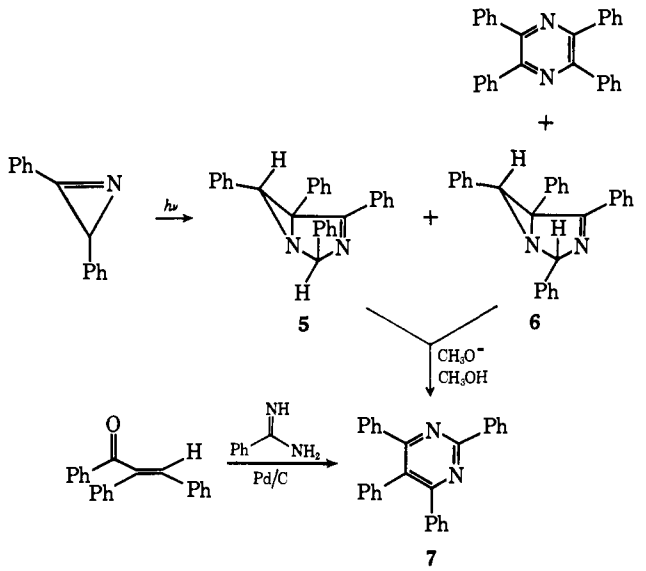
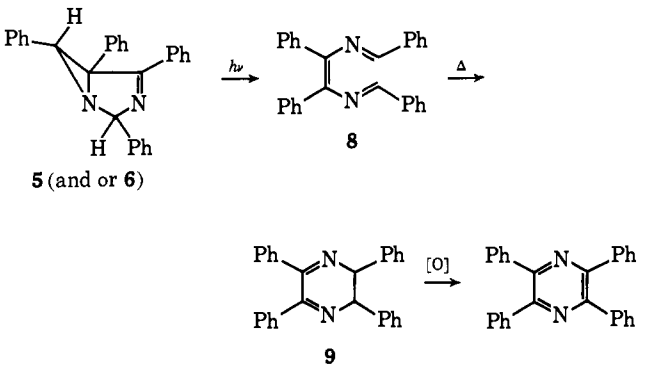
afforded three products which were separated by liquid–liquid partition chromatography. The fastest moving component in the llpc separation proved to be tetraphenylpyrazine (25%). The products with longer retention times were shown by their elemental analyses and by their mass spectra to be dimeric.[6] The nmr spectra ($CDCl_3$) of **5** (τ 3.84 (s, 1 H), 6.86 (s, 1 H), and 2.90 (m, 20 H)) and **6** (τ 4.78 (s, 1 H), 7.04 (s, 1 H), and 2.85 (m, 20 H)) led to their assignment as *endo*- and *exo*-2,4,5,6-tetraphenyl-1,3-diazabicyclo[3.1.0]hex-3-ene. Chemical confirmation of these structures was obtained by treating **5** and/or **6** with sodium methoxide in methanol to give tetraphenylpyrimidine (**7**), mp 183–184°.



Compound **7** was independently synthesized by treating 1,2-diphenylacrylophenone with benzamidine followed by oxidation over palladium on charcoal.

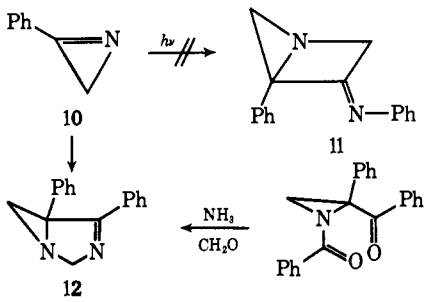
The formation of products **5** and **6** can be interpreted in terms of 1,3-dipolar addition of **2** onto diphenylazirene. On irradiation, dimers **5** and **6** are converted to tetraphenylpyrazine. This latter transformation presumably proceeds by ring opening to enediimine **8** which thermally cyclizes to a dihydropyrazine (**9**) as was previ-



ously observed with related 1,3-diazabicyclohexenes.[7-9] Oxidation of **9** during work-up nicely rationalizes the formation of tetraphenylpyrazine.

(6) All compounds analyzed satisfactorily. Complete spectroscopic and degradative details will be given in our full manuscript.
(7) A. Padwa, S. Clough, and E. Glazer, *J. Amer. Chem. Soc.*, **92**, 1778 (1970).
(8) A. Padwa and E. Glazer, *Chem. Commun.*, 838 (1971).
(9) T. DoMinh and A. M. Trozzolo, *J. Amer. Chem. Soc.*, **92**, 6997 (1970).

Woerner, Reimlinger, and Arnold[10,11] have recently reported that irradiation of 2-phenylazirene (**10**) results in the formation of 4-phenyl-3-phenylimino-1-azabicyclo[2.1.0]pentane (**11**). We have also isolated, from the photolysis of **10**, a dimer consistent with that described by these workers to which we assign an alternate structure, 4,5-diphenyl-1,3-diazabicyclo[3.1.0]-hex-3-ene (**12**), based on the data and an independent



synthesis.[6] Again, the formation of this dimer can be interpreted in terms of 1,3-dipolar addition of the initially generated nitrile ylide onto phenylazirene.

We hope to report on the generality of related 1,3-dipolar additions to azirenes at a future date.

Acknowledgment. We wish to thank the National Science Foundation (Grant No. GP-24449) for financial support.

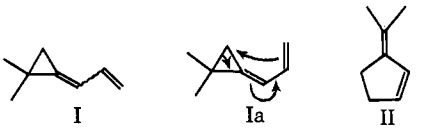
(10) F. P. Woerner, H. Reimlinger, and D. R. Arnold, *Angew. Chem., Int. Ed. Engl.*, **7**, 130 (1968).
(11) F. P. Woerner and H. Reimlinger, *Chem. Ber.*, **103**, 1908 (1970).
(12) Alfred P. Sloan Foundation Fellow, 1968–1970.
(13) NDEA Title IV Fellow, 1969–1971.
(14) NSF Science Faculty Fellow, 1970–1971.

Albert Padwa,*[12] Stuart Clough, Murali Dharan
Joel Smolanoff,[13] S. I. Wetmore, Jr.[14]
Department of Chemistry
State University of New York at Buffalo
Buffalo, New York 14214
Received October 2, 1971

The Allylidenecyclopropane–Methylenecyclopentene Energy Surface. Evidence for a "Conducted Tour" Mechanism

Sir:

Thermal isomerization[1] of allylidenecyclopropane (I) to isopropylidenecyclopentene (II) represents a class of pericyclic rearrangements formally corresponding to $_\sigma2 + {}_\pi4$ addition of a cyclopropane σ bond to a diene system (*cf.* Ia).



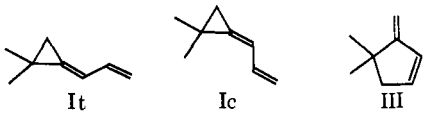
While direct and symmetry allowed, this concerted mechanism fails to explain the reported regiospecificity of the rearrangement. From its mode of synthesis[1] the diene I must be a mixture of isomers It and Ic, and whereas concerted formation of II from It is sterically feasible, the reported absence of cyclopentene III (the expected product from Ic) is difficult to explain.

(1) T. C. Shields, W. E. Billups, and A. R. Lepley, *J. Amer. Chem. Soc.*, **90**, 4749 (1968); T. C. Shields and W. E. Billups, *Chem. Ind. (London)*, 619 (1969).

Table I. Kinetic Data[a] and Activation Parameters for I, V, and VI

Reactant	T, °C	$k \times 10^5$, sec^{-1}	E_a, kcal/mol	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
I[b]	129.9	1.63 ± 0.19			
	141.8	5.28 ± 0.23			
	155.8	18.0 ± 0.7			
	163.0	36.0 ± 1.7			
I,[c] δ_{Me} 1.18	141.8	3.05 ± 0.25	33.2 ± 2.9	32.4 ± 2.9	−1.78 ± 7.14
	163.0	21.6 ± 1.9			
I,[c] δ_{Me} 1.23	141.8	7.35 ± 0.25	32.0 ± 1.2	31.2 ± 1.2	−2.93 ± 2.96
	163.0	48.4 ± 1.9			
V	61.3	9.43 ± 0.37	24.7 ± 0.9	24.0 ± 0.9	−5.43 ± 2.68
	80.0	67.3 ± 2.0			
VI	98.6	4.52 ± 0.10	29.2 ± 0.6	28.4 ± 0.6	−4.41 ± 1.85
	117.5	30.3 ± 0.6			

[a] Kinetic runs were carried out in sealed Pyrex tubes using hexane or benzene solvent; no solvent dependence was observed. [b] Initial first-order rates for 50:50 Ic *vs.* It. [c] Calculated from ratios of nmr methyl resonances during first half-life and from initial rates of 50:50 Ic *vs.* It. Error bounds represent extremes calculated from standard deviations in initial rates and nmr analyses.



Pmr spectra of diene I reveal two methyl singlets of equal intensity at δ 1.18 and 1.23 corresponding to It and Ic.[2] Thermolysis of this mixture produces at low conversions a 90–95% yield of two major products in a 67:33 ratio,[3] characterized as II[4] and the anticipated

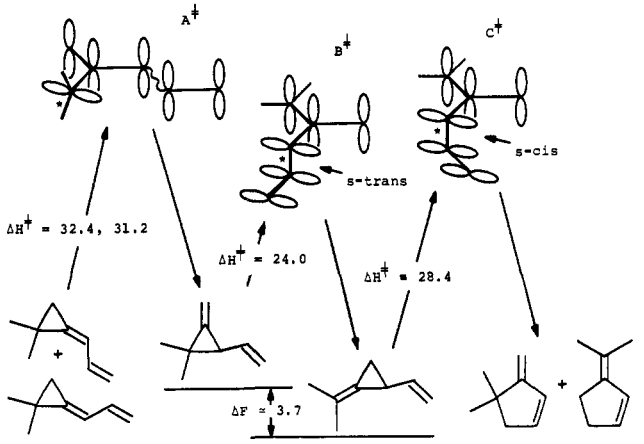
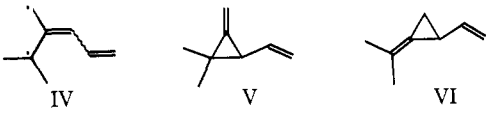


Figure 1. Enthalpy diagram.

III,[5] respectively. Conversion of I shows first-order kinetics over the initial 25% of reaction; pmr analysis at 163° discloses that the two isomers of I disappear at the relative rates of 2.2:1.0, so that at 77% conversion glpc-recovered diene I contains 76 ± 2% of the less reactive isomer having δ_{Me} 1.18. The possibility of a regiospecific transformation of each isomer of I to the corresponding cyclopentene is precluded because repyrolysis at 141.8 or 163.0° of this recovered diene likewise yields the characteristic 67:33 ratio of II and III. Since II and III are stable at 163° and Ic and It are not interconverted, we conclude that rearrangements of Ic and It are *nonregiospecific and probably proceed through a common intermediate.*

Although a stereochemically labile trimethylenemethane (*cf.* IV) could serve as the common precursor to II and III, we propose a sequence of consecutive reactions (Figure 1) whereby stereochemical distinction between It and Ic is lost upon conversion of each into V or VI.[6]



In accord with this postulate, pure V[7] rearranges rapidly at 61.3 and 80.0° with first-order kinetics to give quantitatively the isomer VI. Pure VI[7] in turn rearranges smoothly in 98% yield at 98.6 and 117.5° with first-order kinetics to give the cyclopentenes II and III in a 67:33 ratio. During thermolyses of VI there is formed an equilibrium isomer (0.77 ± 0.17%) identified as V by glc analyses and coinjections.

Evidence confirming the intermediacy of V and VI in the rearrangement of I was obtained by glc reexamination of the minor components of the reaction mixture during 141.8° thermolysis of I. A small peak develops amounting to 1.75 ± 0.20% of the starting concentration of I at *ca.* 30 min of reaction, then slowly declines during the first half-life. Glc collection led to pmr identification of this intermediate as VI. Assuming

(2) No correlation of a methyl chemical shift with any specific isomer is implied. Chemical homogeneity of the mixture I was confirmed by its conversion at −78° with 1 equiv of 4-phenyltriazoline-3,5-dione into a single $_{\pi}4_s + _{\pi}2_s$ adduct, mp 140–142°, in 79% yield. All compounds reported herein gave satisfactory nmr and analytical or mass spectral data.

(3) Analytical and preparative glc were carried out on 1/8 and 1/4 in. columns, respectively, containing 15% Carbowax 20M on Chromosorb P at 80–90°. These product compositions are accurate to ±2%.

(4) Compound II showed λ_{max} 246 nm (ε 15,800): nmr δ 1.66 (3 H, s), 1.72 (3 H, s), 2.5 (4 H, m), 5.88 (1 H, d, $J \simeq 5$ Hz), 6.29 (1 H, d, $J \simeq 5$ Hz).[1]

(5) Compound III showed λ_{max} 233 nm (ε 19,900): nmr δ 1.09 (6 H, s), 2.34 (2 H, m), 4.59 (1 H, s), 4.81 (1 H, s), 5.96 (2 H, m). Formation of III as the minor thermolysis product of I has been independently observed by K. H. Leavell, W. E. Billups, and E. S. Lewis, Abstracts, XXIIIth IUPAC Congress, Boston, Mass., July 26, 1971, Paper No. 108.

(6) Initial formation of V rather than VI from It or Ic is dictated by the kinetically preferred migration of the more substituted ring carbon in the thermal methylenecyclopropane rearrangement; *cf.* W. R. Dolbier, Jr., K. Akiba, M. Bertrand, A. Bezaguet, and M. Santelli, *Chem. Commun.*, 717 (1970).

(7) Compounds V and VI are primary photoisomers formed by 2537-Å light on diene I in acetonitrile or pentane (A. S. Kende, Z. Goldschmidt, R. F. Smith, and E. Riecke, 6th International Conference on Photochemistry, Bordeaux, France, Sept 7, 1971, Paper No. 82).

the consecutive first-order reaction sequence

$$\mathrm{I} \xrightarrow{k_1} \left[\mathrm{V} \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} \mathrm{VI}\right] \xrightarrow{k_3} \mathrm{II} + \mathrm{III}$$

where $k_2 > k_{-2} > k_3 > k_1$ and $k_3/k_1 = 52$ (by extrapolation to 141.8° from Table I), calculations[8] give $[\mathrm{VI}]_{max}/[\mathrm{I}]_0 = 1.77\%$ and $t_{max} = 24$ min. The observed concentration profile of VI demands that the principal energy surface connecting I and cyclopentenes II and III passes through the equilibrium system V $\rightleftarrows$ VI.[9]

The observed $\Delta H^{\pm}$ values (Table I) are consistent with transition states resembling intermediates $A^{\pm}$, $B^{\pm}$, or $C^{\pm}$ in which the migrating carbon (starred) p orbital is orthogonal to a nearly planar pentadienyl or allyl species[10] and thus reflect contributions from (1) the summed delocalization energies of each orthogonal component and (2) nonbonding interactions arising from s-cis *vs.* s-trans conformations of either a migrating allyl group of the initial pentadienyl chain. It is this second contribution, clearly destabilizing $C^{\pm}$ relative to $B^{\pm}$, and precluding direct cyclopentene formation from $A^{\pm}$ by approximately 2.3 kcal/mol,[11] which in effect retards direct closure of either $A^{\pm}$ or $B^{\pm}$ to a five-membered ring.

Acknowledgments. We thank Professor L. E. Friedrich for valuable criticisms during preparation of the manuscript. Partial support of this research by the Petroleum Research Fund, administered by the American Chemical Society, and by the U. S. Public Health Service (Grant No. CA-11326) is gratefully acknowledged.

(8) G. Pannetier and P. Souchay, "Chemical Kinetics," Elsevier, New York, N. Y., 1967, pp 186–188.

(9) Thermodynamic considerations require that $C^{\pm}$ be nearly equally accessible from V and VI.

(10) The probable role of orthogonal trimethylenemethanes in the thermolysis of methylenecyclopropanes has been discussed by W. E. Doering and H. Roth, *Tetrahedron*, **26**, 2825 (1970), and by J. J. Gajewski, *J. Amer. Chem. Soc.*, **93**, 4450 (1971); possibly orthogonal species such as IV have been recently invoked by W. R. Roth and H. Schmidt, *Tetrahedron Lett.*, 3639 (1971), to explain stereoconvergence from thermolysis of 1,2-cis and 1,2-trans ring-disubstituted allylidenecyclopropane derivatives.

(11) *Cf. s-cis- vs. s-trans*-butadiene, $\Delta F_{eq} \simeq 2.3$ kcal/mol: J. G. Aston, G. Szasz, H. W. Wooley, and F. G. Brickwedde, *J. Chem. Phys.*, **14**, 67 (1946).

Andrew S. Kende,* Edgar E. Riecke
Department of Chemistry, University of Rochester
Rochester, New York 14627
Received November 11, 1971

Proton Magnetic Resonance Studies in Trifluoroethanol. Solvent Mixtures as a Means of Delineating Peptide Protons

Sir:

One of the most important steps in determining the secondary structure of small polypeptides by pmr spectroscopy is the separation of peptide protons into groups according to whether they are exposed to the solvent or shielded from the solvent either sterically or through hydrogen bonds. The two most common methods of accomplishing this delineation are through the temperature dependence of the peptide proton chemical shifts[1,2] and by deuterium proton exchange rates. The peptide protons exposed to the solvent will have the higher temperature dependence and the higher deuterium–proton exchange rates. Here we would like to suggest another method of differentiating between these protons in cyclic polypeptides of relatively fixed conformation by using mixtures of TFE (2,2,2-trifluoroethanol) with other solvents.

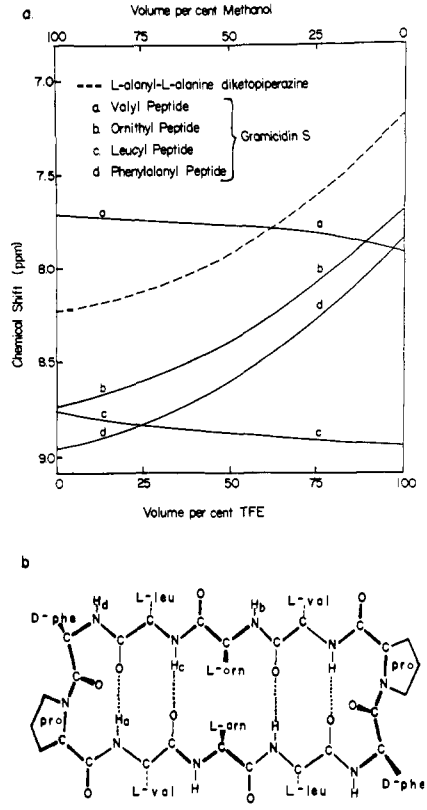


Figure 1. (a) Chemical shifts of the peptide protons of gramicidin S and L-alanyl-L-alanine diketopiperazine as functions of volume per cent of methanol and trifluoroethanol. Spectra were recorded at 220 MHz. (b) Secondary structure of gramicidin S.

As an example we take gramicidin S. Pmr studies on gramicidin S have been conducted by Conti,[3] Stern, *et al.*,[4] and Ohnishi and Urry.[2] A summary of the steps leading to the elucidation of the secondary structure of gramicidin S has been presented by Urry and Ohnishi.[5] The peptide region of the pmr spectrum of gramicidin S in methanol consists of four doublets, each corresponding to two amino acid residues. As the volume per cent of TFE is increased in a methanol–TFE mixture, the phenylalanyl and ornithyl peptide resonances undergo a dramatic upfield shift, the valyl and leucyl, a slight downfield shift (Figure 1). The peptide proton–α-proton coupling constants are independent of the TFE–methanol solvent ratios and the α protons show very little change in splitting patterns. This suggests there is no change in backbone conformation and very little if any change in side chain conformations. Similar behavior is observed in TFE–dimethyl sulfoxide mixtures. The solution conformation of gramicidin S

(1) K. D. Kopple, M. Ohnishi, and A. Go, *J. Amer. Chem. Soc.*, **91**, 4264 (1969).

(2) M. Ohnishi and D. W. Urry, *Biochem. Biophys. Res. Commun.*, **36**, 194 (1969).

(3) F. Conti, *Nature (London)*, **221**, 777 (1969).

(4) A. Stern, W. Gibbons, and L. C. Craig, *Proc. Nat. Acad. Sci. U. S.*, **61**, 734 (1968).

(5) D. W. Urry, "Spectroscopic Approaches to Biomolecular Conformation," American Medical Association, Chicago, Ill., 1970, pp 227–281.