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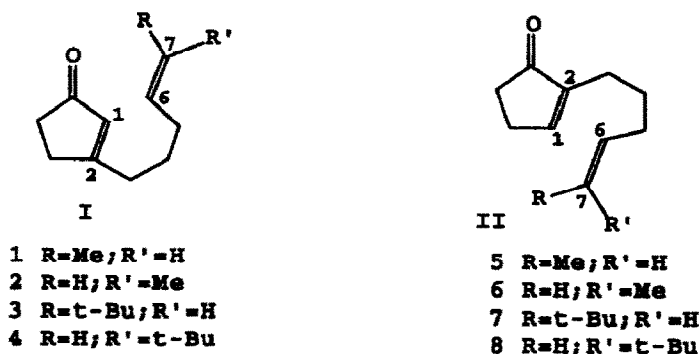
Regio and Stereochemistry in 2+2 Intramolecular Photocycloaddition of Substituted Olefins to Cyclopentenones.

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Abstract: The influence of substituents on the regio- and stereochemistry of the intramolecular [2+2] photocycloaddition of compound 1-8 has been studied. All photoadducts are formed via parallel approach and syn-addition. The endo/exo ratio was used as indicator for the structure of the diradical intermediates.

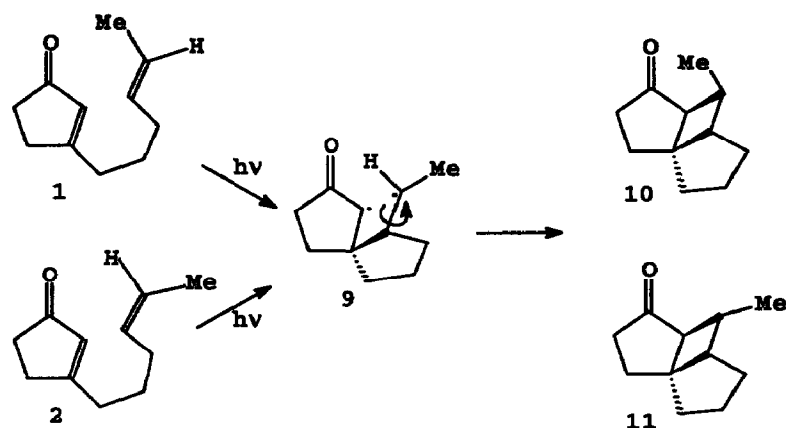
The mechanism of [2+2] photocycloaddition and particularly the 1,4-diradicals intermediates which are involved in the reaction has been carefully studied¹. The intramolecular [2+2] photocycloaddition reaction of olefins to cyclopentenones was investigated by Agosta and Wolff². It was concluded that substituents on carbon 6 can play a significant role in determination of the regiochemistry. The mechanism has been discussed in detail and for some compounds a 1,7-closure has been suggested as an alternative to the common 1,6-process. To our knowledge there is no information on the influence of substituents on carbon 7 on the regioselectivity and the endo/exo ratio in [2+2] intramolecular photocycloaddition of olefins to cyclopentenones. We found previously³ that in intramolecular photocycloaddition of olefins to cyclohexenones the rate of product formation from a 1,4-diradical intermediate is faster than its cleavage to starting material. In addition we found that if a three-methylene chain is tethered to carbon β of the enone the first bond is formed preferentially between 2 and 6 whereas in the system having a chain linked to carbon α , bonding 1,7 competes with the 2,6 process. Our intention was to investigate whether photocycloaddition of E and Z substituted olefins to cyclopentenones would lead to similar conclusions.



Scheme 1

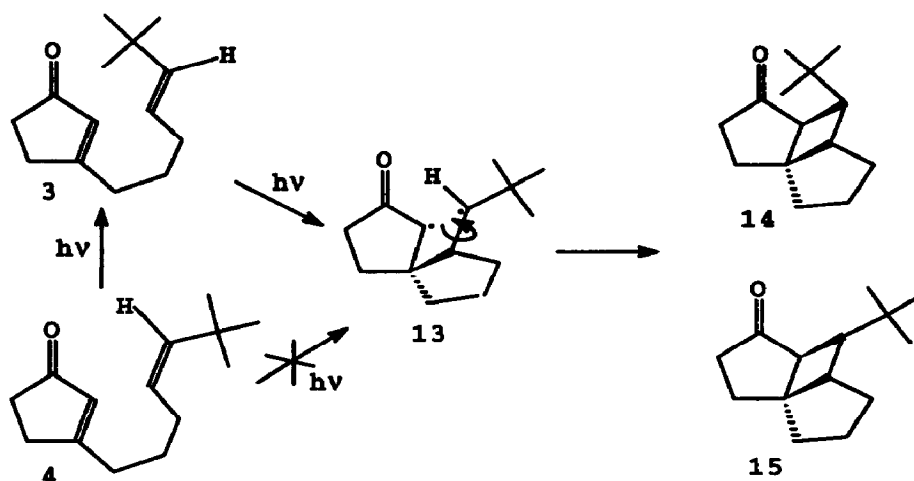
Two systems I⁴ and II⁵ were synthesized by known methods using the corresponding E and Z bromo olefins to give in good yield the corresponding 1-8 cyclopentenones⁶ (see scheme 1). The irradiations were carried out in cyclohexane, using 80 W medium pressure Hg lamp via an Uranium glass filter ($\lambda > 330$ nm). Competition experiments demonstrated that cyclopentenones react photochemically at least twenty times slower than the corresponding cyclohexenones at that range of irradiation. One reason for the slower reaction

of cyclopentenones is presumably due to their lower end absorption at $\lambda > 330$ nm. The photoadducts were formed in high chemical yields (>90%) and are photo-stable (irradiation *via* Pyrex filter leads to secondary reactions). On irradiation of **1** (E isomer) two photoadducts were formed in a 2:1 ratio. The products were separated by chromatography and their structures were determined by spectroscopic methods⁷ to be [2+2] photoadducts **10** (minor Endo) and **11** (major Exo) formed by parallel addition. On irradiation of **2** an identical mixture was formed. GC monitoring of the reaction indicated that equilibration between E and Z during the reaction of **1** and **2** is slower than the [2+2] photocycloaddition. The fact that both **1** and **2** lead to identical mixture of stereoisomer was confirmed by low-conversion experiments (<10%). Based on those results we can suggest that **9** is the common diradical intermediate formed by addition to carbon β of the enone as described in scheme 2. This mechanism is in full agreement with the one we have proposed for cyclohexenones⁸. Hence, it is the first case where substituted olefin tethered by three methylenes to β carbon of an enone leads to formation of [2+2] photoadducts endo and exo in a ratio which is not 1:1. It was assumed that diradicals like **9** would form two stereoisomers (endo:exo) in a 1:1 ratio, but this assumption was not found to be valid in all cases. Further, it was found that the endo:exo ratio is temperature dependent; this effect will be discussed in detail elsewhere.



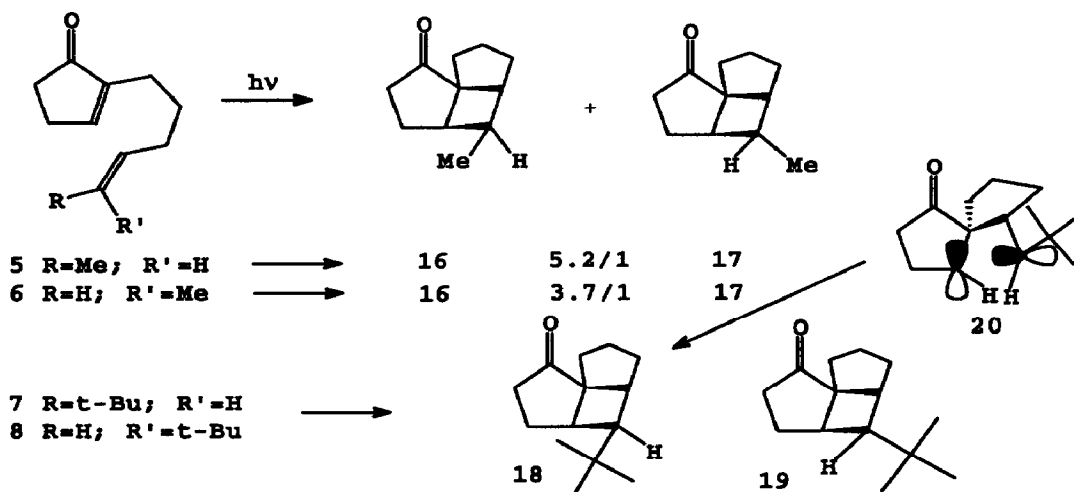
Scheme 2

Irradiation of **3** (E-isomer) having an olefin substituted with a bulky *t*-butyl group led in high yield to two [2+2] photoadducts. Their structures were found to be **14** and **15** formed in a 1.1:1 ratio respectively. It is important to stress at this point that **4** was not formed (<0.5%) during the irradiation of **3**. On the other hand, when **4** was irradiated an identical mixture of photoadducts **14** and **15** was formed, and therefore an intermediate similar to **9** can be proposed. However, we could detect rapid formation (>50% of the enone mixture) of **3** during this reaction. It appears that Z isomer **4** efficiently photoisomerizes to the E isomer **3** *via* a mechanism which is not effective for isomerization of **3** to **4**. In Scheme 3 we propose that **4** has to isomerize to **3** and only **3** can undergo the [2+2] photoaddition process and form **14** and **15**. This sequence is supported by preliminary kinetic and low conversions studies⁹.



Scheme 3

It was interesting to study at this stage the photochemistry of cyclopentenones having an olefin linked *via* three methylenes to carbon α of the enone, since it has been demonstrated⁸ in our work on cyclohexenones that in these systems the first bonding is to both α and β carbons of the enone. Irradiation of **5** (E isomer) gave in high chemical yield a mixture 5.2/1 of two photoadducts. The photoadducts were separated and found to be [2+2] photoadducts by parallel approach and *cis*-addition (**16** (endo) as major, and **17** (exo) as minor constituent). Irradiation of **6** (Z isomer) gave to the same photoadduct mixture, but here with a 3.7/1 endo/exo ratio. The fact that this ratio is dependent whether an E or a Z olefin is used as starting material means that in this system some of the first bonding is to carbon β of the enone *via* a seven membered ring intermediate. Those results are in full agreement to our data obtained for cyclohexenones.



Scheme 4

On irradiation of **7** (E isomer) only one single photoadduct **18** was formed in high chemical yield and found to be the endo product. Irradiation of **8** (Z isomer) gave the same photoadduct as a sole product. Monitoring the reaction by GC established two important phenomena: 1) competition experiments showed **8**

to react twice as fast as 7; 2) no trace of 8 could be detected when 7 was irradiated. Contrastingly, irradiation of 8 led to fast isomerization to 7 (up to 41% of the enone mixture). The mechanism for this effective and highly selective isomerization is being studied. The fact that only one stereoisomer has been formed can not be explained on the basis of their relative stability, since MM2 and semiempirical calculations give similar steric energies for 18 and 19. An attractive way to explain the high tendency to form one stereoisomer is based on a model proposed for oxetanes by Griesbeck¹⁰. It has been assumed that for effective triplet to singlet spin inversion the p orbitals of a 1,4-diradical intermediate have to be perpendicular to each other. It seems reasonable that the bulky t-butyl group will orient itself to the least crowded environment as described in Scheme 4 (20). If this is the dominate factor in the process it might explain why the endo stereoisomer is formed as the sole product. Similar results were obtained in the photocycloaddition of olefins substituted with t-butyl group to cyclohexenones substituted with a t-butyl group at carbon 4¹¹.

In summary, it appears that cyclopentenones react similarly to cyclohexenones with olefins substituted with methyl group on carbon 7. On the other hand bulky substituent like t-butyl enforce a different sequence of bond formation which is currently under investigation.

References and Notes:

- 1 a) Schuster, D. I; Lem, G.; Kaprinidis *Chem. Rev.* **1993**, *93*, 3-22. b) Becker, D.; Haddad, N. *Organic Photochemistry*; Padwa, A., Ed.; Dekker Inc.: New York, 1989; Vol. 10, pp 1-162.
- 2 Matlin, A. R.; George, C. F.; Wolff, S.; Agosta, W. C. *J. Amer. Chem. Soc.* **1986**, *108*, 3385-3394.
- 3 Becker, D.; Nagler, M.; Shahali, Y.; Haddad, N. *J. Org. Chem.* **1991**, *56*, 4537-4543.
- 4 System I was prepared from 3-ethoxy-2-cyclopenten-1-one and the corresponding bromo-olefin as described in ref. 4 for cyclohexenones.
- 5 As described in ref.2.
- 6 All new compounds gave consistent ¹H and ¹³C NMR spectra as well as satisfactory HRMS.
- 7 The stereochemistry of all new photoadducts was determined by 2-D NMR as described in ref. 8. A crystalline derivative was prepared from 11 by aldol condensation with p-bromobenzaldehyde, and its structure was determined by X-ray crystallography.
- 8 Becker, D. Haddad, H. *Tetrahedron* **1993**, *49*, 947-964
- 9 Kinetic measurements are in progress and are in full agreement with the proposed mechanism. A detailed mechanism will be published in due course elsewhere.
- 10 Griesbeck, A. G.; Stadtmuller, S. *J. Amer. Chem. Soc.* **1991**, *113*, 6923-6928.
- 11 Similar results were obtained for cyclohexenones as described in the following Scheme (unpublished):

