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ABOUT THE STEREOCHEMISTRY OF INTRAMOLECULAR [2+2] PHOTOCYCLOADDITIONS

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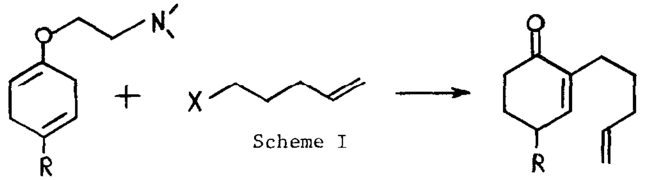
SUMMARY: The stereoselectivity in [2+2] photocycloaddition was studied on System I. Compounds 9, 12a, and 15a cyclize in high yield and the selectivity is higher than 94%.

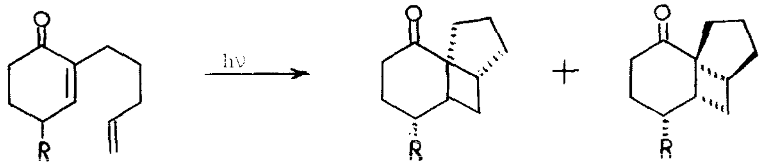
Intramolecular [2+2] photocycloadditions have been used as a key step in synthesis of natural products, in some cases with high regio and stereoselectivity. Although it was found that in similar structures only poor selectivity has been achieved.(1) Since for the time being the conformation of cyclohexenone in a triplet excited state is not known(2), it is impossible to predict the structure of the cycloadducts. We have studied the role of steric effects on the formation of cycloadducts while irradiating system I. The results might be helpful in planning a synthesis based of intramolecular photocycloaddition to cyclohexenone. System I was prepared as described in Scheme I(3)(4) and irradiated through an uranium glass filter (>330 nm) in cyclohexane at room temperature.(5)



Scheme I

I

Cargill(6) has found that the unsubstituted system R=H forms in high regioselectivity the parallel cycloadduct. It was found that 1a and 1b on irradiation cyclize as well in high yield and high regioselectivity although two stereoisomers were identified by gas-chromathography in ratio 1.4:1 2a:3a and 2.3:1 2b:3b respectively. The mixtures were separated by preparative gas-chromatography (15% carb. 20M/chrom Q, 4M) and the structures were determined by spectroscopic methods.(7) An X-ray analysis was carried out on 2c,(8) and the structure obtained was in full agreement with our assignment based on N.M.R. spectroscopy.

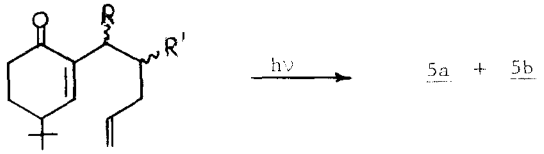


1a R=Me 2a 3a

1b R=Bu^t 2b 3b

The fact that 2a and 2b were formed as the major isomers and the stereoselectivity increased from 1a to 1b substantially, indicate that steric interaction between the approaching olefin and the excited cyclohexenone play a role in controlling the stereoselectivity.

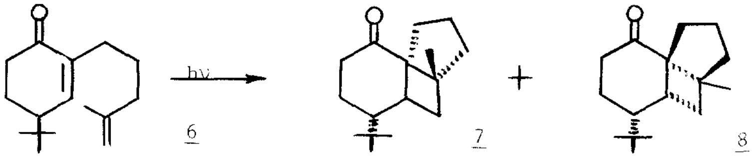
Compounds 4a and 4b were studied in order to find whether methyl substituents on the chain will have any significant effect on the stereoselectivity. Since 4a contains two diastereomeres (in a 1/1 ratio) on irradiation formation of four adducts are to be expected.



4a R=Me R'=H
4b R=H R'=Me

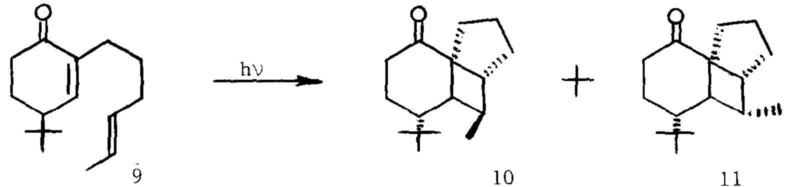
By gas-chromatograph analysis four products were detected in 2:2:1:1 ratio, similar results were obtained for 4b. We conclude at this point that methyl substituent on the chain at position 1' and 2' do not lead to any noticeable improvement of the selectivity in System I.

It was found that methyl at position 4' on the chain had some effect on the stereoselectivity, since two adducts were formed in 2.7/1 ratio on irradiation of 6.



6 7 8

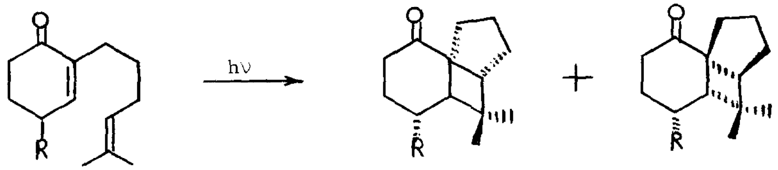
The mixture was separated and the structures were assigned(7) as 7 for the major and 8 for the minor component. High selectivity we have found when 9 having methyl substituted at 5' was irradiated to give in 94% isolated yield two epimers.



9 10 11

The mixture was separated by preparative gas-chromatography and the structures were determined as 10 and 11(7) formed in 4:1 ratio respectively. The assignment of 10 and 11 being epimers was supported by catalytic reduction of 16a over 10% Pd/c in hexane to yield in quantitative yield 10 and 11 in a 1:13 ratio respectively. It means that in the photocyclization of 9 at least 94% of the addition occurs by selective approach of the E disubstituted olefin anti to the Bu^t substituent. The mechanistic significance of the fact that two epimers are formed from an E disubstituted olefin is studied thoroughly in our laboratory.(9a)

The role of steric interaction between substituents on the chain at 5' and 4 on the ring was studied on compounds 12a and 12b.



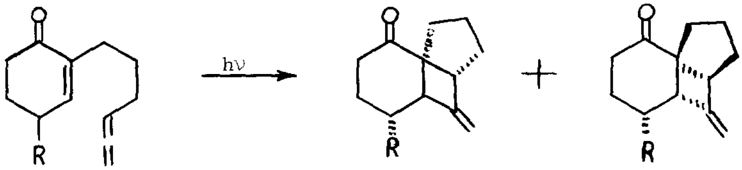
12a R=Bu^t
12b R=Me

13a
13b

14b

High selectivity was expected in photocyclization of 12a. It was found indeed that on irradiation of 12a only one adduct 13a(7) was formed in quantitative yield. The selectivity was diminished by replacing the bulky Bu^t substituted by Me group. When 12b was irradiated two stereo isomers were former 13b and 14b in a 3:1 ratio respectively.

Since it is known(9b) that allenes add intramolecularly to cyclohexenones in high yield and regioselectively, it became interesting to investigate the stereoselectivity as well. It was found that irradiation of 15a yield



15a R=Bu^t
15b R=Me

16a
16b

17b

quantitatively 16a(7) and from 15b two stereoisomers were formed 16b and 17b in a 3:1 ratio respectively.

Based on the results described we can conclude that stereoselectivity higher than 94% can be achieved in [2+2] intramolecular photocycloaddition. The role of the position and the size of the substituents on the system was studied carefully. The photochemistry of system I is further investigated in order to determine the steric requirements of an excited cyclohexenone(10) and the mechanism of the photo-cycloaddition.

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4) All new compounds have H.R. mass spectra and consistent NMR and infrared spectra.

5) Irradiation was carried out in 25 ml immersion vessel, 80W, concentration of the enone < 0.01 Mol.

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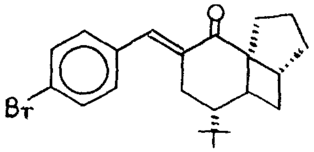
7) 400 MHz H^1-NMR decoupling, N.O.E. experiments and high resolution COSY. (Detailed analysis will be published elsewhere).

8) X-ray analysis was carried out on 2c, prepared according: T.R. Hoye, S.T. Martin and D.R. Peck, J. Org. Chem., 1982, 47, 331.



2c

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