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Topological and Steric Effects in Mechanism of Intramolecular [2+2] Photocycloadditions

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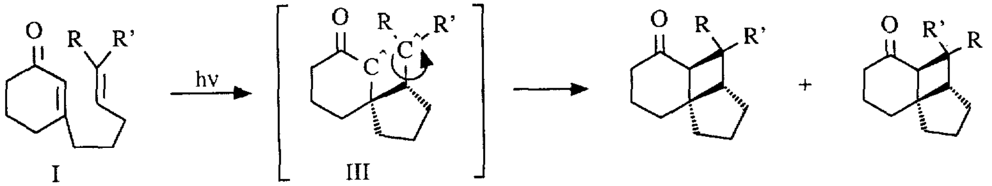
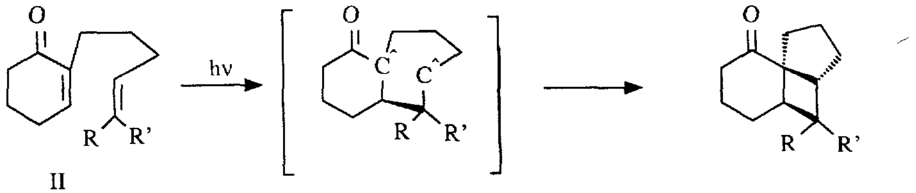
Abstract: It was found that in [2+2] intramolecular photocycloaddition the isomer ratio in system II is different from system I. Compounds 1 and 20 cyclize with high stereoselectivity to give in high yield 3 and 21 respectively. The mechanistic consequences are discussed.

The mechanism of [2+2] photocycloaddition of double bonds to cycloalkenones was proposed by Corey(1) in 1964. It is generally agreed(2) that in most cases a triplet enone will form a diradical intermediate *via* an exciplex(3). The role of the exciplex was questioned lately based on triplet state lifetime measurements(4). The triplet diradical will cyclize to the products after spin inversion to the singlet stste. Prediction of the stereo and the regioselectivity of the cycloaddition reaction is still unsatisfactory.



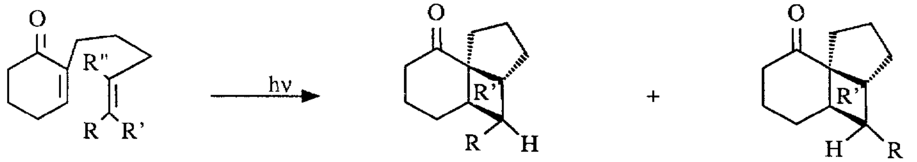
Scheme I



Scheme II

It was proposed(5,6) that when system I is irradiated, it forms the 1,4-diradical III. The first bond is formed between the olefin and carbon-β of the excited cyclohexenone. Rotation around the single bond in the 1,4-diradical intermediate was found to be much faster than cyclization. Therefore Z or E olefins lead to the same product mixture. Corollary, any attempt to transfer structural information from the olefin to the photoadduct will fail. Based on those results, we have studied the following hypothesis. If the first bond formed in system II is to carbon-β, irradiation of Z will lead to one stereoisomer and E will form its epimer. We intend to describe in this paper our preliminary results on the photochemistry of system II and discuss the mechanistic consequences.

The compounds needed for this study were prepared by the method described in our previous paper(7). When 1, having an E double bond, was irradiated(8) it formed mainly isomer 3(9)in high yield (>95%). The ratio of 3 to 4 was determined to be 35:1 respectively. This highly stereoselective process enabled us to prepare 3 in 92% yield and is in full agreement with our working hypothesis. To our surprise, when 2 was irradiated it formed in high yield two epimers 3 and 4 in a 5.8:1 ratio respectively. According to the mechanism in scheme II, 4 was expected to be formed as the main product and not 3. In order to verify how steric interaction effects the epimer ratio the methyl substituent was replaced with an iso-propyl. On irradiation, 5 formed 7 and 8 in a 3.5:1 ratio respectively, and 6 formed the same epimers in a 1.5:1 ratio respectively. In a competition reaction it was found that 2 cyclizes at a rate which is 10% faster than 1. From low conversion (< 10%) experiments it could be concluded that the E to Z isomerization and *vice-versa* is at least ten times slower than the rate of cyclization. Corollary, the "wrong" epimer is formed directly from the starting material.

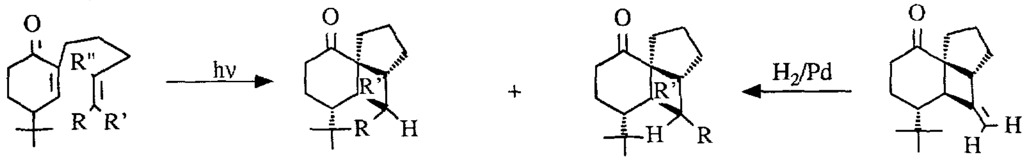


1 R= Me; R'= R''= H	3 R= Me; R'= H	35 / 1	4 R= H; R'= Me
2 R'= Me; R= R''= H	3	5.8 / 1	4
5 R= Pr^i; R'= R''= H	7 R= Pr^i; R'= H	3.5 / 1	8 R= Pr^i; R'= H
6 R'=Pr^i; R= R''= H	7	1.5 / 1	8
9 R= R''= D; R'= H	10 R= R'= D	2 / 1	11 R= R'= D

Scheme III

Olefin 9 was prepared and irradiated in order to study the sterically unhindered system(6). It was found by careful ^{2}H NMR analysis that the ratio of 10 to 11 is 2:1. No geometrical isomer of 9 could be detected in the reaction mixture at 50% conversion (in this measurement if Z isomer was formed its concentration was necessarily below 5%). We can conclude that in this system as well two epimers were formed from one starting material. Based on our results for system I, if the first bond is formed to carbon-α as predicted by the "rule of five", a 1:1 mixture of the epimeric photoadducts was expected. It seems at this point that neither exclusive bonding to carbon-α nor to carbon-β is the first step in the addition process.

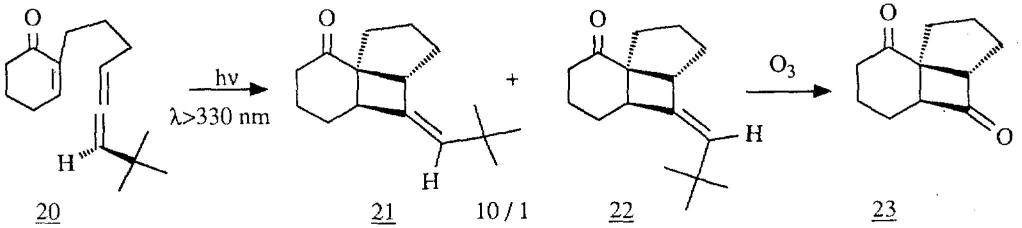
The next stage was to study a system were the approach of the olefin to the surface of the excited enone is controlled by steric effects. It was found that the selectivity of the approach to one side in 12 (E isomer) is over 94% and 86% for 13 (Z isomer)(7). On irradiation 12 cyclizes in quantitative yield to [2+2] photoadducts, 94% of the products are two compounds 14 and 15 which were formed in 4:1 ratio respectively. It was proven unequivocally, by catalytic reduction of 16(7), that 14 and 15 are epimers. On the other hand when the Z isomer 13 was irradiated, it formed 14 and 15 in 1.8:1 ratio. In this system as well, the olefin lost its structure during the addition process. Similarly, the deuterium labeled compound 17 on irradiation formed the epimers 18 and 19 in a 2:1 ratio when the t-butyl is *trans* to the four membered ring. At this stage no conclusive mechanism can be proposed. The assumption that competition between first bonding to carbon-α or carbon-β, a process regulated by steric effects, can not explain the results. Based on trapping results(10)it seems that first bonding to carbon-α as a main route can be ruled out. A competition between parallel and twist(11)approachs of the double bond and first bonding to carbon-β is not an alternative either. Formation of an irreversible exciplex, that enables Z to E isomerization before cyclization, has to be considered as a feasible mechanism. A detailed kinetic study verifying whether an exciplex is formed as an intermediate in system II is essential.



12 R= Me; R'= R''= H	14 R= Me; R'= H	4 / 1	15 R=Me; R'=H	16
13 R'= Me; R= R''= H	14	1.8 / 1	15	
17 R= R''= D; R'= H	18 R= R'= D	2 / 1	19 R= R'= D	

Scheme IV

It was found in our laboratory that substituted allenes (system I) add, on irradiation, to cyclohexenone in high yield(12). A mixture of two geometrical isomers was formed in a ratio close to 1:1. It was suggested that the first bond is formed to carbon-β which leads to a triplet 1,4-diradical intermediate. At that stage, rotation and inversion of the vinyl radical will enable formation of two isomeric adducts. If in system II the "rule of five" regulates the process, the first bond will be formed to carbon-α, which should lead to a mixture of two isomers in a ratio close to 1:1. On the other hand, first bonding to carbon-β should lead to formation of one geometrical isomer preferentially. System 20 was synthesized having a bulky t-butyl group on the allene functionality which should control the approach to one face of the enone system during the addition. It was found that irradiation of 20 *via* uranium glass led to formation (>90% yield) of two geometrical isomers in a 10:1 ratio. It was determined that the structure of the major isomer is 21 (84% yield) and the minor 22 . Cleavage of the mixture by ozone led to one single known diketone 23(13)in 76% yield. By irradiating a 10:1 mixture of 21 and 22 using light filtered through Pyrex glass, an equilibrium of a 1:1.3 ratio respectively has been reached. A probable mechanism for the rearrangement is abstraction of the allylic hydrogen by excited ketone which enables rotation and then recombination(14). The highly stereoselective photocycloaddition can be explained by assuming that fast bonding to carbon-β during the first stage of the cyclization competes with the rotation *via* an exciplex. This might be the preferred mode of reaction in system II when an active and sterically unhindered double bond is approaching the excited enone.



20 | 21 | 10 / 1 | 22 | 23

Scheme V

It can be summarized at this point that the topological effects of the carbon chain being tethered to the α or β position of the enone system (system I versus system II) and steric effects have a dramatic effect on the stereochemistry of the photoadducts.

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8) Irradiations were carried out in cyclohexane (0.01 Mol), using uranium glass filter, 80W Hanovia UV lamp in 25 ml immersion vessel under nitrogen.

9) The spectroscopic properties of all new compounds reported herein are in full agreement with the structures assigned.

10) The results were obtained in preliminary experiments using cyclopropyl as a trapping function. Trapping results for system I were accepted for publication. D. Becker, N. Haddad, Y. Sahali, *Tetrahedron Letters*, (1989).

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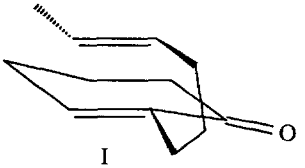

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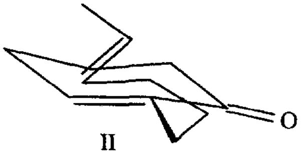

II

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14) The mechanism of this rearrangement is under investigation in our laboratory.

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