

Table I
Relative Intensities of Selected Ions in the EI Spectra

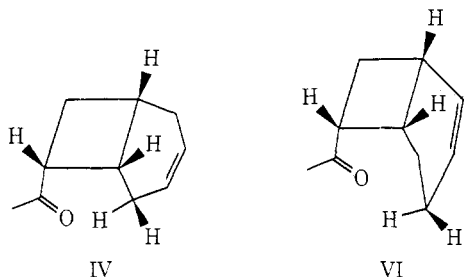
Compd	I	II	III	IV	V	VI
Stereochemistry	Exo	Endo	Exo	Endo	Exo	Endo
M ⁺	0.039	0.008	0.032	0.002	0.042	0.012
(M - 18) ⁺	0.001	0.004	0.010	0.002	0.009	0.005

Table II
Relative Intensities of Selected Ions in the Isobutane CI Spectra

Compd	I	II	III	IV	V	VI
Stereochemistry	Exo	Endo	Exo	Endo	Exo	Endo
(M + 1) ⁺	0.540	0.402	0.633	0.575	0.724	0.562
M ⁻	0.021	0.019	0.016	0.002	0.016	0.006
(M - 1) ⁺	0.051	0.145	0.005	0.011	0.007	0.016
(M + 1 - 18) ⁺	0.026	0.032	0.015	0.131	0.012	0.144
(M - 18) ⁺	0.002	0.002	0.004	0.001	0.003	0.002
(M - 1 - 18) ⁺	0.008	0.001				

six-membered transition state. Hydrogen transfer to the carbonyl group of the unsaturated endo isomers IV and VI could involve the allylic hydrogens of the cyclohexene ring. This suggests that the ready loss of water in the CI spectra of IV and VI reflects the weakness of the allylic C-H bond. The greater aliphatic C-H bond strength results in the weak (M + 1 - 18)⁺ ion of compound II.

It is usually assumed in CI experiments that protonation of aldehydes or ketones occurs on the carbonyl oxygen.^{5e} The evidence presented above indicates that the second proton of the departing H₂O molecule comes from the allylic hydrogens in IV and VI. This means that the loss of water in IV must involve a six-membered transition state, while in VI a seven-membered transition state is required, as shown below. Labeling studies will be necessary to establish these conclusions concerning mechanism with rigor. However, our experimental observations already provide further evidence that CI mass spectrometry can reflect stereochemical differences.¹⁰



Experimental Section

Ketones I-VI were prepared as previously described⁷ and purified by preparative vapor phase chromatography before use.

Mass spectra were obtained with a Du Pont 21-492 mass spectrometer at resolution 2000 or 10,000, source temperature 200°, and at 100 eV ionizing potential for electron ionization and 220 eV for chemical ionization. Samples were introduced via a glass batch inlet system at 200°. Isobutane reactant was Matheson Instrument Grade gas. The repellers were used to optimize the ion current, and were typically zero voltage for CI spectra. The pressure of the source could not be measured, but was about 0.5-1.0 Torr for CI spectra, based on prior experience.

The combined CI-EI source was designed and built in our laboratory under license from Scientific Research Instruments Corp., Baltimore, Md.

The intensities reported have not been corrected for ¹³C isotope contributions. The CI spectra have been corrected for contributions from the reactant gas. Data were obtained with an AEI DS-30 data system to which our own CI programs have been added. A peak with relative intensity 0.001 would typically be three times stronger than the computer threshold level.

Registry No.—I, 24112-75-2; II, 34969-29-4; III, 51222-29-8; IV, 51222-30-1; V, 51222-31-2; VI, 51222-32-3.

Supplementary Material Available. Tabulation of these spectra and high-resolution results will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-74-1752.

References and Notes

- S. Meyerson and A. W. Weitkamp, *Org. Mass Spectrom.*, **1**, 659 (1968).
- J. K. Macleod and R. J. Wells, *J. Amer. Chem. Soc.*, **95**, 2387 (1973).
- (a) H. Ziffer, H. M. Fales, G. W. A. Milne, and F. H. Field, *J. Amer. Chem. Soc.*, **92**, 1597 (1970); (b) P. Longevialle, G. W. A. Milne, and H. M. Fales, *ibid.*, **95**, 6666 (1973), and references cited therein.
- A. N. H. Yeo and D. H. Williams, *Org. Mass Spectrom.*, **2**, 331 (1969).
- (a) R. J. Liedtke and C. Djerassi, *J. Amer. Chem. Soc.*, **91**, 6814 (1969); (b) S. Meyerson, C. Fenselau, J. L. Young, W. R. Landis, E. Selke, and L. C. Leitch, *Org. Mass Spectrom.*, **3**, 689 (1970); (c) P. Brown and C. Fenselau, *ibid.*, **7**, 305 (1973); (d) H. M. Fales, personal communication; (e) T. A. Elwood and J. H. Futrell, *J. Amer. Chem. Soc.*, in press.
- J. Deutsch and A. Mandelbaum, *J. Chem. Soc. B*, 866 (1971).
- R. A. Cormier and W. C. Agosta, *J. Amer. Chem. Soc.*, **96**, 1867 (1974); R. A. Cormier, W. L. Schreiber, and W. C. Agosta, *ibid.*, **95**, 4873 (1973).
- See paragraph at end of paper regarding supplementary material.
- This fraction is calculated by dividing the intensities of the peak by the total intensity of all sample peaks above *m/e* 40 for EI and above *m/e* 60 for CI spectra. The intensities of peaks of the CI reactant gas are not included. The intensities reported are averages of duplicate spectra.
- W. C. A. and R. A. C. acknowledge the partial support of this research by the donors of the Petroleum Research Fund, administered by the American Chemical Society; F. H. F. and D. V. B. thank the Rockefeller Foundation for purchase of the mass spectrometer through a grant to research in reproductive biology.

Synthetic Organic Photochemistry. VI. The Photochemical Ring Expansion of an α -Hydroxy- β,γ -Unsaturated Ketone

Robert G. Carlson*¹ and Ananth V. Prabhu

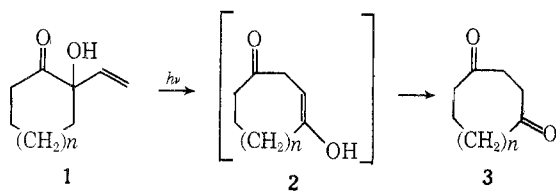
Department of Chemistry, University of Kansas,
Lawrence, Kansas 66045

Received December 11, 1973

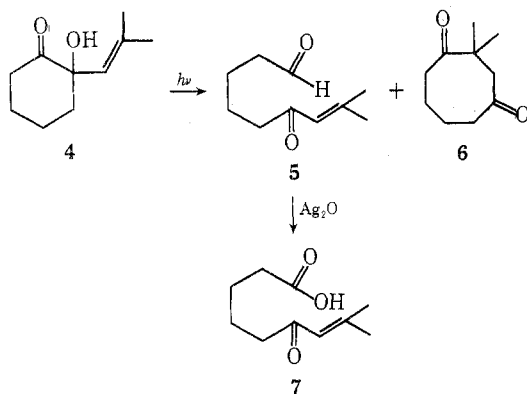
We have recently provided examples of two-carbon photochemical ring expansions of 2-alkenyl- and 2-alkynylcycloalkanes^{2,3} and three-atom photochemical ring expansions of 2-cyclopropyl- and 2-(2-oxiranyl)cycloalkanes.^{4,5} Of these unique methods for ring-size modification, the photochemical ring expansions of 2-alkenylcyclo-

cloalkanones suffer from the disadvantage that the reaction is readily reversible and this necessitates the separation of the starting material and product and the recycling of the starting material to achieve high conversions.

In an attempt to overcome this inherent disadvantage we sought to devise a method which would render the reaction irreversible. One possible solution to this problem would be to design a system in which the double bond of the ring-expanded β,γ -unsaturated ketone would "self-destruct" and thus make the reaction irreversible. The photochemical ring expansion of a 2-alkenyl-2-hydroxycycloalkanone was an attractive choice for such a system because the double bond in the ring-expanded product would be the double bond of an enol and a very rapid ketonization would be expected, removing the double bond ($1 \rightarrow 2 \rightarrow 3$).



In order to examine the photochemical behavior of this type of system, 2-hydroxy-2-(2-methyl-1-propenyl)cyclohexanone (4) was prepared from cyclohexane-1,2-dione by addition of 2-methylpropenyllithium. Ketol 4 proved to be quite stable to photolysis and prolonged irradiations were required to obtain appreciable quantities of the photoproducts. Irradiation of a 1% solution of 4 in hexane with 300-nm lamps for 27 hr produced a mixture whose vpc-volatile fraction consisted of 49% 4, two photoproducts characterized as 5 (30%) and 6 (15%), and 6% of an unidentified product. Further irradiation led to a decrease in the amounts of 5 and 6 present relative to the internal standard.



The aldehyde 5, which was the major photoproduct, proved to be quite unstable and difficult to purify. To circumvent this problem the starting ketol was separated from the photoproducts by column chromatography on silica gel and the photoproduct mixture was oxidized with silver oxide to give the acid 7 as the only acidic product. The structure 7 was readily assigned on the basis of its spectral properties (Experimental Section). The neutral photoproduct 6 was separated by preparative gas chromatography and its structure was assigned on the basis of its spectral properties and mass spectral fragmentation pattern. In particular, in the nmr spectrum the six-proton singlet at δ 1.15 and two-proton singlet at δ 2.48 were of particular significance in the assignment of structure.

It thus appears that the major pathway in the photolysis of 4 involves type I cleavage followed by a 1,5 hydrogen atom shift to give the aldehyde 5. The 1,3-acyl shift characteristic of 2-alkenylcycloalkanones is much less effi-

cient than in the cases in which the hydroxyl group is not present. The reasons for the increased photostability of the ketol 4 are not clear, and, at least in this case, the photolysis of a 2-alkenyl-2-hydroxycycloalkanone does not seem to provide an efficient method of two-atom photochemical ring expansion.

Subsequent to the completion of this work a paper describing photochemical 1,3-acyl shifts of several α -hydroxy ketones appeared.⁶ In one instance reported in this work the reaction proceeded in high yield.

Experimental Section

All boiling points are uncorrected. The infrared spectra were determined in carbon tetrachloride solution and recorded on a Beckman IR-8 spectrophotometer. The nuclear magnetic resonance spectra were recorded on a Varian A-60 or HA-100 instrument using tetramethylsilane as an internal standard. Mass spectra were determined with a Varian MAT CH-5 instrument. Gas chromatography studies utilized F & M Model 700, Aerograph A-90-P, or Bendix 2300 gas chromatographs and recorders equipped with Disc Integrators. Anhydrous potassium carbonate was used as the drying agent and microanalyses were performed by Weiller and Strauss Microanalytical Laboratories, Oxford, England, and Mrs. Kathie Widiger at the University of Kansas.

2-Hydroxy-2-(2-methyl-1-propenyl)cyclohexanone (4). To a suspension of 2.32 g (0.33 mol) of finely cut lithium wire (1% sodium) in 100 ml of dry ether at -12° was added dropwise, under argon, a solution of 15.0 g (0.17 mol) of 1-chloro-2-methylpropene in 15 ml of ether. After stirring for 3.5 hr most of the lithium had reacted and analysis⁷ indicated that the concentration of the lithium reagent was 1.3 M. To this solution of lithium reagent at -12° was added a solution of 7.64 g (0.067 mol) of cyclohexane-1,2-dione in 25 ml of dry ether over a period of 20 min. After stirring overnight, 30 ml of saturated ammonium chloride solution was added carefully. The ether layer was separated, and the aqueous layer was saturated with sodium chloride and extracted with ether. The combined ether layers were washed with brine, dried, and evaporated to afford 6.86 g of crude product which contained 60% of the ketol 4 by vpc analysis.⁸ The crude product was distilled to afford 4.04 g of colorless oil, bp $60-98^\circ$ (0.18 mm), which was chromatographed on silica gel (Silicar CC-7) to give 2.00 g of the pure ketol: ir 3520, 1720, and 1670 cm^{-1} ; nmr δ 1.55 (3 H, d, $J = 1\text{ Hz}$), 1.73 (3 H, d, $J = 1\text{ Hz}$), 1.75-2.5 (8 H, m), 3.81 (1 H, br s), and 5.36 (1 H, m); uv (isooctane) λ_{max} 283 nm (ϵ 207).

Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_2$: C, 71.39; H, 9.59. Found: C, 71.40; H, 9.66.

Irradiation of 4. A solution of 2.00 g of ketol 4 and 0.502 g of cyclododecane (internal standard) in 200 ml of hexane contained in a Vycor vessel was degassed with nitrogen and irradiated at 300 nm in a Rayonet Photochemical Reactor. Aliquots were removed periodically and analyzed by vpc.⁸ Analysis showed that three products were formed. After 27.4 hr the irradiation was stopped because the ratio of products to internal standard was decreasing. Evaporation of the solvent afforded 2.168 g of yellow oil which consisted of 49% 4 and three new products present to the extent of 6% (not characterized), 15% (6), and 30% (5). The starting ketol 4 was readily separated from the other products by column chromatography on silica gel. Dione 6 was separated by preparative vpc⁹ from a portion of the mixture of photoproducts: ir 2900, 1700 cm^{-1} ; nmr δ 1.15 (6 H, s), 1.82 (4 H, m), 2.30 (4 H, m), and 2.48 (2 H, s); mass spectrum (70 eV) m/e (rel intensity) 168 (6), 140 (10), 135 (9), 119 (5), 112 (6), 107 (7), 85 (18), 84 (53), 83 (20), 81 (7), 77 (26), 69 (10), 68 (8), 67 (11), 57 (8), 56 (40), and 55 (100).

Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_2$: C, 71.39; H, 9.59. Found: C, 71.20; H, 9.44.

A portion (0.433 g) of the mixture of photoproducts (free of ketol 4) was oxidized with silver oxide by addition of a methanol solution to a mixture prepared from 0.400 g (10 mmol) of sodium hydroxide in 15 ml of water and 0.853 g (5 mmol) of silver nitrate in 10 ml of water. The resulting mixture was vigorously stirred for 1 hr at 0° . Water (15 ml) was added and the mixture was filtered. The filtrate was extracted with ether and the aqueous solution was cooled to 0° and carefully acidified with dilute nitric acid. The acidic aqueous solution was extracted with ether, and the combined ether extracts were dried (MgSO_4) and evaporated to afford 0.246 g of a brown oil which solidified on standing. A portion of this material was recrystallized twice from hexane to afford the pure sample of 8-methyl-6-oxonon-7-enoic acid (7): mp

46–47°; ir 3650–2500, 1720, 1695, and 1630 cm^{-1} ; nmr δ 1.62 (4 H, m), 1.89 (3 H, d, $J = 1\text{Hz}$), 2.12 (3 H, d, $J = 1\text{Hz}$), 2.40 (4 H, m), 6.03 (1 H, m), and 11.5 (1 H, br s).

Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_3$: C, 65.19; H, 8.75. Found: C, 65.25; H, 8.72.

Sensitized Irradiation of 4. A solution of 108 mg of 4 in acetone was irradiated at 300 nm. After 46 hr no new products had been detected by vpc and removal of the solvent gave a crude product whose spectral properties indicated that it consisted mainly of starting 4.

Acknowledgment. The partial financial support of this work by the National Science Foundation (Grant No. GP-28156) is gratefully acknowledged.

Registry No.—4, 51222-33-4; 5, 51293-25-5; 6, 51222-34-5; 7, 51222-35-6; cyclohexa-1,2-dione, 765-87-7; 1-chloro-2-methylpropene, 513-37-1.

References and Notes

- (1) Alfred P. Sloan Foundation Fellow, 1970–1972.
- (2) (a) R. G. Carlson and J. H. Bateman, *Tetrahedron Lett.*, 4151 (1967); (b) R. G. Carlson, R. L. Coffin, W. W. Cox, and R. S. Givens, *J. Chem. Soc., Chem. Commun.*, 501 (1973).
- (3) R. G. Carlson and D. E. Henton, *Chem. Commun.*, 674 (1969).
- (4) R. G. Carlson and E. L. Biersmith, *Chem. Commun.*, 1049 (1969).
- (5) R. G. Carlson, J. H. Huber, and D. E. Henton, *J. Chem. Soc., Chem. Commun.*, 223 (1973).
- (6) T. Sasaki, K. Kanematsu, K. Hayadawa, and A. Kondo, *J. Org. Chem.*, **38**, 4100 (1973).
- (7) G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Amer. Chem. Soc.*, **93**, 1386 (1971).
- (8) A 6 ft \times 0.25 in. gas chromatography column packed with 15% Dow 710 silicone oil on ABS was utilized for this analysis.
- (9) A 6 ft \times 0.25 in. gas chromatography column packed with 10% DEGS on 60/80 Chromosorb W. was utilized for this separation.

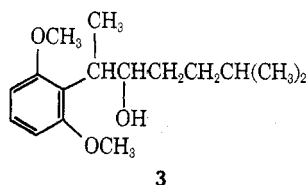
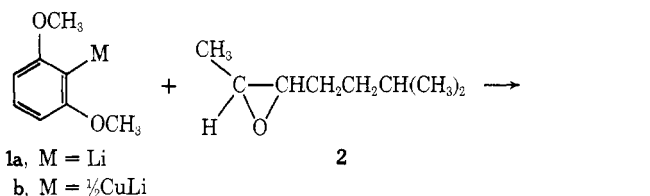
Reactions of Organometallic Derivatives of 1,3-Dimethoxybenzene^{1a}

M. E. Lewellyn^{2b} and D. S. Tarbell*

Department of Chemistry, Vanderbilt University,
Nashville, Tennessee 37235

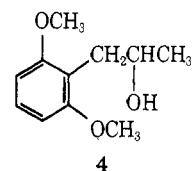
Received November 2, 1973

2-(2,6-Dimethoxyphenyl)-6-methyl-3-heptanol (3), desired in connection with synthetic work on fumagillin,² was to be synthesized by the route below.



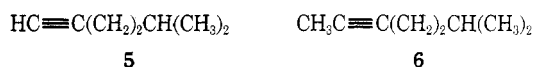
Phenyllithium gives only the secondary alcohol with propylene oxide,³ and it was hoped that 1 would attack the epoxide 2 at the methylated carbon rather than at the carbon carrying the larger isoamyl group.

1,3-Dimethoxybenzene is metalated by *n*-butyllithium in the 2 position,⁴ with only 3–4% in the 4 position, as shown by carbonation⁵ and careful examination of the acid. We have found that 1a with propylene oxide gives a 28% yield of the secondary alcohol 4, along with a considerable amount of 1,3-dimethoxybenzene.



trans-2,3-Epoxy-6-methylheptane (2) was prepared by *m*-chloroperbenzoic acid oxidation⁶ of *trans*-6-methyl-2-heptene; the latter was prepared from the corresponding acetylene, which could serve as the source of both the cis and *trans* ethylene.⁷

5-Methyl-1-hexyne⁸ (5) gave 90% yield of pure 6-methyl-2-heptyne (6) by treatment with *n*-butyllithium at



–78°, addition of a small amount of dimethyl sulfate at this temperature to react with unchanged *n*-butyllithium, and then addition of the remaining dimethyl sulfate at ice–salt temperature. Sodamide and methyl iodide in liquid ammonia gave only a 33% yield of 6. The action of *n*-butyllithium on 5, followed by methyl iodide at –78°, yielded some *n*-butyl iodide. The action of *n*-butyllithium at 0°, followed by dimethyl sulfate at 0°, gave mainly the monomethyl derivative 6, but with about 10% of a higher homolog, probably $\text{CH}_3\text{C}\equiv\text{CCH}(\text{CH}_3)\text{CH}_2\text{CH}(\text{CH}_3)_2$, which would be the result of dianion formation from 6 by the *n*-butyllithium.⁹ The method described above avoids these side products.

Reduction of 6 to the pure *trans*-6-methyl-2-heptene in 57% yield with sodium–liquid ammonia¹⁰ was satisfactory.

2,6-Dimethoxyphenyllithium (1a) did not react with the epoxide 2 after 48-hr refluxing in THF. Heating the mixture in diglyme at 110–120° for 24 hr used up the organometallic,¹¹ but left the epoxide; a crystalline solid, mp 178–180°, isolated from the reaction mixture was shown by nmr, ir, mass spectrum, and elemental analysis to be the known¹² 2,6,2',6'-tetramethoxydiphenylcarbinol, $\text{Ar}_2\text{CH-OH}$, Ar = 2,6-(CH_3O)₂C₆H₃.

It is reported¹³ that lithium dimethylcuprate and lithium diphenylcuprate in ether are better reagents for nucleophilic attack on epoxides than their lithium counterparts. The lithium cuprate of 1,3-dimethoxybenzene (1b), prepared from 0.5 equiv of purified cuprous bromide¹⁴ to 1 equiv of the lithium compound 1a in ether, gave a 45% yield of 4 from propylene oxide. Reaction of the lithium cuprate 1b with the epoxide 2 gave no reaction after 3 hr at 0°; after 12 hr at room temperature, no disappearance of epoxide was observed, but no 1,3-dimethoxybenzene was found by hydrolysis and vpc analysis. A solid, mp 174–176°, different from the solid described above, was isolated, and from its ir and nmr spectra was shown to be the known 2,6,2',6'-tetramethoxybiphenyl.¹⁵ The lithium cuprate compounds couple well with aryl halides.¹⁴

The *trans* epoxide 2 is apparently too highly substituted to react with the diortho-substituted organometallic 1.

Experimental Section¹⁶

6-Methyl-2-heptyne (6). A 2-l., three-neck flask was fitted with a mechanical stirrer (nonsparking motor, glass blade), a condenser, and a dropping funnel fitted with a septum. In the flask were placed 52 g (0.54 mol) of 5-methyl-1-hexyne⁸ in 250 ml of THF. The dropping funnel contained 0.57 mol of *n*-butyllithium, added by means of a syringe; the system had been purged with nitrogen and a nitrogen atmosphere was maintained during the reaction. The flask was cooled by a Dry Ice–acetone bath and the *n*-butyllithium was added dropwise over a 30-min period. The resulting yellow solution was stirred for an additional 45 min at this temperature. About 70 ml of dimethyl sulfate was placed in the dropping funnel, and to the yellow solution was added about 5 ml of dimethyl sulfate to remove any unreacted *n*-butyllithium. The