Tetrahedron Letters,Vol.25,No.49,pp 5615-5618,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

# Thermal, Three-Carbon + Two-Atom Cycloaddition of Cyclopropenone Ketals with Carbon-Heteroatom Double Bonds: Butenolide, Furan, and γ-Keto Ester Preparation.

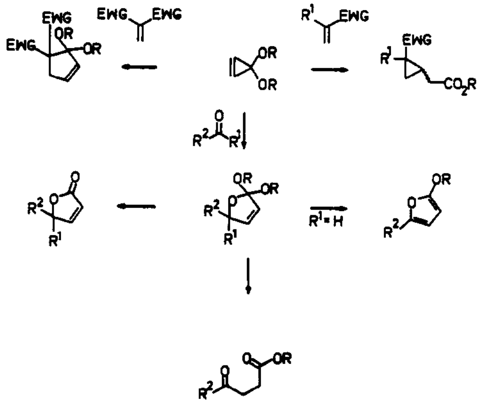
Dale L. Boger,*[1a] Christine E. Brotherton,[1b] and Gunda I. Georg

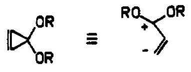
Department of Medicinal Chemistry,
The University of Kansas,
Lawrence, Kansas 66045-2500

**Summary:** A preliminary study of the thermal reaction of cyclopropenone ketals with carbon-heteroatom double bonds is detailed. The reaction with aldehyde and keto carbonyls provide butenolide ortho esters, the product of a formal three-carbon + two-atom cycloaddition of the cyclopropenone ketal across the carbon-oxygen double bond.

Preceding communications have described the thermal reaction of cyclopropenone ketals with electron-deficient olefins,[2] an addition-cyclization reaction which provides either a cyclopentenone ketal product or a cyclopropane product depending upon the degree of electrophilic character of the reactant olefin. The success of the reaction may be attributed to the unusual nucleophilic character of the strained cyclopropenone ketal double bond. Herein we describe a preliminary study of the reaction of cyclopropenone ketals with carbon-heteroatom double bonds, the carbon-oxygen double bond of aldehydes and ketones, which provides butenolide ortho esters, the product of a formal three-carbon + two-atom cycloaddition of I, which in turn may be converted to butenolides, furans, or γ-keto esters, scheme I. The success of this thermal addition-cyclization process of cyclopropenone ketals with simple carbonyl groups underscores the atypical nucleophilic character of the strained double bond of cyclopropenone ketals.

Scheme I.

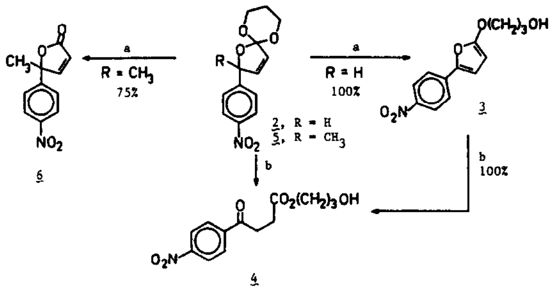




I

**1a** R/R = $(CH_2)_3$
**1b** R = $CH_3$

Table I details the results of an initial survey of the thermal reaction of two cyclopropenone ketals, **1a**[3] and **1b**,[4] with representative carbonyl groups. In the instances detailed in Table I, cycloaddition occurs under mild, thermal conditions (80 °C, 12h) with solvent playing little apparent role in determining the course of reaction. In initial studies with p-nitrobenzaldehyde and p-nitroacetophenone, the butenolide ortho ester adducts **2** and **5** were isolated, pure, by rapid chromatography on silica gel (Method A).[5] Mild, aqueous acid hydrolysis of **2** afforded the furan **3**, whereas mineral acid treatment of **2**, as well as **3**, provided the $\gamma$-keto ester **4**, equation 1. Similarly, mild, aqueous acid hydrolysis of **5** afforded the butenolide **6**. In the subsequent studies detailed in table I no attempt was made to isolate the initial butenolide ortho ester adduct and the crude reaction product was subjected to mineral acid (HCl:acetone, Method B) or mild aqueous acid (HOAc:$H_2O$:THF, Method C) hydrolysis conditions to afford directly the $\gamma$-keto esters or furans/butenolides, respectively.

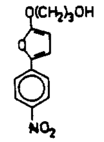
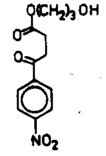
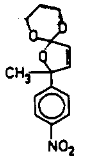
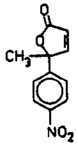
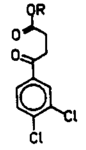
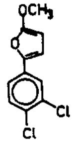
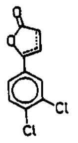


(1)

(a) HOAc, THF-$H_2O$, 25 °C. (b) HCl, acetone, 25 °C.

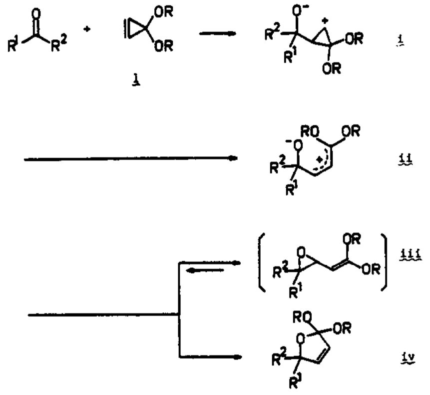
The stepwise formation of the butenolide ortho esters formed from the reaction of cyclopropenone ketals and carbonyl compounds is detailed in scheme II and is consistent with the results of our studies with electrophilic olefins[2] and the initial work of Butler[4]. The potential participation of **iii**, while not being detected, cannot be ruled out.

Table I. Thermal Reaction of Cyclopropenone Ketals **1a** and **1b** with Carbonyl Compounds.

| Cyclopropenone Ketal | Substrate $R^1COR^2$ | Conditions Method,[a] equiv **1**, solvent | Product[b] | % Yield[c] |
|---|---|---|---|---|
| **1a** | $R^1$= H, $R^2$= *p*-$NO_2C_6H_4$ | A, 1, *n*-heptane |  | **3**, 45%[d] |
| | | A, 2, *n*-heptane | | 42% |
| | | A, 2, *n*-heptane[e] | | 44% |
| | | A, 1, neat | | 3% |
| **1a** | | B, 2, *n*-heptane |  | **4**, 44% |
| **1a** | $R^1$= $CH_3$, $R^2$= *p*-$NO_2C_6H_4$ | A, 2, *n*-heptane |  | **5**, 22%[f] |
| **1a** | | C, 2, *n*-heptane |  | **6**, 31% |
| **1a** | $R^1$= H, $R^2$= 3,4-$Cl_2C_6H_3$ | B, 2, *n*-heptane |  | **7**, R = $(CH_2)_3OH$ 53% |
| | | B, 1, $CH_3CN$ | | 37% |
| | | B, 3, $CH_3CN$ | | 52% |
| | | B, 2, benzene | | 46% |
| **1b** | | B, 2, *n*-heptane | | **8**, R = $CH_3$ 49% |
| **1b** | | A, 2, *n*-heptane |  | **9**, 30% |
| **1a** | | C, 2, *n*-heptane |  | **10**, 38% |

(a) Thermal addition-cyclizations were run 0.2-0.6 M in substrate (80 °C, 12 h) under nitrogen; method A: chromatography on $SiO_2$; method B: catalytic concentrated HCl, acetone, 25 °C, 0.5 h; method C: HOAc,THF,$H_2O$ (1:3:1), 25 °C, 3 h (for **10**), 72 h (for **6**). (b) All products exhibited the expected $^1H$ NMR, IR, MS characteristics consistent with the assigned structure and gave satisfactory CHN analysis or HRMS information. (c) All yields are based on purified product isolated by chromatography ($SiO_2$). (d) Variable amounts of **2** could be isolated. Upon standing at 25 °C, **2** is converted to **3** (100%). (e) The reaction was run with slow addition of **1a** (18 h) to the reaction mixture. (f) Compound **5** is unstable to the conditions of isolation.

Scheme II



**Acknowledgments.** This work was assisted financially by the Searle Scholars Program, the National Institutes of Health (CA 00898, GM 07775), and a University of Kansas General Research Allocation (3761-X0-0038).

## References and Notes

1. (a) Searle scholar recipient, 1981-85. Recipient of a National Institutes of Health research career development award, 1983-88 (CA 00898). (b) National Institutes of Health predoctoral trainee (GM 07775).

2. Boger, D. L.; Brotherton, C. E. *J. Am. Chem. Soc.* **1984**, *106*, 805. Idem, preceding communication.

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4. Butler, G. B.; Herring, K. H.; Lewis, P. L.; Sharpe, V. V., III; Veazey, R. L. *J. Org. Chem.* **1977**, *42*, 679. Albert, R. M.; Butler, G. B. *Ibid.* **1977**, *42*, 674.

5. The isolation of **2** was accompanied by the formation and isolation of furan **3**.

(Received in USA 11 September 1984)