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Possible Mechanism for the Stereoselective Double Michael Reaction Catalyzed by Trityl Perchlorate

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The trityl perchlorate catalyzed double Michael reaction forming six-membered ring compounds from  $\alpha$ , $\beta$ -unsaturated ketones and siloxydienes was shown to take place via a two step process.

The Diels-Alder reaction is one of the most useful synthetic methods in organic chemistry due to its easy access to a variety of six-membered ring compounds, and versatile efforts have been made to develop a new combination of dienes and dienophiles.<sup>1)</sup> On the other hand, the similar reaction forming six membered ring systems from cross conjugated dienolates and  $\alpha,\beta$ -unsaturated carbonyl compounds is distinguished from the normal Diels-Alder reaction because the former reaction usually proceeds under milder reaction conditions. It also provides a useful synthetic tool because of its high regio- and stereo-selectivities,<sup>2)</sup> however, the reaction mechanism is still unclear whether it proceeds via a two step process or a concerted one.<sup>3)</sup>

In the previous paper,<sup>4)</sup> we have shown that, in the presence of a catalytic amount of trityl perchlorate,  $\alpha,\beta$ -unsaturated ketones smoothly react with siloxydienes at a low temperature to afford six-membered ring systems stereoselectively in good yields. Although the regio- and stereoselectivities of the above reaction are the same as those of the Diels-Alder reaction, we assumed the stepwise double Michael reaction at that stage from accumulated experimental data.<sup>5)</sup> Now we wish to report here an unambiguous evidence for a two step process.

At first, the reaction of enone  $1-E^{6}$  with 2-t-butyldimethylsiloxy-4-phenyl-1,3-butadiene (2) was carried out in the presence of a catalytic amount of trityl perchlorate (5 mol %) at -78 °C in dichloromethane. The reaction smoothly proceeded to afford the diastereomeric cycloaddition products 3 and 4, separated by flash column chromatography on silica gel, in 33 and 50% yields respectively. On the other hand, the reaction of enone  $1-Z^{6}$  with 2 under identical conditions as above gave only cycloaddition adduct 3 in 83% yield. No isomerization of the starting enones was observed under these reaction conditions. Final stereochemical assignment was made after derivation to the cyclohexanone derivatives  $5^{7}$  and  $6.^{8}$ As the relative stereochemistry of substituents in the dienophile is retained in the addition product formed via the concerted reaction, the above results strongly suggest a two step process.



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We postulate this stepwise double Michael reaction would proceed via the intermediate  $\underline{7}$  shown below. The siloxydiene reacts with the enone  $\underline{1}-Z$  in the presence of a catalytic amount of trityl perchlorate to result in the initial formation of the intermediate silyl enol ether  $\underline{7}$ , whose conformation is kept to minimize the allylic strain. As bond rotation of C3-C4 is faster than ring closure, this intermediate is independent of the geometry of the starting enone. The geometry of  $\alpha,\beta$ -unsaturated ketone part of the intermediate  $\underline{7}$ , which is derived from the siloxydiene, is fixed as stable s-cis,<sup>9)</sup> and the second intra-molecular Michael reaction afforded the cyclohexanone derivative stereoselectively. The different diastereoselectivities between E-enone <u>1</u>-E and Z-enone <u>1</u>-Z are ascribed to the initial Michael reaction.<sup>10</sup>



Synthetic utility of this double Michael reaction is obvious by the result that the reaction of Z-enone 1-Z gave cyclohexanone derivatives with perfectly controlled four chiral centers. Further investigation leading to naturally occuring compounds by utilizing this reaction, is now in progress.

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- 8) <u>6</u>: mp 97 °C.  $[\alpha]_D^{33}$  -17.4° (c 1.35, CHCl<sub>3</sub>). IR (CH<sub>2</sub>Cl<sub>2</sub>) 1715, 1723 cm<sup>-1</sup>. <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) 1.37 (s, 3H), 1.41 (s, 3H), 1.66 (s, 3H), 2.17 (dd, 1H, J=6.5, 15.2 Hz), 2.41 (dddd, 1H, J=3.7, 5.4, 6.5, 9.0 Hz), 2.46 (dd, 1H, J=3.7, 13.7 Hz), 2.80 (dd, 1H, J=5.4, 15.2 Hz), 3.35 (t, 1H, J=13.7 Hz), 3.53 (dt, 1H, J=3.7, 13.7 Hz), 3.56 (t, 1H, J=3.7 Hz), 3.62 (dd, 1H, J=6.1, 8.3 Hz), 4.03 (dt, 1H, J=6.1, 9.0 Hz), 4.15 (dd, 1H, J=6.1, 8.3 Hz), 7.17-7.37 (m, 5H).
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