The crude products were typically light pale yellow or amber.

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(15) Aldrich proton NMR library.

Communications

Stereocontrolled Synthesis of American Cockroach Sex Pheromone, Periplanone B

Summary: The stereoselective synthesis of periplanone B, the sex excitant pheromone of the American cockroach, and a discussion of the diastereoselectivity of C(2),C(3)-epoxidation based on MM2 calculations are presented.

Sir: Periplanone B (**9**), the sex excitant pheromone of the American cockroach, is an attractive synthetic target because of its challenging structural features as well as its high level of biological activity.[1] Syntheses of periplanone B have been achieved by Still[2] and Schreiber[3] in which crucial germacranoid intermediates were constructed by anion-induced oxy-Cope rearrangement.[4] Our approach described here is strategically quite different from the existing ones in the construction of the ten-membered ring. It also presents an epoxidation which is highly stereoselective.

Predictions of stereoselectivity in medium ring systems can be quite difficult since they have many conformational options. Molecular mechanics calculations have proven useful in the prediction of the stereoselectivity in macrocyclic systems.[5] As described below, MM2 calculations[6] of the model compound **10** in respect to strain energies and conformational distributions (Figure 1) suggest that changing the C(5) stereochemistry to the silyloxy methyl **6** from the C(5) exocyclic methylene (Still's intermediate) could provide a highly stereoselective C(2,3)-β-epoxidation. Previous workers[2-4] who used the exocyclic methylene reported only 4:1 stereoselectivity. Thus, in our synthetic plan (Scheme I) the enone **6** is the key intermediate and its ten-membered skeleton is constructed by the intramolecular alkylation[7] of the protected cyanohydrin **4** (X = CN, Y = OCHMeOEt). The cis 1,4-relative stereochemistry[8] between C(5) and C(8) in **6** is constructed by a stereoselective Claisen rearrangement of the allylic alcohol **2** in which the syn-1,2-stereochemical relationship

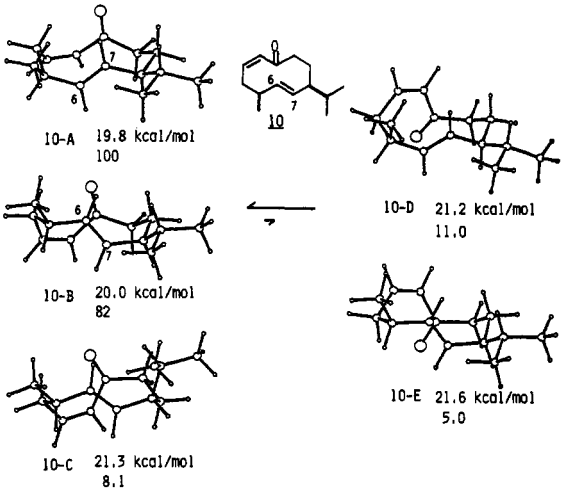
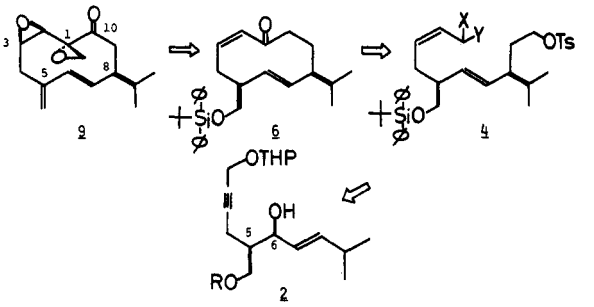


Figure 1. ORTEP drawing of conformers **10A–E** with calculated steric energies and relative ratio (at room temperature).

Scheme I



at C(5) and C(6) is introduced by the reduction of the carbomethoxy ketone **1** with L-Selectride (Aldrich).

With use of the ring-making computer program at 30° dihedral angle resolution and the MM2 molecular mechanics program, the lower energy conformations of the enone **10** were constructed (Figure 1). The calculated lowest energy conformations were qualitatively the same as those found from ^{1}H NMR spectra.[9] When an early transition state was assumed in the peripheral attack epoxidation at C(2),C(3), conformations **10-A,B,C** and **10-D,E** should lead to the α- and β-epoxy ketones, respectively. These conformational distributioins of **10** suggest

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(8) Our epoxidation (**6–7**) is analogous to Still's and Schreiber's epoxidations; however, the stereoselective construction of cis stereochemistry at C(5) and C(8) in **6** is difficult by their methods.

(9) Although conformational distributions (5:4) based on calculation are not consistent with those (3:1) observed in NMR spectrum, significant changes of C(6) and C(7) protons at 25 °C and −30 °C suggest that two lower energy conformations of **10** are **10A** and **10B**. Modification of parameters are necessary to obtain more exact calculations. ^{1}H NMR spectra of **10** at −30 °C to +40 °C and preparative procedures of **1** and **10** are available in supplementary material.

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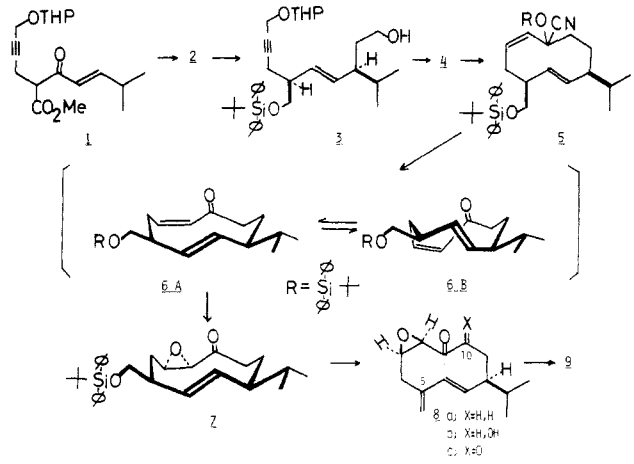
Scheme II



that our intermediate **6** should lead to the α-epoxide with high stereoselectivity.

The enone **6** was prepared in the following way. Stereoselective reduction of the ketone of 1[9] with L-Selectride followed by reduction of the ester group with $LiAlH_4$ gave the syn product **2a** (R = H) in 50% overall yield. The ratio of **2a** to the anti product was approximately 10:1.[10] Selective silylation of the diol **2a** (t-$BuPh_2SiCl/Et_3N$/DMAP; 76% yield), Claisen rearrangement of the silylated product **2b** (R = t-$BuPh_2Si$) with trimethyl orthoacetate, and reduction of the resulting ester with $LiAlH_4$ gave **3** in 50% overall yield. Tosylation of **3** and removal of the THP group (78% yield in two steps) and cis reduction of the triple bond ($Pd-BaSO_4/H_2$) gave **4a** (X = H, Y = OH). Oxidation of **4a** with MnO_2 and protected cyanohydrin formation[7] in three steps gave **4b** (X = CN, Y = OCHMeOEt) in 77% overall yield. Cyclization of **4b** with $LiN(TMS)_2$ in benzene at 80 °C gave **5a** (R = CHMeOEt) in 70% yield. Acid treatment[7] of **5a**, followed by base treatment[7] of the resulting cyanohydrin **5b** (R = H), gave **6** in 85% overall yield.[11]

Stereoselective epoxidation of **6** (t-BuOOH-KH/THF at -20 °C)[2] provided the desired epoxide **7** in 76% yield; none of the stereoisomer was detected in the crude product.[12] Rationalization for this high stereoselectivity was available by MM2 calculations of the model compound **10** as described above. They predict that the peripheral addition of peroxide should proceed through the most likely conformations[13] **6A** and (or) **6B** to give the β-epoxide **7**. Transformation[14] of **7** to periplanone B required three operations; (1) generation of the exocyclic diene at C(5); (2) introduction of the ketone at C(10); (3) epoxidation of the ketone at C(1). Deprotection of the silyl group (Bu_4NF; 81% yield) and selenation of the resulting alcohol (o-$NO_2C_6H_4SeCN$, Bu_3P/THF) and elimination of the o-nitrophenyl selenide (H_2O_2/THF) gave the diene **8a** (mp 83-86 °C) in 82% yield. The regioselective α-oxidation of **8a** ($LiN(TMS)_2$/THF at -70 °C and then $O_2/P(OEt)_3$[15]; 50% yield) and oxidation of the resulting α-hydroxy ketone **8b** (mp 109-111 °C) with PCC afforded the diketone **8c** in 70% yield. Epoxidation at C(1) of **8c** (Me_3SI/Me_2SO/NaH) gave the (±)-periplanone B (**9**) in 54% yield; the C(10)-diepoxide was also formed in 17% yield. None of this triepoxide or any stereoisomer at C(1) were detected. Satisfactory ^1H NMR (300 MHz), IR, and MS spectral properties of the synthetic (±)-periplanone B were obtained.

Acknowledgment. We express our thanks to Prof. Yoshikazu Shizuri (Keio University, Japan), Dr. Katsuhiko Kushida (Varian Instruments Ltd., Japan), and Dr. Yoshiyuki Nakamura (Tokyo Institute of Technology) for measurement of mass and NMR spectra.

Supplementary Material Available: Experimental details and spectral data of compounds in this paper (50 pages). Ordering information is given on any current masthead page.

(10) The stereostructures of syn product **2a** and anti product were determined by ^1H NMR coupling constants after conversion to the corresponding cyclic carbonates.

(11) Cyclization of **4b** (44-g scale), followed by acid and base treatments gave **6** in 58% overall yield (three steps).

(12) ^1H and ^{13}C NMR spectra and GLC, HPLC analyses of the crude reaction mixture showed the absence of the isomeric epoxide. Moreover, the structure of **7** was confirmed by the conversion of **7** to the Schreiber's intermediate.

(13) ^1H NMR spectrum of **6** at -30 °C indicated the presence of two conformers similar to conformers **10A** and **10B**.

(14) These operations were carried out in a similar manner to that reported by Schreiber[3] with several modifications. Details are available in supplementary material.

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Highly Efficient Asymmetric Reduction of α-Tertiary Alkyl Ketones with Diisopinocampheylchloroborane

Summary: (-)-Diisopinocampheylchloroborane, which reduces many aralkyl and heteroaralkyl ketones with remarkably high stereoselectivity, has now been found to reduce α-tertiary alkyl ketones with similar high enantiomeric excess. Such ketones have resisted asymmetric reduction by Alpine-Borane and many other reagents previously described.

Sir: Practical procedures for the synthesis of optically active secondary alcohols, highly useful chiral building blocks, have been actively explored by organic chemists in recent years. One convenient approach has been the chiral reduction of prochiral ketones.[2] Many new reagents have been described in the recent past to achieve such asymmetric reductions. Modifications of lithium aluminum hydride using resolved 2,2'-dinaphthol[3] and of borane, using amino alcohols,[4] are representative examples. Midland and his co-workers introduced the trialkylborane, B-(3-pinanyl)-9-borabicyclo[3.3.1]nonane (Aldrich, Alpine-Borane)[5] and the modified borohydride reagent,

(1) Postdoctoral research associate on Grant DAAG 29-85-K-0062 from the United States Army Research Office.

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