CHEMISTRY LETTERS, pp. 1777-1780, 1988.

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

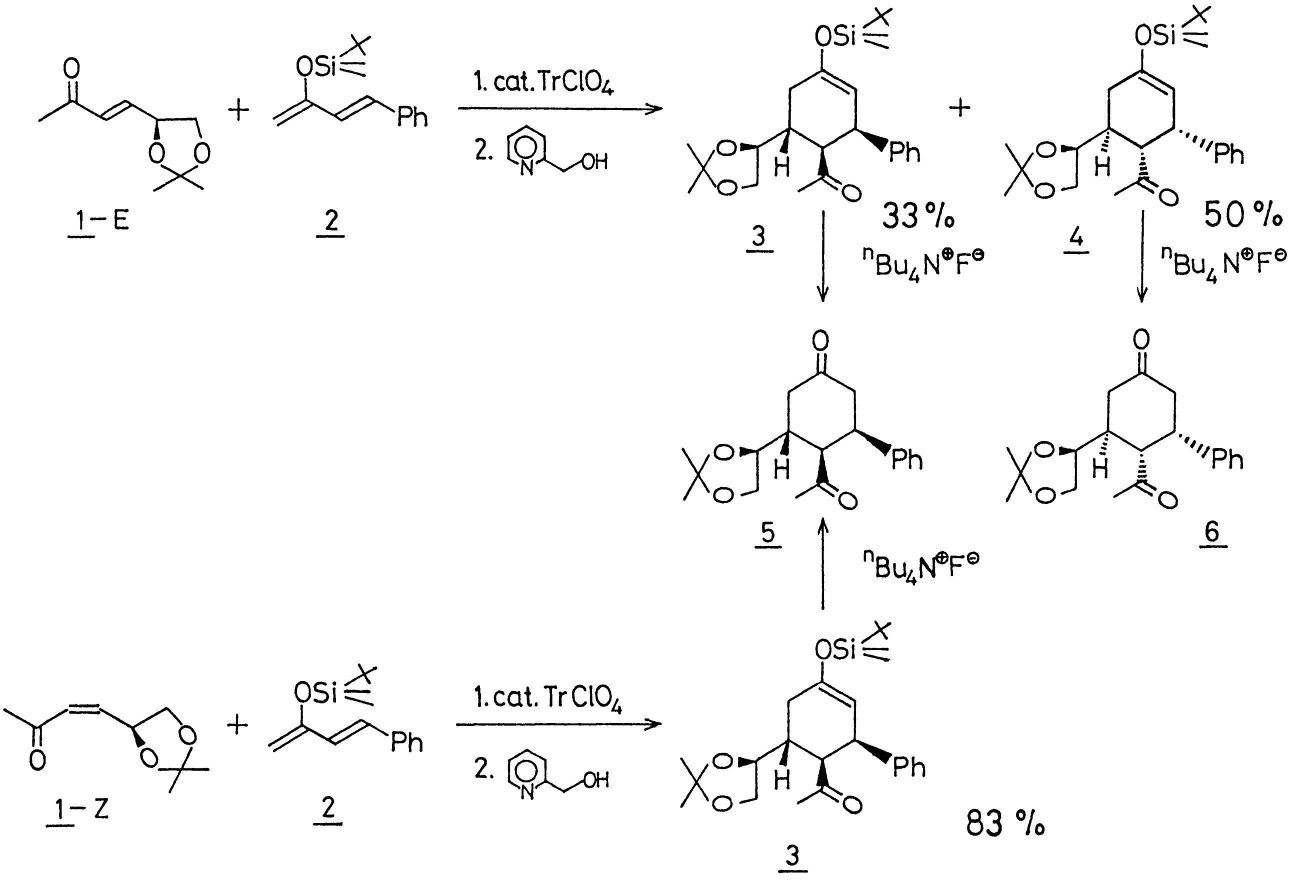
Shū KOBAYASHI, Yukihiro SAGAWA, Hiroshi AKAMATSU, and Teruaki MUKAIYAMA
Department of Applied Chemistry, Faculty of Science,
Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162

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

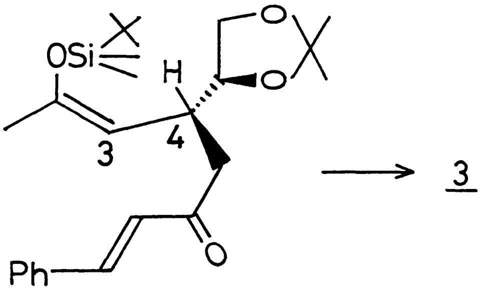
The Diels-Alder reaction is one of the most useful synthetic methods in organic chemistry due to its easy access to a variety of six-membered ring compounds, and versatile efforts have been made to develop a new combination of dienes and dienophiles.[1)] On the other hand, the similar reaction forming six membered ring systems from cross conjugated dienolates and α,β-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 stereoselectivities,[2)] however, the reaction mechanism is still unclear whether it proceeds via a two step process or a concerted one.[3)]

In the previous paper,[4)] we have shown that, in the presence of a catalytic amount of trityl perchlorate, α,β-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.[5)] 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.



We postulate this stepwise double Michael reaction would proceed via the intermediate 7 shown below. The siloxydiene reacts with the enone 1-Z in the presence of a catalytic amount of trityl perchlorate to result in the initial formation of the intermediate silyl enol ether 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 α,β-unsaturated ketone part of the intermediate 7, which is derived from the siloxydiene, is fixed as stable s-cis,[9)] and the second intramolecular Michael reaction afforded the cyclohexanone derivative stereoselectively. The different diastereoselectivities between E-enone 1-E and Z-enone 1-Z are ascribed to the initial Michael reaction.[10)]



7

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.

References

1) W. Carruthers, "Some Modern Methods of Organic Synthesis," 3rd ed, Cambridge University Press, Cambridge (1986), p.184.

2) R. A. Lee, Tetrahedron Lett., 1973, 3333; R. M. Cory and D. M. T. Chan, ibid., 1975, 4441; K. B. White and W. Reusch, Tetrahedron, 34, 2439 (1978); R. M. Cory and R. M. Renneboog, J. Chem. Soc., Chem. Commun., 1980, 1018; R. V. C. Carr, R. V. Williams, and L. A. Paquette, J. Org. Chem., 48, 4976 (1983); M. E. Jung and C. A. McCombs, Tetrahedron Lett., 1976, 2935; G. M.

Rubottom and D. S. Krueger, Tetrahedron Lett., 1977, 611; S. Danishefsky, M. P. Prisbylla, and S. Hiner, J. Am. Chem. Soc., 100, 2918 (1978); F. Richter and H-H. Otto, Tetrahedron Lett., 26, 4351 (1985).

3) G. A. Kraus and P. Gottschalk, J. Org. Chem., 49, 1153 (1984); H. Hagiwara, A. Okano, and H. Uda, J. Chem. Soc., Chem. Commun., 1985, 1047.

4) T. Mukaiyama, Y. Sagawa, and S. Kobayashi, Chem. Lett., 1986,1821.

5) cf. S. Kobayashi, M. Murakami, and T. Mukaiyama, Chem. Lett., 1985, 953; T. Mukaiyama, M. Tamura, and S. Kobayashi, ibid., 1986, 1017; 1817; S. Kobayashi and T. Mukaiyama, ibid., 1986, 221; 1805.

6) I. I. Cubero, M. D. P. Olea, and D. G. Poza, Carbohydr. Res., 138, 135 (1985).

7) 5: $[\alpha]_D^{33}$ +20.9° (c 0.89, $CHCl_3$). IR (KBr) 1715, 1723 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) 1.33 (s, 3H), 1.42 (s, 3H), 1.77 (s, 3H), 2.49 (dddd, 1H, J=3.1, 4.9, 5.3, 7.0 Hz), 2.52 (dd, J=7.0, 14.9 Hz), 2.57 (dd, J=5.3, 15.7 Hz), 2.70 (dd, J=4.9, 14.9 Hz), 3.12 (dd, J=11.4, 15.7 Hz), 3.26 (t, J=5.3 Hz), 3.66 (dd, J= 6.8, 8.2 Hz), 3.71 (dt, J=5.3, 11.4 Hz), 4.05 (dd, J=6.8, 8.2 Hz), 4.19 (dt, J=3.1, 6.8 Hz), 7.10-7.35 (m, 5H).

8) 6: mp 97 °C. $[\alpha]_D^{33}$ -17.4° (c 1.35, $CHCl_3$). IR (CH_2Cl_2) 1715, 1723 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) 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).

9) A. Bienvenue, J. Am. Chem. Soc., 95, 7345 (1973); P. Baas and H. Cerfontain, Tetrahedron, 33, 1509 (1977); N. Thoai and T. M. Chau, Can. J. Chem., 52, 1331 (1974).

10) B. M. Trost, J. Lynch, and P. Renaut, Tetrahedron Lett., 26, 6313 (1985); B. M. Trost and S. M. Mignani, ibid., 27, 4137 (1986); B. M. Trost, S. M. Mignani, and T. N. Nanninga, J. Am. Chem. Soc., 110, 1602 (1988); Y. Yamamoto, S. Nishii, and T. Ibuka, J. Chem. Soc., Chem. Commun., 1987, 464.

(Received July 27, 1988)