In principle, these compounds could be also prepared by the well known Hafner route[13] by using the corresponding 8-(dialkylamino)-substituted 6-vinylpentafulvenes. Whereas this reaction sequence is a three-step procedure (pentafulvene formation, cyclization, and exchange of the dialkylamino substituent), the way described here is a high-yield one-step reaction.

The product types from entries b, d, and e constitute valuable precursors which can be transformed into interesting compounds. Thus, the vinylpentafulvenes **4** and **5** were isomerized to the corresponding 1,5-dihydropentalenes by flash thermolysis. Most effective for this purpose was the flash vacuum thermolysis of the "cyclopentadiene protected" parent vinylpentafulvene **2**. At temperatures between 450 °C and 520 °C[14] cycloadduct **2** loses cyclopentadiene and gives the vinylpentafulvene **10**, which spontaneously cyclizes to the 1,6a-dihydropentalene **11** (Scheme III). This intermediacy product could not be isolated but immediately rearranges to the 1,5-dihydropentalene **12**[15] via 1,5-hydrogen migrations. Although this cyclization–rearrangement sequence was originally reported by Gajewski and Cavender,[4] it was not exploited for synthesis until now (only 10 mg of **12** could be made by direct vinylpentafulvene static thermolysis until now[4]). In our case, **12** could be isolated in 2–3-g quantities by thermolysis of 6 g of **2** in about 30 min. This synthetic methodology competes very well with the cyclooctatetraene thermolysis route developed by Meier and co-workers.[16] Furthermore, it should be easily applied to acceptor-substituted acroleins as starting materials. Investigations using this concept are in progress.

Acknowledgment. I thank the Fonds der Chemischen Industrie (Liebig-Stipendium) and the Universitätsbund Würzburg for financial support.

Supplementary Material Available: Spectral data for pyrrolidine-catalyzed reactions between α,β-unsaturated carbonyl compounds and cyclopentadiene (3 pages). Ordering information is given on any current masthead page.

(13) Kaiser, R.; Hafner, K. *Angew. Chem.* **1970**, *82*, 877. Kaiser, R.; Hafner, k. *Angew. Chem.* **173**, *85*, 361.
(14) 30-cm quartz thermolysis tube, 0.02 Torr of pressure.
(15) Katz, T. J.; Rosenberger, M.; O'Hara, R. K. *J. Am. Chem. Soc.* **1964**, *86*, 249.
(16) Meier, H.; Pauli, A.; Kochhan, P. *Synthesis* **1987**, 573. Meier, H.; Pauli, A.; Kolshorn, H.; Kochhan, P. *Chem. Ber.* **1987**, *120*, 1607.
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A Convergent Synthesis of Polyol Chains

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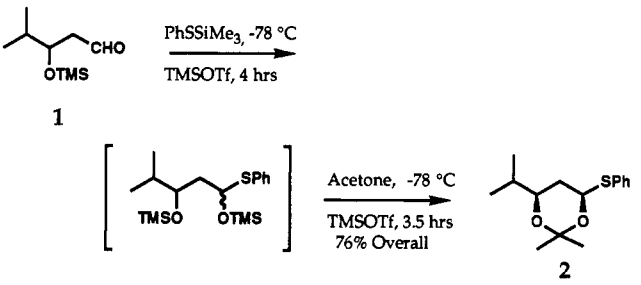
Summary: A new method is described for the convergent synthesis of polyol chains in which two chains are coupled with control of the newly formed stereogenic center.

Sir: Advances in asymmetric synthesis[1] over the last decade have made the construction of many simple polyol chains routine, but larger chains still represent a formidable challenge. A method is described herein which allows polyol chains to be coupled with control of the newly formed stereogenic center. This is a problem for which very few general solutions have been reported.[2,3] Our new method will dramatically simplify the synthesis of large polyol chains because it allows them to be prepared from readily available smaller chains by a *convergent* strategy.

This method is designed around new 1,3-diol synthons: 6-alkyl-4-(phenylthio)-1,3-dioxanes (e.g. **2**). These synthons are protected β-hydroxy aldehydes and can be prepared from either β-hydroxy esters[4,5] or homoallylic alcohols.[6,7] The 1,3-diol synthon **2** was prepared as a single isomer[8] by treating 4-methyl-3-[(trimethylsilyl)oxy]pentanal (**1**) (prepared in two steps from the homoallylic alcohol 2-methyl-5-hexen-3-ol) with (phenylthio)trimethylsilane and catalytic trimethylsilyl triflate to give a mixture of hemithioacetals,[9] followed by treatment with acetone and catalytic trimethylsilyl triflate.[10] This sequence can



be performed in one pot but is more reliable when the intermediate hemithioacetals are isolated. The product slowly decomposes under the reaction conditions, so the

(1) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, New York, 1985; Vol. 1–5.
(2) For a recent approach, see: Mori, Y.; Kuhara, M.; Takeuchi, A.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5419–5422. Mori, Y.; Takeuchi, A.; Kageyama, H.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5419–5422.
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(4) Evans, D. A.; Vogel, E.; Nelson, J. V. *J. Am. Chem. Soc.* **1979**, *101*, 6120–6123. Evans, D. A.; Nelson, J. V.; Vogel, E.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099–3111.
(5) Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 5856–5858. Kitamura, M.; Ohkuma, T.; Inoue, S.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Ohta, T.; Takaya, H.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 629–631.
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(7) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186–8190.
(8) All new compounds were characterized by ^1H and ^{13}C NMR, IR, and C, H analyses or HRMS. Preparation of compounds **2** and **5**, as well as spectral data for compounds **2**, **5**, and **9** are given in the supplementary material.
(9) Evans, D. A.; Truesdale, L. K.; Grimm, K. G.; Nesbitt, S. L. *J. Am. Chem. Soc.* **1977**, *99*, 5099–5017.
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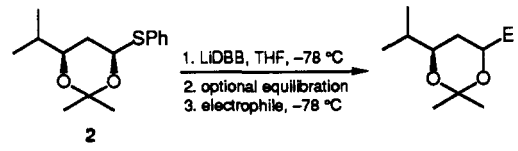
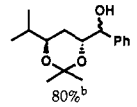
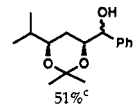
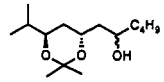
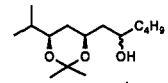
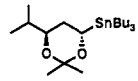
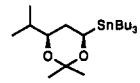
0022-3263/89/1954-4982$01.50/0

Table I. Kinetic and Thermodynamic Coupling Reactions of 1,3-Diol Synthon 2



2

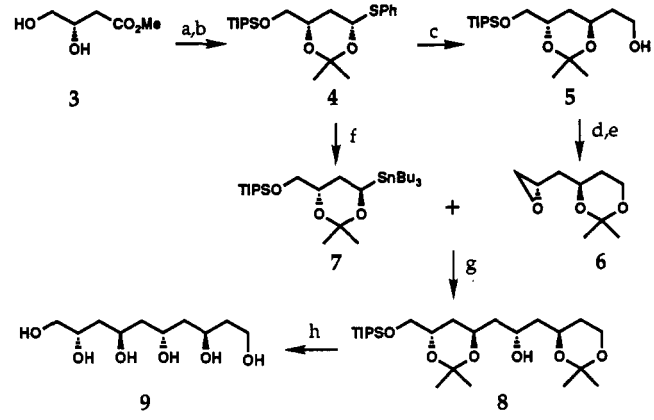
electrophile	axial (kinetic)[a]	equatorial (thermodynamic)[a]
PhCHO	 80%[b]	 51%[c]
	 73% (98 : 2)[d]	 47% (3 : 97)[d]
Bu_3SnCl	 87% (96 : 4)	 65% (5 : 95)

[a] Isolated yields are given, followed by GC ratios (axial/equatorial) in parentheses. All new compounds were characterized by ^1H and ^{13}C NMR, IR, MS, and C, H analyses. [b] 65:35 ratio of carbinol epimers. [c] 61:39 ratio of carbinol epimers. [d] Approximately a 50:50 mixture of carbinol epimers.

reaction must be carefully monitored to achieve optimal yields. We have previously described the reduction of **2** with lithium di-*tert*-butylbiphenylide (LiDBB)[11] to give an axial alkyllithium with 50:1 selectivity; the axial alkyllithium epimerizes to the more stable equatorial alkyllithium on warming to −20 °C for 30 min.[12,13] Coupling either the axial or equatorial alkyllithium with electrophiles (vide infra) leads to protected *anti*- or *syn*-1,3-diols, respectively. In summary, these 1,3-diol synthons are readily prepared from homoallylic alcohols and give either axial or equatorial alkyllithiums by judicious choice of reaction conditions.[12]

The reaction of 1,3-diol synthon **2** with a variety of electrophiles is illustrated in Table I. The initially formed axial alkyllithium couples with representative electrophiles in 73–87% yield, while the more stable equatorial alkyllithium gives 47–65% yields due to competitive protonation of the alkyllithium during equilibration. All of the coupling reactions proceed with retention of stereochemistry at the alkyllithium center.[14] As expected,[15] the additions to benzaldehyde proceed with little selectivity to give protected 1,2,4-triols. The couplings of racemic **2** with racemic 2-butyloxirane according to Ganem's procedure[16] lead to 50:50 mixtures of protected 1,3,5-triols; i.e. no double asymmetric induction[17] is observed. While this precludes the kinetic resolution of a racemic oxirane by an optically active alkyllithium and vice versa, it ensures that all possible diastereomeric products can be prepared by coupling the appropriate optically active components. Reactions of the axial or equatorial alkyllithium with tributyltin chloride give the corresponding tetraalkyltins in good yield. The tetraalkyltins are convenient,[18] stable *syn*- or *anti*-1,3-diol synthons, which return the original alkyllithiums upon treatment with *n*-BuLi;[14] couplings with benzaldehyde give the expected products in excellent yield. Thus the 1,3-diol synthon **2** couples with a variety of electrophiles in good to excellent yield to give protected *syn*- or *anti*-1,3-diols.

Scheme I.[a] Synthesis of Lienomycin Decanehexol 9



[a] (a) (i) TIPSOTf, lutidine, CH_2Cl_2, −20 °C, 71%; (ii) TMSCl, Et_3N, DMAP, CH_2Cl_2, room temperature, 92%; (iii) DIBAL-H, Et_2O, −78 °C, 85%; (b) (i) $PhSSiMe_3$, TMSOTf, CH_2Cl_2, −78 °C; (ii) acetone, TMSOTf, CH_2Cl_2, −78 °C, 51%; (c) LiDBB, THF, −78 °C; ethylene oxide, $BF_3{\cdot}OEt_2$ −78 °C, 77%; (d) PPTS, anhydrous $CuSO_4$, acetone, room temperature; Bu_4NF, THF, room temperature, 84%; (e) TsCl, NaOH, THF, room temperature, 82%; (f) LiDBB, THF, −78 °C; Bu_3SnCl, −78 °C, 82%; (g) 1.0 equiv of **6**, 1.6 equiv of **7**, 1.4 equiv of *n*-BuLi, THF, −78 °C, 10 min; 2.5 equiv of $BF_3{\cdot}OEt_2$, −78 °C, 10 min, 62%; (h) (i) Bu_4NF, THF, room temperature; (ii) MeOH, Amberlyte 15, room temperature, 100%.

The oxirane coupling reaction is particularly well suited to the synthesis of the alternating (1, 3, 5, ...) polyol chains found in the polyene macrolide antibiotics.[19] Lienomycin is an antibacterial and antifungal polyene macrolide antibiotic whose structure[20] and partial stereochemistry[21] have been determined. One of the degradation products of lienomycin was determined to have the structure and stereochemistry of **9** based on extensive ^1H NMR analysis.[21] Decanehexol **9** was chosen to test the effectiveness of this new method in a convergent synthesis (Scheme I). Methyl (*S*)-3,4-dihydroxybutanoate (**3**) was prepared in two steps from (*S*)-malic acid.[22] The primary alcohol was protected as a triisopropylsilyl ether followed by protection of the secondary alcohol as a trimethylsilyl ether. Reduction with DIBAL-H to the corresponding aldehyde

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(13) Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6900–6902. Cohen, T.; Lin, M.-T. *J. Am. Chem. Soc.* **1984**, *106*, 1130–1131. Lancelin, J.-M.; Morin-Allory, L.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1984**, 355–356.

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(18) Reduction of the 1,3-diol synthons produces alkyllithiums contaminated with 1 equiv of lithium thiophenoxide. The thiophenoxide does not affect carbonyl additions but does destroy an equivalent of (precious) alkylating agent. Regenerating the alkyllithiums from tetraalkyltins avoids this problem.

(19) Omura, S.; Tanaka, H. In *Macrolide Antibiotics: Chemistry, Biology and Practice*; Omura, S., Ed.; Academic Press: New York, 1984; pp 351–404.

(20) Pawlack, J.; Zielinsky, J.; Kolodziejczky, P.; Golik, J.; Gumieniak, J.; Jereczek, E.; Borowski, E. *Tetrahedron Lett.* **1979**, *17*, 1533–1536. Pawlack, J.; Zielinsky, J.; Golik, J.; Gumieniak, J.; Borowski, E. *J. Antibiot.* **1980**, *9*, 989–997. Pawlack, J.; Zielinsky, J.; Golik, J.; Jereczek, E.; Borowski, E. *J. Antibiot.* **1980**, *9*, 998–1004.

(21) Pawlak, J.; Nakanishi, K.; Iwashita, T.; Borowski, E. *J. Org. Chem.* **1987**, *52*, 2896–2901.

(22) Saito, S.; Hasegawa, T.; Inaba, M.; Nishida, R. *Chem. Lett.* **1984**, 1389–1392.

followed by sequential treatment with (phenylthio)trimethylsilane and acetone as described above gave the optically active 1,3-diol synthon **4**. The oxirane **6** and the tetraalkyltin **7** were both prepared from synthon **4**. Reduction of **4** and coupling with ethylene oxide gave alcohol **5**.[8] Acid-catalyzed migration of the acetonide to the more stable terminal position, followed by desilylation and dehydration,[23] gave oxirane **6**. Tetraalkyltin **7**[18] and oxirane **6** were coupled by sequentially treating a solution of the two compounds with *n*-BuLi and boron trifluoride etherate at −78 °C to give alcohol **8** in 62% yield. Transmetalation proceeds faster than oxirane opening, and boron trifluoride etherate activates the oxirane for coupling. Desilylation and acid hydrolysis gave decanehexol **9**.[8] The internal bisacetonide prepared from **9** has ^{1}H NMR and COSY spectra consistent with the data reported for the corresponding lienomycin degradation product, confirming the relative stereochemistry. The convergent synthesis of decanehexol **9** from 1,3-diol synthon **4** required only six linear steps and demonstrates the effectiveness of this new method for assembling the alternating polyol chains found in polyene macrolide antibiotics.

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Supplementary Material Available: Preparation of compounds **2** and **5**, as well as spectral data for compounds **2**, **5**, and **9** (1 page). Ordering information is given on any current masthead page.

Articles

Diels–Alder Reactions of 1,2,4-Triazines. Synthesis of Thieno[2,3-*c*]pyridines and 3,4-Dihydro-2*H*-thiopyrano[2,3-*c*]pyridines from 6-(Alkynylthio)-1,2,4-triazines

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Intramolecular Diels–Alder reactions of 6-(alkynylthio)-1,2,4-triazines are shown to give 2,3-dihydrothieno[2,3-*c*]pyridines and 3,4-dihydro-2*H*-thiopyrano[2,3-*c*]pyridines. 1-Oxo-2,3-dihydrothieno[2,3-*c*]pyridines synthesized in this fashion from the corresponding 6-(alkynylsulfinyl)-1,2,4-triazines are readily aromatized to thieno[2,3-*c*]pyridines by an acetic anhydride induced Pummerer reaction.

Inverse electron demand intramolecular Diels–Alder reactions of 1,2,4-triazines tethered to an appropriate dienophilic side chain provide a versatile and remarkably effective route to a broad variety of fused pyridines and pyrimidines.[2,3] Several years ago we developed a convenient synthesis of 1,2,4-triazin-6-ones[4] and their corresponding 6-thiones.[3k] Alkylation of the latter with 4-halo-1-butynes and 5-halo-1-pentynes, utilizing procedures analogous to those previously employed for the preparation of 3-(alkynylthio)-1,2,4-triazines,[3f] provides a family of tethered diene–dienophile pairs that are attractive intermediates for the preparation of thieno[2,3-*c*]pyridines and 3,4-dihydro-2*H*-thiopyrano[2,3-*c*]pyridines. The present paper describes these transformations in full detail.[3a]

It should be noted that thienopyridines, although not found in nature, have attracted considerable attention as components of synthetic antibiotics, as agricultural chemicals, and as dyestuffs. Previous syntheses have invariably utilized preformed pyridines or thiophenes as starting materials and have required strenuous, and often low-yielding, reaction conditions and difficultly accessible starting materials.[5] accessible starting materials.[4,5] By contrast, the conversions described below utilize readily accessible 1,2,4-triazines[3k,4,6] and alkynyl alkylating agents,

(1) Present address: Pfizer Central Research, Chas. Pfizer and Co., Groton, CT 06340.

(2) (a) For a general discussion of intramolecular Diels–Alder reactions of 1,2,4-triazines, see: Boger, D. L.; Weinreb, S. M. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic Press: New York, 1987. (b) Taylor, E. C. *Bull. Soc. Chim. Belg.* **1988**, *97*, 599.

(3) For some specific recent references to intramolecular Diels–Alder reactions of monocyclic 1,2,4-triazines, see the following: (a) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1985**, *26*, 2419. (b) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 431. (c) Taylor, E. C.; French, L. G. *Tetrahedron Lett.* **1986**, *27*, 1967. (d) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 2107. (e) Taylor, E. C.; Pont, J. L. *Tetrahedron Lett.* **1987**, *28*, 379. (f) Taylor, E. C.; Macor, J. E. *J. Org. Chem.* **1987**, *52*, 4280. (g) Taylor, E. C.; Macor, J. E.; Pont, J. L. *Tetrahedron* **1987**, *43*, 5145. (h) Taylor, E. C.; Pont, J. L.; Warner, J. C. *Tetrahedron* **1987**, *43*, 5159. (i) Taylor, E. C.; Pont, J. L.; van Engen, D.; Warner, J. C. *J. Org. Chem.* **1988**, *53*, 5093. (j) Taylor, E. C.; French, L. G. *J. Org. Chem.* **1989**, *54*, 1245. (k) Taylor, E. C.; Macor, J. E. *J. Org. Chem.* **1989**, *54*, 1249. (l) Seitz, G.; Dietrich, S. *Arch. Pharm.* (Weinheim, Ger.) **1984**, *317*, 379. (m) Seitz, G.; Gorge, L.; Dietrich, S. *Tetrahedron Lett.* **1985**, *26*, 4355. (n) Seitz, G.; Dietrich, S. *Arch. Pharm.* (Weinheim, Ger.) **1985**, *318*, 1048 and 1051. (o) Seitz, G.; Dietrich, S.; Gorge, L.; Richter, J. *Tetrahedron Lett.* **1986**, *27*, 2747. (p) Taylor, E. C.; Pont, J. L. *J. Org. Chem.* **1987**, *52*, 4287.

(4) Taylor, E. C.; Macor, J. E. *J. Heterocycl. Chem.* **1985**, *22*, 409.

(5) For a review of the syntheses, uses, and chemistry of thienopyridines, see: Barker, J. M. The Thienopyridines. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1977; Vol. 21, pp 65-119.

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