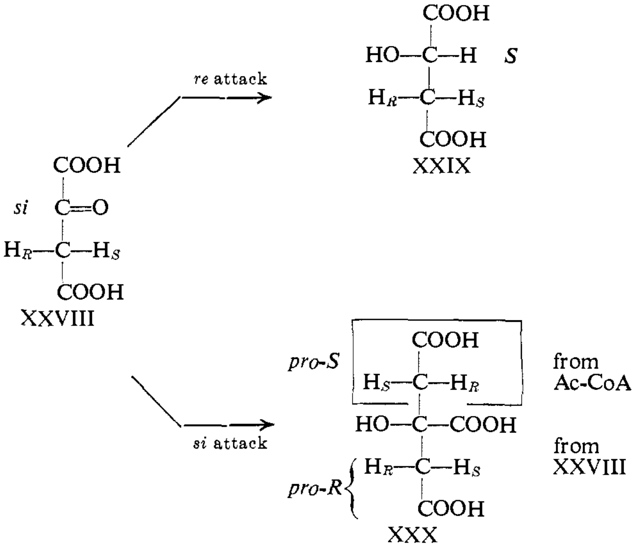

Other Enzymatic Reactions. The *re* and *si* symbols may be employed to describe additions to, or reductions of, carbonyl groups and carbon–carbon double bonds. Although unknown intermediates may be involved in such reactions, the over-all stereochemistry of the process may be specified. Thus malate dehydrogenase (EC 1.1.1.37) catalyzes the transfer of H_R from C-4 of the nicotinamide ring of reduced-NAD (XVIII) to the *re* face of the carbonyl carbon of oxaloacetate (XXVIII) to form L-malate[27] (XXIX), whereas citrate synthase (EC 4.1.3.7) catalyzes the interaction of acetyl-CoA and the *si* face of this same carbon atom, to form the *pro-S* CH_2COOH group of citrate (XXX).[18]

These examples, and the examples of part I, show how the *re*/*si*, *pro-R*/*pro-S*, and *R*/*S* systems, when used in conjunction with standard chemical nomenclature, may serve to transmit stereochemical information without the use of projection or structural formulas. The symbolism is both brief and unambiguous, and as such is suited for use in summaries and abstracts, and in indexing.

Acknowledgment. The writer is greatly indebted to Dr. R. S. Cahn, Professor Sir Christopher Ingold, and Professor V. Prelog for their helpful suggestions and criticisms at all stages in the preparation of this manuscript; also to Drs. H. Hirschmann and H. B. Vickery and to many other colleagues for their valuable comments on drafts of the paper.

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(27) J. L. Graves, B. Vennesland, M. F. Utter, and R. J. Pennington, *J. Biol. Chem.*, **223**, 551 (1956).

The Direct and Sensitized Irradiation of Acyclic Dienes[1-3]

William G. Dauben, Robert L. Cargill, Robert M. Coates,[4] and Jack Saltiel[5]

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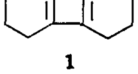
Received February 3, 1966

Abstract: Both the direct and acetophenone-sensitized reaction of 1,1′-bicyclohexenyl (**1**) yielded the valence isomeric cyclobutene **4** as the major product. Myrcene upon direct irradiation yielded mainly the cyclobutene **6** with less than 5% of the bicyclo[2.1.1]hexane isomer **5** which is the sole product of the sensitized reaction. No valence isomerization occurred when 2,3-dimethyl-1,3-butadiene was photosensitized. A possible explanation for this latter result is given. A mechanism for the direct photolysis reaction, based upon the electrocyclization concept of Woodward and Hoffmann, is presented.

The ultraviolet irradiation of cyclic dienes is now a well-established synthetic route to bicyclic compounds containing a cyclobutene ring.[6] Until recently it was not known whether acyclic dienes could similarly be converted into a cyclobutene derivative. The extension of this photochemical reaction to open-chain compounds has been realized in the work of Srinivasan[7] and of Crowley.[8] Parallel studies conducted in this laboratory with 1,1′-bicyclohexenyl (**1**), myrcene (**2**), and 2,3-dimethyl-1,3-butadiene (**3**) yielded similar results which need not be elaborated. In addition, the use of a sensitizer for bringing about the valence isomerization was evaluated.

The direct irradiation of 1,1′-bicyclohexenyl (**1**) formed the valence isomeric cyclobutene **4** and, as was also found by Crowley,[8] at least two other products were formed.[9] Careful fractional distillation gave **4** in about 90% purity, and in order to obtain pure material the distillate had to be purified by tedious,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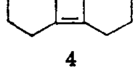
4

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(1) For the previous paper in this series, see W. G. Dauben, 13th Council of Chemistry, International Institute of Chemistry (Solvay), Interscience Press, New York, N. Y., in press.

(2) A preliminary report of a portion of this work has appeared in *Pure Appl. Chem.*, **9**, 539 (1964).

(3) This work was supported in part by Public Health Service Grant No. 00709, National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service.

(4) National Science Foundation Cooperative Fellow, 1960–1963.

(5) National Science Foundation Postdoctoral Fellow, 1964.

(6) For reviews of this reaction see W. G. Dauben and R. M. Coates, *J. Am. Chem. Soc.*, **86**, 2490 (1964), and ref 2.

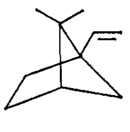
(7) R. Srinivasan, *ibid.*, **84**, 4141 (1962); R. Srinivasan, *ibid.*, **85**, 4045 (1963).

(8) K. J. Crowley, *Tetrahedron*, **21**, 1001 (1964).

(9) On the basis of spectral data the major of the two side products has been assigned the structure of 1,3′-bicyclohexenyl. This product as well as a more extensive study of the sensitized equilibration of **1** and **4** will be the subject of a future communication (W. G. Dauben and J. Saltiel, unpublished results).

inefficient gas–liquid partition chromatography (glpc). Since previous work had shown that both direct and sensitized irradiation of bicyclo[2.2.1]heptadiene[10,11] and 1,3-cyclooctadiene[12-14] yielded similar products, **1** was irradiated in the presence of acetophenone. It was found that the reaction was not complicated by the same side reactions encountered in the direct irradiation and a good yield of pure **4** could be obtained. In fact, up to the point of 50% reaction, **4** was the only product formed; further irradiation, however, initiated some secondary side reactions.

In contrast to the above results where the major product of both the sensitized and direct irradiation is the same, Liu and Hammond[15] found that myrcene (**2**) was converted in high yield to 5,5-dimethyl-1-vinylbicyclo[2.1.1]hexane (**5**) in a benzophenone-sensitized reaction. Crowley[8] has reported that in the direct irradiation the cyclobutene **6** is the principal product and minor amounts of β-pinene and an unidentified material are formed. We also have obtained similar results in the direct irradiation and have shown the minor product (<5%) to be **5** by comparison of the infrared spectra.[16] Furthermore, when 2,3-dimethyl-1,3-butadiene was activated using napthalene as the sensitizer,[17] it was found that no reaction occurred and the starting material remained unchanged. Also, the 1,2-dimethylcyclobutene was stable under the reaction conditions. Upon direct irradiation of the diene, 1,2-dimethyl-1-cyclobutene was formed in high yield.



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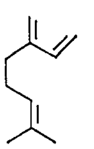

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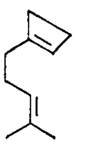

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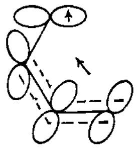
The comparison of the direct and the sensitized irradiations of these three acyclic dienes as well as an earlier demonstration by Srinivasan[7] that the photolysis of 2,3-dimethyl-1,3-butadiene in the vapor phase could not be quenched by oxygen or nitric oxide shows that the triplet state is not required for the valence isomerization of a conjugated diene to a cyclobutene. The results do show, however, that the directly excited singlet state of the diene during its various processes to rid itself of excess energy and return to a low vibrational level of the ground state may have one pathway, varying from efficient to nonefficient, which crosses a pathway in the downward energy cascade from the triplet state. This crossing most likely occurs in the vibrationally excited ground state since intersystem crossing of a diene from the electronically excited singlet to the triplet has not been observed.[18]

In the cases where the same product is obtained from a direct and a sensitized reaction, the geometry of the molecule as it enters the ground state most likely is similar. The failure of the sensitized reaction in the attempted valence isomerization of 2,3-dimethyl-1,3-butadiene could be accounted for by assuming that the triplet may stabilize itself by twisting about the 1,2-bond, as shown in **7**, a configuration suggested by Liu, Turro, and Hammond[19] for the nonspectroscopic triplet of butadiene and isoprene. A triplet of this configuration need not decay to a cyclobutene. On the other hand, such a configuration is not possible for the triplet of 1,1′-bicyclohexenyl since the double bonds are in a six-membered ring. The geometry of this latter triplet might be represented as **8**, a configuration which might be expected to decay to a cyclobutene.



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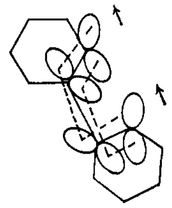

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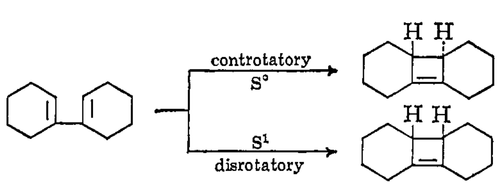
In the valence isomerizations of conjugated dienes brought about by direct irradiation, it is not known whether the transformations occur solely in the electronically excited state, or in coming from this state, or in a vibrationally excited ground state. Since the isomerization is an example of an *electrocyclic reaction*, the postulates of Woodward and Hoffmann[20] can be utilized to predict the reaction route followed. In the case of 1,1′-bicyclohexenyl, the double bonds form part of a *trans–trans* diene system and it would be predicted that reaction in the ground state (S^0) should yield a *trans* product while reaction *within* the electronically excited state (S^1) should furnish a *cis* product. A *cis* stereochemistry has been assigned to the photoproduct **4** on the following basis. Moore[21] has synthesized the stereoisomer of the photoproduct and a comparison of the nmr spectra of the two isomers showed that in both materials the six allylic protons appeared between τ 7.6–8.0. In the photoproduct a four-proton band was centered at τ 7.70 and a two-proton band at 7.85. In Moore's isomer the intensities of these two bands were reversed. In the *trans* isomer the two tertiary allylic protons should be shielded by a *cis* carbon–carbon bond while in the *trans* isomer these two protons should be deshielded by the *trans* carbon–carbon bonds. Thus, the *cis* isomer should have the four-proton band at lower field such as was found for the photoproduct.



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(10) W. G. Dauben and R. L. Cargill, *Tetrahedron*, **15**, 197 (1961).

(11) G. S. Hammond, N. J. Turro, and A. Fischer, *J. Am. Chem. Soc.*, **83**, 4674 (1961).

(12) W. G. Dauben and R. L. Cargill, *J. Org. Chem.*, **27**, 1910 (1962).

(13) S. F. Chappell, III, and R. F. Clark, *Chem. Ind.* (*London*), 1198 (1962).

(14) G. O. Schenck and R. Steinmetz, *Bull. Soc. Chim. Belges*, **71**, 781 (1962).

(15) R. S. H. Liu and G. S. Hammond, *J. Am. Chem. Soc.*, **86**, 1892 (1964).

(16) We are indebted to Professor G. S. Hammond for the infrared spectrum of **5**.

(17) The benzophenone-sensitized reaction of this diene was also studied and the results will be discussed separately since a chemical reaction occurred between the two compounds.

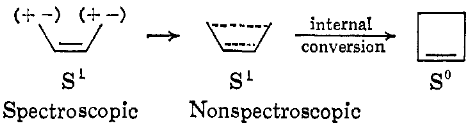
(18) E. Havinga, R. J. deKock, and M. P. Rappoldt, *Tetrahedron*, **11**, 276 (1960); E. Havinga and J. L. M. A. Schlatman, *ibid.*, **16**, 146 (1961); D. F. Evans, *J. Chem. Soc.*, 1735 (1960).

(19) R. S. H. Liu, N. J. Turro, and G. S. Hammond, *J. Am. Chem. Soc.*, **87**, 3406 (1965).

(20) R. B. Woodward and R. Hoffmann, *ibid.*, **87**, 395 (1965).

(21) W. R. Moore, private communication.

The assignment of *cis* stereochemistry to the photoproduct leads to the prediction that the initial bond formation occurs in the electronically exicited state (S^1). From the spectra of the starting material and the product it is known that their spectroscopic singlets are approximately 120 and 140 kcal/mole above their respective ground states. Thus, the formation of the spectroscopic singlet state of the photoisomer **4** from the spectroscopic singlet state of **1** would be endothermic by at least 20 kcal/mole, making the transformation improbable. It is possible, however, to accommodate the stereochemistry of the photoproduct with the prediction based on the electrocyclic concept by assuming that the spectroscopic singlet state of the diene (S^1) decays to a nonspectroscopic S^1 state which is stabilized by partial bond formation between the C_1 and C_4 of the diene such as shown in the scheme.



Since the transformation to the cyclobutene would be partially effected in the S^1 electronic manifold, the initial steric course of the electrocyclic reaction would be dictated by the orbital symmetry demands of this state. If this nonspectroscopic configuration persists through the internal conversion and the loss of vibrational energy in the ground state, a *cis* isomer would be expected. Thus, although the spectroscopic singlet S^1 of the cyclobutene cannot be involved in the photoreaction, sufficient orientation of the atoms toward that molecular arrangement can occur in the electronically excited state of the butadiene so that the stereochemistry of the product is controlled by the orbital symmetry demands of that state, but the cyclobutene itself is formed as the molecule comes out of that state.

Experimental Section

General Irradiation Procedure. All irradiations were performed using a 450-w Hanovia mercury lamp (Type 679A 36) and a Hanovia quartz immersion probe (Type 19434). The cylindrical irradiation flask into which the probe was inserted was of 130- or 450-ml volume and contained two side arms. One arm was fitted with a small condenser capped by a mercury exit seal; the other arm was fitted with a serum cap to permit removal of aliquots. All reaction mixtures were degassed by flushing thoroughly with a stream of helium and the gas flow was continued during the irradiation. The solution was stirred with a magnetic stirring apparatus.

All pentane used in irradiation experiments was washed twice with concentrated sulfuric acid, stirred for 12 hr with 30% fuming sulfuric acid, washed with several portions of water, distilled from phosphorus pentoxide, and stored over sodium wire.

Irradiation of 1,1′-Bicyclohexenyl. A. Direct Irradiation. A solution of 3.77 g (23 mmoles) of 1,1′-bicyclohexenyl[22] [$\lambda_{\max}^{\text{hexane}}$ 239 mμ (ϵ 12,000), λ_{sh} 233 and 246 mμ] in 350 ml of pentane was irradiated under the standard conditions for 115 hr by which time less than 5% of the starting diene remained (determined by ultraviolet spectrum). The irradiation was interrupted every 24 hr to remove deposits which had formed upon the probe. The solvent was distilled, the residue was warmed briefly on a steam bath with 0.5 g (5 mmoles) of maleic anhydride, and the mixture was allowed to stand at room temperature for 12 hr. The mixture was filtered and the precipitate was washed with cold pentane. The combined filtrate was filtered through a column of 17.5 g of neutral Woelm alumina (activity III) and the column washed with pentane. The solvent was removed from the eluates under reduced pressure and the combined residues were distilled, bp 75–77° (4 mm), yield 1.44 g (38%). There was a large distillation residue. The total distillate was analyzed by glpc (DEGS, 110°) and was found to be a mixture of two major and four minor products. Of the two major products, the more rapidly eluted material amounted to ~70% and the slower moving material to ~20%.[23]

The more abundant major product **4** was obtained in pure form by preparative glpc (DEGS, 155°). The material has the following properties: $\lambda_{\max}^{\text{pentane}}$ 205 mμ (ϵ 14,000); $n^{25}\text{D}$ 1.5125; mol wt 162 (mass spectrum[24]) (lit.[8] bp 65° (5 mm), $\lambda_{\max}$ 204 mμ (ϵ 10,400), $n^{23}\text{D}$ 1.5115).

Anal. Calcd for $C_{12}H_{18}$ (162.26): C, 88.82; H, 11.18. Found: C, 88.58; H, 11.14.

A solution of 145 mg (0.88 mmole) of photoproduct **4** (~95% pure) in 25 ml of methanol was ozonized, the reaction mixture diluted with water, and 1.5 g of potassium iodide was added. The crude product was isolated in the usual manner but the material showed only a weak carbonyl absorption in the infrared. This oil was dissolved in 20 ml of 50% aqueous methanol containing 1 drop of 15% sulfuric acid and the solution heated on the steam bath for 15 min. The solution was diluted with water and extracted with ether, and the solvent was removed to yield 125 mg of an oil which possessed an infrared spectrum practically superimposable on that of authentic 2,2′-dioxo-1,1′-bicyclohexyl.[25] The oil was allowed to react with 175 mg (1.6 mmoles) of semicarbazide hydrochloride in a mixture of pyridine and aqueous ethanol, and the precipitate (80 mg) which formed was recrystallized from aqueous ethanol. The 9-ureido-1,2,3,4,5,6,7,8-octahydrocarbazole in an evacuated sealed capillary sublimes at 200–240° and does not melt up to 300°. The infrared spectrum (KBr pellet) was identical with the spectrum of a similar material prepared from an authentic sample of diketone.

Anal. Calcd for $C_{13}H_{19}N_3O_2$ (233.31): C, 66.92; H, 8.21; N, 18.01. Found: C, 67.07; H, 8.11; N, 17.86.

B. **Sensitized Irradiation.** A solution of 1.0 ml (6 mmoles) of 1,1′-bicyclohexenyl and 0.70 ml (6 mmoles) of acetophenone in 125 ml of benzene was irradiated under the standard conditions using a Pyrex filter. The progress of the reaction was followed by glpc (5% Carbowax 400, 115°). The irradiation was stopped after 5 hr at which time 50% of the starting diene had been consumed and the photoproduct **4** was present to the extent of 30%. Further irradiation did not increase appreciably the amount of **4** but other products were slowly formed.

The solvent was removed at 30° under reduced pressure to yield 1.68 g of crude liquid The photoproduct **4** was isolated by preparative glpc (10% Carbowax 6000, 115°). The infrared and nmr spectra of the collected material were identical with the material prepared by direct irradiation

On a large scale, 20 ml of the diene **1** and 20 ml of acetophenone in 40 ml of benzene was irradiated as above for 45 hr at which time the ratio of diene to product was 1:1. The solvent was removed and the residue was allowed to react with an aqueous methanolic solution of 24 g of semicarbazide hydrochloride and 14 g of potassium carbonate. The mixture was allowed to stand 18 hr, the precipitate was filtered, and the solid was washed with cold pentane. The filtrate was extracted with pentane and the combined organic layer was allowed to react with 12.5 g of maleic anhydride The mixture was allowed to stand for 24 hr, the solvent was removed under reduced pressure, and the residue was added to 75 ml of 25% aqueous potassium hydroxide. The mixture was shaken for 1 hr and extracted with pentane, the solvent was removed, and the residue was distilled, bp 55–62° (0.5 mm), 5 g. The infrared spectrum indicated that some acetophenone was still present. A pentane solution of the distillate was passed through 120 g of Woelm basic alumina (activity I), the solvent removed, and the residue distilled through an 18-in. spinning-band column (Nester-Faust), bp 76–78° (4 mm), 3.18 g (in five fractions). No fraction was more than 90% pure and the pure photoproduct was obtained only by preparative glpc (DEGS, 155°).

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(22) A. Mandelbaum and M. Cais, *J. Org. Chem.*, **26**, 2633 (1961).

(23) The slower moving material was isolated by preparative glpc. The nmr spectrum of the material showed absorption between τ 4.2 and 4.7 equivalent to three vinyl protons. This information along with the ultraviolet and infrared spectral data suggests that the compound is the nonconjugated diene, perhaps 1,3′-bicyclohexenyl.

(24) We are indebted to Dr. Richard Teeter of the Chevron Research Corp., Richmond, Calif., for this analysis.

(25) S. G. P. Plant, *J. Chem. Soc.*, 1595 (1930).

Irradiation of Naphthalene in the Presence of 2,3-Dimethyl-1,3-butadiene and 1,2-Dimethylcyclobutene. A solution of 1.38 g (0.011 mole) of naphthalene and 1.0 g (0.012 mole) of 2,3-dimethyl-1,3-butadiene in 135 ml of benzene was irradiated under standard conditions using a Pyrex filter. Samples were removed periodically and were analyzed by glpc (20% TCEP). At the end of 21 hr of irradiation, no 1,2-dimethylcyclobutene could be detected, although there was a slight drop in diene concentration. The irradiation was interrupted, and 1,2-dimethylcyclobutene was added, and the irradiation was continued for another 20 hr. No conversion of the cyclobutene to the diene occurred. Again there was a slight drop in the concentration of diene.

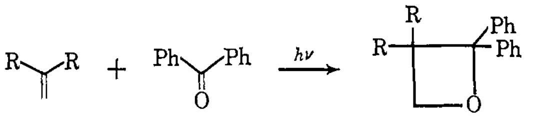
Photochemical Cycloaddition of 2,3-Dimethyl-1,3-butadiene and 1,2-Dimethylcyclobutene to Benzophenone[1,2]

Jack Saltiel,[3] Robert M. Coates,[4] and William G. Dauben

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. *Received February 10, 1966*

Abstract: Conditions are described which permit adduct formation between benzophenone and 2,3-dimethyl-1,3-butadiene although triplet excitation transfer to the diene remains the major path of energy dissipation from the benzophenone triplets. A mechanism is proposed which involves addition of diene triplets to benzophenone in its ground state.

Studies of the photochemistry of mixtures of ketones or aldehydes and olefinic or acetylenic compounds have shown that two major reaction pathways are available. The first involves cycloaddition of the carbonyl moiety to a carbon–carbon double or triple bond[5–8] (eq 1 and 2) and the second involves triplet excitation transfer from the ketone to the hydrocarbon substrate with subsequent reaction of the substrate. Typical examples of the latter path are the sensitized *cis–trans* isomerization of the stilbenes,[9] the sensitized valence isomerization of 1,3-cyclooctadiene[10] and 1,1′-bicyclohexenyl,[11] and the sensitized dimerization of 1,3-butadiene and isoprene.[12]



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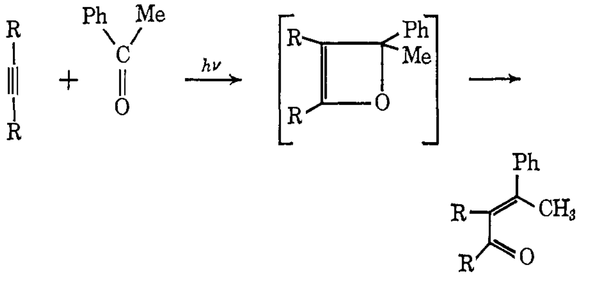

(2)

Two generalizations have been made concerning cycloaddition.[8,13] The first is that only carbonyl compounds whose lowest triplet state is of the $n \rightarrow \pi^*$ type react (*e.g.*, 2-acetonaphthone whose lowest triplet is of the $\pi \rightarrow \pi^*$ type is found to be inert), and the second is that cycloaddition occurs provided triplet excitation transfer from the ketone to the unsaturated substrate is inefficient. In agreement with this second restriction it is found that the most suitable substrates for cycloaddition are compounds which have *isolated* double or triple bonds. In general, the spectroscopic triplet states of these latter unsaturated compounds lie higher in energy than the triplet states of compounds containing the carbonyl moiety,[14] and only the relatively inefficient nonvertical excitation transfer may occur in these systems. An example of the latter process is the benzophenone-sensitized *cis–trans* isomerization of 2-pentene.[9,15]

The favored mechanism for known cycloadditions is shown for reaction 1 in eq 3–5. The process involves attack by the electron-deficient oxygen of the $n \rightarrow \pi^*$ triplet state of the ketone upon the ground state of the unsaturated hydrocarbon. The products can be accounted for if it is assumed that the attack occurs at the position which will lead to the formation of the most stable diradical.[5,16]

As part of a broad program on the mechanism of photochemically induced valence isomerisms of 1,3-butadiene to 1,2-cyclobutenes, an investigation was initiated to see if a triplet state was an essential intermediate.[11] In the course of this work it was found that

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[1] For the previous paper in this series, see W. G. Dauben, R. L. Cargill, R. M. Coates, and J. Saltiel, *J. Am. Chem. Soc.*, **88**, 2742 (1966).

[2] This work was supported in part by PHS Grant No. 00709, National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service.

[3] National Science Foundation Postdoctoral Fellow, 1964.

[4] National Science Foundation Cooperative Fellow, 1960–1963.

[5] G. Büchi, C. G. Inman, and E. S. Lipinski, *J. Am. Chem. Soc.*, **76**, 4327 (1954).

[6] G. Büchi, J. T. Kopron, E. Koller, and D. Rosenthal, *ibid.*, **78**, 876 (1956).

[7] H. E. Zimmerman and L. Craft, *Tetrahedron Letters*, 2131 (1964); D. Bryce-Smith, G. I. Fray, and A. Gilbert, *ibid.*, 2137 (1964).

[8] D. A. Arnold, R. L. Hinman, and A. H. Glick, *ibid.*, 1425 (1964).

[9] G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, and C. Dalton, *J. Am. Chem. Soc.*, **86**, 3197 (1964).

[10] G. O. Schenck and R. Steinmetz, *Bull. Soc. Chim. Belges*, **71**, 781 (1962).

[11] See ref 1.

[12] G. S. Hammond, N. J. Turro, and R. S. H. Liu, *J. Org. Chem.*, **28**, 3297 (1963).

[13] N. C. Yang, *Pure Appl. Chem.*, **9**, 591 (1964).

[14] Compare 82 kcal/mole for ethylene (D. F. Evans, *J. Chem. Soc.*, 1735 (1960)) with 74 kcal/mole for acetophenone (W. G. Herkstroeter, A. A. Lamola, and G. S. Hammond, *J. Am. Chem. Soc.*, **86**, 5437 (1964)).

[15] G. S. Hammond, N. J. Turro, and P. A. Leermarkers, *J. Chem. Phys.*, **66**, 1144 (1962).

[16] G. S. Hammond and N. J. Turro, *Science*, **142**, 1541 (1963).