure is derived from the stereoselective formation of a new C—C bond at the expense of the more readily accessible C—O bond, labeled "a" in the bracketed intermediate. Moreover, the remote carbon centers (*) which become the vicinal sp^3-stereocenters in **4** have readily controlled sp^2-carbon geometry, from which the relative orientation of the substituents R_1 and R_2 in the product are derived. Danishefsky *et al.* have reported[10a] a cyclic ester analog of this process (Eq. 2), by which vinyl lactones of general structure **5** were converted to cyclohexenecarboxylic acids **6**, wherein the stereochemical outcome reflected the bracketed boat-like pericyclic transition state.

Based upon these precedents, it seemed likely that substituted heterocycles should be similarly accessible. It thus became our initial goal to demonstrate that the generalized 6-alkenyl-1,4-dioxan-2-ones in Eqs (3) and (4) (**7** and **9**, respectively) could be transformed into the corresponding polysubstituted dihydropyrans of diastereomeric types **8** and **10**. It should be noted that each of the bracketed intermediates incorporates two boat-like six-atom arrays. Although both the preexisting heterocycle and the locus of the [3,3]-sigmatropic rearrangement would be required to adopt boat-like conformations, this was not expected to prevent the desired reorganization. More troublesome

† Research Fellow of the Alfred P. Sloan Foundation (1984–86); recipient of an NSF Presidential Young Investigator Award (1984–89).



(1)



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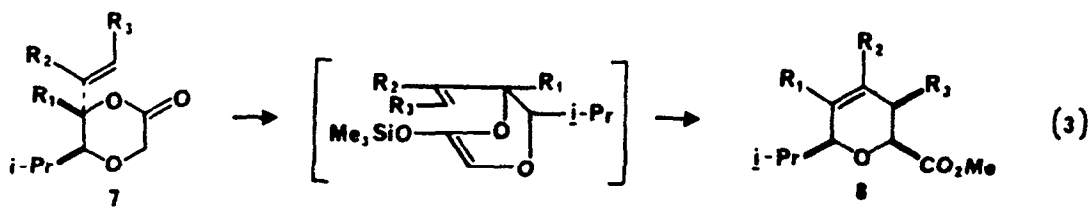
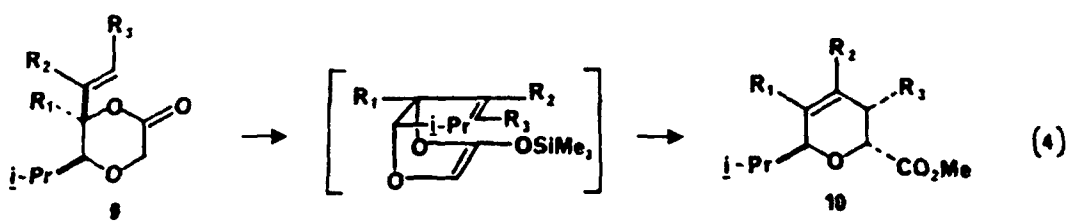


(3)



(4)

was the apparent projection (Eq. 4) of the C5-isopropyl residue into the pericyclic transition state leading to the dihydropyran diastereomer of general structure **10**. In light of the intended application of this method to the production of the ionophore synthon **2**, this concern had to be addressed.

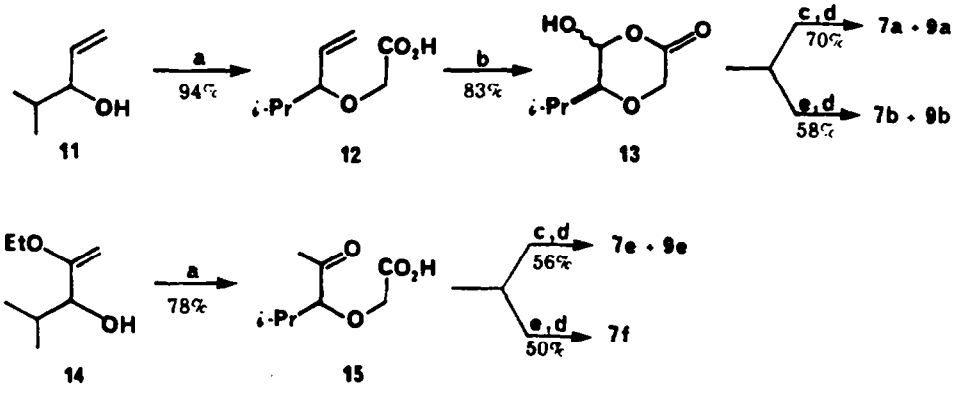
Although a means for selective production of the individual diastereomers **7** and **9** was ultimately desired and developed (*vide infra*), our initial preparations of the oxapyranones **7a–f** and **9a–e** proceeded with low to moderate diastereoselection. This was tolerable since we needed both diastereomeric types for evaluating the scope and limitations of the process, *and* because the diastereomeric 1,4-dioxan-2-ones were easily separated by column chromatography on silica gel and readily differentiated by ^{1}H-NMR spectroscopy (excluding **7e, f** and **9e**).

The sequence outlined in Scheme 1† is representative for these initial substituted 1,4-dioxan-2-one preparations. The ease and versatility of this general sequence rest, in large measure, to the fact that the carbon–carbon bond-forming reactions are simple 1,2-additions of vinylmetallic nucleophiles to aldehyde and/or ketone carbonyls. For example, O-alkylation of 4-methyl-1-penten-3-ol (**11**)‡ with the sodium salt of bromoacetic acid in tetrahydrofuran (THF) gave, after aqueous acid quench, the acetic acid derivative **12**. Cleavage of the vinyl residue in **12** via ozonolysis, followed by Kugelrohr distillation, afforded the lactol **13** in 83% yield. This aldehyde equivalent was reacted with excess vinylmagnesium bromide in THF at −78° to give a mixture of hydroxy acids which was treated directly with camphorsulfonic acid (CSA) in refluxing benzene to afford the *trans*- and *cis*-6-ethenyl-5-(1-methylethyl)-1,4-dioxan-2-ones **7a** and **9a** in 70% yield and in a ratio of 1.53 : 1.§ In analogous fashion, reaction of the lactol **13** with 2-propenylmagnesium bromide followed by acid-catalyzed lactonization gave the dioxanones **7b** and **9b** (2.54 : 1, 58%). Treatment of isobutyraldehyde with (α-ethoxyvinyl)lithium as described by Baldwin[11] afforded 2-ethoxy-4-methyl-1-

† In Schemes 1 and 2 all chiral substances were produced as racemates; a single enantiomer is shown for simplicity, and the names for these compounds in the Experimental section match the isomer shown. Yields cited in all schemes and tables are for chromatographically and spectroscopically pure substances.

‡ 4-Methyl-1-penten-3-ol is commercially available from Wiley Organics, Columbus, Ohio, U.S.A.

§ The diastereomer ratios were determined by glass capillary GLC using 25 m columns coated with either SE-54 or SUPEROX-4.



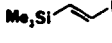
Scheme 1. (a) NaH, THF, 0 → 25°; $BrCH_2CO_2Na$, reflux; H_3O^+ quench. (b) O_3, CH_2Cl_2, −78°; Me_2S. (c) $H_2C{=}CHMgBr$, THF, −78°; H_3O^+ quench. (d) Camphorsulfonic acid, PhH, reflux. (e) $H_2C{=}C(CH_3)MgBr$, THF, −78°; H_3O^+ quench.

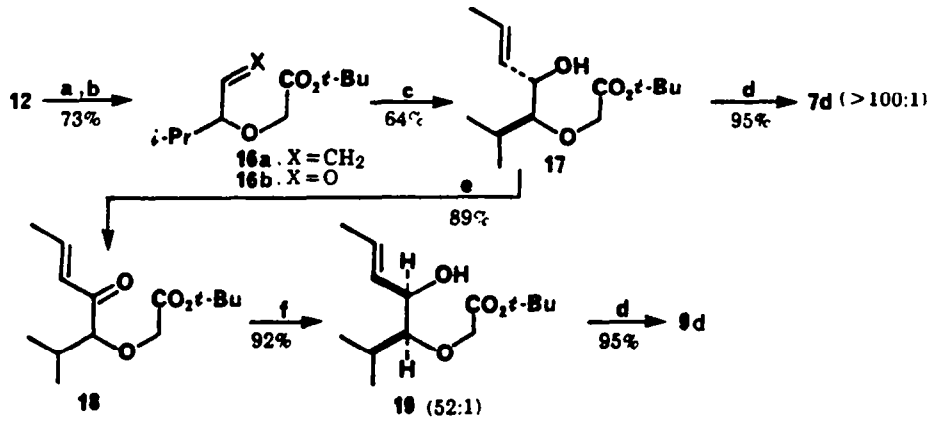
penten-3-ol (**14**), which provided the keto acid **15** upon O-alkylation and aqueous acid hydrolysis as described previously. Keto acid **15** exhibited significantly greater selectivity than the lactol **13** in the addition of vinylmagnesium bromide, leading to dioxanones **7e** and **9e** in a ratio of 9.6:1 (56%). Reaction of **15** with either 2-propenyllithium or the corresponding Grignard reagent gave, after lactonization, the dioxanone Claisen substrate **7f** in the absence of any detectable amount of the diastereomer.

The preparations of the various 6-alkenyl-5-alkyl-1,4-dioxan-2-one rearrangement substrates are summarized in Table 1.§ It should be noted that entry 3, utilizing [*trans*-β-(trimethylsilyl)vinyl]lithium[12] as the vinylmetallic, has not been optimized. In entries 5 and 6, the homogeneous *E*- and *Z*-1-propenylmagnesium bromide reagents were obtained from the corresponding vinyllithium species[13a,b] by treatment with anhydrous $MgBr_2$;[13c,d] direct formation of the Grignard reagents results in a scrambling of olefin geometry, as previously noted.[14]

After we had demonstrated the viability of the sigmatropic reorganization of the 6-alkenyl-1,4-dioxanone derivatives (Eqs 3 and 4 and the subsequent discussion), it became desirable to develop a stereocontrolled route for the selective production of either of the diastereomeric substances generalized as **7** and **9**. Such a sequence is illustrated in Scheme 2. It was clear that increased selectivity could be garnered by attenuating the reactivity of either the nucleophile or the carbonyl substrate, as exemplified by entries 2 and 7–10 in Table 1. Conversion of the acid **12** to the

Table 1. Preparation of 6-alkenyl-5-alkyl-1,4-dioxan-2-ones

Entry	Carbonyl substrate	Nucleophile	Products after lactonization (major/minor)	Yield (%)	Ratio
1	**13**		**7a/9a**, $R_1 = R_2 = R_3 = H$	70	1.53
2	**13**		**7b/9b**, $R_1 = R_3 = H$; $R_2 = Me$	58	2.54
3	**13**		**7c/9c**, $R_1 = R_2 = H$; $R_3 = SiMe_3$	17	1.90
4	**13**		**7d/9d**, $R_1 = R_2 = H$; $R_3 = Me$	63	1.00
5	**13**		**7d/9d**, $R_1 = R_2 = H$; $R_3 = Me$	62	1.31
6	**13**		**20/21**	61	1.30
7	**15**		**7e/9e**, $R_1 = Me$; $R_2 = R_3 = H$	56	9.60
8	**15**		**7e/9e**, $R_1 = Me$; $R_2 = R_3 = H$	61	2.30
9	**15**		**7f**, $R_1 = R_2 = Me$; $R_3 = H$	34	—
10	**15**		**7f**, $R_1 = R_2 = Me$; $R_3 = H$	50	—
11	**16b**		**7d/9d**	61	> 100
12	**18**	$Zn(BH_4)_2$	**9d/7d**	87	52
13	**27c**		**28a/28c**	76	24
14	**28b**	$Zn(BH_4)_2$	**28c/28a**	88	> 100



Scheme 2. (a) t-BuOH, DCC, DMAP, 25°. (b) O_3, CH_2Cl_2, −78°; Me_2S. (c) *trans*-$(MeCH{=}CH)_2CuLi$, Et_2O, −35°. (d) CF_3CO_2H, CH_2Cl_2, 25°. (e) PDC, DMF, 0°. (f) $Zn(BH_4)_2$, Et_2O, 0°.

corresponding t-butyl ester **16a** by the method of Hassner [t-BuOH, dicyclohexylcarbodiimide (DCC), 4-dimethylaminopyridine (DMAP), methylene chloride, 25°][15] (88%) was followed by unmasking the latent aldehyde via ozonolysis as before to give **16b** (83%). Addition of the cuprate derived from *trans*-1-propenyllithium[13a,b] to **16b** gave the Cram-cyclic product **17** (64%) in very high diastereomeric purity.[16] Lactonization was induced by trifluoroacetic acid in methylene chloride to provide the *trans*-5,6-disubstituted dioxanone **7d** in greater than 100:1 diastereomeric ratio. It was reasoned that if **7d** resulted from the addition of the vinylmetallic to the aldehyde carbonyl, then **9d** should be selectively accessible by the addition of a hydride nucleophile to the enone **18**. To effect the reversal in the order of introduction of C6-substituents, the allylic alcohol **17** was oxidized to the enone **18** with pyridinium dichromate (PDC) in dimethylformamide (DMF) at 0° in 89% yield.[17] Reduction proceeded cleanly (92%) with zinc borohydride in ether[18] at 0° to give the hydroxy ester **19** (major) and the epimer **17** in a ratio of 52:1. Trifluoroacetic acid-induced cyclization as before gave the lactone **9d** in 95% yield.

It is worth noting that the 5,6-*trans*-substituted dioxanones **7** invariably had higher R_f values in TLC analysis than the 5,6-*cis*-substituted counterparts **9**, with the ready separations by flash chromatography[19] following the elution order of first **7**, then **9**.

Another characteristic feature distinguishing the diastereomeric *trans*- and *cis*-5,6-disubstituted-1,4-dioxan-2-ones is the vicinal H_5, H_6 coupling in the ^{1}H-NMR spectra. As shown in Table 2, the *trans*-disubstituted isomers showed larger couplings (~ 9 Hz) than the corresponding *cis* isomers (~ 2.5 Hz), as expected.

With the dioxanones **7** and **9** in hand, we systematically investigated the enolate Claisen sequence advanced in Eqs (3) and (4). The substrate lactones were subjected to deprotonation, O-silylation and thermolysis procedures similar to the precedents of Ireland[8] and Danishefsky *et al.*[10a] Typically, deprotonation with lithium diisopropylamide (LDA) in THF at −78° was followed by the addition of chlorotrimethylsilane in Et_3N (−78 → 25°). The volatiles were removed *in vacuo* and the trimethylsilyl ketene acetal was dissolved, without isolation, in dry toluene and heated at 105–110° (bath temperature) for 3–4 h. After aqueous acid hydrolysis and treatment with ethereal diazomethane, the desired dihydropyran products were isolated by chromatography on silica gel in yields ranging from 52 to 91%, as summarized in Table 3. The energetic requirements imposed by the "double boat" transition states (Eqs 3 and 4) for the pericyclic reorganizations are reflected in the temperature and duration necessary for complete reaction. Whereas the typical acyclic Ireland enolate Claisen process occurs at or below ambient temperature in the silyl ketene acetals, rearrangement in the cases detailed herein did not occur at any appreciable rate in refluxing THF. Our observations in this area mirror those of Danishefsky *et al.* in their related studies.[10a]

Significantly, the projection of the isopropyl residue into the presumed pericyclic transition state leading from **9** to **10** seems to offer no impediment to rearrangement. However, a limitation was discovered in the attempted rearrangements of substrates with *cis*-terminal substitution on the alkenyl residue. For example, the substrates **20** and **21** were recovered unchanged after subjection to the rearrangement conditions and subsequent work-up as described.

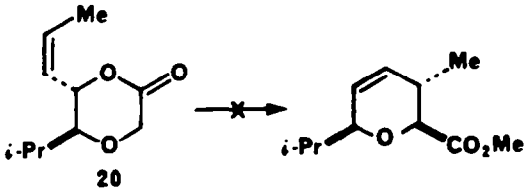
Table 2. Diagnostic ^{1}H-NMR couplings in *cis*- and *trans*-5,6-disubstituted 1,4-dioxan-2-ones

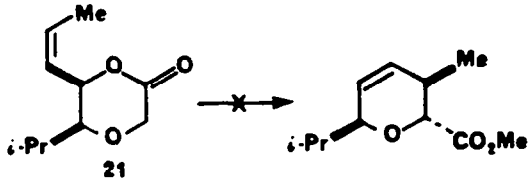
Entry	Compound	$J_{H5,H6}$ in Hz, stereochemistry (determined at 400 MHz in $CDCl_3$)
1	**7a**	8.96, *trans*
2	**7b**	9.22, *trans*
3	**7c**	8.97, *trans*
4	**7d**	9.03, *trans*
5	**20**	9.37, *trans*
6	**33**	9.34, *trans*
7	**9a**	2.28, *cis*
8	**9b**	3.09, *cis*
9	**9c**	2.73, *cis*
10	**9d**	2.34, *cis*
11	**21**	2.38, *cis*
12	**29**	2.46, *cis*

Table 3. 6-Alkenyl-1,4-dioxan-2-one enolate Claisen rearrangements to dihydropyrans[a]

Entry	Substrate	Dihydropyran product	Yield (%)
1	**7a**	**8a**, $R_1 = R_2 = R_3 = H$	67
2	**7b**	**8b**, $R_1 = R_3 = H$; $R_2 = Me$	75
3	**7c**	**8c**, $R_1 = R_2 = H$; $R_3 = SiMe_3$	52
4	**7d**	**8d**, $R_1 = R_2 = H$; $R_3 = Me$	70
5	**7e**	**8e**, $R_1 = Me$; $R_2 = R_3 = H$	90
6	**7f**	**8f**, $R_1 = R_2 = Me$; $R_3 = H$	80
7	**9a**	**10a**, $R_1 = R_2 = R_3 = H$	69
8	**9b**	**10b**, $R_1 = R_3 = H$; $R_2 = Me$	78
9	**9c**	**10c**, $R_1 = R_2 = H$; $R_3 = SiMe_3$	61
10	**9d**	**10d**, $R_1 = R_2 = H$; $R_3 = Me$	81
11	**9e**	**10e**, $R_1 = Me$; $R_2 = R_3 = H$	91
12	**29**	**30**	80
13	**33**	**34**	55

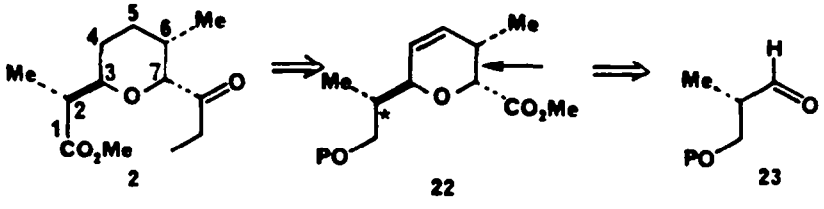
[a] Racemic substrates were used for entries 1–11. Enantiomerically homogeneous substrates were employed for entries 12 and 13. The stereochemical assignments for the products were derived from the known structures of the substrate dioxanones and the geometrical constraints in the rearrangement mechanism. The correlation of dihydropyran **30** with the known substance **2** provided corroboration.



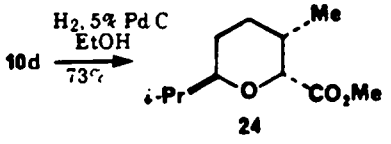


With the scope and limitations thus defined for this method of synthesis of polysubstituted dihydropyrans, we turned our attention to the intended application. The keto ester **2** is a degradation product[7e,k] of the ionophore antibiotic indanomycin (X-14547A) (**1**) and has served as an intermediate in the laboratory synthesis of **1**.[7d,i,k] During the course of this investigation, independent strategies for the synthesis of **2** or its equivalent were revealed by Nicolaou *et al.*,[7d,k] Ho,[7f] Ley and co-workers,[7i] none of which are related to our work. The importance of **2** as a subunit of indanomycin (**1**) and its structural similarity to subunits of other ionophore antibiotics led us to develop an efficient, enantioselective route to the indanomycin "left-wing" synthon, tetrahydropyran **2**.

Dihydropyran **22** was considered to be an appropriate precursor to the "left-wing" synthon **2** in that it possesses all four of the necessary centers of asymmetry and has functionality consistent with **2** by way of adjustment of oxidation state. In light of the preceding discussion, it is apparent that the γ,δ-unsaturated ester **22** should be accessible via an ester enolate Claisen rearrangement of a suitable 6 - alkenyl - 5 - alkyl - 1,4 - dioxan - 2 - one, analogous to the conversion **9** → **10** (Eq. 4). It was thus our intention to form the C6—C7 bond (arrow) in the [3,3]-sigmatropic reorganization, transforming remote sp^2-carbon geometries into vicinal sp^3-carbon stereocenters. Control of relative and absolute stereochemistry at C3, C6 and C7 on the heterocycle **22** (and ultimately **2**) was to be derived from the use of the known (*S*)-3-benzyloxy-2-methylpropionaldehyde (**23**, P = $-CH_2Ph$)[20] as starting material. Again, the use of chelation-controlled 1,2-additions[16] of vinylmetallic reagents was expected to allow the transfer of chirality from the pre-existing center (asterisk in **22**) to the remaining three stereogenic sites. Finally, it should be noted that the lack of substitution at C4 and C5 in the target **2** renders harmless the unnecessary unsaturation at these sites in **22**. In fact, it was anticipated that benzyl protection of the C1 oxygen functionality in **23** would be most desirable in that deprotection would occur in the course of catalytic hydrogenation of the C4—C5 olefinic residue.



The catalytic hydrogenations of the model dihydropyrans **10d** and **8d** proceeded readily as shown below to give the tetrahydropyrans **24** and **25**, respectively, in good yield. Therefore we did not anticipate any problems with the corresponding hydrogenation in the intended application.



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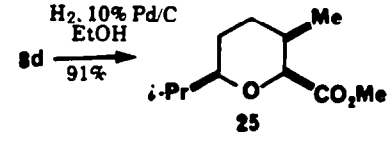

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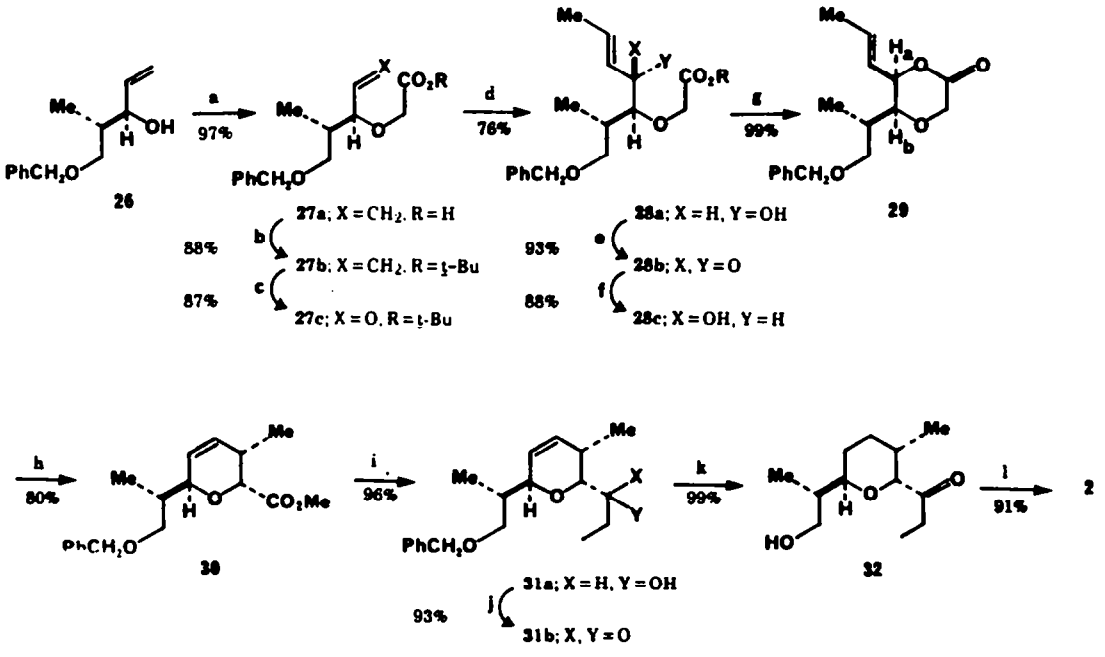
As detailed in Scheme 3, the enantioselective synthesis of the indanomycin precursor **2** proceeded in close analogy to the model studies already described. The allylic alcohol **26** was readily available via the chelation-controlled 1,2-addition of lithium divinylcuprate to (*S*)-3-benzyloxy-2-methylpropionaldehyde by the Still protocol.[16] O-Alkylation (NaH, $BrCH_2CO_2Na$, THF, reflux) proceeded in 97% yield to provide the acid **27a**, which was converted to the corresponding t-butyl ester **27b** by Hassner's method[15] (88%). Ozonolysis of the vinyl residue gave the aldehyde ester **27c** in 87% yield. Treatment of **27c** with the cuprate derived from *trans*-1-propenyllithium[13a,b] and $CuI \cdot PBu_3$ (Et_2O, −78°) gave in 76% yield a 24:1 mixture of allylic alcohol **28a** and its epimer.

A comparison of the stereochemistry of this predominant product and that required for the ultimate production of **2** (see Eq. 4) reveals that the carbinol stereocenter required inversion before lactonization and rearrangement. It should be noted that attempted Mitsunobu-type lactonizations[21] on the corresponding hydroxy acid were unsuccessful. The oxidation/reduction protocol of Scheme 2 was therefore administered to **28a** with good effect. Oxidation with pyridinium dichromate in DMF (−10°, 12 h)[17] gave the enone **28b** in 93% yield. Highly stereoselective reduction with ethereal zinc borohydride[18] gave the allylic alcohol **28c** in greater than 100:1 diastereomeric ratio. Again, this is the expected result of a Cram-cyclic 1,2-addition.

The Claisen rearrangement substrate **29** was formed in near quantitative yield by lactonization of **28c** with 30 mol% trifluoroacetic acid in refluxing benzene. The characteristic *cis* vicinal coupling of 2.46 Hz for the indicated hydrogens confirmed the desired stereochemistry for the 5,6-disubstituted-1,4-dioxan-2-one **29**. Conversion to the trimethylsilyl ketene acetal and thermolysis as previously described gave, after hydrolysis and esterification with ethereal diazomethane, the dihydropyran **30** (80%) and recovered **29** (10.5%).

At this stage, all four sp^3-carbon stereocenters had been established in their correct relative and absolute configurations. It remained to manipulate the



Scheme 3. (a) 3 equiv NaH, 1.1 equiv $BrCH_2CO_2H$, THF, reflux. (b) t-BuOH, DMAP (0.1 equiv), DCC, 25°. (c) O_3, CH_2Cl_2, −78°; Me_2S, −78 → 25°. (d) *trans*-$(MeCH{=}CH)_2CuLi$, Et_2O, −78°. (e) PDC, DMF, −10°, 12 h. (f) $Zn(BH_4)_2$, Et_2O, 0°, 1.5 h. (g) CF_3CO_2H (30 mol%), PhH, reflux, 3 h. (h) LDA, THF, −78°; Me_3SiCl, Et_3N, −78 → 25°; remove THF *in vacuo*, add $PhCH_3$, 110°, 4 h; CH_2N_2, Et_2O. (i) i-Bu_2AlH (1.2 equiv), Et_2O, −78°; EtMgBr (3 equiv), −78 → 25°. (j) $H_2Cr_2O_7$, aq acetone, 25°, 15 min. (k) H_2, 5% Pd/C, EtOH, 25°, 2 h. (l) $H_2Cr_2O_4$, aq acetone, 25°, 20 min; CH_2N_2, Et_2O, 0°.

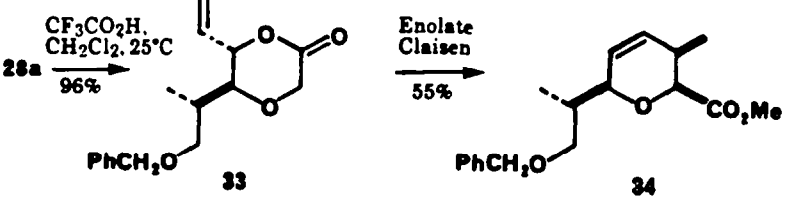
functionality in **30** to afford **2**. Specifically, the C7-carbomethoxy residue had to be converted to the ethyl ketone, the C4—C5 olefin had to be reduced, and the oxidation state at C1 had to be raised to the carboxylic acid level.

The first of these requirements was met by a one-pot procedure in which the ester **30** was treated first with 1.2 equiv of diisobutylaluminum hydride in ether at −78°, followed by 3 equiv of ethylmagnesium bromide (−78 → 25°). This afforded a single secondary alcohol **31a** (configuration unknown) in 96% yield. It has been our experience that α-alkoxyaldehydes are generally quite labile and prone to epimerization, if possible. These complications arose in the aldehyde derived from **30**, thus the development of the one-pot reduction/Grignard addition procedure. The scope and stereochemical implications of this method are under investigation and will be described elsewhere.[22] Jones oxidation of **31a** proceeded quickly at ambient temperature to give the ethyl ketone **31b** in 93% yield after chromatographic purification.

Catalytic hydrogenation of **31b** over 5% Pd/C effected the removal of the C4—C5 unsaturation and the cleavage of the benzyl ether protecting group at C1 to provide the saturated primary alcohol **32** in 99% yield. Finally, Jones oxidation and esterification with ethereal diazomethane gave the targeted ionophore synthon **2**, $[\alpha]_D^{26} = -23.18°$ (*c* 0.91, $CHCl_3$) [lit.[7a,d,k] $[\alpha]_D^{25} = -21.96°$ (*c* 0.85, $CHCl_3$); $-22.20°$ (*c* 1.6, $CHCl_3$)], in 91% yield. This substance was identical by high-field ^{1}H-NMR, IR, and ^{13}C-NMR to the material reported by Nicolaou *et al.*[7a,d,k]

The transformation of **26** → **2** detailed in Scheme 3 proceeded in nearly 30% overall yield. This level of efficiency through twelve synthetic steps was possible in that the poorest step proceeded in 76% yield, while ten of the steps proceeded in 87% yield or better.

The last entry for Table 3 is shown below, wherein the hydroxy ester **28a** was directly lactonized with trifluoroacetic acid to give the *trans*-disubstituted 1,4-dioxan-2-one **33**, which was subjected to the enolate Claisen in the usual manner. The all-*cis*-trisubstituted dihydropyran **34** was thus formed in an unoptimized yield of 55%.



In summary, a versatile and stereospecific synthesis of polysubstituted C-pyranosidic oxygen heterocycles has been developed. The method, based upon the Ireland ester enolate Claisen rearrangement of 6-alkenyl-5-alkyl-1,4-dioxan-2-ones, gives good to excellent yields of dihydropyrans of two diastereomeric types, generalized in Eqs (3) and (4). The production of racemic and optically pure hydropyrans of diverse structure has been demonstrated, and an application to the synthesis of an ionophore synthon proceeded in high overall yield. Future reports from these laboratories will detail further applications of these concepts to the synthesis of C-pyranosidic natural products and densely functionalized acyclic arrays.

EXPERIMENTAL

IR spectra were recorded on a Perkin–Elmer Model 682 or 727B or a Beckman IR 4210 spectrometer. ^{1}H-NMR spectra were recorded at 90 (Varian EM 390) or 400 MHz (Bruker WH-400) as indicated. ^{13}C-NMR spectra were recorded at 20 MHz on an IBM NR-80 spectrometer. Chemical shifts for proton and carbon resonances are reported in ppm (δ) relative to Me_4Si (δ 0.0). Optical rotations were measured on a Perkin–Elmer 243B digital polarimeter. Analytical HPLC was performed on an IBM 9533 liquid chromatograph, and analytical glass capillary gas chromatographic analyses were done on a Hewlett–Packard 5790A GC, utilizing 25 m capillary columns coated with SE-54 or SUPEROX-4 (Alltech Associates, Deerfield, IL).

TLC was done on Analtech TLC plates precoated with silica gel GHLF (250 μm layer thickness). Gravity column chromatography was done on E. Merck silica gel 60 (70–230 mesh) ASTM. Flash chromatography was performed as described by Still *et al.*[19]

THF and diethyl ether (Et_2O) were distilled from sodium benzophenone ketyl immediately before use. C_6H_6 was distilled from CaH_2 and stored over sodium ribbon. CH_2Cl_2 was distilled from P_2O_5 and passed through a column of alumina. Diisopropylamine was distilled from CaH_2 and stored over KOH pellets.

Moisture-sensitive reactions were performed in flame-dried glassware under a positive pressure of argon.

Elemental analyses were performed by Robertson Laboratory, Florham Park, NJ.

([(1-Methylethyl)-2-propenyl]oxy)acetic acid (**12**)

To a slurry of 8.88 g (0.296 mol) of 80% NaH dispersion in 100 ml of THF at 25° was added 10.0 g (0.0988 mol) of **11** in a dropwise fashion as a soln in 100 ml of THF. The mixture was allowed to stir at reflux for 12 h and was then cooled to 0°. Bromoacetic acid, 15.1 g (0.104 mol), was then introduced as a soln in 100 ml of THF and the mixture was stirred at reflux for 35 h. The soln was cooled to 0° and H_2O was added. The aq layer was extracted with Et_2O and the Et_2O extracts were discarded. The aq layer was then acidified to pH 4 with conc HCl and was then extracted repeatedly with Et_2O. The Et_2O extracts were dried ($MgSO_4$) and concentrated to afford 14.7 g (94%) of **12** as an oil: R_f 0.35 (1:4 Et_2O–hexanes, 1% HOAc); IR (film) 2960, 2550, 1720, 1460, 1420, 1380, 1375, 1240, 1110, 995, 970, 930, 890, 840 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.66–5.59 (m, 1H), 5.31 (d, 1H, J = 11.63 Hz), 5.19 (d, 1H, J = 17.26 Hz), 4.07 (ABq, 2H, J_{AB} = 17.02 Hz, $\Delta\nu_{AB}$ = 44.93 Hz), 3.45 (dd, 1H, J = 8.34, 6.69 Hz), 1.86–1.81 (m, 1H), 0.96 (d, 3H, J = 6.79 Hz), 0.87 (d, 3H, J = 6.79 Hz); ^{13}C-NMR ($CDCl_3$) δ 175.35, 135.73, 119.75, 87.96, 65.22, 32.39, 18.62, 18.11; MS (70 eV) base peak 57.

6-Hydroxy-5-(1-methylethyl)-1,4-dioxan-2-one (**13**)

Through a soln of 6.00 g (0.0377 mol) of **12** in 300 ml of CH_2Cl_2 at −78° was passed a stream of O_3 until a blue color persisted. A stream of N_2 was then passed through the soln until the blue color disappeared. Me_2S (50 ml) was then intro-

duced and the soln was allowed to warm to 25° and stir for 12 h. The soln was poured into H_2O and sat $NaHCO_3$ aq was added until pH 8 was achieved. The aq layer was extracted with Et_2O and the Et_2O extracts were discarded. The aq layer was then acidified with conc HCl and extracted repeatedly with Et_2O. The Et_2O extracts were dried ($MgSO_4$) and concentrated to afford the crude hydroxy acid. Kugelrohr distillation afforded 5.14 g (83%) of the lactol **13**: R_f 0.14 (3:2 hexanes–Et_2O, 1% HOAc); IR (film) 3200, 2960, 1730, 1470, 1430, 1390, 1370, 1230, 1120, 1020, 970, 880, 810 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 9.80 (br s, 1H), 8.80 (br s, 1H), 4.25 (s, 2H), 3.55 (m, 1H), 2.20 (m, 1H), 1.12 (d, 3H, J = 6.8 Hz), 1.05 (d, 3H, 6.8 Hz); MS (70 eV) base peak 55.

trans- *and* cis - 6 - *Ethenyl* - 5 - (1 - *methylethyl*) - 1,4 - *dioxan* - 2 - *one* (**7a, 9a**)

To a soln of 3.13 g (19.54 mmol) of **13** in 60 ml of dry THF at −78° was added 15.0 ml (19.5 mmol) of a 1 M soln in THF of vinylmagnesium bromide. The mixture was allowed to stir at −78° for 0.5 h whereupon an additional 18.07 ml (23.49 mmol) of vinylmagnesium bromide was introduced. The resulting cloudy mixture was stirred at −78° for 1.5 h then acidified to pH 2 with 5% HCl aq. The mixture was allowed to warm to 25° and to stir overnight. The mixture was then poured into H_2O and the aq layer was extracted with Et_2O twice. The combined organic extracts were then concentrated and the residue was taken up in 40 ml of C_6H_6 with ~ 30 mg of camphorsulfonic acid. This mixture was heated at reflux for 2 h under a Dean–Stark trap. After removal of the solvent the mixture of lactones was chromatographed on 60–200 mesh silica gel (elution with 4:1 hexanes–Et_2O) to afford 2.29 g (70%) of **7a** and **9a**. The diastereomer ratio **7a/9a** was found to be 1.53:1 by glass capillary GLC. Flash chromatography employing 230–400 mesh silica gel (elution with 7:1 hexanes–Et_2O) afforded pure **7a** and **9a**.

Data for **7a**. R_f 0.45 (2:1 hexanes–Et_2O); IR (film) 2980, 2940, 2890, 1755, 1655, 1475, 1435, 1390, 1375, 1350, 1340, 1310, 1270, 1235, 1160, 1120, 1010, 990, 945, 850, 830 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.82–5.73 (m, 1H), 5.48 (d, 1H, J = 17.11 Hz), 5.39 (d, 1H, J = 10.44 Hz), 4.85 (dd, 1H, J = 8.96, 8.23 Hz), 4.36 (ABq, 2H, J_{AB} = 17.67, $\Delta\nu_{AB}$ = 106.10 Hz), 3.26 (dd, 1H, J = 8.96, 2.74 Hz), 1.94–1.87 (m, 1H), 1.03 (d, 3H, J = 6.91 Hz), 0.92 (d, 3H, J = 6.91 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.05, 131.76, 120.64, 82.16, 79.68, 65.75, 27.74, 19.83, 14.83; MS (70 eV) parent peak 170, base peak 43.

Data for **9a**. R_f 0.43 (2:1 hexanes–Et_2O); IR ($CHCl_3$) 2950, 2860, 1755, 1640, 1476, 1415, 1395, 1356, 1320, 1280, 1240, 1130, 1060, 1020, 990, 950, 890 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.05–5.96 (m, 1H), 5.45 (d, 1H, J = 12.92 Hz), 5.44 (d, 1H, J = 15.00 Hz), 4.88 (dd, 1H, J = 7.65, 2.28 Hz), 4.38 (ABq, 2H, J_{AB} = 17.86 Hz, $\Delta\nu_{AB}$ = 68.92 Hz), 3.34 (dd, 1H, J = 9.83, 2.28 Hz), 1.69–1.60 (m, 1H), 1.01 (d, 3H, J = 6.63 Hz), 0.89 (d, 3H, J = 6.63 Hz); ^{13}C-NMR ($CDCl_3$) δ 166.97, 130.76, 121.34, 81.84, 80.24, 66.44, 29.00, 19.33, 17.74; MS (70 eV) parent peak 170, base peak 43. (Found: C, 63.47; H, 8.21. Calc for $C_9H_{14}O_3$: C, 63.51; H, 8.29%.)

trans- *and* cis - 6 - (1 - *Methylethenyl*) - 5 - (1 - *methylethyl*) - 1,4 - *dioxan* - 2 - *one* (**7b, 9b**)

To a soln of 3.93 g (24.51 mmol) of **13** in 60 ml of THF at −78° was added 40.0 ml (24.52 mmol) of 0.613 M isopropenylmagnesium bromide in THF. The mixture was allowed to stir at −78° for 0.5 h whereupon an additional 48.0 ml (29.42 mmol) of isopropenylmagnesium bromide was introduced. The resulting mixture was stirred at −78° for 1 h then quenched with 5% HCl aq and allowed to warm to 25° and to stir for 2 h. The mixture was poured into H_2O and the aq layer was extracted several times with Et_2O. The combined Et_2O extracts were concentrated and the residue was taken up in 40 ml of C_6H_6 with 50 mg of camphorsulfonic acid. This mixture was heated at reflux for 1 h under a Dean–Stark trap. After the solvent was removed the mixture was chromatographed on 60–200 mesh silica gel (elution with 4:1 hexanes–Et_2O) to afford 2.52 g (58%) of **7b** and **9b**. The diastereomer ratio **7b/9b** was found to be 2.54:1 by glass capillary GLC. Flash chromatography employing 230–400 mesh silica gel (elution with 7:1 hexanes–Et_2O) afforded pure **7b** and **9b**.

Data for **7b**. R_f 0.66 (50:50:1 hexanes–Et_2O–HOAc); IR (film) 3095, 2990, 2960, 2920, 2895, 2850, 1875, 1840, 1750, 1655, 1475, 1455, 1435, 1390, 1370, 1340, 1300, 1270, 1235, 1190, 1160, 1110, 1010, 975, 965, 940, 925, 865, 835, 740, 695 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.12–5.09 (m, 2H), 4.85 (d, 1H, J = 9.22 Hz), 4.36 (ABq, 2H, J_{AB} = 17.68 Hz, $\Delta\nu_{AB}$ = 101.96 Hz), 3.41 (dd, 1H, J = 9.22, 2.57 Hz), 1.86–1.78 (m, 1H), 1.77 (dd, 1H, J = 1.33, 0.87 Hz), 1.03 (d, 3H, J = 6.90 Hz), 0.92 (d, 2H, J = 6.90 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.34, 139.27, 117.83, 85.51, 77.83, 65.86, 22.76, 20.05, 16.91, 14.64; MS (70 eV) parent peak 184, base peak 56. (Found: C, 64.98; H, 9.01. Calc for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75%.)

Data for **9b**. R_f 0.64 (50:50:1 hexanes–Et_2O–HOAc); IR (film) 3090, 2960, 2920, 2870, 2830, 1755, 1680, 1470, 1450, 1430, 1390, 1350, 1325, 1265, 1220, 1185, 1120, 1065, 1010, 965, 955, 900, 875, 790, 730 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.13–5.07 (m, 2H), 4.89 (d, 1H, J = 3.09 Hz), 4.38 (ABq, 2H, J_{AB} = 17.73 Hz, $\Delta\nu_{AB}$ = 77.42 Hz), 3.37 (dd, 1H, J = 9.81, 3.07 Hz), 1.85 (dd, 3H, J = 1.45, 0.85 Hz), 1.67–1.62 (m, 1H), 1.02 (d, 3H, J = 6.60 Hz), 0.92 (d, 2H, J = 6.60 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.25, 139.94, 118.47, 84.67, 80.39, 66.34, 29.04, 19.14, 18.84, 18.72; MS (70 eV) parent peak 184, base peak 56.

[5*β*,6*α*-(*E*)]- *and* [5*β*,6*β* - (*E*)] - 5 - (1 - *Methylethyl*) - 6 - [2 - (*trimethylsilyl*)*ethenyl* - 1,4 - *dioxan* - 2 - *one* (**7c, 9c**)

To a slurry of 0.412 g (0.0138 mol) of 80% NaH dispersion in 15 ml of THF at 0° was added 2.00 g (0.0125 mol) of **13** in 10 ml of THF. The mixture was allowed to stir at 0° for 0.5 h then at 25° for 0.5 h. The mixture was then cooled to −78° and 0.0138 mol of [*trans*-*β*-(trimethylsilyl)vinyl] lithium was introduced. The [*trans*-*β*-(trimethylsilyl)vinyl] lithium reagent was produced by treatment of 5.53 g (0.0142 mol) of [*trans*-*β*-(trimethylsilyl)vinyl] tributyltin in 10 ml of THF at −78° with 8.60 ml (0.138 mol) of 1.6 M n-BuLi in hexanes followed by stirring of the resulting soln at −78° for 1 h then at −30° for 30 min.[12] After addition of the [*trans*-*β*-(trimethylsilyl)vinyl] lithium to the carboxylate the resulting mixture was allowed to stir at −78° for 1.3 h whereupon it was quenched with 5% HCl aq and allowed to warm to 25°. After stirring at 25° for 0.5 h, the mixture was poured into H_2O and the aq layer was extracted with Et_2O. The combined extracts were concentrated and the residue was taken up in 50 ml of C_6H_6 with 50 mg of camphorsulfonic acid. This mixture was heated at reflux for 1.5 h under a Dean–Stark trap. After removal of the solvent the mixture was chromatographed on 60–200 mesh silica gel (elution with 4:1 hexane–Et_2O) to afford 527 mg (17%) of **7c** and **9c**. The diastereomer ratio **7c/9c** was determined to be 1.9:1.0 by glass capillary GLC. Flash chromatography employing 230–400 mesh silica gel (elution with 5:1 hexane–Et_2O) afforded pure **7c** and **9c**.

Data for **7c**. R_f 0.76 (50:50:1 hexanes–Et_2O–HOAc); IR (film) 2960, 2890, 2870, 1750, 1625, 1460, 1425, 1380, 1360, 1340, 1310, 1270, 1240, 1230, 1140, 1110, 1080, 1040, 980, 935, 860, 835, 790, 770, 720, 690 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.15 (dd, 1H, J = 18.68, 1.03 Hz), 5.88 (dd, 1H, J = 18.68, 6.73 Hz), 4.82 (ddd, 1H, J = 8.97, 6.73, 0.96 Hz), 4.34 (ABq, 2H, J_{AB} = 17.64 Hz, $\Delta\nu_{AB}$ = 106.06 Hz), 3.23 (dd, 1H, J = 8.97, 2.85 Hz), 1.89–1.84 (m, 1H), 1.02 (d, 3H, J = 6.91 Hz), 0.92 (d, 3H, J = 6.91 Hz), 0.08 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 167.19, 138.23, 137.24, 83.55, 79.76, 65.75, 27.92, 19.88, 15.16, −1.72; MS (70 eV) parent peak 242, base peak 73.

Data for **9c**. R_f 0.66 (50:50:1 hexanes–Et_2O–HOAc); IR (film) 2950, 2875, 1750, 1620, 1470, 1430, 1385, 1340, 1240, 1220, 1140, 1125, 1050, 1030, 1000, 970, 940, 860, 840, 770, 760, 735, 700, 630 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.11–6.10 (m, 2H), 4.85 (dd, 1H, J = 5.95, 2.73 Hz), 4.39 (ABq, 2H, J_{AB} = 17.82 Hz, $\Delta\nu_{AB}$ = 73.54 Hz), 3.34 (dd, J = 9.76, 2.73 Hz), 1.64–1.60 (m, 1H), 1.03 (d, 3H, J = 6.62 Hz), 0.90 (d, 3H, J = 6.62 Hz), 0.10 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 167.03, 138.39, 137.05, 83.54, 80.30, 66.39, 29.03, 19.33, 17.75, −1.64; MS (70 eV) parent peak 242, base peak 73. (Found: C, 59.62; H, 9.17. Calc for $C_{12}H_{22}SiO_3$: C, 59.46; H, 9.14%.)

[5β,6α-(E)]- and [5β,6β - (E)] - 5 - (1 - Methylethyl) - 6 - (1 - propenyl) - 1,4 - dioxan - 2 - one (**7d, 9d**)

To a slurry of 130 mg (5.21 mmol) of 96% NaH suspension in 10 ml of THF at 0° was added 835 mg (5.21 mmol) of **13** in 20 ml of THF. The mixture was allowed to stir at 0° for 10 min, then allowed to warm to 25° and to stir for 20 min. After the soln had been cooled to −78°, 3.96 ml (6.25 mmol) of a 1.58 M soln of *trans*-propenyllithium in Et_2O was introduced dropwise and the soln was allowed to stir for 1.5 h whereupon it was quenched with 5% HCl aq and allowed to warm to 25° and to stir overnight. The mixture was poured into H_2O and the aq layer was extracted several times with Et_2O. The combined Et_2O extracts were concentrated, and the residue was taken up in 25 ml of C_6H_6 with 30 mg of camphorsulfonic acid. The soln was stirred at reflux for 2.5 h. After removal of the solvent the mixture was chromatographed on 60–200 mesh silica gel (elution with 4 : 1 hexanes–ether) to afford 600 mg (63%) of **7d** and **9d**. The diastereomer ratio **7d/9d** was found to be 1 : 1 by glass capillary GLC. Flash chromatography employing 230–400 mesh silica gel (elution with 7 : 1 hexanes–Et_2O) afforded pure **7d** and **9d**.

Data for **7d**. R_f 0.72 (1 : 1 hexanes–Et_2O); IR ($CHCl_3$) 3030, 2970, 2940, 2850, 2840, 1750, 1675, 1470, 1450, 1430, 1380, 1370, 1330, 1320, 1290, 1250, 1150, 1120, 1070, 1000, 980, 970, 940, 925, 910, 850, 690, 640 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.92 (dq, 1H, J = 15.24, 6.58 Hz), 5.37 (ddd, 1H, J = 15.24, 8.59, 1.53 Hz), 4.78 (dd, 1H, J = 9.03, 8.59 Hz), 4.33 (ABq, 2H, J_{AB} = 17.62 Hz, $\Delta\nu_{AB}$ = 105.81 Hz), 3.23 (dd, 1H, J = 9.03, 2.57 Hz), 1.90–1.83 (m, 1H), 1.75 (dd, 3H, J = 6.58, 1.53 Hz), 1.01 (d, 3H, J = 6.91 Hz), 0.88 (d, 3H, J = 6.91); ^{13}C-NMR ($CDCl_3$) δ 167.39, 133.45, 125.16, 82.64, 79.78, 65.87, 27.91, 19.94, 17.75, 14.82; MS (70 eV) parent peak 184, base peak 69.

Data for **9d**. R_f 0.65 (1 : 1 hexanes–Et_2O); IR ($CHCl_3$) 3010, 2965, 2940, 2920, 2880, 1740, 1645, 1480, 1450, 1430, 1385, 1350, 1310, 1280, 1250, 1230, 1165, 1120, 1035, 990, 970, 930, 920, 890, 830 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.91 (dq, 1H, J = 15.25, 6.44 Hz), 5.69 (ddd, 1H, J = 15.25, 8.66, 1.53 Hz), 4.83 (dd, 1H, J = 8.66, 2.34 Hz), 4.38 (ABq, 2H, J_{AB} = 17.81 Hz, $\Delta\nu_{AB}$ = 72.04 Hz), 3.30 (dd, 1H, J = 9.80, 2.34 Hz), 1.78 (dd, 3H, J = 6.44, 1.53 Hz), 1.75–1.58 (m, 1H), 1.02 (d, 3H, J = 6.63 Hz), 0.86 (d, 3H, J = 6.63 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.18, 133.75, 123.82, 82.12, 80.31, 66.41, 29.01, 19.21, 17.85, 17.68; MS (70 eV) parent peak 184, base peak 69. (Found: C, 65.00; H, 8.87. Calc for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75%.)

(1-Acetyl-2-methylpropoxy)acetic acid (**15**)

To a slurry of 12.5 g (0.416 mmol) of 80% NaH dispersion in 100 ml of THF at 0° was added 20.0 g (0.139 mmol) of **14** in a dropwise fashion as a soln in 100 ml of THF. The mixture was stirred at reflux for 24 h then cooled to 0° and bromoacetic acid (21.2 g, 0.153 mmol) was introduced dropwise as a soln in 100 ml of THF. The mixture was stirred at reflux for 37 h and was then cooled to 0° and H_2O was added. The aq layer was extracted with Et_2O and the Et_2O extracts were discarded. The aq layer was then acidified to pH 4 with conc HCl and extracted repeatedly with Et_2O. The combined Et_2O extracts were then concentrated and the residue was diluted with THF and stirred at 25° with 5% HCl aq for 2 h. The aq layer was then extracted with Et_2O and the Et_2O extracts were dried ($MgSO_4$) and concentrated to afford 19.0 g (78%) of the keto acid **15**: R_f 0.24 (3 : 2 hexanes–Et_2O, 1% HOAc); IR (film) 3500, 3140, 2970, 2940, 2880, 1730, 1460, 1430, 1390, 1370, 1355, 1240, 1130, 1040, 960, 940, 870, 800, 680 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.13 (ABq, 2H, J_{AB} = 16.85 Hz, $\Delta\nu_{AB}$ = 45.92 Hz), 3.64 (d, 1H, J = 5.10 Hz), 2.19 (s, 3H), 2.13–2.10 (m, 1H), 0.99 (d, 3H, J = 6.82 Hz), 0.92 (d, 3H, J = 6.82 Hz); ^{13}C-NMR ($CDCl_3$) δ 210.24, 173.53, 91.97, 68.75, 30.85, 26.10, 18.97, 16.83; MS (70 eV) parent peak 174, base peak 55.

trans- *and* cis - 6 - *Ethenyl* - 6 - *methyl* - 5 - (1 - *methylethyl*) - 1,4 - *dioxan* - 2 - *one* (**7e, 9e**)

To a soln of 330 mg (1.89 mmol) of **15** in 30 ml of THF at 0° was added 1.9 ml (1.9 mmol) of a 1 M soln of vinylmagnesium bromide in THF. The mixture was allowed to stir at 0° for 0.5 h whereupon an additional 2.44 ml (2.44 mmol) of vinylmagnesium bromide was introduced. The resulting cloudy mixture was allowed to stir at 0° for 1.5 h then acidified with 5% HCl aq and warmed to 25°. The mixture was then poured into H_2O and the aq layer was extracted with Et_2O. The combined organic extracts were then concentrated and the residue was taken up in 30 ml of C_6H_6 with 10 mg of camphorsulfonic acid. This mixture was heated at reflux for 2 h under a Dean–Stark trap. After removal of the solvent the mixture was chromatographed on 60–200 mesh silica gel (elution with 4 : 1 hexanes–Et_2O) to afford 195 mg (56%) of **7e** and **9e**. The diastereomer ratio of **7e/9e** was found to be 9.6 : 1 by glass capillary GLC. Flash chromatography on 230–400 mesh silica gel (elution with 5 : 1 hexanes–Et_2O) afforded pure **7e** and **9e**.

Data for **7e**. R_f 0.65 (50 : 50 : 1 hexanes–Et_2O–HOAc); IR (film) 3220, 2960, 2840, 1750, 1480, 1440, 1430, 1410, 1360, 1285, 1190, 1130, 1080, 1050, 1030, 990, 890, 850, 795, 720 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.86 (dd, 1H, J = 17.28, 10.83 Hz), 5.45 (dd, 1H, J = 17.28, 0.52 Hz), 5.32 (dd, 1H, J = 10.83, 0.52 Hz), 4.35 (ABq, 2H, J_{AB} = 17.70 Hz, $\Delta\nu_{AB}$ = 106.73 Hz), 3.18 (d, 1H, J = 5.25 Hz), 1.85–1.61 (m, 3H), 1.53 (s, 3H), 0.99 (d, 3H, J = 6.77 Hz), 0.98 (d, 3H, J = 6.77 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.07, 137.70, 116.87, 85.79, 83.60, 65.99, 28.21, 21.69, 19.12, 17.85; MS (70 eV) parent peak 184, base peak 55. (Found: C, 65.24; H, 8.77. Calc for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75%.)

Data for **9e**. R_f 0.63 (50 : 50 : 1 hexanes–Et_2O–HOAc); IR (film) 3070, 2960, 2850, 1750, 1650, 1470, 1430, 1420, 1390, 1380, 1340, 1300, 1270, 1160, 1140, 1080, 1030, 1000, 980, 950, 940, 860, 820, 780, 710 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.07 (dd, 1H, J = 17.32, 10.90 Hz), 5.35 (d, 1H, J = 17.32 Hz), 5.32 (d, 1H, J = 10.90 Hz), 4.36 (ABq, 2H, J_{AB} = 17.85 Hz, $\Delta\nu_{AB}$ = 95.30 Hz), 3.27 (d, 1H, J = 4.43 Hz), 1.87–1.83 (m, 1H), 1.49 (s, 3H), 1.05 (d, 3H, J = 6.81 Hz), 0.95 (d, 3H, J = 6.81 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.87, 136.11, 116.98, 85.97, 84.97, 66.47, 28.57, 23.43, 22.15, 17.79; MS (70 eV) parent peak 184, base peak 55.

trans - 6 - *Methyl* - 6 - (1 - *methylethenyl*) - 5 - (1 - *methylethyl*) - 1,4 - *dioxan* - 2 - *one* (**7f**)

To a soln of 407 mg (2.33 mmol) of **15** in 50 ml of THF at −78° was added 2.1 ml (2.31 mmol) of 1.10 M isopropenylmagnesium bromide in THF. The mixture was allowed to stir at −78° for 0.5 h whereupon an additional 3.21 ml (3.53 mmol) of isopropenylmagnesium bromide was introduced. The resulting mixture was stirred at −78° for 1 h then quenched with 5% HCl aq and allowed to warm to 25° and to stir for 1 h. The mixture was poured into H_2O and the aq layer was extracted with Et_2O. The combined Et_2O extracts were concentrated and the residue was taken up in 20 ml of C_6H_6 with 20 mg of camphorsulfonic acid. The mixture was heated at reflux for 1.5 h under a Dean–Stark trap. After the solvent was removed the mixture was chromatographed on 60–200 mesh silica gel (elution with 4 : 1 hexane–Et_2O) to afford 225 mg (50%) of **7f** exclusively. R_f 0.63 (50 : 50 : 1 hexanes–Et_2O–HOAc); IR (film) 3085, 2950, 2870, 1750, 1650, 1480, 1390, 1360, 1290, 1215, 1145, 1070, 1035, 1020, 975, 920, 890, 820, 790, 730 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.12 (s, 1H), 5.07 (s, 1H), 4.31 (ABq, 2H, J_{AB} = 17.75 Hz, $\Delta\nu_{AB}$ = 92.33 Hz), 3.42 (d, 1H, J = 5.09 Hz), 1.81 (s, 3H), 1.78–1.70 (m, 1H), 1.56 (s, 3H), 0.95 (d, 3H, J = 6.48 Hz), 0.93 (d, 3H, J = 6.48 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.86, 143.95, 115.72, 88.67, 80.97, 66.29, 28.48, 21.72, 19.30, 19.03, 17.97; MS (70 eV) base peak 56. (Found: C, 66.58; H, 9.15. Calc for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%.)

([1-(1-Methylethyl)-2-propenyl]oxy)acetic acid 1,1-*dimethylethyl ester* (**16a**)

A mixture of 5.0 g (34.41 mmol) of **12**, 7.12 g (34.51 mmol) of 1,3-dicyclohexylcarbodiimide, 3.0 ml (99.20 mmol) of t-butyl alcohol and 384 mg (3.14 mmol) of 4-dimethylaminopyridine in 75 ml of anhydrous CH_2Cl_2 was allowed to stir at room temp for 10 h. Concentration of the reaction mixture *in vacuo*

and purification by flash chromatography (elution with 1:6 Et_2O–hexanes) afforded 5.9 g (88%) of **16a**, homogeneous by TLC and spectroscopic analysis: R_f 0.77 (1:1 Et_2O–hexanes); IR ($CHCl_3$) 3090, 3010, 2980, 2942, 2879, 2117, 1943, 1795, 1686, 1478, 1460, 1433, 1397, 1370, 1311, 1239, 1164, 1121, 1030, 1000, 974, 936, 891, 800 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.68–5.59 (m, 5H), 5.25 (dd, 1H, J = 10.31, 1.94 Hz), 5.16 (dd, 1H, J = 17.40, 1.88 Hz), 3.91 (ABq, 2H, J_{AB} = 16.34 Hz, $\Delta\nu_{AB}$ = 34.21 Hz), 3.44 (dd, 1H, J = 7.97, 6.97 Hz), 1.86–1.79 (m, 1H), 1.46 (s, 9H), 0.97 (d, 3H, J = 6.78 Hz), 0.87 (d, 3H, J = 6.78 Hz); ^{13}C-NMR ($CDCl_3$) δ 169.83, 136.39, 118.65, 87.06, 80.85, 65.99, 32.34, 27.98, 18.49, 17.99; MS (15 eV) base peak 57, parent peak 214. (Found: C, 67.26; H, 10.37. Calc for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35%.)

(1-Formyl-2-methylpropoxy)acetic acid 1,1-*dimethylethyl ester* (**16b**)

A soln of 1.48 g (6.91 mmol) of **16a** in 60 ml of dry CH_2Cl_2 was cooled to −78° and ozone was bubbled through until a distinct blue color persisted. After the mixture had stirred at −78° for 5 min, argon was bubbled through the soln for 5 min to dissipate the excess O_3. The mixture was then treated with 1.0 ml (13.82 mmol) of Me_2S and allowed to warm to room temp and to stir overnight. Concentration and flash chromatography (elution with 1:3 Et_2O–hexanes) gave 1.24 g (83%) of **16b** as a colorless oil, homogeneous by TLC and spectroscopic criteria: R_f 0.52 (1:1 Et_2O–hexanes); IR ($CHCl_3$) 3022, 2979, 2942, 2880, 1741, 1472, 1434, 1395, 1376, 1310, 1235, 1124, 845 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.64 (d, 1H, J = 2.55 Hz), 4.03 (s, 2H), 3.45 (dd, 1H, J = 5.44, 2.55 Hz), 2.08–2.03 (m, 1H), 1.40 (s, 9H), 0.96 (d, 3H, J = 6.84 Hz), 0.95 (d, 3H, J = 6.84 Hz); ^{13}C-NMR ($CDCl_3$) δ 203.47, 169.28, 89.51, 82.00, 68.87, 30.34, 28.03, 18.27, 17.30; MS (15 eV) base peak 57.

[*S*,S** - (*E*)] - ([-2 - *Hydroxy* - 1 - (1 - *methylethyl*) - 3 - *pentenyl*]*oxy*)*acetic acid* 1,1 - *dimethylethyl ester* **17**

To a mixture of 418 mg (1.06 mmol) of CuI · Bu_3P in 5.0 ml of dry Et_2O at −35° was added dropwise 1.62 ml of a 1.31 M ethereal soln of *trans*-propenyllithium.[15a,b] The resulting yellow soln was allowed to stir at −35° for 30 min at which time 115 mg (0.35 mmol) of **16b** was added in 3 ml of Et_2O. After stirring at −35° for 3 h, the mixture was quenched with excess MeOH followed by a 1:1 soln of 3% NH_4OH aq and sat NH_4Cl. The layers were partitioned, and the aq phase was extracted three times with Et_2O. The combined organic extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:7 Et_2O–hexanes) gave 87.3 mg (64%) of **17** as a single diastereomer (> 100:1 by capillary GLC), homogeneous by TLC and spectroscopic criteria: R_f 0.27 (1:1 Et_2O–hexanes); IR ($CHCl_3$) 3440, 3010, 2980, 2940, 2880, 1860, 1680, 1470, 1460, 1435, 1395, 1370, 1295, 1155, 1130, 1085, 1025, 1005, 970, 940, 910, 850 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.78 (dq, 1H, J = 15.26, 6.25 Hz), 5.36 (ddd, 1H, J = 15.26, 7.83, 1.65 Hz), 4.65–4.58 (br s, 1H), 4.12 (ABq, 2H, J_{AB} = 16.86 Hz, $\Delta\nu_{AB}$ = 169.09 Hz), 4.06 (dd, 1H, J = 8.09, 7.83 Hz), 2.97 (dd, 1H, J = 8.09, 2.55 Hz), 1.86–1.78 (m, 1H), 1.69 (dd, 3H, J = 6.52, 1.65 Hz), 1.46 (s, 9H), 0.97 (d, 3H, J = 6.91 Hz), 0.86 (d, 3H, J = 6.91 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.52, 130.04, 128.92, 92.86, 82.45, 73.47, 71.24, 29.90, 28.04, 20.56, 17.82, 15.69; MS (15 eV) base peak 69. (Found: C, 64.87; H, 10.22. Calc for $C_{14}H_{26}O_4$: C, 65.09; H, 10.14%.)

Conversion of **17** *to* **7d**. A mixture of 50 mg (0.193 mmol) of **17** and 5 μl (0.064 mmol) of trifluoroacetic acid in 2 ml of anhydrous CH_2Cl_2 was stirred at room temp for 1 h. Concentration under reduced pressure and flash chromatography (elution with 1:7 Et_2O–hexanes) provided 33.7 mg (95%) of **7d** which was identical in all respects to the material produced previously.

Conversion of **17** *to* **9d**. To a soln of 150 mg (0.58 mmol) of **17** in 4 ml of dry DMF at 0° was added 328 mg (0.87 mmol) of pyridinium dichromate. The resulting mixture was allowed to stir at 0° for 5 h and then poured into 15 ml of H_2O. The aq layer was extracted five times with Et_2O, dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:7 Et_2O–hexanes) gave 132 mg (89%) of **18**, homogeneous by TLC and spectroscopic criteria: R_f 0.54 (1:2 Et_2O–hexanes); IR ($CHCl_3$) 2935, 2889, 1732, 1691, 1610, 1432, 1389, 1382, 1300, 1238, 1220, 1160, 1131, 1069, 1032, 980, 939, 851 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.04 (dq, 1H, J = 15.54, 6.87 Hz), 6.51 (dd, 1H, J = 15.54, 1.72 Hz), 3.93 (ABq, 2H, J_{AB} = 16.36 Hz, $\Delta\nu_{AB}$ = 92.21 Hz), 3.64 (d, 1H, J = 6.41 Hz), 2.04–1.99 (m, 1H), 1.91 (dd, J = 6.87, 1.72 Hz), 1.45 (s, 9H), 1.43 (d, 3H, J = 6.79 Hz), 0.94 (d, 3H, J = 6.79 Hz); ^{13}C-NMR ($CDCl_3$) δ 200.18, 168.95, 144.03, 127.02, 90.27, 81.64, 68.06, 31.17, 28.04, 18.67, 18.39, 17.96; MS (15 eV) base peak 57.

To a soln of 27 mg (0.105 mmol) of **18** in 2 ml of anhydrous Et_2O at 0° was added 0.24 ml of a 0.145 M ethereal soln of zinc borohydride. The mixture was allowed to stir at 0° for 1.5 h and was then poured into sat NH_4Cl aq. The aq layer was extracted three times with Et_2O and the combined Et_2O extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:7 Et_2O–hexanes) yielded 24.8 mg (92%) of esters **19** (major) and **17** (minor) in a ratio of 52:1 as determined by capillary GLC (170°, isothermal, 25 M Superox 4, flow rate 1.5 ml min^{-1}). Analytical data for **19**: R_f 0.42 (1:1 Et_2O–hexanes); IR ($CHCl_3$) 3620, 3540–3300, 3019, 2981, 2960, 2880, 1731, 1472, 1451, 1430, 1397, 1378, 1371, 1250, 1160, 1131, 1048, 972 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.73 (dq, 1H, J = 15.47, 6.32 Hz), 5.69 (ddd, 1H, J = 15.47, 6.72, 1.32 Hz), 4.12 (ABq, 2H, J_{AB} = 17.06 Hz, $\Delta\nu_{AB}$ = 173.53 Hz), 4.08 (m, 1H), 3.05 (dd, 1H, J = 9.14, 2.69 Hz), 1.72 (dd, 3H, J = 6.32, 1.37 Hz), 1.70–1.68 (m, 1H), 1.47 (s, 9H), 0.99 (d, 3H, J = 6.73 Hz), 0.87 (d, 3H, J = 6.73 Hz); ^{13}C-NMR ($CDCl_3$) δ 172.22, 129.49, 128.49, 93.87, 82.69, 73.21, 71.23, 31.22, 28.21, 19.80, 19.09, 18.06; MS (15 eV) base peak 69. (Found: C, 65.15; H, 10.30. Calc for $C_{14}H_{26}O_4$: C, 65.09; H, 10.14%.)

A mixture of 30 mg (0.116 mg) of **19** and 0.04 ml (0.58 mmol) of trifluoroacetic acid in 2 ml of dry CH_2Cl_2 was stirred at room temp for 6 h. Concentration and flash chromatography (elution with 1:7 Et_2O–hexanes) produced 20 mg (95%) of **9d**, identical in all respects to the material produced previously.

cis - 3,6 - *Dihydro* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**8a**)

To a soln of 1.76 mmol of LDA in 1.0 ml of THF at −78° was added 150 mg (0.88 mmol) of **7a** in 3.0 ml of THF. After the mixture had stirred at −78° for 30 min, there was added 0.780 ml of the supernatant from the centrifugation of a 1:1 mixture of Me_3SiCl and Et_3N. The mixture was allowed to stir for an additional 10 min at −78°, it was then warmed to 25°, and stirred for 30 min. The solvent was removed *in vacuo* and replaced with 8 ml of toluene. The soln was stirred at 110° for 4 h wereupon the soln was cooled to 25° and the solvent was removed. The residue was taken up in 20 ml of Et_2O and treated with 5% HCl aq. The soln was stirred at 25° for 2 h whereupon the aq layer was extracted repeatedly with Et_2O. The combined Et_2O extracts were concentrated and the crude carboxylic acid was dissolved in 10 ml of Et_2O at 0° and esterified with an ethereal soln of diazomethane. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 108 mg (67%) of **8a**. R_f 0.44 (1:1 hexanes–Et_2O); IR ($CHCl_3$) 3010, 2925, 2905, 2850, 1745, 1645, 1460, 1435, 1385, 1360, 1335, 1280, 1230, 1200, 1180, 1080, 1025, 840, 825, 750 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.89–5.85 (m, 1H), 5.67 (br d, 1H, J = 9.18 Hz), 4.20 (dd, 1H, J = 10.47, 4.01 Hz), 4.01 (m, 1H), 3.76 (s, 3H), 2.35–2.21 (m, 2H), 1.91–1.66 (m, 1H), 0.95 (d, 3H, J = 7.32 Hz), 0.92 (d, 3H, J = 7.32 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.77, 128.05, 124.35, 79.90, 72.81, 51.95, 32.37, 28.22, 17.82, 17.54; MS (70 eV) parent peak 184, base peak 81.

cis - 3,6 - *Dihydro* - 4 - *methyl* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**8b**)

The dioxanone **7b** (160 mg, 0.87 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 128 mg (74%) of

8b: R_f 0.54 (4:1 hexanes–Et_2O); IR (film) 2910, 2870, 2760, 1745, 1685, 1450, 1430, 1380, 1360, 1350, 1325, 1320, 1270, 1210, 1185, 1170, 1110, 1060, 1040, 1020, 985, 975, 930, 880, 845, 810, 750 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.37 (br s, 1H), 4.17 (dd, 1H, J = 11.13, 3.61 Hz), 3.93 (br s, 1H), 3.76 (s, 3H), 2.25–2.22 (m, 1H), 2.10–2.06 (m, 1H), 1.87–1.81 (m, 1H), 1.72 (d, 3H, J = 0.43 Hz), 0.93 (d, 3H, J = 6.84 Hz), 0.90 (d, 3H, J = 6.84 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.54, 132.07, 121.60, 79.86, 72.97, 51.87, 32.78, 32.56, 22.81, 17.83, 17.58; MS (70 eV) parent peak 198, base peak 95.

(2β,3β,6β) - 3,6 - *Dihydro* - 6 - (1 - *methylethyl*) - 3 - (*trimethylsilyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**8c**)

The dioxanone **7c** (111 mg, 0.457 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 62 mg (52%) of **8c**: R_f 0.60 (4:1 hexanes–Et_2O); IR (film) 3010, 2920, 2860, 2770, 2550, 1755, 1730, 1620, 1460, 1430, 1380, 1360, 1280, 1250, 1200, 1190, 1150, 1100, 970, 950, 850, 840, 790, 760, 750, 710, 680, 620 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.89 (ddd, 1H, J = 10.30, 5.78, 2.11 Hz), 5.60 (dd, 1H, J = 10.30, 1.58 Hz), 4.47 (d, 1H, J = 3.68 Hz), 4.01–3.98 (m, 1H), 3.73 (s, 3H), 1.92–1.89 (m, 1H), 1.87–1.82 (m, 1H), 0.98 (d, 3H, J = 6.81 Hz), 0.93 (d, 3H, J = 6.81 Hz), 0.03 (s, 9H); ^{13}C-NMR δ 171.76, 128.12, 124.97, 81.38, 75.13, 51.36, 32.62, 30.93, 18.56, 18.13, −1.57; MS (70 eV) parent peak 256, base peak 73.

(2β,3β,6β) - 3,6 - *Dihydro* - 3 - *methyl* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**8d**)

The dioxanone **7d** (108 mg, 0.59 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 81 mg (70%) of **8d**: R_f 0.53 (3:1 hexanes–Et_2O); IR (film) 3010, 2935, 2775, 1755, 1650, 1450, 1390, 1370, 1320, 1280, 1200, 1160, 1120, 1080, 1040, 980, 935, 910, 860, 840, 815, 785, 715 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.96 (ddd, 1H, J = 10.22, 5.64, 2.14 Hz), 5.66 (ddd, 1H, J = 10.22, 1.21, 1.21 Hz), 4.36 (d, 1H, J = 3.23), 4.12–4.09 (m, 1H), 3.83 (s, 3H), 2.55–2.49 (m, 1H), 2.05–1.98 (m, 1H), 1.03 (d, 3H, J = 6.88 Hz), 1.02 (d, 3H, J = 7.20 Hz), 1.02 (d, 3H, J = 6.88 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.24, 130.93, 126.78, 80.30, 76.03, 51.63, 32.07, 31.98, 17.79, 17.57, 14.94; MS (70 eV) parent peak 198, base peak 127. (Found: C, 66.51; H, 9.25. Calc for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%.)

cis - 3,6 - *Dihydro* - 5 - *methyl* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**8e**)

The dioxanone **7e** (109 mg, 0.59 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 105 mg (90%) of **8e**: R_f 0.57 (4:1 hexanes–Et_2O); IR (film) 2930, 2870, 2830, 1755, 1620, 1430, 1390, 1370, 1350, 1300, 1230, 1200, 1160, 1130, 1080, 1030, 980, 940, 910, 860, 840, 820, 780 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.59–5.57 (m, 1H), 4.07 (dd, 1H, J = 10.09, 4.23 Hz), 3.99 (m, 1H), 3.74 (s, 3H), 2.24–2.14 (m, 2H), 1.99–1.92 (m, 1H), 1.58 (s, 3H), 1.09 (d, 3H, J = 6.86 Hz), 0.79 (d, 3H, J = 6.86 Hz); ^{13}C-NMR ($CDCl_3$) δ 172.05, 135.45, 120.12, 81.72, 72.27, 51.80, 29.64, 28.25, 19.46, 18.90, 14.33; MS (70 eV) parent peak 198, base peak 95.

cis - 3,6 - *Dihydro* - 4,5 - *dimethyl* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**8f**)

The dioxanone **7f** (120 mg, 0.605 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 103 mg (80%) of **8f**: R_f 0.53 (4:1 hexanes–Et_2O); IR ($CHCl_3$) 2955, 2915, 2875, 2805, 1750, 1600, 1430, 1385, 1370, 1305, 1230, 1135, 1065, 1035, 975, 915, 865 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.04 (dd, 1H, J = 11.17, 3.13 Hz), 3.90 (br s, 1H), 3.70 (s, 3H), 2.22–2.01 (m, 1H), 1.98–1.91 (m, 2H), 1.64 (s, 3H), 1.48 (d, 3H, J = 0.76 Hz), 1.04 (d, 3H, J = 6.86 Hz), 0.69 (d, 3H, J = 6.86); ^{13}C-NMR ($CDCl_3$) δ 172.06, 126.93, 125.02, 82.05, 72.03, 51.68, 33.73, 29.90, 19.61, 18.91, 14.30, 13.61; MS (70 eV) parent peak 212, base peak 109. (Found: C, 67.98; H, 9.65. Calc for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49%.)

trans - 3,6 - *Dihydro* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**10a**)

The dioxanone **9a** (103 mg, 0.605 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 77 mg (69%) of the rearrangement product **10a**: R_f 0.42 (4:1 hexanes–Et_2O); IR (film) 3010, 2930, 2900, 2850, 1745, 1640, 1460, 1435, 1385, 1365, 1335, 1290, 1230, 1200, 1180, 1110, 1080, 1030, 975, 840, 825, 750 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.87–5.82 (m, 1H), 5.74 (ddd, 1H, J = 10.49, 4.08, 1.95 Hz), 4.45 (dd, 1H, J = 5.41, 5.41 Hz), 4.15–4.12 (m, 1H), 3.75 (s, 3H), 2.40–2.37 (m, 2H), 1.88–1.82 (m, 1H), 0.96 (d, 3H, J = 6.78 Hz), 0.93 (d, 3H, J = 6.78 Hz); ^{13}C-NMR ($CDCl_3$) δ 172.55, 128.07, 122.96, 76.66, 69.48, 51.89, 32.48, 26.85, 18.27, 18.03; MS (70 eV) parent peak 184, base peak 81. (Found: C, 65.44; H, 8.94. Calc for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75%.)

trans - 3,6 - *Dihydro* - 4 - *methyl* - 6 - (1 - *methylethyl*) - 2H - *pyran*-2-*carboxylic acid methyl ester* (**10b**)

The dioxanone **9b** (107 mg, 0.58 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) gave 89 mg (78%) of **10b**: R_f 0.45 (1:1 hexanes–Et_2O); IR (film) 2900, 1745, 1680, 1455, 1440, 1380, 1365, 1325, 1280, 1200, 1150, 1120, 1050, 1020, 985, 970, 945, 930, 910, 880, 840, 810, 780, 710 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.42 (br s, 1H), 4.44 (dd, 1H, J = 5.48, 5.48 Hz), 4.06–4.03 (m, 1H), 3.74 (s, 3H), 2.27–2.25 (m, 2H), 1.83–1.75 (m, 1H), 1.72 (s, 3H), 0.93 (d, 3H, J = 6.77 Hz), 0.90 (d, 3H, J = 6.77 Hz); ^{13}C-NMR ($CDCl_3$) δ 172.56, 130.78, 121.44, 76.90, 69.76, 51.84, 32.61, 31.38, 23.11, 18.30, 18.06; MS (70 eV) parent peak 198, base peak 95. (Found: C, 66.54; H, 9.22. Calc for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%.)

(2α,3α,6β) - 3,6 - *Dihydro* - 6 - (1 - *methylethyl*) - 3 - (*trimethylsilyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**10c**)

The dioxanone **9c** (127 mg, 0.52 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 81 mg (61%) of **10c**: R_f 0.64 (4:1 hexanes–Et_2O); IR (film) 3025, 2950, 2880, 1760, 1730, 1460, 1440, 1380, 1365, 1315, 1275, 1250, 1200, 1190, 1145, 1117, 1100, 1080, 1025, 1010, 920, 870, 840, 760, 720 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.98 (ddd, 1H, J = 10.30, 5.94, 2.29 Hz), 5.74 (ddd, 1H, J = 10.30, 2.57, 1.48 Hz), 4.45 (d, 1H, J = 3.38 Hz), 3.92 (br d, 1H, J = 7.42 Hz), 3.75 (s, 3H), 1.98–1.96 (m, 1H), 1.86–1.78 (m, 1H), 0.98 (d, 3H, J = 6.72 Hz), 0.92 (d, 3H, J = 6.72 Hz); ^{13}C-NMR ($CDCl_3$) δ 172.01, 127.60, 125.04, 79.44, 70.50, 51.59, 33.13, 31.01, 19.21, 18.64, −1.921; MS (70 eV) parent peak 256, base peak 73.

(2α,3α,6β) - 3,6 - *Dihydro* - 3 - *methyl* - 6 - (1 - *methylethyl*) - 2H - *pyran*-2-*carboxylic acid methyl ester* (**10d**)

The dioxanone **9d** (188 mg, 1.02 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 163 mg (81%) of **10d**: R_f 0.55 (3:1 hexanes–Et_2O); IR ($CHCl_3$) 3010, 2960, 2930, 2910, 2840, 1755, 1650, 1600, 1460, 1440, 1380, 1370, 1320, 1280, 1230, 1180, 1150, 1120, 1080, 1025, 970, 960, 920, 910, 885, 845, 830, 820, 680, 650 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.05–5.95 (m, 2H), 4.58 (d, 1H, J = 3.61 Hz), 4.10 (br d, 1H, J = 8.34 Hz), 3.96 (s, 3H), 2.65–2.62 (m, 1H), 2.07–2.01 (m, 1H), 1.18 (d, 3H, J = 6.68 Hz), 1.14 (d, 3H, J = 6.98 Hz), 1.11 (d, 3H, J = 6.68 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.38, 129.54, 126.89, 78.88, 71.73, 51.62, 32.01, 31.34, 19.33, 18.63, 14.37; MS (70 eV) parent peak 198, base peak 127.

trans - 3,6 - *Dihydro* - 5 - *methyl* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**10e**)

The dioxanone **9e** (120 mg, 0.65 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography employing 230–400 mesh silica gel (elution with 10:1 hexanes–Et_2O) afforded 117 mg (91%) of **10e**: R_f 0.61 (3:1 hexanes–Et_2O); IR (film) 2960, 2910, 2870, 1745, 1670, 1440, 1385, 1365, 1335, 1290, 1200, 1155, 1030, 970, 920, 900, 860, 830, 810, 770, 670 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.56–5.53 (m, 1H), 4.48 (dd, 1H, J = 5.32, 3.88 Hz), 4.25 (br s, 1H), 3.71 (s, 3H), 2.39–2.35 (m, 2H), 1.97–1.93 (m, 1H), 1.57 (d, 3H, J = 0.74 Hz), 1.08 (d, 3H, J = 6.90 Hz), 0.79 (d, 3H, J = 6.90 Hz); ^{13}C-NMR ($CDCl_3$) δ 173.05, 135.17, 118.47, 78.27, 70.15, 51.68, 30.13, 26.71, 19.61, 19.54, 14.88; MS (15 eV) parent peak 198, base peak 95.

[5β,6α-(*Z*)]- *and* [5β,6β - (*Z*)] - 5 - (1 - *Methylethyl*) - 6 - (1 - *propenyl*) - 1,4 - *dioxan* - 2 - *one* (**20**, **21**)

To a slurry of 201 mg (8.05 mmol) of 97% NaH in 40 ml of THF at 0° was added 1.29 g (8.05 mmol) of **13** as a soln in 10 ml of THF. The mixture was allowed to stir at 0° for 0.5 h then at 25° for 0.5 h before it was cooled to −78°. The cooled soln of the sodium carboxylate was added to a cooled (−78°) soln of 12.08 mmol of *cis*-propenylmagnesium bromide in 10 ml of THF. The *cis*-propenylmagnesium bromide soln was prepared from 7.84 ml (12.08 mmol) of *cis*-propenyllithium and 13.28 ml (13.28 mmol) of a 1 M soln of anhydrous $MgBr_2$ prepared in 3:1 Et_2O–C_6H_6. The cloudy mixture was stirred at −78° for 1 h then acidified with 5% HCl aq and allowed to warm to 25° and to stir for 1 h. The mixture was then poured into H_2O and the aq layer was extracted several times with Et_2O. The combined Et_2O extracts were concentrated and the residue was taken up in 50 ml of C_6H_6 with 40 mg of camphorsulfonic acid. The mixture was heated at reflux for 1.5 h under a Dean–Stark trap. After removal of the solvent, the mixture was chromatographed on 60–200 mesh silica gel (elution with 4:1 hexanes–Et_2O) to afford 893 mg (61%) of **20** and **21**. The diastereomer ratio **20**/**21** was determined to be 1.3:1 by glass capillary GLC. Flash chromatography employing 230–400 mesh silica gel (elution with 7:1 hexanes–Et_2O) afforded pure **20** and **21**.

Data for **20**. R_f 0.71 (1:1 hexanes–Et_2O); IR ($CHCl_3$) 3020, 2975, 2940, 2880, 1745, 1665, 1470, 1450, 1430, 1390, 1370, 1360, 1345, 1335, 1275, 1255, 1215, 1120, 1035, 1000, 980, 845, 820 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.89 (dq, 1H, J = 10.84, 7.04 Hz), 5.36 (ddd, 1H, J = 10.84, 10.19, 1.70 Hz), 5.22 (dd, 1H, J = 10.19, 9.37 Hz), 4.36 (ABq, 2H, J_{AB} = 17.61 Hz, $\Delta\nu_{AB}$ = 108.67 Hz), 3.29 (dd, 1H, J = 9.37, 2.40 Hz), 1.87–1.80 (m, 1H), 1.78 (dd, 3H, J = 7.04, 1.70 Hz), 1.03 (d, 3H, J = 6.91 Hz), 0.91 (d, 3H, J = 6.91 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.58, 132.93, 124.29, 80.01, 66.02, 28.10, 20.15, 15.28, 13.66; MS (70 eV) parent peak 184, base peak 69. (Found: C, 65.41; H, 9.03. Calc for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75%.)

Data for **21**. R_f 0.69 (1:1 hexanes–Et_2O); IR ($CHCl_3$) 3020, 2975, 2880, 1745, 1660, 1475, 1450, 1430, 1390, 1350, 1340, 1280, 1250, 1220, 1120, 1020, 1000, 970, 955, 930, 925, 890 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.93 (dq, 1H, J = 10.86, 7.00 Hz), 5.71 (ddd, 1H, J = 10.86, 10.17, 1.72 Hz), 5.23 (dd, 1H, J = 10.17, 2.38 Hz), 4.37 (ABq, 2H, J_{AB} = 17.81 Hz, $\Delta\nu_{AB}$ = 65.37 Hz), 3.37 (dd, 1H, J = 9.77, 2.38 Hz), 1.78 (dd, 2H, J = 7.00, 1.77 Hz), 1.65–1.60 (m, 1H), 1.01 (d, 3H, J = 6.66 Hz), 0.83 (d, 3H, J = 6.66 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.37, 132.86, 122.50, 80.28, 75.39, 66.32, 29.18, 19.30, 17.86, 13.39; MS (70 eV) parent peak 184, base peak 69.

(2α,3α,6β) - *Tetrahydro* - 3 - *methyl* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**24**)

A mixture of 116 mg (0.585 mmol) of **10d**, 28 mg of 5% Pd/C and 15 ml of absolute EtOH was evacuated by aspiration and purged with H_2 several times. This suspension was then stirred vigorously for 2 h at room temp. Filtration through a pad of Celite followed by evaporation of the solvent provided a colorless oil. Flash chromatography (elution with 1:14 Et_2O–hexanes) provided 85.2 mg (73%) of **24**, homogeneous by TLC and spectroscopic criteria: R_f 0.73 (1:2 Et_2O–hexanes); ^{1}H-NMR (90 MHz, $CDCl_3$) δ 4.31 (d, 1H, J = 5.3 Hz), 3.82–3.60 (m, 1H), 3.68 (s, 3H), 2.10–1.31 (m, 6H), 0.89 (m, 9H).

(2β,3β,6β) - *Tetrahydro* - 3 - *methyl* - 6 - (1 - *methylethyl*) - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**25**)

A mixture of 245 mg (1.24 mmol) of **8d**, 40 mg of 10% Pd/C and 20 ml of absolute EtOH was evacuated by aspiration and purged with H_2 several times. This suspension was then stirred for 3 h at room temp. Filtration through a pad of Celite followed by evaporation of the solvent provided 224 mg (91%) of **25** as a colorless oil, homogeneous by TLC and spectroscopic criteria: R_f 0.62 (1:2 Et_2O–hexanes); IR ($CHCl_3$) 3685, 3013, 2964, 2935, 2880, 2864, 1752, 1732, 1604, 1463, 1439, 1393, 1386, 1368, 1350, 1341, 1303, 1288, 1204, 1161, 1151, 1123, 1091, 1079, 1066, 1045, 1032, 1002, 904, 859, 832 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 4.09 (d, 1H, J = 2.0 Hz), 3.74 (s, 3H), 2.98 (m, 1H), 2.13 (m, 1H), 1.95–1.15 (m, 5H), 1.05–0.80 (m, 9H).

(3*R*,4*S*) - 5 - (*Benzyloxy*) - 3 - *hydroxy* - 4 - *methyl* - 1 - *pentene* (**26**)

To a soln of 16.0 g (40.39 mmol) of CuI · Bu_3P in 120 ml of dry Et_2O at −35° was added 50.2 ml of vinyllithium (1.61 M in THF). The resulting dark blue soln was allowed to stir at −35° for 30 min at which time 6.0 g (33.66 mmol) of **23** was added in 60 ml of THF. After stirring at −35° for 1 h, excess MeOH was added followed by a 1:1 soln of 3% NH_4OH aq and sat NH_4Cl aq. The mixture was warmed to room temp and then stirred vigorously overnight. The two layers were partitioned and the aq layer was extracted three times with Et_2O, dried ($MgSO_4$) and concentrated. Chromatography on 70–230 mesh silica gel (elution with 1:5 Et_2O–hexanes) provided 5.97 g (86%) of **26** (major) and the *erythro*-isomer (minor) in a ratio of *ca* 4:1 as determined by ^{13}C-NMR. Flash chromatography of this mixture (elution with 1:7 Et_2O–hexanes) gave 3.4 g of the *threo*-isomer **26** along with 2.2 g of a mixture of **26** and the *erythro*-isomer which was rechromatographed. Analytical data for the *threo*-isomer **26**: R_f 0.56 (1:1 Et_2O–hexanes); $[\alpha]_D^{25}$ +27.5° (*c* 1.70, $CHCl_3$); IR ($CHCl_3$) 3600, 3480, 3010, 2801, 2860, 1499, 1460, 1451, 1368, 1231, 1101, 1028, 995, 930, 701 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 7.33 (s, 5H), 6.08–5.33 (m, 1H), 5.22–5.06 (m, 2H), 4.52 (s, 3H), 4.11–3.95 (m, 1H), 3.72–3.23 (m, 3H), 1.98–1.76 (m, 1H), 0.92 (d, 3H, J = 6.96 Hz); ^{13}C-NMR ($CDCl_3$) δ 139.19, 137.80, 128.00, 127.21, 115.12, 76.02, 73.53, 72.90, 38.42, 13.17; MS (15 eV) base 91, parent peak 206. (Found: C, 75.41; H, 8.83. Calc for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79%.)

(1*R*,2*S*) - [3 - (*Benzyloxy*) - 2 - *methyl* - 1 - (*ethenyl*)*propoxy*]*acetic acid* (**27a**)

To a slurry of 2.10 g (86.52 mmol) of 97% NaH in 50 ml of THF at 0° was added 5.10 g (24.72 mmol) of **26** in 20 ml of THF. The resulting gray suspension was heated at reflux for 1 h and then cooled to 0°. To this heterogeneous mixture was added 4.10 g (29.70 mmol) of bromoacetic acid in 15 ml of THF and this was then heated at reflux for 12 h. After the mixture was allowed to cool to room temp, it was carefully poured into sat Na_2CO_3 aq and the aq layer was washed with Et_2O. The aq phase was acidified to pH 2 with conc HCl at 0° and was extracted repeatedly with Et_2O. The combined extracts were dried ($MgSO_4$) and concentrated. Column chromatography on 70–230 mesh silica gel (elution with 1:5 Et_2O–hexanes containing 1% HOAc) gave 6.3 g (97%) of the acid **27a**, homogeneous by TLC and spectroscopic analysis: $[\alpha]_D^{25}$ −11.27° (*c* 2.44, $CHCl_3$); IR ($CHCl_3$) 3410, 3095, 3039, 3028, 2998, 2919, 2874, 1760, 1730, 1500, 1455, 1422, 1360, 1348, 1245, 1110, 1061, 970, 700 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.22–9.86 (br s, 1H), 7.37–7.25 (m, 5H), 5.67–5.57 (m, 1H), 5.33 (d, 1H, J = 10.21 Hz), 5.23 (d, 1H, J = 17.18 Hz), 4.55 (ABq, 2H, J_{AB} = 12.09 Hz, $\Delta\nu_{AB}$ = 18.43 Hz), 4.04 (ABq, 2H, J_{AB} = 17.13 Hz, $\Delta\nu_{AB}$ = 53.11 Hz), 3.69–3.63 (m, 2H), 3.49–3.42 (m, 1H), 2.06–2.00 (m, 1H), 0.89 (d, 3H, J = 7.00 Hz); ^{13}C-NMR ($CDCl_3$) δ 173.19, 137.54, 135.40, 128.39, 127.97, 127.82,

120.38, 84.93, 73.33, 72.48, 65.27, 37.51, 13.61; MS (15 eV) parent peak 264, base peak 91. (Found: C, 67.96; H, 7.93. Calc for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63%.)

(1*R*,2*S*) - [3 - (*Benzyloxy*) - 2 - *methyl* - 1 - (*ethenyl*)*propoxy*]*acetic acid* 1,1 - *dimethylethyl ester* (**27b**)

A mixture of 1.10 g (4.16 mmol) of acid **27a**, 944 mg (4.57 mmol) of 1,3-dicyclohexylcarbodiimide, 0.43 ml (4.57 mmol) of t-BuOH and 51 mg (0.412 mmol) of 4-dimethylaminopyridine in 30 ml of dry CH_2Cl_2 was stirred at room temp for 3 h. The mixture was washed three times with 5% HOAc aq, three times with H_2O, dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:12 Et_2O–hexanes) provided 1.15 g (88%) of **27b** as an oil which was homogeneous by TLC and spectroscopic analysis: R_f 0.87 (1:1 Et_2O–hexanes); $[\alpha]_D^{25}$ −11.26° (*c* 1.64, $CHCl_3$); IR ($CHCl_3$) 3035, 3017, 3008, 2982, 2937, 2906, 2859, 1748, 1720, 1496, 1478, 1457, 1422, 1396, 1371, 1309, 1232, 1161, 1117, 1028, 999, 937, 848, 700 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$), δ 7.34–7.26 (m, 5H), 5.71–5.62 (m, 1H), 5.27 (d, 1H, J = 10.27 Hz), 5.19 (d, 1H, J = 16.87 Hz), 4.50 (s, 2H), 3.91 (ABq, 2H, J_{AB} = 16.29 Hz, $\Delta\nu_{AB}$ = 38.05 Hz), 3.75 (dd, 1H, J = 7.58, 7.58 Hz), 3.55 (dd, 1H, J = 9.21, 5.80 Hz), 3.44 (dd, 1H, J = 9.21, 6.43 Hz), 2.16–2.09 (m, 1H), 1.46 (s, 9H), 0.94 (d, 3H, J = 6.97 Hz); ^{13}C-NMR ($CDCl_3$) δ 169.81, 138.84, 135.85, 128.21, 127.49, 127.33, 119.17, 83.31, 81.10, 72.93, 72.27, 66.21, 37.97, 28.08, 12.98; MS (15 eV) parent 320, base peak 82. (Found: C, 70.98; H, 8.89. Calc for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81%.)

(1*S*,2*S*) - [3 - (*Benzyloxy*) - 1 - *formyl* - 2 - *methylpropoxy*]*acetic acid* 1,1 - *dimethylethyl ester* (**27c**)

The ester **27b** (1.0 g, 3.12 mmol) was placed in 100 ml of dry CH_2Cl_2 and this was cooled to −78°. O_3 was then bubbled through the soln until a distinct blue color persisted. After stirring at −78° for 5 min, argon was bubbled through the soln for 5 min to dissipate the excess O_3. The soln was then treated with 0.45 ml (6.14 mmol) of Me_2S and allowed to warm to room temp over 2 h. The mixture was dried (Na_2SO_4) and the solvent was removed under reduced pressure. Flash chromatography (elution with 1:6 Et_2O–hexanes) gave 867.5 mg (87%) of **27c**, homogeneous by TLC and spectroscopic criteria: R_f 0.59 (1:1 Et_2O–hexanes); $[\alpha]_D^{25}$ −28.10° (*c* 3.42, $CHCl_3$); IR 3019, 2984, 2940, 2862, 1739, 1499, 1478, 1457, 1397, 1381, 1372, 1310, 1238, 1163, 1141, 1122, 1031, 947, 848, 701 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.72 (d, 1H, J = 1.66 Hz), 7.34–7.23 (m, 5H), 4.45 (ABq, 2H, J_{AB} = 12.02 Hz, $\Delta\nu_{AB}$ = 15.52 Hz), 4.11 (ABq, 2H, J_{AB} = 16.66 Hz, $\Delta\nu_{AB}$ = 13.53 Hz), 3.53 (dd, 1H, J = 9.24, 9.24 Hz), 3.38 (dd, 1H, J = 9.24, 4.99 Hz), 2.43–2.39 (m, 1H), 1.46 (s, 9H), 1.05 (d, 3H, J = 7.08 Hz); ^{13}C-NMR ($CDCl_3$) δ 202.76, 169.17, 138.12, 128.21, 127.41, 86.67, 81.88, 72.85, 70.40, 68.99, 37.10, 27.98, 13.39; MS (15 eV) parent 322, base peak 251.

[1*S*,2*S* - 3(*E*)] - ([1 - ([2 - (*Benzyloxy*) - 1(*S*) - *methyl*]*ethyl*) - 2 - *hydroxy* - 3 - *pentenyl*] - *oxy*)*acetic acid* 1,1 - *dimethylethyl ester* (**28a**)

To a soln of 1.66 g (4.23 mmol) of CuI·Bu_3P in 15 ml of anhydrous Et_2O at −35° was added 5.13 ml of *trans*-propenyllithium (1.65 M in Et_2O).[13a,b] The resulting yellow soln was allowed to stir at −35° for 30 min and then cooled to −78° at which time 910 mg (2.82 mmol) of **27c** was added in 7 ml of Et_2O. After the mixture had stirred at −78° for 2 h, excess MeOH was added followed by a 1:1 soln of 3% NH_4OH aq and sat NH_4Cl aq. The mixture was warmed to room temp and then stirred vigorously for 2 h. The two layers were partitioned and the aq layer was extracted three times with Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:7 Et_2O–hexanes) yielded 779 mg (76%) of **28a** (major) and **28c** (minor) in a ratio of 24:1 as determined by capillary GLC (240°, isothermal). Analysis data for **28a**: R_f 0.5 (1:1 Et_2O–hexanes); $[\alpha]_D^{25}$ +24.61° (*c* 1.04, $CHCl_3$); IR ($CHCl_3$) 3530–3300, 3010, 2985, 2932, 2866, 1734, 1429, 1470, 1458, 1398, 1371, 1315, 1249, 1160, 1128, 1026, 971, 909, 842, 700 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36–7.26 (m, 5H), 5.73 (dq, 1H, J = 15.29, 6.86 Hz), 5.40 (ddd, 1H, J = 15.29, 7.39, 1.41 Hz), 4.15 (dd, 1H, J = 7.17, 7.17 Hz), 4.09 (ABq, 2H, J_{AB} = 16.71 Hz, $\Delta\nu_{AB}$ = 117.63 Hz), 3.52 (dd, 1H, J = 9.16, 5.76 Hz), 3.37 (dd, 1H, J = 9.16, 6.78 Hz), 3.18 (dd, 1H, J = 7.17, 3.58 Hz), 2.13–2.08 (m, 1H), 1.67 (dd, 3H, J = 6.86, 1.41 Hz), 1.47 (s, 9H), 1.04 (d, J = 7.04 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.04, 138.52, 130.42, 128.87, 128.27, 127.52, 127.46, 89.67, 82.31, 73.03, 72.85, 71.45, 70.64, 35.80, 28.04, 17.77, 15.04; MS (15 eV) parent 364, base peak 91. (Found: C, 68.96; H, 8.92. Calc for $C_{21}H_{32}O_5$: C, 69.14; H, 8.84%.)

[1*S* - 3(*E*)] - ([1 - ([2 - (*Benzyloxy*) - 1(*S*) - *methyl*]*ethyl*) - 2 - *oxo* - 3 - *pentenyl*]*oxy*)*acetic acid* 1,1 - *dimethylethyl ester* (**28b**)

To a cooled (−10°) soln of 290 mg (0.795 mmol) of **28a** in 15.0 ml of dry DMF was added 444 mg (1.19 mmol) of pyridinium dichromate. The resulting mixture was stirred at −10° for 12 h and then poured into 45 ml of H_2O. The aq layer was extracted five times with Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:7 Et_2O–hexanes) provided 267 mg (93%) of **28b**, homogeneous by TLC and spectroscopic analysis: R_f 0.74 (1:1 Et_2O–hexanes); $[\alpha]_D$ −56.1° (*c* 1.36, $CHCl_3$); IR ($CHCl_3$) 3190, 3165, 3016, 2980, 2938, 2865, 1743, 1693, 1618, 1496, 1479, 1453, 1441, 1392, 1369, 1312, 1296, 1231, 1160, 1120, 1028, 971, 938, 907, 842, 699 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 5H), 6.98 (dq, 1H, J = 15.53, 6.89 Hz), 6.52 (dd, 1H, J = 15.53, 1.65 Hz), 4.47 (ABq, 2H, J_{AB} = 6.88 Hz, $\Delta\nu_{AB}$ = 13.93 Hz), 3.94 (ABq, 2H, J_{AB} = 16.29 Hz, $\Delta\nu_{AB}$ = 87.52 Hz), 3.86 (d, 1H, J = 6.28 Hz), 3.60 (dd, 1H, J = 9.29, 5.83 Hz), 3.45 (dd, 1H, J = 9.29, 6.15 Hz), 2.29–2.13 (m, 1H), 1.87 (dd, 3H, J = 6.89, 1.65 Hz), 1.45 (s, 9H), 0.99 (d, 3H, J = 6.99 Hz); ^{13}C-NMR ($CDCl_3$) δ 199.51, 168.83, 143.69, 138.48, 128.12, 127.45, 127.27, 127.06, 86.85, 81.64, 72.88, 71.26, 68.08, 36.96, 27.98, 18.31, 13.63; MS (15 eV) parent 362, base peak 237. (Found: C, 69.34; H, 8.42. Calc for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34%.)

[1*S*,2*R* - 3(*E*)] - ([1 - ([2 - (*Benzyloxy*) - 1(*S*) - *methyl*]*ethyl*) - 2 - *hydroxy* - 3 - *pentenyl*] - *oxy*)*acetic acid* 1,1 - *dimethylethyl ester* (**28c**)

To a soln of 112 mg (0.309 mmol) of **28b** in 8.0 ml of anhydrous Et_2O at 0° was added 0.71 ml of a 0.145 M ethereal $Zn(BH_4)_2$ soln. After stirring at 0° for 1 h, the mixture was poured into sat NH_4Cl aq and extracted three times with Et_2O. The combined organic extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:6 Et_2O–hexanes) afforded 99.2 mg (88%) of **28c** as a single diastereomer which was homogeneous by TLC and spectroscopic analysis: R_f 0.53 (1:1 Et_2O–hexanes); $[\alpha]_D^{25}$ +12.06° (*c* 2.16, $CHCl_3$); IR ($CHCl_3$) 3601–3309, 3002, 2980, 2938, 2919, 2857, 1729, 1495, 1452, 1431, 1391, 1385, 1368, 1247, 1154, 1142, 1133, 1025, 990, 968, 907, 840, 693 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 5H), 5.75–5.68 (m, 1H), 5.60 (ddd, 1H, J = 15.40, 7.54, 1.15 Hz), 4.81–4.66 (br s, 1H), 4.50 (s, 2H), 4.07 (br d, 1H, J = 6.18 Hz), 4.06 (ABq, 2H, J_{AB} = 17.03 Hz, $\Delta\nu_{AB}$ = 73.55 Hz), 3.56 (dd, 1H, J = 8.98, 4.29 Hz), 3.46 (dd, 1H, J = 8.98, 3.60 Hz), 3.42 (dd, 1H, J = 9.07, 3.00 Hz), 1.85–1.78 (m, 1H), 1.71 (dd, 3H, J = 6.18, 1.15 Hz), 1.46 (s, 9H), 0.98 (d, 3H, J = 6.95 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.96, 138.21, 129.36, 128.93, 128.26, 128.12, 127.57, 127.52, 125.21, 88.35, 82.22, 73.09, 72.82, 71.83, 70.09, 36.38, 27.98, 17.82, 14.37; MS (15 eV) parent 364, base peak 237. (Found: C, 69.36; H, 8.85. Calc for $C_{21}H_{32}O_5$: C, 69.14; H, 8.84%.)

(5*S*,6*R*) - 5 - [2 - (*Benzyloxy*) - 1(*S*) - *methyl*]*ethyl* - 6 - [1(*E*) - *propenyl*] - 1,4 - *dioxan* - 2 - *one* (**29**)

A mixture of 160 mg (0.438 mmol) of **28c** and 10 μl (0.131 mmol) of trifluoroacetic acid in 5 ml of anhydrous C_6H_6 was heated at reflux for 3 h at which time TLC analysis showed complete consumption of starting material. The solvent was removed under reduced pressure and the residue was purified by flash chromatography. Elution with 1:6 Et_2O–hexanes gave 126.2 mg (99%) of **29**, homogeneous by TLC and spec-

troscopic criteria: R_f 0.56 (CH_2Cl_2); $[\alpha]_D^{25}$ +45.64° (*c* 1.82, $CHCl_3$); IR ($CHCl_3$) 3100–2900, 1738, 1459, 1388, 1370, 1358, 1260, 1239, 1218, 1125, 1079, 1039, 1005, 979, 900 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H), 5.92 (dq, 1H, J = 15.26, 6.00 Hz), 5.69 (ddd, 1H, J = 15.26, 8.76, 1.67 Hz), 4.80 (dd, 1H, J = 8.76, 2.46 Hz), 4.50 (ABq, 2H, J_{AB} = 12.10 Hz, $\Delta\nu_{AB}$ = 25.63 Hz), 4.30 (ABq, 2H, J_{AB} = 17.76 Hz, $\Delta\nu_{AB}$ = 80.62 Hz), 3.70 (dd, 1H, J = 10.23, 2.46 Hz), 3.56 (dd, 1H, J = 8.84, 5.19 Hz), 3.49 (dd, 1H, J = 8.84, 2.91 Hz), 1.77 (dd, 3H, J = 6.00, 1.50 Hz), 1.75–1.63 (m, 1H), 0.98 (d, 3H, J = 6.92 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.14, 138.48, 134.17, 128.33, 127.52, 123.63, 82.11, 73.18, 70.85, 66.30, 34.93, 17.95, 12.94; MS (15 eV) parent 290, base peak 68. (Found: C, 70.49; H, 7.64. Calc for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%.)

(2*R*,3*S*,6*R*) - 6 - [2 - (*Benzyloxy*) - 1(*S*) - *methyl*]*ethyl* - 3,6 - *dihydro* - 3 - *methyl* - 2H - *pyran* - 2 - *carboxylic acid methyl ester* (**30**)

The dioxanone **29** (194 mg, 0.67 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography (elution with 1:10 Et_2O–hexanes) provided 163 mg (80%) of **30** along with 20.1 mg (10.5%) of recovered starting material. The ester **30** produced was homogeneous by TLC and spectroscopic analysis: R_f 0.74 (1:1 Et_2O–hexanes); $[\alpha]_D^{25}$ +134.26° (*c* 1.38, $CHCl_3$); IR ($CHCl_3$) 3021, 3010, 2964, 2958, 2909, 2879, 1752, 1733, 1495, 1451, 1439, 1392, 1371, 1362, 1280, 1278, 1188, 1115, 1080, 1024, 691 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33–7.31 (m, 5H), 5.87 (ddd, 1H, J = 10.38, 5.22, 2.02 Hz), 5.79 (ddd, 1H, J = 10.38, 2.90, 1.2 Hz), 4.50 (s, 2H), 4.39 (d, 1H, J = 3.64 Hz), 4.19 (d, 1H, J = 8.99 Hz), 3.74 (s, 3H), 3.64 (dd, 1H, J = 9.10, 4.28 Hz), 3.40 (dd, 1H, J = 9.10, 7.04 Hz), 2.48–2.44 (m, 1H), 2.09–2.04 (m, 1H), 1.01 (d, 3H, J = 6.80 Hz), 0.96 (d, 3H, J = 6.97 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.13, 138.57, 129.78, 128.09, 127.34, 127.20, 126.49, 72.97, 72.57, 71.65, 51.54, 37.48, 31.24, 14.31, 13.88; MS (15 eV) parent 304, base peak 91. (Found: C, 71.05; H, 8.05. Calc for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95%.)

(2*R*,3*S*,6*R*) - 6 - [2 - (*Benzyloxy*) - 1(*S*) - *methyl*]*ethyl* - 3,6 - *dihydro* - 2 - (1 - *hydroxypropyl*) - 3 - *methyl* - 2H - *pyran* (**31a**)

To a soln of substrate ester **30** (106 mg, 0.348 mmol) in 5.0 ml of anhydrous Et_2O at −78° was added 0.42 ml of diisobutylaluminum hydride (0.95 M in hexanes). After the mixture had stirred for 1.5 h at −78°, there was added 0.37 ml of EtMgBr (2.82 M in THF). The mixture was stirred at −78° for 15 min and then allowed to warm to room temp over a 2 h period. The soln was poured into 5% HCl aq and extracted three times with Et_2O. The combined extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:10 Et_2O–hexanes) gave 101.9 mg (96%) of **31a** as a single diastereomer, homogeneous by TLC and spectroscopic criteria: R_f 0.71 (1:1 Et_2O–hexanes); $[\alpha]_D^{26}$ +119.56° (*c* 1.60, $CHCl_3$); IR ($CHCl_3$) 3579, 3422, 3091, 3065, 3018, 3004, 2963, 2957, 2878, 1494, 1452, 1405, 1395, 1370, 1318, 1291, 1232, 1190, 1153, 1086, 1061, 1022, 991, 965, 918, 887, 841, 691 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H), 5.89 (ddd, 1H, J = 10.26, 5.80, 2.17 Hz), 5.77 (ddd, 1H, J = 10.26, 3.07, 1.02 Hz), 4.54 (s, 2H), 4.05 (br d, 1H, J = 9.33 Hz), 3.55–3.50 (m, 2H), 3.46–3.44 (m, 2H), 3.44–3.42 (br s, 1H), 2.12–2.04 (m, 2H), 1.57–1.51 (m, 1H), 1.37–1.25 (m, 1H), 1.02 (t, 3H, J = 7.40 Hz), 0.95 (d, 3H, J = 6.95 Hz), 0.94 (d, 3H, J = 6.85 Hz); ^{13}C-NMR ($CDCl_3$) δ 183.31, 131.50, 128.17, 127.52, 127.36, 126.53, 75.40, 74.62, 73.46, 73.05, 72.18, 36.91, 29.90, 24.68, 14.18, 13.07, 9.64; MS (15 eV) parent 304, base peak 155. (Found: C, 74.70; H, 9.43. Calc for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27%.)

(2*R*,3*S*,6*R*) - 6 - [2 - (*Benzyloxy*) - 1(*S*) - *methyl*]*ethyl* - 3,6 - *dihydro* - 3 - *methyl* - 2 - (1 - *oxopropyl*) - 2H - *pyran* (**31b**)

To a soln of 90 mg (0.295 mmol) of **31a** in 3 ml of Me_2CO was added 110 μl of 2.67 M Jones reagent. The soln was stirred at room temp for 10 min, quenched with 4 drops of isopropyl alcohol, and then concentrated under reduced pressure. The crude residue was diluted with Et_2O, poured into sat $NaHCO_3$ aq, and extracted three times with Et_2O. The combined extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (elution with 1:10 Et_2O–hexanes) afforded 83.1 mg (93%) of **31b** as an oil, homogeneous by TLC, gas capillary GLC, and spectroscopic criteria: R_f 0.84 (1:1 Et_2O–hexanes); $[\alpha]_D^{24}$ +177.39° (*c* 1.64, $CHCl_3$); IR ($CHCl_3$) 3030, 3011, 2969, 2940, 2903, 2880, 1713, 1495, 1452, 1400, 1380, 1373, 1362, 1192, 1111, 1093, 1062, 873, 629 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37–7.30 (m, 5H), 5.91 (ddd, 1H, J = 10.29, 5.63, 2.17 Hz), 5.78 (ddd, 1H, J = 10.29, 3.07, 1.01 Hz), 4.52 (ABq, 2H, J_{AB} = 12.12 Hz, $\Delta\nu_{AB}$ = 6.03 Hz), 4.15–4.12 (m, 1H), 4.11 (d, 1H, J = 3.31 Hz), 3.58 (dd, 1H, J = 9.00, 3.78 Hz), 3.43 (dd, 1H, J = 9.00, 6.53 Hz), 2.47 (q, 2H, J = 7.28 Hz), 2.47–2.43 (m, 1H), 2.06–1.99 (m, 1H), 1.03 (d, 3H, J = 6.81 Hz), 0.99 (t, 3H, J = 7.28 Hz), 0.86 (d, 3H, J = 6.88 Hz); ^{13}C-NMR ($CDCl_3$) δ 212.27, 138.54, 130.81, 128.26, 127.51, 127.43, 126.52, 77.15, 73.12, 72.45, 37.37, 32.83, 31.25, 14.15, 13.83, 6.73; MS (15 eV) parent 302, base peak 245. (Found: C, 75.41; H, 8.87. Calc for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67%.)

(2*R*,3*S*,6*R*) - 6 - (2 - *Hydroxy* - 1(*S*) - *methyl*)*ethyl* - 3 - *methyl* - 2 - (1 - *oxopropyl*) - *tetrahydropyran* (**32**)

A mixture of 77 mg (0.254 mmol) of **31b**, 20 mg of 5% Pd/C and 2 ml of absolute EtOH was evacuated by aspiration and purged with H_2 several times. This suspension was then stirred vigorously under 1 atm of H_2 for 2 h at room temp. Filtration through a pad of Celite followed by evaporation of the solvent provided 56 mg of a colorless oil. Flash chromatography (elution with 1:3 Et_2O–hexanes) gave 53.2 mg (99%) of **32**, homogeneous by TLC and spectroscopic analysis: R_f 0.36 (1:1 Et_2O–hexanes); $[\alpha]_D^{25}$ −26.21° (*c* 1.02, $CHCl_3$); IR ($CHCl_3$) 3630, 3515, 3010, 2960, 2938, 1717, 1460, 1381, 1109, 1180, 1033 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.20 (d, 1H, J = 4.67 Hz), 3.61–3.59 (m, 2H), 3.51 (dt, 1H, J = 8.74, 3.32 Hz), 2.53 (q ABq, 2H, J = 7.30 Hz, J_{AB} = 18.20 Hz, $\Delta\nu_{AB}$ = 58.61 Hz), 2.03–1.97 (m, 1H), 1.86–1.75 (m, 2H), 1.69–1.64 (m, 2H), 1.44–1.35 (m, 1H), 1.04 (t, 3H, J = 7.30 Hz), 0.98 (d, 3H, J = 7.10 Hz), 0.85 (d, 3H, J = 6.96 Hz); ^{13}C-NMR ($CDCl_3$) δ 210.94, 79.70, 78.28, 67.15, 38.36, 34.17, 31.99, 27.32, 26.33, 15.79, 13.65, 7.27; MS (15 eV) base peak 69. (Found: C, 67.45; H, 10.56. Calc for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35%.)

Methyl (α*R*,2*R*,5*S*,6*R*) - *tetrahydro* - α,5 - *dimethyl* - 6 - (1 - *oxopropyl*) - 2H - *pyran* - 2 - *acetate* (**2**)

To a soln of 38 mg (0.178 mmol) of **32** and 1.0 ml of Me_2CO was added 133 μl of 2.67 M Jones reagent. The soln was allowed to stir at room temp for 20 min and was then treated with 3 drops of isopropyl alcohol. The crude mixture was concentrated under reduced pressure, diluted with Et_2O, filtered through a Celite pad, and concentrated. The crude product thus obtained was dissolved in 2 ml of Et_2O and esterified with excess ethereal diazomethane. Flash chromatography on 230–400 mesh silica gel (elution with 1:7 Et_2O–hexanes) gave 39.1 mg (91%) of **2**, homogeneous by TLC and spectroscopic criteria: R_f 0.85 (1:1 Et_2O–hexanes); $[\alpha]_D^{26}$ −23.18° (*c* 0.91, $CHCl_3$); IR ($CHCl_3$) 3020, 2981, 2955, 2880, 1732, 1720, 1460, 1437, 1380, 1350, 1271, 1163, 1142, 1080, 1051 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.14 (d, 1H, J = 4.91 Hz), 3.72–3.67 (m, 1H), 3.67 (s, 3H), 2.71 (dq, 1H, J = 9.64, 6.98 Hz), 2.47 (q ABq, 2H, J = 7.30 Hz, J_{AB} = 18.36 Hz, $\Delta\nu_{AB}$ = 72.91 Hz), 2.04–1.97 (m, 1H), 1.86–1.79 (m, 1H), 1.68 (dt, 2H, J = 6.55, 6.55 Hz), 1.37–1.28 (m, 1H), 1.07 (d, 3H, J = 6.98 Hz), 1.01 (t, 3H, J = 7.30 Hz), 0.95 (d, 3H, J = 7.09 Hz); ^{13}C-NMR ($CDCl_3$) δ 211.30, 175.26, 79.37, 75.25, 51.47, 43.29, 33.49, 31.35, 26.00, 25.12, 14.95, 13.55, 7.08; MS (15 eV) parent 242, base peak 185. (Found: C, 64.27; H, 9.36. Calc for $C_{13}H_{22}O_4$: C, 64.43; H, 9.15%.)

(5*S*,6*S*) - 5 - [2 - (*Benzyloxy*) - 1(*S*) - *methyl*]*ethyl* - 6 - [1(*E*) - *propenyl*] - 1,4 - *dioxan* - 2 - *one* (**33**)

To a soln of 86 mg (0.236 mmol) of **28a** in 2 ml of anhydrous CH_2Cl_2 was added 4.0 μl (0.047 mmol) of trifluoroacetic acid. The resulting clear soln was stirred at room temp for 3 h and then concentrated under reduced pressure. Flash chromatography (elution with 1:5 Et_2O–hexanes) provided 65.7 mg

(96%) of **33** as an oil which was homogeneous by TLC and spectroscopic criteria: TLC 0.46 (1:3 Et_2O–hexanes); IR ($CHCl_3$) 3002, 2947, 2899, 2841, 1739, 1668, 1493, 1452, 1434, 1380, 1360, 1309, 1241, 1141, 1101, 1036, 992, 963, 938, 857, 782, 742, 701 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38–7.27 (m, 5H), 5.85 (ddq, 1H, J = 15.22, 6.60, 0.63 Hz), 5.41 (ddd, 1H, J = 15.22, 8.18, 1.62 Hz), 5.13 (dd, 1H, J = 9.00, 8.18 Hz), 4.47 (s, 2H), 4.33 (ABq, 2H, J_{AB} = 17.53 Hz, $\Delta\nu_{AB}$ = 101.86 Hz), 3.59 (dd, 1H, J = 9.00, 8.01 Hz), 3.37 (dd, 1H, J = 9.38, 2.41 Hz), 3.28 (dd, 1H, J = 9.38, 5.44 Hz), 2.19–2.16 (m, 1H), 1.76 (dd, 3H, J = 6.60, 1.62 Hz), 1.02 (d, 3H, J = 7.08 Hz); ^{13}C-NMR ($CDCl_3$) δ 167.52, 138.14, 133.80, 128.35, 127.62, 127.57, 125.14, 82.25, 98.97, 73.18, 70.50, 65.96, 33.92, 17.85, 15.26; MS (15 eV) parent 290, base peak 91. (Found: C, 70.47; H, 7.84. Calc for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%.)

(2S,3R,6R) - 6 - [2 - (Benzyloxy) - 1(S) - methyl]ethyl - 3,6 - dihydro - 3 - methyl - 2H - pyran - 2 - carboxylic acid methyl ester (**34**)

The dioxanone **33** (147 mg, 0.51 mmol) was rearranged and esterified by the procedure described for the production of **8a**. Flash chromatography (elution with 1:8 Et_2O–hexanes) produced 84.6 mg (55%) of **34** as an oil, homogeneous by TLC and spectroscopic criteria: R_f 0.47 (1:1 Et_2O–hexanes); IR ($CHCl_3$) 3017, 3009, 2965, 2938, 2880, 2861, 1758, 1732, 1456, 1441, 1399, 1371, 1362, 1320, 1283, 1271, 1192, 1188, 1121, 1090, 1081, 1030, 700 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36–7.26 (m, 5H), 5.88 (m, 1H), 5.59 (d, 1H, J = 10.24 Hz), 4.50 (ABq, 2H, J_{AB} = 12.10 Hz, $\Delta\nu_{AB}$ = 9.31 Hz), 4.33–4.31 (m, 1H), 4.29 (d, 1H, J = 3.25 Hz), 3.76 (s, 3H), 3.48 (d ABq, 2H, J = 6.41 Hz, J_{AB} = 9.47 Hz, $\Delta\nu_{AB}$ = 20.48 Hz), 2.48–2.44 (m, 1H) 2.25–2.20 (m, 1H), 0.99 (d, 3H, J = 6.90 Hz), 0.95 (d, 3H, J = 6.89 Hz); ^{13}C-NMR ($CDCl_3$) δ 171.13, 138.69, 130.99, 128.27, 127.47, 127.42, 126.68, 76.14, 75.41, 73.01, 72.13, 51.65, 37.73, 31.92, 14.97, 12.76; MS (15 eV) parent 304, base peak 91.

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