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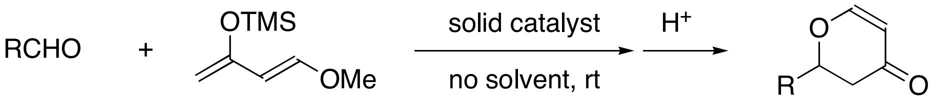
HETERO-DIELS–ALDER REACTION CATALYZED BY SELF-ORGANIZED POLYMERIC RARE EARTH COMPLEXES UNDER SOLVENT-FREE CONDITIONS

Shuichi Ishida,[a] Tetsuji Hayano,[a] Hiroshi Furuno,[b] and Junji Inanaga[b],*

[a]Department of Molecular Chemistry, Graduate School of Sciences, and
[b]Institute for Materials Chemistry and Engineering (IMCE), Kyushu University,
Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan;
inanaga@ms.ifoc.kyushu-u.ac.jp

Abstract – 2-Substituted 2,3-dihydropyran-4-one derivatives were conveniently synthesized under solvent-free conditions by Lewis acid-catalysis with a polymeric scandium sulfonate complex, which can be prepared in a self-organized manner in one step and successfully reused for the next round of reactions.

The hetero-Diels–Alder reaction is a useful reaction for synthesizing six-membered heterocyclic compounds in one step.[1] Thus, many examples of Lewis acid-promoted hetero-Diels–Alder reactions of heterodienes with dienophiles and those of dienes with heterodienophiles have been accumulated.[2] However, efficient heterogeneous catalysis of the hetero-Diels–Alder reaction under solvent-free conditions has never been realized, although the development of such methods is highly desired from the viewpoint of green-sustainable chemistry.[3] We report here the first successful example of a recyclable coordination polymer-catalyzed hetero-Diels–Alder reaction of aldehydes with the Danishefsky's diene under solvent-free conditions (Scheme 1).



Scheme 1. Heterogeneous catalysis of hetero-Diels–Alder reaction under solvent-free conditions

The development of efficient heterogeneous catalysts that can be easily prepared, recovered, and reused without losing their activities has currently received much attention from a practical as well as an

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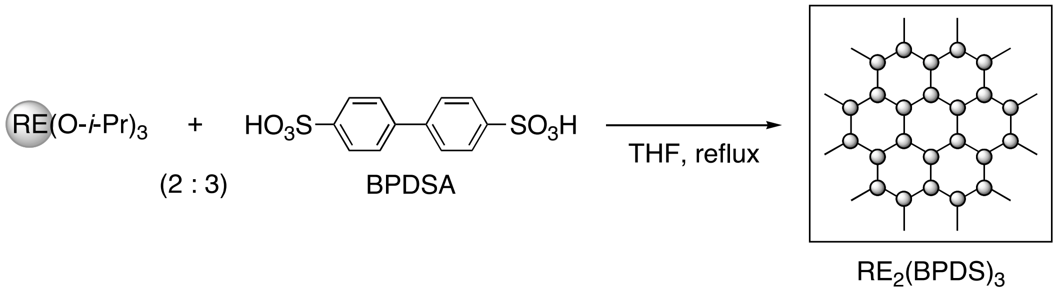
This paper is dedicated to the memory of the Emeritus Professor Kenji Koga of Tokyo University.

environmental point of view, and more than a few such reusable heterogeneous catalysts (e.g., supported on inorganic materials or insoluble polymers) have been reported.[4,5] In general, however, they tend to have lower catalytic activities and selectivities compared to the corresponding homogeneous ones, and their preparations are often tedious. To solve such problems, we tried to prepare porous coordination polymer-type rare earth complexes in one step *via* a self-organized process[6,7] and examined the catalytic abilities and reusabilites of them as a novel heterogeneous catalyst for the hetero-Diels–Alder reaction.



Scheme 2. Preparation of the coordinated polymer catalysts

Four rare earth (RE) metal ions (Sc, Yb, Y, and La) and a two-way spacer ligand (biphenyl-4,4'-disulfonic acid: BPDSA) were employed for the preparation of the catalysts as shown in Scheme 2. The catalytic activity of $RE_2(BPDS)_3$[8] thus obtained was examined in the hetero-Diels–Alder reaction of benzaldehyde with the Danishefsky's diene using 5 mol% of the catalyst at room temperature either in the presence or absence of solvents. The results are summarized in Table 1.

Table 1. Effect of metal ions and a solvent on the hetero-Diels–Alder reaction[a]

Entry	RE	Solvent	Yield (%)[b]	Entry	RE	Solvent	Yield (%)[b]
1	Sc	CH_2Cl_2	61	5	La	CH_2Cl_2	9
2	Sc	None	90	6	La	None	28
3	Y	CH_2Cl_2	18	7	Yb	CH_2Cl_2	14
4	Y	None	36	8	Yb	None	51

[a] The reaction of benzaldehyde with the Danishefsky's diene was carried out using 5 mol% of $RE_2(BPDS)_3$ at rt for 48 h. [b] Isolated yield.

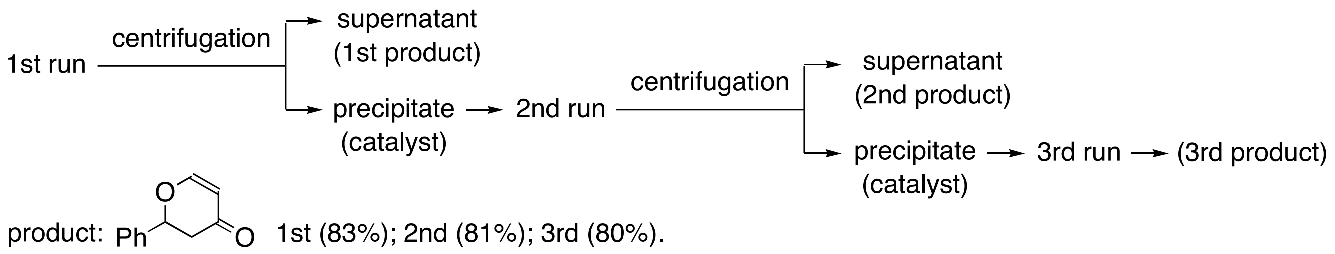
As a general trend, the metal complexes with smaller ionic radii afforded better results and performing the reaction in solvent-free conditions was found to be superior to performing the reaction in solution. Thus, the $Sc_2(BPDS)_3$ catalyzed reaction under solvent-free conditions gave the best result. Although strong Lewis acids tend to polymerize active dienes like the Danishefsky's diene, this side reaction was not observed in the above reaction. Under optimal conditions, various aromatic aldehydes were converted to the corresponding dihydropyranone derivatives in good yields regardless of the electron-donating or electron-withdrawing nature of the substituents as shown in Table 2.

Table 2. Application to various aldehydes[a]

Entry	R	Yield (%)[b]	Entry	R	Yield (%)[b]
1	4-F-C_6H_4	82	4	4-NO_2-C_6H_4	87
2	4-Cl-C_6H_4	82	5	4-Me-C_6H_4	81
3	4-Br-C_6H_4	85	6	4-MeO-C_6H_4	81

[a] The reactions were carried out using 5 mol% of $Sc_2(BPDS)_3$ at rt under solvent-free conditions (see Scheme 1). [b] Isolated yield.

Finally, recovery and reuse of the catalyst was investigated. As shown in Scheme 3, after completion of the reaction, the scandium catalyst was recovered by centrifugation and, after drying under a vacuum, it could be successfully used for the next round of reactions. Essentially neither deactivation of the catalyst nor leaching of the metal ion was observed even in the third round of reactions.



Scheme 3. Recovery and reuse of the catalyst

In summary, we have developed an efficient and environmentally benign method to obtain dihydropyranone derivatives. The coordined polymer catalyst prepared here is stable in the air, does not require any solvents, and can be reused several times without losing its catalytic activity.

EXPERIMENTAL

Preparation of $Sc_2(BPDS)_3$. To a refluxing solution of $\mathrm{Sc(O\text{-}}i\mathrm{\text{-}Pr)_3}$ (444 mg, 2 mmol) in THF (20 mL) was added slowly a solution of BPDSA (943 mg, 3 mmol) in THF (20 mL), and the resulting mixture was stirred for 18 h under the same conditions. After cooling, the resulting precipitates were filtered, washed with THF and dried at 200 ˚C for 24 h *in vacuo* to give the complex $Sc_2(BPDS)_3$ (911 mg, 83%) as a colorless amorphous solid. IR (KBr): 3399, 1599, 1388, 1279, 1161, 1112, 1048, 997, 818, 728, 610 cm^{-1}. Anal. Calcd for $C_{36}H_{24}O_{18}S_6Sc_2{\bullet}4H_2O$: C, 39.35; H, 2.94. Found: C, 39.48; H, 2.89.

Typical Hetero-Diels–Alder Reaction. To a reaction tube containing $Sc_2(BPDS)_3$ (5.1 mg, 0.01 mmol for Sc) were added benzaldehyde (21.2 mg, 0.2 mmol) and the Danishefsky's diene (51.7 mg, 0.3 mmol). The mixture were stirred for 48 h at rt, and then successively treated with three drops of trifluoroacetic acid and four drops of diisopropylamine. The resulting mixture was directly subjected to column chromatography on silica gel (hexane/AcOEt 9:1) to give 2,3-dihydro-2-phenylpyran-4-one (31.5 mg, 90%). CAS registry no. 40989-96-6.

Recovery and Reuse of the Catalyst. After the reaction, the reaction mixture was treated with Et_2O (3 mL) and subjected to centrifugation. The supernatant was collected and the precipitates were washed with Et_2O (three times, total 12 mL). The recovered catalyst was dried at rt *in vacuo* and used again for the next round of reactions.

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