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INTRAMOLECULAR [2+2] PHOTOCYCLOADDITION OF 4-(ALLENIC-SUBSTITUTED)-2-CYCLOALKEN-1-ONES. RING SIZE, LENGTH OF SIDECHAIN AND TEMPERATURE EFFECTS

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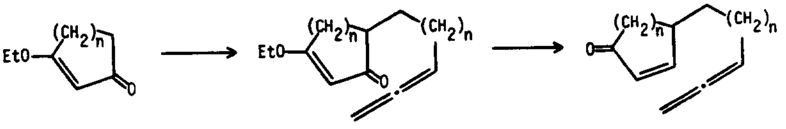
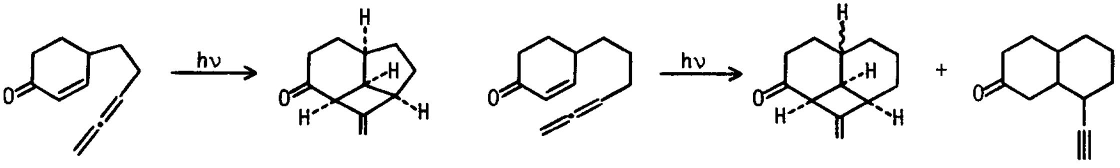
Abstract. The intramolecular [2+2] photocycloaddition of 4-(allenic-substituted)-2-cycloalken-1-ones has been shown to be controlled by the ring size of the cycloalkenone, the chain length and the temperature of the reaction.

The preparative value of intramolecular [2+2] photocycloaddition reactions is well established[1] but few 4-substituted-2-cyclohexen-1-ones have been studied. Using the allenic grouping as the addend, the effect of the ring size, the chain length and the reaction temperature have been evaluated in this latter grouping. Simple 4-(allenic-substituted)-2-cycloalken-1-ones are readily available by alkylation of the lithium enolate of a 3-alkoxy-2-cycloalken-1-one[2a,b] with the requisite allenic iodide,[2c,d] followed by reductive enone transposition with LAH or Dibal and hydrolysis.



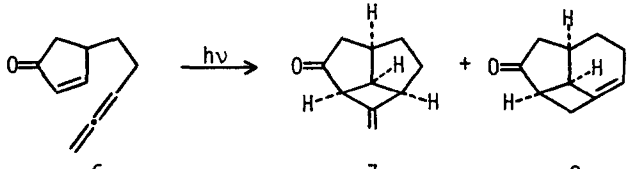
n = 1,2

Irradiation of the 1,6-unsaturated enone 1[3] with three carbon atoms separating the unsaturations gave the straight cycloadduct 2 as the sole product.[4] The hydrindane fusion in 2 is almost certainly cis based upon thermodynamic considerations. Five products were formed in the irradiation of the 1,7-unsaturated homolog 3 in 29, 25, 21, 13 and 7% yields, as determined

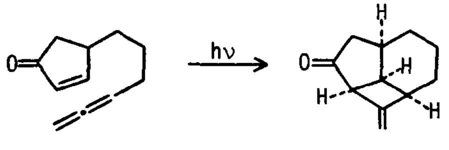


1 2 3 4 5

by capillary GC analysis of compounds listed in elution order. The two major products were shown to be straight cycloadducts 4,[3] undoubtedly containing *cis*- and *trans*-decalin fusions by conversion to the corresponding 1,3-diones which readily underwent retro-Claisen reaction. The third and fifth components could not be obtained in sufficient purity to permit structure evaluation. The fourth component (13%) was shown, by spectroscopy, to possess a mono-substituted acetylenic group and structure 5 has been assigned. Clearly, there is a loss in selectivity as one proceeds from 1,6- to 1,7-unsaturation with the 4-(allenic-substituted)cyclohexenones.[5]



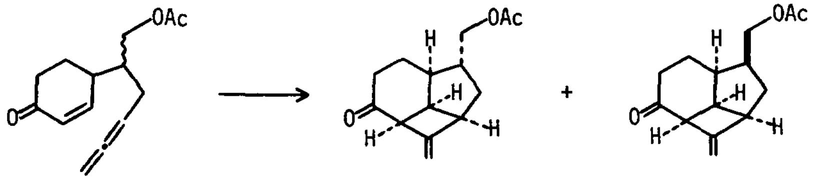
6 7 8



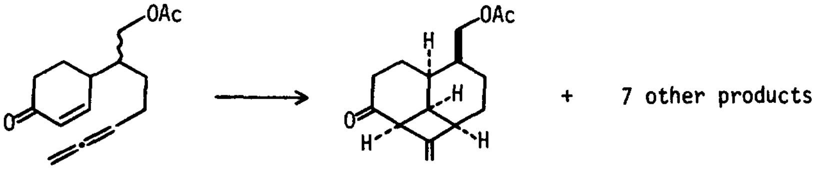
9 10

The opposite effect is observed in the intramolecular photocycloaddition of the analogous 1,6- and 1,7-unsaturated-cyclopentenones 6 and 9. Irradiation of 6 gave a 3:1 mixture of the straight cycloadduct 7 to the bridgehead olefin 8.[6] The irradiation of 9 gave the straight product 10 as the sole product.[6] These results show that the ring size of the cycloalkenone is important, and a simple rule of selectivity based on the sidechain length cannot be formulated.

The effect of sidechain substitution on the photocycloaddition of these allenic-substituted-cyclohexenones has also been investigated. Placement of an acetoxymethyl group at the 1-position of the sidechain[7] has little effect on the selectivity at room temperature. Irradiation of 11, as an equal mixture of diastereomers, gave a 1:1 mixture of straight cycloadducts 12 and 13.



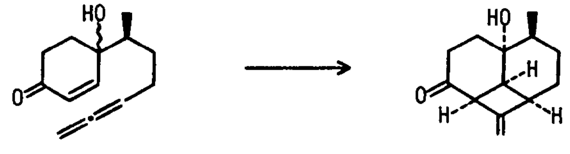
11 12 13



14 15

Room temperature irradiation of 14, as a 1:1 mixture of diastereomers, gave eight products (in retention time order) of 30, 20, 14, 13, 7, 6, 6 and 5 relative abundance. The major product is a straight cycloadduct which is assigned structure 15 by analogy with the unambiguous results obtained with the methyl analog of 14.[8]

When a γ-hydroxyl group and a methyl substituent at the 1-position in the sidechain are incorporated to give **16**, a very selective cycloaddition is observed with the anti diastereomer.[2d] Room temperature irradiation of **16**, as a 60:40 mixture of anti:syn diastereomers, gave a 47% yield of **17** (84% based on anti diastereomer),[8] while at -70 °C irradiation resulted in a quantitative conversion of the anti diastereomer to **17**. The syn diastereomer gave rise to three uncharacterized products. This selective cycloaddition of the antiisomer has been utilized for the synthesis of decipiane diterpenes.[2d]



16 **17**

In conclusion, it is clear that both the ring size of the cycloalkenone and the length of the sidechain, and the reaction temperature have significant effects on the intramolecular photocycloaddition. Substitution on the ring and the sidechain have been shown to affect the selectivity of the reaction with the stereochemistry of the substitution pattern being of primary importance.

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References and Notes

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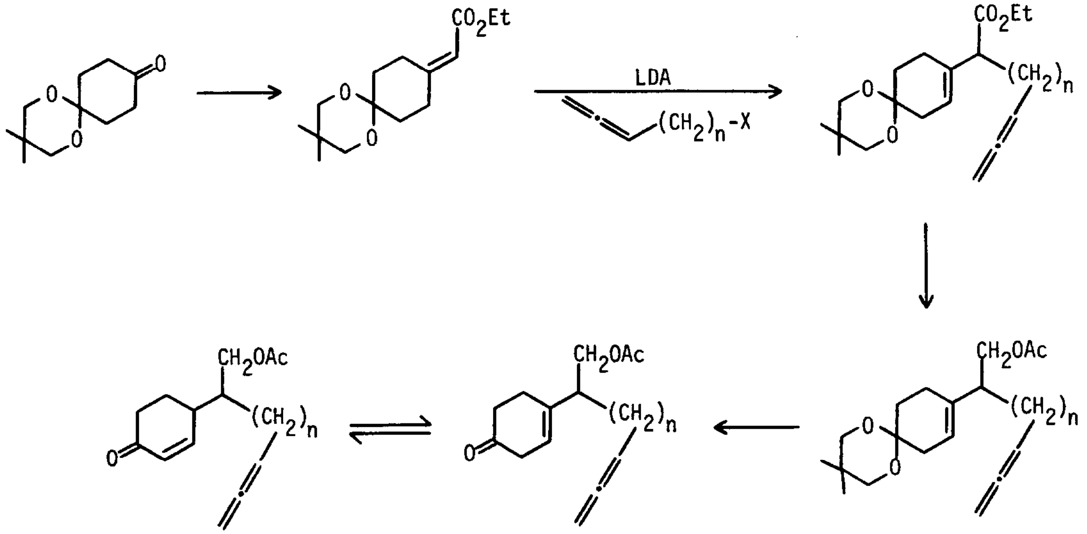
3. The systems studied have either 1,6 or 1,7 unsaturation as defined by numbering from C-alpha of the enone until the first unsaturated atom of the allene function is reached. Cycloaditions involving bonding between the central allenic carbon with C-alpha of the enone are called straight, while bonding involving the central allenic carbon and C-beta of the enone are called crossed.

4. a) All irradiations were performed with 450 watt Hanovia light filtered through uranium glass to prevent product decomposition. Isolated material balance after chromatography is typically 80%. b) The structure of the straight cycloadducts is readily assigned by the presence of a

signal at δ 3.5 for the cyclobutyl proton α to the carbonyl group. The structure of **2** was also verified by ozonolysis to 1,3 dione which underwent retro-Claisen reaction.

5. A similar, less dramatic loss in selectivity has been reported in the intramolecular photocycloaddition of 1,6- and 1,7-unsaturated 3-substituted allenic cyclohexenones. Becker, D.; Harel, Z.; Nagler, M.; Gillon, A. *J. Org. Chem.* **1982**, *47*, 3297.
6. The structures of these products are assigned on the basis of ^1H NMR and off resonance ^{13}C NMR data.
7. These materials were obtained as shown in the following scheme.



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