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INTRAMOLECULAR PHOTOCHEMICAL [2+2] CYCLOADDITIONS. REGIOCHEMISTRY OF THE PHOTOCYCLIZATIONS OF SOME OXYGEN-SUBSTITUTED 6-ALLYLCYCLOHEXENONES.

Stephen F. Martin*[1] and James B. White

Department of Chemistry, The University of Texas, Austin, Texas 78712

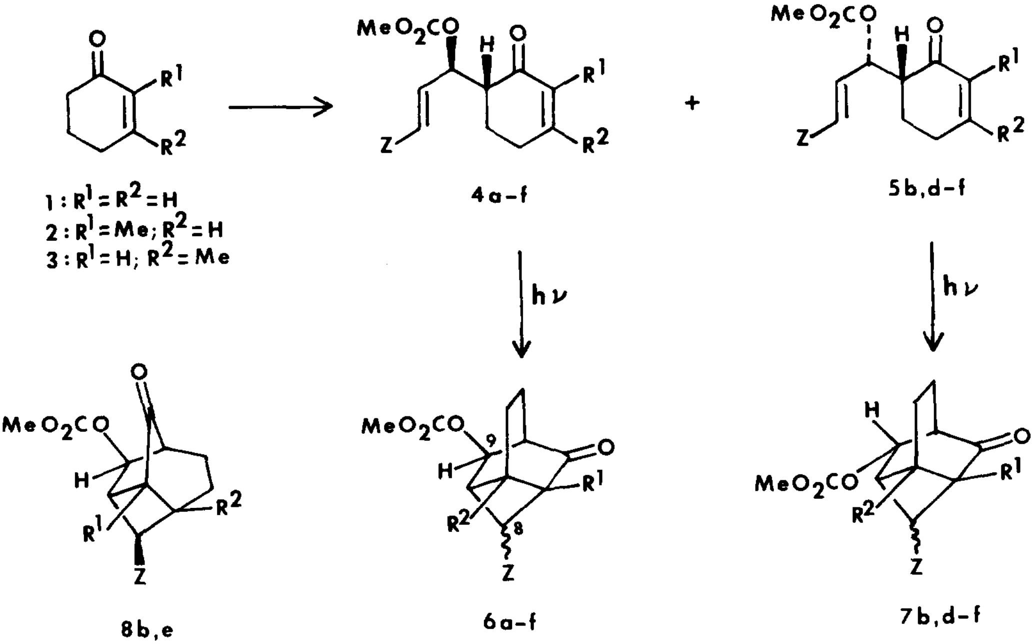
Abstract: The regioselectivity of the intramolecular [2+2] photocycloadditions of certain 6-allylcyclohexenones appears to be largely independent of the substituent (H,OR) on the distal terminus of the isolated double bond.

During the course of an investigation of the intramolecular photochemical [2+2] cycloadditions[2] of unconjugated dienones, we examined the regioselectivity of the photocyclizations of several functionalized 6-allylcyclohexenones to determine the effect of placing various substituents on the isolated carbon-carbon double bond. Based upon the preferred orientation observed in the bimolecular photoadditions of cyclic enones to enol ethers and enol esters,[3] we expected that the regiochemistry of the photocyclization of 6-allylcyclohexenones might be inverted when an oxygen substituent was introduced at the remote terminus of the isolated carbon-carbon double bond. However we discovered that the intramolecular photocycloadditions of certain enol esters proceed in a regiochemical sense opposite to that generally observed in the related intermolecular processes, and we now wish to report the preliminary results of some of these studies.

The requisite substrates for the photocyclizations in this investigation were readily prepared by directed aldol reactions. Thus, treatment of the cyclohexenones 1-3 with lithium diisopropylamide (1.2 equiv., THF, -78°C) followed by the sequential reaction of the kinetic enolates thus generated with either acrolein or β-pivaloyloxyacrolein[4] and then methyl chloroformate gave variable mixtures of the corresponding protected threo- and erythro-aldols 4a-f and 5b, d-f in very good overall yields (Table 1).[5] As anticipated,[7] these crossed-aldol reactions proceeded with a moderate to high degree of stereoselectivity producing the threo-isomers 4a-f as either the major or exclusive products.[8]

Irradiation of the threo-aldols 4a-c (0.1-0.2% in cyclohexane using a 450W medium pressure Hanovia lamp with a uranium filter) afforded good yields of the expected[11] cycloadducts 6a-c as the only identifiable photoproducts (Table 1).[12] Interestingly, when the erythro-aldol 5b was photolyzed, an approximately 2:1 mixture of photoadducts was obtained (42%).

SCHEME 1



Series a-c: Z = H
d-f: $Z = O_2C\text{-}t\text{-}Bu$

The major product appears to be 7b, but the minor component has not yet been fully characterized although it is probably the regioisomeric cycloadduct 8b.

Unfortunately, all efforts to separate the threo- and erythro-aldols 4d-f and 5d-f have been singularly unsuccessful, and it was therefore necessary to photolyze the threo/erythro- mixtures. Surprisingly, the principal photoproducts formed upon irradiation of the aldols 4d-f/5d-f were the cycloadducts 6d-f which were obtained as mixtures of exo-and endo-diastereoisomers epimeric at C(8).[12] The introduction of a pivaloyloxy group on the terminus of the isolated olefinic moiety did not affect the orientation of the intramolecular [2+2] photocycloaddition as originally anticipated. Since any other photoproducts from the irradiation of 4d/5d and 4f/5f are formed in only exiguous quantities (<5%), none have been isolated. On the other hand, three minor components (ca. 10%) have been isolated from the photolysis of 4e/5e, two of which appear to be exo- and endo-7e. Although the other has not been fully characterized, it is probably the regioisomeric photocycloadduct 8e.

Table 1. Preparation and Photocyclizations of Oxygenated 6-Allyl-2-Cyclohexenones

Entry	R^1	R^2	Z	Yield (%)[a] **4+5**	*threo/erythro* ratio (**4**:**5**)	Yield (%) **6**	*exo/endo* Z
a	H	H	H	74	>95:5	74	
b	Me	H	H	71	4.7:1	77	
c	H	Me	H	72	>95:5	80	
d	H	H	O_2C-*t*-Bu	81	6:1[b]	60[c]	2.7:1
e	Me	H	O_2C-*t*-Bu	69	3:1[b]	73[c]	2:1
f	H	Me	O_2C-*t*-Bu	76	5:1[b]	61[c]	1:2.7[b]

[a] Combined yield of *threo-* and *erythro-* diastereoisomers.
[b] Obtained as an inseparable mixture, and the ratio was determined by ^{13}C NMR
[c] Based upon relative amount of **4** in the mixture of aldols **4**/**5**

There are several aspects of these photocyclizations that merit attention: (1) Owing to conformational, steric and/or other factors, an oxygen substituent on the isolated double bond of an unconjugated dienone may not direct the orientation of intramolecular photocycloadditions in the same manner as is observed in the related bimolecular processes; (2) The outcome of photocyclizations may be affected by the configuration of chiral carbon atoms in the chain linking the two olefinic moieties; (3) The stepwise nature of some of these photocyclizations is evident as the geometry about the carbon-carbon double bond in the starting materials **4d-f** is not completely retained in the photoproducts *exo-* and *endo*-**6d-f**. Since photoinduced *cis-/trans* isomerization of the enol ester seems unlikely, biradical intermediates are doubtless involved in these reactions.

Further studies of related photocyclizations are in progress to define more completely the factors involved in determining the regiochemical course of intramolecular photocycloadditions, and the results of these studies will be reported in due course.

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References and Notes

1. Recipient of a National Institute of Health (National Cancer Institute) Research Career Development Award, 1980-1985.
2. For a review of photocycloadditions see (a) Meier, H. in "Houben-Weyl, Methoden der Organischen Chemie," Vol 4/5b, Müller, E., Ed., Georg Thieme Verlag, Stuttgart, 1975, p. 898 ff. (b) Kossanyi, J. *Pure Appl. Chem.* **1979**, *51*, 181.
3. *Cf.* (a) Corey, E.J.; Bass, J.D.; LeMahieu, R.; Mitra, R.B. *J. Am. Chem. Soc.* **1964**, *86*, 5570. (b) Yamada, Y.; Uda, H.; Nakanishi, K. *J. Chem. Soc. Chem. Commun.* **1966**, 423. (c) Cantrell, T.S.; Haller, W.S.; Williams, J.C. *J. Org. Chem.* **1969**, *34*, 509. (d) Singh, P. *Ibid.* **1971**, *36*, 3334. (e) Liu, H.J.; Ogino, T. *Tetrahedron Lett.* **1973**, 4937. (f) Mori, K.; Susaki, M. *Tetrahedron* **1980**, *36*, 2197. (g) Shih, C; Fritzen, E.L.; Swenton, J.S. *J. Org. Chem.* **1980**, *45*, 4462.
4. Prepared according to procedure of Protopopova T.V.; Skoldinov, A.P. *J. Gen. Chem. USSR.* **1958**, *28*, 241.
5. The spectral data (^{1}H NMR, ^{13}C NMR, IR, low resolution mass) for all compounds are in accord with the proposed structures, and all new compounds gave satisfactory analytical data (high resolution mass spectra and/or combustion analysis). The structure of *exo*-**6e** has been confirmed by X-ray crystallography.[6]
6. We wish to thank Professor S.H. Simonsen and Dr. M. Kimura for this determination.
7. *Cf.* Torii, S.; Inokuchi, T.; Ogawa, H. *Bull Chem. Soc. Jap.* **1979**, *52*, 1233.
8. Since the aldols are isolated as their carbonates, the analysis of the stereochemistry of the aldol reactions by ^{1}H NMR is problematic,[9] and ^{13}C NMR[10] was therefore employed. The carbinol carbons of the *threo*- aldols **4** are observed downfield (2-2.5ppm) from the carbinol carbons of the *erythro*-aldols **5** whereas the methine carbons of the *threo*-aldols are slightly upfield (.1-.3ppm) relative to those of the *erythro*-aldols.
9. Stiles, M.; Winkler, R.R.; Chang, Y.; Traynor, L. *J. Am. Chem. Soc.* **1964**, *86*, 3337.
10. Heathcock, C.H.; Pirrung, M.C.; Sohn, J.E. *J. Org. Chem.* **1979**, *44*, 4294.
11. *Cf.* (a) Fröstl, W.; Margaretha, P. *Helv. Chim. Acta* **1976**, *59*, 2244. (b) Altmeyer, I; Margaretha, P. *Ibid.* **1977**, *60*, 874.
12. The proton at C(9) appears as a doublet in the cycloadducts **6a-f** (J=5 Hz), as a broadened doublet in **7b,e** (J=7 Hz), and as a broadened singlet in **8b,e**. The proton at C(8) in *exo*-**6d-f** appears as a broadened singlet, in *endo*-**6d,f** as a triplet (J=7 Hz), and in *endo*-**6e** as a doublet (J=7 Hz).

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