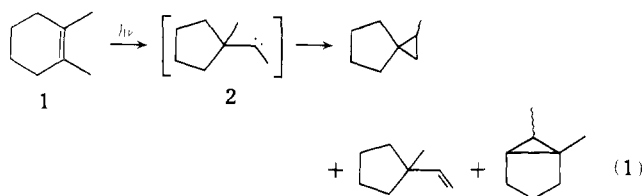


Organic Photochemistry with High Energy (6.7 eV) Photons: Duality of Carbene Intermediates from Cyclic Olefins

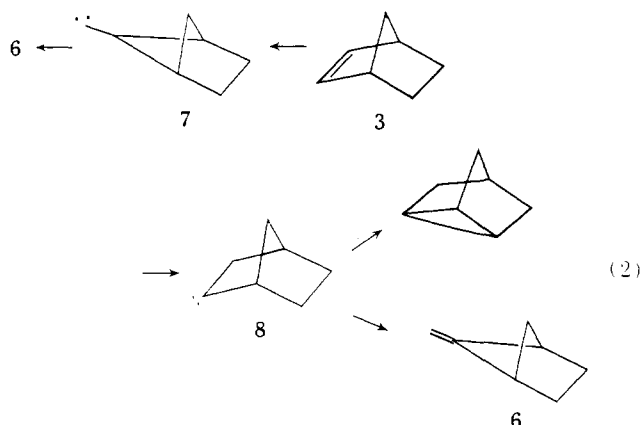
Sir:

The photochemistry of tri- and tetrasubstituted olefins in hydrocarbon solution has been investigated by Kropp and co-workers¹ using a high-pressure mercury arc and quartz optics (presumably radiation of wavelength >200 nm). More recently, the photochemistry at 185 nm of cyclic monoolefins with six, seven, and eight members has been investigated in solution and in the gas phase by Inoue, Takamuka and Sakurai.² A reaction which both groups have identified as a general one under these conditions is the formation of a carbene which subsequently rearranges by insertion or hydrogen migration. In the case of 1,2-dimethylcyclohexene (**1**), this reaction was formulated by Fields and Kropp^{1b} as shown in eq 1. We present



evidence here to show that, in addition to a carbene such as **2** which is formed by an initial migration of a C-C bond, in the case of certain disubstituted cyclic olefins, a second carbene which is formed by the initial migration of a C-H bond is also operative.

The photolysis of the bicyclic olefins, **3**, **4**, and **5**, gave the products listed in Table I. Quantum yields for these isomerizations are reported along with similar measurements for cyclohexene and cycloheptene since these have not been reported before. It can be seen that the sum of the isomerization quantum yields are comparable in all instances, although the ratios between the two products from a given olefin vary widely. The saturated products from the bicyclic olefins must come from a different carbene from that formed by initial C-C bond migration. Thus norbornene **3** can give **6** via carbene **7** (eq 2), but nortricyclene which is a major product probably comes from carbene **8**, a path that is well documented in the literature.³ Analogous arguments apply to **4** and **5** as well.



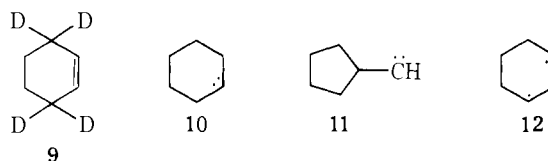
Therefore, a convincing case can be made in all three instances for the intermediacy of one new carbene formed by C-H bond migration or the presence of two carbene intermediates. It is interesting to note that, if two carbene intermediates are present in the same system, they can interconvert only through the excited state of the reactant.

In order to probe if such carbenes of the second kind are limited to bicyclic systems and to obtain further insight into the mechanism of these isomerizations, the photolysis of cy-

Table I. Photochemical Products from some Monoolefins at 185 nm^a

Reactant	Products			
	Structure	ϕ	Structure	ϕ
		0.05		0.07
		0.10		0.02
		0.07		0.07
		0.20		0.01
		0.09		0.02

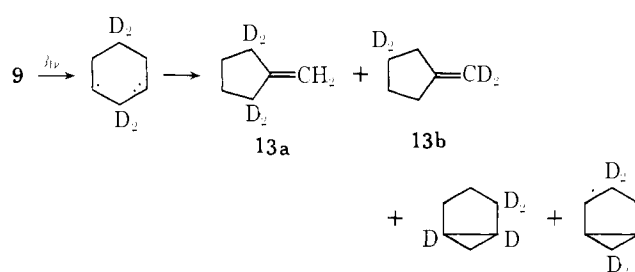
^a Concentration of reactant: 4×10^{-2} M; absorbed intensity 2.5×10^{17} photons/mL⁻¹ min⁻¹. ^b See Ref 9 for spectral data. ^c R. W. Hoffman, *Chem. Ber.*, **108**, 109 (1975). ^d C. A. Grob and J. Hostynek, *Helv. Chim. Acta.*, **180**, 1676 (1963). ^e J. H. Lukas, A. P. Kouwenhoven, and F. Baardman, *Angew. Chem.*, **14**, 709 (1975). We thank Dr. Lukas for the NMR spectrum of the compound.



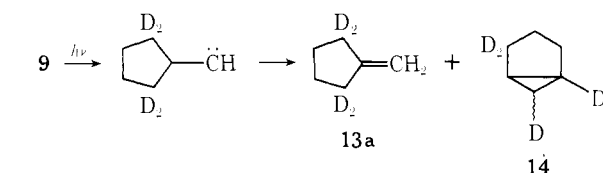
clohexene-3,3,6,6-*d*₄ (**9**) was investigated.^{4,5} Three intermediates derived from cyclohexene can be considered. Both **10** and **11** could lead to either or both of the observed products, while **12** could lead only to bicyclo[3.1.0]hexane. In the case of the deuterated material, these intermediates and their reaction paths can be formulated according to Schemes I-III.

Analysis of the NMR spectrum of methylene cyclopentane-*d*₄ that was isolated showed that it was made up of 92%

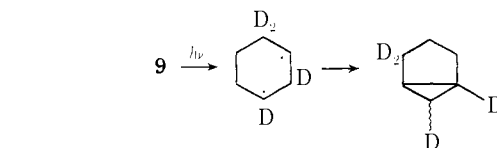
Scheme I



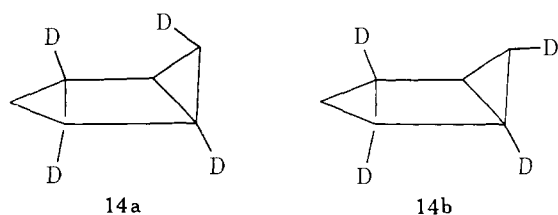
Scheme II



Scheme III



13a and 8% **13b**⁶ which corresponds a 5:1 preference⁷ for Scheme II over I for the formation of this product. In the NMR spectrum of the bicyclo[3.1.0]hexane-*d*₄ that was isolated, the intensities of the absorptions at δ 0.15, 1.2, and 1.6 were in the ratio 1:2:3 instead of 2:3:5 as in bicyclo[3.1.0]hexane. This showed that there was one deuterium atom each in the methylene and one of the methine groups on the cyclopropane ring and two deuterium atoms at C-2. In order to find out if the compound was homogenous in terms of its deuterium distribution, the NMR spectrum was studied at high resolution (220 MHz). In the spectrum of bicyclo[3.1.0]hexane, the two protons at C-6 occur at δ 0.10 and 0.23. The former which is presumably the endo hydrogen is coupled less strongly ($J = 4$ Hz) to the two methine protons than the exo hydrogen ($J = 8$ Hz). The geminal coupling is ~ 4 Hz.⁸ In the spectrum of the tetradeuterio derivative, absorptions due to both protons at C-6 are present, but the geminal coupling between them is absent. The intensities of these absorptions correspond to the composition **14a**:**14b**::1:2. This distribution of the deuterium at C-6 indicates much stereoselectivity in the formation of this product



which in turn argues against the intermediacy of a diradical as in Scheme III. It is not surprising that carbene **10** does not lead to bicyclo[3.1.0]hexane, a fact that is well known.³ If the formation of bicyclo[3.1.0]hexane is also included, the partition of the excited state of cyclohexene between carbenes **10** and **11** will be 1:14.

The intriguing question that remains unanswered is the factor (or factors) which determines the direction of the excited state between these two pathways.

Acknowledgment. The authors thank Drs. J. J. Wynne and J. A. Armstrong for their advice and encouragement.

References and Notes

- (a) P. J. Kropp, H. G. Fravel, Jr., and T. R. Fields, *J. Am. Chem. Soc.*, **98**, 86 (1976); (b) T. R. Fields and P. J. Kropp, *ibid.*, **96**, 7559 (1974); (c) P. J. Kropp, E. J. Reardon, Jr., Z. L. F. Gaibel, K. F. Williard, and J. H. Hattaway, Jr., *ibid.*, **95**, 7058 (1973).
- (a) Y. Inoue, S. Takamuku, and H. Sakurai, *J. Chem. Soc., Chem. Commun.*, 577 (1975), and 423 (1976); (b) *J. Phys. Chem.*, **81**, 7 (1977); (c) *J. Chem. Soc., Perkin Trans. 2*, 1635 (1977).
- W. Kirmse, "Carbene Chemistry", Academic Press, New York, N.Y., 1964, p 56.
- Deuterium-labeling experiments with cycloheptene-1,2-*d*₂ were conducted in ref 2a and 2c. The formation of only one kind of methylenecyclohexane was reported. No stereochemical information on the bicyclo[4.1.0]heptane-*d*₂ that was also formed was given.
- Cyclohexene-3,3,6,6-*d*₄ was obtained from Merck & Co. Its isotopic purity as verified by NMR was >98%. Its NMR spectrum was unchanged after a part of it had been photoisomerized.
- In the NMR spectrum of methylenecyclopentane, the absorptions corresponding to the three kinds of protons are distinctly separate. The composition of the mixture of **13a** and **13b** can be estimated from the area of any of these peaks (if the total = 6 H). The composition that was calculated was internally consistent to $\pm 1\%$.
- It is uncertain what, if any, isotope effect should be attributed to Schemes I or II. The preference reported here assumes that no isotope effect was operative.
- D. J. Patel, M. F. H. Howden, and J. D. Roberts, *J. Am. Chem. Soc.*, **85**, 3218 (1963). These assignments were made by comparing the NMR spectrum of bicyclo[3.1.0]hexane with that of its derivative listed here.
- IR 870, 1675 cm^{-1} ; NMR δ 4.22 (2 H), 2.88 (2 H), 2.24 (1 H), 1.2-1.8 (5 H).

R. Srinivasan,* K. H. Brown
IBM Thomas J. Watson Research Center
Yorktown Heights, New York 10598
Received November 23, 1977

Two Antiparallel Tripeptide Chains Stabilized by an SS Unit: *S,S'*-Bis(Cbz-L-Ala-L-Cys-L-Ala-OMe) in Chloroform Solution

Sir:

Recent developments^{1,2} in the study of folding pathways for SS-containing globular proteins indicate the importance of thermodynamic stability of the peptide conformations before and after disulfide bond formation. Studies on relative thermodynamic stabilities of different disulfide intermediates have been needed in this area. This report concerns the fundamental aspect of conformational stability of SS-containing oligopeptides. It has been known that many natural proteins containing cystine take antiparallel arrangements in the close proximity of the SS linkage, and that the most stable dihedral angle of the CSSC group is restricted to $\sim 90^\circ$.³ Restricted rotation of this group significantly reduces the number of possible conformers of cystine itself, and, more importantly, as herein reported, it stabilizes intramolecular hydrogen bonds between open oligopeptide chains leading to an antiparallel conformation. Although our study was made on specific cases, the problem of antiparallel conformation in a globular protein can be understood more comprehensively than previously by combining the present results with information on antiparallel chain-forming processes without an SS linkage (e.g., β turn or association).⁴

We investigated the solution conformation of open-chain tetra- and hexapeptides having a cysteinyl SS linkage and found that a hexapeptide, *S,S'*-bis(Cbz-L-Ala-L-Cys-L-Ala-OMe) (I), readily takes an antiparallel ladder-like conformation possessing four intramolecular hydrogen bonds between the tripeptide chain moieties. In contrast, tetrapeptides containing cystine and alanine, i.e., *S,S'*-bis(Cbz-L-Ala-L-Cys-OMe) (II) and *S,S'*-bis(Cbz-L-Cys-L-Ala-OMe) (III), have decreasing trends in forming such specific conformations. Hence, we suggest that at least three amino acid residues in each chain are required to stabilize an antiparallel sheet structure containing hydrogen bonds in close proximity to a cystine SS linkage.

The oligopeptides were prepared stepwise from cystine by mixed anhydride methods, carefully preventing cleavage of the SS group, and resulting in powdery crystallines after recrystallization. The purity of the products was checked by high-speed liquid chromatography and elemental analysis.

In CDCl_3 solution, the hexapeptide I shows a ¹H NMR spectrum (Figure 1) corresponding to an almost entirely symmetrical structure. The Cys-NH proton signal depends

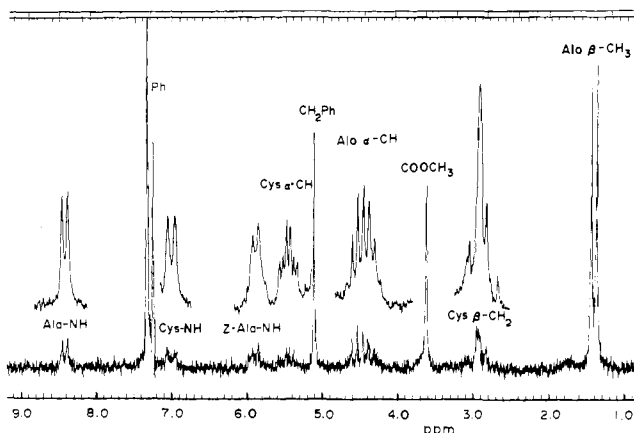


Figure 1. 100-MHz ¹H NMR spectrum of *S,S'*-bis(Cbz-L-Ala-L-Cys-L-Ala-OMe) (I) in CDCl_3 solution: concentration 2.4×10^{-2} M, 37 °C. The spectrum was recorded with a Varian XL-100 spectrometer. The inset spectra ($\times 4$ intensity) were taken by changing the radio frequency from 60 to 70 dB, the filter value from 4 to 1 Hz, and the sweep time from 500 to 1000 s, so that the noise level of the spectra was minimized.