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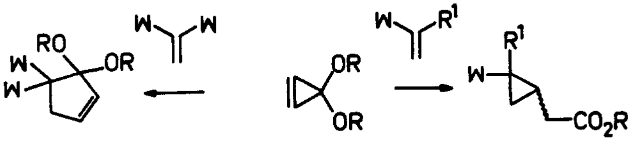
Effective, Thermal One-Carbon + Two-Carbon Cycloaddition of Cyclopropenone Ketals with Electron-Deficient Olefins: Cyclopropane Formation.

Dale L. Boger*[1a] and Christine E. Brotherton[1b]

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

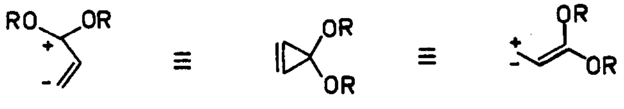
Summary: Treatment of olefins bearing one electron-withdrawing substituent with cyclopropenone ketals under mild, thermal conditions provide cyclopropane products.

Recently, we disclosed the results of a study of the thermal reaction of cyclopropenone ketals with electron-deficient olefins bearing two electron-withdrawing substituents, a reaction which provides cyclopentenone ketal products,[2] equation 1. The preliminary studies suggested that the reaction: formally a three-carbon + two-carbon cycloaddition of the 1,3-dipole **I**; proceeds by nucleophilic attack of the strained cyclopropenone ketal onto the electron-deficient olefin, rearrangement of the cyclopropyl carbocation to the allyl cation, and collapse of the resulting dipole to the observed products, scheme I. Herein, a preliminary study of the thermal reaction of cyclopropenone ketals with simple electron-deficient olefins, those bearing one electron-withdrawing substituent, is detailed and further implicates the intermediacy of the dipole **ii** in the course of the reaction. The reaction, which provides cyclopropane products derived from **iii** exclusive of cyclopentenone ketal products **iv**,[2] formally constitutes a cycloaddition of the 1,1-dipole **II** with simple electron-deficient olefins.



(1)

W = electron-withdrawing substituent



I

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

II

Scheme I

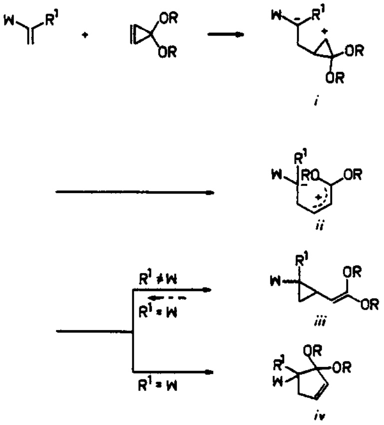
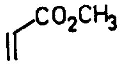
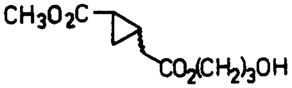
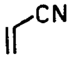
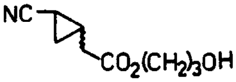
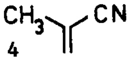
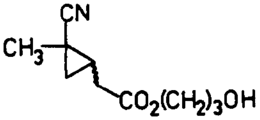
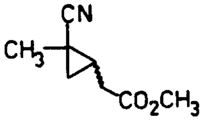
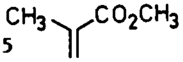
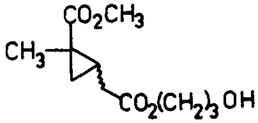


Table I details preliminary results of a study of the thermal reaction of two cyclopropenone ketals, **1a**[3a] or **1b**,[4] with representative, simple electron-deficient olefins **2** - **5**, each bearing one electron-withdrawing substituent. In each instance, thermal reaction (benzene, 70 - 80 °C, 16 - 20 h) of **1** with **2** - **5** provided products derived from the cyclopropane ketene acetal **iii** (**6** - **11**, 36 - 80%), exclusive of cyclopentenone ketal product **iv**. The cyclopropane ketene acetal products, which could be detected by ^{1}H NMR, were converted directly to the corresponding esters by chromatography on silica gel or brief aqueous acid treatment. Unexpectedly, the reaction provides predominantly the *cis*-substituted cyclopropane derivatives. Comparison of the major (*cis*, 85%) and minor (*trans*, 15%) adducts isolated (49% combined yield) from the reaction of 3,3-dimethoxycyclopropene (**1b**) with methyl acrylate (**2**) with authentic *cis* and *trans*-1-(methoxycarbonyl)-2-[(methoxycarbonyl)methyl]-cyclopropane[5] confirmed the structure and isomer assignments. The isomer ratios and assignments of the isolated cyclopropane products were readily determined and by ^{1}H NMR and *cis* stereoisomer was determined to be the major product in each entry in Table I.[6]

The clean partitioning of the reaction products: exclusive formation of products derived from **iii** if R^1 ≠ electron-withdrawing substituent or exclusive formation of the cyclopentenone ketal product[2] **iv** if R^1 = electron-withdrawing substituent; may be the result of kinetic ring closure (**ii** → **iii**, R^1 ≠ electron-withdrawing substituent) versus closure to the thermodynamically preferred product (**ii** → **iv**, R^1 = electron-withdrawing substituent). The relative stability of the dipole **ii** may account for the difference in the rate of closure and thus determine the observed products. However, the exclusive formation of **iii** *or* **iv**, with no detectable mixtures, further suggests that **iii** may be the primary product in both instances, and that under the reaction conditions the dipolar closure to cyclopropane is reversible (**iii** $\rightleftarrows$ **ii** → **iv**) if the cyclopropane is substituted with

Table I. Thermal Reaction of Cyclopropenone Ketals with Olefins Bearing One Electron-withdrawing Substituent.

Cyclopropenone Ketal	Substrate	Conditions[a] equiv 1, Temp °C(time h)	Product[b]	% Yield[c] ( )[d]
1a	2 	2, 80(20)		6, 69(>95:5)
1b	2	2, 80(16)		7, 49(5:1)[e]
1a	3 	2, 80(16)		8, 65(10:1)
1a	4 	2, 80(16)		9, 80(9:1)
1b	4	2, 75(16)		10, 63(5:1)
1a	5 	2, 80(16)		11, 36(1:1)

(a) Each reaction was run in benzene (0.8-1.0 M in substrate) under nitrogen and the crude reaction mixture was exposed to 9:1 tetrahydrofuran:water containing acetic acid (10-12 uL/mmole, 25 °C, 20-30 min). (b) All products exhibited the expected ^{1}H NMR, IR and mass spectral consistent with the assigned structure. (c) All yields are based on purified product isolated by chromatography (SiO_2). (d) Ratio of cis:trans isomer determined by ^{1}H NMR. (e) Cis and trans-7 displayed the identical properties as reported for authentic materials, see reference 5.

two, geminal electron-withdrawing substituents.

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References and Notes

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

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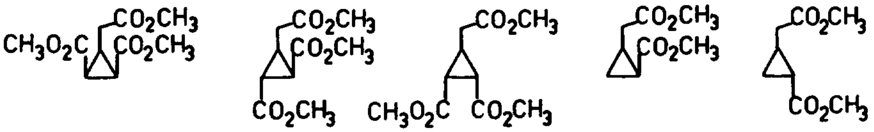
6. The *cis:trans* isomer ratios of the cyclopropane products were determined by ^1H NMR integration of the $C\underline{H}_2CO_2R$ signal. The presence of a vicinal electron-withdrawing substituent *cis* to this methylene produces an *ca.* 0.2 ppm downfield shift in this signal. This characteristic shift was used to distinguish the *cis* isomers.



$-C\underline{H}_2CO_2CH_3$ (ppm)	2.84	2.65	2.40	2.55	2.26

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