viously described sample by comparison of IR, ^{1}H NMR, and TLC data.

The earlier fractions containing (TLC) a mixture of adducts **15** (R_f 0.64), **16** and other unidentified components was rechromatographed on silica gel to separate early fractions containing the crude cycloadduct **15**. Recrystallization from hexane separated 47 mg (2%) of the adduct **15** as colorless prisms, mp 121-122 °C, that were identified with a previously described sample by comparison of IR, ^{1}H NMR, and TLC data.

The middle chromatographic fractions containing (TLC) the adduct **16** and other unidentified materials were chromatographed on silica gel impregnated with $AgNO_3$ by employing an ethyl acetate-hexane eluent (1:1, v/v). The center fractions were collected and rechromatographed on plain silica gel to separate 242 mg (9%) of the crude adduct **16** as a colorless liquid. This sample of the cycloadduct **16** was identified with the previously described sample by comparison of ^{1}H NMR spectra and by reaction of this sample with bromine to form the crude tribromide **18**, mp 149-153 °C dec, that was identified with the previously described sample by comparison of ^{1}H NMR and mass spectral data.

Reaction of Enone 1c with Oxygen. A mixture of 324 mg (1.11 mmol) of the bromo ketone **2** and 20 mL of anhydrous oxygen-free Et_3N was stirred at 25 °C under an N_2 atmosphere for 12 h. The resulting slurry was centrifuged, and the supernatant liquid was separated and then concentrated under reduced pressure. The residual enone **1c**, a yellow liquid, was dissolved in 30 mL of anhydrous oxygen-free CH_3CN. After the solution had been cooled to -20 °C, a slow stream of anhydrous O_2 gas was passed through the cold solution for 1.5 h. The resulting yellow-tan suspension was filtered through a glass frit, and the residual tan solid was washed with two additional portions of cold (0 °C) CH_3CN. The residue was dried under reduced pressure to leave 154 mg (54%) of a tan solid, mp 75-80 °C dec, believed to be a mixture of peroxides **9** and **11** mixed with some residual CH_3CN. Solutions of this material in $CHCl_3$ or $CDCl_3$ exhibited the following spectral properties: IR ($CHCl_3$) 1725 cm^{-1} (nonconjugated C=O); ^{1}H NMR ($CDCl_3$) δ 6.3-8.2 (br m, ca. 5 H, aryl CH), 0.8-3.4 (br m, ca. 12 H aliphatic CH including a sharp CH_3CN singlet at 1.97); ^{13}C NMR ($CDCl_3$ at -20 °C) broad peaks at 201.9, 130.8, 130.2, 128.9 (2 C atoms), 126.1 (2 C atoms), 89.5, 85.6, 43.9, 33.5, 30.3 (3 C atoms, ?), 19.6 ppm, accompanied by sharp peaks at 117.0 and 2.1 ppm for CH_3CN, at 0.0 ppm for Me_4Si, and at 77.6, 77.2, and 76.8 ppm for $CDCl_3$. When the sample was allowed to warm to 25 °C and then the ^{13}C NMR spectrum determined at 35 °C during a 1-h period, the spectrum exhibited a set of sharp NMR peaks attributable to presence of CH_3CN and ca. 20% of the triketone **6**. In addition, broad peaks attributable to the peroxide **9**-dioxetane **11** mixture were evident at 201.4, 89.8, 85.9, 44.2, 30.5, and 19.7 ppm. After the $CDCl_3$ solution had been heated to 55 °C for 30 min, the ^{13}C NMR spectrum exhibited a set of sharp signals corresponding to the triketone **6**, and the broad peaks attributable to the peroxide-dioxetane mixture were no longer present. In a comparable experiment, a solution of 140 mg (0.57 mmol) of the crude peroxide **9**-dioxetane **11** mixture in 1.5 mL of $CDCl_3$ was heated to 55 °C for 30 min during which time the solution became bright yellow in color. This solution was concentrated to leave 139 mg of the crude triketone **6**. Chromatography on silica gel followed by recrystallization from Et_2O separated 119 mg (85%) of the triketone **6** as yellow prisms, mp 71.0-72.5 °C, that were identified with an authentic sample by comparison of IR and ^{1}H NMR spectral data.

Registry No. **1a**, 71370-30-4; **1b**, 74262-53-6; **1c**, 85319-04-6; **1d**, 85319-05-7; **2**, 81408-13-1; **3**, 38259-33-5; **4**, 85319-06-8; **5**, 85335-10-0; **6**, 85319-07-9; **7**, 81408-12-0; **8**, 4556-09-6; **9** (polymer), 85319-13-7; **9** (replating unit), 85319-14-8; **11**, 85319-08-0; **13**, 85319-09-1; **15**, 85319-10-4; **16** (isomer 1), 85319-11-5; **16** (isomer 2), 85354-05-8; **18**, 85319-12-6; **21**, 81408-15-3; CH_2=CHCH=CH_2, 106-99-0.

Supplementary Material Available: Descriptions of determination of crystal structures for the diol **5** and the adduct **15**, including tables of atomic coordinates for each compound (8 pages). Ordering information is given on any current masthead page.

Perhydroazulenes. 3. Conformations of the 4-Oxoperhydroazulenes[1]

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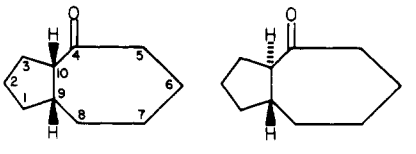
Received June 4, 1982

The conformations of cis (**1**) and trans (**2**) 4-oxoperhydroazulenes have been studied by employing data from X-ray crystal structures of solid derivatives, ^{1}H NMR spectra, ^{13}C NMR spectra, and molecular mechanics calculations. Related studies have been performed with the 2-*tert*-butyl-4-oxoperhydroazulenes **8a** and **9a** and the 10-methyl-4-oxoperhydroazulenes **10** and **11**. Those studies suggest that the trans ketone **2** exists in solution as the conformer TC-1 while the cis ketone **1** exists in a solution as a mixture of equilibrating conformers probably including conformer B-3 and the closely related pair of conformers C-3 and TC-7.

In continuing our studies of the synthesis and conformation of perhydroazulene derivatives,[2,3] we wished to determine the probable conformations for cis (**1**) and trans (**2**) 4-oxoperhydroazulenes. To pursue this investigation, we used the procedure recently devised by DeClercq[4] to



1 2

systematize the earlier conformational study of perhydroazulenes by Hendrickson.[5] This procedure allows all reasonable conformations for a perhydroazulene to be considered and provides a system of nomenclature for the

(1) A portion of this research was supported by Public Health Service Grant R01-GM-30735 from the National Institute of General Medical Science. The execution of this research was also aided by Institutional Research Grants from the National Science Foundation for the purchase of a mass spectrometer and a NMR spectrometer.

(2) House, H. O.; Sayer, T. S. B.; Yau, C. C. *J. Org. Chem.* **1978**, *43*, 2153.

(3) House, H. O.; Yau, C. C.; VanDerveer, D. *J. Org. Chem.* **1979**, *44*, 3031.

(4) DeClercq, P. J. *J. Org. Chem.* **1981**, *46*, 667.

(5) Hendrickson, J. B. *Tetrahedron* **1963**, *19*, 1387.

0022-3263/83/1948-1661$01.50/0

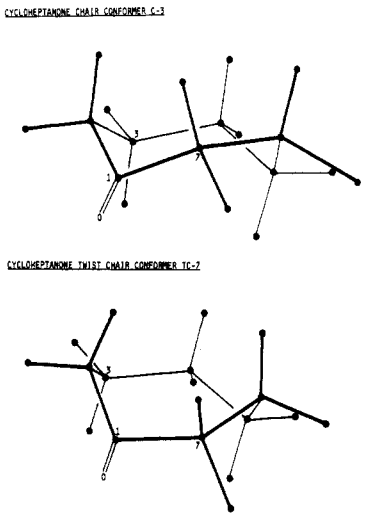


Figure 1. Examples of related chair and twist-chair conformers of cycloheptanone.

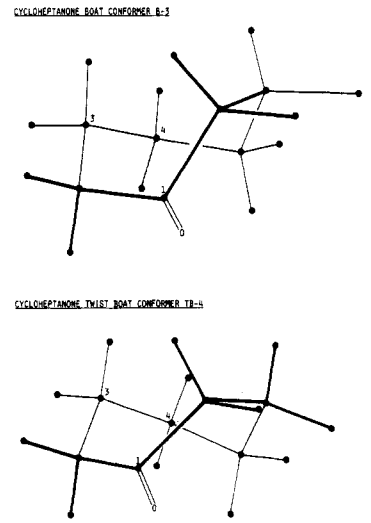


Figure 2. Examples of related boat and twist-boat conformers of cycloheptanone.

various conformations based upon the magnitudes and the signs of the dihedral angles contained within the 7-membered ring. Although DeClercq's procedure[4] also provides a qualitative estimate of the relative energies for various perhydroazulene conformations, we conclude that much more reliable energy estimates could be obtained from force field calculations employing Allinger's MM2 program.[6] Consequently, our computational procedure involved assembly of Drieding molecular models (scale 0.4 Å/cm) for all reasonable conformations suggested by DeClercq's procedure. The carbon atom and oxygen atom coordinates obtained from these molecular models were entered as initial coordinates for energy minimization by the MM2 program. Alternatively, the initial coordinates for certain conformations could be obtained from X-ray crystallographic data.

After energy minimization for a given set of starting coordinates was complete, the designation of the final conformation (which may have changed from the initial imput conformation) was determined by considering the magnitude and signs[7] of the seven dihedral angles con-

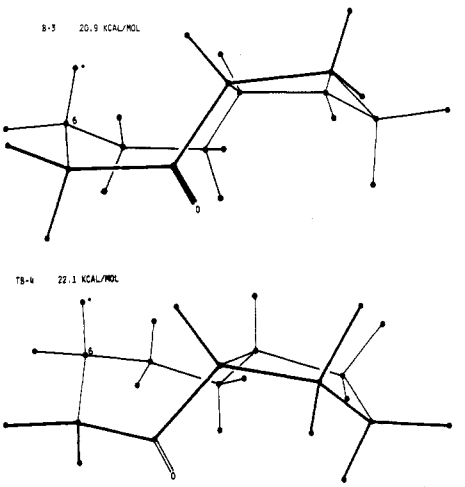


Figure 3. Low-energy conformers of 4-oxo-*cis*-perhydroazulene.

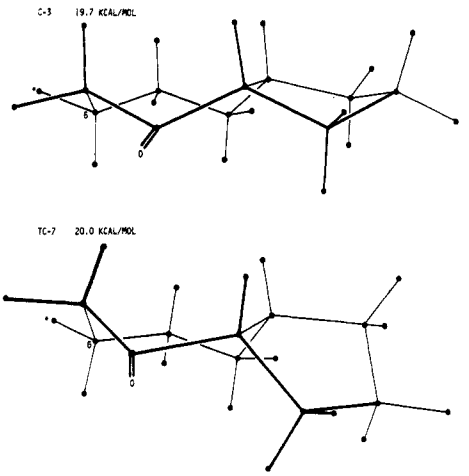
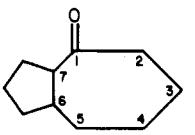


Figure 4. Low-energy conformers of 4-oxo-*cis*-perhydroazulene.

tained within the perhydroazulene seven-membered ring. For purposes of conformational designation, the numbering system illustrated in structure **3** was employed and cycloheptane conformational notation was employed. As illustrated in Figures 1 and 2, each cycloheptanone boat or chair conformer has one or more closely related twist-boat or twist-chair conformers that is formed by slight twisting of a fully eclipsed dihedral angle in the chair or boat conformer. The chair and boat conformers have a plane of symmetry passing through one carbon atom (e.g., C-3 in the chair conformer in Figure 1) while the twist conformers have a C_2 axis of symmetry passing through one carbon atom (e.g., C-4 in the twist-boat conformer in Figure 2).



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Application of the above computational procedures to 4-oxo-*cis*-perhydroazulene (**1**) indicated that two pairs of conformations (B-3 and TB-4 (Figure 3) and C-3 and TC-7 (Figure 4)) had calculated final steric energies significantly lower than the calculated energies (24.3–29.6 kcal) for other

(6) For a review, see: Allinger, N. L. *Adv. Phys. Org. Chem.* **1976**, *13*, 1. We are most grateful to Professor Allinger and his associates and to the University of Georgia Computer Center for allowing us to use the current version of the MM2 program for these calculations.

(7) By convention for a dihedral angle A–B–C–D (180° or less) observed looking through B toward C, the sign is negative if a counterclockwise rotation of line AB is required to superimpose AB upon line CD.

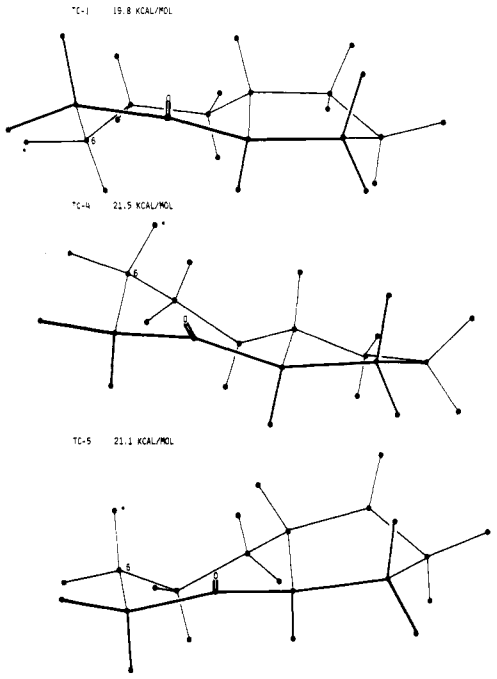


Figure 5. Low-energy conformers of 4-oxo-*trans*-perhydroazulene.

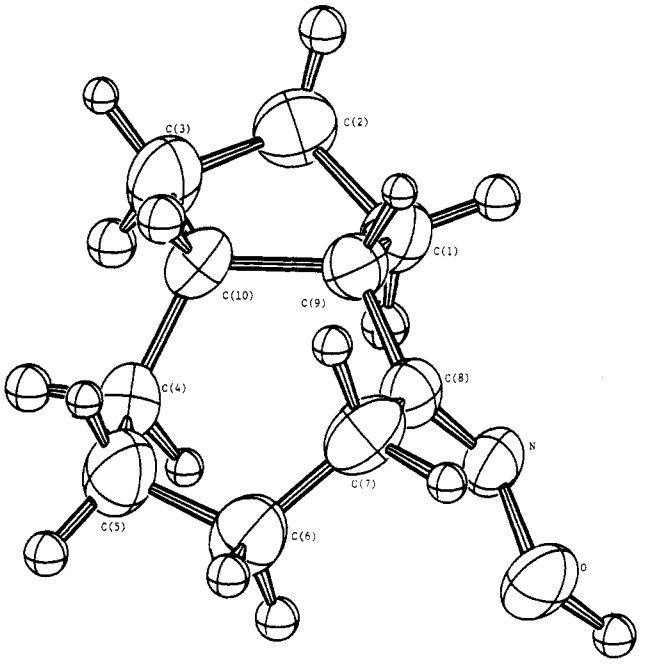
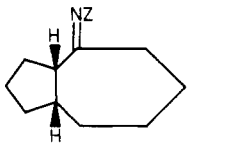
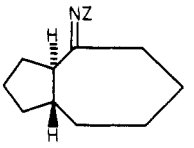


Figure 6. Perspective view of the molecular structure of the oxime of 4-oxo-*cis*-perhydroazulene.

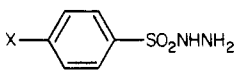
Chart I



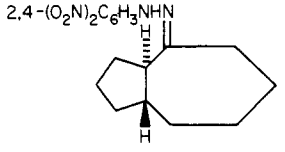
4a, Z = OH
b, Z = $NHSO_2C_6H_4CH_3$-*p*



5a, Z = $NHSO_2C_6H_4Br$-*p*
b, Z = $NHSO_2C_6H_4CH_3$-*p*
c, Z = $NHSO_2C_6H_4Cl$-*p*
d, Z = $NHC_6H_3(NO_2)_2$-2,4



6a, X = CH_3
b, X = Br
c, X = Cl



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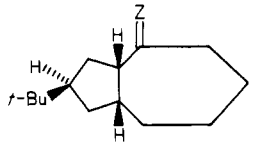
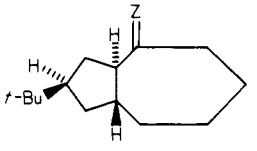


8a, Z = O
b, Z = $NNHSO_2C_6H_4Br$-*p*



9a, Z = O
b, Z = $NNHSO_2C_6H_4CH_3$-*p*

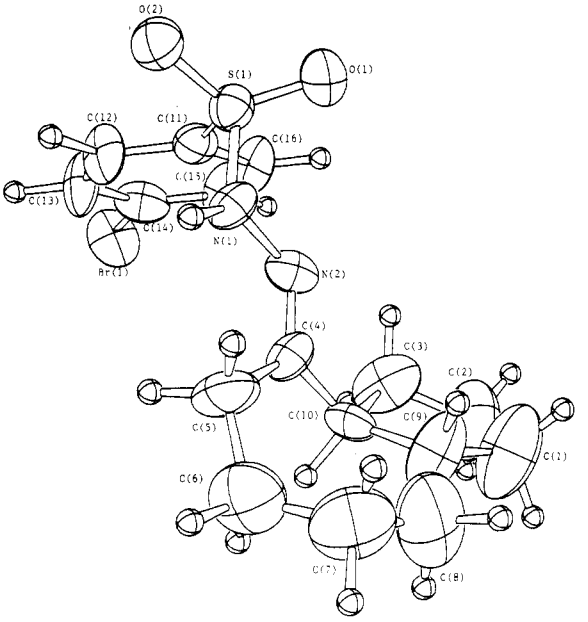


Figure 7. Perspective view of the molecular structure of the brosylhydrazone of 4-oxo-*trans*-perhydroazulene.

reasonable conformations of the ketone **1**. Among the low-energy conformers for the cis ketone **1**, the calculated energies of the chair and twist-chair conformers (Figure 4) are slightly lower than the corresponding boat conformers (Figure 3). When similar computations were done with conformers of the *trans* ketone **2**, three twist-chair conformers (TC-1, TC-4, and TC-5 (Figure 5)) were found to have calculated final steric energies lower than calculated energies (23.1–24.8 kal) for other reasonable conformers. Among these three conformers the calculated final steric energy is lower for the TC-1 conformer than for the closely related pair of conformers TC-4 and TC-5.

An interesting feature emerges when the various low-energy conformations (Figures 3–5) are considered. The conformers fall into two categories. In one group (C-3 and TC-7 of Figure 4 and TC-1 of Figure 5) a β substituent at C-6 (designated as *) will be located in an equatorial position. In the second group of conformers (B-3 and TB-4 of Figure 3 and TC-4 and TC-5 of Figure 5) a corresponding β substituent at C-6 is located in an axial position. These observations suggest that stereochemically correct placement of a sterically bulky substituent at C-6 would allow control of the conformation in the seven-membered ring of these perhydroazulene systems. This implication will be explored further in a subsequent publication.

To examine the actual conformational preferences of the 4-oxoperhydroazulenes, each of the previously prepared[2] ketones **1** or **2** was converted to several solid derivatives **4** or **5** (Chart I), and the suitability of these derivatives for X-ray crystallography was explored. The cis oxime **4a** and the trans brosylhydrazone **5a** were found to be satisfactory, and their crystal structures were determined (see Figures

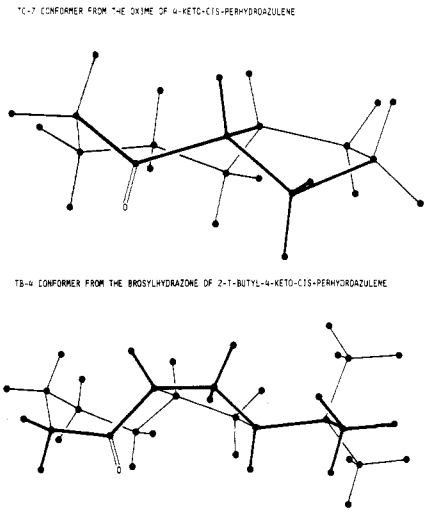


Figure 8. Perspective view of the 4-oxo-*cis*-perhydroazulene conformers present in crystalline derivatives.

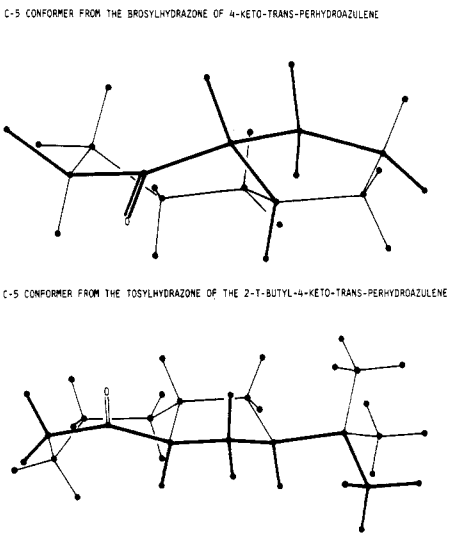


Figure 9. Perspective view of the 4-oxo-*trans*-perhydroazulene conformers present in crystalline derivatives.

6 and 7). The coordinates of the ketone moieties present in these crystal structures were used to prepare the perspective drawings of the cis (Figure 8) and trans (Figure 9) ketone conformations present in these solid derivatives. Figures 8 and 9 also include perspective drawings of the conformations of the 2-*tert*-butyl-4-oxoperhydroazulenes **8a** and **9a** that were found in the crystalline derivatives **8b** and **9b**.[3] Both trans ketone derivatives **5a** and **9b** (Figure 9) correspond to chair conformers C-5, conformations closely related to the twist-chair conformer TC-1 predicted from calculations to the most favorable energetically. While one cis ketone derivative **4a** (Figure 8) has the twist-chair conformer TC-7 predicted from computations to be the more favorable, the second cis ketone derivative **8b** exists as the twist-boat conformer TB-4 that is predicted by calculation[3] to be slightly less stable than a C-3 or TC-7 conformer.

Equilibration studies at 25.0 °C in a MeOH–PhH solution indicate that the energy differences between the cis and trans conformers present in solution are very similar in these two series. The equilibrium composition of the 2-tert-butyl ketones is 11.0% cis ketone **8a** and 89.0% trans ketone **9a**;[3] the corresponding values for the parent ketone are 12.9% cis ketone 1 and 87.1% trans ketone **2**.

The 10-methyl-4-oxoperhydroazulenes (**10** and **11**, Scheme I) were also examined as part of this study. The

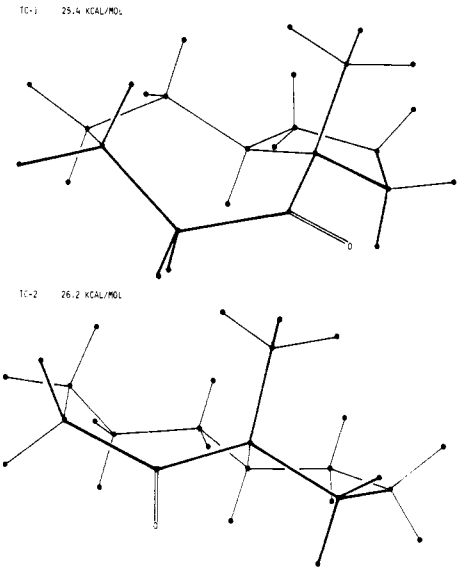


Figure 10. Low-energy conformers of 10-methyl-4-oxo-*trans*-perhydroazulene.

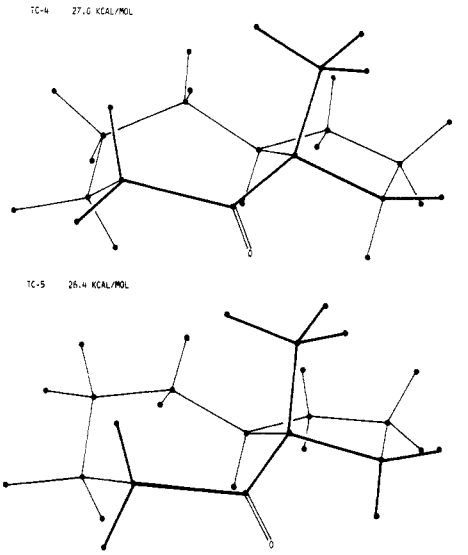


Figure 11. Low-energy conformers of 10-methyl-4-oxo-*trans*-perhydroazulene.

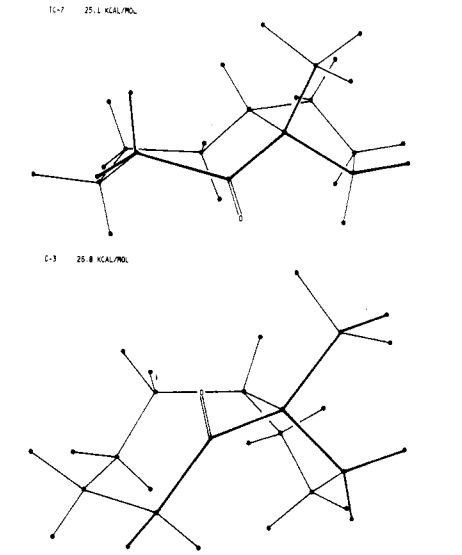
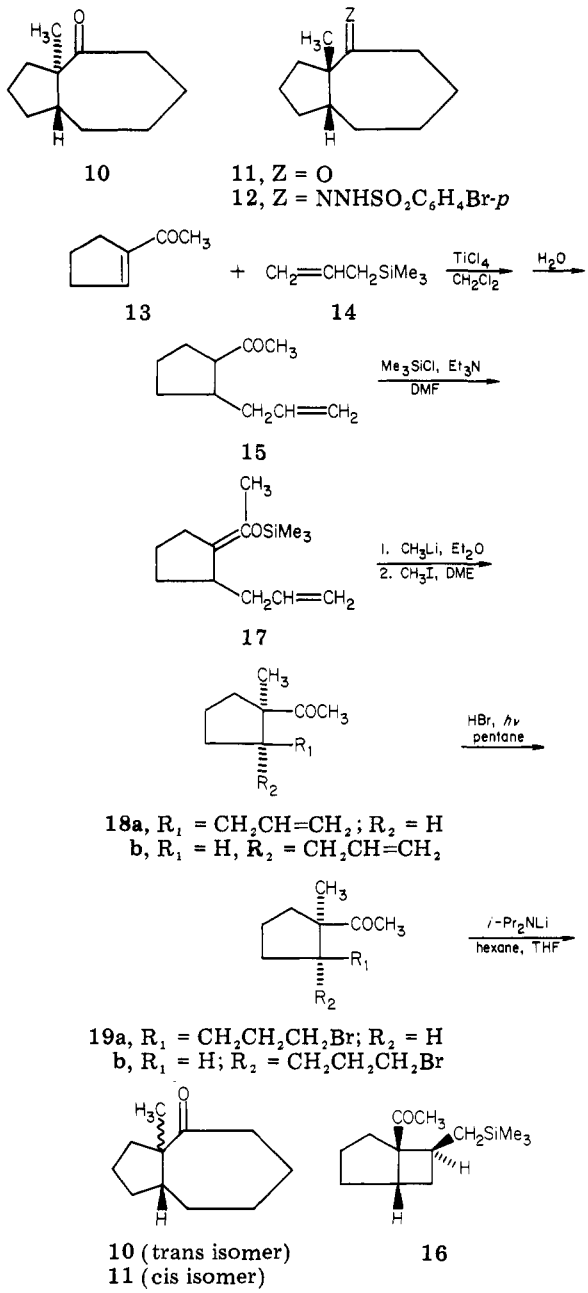


Figure 12. Low-energy conformers of 10-methyl-4-oxo-*cis*-perhydroazulene.

Scheme I



lowest energy conformations found by computation for the trans ketone **10** (TC-1 and TC-2 in Figure 10, TC-4 and TC-5 in Figure 11) correspond to the conformers found for the parent trans ketone **2** with conformer TC-1 again having the smallest computed final steric energy. The low-energy conformers of the cis ketone **11** (TC-7 and C-3 in Figure 12, TC-3 and B-3 in Figure 13) also correspond to the conformers found for the parent cis ketone **1** except that the twist-boat conformer TB-4 found for the parent ketone **1** was replaced by a twist-chair conformer TC-3. The TC-7 conformer of the cis ketone **11** had a slightly smaller computed final steric energy than did the other conformers.

The two 10-methyl ketones **10** and **11** were prepared from the unsaturated ketone **15** by the procedure outlined in Scheme I). The cis and trans isomers were most readily separated at the stage of the unsaturated ketones **18**, and each was converted separately to the 10-methyl ketone **10** or **11**. The stereochemical assignment for the cis ketone **11** was confirmed by conversion to the brosylhydrazone **12** for X-ray crystallographic analysis (see Figure 14). As

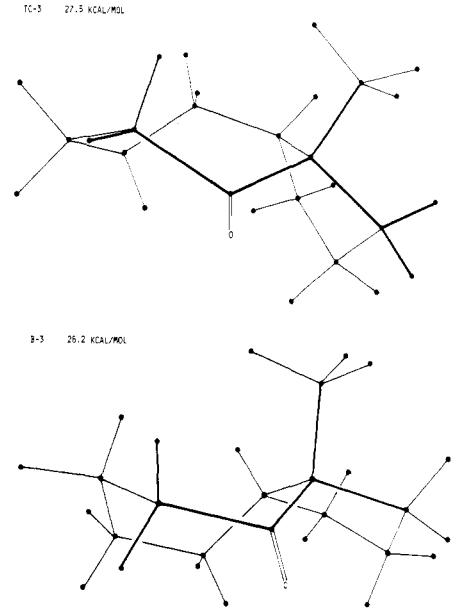


Figure 13. Low-energy conformers of 10-methyl-4-oxo-*cis*-perhydroazulene.

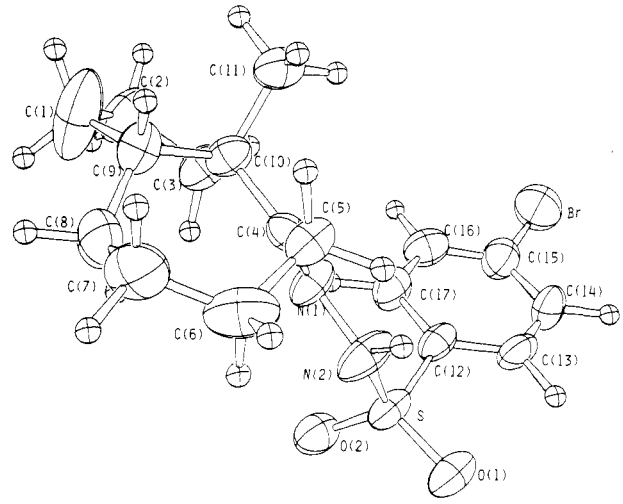


Figure 14. Perspective view of the molecular structure of the brosylhydrazone of 10-methyl-4-oxo-*cis*-perhydroazulene.

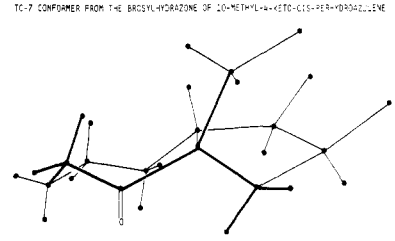


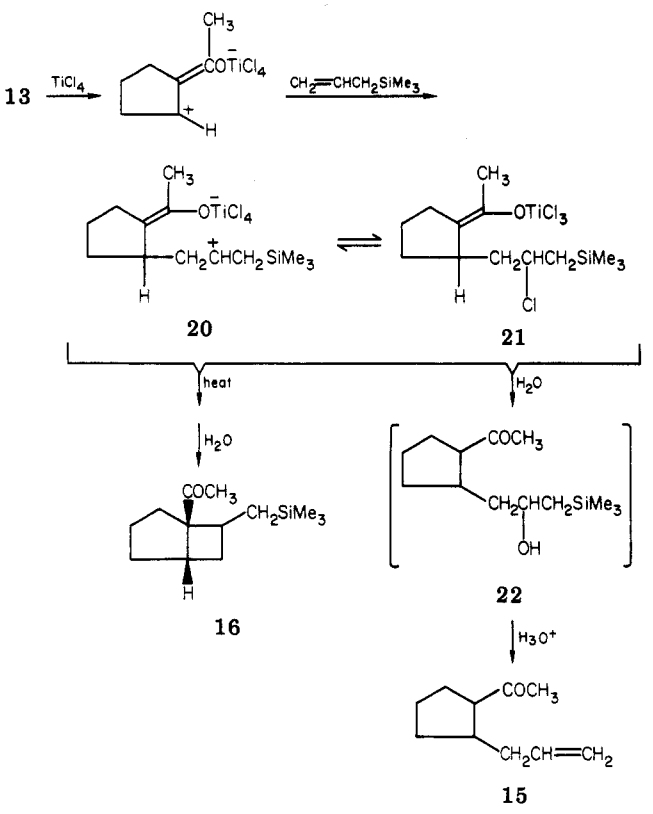
Figure 15. Perspective view of the 10-methyl-4-oxo-*cis*-perhydroazulene conformer present in a crystalline derivative.

illustrated in Figure 15, the perhydroazulene conformer present in this solid derivative **12** is the TC-7 conformer, the conformer calculated to have the lowest final steric energy.

In the course of this study, we were prompted to investigate a recent report[8] that reaction of the enone **13** with the allylsilane **14** in the presence of $TiCl_4$ formed both the unsaturated ketone **15** and a keto silane byproduct assigned the structure and stereochemistry shown in structure **16**. This report was puzzling because the byproduct

(8) Pardo, R.; Zahra, J. P.; Santelli, M. *Tetrahedron Lett.* **1979**, 4557.

Scheme II

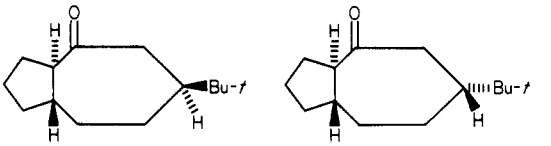


16 had not been present in several previous preparations of ketone **15** in our laboratory[2a] and yet analogous byproducts had been noted[9] in other reactions of enones with allylsilanes. We have now found that the presence or absence of the byproduct **16** is determined by the time and temperature used in generating and subsequently hydrolyzing the reaction mixture. In our standard isolation procedure, H_2O was added to the cold (−30 to −78 °C) reaction mixture and the mixture was stirred until it warmed to 25 °C before the organic phase was separated. With these conditions, we found only the stereoisomeric ketones **15** as reaction products in 83–94% yield. However, if water was added to the cold (−30 to −78 °C) reaction solution and the organic phase was separated rapidly from the aqueous phase (present mainly as ice), then the products were the ketones **15** (71% yield) and the keto silane **16** (22% yield). In another experiment, the cold (−78 °C) reaction solution obtained from the enone **1**, the silane **3**, and $TiCl_4$ were rapidly added to boiling CH_2Cl_2 and then this warm solution was hydrolyzed. From this procedure, the yield of the keto silane **16** (37%) was increased at the expense of the yield of the unsaturated ketone **15** (35%). Appropriate control experiments demonstrated that the keto silane **16** in CH_2Cl_2 solution was not converted to the unsaturated ketone **15** either by treatment with $TiCl_4$ followed by treatment with H_2O or by treatment with a mixture prepared from $TiCl_4$ and H_2O. The spectral data for our product correspond to the previously described[8] data; however, in our opinion the stereochemical assignment[8] is not unambiguously established by the spectral data available.

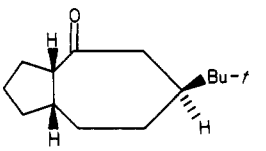
Our data are consistent with the reaction path illustrated in Scheme II in which one or more intermediates such as **20** or **21** can react with water to form successively a β-hydroxy silane **22** and an unsaturated ketone **15**. If the intermediates **20** and/or **21** are warmed to 25 °C prior to complete hydrolysis, competing cyclization to form the keto silane **16** can occur.

Several lines of evidence suggest that both the solid-state and the solution conformations of the trans ketones **2** and **9a** correspond to one of the closely related conformers TC-1 (calculated to be of lowest energy, see Figure 5) or C-5 (see Figure 9). The solution and solid-state[10] ^{13}C NMR spectra for the trans ketone brosylhydrazone **5a** resemble each other very closely with the maximum difference between any corresponding peaks being 2.2 ppm for a peak at 129.7 ppm; the average difference between corresponding peaks is ±0.9 ppm. By contrast, the solution and solid-state ^{13}C NMR spectra of the cis ketone oxime **4a** differ significantly. The largest difference between two corresponding peaks is 4.2 ppm of a peak at 20.5 ppm, and the average difference between corresponding peaks is ±2.2 ppm. Also, the locations of the ^{13}C NMR peaks for the trans ketones **2** and **9a** correspond more closely than the locations of the corresponding peaks in the cis ketones **1** and **8a**. Although examination of the ^{13}C NMR spectra of both ketones **1** and **2** at temperatures down to −58 °C failed to provide evidence for two or more conformations, we are presently inclined to believe that solutions of the cis ketones **1** and **8a** are mixtures of two types of low-energy conformers as illustrated in Figures 3 and 4.

Although our efforts to extract useful proton–proton coupling constants from the 300-MHz ^1H NMR spectra of ketones **1**, **2**, **8a**, and **9a** have not yet been successful, the lower field portions of the ^1H NMR spectra (δ 2.0–3.0) for the trans ketones **2** and **9a** are strikingly similar to one another, again suggesting that the two molecules have the same conformation in the perhydroazulene ring. Comparison with the lower field regions of the ^1H NMR spectra for the ketones **23** and **24** (to be described in a subsequent paper) reveals a marked similarity among the spectra for ketones **2**, **9a**, and **23** and a distinct difference from the corresponding spectrum for ketone **24**. As discussed earlier and illustrated in Figure 5, ketone **23** is expected to be held in a TC-1 conformation while ketone **24** is expected to be held in one of the closely related conformations TC-4 or TC-5. Consequently, all of our presently available evidence supports the view that the trans ketones **2** and **9a** are present as TC-1 conformers both in the solid state and in solution.



23 24



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The lower field portions of the 300-MHz ^1H NMR spectra (δ 2.0–3.3) of the cis ketones **1** and **8a** are very similar, again suggesting that these ketones have the same conformation (or mixture of conformations) in solution. However, the NMR spectral data of ketones **1** and **8a** differ

(9) (a) Hosomi, A.; Kobayashi, H.; Sakurai, H. *Tetrahedron Lett.* **1980**, *21*, 955. (b) Jellal, A.; Santelli, M. *Ibid.* **1980**, *21*, 4487. (c) Danishefsky, S.; Kahn, M. *Ibid.* **1980**, *22*, 485.

(10) The solid-state ^{13}C NMR spectra were determined at 50-MHz by Dr. Paul D. Ellis and his associates at the South Carolina Magnetic Resonance Laboratory, Columbia, SC 29208.

substantially from the corresponding NMR data for cis ketone **25**, a ketone to be described in a subsequent paper that is expected to exist in one of the closely related conformations C-3 or TC-7 (see Figure 3). Thus, our present evidence all suggests that the cis ketones **1a** and **8a** exist in solution as a mixture of the closely related pair of conformers C-3 and TC-7 (Figure 3) and an additional low-energy conformer such as B-3 (Figure 2).

Experimental Section[11]

Preparation of the 4-Oxoperhydroazulenes 1 and 2. Previously described procedures[2,3] were used to synthesize the enone **13** and the allylsilane **14**. In the subsequent $TiCl_4$-promoted addition of the allylsilane **14** to the enone **13**, the only products found previously[2] and initially in the present study were the cis and trans isomers of the unsaturated ketone **15** [bp 84–85 °C (10 mm), n^{25}_D 1.4631, 86% yield]. Since other workers have reported[8,9] the formation of the keto silane **16** or related byproducts in reactions of this type, we investigated the reaction in more detail. The difference in the two procedures proved to involve the time and temperature used for hydrolysis in the reaction. In our earlier studies,[2] water was added to the cold (−30 to −70 °C) reaction mixture and the hydrolyzed mixture was allowed to warm to 25 °C *before* the organic layer was separated, dried, and distilled. Under these circumstances only the stereoisomeric ketones **15** were found in the reaction product. However, if the organic layer was separated from the "hydrolyzed" mixture before the temperature of the mixture (ice and a CH_2Cl_2 solution) had warmed to 0 °C, then significant amounts of the byproduct **16** were found. For example, after a cold (−78 °C) solution of 35.0 g (0.318 mol) of enone **13** in 700 mL of CH_2Cl_2 had been treated successively with 60.3 g (0.318 mol) of $TiCl_4$ and with a solution of 39.9 g (0.349 mol) of silane **14** in 500 mL of CH_2Cl_2, the resulting purple solution was stirred at −78 °C for 1.5 h. Then 350 mL of H_2O was added and the mixture was rapidly transferred to a separatory funnel. At this stage, the mixture was mainly ice and a CH_2Cl_2 solution. The pink-colored organic layer was rapidly separated, dried, and concentrated. Fractional distillation of the residual pale green liquid separated 34.3 g (71%) of unsaturated ketone **15** [bp 45–47 °C (1.5 mm), n^{25}_D 1.4628] that was identified by comparison of IR and NMR spectra. Later fractions contained 15.5 g (21.7%) of the keto silane **16** as a colorless liquid: bp 65–68 °C (1.5 mm); n^{25}_D 1.4732; IR (CCl_4) 1695 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 0.9–3.0 (15 H, m, aliphatic CH including a CH_3CO singlet at 2.20), 0.00 (9 H, s, Me_3Si); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 211.2 (s), 69.0 (s), 47.6 (d), 39.5 (t), 36.9 (t), 32.9 (t), 28.0 (d), 25.5 (q), 24.7 (t), −3.3 ppm (q, 3 C atoms); mass spectrum, *m/e* (rel intensity) 224 (M^+, 8), 183 (43), 111 (50), 73 (100), 43 (27). On GLC analysis (silicone fluid SE-30 on Chromosorb P), the keto silane **16** exhibited a single peak at t_r = 22.2 min under conditions where the unsaturated ketone **15** exhibited a peak at t_r = 7.2 min. Our ^{13}C NMR and mass spectra match closely the spectra reported[8] earlier, confirming the identity of the two samples. However, we find no compelling evidence to confirm the assigned[8] stereochemistry either in the previous report or in our spectral measurements.

In a related experiment, a cold (−78 °C) purple reaction solution was prepared in the usual way from 200 mg (1.8 mmol) of enone **13**, 379 mg (2.0 mmol) of $TiCl_4$, 249 mg (2.2 mmol) of the silane **14**, and 8 mL of CH_2Cl_2. One-half of this cold reaction solution was added to 10 mL of refluxing CH_2Cl_2 and refluxed for 20 min. The resulting solution, whose color changed from deep purple to pale purple during this heating, was then mixed with water, subjected to the usual isolation procedure, and finally chromatographed on silica gel to separate 43 mg (35%) of the unsaturated ketone **15** (n^{25}_D 1.4610) and 68 mg (37%) of the silyl ketone **16** (n^{25}_D 1.4732). The second half of the cold (−78 °C) reaction solution was allowed to warm to 25 °C during 85 min, after which H_2O was added and the usual isolation procedure was followed. The crude liquid product (131 mg) contained (TLC on silica gel with an ethyl acetate–hexane eluent, 1:9, v/v) the silyl ketone **16** (R_f 0.56), the unsaturated ketone **15** (R_f 0.47), and a series of more polar unidentified components (R_f 0.0–0.15). Chromatography on silica gel separated 55 mg (43%) of the unsaturated ketone **15** (n^{25}_D 1.4611) and 12 mg (6%) of the silyl ketone **16** (n^{25}_D 1.4730).

A solution prepared from adding 84 mg (0.45 mmol) of $TiCl_4$ to 0.5 mL of H_2O was added to a solution of 100 mg (0.45 mmol) of the keto silane **16** in 1.0 mL of CH_2Cl_2. After the mixture had been stirred at 25 °C for 45 min, it was washed with aqueous NaCl, dried, and concentrated. The residual liquid (95 mg, n^{25}_D 1.4730) was identified as the starting keto silane **16** by TLC analysis and by comparison of IR and ^1H NMR spectral data. Similarly, a cold (−78 °C) yellow solution prepared from 100 mg (0.45 mmol) of the keto silane, 84 mg (0.45 mmol) of $TiCl_4$, and 1.0 mL of CH_2Cl_2 was stirred at −78 °C for 1 h, and then 0.5 mL of H_2O was added. The temperature of the mixture was allowed to rise to 25 °C with stirring during 20 min, and then the mixture was subjected to the previously described isolation procedure. The residual liquid (93 mg, n^{25}_D 1.4733) was identified as the unchanged keto silane **16** by comparison of IR and ^1H NMR spectral data.

The unsaturated ketone **15** (a mixture of stereoisomers) was converted successively via the bromo ketone [bp 76–77 °C (0.05 mm), n^{25}_D 1.4927, 82% yield] and to the perhydroazulenones **1** and **2** [bp 103–104 °C (10 mm), n^{25}_D 1.4875, 93% yield] by previously described procedures.[2] This product contained[12] a mixture of ca. 15% of the cis ketone **1** (t_r 135.0 min) and ca. 85% of the trans ketone **2** (t_r 153.7 min).

The isomeric ketones were separated by HPLC employing a Waters Model ALC 202 chromatograph fitted with a LDC RefractoMonitor detector and a 12 mm × 25 cm column packed with C-18 reverse-phase packing. Employing a 4:1 (v/v) H_2O–MeOH eluent with a flow rate of 1 mL/min, the retention times of the cis and trans ketones **1** and **2** were 5.5 and 8.3 min, respectively. Pure samples of cis ketone **1** (n^{25}_D 1.4881), and trans ketone **2** (n^{25}_D 1.4869) were identified with previously described[2] samples by comparison of IR, ^1H NMR, ^{13}C NMR, and mass spectral data. The ^{13}C NMR spectrum ($CDCl_3$) of each ketone **1** and **2**, determined at −58 °C, was not appreciably different from the ^{13}C NMR spectrum determined at 30 °C. The ^1H NMR spectra of ketones **1** and **2**, determined in $CDCl_3$ at 300 MHz, exhibited the following features: trans isomer **2** δ 2.76 (1 H, m, 838.6, 830.5, 828.0, 822.1 Hz, CHCO), 2.53 (1 H, m, 775.7, 772.1, 768.8, 767.3, 758.2, 757.1, 753.8, 750.5 Hz, CHCO), 2.35 (1 H, m, 724.9, 721.3, 712.5, 708.8, 706.6, 702.6, 694.2, 690.2 Hz, CHCO), 0.8–2.2 (13 H, m, aliphatic CH); cis- isomer **1** δ 3.10 (1 H, m, 939.3, 931.0, 928.9, 922.8, 920.5, 912.3 Hz, CHCO), 2.40 (3 H, m, 755.1, 751.2, 745.6, 741.6, 737.6, 731.9, 728.3, 718.4, 715.5, 709.8, 706.8, 704.8, 702.0, 696.1, 693.2, 689.8, 685.4, 683.8, 675.7, 674.2, 671.9, 637.2 Hz, CHCO and aliphatic CH), 0.9–2.1 (12 H, m, aliphatic CH).

A solution of 20 mg (0.13 mmol) of ketone **2** and 0.50 mmol of NaOMe in 1.0 mL of PhH and 1.0 mL of MeOD was stirred for 7 days and then quenched with an aqueous phosphate buffer (pH 6.9). The recovered ketone (mainly **2**, 18 mg or 85%) contained 1.7% d_0 species, 2.5% d_1 species, 18.9% d_2 species, and 76.9% d_3 species (mass spectral analyses). The absence of appreciable ^1H NMR absorption in the region δ 2.2–3.0 confirms our assignment of multiplets at δ 2.76, 2.53, and 2.35 to protons α to the C=O function.

Equilibration of Stereoisomeric Ketones 1 and 2. Mixtures of the isomeric ketones and the internal standard were analyzed by GLC[12] with the following retention times: cis ketone **1**, 135.0 min; trans ketone **2**, 153.7 min; *n*-$C_{15}H_{32}$, 71.0 min. A solution of 11.1 mg (0.073 mmol) of trans ketone **2** and 10.0 mg of *n*-$C_{15}H_{32}$

(11) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated $MgSO_4$ was employed as a drying agent. The IR spectra were determined with a Perkin-Elmer Model 299 infrared recording spectrophotometer fitted with a grating. The UV spectra were determined with a Cary Model 14 or a Perkin-Elmer Model 202 recording spectrophotometer. The ^1H NMR spectra were determined at 60 MHz with a Varian Model T-60A NMR spectrometer or at 300 MHz with a Bruker Model WM-300 NMR spectrometer. The ^{13}C NMR spectra were determined at 25 MHz with a JEOL Model PFT-100 NMR spectrometer or at 75 MHz with a Bruker Model WM-300 spectrometer. The chemical shift values are expressed in δ values (ppm) relative to a Me_4Si internal standard. The mass spectra were obtained with either a Hitachi Perkin-Elmer Model RMU-7 or a Varian MAT Model 112S mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.

(12) A GLC column was packed with FFAP on Chromosorb P; the GLC apparatus was calibrated with known mixtures.

in 1.5 mL of PhH was mixed with 1.5 mL of a MeOH solution containing 0.15 mmol of NaOMe. The resulting solution was kept at 25.0 °C, and 0.8-mL aliquots were removed at intervals and quenched in an aqueous phosphate buffer (pH 6.9). The organic layer from each aliquot was dried and subjected to GLC analysis. The composition of the ketones was constant after 12 h and contained 12.9% of the cis isomer **1** and 87.1% of the trans isomer **2**; the calculated yield of recovery of ketones **1** and **2** was 98%. A comparable experiment was performed with 11.1 mg of the cis ketone **1**, 10.0 mg of n-$C_{15}H_{32}$, 1.5 mL of PhH, and 1.5 mL of MeOH solution containing 0.15 mmol of NaOMe. The composition of the ketone mixture (98% recovery) was constant after 24 h; the mixture contained 12.9% of the cis ketone **1** and 87.1% of the trans ketone **2**.

Properties of Cis-Ketoxime 4a. A sample of this oxime **4a** (mp 118–119 °C) was prepared as previously described[2] and recrystallized from EtOH. The spectral data for the oxime **4a** follow: ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 162.6 (s), 48.0 (d), 41.3 (d), 34.5 (t), 32.5 (t), 28.9 (t), 28.3 (t), 28.0 (t), 25.7 (t), 24.7 ppm (t); ^1H NMR ($CDCl_3$, 300 MHz) δ 2.95 (1 H, m, 899.4, 896.5, 890.7, 886.3, 883.4, 877.5, 874.9 Hz, CHC=N), 2.84 (1 H, m, 865.1, 856.7, 847.2, 838.4 Hz, CHC=N), 2.21 (1 H, m, 675.4, 667.4, 665.2, 659.3, 657.1, 654.9, 652.7 Hz, CHC=N), 1.1–2.1 (14 H, m, OH and aliphatic CH). The solid-state ^{13}C NMR spectrum[10] of the cis ketoxime **4a** exhibited the following peaks (and differences in ppm from the spectrum in $CDCl_3$ solution): 45.7 (2.3), 43.2 (1.9), 37.4 (2.9), 35.6 (3.1), 31.0 (2.1), 27.9 (0.4), 26.5 (1.5), 24.2 (1.5), and 20.5 (4.2) ppm.

Preparation of Sulfonylhydrazone 6b. Following previously published general directions,[13] the reaction of 100 g (0.40 mol) of p-$BrC_6H_4SO_2Cl$ with 56.1 g (1.11 mol) of hydrazine hydrate in 175 mL of THF at 10–20 °C yielded 79 g (80%) of the crude hydrazide **6b** as colorless needles, mp 115–117 °C dec. Recrystallization from absolute EtOH afforded 60.2 g (61.5%) of the pure hydrazide **6b**: mp 118–119 °C dec. (lit.[14] mp 117–118 °C); IR ($CHCl_3$) 3355 (NH), 1340, 1165 cm^{-1} (SO_2); NMR (Me_2SO-d_6) δ 8.50 (1 H, br, NH), 7.79 (4 H, s, aryl CH), 4.18 (2 H, br, NH_2).

Preparation of Tosylhydrazones 4b and 5b. After a mixture of 1.34 g (7.2 mmol) of $TsNHNH_2$ and 25 mL of EtOH had been warmed to 40 °C, the resulting solution was treated with 0.15 mL of HOAc, cooled to 25 °C, and then stirred and treated with 0.91 g (6.0 mmol) of *trans*-1-decalone. The white solid that separated within 15 min was collected and recrystallized from EtOH to separate 1.7 g (89%) of the **tosylhydrazone of *trans*-1-decalone** as colorless needles: mp 150–151 °C; IR ($CHCl_3$) 3260 (NH), 1330, 1160 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ 7.2–8.1 (4 H, m, aryl CH), 2.8–3.0 (1 H, br, NH), 2.46 (3 H, s, aryl CH_3), 1.1–2.1 (16 H, m, aliphatic CH); UV max (95% EtOH), 232 nm (ϵ 10500), 277 (885); mass spectrum, m/e (rel intensity) 298 (26), 150 (24), 139 (27), 92 (52), 91 (100), 79 (33), 77 (26), 67 (23), 65 (40), 41 (31), 39 (27).

Anal. Calcd for $C_{16}H_{24}N_2O_2S$: C, 63.71; H, 7.55; N, 8.74; S, 10.01. Found: C, 63.70; H, 7.56; N, 8.75; S, 10.00.

The same procedure was employed with 0.34 g (2.0 mmol) of $TsNHNH_2$, 0.15 mL of HOAc, 25 mL of EtOH, and 0.24 g (1.6 mmol) of either cis ketone **1** or trans ketone **2**. The trans derivative **5b** separated as 0.45 g (88%) of colorless prisms, mp 127–128 °C, and the cis derivative **4b** separated as 0.43 g (85%) of colorless prisms, mp 121–122 °C. The spectral properties of the trans derivative **5b** follow: IR (CCl_4) 3220 (NH), 1345, 1170 cm^{-1} (SO_2); ^1H NMR (CCl_4) δ 7.2–8.0 (4 H, m, aryl CH), 0.9–2.8 (20 H, m, NH, aliphatic CH, and an aryl CH_3 singlet at 2.45); UV max (95% EtOH) 234 nm (ϵ 10600), 275 (1050); mass spectrum, m/e (rel intensity) 300 (72), 299 (43), 298 (57), 278 (40), 271 (30), 166 (23), 165 (27), 157 (28), 156 (35), 152 (30), 150 (32), 139 (45), 135 (35), 107 (21), 93 (28), 92 (65), 91 (100), 79 (33), 77 (22), 67 (46), 65 (45), 55 (23), 41 (53), 39 (34).

Anal. Calcd for $C_{16}H_{24}N_2O_2S$: C, 63.71; H, 7.55; N, 8.74; S, 10.01. Found: C, 63.70; H, 7.57; N, 8.75; S, 10.01.

The spectral properties of the cis derivative **4b** follow: IR ($CHCl_3$) 3290 (NH), 1330, 1165 cm^{-1} (SO_2); ^1H NMR (CCl_4) δ 7.2–8.0 (4 H, m, aryl CH), 0.9–2.8 (20 H, m, NH, aliphatic CH, and an aryl CH_3 singlet at 2.45); UV max (95% EtOH) 229 nm (ϵ 10100), 275 (1250); mass spectrum, m/e (rel intensity) 298 (15), 150 (23), 139 (55), 124 (32), 123 (35), 93 (26), 91 (100), 79 (27), 77 (20), 67 (23), 65 (26), 41 (36), 39 (25).

Anal. Calcd for $C_{16}H_{24}N_2O_2S$: C, 63.71; H, 7.55; N, 8.74; S, 10.01. Found: C, 63.65; H, 7.56; N, 8.71; S, 10.09.

Preparation of Sulfonylhydrazide 6c. Use of previously described[13] general procedure with 8.0 g (38 mmol) of p-$ClC_6H_4SO_2Cl$, 25 mL of THF, and 4.1 g (80 mmol) of hydrazine hydrate at 10–20 °C for 15 min yielded 7.14 g (91%) of the crude hydrazide **6c** as a colorless solid, mp 105–106 °C. Recrystallization from EtOH separated 7.01 g (89%) of the pure hydrazide **6c** as a colorless solid, mp 115–116 °C (lit.[14] mp 113–114 °C). The spectral properties of the hydrazide **6c** follow: IR ($CHCl_3$) 3370 (NH), 1345, 1167 cm^{-1} (SO_2); ^1H NMR (Me_2SO-d_6) δ 7.86 (2 H, d, J = 8 Hz, aryl CH), 7.61 (2 H, d, J = 8 Hz, aryl CH), 7.34 (1 H, br, NH), 3.70 (2 H, br, NH); mass spectrum, m/e (rel intensity) 208 (M^+, 3), 206 (M^+, 8), 117 (34), 112 (52), 111 (47), 75 (47), 75 (47), 31 (100).

Preparation of Sulfonylhydrazones 5a and 5c. A solution of 1.81 g (7.2 mmol) of the hydrazide **6b**, 0.1 mL of HOAc, and 912 mg (6.0 mmol) of *trans*-1-decalone in 25 mL of EtOH was stirred at 25 °C for 30 min and then concentrated under a stream of N_2. The residual colorless solid was recrystallized from MeOH to separate 1.20 g (88%) of the **(*p*-bromophenyl)sulfonylhydrazone of *trans*-1-decalone**: mp 145–146 °C; IR ($CHCl_3$) 3380 (NH), 1340, 1172 cm^{-1} (SO_2); NMR ($CDCl_3$) δ 7.4–8.0 (4 H, m, aryl CH), 0.6–3.0 (16 H, m, aliphatic CH).

Anal. Calcd for $C_{16}H_{21}BrN_2O_2S$: C, 49.87; H, 5.49; Br, 20.74; N, 7.27; S, 8.32. Found: C, 49.80; H, 5.53; Br, 20.68; N, 7.26; S, 8.29.

A comparable reaction with 121 mg (0.48 mmol) of the hydrazide **6b**, 0.05 mL of HOAc, and 70 mg (0.46 mmol) of the trans ketone **2** in 11 mL of EtOH yielded, after recrystallization from MeOH, 168 mg (95%) of the sulfonylhydrazone **5a**: mp 147–148 °C; IR ($CHCl_3$) 3300 (NH), 1340, 1165 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.83 (2 H, d, J = 8.7 Hz, aryl CH), 7.64 (2 H, d, J = 8.7 Hz, aryl CH), 2.8 (1 H, m, CHC=N), 2.43 (2 H, m, CH_2C=N), 0.6–2.2 (13 H, m, aliphatic CH); ^{13}C NMR ($CDCl_3$) 163.6, 136.6, 131.3 (2 C atoms), 129.1 (2 C atoms), 127.5, 51.1, 45.9, 37.0, 34.6, 31.2, 29.2, 28.6, 23.8, 23.6 ppm; mass spectrum, m/e (rel intensity) 386 (M^+, 0.4), 384 (M^+, 0.4), 298 (28), 165 (100), 158 (21), 157 (33), 156 (21), 155 (33), 150 (39), 149 (24), 148 (24), 135 (34), 93 (39), 91 (34), 79 (49), 77 (51), 76 (35), 67 (52), 55 (24), 50 (36), 41 (60), 39 (28). The solid-state ^{13}C NMR spectrum[10] of the sulfonylhydrazone **5a** exhibited the following peaks (and differences in ppm from the spectrum in $CDCl_3$ solution): 164.1 (0.5), 137.9 (1.3), 132.4 (1.1), 129.7 (0.6), 129.7 (2.2), 49.8 (1.3), 46.7 (0.8), 36.8 (0.2), 35.0 (0.4), 30.2 (1.0), 27.3 (1.9), 27.3 (1.3), 23.4 (0.4), 23.4 (0.2) ppm.

Anal. Calcd for $C_{16}H_{21}BrN_2O_2S$: C, 49.87; H, 5.49; Br, 20.74; S, 8.32. Found: C, 49.83; H, 5.53; Br, 20.73; S, 8.32.

Similarly, a solution of 83 mg (0.40 mmol) of the hydrazide **6c**, 0.05 mL of HOAc, and 56 mg (0.37 mmol) of the trans ketone **2** in 10 mL of EtOH was stirred at 25 °C for 1 h and then concentrated and recrystallized from MeOH. The colorless sulfonylhydrazone **5c** amounted to 115 mg (91%): mp 122–123 °C; IR ($CHCl_3$) 3310 (NH), 1340, 1170 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ 7.2–8.0 (4 H, m, aryl CH), 0.8–3.0 (17 H, m, NH and aliphatic CH); mass spectrum, m/e (rel intensity) 339 (M^+, 0.5), 237 (23), 134 (17), 73 (100).

Anal. Calcd for $C_{16}H_{21}ClN_2O_2S$; C, 56.37; H, 6.21; Cl, 10.40. Found: C, 56.21; H, 6.23; Cl, 10.35.

Preparation of (2,4-Dinitrophenyl)hydrazone 5d. A solution of 130 mg (0.65 mmol) of (2,4-dinitrophenyl)hydrazine, 100 mg (0.65 mmol) of the ketone **2**, and 1 mL of aqueous 12 M HCl in 15 mL of MeOH was refluxed for 10 min and then cooled. The crude DNP **5d** was collected as 210 mg (97%) of orange-red solid, mp 219–220 °C, that contained (TLC analysis) major and minor components. The sample was chromatographed on silica gel with an ethyl acetate–hexane eluent. The more rapidly eluted component was recrystallized from EtOH to separate 198 mg (91%) of the major stereoisomer of **5d** as orange plates, mp 220–221 °C. The more slowly eluted component was recrystallized from EtOH to separate 6 mg (3%) of the minor stereoisomer of **5d** as orange plates, mp 219–220 °C. The spectral properties of the major

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isomer of **5d** follow: IR ($CHCl_3$) 3430 (NH), 1618 cm^{-1} (C=N); ^1H NMR ($CDCl_3$, 300 MHz) δ 11.06 (1 H, s, NH), 9.12 (1 H, d, J = 2.5 Hz, aryl CH), 8.30 (1 H, dd, J = 2.5, 10 Hz, aryl CH), 7.98 (1 H, d, J = 10 Hz, aryl CH), 2.70 (2 H, m, CH_2C=N), 1.2–2.5 (14 H, m, aliphatic CH); ^{13}C NMR ($CDCl_3$) 163.3, 145.6, 137.7, 129.9, 129.3, 123.5, 116.6, 51.9, 47.0, 37.3, 35.0, 31.9, 30.8, 29.6, 29.0, 24.0 ppm; mass spectrum, m/e (rel intensity) 332 (M^+, 45), 297 (22), 135 (88), 93 (62), 91 (49), 81 (42), 79 (74), 67 (100), 55 (45), 41 (76); UV max (95% EtOH) 235 nm (ϵ 11900), 379 (14000).

Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.85; H, 6.10; N, 16.87.

The spectral properties of the minor isomer of **5d** follow: IR ($CHCl_3$) 3330 (NH), 1615 cm^{-1} (C=N); mass spectrum, m/e (rel intensity) 332 (M^+, 45), 297 (21), 135 (88), 93 (62), 91 (48), 81 (44), 79 (68), 67 (100), 55 (47), 41 (74).

Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.87; H, 6.09; N, 16.82.

^1H NMR Spectra of the 2-*tert*-Butyl Ketones 8a and 9a. Previously described[3] samples of the ketones **8a** and **9a** were used to obtain 300-MHz ^1H NMR spectra in $CDCl_3$ solution. The cis ketone **8a** exhibited the following peaks: δ 3.05 (1 H, m, 926.2, 921.0, 916.6, 912.2, 908.2, 903.0 Hz, CHCO), 2.41 (3 H, m, 775.1, 771.8, 762.9, 759.6, 751.9, 748.6, 744.9, 736.4, 730.9, 725.1, 722.9, 716.6, 715.1, 703.0, 693.8, 691.2 Hz), 2.15 (1 H, m, 654.8, 650.4, 647.5, 642.0, 637.2, 634.3, 629.1 Hz), 1.1–1.9 (10 H, m, aliphatic CH), 0.84 (9 H, s, t-Bu). The trans ketone **9a** exhibited the following peaks: δ 2.74 (1 H, m, 837.2, 826.6, 819.5, 817.0, 809.6 Hz), 2.53 (1 H, m, 778.0, 764.0, 762.9, 759.6, 756.3 Hz), 2.37 (1 H, m, 725.1, 721.4, 712.6, 708.9, 706.7, 703.0, 693.5, 690.5 Hz), 1.2–2.0 (12 H, m, aliphatic CH), 0.84 (9H, s, t-Bu).

After a solution of 15 mg (0.072 mmol) of the ketone **9a** and 0.5 mmol of NaOMe in 1.0 mL of PhH and 1.0 mL of MeOD had been stirred for 7 days, it was quenched with an aqueous phosphate buffer (pH 6.9). The recovered ketone (mainly **9a**, 11 mg or 68%) contained 0.7% d_0 species, 3.0% d_1 species, 26.7% d_2 species, and 69.6% d_3 species (mass spectral analyses). The absence of appreciable ^1H NMR absorption ($CDCl_3$, 300 MHz) in the region δ 2.2–3.0 confirms our assignment of multiplets at δ 2.74, 2.53, and 2.37 to protons α to the C=O function.

Preparation of Silyl Ether 17 and Methylated Ketones 18. A solution of 3.00 g (19.7 mmol) of the ketone **15**, 3.98 g (39.4 mmol) of Et_3N (distilled from $LiAlH_4$), and 4.10 g (37.8 mmol) of Me_3SiCl (distilled from quinoline) in 9.0 mL of DMF was heated to 90 °C for 11 h and then cooled and partitioned between hexane and cold (0 °C) aqueous $NaHCO_3$. The organic layer was dried and concentrated to leave a liquid residue containing (TLC, silica gel with diethyl ether–hexane eluent, 1:19, v/v) the starting ketone **15** (R_f 0.46) and the silyl ether **17** (R_f 0.92). This crude product was chromatographed on silica gel to separate 2.07 g (47%) of the crude silyl ether **17**. A 1.20-g sample of this crude product was chromatographed on silicic acid with an ethyl acetate–hexane eluent to separate 0.12 g of the starting ketone **15** and 1.05 g (41%) of the enol ether **17**. Distillation afforded 0.99 g of the pure enol ether **17**: bp 100–103 °C (10 mm), n^{25}_D 1.4580; IR (CCl_4) 1687 (enol ether C=C), 1639 (C=C), 910 cm^{-1} (CH=CH_2); ^1H NMR (CCl_4) δ 4.8–6.0 (3 H, m, vinyl CH), 1.5–3.0 (12 H, m, aliphatic CH), 0.20 (9 H, s, Me_3Si); mass spectrum, m/e (rel intensity) 224 (M^+, 1.2), 183 (65), 147 (13), 75 (49), 73 (100), 43 (39).

Anal. Calcd for $C_{13}H_{24}OSi$: C, 69.57; H, 10.78. Found; C, 69.60; H, 10.80.

A solution of 5.00 g (22.3 mmol) of the silyl enol ether **17**, 25.0 mmol of MeLi (halide free), and 1 mg of 2,2-bipyridyl (an indicator) in 46 mL on Et_2O was stirred at 25 °C for 1 h and then concentrated under reduced pressure. The residual lithium enolate was redissolved in 25 mL of anhydrous DME, and the resulting red (excess MeLi) solution was cooled to 0 °C and then treated with 9.40 g (66.8 mmol) of MeI (dried over activated alumina). After the reaction mixture had been stirred at 0 °C for 2 min, it was quenched by the addition of 25 mL of aqueous 5% HCl and then partitioned between pentane and aqueous NaCl. The organic layer was dried and concentrated to leave 3.65 g of crude liquid product containing (TLC, silica gel coating with an ethyl acetate–hexane eluent, 1:9, v/v) the olefinic ketone **15** (R_f 0.65) and the methylated ketones **18a** (R_f 0.60) and **18b** (R_f 0.57). This material was chromatographed on silica gel with an ethyl acetate–hexane eluent (1:19, v/v) to separate the three components, each of which was distilled in a short-path still.

Following separation of 219 mg (6% yield) of the ketone **15**, the methyl ketone **18a** was separated as 1.41 g (39%) of colorless liquid: bp 90–93 °C (19 mm); n^{25}_D 1.4614; IR (CCl_4) 1705 (C=O), 1641 (C=C), 917 cm^{-1} (CH=CH_2); ^1H NMR ($CDCl_3$) δ 4.9–5.7 (3 H, m, vinyl CH), 0.9–2.3 (15 H, m, aliphatic CH including CH_3 singlets at 2.12 and 1.22); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 211.7 (s), 137.0 (d), 115.0 (t), 58.0 (s), 50.1 (d), 35.6 (t), 35.0 (t), 29.7 (t), 28.0 (q), 24.5 (q), 21.8 ppm (t); mass spectrum, m/e (rel. intensity), 166 (M^+, 1), 123 (43), 94 (31), 85 (29), 81 (100), 79 (22), 67 (32), 43 (31).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.46; H, 10.93.

The methyl ketone **18b** was separated as 1.44 g (39%) of colorless liquid: bp 92–95 °C (10 mm); n^{25}_D 1.4617; IR (CCl_4) 1700 (C=O), 1639 (C=C), 910 cm^{-1} (CH=CH_2); ^1H NMR ($CDCl_3$) δ 4.9–5.7 (3 H, m, vinyl CH), 0.9–2.3 (15 H, m, aliphatic CH including CH_3 singlets at 2.18 and 1.03); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 211.0 (s), 137.0 (d), 115.0 (t), 57.9 (s), 50.1 (d), 35.4 (t), 35.1 (t), 29.7 (t), 28.0 (q), 24.5 (q), 21.8 ppm (t); mass spectrum, m/e (rel intensity) 166 (M^+, 0.6), 123 (25), 94 (18), 81 (100), 79 (21), 67 (58), 55 (22), 43 (70), 41 (30).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.46; H, 10.91.

Preparation of Bromo Ketones 19. A stream of anhydrous HBr gas was passed through a solution of 640 mg (3.50 mmol) of the olefinic ketone **18a** in 100 mL of pentane for 15 min while the mixture was irradiated with the light from a Hanovia 450-W medium-pressure Hg lamp. The resulting pale yellow solution was washed successively with aqueous $Na_2S_2O_3$, with aqueous $NaHCO_3$, and with aqueous NaCl and then dried and concentrated. The crude bromo ketone **19a**, 950 mg (99%) of dark colored liquid, was used without purification. The spectral properties of the crude bromo ketone **19a** follow: IR (CCl_4) 1710 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 3.33 (2 H, t, J = 6 Hz, CH_2Br), 0.8–3.0 (17 H, m, aliphatic CH including CH_3 singlets at 2.03 and 1.20); mass spectrum, m/e (rel intensity) 149 (30), 123 (100), 95 (15), 85 (33), 81 (74), 79 (16), 69 (39), 67 (43), 55 (53),43 (85), 41 (49), 39 (22).

The same procedure was followed with a solution of 750 mg (4.51 mmol) of the unsaturated ketone **18b** in 300 mL of pentane with a total reaction time of 10 min. The crude bromo ketone **19b**, 1.10 g (98%) of dark colored liquid, was used without further purification. The spectral properties of this crude product follow: IR (CCl_4) 1705 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 3.36 (2 H, t, J = 7 Hz, CH_2Br), 0.7–2.5 (17 H, m, aliphatic CH including CH_3 singlets at 2.06 and 1.03); mass spectrum (chemical ionization), m/e (rel intensity) 249 (M + 1, 100), 247 (M + 1, 90), 231 (42), 229 (43), 167 (94), 123 (39), 109 (33); mass spectrum (electron impact), m/e (rel intensity) 123 (93), 85 (48), 81 (91), 69 (43), 67 (40), 55 (65), 43 (100), 41 (69).

Preparation of Ketones 10 and 11. A. Cis Isomer 11. To a cold (−78 °C) solution of 5.7 mmol of i-Pr_2NLi in 11 mL of hexane and 60 mL of THF was added, dropwise and with stirring, a solution of 951 mg (3.85 mmol) of the crude bromo ketone **19a** in 10 mL of THF. After the resulting solution had been stirred at −78 °C for 20 min, it was rapidly heated to boiling and then refluxed for 2 h. The reaction mixture was partitioned between Et_2O and aqueous NH_4Cl, and the organic layer was dried and concentrated. The residual crude product (625 mg of dark colored liquid) contained (TLC on silica gel with ethyl acetate–hexane eluent, 1:9, v/v) a number of minor components (R_f 0.90, 0.70, 0.30, 0.1), including the unsaturated ketone **18a** (R_f 0.61) and the cyclic ketone **11** (R_f 0.52). Chromatography on silica gel with an ethyl acetate–hexane eluent separated 521 mg (82%) of the crude ketone **11** containing ca. 7% of the ketone **18a**. A second chromatography on silica gel impregnated with $AgNO_3$[15] by employing an ethyl acetate–hexane eluent (1:9, v/v) separated 18 mg (3.4%) of the unsaturated ketone **18a** (identified by comparison of IR spectra) and 501 mg (79%) of the ketone **11** as a colorless liquid: bp 50–54 °C (0.05 mm); n^{25}_D 1.4921; IR (CCl_4), 1705 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 300 MHz) 2.75 (1 H, m, COCH), 2.35 (1 H, m,

(15) Algner, R.; Spitzy, H.; Frei, R. W. *J. Chromatogr. Sci.* **1976**, *14*, 381.

COCH), 2.14 (2 H, m, aliphatic CH), 1.2–1.9 (11 H, m, aliphatic CH), 1.17 (3 H, s, CH_3); mass spectrum, m/e (rel intensity) 166 (M^+, 13), 125 (29), 122 (24), 111 (40), 95 (81), 82 (33), 81 (89), 79 (24), 67 (100), 55 (42), 53 (25), 41 (71), 39 (50).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.70; H, 11.19.

B. Trans Isomer 10. The same procedure was followed—adding a solution of 939 mg (3.80 mmol) of the crude bromo ketone **19b** in 10 mL of THF to a cold solution of 5.3 mmol of *i*-Pr_2NLi in 10 mL of hexane and 75 mL of THF. The crude liquid product (602 mg) contained (TLC) the unsaturated ketone **18b** (R_f 0.58), the cyclic ketone **10** (R_f 0.49), and several minor unidentified components (R_f 0.91, 0.71, and 0.22–0.05). Chromatography first on silica gel and then on a silica gel–$AgNO_3$ column[15] separated 15 mg (3%) of the unsaturated ketone **18b** and 481 mg (76%) of a product believed to be the cyclic ketone **10** as a colorless liquid: bp 55–57 °C (0.05 mm); n^{25}_D 1.4891. An analytical sample of the ketone **10**, collected from an HPLC column packed with silica gel (10 μm), and eluted with ethyl acetate–hexane (3:97, v/v), was a colorless liquid: n^{25}_D 1.4901; IR (CCl_4) 1705 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.8–2.0 (18 H, m, aliphatic CH including a CH_3 singlet at 1.18); mass spectrum, m/e (rel intensity) 166 (M^+, 32), 125 (35), 122 (35), 111 (40), 95 (89), 82 (40), 81 (95), 79 (35), 67 (100), 57 (95), 56 (95), 55 (81), 53 (45), 43 (75), 41 (71), 39 (61).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.59; H, 10.95.

Preparation of Hydrazone 12. A solution of 20.0 mg (0.12 mmol) of the cis ketone **11**, 30.2 mg (0.12 mmol) of the bromo hydrazide **6b**, and 1 μL of HOAc in 5 mL of EtOH was stirred at 25 °C for 45 min and then cooled to 0 °C. The crude derivative **12** separated as 35 mg (73%) of colorless solid, mp 175–181 °C. Recrystallization from MeOH afforded 28.1 mg (58%) of the pure hydrazone **12** as colorless prisms: mp 217–218 °C; IR ($CHCl_3$) 3300, 3240 cm^{-1} (NH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.6–7.8 (4 H, m, aryl CH), 2.33 (1 H, m, aliphatic CH, 700.3 Hz), 2.0–2.1 (2 H, m, aliphatic CH, 639.3, 628.5, 626.1, 615.3, 612.9, 607.0 Hz), 1.1–1.7 (13 H, m, aliphatic CH), 1.00 (3 H, s, CH_3); mass spectrum (chemical ionization), m/e (rel intensity) 401 ($M^+ + 1$, 83), 399 (52), 283 (57), 236 (54), 191 (56), 189 (66), 181 (100).

Anal. Calcd for $C_{17}H_{23}BrN_2O_2S$: C, 51.13; H, 5.80; Br, 20.01; N, 7.02; S, 8.03. Found: C, 51.05; H, 5.79; Br, 20.10; N, 6.99; S, 8.07.

Registry No. 1, 5365-37-7; 2, 5365-38-8; 4a, 5365-39-9; 4b, 85318-90-7; 5a, 85318-91-8; 5b, 85318-92-9; 5c, 85318-93-0; (*Z*)-5d, 85354-01-4; (*E*)-5d, 85354-02-5; 6a, 1576-35-8; 6b, 2297-64-5; 6c, 2751-25-9; 8a, 70775-28-9; 9a, 70775-29-0; 10, 85318-94-1; 11, 85318-95-2; 12, 85335-03-1; 13, 16112-10-0; 14, 762-72-1; *cis*-15, 65682-09-9; *trans*-15, 65682-10-2; 16, 74272-08-5; 17, 85318-96-3; 18a, 85318-97-4; 18b, 85318-98-5; 19a, 85318-99-6; 19b, 85335-09-7; *trans*-1-decalone, 21370-71-8; *trans*-1-decalone tosylhydrazone, 85319-00-2; *trans*-1-decalone (*p*-bromophenyl)sulfonylhydrazone, 85319-01-3.

Supplementary Material Available: Description of determination of crystal structures for the ketone derivatives **4a**, **5a**, and **12**, including tables of atomic coordinates for each compound (12 pages). Ordering information is given on any current masthead page.

Perhydroazulenes. 4. The 6-*tert*-Butyl-4-oxoperhydroazulene System[1]

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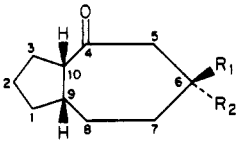
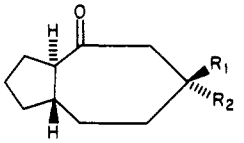
The four diastereoisomeric 6-*tert*-butyl-4-oxoperhydroazulenes (**3–6**) have been prepared and characterized. Molecular mechanics calculations suggest that each of these ketones will exist as one or both of a pair of closely related conformers as follows: **3**, C-3 or TC-7; **4**, TC-1 or TC-2; **5**, B-3 or TB-4; **6**, TC-4 or TC-5. A combination of ^1H NMR data and X-ray crystallographic data support the correctness of these predictions.

Our earlier studies[2-4] of the 4-oxoperhydroazulenes indicated that the cis isomer **1** was expected to exist as one





1, $R_1 = R_2 = H$
3, $R_1 = t$-Bu; $R_2 = H$
5, $R_1 = H$; $R_2 = t$-Bu

2, $R_1 = R_2 = H$
4, $R_1 = t$-Bu; $R_2 = H$
6, $R_1 = H$; $R_2 = t$-Bu

or both of two pairs of closely related conformers, either the pair B-3 or TB-4 or the pair C-3 or TC-7.[5] Similarly, the trans isomer **2** was expected to exist either as the conformer TC-1 or as one of the less stable pair of closely related conformers TC-4 or TC-5. In both the cis and the trans series, consideration of these low-energy conformations suggested that introduction of sterically bulky substituent at C-6 with the correct stereochemistry would allow one closely related pair of conformers to be distinctly favored over the other pair.

Support for this idea was gained from calculations that employed Allinger's MM2 molecular mechanics program[7b] to minimize the energies and compute the relative sta-

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(2) House, H. O.; Sayer, T. S. B.; Yau, C. C. *J. Org. Chem.* **1978**, *43*, 2153.

(3) House, H. O.; Yau, C. C.; VanDerveer, D. *J. Org. Chem.* **1979**, *44*, 3031.

(4) House, H. O.; Gaa, P. C.; VanDerveer, D. *J. Org. Chem.*, preceding paper in this issue.

(5) (a) The conformational designations being used are those suggested by DeClercq[6] on the basis of the earlier cycloheptane designations of Hendrickson.[7a] In this scheme the cycloheptanone ring of the ketoperhydroazulene is numbered as shown below. The number in each conformational designation indicates the atom through which the plane of symmetry [in a chair (C) or boat (B) conformer] or the axis of symmetry [in a twist-chair (TC) or twist-boat (TB) conformer] passes. (b) We arbitrarily designate the stereochemistry of the *t*-Bu group as either syn (e.g., **3**) or anti (e.g., **5**) to the hydrogen atom at C-9.