Tetrahedron Letters, Vol.29, No.2, pp 163-166, 1988
Printed in Great Britain

0040-4039/88 $3.00 + .00
Pergamon Journals Ltd.

# PHOTOCHEMICAL REARRANGEMENTS OF QUINONE MONOKETALS. SYNTHESIS OF SUBSTITUTED CYCLOPENTENONES

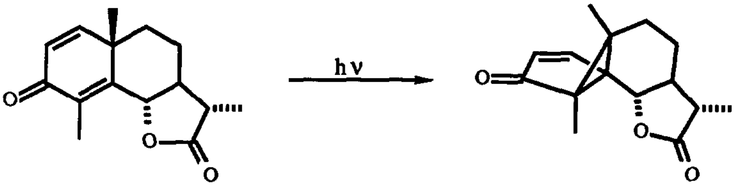
*Michael C Pirrung*[1] and David S Nunn*

*Department of Chemistry, Stanford University*

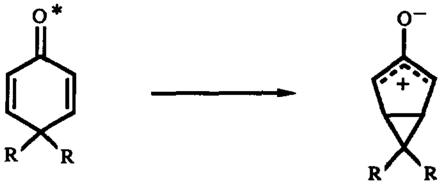
*Stanford, California 94305*

Summary The irradiation of quinone ethylene monoketals in acetic acid leads in high yield to substituted 4-(alkoxycarbonyl)cyclopentenones

The photochemical rearrangement of cyclohexadienones, exemplified by the prototypical santonin to *lumi*-santonin conversion (Eq 1), has been extensively studied since this initial report [2] The reactive excited state is believed to be the n->π* triplet, which by β-bond formation and intersystem crossing leads to zwitterion **1** Depending on reaction conditions, this intermediate may give either a bicyclo[3 1 0]hexenone or solvolysis products Several useful synthetic applications of this reaction in the sesquiterpene field have been reported,[3] and recently reports have appeared concerning general synthetic methodology using 4-methoxycarbonyldienones [4] One of the major factors limiting the previous use of these reactions in synthesis is the limited availability of cyclohexa-2,5-dienones A general route to such dienones in the form of quinone monoketals has become available, however [5] Indeed, the photorearrangements of dialkoxycyclohexadienones have been reported,[6] but the yield and selectivity observed were not encouraging In our hands, photoreaction of **2** utilizing methanol as solvent permits the isolation of 2-(trimethoxymethyl)-2-cyclopentenone (**3**) in 75% yield, but this result is not generalizable Reasoning that compound **3** is derived from an intermediate bicyclo[3 1 0]hexenone, it was desirable to trap the intermediate zwitterion **1** with a protic solvent before the bicyclohexenone could be formed While quinone dimethyl ketals **2** are

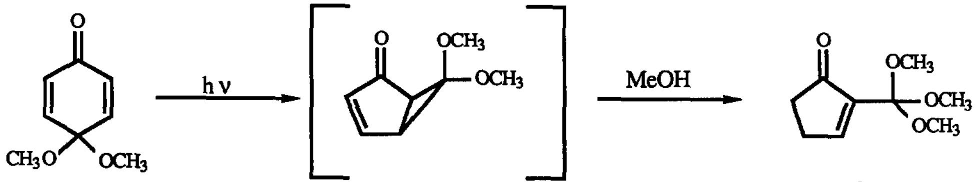


(1)



**1**

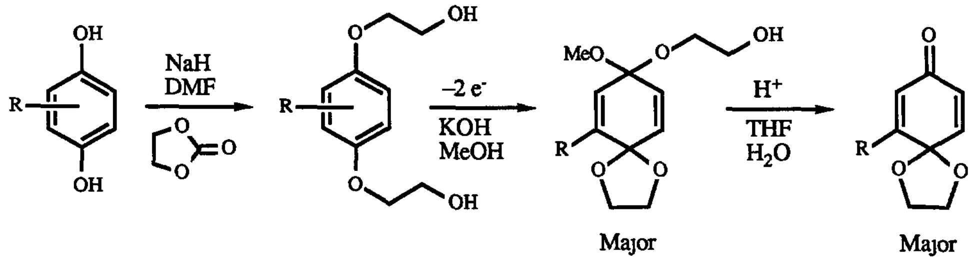
unstable to acetic acid, the corresponding ethylene ketals are more stable[5] In this instance, it has proved possible to conduct the photoreaction in the presence of acid to give selectively 4-alkoxycarbonylcyclopentenones



2

3

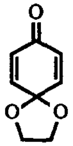
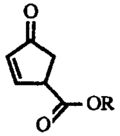
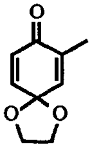
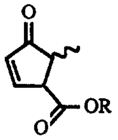
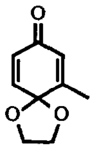
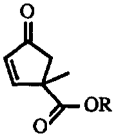
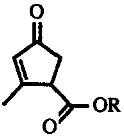
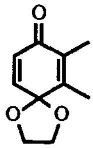
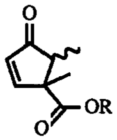
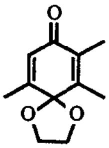
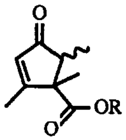
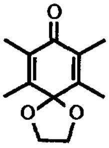
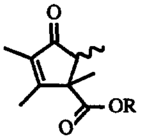
The required quinone ethylene ketals are prepared in a three-step procedure from the hydroquinone O-Alkylation with ethylene carbonate and sodium hydride under the conditions of Yoshino[7] gives the diether, which is oxidized electrochemically to give a mixture of quinone-*bis*-ketals[8] The experimental apparatus for the oxidation is an exceedingly simple one, consisting of a concentric nickel sheet cathode and carbon cloth anode in a 180mL beaker These are connected to an automobile battery charger whose output is adjusted to 6V by powering the charger through a Variac™ The reaction is usually cooled on ice to dissipate the ohmic heat 1% KOH in methanol is used as the supporting electrolyte Oxidations are usually complete in 18 h. Workup consists of dilution with water, extraction into $CH_2Cl_2$, drying and evaporation Hydrolysis of the *bis*-ketal to the monoketal is accomplished in refluxing THF/aqueous acetic acid (14 h)



The photorearrangements are conducted at 50mM concentration in glacial acetic acid through uranium glass with a 450W Hanovia source After consumption of starting material is complete (TLC), the reaction mixture is diluted with water, extracted with $CH_2Cl_2$, and washed with $NaHCO_3$ From the results summarized in the Table, one can see the generally high yields and high regioselectivity in the reaction The only exception is **6**, which gives a 2 1 mixture In general, the product with the <u>less</u> substituted enone double bond is favored This preference can be best understood through study of putative intermediate **17**, which undergoes selective bond cleavage at *b* The solvolysis of **17** prevents the formation of a bicyclo[3 1 0]hexenone and enforces the location of the carboxyl group at the 4-position of the cyclopentenone Selective cleavage of bond *b* is contrary to the precedents from bicyclic systems, where products which retain the more substituted enone double bond are favored.[2] The intermediacy of enol **18** results in a mixture of isomers (about 2 1, major stereochemistry undefined) at the α-position

**17** **18**

Table

| Quinone Monoketal[a] | | | Cyclopentenone[c,10] | | | | | |
|---|---|---|---|---|---|---|---|---|
|  | (76%) | **4** |  | (82%) | **10** | | | |
|  | (20%)[b] | **5** |  | (79%) | **11** | | | |
|  | (46%)[b] | **6** |  | (23%) | **12** |  | (44%) | **13** |
|  | (77%) | **7** |  | (89%) | **14** | | | |
|  | (67%) | **8** |  | (84%) | **15** | | | |
|  | (25%) | **9** |  | (81%) | **16** | | | |

R = $CH_2CH_2OH$

a Yield from the hydroquinone b These compounds are derived from a common precursor, tolhydroquinone, which gives a 2 2 1 mixture on hydrolysis of the bis-ketals c Isolated yield

In conclusion, a general, high yielding, simple approach to substituted cyclopentenones from readily-available aromatic compounds has been developed. Considering the recent burgeoning interest in five-membered ring synthesis,[8] this method should find use in the preparation of natural products, for example the gingkolide and bilobalide class of terpenes [9]

**Acknowledgments** This work was supported by the Alfred P Sloan Foundation and a Presidential Young Investigator Award (NSF CHE 84-51324), with matching contributions from Pfizer, Syntex, and Johnson & Johnson NMR spectra were obtained on an instrument purchased with NSF equipment grant CHE 84-14329

**References and Notes.**

1 Research Fellow of the Alfred P. Sloan Foundation, 1986-88. Presidential Young Investigator, 1986-89

2 Kropp, P. *Org Photochem* **1967** *1*, 1 Schaffner, K. *Adv Photochem* **1966** *4*, 81 Chapman, O L , Weiss, D S *Org Photochem* **1973**, *3*, 197. Schuster, D. I *Acc Chem Res* **1978** *11*, 65 Schaffner, K , Demuth, M M In *Rearrangements in Ground and Excited States*, deMayo, P , Ed , Academic Press, N Y , 1980; Vol 3.

3. Caine, D.; Chu, C.-Y ; Graham, S. *J Org Chem* **1980** *45*, 3790 Caine, D ; Chu, C.-Y. *Tetrahedron Lett* **1974**, 703. Caine, D., Boucugnani, A. A.; Chao, S. T ; Dawson, J B.; Ingwalson, P. F *J Org Chem* **1976** *41*, 1539 Caine, D., Deutsch, H. *J Am Chem Soc* **1978** *100*, 8030. Caine, D , Gupton, J T *J Org Chem* **1975** *40*, 809 Caine, D., Ingwalson, P F. *J Org Chem* **1972** *37*, 3751 Caine, D ; Tuller, F *J Org Chem* **1973** *38*, 3663. Caine, D., Frobese, A. S , *Tetrahedron Lett* **1977**, 3107.

4. Schultz, A G., Lavieri, F. P ; Macielag, M. *Tetrahedron Lett* **1986**, *27*, 1481. Schultz, A G ; Lavieri, F P , Macielag, M , Plummer, M. *J Am Chem Soc* **1987** *109*, 3991

5 Dolson, M. G , Swenton, J S *J Org Chem* **1981** *46*, 177

6 Hewitt, D G ; Taylor, R. F *J Chem Soc , Chem Commun.* **1972**, 493 Margaretha, P *Helv Chim Acta* **1976** *59*, 661 Feldman, K *Ph D Thesis*, **1984**, Stanford University.

7. Yoshino, T ; Inaba, S., Ishido, Y *Bull Chem Soc Jpn* **1973** *46*, 553

8. Paquette, L *Top Curr Chem* **1984** *119*, 1.

9. Nakanishi, K., Habaguchi, K.; Nakadaira, Y , Woods, M C ; Maruyama, M.; Major, R. T , Alauddin, M , Patel, A R , Weinges, K , Bahr, W *J Am Chem Soc* **1971** *93*, 3544

10. $^1$H NMR (CDCl$_3$) **10**: δ 7 71 (dd, J=6,3, 1H), 6 29 (dd, J=6,2, 1H), 4.28 (m, 2H), 3 95 (m, 1H), 3 87 (m, 2H), 2 79 (dd, J=19,3, 1H), 2.64 (dd, J=19,7, 1H) **11** δ 7 64 (dd, J=6,2 5, 1H), 6 27 (dd, J=6,2 5, 1H), 4.33 (m, 2H), 3.89 (m, 2H), 3.49 (m, 1H), 2.70 (dq, J=3,7, 1H), 1 30 (d, J=7, 3H) **12** δ 7 62 (d, J=6, 1H), 6.17 (d, J=6, 1H), 4 24 (m, 2H), 3.84 (m, 2H), 3 01 (d, J=19, 1H), 2 28 (d, J=19, 1H), 1.54 (s, 3H) **13**. δ 6.05 (m, 1H), 4 29 (m, 2H), 3.88 (m, 2H), 3 73 (m, 1H), 2.74 (dd, J=18,3, 1H), 2 66 (dd, J=18,7, 1H), 2 19 (s, 3H) **14** (major) δ 7 66 (d, J=6, 1H), 6 18 (d, J=6, 1H), 4 27 (m, 2H), 3.86 (m, 2H), 2.80 (q, J=7, 1H), 1.35 (s, 3H), 1.21 (d, J=7, 3H), (minor) δ 7 50 (d, J=6, 1H), 6 26 (d, J=6, 1H), 4 22 (m, 2H), 3 81 (m, 2H), 2.27 (q, J=7, 1H), 1.52 (s, 3H), 1 14 (d, J=7, 3H) **15** (major) δ 5.98 (d, J=1, 1H), 4 27 (m, 2H), 3.84 (m, 2H), 2 84 (q, J=7, 1H), 2 11 (d, J=1, 3H), 1 33 (s, 3H), 1 14 (d, J=7, 3H), (minor) δ 6 05 (d, J=1, 1H), 4 22 (m, 2H), 3.80 (m, 2H), 2 32 (q, J=7, 1H), 2 07 (d, J=1, 3H), 1 49 (s, 3H), 1 12 (d, J=7, 3H). **16** (major) δ 4 27 (m, 2H), 3.83 (m, 2H), 2 77 (q, J=7, 1H), 2 00 (s, 3H), 1.73 (s, 3H), 1.59 (s, 3H), 1.14 (d, J=7, 3H), (minor) δ 4 20 (m, 2H), 3.78 (m, 2H), 2 25 (q, J=7, 1H), 1.97 (s, 3H), 1 75 (s, 3H), 1.28 (s, 3H), 1.12 (d, J=7, 3H)

(Received in USA 15 September 1987)