Registry No. 1, 935-56-8; 2, 7677-24-9; 3, 22110-53-8; 4, 3405-48-9; 6, 2290-65-5; 7, 39825-84-8; 8, 4411-26-1; 10, 1118-02-1; 11, 62139-68-8; 13, 25348-10-1; 14, 79664-52-1; 15, 4648-54-8; 16, 24886-73-5; *N*-methylodamantanamine, 3717-38-2; cyanogen bromide, 506-68-3.

Communications

New Sigmatropic Sequences Based on the [2,3] Wittig Rearrangement of Bis-Allylic Ethers. Regiocontrolled Joining Reactions of Two or Three Allylic Moieties Leading to Unsaturated Carbonyl Compounds

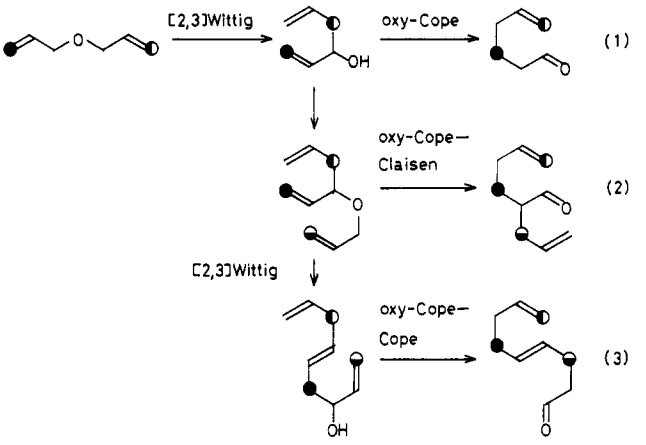
Summary: Three new sigmatropic sequences based on the [2,3] Wittig rearrangement of bis-allylic ethers are described which provide unique, regiocontrolled methods for the synthesis of a variety of unsaturated carbonyl compounds possessing interesting molecular frameworks.

Sir: Recently we have found that the [2,3] Wittig rearrangement of unsymmetrical bis-allylic ethers **1** is exceedingly useful for regio- and stereoselective preparations of 1,5-dien-3-ols **2**.[1] To expand further the synthetic potential of the rearrangement, our efforts have now been directed toward development of new sigmatropic sequences triggered by the [2,3] Wittig variant. While a number of tanden [3,3]–[3,3] sigmatropic sequences such as the Claisen–Cope[2] and the Cope–Claisen rearrangements[3] have currently been developed and have found substantial utility in the methodology for organic synthesis, only a few [2,3] sigmatropic rearrangements have been exploited in tandem or in series for effecting carbon–carbon bond formations.[4]

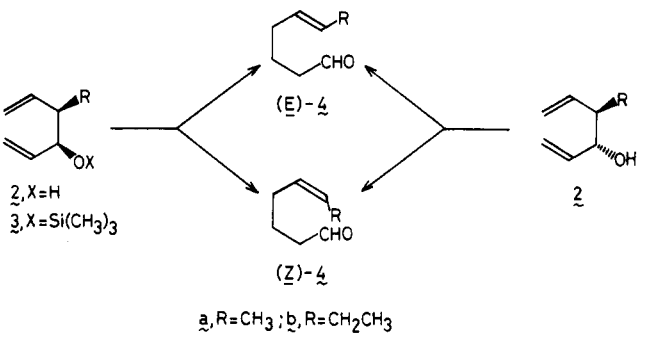
Herein we describe three new sigmatropic sequences based on the [2,3] Wittig rearrangement which provide unique, facile methods for the synthesis of various kinds of unsaturated carbonyl compounds possessing interesting molecular frameworks. The overall bond organizations are shown in Scheme I. Significantly, the net effect of these sequences allows two or three allylic moieties initially linked by a readily formed ether bond(s) to be recombined by a newly created carbon–carbon bond(s) in a regiospecific fashion.

First, the accessibility of diastereomerically defined 1,5-dien-3-ols by virtue of the [2,3] Wittig rearrangement[1]

Scheme I



Scheme II



a, R=CH_3; b, R=CH_2CH_3

has prompted us to investigate the unresolved stereochemistry of the *acyclic* oxy-Cope rearrangement.[5] Thus we carried out the rearrangement of both erythro- and threo-rich mixtures[6] of **2a** and **2b** (Scheme II) by applying the four current procedures: the anionic oxy-Cope[7] and the siloxy-Cope[8] modifications and thermolysis in *N*-methylpyrrolidone (NMP)[9] and in refluxing decane.

The experimental results thus obtained[10] reveal stereochemical features of the acyclic oxy-Cope rearrangement

(1) Nakai, T.; Mikami, K.; Taya, S.; Fujita, Y. *J. Am. Chem. Soc.*, in press.

(2) Thomas, A. F. *J. Am. Chem. Soc.* **1969**, *91*, 3281. Thomas, A. F.; Ohloff, G. *Helv. Chim. Acta* **1970**, *53*, 1145. Fráter, G. *Ibid.* **1975**, *58*, 442. Fráter, G. *Chimia* **1975**, *29*, 528. Wilson, S. R.; Myers, R. S. *J. Org. Chem.* **1975**, *40*, 3309. Bowden, B.; Cookson, R. C.; Davis, H. A. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2634. Cookson, R. C.; Rogers, N. R. *Ibid.* **1973**, 2741. Fujita, Y.; Onishi, T.; Nishida, T. *Synthesis* **1978**, 523. Thio-Claisen–Cope: Tamaru, Y.; Harada, T.; Yoshida, Z. *J. Am. Chem. Soc.* **1980**, *102*, 2392. Claisen–aza-Cope: Holmes, B. N.; Leonard, N. J. *J. Org. Chem.* **1976**, *41*, 568.

(3) Ziegler, F. E.; Piwinski, J. J. *J. Am. Chem. Soc.* **1979**, *101*, 1611; **1980**, *102*, 880. Raucher, S.; Burks, J. E., Jr.; Hwang, K.-J.; Svedberg, D. P. *Ibid.* **1981**, *103*, 1853.

(4) (a) *S*-Ylide [2,3]-Cope: Labuschange, A. J. H.; Meyer, C. J.; Spies, H. S. C.; Schneider, D. F. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2129 and references therein. (b) *N*-Ylide [2,3]-Cope: Jemison, R. W.; Laird, T.; Ollis, W. D.; Sutherland, I. O. *Ibid.* **1980**, 1436; Büchi, G.; Wüest, H. *J. Am. Chem. Soc.* **1974**, *96*, 7573. (c) *N*-Oxide [2,3]-Claisen: Thyagarajan, B. S.; Hillard, J. B.; Reddy, K. V.; Majumdar, K. C. *Tetrahedron Lett.* **1974**, 1999. (d) *S*-Oxide [2,3]-Claisen: Majumdar, K. C.; Thyagarajan, B. S. *Chem. Commun.* **1972**, 83. (e) [2,3] Wittig–oxy-Cope: Garbers, C. F.; Scott, F. *Tetrahedron Lett.* **1976**, 507.

(5) Recent reviews include: Marvell, E. N.; Whalley, W. In "Chemistry of the Hydroxy Group"; Patai, S., Ed.; Interscience: New York, 1971; Vol. 2, Chapter 13. Bennett, G. B. *Synthesis* **1977**, 589.

(6) Two diastereomeric mixtures of **2a** (88% erythro and 79% threo) and a mixture of **2b** (80% threo) were used as substrates.

(7) The potassium alkoxide (prepared with KH) was heated in DME at 85 °C. Cf.: Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765. Evans, D. A.; Nelson, J. V. *Ibid.* **1980**, *102*, 774.

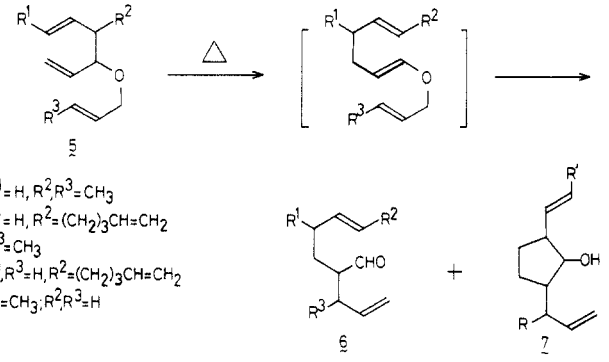
(8) The silyl ether **3** was heated in refluxing decane. Cf.: Thies, R. W. *Chem. Commun.* **1971**, 237. Thies, R. W.; Wills, M. T.; Chin, A. W.; A. W.; Schick, L. E.; Walton, E. S. *J. Am. Chem. Soc.* **1973**, *95*, 5281.

(9) Alcohol **2** was heated in NMP at 202 °C. Cf.: Fujita, Y.; Onishi, T.; Nishida, T. *Synthesis* **1978**, 612. Fujita, Y.; Amiya, S.; Onishi, T.; Nishida, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1983.

(10) For details of the experimental results, see the supplementary material.

0022-3263/81/1946-5447$01.25/0

Scheme III



Scheme IV

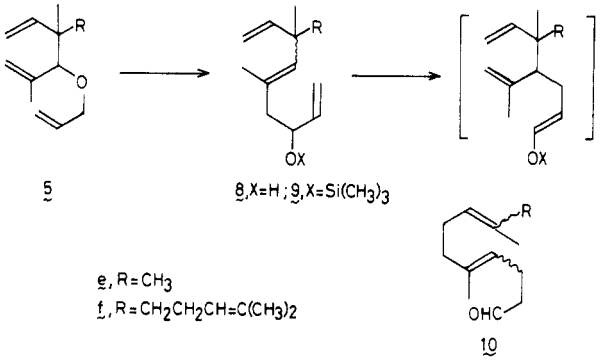


Table I.[15] Tandem Oxy-Cope-Claisen Rearrangement of 5

entry	substrate[a] (threo/erythro ratio)[b]	conditions[c] temp, °C	time, h	product[d] (% yield)[e]
1	5a (79:21)	250	10	6a (36), 7[R = CH_3, R′ = H] (20)
2	5a (79:21)	250	5[f]	6a (46), 7[R = CH_3, R′ = H] (12)
3	5b[g] (80:20)	200	4	6b (45)
4	5c[g] (80:20)	200	4	6c (45), 7[R = H, R′ = $(CH_2)_2CH=CH_2$] (13)
5	5d	250	10	6d (41)

[a] Prepared by etherification of the corresponding 1,5-dien-3-ol (2) with the allylic halide following the literature procedure: Freeman, H. H.; Dubois, R. A. *Tetrahedron Lett.* **1976**, 95. [b] The diastereomeric ratio refers to that of 2. [c] All reactions were run in a sealed tube. [d] Fully characterized by IR and NMR spectra (see the supplementary material). [e] Isolated yield. [f] Thermolysis was conducted in NMP. [g] Prepared from (*E*)-2,7-octadienol as the starting material. We thank Professor J. Tsuji for providing the butadiene telomer. Cf.: Tsuji, J. *Pure Appl. Chem.* **1979**, *51*, 5070.

in general. (1) Both the erythro- and threo-rich substrates afforded essentially the same stereochemical outcomes under a given rearrangement condition. (2) Applications of the first three procedures described above gave geometric mixtures of **4** in yields of 42–84% with moderate degrees of *E* selectivity ranging from 79% to 67%. (3) Of synthetic value are higher levels of *E* selectivity (90–95%) observed with the thermolysis in decane. It thus appears that *the olefinic stereochemistry of product in the acyclic oxy-Cope rearrangement is independent of relative stereochemistry of substrate* and that levels of the observed *E* selectivity depends largely on the rearrangement procedure employed.[11]

From the standpoint of synthetic value, the tandem [2,3] Wittig–oxy-Cope sequence is of special interest since the net effect allows the allyloxy moiety to serve as a homoenolate anion equivalent[12] and thereby accomplishes the selective α substitution[13] of allylic halides (or alcohols) with the homoenolate equivalent. Therefore, this sequence provides a versatile synthetic route to δ,ϵ-unsaturated carbonyl compounds which have currently found widespread use in synthetic transformations.[14]

Second, we have studied thermolysis of the allylic ethers **5**, readily obtainable via etherification of **2**. Thermolysis of **5** (neat, 200–250 °C, N_2) gave rise to aldehyde **6** as the major product.[15] The formation of **6** is best explained by the tandem oxy-Cope–Claisen sequence (Scheme III). The examples are given in Table I. In certain cases, the cyclic alcohol **7** was also formed which was independently shown to arise from **6** via an intramolecular ene reaction.[16] Interestingly, the use of NMP as the reaction medium depresses the subsequent ene reaction (entry 2, Table I).

These transformations not only offer the first example of the unprecedented tandem sequence in which *the oxy-Cope triggers the Claisen rearrangement* but also furnish the overall sequence represented by eq 2 in Scheme I. The stereochemical outcome of the sequence, though not extensively studied, appears predictable from combination of the well-known stereochemistry of the respective process involved. In fact, the newly created olefinic bond possesses exclusively the *E* geometry (entries 1–4, Table I).

Finally, we have explored thermolysis of the trienol **8**,[15] readily prepared via the regiocontrolled [2,3] Wittig rearrangement of the allylic ether **5**. Trienol **8e** was subjected to the oxy-Cope conditions (202 °C, NMP, N_2) to produce a geometric mixture (*E*/*Z* ratio of 2.0) of geranylacetaldehyde (**10e**)[17] in 41% of isolated yield. Significantly, an increased yield (86%) was obtained when siloxy triene **9e** was heated in neat at 250 °C. The formation of **10e** is best explained by the tandem (sil)oxy-Cope–Cope rearrangement (Scheme IV). A similar thermolysis of a diastereomeric mixture (72:28)[18] of **8f**, derived from geraniol via the above-mentioned sequence, gave rise to a geometric mixture of farnesylacetaldehyde (**10f**) in a 46% isolated yield.[19] In a like manner, another diastereomeric mixture (44:56)[18] of **8f** derived from nerol afforded a nearly identical stereomixture in 34% yield. The stereomixture was found to be a mixture of the four possible geometric isomers through GLC comparisons with a stereomixture (4*E*/4*Z*, 2:1) of (8*E*)-**10f** independently

(11) These stereochemical features will be discussed on mechanistic grounds in a full paper.

(12) For leading references of homoenolate anion equivalents, consult: Ehlinger, E.; Magnus, P. *J. Am. Chem. Soc.* **1980**, *102*, 5004.

(13) For a recent review on regio- and stereochemistry of organometallic displacement reactions of allylic compounds, see: Magid, R. M. *Tetrahedron* **1980**, *36*, 1901.

(14) Conia, J. M.; Le Perchec, P *Synthesis* **1975**, 1 and references therein. Shono, T.; Nishiguchi, I.; Ohmizu, H.; Mizutani, M. *J. Am. Chem. Soc.* **1978**, *100*, 545. Corey, E. J.; Boger, D. L. *Tetrahedron Lett.* **1978**, 2461. Sowinski. A. F.; Whitesides, G. M. *J. Org. Chem.* **1979**, *44*, 2369.

(15) All products were fully characterized by IR and NMR spectra (see the supplementary material).

(16) For a review, see: Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556.

(17) Determined by GLC comparison with an authentic mixture prepared from linalool via the Claisen rearrangement. Cf.: Marbet, R.; Saucy, G. *Helv. Chim. Acta* **1967**, *50*, 2095.

(18) The stereochemistry of the major diastereomer has not been determined yet.

(19) In this case, no increased yield was obtained with the attempted siloxy-Cope rearrangement.

prepared from (6*E*)-neroridol via the Claisen rearrangement.[20]

The transformation of **5** to **10** not only presents the first example of the unprecedented tandem sequence in which *the oxy-Cope triggers the Cope rearrangement* but also furnishes the overall sequence depicted by eq 3 in Scheme I. Furthermore, the new sequence provides a novel, versatile method for the synthesis of functionalized 1,5-diene derivatives which are commonly found in many terpenoid natural products. In particular, farnesylacetaldehyde obtained above is a promising precursor of geranyl farnesylacetate (so-called Gefarnate), a commercial antiulser agent.[21]

Further stereochemical studies of the three new sigmatropic sequences outlined in this study and their applications to natural product synthesis are in progress.

Registry No. *erythro*-**2a**, 79705-03-6; *threo*-**2a**, 79705-02-5; *erythro*-**2b**, 79803-44-4; *threo*-**2b**, 79803-45-5; *erythro*-**3a**, 79803-46-6; *threo*-**3a**, 79803-47-7; (*E*)-**4a**, 21662-19-1; (*Z*)-**4a**, 21661-98-3; (*E*)-**4b**, 41547-29-9; (*Z*)-**4b**, 41547-22-2; *erythro*-**5a**, 79803-48-8; *threo*-**5a**, 79803-49-9; *erythro*-**5b**, 79803-50-2; *threo*-**5b**, 79803-51-3; *erythro*-**5c**, 79803-52-4; *threo* **5c**, 79803-53-5; **5d**, 79803-54-6; **5e**, 79803-55-7; **5f**, 79803-56-8; **6a**, 79803-57-9; **6b**, 79761-79-8; (*E*)-**6c**, 79803-58-0; **6d**, 79772-67-1; **7** (R = CH_3; R′ = H), 79803-59-1; **7** (R = H; R′ = $(CH_2)_2CH{=}CH_2$, 79803-60-4; **8e**, 79803-61-5; **8f**, 79803-62-6; **9e**, 79803-63-7; **9f**, 79803-64-8; (*E*)-**10e**, 18445-88-0; (*Z*)-**10e**, 18445-81-3; (*Z*,*E*)-**10f**, 79803-65-9; (*E*,*E*)-**10f**, 67858-78-0; (*Z*,*Z*)-**10f**, 79803-66-0; (*E*,*Z*)-**10f**, 79803-67-1; 3,4-dimethyl-1,5-hexadien-3-ol, 30884-86-7; (*E*)-oct-6-en-2-one, 51193-76-1; (*Z*)-oct-6-en-2-one, 74810-53-0; (*E*)-2,7-octadienol, 62179-18-4; geraniol, 106-24-1; nerol, 106-25-2; (*E*)-nerolidol, 40716-66-3; (*Z*)-nerolidol, 3790-78-1.

Supplementary Material Available: Tables containing experimental results of the oxy-Cope rearrangement and spectral data for new compounds (6 pages). Ordering information is given on any current masthead page.

(20) In a similar manner, another authentic mixture (4*E*/4*Z*, 2:1) of (8*Z*)-**10f** was prepared from (6*Z*)-neroridol.

(21) Activity: Adami, E. *Experimentia* **1962**, *18*, 461. Takagi, K.; Okabe, S. *Jpn. J. Pharmacol.* **1968**, *18*, 9. Synthesis: Pala, G; Mantegani, A.; Bruzzese, T.; Sekules, G. *Helv. Chim. Acta* **1970**, *53*, 1827. Fujita, Y.; Ohmura, Y.; Nishida, T.; Itoi, K. U.S. Patent 3 928 403.

K. Mikami, S. Taya, T. Nakai*
Department of Chemical Technology
Tokyo Institute of Technology
Meguro, Tokyo 152, Japan

Y. Fujita
Central Research Laboratories
Kuraray Co. Ltd.
Kurashiki, Okayama 710, Japan
Received August 10, 1981

Lasidiol Angelate: Ant Repellent Sesquiterpenoid from *Lasiantheae fruticosa*

Summary: Lasidiol angelate, a new sesquiterpenoid containing a carotane skeleton, has been isolated from *Lasiantheae fruticosa* (Compositae). A structure was proposed on the basis of spectral evidence and confirmed by a synthesis which achieves oxidation α to the less substituted terminus of a trisubstituted double bond by a double-reverse strategy. The natural products and several of the synthetic compounds are potent ant repellents.

Sir: The leafcutter ants, which are abundant from Texas to Argentina, are polyphagous herbivores. Among their preferred host plants are many of commercial value, including citrus, banana, and coffee.[1] This has led to the classification of leafcutter ants as serious agricultural pests in most of the New World, including the United States.

While the leafcutter ants are broadly polyphagous, many native plants do escape their attack. Plant defenses against their herbivory might take many forms, but it is reasonable to postulate that some plants have evolved chemical defenses.[2] We have developed bioassays to measure the relative acceptability of various species and the palatability of plant extracts to leafcutter ants.[3] Using these bioassays to direct an isolation sequence, we have isolated an ant repellent sesquiterpenoid from *Lasiantheae fruticosa* (Compositae), a plant common within the range of *Atta cephalotes* Hymenoptera, Formicidae, Attini) but not attacked by this ant.

The active compound (ca. 35 mg) was isolated from the chloroform extract of *L. fruticosa* leaves (2.3 kg) by a sequence of column and preparative layer chromatography. The electron impact (EI) mass spectrum of this compound does not show a molecular ion, but the chemical ionization (CI) mass spectrum revealed a molecular weight of 320. Because the ^{13}C NMR spectrum shows 20 carbons, including an ester group and a hydroxylic carbon (δ 167.3, 83.2, 77.3), a molecular formula of $C_{20}H_{32}O_3$ could be deduced. The delayed decoupled[4] ^{13}C NMR spectrum allowed recognition of two trisubstituted double bonds (δ 142.3, 122.2, 138.4, 127.8) and six methyl groups (δ 25.7, 24.3, 22.7, 21.3, 20.9, 15.7). Therefore, this compound, with a total of five degrees of unsaturation, must be bicyclic. The upfield portion of the ^1H NMR spectrum revealed three methyl groups attached to double bonds, a methyl singlet, and an isopropyl group. In the downfield region of the spectrum a quartet (δ 6.04, 1 H, J = 6 Hz) and two doublets (δ 5.16, 1 H, J = 6 Hz; δ 5.42, 1 H, J = 6 Hz) are visible. Homonuclear decoupling experiments confirmed spin–spin coupling between the two doublets and also established coupling between the quartet and an upfield methyl group (δ 1.9, 3 H, J = 6 Hz). The ^1H and ^{13}C NMR data indicate that this compound is a sesquiterpenoid containing a tertiary hydroxyl group and bearing a secondary angelate ester.[5,6]

To further characterize this sesquiterpenoid, a small portion of our sample (6 mg) was reduced with $LiAlH_4$ to afford a C_{15} diol. The CI mass spectrum confirmed the expected molecular weight of 238. As predicted, in the ^{13}C NMR spectrum the carbon bonded to the newly formed hydroxyl group shifted upfield by ca. 2 ppm (to δ 75.4). Because the carbons of the double bond and a quaternary carbon also shifted, it appeared as though this secondary hydroxylic carbon was flanked by these two groups. The ^1H NMR spectrum also is consistent with these conclusions. One methyl signal had shifted slightly upfield, while the two methyl signals of the angelate were absent. The signal for the proton geminal to the newly formed hydroxyl group was observed at δ 4.0 vs. a chemical shift of δ 5.4 in the ester. These facts are summarized by part structure 1.

For completion of a structure assignment, the diol (all 3 mg) was oxidized with pyridinium chlorochromate (PCC) to afford a keto alcohol. The EI mass spectrum showed

(1) Weber, N. A. "Gardening Ants, the Attines"; American Philosophical Society: Philadelphia, 1972.

(2) Schildknecht, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 164–84.

(3) Hubbell, S. P.; Wiemer, D. F. In "Social Insects in the Tropics"; Jaisson, P., Ed.; University of Paris Press: 1981, in press.

(4) Anet, F.; Strouse, J.; Jaffer, W. 21st Experimental NMR Conference, Tallahassee, FL, 1980.

(5) Culvenor, C. C. J.; Johns, S. R.; Lamberton, J. A.; Smith, L. W. *Aust. J. Chem.* **1970**, *23*, 1279–82.

(6) Bohlmann, F.; Zdero, C.; Grenz, M. *Chem. Ber.* **1974**, *107*, 3928–45.

0022-3263/81/1946-5449$01.25/0