The Catalytic Diels-Alder Reaction Using Combined Catalyst System of Diphenyltin Sulfide or Lawesson's Reagent and Silver Perchlorate

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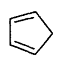
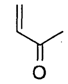
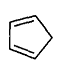
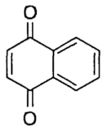
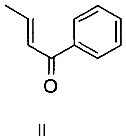
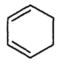
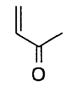
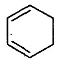
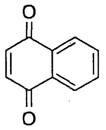
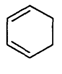
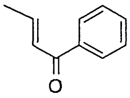
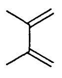
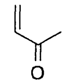
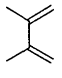
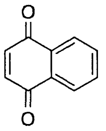
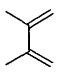
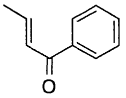
Catalytic Diels-Alder reactions between several 1,3-dienes and α,β-unsaturated ketones are effectively promoted by the combined use of diphenyltin sulfide ($Ph_2Sn=S$) and silver perchlorate or Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide) and silver perchlorate under mild conditions.

The Diels-Alder reaction is one of the most fundamental and useful reactions in synthetic organic chemistry and is widely used for the synthesis of six-membered ring compounds via representative [4+2] cycloaddition in which a conjugated diene component undergoes a stereospecific addition reaction with dienophiles.[1] In most cases, the Diels-Alder reactions proceed at relatively high temperature without using any catalysts. There is obvious limitation in carrying out the Diels-Alder reaction at high temperature since synthetic intermediates in the multi-step synthesis of complex molecules are often heat sensitive. On the other hand, Yates and Eaton, as well as Fray and Robinson, reported that Lewis acid catalysts such as $AlCl_3$, $BF_3{\cdot}OEt_2$, $SnCl_4$, etc. efficiently accelerate certain Diels-Alder reactions.[2] Though the above reactions generally take place at room temperature and give satisfactory yields, acid catalysts sometimes induce the polymerization of dienes. Moreover, in the case of carbonylcontaining dienophiles, 2 molar amounts of Lewis acids are needed for the completion of the reaction since at least 1 molar amount of the catalyst is tied up owing to 1 : 1 complex formation between the Lewis acid and the carbonyl oxygen atom. Requirement of larger amount of Lewis acid induce side reactions such as isomerizations and rearrangements when substrates having acid sensitive functionalities are employed. Therefore, exploration of a new catalyst system to promote the Diels-Alder reaction under mild conditions at a low temperature is demanded in order to expand the scope and applications of this reaction.

Recently, an efficient method for the stereoselective synthesis of β-D-ribofuranosides from 2,3,5-tri-O-benzyl-1-O-iodoacetyl-D-ribofuranose or 2,3,5-tri-O-benzyl-D-ribofuranose and trimethylsilylated alcohols or free alcohols was reported by using the combined catalyst system of [$Ph_2Sn=S$/silver salt] or [Lawesson's reagent/silver salt].[3] The above system was successfully applied to the synthesis of β-ribonucleosides from methyl ribofuranosyl carbonate and trimethylsilylated nucleoside bases and also to the catalytic aldol reactions between aldehydes and trimethylsilyl enol ethers or silyl ketene acetals under mild conditions affording the corresponding aldols in high yields.[4] Now, we would like to describe the effective catalytic Diels-Alder reactions between 1,3-dienes and α,β-unsaturated ketones using the above catalyst systems.

In the first place, solutions of cyclopentadiene in dichloromethane and methylvinylketone in dichloromethane were successively added to a suspension of 3 mol% of $Ph_2Sn=S$ and 1 mol% of $AgClO_4$ in dichloromethane at -78 °C, and the corresponding adduct (Endo / Exo = 98 / 2) was obtained in 69% yield after 3h. Next, the order of addition was examined. When a mixture of cyclopentadiene and methylvinylketone was added to the catalyst system, the corresponding adduct was produced in

Table 1. Catalytic Diels-Alder Reaction in CH_2Cl_2 [a]

Entry	Diene	Dienophile	Condition[b]	Time / h	Yield / %
1			A	0.17	92[d]
2			B	0.17	76[d]
3			A	2	91[e]
4			B	2	92[e]
5			C	18	90[d]
6			D	18	87[d]
7			C	6	95[e]
8			D	6	77[e]
9			C	0.5	90[e]
10			F	1	79[e]
11			E	48	83[e]
12			F	24	80[e]
13[c]			C	6	90
14			D	6	78
15			E	0.5	90
16			F	0.5	75
17[c]			E	24	57
18[c]			F	24	72

[a] 1.1 molar amount of dienes was used.
[b] A: 4 mol% of [3 $Ph_2Sn=S$ / $AgClO_4$] was used at -78 °C.,
B: 4 mol% of [0.5 L. R. / $AgClO_4$] was used at -78 °C.,
C: 10 mol% of [3 $Ph_2Sn=S$ + $AgClO_4$] was used at -78 °C.,
D: 10 mol% of [0.5 L. R. + $AgClO_4$] was used at -78 °C.,
E: 10 mol% of [3 $Ph_2Sn=S$ + $AgClO_4$] was used at 0 °C.,
F: 10 mol% of [0.5 L. R. + $AgClO_4$] was used at 0 °C.,
L. R. = Lawesson's reagent.
[c] 3 molar amount of diene was used.
[d] Endo / Exo = 99 / 1. [e] Endo / Exo = >99 / 1.

almost the same yield with that of the former reaction. However, the yield apparently decreased when methylvinylketone and cyclopentadiene were added to a suspension of catalyst system in this order (41%). Based on these results, subsequent experiments were carried out by adding cyclopentadiene and methylvinylketone successively to the catalyst systems.

Secondly, the reaction conditions such as temperature and time were examined in detail. When the reaction of cyclopentadiene with methylvinylketone was carried out at temperatures ranging from -78 °C to -23 °C for 3 h, the desired adduct was afforded in almost the same yields (70-80%). Further, the increase in yield was observed when the reaction time was shortened to 1 h, and the corresponding adduct (Endo / Exo = 99 / 1) was obtained in 92% yield by quenching the reaction after stirring for 10 min. These tendencies caused by reaction conditions such as temperature and time are somewhat dependent on the kind of substrates employed in the reactions (Table 1). It is noteworthy that the above reaction was efficiently catalyzed even at -78 °C in some cases while the previously reported Diels-Alder reactions between 1,3-dienes and α,β-unsaturated ketones by using typical Lewis acid catalysts such as $AlCl_3$, $BF_3 \cdot Et_2O$ and $SnCl_4$ were generally carried out at higher than room temperature.[5] For example, the Diels-Alder reaction between 3 molar of cyclopentadiene and 1 molar of chalcone using 20 mol% of $AlCl_3$ gave the desired adduct in 4% yield at -78 °C and in 15% yield at 0 °C, respectively. On the other hand, the same reaction was promoted by using 20 mol% of the present combined catalyst system at -78 °C to give the corresponding adduct in 64% yield.[6]

Though the detailed study on the structure of active species has not yet been made clear, it is assumed that active charged species stabilized by perchlorate anion is possibly generated in situ by the interaction between $AgClO_4$ and $Ph_2Sn{=}S$ because neither $AgClO_4$ nor $Ph_2Sn{=}S$ alone is effective in the present reaction.

When Lawesson's reagent was used in stead of $Ph_2Sn{=}S$ as a partner of $AgClO_4$ in the above experiments, the catalyst was generated from 1 molar amount of $AgClO_4$ and 0.5 molar amount of Lawesson's reagent because Lawesson's reagent exists as a dimeric structure. The reaction of cyclopentadiene and methylvinylketone was carried out by using 4 mol% of above combined catalyst system in dichloromethane at -78 °C and the corresponding adduct (Endo / Exo = 99 / 1) was obtained in 76% yield. When the catalyst generated from equimolar amounts of Lawesson's reagent and $AgClO_4$ was employed in the above reaction, the yield slightly decreased to 67%.

Several examples of the present Diels-Alder reactions show that the desired adducts were obtained in high yields by using the combined catalyst system of [$Ph_2Sn{=}S/AgClO_4$] or [Lawesson's reagent/$AgClO_4$] under mild conditions (see Table 1).

A typical experimental procedure is described for the reaction of cyclopentadiene with methylvinylketone; to a suspension of $AgClO_4$ (0.049 mmol) in dichloromethane (1.0 ml) was added a solution of $Ph_2Sn{=}S$ (0.148 mmol) in dichloromethane (1.0 ml) at -78 °C. After stirring for 20 min, solutions of cyclopentadiene (1.352 mmol) in dichloromethane (1.0 ml) and methylvinylketone (1.230 mmol) in dichloromethane (1.0 ml) were successively added. Then the reaction was quenched with phosphate buffer (pH=7) after stirring for 10 min. Usual work up and purification by TLC on silica gel afforded the Diels-Alder adduct in 92% yield.

It is noted that the Diels-Alder reactions between several 1,3-dienes and α,β-unsaturated ketones proceed smoothly in the presence of the combined catalyst system such as [$Ph_2Sn{=}S/AgClO_4$] or [Lawesson's reagent/$AgClO_4$] under mild conditions.

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References and Notes

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5 F. Fringuelli, F. Pizzo, A. Taticchi, and E. Wenkert, *J. Org. Chem.*, **48**, 2802 (1983).

[6] Though the Diels-Alder reaction between 3 molar of 2-trimethylsiloxy-1,3-butadiene and 1 molar of chalcone using 20 mol% of $AlCl_3$ gave the corresponding adduct in 69% yield at 0 °C, the reaction provided the adduct in 13% yield at -78 °C. This reaction was promoted by using 20 mol% of the catalyst generated from 1 molar amount of $AgClO_4$ and 0.5 molar amount of Lawesson's reagent to give the corresponding adduct in 41% yield at -78 °C.