

**REVERSAL OF REGIOSELECTIVITY WITH INCREASING RING SIZE
OF ALKENE COMPONENT IN [2+2] PHOTOADDITIONS**

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ABSTRACT: Photoaddition of cyclohexenones **1a** or **1b** to methyl cyclobutene- (**2**), cyclopentene- (**5**) or cyclohexenecarboxylate (**9**) shows a gradual reversal of regioselectivity from head-to-head (**3a/b**) to head-to-tail adducts (**11a/b**). These results are inconsistent with the generally accepted dipolar interaction model.

Photochemical cycloaddition of 2-cyclohexenones with unsymmetric alkenes leads to the formation of head-to-head (HH) and/or head-to-tail (HT) regioisomers. Corey proposed that in these photoadditions an initially formed "oriented π -complex"¹ (later proposed to be an exciplex²) proceeded via a 1,4-diradical to a cyclobutane adduct. It was further suggested that the regiochemistry of the adducts was derived from the dipolar interaction of the ground-state alkene and the triplet excited state enone. Recently the exciplex hypothesis and the existence of a π -complex has been questioned.³ In this letter we report a gradual reversal of regioselectivity in photoadditions of cyclohexenones with cycloalkene esters of increasing ring size. These results are not consistent with the dipolar interaction model.

We have examined the photoaddition of the 3-substituted cyclohexenones **1a** or **1b** with cycloalkenecarboxylates **2,5** and **9**.⁴ Irradiation of **1a** with methyl 1-cyclobutene-1-carboxylate, **2**⁵ (or the corresponding carboxylic acid⁶), gave the HH adduct **3a** while photoaddition of **1b** with the acid of **2** gave, after esterification with diazomethane, adduct **3b**⁷ (see Figure and Table). The HH regiochemistry and cis-anti-cis stereochemistry of these adducts was established by borohydride reduction of the ketone followed by spontaneous lactonization to yield adducts **4a** or **4b**, respectively. Previously, 3,6-disubstituted cyclohexenones were shown to give HH, cis-anti-cis adducts upon photoaddition with **2** (or the corresponding acid)^{5,8-10}.

Next, we investigated irradiation of **1a/b** with methyl 1-cyclopentene-1-carboxylate, **5**. From **1a** about equal amounts of the HH (**6a**) and HT (**7a**) products were formed, although the majority of the HT portion was the disproportionation product **8**, presumably formed from the diradical **12** (see Figure). Products such as **8** are not uncommon in photoadditions and provide evidence for the intermediacy of diradicals in these reactions.^{1,11,12} Irradiation of ester **1b** with **5** gave a 60:40 ratio of the HH adduct **6b** and the HT adduct **7b**. The structures of **6a** and

Figure: Photoaddition Products

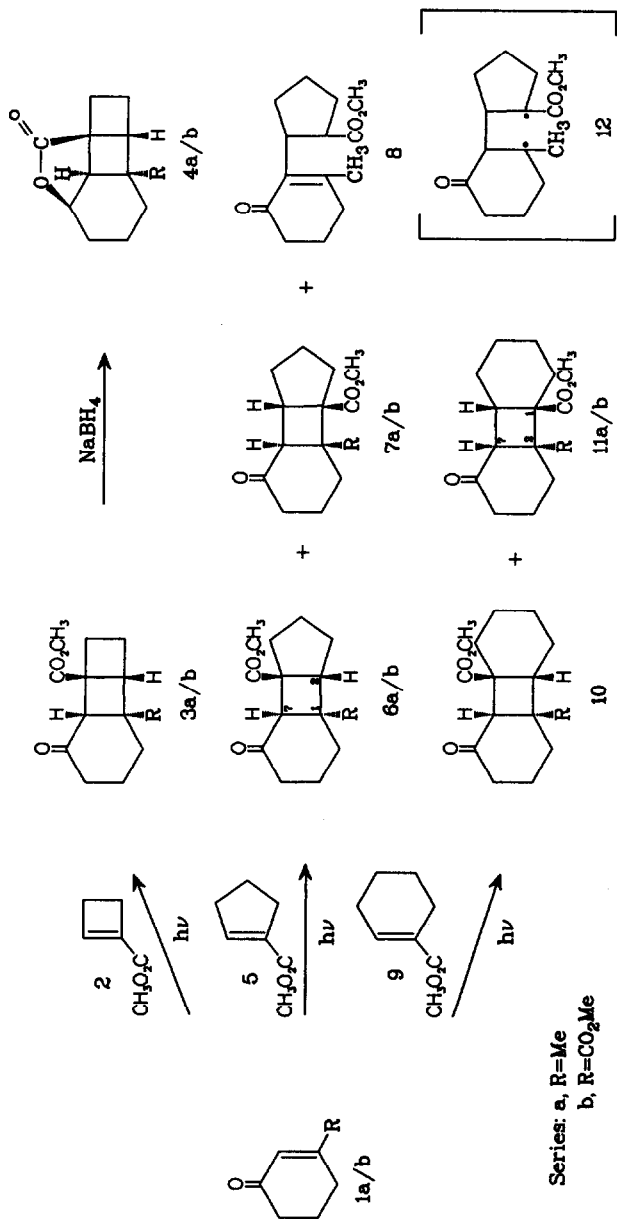


Table Yields of Photoadducts and Ratios of HH:HT Adducts

<u>Enone</u>	<u>Alkene</u>	<u>Adduct(s)</u>	<u>Total % Yield of Adduct(s)^a</u>	<u>Ratio of HH:HT Adduct(s)</u>
1a	2	3a	78 ^b (60 ^c)	>95:5 ^d
1b	2	3b	(55 ^c) ^e	>95:5 ^d
1a	5	6a&7a&8	35 ^a	50:50 ^f
1b	5	6b&7b	22 ^a	60:40
1a	9	10a&11a	49	11:89
1b	9	11b	87	<5:95 ^d

^a Yields are based on products isolated by flash chromatography and are not corrected for unreacted enone. All irradiations were conducted for the same length of time and in some reactions (e.g. with 5) significant amounts of enones 1a or 1b did not react.

^b See ref.5 for this experiment.

^c The carboxylic acid rather than ester 2 was used for this experiment.

^d Minor regioisomer was not observed.

^e See ref.7 for this experiment.

^f Two-thirds of the HT portion was disproportionation product 8.

6b were assigned on the basis of their ¹H NMR spectra and their reduction products. The proton spectra exhibited singlets for H-7 at 2.33 and 3.24 ppm, respectively, and upon borohydride reduction both adducts spontaneously formed lactones. The HT regiochemistry of adducts 7a and 7b was indicated by doublets for H-7 at 2.08 (J=7.3 Hz) and 3.10 ppm (J=7.3 Hz), respectively. The pronounced downfield shift of H-7 in the latter case is the result of deshielding of the proton by the methyl ester at C-1, as compared with the shielding effect of the methyl substituent in the former. The smaller coupling constants of about 7 Hz suggested anti rather than syn stereochemistry for the adducts.¹³

Finally, irradiation of 1a with the 6-membered unsaturated ester 9 gave only a small amount of the HH adduct 10 with the HT adduct 11a predominating, while with 1b and 9 only the HT adduct 11b was formed in high yield (87%). The structure of 10 was established in the same manner as described above for 6a/b. The ¹H NMR spectra of 11a and 11b again displayed doublets for H-7 at 2.49 (J=10.9 Hz) and 3.12 ppm (J=11.3 Hz). The doublets for H-7 established the HT regiochemistry of the adducts but the larger coupling constants of about 11 Hz left in doubt the assignment of the cyclobutane stereochemistry.¹³ Consequently, a single crystal X-ray analysis of 11b was performed and unambiguously established the cis-anti-cis stereochemistry of the adduct.¹⁴ Because of the greater flexibility in adducts containing two cyclohexane rings, drawing conclusions about the stereochemistry of the cyclobutane ring from vicinal coupling constants appears to be risky.

In this study we have shown there is a gradual reversal of regioselectivity from HH to HT adducts as the alkene component is changed from a 4- to a 5- to a 6-membered ring unsaturated ester. The irradiations reported in the Table were

all run in toluene solvent and when we conducted the photoaddition of **1b** to **9** in methylene chloride or methanol the HT adduct **11b** was formed again in high yield. The excellent yield of this adduct obtained supports Schuster's contention that electron-poor alkenes should not be ignored in these photoadditions.³ All irradiations were carried out for the same length of time so, in many cases, the yields are not maximized but they do give some rough idea of the comparative efficiencies of the cycloadditions.

The reversal of regioselectivity with a change in ring size of the alkene component is not consistent with the dipolar interaction hypothesis discussed in the first paragraph as the dipolar effects of alkenes **2,5** and **9** should be very similar. It could be argued that dipolar effects should not be significant in the photoaddition of an electron-deficient alkene to an enone, but if that is the case, then what factor dictates the regioselectivity of the adducts? Possibly more consideration should be given to the suggestions of Bauslaugh regarding the stability of the intermediate diradicals formed in these photoadditions, i.e., the most stable diradicals revert to the starting materials, the least stable are not formed in significant amount, and those radicals of moderate stability close more often to give adducts.^{15,16} A complete discussion of these arguments will be presented in a full paper, which outlines additional details of our investigation.

References and Notes

1. Corey, E.J.; Bass, J.D.; Le Mathieu, R.; Mitra, R.B. J. Am. Chem. Soc. **1964**, *86*, 5570.
2. de Mayo, P. Acc. Chem. Res. **1971**, *4*, 41.
3. Schuster, D.I.; Heibel, G.E.; Brown, P.B.; Turrow, N.J.; Kumar, C.V. J. Am. Chem. Soc. **1988**, *110*, 8261.
4. Irradiations were conducted for 72 hours in a Rayonet Preparative Reactor with 350 nm lamps. Toluene solutions with a 2:1 ratio of cycloalkene: cycloalkenone were placed in Pyrex tubes and deoxygenated with argon before irradiation.
5. Wender, P.A.; Hubbs, J.C. J. Org. Chem. **1980**, *45*, 365.
6. Experiment done in this study.
7. Lange, G.L.; Otulakowski, J.A. J. Org. Chem. **1982**, *47*, 5093.
8. Lange, G.L.; McCarthy, F.C. Tetrahedron Lett. **1978**, 4749.
9. Lange, G.L.; So, S.; Lautens, M.; Lohr, K. Tetrahedron Lett. **1981**, *22*, 311.
10. Wilson, S.R.; Phillips, L.R.; Pelister, Y.; Huffman, J.C. J. Am. Chem. Soc. **1979**, *101*, 7373.
11. Lange, G.L.; Campbell, H.M.; Neidert, E. J. Org. Chem. **1973**, *38*, 2117.
12. Greenlee, M.L.; Fritzen, E.L.; Swenton, J.S. J. Org. Chem. **1978**, *43*, 4512.
13. In relatively rigid cyclobutane systems the *cis* vicinal coupling constant is larger than the *trans*: Rinaldi, P.L.; Salomon, R.G. J. Org. Chem. **1983**, *48*, 3182; Bourhis, M.; Goursolle, M.; Leger, J.-M.; Duboudin, J.-G.; Duboudin, F.; Picard, P. Tetrahedron Lett. **1989**, *30*, 4665; Lewis, F.D.; Barancyk, S.V. J. Am. Chem. Soc. **1989**, *111*, 8653.
14. Performed by G.F. Ferguson, University of Guelph. Details will be published in our full paper.
15. Bauslaugh, P.G. Synthesis **1970**, 287.
16. Schuster, D.I. In The Chemistry of Enones, Part 2; Patai, S., Rappoport, Z., Eds. John Wiley and Sons: New York, N.Y., **1989**, p. 623.