

## Intramolecular Photocycloaddition of Cyclopropenes. Ring Strain-Driven Hydrogen Transfer of 1,4-Biradical Intermediates

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**Abstract:** Intramolecular photocycloaddition of cyclopropene carboxylic acid allylic esters **1** results in an exclusive formation of 5-oxaspiro[2.4]hepta-4-ones **2**, the hydrogen transferred rearrangement products, with induction of three stereogenic centers. Ring strain is crucial to alter the course of reaction from the [2+2] photocycloaddition to the hydrogen transfer.  
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In [2 + 2] photocycloaddition of enones with alkenes, a stepwise mechanism involving a 1,4-biradical intermediate has been widely accepted.<sup>1</sup> Its existence was chemically proven by trapping with hydrogen selenide.<sup>2</sup> The resulting 1,4-biradical can rearrange using an adjacent cyclopropyl group,<sup>3</sup> a radical clock.<sup>4</sup> A carbene was generated if the resulting 1,4-biradical was conjugated with an alkynyl group.<sup>5</sup> These successful trapping experiments suggest that introduction of a process faster than the  $\sigma$ -bond formation between the two radical sites can change the course of reaction from a cycloaddition to a rearrangement. Hydrogen transferred rearrangement products,<sup>6</sup> sometimes reported as byproducts accompanying [2 + 2] adducts, can be considered as the result of such a process. Since quantitative arguments on how the course of [2 + 2] cycloaddition can be controlled leading to cycloaddition or hydrogen transferred rearrangement, have never been cited, establishment of a simple index for differentiating the course of cycloaddition is indeed worthwhile. This kind of control of the course of cycloaddition is not only interesting from mechanistic viewpoints but also useful for preparative organic photochemistry. In this paper, we report on our approach to this problem in the intramolecular photocycloaddition of cyclopropene carboxylic acid allylic esters.

An introduction of a cyclopropene ring as a double bond unit should result in large ring strain in an intramolecular [2+2] cycloadduct due to an involvement of the cyclopropane ring fusion. If an alkene possesses a hydrogen atom available for the hydrogen transfer rearrangement, the above-mentioned ring strain might become the driving force to alter the course of photochemical reaction. Based on this idea, we designed a photochemical reaction of cyclopropene carboxylic acid allylic esters **1**. Photochemical intramolecular [2+2] cycloaddition of cyclopropene derivatives was intensively studied by Padwa et al; however, their system lacked a hydrogen atom for the hydrogen transfer rearrangement to result in the formation of [2+2] cycloadducts.<sup>7</sup>

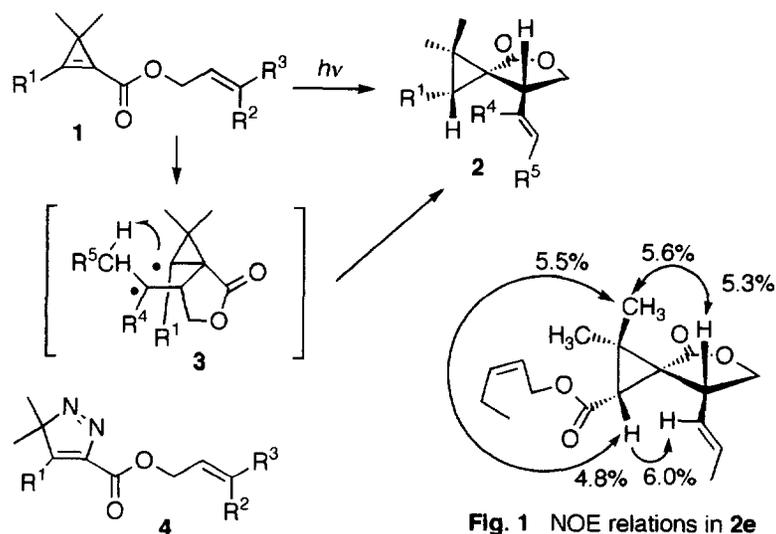


Fig. 1 NOE relations in **2e**

**Table 1** Isolated yields of the hydrogen transferred rearrangement products **2**

Compd.	$R^1$	$R^2$	$R^3$	Products	$R^4$	$R^5$	Irradiation time (min)	Yield <b>2</b> (%)	Recovery <b>1</b> (%)
<b>1a</b>	H	Me	Me	<b>2a</b>	Me	H	60	79	11
<b>1b</b>	Ph	Me	Me	<b>2b</b>	Me	H	60	73	10
<b>1c</b>		H	Me	<b>2c</b>	H	H	60	71	12
<b>1d</b>	$\text{Me}_2\text{C}=\text{CHCH}_2\text{OCO}-$	Me	Me	<b>2d</b>	Me	H	90	90	5
<b>1e</b>		Et	H	<b>2e</b>	H	Me	20	81	10

Alkenes **1** were synthesized by the photochemical denitrogenation of 3H-pyrazole derivatives **4** prepared from the corresponding acetylene carboxylic acid esters and 2-diazopropane. Photochemical reaction of **1** (0.8 - 1.0 mmol) was carried out in benzene (15 ml) under bubbling of argon irradiated with a 400W high pressure mercury lamp through a Pyrex glass filter. After evaporation of the solvent, the residue was chromatographed on a silica gel column to result in the formation of the rearrangement product **2** as a single product with three stereogenic centers for **2c-e**.<sup>8</sup> No reaction occurred when alkenes **1** were irradiated with 366 nm light wavelength (with combination of filters: 340 nm <  $\lambda$  < 380 nm). However, the reaction proceeded in the presence of a triplet sensitizer (benzophenone or thioxanthone) with 366 nm irradiation to result in a quantitative formation of **2**. Its stereochemistry was deduced from the NOE difference spectrum. Figure 1 shows the typical NOE relations observed for **2e** as a representative example. Irradiation of one of

the methyls of *gem*-dimethyl groups caused enhancement of the methine proton of the cyclopropane ring and the methine proton of the  $\gamma$ -lactone ring. The other methyl protons did not show these NOE enhancements. Furthermore, a NOE relation was observed between the cyclopropane methine proton and the vinyl proton. It was found that the formation of **2** could be accomplished in one-pot directly from **4** without isolation of **1**. The formation of hydrogen transferred product **2** can be best explained by the intermediacy of a 1,4-biradical intermediate **3** which has an option either to cyclize or hydrogen transfer.

It is reported that the formation of hydrogen transferred products is the result of photochemical rearrangement of the initially formed [2+2] cycloadducts.<sup>6c</sup> In our case, we could not detect the formation of the corresponding [2+2] cycloadducts. If the 1,4-biradical intermediate is considered as the common intermediate for both the cycloadduct and the hydrogen transferred product,<sup>5a,b</sup> the efficiency of the path there from governs the course of the reaction, i.e., either the [2+2] cycloaddition or the hydrogen transferred rearrangement. This efficiency should depend largely on the stability of the products. The AM1 calculations<sup>9</sup> on the heat of formation ( $\Delta H_f$ ) showed that **2a** and **2b** are 20.7 and 20.3 kcal/mol more stable than the corresponding [2+2] cycloadducts, respectively. The ring strain might alter the course of reaction. Thus,  $\Delta\Delta H_f$  (the difference in the heats of formation between the [2+2] cycloadduct and the hydrogen transferred product) might be a convenient index to predict the course of reaction from the 1,4-biradical intermediate.

We are currently comparing the reported results on the hydrogen transferred rearrangement with their calculated  $\Delta\Delta H_f$  to generalized this idea.

## References and Notes

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8. Spectroscopic data of the hydrogen transferred rearrangement products **2c** - **2e**.  
**2c**: colorless oil; IR (NaCl) 2970, 1766, 1737, 1372, 1215, 1170, 1075  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  5.84 (dt,  $J = 17.0, 9.7$  Hz, 1H), 5.77 (dtq,  $J = 15.3, 6.4, 1.1$  Hz, 1H), 5.58 (dtq,  $J = 15.3, 6.4, 1.1$  Hz, 1H), 5.20 (dd,  $J = 9.7, 1.0$  Hz, 1H), 5.14 (d,  $J = 17.0$  Hz, 1H), 4.57 (ddt,  $J = 12.4, 6.4, 1.1$  Hz, 1H), 4.47 (m, 2H), 4.13 (dd,  $J = 9.4, 4.3$  Hz, 1H), 3.04 (ddd,  $J = 9.7, 8.0, 4.3$  Hz, 1H), 1.91 (s, 1H), 1.71 (ddd,  $J = 6.4, 2.5, 1.1$  Hz, 3H), 1.49 (s, 3H), 1.23 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 22.4 MHz)  $\delta$  174.12 (s), 167.11(s), 137.23 (d), 130.98 (d), 125.22 (d), 118.18 (t), 70.05 (t), 65.61 (t), 42.16 (d), 36.93 (d), 36.62 (s), 30.71 (s), 23.47 (q), 17.74 (q), 16.14 (q); HRMS (EI) calcd for  $\text{C}_{15}\text{H}_{20}\text{O}_4$  ( $\text{M}^+$ ) 264.1360, found 264.1362.  
**2d**: colorless oil; IR (NaCl) 2968, 2920, 1766, 1738, 1384, 1218, 1170, 1078  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  5.33 (tm,  $J = 7.0$  Hz, 1H), 4.85 (t,  $J = 1.4$  Hz, 1H), 4.76 (br. s, 1H), 4.66 (dd,  $J = 12.0, 7.0$  Hz, 1H), 4.57 (dd,  $J = 12.0, 7.0$  Hz, 1H), 4.42 (dd,  $J = 9.8, 8.3$  Hz, 1H), 4.27 (dd,  $J = 9.8, 2.0$  Hz, 1H), 3.03 (dd,  $J = 8.3, 2.0$  Hz, 1H), 1.86 (s, 3H), 1.78 (s, 1H), 1.74 (s, 3H), 1.69 (s, 3H), 1.51 (s, 3H), 1.23 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 22.4 MHz)  $\delta$  174.47 (s), 167.25 (s), 144.46 (s), 138.58 (s), 118.41 (t), 114.44 (d), 68.97 (t), 61.67 (t), 45.52 (d), 36.78 (s), 36.16 (s), 31.17 (d), 25.57 (q), 23.66 (q), 17.93 (q), 17.00 (q), 16.14 (q); HRMS (FAB) calcd for  $\text{C}_{17}\text{H}_{25}\text{O}_4$  ( $\text{MH}^+$ ) 293.1753, found 293.1748.  
**2e**: colorless oil; IR (NaCl) 3024, 2968, 2938, 2872, 1762, 1733, 1461, 1418, 1375, 1258, 1217, 1169  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  5.67-5.41 (m, 4H), 4.70 (dd,  $J = 12.8, 6.7$  Hz, 1H), 4.61 (dd,  $J = 12.8, 6.7$  Hz, 1H), 4.44 (dd,  $J = 9.0, 8.9$  Hz, 1H), 4.07 (dd,  $J = 8.9, 4.8$  Hz, 1H), 3.02 (ddd,  $J = 9.0, 8.9, 4.8$  Hz, 1H), 2.12 (quintet,  $J = 7.1$  Hz, 2H), 1.82 (s, 1H), 1.71 (dd,  $J = 6.4, 1.6$  Hz, 3H), 1.48 (s, 3H), 1.20 (s, 3H), 0.99 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 22.4 MHz)  $\delta$  174.35 (s), 167.31 (s), 136.64 (d), 129.99 (d), 129.39 (d), 122.76 (d), 70.47 (t), 60.65 (t), 41.08 (d), 36.75 (s), 36.54 (s), 31.52 (s), 23.18 (q), 20.82 (t), 17.75 (q), 16.11 (q), 14.02 (q); HRMS (FAB) calcd for  $\text{C}_{17}\text{H}_{25}\text{O}_4$  ( $\text{MH}^+$ ) 293.1753, found 293.1759.
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