

FACE SELECTIVITY IN THE [2+2] PHOTOANNELATION OF  
CHIRAL 3(2H)-FURANONES WITH ALKENES

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Summary: The photocycloadditions of a series of chiral 3(2H)-furanones with alkenes show facial selectivities which parallel the steric bulk of the furanone substituents. Selectivities approaching 50:1 are observed in some instances.

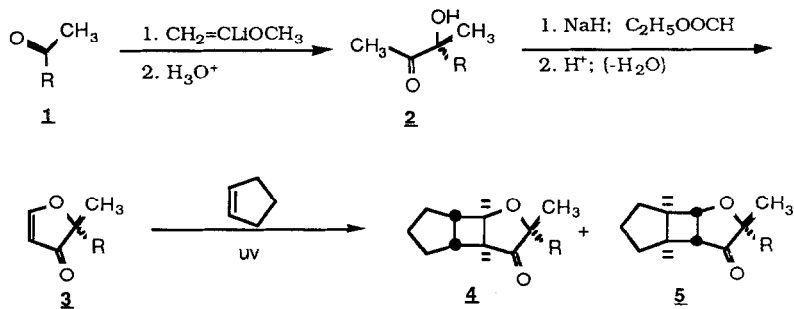
As part of an ongoing effort directed at the synthesis of natural products by photochemical techniques, we sought a refinement of our previously published photoannulation technique which would result in the preparation of optically active target molecules. In particular we were interested in developing optically active reagents capable of undergoing face-selective [2+2] photochemical reactions with alkenes.

From a practical point of view, it was reasoned that a chiral 3(2H)-furanone would be an ideal candidate for such a process. In previous reports it had been shown that the achiral 2,2-dimethyl-3(2H)-furanone (**3a**) undergoes photochemical cycloaddition reactions with alkenes with high regio- and stereoselectivity, and that the photoproducts can be converted to useful synthetic intermediates in a variety of ways.<sup>2,3</sup> Described here are the results of an investigation of the photochemical reaction between several alkenes and a series of 2-methyl-2-substituted-3(2H)-furanones **3** which show that high alkene face selectivity can indeed be obtained in many instances.

The most generally useful synthetic route to the racemic 2,2-disubstituted furanones involved the formylation and subsequent dehydration of  $\alpha$ -hydroxy methyl ketones **2** which were themselves available by the addition of 1-methoxyvinyl lithium<sup>4</sup> to the parent methyl ketones followed by acidic hydrolysis. By this three step procedure the seven 2,2-disubstituted furanones shown in Table I were prepared. Alternatively, most of the furanones were also available by the method of Nozaki.<sup>5</sup>

Cyclopentene was chosen as the initial alkene substrate because of the complete stereospecificity of its reaction with the parent furanone **3a** (*cis/anti/cis*)<sup>2</sup> which was expected to be carried over to the other members of the series. Thus, irradiation of pentane solutions of furanones **3a-3f** in the presence of excess cyclopentene at room temperature ( $\lambda > 280$  nm; pyrex glass filter) led to their rapid consumption and the simultaneous appearance of products **4** and **5**. In the case of Me/*t*-Bu furanone **3d**, it was necessary to employ longer wave length irradiation ( $\lambda > 350$  nm; uranium glass filter) since both starting furanone and product underwent decomposition at the shorter wavelengths employed in the other photocycloadditions.<sup>6</sup> Under these conditions the yields of crude photoproducts were uniformly and reproducibly high (93-100%).

The ratio of photoproducts (**4**:**5**) in each case was determined by capillary gas chromatographic analysis of the crude reaction mixtures and confirmed by the 250 MHz  $^1\text{H}$  NMR spectra. As can be seen, the product ratios ranged from modest (1.4:1) to significant (23:1) as the steric bulk of **R** was increased from ethyl to *t*-butyl. Of further interest was the observation that the increase in facial selectivity of the photoaddition paralleled the increase in the effective size of the **R** group. For instance, a plot of the log of the product ratio *vs.* the Taft steric parameter  $E_s$ <sup>7</sup> for the series Me/Me ( $E_s = 0.00$ ), Me/Et ( $E_s = -0.07$ ), Me/*i*-Pr ( $E_s = -0.47$ ), Me/*t*-Bu ( $E_s = -1.54$ ) affords a straight line indicating that successive methyl substitution at the carbon adjacent to the furanone ring exerts a regular incremental increase in the effective size of the resulting group. Not surprisingly, substitution at sites more remote from the furanone ring such as *i*-Br ( $E_s = -0.93$ ) and *n*-Pent ( $E_s = -0.40$ ) resulted in diminished ratios relative to those expected from the  $E_s$  numbers alone. It was also found that the product ratios were insensitive to changes in temperature ( $-30^\circ\text{C}$  --  $+25^\circ\text{C}$ ) and solvent (pentane, acetonitrile).



**Table I:** Facial Selectivity of Furanones **3** with Cyclopentene

<b>3</b>	Yield(%) <sup>a</sup>	<b>R</b>	Yield(%) <sup>b</sup>	Ratio <sup>c</sup>	$-E_s$ <sup>d</sup>
<b>a</b>	77	$\text{CH}_3$	99	1:1	0.00
<b>b</b>	63	$\text{C}_2\text{H}_5$	99	1:1.4	0.07
<b>c</b>	47	$\text{CH}(\text{CH}_3)_2$	93	1:4.0	0.47
<b>d</b>	74	$\text{C}(\text{CH}_3)_3$	95	1:23	1.54
<b>e</b>	57	$\text{CH}_2\text{CH}(\text{CH}_3)_2$	99	1:3.5	0.93
<b>f</b>	61	$(\text{CH}_2)_4\text{CH}_3$	97	1:1.3	0.40
<b>g</b>	59	$\text{C}_6\text{H}_5$	—	—	2.55

<sup>a</sup>Yield of **3** from **1** (4 steps). <sup>b</sup>Yield of crude photoproducts **4** + **5**. <sup>c</sup>Determined by 250 MHz  $^1\text{H}$  NMR and capillary gc. <sup>d</sup>Reference 7.

Other alkenes exhibited similar face selectivity in their reactions with the furanones **3** (Table II). For instance isobutylene reacted with furanones **3b**, **3c**, and **3d** to give the head/tail adducts with stereochemical ratios (chemical yields) of 2.1:1 (94%), 4.9:1 (97%), and 30:1 (87%), respectively. Similarly the Me/*t*-Bu furanone **3d** reacted with cyclohexene and tetramethylethylene to give product ratios of 25:1 (98%)

and 50:1 (97%), respectively. It was expected that the Me/Ph furanone **3g**, potentially derivable in optically active form from atrolactic acid, would also afford high face selectivity because of the large effective bulk of the phenyl group ( $E_S = -2.55$ ).

Unfortunately, irradiation of **3g**, either alone or the presence of alkenes, gave rise to rearranged materials, presumably through the intermediacy of an epoxy ketene in a process similar to that reported by Padwa.<sup>8</sup>

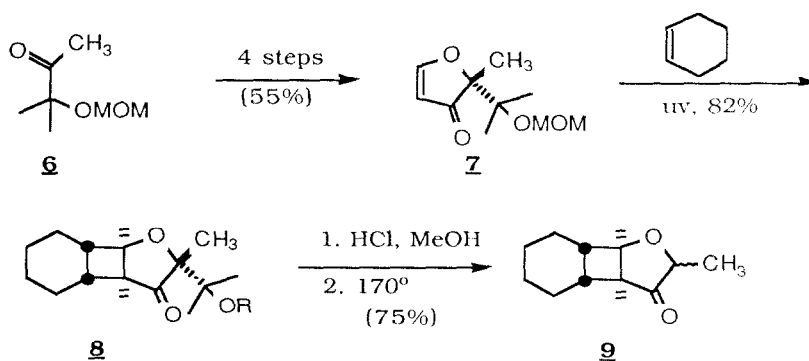
**Table II:** Furanone Face Selectivities with Several Alkenes<sup>a</sup>

Furanone	R	alkene	ratio <sup>b</sup>
<b>3b</b>	C <sub>2</sub> H <sub>5</sub>	isobutylene	2.1:1
<b>3c</b>	CH(CH <sub>3</sub> ) <sub>2</sub>	isobutylene	4.9:1
<b>3d</b>	C(CH <sub>3</sub> ) <sub>3</sub>	isobutylene	30:1
<b>3d</b>	C(CH <sub>3</sub> ) <sub>3</sub>	tetramethylethylene	50:1
<b>3d</b>	C(CH <sub>3</sub> ) <sub>3</sub>	cyclohexene	25:1
<b>7</b>	C(CH <sub>3</sub> ) <sub>2</sub> OMOM	cyclopentene	24:1
<b>7</b>	C(CH <sub>3</sub> ) <sub>2</sub> OMOM	cyclohexene	25:1
<b>7</b>	C(CH <sub>3</sub> ) <sub>2</sub> OMOM	isobutylene	28:1

<sup>a</sup>Photoadditions run with excess alkene at room temperature in pentane. <sup>b</sup>Ratios determined by 250 MHz <sup>1</sup>H NMR and by capillary gc.

Although the above results, particularly with the highly biased Me/*t*-Bu furanone **3d**, were encouraging with regard to our ultimate goal, problems were encountered on attempted elaboration of the photoproducts. It had previously been shown that dimethylfuranone photoadducts such as **4a** (R=Me) reacted readily with peracids,<sup>3a</sup> hydroxylamine,<sup>3a</sup> and organometallic reagents<sup>3b</sup> to give high yields of oximes, lactones, and tertiary alcohols, respectively, which could be conveniently transformed into a variety of valuable materials. In the cases of the photoproducts derived from the more bulky furanones such as **3c** and **3d**, it was impossible to effect reaction of the carbonyl with any of these reagents even under the most forcing conditions. Apparently both faces of the carbonyl are sufficiently hindered as to preclude attack from even the most robust reagents.

A solution to this problem was found in furanone **7**, available in four steps from MOM-protected 3-hydroxy-3-methylbutanone **6**. Irradiation of **7** in the presence of cyclohexene as before (uranium glass filter) led to an 82% yield of photoproduct **8** (R = MOM) which was shown to be a 25:1 ratio of stereoisomers. Similar ratios were obtained with cyclopentene (24:1) and isobutylene (28:1). Treatment of **8** (R = MOM) with methanolic HCl at room temperature for six hours afforded the β-hydroxy ketone **10** (R = H) (95%) which underwent a smooth retroaldol loss of acetone on heating at 170°C for 45 minutes to give tricyclic ketone **9** (83%). Reaction of **9** with the various reagents previously mentioned now proceeded without incident.



In conclusion, facially biased 3(2H)-furanones undergo photochemical cycloadditions with alkenes in a regular and predictable manner. Synthetically useful ratios (>20:1) can be obtained on a routine basis, opening the door for the preparation of optically active products. The results of our studies investigating a variety of routes to the starting furanones in optically active form are forthcoming.

#### References and Notes

1. (a) Paper number 17 in the series. For Number 16 see S. W. Baldwin, G. F. Martin, Jr., and D. S. Nunn, *J. Org. Chem.*, **50**, 5720 (1985). (b) Partial financial support from the National Institutes of Health is gratefully acknowledged (GM 26266).
2. P. Margaretha, *Chimia*, **29**, 1317 (1975).
3. (a) S. W. Baldwin and M. T. Crimmins, *Tetrahedron Lett.*, 4197 (1978). (b) S. W. Baldwin and J. M. Wilkinson, *Ibid.*, 2657 (1979). (c) S. W. Baldwin and H. R. Blomquist, Jr., *J. Am. Chem. Soc.*, **104**, 4990 (1982).
4. J. E. Baldwin, G. A. Hofle, and O. W. Lever, Jr., *J. Am. Chem. Soc.*, **96**, 7125 (1974).
5. (a) T. Hiyama, M. Shinoda, H. Saimoto, and H. Nozaki, *Heterocycles*, **15**, 263 (1981). (b) D. R. Williams, A. Abbaspour, and R. M. Jacobson, *Tetrahedron Lett.*, **22**, 3565 (1981).
6. Control experiments demonstrated that the product ratio for furanones **3a** and **3b** were independent of the wavelength of the incident irradiation.
7. J. Shorter, *Quart. Rev.*, **24**, 433 (1970).
8. (a) A. Padwa and T. Brookhart, *J. Org. Chem.*, **44**, 4021 (1979). (b) A. Padwa, T. Brookhart, D. Dehm, and G. Wuebels, *J. Am. Chem. Soc.*, **100**, 8247 (1978). The product of the photochemical rearrangement of **3g** was 2-methyl-2-phenyl-2(5H)-furanone.

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