

## STEREOCONTROLLED PHOTOCHEMICAL [2 + 2] CYCLOADDITION

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*Summary:* Dimethyldicinnamyl- and diphenyldicinnamylsiloxane were synthesized from cinnamyl alcohol and dimethyl- and diphenyldichlorosilane, respectively. After photolysis, one cyclobutane product, the all trans isomer, was observed in nearly quantitative yield. Photolysis of cinnamyl alcohol under the same conditions results in very little cyclobutane formation.

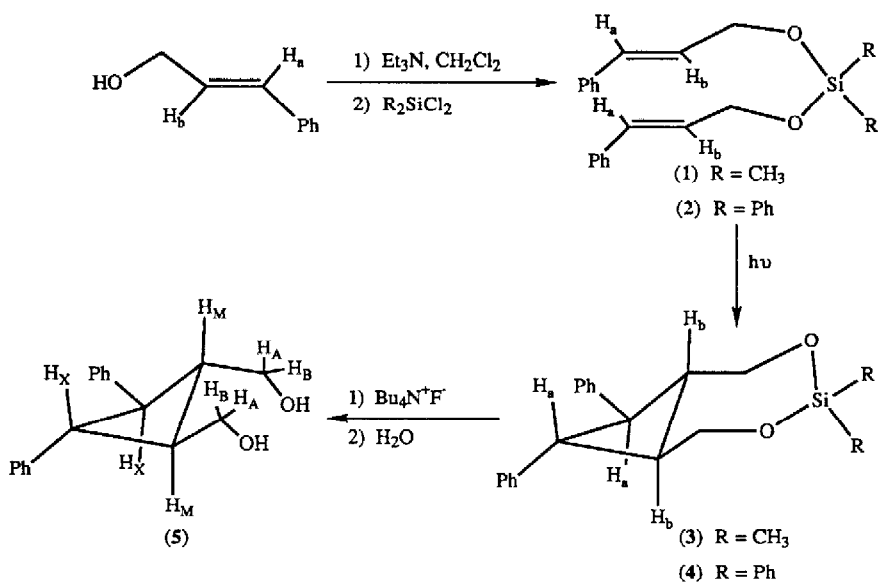
The [2 + 2] photocycloaddition is a powerful carbon-carbon bond forming reaction. It is probably the most synthetically useful photochemical reaction. Recently, much attention has been focused on intramolecular [2 + 2] reactions, where selective coordination of different alkenes to a template or covalent bonding to a tether is used to preorganize reactant alkenes. This methodology provides a means for controlling the regio- and stereochemistry of the reaction, as well as eliminating competing reactions, such as cis/trans isomerization. Included in these studies have been copper catalyzed reactions,<sup>1</sup> Lewis acid catalysis,<sup>2,3</sup> and cycloaddition of alkenes coupled to a polymer backbone<sup>4</sup> or hydrocarbon chain.<sup>5</sup>

The use of silicon as a tether for various intramolecular reactions has been explored, including radical cyclization reactions<sup>6</sup> and [4 + 2] reactions.<sup>7</sup> Some studies have focused on alkyl silanes,<sup>8</sup> where the silicon is tethered to the reacting molecules by way of a silicon-carbon bond. One limitation to this approach is the difficulty of desilylation after reaction. A more synthetically useful and versatile approach utilizes siloxanes.<sup>6</sup> Here, the reacting molecules are attached to silicon via a silicon-oxygen bond, which is easily cleaved after reaction.

We now report our results from the use of siloxanes as tethers in photochemical [2 + 2] reactions. The silaketals were prepared from the commercially available dialkyldichlorosilane and various alcohols or enolates. Because of the wealth of information available on the photochemistry of cinnamic acid and related compounds, we chose to initiate our studies with cinnamyl alcohol.<sup>9</sup> When irradiated in solution,<sup>10</sup> cinnamyl alcohol gives a 1:2 ratio of the cis and trans isomers, respectively, as well as a minor amount (2-3%) of cyclobutane products. Undoubtedly for this reason, the dimer of cinnamyl alcohol has not been reported previously.

The dicinnamyl siloxane (**1**) was easily prepared by adding dimethyldichlorosilane to a solution containing 2 equivalents of cinnamyl alcohol and triethylamine in methylene chloride at room temperature. The mixture was allowed to stir for two hours, after which it was concentrated, washed with pentane and filtered. After chromatography, **1** was isolated in 60% yield.<sup>11</sup> The corresponding dicinnamyl siloxane (**2**) made from diphenyldichlorosilane was prepared in the same fashion, in 57% isolated yield. These compounds were fully characterized.<sup>12</sup>

When **1** or **2** was irradiated,<sup>13</sup> the cyclobutane dimers (**3** and **4**, respectively) were formed in nearly quantitative yields. It is noteworthy that only one stereoisomer, the all trans isomer, was formed. Coincidentally, energy calculations indicate that this is the most stable isomer.<sup>14</sup> The tethered dimers (**3,4**) were identified by NMR (<sup>1</sup>H and <sup>13</sup>C).<sup>15</sup> Desilylation of **3** or **4** with standard conditions gave diol (**5**), which was characterized by NMR (<sup>1</sup>H and <sup>13</sup>C) and mass spectrometry.<sup>16</sup> Overall yields were ca. 95%, based on HPLC analysis.<sup>17</sup>



In conclusion, we have demonstrated that the [2 + 2] photochemical cycloaddition can be accelerated and controlled by the use of a silicon tether. We are investigating the synthesis of previously inaccessible cyclobutane compounds using this methodology. We are also exploring

other tethered photochemical cycloadditions.

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9. Attempts to accelerate this [2 + 2] photocycloaddition reaction using titanium as both a Lewis acid catalyst and a tether gave very low conversions. With cinnamic acid, we observed the formation of two cyclobutane products ( $\beta$ - and  $\delta$ -truxinic acid) in 5% yield. With cinnamyl alcohol, we observed no dimerization. Further experimentation indicated that titanium(IV) is an effective quencher of the excited state for these complexes.
10. A 0.01M solution in CH<sub>3</sub>CN was irradiated with a Hanovia 450 W mercury medium pressure lamp through quartz for 2 hours. The test tube was approximately 1 inch from the lamp.
11. Column chromatography was performed on SiO<sub>2</sub> with EtOAc/C<sub>5</sub>H<sub>12</sub> (95:5) elution.
12. The spectral data for **1** were: <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>)  $\delta$  7.2-7.4 (m, 10, arom.), 6.62 (bd, J = 16 Hz, 2, H<sub>a</sub>), 6.33 (dt, J = 16 Hz, J = 6.7 Hz, 2, H<sub>b</sub>), 4.44 (d, J = 6.7 Hz, 4, CH<sub>2</sub>), 0.26 (s, 6, CH<sub>3</sub>); <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>)  $\delta$  136.98, 130.51, 128.62, 128.33, 127.58, 126.55, 63.21, -3.21; IR: 3025, 1258 (Si-CH<sub>3</sub>), 1114, 1055 (Si-O-C), 965 cm<sup>-1</sup>; UV (CH<sub>2</sub>Cl<sub>2</sub>)  $\lambda_{\max}$  236 nm ( $\epsilon$  38,138); *Anal.* Calcd. for C<sub>20</sub>H<sub>24</sub>O<sub>2</sub>Si: C, 74.03; H, 7.46. Found: C, 74.05; H, 7.67.

The spectral data for **2** were:  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  7.73 (d, 4, arom.), 7.1-7.5 (m, 16, arom.), 6.62 (bd,  $J = 16$  Hz, 2,  $\text{H}_a$ ), 6.33 (dt,  $J = 16$  Hz,  $J = 6.8$  Hz, 2,  $\text{H}_b$ ), 4.52 (d,  $J = 6.8$  Hz, 4,  $\text{CH}_2$ );  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  138.86, 134.94, 132.48, 130.44, 128.48, 128.02, 127.93, 127.43, 126.44, 63.94; IR: 3024, 1429 (Si-Ph), 1116, 1054 (Si-O-C), 965, 735, 719, 700  $\text{cm}^{-1}$ ; UV ( $\text{CH}_2\text{Cl}_2$ )  $\lambda_{\text{max}}$  254 nm ( $\epsilon$  43,007); *Anal.* Calcd. for  $\text{C}_{30}\text{H}_{28}\text{O}_2\text{Si}$ : C, 80.32; H, 6.29. Found: C, 80.32; H, 6.38.

13. See ref. 10. Solvents were deoxygenated by bubbling nitrogen through the solution before photolysis. When oxygen was bubbled through the solution, there was no change in photoproducts or conversions. This implies that dimerization proceeds through the singlet excited state.
14. The calculations were performed using MM2 on all possible cyclobutane isomers. The all trans isomer was calculated to have a conformational energy of 57.33 kcal/mol. The other isomers ranged from 61.02 to 72.11 kcal/mol. Thermodynamic stability is not expected to control photoproduct formation.
15. The spectral data for **3** were:  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  6.9-7.4 (m, 10, arom.), 4.15 (m, 4,  $\text{CH}_2$ ), 3.82 (d,  $J = 6$  Hz, 2,  $\text{H}_a$ ), 3.2 (m, 2,  $\text{H}_b$ ), 0.12-0.35 (m, 6,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  139.53, 127.70, 127.52, 125.57, 62.84, 43.39, 41.13, -3.63. Cyclobutane NMR assignments were verified by COSY.  
  
The spectral data for **4** were:  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  7.6-7.8 (m, 4, arom.), 6.8 - 7.5 (m, 16, arom.), 4.25 (m, 4,  $\text{CH}_2$ ), 3.78 (d,  $J = 5.9$  Hz, 2,  $\text{H}_a$ ), 3.3 (m, 2,  $\text{H}_b$ );  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  139.80, 134.83, 134.65, 130.58, 128.49, 128.0, 127.76, 125.80, 63.98, 43.52, 41.53.
16. The spectral data for **5** were:  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  6.9-7.35 (m, 10, arom.), 4.05 (dd, ABMX system,  $J_{\text{AB}} = 11.26$  Hz,  $J_{\text{AM}} = 9.50$  Hz, 2,  $\text{H}_A$ ), 3.87 (dd,  $J_{\text{AB}} = 11.26$  Hz,  $J_{\text{BM}} = 4.03$  Hz, 2,  $\text{H}_B$ ), 3.60 (d,  $J_{\text{MX}} = 4.30$  Hz, 2,  $\text{H}_X$ ), 3.20 (m,  $J_{\text{AM}} = 9.5$  Hz,  $J_{\text{BM}} = 4.03$  Hz,  $J_{\text{MX}} = 4.30$  Hz, 2,  $\text{H}_M$ ), 2.95 (bs, 2, OH); NMR assignments were verified with COSY and  $\text{D}_2\text{O}$  exchange experiments. The ABMX system was identified and confirmed with the Gemini 6.3C Spin Simulation program.  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  128.76, 128.14, 127.98, 126.04, 62.61, 44.06, 40.28; MS, 20 eV,  $m/z$  268 (M+), 134 (M/2), 133 ( $m/2 - \text{H}$ ).  $^1\text{H}$  NMR assignment was consistent with data for the corresponding cinnamic acid dimer. See a) Montaudo, G.; Caccamese, S. *J. Org. Chem.* **1973**, *38*, 710; b) Montaudo, G.; Caccamese, S.; Librando, V. *Org. Mag. Res.* **1974**, *8*, 534. For cyclobutane NMR assignments see also: Bovey, Frank A. *Nuclear Magnetic Resonance Spectroscopy*, Academic Press, New York: 1988; p. 200.
17. Reverse phase C18 HPLC with  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$  (38:62) elution. Retention time = 14.43 minutes.  $\alpha$ -Chloro-4-nitrotoluene was used as an internal standard.

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