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ON THE COMMUNICATION OF CHIRALITY FROM FURANOSE AND PYRANOSE RINGS TO MONOSACCHARIDE SIDE CHAINS: ANOMALOUS RESULTS IN THE GLUCOSE SERIES

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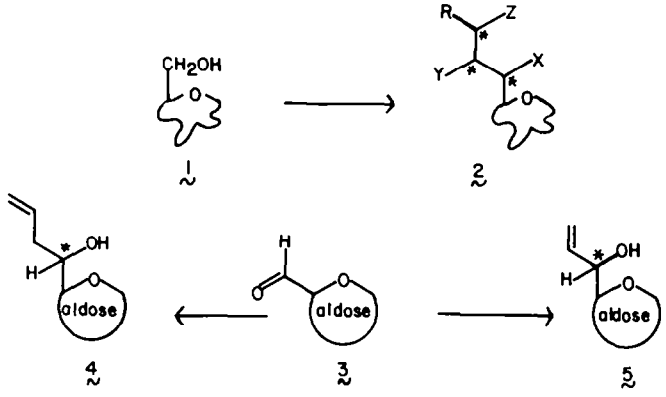
Abstract—The reactions of allyltrimethylsilane with dialdose derivatives occur, under catalysis by boron trifluoride etherate or titanium tetrachloride, with high stereoselectivity, thereby providing simple routes to the corresponding allyl carbinols. The sense of this Sakurai reaction is very dependent on the nature of the Lewis acid. The same aldehydes react with β-trimethylsilylethylidenetriphenylphosphorane to afford 3-trimethylsilylprop-1-ene-1-yl-furanosides and pyranosides. Reactions of these compounds with osmium tetroxide, followed by elimination of trimethylsilanol, afford the corresponding vinyl carbinols.

Our objective in this study was the attainment of stereoselective processes to allow for the communication of chirality from the furanose and pyranose sectors of monosaccharides to emerging side chains. Several considerations converged to render this objective, summarized in the formalism **1** → **2**, worthy of pursuit. The use of monosaccharides as "chiral synthons" (or "chirons") in the assembly of more complex targets is, by now, well established.[1,2] The capacity to convey the chiral imprint of the ring structure to an emerging side chain would add considerable flexibility to this synthetic strategy.

RESULTS AND DISCUSSION

In the work described herein, we focused on dialdose derivatives of type **3** and concerned ourselves with their transformation to generic systems **4** and **5**. Such carbinols might serve as substrates for newly emerging technology in acyclic stereoselection en route to reaching target systems **2**. However, examination of the literature reveals that, with few exceptions, the reactions of organometallic reagents with such dialdose derivatives have not exhibited high margins of diastereofacial preference.[6]



Moreover, there exists a variety of complex monosaccharides (C_8–C_{11}) of diverse biological function.[3] Clearly, the capability envisioned herein would be helpful in expediting the synthesis of such systems from the more available pentose and hexose sugars.

Also, as a consequence of earlier investigations from our laboratory, pyranose compounds bearing diverse functionality and stereochemical patterns can be readily synthesized.[4,5] If the dissymmetry available through the cyclocondensation reaction can be effectively conveyed to the side chain, some exciting possibilities for the rapid build-up of systems bearing centers of stereogenicity can be envisioned.

A clue as to a potential solution to this type of problem arose from previous work in our laboratory with 2-phenylpropanal.[7] Although this aldehyde had exhibited poor facial selectivity in reactions with various nucleophiles, it exhibited striking stereospecificity (in the Cram[8]–Felkin[9] sense) in cycloadditions with enoxysilanes in the presence of Lewis acids. Subsequent investigations by Heathcock and coworkers served to reinforce, broaden and interpret[10] these findings. Accordingly, we wondered whether Lewis acid induced nucleophilic attacks on a dialdose might allow for more acceptable stereoselectivity. Given the commercial availability of allyltrimethylsilane (**6**), and given the fact that the reaction of this

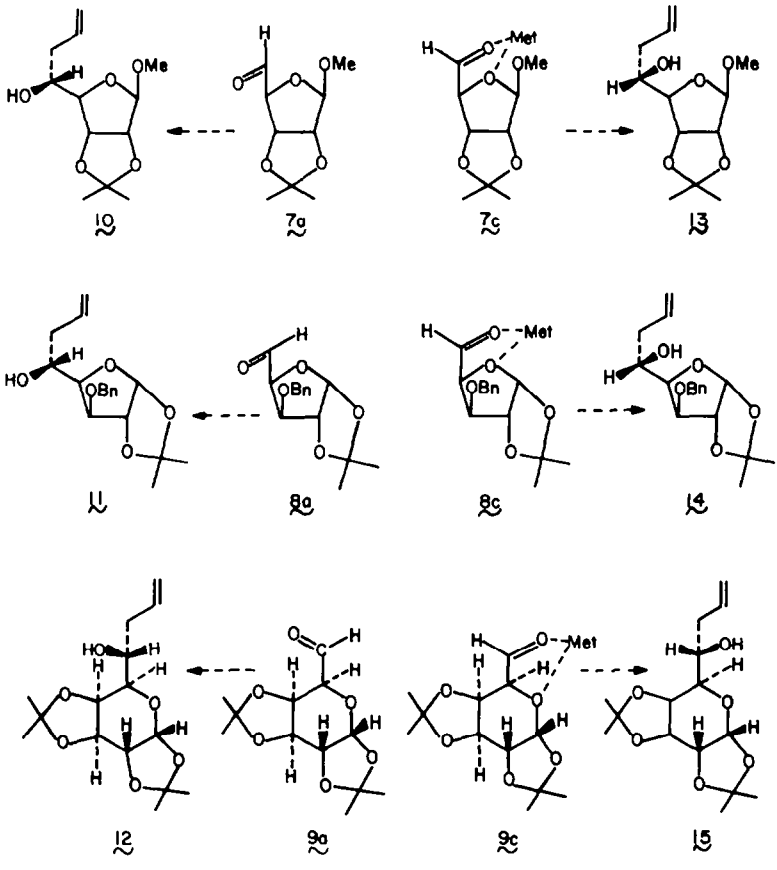
compound with aldehydes is normally carried out under mediation by Lewis acids, it was natural to begin our inquiry with this (Sakurai) reaction.[11,12] The dialdoses which were employed first were the ribose derivative **7**,[13a] the xylose **8**[13b] and the galactose derivative **9**.[13c] With $BF_3 \cdot OEt_2$ as the catalyst, in methylene chloride, high margins of Cram–Felkin selectivity were realized in good to excellent yields. The configurations of these products are securely established (*vide infra*). In each case, the major product is the one which would have arisen from attack by the allylic nucleophile on the *s-trans* aldo conformer (implied in structures **7a**, **8a**, **9a**) *anti* to the face containing the sugar residue.

In this connection it was of interest to find that an X-ray crystallographic determination of starting aldehyde **7** reveals that the dihedral angle of the carbonyl group of the aldehyde with the C—O bond of the furanose indeed corresponds to 157.4°.† Of course, this determination does not define the nature of the reacting (Curtin–Hammett) conformer under the influence of the Lewis acid, $BF_3 \cdot OEt_2$, but the formation of major products, **10–12** is certainly not inconsistent with such a view.

It was of importance to determine whether recourse to a different Lewis acid might provide access to the alternative stereoisomer. Since attack by the nucleophile from the α-face of any of the **7a–9a** (a = *anti*) rotamers would appear to be much more probable than attack from the β-face, reversal of the stereochemical outcome would appear to require a change in the reactive (Curtin–Hammett) conformation. In principle, this could be achieved by a catalyst which would be chelated between the aldehydo and ring oxygens, thereby favoring conformers **7c**, **8c** and **9c** (c = *cisoid*) in the stereochemically determinative step. In the event, recourse to either magnesium bromide or titanium tetrachloride led to a dramatic reversal, producing very strong preferences of the apparent Cram cyclic model products[8] **13–15**. Thus, by the simple expedient of varying the Lewis acid catalyst, access to either side-chain stereochemical series becomes available (see Table 1).[14]

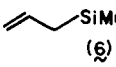
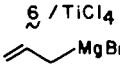
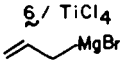
These data strongly point to an important role for the Lewis acid in the communication of stereochemistry. This role is further underscored by comparison of the results of the Lewis acid dependent Sakurai reaction with those of the reactions of the same dialdoses with allylmagnesium bromide (see Table 1). While there is undoubtedly a Lewis acid component to the mechanism of action of the Grignard reagent, its more subtle nature is apparently much less influential on the stereochemical outcome.

With an acceptable solution to the synthesis of both allylic carbinol types (**4**) in hand, attention was directed to the epimeric vinyl carbinols (**5**). Such systems are attractive materials for the goals defined above since the vicinal relationship between the hydroxylic and



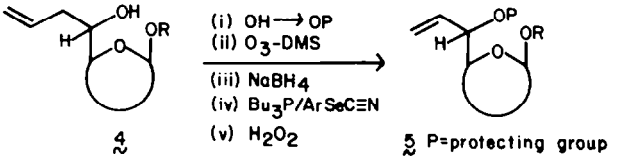
† This compound was crystallized by Dr. R. Hungate of these laboratories and a crystallographic determination was carried out by Gayle Schulte of Yale University. The full results of this determination will be published in due course.

Table 1

Aldulose	Reagent / Cat	Ratio of Products
7	 (6)	10:13 >20:1
7	6 / $TiCl_4$	10:13 ca 1:20
7		10:13 ca 2:1
8	6 / BF_3	11:14 >20:1
8	6 / $TiCl_4$	11:14 < 1:20
8		11:14 1.5:1
9	6 / BF_3	12:15 20:1
9	6 / $TiCl_4$	12:15 1:10
9		12:15 1:2

olefinic portions lends itself to various stereoselective operations at the double bond. One approach would involve conversion of the allylic carbinols to the vinylic carbinols (**4** → **5**). Indeed, in two cases (*vide infra*), this was accomplished by a simply executed sequence. After protection of the secondary hydroxyl group (either as a benzyl ether or as an acetate) the double bond was subjected to ozonolysis to afford an aldehyde, which was reduced with sodium borohydride. The primary alcohol was converted to its *o*-nitrophenylselenide by the method of Grieco *et al.*[15] Oxidative de-selenylation afforded the vinylic substrates **5**, wherein P = Bn or Ac.

investigation from our laboratory,[18] indicated high facial selectivity in the attack of various electrophilic reagents (E^+) on such double bonds in the galactose series. The overall stereochemical outcome was such that it could be accommodated via α-face on rotamer **16c**, in which the pyranose oxygen atom and the double bond are disposed in an *s-cis* fashion, affording an intermediate generalized as **17**. An example of stereospecific epoxidation of a *Z*-alkenyl group (in the same sense) was described by Perlin[19,20] who also found that the corresponding *E*-isomer exhibited virtually no selectivity. An instance of high specificity in



4 **5** P=protecting group

Although this method was sound, we explored an alternative route which would produce the desired products more quickly from the aldehyde without recourse to degradation. The obvious possibility, i.e. the reaction of a vinylic Grignard reagent with the aldehyde was shown, as expected,[6] to be lacking in useful margins of selectivity (see Table 2).

Toward this end, the stereoselectivity of electrophilic attacks on side-chain allylic silanes was investigated. The requisite allylic silanes **19–21** were synthesized in one step from the reaction of aldehydes **7–9** with phosphorane **18**.[16] Although the yields of these conversions were far from ideal (see Experimental), very rapid access to the required substrates† was in hand.

Before focusing on the selectivity of the electrophilic reactions on these rather special allylic silanes, it is well to consider, as background, the situation with respect to the more common alkenylsaccharides. An early result due to Szarek and co-workers,[17] as well as an

the corresponding sense in the osmylation of the 4-deoxy-4-azidogluco series was reported by Secrist and Barnes.[21] Finally, there should be noted the detailed investigations of Kishi and co-workers[22] and of Jarrell and Szarek[23] with related substrates. It was found that highly selective osmylation processes can be realized, though the overall result can be strongly influenced by subtle variations of the substrates and manipulation of reaction conditions.

Following our initial observations,[18] we theorized that in the *s-cis* (**16c**) rotamer, the nucleophilic character of the double bond is maximized in that the stereoelectronic consequences of the electron-withdrawing allylic oxygen group are minimized. These conjectures were placed into a broader conceptual framework by Houk *et al.*[24] Thus, the assessment of the facial selectivity in the osmylation reactions of the allylic silanes was of theoretical, as well as synthetic, interest.

The diols resulting from the action of osmium tetroxide on compounds **19–21** were subjected to elimination under two sets of conditions (see Methods A and B). The results are shown in Table 2. In each case, the major products were those predicted from the precedents and were consistent with a model wherein

† Aldehydes **7**, **8** and **9** provided the *Z*-substituted allylsilanes as the sole product, whereas aldehyde **28** gave rise to a 3:1 (*Z*:*E*) ratio of allylsilanes by 250 MHz ^{1}H-NMR analysis.

rotamer type **16c** undergoes α-face attack leading to **17** (E = osmate ester). For substrates **20** and **21**, the selectivity was quite high. In the case of the ribose derivative **19**, some modification of the experimental conditions was necessary (see Experimental) to reach high levels of selectivity. The assignments of configuration are rigorous (*vide infra*). As is seen in Table 2, the reactions of the aldehydes **7–9** with vinylmagnesium bromide are devoid of significant selectivity.

While the complex monosaccharide synthetic targets which served to motivate this study were largely those

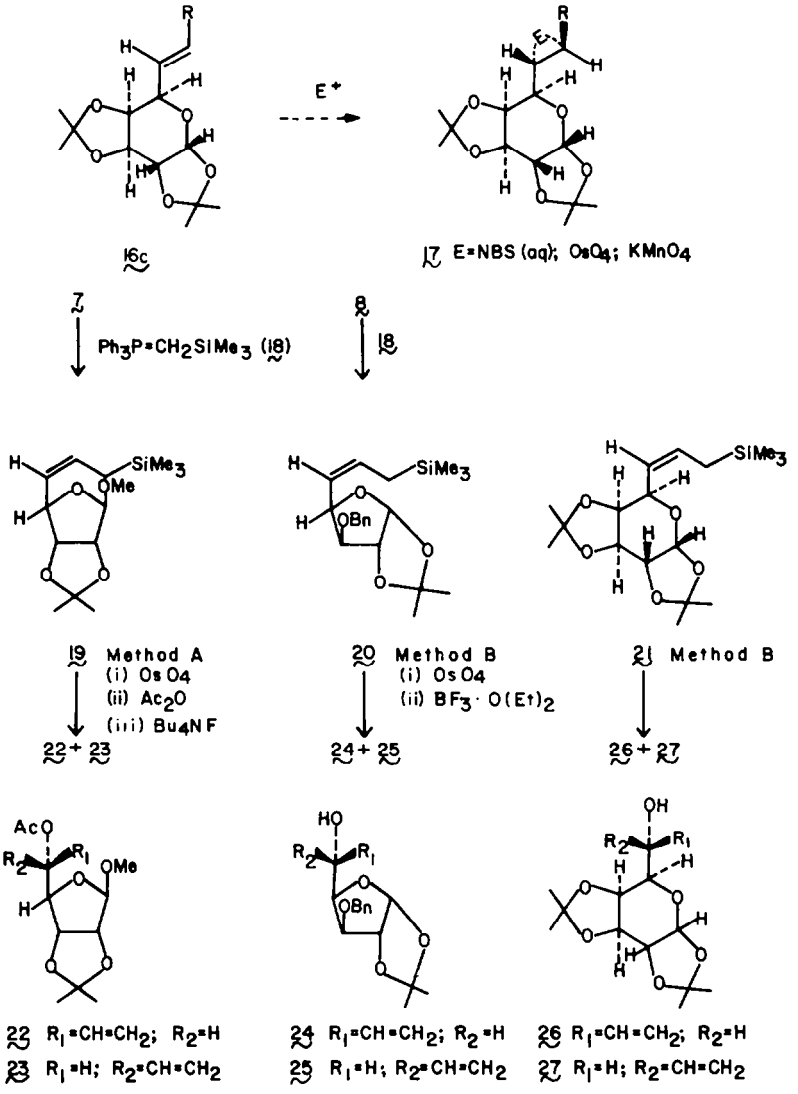


Table 2

Starting Material	Ratio of Vinyl Carbinols		Yield
	22	23	
19 →	8	1	96
7 —MgBr→	2	1	68
	24	25	
20 →	> 20	1	85
8 —MgBr→	1	1.5	81
	26	27	
21 →	20	1	80
9 —MgBr→	2	1	—

Table 3

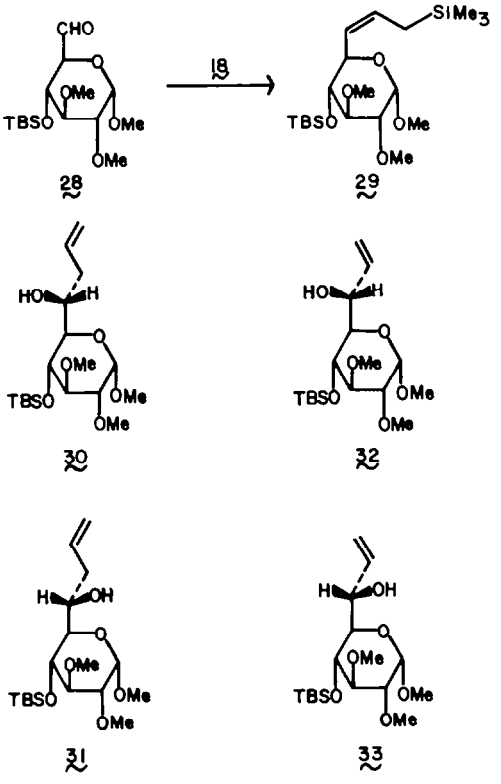
		30	31			32	33
28+6	BF_3 →	1	20	29	(i) OsO_4 → (ii) BF_3	1	2
28+6	$TiCl_4$ →	<1	20	28	MgBr →	1	2.5
28 +	MgBr →	1	2.5				

in which we would contemplate starting with a ribosyl or galactosyl precursor,[3] it was of interest to investigate the sense and quality of the chirality transfer in the case of a glucosyl derivative. With an eventual view towards a possible synthesis of apramycin,[25] we had occasion to prepare (*vide infra*) the aldehyde **28** and thence its allylsilane derivative **29**. Once again, as seen in Table 3, the reactions of **28** with allyl and vinyl magnesium bromides were not strongly selective though such modest selectivity as did exist tended to favor the apparent "cyclic Cram model" attack,[8] leading to a preference for **31** relative to **30** and for **33** relative to **32**.

The Sakurai reaction[11] of **28** with **6** under the influence of titanium tetrachloride, a chelation-promoting catalyst, did indeed produce **31** with very high selectivity. This was in keeping with previous precedents (*vide supra* Tables 1 and 2). *However, most unexpected was the finding that the same product predominated quite heavily even when* $BF_3 \cdot OEt_2$ *was the catalyst.* Thus, aldehyde **28** is the first in which the apparent chelation-promoting catalyst ($TiCl_4$) and the apparent Cram–Felkin catalyst (BF_3) afford substantially the same product. Put differently, it is the only case of the four in which the BF_3-catalyzed Sakurai reaction affords the apparent "*anti*-Cram" product, **31**.

Another surprise was encountered when allylsilane **29** was subjected to hydroxylation with osmium tetroxide. The major product was the vinyl carbinol **33**. Thus, as in the case of the ribose, xylose and galactose series, the Sakurai sequence with BF_3 catalysis and the osmylation of the side-chain alkenylsilanes afford products of the same configuration. In the previous cases, we took this convergence to reflect the involvement of opposite rotamers (cf. **16c** vs **7a**), each being attacked from the same α-face with opposite order of introduction of the carbon and oxygen atoms. Similarly, in the gluco series both sequences lead to the same major product. *However, in the gluco derivatives, the sense of the stereochemical induction in both sequences is reversed from that of the three previous cases.* To what extent this represents some very special effect of the large OTBS group, or is general to the gluco series, is not presently known.

The assignments of configurations to the various carbinols are based on chemical inter-correlations and correlation of at least one member of the series with a substance of proven stereochemistry. In each instance, the corresponding allylic and vinylic carbinols could be correlated with one another. In the ribose series, **10** was converted to its BOM ether which, upon ozonolysis and reductive workup, gave rise to aldehyde **34**. The

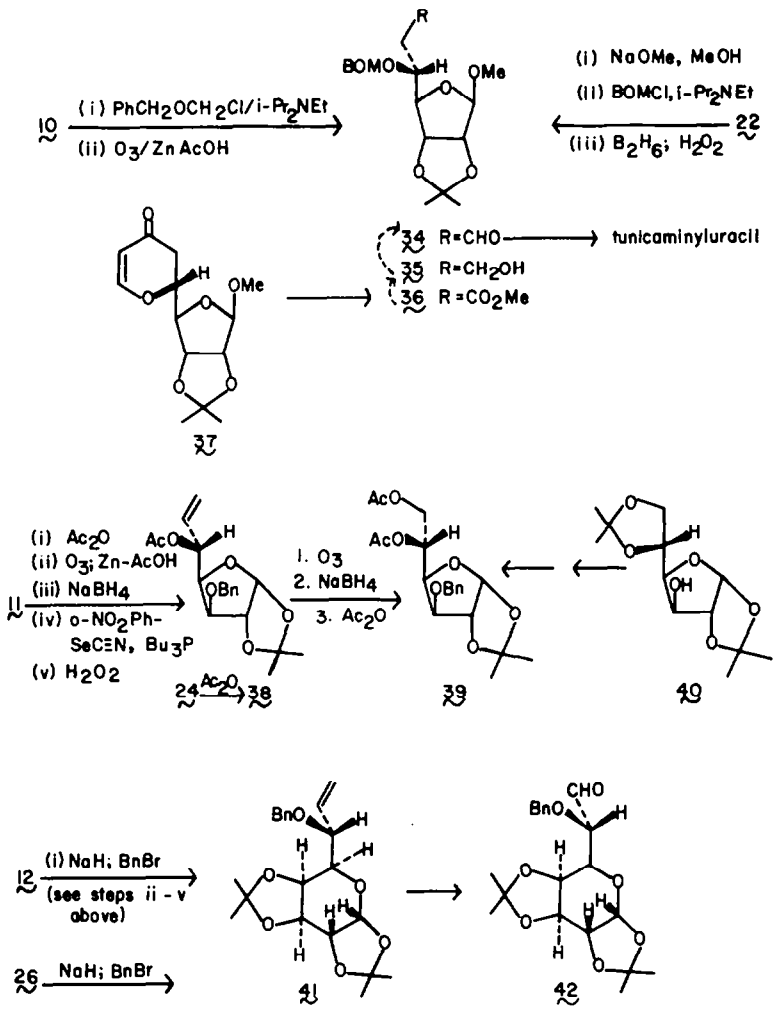


configuration at C_5 in this heptose is secure in that **34** was eventually[26] converted to a tunicaminyluracil derivative of known configuration. Moreover, the same aldehyde was synthesized from carbinol **35** via methyl ester **36**. This methyl ester, in turn, was obtained in four steps [(i) O_3; (ii) H_2O_2–NaOH; (iii) CH_2N_2; (iv) i-Pr_2NEt–$PhCH_2OCH_2Cl$] from dihydropyrone **37**. This compound was obtained by cyclocondensation of aldehyde **7** with *E*-1-methoxy-3-trimethylsilyloxybutadiene. The configuration at C_5 in **37**, and therefore in **36**, was proven by an X-ray crystallography determination.†

In the xylose series, the configurations of allyl carbinol **11** and vinyl carbinol **15** were interrelated as shown via the acetate **38**. This compound was, in turn, converted to the benzyl diacetate **39**. The latter was itself synthesized from diacetone glucose (**40**) by benzylation, selective deprotection and bis-acetylation.

In the galactose series, the configurations of carbinols **12** and **26** were interrelated in a similar way. In this case, the linkage point was the benzyl ether, **41**. Degradation of the vinyl group gave the corresponding aldehyde **42**. Rigorous evidence for the stereochemistry at C_5 in this compound had already been obtained via its cyclocondensation product with *Z,E*-1-*benzoyloxy-*

† The crystallographic determination was provided by Gayle Schulte of Yale University.

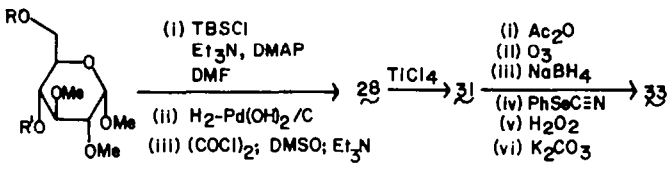


2 - *trimethylsilyloxy* - 4 - *methoxy* - 1,3 - *butadiene*.[27] A single-crystal X-ray determination of that cyclocondensation product parenthetically serves to define the configuration at C_6 of aldehyde **42** and, therefore, of **12** and **26**.

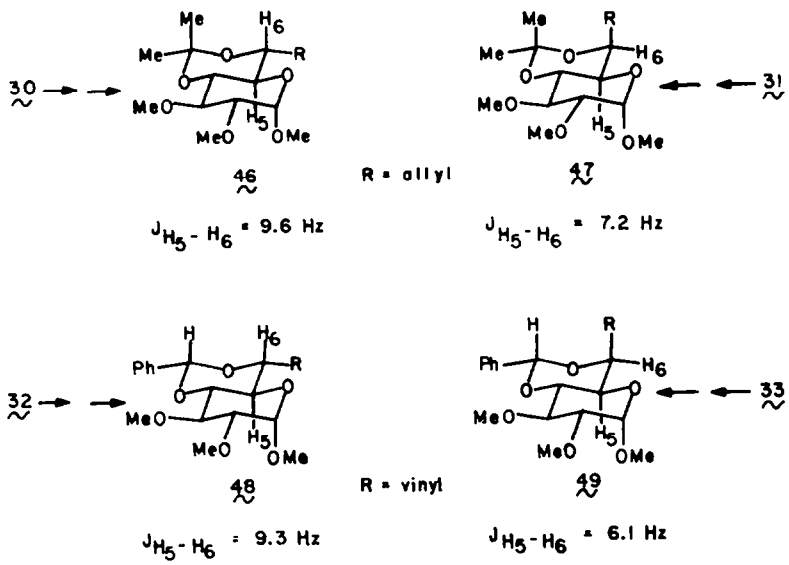
The glucose aldehyde **28** used in this work was synthesized from **43** (in turn obtained from its benzylidine precursor, see Experimental). Allylic carbinol **31** was interrelated with the vinylic carbinol **33** through the usual degradation. In fact, this is, at present, our only stereospecific route to **33**, since neither of the two direct routes (Table 3) were stereospecific.

The assignments of stereochemistry to **30** and **31** were based on their conversion to isopropylidene derivatives **46** and **47**. In each case, this was accomplished by desilylation (TBAF), followed by engagement of 2,2'-dimethoxypropane in the presence of camphorsulfonic acid. The crucial coupling consists of H_5 and H_6 in these compounds defines the configuration of the C-allyl group in both compounds and, therefore, in the related vinylic **32** and **33**. The assignments were cross-checked by conversion of **32** and **33** to their corresponding benzylidene derivatives, **48** and **49**. The critical coupling constants in these vinylic acetals are also provided.

In summary, through the reactions described herein, highly stereoselective routes to 14 of the hypothetical 16 allylic and vinylic carbinols derivable from the four basic aldehyde types have been developed. The two carbinols which do not yet fall within the scope of our methodology are the "Cram–Felkin-*anti*" carbinols **30** and **32**, derivable from the glucoaldehyde. At present, these are available only as minor products from our chemistry. The excellent routes developed



43 R=Bn, R'=H
44 R=Bn, R'=TBDMS
45 R=H, R'=TBDMS



to the other systems are proving to be very helpful in more complex undertakings.

EXPERIMENTAL

General. Reagents and solvents were purified and dried using standard methods. ^{1}H-NMR spectra were recorded on a Brucker WM-250 or WM-500 spectrometer, as indicated. Chemical shifts are reported in ppm (δ) relative to $CHCl_3$ (δ 7.270). Mass spectroscopic studies were conducted on a Hewlett–Packard Model 5985 mass spectrometer using electron-impact techniques. High-resolution mass spectra were recorded on a Kratos MS-80RFA. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. IR spectra were taken on a Perkin–Elmer 1420 spectrometer in $CHCl_3$, $CDCl_3$, or neat, as indicated. Optical rotations ($[\alpha]_D$) were obtained on a Perkin–Elmer 241 variable-wavelength polarimeter with a 1 ml quartz window cell. M.ps were determined with a Thomas–Hoover m.p. apparatus and are uncorrected. E. Merck silica gel No. 9385 (230–400) was used for column chromatography.

Preparation of alcohol **43**.[28] A soln of 6.70 g (0.092 mmol) of triethylamine–borane complex in 250 ml of dry THF containing 6.0 g of 4 Å molecular sieves under N_2 was stirred for 20 min at room temp, after which 12.2 g (0.092 mmol) of anhydrous $AlCl_3$ was slowly added via a powder addition funnel. After the addition was complete, 5.0 g (0.015 mmol) of β - methyl - 4,6 - O - benzylidene - 2,3 - O - dimethyl-glucopyranoside[29] was added in one portion. After 7 h at room temp, the reaction was filtered through Celite and treated with Dowex-50-X8 (H^+) resin. The mixture was filtered after 10 min and the solvent removed. The residue was co-concentrated with MeOH (3 × 60 ml) followed by chromatography on 200 g of silica gel (elution with 2:3, 1:1; EtOAc–hexanes) to afford 4.69 g (93%) of **43** as a viscous oil: $[\alpha]_D$ +85.6° (*c* 1.95, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.29 (m, 5H), 4.83 (d, 1H, J = 4.5 Hz), 4.56 (ABq, 2H, J = 12.0 Hz, $\Delta\nu_{AB}$ = 10.6 Hz), 3.68 (m, 3H), 3.60 (s, 3H), 3.58–3.46 (m, 1H), 3.46 (s, 3H), 3.39 (m, 1H), 3.40 (s, 3H), 3.22 (dd, 1H, J = 4.5, 10.2 Hz), 2.71 (br m, 1H); IR ($CHCl_3$) 3590, 3550–3400, 3010, 2930, 2910, 2840, 1155 and 1060 cm^{-1}.

Preparation of silyl ether **44**. A soln of 4.60 g (0.0147 mmol) of **43** and 3.9 ml (0.028 mmol) of Et_3N in 20 ml of dry DMF containing 170 mg (1.40 mmol) of dimethylaminopyridine under N_2 was treated with 3.26 g (0.021 mmol) of t-butyldimethylsilyl chloride. After 36 h, the reaction was diluted with EtOAc (400 ml), washed with H_2O (2 × 60 ml), brine (60 ml), dried ($MgSO_4$) and the solvent removed. Chromatography of the residue on 60 g of silica gel (elution with 1:9 EtOAc–hexanes) afforded 5.65 g (90%) of silyl ether **44** as a colorless oil: $[\alpha]_D$ +81.8° (*c* 1.95, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.31 (m, 5H), 4.82 (d, 1H, J = 3.5 Hz), 4.54 (ABq, 1H, J = 12.1 Hz, $\Delta\nu_{AB}$ = 25.3 Hz), 3.61 (m, 3H), 3.52 (s, 3H), 3.52–3.46 (m, 1H), 3.46 (s, 3H), 3.41 (s, 3H), 3.32 (t, 1H, J = 9.4 Hz), 3.20 (dd, 1H, J = 3.5, 9.5 Hz), 0.82 (s, 9H), 0.07 (s, 3H), −0.02 (s, 3H); IR ($CHCl_3$) 3020, 2960, 2935, 2860, 1160, 1095 and 1050 cm^{-1}.

Preparation of alcohol **45**. A mixture of 4.86 g (0.0113 mmol) of **44** and 120 mg of 5% palladium hydroxide on carbon in 70 ml of absolute MeOH was stirred under an H_2 atmosphere for 90 min. The H_2 was replaced with N_2 and the reaction filtered through Celite with washing with EtOAc (70 ml). The solvent was removed to afford 3.69 g (96%) of **45** as a white solid. Recrystallization from pentane afforded pure alcohol, m.p. 54–55°; $[\alpha]_D$ +115.2° (*c* 4.20, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 4.79 (d, 1H, J = 3.5 Hz), 3.78 (ddd, 1H, J = 2.6, 6.4, 11.6 Hz), 3.70–3.61 (m, 1H), 3.57–3.40 (m, 2H), 3.52 (s, 3H), 3.48 (s, 3H), 3.40 (s, 3H), 3.33 (t, 1H, J = 9.3 Hz), 3.15 (dd, 1H, J = 3.5, 9.4 Hz), 1.78 (br t, 1H, J = 6.4 Hz), 0.87 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H); IR ($CHCl_3$) 3690, 3640–3580, 3020, 2860, 2840, 2865, 1095 and 1055 cm^{-1}.

Preparation of aldehyde **28**. To a soln of 155 μl (1.79 mmol) of oxalyl chloride in 2 ml of dry CH_2Cl_2 at −78° under N_2 was added dropwise 317 μl (4.47 mmol) of dimethyl sulfoxide. After 5 min, a soln of 300 mg (0.89 mmol) of **45** in 2.0 ml of dry CH_2Cl_2 was added dropwise. After 1 h at −78°, 620 μl (4.46 mmol) of Et_3N was added and the reaction warmed to room temp. The mixture was poured into sat $NaHCO_3$ aq (5 ml) and extracted with CH_2Cl_2 (2 × 10 ml). The extracts were combined, dried ($MgSO_4$) and the solvent removed. Chromatography of the residue on 30 g of silica gel (elution 3:7, 1:1 EtOAc–hexanes) afforded 264 mg (89%) of **28** as a colorless oil: $[\alpha]_D$ +112.9° (*c* 2.68, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 9.71 (d, 1H, J = 0.9 Hz), 4.87 (d, 1H, J = 3.5 Hz), 4.05 (d, 1H, J = 9.9 Hz), 3.62–3.38 (m, 2H), 3.53 (s, 3H), 3.48 (s, 3H), 3.41 (s, 3H), 3.17 (dd, 1H, J = 3.5, 9.5 Hz), 0.86 (s, 9H), 0.09 (s, 3H), 0.00 (s, 3H); IR ($CHCl_3$) 3010, 2960, 2940, 2860, 1740, 1160, 1095 and 1050 cm^{-1}.

Reaction of aldehyde **7** *with silane* **6** *in the presence of* $BF_3 \cdot OEt_2$

Formation of compound **10**. A soln of 38 mg (0.20 mmol) of **7** in 10 ml of dry CH_2Cl_2 at −78° under N_2 was treated with 37 μl (0.30 mmol) of $BF_3 \cdot OEt_2$. After 15 min, allyltrimethylsilane (40 μl, 0.25 mmol) was added and the resulting soln stirred for 3 h at −78°. The reaction was poured into sat $NaHCO_3$ aq (5 ml) and extracted with Et_2O (2 × 10 ml). The extracts were combined, washed with brine (5 ml) and dried ($MgSO_4$).

Concentration *in vacuo* afforded **10** as the sole observable product, as judged by ^{1}H-NMR (250 MHz) analysis. Chromatography on 5 g of silica gel (elution with 1:4 EtOAc–hexanes) afforded 38 mg (80%) of pure **10**: ^{1}H-NMR (250 MHz, $CDCl_3$) δ 5.8–5.6 (m, 1H), 5.1–5.25 (m, 2H), 4.98 (s, 1H), 4.8 (d, 1H, J = 6 Hz), 4.58 (d, 1H, J = 6 Hz), 4.27 (d, 1H, J = 2 Hz), 3.75 (m, 1H), 3.61 (s, 1H), 3.44 (s, 3H), 2.3 (t, 2H, J = 7 Hz), 1.5 (s, 3H), 1.33 (s, 3H); IR ($CDCl_3$) 3500, 1380, 1250, 1200, 1050 cm^{-1}; MS *m/z* 229 ($M^+ - 15$), 203 ($M^+ -$ allyl); anal. ($C_{12}H_{20}O_5$) C, H.

Reaction of aldehyde **7** *with silane* **6** *in the presence of* $TiCl_4$ gave an 89% yield of **10** and **13** as a 1:20 mixture.

Compound **13**. ^{1}H-NMR (250 MHz, $CDCl_3$) δ 5.95–5.75 (m, 1H), 5.2–5.05 (m, 2H), 5.0 (s, 1H), 4.55 (d, 1H, J = 6 Hz), 4.6 (t, 1H, J = 6 Hz), 4.4 (d, 1H, J = 2 Hz), 3.6 (s, 1H), 3.5 (s, 3H), 3.4 (m, 1H), 2.3 (t, 2H, J = 7 Hz), 1.55 (s, 3H), 1.35 (s, 3H); IR ($CDCl_3$) 3400, 1375, 1250, 1080 cm^{-1}; MS *m/z* 299 ($M^+ - 15$), 203 ($M^+ -$ allyl); anal. ($C_{12}H_{20}O_5$) C, H.

Reaction of aldehyde **8** *with silane* **6** *in the presence of* $BF_3 \cdot OEt_2$ gave a 69% yield of **11** as the only observable product by ^{1}H-NMR (250 MHz) analysis.

Compound **11**. ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.4–7.3 (m, 5H), 5.97 (d, 1H, J = 4 Hz), 5.95–5.8 (m, 1H), 5.18 (m, 1H), 5.1 (m, 1H), 4.75 (d, 1H, J = 8 Hz), 4.65 (d, 1H, J = 4 Hz), 4.55 (d, 1H, J = 8 Hz), 4.1 (m, 1H), 4.0 (m, 2H), 2.55–2.4 (m, 1H), 2.3–2.15 (m, 2H), 1.5 (s, 3H), 1.34 (s, 3H); IR ($CDCl_3$) 3550, 1080, 1040 cm^{-1}; MS *m/z* 320 (M^+), 305, 279; anal. ($C_{18}H_{24}O_5$) C, H.

Reaction of aldehyde **8** *with silane* **6** *in the presence of* $TiCl_4$ gave a 74% yield of **14** as the only observable product by ^{1}H-NMR (250 MHz) analysis.

Compound **14**. ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.4–7.25 (m, 5H), 6.0 (d, 1H, J = 4 Hz), 6.0–5.8 (m, 1H), 5.15 (m, 1H), 5.05 (s, 1H), 4.75 (d, 1H, J = 11 Hz), 4.68 (d, 1H, J = 4 Hz), 4.48 (d, 1H, J = 11 Hz), 4.1–4.0 (m, 2H), 3.9 (d, 1H, J = 3 Hz), 2.85 (s, 1H), 2.25 (t, 2H, J = 6 Hz), 1.5 (s, 3H), 1.34 (s, 3H); IR ($CDCl_3$) 3500, 1740, 1070, 1020 cm^{-1}; MS *m/z* 305 ($M^+ - 15$), 279.

Reaction of aldehyde **9** *with silane* **6** *in the presence of* $BF_3 \cdot OEt_2$ gave a 78% yield of **12** and **15** as a 20:1 mixture.

Compound **12**. ^{1}H-NMR (250 MHz, $CDCl_3$) δ 5.9–5.7 (m, 1H), 5.5 (d, 1H, J = 6 Hz), 5.2–5.05 (m, 2H), 4.6 (dd, 1H, J = 7, 2 Hz), 4.4 (dd, 1H, J = 7, 2 Hz), 4.3 (dd, 1H, J = 6, 2 Hz), 3.8 (m, 1H), 3.6 (dd, 1H, J = 7, 2 Hz), 2.4 (m, 2H), 2.2 (m, 1H), 1.5 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H), 2.3 (s, 3H); IR ($CDCl_3$) 3500, 1380, 1250, 1200, 1070 cm^{-1}; MS *m/z* 300 (M^+), 285 ($M^+ - 15$), 259 ($M^+ -$ allyl); anal. ($C_{15}H_{24}O_6$) C, H.

Reaction of aldehyde **9** *with silane* **6** *in the presence of* $TiCl_4$ gave a 64% yield of **12** and **15** as a 1:10 mixture.

Compound **15**. ^{1}H-NMR (250 MHz, $CDCl_3$) δ 6.05–5.8 (m, 1H), 5.7 (d, 1H, J = 6 Hz), 5.25–5.05 (m, 2H), 4.6 (dd, 1H, J = 7, 2 Hz), 4.33 (dd, 1H, J = 7, 2 Hz), 4.3 (d, 1H, J = 2 Hz), 4.0 (q, 1H, J = 7 Hz), 3.7 (m, 1H), 3.15 (s, 1H), 2.4 (m, 2H), 1.55 (s, 3H), 1.5 (s, 3H), 1.37 (s, 3H), 1.3 (s, 3H); IR ($CHCl_3$) 3750, 3450, 1200, 1075 cm^{-1}; MS *m/z* 300 (M^+), 285 ($M^- - 15$), 259 ($M^- -$ allyl); anal. ($C_{15}H_{24}O_6$) C, H.

Reaction of aldehyde **28** *with silane* **6** *in the presence of* $TiCl_4$ gave an 80% yield of **31** as the sole observable product by ^{1}H-NMR (250 MHz) analysis.

Compound **31**. M.p. 121–122.5° (Et_2O, pentane); $[\alpha]_D$ +90.41° (*c* 0.97, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.83 (tdd, 1H, J = 7.0, 10.7, 16.6 Hz), 5.16–5.12 (m, 2H), 4.85 (d, 1H, J = 3.6 Hz), 3.93 (br q, 1H, J = 8.3 Hz), 3.65 (t, 1H, J = 9.3 Hz), 3.55 (s, 3H), 3.51 (s, 3H), 3.43 (s, 3H), 3.42 (d, 1H, J = 8.8 Hz), 3.36 (t, 1H, J = 9.5 Hz), 3.19 (dd, 1H, J = 3.6, 9.7 Hz), 2.46 (br td, 1H, J = 7.0, 13.7 Hz), 2.31 (br td, 1H, J = 7.0, 13.7 Hz), 1.69 (d, 1H, J = 9.0 Hz), 0.908 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); IR ($CHCl_3$) 3600, 3030, 2975, 2945, 2875, 1600, 1170, 1100, 1060 cm^{-1}.

Reaction of aldehyde **28** *in the presence of* $BF_3 \cdot OEt_2$ under the usual conditions in CH_2Cl_2 gave an 80% yield of **30** and **31** as a 3:7 mixture which was unseparable by column chromatography. In toluene at −78° the ratio of **30**:**31** was 1:20.

Formation of allylsilane **21**. A suspension of 2.46 g (6.9 mmol) of methyltriphenylphosphonium bromide in 30 ml of dry THF at 0° under N_2 was treated with 4.0 ml (10 mmol) of 2.5 M n-BuLi in hexane followed by warming to room temp. After 1 h, the clear red soln was cooled to 0° and treated with 1.7 g (8.1 mmol) of iodomethyltrimethylsilane, followed by warming to room temp. After 1 h, the reaction was cooled to −78° and treated with 4.0 ml (10 mmol) of 2.5 M n-BuLi in hexane. The resulting dark red soln was warmed to room temp, stirred for 2.5 h, recooled to −78° and treated with a soln of 988 mg (3.8 mmol) of **9** in 5 ml of dry THF, followed by warming to room temp. After 19 h, the reaction was diluted with Et_2O and washed with sat NH_4Cl aq. The organic phase was washed with brine, dried ($MgSO_4$) and the solvent removed *in vacuo*. Chromatography on 30 g of silica gel (elution with 95:5 hexane–EtOAc) gave 560 mg (44%) of allylsilane and 195 mg of a mixed fraction which contains the allylsilane and **26** protected as its trimethylsilyl ether. The ether could be separated from the allylsilane by hydrolysis to the alcohol with citric acid in MeOH and rechromatography.

Compound **21**. $[\alpha]_D$ −70° (*c* 1.2, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 5.73 (dt, 1H, J = 11, 8 Hz), 5.58 (d, 1H, J = 5.1 Hz), 5.5–5.6 (m, 1H), 4.62 (dd, 1H, J = 7.9, 2.3 Hz), 4.54 (dt, 1H, J = 8.4, 0.8 Hz), 4.32 (dd, 1H, J = 5.1, 2.3 Hz), 4.14 (dd, 1H, J = 7.9, 2.0 Hz), 1.6 (m, 2H), 1.58 (s, 3H), 1.49 (s, 3H), 1.36 (br s, 6H), 0.04 (s, 9H); IR ($CHCl_3$) 1245, 1062, 854 cm^{-1}; MS *m/z* (%) 343 ($M^+ + 1$, 1), 327 ($M^+ - 15$, 17), 131 (55), 113 (100).

Reaction of aldehyde **7** as above gave a 58% yield of allylsilane **19**.

Compound **19**. $[\alpha]_D$ −9.25° (*c* 1.06, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 5.50–5.62 (br t, 1H, J = 8.8 Hz), 5.33–5.41 (br d, 1H, J = 10 Hz), 4.96 (s, 1H), 4.92 (d, 1H, J = 9.5 Hz), 4.64 (d, 1H, J = 5.9 Hz), 4.55 (d, 1H, J = 5.9 Hz), 3.31 (s, 3H), 1.58–1.62 (m, 2H), 1.50 (s, 3H), 1.31 (s, 3H), 0.05 (s, 9H); IR ($CHCl_3$) 3010, 1215, 1100 cm^{-1}.

Reaction of aldehyde **8** as above gave a 29% yield of allylsilane **20** and a 29% yield of allyl alcohol **24** after hydrolysis with citric acid.

Compound **20**. $[\alpha]_D$ −83° (*c* 1.5, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.3 (m, 5H), 5.96 (d, 1H, J = 3.9 Hz), 5.78 (dt, 1H, J = 11.0, 9 Hz), 5.63 (dd, 1H, J = 11, 8.6 Hz), 4.93 (dd, 1H, J = 8.6, 3.0 Hz), 4.67 (d, 1H, J = 12.0 Hz), 4.64 (d, 1H, J = 3.9 Hz), 4.57 (d, 1H, J = 12.0 Hz), 3.83 (d, 1H, J = 3.0 Hz), 1.65 (dd, 1H, J = 12, 9 Hz), 1.57 (dd, 1H, J = 12, 9 Hz), 1.54 (s, 3H), 1.34 (s, 3H), 0.04 (s, 9H); IR (neat) 1073, 855 cm^{-1}; MS *m/z* (%) 362 (M^+, 0.1), 347 (1), 173 (83), 91 (100). Exact mass calc for $C_{20}H_{30}O_4Si$: 362.1913. Found: 362.1867.

Reaction of aldehyde **28** afforded a 27% yield of allylsilane **29** as a 3:1 *Z*:*E* mixture and a 37% yield of vinyl carbinol **33** after hydrolysis with citric acid.

Formation of vinyl carbinol **26** (*Method A*)

The allylsilane **21** (163.7 mg, 0.48 mmol) was dissolved in THF (5 ml)–H_2O (1 ml) and OsO_4 (6 mg, 0.02 mmol) and 4-methylmorpholine N-oxide monohydrate (108 mg, 0.92 mmol) were added. After stirring 24 h, sat $NaHSO_3$ (1 ml) was added. After stirring 6 h, the aq phase was extracted with Et_2O. The Et_2O extract was washed with brine, dried (Na_2SO_4) and the solvent was removed. The residue was filtered through silica and the solvent was removed to give 168.5 mg of crude diol.

The diol was dissolved in CH_2Cl_2 (4 ml) under N_2 and cooled to −78°. $BF_3 \cdot OEt_2$ (65 mg, 0.46 mmol) was added and the soln slowly warmed to −5° over 2.5 h. Sat $NaHCO_3$ and Et_2O were added and the organic layer was separated, washed with brine, dried (Na_2SO_4) and the solvent was removed. Flash chromatography on silica (5 g) with 3:1

hexanes–EtOAc gave 110.0 mg (80%) of **26** and **27** as a 20:1 mixture.

Formation of acetates of alcohols **22** *and* **23** *(Method B)*

To a soln of **19** (100 mg, 0.35 mmol) in 10 ml of dry THF was added 40 mg (0.34 mmol) of 4-methylmorpholine N-oxide monohydrate dissolved in 2 ml of H_2O. OsO_4 (5 mg, 0.02 mmol) was added and the mixture stirred at room temp for 24 h under N_2. The reaction was quenched by addition of 10 ml of sat sodium dithionite aq and the mixture stirred for 1 h. The mixture was poured into 100 ml of EtOAc and partitioned with 50 ml of sat $NaHCO_3$ aq and twice with 25 ml of H_2O. The EtOAc extract was dried ($MgSO_4$), filtered and evaporated *in vacuo* to afford 103.7 mg (92.6%) of the crude epimeric mixture of diols.

The crude diol (68.4 mg, 0.22 mmol) was redissolved in 5 ml of dry pyridine. Ac_2O (1 ml) and 2 mg of *p*-dimethylaminopyridine were added and the mixture stirred at room temp for 4 h. Pyridine was removed *in vacuo* and the residue redissolved in 25 ml of $CHCl_3$. The $CHCl_3$ soln was partitioned with 10 ml of sat $NaHCO_3$ aq and washed twice with 10 ml of H_2O. The $CHCl_3$ extract was dried ($MgSO_4$), filtered and evaporated *in vacuo* to yield 75 mg (86%) of the crude epimeric mixture of diacetates.

The crude diacetates (27 mg, 0.06 mmol) were dissolved in 5 ml of CH_3CN. Tetrabutylammonium fluoride (0.5 ml) was added and the mixture stirred at room temp and under N_2 for 3 h. Solvent was removed *in vacuo* and the residue redissolved in 50 ml of $CHCl_3$. The $CHCl_3$ soln was washed twice with 25 ml of H_2O, dried ($MgSO_4$), filtered and evaporated *in vacuo*. The syrupy residue was purified by chromatography over silica gel (hexane–EtOAc, 4:1) to afford 18 mg (95.6%) of the epimeric mixture of acetates as an 8:1 mixture. The two epimers were separated by HPLC (μ Porasil, hexane–EtOAc, 9:1).

Compound **22** *acetate*. $[\alpha]_D$ −54.1° (*c* 1.0, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 5.80–5.94 (m, 1H), 5.37 (d, 1H, J = 12.8 Hz), 5.36 (d, 1H, J = 7 Hz), 5.33 (d, 1H, J = 17.4 Hz), 4.97 (s, 1H), 4.69 (d, 1H, J = 6.0 Hz), 4.58 (d, 1H, J = 6.0 Hz), 4.25 (d, 1H, J = 7.0 Hz), 3.32 (s, 3H), 2.11 (s, 3H), 1.49 (s, 3H), 1.33 (s, 3H); IR ($CHCl_3$) 3010, 1740 cm^{-1}. Exact mass calc for $C_{13}H_{20}O_6$: 272.1260. Found: 272.1258.

Compound **23** *acetate*. $[\alpha]_D$ −50.0° (*c* 0.31, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 5.72–5.86 (m, 1H), 5.45 (d, 1H, J = 18.2 Hz), 5.39 (d, 1H, J = 10.8 Hz), 5.22–5.29 (m, 1H), 5.01 (s, 1H), 4.67 (d, 1H, J = 6.0 Hz), 4.64 (d, 1H, J = 6.0 Hz), 4.23 (d, 1H, J = 7.9 Hz), 3.31 (s, 3H), 2.12 (s, 3H), 1.50 (s, 3H), 1.33 (s, 3H); IR ($CHCl_3$) 3010, 1740 cm^{-1}.

Reaction of allylsilane **20** as above (Method A) gave an 85% yield of **24** as the only compound observable by ^{1}H-NMR (250 MHz) analysis.

Compound **24**. $[\alpha]_D$ −34° (*c* 1.17, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.98 (d, 1H, J = 3.8 Hz), 5.96 (ddd, 1H, J = 17.2, 10.5, 5.2 Hz), 5.37 (dt, 1H, J = 17.2, 1.6 Hz), 5.20 (dt, 1H, J = 10.5, 1.6 Hz), 4.68 (d, 1H, J = 11.6 Hz), 4.61 (d, 1H, J = 3.8 Hz), 4.51 (d, 1H, J = 11.6 Hz), 4.52 (m, 1H), 4.13 (d, 1H, J = 3.4 Hz), 4.10 (dd, 1H, J = 3.4, 6.4 Hz), 2.6 (d, 1H, J = 7.1 Hz), 1.47 (s, 3H), 1.31 (s, 3H); IR (neat) 3500, 1218, 1076 cm^{-1}; MS *m/z* (%) 291 (M^+ − 15, 1), 249 (19), 91 (100); anal. ($C_{17}H_{22}O_5$) C, H.

Reaction of allylsilane **29** as above (Method A) gave an 84% yield of **32** and **33** as a 1:3 mixture.

Compound **33**. M.p. 129.5–13.5° (Et_2O, pentane); $[\alpha]_D$ +77.06° (*c* 1.80, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.99 (ddd, 1H, J = 5.4, 10.6, 17.2 Hz), 5.33 (br d, 1H, J = 17.2 Hz), 5.20 (br d, 1H, J = 10.6 Hz), 4.83 (d, 1H, J = 3.6 Hz), 4.40 (m, 1H), 3.38 (s, 3H), 3.36 (t, 1H, J = 9.0 Hz), 3.67 (t, 1H, J = 9.0 Hz), 3.56 (s, 3H), 3.51 (s, 3H), 3.48 (t, 1H, J = 9.0 Hz), 3.24 (dd, 1H, J = 3.6, 9.6 Hz), 1.82 (d, 1H, J = 9.6 Hz), 0.92 (s, 9H), 0.16 (s, 6H); IR ($CHCl_3$) 3630, 3590, 3030, 2975, 2945, 2875, 1170, 1100, 1060 cm^{-1}.

Compound **32**. $[\alpha]_D$ +103.74 (*c* 0.99, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.01 (ddd, 1H, J = 5.9, 10.6, 17.2 Hz), 5.42 (td, 1H, J = 1.5, 17.2 Hz), 5.32 (td, 1H, J = 1.4, 10.6 Hz), 4.84 (d, 1H, J = 3.5 Hz), 4.42 (m, 1H), 3.75 (m, 1H), 3.56 (s, 3H), 3.49 (s, 3H), 3.45 (s, 3H), 3.38 (m, 2H), 3.18 (m, 1H), 2.27 (d, 1H, J = 8.4 Hz), 0.90 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); IR ($CHCl_3$) 3580, 3540–3400, 3010, 2960, 2930, 2860, 1160, 1090, 1050 cm^{-1}.

Reaction of aldehyde **8** *with vinylmagnesium bromide* gave an 81% yield of a 1:1.5 mixture of **24** and **25**.

Compound **25**. M.p. 78–79°; $[\alpha]_D$ −55° (*c* 0.79, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.3 (m, 5H), 6.00 (d, 1H, J = 3.8 Hz), 5.84 (ddd, 1H, J = 17.2, 10.5, 5.6 Hz), 5.42 (dt, 1H, J = 17.2, 1.5 Hz), 5.21 (dt, 1H, J = 10.5, 1.5 Hz), 4.70 (d, 1H, J = 11.7 Hz), 4.65 (d, 1H, J = 3.8 Hz), 4.54 (m, 1H), 4.48 (d, 1H, J = 11.7 Hz), 4.07 (dd, 1H, J = 6.5, 3.4 Hz), 4.97 (d, 1H, J = 3.4 Hz), 2.74 (br, 1H), 1.50 (s, 3H), 1.34 (s, 3H); IR ($CDCl_3$) 1073, 1020 cm^{-1}; MS *m/z* (%) 291 (M^+ − 15, 0.5), 249 (8), 91 (100). Exact mass calc for $C_{17}H_{22}O_5$: 306.1467. Found: 306.1491.

Acetate of **11**. ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.40–7.28 (m, 5H), 5.92 (d, 1H, J = 3.7 Hz), 5.80 (m, 1H), 5.27 (m, 1H), 5.12 (br d, 1H, J = 8.8 Hz), 5.05 (br s, 1H), 4.60 (d, 1H, J = 4.0 Hz), 4.53 (ABq, 2H, J = 11.6 Hz, $\Delta\nu_{AB}$ = 40.1 Hz), 4.20 (dd, 1H, J = 3.1, 8.6 Hz), 3.90 (d, 1H, J = 3.2 Hz), 2.69 (m, 1H), 2.40 (dt, 1H, J = 7.6, 14.7 Hz), 1.90 (s, 3H), 1.50 (s, 3H), 1.30 (s, 3H); IR ($CHCl_3$) 1740, 1375, 1248, 1080, 1025 cm^{-1}; MS *m/z* (%) 347 (P^+ − 15 (Me)), 302 (P^+ − 60 (HOAc)).

Benzyl ether **12**. ^{1}H-NMR (250 MHz, $CDCl_3$) δ 7.43–7.25 (m, 5H), 5.95 (tdd, 1H, J = 7.5, 9.8, 17.1 Hz), 5.61 (d, 1H, J = 5.0 Hz), 5.17 (br d, 1H, J = 17.1 Hz), 5.07 (br d, 1H, J = 9.8 Hz), 4.72 (ABq, 2H, J = 11.6 Hz, $\Delta\nu_{AB}$ = 59.6 Hz), 4.59 (dd, 1H, J = 2.4, 7.9 Hz), 4.32 (dd, 1H, J = 2.4, 5.0 Hz), 4.28 (dd, 1H, J = 1.8, 8.0 Hz), 3.87 (dd, 1H, J = 1.5, 7.8 Hz), 3.75 (dt, 1H, J = 3.6, 7.5 Hz), 2.52 (m, 1H), 2.33 (dt, 1H, J = 7.5, 14.6 Hz), 1.54 (s, 3H), 1.47 (s, 3H), 1.35 (s, 3H), 1.34 (s, 3H); IR ($CHCl_3$) 3060, 2980, 2925, 2865, 1640, 1380, 1250, 1210, 1165, 1110, 1070 cm^{-1}; MS (20 eV) *m/z* 390 (P^+), 375 (P^+ − 15 (Me)), 349 (P^+ − 41 (allyl)), 299 (P^+ − 91 (benzyl)); anal. C, H.

Acetate of **31**. $[\alpha]_D$ +82.3° (*c* 1.65, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 5.73 (tdd, 1H, J = 7.2, 9.8, 17.2 Hz), 5.11 (br d, 1H, J = 9.8 Hz), 5.06–5.01 (m, 2H), 4.88 (d, 1H, J = 3.3 Hz), 3.56 (t, 1H, J = 9.3 Hz), 3.51 (s, 3H), 3.47 (s, 3H), 3.45 (t, 1H, J = 9.0 Hz), 3.43 (s, 3H), 3.32 (t, 1H, J = 9.5 Hz), 3.21 (dd, 1H, J = 3.3, 9.5 Hz), 2.50 (m, 2H), 2.05 (s, 3H), 0.86 (s, 9H), 0.06 (s, 3H), −0.05 (s, 3H); IR ($CHCl_3$) 3020, 2970, 2940, 2880, 1745, 1650, 1255, 1100, 1055 cm^{-1}.

Conversion of benzyl ether **12** *to benzyl ether* **41**

Ozone was bubbled through a soln of 218 mg (0.555 mmol) of **12** in 50 ml of dry CH_2Cl_2 at −78° until the soln remained blue. The soln was then purged with N_2, discharging the blue color. The reaction was warmed to room temp and treated with Zn (dust) followed by HOAc. After 90 min, the reaction was filtered through Celite and the solvent removed *in vacuo*. The residue was filtered through silica gel (elution 1:4 EtOAc–hexane) to afford 218 mg of aldehyde which was used directly in the next reaction.

To a soln of the above aldehyde in 5.0 ml of CH_2Cl_2 containing 5.0 ml of absolute EtOH at 0° was added 21 mg (0.55 mmol) of $NaBH_4$. After 30 min, the reaction was quenched by the addition of sat NH_4Cl (5 ml), and the product extracted with Et_2O (3 × 10 ml). The extracts were combined, dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. Filtration of the residue through silica gel (elution with 1:4 EtOAc–hexane) afforded 185 mg of alcohol which was used directly in the next reaction.

To a soln of the above alcohol in 2.0 ml of dry THF was added 150 mg (0.66 mmol) of *o*-nitrophenyl selenocyanate followed by the dropwise addition of 164 μl (0.66 mmol) of tri-n-butylphosphine. After 30 min at room temp, the reaction was cooled to 0° and treated with 200 μl of 30% H_2O_2 over a 1 h period. The mixture was warmed to room temp and stirred for 6 h. The reaction was diluted with 5 ml of CH_2Cl_2, solid $NaHCO_3$ was added and the suspension allowed to stir overnight. The mixture was diluted with sat $NaHCO_3$ aq (5 ml) and extracted with Et_2O (3 × 10 ml). The extracts were

combined, dried ($MgSO_4$) and the solvent was removed *in vacuo*. Chromatography (elution with 1:9 EtOAc–hexane) afforded 123 mg (60%) of **12** which was identical to a sample of **12** prepared previously.

Conversion of the acetate of **31** *into* **33**

Treatment of the acetate of **31** under the above conditions followed by methanolysis afforded a vinyl carbinol (30% overall yield) which was identical to **33** prepared previously.

Desilylation of **30** *and* **31**. A soln of 60 mg (0.160 mmol) of a mixture of **30** and **31** in 250 μl of dry THF at 0° was treated with 256 μl (0.256 mmol) of a 1 M soln of tetrabutylammonium fluoride in THF. After 4 h, the reaction was poured into sat NH_4Cl (5 ml) and extracted with CH_2Cl_2 (3 × 10 ml). The extracts were combined, dried ($MgSO_4$) and the solvent was removed *in vacuo*. Chromatography of the residue on 10 g of silica gel (elution with 50:50:1 EtOAc–hexane–i-PrOH) afforded 12 mg (29%) of Cram diol **30** (R = H) as an oil: $[\alpha]_D$ +123.83° (*c* 0.94, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.91 (m, 1H), 5.21–5.16 (m, 2H), 4.82 (d, 1H, J = 3.6 Hz), 3.83 (m, 1H), 3.65 (s, 3H), 3.56 (m, 1H), 3.51 (s, 3H), 3.48 (t, 1H, J = 9.4 Hz), 3.44 (s, 3H), 3.26 (d, 1H, J = 1.5 Hz), 3.21 (dd, 1H, J = 3.6, 9.3 Hz), 2.82 (d, 1H, J = 3.4 Hz), 2.62–2.57 (m, 1H), 2.26 (td, 1H, J = 8.3, 14.3 Hz); IR ($CHCl_3$) 3585, 3540–3460, 3010, 2935, 2910, 2840, 1645, 1605, 1155, 1090, 1055 cm^{-1}.

Further elution with 60:40:1 EtOAc–hexane–i-PrOH afforded 28 mg (67%) of *anti*-Cram diol **31** (R = H) as a crystalline material, m.p. 96.0–97.0°; $[\alpha]_D$ +101.30° (*c* 2.53, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.87 (tdd, 1H, J = 7.00, 10.17, 17.15 Hz), 5.16 (br d, 1H, J = 17.15 Hz), 5.13 (br d, 1H, J = 10.17 Hz), 4.88 (d, 1H, J = 3.52 Hz), 4.00 (dq, 1H, J = 2.80, 8.30 Hz), 3.67 (dt, 1H, J = 2.86, 9.04 Hz), 3.64 (s, 3.54 (dd, 1H, J = 1.59, 9.87 Hz), 3.51 (s, 3H), 3.47 (t, 1H, J = 9.41 Hz), 3.44 (s, 3H), 3.23 (dd, 1H, J = 3.48, 9.58 Hz), 2.59 (d, 1H, J = 2.80 Hz), 2.46 (m, 1H), 2.36 (m, 1H), 1.95 (d, 1H, J = 8.23 Hz); IR ($CHCl_3$) 3600, 3560 3300, 3095, 3030, 2950, 2930, 2855, 1650, 1165, 1105, 1075, 1060, 1035 cm^{-1}.

Formation of acetonide **46**. A soln of 12 mg (0.0458 mmol) of diol **30** (R = H) and 1 mg of PPTS in 250 μl of dry CH_2Cl_2 containing 100 μl of 2,2-dimethoxypropane was stirred at room temp for 90 min. The reaction was directly chromatographed on 5 g of silica gel (elution with 1:3 EtOAc–hexane) to afford 13 mg (96%) of acetonide **46** as a crystalline material: $[\alpha]_D$ +95.6° (*c* 1.47, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.90 (m, 1H), 5.12 (dd, 1H, J = 1.6, 17.2 Hz), 5.07 (dd, 1H, J = 1.6, 10.2 Hz), 4.81 (d, 1H, J = 3.8 Hz), 3.79 (ddd, 1H, J = 3.5, 7.2, 9.6 Hz), 3.58 (s, 3H), 3.56 (t, 1H, J = 9.6 Hz), 3.53 (s, 3H), 3.50 (t, 1H, J = 9.1 Hz), 3.41 (s, 3H), 3.28 (t, 1H, J = 9.6 Hz), 3.23 (dd, 1H, J = 3.8, 9.1 Hz), 2.50 (m, 1H), 2.23 (dt, 1H, J = 7.2, 14.6 Hz), 1.51 (s, 3H), 1.43 (s, 3H); IR ($CHCl_3$) 3020, 2940, 2845, 1645, 1100, 1070 cm^{-1}.

Formation of acetonide **47**. Treatment of diol **31** (R = H) under the above conditions afforded the acetonide **47** (89%): $[\alpha]_D$ +96.0° (*c* 1.36, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.88 (m, 1H), 5.14 (dd, 1H, J = 1.6, 17.2 Hz), 5.06 (dd, 1H, J = 1.6, 10.2 Hz), 4.83 (d, 1H, J = 3.8 Hz), 4.12 (m, 1H), 3.87 (dd, 1H, J = 7.2, 9.8 Hz), 3.60 (t, 1H, J = 9.6 Hz), 3.58 (s, 3H), 3.55 (t, 1H, J = 9.1 Hz), 3.53 (s, 3H), 3.40 (s, 3H), 3.24 (dd, 1H, J = 3.8, 9.0 Hz), 2.45–2.37 (m, 2H), 1.45 (s, 3H), 1.37 (s, 3H); IR ($CHCl_3$) 3020, 2940, 2920, 2840, 1645, 1205, 1165, 1095, 1070, 1050 cm^{-1}.

Formation of benzylidene acetal **48**. A soln of 13.5 mg (0.0373 mmol) of **32** in 100 μl of dry THF at room temp was treated with 75 μl (0.0746 mmol) of a 1 M soln of tetrabutylammonium fluoride in THF. After 2 h, the reaction was directly chromatographed on 5 g of silica gel (elution with 3:2 EtOAc–hexane) to afford 8.2 mg of diol which was used directly in the next reaction.

A soln of the above diol in 200 μl of dry CH_2Cl_2 containing 100 μl of benzaldehyde dimethylacetal was treated with 1 mg of CSA. After 24 h the reaction was directly chromatographed on 5 g of silica gel (elution with 5:95 EtOAc–hexane) to afford 8.5 mg (80%) of **48** as a crystalline material: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.52 7.35 (m, 5H, 5.99 (dd, 1H, J = 5.8, 10.7, 17.2 Hz), 5.69 (s, 1H), 5.50 (td, 1H, J = 1.5, 17.2 Hz), 5.33 (td, 1H, J = 1.5, 10.7 Hz), 4.87 (d, 1H, J = 3.7 Hz), 4.21 (br dd, 1H, J = 5.8, 9.3 Hz), 3.69 (t, 1H, J = 9.2 Hz), 3.65 (s, 3H), 3.61 (t, 1H, J = 9.3 Hz), 3.56 (s, 3H), 3.48 (t, 1H, J = 9.3 Hz), 3.40 (s, 3H), 3.32 (dd, 1H, J = 3.7, 9.2 Hz); IR ($CHCl_3$) 3005, 2930, 2835, 1090, 1055, 995 cm^{-1}.

Formation of benzylidene acetal **49**. Desilylation and acetal formation of **33** as described above afforded **49** (63%): $[\alpha]_D$ +14.89° (*c* 3.15, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.52–7.35 (m, 5H), 6.20 (ddd, 1H, J = 4.6, 11.0, 17.5 Hz), 5.93 (s, 1H), 5.60 (td, 1H, J = 1.8, 17.6 Hz), 5.55 (td, 1H, J = 1.8, 11.0 Hz), 4.90 (d, 1H, J = 3.6 Hz), 4.81 (m, 1H), 4.08 (dd, 1H, J = 6.1, 10.2 Hz), 3.75 (dd, 1H, J = 9.2, 10.2 Hz), 3.68 (t, 1H, J = 9.2 Hz), 3.63 (s, 3H), 3.55 (s, 3H), 3.47 (s, 3H), 3.27 (dd, 1H, J = 3.6, 9.2 Hz); IR ($CHCl_3$) 3005, 2930, 2830, 1090, 1060, 995 cm^{-1}.

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