in **2** are well documented.[18] The higher homologues **3** and **4** did not react with Moore's ketene. For example bicyclo[4.1.0]heptane (**4**) and Moore's ketene showed no reaction (reflux in toluene, 20 h), when monitored by IR and ^{1}H NMR spectroscopy.

Quadricyclane (**5**) gave the oxetane **8**, as the sole reaction product (quantitative yield) when treated with Moore's ketene.[17] At 19 °C, the cycloaddition occurred in 2 min. Norbornadiene was reported to react with Moore's ketene with comparable readiness[19] as its valence isomer quadricyclane, resulting the cyclobutanone **11** and the ether **12**, both isomers of oxetane **8**. Tentatively, the configurations of the *exo*-methylene fragment and of the four-membered ring is provided by ^{1}H NMR spectra without and with Eu(fod)$_3$d$_{27}$.

Naphtho[*b*]cyclopropane (**6**) gave the benzoindanone **9** when treated with Moore's ketene (90% yield). However, the reactivity of the cyclopropane ring annelated to the naphthalene was less than of quadricyclanic rings. For example at room temperature the cycloaddition took ca. 24 h as compared to 2 min in the case of quadricyclane.

The strain energy prerequisite threshold established with the present array of ketenophiles was estimated at about 31 kcal mol^{-1}.

We are actively engaged in testing new substrates and other ketenes in order to illustrate phenomenologically the reaction of ketenes with C–C σ bonds, as well as to uncover various aspects of the reaction mechanism.

Acknowledgment. We are grateful to the referees, especially for the constructive suggestions to revise the manuscript, and Prof. Dieter Cramer (Köln, West Germany) and Armin de Meijere (Hamburg, West Germany) for informing us prior to publication on topics of interest to us, as well as for reprints of their earlier works.

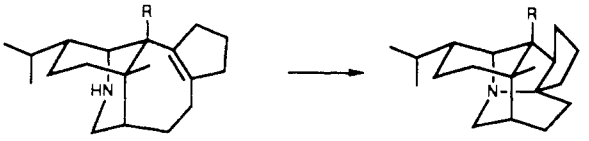
(18) Gajewski, J. J.; Chang, M. J.; Stang, P. J.; Tremeling, M. *J. Am. Chem. Soc.* **1980**, *102*, 2096 and literature cited therein.
(19) Brook, P. R.; Hunt, K. J. *J. Chem. Soc., Chem. Commun.* **1974**, 989. Gheorghiu, M. D.; Drăghici, C.; Pârvulescu, L. *Tetrahedron* **1977**, *33*, 3295.

Biomimetic Total Synthesis of (±)-Methyl Homodaphniphyllate[1]

Roger B. Ruggeri and Clayton H. Heathcock*
Department of Chemistry, University of California, Berkeley, California 94720
Received March 19, 1990

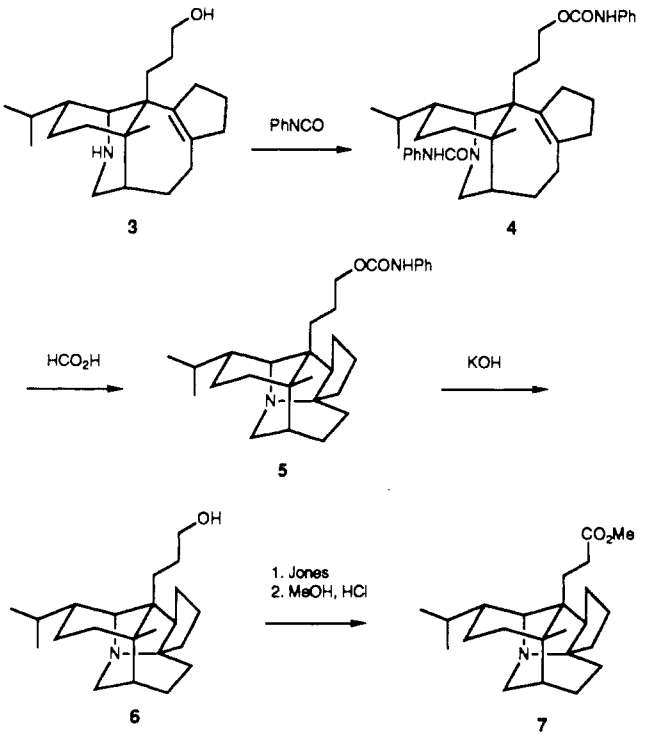
Summary: Bis-carbamoyl derivative **4**, prepared from the known amino alcohol **3** by reaction with phenyl isocyanate, is converted into carbamate **5** in refluxing formic acid. A similar process, involving carbamoyl phosphate as the carbamoylating agent, might operate in the biosynthesis of the daphniphylline skeleton.

It has been suggested that the daphniphylline skeleton **2** might arise by cyclization of an unsaturated amine **1**.[2] We have attempted to bring about this transformation in vitro by treatment of compounds of type **1** under various acidic conditions, without success. This failure to cyclize presumably results from preferential protonation of the amine under the attempted acidic conditions.



1 **2**

In contrast, the bis-carbamoyl derivative **4**, obtained by treatment of amino alcohol **3**[3] with phenyl isocyanate, cyclizes smoothly in refluxing formic acid to provide the carbamate **5**. Saponification of **5** affords alcohol **6** in 94% overall yield for the three-step conversion. Amino alcohol **6** is converted into (±)-methyl homodaphniphyllate (**7**) by Jones oxidation and Fischer esterification (73% yield). The conversion of **3** into **7** completes a 13-step stereocontrolled total synthesis of the alkaloid (13% overall yield) and completely solves our earlier problem in controlling the stereochemistry at the isopropyl-bearing carbon.[4]



The ease of cyclization of **4** raises the interesting question of whether a similar process might be involved in the actual biosynthetic formation of the daphniphylline

(1) Part 7 in a series of papers on the *Daphniphyllum* alkaloids. For part 6, see: Piettre, S.; Heathcock, C. H. *Science (Washington, D.C.)*, in press.
(2) (a) Niwa, H.; Toda, M.; Ishimaru, S.; Hirata, Y.; Yamamura, S. *Tetrahedron* **1974**, *30*, 3031. (b) Ruggeri, R. B.; Heathcock, C. H. *Pure Appl. Chem.* **1989**, *61*, 289.
(3) Ruggeri, R. B.; McClure, K. F.; Heathcock, C. H. *J. Am. Chem. Soc.* **1989**, *111*, 1530.
(4) Heathcock, C. H.; Davidsen, S. K.; Mills, S.; Sanner, M. A. *J. Am. Chem. Soc.* **1986**, *108*, 5650.

0022-3263/90/1955-3714$02.50/0

skeleton from 1. The biogenic carbamoylating agent could be carbamoyl phosphate.[5]

Acknowledgment. This work was supported by a grant from the National Science Foundation (CHE-84-18437) and by fellowships granted to R.B.R. by Smith, Kline, and French Research Laboratories (administered by the ACS Division of Organic Chemistry) and Pfizer, Inc. We thank Professor S. Yamamura for a sample of natural methyl homodaphniphyllate.

(5) (a) Jones, M. E. *Science (Washington, D.C.)* **1963**, *140*, 1373. For general discussions of carbamoyl phosphate, see: (b) Stryer, L. *Biochemistry*; Freeman: San Francisco, 1981; pp 411–414. (c) Brucie, T. C.; Benkovic, S. J. *Bioorganic Mechanisms, Vol II*; Benjamin: New York, 1966; pp 84–88.

Supplementary Material Available: Experimental procedure for the conversion of 3 into 7 and ^{1}H NMR spectra of synthetic and natural methyl homodaphniphyllate (4 pages). Ordering information is given on any current masthead page.

Enantioselective Synthesis of Tertiary α-Hydroxy Carbonyl Compounds Using ((8,8-Dichlorocamphoryl)sulfonyl)oxaziridine

Franklin A. Davis* and Michael C. Weismiller

Department of Chemistry, Drexel University, Philadelphia, Pennsylvania 19104

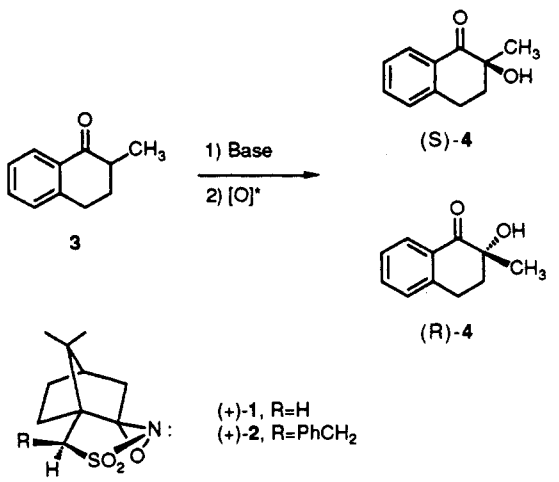
Received March 5, 1990

Summary: Very high stereoinduction, generally 90–95% ee, is observed for the asymmetric oxidation of 2-substituted-1-tetralone enolates to 2-hydroxy-2-substituted-1-tetralones by chiral nonracemic oxaziridine (+)-7. Not only are these α-hydroxy carbonyl compounds difficult to prepare enantiomerically pure via other methods, but they are also models for several biologically active compounds.

The development of highly enantioselective methods for the construction of tertiary α-hydroxy carbonyl compounds is of current interest because such compounds are common to many biologically active natural products. This is particularly true of the tetralin(tetralone) ring system where this structural unit is featured in the anthracycline antitumor antibiotics,[1] the phytoalexin lacinilene C,[2] the antitumor alkaloid campthothecin,[3] and the homoisoflavanone eucomol.[4]

Efforts in our laboratory have been directed toward developing methodology for the reagent controlled asymmetric oxidation of enolates to α-hydroxy carbonyl compounds using chiral nonracemic *N*-sulfonyloxaziridines such as 1 and 2.[5,6] These reagents afforded synthetically useful enantioselectivities, 60–95% ee, for the asymmetric oxidation of prochiral acyclic ketone,[6,7] ester,[8] amide,[8] and α-keto ester[9] enolates to the corresponding α-hydroxy carbonyl compounds. However, the stereoselectivity for the asymmetric oxidation of the tetrasubstituted enolate of 2-methyl-1-tetralone (3) to 2-hydroxy-2-methyl-1-tetralone (4), a model for the aforementioned tetralin ring system, is only 16–30% ee using (+)-1.[6,7]

Scheme I



Studies of the oxidation of ketone enolate anions by (+)-1 suggest that the enolate geometry, the enolate substitution pattern, and the enolate solution structure strongly influence the product stereochemistry.[6,10] To explain the chiral recognition a mechanism involving an S_N2 type substitution of the enolate on (+)-1 via an "open" transition controlled by nonbond steric interactions was formulated.[6] In cyclic systems control of enolate geometry is unimportant and options for improving reaction stereoselectivities by varying the enolate substitution pattern are limited. While there are greater opportunities for increasing the stereoinduction by altering counterion and solvent, i.e. the enolate solution structure, this approach also appears limited. For example, optimization of the reaction conditions resulted in only a modest improvement in the stereoinduction of 4 when the solvent was changed from THF to toluene, i.e. 30–60% ee, respectively.[6]

An approach that offers much greater flexibility and promise for improving enolate oxidation stereoselectivities

(1) Krohn, K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 790. Krohn, K. *Foretschr. Chem. Org. Naturst.* **1989**, *55*, 37.
(2) Stipanovic, R. D.; McCormick, J. P.; Schlemper, E. O.; Hamper, B. C.; Shinmyozu, T.; Pirkle, W. H. *J. Org. Chem.* **1986**, *51*, 2500.
(3) Schultz, A. G. *Chem. Rev.* **1973**, *73*, 385.
(4) Tamm, C. *Foretschr. Chem. Org. Naturst.* **1981**, *40*, 105.
(5) For a review on the chemistry of *N*-sulfonyloxaziridines, see: Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703.
(6) Davis, F. A.; Sheppard, A. C.; Chen, B. C.; Haque, M. S. *J. Am. Chem. Soc.* In press.
(7) (a) Davis, F. A.; Haque, M. S. *J. Org. Chem.* **1986**, *51*, 4083. (b) Davis, F. A.; Haque, M. S.; Prezeslawski, R. M. *J. Org. Chem.* **1989**, *54*, 2021.
(8) Davis, F. A.; Haque, M. S.; Ulatowski, T. G.; Towson, T. G. *J. Org. Chem.* **1986**, *51*, 4083.
(9) Chen, B. C.; Davis, F. A.; Boschelli, D.; Empfield, J. R.; Smith, A. B., III Submitted.
(10) Davis, F. A.; Weismiller, M. C.; Lal, G. S.; Chen, B. C.; Przeslawski, R. M. *Tetrahedron Lett.* **1989**, 1613.

0022-3263/90/1955-3715$02.50/0