dibromoheptan-4-one (98 mg, 0.36 mmol), and $Fe_2(CO)_9$ (146 mg, 0.40 mmol) was heated at reflux under argon for 24 h. After the mixture was cooled, 15 mL of EtOAc was added, the solution washed with 10 mL of saturated $NaHCO_3$ and then 10 mL of saturated brine and dried ($MgSO_4$), and the solvent removed in vacuo. Preparative TLC (3:1 hexane/EtOAc: R_f 0.52) yielded 78 mg (68%) of the product as a gummy semisolid: ^1H NMR (360 MHz) δ 0.55, 0.74, 0.76, 0.86, 0.92, 0.94, 1.00, 1.07 (6, multiple t, CH_2CH_3), 1.3–2.3 (15, m, CH_2, CH), 1.56, 1.58 (3, 2 s, $NCCH_3$), 2.41, 2.43 (3, 2 s, $PhCH_3$), 2.96 (1, m, CH), 4.15–4.30 (1, m, CH), 7.3 (2, m, Ar H), 7.7 (2, m, Ar H); IR ($CHCl_3$) 1734 (C=O), 1600, 1495, 1450, 1344, 1153 cm^{-1}. Anal. Calcd for $C_{22}H_{31}NO_3S$: C, 67.83; H, 8.02; N, 3.60. Found: C, 67.79; H, 8.05; N, 3.54.

1,3,3a,4,4a,5,6,7,7a,7b-Decahydro-2-keto-1,3,3a-trimethyl-4-[(4-methylphenyl)sulfonyl]dicyclopenta[*b*,*d*]pyrrole (12). Under argon, a solution of benzene (7 mL), *cis*-*N*-tosyl-3-methyl-2-azabicyclo[3.3.0]oct-3-ene (100 mg, 0.36 mmol), 2,4-dibromopentan-3-one (88 mg, 0.36 mmol), and $Fe_2(CO)_9$ (146 mg, 0.40 mmol) was heated at reflux for 24 h. After the mixture was cooled, 15 mL of EtOAc was added, the solution washed with 10 mL of saturated $NaHCO_3$ and then 10 mL of saturated brine and then dried ($MgSO_4$), and the solvent removed in vacuo. Preparative TLC (3:1 hexane/EtOAc, R_f 0.35) yielded the product as a clear, colorless oil that solidified upon standing (79 mg, 61%). The analytical sample was obtained by recrystallization from hexanes: mp 144–147 °C; ^1H NMR (360 MHz, $CDCl_3$) δ 1.40–1.61 (m, 3, *H*CH), 1.63–1.77 (m, 3, HC*H*), 1.11 (d, J = 6.9 Hz, 3, $CHCH_3$) 1.29 (d, J = 6.9 Hz, 3 $CHCH_3$), 1.53 (s, 3, CCH_3), 2.22–2.24 (m, 2, COCH), 2.39–2.44 (m, 2, CH), 2.43 (s, 3, $PhCH_3$), 4.14–4.19 (m, 1, NCH), 7.29 (d, 2, J = 8.1 Hz, Ar H), 7.76 (d, 2, J = 8.1 Hz, Ar H); IR (KBr) 1736 (C=O), 1600, 1457 (Ar), 1307, 1152 cm^{-1}. Anal. Calcd for $C_{20}H_{27}NO_3S$: C, 66.45; H, 7.53; N, 3.87. Found: C, 66.58; H, 7.70; N, 3.64.

1,3,3a,4,4a,5,6,7,7a,7b-Decahydro-2-keto-3a-methyl-4-[(4-methylphenyl)sulfonyl]-1,3-diphenyldicylopenta[*b*,*d*]pyrrole (13). Under argon, a solution of benzene (7 mL), *cis*-*N*-tosyl-3-methyl-2-azabicyclo[3.3.0]oct-3-ene (100 mg, 0.36 mmol), 1,3-dibromo-1,3-diphenylacetone (1.33 mg, 0.36 mmol), and $Fe_2(CO)_9$ (146 mg, 0.40 mmol) was heated at reflux for 22 h. After the mixture was cooled, 15 mL of EtOAc was added, the solution washed with 10 mL of saturated $NaHCO_3$ and 10 mL of saturated brine and then dried ($MgSO_4$), and the solvent removed in vacuo. Preparative TLC (3:1 hexane/EtOAc, R_f 0.31) gave 73 mg (42%) of the product as a white solid: mp 94–97 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 0.8–2.0 (m, 9, CH_2, $NCCH_3$), 2.3–2.6 (m, 2 CH), 2.39 (s, 3 $PhCH_3$), 4.0–4.4 (m, 3 PhCH, NCH), 7.1–7.4 (m, 12, Ar H), 7.6–7.9 (m, 2, Ar H); IR (KBr) 1742 (C=O), 1598, 1494, 1450, 1332, 1151 cm^{-1}. Anal. Calcd for $C_{30}H_{31}NO_3S$: C, 74.20; H, 6.43; N, 2.88. Found: C, 74.07; H, 6.63; N, 2.75.

1,3,3a,4,4a,5,6,7,7a,7b-Decahydro-2-keto-1,1,3,3,3a-pentamethyl-4-[(4-methylphenyl)sulfonyl]dicyclopenta[*b*,*d*]pyrrole (14). Under argon, a solution of benzene (7 mL), *cis*-*N*-tosyl-3-methyl-2-azabicyclo[3.3.0]oct-3-ene (100 mg, 0.36 mmol), 2,4-dibromo-2,4-dimethylpentan-3-one (98 mg, 0.36 mmol), and $Fe_2(CO)_9$ (146 mg, 0.40 mmol) was heated at reflux for 60 h. After the mixture was cooled, 15 mL of EtOAc was added, the solution washed with 10 mL of saturated $NaHCO_3$ and 10 mL of saturated brine and then dried ($MgSO_4$), and the solvent removed in vacuo. Purification by chromatotron (7:2 hexane/EtOAc, second UV visible band) gave 62 mg (44%) of the product as a white solid. The analytical sample was obtained by recrystallization from hexanes: mp 135–137 °C; ^1H NMR (360 MHz, $CDCl_3$) δ 0.67, 0.69, 0.95, 0.98, 1.15, 1.17, 1.21, 1.23, 1.25, 1.29 (multiple s, 12, O=$CCCH_3$), 1.68, 1.74 (2 s, 3, $NCCH_3$), 1.4–1.7 (m, 3, CH_2), 2.0–2.15 (m, 3, CH_2, CH), 2.41, 2.43 (2 s, 3, $PhCH_3$), 2.63 (m), 3.23 (br s, 1, CH), 4.26, 4.42 (2 m, 1, CH), 7.28 (d, 2, J = 8.3 Hz, Ar H), 7.69 (d, 1, J = 8.3 Hz, Ar H), 7.81 (d, 1, J = 8.3 Hz, Ar H); IR (KBr) 1734 (C=O), 1599, 1494, 1468, 1342, 1151 cm^{-1}. Anal. Calcd for $C_{22}H_{31}NO_3S$: C, 67.83; H, 8.02; N, 3.60. Found: C, 67.88; H, 8.07; N, 3.78.

1,2,3,3a,4,5,6,6a-Octahydro-5-keto-4,6,6a-trimethyl-1-[(4-methylphenyl)sulfonyl]cyclopenta[*b*]pyrrole-3-spirocyclohexane (18). A solution of benzene (7 mL), *N*-tosyl-3-methyl-2-azaspiro[5,6]undec-3-ene (90 mg, 0.29 mmol), 2,4-dibromopentan-3-one (72 mg, 0.29 mmol), and $Fe_2(CO)_9$ (118 mg, 0.32 mmol) was heated at reflux under argon for 23 h. After the mixture was cooled, 15 mL of EtOAc was added, the solution washed with 2 × 10 mL of saturated aqueous $NaHCO_3$ and then 10 mL of saturated brine and dried ($MgSO_4$), and the solvent removed in vacuo. Purification by chromatotron (4:1 hexane/EtOAc, second UV visible band) gave 67 mg (58%) of the product as a white solid. The analytical sample was obtained by recrystallization from hexanes: mp 154–156 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 0.81 (d, 3, J = 6.8 Hz, $CHCH_3$), 1.19 (d, 3, J = 6.8 Hz, $CHCH_3$), 1.0–1.7 (m, 13, CH_2, $NCCH_3$), 2.15–2.30 (m, 1, O=CCH), 2.44 (s, 3, $PhCH_3$), 2.50–2.65 (m, 1, O=CCH), 2.95–3.05 (m, 1, CH), 3.30–3.50 (m, 2, NCH_2), 7.31 (d, 2, J = 8.1 Hz, Ar H), 7.73 (d, 2, J = 8.1 Hz, Ar H); IR (KBr) 1741 (C=O), 1598, 1494, 1451, 1342, 1153 cm^{-1}. Anal. Calcd for $C_{22}H_{31}NO_3S$: C, 67.83; H, 8.02; N, 3.60. Found: C, 67.99; H, 8.01; N, 3.64.

1,2,3,3a,4,5,6,6a-Octahydro-5-keto-4,6,6a-trimethyl-3-phenyl-1-[(4-methylphenyl)sulfonyl]cyclopenta[*b*]pyrrole (19). A solution of benzene (7 mL), *N*-tosyl-2-methyl-4-phenyl-Δ^2-pyrroline (90 mg, 0.29 mmol), 2,4-dibromopentan-3-one (70 mg, 0.29 mmol), and $Fe_2(CO)_9$ (115 mg, 0.32 mmol) was heated at reflux for 24 h under an argon atmosphere. Upon cooling, 15 mL of EtOAc was added, the solution washed with 2 × 10 mL of saturated aqueous $NaHCO_3$ and then 10 mL of saturated brine and dried ($MgSO_4$), and the solvent removed in vacuo. Preparative TLC (3:1 hexane/EtOAc, R_f 0.28) gave 58 mg (51%) of the product as a clear, colorless oil, which solidified on standing: mp 48–51 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 0.8–1.6 (m, 9, $CHCH_3$, $NCCH_3$), 2.1–2.6 (m, 2, O=CCH), 2.43 (s, 3, $PhCH_3$), 3.2–4.2 (m, 4, PhCH, NCH_2, CH), 7.1–7.4 (m, 2, Ar H), 7.31 (s, 5, Ar H), 7.6–7.8 (m, 2, Ar H); IR (KBr) 1739 (C=O), 1598, 1491, 1450, 1340, 1152 cm^{-1}. Anal. Calcd for $C_{23}H_{26}NO_3S$: C, 69.67; H, 6.61; N, 3.53. Found: C, 69.69; H, 6.76; N, 3.61.

Registry No. 1, 97486-45-8; 2, 97486-46-9; 3, 97486-47-0; 4, 97486-48-1; 5, 97486-49-2; 6, 97486-50-5; 7, 97486-51-6; 11, 97486-52-7; 12, 97486-53-8; 13, 97486-54-9; 14, 97486-55-0; 18, 97486-56-1; 19, 97486-57-2; (allyl)Fp, 38960-10-0; 1,3-dibromo-1,3-diphenylpropan-2-one, 958-79-2; diiron nonacarbonyl, 15321-51-4; 2,4-dibromo-2,4-dimethylpentan-3-one, 17346-16-6; 3,5-dibromo-2,6-dimethylheptan-4-one, 30957-25-6; 3,5-dibromoheptan-4-one, 36461-40-2; 2,4-dibromohexan-3-one, 97486-44-7; 2,4-dibromopentan-3-one, 815-60-1; 2,4-dibromo-2-methylpentan-3-one, 37010-00-7; *cis*-*N*-tosyl-3-methyl-2-azabicyclo[3.3.0]oct-3-ene, 81097-07-6; *N*-tosyl-3-methyl-2-azaspiro[4.5]undec-3-ene, 81097-23-6; *N*-tosyl-2-methyl-4-phenyl-Δ^2-pyrroline, 81120-69-6.

The Regioselectivity of Epoxide-Opening Reactions Using Alkynylaluminum Reagents

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The reaction of dialkylalkynylalanes with epoxides is a general route to β-hydroxyacetylenes that has found important application in organic synthesis.[1,2] This epoxide-opening reaction is particularly useful in constructing intermediates to prostaglandins and prostaglandin analogues,[3,4] as illustrated in the two examples in Scheme I. The opening of diol epoxide **4** is a key reaction in Fried's general approach to prostanoids,[5] and the opening of ketal epoxide **7** has been reported by several groups[6,7] as an

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(2) Zweifel, G.; Miller, J. A. *Org. React.* (*N.Y.*) **1984**, *32*, 375.
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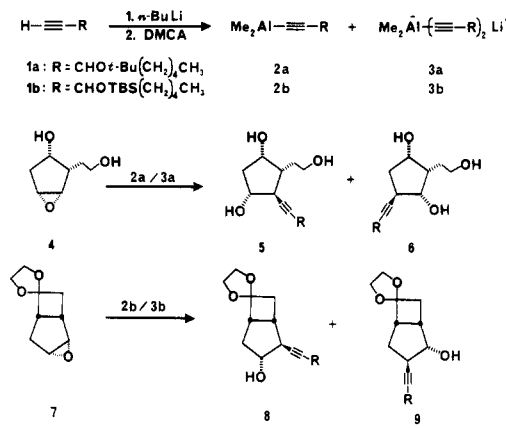
0022-3263/85/1950-3923$01.50/0

Scheme I



approach to the important prostanoid intermediate **8**. Alkynylalanes for such reactions are usually made by Fried's method,[8] where the appropriate alkyne is deprotonated with *n*-butyllithium and then treated with dimethylchloroalane (DMCA) to give the desired dialkylalkynylalane reagent as shown in Scheme I.

The synthetic utility of the alkynylalane reagent is often greatly enhanced by its regioselectivity. For example, exclusive formation of desired isomer **5** from the opening of epoxide **4** was reported.[5] This selectivity was rationalized by assuming reaction of the alane with the primary alcohol of **4** to give an alkoxymethylalkynylalane, followed by intramolecular delivery of the alkynyl group to the correct end of the epoxide. However, in a subsequent paper[8] Fried reported that this result is not reproducible. When new bottles of DMCA were used, the reaction rate increased, and the selectivity decreased to ratios ranging from 4:1 to 1:1 (**5**/**6**). Speculating that their original DMCA might have been contaminated by air to produce the less reactive, more selective methoxymethylchloroalane (MMCA), Fried found that the reaction of 1 equiv of methanol with fresh DMCA produced MMCA which reproducibly gave the highly selective results originally reported. This example shows that the exact structure of the alkynylaluminum species can critically affect the regioselectivity. In the second example involving ketal epoxide **7**, alane **2b** is reported[6,7] to give the desired regioselectivity although the ratio **8**/**9** is only about 2:1. This regioselectivity seems to be general for nucleophilic reactions on **7** and is rationalized by an argument based on conformational requirements of ketal **7** that lead to a favored transition state for the desired mode of attack on the epoxide.[6]

For our prostaglandin synthesis program, we needed large quantities of both intermediates **5** and **8**. Repeating the two reactions above, however, we could not achieve the selectivities reported. In the opening of epoxide **4**, product ratios of 3:1–4:1 favoring the desired isomer **5** were consistently observed, regardless of the source of our DMCA. This is not too different from the literature reports,[5] and since the reaction could be used to produce large amounts of **5** with reasonable selectivity, we did not pursue the matter. However, the alane reaction on ketal epoxide **7** led, in our hands, to a ratio of 0.7:1 favoring the undesired isomer **9**. Moreover, our reaction seemed much too fast, reaching completion in about 3 h at 25 °C as opposed to 8 h at 80 °C as reported in the literature. This poor isomer ratio was unacceptable for our needs, and thus we initiated a study of the reaction to determine what was causing the unfortunate reversal of regioselectivity.

Table I. Ratios of Regioisomers from Epoxide-Opening Reactions Using Alanes and Alanates Derived from Ether 1a

	product ratio		
epoxide	alane	alanate	products
4	3.3	0.2	**5**/**6**
7	0.7	3.3	**8**/**9**

Results and Discussion

Over 30 reactions were run to determine the effects of solvent, temperature, order of addition, timing, stoichiometry, and substrate structure (different protective groups on **1** and **7**) on the regioselectivity of the reaction. Our results can be summarized by saying that most of these changes either suppressed the reaction completely (for example, the use of ether solvents like THF) or gave **8**/**9** ratios of 0.6:1–0.7:1 as in the initial run. In one case, however, a dramatic change was observed: when the stoichiometry was adjusted so that the ratio of lithium acetylide to DMCA was 2:1, instead of the usual[5-9] 1.5:1, the reaction slowed down to a rate consistent with the literature, and the product ratio **8**/**9** was 3.3:1, now favoring the desired isomer even more than the reported 2:1 ratio. We believe that this result can be explained by considering the dimethyldialkynylalanate **3a** that is produced along with the alane **2a**. Under the usual conditions (1.5:1 lithium acetylide/DMCA), approximately equal amounts of the two aluminum species **2a** and **3a** should be present (the purpose of the 0.5 equiv of excess lithium acetylide under the original conditions was to avoid chlorohydrin formation.[11]) On the other hand, increasing the acetylide/DMCA ratio to 2:1 should result in virtually complete conversion to the alanate **3a**. It is known that alanes are Lewis acids that strongly bind ether oxygens, a property that accounts for the ease with which alanes open epoxides.[10] When only the alanate **3a** is present, with little of the electrophilic **2a** around, the reaction becomes much slower, allowing the conformational factors mentioned above[6] to predominate.[13] Although alkyl- and alkenylalanates have previously been used to open epoxides, we are unaware that alkynylalanate epoxide-opening reactions have received attention before.

That observation in hand, it was of interest to try opening diol epoxide **4** under the alanate conditions. In side-by-side reactions comparing the alane with the alanate reagent, the ratio of regioisomers again changed. In this case the favorable alane ratio of 3.3:1 reversed for the alanate to 1:4.4, now favoring the undesired isomer **6**. Even though the alanate can form a covalent bond to the primary hydroxyl oxygen of **4**, just as the alane does, the lack of the electrophilic Lewis acid component apparently

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(7) (a) O-Yang, C.; Kertesz, D. J.; Kluge, A. F.; Kuenzler, P.; Li, T.; Marx, M. M.; Bruno, J. J.; Chang, L. *Prostaglandins* **1984**, 851. (b) Li, T.; Marx, M. U.S. Patent 4 423 068, 1983.

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(9) Fried, J.; Lin, C, H.; Mitra, M. M.; Kao, W. L.; Dalven, P. *Ann. N.Y. Acad. Sci.* **1971**, *180*, 38.

(10) Fried, J.; Lin, C, H. Ford, S. H.; *Tetrahedron Lett.* **1969**, 1379.

(11) See footnote 7 in ref 8.

(12) Fried, J.; Lin, C. H.; Sih, J. C.; Dalven, P.; Cooper, G. F. *J. Am. Chem. Soc.* **1972**, *94*, 4342.

(13) A further increase of the lithium acetylide/DMCA ratio to 2.5:1 (resulting in production of the alanate **3a** plus excess acetylide) gave a reaction that still favored the desired isomer **8**, but to a lesser extent (2.4:1). The 2:1 ratio of acetylide/DMCA appears optimal in this case.

deactivates the system to the extent that the alkoxyaluminate does not react, and merely serves to sterically block attack on that side of the epoxide. This observation is consistent with Fried's results,[5a] where he found that blocking the primary alcohol of **4** with a bulky ether group led to a ratio of about 1:3 also favoring the wrong isomer **6**.

In summary, we have found that superficially innocuous changes in the amount of "excess"[11] reagent used to prepare alkynylalanes for epoxide-opening reactions can lead to great changes in the resulting regioselectivity, even to the extent of reversing the isomer ratios. As a consequence, the substitution of an alanate for the usual alane reagent can sometimes be useful in achieving desired regioselectivity. Our data on the opening of epoxides **4** and **7** are tabulated in Table I. It has been our experience in general that the regioselectivity of these reactions is often governed by effects more subtle than one might anticipate from the literature; this should be considered by those who want to use these reactions synthetically.[14]

Experimental Section

The Alanate Opening of Epoxide 4. To a solution of 2.275 g (12.5 mmol, 8 equiv) of octyne ether **1a** in 10 mL of dry toluene, stirred under argon at 0 °C, was added 8.06 mL of 1.55 M *n*-butyllithium (12.5 mmol, 8 equiv) dropwise via syringe. After 15 min, 6.25 mL of 1.0 M DMCA (6.25 mmol, 4 equiv) was added dropwise via syringe, and the stirring was continued at 0 °C for 50 min more. Epoxide **4** (225 mg, 1.56 mmol) was then added as a solution in 2–3 mL of toluene, dropwise via syringe. The reaction was allowed to warm to room temperature overnight and was then heated in a 60 °C oil bath for 4 h. After careful quenching (saturated sodium sulfate at 0 °C), the mixture was added to 100 mL of water and 100 mL of ether and was filtered through a Celite pad to clarify. The water layer was separated and extracted with two 50-mL portions of ether. The combined ether layers were dried over molecular sieves and concentrated in vacuo. The ratio of the two isomers **5**/**6** was determined to be 1:4.4 by HPLC (1:1 acetone/hexane as solvent). The structures were verified by NMR as in ref 12. The two isomers were very difficult to separate chromatographically and were normally carried on as a mixture for synthetic purposes.

The Alanate Opening of Epoxide 7. To a solution of 2.609 g (14.3 mmol, 3 equiv) of octyne ether **1a** in 10 mL of dry toluene, stirred under argon at 0 °C, was added 9.21 mL of 1.55 M *n*-butyllithium (14.3 mmol, 3 equiv), dropwise via syringe. After the mixture was stirred 15 min, 7.13 mL of 1.0 M DMCA (7.13 mmol, 1.5 equiv) was added dropwise via syringe. After the mixture was stirred 50 min more, a solution of epoxide **7** (0.8 g, 4.76 mmol) in 10 mL of dry toluene was added dropwise via syringe. The ice bath was removed, and the mixture was warmed to 80 °C and stirred for 8 h. After cooling to room temperature, the mixture was worked up as described in the example above. By HPLC (7:3 hexane/ethyl acetate solvent), the ratio of isomers **8**/**9** was 3.35:1. To further verify the structural assignments and ratio, the crude product was hydrolyzed to a mixture of the corresponding ketones with acetonitrile/sulfuric acid/water (12 h at 25 °C), as described in ref 6b. The isomers were then separated by flash chromatography to afford the ketones corresponding to **8** and **9**, 809 and 258 mg, respectively. The total, chromatographed yield of the two isomers, overall for the two steps, was 74%.

Acknowledgment. We gratefully acknowledge helpful discussions with Professor Ernest Wenkert.

(14) Some related epoxide-opening reactions with alkynyl species have been reported: (a) Murray, T. F.; Samsel, E. G.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 7520. (b) Brown, H. C.; Racherla, U. S.; Singh, S. M. *Tetrahedron Lett.* **1984**, 2411. (c) Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, 391. In the case of epoxide **7**, use of the alkynyl borate method described in ref 14b and c resulted in a ratio of 1.7:1 for isomers **8**/**9**, a value midway between the alane and the alanate results in Table I.

4-Chlorooctahydro-2*H*-1-benzopyrans and 4-Chloro-4a,5,6,7,8,8a-hexahydro-2*H*-1-benzopyrans via the Lewis Acid Promoted Cyclization of Acetals Derived from *trans*-2-Vinylcyclohexanol and *trans*-2-Ethynylcyclohexanol: Synthesis, Structure, and Mechanism[1]

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There is current interest in the tetrahydropyran and dihydropyran nuclei as they occur in a number of natural products which have received recent attention.[2] The major route to hydropyrans has been the *carbon–oxygen* bond-forming cyclization of 1,5-diols and closely related structures or difunctional compounds prepared from 1,5-diols.[3] We wish to report a facile and selective synthetic route to substituted octahydro-2*H*-1-benzopyrans and 4a,5,6,7,8,8a-hexahydro-2*H*-1-benzopyrans via a Lewis acid promoted *carbon–carbon* bond-forming cyclization of acetals derived from 2-vinyl- and 2-ethynylcyclohexanol and the acetal-forming reagents ethyl vinyl ether and MEM chloride. The syntheses described herein with our earlier work[4] should have general applicability for entry into the tetrhydropyran and 5,6-dihydro-2*H*-pyran subunits. Additionally, the product distributions and structures for the ethyl vinyl ether based acetals of the two trans cyclohexanols give substantial insight into the cyclization pathway.

Results and Discussion

The ethyl vinyl ether and MEM acetals of *trans*-2-vinyl- and *trans*-2-ethynylcyclohexanol are formed readily by well-known methods.[5] The acetals derived from ethyl vinyl ether are isolated as an approximately equal (50:50 ± 5) mixture of diastereomers. Cyclization of the unsaturated acetals is effected in a straightforward fashion by adding the substrate to a methylene chloride solution of titanium tetrachloride. The ethynyl–acetal cyclizations are optimal at −63 °C; the vinyl–acetals give excellent yields at −45 °C. Products and yields are listed in Chart I.

A noteworthy feature of the cyclizations is that the diastereomeric mixture of the ethyl vinyl ether–acetal of *trans*-2-vinylcyclohexanol leads essentially (97%) to only one of four possible stereoisomeric products. Likewise, the diastereomeric mixture of the *trans*-2-ethynylcyclohexanol ethyl vinyl ether acetal leads to only one (98%) of two possible diastereomeric products. The structures of these products as determined by NMR are shown in Chart I. For both stereoisomeric products the 2-methyl groups in the ^{13}C NMR spectra are at ca. 22 ppm (relative to Me_4Si). From the work of Eliel et al.[6] and Kleinpeter et al.,[7] this establishes the positions of the methyl groups as equatorial, consistent with the large conformational energy for a 2-methyl substituent of ca. 2.9 kcal/mol.[6] The chloride substituent in the saturated product is also equatorial as indicated by the splitting pattern of the axial 4-hydrogen (3.0 ppm, $J_{a-a} \sim 10$ Hz, $J_{a-e} \sim 3.5$ Hz). This equatorial preference for chloride is surprising given its conformational energy in tetrahydropyrans of ca. 0.3 kcal/mol[6] and when compared with observations of mixed axial–equatorial attachments in cyclohexane chemistry.[8,9] This

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