*S**)-4-methoxy-2-heptanol, 94904-81-1; (*R**,*R**)-4-methoxy-2-heptanol, 94904-82-2; (*R**,*S**)-2,4-heptanediol, 94904-83-3; (*R**,*R**)-2,4-heptanediol, 94904-84-4.

Supplementary Material Available: Erythro/threo correlations and ratio determinations for Table II; experimental details for the relative rate experiments outlined in ref 8 (6 pages). Ordering information is given on any current masthead page.

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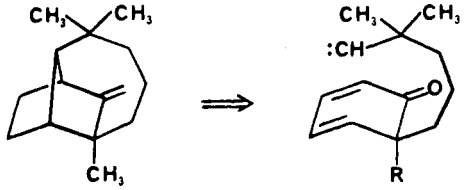
The Intramolecular Diene–Carbene Cycloaddition Equivalence and an Enantioselective Birch Reduction–Alkylation by the Chiral Auxiliary Approach. Total Synthesis of (±)- and (–)-Longifolene

Summary: Total syntheses of racemic and optically pure (–)-longifolene (1) illustrate (1) a preparation of 6-alkyl-6-(methoxycarbonyl)-2,4-cyclohexadien-1-ones (e.g., **5a**) by Birch reduction–alkylation of methyl *o*-methoxybenzoate and the chiral benzoic acid derivative **10** and (2) seven-membered ring construction by use of the synthetic equivalence of an intramolecular Diels–Alder reaction between a diene and a carbene (e.g., **5a** → **8**).

Sir: The tricyclic sesquiterpene (+)-longifolene (1) has provided a challenging test of proximity effects in the development of new annelation methodology.[1,2] We have considered the possibility of constructing longifolene (and other tricyclic frameworks) by performing the synthetic equivalence of an intramolecular cycloaddition between a diene and a carbene, e.g., **2** → **1**. Such a construction

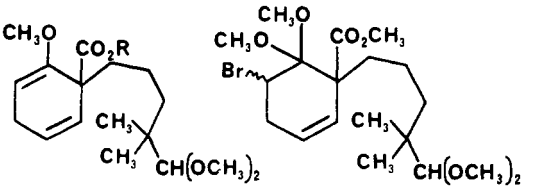


1 **2**

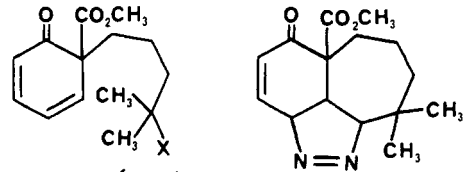
would be of value, because relatively few methods are available for direct synthesis of seven-membered rings. Only the Johnson synthesis of longifolene[1c] incorporates a direct seven-membered ring construction by use of a variation of the cation–polyene cyclization technique; the intramolecular Diels–Alder approach with a substituted cyclopentadiene has failed thus far because of a competing rearrangement pathway.[2e,f]

Realization of the synthesis plan required the development of a practical synthesis of 6,6-disubstituted 2,4-cyclohexadien-1-ones.[3] The diene–carbene synthetic equivalence has been demonstrated in the construction of tricyclo[4.3.0.0^{3,7}]non-4-en-2-ones by intramolecular cycloaddition of a diazoalkane to the C(4)–C(5) double bond of a 2,4-cyclohexadien-1-one and photorearrangement of the resulting pyrazoline (and derived vinylcyclopropane).[4] We now report a new total synthesis of (±)-longifolene patterned after the retrosynthetic analysis **2** → **1**. An enantiospecific synthesis of (–)-longifolene, via Birch reduction–alkylation of a chiral benzoic acid derivative, **10**, also is presented. This route to optically active cyclohexanes from *o*-hydroxybenzoic acids should find extensive use in organic synthesis.

Cyclohexadiene **3a** was prepared by Birch reduction–alkylation of methyl 2-methoxybenzoate[3] with the dimethyl acetal of 2,2-dimethyl-5-iodopentanal[5] (98%, oil). Conversion of **3a** to the key 2,4-cyclohexadien-1-one **5b** was



3a R = CH_3 **4**
b R = $C_7H_{12}NO_2$



5a X = $CH(OCH_3)_2$ **6**
b X = CHO
c X = CHN–NCHPh–CHPh
d X = CN

accomplished by (1) treatment of **3a** with *N*-bromoacetamide in methanol to give a diastereoisomeric mixture of bromo ketals **4** (95%, oil), (2) dehydrobromination of **4** with 1,5-diazabicyclo[4.3.0]non-5-ene in refluxing toluene followed by ketal hydrolysis during silica gel chromatography to give **5a** (85%, oil), and (3) acetal exchange by refluxing an acetone solution of **5a** in the presence of *p*-toluenesulfonic acid for 3 h (86%, oil).

The aziridinyl imine **5c** generated by reaction of **5b** with 1-amino-*trans*-2,3-diphenylaziridine,[6] on thermolysis in refluxing toluene solution, gave pyrazoline **6**. As anticipated,[4] **6** was converted to vinylcyclopropane **7** (mp 78–80 °C) on irradiation with 366-nm light in benzene solution.

(1) For total syntheses of longifolene, see: (a) Corey, E. J.; Ohno, M.; Mitra, R. B.; Vatakencherry, P. A. *J. Am. Chem. Soc.* **1964**, *86*, 478. (b) McMurry, J. E.; Isser, S. J. *J. Am. Chem. Soc.* **1972**, *94*, 7132. (c) Volkmann, R. A.; Andrews, G. C.; Johnson, W. S. *J. Am. Chem. Soc.* **1975**, *97*, 4777. (d) Oppolzer, W.; Godel, T. *J. Am. Chem. Soc.* **1978**, *100*, 2583.

(2) For additional synthetic studies, see: (a) Scherrer, R. A. Ph.D. Thesis, University of Illinois, 1958; *Diss. Abstr.* **1958**, *19*, 960. (b) Hudak, N. J. Ph.D. Thesis, Cornell University, 1959; *Diss. Abstr.* **1959**, *20*, 79. (c) Napier, R. P. Ph.D. Thesis, University of Rochester, 1964; *Diss. Abstr.* **1964**, *25*, 1577. (d) Grant, J. E., Jr.; Ph.D. Thesis, Pennsylvania State University, 1969; *Diss. Abstr. B.* **1969**, *29*, 3653. (e) Brieger, G. *J. Am. Chem. Soc.* **1963**, *85*, 3783. (f) Glass, R. S.; Herzog, J. D.; Sobczak, R. L. *J. Org. Chem.* **1978**, *43*, 3209.

(3) (a) Schultz, A. G.; Dittami, J. P. *Tetrahedron Lett.* **1983**, *24*, 1369. (b) Schultz, A. G.; Dittami, J. P.; Lavieri, F. P.; Salowey, C.; Sundararaman, P.; Szymula, B. *J. Org. Chem.* **1984**, *49*, 4429.

(4) Schultz, A. G.; Dittami, J. P.; Eng, K. K. *Tetrahedron Lett.* **1984**, *25*, 1255.

(5) The dimethyl acetal of 2,2-dimethyl-5-iodopentanal was prepared from the dimethyl acetal of 2,2-dimethylpent-4-en-1-al (Brannock, K. C. *J. Am. Chem. Soc.* **1959**, *81*, 3379) by (1) hydroboration (BH_3)–oxidation (H_2O_2) to give the dimethyl acetal of 2,2-dimethyl-5-hydroxypentanal (94%, oil, C, H analysis), (2) conversion to the mesylate with methanesulfonyl chloride–triethylamine (95%, oil), and (3) substitution with sodium iodide in acetone (91%, oil, C, H analysis).

(6) (a) Felix, D.; Müller, R. K.; Horn, U.; Joos, R.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1972**, *55*, 1276. (b) Padwa, A.; Ku, H. *Tetrahedron Lett.* **1979**, 4425. (c) Padwa, A.; Ku, H. *J. Org. Chem.* **1980**, *45*, 3756.

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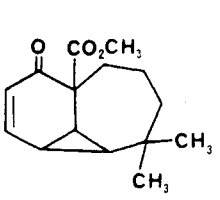

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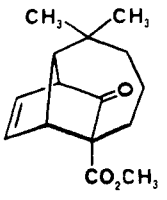

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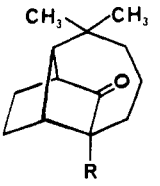
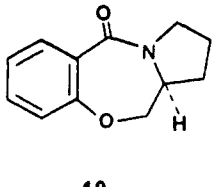


9a R = CO_2CH_3
b R = CO_2H
c R = H
d R = CH_3



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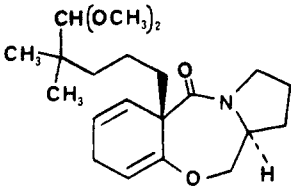

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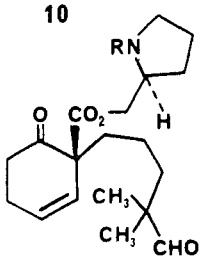

12a R = H
b R = CO_2CH_3

On the other hand, **6** and **7**, in refluxing xylene solution, both rearranged to tricyclic ketone **8** (oil) in ~90% yield.[7] The most efficient protocol for conversion of aldehyde **5b** into tricyclic ketone **8** (~40% overall yield) involves two experimental steps (preparation and thermolysis of **5c**) and is performed without isolation of reaction intermediates.

The efficiency of formation of **6** (43%) may not reflect problems inherent in the cyclization step. A major byproduct in the decomposition of the aziridinyl imine **5c** is the nitrile **5d**, presumably formed by Beckmann-like elimination of *trans*-2,3-diphenylaziridine from **5c**.

Tricycle **8** was converted to **9c**, an intermediate in both the Johnson[1c] and Oppolzer[1d] syntheses of longifolene, by (1) olefin hydrogenation at atmospheric pressure in ethanol with 5% Pd on carbon to give **9a** (92%, mp 101 °C), (2) saponification of **9a** with KOH in methanol–water at 25 °C to give carboxylic acid **9b** (85%, mp 160 °C), and (3) decarboxylation of **9b** in refluxing toluene solution (86%). ^1H NMR, ^{13}C NMR, IR, and mass spectra obtained with our synthetic **9c** compared favorably with spectra kindly provided by Professors Johnson and Oppolzer. Transformation of racemic **9c** to (±)-longicamphenylone (**9d**) and thence to (±)-longifolene (**1**) followed literature procedures.[1]

Benzoxazepenone **10**[8] provided the means for an enantiospecific preparation of (−)-longifolene. Reductive alkylation of **10** gave **11**, isolated as a single diastereoisomer in 96% yield. This substance was converted to enantiomerically pure **3a** by (1) treatment with methanol–hydrochloric acid to give carboxylic ester **12a**, (2) N-acylation of **12a** with methyl chloroformate–sodium bicarbonate to give urethane **12b**, (3) conversion of **12b** to acetal–enol ether **3b** in refluxing methanol–trimethyl orthoformate–hydrogen chloride, and (4) transesterification of **3b** with sodium methoxide in methanol (~75% overall from **11**).

Conversion of optically active **3a** to (−)-longicamphenylone (**9d**) [(+) configuration shown] followed the procedure already described for transformation of racemic **3a** to racemic **9d**. The isolated product was found to have optical rotation equal but opposite to that of (+)-**9d** prepared from (+)-longifolene.[1a,9] Finally, conversion of (−)-**9d** to (−)-longifolene[10] by the literature procedure[1a] confirmed the sense of stereoselection in the Birch reduction–alkylation step.

Acknowledgment. This work was supported by the National Institutes of Health (GM 33061). We thank W. S. Johnson and W. Oppolzer for providing us with spectral data for **9c**. We thank J. P. Dittami for preparation of the dimethyl acetal of 2,2-dimethyl-5-hydroxypentanal.

Supplementary Material Available: Listing of spectral and analytical data for all new compounds prepared in this work (6 pages). Ordering information is given on any current masthead page.

(7) For an earlier report of a vinyl cyclopropane rearrangement in this tricyclic ring system, see: Aumann, R. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 376.

(8) Schultz, A. G.; Sundararaman, P. *Tetrahedron Lett.* **1984**, *25*, 4591.

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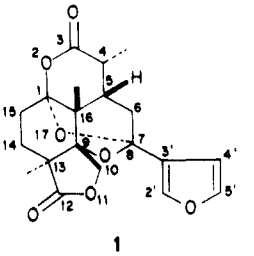
Saudin, a Hypoglycemic Diterpenoid with a Novel 6,7-Secolabdane Carbon Skeleton, from *Cluytia richardiana*

Summary: A novel hypoglycemic diterpene named saudin (**1**) was isolated from the petroleum ether extract of *Cluytia richardiana* (Euphorbiaceae) growing in Saudi Arabia and was shown to be a novel 6,7-secolabdane with an unusual arrangement of lactone groups presumably formed via oxidation of the B-ring ketone to an ϵ-lactone followed by hydrolysis, rearrangement, and cyclization to give a highly caged structure.

Sir: We report the isolation and structural elucidation of the hypoglycemic agent saudin (**1**; (−)-(1*R*,4*R*,5*S*,7*R*,9*S*,13*S*,16*R*)-7-(3′-furanyl)-4,13,16-trimethyl-2,8,11,17-tetraoxapentacyclo[7.6.1.$1^{1,7}$.$0^{5,16}$.$0^{9,13}$]-heptadeca-3,12-dione). Saudin (**1**) was isolated from the



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leaves of the toxic plant *Cluytia richardiana* (L.) family Euphorbiaceae, which grows in the mountainous regions of western and southern Saudi Arabia. Compound **1** apparently derives from the labdane group of prefuranoid diterpenes and is a very novel, highly oxygenated and

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