wt, 315.1440. Found: C, 68.45; H, 6.88; N, 4.43; mol wt, 315.1467 (HRMS).

Continuation of the chromatography of the "liberated" alkaloids from *E. salviiflora* eluted a small amount of erysodine (**6**) and erysovine (**7**), mainly the former, then 0.44 g of a mixture of erysotine (**11**) and erysosalvine (**12**) which could not be resolved by chromatography on either silica gel or alumina columns. Extraction of the purified mixture (0.17 g) with boiling ether left 42 mg of an insoluble residue which, after two recrystallization from chloroform–ether, gave 18 mg of pure erysotine (**11**) as colorless crystals, mp 225–227°.

Anal. Calcd for $C_{18}H_{23}NO_4$: mol wt, 317.1628. Found: mol wt, 317.1630 (HRMS).

Erysosalvine (**12**) was not obtained pure, the best sample being contaminated with about 20% of erysotine as shown by gc. Its mass spectrum showed a molecular ion at *m/e* 317, and was identical with that of pure erysotine (Table II).

Reduction of Erysotinone with Sodium Borohydride.[6a] Erysotinone (**17**, 100 mg) was warmed at 65° with 150 mg of sodium borohydride in 3 ml of methanol until tlc indicated complete reaction after about 30 min. The solution was then diluted with 30 ml of water, heated to 100°, cooled, and extracted repeatedly with chloroform. The combined extracts were dried over magnesium sulfate, filtered, and evaporated to yield 65 mg of erysotine (**11**), presumably mixed with its C-2 epimer. No further purification could be achieved by chromatography on silica gel or alumina. Gas chromatography of the trimsyl derivative gave a single peak, coincident in retention time with ditrimsylerysotine [**11**-$(TMS)_2$].

Preparation of Dihydroerysodine (15). A. From Erysodine (6).[11] Erysodine (**6**, 60 mg) was hydrogenated for 2 hr over 25 mg of 5% palladium–barium sulfate catalyst in 12 ml of ethanol. The solution was filtered through Celite, solvent was removed, and the residue was chromatographed on silica gel, eluting with chloroform–methanol (98:2) to afford 40 mg (60%) of pure dihydroerysodine (**15**), mp 208–209° (lit.[6] 212°).

Anal. Calcd for $C_{18}H_{23}NO_3$: mol wt, 301.1678. Found: mol wt, 301.1692 (HRMS).

B. From Erysotinone (17). Erysotinone (**17**, 60 mg) was dissolved in 0.15 ml of ethanedithiol, and 0.1 ml of boron trifluoride etherate was added. After standing 14 hr at 20° the solution was diluted with ether and the resulting precipitate was washed with dry ether. The oily residue (45 mg) was homogeneous on tlc ($CHCl_3$–MeOH, 9:1): ir 1517 cm^{-1} (but no absorption at 1675 cm^{-1}); nmr (60 MHz) δ 6.73, 6.51 (s, 1, aromatic H), 6.11 (m, 1, H-1), 3.84 (s, 3, 15-OCH_3), 3.56 (s, 3, 3-OCH_3) ppm. Without further purification, the thioketal derivative was heated for 0.5 hr with 1.5 g of Raney nickel (W-2) in 10 ml of refluxing ethanol. The solution was then filtered through Celite, concentrated, and chromatographed on a silica gel preparative tlc plate to give 6 mg of dihydroerysodine (**15**), mp 204–206°, whose ir and mass spectra, tlc behavior ($CHCl_3$–MeOH:9:1), and gc retention time (as its trimsyl derivative) were identical with those of the authentic sample of dihydroerysodine (**15**) prepared in part A.

Conversion of Erysotine (11) and Erysosalvine (12) into Erythratidine (13). A mixture of erysotine (**11**) and erysosalvine (**12**) (4:1, 15 mg) was dissolved in methanol (0.1 ml) and excess ethereal diazomethane was added to the solution, which was allowed to stand until tlc indicated complete reaction. The product was recrystallized from ether to give erythratidine (**13**, 5 mg), with melting point, tlc behavior, and gc retention time (after trimsylation) identical with those of authentic erythratidine described above.

Identification of Erythrina Seeds. The seeds used in these studies were collected and identified by B. A. Krukoff, Consulting Botanist of Merck Research Laboratories and Honorary Curator of New York Botanical Garden. They are as follows: *Krukoff 1969–239* identified as *Erythrina folkersii* Krukoff and Moldenke; *Krukoff 1969–58*, as *E. salviiflora* Krukoff and Barneby; *Krukoff 1969–167* as *E. macrophylla* Alph. De Candolle; *Krukoff 1969–246* as *E. guatemalensis* Krukoff; *Krukoff 1967–3* as *E. berteroana* Urban; *Krukoff 1969–145* as *E. steyermarkii* Krukoff and Barneby; and *Krukoff 1969–104* (a not yet identified Erythrina species).

All samples of seeds are authentic, that is, backed by herbarium material deposited at the New York Botanical Garden and other herbaria of the world.

Acknowledgment. We thank Dr. N. G. Brink and Dr. D. E. Wolf of Merck and Co. for supplying us with *Erythrina* seeds. We also thank Dr. R. D. Johnson and Dr. R. T. Hargreaves for valuable advice and assistance. This work was supported in part by U. S. Public Health Service Grants AI 04769, from the National Institute of Allergy and Infectious Diseases, and CA 11388, from the National Cancer Institute.

Stereoselective Total Synthesis of (±)-Longipinenes

Masaaki Miyashita and Akira Yoshikoshi*

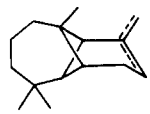
Contribution from the Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, Sendai 980, Japan. *Received September 11, 1973.*

Abstract: A total synthesis of racemic α- and β-longipinenes (**1a** and **1b**, respectively) is described. The key step is the photocyclization of a cyclodeca-1,5-diene derivative (**5b**) to a tricyclo[5.3.0.$0^{2,8}$]decane structure (**24**). The photocyclization product was converted to longipinenes *via* Tiffeneau–Demjanov ring expansion of an amino alcohol (**30a**) derived therefrom.

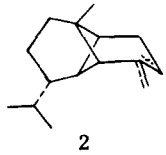
The (+)-α isomer of longipinene has been isolated from the wood of *Pinus silvestris*,[1] Swedish sulfate turpentine,[2] and *P. longifolia*,[3] and the structure **1a** has been assigned on the basis of spectral similarities with those of α-pinene and by chemical transformation, chiefly conversion into (+)-longibornyl chloride on the action of hydrogen chloride.[1,4] Recently, (−)-β-longipinene (enantiomer of **1b**),[5] along with (−)-α isomer,[5,6] has been found in liverwort (*Scapania undulata*).

Longipinenes, as well as copaenes **2**,[7] ylangenes **3**,[8] and bergamotenes **4**,[9] comprise a pinane moiety in the carbon framework as a conspicuous structural feature.

(1) L. Westrfelt, *Acta Chem. Scand.*, 17, 2351 (1963); 20, 2826 (1966).
(2) L. Westfelt, *Acta Chem. Scand.*, 20, 2841 (1966).
(3) S. Dev, personal communication.
(4) L. Westfelt, *Acta Chem. Scand.*, 21, 159 (1967).
(5) N. H. Andersen, personal communication.
(6) A. Matsuo, M. Nakagawa, S. Sato, R. Utosei, and S. Hayashi, Annual Meeting of the Chemical Society of Japan, Tokyo, Apr 1973.
(7) (a) (α-Copaene) P. de Mayo, R. E. Williams, G. Büchi, and S. H. Feairheller, *Tetrahedron*, 21, 619 (1965); V. H. Kapadia, B. A. Nagasampagi, V. G. Naik, and S. Dev, *ibid.*, 21, 607 (1965); (b) (β-copaene) L. Westfelt, *Acta Chem. Scand.*, 21, 152 (1967).
(8) (α-Ylangene) O. Motl, V. Herout, and F. Sorm, *Tetrahedron Lett.*, 451 (1965); (β-ylangene) see ref 7b.
(9) V. Herout, V. Ruzicka, M. Vrany, and F. Sorm, *Collect. Czech. Chem. Commun.*, **15**, 373 (1950). See also ref 10c.



(+)-1a (endo double bond)
(+)-1b (exo double bond)



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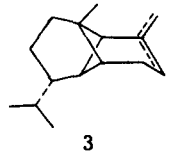
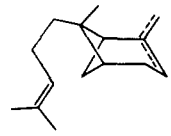


3

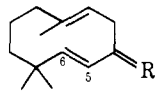


4

In the synthetic study of these sesquiterpenes, elaboration of the pinane skeleton is the most essential problem throughout the synthetic course.[10]

In this paper we report the stereoselective total synthesis of (±)-α- (**1a**) and (±)-β-longipinenes (**1b**) *via* the intramolecular photocyclization of methylenecyclodecadiene **5b**.[11] Our attention focused on the cross photocyclization of cyclic nonconjugated dienes and related compounds.[12] Only little has been known on the photocyclization of medium-size cyclic nonconjugated dienes,[13] while relatively abundant examples are available in the photocyclization of acyclic dienes.[14]

Previous works[13] demonstrate that the "Rule of Five," an empirical rule proposed to propensity for the photocyclization of acyclic nonconjugated dienes,[14a,b] does not necessarily show straightforward applicability to the medium-size cyclic 1,5-dienes in contrast with acyclic systems. Although there was no precedent that has reported the successful formation of cross photocyclization product from cyclodeca-1,5-dienes, we decided to examine photocyclization of trimethylcyclodecadienone (**5a**) and trimethylmethylenecyclodecadiene (**5b**) as the key step for the synthesis of longipinenes **1** in the hope that the desired cross cycloaddition might take place, because model inspections demonstrate possible transannular approach of the endo double bonds in these cyclodecadiene derivatives leading to the formation of stabilized 1,4-diradicals, such as **29**, on irradiation.



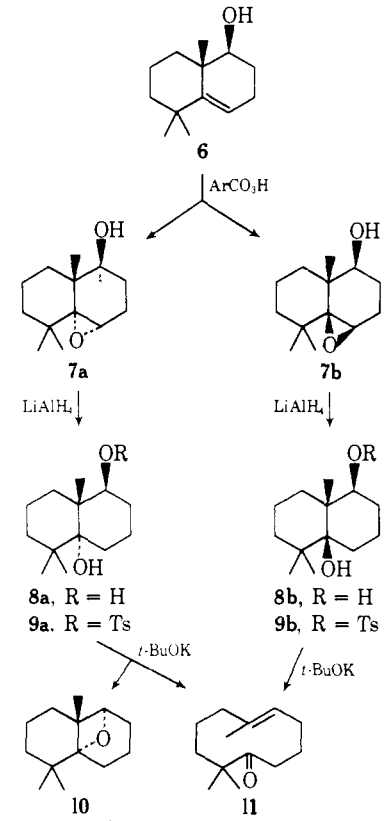
5a, R = O
5b, R = CH_2

Results

To obtain the ten-membered cyclic intermediates **5a** and **5b**, the preparation and base-induced fragmentation of 1,3-diol monosulfonate, such as **15b**, were attempted. This fragmentation has been frequently applied as a useful method for the synthesis of medium-size carbocycles.[15] According to Wharton and Hiegel,[15f] an antiperiplanar relationship between breaking carbon–carbon bond and carbon–leaving group bond is required for this synchronous fragmentation, as they clarified by the examination of the reaction of four isomeric decalin-1,4-diol tosylates and base. As a model, we prepared two isomeric diol monosulfonates, **9a** and **9b**, and subjected them to the fragmentation reaction.

Epoxidation of octalol **6**[16] with *m*-chloroperbenzoic acid in methylene chloride gave a mixture of trans and cis epoxides, **7a** and **7b**, in a ratio of 80:20, and the mixture was separated into the respective isomers (Scheme I). Assignment of the stereochemistry of

Scheme I



(10) Construction of the pinane structures has been achieved by intramolecular base-catalyzed cyclization of substituted ketones [(a) C. H. Heathcock, R. A. Badger, and J. W. Patterson, Jr., *J. Amer. Chem. Soc.*, **89**, 4133 (1967); (b) E. Wenkert, P. Bakuzis, R. J. Baumgarten, D. Doddrell, P. W. Jeffs, C. L. Leicht, R. A. Mueller, and A. Yoshikoshi, *ibid.*, **92**, 1617 (1970); (c) E. J. Corey and D. S. Watt, *ibid.*, **95**, 2303 (1973)] or by photochemical cyclization of an acyclic triene [(d) E. J. Corey, D. E. Cane, and L. Libit, *ibid.*, **93**, 7016 (1971)].

(11) For preliminary communications regarding part of this work, *cf.* M. Miyashita and A. Yoshikoshi, *Chem. Commun.*, 1091 (1971); *J. Chem. Soc., Chem. Commun.*, 1173 (1972).

(12) For a pertinent review regarding intramolecular photocyclizations of nonconjugated olefins, *cf.* W. L. Dilling, *Chem. Rev.*, **66**, 373 (1966).

(13) Successful photocyclization of medium-size cyclic nonconjugated dienes, to our knowledge, has been reported for 1,5-cyclooctadiene [R. Srinivasan, *J. Amer. Chem. Soc.*, **85**, 3048 (1963); **86**, 3318 (1964); J. Meinwald and B. E. Kaplan, *ibid.*, **89**, 2611 (1967)], isabelin [H. Yoshioka, J. T. Mabry, and A. Higo, *ibid.*, **92**, 923 (1970)], and 2-methylcyclodeca-1,6-dien-5-one [C. H. Heathcock and R. A. Badger, *J. Org. Chem.*, **37**, 234 (1972)]. Photolysis of (*E,Z*)-1,5-cyclodecadiene [J. G. Traynham and H. H. Hsieh, *Tetrahedron Lett.*, 3905 (1969)] and of germacrone [K. Takeda, I. Horibe, and H. Minato, *Chem. Commun.*, 87 (1971)] resulted merely in double bond isomerization.

(14) (a) R. Srinivasan and K. H. Carlough, *J. Amer. Chem. Soc.*, **89**, 4932 (1967); (b) R. S. Liu and G. S. Hammond, *ibid.*, **89**, 4932 (1967); (c) J. L. Charlton, P. de Mayo, and L. S. Skattobøl, *Tetrahedron Lett.*, 4679 (1965); (d) R. C. Cookson, *Pure Appl. Chem.*, **9**, 575 (1964); (e) J. R. Scheffer and R. A. Wostradowski, *Chem. Commun.*, 144 (1971); (f) F. T. Bond, H. L. Jones, and L. Scerbo, *Tetrahedron Lett.*, 4685 (1965); (g) J. Meinwald and R. A. Chapman, *J. Amer. Chem. Soc.*, **90**, 3218 (1968).

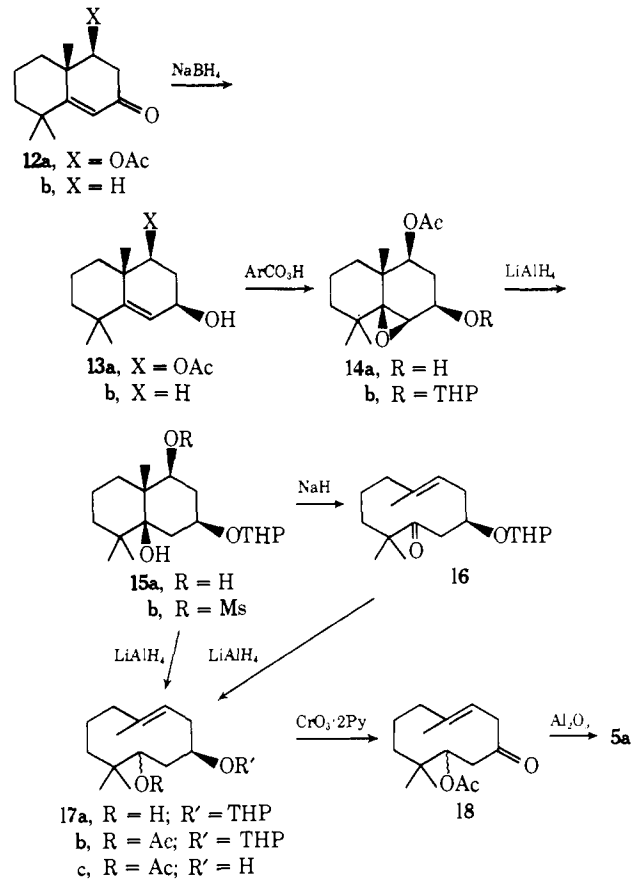
(15) For example, *cf.* (a) P. S. Wharton, *J. Org. Chem.*, **26**, 4781 (1961); (b) M. E. Kosower, W. D. Closson, H. L. Goering, and J. C. Cross, *J. Amer. Chem. Soc.*, **83**, 2013 (1961); (c) E. J. Corey, R. B. Mitra, and H. Uda, *ibid.*, **86**, 485 (1964); (d) H. H. Weston, *Helv. Chim. Acta*, **47**, 575 (1964); (e) M. Tanabe and D. F. Crowe, *Tetrahedron Lett.*, 2955 (1964); (f) P. S. Wharton and G. A. Hiegel, *J. Org. Chem.*, **30**, 3254 (1965); (g) J. A. Marshall and C. J. V. Scanio, *ibid.*, **30**, 3019 (1965); (h) R. Zerfluh, E. N. Wall, J. B. Siddall, and J. A. Edwards, *J. Amer. Chem. Soc.*, **90**, 6224 (1968).

(16) (a) J. D. Cocker and T. G. Halsall, *J. Chem. Soc.*, 3441 (1957); (b) F. Sondheimer and D. Elad., *J. Amer. Chem. Soc.*, **79**, 5542 (1957).

these epoxides is based on the following: (1) the major product must be formed by attack of the peracid on the less hindered face, (2) in the nmr spectra, the C(1) proton of the major epoxide shows a remarkably lower chemical shift than that of the minor epoxide, the results showing a magnetic deshielding due to the *cis*-oxirane ring, (3) as will be mentioned later, diol monotosylate **9a** derived from the major epoxide gives oxetane **10** as one of the products upon treatment with base. The epoxides, **7a** and **7b**, were treated with lithium aluminum hydride to yield crystalline diols, **8a** and **8b**, in high yields, respectively. Tosylate **9a** obtained from **8a**, on treatment with potassium *tert*-butoxide, gave a mixture of oxetane **10** and cyclodecenone **11** in a 63:37 ratio quantitatively. The *E* geometry of the newly created double bond of the latter is assigned on the basis of the known stereoselectivity of the fragmentation.[15] The formation of oxetane such as **10** has been rarely found in the base-induced fragmentation of bicyclic 1,3-diol monosulfonates, although some instances have been reported for steroids.[17] The base treatment of cis tosylate **9b** yielded only **11** quantitatively. In our synthesis a derivative of **11** having an extra oxygen function in an appropriate position, such as **16**, is required. The above model experiment indicates that a precursor adequate to the preparation of such a medium-size carbocycle is cis-fused decalindiol monosulfonate such as **15b**.

Acetoxyoctalone **12a** was prepared from the octalol **6** according to the known procedure.[18] The former was treated with sodium borohydride to give an epimeric mixture of acetoxyoctalols, from which **13a** was separated as crystals (79% yield) (Scheme II). The configurational assignment of the hydroxyl group of **13a** is based on that quasiequatorial alcohol **13b** is the major reduction product of **12b** and that a similar coupling pattern is observed in the nmr spectra of **13a** and reference alcohol **13b**.[19] Epoxidation of the acetoxyoctalol **13a** with *m*-chloroperbenzoic acid in a low concentration (0.13 *M*) in methylene chloride resulted in the predominant formation of cis epoxide **14a**. The use of the peracid in higher concentration decreased the cis to trans ratio, the results harmonizing with Henbest's findings which have been interpreted by an interaction between the hydroxyl group and peracid.[20] Hence the major epoxide isolated in 78% yield was assigned to the cis isomer **14a**. After the hydroxyl group of **14a** was protected as the THP ether, the resulting diastereomeric mixture of THP ethers **14b** was treated with lithium aluminum hydride giving diol **15a** in excellent overall yield from **14a**. Under standard conditions **15a** yielded methanesulfonate **15b** (80% yield) as a mixture of diastereomers. When **15b** was treated with sodium hydride in tetrahydrofuran, cyclodecenone **16** was produced as an unstable oil, which was immediately reduced with lithium aluminum hydride to give cyclodecanol **17a** in good overall yield. On the other hand, on treatment with lithium aluminum hydride in dimethoxyethane, **15b** gave directly **17a**

Scheme II



quantitatively.[21] After cyclodecenol **17a** was acetylated to **17b** on treatment with acetyl chloride in pyridine (74%), the ether linkage was cleaved by *p*-toluenesulfonic acid in wet methanol to give hydroxyacetate **17c** in quantitative yield. Oxidation of the latter with Collins' reagent[22] afforded crystalline acetoxycyclodecenone **18** (82% yield). Introduction of the second double bond into the cyclodecene ring was achieved in excellent yield by passing **18** through an activated alumina column leading to **5a**, which is sensitive toward heat and silica gel column chromatography. An *E* geometry is assignable to the conjugated double bond of the product from the nmr coupling constant (J = 18 Hz) of an AB-patterned olefinic proton signal. Triene **5b** was derived from **5a** by the reaction with methylenetriphenylphosphorane in ether (87% overall yield from **18**), and no isomerization of the $\Delta^{5,6}$-double bond was observed during the Wittig reaction as disclosed by nmr (Scheme III). The uv spectrum of **5b** tails remarkably toward the red manifesting a transannular interaction between the isolated and conjugated double bonds. Interestingly, the Wittig reaction of **5a** in dimethyl sulfoxide (Corey's modification)[23] resulted in the formation of a mixture of **5b** and cis-fused methyleneoctalin **19a** in variable ratios, and trans isomer **20a** has never been detected. The structure of **19a** was unambiguously assigned by the synthesis of the authentic cis and trans compounds, **19a** and **20a**, from cis and trans octalones,

(17) For a review, *cf.* D. N. Kirk ad M. P. Harthorn, "Steroid Reaction Mechanisms," Elsevier, Amsterdam, 1968, pp 272–277.

(18) P. Beak and B. M. Monroe, *J. Org. Chem.*, 32, 2778 (1967).

(19) W. G. Dauben and A. C. Ashcraft, *J. Amer. Chem. Soc.*, 85, 3673 (1963).

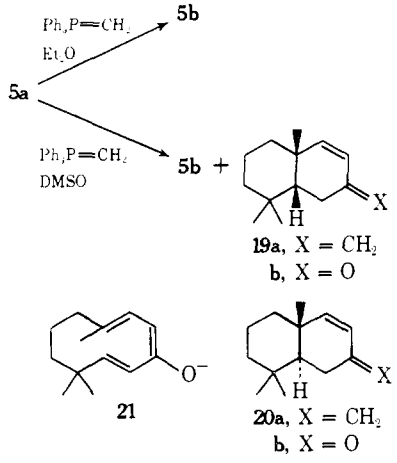
(20) H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 1958 (1957); H. B. Henbest, *Proc. Chem. Soc., London*, 159 (1963).

(21) This procedure was previously employed in the fragmentation reaction of a bicyclo[5.3.1]undecane derivative by Marshall and Scanio (ref 15g).

(22) J. C. Collins, *Tetrahedron Lett.*, 3363 (1968).

(23) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, 28, 1128 (1963).

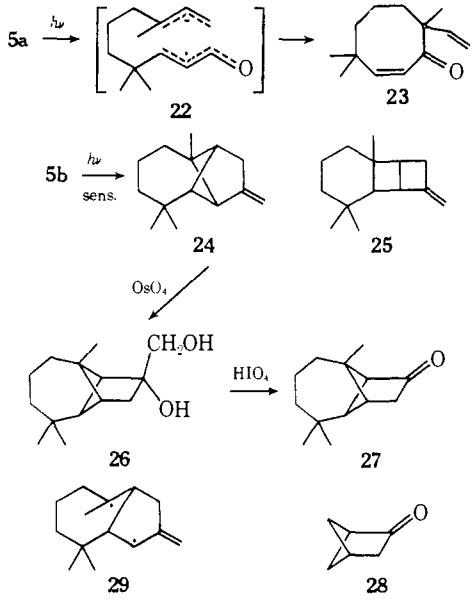
Scheme III



19b and **20b**,[24] *via* Wittig reaction, respectively. The stereoselective formation of **19a** may be rationalized in terms of thermal cyclization of cyclodecadienone enolate **21** to **19b**, followed by methylenation.

Photolysis of the cyclodecadienone **5a** was discouraging (Scheme IV). Irradiation of an ethereal

Scheme IV



solution of **5a** with a high-pressure mercury lamp was executed under various conditions (with or without a Pyrex or Vycor filter in the presence of cuprous chloride or sensitizers). Only a product was isolated on activated alumina column chromatography (13% yield), and the structure **23** was allowed to be assigned from its spectral characteristic. The absorption maximum (225 nm) of a low intensity in the uv spectrum of **23**, as well as the β-olefinic proton signal of the enone system shifted to unusually high magnetic field, would be indicative of lowered π-orbital overlapping in the conjugated enone grouping, which may be ascribable to steric distortion of the cyclooctenone ring by the crowded substituents. The formation of **23** would be interpreted in terms of cyclization of ketene diradical **22** formed by photofission of **5a** (Norrish type I) or of photochemical 1,3-acyl migration,[25,26] although we did not intend to elucidate the mechanism. On the other hand, an ethereal solution of **5b** was irradiated with a high-pressure mercury lamp through a Pyrex filter using β-acetonaphthone as the sensitizer, leading to a mixture of cross cycloadduct **24**, the starting triene **5b**, and an unidentified olefin in a ratio of 75:15:10. Since the spectra of the photoproduct **24** cannot differentiate between the structures **24** and **25**, the photoproduct was converted, *via* glycol **26**, to its nor ketone **27** by osmium tetroxide oxidation followed with periodic acid. The carbonyl absorption (1755 cm^{-1}) in the ir spectrum of **27** is in good agreement with that of bicyclo[2.1.1]hexanone **28**.[14f] This result demonstrates that the photocyclization proceeds almost unidirectionally to produce the cross adduct, probably by a nonconcerted path *via* stabilized diradical **29**. To test the multiplicity of this photoreaction, irradiation of the triene **5b** was carried out in the presence of piperylene or in the absence of the sensitizer. In the former case the formation of the photoproduct **24** was completely prevented, and the triene was left unchanged, while irradiation in the absence of β-acetonaphthone showed the greatly reduced formation rate of **24**. These results clearly demonstrate that the photocyclization must proceed *via* a triplet excited state. Photocyclization of **5b**, to our knowledge, is the first example of successful cross photocyclization in the cyclodeca-1,5-diene system.

The photoproduct **24** contains 14 carbon atoms available for the construction of the 2,6,6-trimethyltricyclo[5.4.0.0^{2,8}]undecane framework, if its five-membered ring containing an sp^2-hybridized carbon could be expanded to a six-membered ring by some way. Many attempts of the ring enlargement of **24**,[27] for example, lead tetraacetate oxidation,[28] solvolytic rearrangement of a monotosylate of **26**, etc., were unsuccessful. Then we turned to the nor ketone **27** to employ as the intermediate. The ketone **27** hardly reacted with diazomethane to give ring expanded product even under influence of boron trifluoride etherate,[29] while the reaction catalyzed with anhydrous aluminum chloride gave a complex mixture.[29b,c,30] Tiffeneau–Demjanov rearrangement has been known as an efficient ring enlargement method *via* ketones.[31]

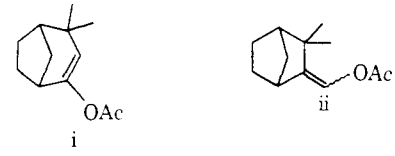
(24) M. Miyashita, H. Uda, and A. Yoshikoshi, *Chem. Commun.*, 1396 (1969).

(25) For example, see D. I. Schuster, G. R. Underwood, and T. P. Knudsen, *J. Amer. Chem. Soc.*, 93, 4307 (1971).

(26) We thank Professor T. Mukai for his helpful discussion of this photochemical reaction.

(27) For a review, *cf.* D. C. Gutsche and D. Redmore, "Carbocyclic Ring Expansion Reactions," Academic Press, New York, N. Y., pp 101–103.

(28) With this reagent, camphene gives enol acetate (i) accompanied by ii: J. Wolinsky, *J. Org. Chem.*, 26, 704 (1961), and references cited therein.



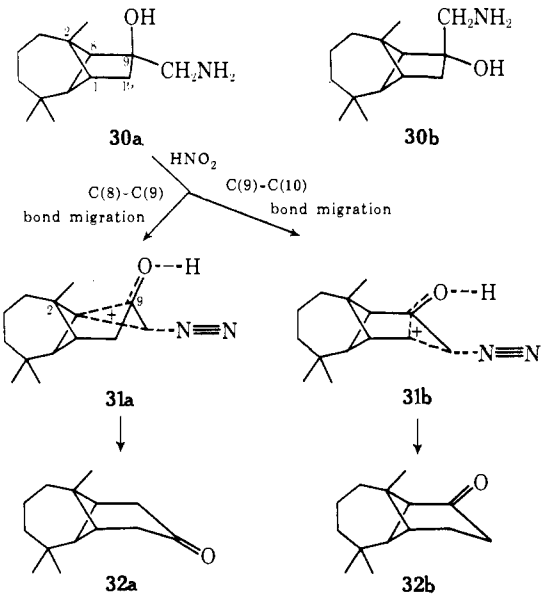
(29) (a) H. O. House, E. J. Grubbs, and W. F. Gannon, *J. Amer. Chem. Soc.*, 82, 4099 (1960); (b) E. Müller, M. Bauer, and W. Rundel, *Tetrahedron Lett.*, No. 13, 30 (1960); (c) E. Müller, M. Bauer, and W. Rundel, *Z. Naturforsch. B*, 15, 268 (1960); (d) W. S. Johnson, M. Neeman, S. P. Birkeland, and N. A. Fedoruk, *J. Amer. Chem. Soc.*, 84, 989 (1962).

(30) E. Müller, M. Bauer, and W. Rundel, *Tetrahedron Lett.*, 136 (1961).

(31) For a review, *cf.* P. A. S. Smith and D. R. Baer, *Org. React.*, 11, 157 (1960).

Prior to the description of experimental results, we will discuss stereoelectronic aspects in Tiffeneau–Demjanov rearrangement of amino alcohols **30a** and **30b**, which would be accessible from the nor ketone **27** (Scheme V).

Scheme V



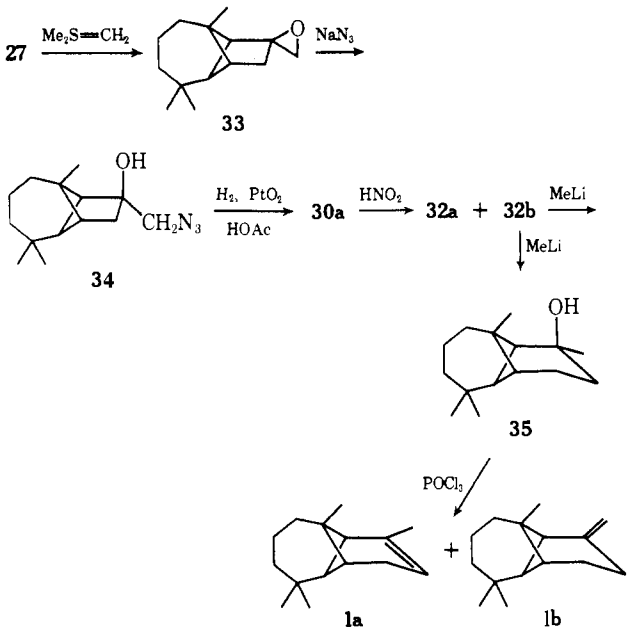
Deaminative rearrangement of these amino alcohols may proceed to give two isomeric ketones, **32a** and **32b**, *via* the distinct transition states **31a** and **31b**, respectively. Although migration of the more highly substituted C(8)–C(9) bond is electronically favorable than that of the less substituted C(9)–C(10) bond, in the transition state **31a**, so produced, a severe nonbonded interaction may be anticipated between the C(2)–methyl and the C(9) position. Migration of the C(9)–C(10) bond, meanwhile, leads to the sterically more stable transition state **31b**. Assuming the steric control is dominant over the electronic control, the ketone **32b**, which is more favorable than **32a** to attain to longipinenes in shorter course, would be obtained as the major product. A similar argument may be also given to the amino alcohol **30b** and leads us to anticipate the predominant formation of **32a**. We thus endeavored to obtain the amino alcohol **30a**.

Recently Kirk and Wilson have reported a useful method for the preparation of amino alcohols from ketones *via* epoxide, hydroxy azide, and hydroxy amine stages.[32] A single epoxide **33**, whose stereochemistry was given on the basis of the presumable stereoselective attack of the reagent caused by the C(2)–methyl group, was obtained from the ketone **27** by the reaction with dimethylsulfonium methylide[33] (Scheme VI). The epoxide **33** was treated with sodium azide in boiling dimethylformamide containing boric acid as catalyst giving hydroxy azide **34** (85% yield from **27**). Although chromous chloride reduction of **34**, the procedure recommended by Kirk and Wilson,[32] was fruitless under various conditions, catalytic hydrogenation of **34** over platinum oxide in acetic acid gave a solution of the amino alcohol **30a**, which was immediately treated with aqueous sodium nitrite to afford a mixture of the

(32) D. N. Kirk and M. A. Wilson, *Chem. Commun.*, 64 (1970).

(33) E. J. Corey and M. Chaykovsky, *J. Amer. Chem Soc.*, 87, 1353 (1965).

Scheme VI



ketones **32a** and **32b** in a ratio of 6:90 (quantitative yield from **34**). The structure assignment to these ketones was made with spectral data and deuterium incorporation upon treatment with methyl deuterioxide under basic conditions. The predominant formation of **32b** obviously demonstrates the overwhelming steric control in the rearrangement of **30a**. The reaction of **32b** and methyllithium produced a homogeneous carbinol, longipinanol **35** (80% yield), whose stereoformula was given as depicted taking into consideration a steric control due to the C(2)–methyl of **32b**. Dehydration of **35** with phosphorus oxychloride in pyridine gave an olefin mixture, from which (±)-α- (**1a**) (48%) and (±)-β-longipinenes (**1b**) (36%) were separated by preparative glc or tlc (silver nitrate impregnated silica gel), and these were identified spectroscopically.[34] The accomplishment of this synthesis fully corroborates the proposed structures of natural longipinenes.

Experimental Section

All melting points and boiling points are uncorrected. Ir spectra were taken on a Hitachi EPI-S2 or a G-2 spectrometer. Nmr spectra were obtained on a JEOL Model C-60HL or PS-100 instrument using TMS as an internal standard and CCl_4 as the solvent unless otherwise indicated. Reported values are on the δ scale. Uv spectra were taken on a Cary Model 14 spectrometer. Mass spectra were recorded on a Hitachi RMU-6D, and high-resolution mass spectra were obtained on a JEOL JMS-OISC spectrometer. Glpc analyses were performed on a JEOL Model JGC-750 instrument using the following columns: A (20% PEG, 2 m × 3 mm) and B (10% SE-30, 2m × 3 mm). Elemental analyses were performed in the microanalytical laboratory of this institute.

2,3,4,4a,5,6,7,8-Octahydro-4aβ,8,8-trimethyl-4β-naphthol (6). This alcohol was prepared from Wieland–Miescher ketone[35] according to Cocker and Halsall's procedure,[16a] which was somewhat modified to obtain a better overall yield. Wieland–Miescher ketone was treated, according to Heathcock, *et al.*,[10a] with sodium borohydride in dry ethanol to give 4,4a,5,6,7,8-hexahydro-5β-hydroxy-4aβ-methyl-2(3*H*)-naphthalenone (**36**) in almost quantitative yield.

(34) We thank Dr. S. Dev (National Chemical Laboratory, India) for his generous gift of a sample of the authentic (+)-α-longipinene and are indebted to Dr. N. H Andersen (University of Washington) for the identification of β-longipinene.

(35) P. Wieland and K. Miescher, *Helv. Chim. Acta*, **33**, 2215 (1950); R. Ramachandran and M. S. Newman, *Org. Syn.*, **41**, 38 (1961).

The product was used, without further purification, in the next step.

Phosphorus oxychloride (7 ml) was added dropwise to a stirred solution of **36** (120 g, 0.67 mol) and dihydropyran (168 g, 2.01 mol) in dry methylene chloride (3 l.) in an ice–salt bath. After stirring for an additional 1.5 hr at −3–0°, the mixture was washed with aqueous sodium carbonate and brine. Evaporation of the solvent and excess dihydropyran gave tetrahydropyranyl ether (**37**) (177 g) as a viscous oil. An aliquot of the product was purified by preparative tlc using petroleum ether as eluent to give the diastereomers as crystals (mp 61–67°), which were recrystallized from petroleum ether to give a pure specimen as prisms, mp 63–69° (lit.[16a] mp 68–74°).[36]

A solution of the diastereomeric mixture of **37** (177 g, 0.67 mol) in dry *tert*-butyl alcohol (1 l.) was added, in an ice bath, to a stirred solution of potassium *tert*-butoxide (0.87 *M*, 3 l., 2.61 mol) at such a rate that the solvent just began to crystallize. This process was slightly exothermic. After the mixture was stirred for a further 10 min, methyl iodide (370 g, 2.61 mol) was added. Stirring was continued for 0.5 hr, and the temperature was then allowed to rise to room temperature. After the mixture was stirred at room temperature for 3.5 hr, 10% hydrochloric acid (1050 ml) was added to quench the reaction, and the mixture was stirred at room temperature for 12 hr to hydrolyze the THP protective group. The solvent was evaporated *in vacuo* on a steam bath, and the residue was poured into cold water. The product was extracted three times with ether (600 ml each). The combined extracts were successively washed with water, aqueous sodium carbonate, aqueous sodium hyposulfite, water, and brine, and dried ($MgSO_4$). Evaporation of the solvent left an oil (170 g), which was distilled *in vacuo* (bp 143° (0.4 mm) to give a yellow oil. The oil crystallized on standing. Recrystallization from petroleum ether–ethyl acetate (1:1) gave 3,4,4a,5,6,7-hexahydro-5β-hydroxy-1,1,4aβ-trimethyl-2(1*H*)-naphthalenone (**38**) (64 g, 46% from **36**) as prisms, mp 89.5–90.5° (lit.[16a] mp 92–94°).[36]

A mixture of **38** (56 g, 0.27 mol), 100% hydrazine hydrate (237 ml), and hydrazine hydrochloride (2 g) in diethylene glycol (3 l.) was heated at 100–110° for 2.5 hr. Potassium hydroxide (54 g) was added, and the mixture was heated to 210° to distill off water formed. Heating was continued for a further 6 hr. The mixture was then diluted with water (10 l.), and the precipitate was collected by filtration. The precipitate was recrystallized from aqueous methanol giving **6** (39.2 g, 75%) as needles, mp 121–122° (lit. mp 122–122.5°,[16a] 122–123°[16b]).

Decahydro-4α,4aα-epoxy-5,5,8aβ-trimethyl-1β-naphthol (7a) and Decahydro-4β,4aβ-epoxy-5,5,8aβ-trimethyl-1β-naphthol (7b). To a stirred solution of **6** (3.0 g, 154 mmol) in dry methylene chloride (90 ml) was added dropwise a solution of commercial *m*-chloroperbenzoic acid (3.67 g, *ca.* 180 mmol) in dry methylene chloride (30 ml) in an ice bath. After stirring for an additional hour at the same temperature, the mixture was kept at 5° for 6 hr until no **6** could be detected in tlc or glpc. The solution was washed with aqueous sodium bicarbonate, water, and brine, and dried ($MgSO_4$). Evaporation of the solvent gave a crystalline mixture of **7a** and **7b** (3.23 g, 100%). Glpc analysis (column A at 200°) showed two peaks in a ratio of 80:20. Recrystallization of the mixture from petroleum ether gave crystalline **7a** (2.09 g, 65%), mp 97–98°, which corresponded to the main peak in glpc: ir (KBr) 3275 and 914 cm^{-1}; nmr 0.62, 1.05, and 1.13 (s, 3 H each), 2.94 (t, 1 H, J = 1.5 Hz, epoxy H), and 3.79 (q, 1 H, J = 7.5 Hz, C*H*OH).[36]

The oily **7b** (290 mg, 9%) was separated from the recrystallization filtrate by preparative tlc using chloroform as eluent: ir (film) 3450 and 915 cm^{-1}; nmr 0.75, 1.02, and 1.19 (s, 3 H each), 3.00 (br, t, 1 H, J = 4.5 Hz, epoxy H), and 3.20 (q, 1 H, J = 1.5 Hz, C*H*OH). An analytical sample was obtained by distillation (bath temperature, 80°) *in vacuo* (0.2 mm).[36]

Decahydro-5,5,8aβ-trimethyl-1β,4aα-naphthalenediol (8a). A solution of **7a** (2.09 g, 10 mmol) in dry tetrahydrofuran (20 ml) was added dropwise to a stirred solution of lithium aluminum hydride (767 mg, 20 mmol) in dry tetrahydrofuran (40 ml) over 0.5 hr at room temperature. The mixture was then refluxed for 6 hr, and the excess reagent was destroyed by adding wet ether followed by water in an ice bath. After usual work-up, removal of the solvent left crystals, which were recrystallized from methanol to give **8a** (1.74 g, 82%) as colorless needles: mp 109–110°; ir (KBr) 3450 cm^{-1}; nmr ($CDCl_3$) 0.90 (s, 3 H), 1.05 (s, 6 H), and 3.80–4.20 (m, 1 H, C*H*OH).[36]

(36) Satisfactory combustion analysis has been obtained for this compound.

Decahydro-5,5,8aβ-trimethyl-1β,4aβ-naphthalenediol (8b). A solution of **7b** (126 mg, 0.6 mmol) and lithium aluminum hydride (90 mg, 2.4 mmol) in dry ether (20 ml) was refluxed for 14 hr. After similar treatment as described for **8a**, an oil (128 mg) was given upon removal of the solvent. The oil was purified by preparative tlc using chloroform–ether (7:5) as eluent to give crystalline **8b** (88 mg, 70%): ir (KBr) 3300 cm^{-1}; nmr ($CDCl_3$) 0.85, 1.10, and 1.26 (s, 3 H each), and 3.32 (br s, 1 H, C*H*OH). An analytical sample, mp 99.5–100°, was obtained by recrystallization from *n*-hexane.

Decahydro-5,5,8,8aβ-trimethyl-1β,4aα-naphthalenediol *p*-Toluenesulfonate (9a). A solution of **8a** (140 mg, 0.66 mmol) and *p*-toluenesulfonyl chloride (252 mg, 1.32 mmol) in dry pyridine (2 ml) was allowed to stand overnight at room temperature. The mixture was poured into ice–water, and the product was thoroughly extracted with ether. The extracts were washed with dilute hydrochloric acid, water, and brine. After the extracts were dried over magnesium sulfate, evaporation of the solvent afforded crystals, which were recrystallized from ether–petroleum ether to give **9a** (233 mg, 97%) as colorless needles: mp 100–101° dec; ir (KBr) 3520, 1600, 1320, 1179, and 900 cm^{-1}; nmr ($CDCl_3$) 0.86, 1.00, and 1.09 (s, 3 H each), 2.47 (s, 3 H, aromatic Me), and 4.80–5.20 (m, 1 H, C*H*OTs).[36]

Decahydro-5,5,8aβ-trimethyl-1β,4aβ-naphthalenediol *p*-Toluenesulfonate (9b). A solution of **8b** (40 mg, 0.19 mmol) and *p*-toluenesulfonyl chloride (100 mg, 0.52 mmol) in dry pyridine (1 ml) was allowed to stand at room temperature for 24 hr in the dark. The reaction mixture was poured into cold water and extracted three times with ether. The extracts were washed with water, aqueous cupric sulfate, and brine, and dried ($MgSO_4$). Evaporation of the solvent gave an oil (50 mg). Since the crude product still contained a considerable amount of unreacted **8b**, it was redissolved in dry pyridine (1 ml), and *p*-toluenesulfonyl chloride (100 mg) was added. After the mixture was allowed to stand at room temperature for 3 days, more *p*-toluenesulfonyl chloride (100 mg) was added. The solution was kept at the same temperature for an additional 20 hr. Work-up as mentioned above gave crystals (51 mg), which were recrystallized from ether–petroleum ether to afford pure **9b** (42 mg): mp 87–88°; ir (KBr) 3600, 1600, 1350, 1175, 900, and 877 cm^{-1}; nmr 0.85, 1.00, and 1.03 (s, 3 H each), 2.47 (s, 3 H, aromatic Me), 4.35 (br s, 1 H, C*H*OTs), and 7.25–7.90 (q of an AB type, 4 H, aromatic H).[36] This tosylate is unsuitable on standing or on chromatographic purification.

Solvolysis of Tosylate 9a to 2,6,6-Trimethyl-11-oxatricyclo-[5.3.1.$0^{2,7}$]undecane (10) and 2,6,6-Trimethyl-(*E*)-1-cyclodecen-7-one (11). A solution of potassium *tert*-butoxide (609 mg, 5.44 mmol) in dry *tert*-butyl alcohol (10 ml) was added dropwise to a stirred solution of **9a** (500 mg, 1.37 mmol) in dry *tert*-butyl alcohol (3 ml) at room temperature under nitrogen. The mixture was further stirred for an additional 3 hr at 60° and then poured into water. The product was extracted with ether, and the extracts were washed with water and brine, and dried ($MgSO_4$). Removal of the solvent left an oil (267 mg), which showed two peaks in a ratio of 37:63 in glpc (column A at 180°). These products were separated by preparative tlc using chloroform as eluent. The less polar product was **11**: ir (film) 1697 cm^{-1}; nmr 1.01 (s, 6 H), 1.58 (d, 3 H, J = 1.5 Hz, olefinic Me), and 4.90 (unresolved br t, 1 H, olefinic H).[36]

The polar product was **10**: ir (film) 998, 990, and 908 cm^{-1}; nmr 1.17, 1.31, and 1.51 (s, 3 H each), and 3.76 (m, 1 H, CH–O).[36]

Solvolysis of Tosylate (9b) to Cyclodecenone (11). A solution of **9b** (20 mg, 0.06 mmol) and potassium *tert*-butoxide (25 mg, 0.22 mmol) in dry *tert*-butyl alcohol (1.5 ml) was stirred at room temperature under nitrogen and was then heated at 60° for 1 hr. The mixture was poured into cold water and extracted with ether. The extracts were washed with water and brine, and dried ($MgSO_4$). Removal of the solvent gave an oil (10 mg). Glpc (column A at 180°) of the product showed a single peak, and its spectra were in good agreement with those of **11**.

2,3,4,4a,5,6,7,8-Octahydro-4aβ-acetoxy-4aβ,8,8-trimethyl-2β-naphthol (13a). Sodium borohydride (2.16 g, 57 mmol) was added to a stirred solution of acetoxyoctalone (**12a**)[18] (14.34 g, 57 mmol) in methanol (300 ml) in an ice bath. The mixture was stirred for 30 min with cooling and then for 4.5 hr at room temperature. Acetic acid (4.4 ml) was added, and the mixture was concentrated to half the volume at 60°. The residue was diluted with water and extracted with ether. The extracts were washed with water and brine, and dried ($MgSO_4$). Evaporation of the solvent gave a colorless oily residue. Petroleum ether was added, and the residue was scratched to induce crystallization at an ice–salt temperature. A crystalline mass (11.32 g, 79%) thus obtained was washed three

times with cold petroleum ether. This was sufficiently pure to be used in the next step: ir (KBr) 3430, 1713, and 1635 cm^{-1}; nmr 1.11, 1.17, and 1.25 (s, 3 H each), 2.02 (s, 3 H, Ac), 4.35 (br t, C*H*OH), 4.60 (q, 1 H, J = 2.7 and 12 Hz, C*H*OAc), and 5.49 (d, 1 H, J = 2 Hz, olefinic H). An analytical sample, mp 75–76°, was obtained by recrystallization from petroleum ether.[36]

Decahydro-4β-acetoxy-1β,8aβ-epoxy-4aβ,8,8-trimethyl-2β-naphthol (14a). A solution of *m*-chloroperbenzoic acid (18.20 g, 85% in purity, 89.6 mmol) in dry methylene chloride (340 ml) was added dropwise to a solution of **13a** (17.6 g, 70 mmol) in dry methylene chloride (500 ml) over 1.5 hr in an ice bath. The mixture was stirred for an additional 0.5 hr at the same temperature and was then kept at 3° for 18 hr. After the solution was washed with 1% aqueous sodium hydroxide, water, and brine, and dried ($MgSO_4$), removal of the solvent gave a crystalline residue, which showed two peaks in a ratio of 88:12 in glpc (column A at 230°). Recrystallization of the residue from methanol gave **14a** (14.50 g, 78%): mp 173–177°; ir (KBr) 3415, 1716, 1269, 920, 906, and 892 cm^{-1}; nmr ($CDCl_3$) 0.90, 0.96, and 1.17 (s, 3 H each), 3.40 (d, 1 H, J = 2.3 Hz, epoxy H), 4.15 (br m, 1 H, C*H*OH), and 4.43 (q, 1 H, J = 9.8 and 5.3 Hz, C*H*OAc).[36]

Decahydro-4β-acetoxy-1β,8aβ-epoxy-4aβ,8,8-trimethyl-2β-naphthol Tetrahydropyranyl Ether (14b). A solution of **14a** (8.15 g, 30.4 mmol), dihydropyran (7.66 g, 91.2 mmol), and phosphorus oxychloride (0.5 ml) in methylene chloride (320 ml) was stirred for 3.5 hr in an ice bath. The solution was washed with 10% aqueous sodium carbonate, water, and brine. Evaporation of the solvent left a diastereomeric mixture of **14b** (11.0 g, 100%) as an oil, which was sufficiently pure to be used in the next step. An aliquot of the product gave one of the diastereomers as crystals (mp 75–78°) on silica gel column chromatography using a mixture of ether and petroleum ether (1:1) as eluent. An analytical sample (mp 81–82°) was obtained by recrystallization from petroleum ether in a Dry Ice–methanol bath: ir (KBr) 3030, 1727, 1245, and 1020 cm^{-1}; nmr 0.89, 1.07, and 1.24 (s, 3 H each), 2.00 (s, 3 H, Ac), 3.25 (d, 1 H, J = 2.5 Hz, epoxy H), and 4.80 (br s, 1 H, O–CH–O).[36]

Decahydro-4aβ,8,8-trimethyl-2β,4β,8aβ-naphthalenetriol Tetrahydropyranyl Ether (15a). A solution of **14b** (10.6 g, 30 mmol) in dry tetrahydrofuran (300 ml) was added dropwise to a stirred solution of lithium aluminum hydride (4.60 g, 121 mmol) in the same solvent (300 ml) over 0.5 hr at room temperature. The mixture was then refluxed for 7 hr, and the excess reagent was quenched by adding wet ether (500 ml) and then 1% aqueous sodium hydroxide in an ice bath. Removal of the solvent left **15a** (9.5 g, 98%) as a viscous oil. The product was sufficiently pure to be used in the next step. An analytical sample was obtained by distillation (bath temperature, 135°) *in vacuo* (10^{-3} mm): ir (film) 3450 cm^{-1}; nmr 0.88, 1.07, and 1.25 (s, 3 H each), 2.50–4.30 (unresolved m, 6 H), and 4.69 (unresolved t, 1 H, O–CH–O).

Decahydro-4β-methylsulfonyloxy-4aβ,8,8-trimethyl-2β,8aβ-naphthalenediol Tetrahydropyranyl Ether (15b). After methanesulfonyl chloride (7.0 g, 61.0 mmol) was added to a solution of **15a** (9.5 g, 30 mmol) in pyridine (280 ml) in an ice bath, the resulting solution was stirred for 3 hr at the same temperature and then allowed to stand for 13 hr at room temperature. The mixture was poured into ice–water (1.5 l.) and stirred for 1 hr. The precipitate was filtered and dissolved in ether (700 ml). The ethereal solution was washed with brine and dried ($MgSO_4$). Evaporation of the solvent gave colorless crystals (8.10 g). The filtrate was extracted twice with ether, and the combined extracts were washed with aqueous cupric sulfate solution and brine. Removal of the solvent left a yellow oil (4.0 g), which was then chromatographed on neutral alumina (Woelm, activity III). Petroleum ether and petroleum ether–ether (9:1–1:2) eluted crystals (1.20 g). The combined crystals weighed 9.30 g (80%). Tlc of the crystals showed closely neighboring two spots indicative of a mixture of diastereomers regarding the tetrahydropyranyl ether moiety. One of the diastereomers, mp 105.5–106.5° dec, was obtained by recrystallization from ether: ir (KBr) 3520, 1312, 1176, and 900 cm^{-1}; nmr 1.00, 1.10, and 1.29 (s, 3 H each), 3.03 (s, 3 H, Ms), 4.56 (unresolved t, 1 H, O–CH–O), and 4.87 (br s, 1 H, C*H*OMs).[36]

9-Oxo-4,8,8-trimethyl-(*E*)-3-cyclodecen-1-ol Tetrahydropyranyl Ether (16). A solution of **15b** (a mixture of the diastereomeric isomers) (225 mg, 0.57 mmol) in dry tetrahydrofuran (5 ml) was added to a suspension of sodium hydride (56 mg, 1.17 mmol) in the same solvent (5 ml), and the mixture was stirred for 15 hr at room temperature under nitrogen. The reaction mixture was poured into cold dilute sodium hydroxide solution and extracted with ether. The extracts were washed with water and brine. Removal of the solvent afforded an oil (205 mg), which was chromatographed on neutral alumina (10 g, Woelm, activity III). Elution with petroleum ether gave **16** (140 mg, 83%) as an oil: ir (film) 1695 cm^{-1}; nmr 0.92 and 1.12 (s, 3 H each), 1.60 (br s, olefinic Me overlapped with methylene protons), and 4.95 (br t, 1 H, olefinic H). Since this compound is unstable on standing and toward heat, no analytically pure sample could be prepared.

9-Hydroxy-4,8,8-trimethyl-(*E*)-3-cyclodecen-1-ol Tetrahydropyranyl Ether (17a). Fragmentation of 15b by Lithium Aluminum Hydride. A solution of lithium aluminum hydride (2.28 g, 60 mmol) in dry dimethoxyethane (120 ml) was added dropwise to a stirred solution of **15b** (7.80 g, 20 mmol) in the same solvent (180 ml) in an ice bath under nitrogen. The mixture was allowed to warm to room temperature, and stirring was continued for 17 hr. The mixture was cooled in an ice bath again, and the excess reagent was decomposed with 10% aqueous sodium hydroxide. A usual work-up gave **17a** (6.0 g, 100%) as a colorless oil: ir (film) 3560 cm^{-1}; nmr 0.70 and 0.88 (s, 3 H, each), 1.70 (br s, 3 H, olefinic Me), and 5.15 (br t, 1 H, J = 9 Hz). The product was sufficiently pure to be used in the next step. An analytical sample was obtained by distillation (bath temperature, 120°) *in vacuo* (0.15 mm).[36]

Reduction of 16. A solution of **16** (140 mg, 0.48 mmol) in dry dimethoxyethane (3 ml) was added dropwise to a stirred solution of lithium aluminum hydride (38 mg, 1.0 mmol) in the same solvent (4 ml) in an ice bath. The mixture was allowed to warm to room temperature and stirred for 17 hr. The reaction mixture was cooled in an ice bath again, and water was added. A usual work-up gave **17a** (140 mg), which was identified by ir.

9-Acetoxy-4,8,8-trimethyl-(*E*)-3-cyclodecen-1-ol Tetrahydropyranyl Ether (17b). Acetyl chloride (1.5 ml) was added to a stirred solution of **17a** (400 mg, 1.4 mmol) in dry pyridine (16 ml) in an ice bath. After stirring for 30 min in the cold and then for an additional 3.5 hr at room temperature, the mixture was poured into ice water and extracted thoroughly with ether. The combined extracts were washed with water, aqueous cupric sulfate, and brine, and dried ($MgSO_4$). Removal of the solvent left an oil, which was chromatographed on silica gel (30 g). Elution with petroleum ether and petroleum ether–ether (9:1–2:1) afforded oily **17b** (348 mg, 74%): ir (film) 1736 and 1250 cm^{-1}; nmr 0.75 and 0.79 (s, 3 H each), 1.82 (br s, 3 H, olefinic Me), 1.91 (s, 3 H, Ac), and 5.02 (q, 1 H, J = 6 and 2.3 Hz, olefinic H). An analytical sample was obtained by distillation (bath temperature, 120°) *in vacuo* (0.17 mm).[36]

9-Acetoxy-4,8,8-trimethyl-(*E*)-3-cyclodecen-1-ol (17c). A solution of **17b** (2.0 g, 5.9 mmol) and *p*-toluenesulfonic acid (230 mg) in wet methanol (100 ml) was stirred for 2 hr at room temperature. The mixture was poured into cold aqueous sodium carbonate and extracted with ether. The extracts were washed with water and brine, and dried ($MgSO_4$). Removal of the solvent left oily **17c** (1.50 g, 100%), which was homogeneous as demonstrated by nmr and tlc. An analytical sample was obtained by distillation (bath temperature, 120°) *in vacuo* (0.15 mm). The distillate solidified by scratching and was recrystallized from petroleum ether: mp 66.5–67.5°; ir (KBr) 3500, 1705, and 1250 cm^{-1}; nmr 0.76 and 0.80 (s, 3 H each), 1.81 (br s, 3 H, olefinic Me), 2.00 (s, 3 H, Ac), and 4.60–5.40 (m, 2 H, C*H*–O).[36]

9-Acetoxy-4,8,8-trimethyl-(*E*)-3-cyclodecen-1-one (18). A mixture of **17c** (3.7 g, 14.5 mmol), chromic anhydride–dipyridine complex[22] (20 g, 77.7 mmol), and dry methylene chloride (350 ml) was stirred for 15 min at room temperature and then passed through a column of silica gel (50 g) by the aid of ether. Removal of the solvent gave an oil, which solidified by scratching in an ice–salt bath. Recrystallization from petroleum ether afforded **18** (3.00 g, 82%): mp 51–52°; ir (KBr) 1726, 1710, and 1248 cm^{-1}; nmr 0.78 and 0.80 (s each, 6 H in total), 1.81 (br s, 3 H, olefinic Me), 1.97 (s, 3 H, Ac), 4.86 (d, 1 H, J = 9.0 Hz, C*H*OAc), and 5.56 (br t, 1 H, J = 8.3 Hz, olefinic H).[36]

4,8,8-Trimethyl-(*E*)-3,(*E*)-9-cyclodecadien-1-one (5a). A solution of **18** (330 mg, 1.2 mmol) in ether (1 ml) was poured on a column of activated alumina (20 g). After the solution was allowed to stand for 15 min, petroleum ether (40 ml) was passed through the column. Elution with ether (100 ml) gave oily **5a** (229 mg, 100%): ir (film) 3050, 1679, 1640, and 862 cm^{-1}; nmr 0.93 and 1.00 (s each, 6 H in total), 1.37 (br s, 3 H, olefinic Me), 5.23 and 6.05 (q of an AB type, 2 H, J = 18 Hz, C(9) and C(10) protons), and 5.56 (br t, 1 H, J = 9 Hz, C(3)–H).[36]

1,7,7-Trimethyl-4-methylene-(*E*)-1,(*E*)-5-cyclodecadiene (5b). A 20% *n*-hexane solution of *n*-butyllithium (2.2 ml, 4.1 mmol) was added dropwise to a stirred suspension of methyltriphenylphosphonium bromide (1.50 g, 4.1 mmol) in dry ether (20 ml) under nitrogen, and the mixture was stirred for 7 hr at room temperature.

The mixture was then cooled in an ice bath, and a solution of freshly prepared **5a** (440 mg, 2.3 mmol) in dry ether (9 ml) was added under nitrogen. The resulting mixture was allowed to warm to room temperature and stirred for an additional 15 hr. The mixture was poured into cold water, and the organic layer was separated. The aqueous layer was extracted thoroughly with pentane, and the combined organic layers were washed with water and brine. After the layers were dried ($MgSO_4$), the solvent was removed to leave an oil, which was passed through a column of neutral alumina (Woelm, activity III) by the aid of pentane. Distillation of the solvent through a Vigreux column left oily **5b** (350 mg, 87%): uv (MeOH) 213 nm (ϵ 10,700), 245 (3750), 260 (2520), and 280 (240); ir (film) 3100, 3030, 1645, 1605, 980, 886, and 862 cm^{-1}; nmr 0.98 (s, 6 H), 1.57 (br s, 3 H, olefinic Me), 4.80–5.20 (m, 3 H, C(2) and *exo*-methylene protons), and 5.15 and 5.50 (q of an AB type, 2 H, J = 16.5 Hz, C(5) and C(6) protons). An analytical sample was obtained by distillation (bath temperature, 125–130°) *in vacuo* (34 mm).[36]

Wittig Reaction of 5a Leading to 19a. Dry dimethyl sulfoxide (7 ml) was added to sodium hydride (216 mg, 9.0 mmol), and the mixture was stirred at 70–75° for 45 min under nitrogen. The mixture was cooled to room temperature, and a solution of methyltriphenylphosphonium bromide (4.284 g, 12 mmol) in dry dimethyl sulfoxide (17 ml) was added. After the resulting light brown solution was stirred for 30 min at room temperature, a solution of **5a** (1.152 g, 6.0 mmol) in dry dimethyl sulfoxide (13 ml) was added. Stirring was continued for an additional 3.5 hr at room temperature, and the mixture was diluted with water. The product was extracted with pentane and washed with 50% aqueous dimethyl sulfoxide and then brine. After evaporation of the solvent, the residue was passed through a column of neutral alumina (Woelm, activity IV, 25 g) by the aid of pentane. Distillation of the solvent through a Vigreux column left an oil (1.15 g), which was chromatographed on a silver nitrate impregnated silica gel column. Petroleum ether eluted **19a** (*vide post*), and subsequent elution with ether gave **5b**. Both the products were identified by glpc and spectral comparison.

Preparation of 1,2,4a,5,6,7,8,8aβ-Octahydro-4aβ,8,8-trimethyl-2-methylenenaphthalene (19a) from 19b. A mixture of sodium hydride (20 mg, 0.85 mmol) and dry dimethyl sulfoxide (1 ml) was stirred at 70–75° for 45 min under nitrogen. The mixture was cooled in an ice bath, and a solution of methyltriphenylphosphonium bromide (320 mg, 0.9 mmol) in the same solvent (2 ml) was added rapidly with stirring. After the resulting mixture was stirred for 30 min at room temperature, a solution of **19b**[24] (64 mg, 0.3 mmol) in dry dimethyl sulfoxide (3 ml) was added. Stirring was continued for an additional 4 hr at room temperature. The reaction mixture was poured into cold water and extracted with pentane. The extracts were washed with 50% aqueous dimethyl sulfoxide and brine, and dried ($MgSO_4$). Distillation of the solvent through a Vigreux column left oily **19a** (50 mg, 87%): ir (CCl_4) 3075, 3000, 1631, 1593, 889, 877, and 869 cm^{-1}; nmr 0.85, 0.94, and 1.04 (s, 3 H each), 4.72 (unresolved q, 2 H, *exo*-methylene protons), and 5.52 and 6.02 (q of an AB type, 2 H, J = 9.8 Hz, C(3) and C(4) olefinic protons); *m/e* 190 (M^+).[36]

1,2,4a,5,6,7,8,8aα-Octahydro-4aβ,8,8-trimethyl-2-methylenenaphthalene (20a). An ylide solution was prepared from a solution of sodium hydride (48 mg, 1 mmol) in dimethyl sulfoxide (1 ml) and a solution of methyltriphenylphosphonium bromide (357 mg, 1.0 mmol) in dimethyl sulfoxide (2 ml) as described above. A solution of **20b**[24] (134 mg, 0.7 mmol) in dimethyl sulfoxide (1.5 ml) was added, and the whole mixture was stirred for 2 hr at room temperature. Work-up as described for **19a** gave oily **20a** (130 mg, 97%): ir (film) 3100, 3010, 1634, 1597, 874, and 791 cm^{-1}; nmr 0.90, 0.94, and 0.99 (s, 3 H each), 4.77 (unresolved q, 2 H, *exo*-methylene protons), and 5.66 and 5.90 (q of an AB type, 2 H, J = 10 Hz, C(3) and C(4) olefinic protons). An analytical sample was obtained by distillation (bath temperature, 110°) *in vacuo* (53 mm).[36]

4,4,8-Trimethyl-8-vinyl-2-cyclooctен-1-one (23). A solution of **5a** (120 mg, 0.62 mmol) in dry ether (100 ml) in a quartz vessel was irradiated with a 400-W high-pressure mercury lamp at 0° for 1 hr under nitrogen. After removal of the solvent, the residue was chromatographed on a column of neutral alumina (Woelm, activity I, 20 g). Elution with ether gave oily **23** (15 mg, 13%): uv (MeOH) 225 nm (ϵ 2050); ir 3100, 1688, 1632, 999, and 915 cm^{-1}; nmr 1.00, 1.05, and 1.17 (s, 3 H each), 4.85–6.07 (m of an ABX type, 3 H, vinyl), and 5.56 (br s, 2 H, C(1) and C(2) protons); *m/e* 192 (M^+).[36]

2,6,6-Trimethyl-9-methylenetricyclo[5.3.0.0^{2,8}]decane (24). A solution of **5b** (700 mg, 3.7 mmol) and β-acetonaphthone (100 mg) in dry ether (400 ml) was irradiated with a 400-W high-pressure mercury lamp through a Pyrex filter at 5–10° under nitrogen. After 19 hr, glpc (column B at 172°) showed three peaks in a ratio of 75:10:15. The peak formed 15% of the product was identified to be unchanged **5b** by glpc retention time. After the solvent was distilled through a Vigreux column, the residue was dissolved in pentane and passed through a column of neutral alumina (Woelm, activity III, 10 g). Pentane was removed by distillation through a Vigreux column leaving a colorless oil. The main photoproduct was purified by preparative glpc and was obtained as a colorless oil: ir (CCl_4) 3075, 1670, and 869 cm^{-1}; nmr 0.76 (s, 3 H), 0.91 (s, 6 H), and 4.59 and 4.83 (br s, 1 H each, C=CH_2). An exact mass determination gave *m/e* 190.1749 (calcd for $C_{14}H_{22}$, 190.1721).

Quenching Experiment. A solution of **5b** (8 mg) and *trans*-piperylene (0.4 ml) in dry ether (8 ml) was irradiated under similar irradiation conditions as described above. After irradiation for 25 hr, glpc demonstrated that **5b** remained unchanged.

9-*exo*-Hydroxymethyl-2,6,6-trimethyltricyclo[5.3.0.0^{2,8}]decan-*endo*-9-ol (26). After a solution of the crude **24** (155 mg, 0.81 mmol) and osmium tetroxide (320 mg, 1.26 mmol) in dry pyridine (5 ml) was stored at room temperature for 63 hr in the dark, a 25% aqueous solution of sodium bisulfite (6 ml) was added. The mixture was stirred for 4.5 hr at room temperature and poured into cold water. The product was extracted with methylene chloride. The combined extracts were washed with water and brine, and dried ($MgSO_4$). Removal of the solvent gave an oil (130 mg), which was purified by preparative tlc using chloroform–ether (1:1) as eluent to afford crystalline **26** (120 mg, 66% from **5b**), mp 99–101°. An analytical sample was obtained by recrystallization from *n*-hexane as prisms: mp 103°; ir (KBr) 3500 sh and 3300 cm^{-1}.[36]

2,6,6-Trimethyltricyclo[5.3.0.0^{2,8}]decan-9-one (27). A solution of periodic acid (410 mg, 1.8 mmol) in dry tetrahydrofuran (5 ml) was added to a solution of crude **26** (270 mg, 1.2 mmol) in the same solvent (5 ml) at room temperature. The mixture was stirred for 1.25 hr at the same temperature and was passed through a column of neutral alumina (Woelm, activity III, 8 g). Ether eluted oily **27** (213 mg, 92%): ir (film) 1755 cm^{-1}; nmr 0.90, 0.95, and 1.00 (s, 3 H each). An analytical sample was obtained by distillation (bath temperature, 111–120°) *in vacuo* (1.5 mm).[36]

9-*endo*-Azidomethyl-2,6,6-trimethyltricyclo[5.3.0.0^{2,8}]decan-*exo*-9-ol (34). A mixture of sodium hydride (72 mg, 3.0 mmol) and dry dimethyl sulfoxide (2 ml) was stirred at 75–80° for 30 min under nitrogen. Dry tetrahydrofuran (2 ml) was added, and the whole mixture was cooled to −5°. A solution of trimethylsulfonium iodide (615 mg, 3.0 mmol) in dry dimethyl sulfoxide (2.5 ml) was added to the above mixture with stirring, and then a solution of **27** (290 mg, 1.50 mmol) in dry tetrahydrofuran (5 ml) was added. After stirring for 2 hr at 0°, the mixture was poured into water and extracted with ether. The extracts were washed with water and brine, and dried ($MgSO_4$). Removal of the solvent gave oily **33** (310 mg): ir (film) 3030, 902, and 815 cm^{-1}; nmr 0.89, 0.95, and 1.05 (s, 3 H each), 2.64 (s, 2 H, epoxy H). The product was used, without further purification, in the next step.

A mixture of the crude **33** (310 mg, 1.5 mmol), sodium azide (293 mg, 4.5 mmol), boric acid (35 mg), and dimethylformamide (13 ml) was refluxed for 3 hr.[32] The mixture was then diluted with water and extracted with ether. The combined extracts were washed with water and brine, and dried ($MgSO_4$). After the solvent was removed, the residue was chromatographed on silica gel (8.5 g). Ether–petroleum ether (1:5) eluted oily **34** (270 mg, 85% from **27**): ir (film) 3420, 3050, and 2100 cm^{-1}; nmr 0.90 (s, 6 H), 1.14 (s, 3 H), and 3.59 (q of an AB type, 2 H, J = 12 Hz, CH_2N_3). An analytical sample was obtained by distillation (bath temperature, 95°) *in vacuo* (0.21 mm).[36]

2,6,6-Trimethyltricyclo[5.4.0.0^{2,8}]undecan-9-one and -10-one (32b and 32a). A solution of **34** (63 mg, 0.27 mmol) in acetic acid (5 ml) was hydrogenated over Adams' catalyst (38 mg). After hydrogen uptake ceased, the catalyst was filtered off, and the filtrate was diluted with water (21 ml). A cold 4% aqueous solution of sodium nitrite (260 mg) was added dropwise to the above hydroxyamine solution in an ice bath, and the mixture was stirred for 1 hr in the cold. Stirring was continued for an additional 1.5 hr at room temperature. Finally the mixture was heated at 60° for 1 hr. An oil (57 mg) obtained by usual work-up showed three peaks in a ratio of 90:6:3 in glpc (column A at 175°). The main product (**32b**) (42 mg, 76% from **34**) was separated by preparative tlc using ether–petroleum ether (1:5) as eluent: ir (film) 1710 cm^{-1}; nmr 0.80, 0.90, and 0.92 (s, 3 H each); *m/e* 206 (M^+).[36]

Two other minor ketones were separated by preparative glpc (column A at 175°). The ketone which formed 6% of the mixture was the isomeric ketone **32a**: ir (CCl_4) 1720 cm^{-1}; nmr 0.86 (s, 3 H) and 0.93 (s, 6 H). An exact mass determination gave *m/e* 206.1670 (calcd for $C_{14}H_{22}O$, 206.1670).

The least ketone was **27** as identified by glpc and ir.

Deuteration of 32b. A solution of **32b** (9 mg) in methanol-d_1 (0.5 ml) was added to a sodium methoxide solution prepared from sodium (10 mg) and methanol-d_1 (0.5 ml), and the mixture was refluxed for 1 hr under nitrogen. Deuterium oxide (3 drops) was added, and the solvent was evaporated *in vacuo*. The residue was dissolved in pentane and dried ($MgSO_4$). Removal of the solvent gave an oil, *m/e* 208 (M^+).

2,6,6,9-Tetramethyltricyclo[5.4.0.0^{2,8}]undecan-*exo*-9-ol (35). A solution of **32b** (52 mg, 0.25 mmol) in dry ether (3 ml) was added to a methyllithium solution, prepared from lithium (70 mg, 5 mmol) and methyl iodide (0.31 ml) in dry ether (4 ml), under nitrogen. The mixture was stirred for 5.5 hr at room temperature, and the reaction was then quenched with cold aqueous ammonium chloride. The organic layer was separated and washed with water and brine. Removal of the solvent left crystals, which were recrystallized from pentane at a Dry Ice–methanol temperature affording pure longipinanol (**35**) (44 mg, 80%): mp 98.0–98.5°; ir (KBr) 3370, 3025, 1109, 915, and 879 cm^{-1}; nmr 0.88 (s, 6 H), and 1.05 and 1.22 (s, 3 H each).[36]

α- and β-Longipinenes (1a and 1b). Phosphorus oxychloride (0.16 ml) was added to a solution of **35** (42 mg, 0.19 mmol) in dry pyridine (1 ml). The mixture was heated to 100° and kept at this temperature for 5 min. After cooling to room temperature, the mixture was poured into a stirred mixture of pentane (30 ml) and cold water (20 ml). Stirring was continued for further 20 min, and the organic layer was separated. The aqueous layer was extracted with two 30-ml portions of pentane. The combined organic layers were successively washed with water, dilute sodium carbonate, water, aqueous cupric sulfate, water, and brine, and dried ($MgSO_4$). The solvent was distilled off through a Vigreux column to leave an oil, whose pentane solution was passed through a column of neutral alumina (Woelm, activity II, 4 g). Removal of the solvent left a clear colorless oil. Glpc analysis (column B at 157°) indicated that the oil consisted of two main olefins (48 and 36%), along with two unidentified minor products (16%). The most abundant olefin was presumed to be α-longipinene by glpc. The products were separated by preparative glpc to give two main olefins. One of them was (±)-α-longipinene as identified by comparison of the ir and nmr spectra with those of (+)-α-longipinene: ir (film) 3030, 1656, and 786 cm^{-1}; nmr 0.82 (s, 6 H), 0.89 (s, 3 H), and 5.12 (m, 1 H).[36]

The second olefin, (±)-β-longipinene, was identified by comparison of the ir and nmr spectra with those of (−)-β-longipinene: ir (film) 3070, 1642, and 973 cm^{-1}; nmr 0.68 (s, 3 H), 0.88 (s, 6 H), and 4.50 (m, 2 H, $W_{1/2}$ = 6 Hz).[36]

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Structure and Conformation of Amino Acids Containing Sulfur. II.[1a] The Crystal Structure of *meso*-Lanthionine Dihydrochloride; a Short Intermolecular S···S Contact Distance

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Abstract: The crystal structure of *meso*-lanthionine dihydrochloride ($C_6H_{12}N_2O_4S \cdot 2HCl$) has a remarkably short $S^{\gamma}\cdots S^{\gamma}$ contact distance, 3.251 (2) Å, between two sulfide ($C^{\beta'}$–S^{γ}–C^{β}) groups that are almost coplanar. A second sulfur contact, 3.515 (2) Å to Cl^-, is also directed close to the plane through $C^{\beta'}$–S^{γ}–C^{β}. Two intramolecular $S^{\gamma}\cdots$H–N contacts, each 2.75 (8) Å long, are directed, in contrast, nearly normal to this plane. These results are interpreted in terms of the orbital geometry of S^{γ}'s unshared pair of 3p electrons, and they suggest a smaller van der Waals radius for sulfur in the plane of the sulfide group. Both carboxyl carbon atoms are ± antiperiplanar to S^{γ}, an unusual conformation in structures of amino acids containing sulfur. Two carboxyl and one amino hydrogen atoms form short hydrogen bonds, 2.11 (7) Å long, to Cl^- ions. Each of five amino hydrogen atoms has two contacts with electronegative atoms, and lies in the plane through these atoms and its bonded nitrogen. The crystals have the space group $P2_1/a$. The cell constants [T = 22 ± 3°, λ(Cu Kα$_1$) 1.54051 Å] are a = 9.821 (1), b = 20.158 (1), and c = 5.706 (1) Å, β = 93.37 (1)°, V_c = 1127.7 Å^3, and Z = 4; d_{obsd} is 1.67 (1) g/cm^3 (flotation), d_{calcd} is 1.656 g/cm^3, and μ is 68.4 cm^{-1}. Data were measured (Cu Kα, $2\theta \leq 160°$) on a G. E. XRD-6 diffractometer, and were corrected for absorption. The structure, solved by the heavy atom method, was refined by least squares to an R of 0.056, using 1606 reflections.

Lanthionine (3,3′-thiodialanine) is a rare, naturally occurring amino acid, the sulfide analog of cystine. It was isolated originally from wool, chicken feathers, lactalbumin, and human hair, after treatment with dilute alkali;[2] and it has also been found in the peptide antibiotics subtilin[3a] and nisin.[3b] du Vigneaud and Brown were the first to synthesize the D, L, and *meso* forms.[4] We decided to study lanthionine's crystal structure in order to compare it with the several structures already reported for L-cystine, L-cysteine, and

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