CHAPTER I

PHOTO-INDUCED VINYL CYCLOPROpane
CYCLOPENTENE REARRANGEMENT:
A LITERATURE SURVEY.
INTRODUCTION

During the last twentyfive years since its discovery, thermal vinylcyclopropane-cyclopentene rearrangement (VCR, Chart1.01, Eq.1) has been the subject of many mechanistic and theoretical studies. This rearrangement has also been incorporated into many synthetic designs directed towards the total synthesis of a variety of natural products. A few selected examples have been listed in Chart1.01. This topic has been excellently reviewed recently.

The photochemical version of this well known rearrangement (photo-VCR) was observed in 1962 during the addition of photochemically generated methylene diradical to butadiene. This reaction has attracted the attention of many photochemists and has become the topic of current interest.

ULTRAVIOLET ABSORPTION OF VINYL CYCLOPROPANES

The similarity of a cyclopropane to a carbon-carbon double bond in its physical and chemical properties is well documented. The three-membered carbocycle is known to effectively conjugate with C=C linkages and thus become prone to undergo certain ionic reactions typical of conjugated dienes. An isolated cyclopropane chromophore is known to absorb around

*We have made use of this abbreviation in our recent publications and we continue to use the same throughout the present dissertation.
APPLICATION OF VCR IN THE SYNTHESIS OF SOME NATURAL PRODUCTS

![Equation](image)

VINYL CYCLOPROPANE. REARRANGED PRODUCT. NATURAL PRODUCT.

![Chemical Structures](image)

"Prostaglandin Precursors: SALAûM & OLLIVIER"^2

Cis-Sativene diol
McMURRY & SILVESTRI^3

Zizaene
PIERS & BANVILLE^4
CHART 1.01 (contd.)

VINYL CYCLOPROPANE.  REARRANGED PRODUCT.  NATURAL PRODUCT.

Aphidicolin
TROST et al. 5

Hirsutene
HUDLICKY et al. 6

α-Vetispirene
YAN & PAQUETTE 7
≤200 nm and hence it is inaccessible for photochemical studies in UV-region. However, when conjugated with an olefinic function, the resulting system absorbs in the range 205-223 nm enabling its photochemical study in the ultraviolet region. In fact this characteristic UV absorption has been used as a diagnostic tool in structural elucidation of products in certain photochemical cycloadditions. It has also been utilized to distinguish between certain types of carbocyclic vinylcyclopropanes. For instance, in a bicyclo[4.1.0]heptene system a maxima occurs at 222-224 nm (ε 4000 - 6000) while no such maxima is observed for a bicyclo[3.1.0]hexene system down to 205 nm though a high extinction coefficient (5000) is noticed. Representative UV absorptions of vinylcyclopropanes are included in Chart 1.02.

PHOTOChemistry OF VInylcyclopropanes

In addition to the above mentioned photo-VCR, other important reactions of this chromophore include bicyclopentane formation, olefin formation, cis-trans isomerization, hydrogen abstraction and Walk-rearrangement etc. All these reactions seem to be highly dependent on the structural features of the molecule. As photo-VCR constitutes a significant part of the work presented in this thesis, it is pertinent to provide a brief survey of literature of this reaction.
REPRESENTATIVE UV-ABSORPTIONS OF SOME VINYLCYCLOPROPANES

206 nm (ε, 510)\textsuperscript{16}

208 nm (ε, 5300)\textsuperscript{16}

220 nm (ε, 3000)\textsuperscript{17}

207 nm (ε, 12300)\textsuperscript{16}

224 nm (ε, 4360)\textsuperscript{18}

220 nm (ε, 5250)\textsuperscript{19}

207 nm (ε, 5090)\textsuperscript{15}
An early report of this rearrangement can be seen in the benzene sensitized photolysis of 1,2-diphenylcyclopropane 1 wherein the aromatic double bond participated in the rearrangement giving rise to the VCR product 2, although in a low yield\(^{20}\), in addition to the products 3, 4 and 5 (Chart 1.03). The formation of these products has been rationalized on the basis of the diradical intermediate 6. Another interesting example\(^{21}\) of photo-VCR is the isomerization of vinylcyclopropane 7 into 8. The latter could be converted into the former under thermal conditions.

The direct photolysis of 9 afforded\(^{22}\) the cyclopentene 10 as a major product along with a few minor ones. As benzene and acetone-sensitized irradiations furnished 10 in only trace quantities the formation of this product was attributed to the singlet excited state. Mazzocchi and Ladenson\(^ {23}\) have investigated the photochemistry of a number of styrylcyclopropanes 11 - 13 (Chart 1.03). Irradiation of 11 and 12 furnished cyclopentenes 14 and 15 respectively as the only products whereas similar irradiation of 13 led to only cis-trans isomerization and slow polymerization. The failure of 13 to undergo rearrangement was attributed to the fact that both the isomers of the substrate exist essentially in transoid conformation and the diradical generated, 13A, is constrained from undergoing cyclization to cyclopentene. In contrast to this, the diradical, 11A, formed from 11 and 12 can easily
CHART 1.03

1. Ph\[\overset{\text{h} \nu, \text{Benzene}}{\rightarrow}\] Ph

2. Ph

3. Ph

4. Ph

5. Ph

6. Ph

7. \(\text{H}_3\text{CO}_2\text{C} \rightarrow \text{CO}_2\text{CH}_3\)

8. \(\text{CO}_2\text{CH}_3\)

9. \(\text{Hexane}\)

10. \(+ \text{Other products}\)

11. \(R_1 = R_2 = \text{H}\)

12. \(R_1 = \text{H}, R_2 = \text{CH}_3\)

13. \(R_1 = \text{CH(CH}_3)_2, R_2 = \text{H}\)

14. \(R_1 = R_2 = \text{H}\)

15. \(R_1 = \text{H}, R_2 = \text{CH}_3\)

Polymerization

11 A

13 A
undergo cyclization due to the favourable geometry.

The photochemistry of a group of open chain vinyl cyclopropanes 16 a b c (cis isomers) possessing carbonyl groups has been studied\textsuperscript{24}. In addition to cis-trans isomerization, the substrates furnished substituted dihydrofurans 17 (a, b & c) and the VCR product 18 (a & c) (Chart 1.04). It is interesting to note that the VCR product is not obtained with the substrate 16b which yielded only the dihydrofuran. Zimmerman and Epling\textsuperscript{25} have investigated the rearrangements of 19, 20 and 21 (Chart 1.04) in depth and established the nature of the excited states responsible for the internal and external bond ruptures of the cyclopropane ring. The use of optically active 19 and 21 as well as the quantum yield measurements showed that the triplets prefer to react via external bond fission whereas the singlets have a greater propensity to react by cleavage of the internal bond. It was also suggested that the singlet rearrangements involve concerted mechanism and the triplet results are consistent with a diradical pathway.

Kaplan et al.\textsuperscript{26} however, observed an opposite multiplicity-reactivity relationship in their study on the photochemistry of 22 and 25. These bicyclic ethers furnished rearranged products 23 and 24 on triplet-sensitized irradiation.
Apparently, the rearrangement occurs via the diradical intermediate, 22A, since the ratio of rearranged products 23 and 24 remains the same regardless of whether 22 or 25 is used (Chart 1.04). These results revealed that most of the triplets of both 22 and 25 react via internal bond fission. It was also shown that the starting vinylcyclopropanes do not interconvert when irradiated separately.

The dependence of excited state multiplicity on the structural features has also been examined by Paquette. Direct irradiation of 26 (Chart 1.05) led to the formation of 27 and this product was found, by sensitization and quenching studies, to be singlet-derived. In contrast, the photosensitization of 28 offered 29 in a very high yield; whereas upon direct irradiation, 28 did offer 29 but in much lower proportion, together with a number of other products. These results indicated that transformation of 26 to 27 is a singlet state process while that of 28 to 29 seems to be mostly through triplet state. Though both the substrates undergo the same rearrangement to the corresponding cyclopentenes, the involvement of different excited states was attributed to the structural difference in these molecules.

The photochemistry of ketones 30 and 32 was also investigated by the same authors under direct and sensitized conditions. It was concluded that n - π* singlets were
involved in the isomerization of $^{30}$ while an efficient isomerization of $^{32}$ was found to occur from its triplet manifolds. However, the authors could not rule out the involvement of the singlet excited state in the formation of $^{33}$ from $^{32}$ in the direct irradiation.

Jorgenson$^{28}$ studied the photochemistry of a series of $^\beta$-cyclopropyl acrylic esters $^{34a-f}$ under both direct and sensitized conditions. It is significant to note that of the six cyclopropyl acrylates studied, only those with a methyl group instead of hydrogen at C-2 formed bicyclopentane $^{36}$ as major product on direct irradiation. On the other hand, those substrates with just a hydrogen on C-2 carbon essentially furnished the VCR product $^{35}$. It is interesting to observe that these substrates gave mostly VCR products on sensitized irradiation. These differences in their photobehaviour have been rationalized on the basis of their energy difference of the ground state conformations.

Hart and Takino$^{29}$ observed that the photolysis of the ketone $^{37}$ in a highly polar medium viz silica gel suspended in cyclohexane resulted in the formation of the VCR products $^{38}$ and $^{39}$ in a 2:1 ratio (Chart 1.06). It is noteworthy that both the internal and external bonds of cyclopropanes have cleaved affording two different types of products. The same group of workers reported$^{30}$ that the
(a) $R = R' = R'' = H$
(b) $R = R'' = H$, $R' = CH_3$
(c) $R = R' = CH_3$, $R'' = H$
(d) $R' = R'' = H$, $R = CH_3$
(e) $R = H$, $R' = R'' = CH_3$
(f) $R = R' = H$, $R' = \text{Cyclopropyl}$
photochemistry of certain types of vinylcyclopropanes depends on both the wavelength of irradiation and substituents on the cyclopropane ring. For instance, irradiation of the dichlorocyclopropyl enones 40 and 41 with a light of >340 nm wavelength resulted in photoisomerization furnishing the products 42 and 43 respectively. These products however underwent dehydrochlorination yielding 44, 45 and 46 during the work up. On the other hand, it is interesting to note that the same two ketones, on irradiation of >270 nm furnished altogether two different sets of products viz. 47, 48 and 49, 46 respectively. An independent photolysis of 42 under Corex filtered light afforded the products 47 and 48 indicating the intermediacy of 42 in the photolysis of 40. It can be noticed that no VCR reaction occurred with these substrates. However, the corresponding ketone 50, lacking the chlorine substituents when irradiated at >340 nm essentially furnished the VCR product 51.

Jeger and coworkers in their study of the photochemistry of \( \xi \)-cyclopropyl-\( \alpha,\beta \)-dienone 52 and the corresponding triene 54, demonstrated that the nature of the excited state controls the type of reaction (Chart 1.07). For example, the ketone 52, on direct excitation, afforded mainly the VCR product 53 along with other minor ones arising from 1,5-sigmatropic shift and ring opening. However, on singlet excitation, the triene 54 gave mostly 1,5-shift product 55.
along with the VCR product 56. Benzophenone-sensitized photolysis of 54 resulted essentially in 56 suggesting the involvement of the triplet excited state in its formation.

Upon benzene-sensitized photolysis,32 (+)-2-carene-4\-methanol 57, clearly underwent VCR reaction affording isomeric bicyclo [3.2.0]hept-2-enes 58 and 59 in an approximately 1:5 ratio. However, direct irradiation of 57 with a high pressure mercury lamp gave a complex mixture of products in which 58, 59 and a new product 60 were present. Based on these results, it was concluded that the cleavage of internal 1,6-bond in 57 leading to 58 and 59 is a triplet state reaction while a higher singlet state could be responsible for the external 1,6-bond fission leading to 60.

Leigh and Srinivasan12 have studied the photochemistry of bicyclo[4.1.0]hept-2-ene 61 under both direct and sensitized conditions (Chart 1.07). Direct irradiation of 61 with a monochromatic light led to a variety of products of which the major product was cis-1,3,6-heptatriene 62. This product was shown to arise from an electrocyclic ring opening reaction by deuterium labelling studies. It has also been shown that this ring opening is a concerted process arising from the singlet excited state. The VCR product 63 was one among the minor products.

Interestingly enough, toluene-sensitized photolysis
of 61 in deoxygenated pentane solution afforded 62 and 63 in different amounts depending on the extent of irradiation. At low conversions (<2%) almost equivalent amounts of 62 and 63 were obtained. However, 63 was a major product at higher conversions. The formation of these two products has been rationalized by assuming a common biradical intermediate.

In order to ascertain the stereochemical implications of these reactions, the photochemistry of 64 and 65 has also been investigated by the same authors. The formation of cis-5-methyl-1,3,6-heptatriene 66 and exo/endo isomerization were the major decomposition pathways in both cases in direct irradiation (Chart 1.08). The stereospecific formation of VCR products exo-68 and endo-68, the other products syn-67 and anti-67 from 64 and 65 respectively indicated that common biradical intermediates were not involved in this reaction. On the contrary, toluene-sensitized irradiation of both isomers 64 and 65 resulted in VCR reaction yielding exo-68 (no traces of endo) and photo-interconversion. The exclusive formation of exo-68 from either of the substrates suggested the involvement of the triplet biradical 69 which must be sufficiently long-lived to lose its stereochemical integrity at C-7 and undergo cyclization. The conformation of endo-68 has been attributed to steric factors since the required closure would necessarily proceed through a transition state in which the methyl group at C-7 is brought into close contact.
CHART 1.07

52 \[ \text{h} \gamma > 347 \text{nm} \] \rightarrow 53

55 \[ \text{h} \gamma > 280 \text{nm} \] \rightarrow 54

\[ \text{h} \gamma > 347 \text{nm} \] \rightarrow Benzophenone

56

57 \[ \text{h} \gamma, \text{sens.} \] \rightarrow 58

\[ \text{h} \gamma, \text{direct} \] \rightarrow 254 nm

58 + 59 + 60

61 \[ \text{h} \gamma/214 \text{nm} \] \rightarrow pentane

62 + 63

\[ \text{h} \gamma/\text{sens.} \] \rightarrow pentane

62 + 63

OTHER MINOR PRODUCTS

OTHER PRODUCTS
with the developing cyclobutane ring.

A successful utilization of photo-VCR can be seen in the transformation of certain tricyclo[4.3.0^5,7]non-3-en-2-one 70 into tricyclo[4.3.0^3,7]non-4-en-2-one 71 in almost quantitative yield effected by irradiating 70 using 366 nm light (Chart 1.09). The choice of this wavelength of light is important as the \( \alpha,\beta \)-eneone chromophore in 70 absorbs in this region while the \( \beta,\gamma \)-unsaturated ketone 71 does not. The same type of photobehaviour was displayed by the pyrozolline 72 apparently involving 70 as an intermediate. On the other hand, trimethyl substituted analogues 73 and 74 under similar conditions of irradiation, displayed an entirely different photorearrangement affording 1,3,5-trimethyltricyclo[4.2.1.0^3,9]non-4-en-2-one 75 in excellent yield. This strikingly divergent photochemical behaviour still remains to be understood.

Wender and Dreyer\(^{18}\) have studied the arene-olefin \textit{meta}-photocycloaddition and synthesized a number of natural products incorporating a polyquinane system. For instance, the intramolecular \textit{meta} addition of the double bond to the arene of 76 resulted in a 4.5:1 mixture of 77 and 78 when the irradiation was done for a short duration. However, on prolonged irradiation it was found that there was a photo-isomerization of 77 to 78 resulting in a 1:1 mixture of the
same, involving a VCR reaction. Both the isomers have been utilized in the synthesis of isocomene 79.
CHART 1.09

70

\[ R = \text{t-Bu, SiMe}_3 \]

\[
\begin{array}{c}
\text{h}\gamma \\
> 366 \text{ nm}
\end{array}
\]

71

\[
\begin{array}{c}
\text{h}\gamma \\
> 366 \text{ nm}
\end{array}
\]

72

\[ R = \text{t-Bu} \]

73

\[
\begin{array}{c}
\text{h}\gamma \\
> 366 \text{ nm}
\end{array}
\]

74

75

76

\[ \text{hv} \quad \text{meta-addition} \]

77

78

79
REFERENCES

1  N.P. Neureiter  
    J. Org. Chem., 24, 2044 (1959);  
    B.M. Trost and P.H. Scudder  

2  J. Salaum and J. Ollivier  

3  J.E. McMurry and M.G. Silvestri  

4  E. Piers and J. Banville  

5  B.M. Trost, Y. Nishimura, K. Yamamoto and S.S. McElvain  

6  T. Hudlicky, F.J. Koszyk, T.M. Kutchan and J.P. Sheth  

7  T.H. Yan and L.A. Paquette  

8  T. Hudlicky, T.M. Kutchan and S.M. Naqvi  

9  See: S.S. Hixon in Organic Photochemistry, Vol. 4  
    (Ed. A. Padwa), Dekker, 1979, Chapter 3, p. 218.

10 H.M. Frey  

11 W.J. Leigh and R. Srinivasan  

12 W.J. Leigh and R. Srinivasan  

13 See: Charton, M., in "The chemistry of Alkenes"  

14 W.G. Dauben and G.J. Fonken  
15 W. Ferree, Jr., J.B. Grutzner and H. Morrison
16 O.L. Chapman, G.W. Borden, R.W. King and B. Winkler
17 K.E. Wilzbach and L. Kaplan
18 A. Zurcher, O. Jeger and L. Ruzicka
19 P.A. Wender and G.B. Dreyer
20 G.W. Griffin, J. Covell, R.C. Petterson, R.M. Dodson and
   C. Klose
21 H. Prinzbach and E. Druckrey
22 R.S. Cooke
23 P.H. Mazzocchi and R.C. Ladenson
24 P.Y. Bahurel, F. Pautet and G. Descotes
25 H.E. Zimmerman and G.A. Epling
26 L. Kaplan, D.J. Rausch and K.E. Wilzbach
27 L.A. Paquette, G.V. Meehan, R.P. Henzel and R.F.
   Eizember
28 M.J. Jorgenson
29 H. Hart and T. Takino
30 H. Hart and M. Weiner
31  K. Ishii, B. Frei, H.R. Wolf and O. Jeger

32  P.J. Kropp

33  A.G. Schultz, J.P. Dattam and K.K. Eng