their superb NMR, mass spectroscopic, and X-ray crystallographic assistance and useful comments. We also thank Professor Kurt Mislow, Princeton University, for stimulating discussions concerning stereochemical consequences in this work. This work was financially supported by the National Institutes of Health, Merck Sharp and Dohme, and Hoffman-La Roche.

Registry No. 1a, 103710-72-1; **1b**, 103710-73-2; **2**, 103710-74-3; **3**, 103710-75-4; **3** (analogue 1), 103710-80-1; **3** (analogue 2), 103710-81-2; **3** (analogue 3), 103710-82-3; **3** (analogue 4), 103710-83-4; **3** (analogue 6), 103710-84-5; **3** (analogue 7), 103710-85-6; **4**, 103710-76-5; **4** (analogue 1), 103710-86-7; **4** (analogue 2), 103710-87-8; **4** (analogue 3), 103710-88-9; **4** (analogue 4), 103710-89-0; **4** (analogue 6) (isomer 1), 103710-90-3; **4** (analogue 6) (isomer 2), 103774-02-3; **4** (analogue 7), 103710-91-4; **5**, 103710-77-6; **5** (analogue 1), 103710-93-6; **5** (analogue 3), 103710-94-7; **5** (analogue 4), 103710-95-8; **5** (analogue 6), 103710-96-9; **5** (analogue 7), 103710-97-0; **6**, 103710-78-7; **7**, 103774-01-2; **8**, 103710-79-8; **8** (analogue 4), 103694-13-9; **8** (analogue 6), 103694-15-1; **8** (analogue 7), 103710-92-5.

Supplementary Material Available: Experimental procedure (**3** → **4**), listing of ^1H and ^{13}C NMR, IR, and mass spectroscopic data for compounds **4**–**7**, and X-ray crystallographic analysis data for compound **5** (8 pages). Ordering information is given on any current masthead page.

Total Synthesis of (-)-Xylomollin

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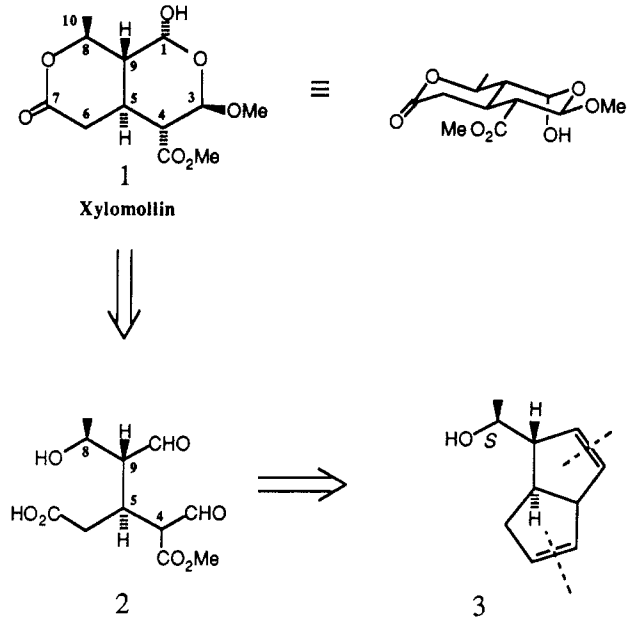
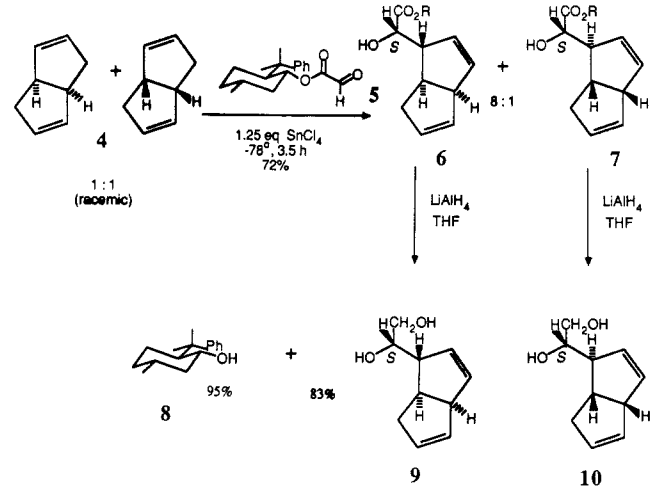
In 1976 Kubo and Nakanishi[1] described the isolation and characterization of the iridoid terpene xylomollin. Interest was immediately drawn to this compound because of its demonstrated biological activity as an insect antifeedant and as a decoupler of respiration in rat liver mitochondria and because xylomollin was the first and as of this date is the only iridoid terpene with the trans relative configuration at carbons 5 and 9.[2,3] We wish to describe here a short and efficient entry into this terpene system (Scheme I).[4]

In 1982 we communicated[5] a powerful tool for the control of absolute stereochemistry and further studies[6] expanded the scope of this method and placed it among the few practical transformations that form carbon–carbon bonds with high levels of asymmetric induction. The homoallylic alcohol functionality formed in this reaction represents a versatile synthetic building block that can be elaborated in a variety of ways. In the present context the aldol subunit present in the natural product (best visualized in **2**, the unraveled form of xylomollin) could be readily prepared by oxidative cleavage of such a homoallylic alcohol. This would provide the opportunity to create both the C-1 and C-3 aldehyde functionalities simultaneously. Such a retrosynthetic reconnection can be coupled with the joining of the carbomethoxy group carbon and C-7, leading to **3** as a key synthetic intermediate (Scheme II).

Scheme I



Scheme II



Synthesis of the homoallylic alcohol **3** was accomplished by an ene reaction between the glyoxylate **5** and 1 equiv of the racemic, bicyclic diene **4**.[7] Control of stereochemistry in this reaction led to production of two adducts (**6** and **7**)[8] in a ratio of 8:1[9] and a combined yield of 72%. The separated adducts were independently reduced to glycols **9** and **10**, respectively. Further conversion of **9** to **3** required reduction of the primary carbinol carbon to a methyl group with simultaneous inversion of stereochemistry at the secondary carbinol carbon. This was accomplished by sequence (b) shown in Scheme III involving protection of the primary hydroxyl followed by tosylation of the secondary hydroxyl group, removal of the silyl protecting group to form an intermediate epoxide with inversion, and reduction of the epoxide with lithium triethylborohydride. The minor ene adduct **10** was converted by an alternate sequence that effected that same reduction without inversion of stereochemistry (a, Scheme III) to a homoallylic alcohol (**11**) that was identical with **3** except for absolute stereochemistry, thus establishing the stereochemical relationship

(1) Kubo, I.; Miura, I.; Nakanishi, K. *J. Am. Chem. Soc.* **1976**, *98*, 6704.
(2) Whitesell, J. K.; Matthews, R. S.; Wang, P. K. S.; Helbling, A. M. *Abstracts of Papers*, 175th National Meeting of the American Chemical Society, Anaheim, CA, March, 1978; American Chemical Society: Washington, DC, 1978; ORGN 176.
(3) Nakane, M.; Hutchinson, C. R.; VanEngen, D.; Clardy, J. *J. Am. Chem. Soc.* **1978**, *100*, 7079.
(4) For a previous synthetic effort, see: Whitesell, J. K.; Wang, P. K. S.; Aguilar, D. A. *J. Org. Chem.* **1983**, *48*, 2511.
(5) Whitesell, J. K.; Bhattacharya, A.; Aguilar, D. A.; Henke, K. *J. Chem. Soc., Chem. Commun.* **1982**, 989.
(6) Whitesell, J. K.; Bhattacharya, A.; Buchanan, C. M.; Chen, H. H.; Deyo, D.; James, D.; Liu, C.-L.; Minton, M. A. *Tetrahedron* **1986**, 2993. Whitesell, J. K.; Chen, H. H.; Lawrence, R. M. *J. Org. Chem.* **1985**, *50*, 4663. Whitesell, J. K.; Allen, D. A. *J. Org. Chem.* **1985**, *50*, 3025. Whitesell, J. K.; Liu, C.-L.; Buchanan, C. M.; Chen, H. H.; Minton, M. A. *J. Org. Chem.* **1986**, *51*, 551.
(7) Baldwin, J. E.; Kaplan, M. S. *J. Am. Chem. Soc.* **1971**, *93*, 3969. We have made substantial improvements to this literature procedure for the preparation of diene **4**.
(8) Spectral data in full accord with the proposed structures of all intermediates were obtained. In addition, high-resolution mass spectral analyses were obtained for key, stable, and nonvolatile intermediates.
(9) The ratio of diastereomers was unchanged when a 10-fold excess of diene was used.

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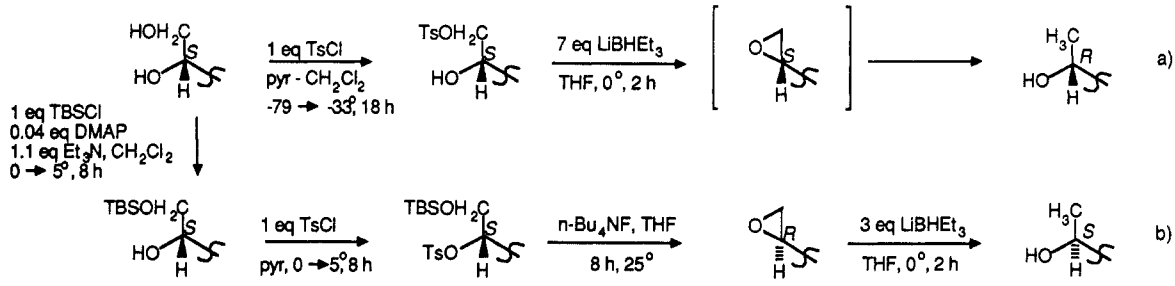
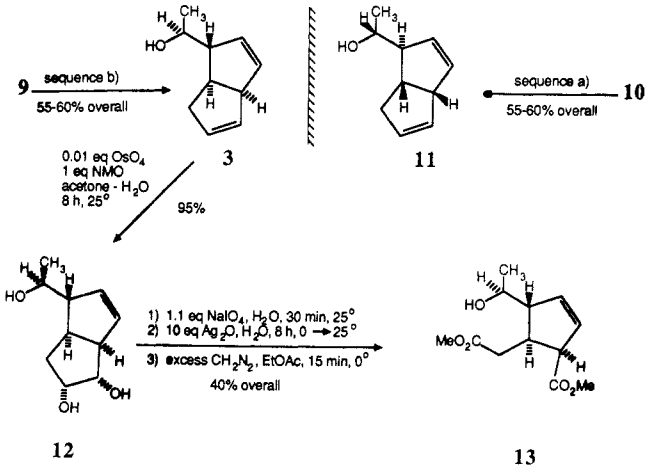
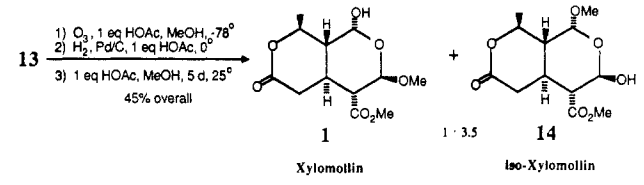
Scheme III



Scheme IV



Scheme V



between **6** and **7** to be as shown.

Reaction of **3** with catalytic osmium tetraoxide and *N*-methylmorpholine *N*-oxide afforded the triol **12** in high yield with excellent stereo- and regiochemical control (Scheme IV). Cleavage with periodate and further oxidation with nonbasic silver oxide[10] followed by esterification with excess diazomethane afforded diester **13**.[11] Oxidation of **13** with ozone followed by catalytic reduction exposed all of the functionality represented in **2**. The unique lactone, acetal–hemiacetal system present in the natural product was then formed upon extended treatment with mild acetic acid in methanol (Scheme V).[13,14] A regioisomer, isoxylomollin (**14**), was also produced with the same stereochemistry at carbons 1, 3, and 4[15] as in **1** but where the methoxy and hydroxy groups at C-1 and C-3 have been interchanged. The preferential formation of **14** is reasonable[16] and indeed, prolonged treatment with mild acid only further enriched the mixture in **14** at the expense of **1**.

We have accomplished a total synthesis of this highly unusual and biologically active iridoid terpene in optically active form by a unique combination of stereochemical methods. In particular, two new stereochemical centers were formed with high levels of absolute as well as relative asymmetric induction at the same time that a third was controlled by kinetic resolution. In addition, the development of divergent schemes for further elaboration of the adduct with either net inversion or retention at the secondary carbinol center expands the scope of applications for our asymmetric ene reaction.

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Supplementary Material Available: Experimental details for the preparation of and spectral data for all intermediates (16 pages). Ordering information is given on any current masthead page.

(10) The use of nonbasic silver oxide is critical here. Standard procedures for the preparation of this reagent invariably employ excess base and use of such material for the oxidation of the intermediate dialdehyde derived from **12** afforded very low yields of diacid.

(11) Repeated attempts to effect lactonization of **13** by using a variety of reaction conditions were unsuccessful, with migration of the double bond into conjugation with the ester functionality occurring more rapidly than ring closure. Apparently the strain induced by the presence of the double bond in the bicyclic, trans-fused hydrindane lactone is substantial. A simpler model, lacking the unsaturation, closed spontaneously.[12]

(12) Baldwin, S. W.; Crimmins, M. T. *Tetrahedron Lett.* **1978**, 4197.

(13) It is not clear at this time whether xylomollin is an artifact of the isolation procedure (that involved extraction with methanol) or is present in the fruit.

(14) Both carbon-13 and proton NMR spectra of synthetic xylomollin were identical with those obtained on a sample of natural material kindly provided by Professor Nakanishi. The melting points were also essentially identical (137–139 °C (MeOH), synthetic; 138–139 °C (EtOH, authentic), while the optical rotation was slightly low ($[\alpha]_D$ −40.0° (*c* 0.42, MeOH) vs. −44.3° (concentration not specified, MeOH)). However, the synthetic sample slowly converted to isoxylomollin in neutral methanol over time and the rotation of the latter is lower ($[\alpha]_D$ −25.2 (*c* 0.5, MeOH). The sample recovered after the rotation measurement was in fact contaminated with isoxylomollin.

(15) The axial orientation of the Cl hydroxyl group is presumably dictated by the anomeric effect and avoidance of a peri interaction with the C-10 methyl group. Equatorial orientations for the remaining groups would then be expected.

(16) Assuming fixed stereochemistry,[15] it might be anticipated that the methoxy group would be preferred in an axial and the hydroxy group in an equatorial orientation based on the preference for β- over α-glucose and α- over β-methyl glucoside.

Use of Pulsed Time-Resolved Photoacoustic Calorimetry To Determine the Strain Energy of *trans*-1-Phenylcyclohexene and the Energy of the Relaxed 1-Phenylcyclohexene Triplet

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The energetics of nonspectroscopic species on excited-state surfaces, as well as the energies of highly strained, short-lived transients on ground-state surfaces, have generally been accessible only through indirect arguments.[3,4] Such information, however,

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