Pergamon

Tetrahedron Letters, Vol. 35, No. 5, pp. 663-664, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(93)E0313-9

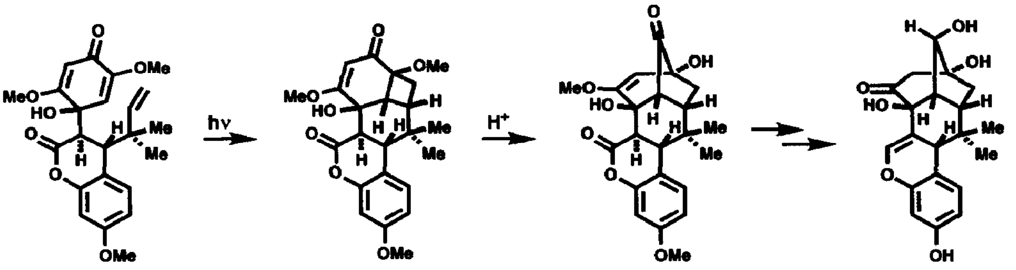
PREFERENCE FOR PHOTODISSOCIATION OVER INTERNAL [2 + 2]-CYCLOADDITION DURING IRRADIATION OF AN UNSATURATED α,β-ENONE

E. J. Corey and Laurence I. Wu

Department of Chemistry, Harvard University, Cambridge, Massachusetts, 02138

Summary: *Irradiation of 2, its trimethylsilyl ether or acetate ester using ultraviolet light of wavelength > 290 nm results not in internal olefin–α,β-enone cycloaddition, but exclusively in photodissociation either of the intercyclic bond (for 2 or the TMS ether) or the C–OAc bond for the acetate ester.*

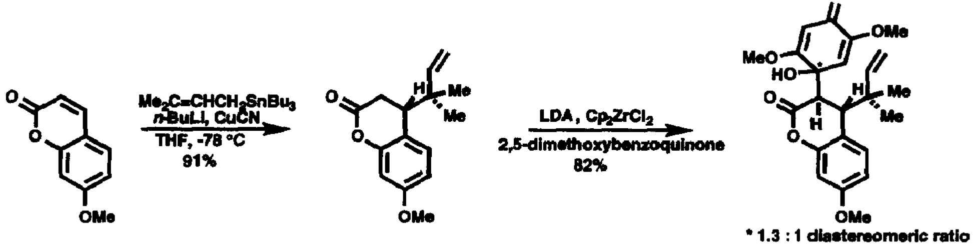
We have recently described a total synthesis of the unusual natural product miroestrol (**1**, obtained from the Thai plant *Pueraria mirifica*) using as a key step a novel internal transannular double cation-olefin cyclization.[1,2] In connection with this project we were interested in the possibility of constructing miroestrol by an approach involving a combination of internal [2 + 2]-photocycloaddition and cationic 1,2-rearrangement of carbon as shown in the following scheme.



2 **1**

The synthesis of the required substrate for the internal [2 + 2]-photocycloaddition step (**2**) was carried out as follows. Reaction of 7-methoxycoumarin (**3**) (Aldrich Co.) in tetrahydrofuran (THF) with 1.6 equiv of the Gilman reagent prepared from prenyllithium[3] and cuprous cyanide (1 : 1, -78 °C, 1 h) was carried out at -78 °C for 30 min and then at -78° to 0 °C over 30 min to give, after quenching with saturated NH_4Cl solution buffered to pH 9 with NH_4OH and extractive isolation, the conjugate addition product **4** in 91% yield. Although treatment of **4** with 1 equiv of lithium diisopropylamide in THF at -78 °C generated the corresponding lithium enolate, the reaction of this enolate with 2,5-dimethoxy-1,4-benzoquinone[4] (THF, -78 °C) produced very little of the aldol adduct **2**, but instead a mixture of 2,5-dimethoxy-1,4-hydroquinone (evidently by a pathway involving electron transfer from the enolate to the quinone) and the Michael adduct. Two diastereomeric aldol adducts **2** (ratio 1.3 : 1) were obtained in good yield, however, when the lithium enolate of **4** was converted to the less electron-rich zirconium enolate by reaction with 1 equiv of Cp_2ZrCl_2 prior to reaction with 2,5-dimethoxy-1,4-benzoquinone.

Irradiation of the aldol diastereomers **2** in ether solution under argon using a Hanovia medium-pressure mercury lamp with a Corex filter as ultraviolet source ($\lambda > 290$ nm) resulted in fragmentation to form the 7-methoxycoumarin derivative **4** and 2,5-dimethoxy-1,4-hydroquinone and no detectable amount of any internal [2 + 2]-cycloadduct.[5] The same reaction pathway was observed using the trimethylsilyl ether of **2** which afforded after aqueous workup **4** and 2,5-dimethoxy-1,4-hydroquinone.[5] The formation of these photoproducts from **2** is clearly the result of photodissociation of **2** to form the radicals **5** and **6** which then abstract hydrogen from solvent. In experiments using cyclohexane as solvent further fragmentation of **5** to 7-methoxycoumarin was observed in addition to formation of **4**.

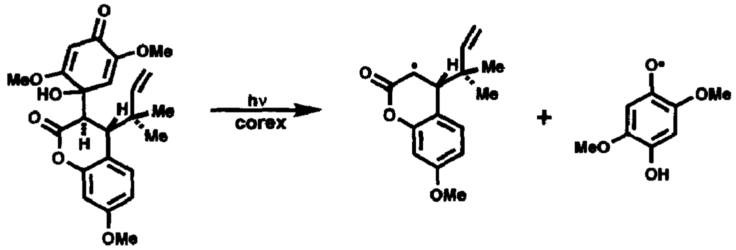


* 1.3 : 1 diastereomeric ratio

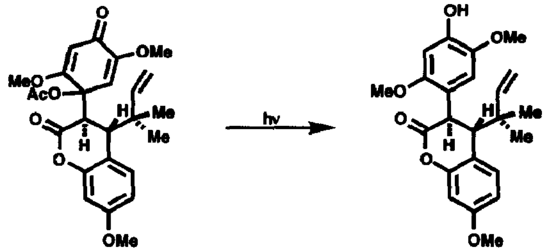
3 4 2

Ultraviolet irradiation (>290 nm) of the acetate **7** in ether took still another course: loss of acetoxy radical to form a tricyclic phenoxy radical which abstracted hydrogen from solvent to form the corresponding phenol **8**.

It is quite interesting that in these experiments dissociation pathways took precedence over the normally very favorable internal olefin–α,β-enone [2 + 2]-cycloaddition. Two factors which clearly favor fragmentation over cycloaddition are (1) dissociation results in a strongly stabilized phenoxy radical and (2) dissociation leads to a relief of the steric repulsion between the bulky vicinal cyclohexadienyl and α,α-dimethylallyl substituents. It is apparent that the behavior of substrate **2** under irradiation is highly instructive with regard to defining critical limits on the scope of the internal [2 + 2]-photoaddition reaction as a key element in the construction of polycyclic systems such as **1**.[6]



2 5 6



7 8

References and Notes

1. Corey, E. J.; Wu, L. I. *J. Am. Chem. Soc.* **1993**, *115*, 9327.
2. For the structure of miroestrol see Taylor, N. E.; Hodgkin, D. C.; Rollett, J. S. *J. Chem. Soc.* **1960**, 3685.
3. Prenyllithium was prepared from tri-*n*-butylprenyltin and *n*-butyllithium (1 : 1) in THF at -78 °C for 1 h.
4. Davidge, H.; Davies, A. G.; Kenyon, J.; Mason, R. F. *J. Chem. Soc.* **1958**, 4569.
5. Control experiments demonstrated that 2,5-dimethoxy-1,4-benzoquinone is not an intermediate in this reaction since it is not converted to the corresponding hydroquinone upon irradiation in ether solution.
6. This research was supported by the National Science Foundation and the National Institutes of Health.

(*Received in USA* 19 *October* 1993; *revised* 12 *November* 1993; *accepted* 23 *November* 1993)