The total acquisition time for Figure 1 was 8 h. However, adequate kinetic data could be obtained in 2 h and trial spectra in 30 min. Thus this technique can be competitive with the previous saturation-transfer technique. Moreover, the time required for the 2D experiments is nearly independent of the number of sites (if chemical shifts are well separated), whereas the time required for the multiple saturations increases with the number of sites. Therefore, the 2D technique is likely to be preferable with many sites, but not with only two sites.

The 2D technique is essential for thioacetamide. Hydroxylic solvents are required for proton exchange, and viscous solvents are required to sharpen NH resonances. In such solvents the peak separation between H_E and H_Z is quite small—0.06 ppm in the solvent mixture used here. Such a close spacing would not permit selective irradiation for a saturation-transfer study. However, the 2D technique does provide quantitative kinetic data.

Acknowledgment. We are greatly indebted to Dr. John Wright for programming the Nicolet 293-B programmer and 1180-E computer to cycle through the pulse phases and to manipulate the data efficiently. Dr. Eric R. Johnston performed some preliminary experiments. This research was supported by National Science Foundation Grant CHE 81-16800.

Registry No. $CH_3C(SH)=NH$, 65680-21-9; acrylamide, 79-06-1; thioacetamide, 62-55-5.

Cyclobutene Bridgehead Olefin Route to the American Cockroach Sex Pheromone, Periplanone-B

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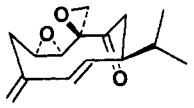
Periplanone-B, the potent sex attractant and sex excitant pheromone of the American cockroach, *Periplaneta americana*, escaped complete stereochemical assignment of structure for the first 25 years of combined studies from several research groups. Persoons and his co-workers were able to isolate and purify a small quantity (200 μg) of periplanone-B, and in 1976, on the basis of their extensive spectroscopic studies, established the constitution as shown in **1**.[2] Through conformational analysis of germacranoid



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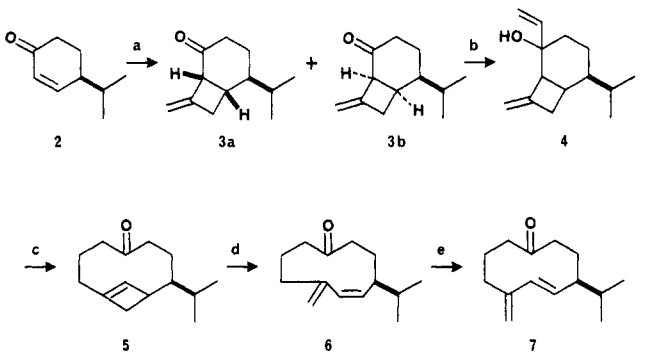
synthetic intermediates, Still was able to deduce the relative stereochemistry of periplanone-B on route to the first total synthesis of this substance.[3] A combination of X-ray, synthetic, and chiroptical techniques finally established the absolute configuration of periplanone-B as shown in **1**.[4]

The challenging structural features of periplanone-B in combination with the practical implications of the potent attractant property[5] of the cockroach pheromone render **1** as an attractive target for further synthetic studies. Herein, we report on our investigations which have resulted in a new total synthesis of (±)-periplanone-B.

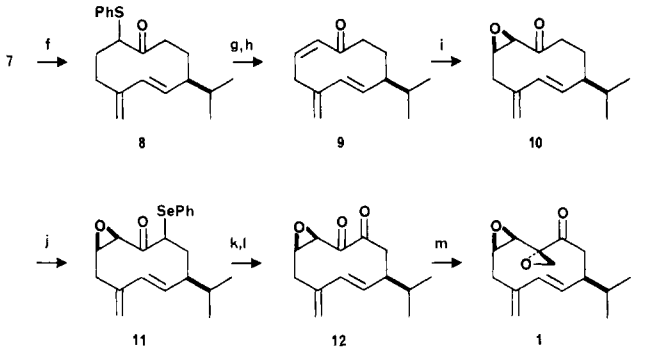
Our synthesis commenced with photocycloaddition of allene and 4-isopropyl-2-cyclohexen-1-one[6] (10.6 g), which provided a 2:1 mixture of the anti (**3a**)[7] and syn (**3b**)[8] head-to-head[9] photoadducts (9.9 g, 72% yield)[10] (Scheme I). Although **3a** and **3b** can be isolated by HPLC (10-μm Porasil, 9% EtOAc/hexane)

Scheme I[a]



[a] (a) $CH_2=C=CH_2$, Et_2O, $h\nu$ (450-W Hanovia lamp equipped with a Pyrex filter), 72% (**3a:3b** = 2:1), 30 °C. (b) $CH_2=CHMgBr$, Et_2O, -78 °C, 63%. (c) KH, 5 equiv of 18-Cr-6, THF, 60 °C, 25 min. (d) Toluene, 175 °C, 20 h, 77%. (e) Benzene, $h\nu$ (450-W Hanovia lamp equipped with a Vycor filter), 82%.

Scheme II[a]



[a] (f) THF, $LiN(SiMe_3)_2$, -78 °C, $PhSSO_2Ph$, regioselectivity = 16:1. (g) aqueous MeOH, $NaIO_4$, 71% from 7. (h) Toluene, 110 °C, 45%. (i) THF, *t*-BuOOH, KH, 0 °C, 83% (4:1) mixture of β:α epoxides). (j) THF, $LiN(SiMe_3)_2$, -78 °C, PhSeBr, 83%. (k) 30% H_2O_2, THF, 97%. (l) THF, Ac_2O, NaOAc; then MeOH, H_2O, K_2CO_3, 60%. (m) Me_2SO, THF, $(Me)_3S^+I^-$, dimsyl (NaH), 62%.

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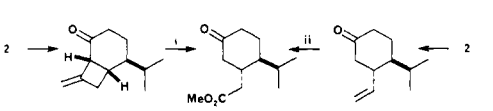

i: O_3, MeOH, K_2CO_3. ii: (1) disiamylborane; $H_2O_2^-$, OH; (2) Jones oxidation; (3) CH_2N_2.

(1) Searle Scholar, 1982–1985.
(2) (a) Persoons, C. J.; Verwiel, P. E. J.; Ritter, F. J.; Talman, E.; Nooijen, P. F. J.; Nooijen, W. J. *Tetrahedron Lett.* **1976**, 2055. (b) Talman, E.; Verwiel, J.; Ritter, F. J.; Persoons, C. J. *Isr. J. Chem.* **1978**, *17*, 227. (c) Persoons, C. J.; Verwiel, P. E. J.; Talman, E.; Ritter, F. J. *J. Chem. Ecol.* **1979**, *5*, 219.
(3) Still, W. C. *J. Am. Chem. Soc.* **1979**, *101*, 2493.
(4) Adams, M. A.; Nakanishi, K.; Still, W. C.; Arnold, E. V.; Clardy, J.; Persoons, C. J. *J. Am. Chem. Soc.* **1979**, *101*, 2495.
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(6) Prepared by either of two methods: (a) Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207. (b) Krapcho, A. P.; Bothner-By, A. A. *Ibid.* **1959**, *81*, 3658.
(7) The stereochemistry was assigned on the basis of chemical correlation (eq 1) with the product of the copper-catalyzed conjugate addition of vinylmagnesium bromide to cryptone 2, a reaction process known to occur with trans stereoselectivity.[11]
(8) For another example of predominant "anti" addition and a discussion, see: Cargill, R. L.; Morton, G. H.; Bordner, J. *J. Org. Chem.* **1980**, *45*, 3929.
(9) (a) Corey, E. J.; Bass, J. D.; LaMahieu, R.; Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570. (b) Eaton, P. E. *Tetrahedron Lett.* **1964**, 3695.
(10) For a preliminary account of this approach, see: Schreiber, S. L.; Santini, C. *Tetrahedron Lett.* **1981**, *22*, 4651.
(11) Posner, G. H. In "Organic Reactions"; Dauben, W. G., Ed.; Wiley: New York, 1972, Vol. 19, p 1.

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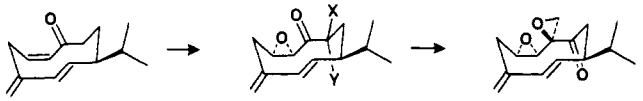
Scheme III



and have been converted separately to the *trans*-butadiene **7**, a more convenient procedure avoided the chromatography. The two ring fusion stereocenters are returned to achiral, trigonal centers in the reaction sequence; thus both photoadducts converge on the same end product. Consequently, on large runs the 2:1 mixture of **3a** and **3b** was employed, allowing for greater material throughput. Stereospecific addition of vinylmagnesium bromide to the convex face of **3a** and **3b** provided the expected 2:1 mixture of allylic carbinols **4**.[10] Anion-accelerated oxy-Cope rearrangement[12] proceeded smoothly to provide the 2:1 mixture of cyclobutene bridgehead olefins **5** in 75% yield, despite the poor overlap of the 1,5-diene system present in **4** as judged by inspection of molecular models.[13] Electrocyclic ring opening provided a 2:1 mixture of cis- and trans-diene isomers (**5a** → 3:1 (**6**:**7**), **5b** → 2:3 (**6**:**7**)),[10] which could be separated by flash chromatography.[14] Photoisomerization of cis-diene **6** or trans-diene **7** in benzene established a photostationary equilibrium consisting of a 15:1 mixture enriched in the trans isomer.[10] Chromatography of thermolysis mixture was not required; the mixture could be directly photoisomerized to provide **7** in 70–75% isolated yield.

We have observed a high degree of regio- and stereoselectivity in the formation and trapping of 10-membered ring ketone enolates; one of these reactions provided the basis for the successful completion of the periplanone-B synthesis (Scheme II).[15] Lithium hexamethyldisilazide promoted enolization of **7** at −78 °C for 60 min and sulfenylation with Trost's reagent[16] provided a 16:1 regioisomeric mixture of monosulfenylated ketones (each as a single stereoisomer). The major C_2 (periplanone-B numbering) sulfide **8** was not separated from its minor regioisomer, since pyrolysis of the corresponding sulfoxides exhibited a substantial difference in rate, affording the readily separable cis enone and the more polar unreacted minor C_{10} sulfoxide.

At this stage, completion of the synthesis required incorporation of the two remaining epoxides and the C_{10} ketone. The Still synthesis of periplanone-B provided the expectation that stereochemically controlled bisepoxidation of the enone could be achieved (Scheme III).[3] Support for this premise was forthcoming.

Stereoselective epoxidation of **9** provided a 4:1 mixture of cis epoxides in which the major component was the desired isomer **10**.[3] Introduction of the C_{10} keto functionality began with the regio- and stereospecific selenenylation of epoxy ketone **10** to provide the selenide **11**. Oxidation afforded the corresponding selenoxides which could be isolated without complications resulting from selenoxide elimination. Selena–Pummerer rearrangement[17] and saponification afforded the α-diketone **12**. Monoepoxidation with dimethylsulfonium methylide provided, as the major product, (±)-periplanone-B, which exhibited spectral properties (UV, MS, IR, ^{13}C NMR, ^1H NMR) in accord with the structure. Comparison with the 300-MHz ^1H NMR spectrum of the natural material[2c] indicated these substances were the same. Furthermore, bioassay of the synthetic material, according to the reported method,[4] provided the response expected for the sex pheromone.

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(14) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
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Tunneling in the Automerization of Cyclobutadiene

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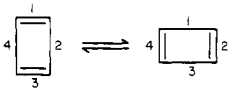
Carpenter[1] recently has communicated the possiblity that tunneling is the major pathway for the automerization (1) of



(1)

cyclobutadiene below 0 °C. He emphasized that the narrowness of the barrier makes this bond-shifting reaction "especially susceptible to tunneling" although heavy (carbon) atoms are involved. Carpenter carried out a one-dimensional tunneling calculation based on a vibrational frequency of cyclobutadiene multiplied by the transmission coefficient (TC) expression of Bell[2] for a barrier that is an inverted truncated parabola. The purpose here is to point out that such tunneling rates are much lower than those obtained by considering one-dimensional tunneling in a symmetric double-minimum potential in terms of the energy splittings (ES) ΔE_i characteristic of the levels of such a potential; $\Delta E_i = E_{i^-} - E_{i^+}$ where + and − refer to symmetries of the wave functions, 0^+ is the ground state, $E_{i\pm} < E_{(i+1)\pm}$ and $\Delta E_i < \Delta E_{i+1}$. For a one-dimensional symmetric potential, the ES method is the correct one for calculating tunneling rates. The finding that the TC method underestimates the tunneling rates confirms earlier calculations[3] and has been rationalized in terms of quantum mechanical resonance between the levels in the two symmetric wells, ignored in the TC method.

Carpenter modeled the reaction coordinate as a single stretching motion; in his model an inverted parabolic potential energy barrier separates the diatomic molecule (26–26) configuration with internuclear separation corresponding to the minimum energy of the C=C bond from the configuration with internuclear separation corresponding to the C—C bond. The potential and correspondingly the transmission coefficients are completely determined by the height of the potential barrier and the difference between the lengths of the single and the double bonds, chosen by Carpenter as 10.8 kcal/mol and 0.198 Å, respectively. Carpenter assumed a harmonic oscillator frequency of 1000 cm^{-1} along the reaction coordinate in the initial configuration, a Boltzmann distribution of pseudo-diatomic molecules among states corresponding to this frequency, and a tunneling rate from each of these states equal to the frequency times the transmission coefficient. Rates obtained at −50 and −10 °C were 8.08×10^4 and 4.65×10^5 s^{-1}, respectively.

The ES calculations here were carried out with a symmetric double-minimum potential, $V(R) = AR^2 + Be^{-CR^2}$, where A, B, and C are parameters, and $R = r_1 + r_3 - r_2 - r_4$, with r_i the ith carbon–carbon distance as indicated in (1). The parameters A,

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