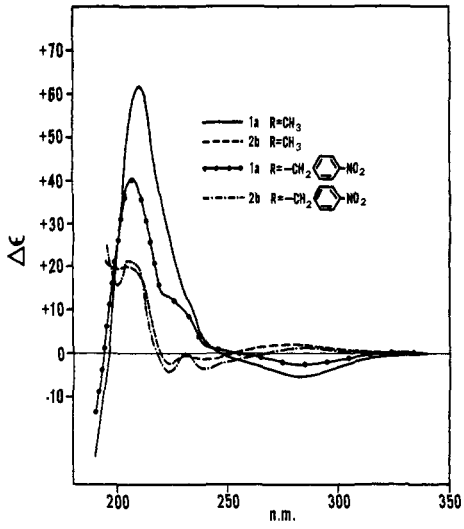

Figure 1. Circular dichroism curves in acetonitrile.

observation that an NOE exists between H-2 and the high-field methyl (16–20%) and not between H-2 and the low-field methyl in the spectra of **2** strongly supports conformation **2b** over **2a**. This conformational assignment is supported further by the observed long-range, five-bond coupling between H-2 and H-7 in **2** ($^5J_{4,7} \simeq 1.0$ Hz). Similar long-range coupling between H-2 and H-7 has been observed in cepham where the C-4 proton occupies an α-axial configuration.[9] Accordingly, trans isomer **2** must adopt a conformation where H-2 is axially oriented and is in the same geometrical relationship to H-7 as in cepham systems where coupling of this nature has been previously observed. Such a geometrical relationship is satisfied by stereoformula **2b**.

Clear conformational and configurational assignments for thiazolidine derivative **3**, obtained as a by-product in the synthesis of **1a** and **2b**, can be made from an analysis of the 100-MHz DMSO-d_6 spectrum of this compound. The following nmr data are offered as evidence for the assignment of this product to structure **3**: δ 1.13 (s, 3, CH_3), 1.61 (s, 3, CH_3), 3.51 (d of d, 1, J = 5.5; 14.5 Hz, H-6), 3.84 (d of d, 1, J = 10, 14.5 Hz, H-6), 3.84 (d, 1, J = 13.5 Hz, H-4), 4.25 (d of d, 1, J = 7.5, 13.5 Hz, NH, D_2O exchangeable), 4.95 (m, 1, J = 5.5, 10, 7.5 Hz, H-2). The observed couplings of 13.5 Hz between NH and H-4 and 7.5 Hz between NH and H-2 require dihedral angles of approximately 180 and 30°, respectively, between these protons[10] and establish the C-2 configurations and thiazolidine conformation shown in structure **3**. Other thiazolidine conformational and C-2 configurational possibilities are eliminated readily on the basis of incompatibility with recorded NH coupling information.

Unfortunately, the nmr spectrum of **4** in DMSO-d_6 does not reveal a discernible NH signal. As a result vicinal NH couplings cannot be measured and a complete stereochemical assignment for **4** could not be determined unequivocally. However, on the basis of nmr data[11] and mechanistic considerations, we believe that **4** has the structure shown above.

(9) (a) D. O. Spry, Eli Lilly & Co., private communication; (b) P. V. Demarco and R. Nagarajan in "Cephalosporins and Penicillins—Chemistry and Biology," E. H. Flynn, Ed., Academic Press, New York, N. Y., 1972, Chapter 8.

(10) V. F. Bystrov, S. L. Portnova, T. A. Balashova, V. I. Tsetlin, V. T. Ivanov, P. V. Kostetzky, and Yu. A. Ovchinnikov, *Tetrahedron Lett.*, 5225 (1969); K. G. R. Pachler, *Spectrochim. Acta*, **19**, 2085 (1963); **20**, 581 (1964).

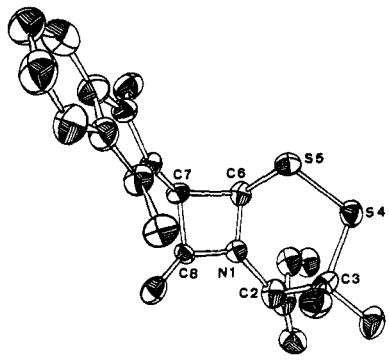

Figure 2. Skeletal conformation of the cis isomer in the crystalline state. Thermal ellipsoids are drawn to include 50% probability.

Acknowledgments. We thank Mr. R. D. Miller for circular dichroism measurements and Mr. D. W. Smith for computer assistance.

(11) Compound **4** shows the following nmr data in $CDCl_3$: δ 1.20 (s, 3, CH_3), 1.60 (s, 3, CH_3), 3.95 (d of d, 1, J = 4.5, 14.5 Hz, H-6), 4.05 (d of d, 1, J = 7.5, 14.5 Hz, H-6), 3.59 (s, 1, H-4), 3.20 (m, NH), and 4.95 (d of d, 1, J = 4.5, 7.5 Hz, H-2).

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2,3-Dimethylenebicyclo[2.2.0]hexane and Its Cycloreversion to 2,3-Dimethylenecyclohexa-1,3-diene

Sir:

Vapor phase thermolysis at 250–300° of 1,2-dimethylenecyclobutane (**1**) appears to generate tetramethyleneethane (**2**) as a transient intermediate.[1,2] The chemistry of this latter species is of considerable current interest.[1–8] The bicyclic diene **3** of the title seemed to offer an ideal means for producing a simple tetramethyleneethane derivative **4** in solution at moderate temperatures, thus providing an unprecedented opportunity to study the bimolecular reactions, particularly the cycloadditions, of a member of this novel class of compounds. Such a study might also be expected to yield valuable insights into the electronic configurations of tetramethyleneethanes. The activation enthalpy for the cycloreversion **1** → **2** is 45.7 kcal/mol.[2] In view of the additional cyclobutane ring strain energy present

(1) J. J. Gajewski and C. N. Shih, *J. Amer. Chem. Soc.*, **89**, 4532 (1967).
(2) W. von E. Doering and W. R. Dolbier, *ibid.*, **89**, 4534 (1967).
(3) J. J. Gajewski and C. N. Shin, *ibid.*, **91**, 5900 (1969).
(4) W. R. Moore, R. D. Bach, and T. M. Ozretich, *ibid.*, **91**, 5918 (1969).
(5) P. Dowd, *ibid.*, **92**, 1066 (1970).
(6) J. J. Gajewski and C. N. Shih, *ibid.*, **92**, 4457 (1970).
(7) B. G. Odell, R. Hoffman, and A. Imamura, *J. Chem. Soc. B*, 1675 (1970).
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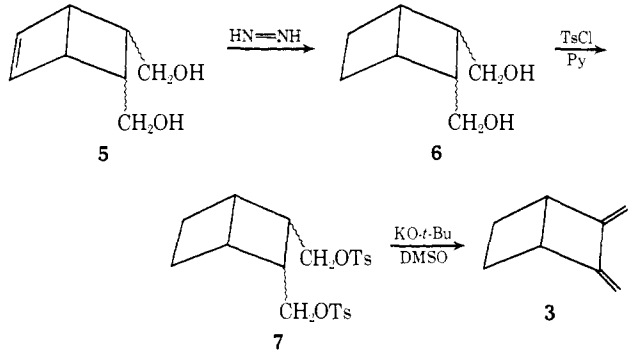
in **3**, the cycloreversion **3** → **4** should be much (at least 28 kcal) more exothermic. Were all of this strain to be released in the transition state for the latter cycloreversion, the activation enthalpy could be less than 18 kcal, a barrier sufficiently small for the expressed purposes. Both experimental and theoretical evidence suggests that the disrotation necessary for maximum strain release is not powerfully[3] (or even at all[8]) opposed by symmetry factors.

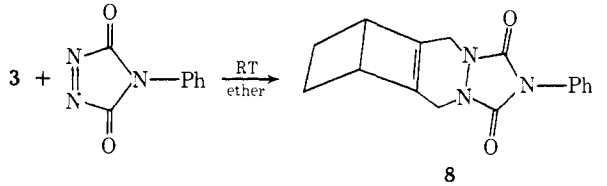
The synthesis of **3** was accomplished as shown in Scheme I. The diol **5**[9] was reduced (diimide, acetic

Scheme I



acid, room temperature; 94% yield) to the saturated diol **6**: nmr ($CDCl_3$) τ 4.9 (s, 2 H), 6.2–6.6 (m, 4 H), 7.0–8.2 (m, 8 H). Tosylation (tosyl chloride, pyridine, 0–5°, overnight) of the latter gave 66% of the ditosylate **7**: mp 143–145° (MeOH); nmr ($CDCl_3$) τ 2.2 (d, 2 H, J = 8.5 Hz), 2.6 (d, 2 H, J = 8.5 Hz), 5.8–6.0 (m, 4 H), 7.0–8.2 (m, plus s at 7.55, 14 H). Addition of the ditosylate to potassium *tert*-butoxide in DMSO on a vacuum line gave 40–60% of the desired diene (**3**): nmr (CCl_2=CCl_2) τ 4.8 (s, 2 H), 5.3 (s, 2 H), 6.75 (br s, 2 H), 7.3–8.4 (m, 4 H); uv (MeOH) λ max 238 nm (log ϵ 3.98), 247 (log ϵ 4.05), 257 (sh, log ϵ 3.90); ir (CCl_4) ν 2950 (s), 2875 (s), 1765 (w), 1650 (w), 882 (s), 825 cm^{-1} (s); mass spectrum *m/e* 105, 106, 107 (M − 1, M, M + 1). The uv spectrum of **3** is very similar to that of **1**.[10] Operations involving **3** were performed on a vacuum line, and it was routinely stored at or below −78°.

Reaction with 1-phenyl-1,3,4-triazoline-2,5-dione converts **3** to a bicyclo[2.2.0]-hex-2-ene adduct (**8**) in



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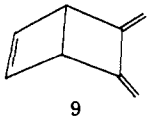

9

quantitative yield: mp ($CHCl_3$–Skelly B) 158–160°; nmr ($CDCl_3$) τ 2.3–2.6 (m, 5 H), 5.77 (s, 4 H), 6.5 (br s, 2 H), 7.55–8.4 (m, 4 H); mass spectrum *m/e* 280, 281, 282 (M − 1, M, M + 1).

The kinetics of the decomposition of **3** in tetrachloroethylene were investigated by means of nmr spectroscopy, measuring the rate of disappearance of the τ 4.8 absorption. Kinetic runs were carried out to greater than 3 half-lives and were treated by least-squares regression analyses of the simple rate equation $\ln (A_0 - A_\infty/A_t - A_\infty) = kt$. The decompositions were strictly first order, yielding $k_1 \times 10^4$ sec^{-1} = 1.319 ± 0.002 (51.5 ± 0.5°, 0.5 m*M* **3**), 2.761 ± 0.029 (60.5 ± 0.5°, 0.5 m*M* **3**), 2.893 ± 0.027 (60.5 ± 0.5°, 0.25 m*M* **3**), and 2.107 ± 0.006 (5.65 ± 0.5°, 0.7 m*M* **3**). The activation parameters calculated from all kinetic runs using a least-squares analysis of the Eyring equation are $\Delta H^{\pm}$ = 17.46 ± 0.98 kcal/mol and $\Delta S^{\pm}$ = −22.66 ± 2.97 eu. The activation enthalpy for the cycloreversion of **3** → **4** is thus 30 kcal less than that for **1** → **2**. It emerges that there is indeed no very large symmetry-engendered barrier to this reaction and that close to the full amount of the additional strain energy must be released in the transition state. The kinetics indicate that **3** is, in fact, a convenient and facile source for the tetramethylenethane **4** in solution.

It may be worth noting that neither **4** nor *o*-xylylene cyclize appreciably (**4** to bicyclo[4.2.0]octa-1,5-diene; *o*-xylylene to benzocyclobutene) at these temperatures in the liquid phase, though *o*-xylylene does in the vapor phase at elevated temperatures. Apparently these cyclizations have activation requirements that are best satisfied at high temperatures and low concentrations.

It is interesting to note that the much more exothermic cycloreversion of Dewar *o*-xylylene (**9**) to *o*-xylylene also has $\Delta H^{\pm} \approx 17$ kcal.[11] Apparently, as predicted by theory, the disrotatory cycloreversion of **9** does have a substantial symmetry imposed barrier, and this approximately nullifies the thermodynamic advantage. The kinetics of the decomposition of bicyclo[2.2.0]hex-2-ene have not been reported, but, as would be expected on the basis of a strongly forbidden disrotatory cleavage mode, it appears substantially more stable than **3**.[12]

Acknowledgments. We thank the Welch Foundation (F-149) for generous support of this work.

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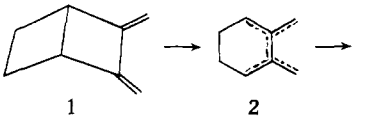
Cycloadditions of 2,3-Dimethylenecyclohexa-1,3-diene, a Tetramethyleneethane Derivative

Sir:

The formation in solution at 40–60° of the novel title compound **2** from a bicyclic precursor **1** has been ac-



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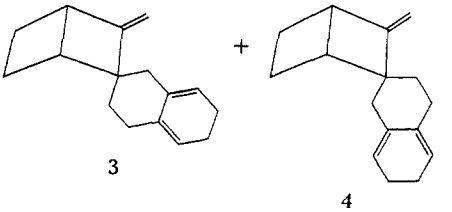

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