were identical with those of the natural product.[9,10] The total synthesis of bigelovin confirms the structural assignment of the natural material put forth some years ago by Professor Herz.[1b]

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Registry No. 1, 70981-13-4; **3**, 68241-54-3; **4**, 70913-22-3; **6**, 70981-14-5; **7**, 70913-23-4; **8**, 70913-24-5; **9**, 70981-15-6.

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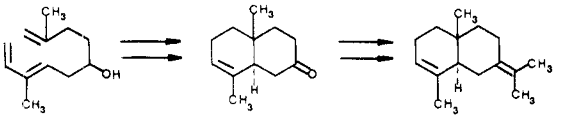
[9] *dl*-Bigelovin: IR ($CHCl_3$) 1758, 1730, 1707, 1662, 1585, 1241 cm^{-1}; NMR (250 MHz) ($CDCl_3$) δ 7.72 (dd, 1 H, J = 1.8, 6.1 Hz, H-2), 6.23 (d, 1 H, J = 3.5 Hz, exocyclic methylene), 6.11 (dd, 1 H, J = 3.0, 6.1 Hz, H-3), 5.93 (d, 1 H, J = 3.5 Hz, exocyclic methylene), 5.62 (d, 1 H, J = 7.6 Hz, H-6), 4.61 (ddd, 1 H, J = 3.0, 10.9, 12.2 Hz, H-8), 3.14–3.00 (m, 2 H), 2.58 (dt, 1 H), 2.15–1.90 (m, 4 H), 1.97 (s, 3 H), 1.54 (m, 1 H), 1.29 (d, 3 H, J = 7.2 Hz), 1.21 (s, 3 H).

[10] We are indebted to Professors Werner Herz and T. J. Mabry for spectra of natural bigelovin.

An Intramolecular Diels-Alder Approach to Diterpenes

Summary: The synthesis of three dienes **4a**, **4b**, and **4c**, suitably constituted for intramolecular Diels–Alder cyclization to tricyclic compounds **6a**, **6b**, and **6c**, is described. The newly formed rings are mainly cis fused. The method results in the addition of two fused six-membered rings to *o*-vinylbenzaldehyde derivatives in a two-step bis annelation sequence.

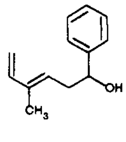
Sir: The Diels–Alder reaction is one of the most useful reactions in organic synthesis. Although the intramolecular Diels–Alder reaction[1] has been used in several terpene syntheses before,[2] the only *general* application of the reaction to polycyclic terpenes centers on reactions of the *o*-quinodimethane type.[3] We have recently reported[4] a synthesis of the Eudesmane sesquiterpene (±)-selenadiene via the scheme shown in eq 1. We now report preliminary



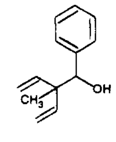
(1)

studies in the extension of this methodology to the synthesis of tricyclic compounds related to diterpenes.

The requisite dienes for our Diels–Alder strategy are readily available via the addition of 3-methylpentadienyllithium (3-MPL)[5] to an aldehyde. For example, benzaldehyde reacts with 3-MPL to give 51% **1** and 36% **2**. As reported earlier,[6] the undesired branched isomer



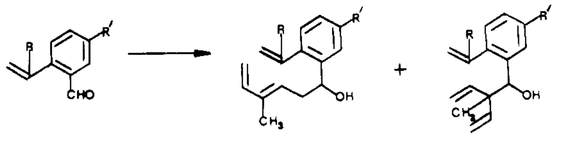
1



2

2 can be isomerized to **1** by KH/THF/0 °C.

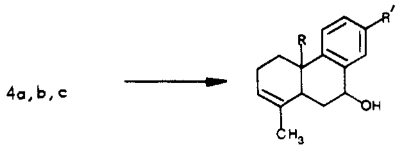
Substituted dienes **4a** and **4b** were prepared as follows. *o*-Vinylbenzaldehyde **3a**[7] reacts with 3-MPL (THF, 0 °C) to give 48% of **4a**[8] and 22% of **5a**. In contrast to the bicyclic series,[4] compound **4a** cyclizes readily. Pure **4a** reacts to give **6a** cleanly at 100 °C ($T_{1/2}$ = 2 h, 72% yield).



3a, R=H, R′=H
3b, $R=CH_3, R'=H$
3c, $R=CH_3, R'=\underset{CH_3}{\underset{|}{CH}}-CH_3$

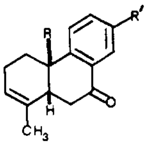
4a, R=H, R′=H
4b, $R=CH_3, R'=H$
4c, $R=CH_3, R'=\underset{CH_3}{\underset{|}{CH}}-CH_3$

5a, R=H, R′=H
5b, $R=CH_3, R'=H$
5c, $R=CH_3, R'=\underset{CH_3}{\underset{|}{CH}}-CH_3$

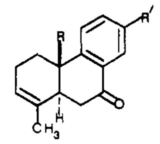


6a, R=H, R′=H
6b, $R=CH_3, R'=H$
6c, $R=CH_3, R'=\underset{CH_3}{\underset{|}{CH}}-CH_3$

Compound **3b**[9] reacts with 3-MPL to produce a 50% yield of **4b** and 11% of **5b**. As expected, the presence of an incipient angular methyl slows the Diels–Alder reaction markedly. Compound **4b** does not undergo cyclization below 140 °C, where it begins to decompose. However, the trimethylsilyl ether of **4b** undergoes intramolecular Diels–Alder reaction (180 °C, 24 h) giving the expected **6b** (silyl ether) which was hydrolyzed (KF/CH_3OH) and oxidized (Jones) to **7b**/**8b**. The overall yield of tricyclic



7a, R=H, R′=H
7b, $R=CH_3, R'=H$
7c, $R=CH_3, R'=\underset{CH_3}{\underset{|}{CH}}-CH_3$



8a, R=H, R′=H
8b, $R=CH_3, R'=H$
8c, $R=CH_3, R'=\underset{CH_3}{\underset{|}{CH}}-CH_3$

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[1] (a) Carlson, R. G. *Ann. Rep. Med. Chem.*, **1974**, *9*, 270. (b) Oppolzer, W. *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 10.

[2] Himachelene: Wenkert, E.; Naemura, K. *Synth. Commun.* **1973**, *3*, 45. Patchouli alcohol: Näf, R.; Ohloff, G. *Helv. Chim. Acta.* **1974**, *57*, 1868. Seychelline: Frater, G. *Ibid.* **1974**, *57*, 172. Cedrane: Breitholle, E. G.; Fallis, A. G. *J. Org. Chem.* **1978**, *43*, 1964. Khusitene: Vig, O. P.; Trehan, I. R.; Kumar, R. *Indian J. Chem.* **1977**, *15*, 319.

[3] (a) Review: Oppolzer, W. *Synthesis* **1978**, 793. (b) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1978**, *100*, 5483. (c) Kametani, T.; Tusbuki, M.; Shiratori, Y.; Kato, Y.; Nemoto, H.; Ihare, M.; Fukumoto, K. *J. Org. Chem.* **1977**, *42*, 2672. (d) Kametani, T.; Hirai, Y.; Satoh, F.; Fukumoto, K. *J. Chem. Soc., Chem. Commun.* **1977** 16. (e) Kametani, T.; Nemoto, Ishidawa, H.; Shiroyama, K.; Fukumoto, K. *J. Am. Chem. Soc.* **1976**, *98*, 3378.

[4] Wilson, S. R.; Mao, D. T. *J. Am. Chem. Soc.* **1978**, *100*, 6289.

[5] Wilson, S. R.; Jernberg, K. M.; Mao, D. T. *J. Org. Chem.* **1976**, *41*, 3209.

[6] Wilson, S. R.; Mao, D. T.; Jernberg, K. M.; Ezmirly, S. T. *Tetrahedron Lett.* **1977**, 2559.

[7] Dale, W. L.; Starr, L.; Strobel, C. W. *J. Org. Chem.* **1961**, *26*, 2225.

[8] All new compounds possessed spectral and analytical data consistent with the assigned structures.

[9] Brown, R. F. C.; Butcher, M. *Aust. J. Chem.* **1969**, *25*, 1457.

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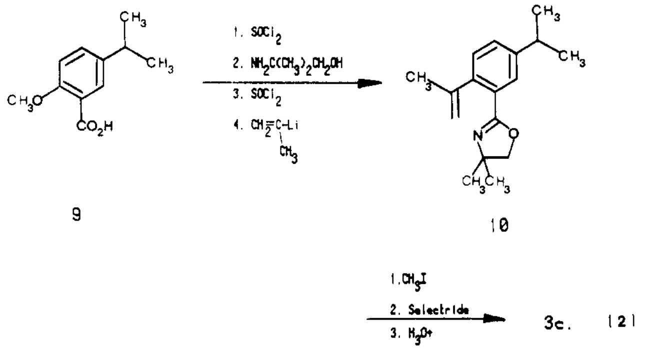
ketones **7b**/**8b** from **4b** was 43%. Inspection of the NMR spectrum of the ketone mixture **7b**/**8b** showed a cis/trans ratio[10] of 2:1. GLC analysis (OV101) showed two peaks in a 2:1 ratio, but the isomers could not be separated by silica gel chromatography. Oxidation of tricyclic **6a** gave a mixture of ketones **7a**/**8a** in a ratio of 4:1.[11]

Application of this strategy to the synthesis of the Abietane skeleton is now described. The synthesis of the requisite aldehyde **3c** was carried out as outlined in eq 2.



9

10

3c. (2)

The acid **9** (obtained by metalation/carboxylation of *p*-isopropylanisole) was converted to oxazoline **10** by the method of Meyers[12] (90% overall). Conversion of **10** to aldehyde **3c** was accomplished (eq 2) in about 90% yield.[13]

When aldehyde **3c** was reacted with 3-MPL, compounds **4c** (41%) and **5c** (27%) were formed. Intramolecular Diels–Alder cyclization of **4c** (Me_3Si ether) at 180 °C for 22 h gave, after hydrolysis and Jones oxidation, ketones **7c**/**8c** (1:1)[15] in 77% yield from **4c**. Thus, the stereoselectivity observed in the (±)-selenadiene synthesis[4] has now turned against us. It is well known[1b] however that subtle changes in the conformation of the bridging atoms can have a dramatic effect on intramolecular Diels–Alder selectivities. Such cis preference could also be related to the known (and unexpected) thermodynamic preference for *cis*-AB ring fusion in the Abietanes.[16,17]

In conclusion, we have shown that a synthetic approach which involves the simultaneous formation of two six-membered rings *and an angular methyl group* is a quite reasonable one. More importantly, we should point out that there is not a requirement for an activating substituent on the diene or the dienophile.

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Registry No. 1, 70897-96-0; **2**, 60462-68-2; **3a**, 28272-96-0; **3b**, 23417-79-0; **3c**, 70897-97-1; **4a**, 70897-98-2; **4b**, 70897-99-3; **4b** Me_3Si derivative, 70898-00-9; **4c**, 70898-01-0; **5a**, 70898-02-1; **5b**, 70898-03-2; **5c**, 70898-04-3; **6a**, 70898-05-4; **6b** Me_3Si derivative, 70898-06-5; **7a**, 70898-07-6; **7b**, 70898-08-07; **8a**, 70898-09-8; **8b**, 70898-10-1; **9**, 68014-67-5; **10**, 70898-11-2; 3-MPL, 51852-87-0; benzaldehyde, 100-52-7; *p*-isopropylanisole, 4132-48-3.

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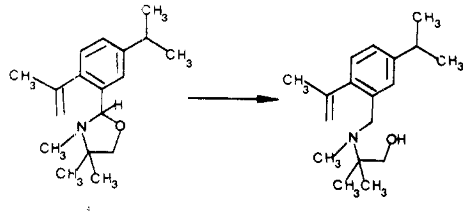
[10] The angular methyl signal of **5b** comes at δ 1.39 whereas **6b** comes at δ 1.14.

[11] A referee suggested that "the apparent low selectivity of the isopropenyl cases, which involve considerably harsher thermal conditions than the vinyl examples, arises not from a low kinetic stereoselectivity, but by equilibration via retro-Diels–Alder reaction and readdition". Unfortunately, the cis/trans isomers could not be separated to test this hypothesis.

[12] Meyers, A. I.; Gabel, R.; Michelich, E. D. *J. Org. Chem.* **1978**, *43*, 1372.

[13] i is very readily overreduced[14] to amine ii.



i

ii

This is more of a problem in the preparation of *o*-isopropenylbenzaldehydes than *o*-vinylbenzaldehydes. The explanation could either be steric or electronic. (Wilson, S. R.; Mao, D. T.; manuscript in preparation.)

[14] Bergmann, E. D. *Chem. Rev.* **1953**, *53*, 309.

[15] Angular methyl signal of **5c** comes at δ 1.36 and that of **6c** at δ 1.11.

[16] Bennett, C. R.; Cambie, R. C.; Franich, R. A.; Fullerton, T. J. *Aust. J. Chem.*, **1979**, *22*, 1711.

[17] Certainly fusion of an additional ring (ring C) tends to "flatten out" the transition states leading to cis or trans products (endo/exo) and makes the non-bonded interactions observed previously less severe. Specifically, the C-7 hydrogen is not axial but pseudoaxial.

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