Tetrahedron Letters,Vol.28,No.43,pp 5083-5086,1987
Printed in Great Britain

0040-4039/87 $3.00 + .00
Pergamon Journals Ltd.

INTRAMOLECULAR PHOTOCHEMICAL REACTIONS OF 2-ACYL-4-OXA-1,5-HEXADIENES

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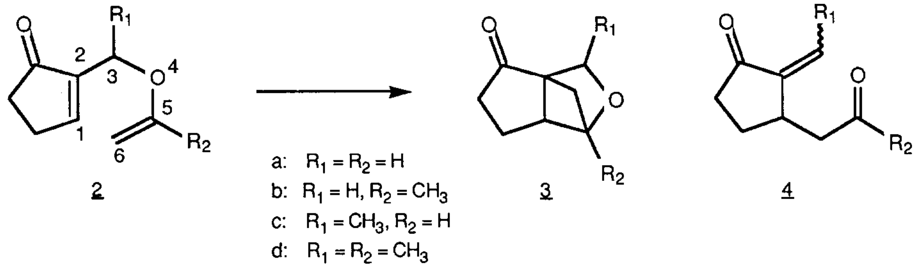
Abstract: Photolysis of alkyl-substituted 2-(2-oxa-3-butenyl)cyclopent-2-enones gives rise to derivatives of bicyclo[2.1.1]hexanes ("rule of five" product), and α - methylenecyclopentanones (photo-Claisen rearrangement). Methyl substitution remote from the bond forming centers produces a regioselective reaction yielding only the "rule of five" product.

Intramolecular [2 + 2] photocycloadddition reactions have been the focus of many mechanistic and synthetic studies.[1] These reactions produce, in general, multi-cyclic photoproducts via stepwise formation of two new σ-bonds. It has long been noted that the reaction of 1,5-hexadienes and 1,6-heptadienes is highly regioselective and gives rise to products containing 5-membered rings.[2] The empirically based "rule of five" has recently been extensively investigated by Wolff and Agosta for three distinct classes of carbonyl substituted 1,5-hexadienes: 1-acyl, 2-acyl and 3-keto.[3] Their results demonstrate that the mode of cyclization of the 1-acyl and 3-keto series can be tuned from initial 1,5 closure (crossed) to 1,6 closure (straight) by the appropriate combination of alkyl group substitution at C-5 and incorporation of the enone double bond into a ring. In light of these results, we sought to explore the effect of oxygen substitution on the mechanism and regioselectivity of the photocycloaddition of 1,5-hexadienes. We report here our initial studies with the 2-acyl series.[4]



2

a: $R_1 = R_2 = H$
b: $R_1 = H, R_2 = CH_3$
c: $R_1 = CH_3, R_2 = H$
d: $R_1 = R_2 = CH_3$

3

4

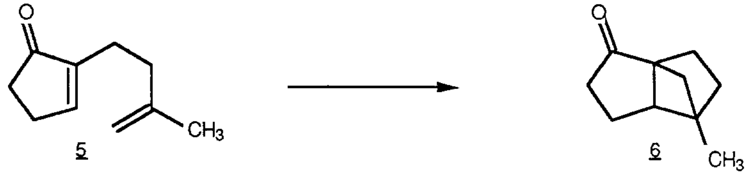
Dienones **2a,b,c** were prepared in 10-20% yield by refluxing 2-(hydroxymethyl)-2-cyclopentenone[5a], **1a**, and 2-(1-hydroxyethyl)-2-cyclopentenone[5b], **1c**, with either ethyl vinyl ether or 2-methoxypropene in the presence of mercuric acetate.[6,7,8] Photolysis ($\lambda \geq$ 340 nm) of ~0.01M hexane or benzene solutions of dienones **2a,b,c** gave rise to 1,5 and 1,6 closure products in 20-65% yield . These results are summarized in Table 1.[7]

Table 1.

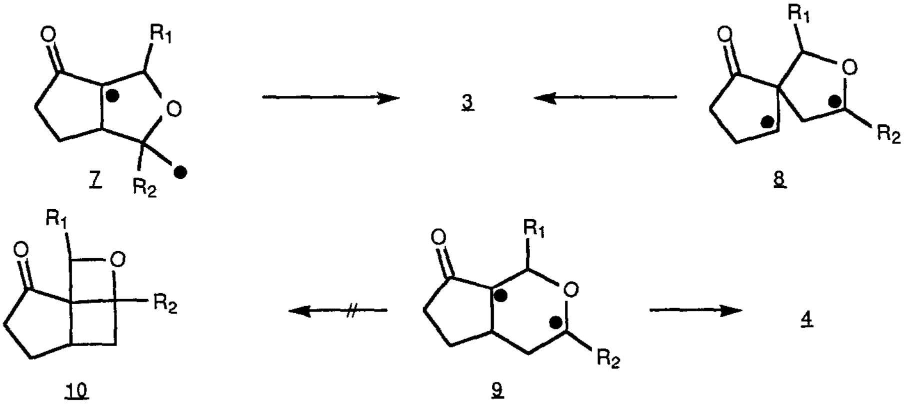
		Photoproducts		ratio	
Dienone	hv time, (h)	1,5 closure	1,6 closure	1,5 : 1,6	yield
2a	66	3a	4a	1.6 : 1	20
2b	30	3b	4b	1.1 : 1	25
2c	15	3c	---	>50 : 1	65[a]

a. Only one diastereomer is formed.

Oxa-substitution results in dramatic changes in the photolysis rate and regiochemistry of the reaction when compared to the alkenyl members of the 2-acyl series. For example, photolysis of enone **5** under similar conditions requires 14 days to reach completion and produces the crossed product **6**.[3b] The observation of photo-Claisen rearrangement[9] products **4a** and **4b** are the first examples of 1,6 closure in the 2-acyl series.[10]



At the outset, we conjectured that 4-oxa substitution would stabilize biradical intermediates **9** (initial 1,6 closure) and **8** (initial 2,6 closure, "rule of five"), but would have little effect on biradical **7** (initial 1,5 closure). The observed rate enhancement in the 4-oxa substituted series is consistent with the formation of biradicals **8** and **9**. Alkyl substitution at C-5 might be expected to sterically retard 1,5 closure (formation of **7**) and stabilize biradicals **8** and **9**. Our results show that methyl substitution at C-5 (**2a** vs. **2b**) has little effect on the regiochemical selectivity of the cycloaddition but gives rise to a small rate enhancement. The response to substitution at C-5 is similar to that seen in the alkenyl systems. Our results support Wolff and Agosta's suggestion that photolysis of 2-acyl-1,5-hexadienes proceeds via initial 2-6 closure in route to crossed products.



Although 4-oxa substitution promotes 1,6 closure, there is a very small energy difference between the two reaction pathways and subtle structural changes can affect the product distribution. Methyl substitution at C-3 (**2c**), which is remote from the bond breaking and forming centers, tips the balance to produce solely crossed closure. In addition, the rate of photolysis increases by a factor of ~4 and the yield rises to a synthetically serviceable 65%. The rate enhancement engendered by C-3 substitution is reminiscent of that seen in the cyclization of 5-hexenyl radicals. In these systems, Beckwith observed that methyl substitution at C-2 and C-3 results in an increase in the rates of cyclization by a factor of 2.5 and 3.2 respectively.[11] While the exact nature of the effect of remote alkyl substitution is unclear, it may be due in part to conformational factors in the acyclic portion of the hexadiene system affecting the relative reaction coordinate energy profiles (2,6 vs. 1,6 closure) of the initial bond closure.

Acknowledgements. This research was supported by a Penta Corporation Grant of Research Corporation. Partial support was provided by the National Science Foundation (CHE-8508737) for the purchase of a 200 MHz NMR. Support from the NSF's College Science Instrumentation Program (CSI-8551703), Hewlett-Packard and Johnson Wax for the purchase of a GC-MS system is gratefully acknowledged.

Notes and References

1. a) Baldwin,S.W. Org. Photochem. **1981**, 5, 123. b) Weedon, A.C. in "Synthetic Organic Photochemistry", Horspool, W.M., Ed., Plenum: New York, 1984, pp 61-143. c) Margaretha, P. Topic in Current Chem. **1982**, 103,
2. a) Oppolzer,W. Acc. Chem. Res. **1981**, 15, 135 and references therein. b) Matlin, A.R.; George, C.F.; Wolff, S.; Agosta, W.C. J. Am. Chem. Soc. **1984**, 108, 3385, and references therein.
3. a) Wolff, S.; Agosta, W.C. J. Am. Chem. Soc. **1983**, 105, 1292. b) Wolff, S.; Agosta, W.C. J. Am. Chem. Soc. **1983**, 105, 1299.
4. For our initial studies with the 1-acyl-3-oxa series see the following communication.
5. a) Smith, A.B.; Branca, S.J.; Guaciaro, M.A. Org. Synth. **1983**, 61, 65. b) Alcohol **1c** was prepared by treating the α-keto vinyl anion of 2-cyclopentenone ethylene ketal with acetaldehyde. For related alkylations of α-keto vinyl anions see: Smith, A.B.; Guaciaro, M.A.; Workulich, P.M. Tetrahedron Lett. **1978**, 4661.
6. Watanabe, W.H.; Conlon, L.E. J. Am. Chem. Soc. **1957**, 79, 2828.
7. All new compounds have been characterized by ^{1}H and ^{13}C NMR, IR and MS.
8. We have been unable to prepare dienone **2d** using these conditions.
9. a) To our knowledge, this is the first example of a non-aromatic photo-Claisen rearrangement. b) For a related example; photo-rearrangement of 3,5-dimethyl-4-oxa-5-hexen-2-one see: Dalton, J.C.; Tremont, S.J. J. Am. Chem. Soc. **1975**, 97, 6916. c) For an example with an aromatic system see: Pinhey, J.T.; Rigby, R.D.G. Aust. J. Chem. **1969**, 22, 977.
10. In principle, biradical **9** could collapse to bicyclo[2.2.0]hexane derivative **10** (straight closure) or fragment to rearrangement product **4** or fragment to starting material **2**. GC-MS analysis of photolysis aliquots suggest that **10** may be formed, but not survive the purification procedures (preparative GC and column chromatography).
11. a) Beckwith, A.L.J.; Blair, I.A.; Phillipou, G. Tetrahedron Lett. **1974**, 2251. b) Wolff and Agosta have previously noted that the cyclization of 5-hexenyl radicals serves as a model for the regiochemical selectivity of the photocyclization of 1,5-hexadien-3-ones. Wolff, S.; Agosta, W.C. J. Org. Chem. **1980**, 45, 3139.

(Received in USA 10 July 1987)