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Supplementary Material Available: IR, NMR, and mass spectrometry data for compounds **7**, **11**, **12a**, **12b**, **13a**, **13b**, **14**, and **15a** (7 pages). Ordering information is given on any current masthead page.

Biogenetically Inspired Stereospecific Synthesis of the Dienylvinylcyclopropane Gamete Attractant Dictyoptere B

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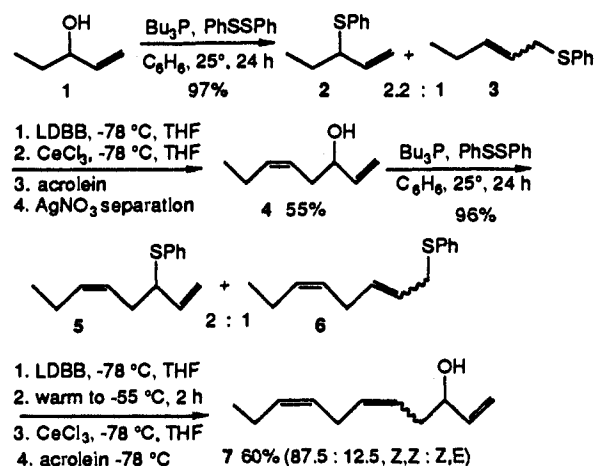
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Although *cis,cis*-undeca-1,5,8-trien-3-ol (the *Z,Z* isomer of **7**) has been proposed as a biosynthetic precursor of the marine gamete attractants dictyoptere B (**10**), dictyoptere D (**13**), and the two $C_{11}H_{16}$ tetraenes **11** and **12**,^{1,2} **7** has never been converted to these gamete attractants. We now disclose that such conversions can be executed in a highly efficient and stereospecific manner, especially with regard to the formation of **10**.

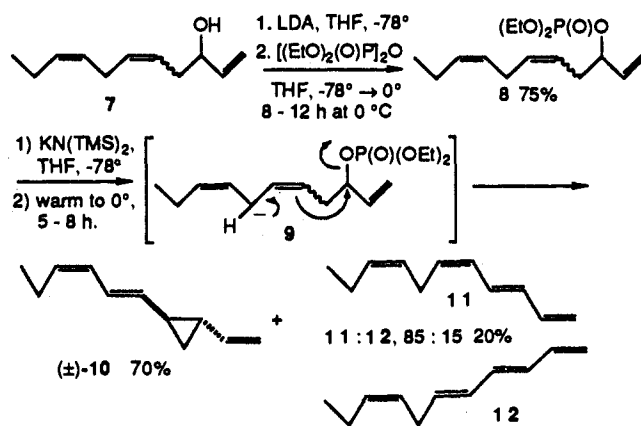
7 (mainly the *Z,Z* isomer) is now readily available by a modification and refinement (Scheme I) of the synthesis reported recently from this laboratory.³ Commercially available 1-penten-3-ol (**1**) was efficiently converted⁴ to a mixture of sulfides **2** and **3**, which was reductively lithiated⁵ with lithium *p,p'*-di-*tert*-butylbiphenylide⁶ (LDBB) followed by transmetalation with $CeCl_3$ and quenching of the resulting allylcerium(III) η^3 complex in situ with acrolein to afford 68% of a mixture of **4** and its trans isomer in a ratio of 89:11. The desired *cis* isomer **4** was separated from the trans isomer by flash chromatography using silica gel impregnated with a low concentration of $AgNO_3$ to provide a 55% yield from **2** and **3**. The alcohol **4** was subjected to the same reactions as **1** except that the intermediate allyllithium was warmed to $-55^\circ C$ for 2 h in order to accomplish stereochemical equilibration, which was more sluggish than that of the allyl anion derived from **2** and **3**. The product **7** was a mixture of *Z,Z* and *Z,E* isomers in a ratio of 87.5:12.5. It was assumed that separation of the isomers of **7**, which was found to be very difficult at best, would be unnecessary since the internal double bond is destroyed during the ring closure to (\pm)-dictyoptere B (**10**) and that double bond that occurs in **7** in both *cis* and *trans* forms appears in the tetraenes **11** and **12** also as a mixture of *cis* and *trans* isomers. It should be noted that this route (four synthetic steps, 31% overall yield) to the putative biogenetic precursor **7** is the most efficient to date.^{2,7}

Dictyoptere B, the most abundant and interesting of these gamete attractants, was prepared from **7** in two steps. Treatment of the alkoxide derivative of **7** with tetraethyl pyrophosphate produced the phosphate ester **8**.⁸ Upon addition of potassium bis(trimethylsilyl)amide to **8** and subsequent warming of the

Scheme I



Scheme II



reaction mixture, a remarkably stereospecific and efficient [1,2,(3,5)]-elimination⁹ occurred to provide (\pm)-dictyoptere B (**10**) in 70% yield (Scheme II).^{10,11} The only separable byproduct isolated from the reaction by chromatography was an oil consisting of a mixture of the two natural tetraenes **11** and **12**. Interestingly, no production of the *cis*-disubstituted cyclopropane corresponding to **10** was formed since it is known¹² to rearrange at room temperature to dictyoptere D (**13**), which was not an observed product. Molecular models indicate that, in the transition state for the elimination leading to the *cis*-disubstituted cyclopropane, serious nonbonded interactions occur between the protons on the sp^2 carbon atoms closest to the developing ring; the transition state leading to **10** appears to be strain free.

Although S_N2 displacements of phosphate groups appear to be very rare, there is a well-documented procedure for cyclopropane formation that involves displacement of this group by an enolate anion in a special system in which the phosphate ester is generated by a rearrangement.¹³ Allyl diethyl phosphates undergo nucleophilic displacement of the phosphate group by ligands of aluminum, but this process appears to follow an S_N1 course.¹⁴

(1) Moore, R. E. *Acc. Chem. Res.* 1977, 10, 40 and citations therein.

(2) After Moore made this suggestion, the acetate of *cis,cis*-**7** in the correct enantiomeric configuration was isolated from *Dictyoptera prolifera*. Yamada, K.; Tan, H.; Tatamatsu, H.; Ojika, M. *Tetrahedron* 1986, 42, 3775 and citations therein.

(3) Guo, B.-S.; Doubleday, W.; Cohen, T. *J. Am. Chem. Soc.* 1987, 109, 4710.

(4) Nakagawa, I.; Hata, T. *Tetrahedron Lett.* 1975, 1409.

(5) Cohen, T.; Bhupathy, M. *Acc. Chem. Res.* 1989, 22, 152.

(6) Freeman, P.; Hutchinson, L. *J. Org. Chem.* 1980, 45, 1924.

(7) A five-step route to racemic *cis,cis*-**7** in poor yield has been reported: Marner, F. J. Ph.D. Thesis, University of Cologne, Cologne, 1975. Cited in the following: Moore, R. E. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic Press: New York, 1978; Vol. 1, pp 43-124.

(8) Preparation of dialkyl phosphates from pyrophosphates: Chouinard, P. M.; Bartlett, P. A. *J. Org. Chem.* 1986, 51, 75 and citations therein.

(9) Review of such eliminative cyclizations: Kaupp, G. *Top. Curr. Chem.* 1988, 146, 58.

(10) The 1H NMR, ^{13}C NMR, and mass fragmentation spectra of (\pm)-**10** were identical with the spectra of the natural gamete attractant, dictyoptere B.

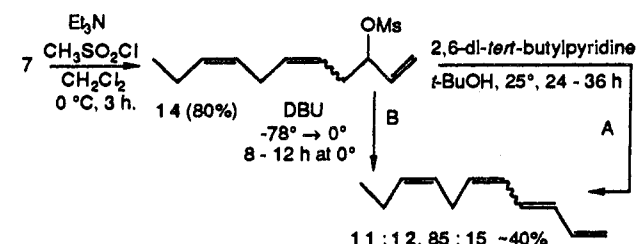
(11) According to capillary GC and 1H NMR (500 MHz), the isolated cyclopropane (\pm)-**10** was contaminated with ~5% of an unknown and inseparable impurity.

(12) Schneider, M. P.; Goldbach, M. *J. Am. Chem. Soc.* 1980, 102, 6114.

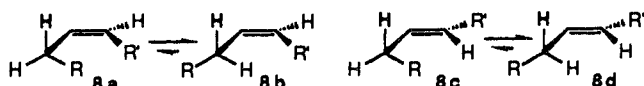
(13) Izydore, R. A.; Ghirardelli, R. G. *J. Org. Chem.* 1973, 38, 1790. Petter, R. C. *Tetrahedron Lett.* 1989, 30, 399.

(14) Kitagawa, Y.; Hashimoto, S.; Iemura, S.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* 1976, 98, 5030. Itoh, A.; Ozawa, S.; Oshima, K.; Sasaki, S.; Yamamoto, H.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* 1980, 53, 2357.

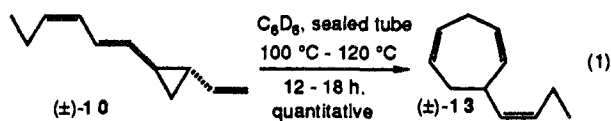
Scheme III



The exclusive formation of the *cis,trans* geometry of the conjugated diene in **10** suggests the following about the reaction mechanism: (1) The lack of change in the *Z*-olefin geometry ($C_{8,9}$) of **8** signified that either elimination in the anion **9** to form the cyclopropane **10** occurs faster than stereochemical equilibration of the pentadienyl anion or the *cis,trans* configuration of the pentadienyl anion is thermodynamically favored. On the basis of studies by Schlosser¹⁵ of closely related systems, both of these possibilities seem likely. (2) The exclusive *E* geometry of the newly formed double bond in **10** may be attributed to steric interactions during deprotonation. Removal of that diallylic proton from **8** which results in a pentadienyl anion (indicated in bold type) most likely occurs in **8b** rather than **8a** in the case of the predominant *cis* isomer and in **8d** rather than **8c** in the case of the *trans* isomer since the resulting transition states would be less crowded in each case. **8b** and **8d** would afford dictyopterene B (**10**) while **8a** and **8c** would produce the *cis,cis* isomer of **10**.



(±)-Dictyopterene B (**10**) was quantitatively converted to (±)-dictyopterene D (**13**)^{16,17} through the known procedure of heating (±)-**10** in a sealed tube for several hours (eq 1).



When the methanesulfonate ester **14** of **7** was solvolysed (path A, Scheme III) or treated with excess 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) (path B¹⁸), a mixture of tetraene gamete attractants **11** and **12**¹⁹ was produced in 40% yield and no dictyopterene B was detected. It is not surprising that **14** undergoes β -elimination under essentially neutral solvolytic conditions whereas **9**, in the presence of a strong base, undergoes deprotonation followed by an intramolecular S_N2 reaction. The solvolysis of **14**, bearing an excellent leaving group, presumably involves an $E1$ process in which the most acidic (β) proton of the carbocationic intermediate is removed.

The production of racemic dictyopterene B (**10**)²⁰ and dictyopterene D (**13**) in six and seven steps, respectively, in 16%

(15) Schlosser, M.; Rauchschalbe, G. *J. Am. Chem. Soc.* **1978**, *100*, 3258. Bosshardt, H.; Schlosser, M. *Helv. Chim. Acta* **1980**, *63*, 2393. Schlosser, M. *Proc. Jpn. Chem. Soc. (Tokyo)* **1984**, *3*, 1820. Schlosser, M. *Pure Appl. Chem.* **1988**, *60*, 1627.

(16) According to capillary GC and ¹H NMR (500 MHz), the isolated cycloheptadiene (±)-**13** was contaminated with ~5% of the same unknown and inseparable impurity that was in reactant **10**.

(17) The ¹H NMR, ¹³C NMR, and mass fragmentation spectra of (±)-**13** were identical with those of the enantiomer of natural dictyopterene D.¹⁰

(18) Corey, E. J.; Su, W.; Mehrotra, M. *Tetrahedron Lett.* **1984**, *25*, 5123.

(19) According to both the 500-MHz ¹H NMR spectrum and the capillary GC analysis, the mixture of tetraenes **3** and **4**, isolated from procedure A, contained 10-15% of unidentifiable impurities along with a considerable amount of 2,6-di-*tert*-butylpyridine (~35%), while that from procedure B (DBU) contained 10-20% of unidentifiable impurities.

(20) It should be noted that even though the ova in most Pacific seaweeds secrete only (*R,R*)-(-)-**10**, the male gametes in some of the brown algae do not distinguish between *R,R* and *S,S* forms and thus are attracted to both enantiomers of **10**.¹

overall yield starting with commercial **1** is the most efficient synthesis to date.²¹ It is also truly unique as all previous syntheses utilize a Wittig reaction to generate C-C unsaturation in a stereochemically controlled manner, usually in poor yield. More importantly, it has now been demonstrated for the first time that these gamete attractants can be prepared from their proposed¹ biogenetic precursor **7** in good yield. While the conditions used in the conversion of **7** to **10** do not resemble those in a biological system, our results render plausible a biosynthesis involving electrophilic enzymatic assistance to removal of a good leaving group such as a pyrophosphate with simultaneous enzymatic deprotonation of the developing cation.²² The [1,2,(3),5]-elimination described here is apparently the only example of this rare type of ring closure in a noncyclic system⁹ in which the entropy of activation should be less favorable than in the few known cases.

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Supplementary Material Available: Sample procedures for the reactions described herein and spectral data and copies of the ¹H NMR spectra for the products (22 pages). Ordering information is given on any current masthead page.

(21) Ali, A.; Sarantakis, D.; Weinstein, B. *J. Chem. Soc., Chem. Commun.* **1971**, 940. Jaenicke, L.; Akintobi, T.; Müller, D. G. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 492. Jaenicke, L.; Akintobi, T.; Marner, F.-J. *Justus Liebigs Ann. Chem.* **1973**, 1252. Kajiwara, T.; Nakatomi, T.; Sasaki, Y.; Hatanaka, A. *Agric. Biol. Chem.* **1980**, *44*, 2099. Schotten, T.; Boland, W.; Jaenicke, L. *Helv. Chim. Acta* **1985**, *68*, 1186. Dorsch, D.; Kunz, E.; Helmchen, G. *Tetrahedron Lett.* **1985**, *26*, 3319.

(22) An alternative biogenetic hypothesis involves hydrogen atom abstraction from a methylene-interrupted triene. Jaenicke, L.; Boland, W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 643.

Preparation, X-ray Molecular Structure, and Electronic Structure of the First 16-Electron Dihydrogen Complexes $RuH(H_2)X(PCy_3)_2$

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Since the first demonstration by Kubas of the coordination of dihydrogen to a transition metal,¹ numerous examples of such compounds have appeared in the literature.² A large number of these resulted from the reinvestigation of complexes that had been previously assigned a polyhydride structure. This is the case for the polyhydrides $FeH_4(PR_3)_3$, $RuH_4(PR_3)_3$, and $RuH_6(PCy_3)_2$, which were shown to adopt a d^6 octahedral structure ($FeH_2(H_2)(PR_3)_3$,^{3,4} $RuH_2(H_2)(PR_3)_3$,^{3,5} and $RuH_2(H_2)_2(PCy_3)_2$,⁵ re-

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(1) Kubas, G. J. *Acc. Chem. Res.* **1988**, *21*, 120.

(2) (a) Crabtree, R. H. *Adv. Organomet. Chem.* **1988**, *28*, 295. (b) Crabtree, R. H. *Acc. Chem. Res.* **1990**, *23*, 95.

(3) Hamilton, D. G.; Crabtree, R. H. *J. Am. Chem. Soc.* **1988**, *110*, 4126.