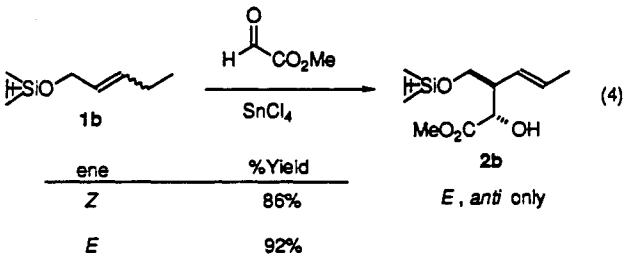
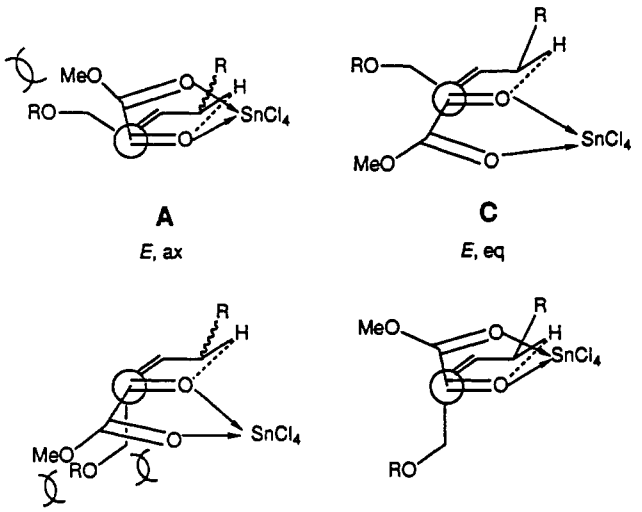
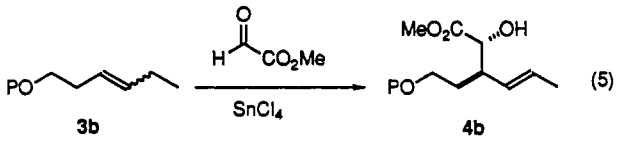


ene	%Yield	
Z	86%	E, anti only
E	92%	



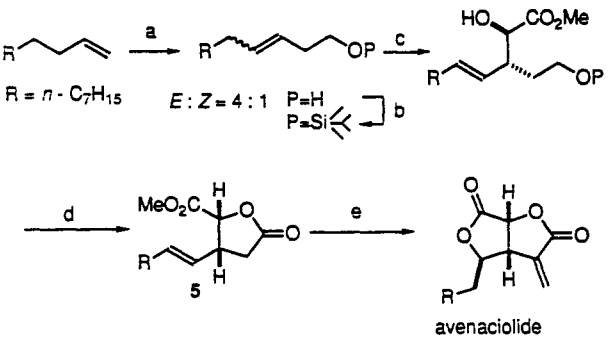
with **3b** gave *E*,anti ester **4b** as a single isomer,[6] *irrespective of the ene geometry*. Taking advantage of this



ene	P	%Yield
Z	Si	72%
	Si	77%
E	Si	54%

highly regio- and stereoselective glyoxylate–ene reaction, we carried out a formal synthesis of (±)-avenaciolide

Scheme I[a]



[a] (a) CH_2O, $EtAlCl_2$, CH_2Cl_2, 0 °C (quant).[13] (b) i-$PrMe_2SiCl$, imidazole, DMF (92%). (c) MeO_2CCHO, $SnCl_4$, CH_2Cl_2, −78 °C (34%). (d) Jones reagent, 0 °C to rt (64%). (e) Reference 12b.

(Scheme I).[11,12] Thus, the formaldehyde–ene/glyoxylate–ene sequence starting from 1-undecene followed by highly chemoselective oxidation furnished directly *E,cis*-lactone **5** as a single isomer, which is a key intermediate in a recent synthesis of avenaciolide.[12b]

In conclusion, we have demonstrated that the Lewis acid promoted glyoxylate–ene reaction of properly protected allylic and homoallylic alcohols allows the introduction of polyoxy functionality in a high regio- and stereocontrolled fashion.

Acknowledgment. This research was partially supported by a Grant-in-Aid for Priority Research from the Ministry of Education, Japan, and the Asahi-Kasei Award in Synthetic Organic Chemistry, Japan.

Supplementary Material Available: Experimental details of the glyoxylate–ene reactions, lactonizations, and the formal total synthesis of (±)-avenaciolide (5 pages). Ordering information is given on any current masthead page.

(11) For the isolation and antifungal and antibacterial activities of avenaciolide, see: (a) Brookes, D.; Tidd, B. K.; Turner, W. B. *J. Chem. Soc.* **1963**, 5385. (b) Ellis, J. J.; Stodola, F. H.; Vesonder, R. F.; Glass, C. A. *Nature (London)* **1964**, *203*, 1382. (c) Brookes, D.; Sternhell, S.; Tidd, B. K.; Turner, W. B. *Aust. J. Chem.* **1967**, *18*, 373.

(12) For syntheses, see: (a) Schreiber, S. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1984**, *106*, 7200. (b) Kallmerten, J.; Gould, T. J. *J. Org. Chem.* **1985**, *50*, 1128. (c) Anderson, R. C.; Fraser-Reid, B. *Ibid.* **1985**, *50*, 4781. (d) Suzuki, K.; Miyazawa, M.; Shimazaki, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1986**, *27*, 6237. (e) Sharma, G. V. M.; Vepachedu, S. R. *Ibid.* **1990**, *31*, 4931 and references cited therein.

(13) For the rate acceleration with $EtAlCl_2$ instead of Me_2AlCl, see: Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. *J. Am. Chem. Soc.* **1982**, *104*, 555.

Synthesis of (−)-(6*R*,10*R*)-Matsuone. Assignment of Relative Stereochemistry to a Pheromone of *Matsucoccus* Pine Bast Scales

Charles L. Cywin,[†] Francis X. Webster,[‡] and James Kallmerten*,[†]

Department of Chemistry, Syracuse University, Syracuse, New York 13244-4100, and Department of Chemistry, SUNY College of Environmental Science and Forestry, Syracuse, New York 13210

Received February 4, 1991

Summary: A convergent, enantioselective synthesis of (−)-matsuone (1, (2*E*,4*E*,6*R*,10*R*)-4,6,10,12-tetramethyl-2,4-tridecadien-7-one), the primary sex attractant pheromone of the red pine scale *Matsucoccus resinosae*, is described.

Infestations of pine bast scales in the United States and worldwide present a serious threat to the viability of af-

[†] Syracuse University.
[‡] SUNY College of Environmental Science and Forestry.

0022-3263/91/1956-2953$02.50/0

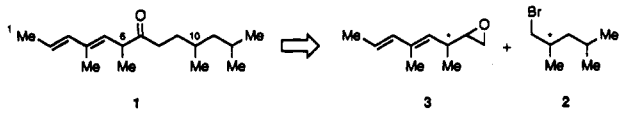
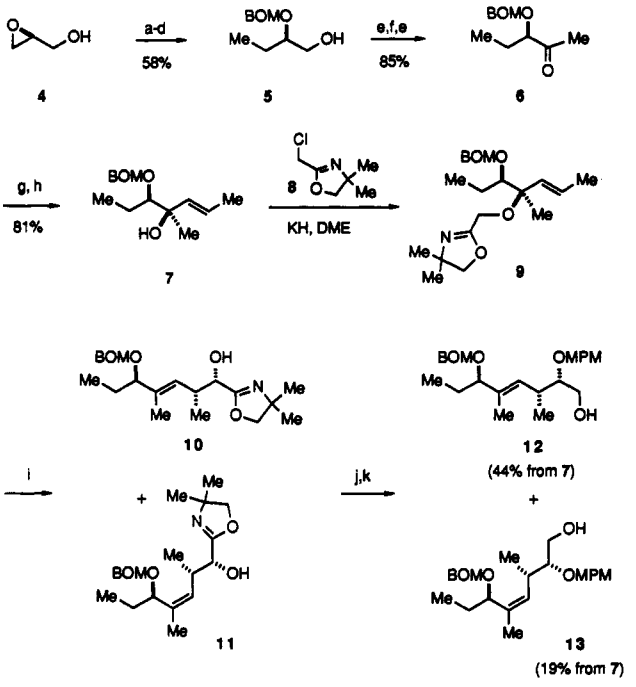


Figure 1.

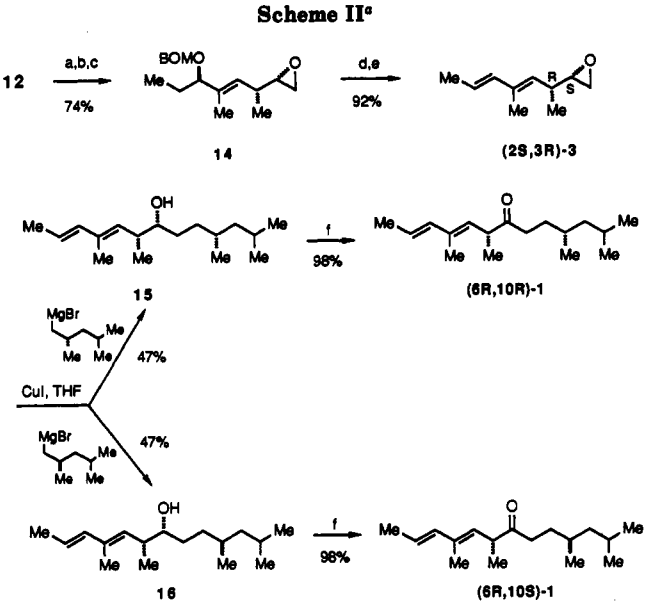
Scheme I[a]



[a] Reagents: (a) *t*-BuMe$_2$SiCl, imidazole, CH_2Cl_2, 0 °C; (b) CH_3MgBr, CuI, THF; (c) $PhCH_2OCH_2Cl$, Et*i*-PrN, CH_2Cl_2; (d) *n*-Bu$_4$NF, THF; (e) $(COCl)_2$, NEt_3, DMSO, CH_2Cl_2; (f) CH_3MgBr, THF; (g) $CH_3CCMgBr$, THF; (h) $LiAlH_4$, THF; (i) *n*-BuLi, THF, −78 °C; (j) *p*-MeOPhCH_2Cl, KH, DME; (k) TFA, H_2O, 24 h, then $LiAlH_4$, THF.

fected forestlands. Recent studies have identified matsuone **1** as the primary sex attractant pheromone of the red pine scale *Matsucoccus resinosae* and two related species indigenous to Asia, *M. matsumurae* (China) and *M. thunbergianae* (Korea).[1,2] The potential importance of synthetic matsuone as one component of a bioethical strategy for control of *Matsucoccus* predation, combined with the limited availability of the pheromone[3] and the unresolved structural and stereochemical issues surrounding the natural product fostered our interest in the development of a preparative route to the individual stereoisomers of **1**. Herein we report the enantioselective synthesis of (−)-(6*R*,10*R*)-**1** and its 6*R*,10*S* diastereomer, confirming the structure of matsuone as (2*E*,4*E*,6*R**,10*R**)-4,6,10,12-tetramethyl-2,4-tridecadien-7-one and establishing the C_6–C_{10} stereochemical relationship of the naturally occurring pheromone as *priority-reflective*[4] (Figure 1).

Scheme II[a]

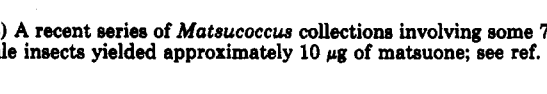


[a] Reagents: (a) TsCl, pyridine; (b) 1 M aqueous $Ce(NH_4)_2(NO_3)_6$, MeCN; (c) NaOMe, MeOH; (d) Na, NH_3, −78 °C; (e) MeOC(O)NSO_2NEt_3, benzene, 50 °C; (f) (*n*-Pr)$_4$NRuO_4, *N*-methylmorpholine *N*-oxide, 4-Å sieves, CH_2Cl_2.

The copper-assisted coupling of an organomagnesium reagent derived from optically active bromides **2** to epoxide **3**, comprising the C_1–C_8 fragment of the pheromone, presented an attractive strategy for enantioselective synthesis of the individual stereoisomers of **1**. Given the anticipated availability of either antipode of bromide **2**,[5] the preparation of epoxide (2*S*,3*R*)-**3** became the focus of our synthetic efforts. Our approach to this intermediate, based on our recent observation that the [2,3] Wittig rearrangement of tertiary allylic ethers provides a stereorational entry to trisubstituted acyclic olefins,[6] is depicted in Scheme I. Commercially available (*S*)-(−)-glycidol **4** (ee 85%) was transformed to its *tert*-butyldimethylsilyl ether, which was subjected to regioselective copper-catalyzed addition by methyl Grignard reagent. Alkylation of the resulting alcohol and desilation yielded, as the only observed product, **5**.[7] Conversion of **5** to methyl ketone **6** was followed by final elaboration of the tertiary allylic alcohol **7**, via chelation-controlled addition[6] of propynyl Grignard reagent and reduction of the resulting propargylic alcohol with $LiAlH_4$. Alkylation of alcohol **7** with 2-(chloromethyl)oxazoline **8** and treatment of the resulting ether **9** with *n*-BuLi resulted in [2,3] Wittig rearrangement to give a mixture of (*E*)- and (*Z*)-hydroxyoxazolines **10** and **11**. Protection as the *p*-methoxybenzyl ether and reductive cleavage of the oxazoline system[8] yielded the corresponding

(1) Lanier, G. N.; Qi, Y.; West, J. R.; Park, S. C.; Webster, F. X.; Silverstein, R. M. *J. Chem. Ecol.* **1989**, *15*, 1645.

(2) The isolation of the structurally related pheromones i and ii from *M. feytaudi* was recently described: Einhorn, J.; Menassieu, P.; Malosse, C.; Ducrot, P.-H. *Tetrahedron Lett.* **1990**, *31*, 6633.



(3) A recent series of *Matsucoccus* collections involving some 77 000 female insects yielded approximately 10 μg of matsuone; see ref. 1.

(4) Carey, F. A.; Kuehne, M. E. *J. Org. Chem.* **1982**, *47*, 3811.

(5) Bromides (2*S*)-**2** and (2*R*)-**2** were prepared from the corresponding optically pure (ee >98%) 2,4-dimethylpentanoic acids (Evans, D. A.; Dow, R. L.; Shih, T. L.; Takacs, J. M.; Zahler, R. *J. Am. Chem. Soc.* **1990**, *112*, 5290) using a modified literature procedure, see: Bergmann, E. D.; Blum, S.; Levinson, Z. H. *Steorids* **1966**, *7*, 415.

(6) Wittman, M. D.; Kallmerten, J. *J. Org. Chem.* **1988**, *53*, 4631.

(7) All compounds reported herein were fully characterized by IR and ^{1}H and ^{13}C NMR spectroscopy. Satisfactory combustion analyses and/or high-resolution mass spectra were obtained for all new compounds.

(8) Meyers, A. I.; Flisak, J. R.; Aitken, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 5446.

alcohols 12 and 13, which were readily separable by flash chromatography.[9]

The requisite epoxide unit was introduced by the conversion of alcohol 12 to the primary tosylate, followed by oxidative deprotection of the *p*-methoxybenzyl ether and treatment of the resulting alcohol with sodium methoxide to yield epoxide 14 (Scheme II). Final installation of the *E,E* diene system was accomplished by reductive cleavage of the (benzyloxy)methyl ether and dehydration using the Burgess protocol,[10] affording the sensitive diene epoxide (2*S*,3*R*)-3.

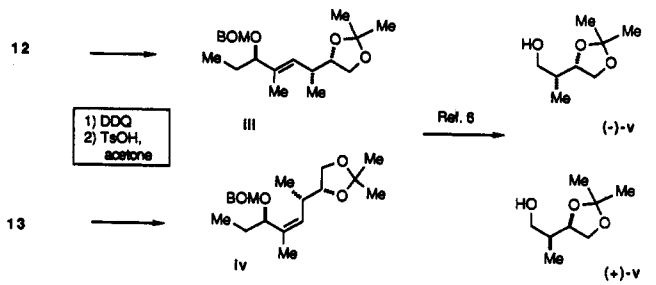
Treatment of epoxide (2*S*,3*R*)-3 with the Grignard reagents[11] derived from (*S*)- and (*R*)-1-bromo-2,4-dimethylpentanes afforded alcohols 15 and 16, respectively, each of which was accompanied by ca. 7% of an inseparable minor diastereomer.[12] Oxidation of 15 with catalytic tetrapropylammonium perruthenate[13] in the presence of *N*-methylmorpholine *N*-oxide gave a 98% yield of the ketone (6*R*,10*R*)-1 accompanied by the minor 6*S*,10*R* diastereomer. Similarly, oxidation of 16 afforded (6*R*,10*S*)-1 and the minor 6*S*,10*S* ketone product. The 500-MHz ^{1}H NMR, mass spectroscopic, and chromatographic properties of (6*R*,10*R*)-1 correspond to those of authentic matsuone; in contrast, the properties of the diastereomeric (6*R*,10*S*)-1 were clearly distinct from those of the natural pheromone.[14] Particularly diagnostic are the 500-MHz ^{1}H chemical shifts of signals assigned to the diastereotopic protons of the C_8 methylene group of matsuone diastereomers. Signals assigned to the C_8 protons of matsuone and (6*R*,10*R*)-1 appear at δ 2.19 (ddd, J = 16.8, 9.3, 5.5 Hz) and 2.29 (ddd, J = 16.8, 8.6, 6.4 Hz), while the corresponding protons of (6*R*,10*S*)-1 are observed at δ 2.13 (ddd, J = 16.8, 8.7, 6.1 Hz) and 2.32 (ddd, J = 16.8, 9.3, 5.5 Hz); the latter signals are notably absent from the spectrum of authentic 1.[15]

The relative configuration of matsuone is thus established as *priorty-reflective*. We note that the availability of both antipodes of matsuone[12] is expected to faciltate assignment of the absolute configuration to the natural pheromone by chiral-phase gas chromatographic analysis.[16] These studies, and the results of field tests utilizing individual stereoisomers of 1, will be the subject of future reports.

Acknowledgment. Support for this work was provided by a grant from the National Institutes of Health (GM-39990). We thank Arco Chemicals for a generous gift of (*S*)-(−)-glycidol. The support of Syracuse University in the form of a University Fellowship (C.L.C.) is gratefully acknowledged.

Supplementary Material Available: Experimental procedures and full characterization data for all new compounds and 500-MHz ^{1}H NMR spectra of matsuone and synthetic stereoisomers (23 pages). Ordering information is given on any current masthead page.

(9) Stereochemical assignments for 12 and 13 were confirmed by NOE studies and by conversion to the known triol derivatives v, as previously described.[6]



(10) Burgess, E. M.; Penton, H. R.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.

(11) Zimmerman, M. P.; Li, H.; Duax, W. L.; Weeks, C. M.; Djerassi, C. *J. Am. Chem. Soc.* **1984**, *106*, 5602.

(12) The minor diastereomeric products observed from Grignard couplings of (2*S*,3*R*)-3 reflect the stereochemical heterogeneity of this epoxide and are consistent with the optical purity of starting glycidol 4 (ee ca. 85%). We note that the presence of these minor diastereomers provides access to all four stereoisomers of ketone 1; thus, the ketone obtained from oxidation of 15 (and the accompanying minor diastereomer) contains 7% of the 6*S*,10*R* diastereomer, while oxidation of 16 affords (6*R*,10*S*)-1 accompanied by 7% of the 6*S*,10*S* diastereomer.

(13) Griffith, W. P.; Ley, S. V. *Aldrichimica Acta* **1990**, *23*, 13.

(14) The 500-MHz ^{1}H NMR spectrum of authentic matsuone,[1] obtained in benzene-d_6 with ca. 1–2 μg of material, exhibits signal envelopes in the δ 1.0–1.2 and 1.9–2.2 regions that are not present in either synthetic diastereomer. Our NMR sample of matsuone was purified to homogeneity prior to use, and we attribute these signals to the presence of minor solvent impurities.

(15) A similar chemical-shift pattern is observed for diastereomers of the *M. feytaudi* pheromone i (Cywin, C. L. Unpublished results).

(16) Schurig, V.; Nowothy, H. P. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 939. The limited availability of authentic 1 has to date precluded either a determination of optical rotation or NMR analysis using chiral shift reagents.

Lithiation and Isomerization of Allylic Amines as a General Route to Enamines and Their Carbonyl Derivatives[1]

John J. Eisch* and Jamshed H. Shah

Department of Chemistry, The State University of New York at Binghamton, Binghamton, New York 13902-6000

Received January 30, 1991

Summary: [3-(Diphenylamino)-2-propenyl]lithium, readily prepared by the lithiation of allyldiphenylamine with *n*-butyllithium in THF, undergoes alkylation either with organic halides or with carbonyl or azomethine derivatives to yield enamines, which can be converted by protons or other electrophiles into aldehydes or into five-membered heterocycles; lithiation of such allyldiarylamines with other reagents leads principally to isomerization to enamines (with lithium diisopropylamide) or to carbenoid intermediates (*tert*-butyllithium and potassium *tert*-butoxide).

Previous studies[2] have demonstrated that attempted metalation of tertiary allylamines (1) can lead both to

(1) Part 9 of the series of publications devoted to Functionalized Organolithium Reagents. Part 8: Eisch, J. J.; Galle, J. E. *J. Org. Chem.* **1990**, *55*, 4835. For general reference to the use of heteroatom-substituted allyllithium reagents as homoenolates, see: Barluenga, J. *Pure Appl. Chem.* **1990**, *62*, 595. This should lead the interested reader to the considerable literature on this topic.

0022-3263/91/1956-2955$02.50/0