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Studies on the Intramolecular [2+2] photocycloaddition of Dihydro-4-pyrones

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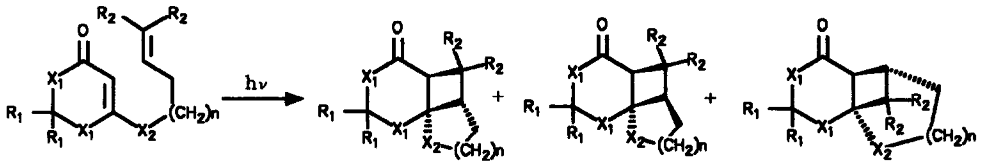
Abstract: Dihydropyrones **3** shown to undergo intramolecular photocycloaddition in high regioselectivity and good yields. The oxygen-heteroatom plays an important role in the regioselectivity of this reaction and in the subsequent fragmentations. Two possible approaches of the olefin to the cyclic enone have been described.

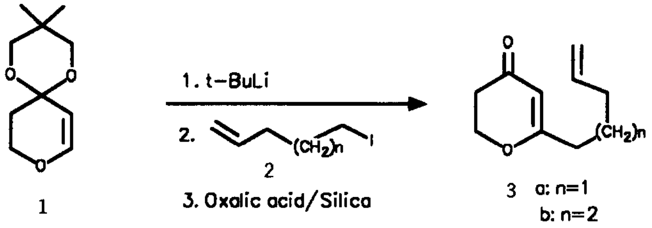
The intramolecular [2+2] photocycloaddition of C=C double bonds to cyclic enones is well documented. Several investigations of the mechanism and applications[1] of this reaction to the synthesis of naturally occurring compounds have been reported in the last decade. Recently, more attention has been directed towards the effect of heteroatoms on the regio- and stereoselectivity of [2+2] photocycloaddition reactions[2]. In contrast to cyclohexenones, in which the length of the olefinic chain has a noticeable effect on the regioselectivity of the intramolecular photocycloaddition reaction of olefins and allenes to cyclohexenones[3], Winkler's group have found that intramolecular photocycloaddition of olefins to dioxenones occurs with parallel regioselectivity in high yields, even though the olefin and the enone double bonds were three, four or five methylene groups apart[4].



I	II	III	IV	
a: $n=1$, $X=CH_2$, $R_1=R_2=H$ or CH_2 (allene)	100%	0%	0%	(>95%, ref. 3a)
b: $n=2$, $X=CH_2$, $R_1=R_2=H$	66%	17%?	17%?	(90%, ref. 3b)
c: $n=2$, $X=CH_2$, $R_1=H$, $R_2=CH_2$ (allene)	85%	0%	15%	(>95%, ref. 3a)
d: $n=2$, $X_1=CH_2$, $X_2=O$, $R_1=R_2=H$	100% (II and/or III)		0%	(60%, ref. 3c)
e: $n=2$, $X_1=O$, $X_2=CH_2$, $R_1=R_2=H$	98%	0%	2%	(>73%, ref. 4)

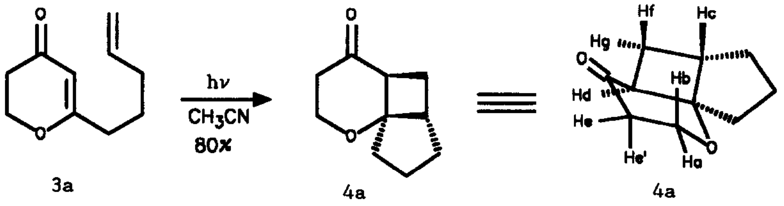
Scheme I

We have investigated the effect of the oxygen-heteroatom in the cyclic enones **3** on the regio- and stereoselectivity of the intramolecular photocycloaddition reaction. Compounds **3**, with different chain lengths, were prepared by coupling of the vinylic anion[5] derived from **1** (tBuLi, THF, HMPA) with the appropriate alkenyl iodides **2** (2 eq), followed by mild hydrolysis of the ketal group (oxalic acid on wet silica, CH_2Cl_2, r.t., 3h) to provide the desired pyrones[6] **3a** and **3b** in 65% and 57% total yields respectively.



Scheme II

Irradiation of enone **3a** (λ=260 nm) in acetonitrile solution was carried out at 0°C, using 80-W Hanau mercury vapor lamp (Q-81) *via* a pyrex glass filter, and followed by GLC[7] (ca. 20 minutes). A single product **4a** was obtained in 80% isolated yield. The structure of **4a** was determined by one- and two-dimensional NMR techniques[6]. Selected NOE and COSY data are presented in table I.

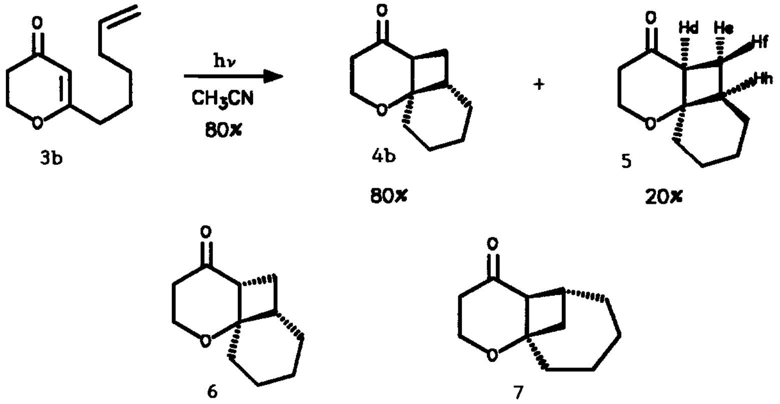


scheme III

Table 1. Selected Chemical Shifts, COSY, NOE and Coupling Constants of 4a.

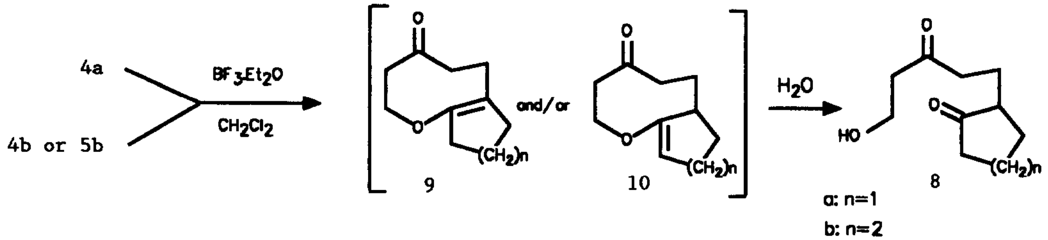
Proton	$\delta(C_6D_6)$	COSY	NOE (%)	J	He	He'
a	3.60	Hb, He	Hb(9.7), He(2.5)	J_a= 12.3,	5.0	5.0
b	3.45	Ha, He	Ha(15.3), He(4.9), Hc(4.3)	J_b= 12.3,	5.4,	8.2
c	2.52	Hf, Hg	Hb(2.0), Hf(2.4), Hcp(1.3)			
d	2.36	Hf, Hg	Hg (1.1)			
e	2.09	Hb, Ha				
f	2.02	Hc, Hd				
g	1.30	Hc, Hd				

Irradiation of compound **3b** under similar conditions led to the formation of two isomeric chromatographically separable products in a 4:1 ratio and 80% total yield.



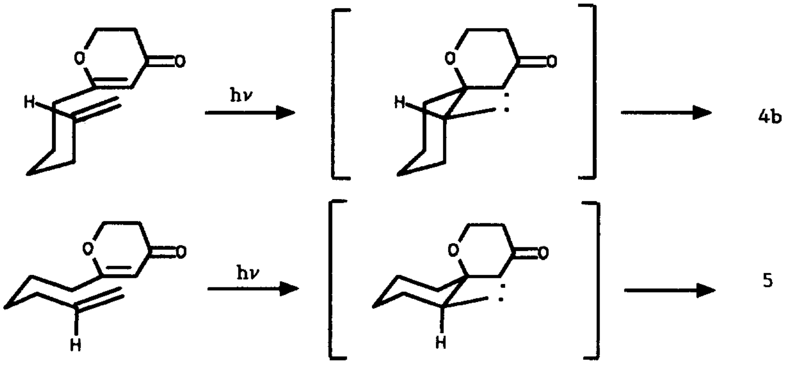
Scheme IV

The stereochemistry of the separated products was determined by NMR[6]. The major photoadduct found to be the expected parallel *cis*-fused photoadduct **4b**. The minor product was found to be **5** rather than alternatives **6** and **7**. The structure assignment of this photoadduct was supported by exchanging H(d) (2.75 ppm, Quartet, J_{de}= 9.0 Hz, J_{df}= 7.5 Hz) with deuterium (CD_3ONa/CD_3OD) which occurred with no detected epimerization to **4b**. This result precludes structure **6**. Further support was achieved upon treatment of each one of photoadducts **4b** and **5b** with boron trifluoride etherate[8] (CH_2Cl_2, 0°C, 15 min, 70% yield) to give the same product **8b**, presumably *via* enolethers **9b** and/or **10b**. This result precludes structure **7**.



Scheme V

The high regioselectivity of the parallel photocycloaddition of the systems studied can be attributed to the preferred formation of the first bond on the oxygen-substituted carbon[2a].The formation of the less stable photoadduct **5** (5.7 Kcal/mol)[9] is consistent with the formation of the first bond at the β-carbon of the enone. The isomeric distribution of the photoadducts is attributed to the two possible approaches of the C=C double bond to the cyclic enone as described in the scheme VI.



Scheme VI

The high yield cycloaddition and subsequent conversion of the photoadducts to the corresponding diketones **8** extends the applications of this reaction in the synthesis of oxygen-containing spirosystems, macrolactones and bridged bicyclic systems which might be derived from **8**.

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References and Notes

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6. All new conpounds were charactarized by full spectroscopic data, yields refer to chromatographed materials with purity of >95%.
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