

Photochemical Transformations of Small-Ring Carbonyl Compounds

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The ground-state chemistry of small-ring heterocyclic compounds has fascinated chemists not only because of its theoretical implications but also for the diversity of its synthetic procedures and the unusual nature of its transformations. The high degree of strain present in small rings is responsible for many of the chemical properties of these compounds. These properties, in turn, have been associated with the different orbital hybridization present in small-membered ring compounds as compared with their "strainless" analogs.

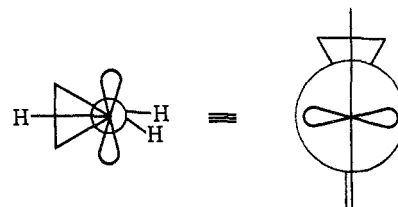
The great reactivity of these systems was explained in terms of steric strain by Baeyer as early as 1885. He reasoned that small rings, such as cyclopropane, could be formed only by compressing the C-C-C bond far below the normal tetrahedral angle of 109° . Ring opening, of course, would relieve the strain. Thus, cyclopropane is cleaved more easily than other cycloalkanes. Three-membered heterocyclic rings are similarly reactive, the ring being opened by many reagents.

Three-membered-ring molecules with severe angle strain are faced with the alternatives of keeping the interorbital angles at $\sim 109^\circ$ to minimize interelectron repulsion with sacrifice of maximum overlap of bonding orbitals or of achieving maximum overlap by placing the bonding orbitals coaxial with the line between nuclei in the normal way, with the disadvantage of higher interelectron repulsions between orbitals only 60° apart. It appears that these rings adopt an intermediate orbital geometry which minimizes the overall energy. The bonds are intermediate in character between σ and π , and are called bent or banana bonds.

Considerable attention has been focused in recent years on the conjugative properties of small rings when joined directly to an unsaturated grouping. Among these studies have been many concerned with the conjugative interaction of small rings with adjacent carbonium ions. Cyclopropylcarbinyl derivatives solvolyze with markedly enhanced rates¹ to give rearranged and position-scrambled products of the allylcarbinyl, cyclobutyl, and cyclopropylcarbinyl types. There appears to be extensive charge delocalization from the carbinyl carbon of the cyclopropyl carbonium ion to the cyclopropane ring. The available evidence indicates that the maximum interaction between a cyclopropyl ring and an adjacent electron-deficient carbon occurs when the plane of the three-membered

ring is parallel to the adjacent p orbital, *i.e.*, the bisected conformation (see Scheme I).

Scheme I



The electronic absorption spectra of molecules containing a small-membered ring adjacent to a carbonyl group have also provided an effective method of demonstrating the conjugative properties arising from the unsaturated character of these rings. The nature of the electrical interaction between the small ring and the carbonyl group has been described as a type of hyperconjugation which results from orbital overlap of the bent bonds of the small ring with the orbitals of the attached carbonyl group.²

In addition to these spectroscopic studies, increased emphasis has been given during the past few years to the photochemistry of small-ring compounds which have an unsaturated grouping attached to one of the ring atoms. It might be anticipated that the bond angle strain present in these small rings would also have a pronounced effect upon the reactivity of molecules in an electronically excited state. In an attempt to assess the importance of this effect as well as the chemical consequences of the conjugative interaction of the small ring with the adjacent π bond, we have studied the photochemical transformations of a number of small-ring carbonyl compounds. This Account sets forth some of the main results that have been obtained in this laboratory during the past few years.

Photochemistry of Three-Membered-Ring Carbonyl Compounds

Cyclopropyl Ketones. Three-membered rings are known to possess a somewhat delocalized electronic system. These delocalized electrons lie in the plane of the ring and have been attributed to the overlap of bent bonding orbitals.³ This type of bonding is intermediate in character between the sideways π -bonding overlap and an endways σ -bonding overlap. When

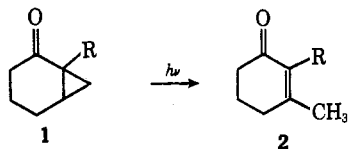
(1) For a review see R. Breslow in "Molecular Rearrangements," Vol I, P. de Mayo, Ed., Interscience, New York, N. Y., 1963, Chapter 4.

(2) N. H. Cromwell and M. A. Graff, *J. Org. Chem.*, **17**, 414 (1952).

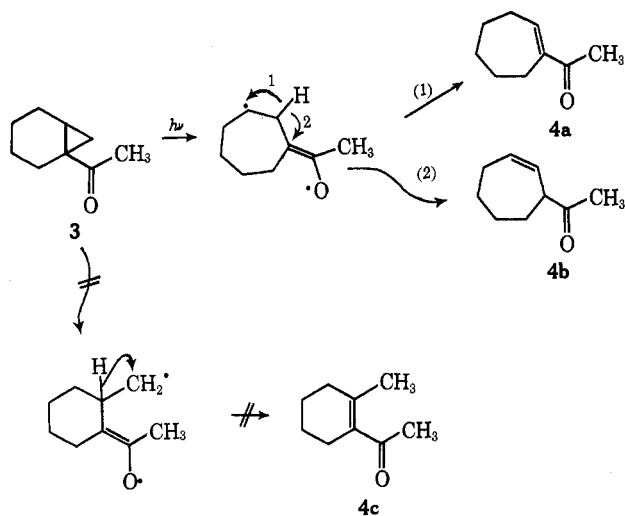
(3) R. Parker and N. Issacs, *Chem. Rev.*, **59**, 737 (1959).

atoms with π -bonding electrons, such as a carbonyl group, are attached to the carbon atom of these bent bonds, some overlapping and interaction between the bent bonds and the π orbitals are to be expected. Evidence for such delocalization has been obtained from theoretical^{4,5} and ultraviolet,^{6,7} infrared,⁶ and nuclear magnetic resonance spectral studies.⁸

Dauben and Berezin⁹ have studied conjugative effects in various cyclopropyl conjugated ketones and have concluded that the degree of conjugation between the cyclopropane ring and the carbonyl group is related to the steric orientation of the groupings. For maximum interaction, the plane of the three-membered ring should lie parallel to the π orbital of the carbonyl group (see Scheme I). Irradiation of conformationally rigid conjugated cyclopropyl ketones (such as ketone **1**) generally results in cleavage of the external β cyclopropyl bond, a fact which may be attributed to better overlap of the π^* orbital with this bond than with the internal β cyclopropyl bond.^{10,11} When free rotation is

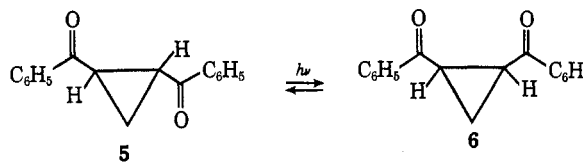


possible and when both cyclopropane bonds are able to overlap with the carbonyl group, the stability of the radical formed determines the direction of ring opening.^{12,13} Ketone **3**, with a freely rotating acetyl group,

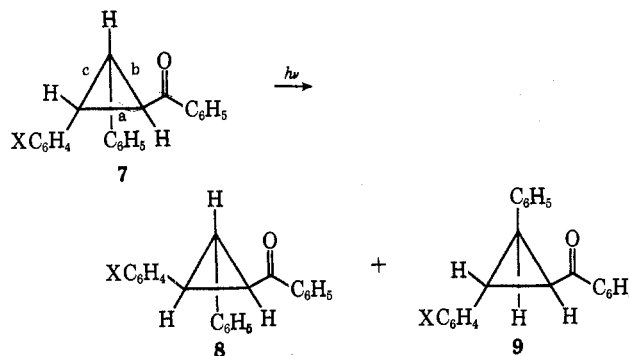


allows the carbonyl function to overlap equally well with both conjugated bonds of the cyclopropane ring. In this case thermodynamic control of the ring opening (stability of a secondary *vs.* a primary radical) is the major factor responsible for the formation of ketones **4a** and **4b** rather than **4c**.

In view of the related behavior of a large number of cyclopropyl and olefinic systems, it is not surprising that cyclopropyl ketones undergo *cis*-*trans* isomerization upon ultraviolet irradiation. For example, irradiation of *trans*-1,2-dibenzoylcyclopropane (**5**) affords *cis*-1,2-dibenzoylcyclopropane (**6**).¹⁴



Zimmerman and coworkers have recently examined the effects of substituents on the photochemical stereoisomerization of 2,3-diphenyl-1-benzoylcyclopropanes (**7**).^{15,16} The preferential formation of the *cis*,*trans*



isomer **8** has been interpreted as arising from an electronically excited state which has odd electron density in the three-membered ring. The reaction has been suggested to proceed with selective homolytic fission of bond a followed by a single rotation about the benzylic-benzylic bond c and subsequent closure.

Epoxy Ketones. Recent investigations on the structurally related α,β -epoxy ketones have demonstrated that these species are exceptionally reactive under the influence of ultraviolet light.^{17,18} Irradiation may lead to geometrical isomerization,¹⁹ to rearrangement,²⁰ to internal hydrogen abstraction,²¹ to photofragmentation,²² or to photochemical valence tautomerization.²³

(14) G. W. Griffin, E. J. O'Connell, and H. A. Hammond, *ibid.*, **85**, 1001 (1963).

(15) H. E. Zimmerman, S. S. Hixson, and E. F. McBride, *ibid.*, **92**, 2000 (1970).

(16) H. E. Zimmerman and C. M. Moore, *ibid.*, **92**, 2023 (1970).

(17) A. Padwa in "Organic Photochemistry," Vol. I, O. L. Chapman, Ed., Marcel Dekker, New York, N. Y., 1967, p 92.

(18) O. Jeger, K. Schaffner, and H. Wehrli, *Pure Appl. Chem.*, **9**, 555 (1964).

(19) C. L. Johnson, B. Dominy, and W. Reusch, *J. Amer. Chem. Soc.*, **85**, 3895 (1963).

(20) S. Bodforss, *Chem. Ber.*, **51**, 214 (1918).

(21) H. E. Zimmerman, B. R. Cowley, C. Y. Tseng, and J. W. Wilson, *J. Amer. Chem. Soc.*, **86**, 947 (1964).

(22) P. C. Petrellis and G. W. Griffin, *Chem. Commun.*, 691 (1967).

(23) A. Padwa, *Tetrahedron Lett.*, 813 (1964).

(4) A. D. Walsh, *Trans. Faraday Soc.*, **45**, 179 (1949).

(5) C. A. Coulson and W. Moffitt, *Phil. Mag.*, **40**, 1 (1949).

(6) R. H. Eastman, *J. Amer. Chem. Soc.*, **76**, 4115, 4118 (1954); **77**, 6643 (1955).

(7) E. M. Kosower and M. Ito, *Proc. Chem. Soc.*, 25 (1962).

(8) T. Shono, T. Morikawa, A. Oku, and R. Oda, *Tetrahedron Lett.*, 791 (1964).

(9) W. G. Dauben and G. H. Berezin, *J. Amer. Chem. Soc.*, **89**, 3449 (1967).

(10) L. D. Hess and J. N. Pitts, Jr., *ibid.*, **89**, 1973 (1967).

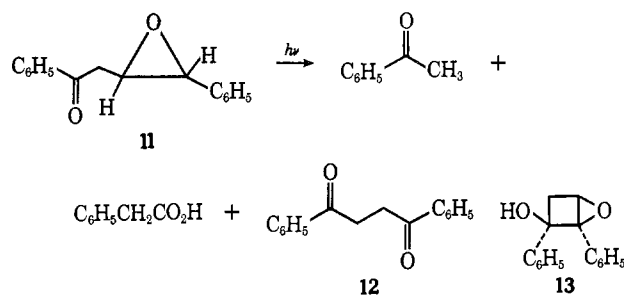
(11) W. G. Dauben and G. W. Shaffer, *Tetrahedron Lett.*, 4415 (1967).

(12) R. E. K. Winter and R. F. Lindauer, *ibid.*, 2345 (1967).

(13) W. G. Dauben, G. W. Shaffer, and E. J. Deving, *J. Amer. Chem. Soc.*, **92**, 6273 (1970).

In those cases which have been fully investigated, it has usually been found that the photolysis can best be described by a cleavage of the α C-O bond of the oxide ring followed by a multitude of possible second steps. The driving force for the fission of the epoxide ring was attributed to the tendency of the excited $n-\pi^*$ state to eliminate α substituents as odd-electron or anionic species depending on the reaction medium.²¹ However, it has recently been demonstrated that a number of the photochemical reactions in this series may be envisaged as proceeding *via* scission of the α,β C-C bond.²⁴⁻²⁷

In contrast to the exhaustive studies concerned with the photochemistry of α,β -epoxy ketones, there has been little effort directed toward examining the photochemical transformations of the related β,γ -epoxy ketone system. In order to obtain a better understanding of this system, we investigated the photochemistry of *cis*- (10) and *trans*-1,4-diphenyl-3,4-epoxybutan-1-one (11).²⁷ Irradiation of the *trans* isomer in benzene gave dibenzoyl ethane (12), *cis*-1,2-diphenyl-2,3-epoxy-1-cyclobutanol (13), acetophenone, and phenylacetic acid. The for-



mation of the products may be rationalized by intramolecular γ -hydrogen abstraction to produce a spin-unpaired 1,4 biradical which subsequently undergoes ring closure or β scission.²⁸ Photoelimination yields the enol form of acetophenone and phenylloxirene as a transient intermediate. Rearrangement of the oxirene to phenylketene followed by reaction with water accounts for the presence of phenylacetic acid. The isolation of dibenzoyl ethane (12) in addition to acetophenone and cyclobutanol 13 makes the intermediacy of a 1,4 biradical, from which both types of product could result, especially appealing. Opening of the three-membered oxide ring should occur with considerable ease, and the 1,3 diradical thus formed easily accommodates formation of dibenzoyl ethane. The isolation of both 12 and 13 adds strong support for Yang's stepwise mechanism for cyclobutanol formation.²⁹ The related *cis* ketone 10 was inert to photolysis due to the lack of an available γ hydrogen.

Aziridinyl Ketones. In view of the structural rela-

(24) A. Padwa and R. Hartman, *J. Amer. Chem. Soc.*, **88**, 1518 (1966).

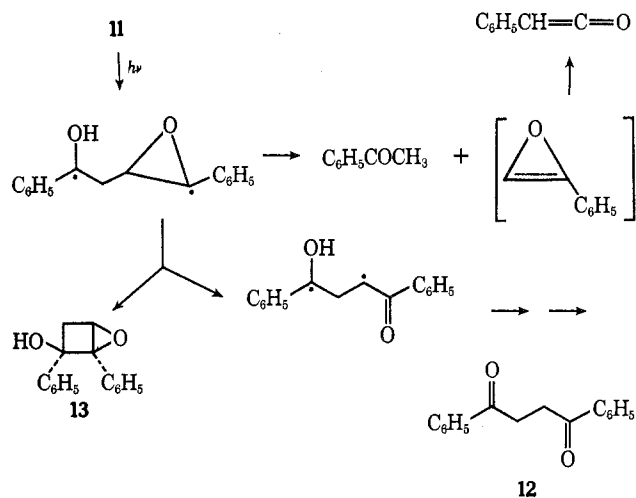
(25) E. F. Ullman and J. E. Milks, *ibid.*, **86**, 3814 (1964).

(26) J. M. Dunston and P. Yates, *Tetrahedron Lett.*, 505 (1964).

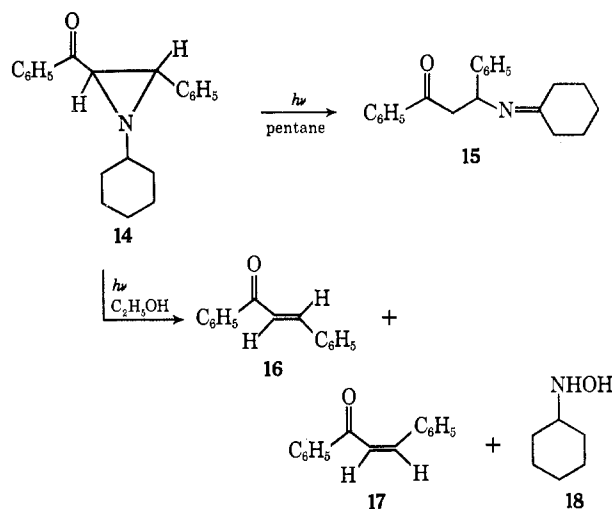
(27) A. Padwa, *J. Amer. Chem. Soc.*, **87**, 4205 (1965).

(28) A. Padwa, D. Crumrine, R. Hartman, and R. Layton, *ibid.*, **89**, 4435 (1967).

(29) N. C. Yang and D. D. H. Yang, *ibid.*, **80**, 2913 (1958).



tionship between aziridinyl ketones and the epoxy ketones and as a logical extension of our photochemical work with small-ring carbonyl compounds, studies were initiated to determine whether the photochemical properties of 2-benzoylaziridines would parallel those of benzoyl epoxides. In our studies we have found that the nature and position of substituents about the aziridine ring produce markedly different chemical effects.^{30,31} Aziridine 14 was found to rearrange photochemically to 15 in pentane, while in ethanol products 16, 17, and 18 were formed.³² Irradiation of *trans*-



aziridinyl ketone 19 produces 20, the analog of 15. The formation of 15 and 20 involves abstraction of a hydrogen from the nitrogen substituent to form a diradical intermediate which can ring-open by a type II process.

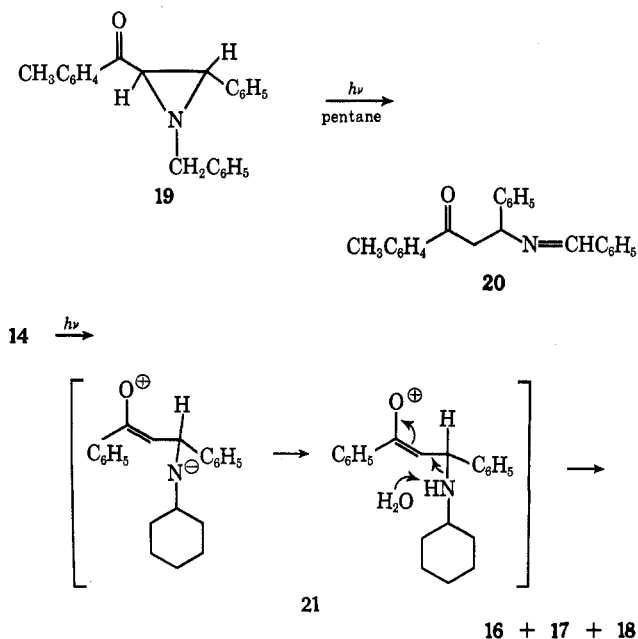
These reactions occur with good efficiency ($\Phi = 0.25$ for 14, $\Phi = 0.60$ for 19) and appear to proceed from an $n-\pi^*$ triplet state. The photolysis of 14 in ethanol may involve a zwitterionic intermediate such as 21.

The course of the overall photoreaction was noted

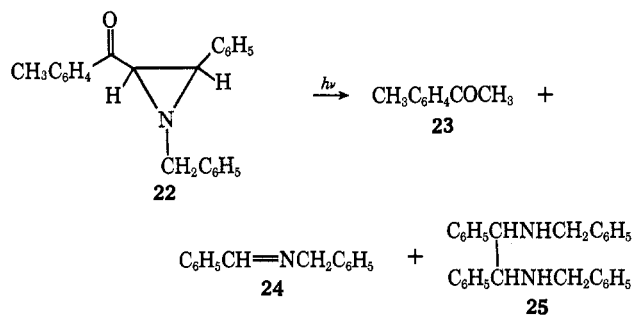
(30) A. Padwa and L. Hamilton, *ibid.*, **87**, 1821 (1965).

(31) A. Padwa and W. Eisenhardt, *ibid.*, **90**, 2442 (1968).

(32) A. Padwa and L. Hamilton, *ibid.*, **89**, 102 (1967).

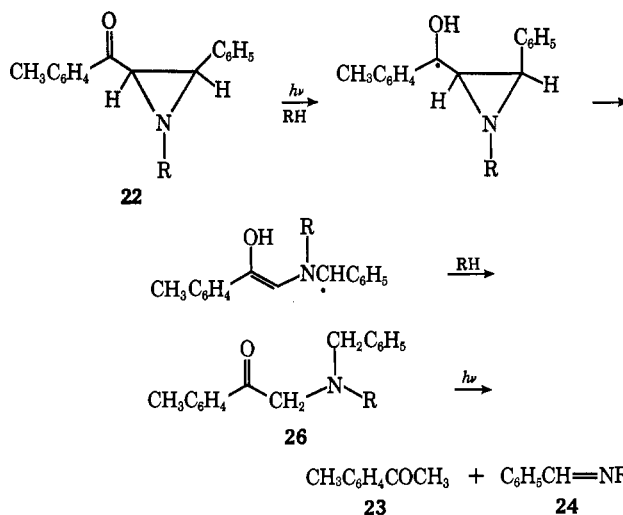


to be drastically altered for the *cis* isomers. Irradiation of *cis-N*-benzyl-2-phenyl-3-*p*-toluylaziridine (**22**) in 95% ethanol gave 4-methylacetophenone (**23**), *N*-benzylbenzalimine (**24**), and *N,N'*-dibenzyl-1,2-diphenyl-1,2-diaminoethane (**25**) as the major products.



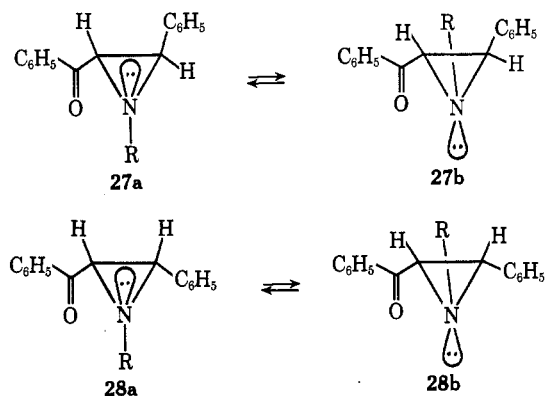
Compound **25** was shown to be a secondary photo-product formed by the photoreduction of **24** in ethanol, a reaction demonstrated by independent experiments.³³ Further studies on the photoreductive dimerization of a series of benzaldehyde *N*-alkylimines showed that the photoreduction did not involve the excited states of the imines at all, but was the result of a most interesting set of circumstances.³⁴ To account for the products obtained from the *cis* isomer, we proposed that the excited state abstracts hydrogen from solvent and then undergoes homolytic ring cleavage to give a radical which leads to the observed products by a succession of hydrogen abstraction and photoelimination reactions.

The failure to observe α -amino ketone **26** from the photolysis runs can be ascribed to its further photo-reaction under the reaction conditions. In agreement with this interpretation, it was observed that indepen-



dent irradiation of **26** afforded **23** and **24**.³⁵ Furthermore, it was shown that the photoreaction of **26** occurred more rapidly than did that of *cis*-aziridine **22**.

In order to account for the difference in photochemistry of the *cis* and *trans* isomers it will be fruitful to discuss the configurational mobility of the aziridinyl ketones in question. Rapid pyramidal inversion of groups bonded to nitrogen in ammonia and related molecules has been known for a long time. The data so far obtained indicate that *N*-alkyl-substituted aziridines with molecular asymmetry due to trivalent nitrogen are likely only to be resolved into stable optical antipodes at temperatures below -50° .³⁶ The configurations of the *trans*-aziridinyl ketones under consideration may be represented by **27a,b** and those of the *cis* isomers by **28a,b**.



In the two configurations of the *trans* compound the amount of steric crowding should be approximately equal, and consequently the *trans* isomer should exist as a rapidly inverting mixture of both forms. In diastereomer **27a** the benzoyl group and the substituent on nitrogen are on the same side of the plane of the three-membered ring. In this configuration hydrogen abstraction by the $n-\pi^*$ excited state can proceed via a six-membered transition state. It seems probable, however, that steric crowding would allow the *cis*

(33) A. Padwa, W. Bergmark, and D. Pashayan, *J. Amer. Chem. Soc.*, **90**, 4458 (1968).

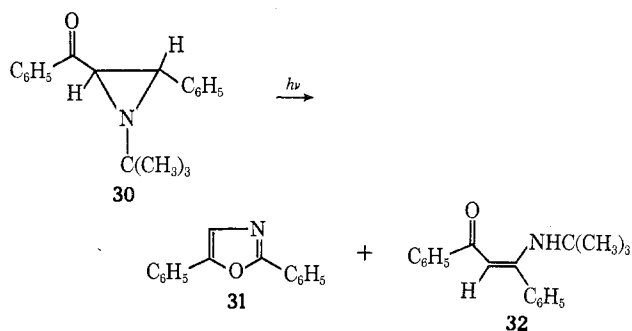
(34) A. Padwa, W. Bergmark, and D. Pashayan, *ibid.*, **91**, 2653 (1969).

(35) A. Padwa, W. Eisenhardt, R. Gruber, and D. Pashayan, *ibid.*, **91**, 1857 (1969).

(36) A. T. Bottini and J. D. Roberts, *ibid.*, **80**, 5203 (1958).

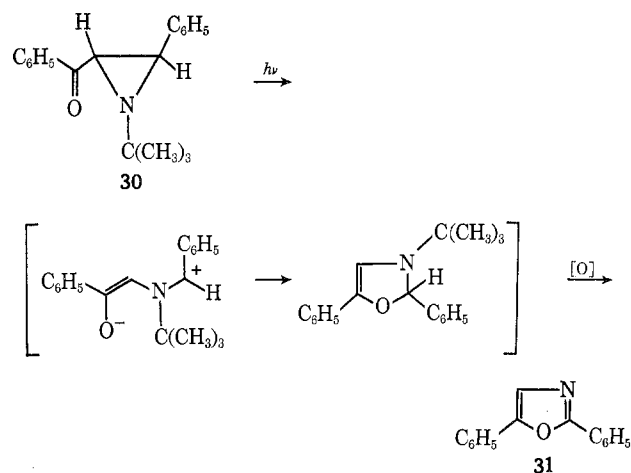
form to exist predominantly as **28b**, especially since the group on nitrogen is large. In this case the excited $n-\pi^*$ state is incapable of internal hydrogen abstraction, and instead other, less efficient, processes occur. In agreement with this rationalization, it was observed that the photoefficiency of the trans isomer ($\Phi = 0.62$) was much greater than that of the cis isomer ($\Phi = 0.05$). In benzene, which shows virtually no reactivity as a hydrogen donor, *cis*-aziridine **22** is converted very slowly to **20**. This reaction may involve photoepimerization of **22** to *trans*-aziridine **19**.

Because such strikingly different photobehavior was observed with the above *cis*- and *trans*-aziridinyl ketones, a more thorough investigation of *N*-substituted 2-phenyl-3-benzoylaziridines seemed desirable. In particular, it became of interest to inspect the photochemistry of a related aziridine in which the group attached to the nitrogen atom is devoid of α hydrogens. To this end *cis*- and *trans*-*N*-*tert*-butyl-2-phenyl-3-benzoylaziridines **29** and **30** were studied.³¹ Irradiation of trans isomer **30** in moist pentane gave 2,5-diphenyloxazole (**31**) and (β -*tert*-butylamino)-*trans*-benzalacetophenone (**32**) as the major photoproducts.

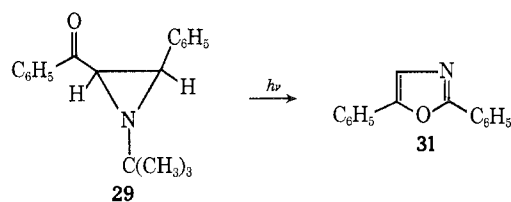


From the above results it is quite clear that the mode of reaction of the 2-benzoylaziridine system is dependent not only on the initial stereochemistry but also on the nature of the substituent attached to nitrogen. With a *tert*-butyl group the intramolecular hydrogen transfer step is precluded on structural grounds, and instead other processes occur. The formation of diphenyloxazole may be rationalized by C-C bond scission followed by ring closure to a transient 2,3-dihydrooxazole which is subsequently oxidized. The ready oxidation of the transient 2,3-dihydrooxazole may be attributed both to the extremely low bond dissociation energy of the tertiary C-H bond and the stability of the heteroatomic system formed. The formation of a stabilized 1,3-dipole intermediate³⁷⁻³⁹ provides a reasonable explanation for the direction of ring opening. A similar transformation has been encountered in the thermolysis of a variety of arylaroylaziridines.⁴⁰ This reaction may be considered to be

structurally analogous to the vinylocyclopropane-cyclopentene isomerization.

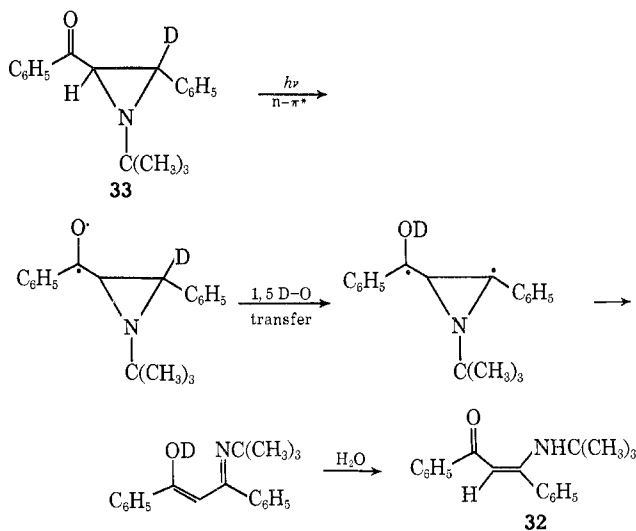


In order to help elucidate the mechanism for formation of **32**, the photochemistry of *trans*-*N*-*tert*-butyl-2-phenyl-3-benzoylaziridine-2- d_1 (**33**) was examined. Irradiation of **33** afforded product **32** that was devoid of better than 98% deuterium. Control experiments demonstrated that no isotope exchange of product **32** occurred under comparable photolytic conditions. The quantum yield for appearance of **32** from **33** is 0.006, one-third the value obtained from **30**. It was also noted that irradiation of *cis*-aziridine **29** produced only oxazole **31** with no detectable quantities of **32**.



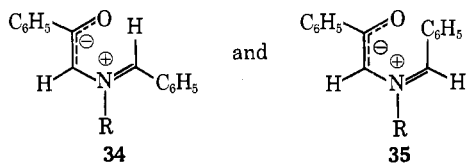
The deuterium-labeling experiments and the total absence of **32** from the irradiation of **29** suggests that the formation of **32** involves a prior 1,5-hydrogen transfer followed by subsequent ring opening, as shown below.

In connection with the photochemical studies of 2-



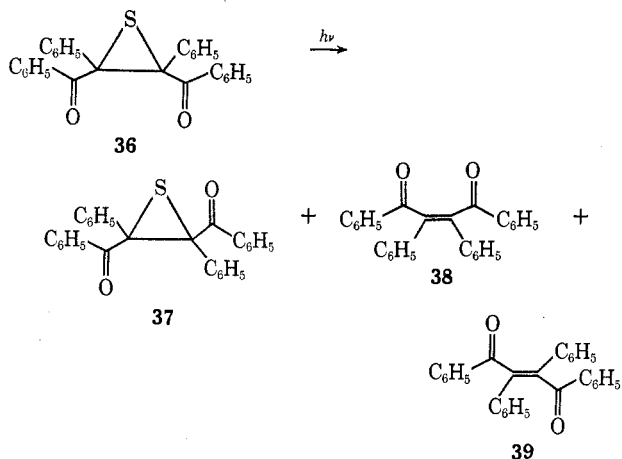
(37) A. Padwa and L. Hamilton, *Tetrahedron Lett.*, 4363 (1965).
 (38) H. W. Heine, R. Peavy, and A. J. Durbetaki, *J. Org. Chem.*, **31**, 3924 (1966).
 (39) R. Huisgen, W. Scheer, and H. Huber, *J. Amer. Chem. Soc.*, **89**, 1753 (1967).
 (40) A. Padwa and W. Eisenhardt, *Chem. Commun.*, 380 (1968).

benzoylaziridines, we noticed that these systems developed a deep pink color on exposure to light and that this pink coloration faded on standing in the dark. From low-temperature absorption studies, we noted that the magnitude of the molar absorptivity and position of the absorption maximum of the colored species produced on irradiation were dependent on the initial orientation of the carbonyl group in the three-membered ring.⁴¹ The position of the absorption maximum in the visible region suggests that there is an extensive electrical interaction between the bent bonds of the aziridine ring and the π orbitals of the benzoyl and phenyl groups. The Lewis structures shown below can be used to describe pictorially the resonance representations of such electronic interactions. Trozzolo and DoMinh have also suggested similar representations.⁴²

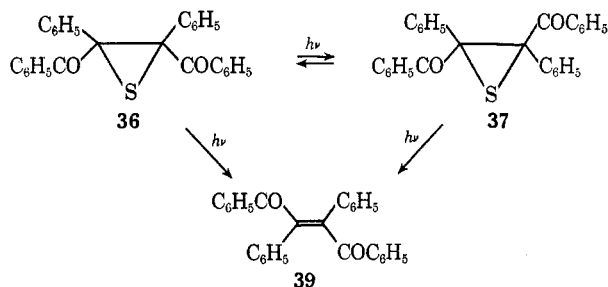


On the assumption that **34** and **35** represent the correct structures for the colored material, and since they are 1,3-dipolar intermediates, it seemed reasonable to trap them with an unsaturated system. At the time we began these studies there were no reports in the literature which described the cycloaddition of aziridines with various alkenes and alkynes.³⁷ Since the commencement of our work, other aziridines were also noted to form adducts with various multiple bonds by carbon-carbon cleavage of the aziridine ring.^{43,44}

Benzoyl Episulfides. In 1965 our laboratory turned its attention to the photochemistry of benzoyl episulfides. Our ultimate goal was to determine whether the irradiation of episulfides would parallel the photoextrusion of the hetero atom observed with aziridiny ketones. Photolysis of *cis*-dibenzoylstilbene episulfide (**36**) gave the corresponding *trans* isomer **37** and *cis*-(**38**) and *trans*-dibenzoylstilbene (**39**).⁴⁵⁻⁴⁷ Consideration of the product distribution as a function of time showed that, at short exposures, *trans*-dibenzoylstilbene (**39**) accounts for nearly all the product produced. At longer exposures, owing to secondary reactions, the yield of the *trans* olefin gradually decreases. From the time studies, it became clear that the desulfurization



of *cis* episulfide **36** is almost totally stereoselective and that *trans*-dibenzoylstilbene (**39**) was the primary reaction product. Irradiation of *trans* episulfide **37** gave only *trans* olefin **39** and *cis* episulfide **36**. It appears therefore that both episulfides afford only one stereoisomeric olefin.



The loss of sulfur from the episulfide upon photolysis is most simply explained by assuming a cleavage of the C_{α} -S bond of the three-membered ring followed by loss of atomic sulfur. The driving force for the fission of the episulfide ring can be attributed to the tendency of the excited $n-\pi^*$ state to eliminate α substituents as odd-electron species.

The high stereoselectivity observed in the reaction demands that rotational isomerization be a relatively efficient process compared to sulfur extrusion. In addition, the diradical formed must possess a relatively long lifetime for efficient loss of sulfur to occur. Since *trans*-dibenzoylstilbene (**39**) is formed to the exclusion of the *cis* isomer, it may be concluded that the overall rate of formation of **39** is greater than the overall rate for **38**, and that the free energy of the sulfur extrusion transition state from **39** is lower than that from **38**.

Since phenyl is a more bulky group than benzoyl, it is tempting to suggest that the transition state in which the phenyl and benzoyl groups are *cis*oid would be of lower energy than the transition state in which the two phenyl groups are *cis*oid. Hence, the van der Waals repulsive forces between two large groups appear to be the decisive factor for the exclusive formation of the *trans* olefin.

Ultraviolet irradiation of the related dibenzoylstilbene episulfoxide (**40**) in benzene affords monothio-

(41) A. Padwa and L. Hamilton, *J. Heterocycl. Chem.*, **4**, 118 (1967).

(42) A. M. Trozzolo and T. DoMinh, Abstracts of the Chemical Institute of Canada-American Chemical Society Joint Meeting, Toronto, Canada, 1970, p 60.

(43) H. W. Heine and R. E. Peavy, *Tetrahedron Lett.*, 3123 (1965).

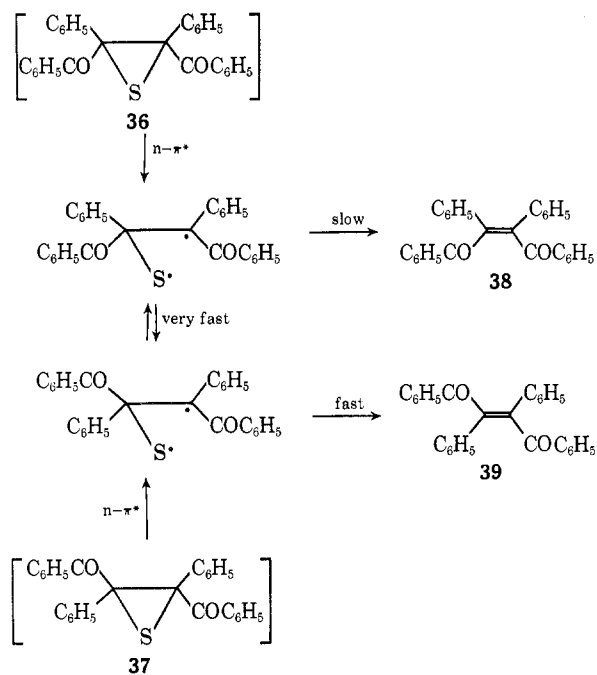
(44) R. Huisgen, W. Scheer, G. Szeimies, and H. Huber, *ibid.*, 397 (1966).

(45) A. Padwa and D. Crumrine, *Chem. Commun.*, 506 (1965).

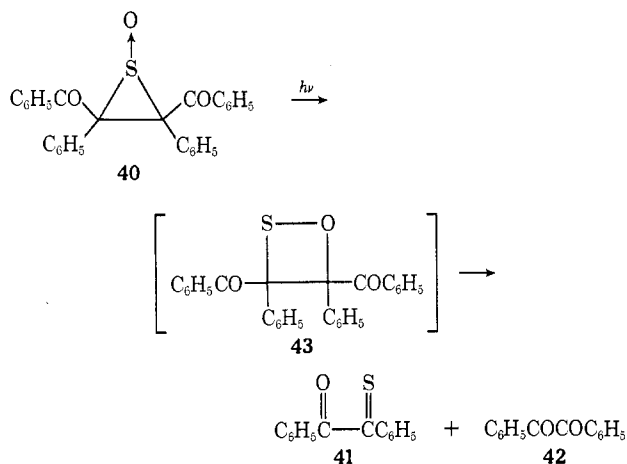
(46) A. Padwa, D. Crumrine, and A. Shubber, *J. Amer. Chem. Soc.*, **88**, 3064 (1966).

(47) We originally based our structural assignments for *cis*- and *trans*-dibenzoylstilbene episulfides on Dittmer's tentative assignments.⁴⁸ However, recent unpublished results by Dittmer and co-workers indicate that the original structural assignments made were incorrectly and should be reversed.

(48) D. C. Dittmer and G. C. Levy, *J. Org. Chem.*, **30**, 636 (1965).



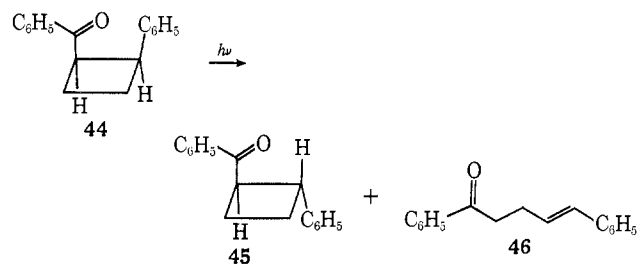
benzil (41) and benzil (42) presumably by rearrangement of an oxathietane intermediate 43.⁴⁹



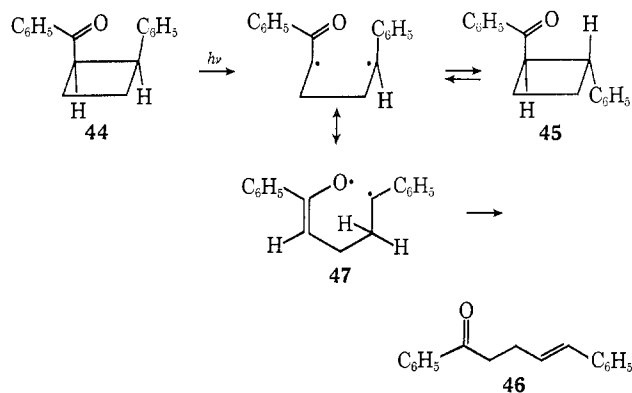
Photochemistry of Four-Membered Ring Carbonyl Compounds

Cyclobutyl Ketones. Although much still remains to be learned about the electronic state of three-membered-ring carbonyl compounds, a fair understanding of the potential reactivity of this class of compounds had emerged by the middle sixties. On the other hand, relatively little was known about the photochemistry of the homologous four-membered ring at the beginning of our investigations in 1967. At that time we began some systematic attempts to obtain more information on the photoreactivity of four-membered ring ketones. At the inception of our work on four-membered-ring photochemistry, priority was given to establishing the photobehavior of cyclobutyl ketones. We found that irradiation of *cis*-2-phenylcyclobutyl phenyl ketone (44)

in benzene gave *trans*-2-phenylcyclobutyl phenyl ketone (45) and 1,5-diphenyl-4-penten-1-one (46).⁵⁰ By fol-



lowing the reaction as a function of time one could show that a rapid photoisomerization of 44 and 45 first occurs and is then followed by further intramolecular reaction to form 46. The isomerization and the formation of 46 may be rationalized on the assumption that the reaction proceeds *via* diradical 47, a species derived by homolysis of the C-C bond β to the carbonyl group.



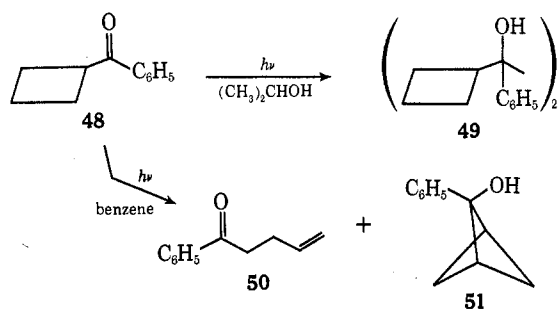
Such a process is not without analogy and is related to the reversible photoisomerization of arylaroylcyclopropanes.¹⁴ The isolation of 46 in addition to the *trans* isomer 45 makes the intermediacy of a 1,4 biradical, from which both products could result, especially appealing. Internal hydrogen abstraction followed by tautomerization readily explains the formation of 46 from diradical 47.

With the above results in hand, we considered it relevant to explore the photochemistry of the simpler cyclobutyl phenyl ketone system. Irradiation of cyclobutyl phenyl ketone (48) in isopropyl alcohol afforded the pinacol 49 as the virtually exclusive photoproduct. When the irradiation of 48 was carried out in benzene, 1-phenyl-4-penten-1-one (50) and 2-phenylbicyclo[1.1.1]pentan-2-ol (51) were the major products.⁵¹ The bicyclo[1.1.1]pentane derivative was easily identified because of its unique nmr spectrum. The bridgehead-bridgehead long-range coupling constant ($J = 18$ cps) determined from ¹³C-H coupling is the largest thus far measured. An X-ray single-crystal structure analysis of a derivative of 51 indicated that the bridgehead carbons were separated by only 1.89 Å.⁵² The

(49) D. C. Dittmer, G. C. Levy, and G. E. Kuhlmann, *J. Amer. Chem. Soc.*, **89**, 2793 (1967).

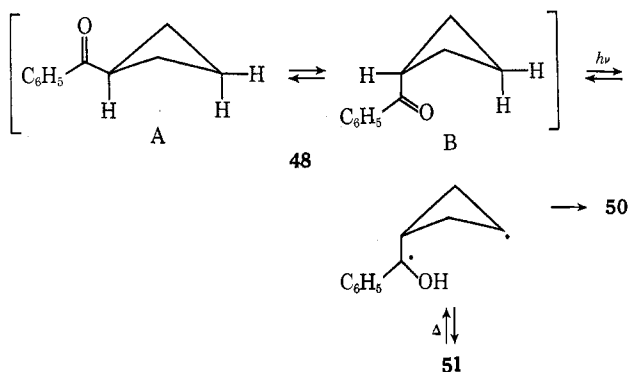
(50) A. Padwa, E. Alexander, and M. Niemczyk, *ibid.*, **91**, 456 (1969).

(51) A. Padwa and E. Alexander, *ibid.*, **89**, 6376 (1967).



rationalization offered by Meinwald and Lewis⁵³ involving extensive overlap between the back lobes of the orbitals rationalizes the large four- σ -bond coupling in this system.

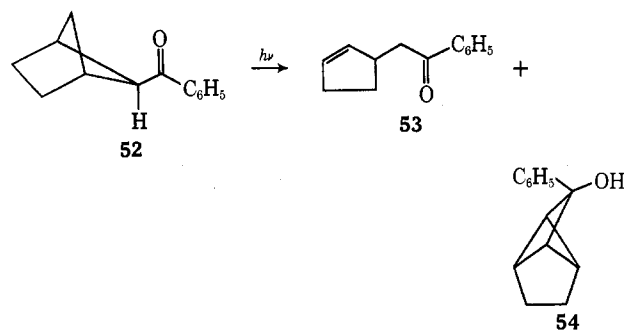
The formation of the bicyclopentanol was proposed to occur by a novel transannular hydrogen abstraction by the excited $n-\pi^*$ triplet state of cyclobutyl phenyl ketone. The cyclobutane ring is known to be puckered



by about 30° , leading to both pseudoaxial and pseudo-equatorial positions which may be occupied by substituents. In one of the two possible conformations of 48 (conformer B) hydrogen abstraction by the $n-\pi^*$ excited state can proceed *via* a six-membered transition state. Once formed, the biradical intermediate undergoes spin inversion prior to ring closure (51) or elimination (50). Interestingly, thermolysis of bicyclopentanol 51 afforded a mixture of 48 and 50. Kinetic data and deuterium labeling studies showed that the rearrangement proceeded predominantly *via* a 1,5 hydrogen transfer from the diradical obtained from cleavage of the bridgehead carbon-carbon bond.⁵⁴ The formation of a mixture of 48 and 50 from 51 implies that the thermally generated diradical behaves in a fashion analogous to that observed in the Norrish type II elimination of cyclobutyl phenyl ketone (48) and supports Wagner's claim that γ -hydrogen abstraction is reversible in type II photoeliminations.⁵⁵

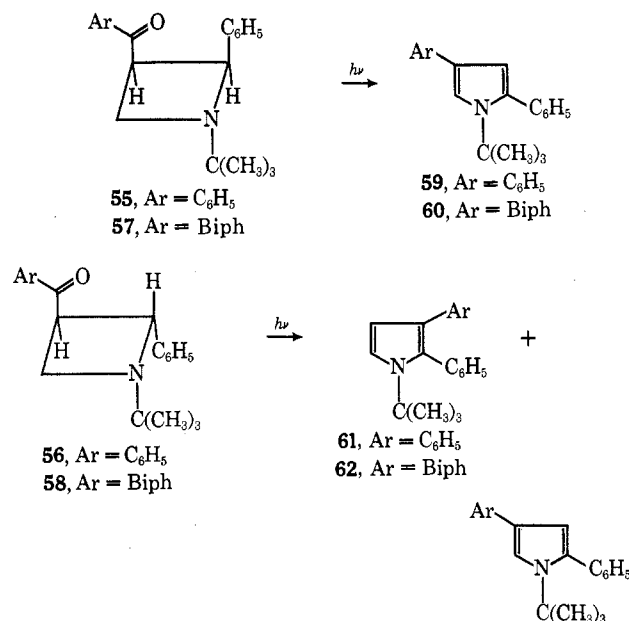
The inefficiency ($\Phi_{51} = 0.02$) and remarkably low unimolecular rate constant for bicyclopentanol (51) formation ($k = 5.5 \times 10^3 \text{ sec}^{-1}$) may be related to the low concentration of conformer B, thereby allowing for

a high rate of internal decay. In order to obtain additional support for this interpretation, we investigated the photochemistry of *exo*-5-benzoylbicyclo[2.1.1]hexane (52).⁵⁶



Bicyclic ketone 52 is an appropriate model for the reactive conformer of 48 (conformer B), since the benzoyl group is now locked into the pseudoaxial position. If the low triplet reactivity of 48 was due to the low population of the reactive conformer, we would expect that the triplet state of 52 would be much more reactive than that of 48. This turns out to be the case since the value for the unimolecular rate constant for formation of 54 is comparable to that of valerophenone.⁵⁷

Azetidinyl Ketones. Since we had previously observed that three-membered nitrogen heterocycles exhibited versatile and intriguing properties upon electron excitation, we were motivated to investigate the photochemistry of the homologous four-membered ring. We found that under the influence of ultraviolet light arylaroylazetidines undergo deep-seated rearrangements to diarylpyrroles.⁵⁸ The most remarkable result obtained is perhaps the specificity of the rear-



(52) A. Padwa, E. Shefter, and E. Alexander, *J. Amer. Chem. Soc.*, **90**, 3717 (1968).

(53) J. Meinwald and A. Lewis, *ibid.*, **83**, 2769 (1961).

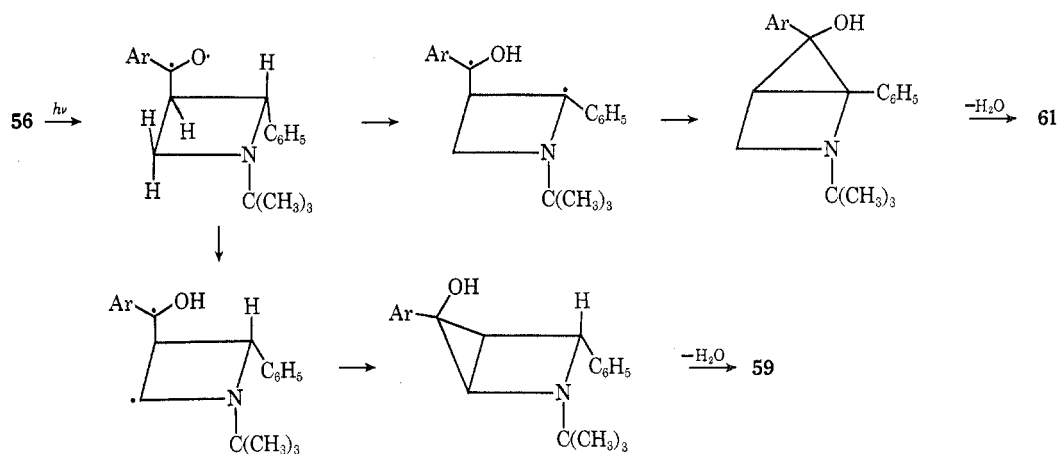
(54) A. Padwa and E. Alexander, *ibid.*, **90**, 6871 (1968).

(55) P. J. Wagner, *ibid.*, **89**, 5898 (1967).

(56) A. Padwa and W. Eisenberg, *ibid.*, **92**, 2590 (1970).

(57) W. Eisenberg, unpublished results.

(58) A. Padwa, R. Gruber, and L. Hamilton, *J. Amer. Chem. Soc.*, **89**, 3077 (1967).



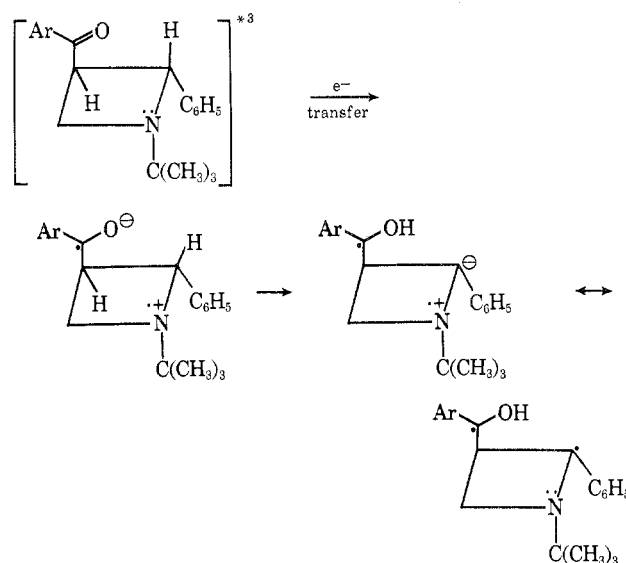
rangement, leading to one primary product from *cis* starting material and a mixture of two primary products from the *trans* isomer.⁵⁹ The distribution of pyrroles appears to favor 2,3-diarylpyrroles over 2,4-diarylpyrroles (2:1). The more readily derived facts about the azetidine rearrangement are the following. (a) The rearrangement of several aroyl- and deuterioazetidines occurs with a high degree of specificity and pinpoints the location of all the carbon atoms in the pyrrole ring. (b) The quantum efficiency of the rearrangement is low ($\Phi = 0.05$) and increases slightly with deuterium substitution on the azetidine ring. (c) Sensitization and emission studies indicate that the reaction is derived from the lowest triplet state. (d) The lack of quenching indicates that the triplet state rearranges at a particularly rapid rate.

The simplest mechanism consistent with the observed rearrangement patterns of the substituted azetidines involves an intramolecular hydrogen transfer and subsequent formation of a spin-unpaired 1,3-biradical intermediate. Spin inversion followed by ring closure affords a transient azabicyclo[2.1.0]pentane that may readily lose water to give a disubstituted pyrrole.

The fact that the 2,3-disubstituted pyrrole is formed in preference to the 2,4 isomer from the irradiation of *trans*-azetidine **56** can be attributed to the lower bond dissociation energy of the tertiary benzylic hydrogen. Also, the exclusive formation of the 2,4-diarylpyrrole from the irradiation of the *cis* isomer is fully compatible with the above scheme. In this case the geometry of the ring only allows for abstraction of the methylene hydrogens. This mechanism also satisfactorily explains the rearrangement paths of the deuterio- and aroyl-substituted arylazetidines.

It is especially noteworthy that ketones **57** and **58**, which possess low-lying $\pi-\pi^*$ triplet states, exhibit photoreactivity comparable to that observed with azetidines **55** and **56**. The latter ketones possess low-lying $n-\pi^*$ triplet states. It has been suggested that the tendency of an excited ketone to abstract hydrogen depends on the nature of the lowest triplet, with $^3(n-\pi^*)$ states being generally reactive and $^3(\pi-\pi^*)$ states non-

reactive.⁶⁰ To account for the photoreactivity of azetidines **57** and **58** we suggest that the above transformations proceed by an initial charge-transfer interaction between the ketone triplet and the electron pair on nitrogen followed by proton transfer and electron reorganization. This series of steps will produce the same biradical intermediate as would be obtained by simple hydrogen abstraction; these steps would



predict a decrease in the quantum efficiency of photorearrangement as the pair of electrons on nitrogen becomes less available. In accord with this expectation, we find that the corresponding protonated azetidines are photochemically inert.

Thiacyclobutyl Ketones. At this stage of our study we recognized that the influence of the heteroatom in the photochemistry of four-membered-ring ketones needed to be assessed. We therefore turned our attention to the related thietane ring in order to make a comparison with the photochemistry of the azetidine system. Our initial experiments were involved with the photochemistry of *trans*-2-phenyl-3-benzoylthietane^{61,62} (**63**). Irradiation of **63** afforded *cis*- and

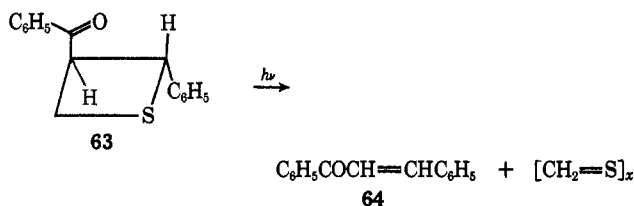
(60) A. Beckett and G. Porter, *Trans. Faraday Soc.*, **59**, 2038 (1963).

(61) A. Padwa and R. Gruber, *Chem. Commun.*, **5** (1969).

(62) A. Padwa and R. Gruber, *J. Org. Chem.*, **35**, 1781 (1970).

(59) A. Padwa and R. Gruber, *J. Amer. Chem. Soc.*, **90**, 4456 (1968); **92**, 100 (1970).

trans-benzalacetophenone (64). The anticipated 2,3- and 2,4-diphenylthiophenes were not detected in the reaction mixture. This result indicates that the photo-



chemistry of the thietane system proceeds by an entirely different path from that encountered in the azetidine series. The formation of *cis*- and *trans*-benzalacetophenone may be envisaged as proceeding by way of a homolytic cleavage of the benzylic carbon-sulfur bond. The resulting diradical undergoes subsequent fragmentation to thioformaldehyde and benz-

alacetophenone. The low bond dissociation energy of the C-S bond appears to be the major factor responsible for the difference in photochemistry of the two heterocyclic systems.

The foregoing examples have been considered in order to provide at least a partial indication of the intriguing and unusual transformations that small-ring ketones undergo upon electronic excitation. Considerable work in this area has been carried out by many investigators, and it may be safely anticipated that significant and new findings in small-ring photochemistry will be forthcoming in the future.

It is a pleasure to acknowledge the vital contribution of my co-workers, whose names are to be found in the references. I wish also to express my thanks to the National Science Foundation, the U. S. Public Health Service, and the Alfred P. Sloan Foundation for their financial support.

Recognition of Stereochemical Paths by Orbital Interaction

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The importance of orbital interactions, particularly between the HO (highest occupied) MO (molecular orbital) of one reactant and the LU (lowest unoccupied) MO of the other, in rationalizing chemical reactions is now invincibly evident.^{2,3} Several papers have discussed this problem, giving a fair reasoning of the orbital interaction scheme.⁴⁻⁶ The physical grounds for differentiation of the HOMO and LUMO from the other MO's have also been disclosed.⁷

The scheme of the HOMO-LUMO interaction between reacting species²⁻⁴ has drawn the attention of organic chemists to the interpretation of the steric course of concerted processes, mainly through the elegant generalization of stereoselection rules and the classification of various stereospecific reactions by Woodward and Hoffmann.⁵ Although a large part of their interpretation is based on the correlation diagram method, the orbital interaction scheme is also used in some parts, namely, in the explanation of the preferable paths of ring opening for cyclobutenes and for cyclopropyl derivatives, the dimerization of two ethylene molecules by an orthogonal approach, the migration of hydrogen or alkyl across a conjugated chain, the exo-endo selectivity in Diels-Alder-type cycloadditions, and the addition of ketenes to olefins. Obviously the correlation diagram criteria are not employed in some cases, such as interpretation of "sigmatropic" reactions, in which the reaction path has no usable symmetric character.

The purpose of this Account is to show that the HOMO-LUMO interaction scheme can in a unified manner be applied to various processes which have been mentioned and discussed by Woodward and Hoffmann,⁵ and also to present, at the same time, an extremely simple and practical method to interpret or predict the favorable steric pathway. While this method is general in character, it is particularly suitable

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(2) For instance, see K. Fukui, "Molecular Orbitals in Chemistry, Physics, and Biology," P.-O. Löwdin and B. Pullman, Ed., Academic Press, New York, N. Y., 1964, p 513, and references cited therein, and subsequent papers on the frontier electron theory.

(3) (a) K. Fukui, *Bull. Chem. Soc. Jap.*, **39**, 498 (1966); (b) K. Fukui and H. Fujimoto, *ibid.*, **39**, 2116 (1966); (c) K. Fukui and H. Fujimoto, "Mechanisms of Molecular Migrations," Vol. 2, B. S. Thyagarajan, Ed., Interscience, New York, N. Y., 1969, p 118; (d) K. Fukui, "Theory of Orientation and Stereoselection," Springer-Verlag, Heidelberg, 1970.

(4) (a) G. Klopman and R. F. Hudson, *Theor. Chim. Acta*, **8**, 165 (1967); (b) R. F. Hudson and G. Klopman, *Tetrahedron Lett.*, 1103 (1967); (c) G. Klopman, *J. Amer. Chem. Soc.*, **90**, 223 (1968); (d) L. Salem, *ibid.*, **90**, 543 (1968); (e) L. Salem, *ibid.*, **90**, 553 (1968); (f) L. Salem, *Chem. Brit.*, 449 (1969); (g) A. Devaguet and L. Salem, *J. Amer. Chem. Soc.*, **91**, 3793 (1969).

(5) R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969); *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969); "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1969; and their preceding papers cited therein.

(6) R. G. Pearson, *Theor. Chim. Acta*, **16**, 107 (1970).

(7) (a) K. Fukui and H. Fujimoto, *Bull. Chem. Soc. Jap.*, **41**, 1989 (1968); (b) K. Fukui and H. Fujimoto, *ibid.*, **42**, 3399 (1969).