The Polymer Effect on Catalysts. Aldimine-Selective Reactions in the Coexistence of Aldehydes Using a Polymer-Supported Scandium Catalyst

Shu Kobayashi* and Satoshi Nagayama

Department of Applied Chemistry, Faculty of Science, Science University of Tokyo (SUT), CREST, Japan Science and Technology Corporation (JST), Kagurazaka, Shinjuku-ku, Tokyo 162, Japan

Fax 3-3260-4726

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Abstract: Aldimine-selective reactions in the coexistence of aldehydes using a polymer-supported scandium catalyst have been developed. These are remarkable examples of the polymer effect on catalysts to increase selectivities, which can be explained by the stability of the aldimine-polymer-supported catalyst complexes.

Use of polymer-supported catalysts offers several advantages in synthesis such as simplification of reaction procedures, easy separation of catalysts and products, application to automation systems, etc.[1] As for achieving high selectivities in synthesis (one of the most important topics in modern organic chemistry), development of highly selective reactions using polymer-supported catalysts is desired by utilizing the bulkiness of polymers, the stability of polymer-coordinated complexes, etc.[1,2] In this paper, we report such an example: aldimine-selective reactions in the coexistence of aldehydes using a polymer-supported scandium catalyst.

It is well-recognized that aldimines are less reactive than aldehydes towards nucleophilic addition because of the difference in electronegativity between oxygen and nitrogen, the steric hindrance of aldimines, etc.[3] In fact, in the model competition reaction of benzaldehyde and *N*-benzylideneaniline with propiophenone lithium enolate, the enolate attacks the aldehyde exclusively in the coexistence of the aldimine.[4] On the other hand, we have recently found that in the presence of a catalytic amount of Yb(OTf)$_3$, aldimines reacted with silyl enolates selectively to afford the corresponding adducts in high yields, even in the coexistence of aldehydes.[4] We then used scandium salts in the same competition reactions. Although both scandium and ytterbium elements belong to group 3, the competition reaction of benzaldehyde and *N*-benzylideneaniline with the silyl enol ether of propiophenone in the presence of 20 mol% of Sc(OTf)$_3$ gave a mixture of aldehyde-adduct **1a** (13%) and aldimine-adduct **2a** (58%).[5] Interestingly, when a polymer-supported scandium catalyst (PA-Sc-TAD),[6] which was recently developed in our laboratory, was used, the aldimine-selectivity was improved dramatically, and the aldimine reacted with the silyl enolate to give the corresponding adduct in excellent selectivity (Table 1). Other combinations of aldehydes, aldimines, and silyl enolates were then tested, and the results are summarized in Table 2. In all cases, aldimines reacted with silyl enolates selectively in the coexistence of aldehydes to afford the corresponding adducts in high yields.

In order to make clear the origin of these unique selectivities, we first examined the effect of counter anions of scandium catalysts in the competition reaction between an aldehyde and an aldimine. When Sc(OTf)$_2$NTf$_2$ was used in the reaction of benzaldehyde, *N*-benzylidenaniline, and the silyl enol ether of propiophenone, a mixture of aldehyde-adduct **1a** (16%) and aldimine-adduct **2a** (77%) was obtained (the aldehyde-adduct/imine-adduct ratio (**1a**/**2a**) = 17/83). On the other hand, equimolar amounts of **1a** and **2a** were produced when using Sc(NTf$_2$)$_3$ as a catalyst. It was indicated from these experiments that the almost perfect selectivities obtained using the polymer-supported catalyst were not mainly caused by the effect of counter anions, but by the polymer effect (*vide infra*). It was also found that other counter anions influenced the selectivities, and these effects are summarized in Table 3. It is noted that when Sc(PF$_6$)$_3$ was used as a catalyst, only aldimine reacted in the coexistence of the aldehyde to give the corresponding adduct in a good yield.

The unique selectivities obtained using the polymer-supported catalyst can be explained by the following equations. A catalytic amount of a scandium Lewis acid first coordinates an aldimine, but the coordination occurs under equilibrium conditions (eq. 1). Aldehyde-Lewis acid or aldimine-Lewis acid complexes should be stabilized by counter anions

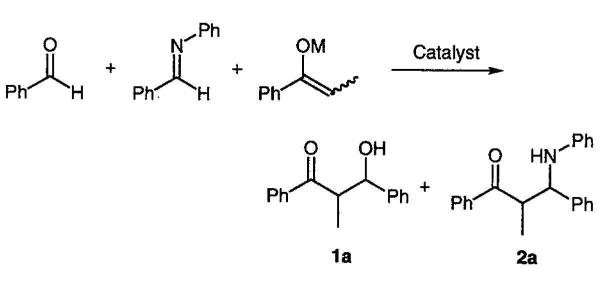


Table 1. A Competition Reaction between an Aldehyde and an Aldimine

M	Catalyst /equiv	Solvent /temp(°C)	Yield (%) 1a	Yield (%) 2a	1a/2a
Li	——	THF/-78	97	trace	>99/1
TMS	Yb(OTf)$_3$/0.2	CH$_3$CN/-23	2	92	2/98[a)]
TMS	Sc(OTf)$_3$/0.2	CH$_3$CN/-23	13	58	18/82
TMS	PA-Sc-TAD/0.06	CH$_2$Cl$_2$:CH$_3$CN (2:1)/0	1	95	1/99

a) Ref. 4.

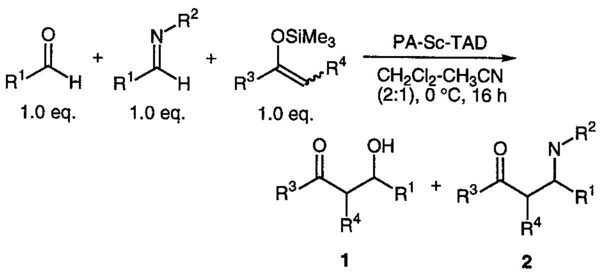


Table 2. Aldimine-selective Reactions Using a Polymer-supported Catalyst

R^1	R^2	R^3	R^4	Yield (%)[a)] 1	2	1/2
Ph	Ph	Ph	Me	1	97	1/99
c-C$_6$H$_{11}$	Ph	Ph	Me	trace	91	<1/>99
2-furyl	Ph	Ph	Me	trace	>99	<1/>99
c-C$_6$H$_{11}$	(p-Cl)Ph	Ph	Me	trace	97	<1/>99
Ph	Ph	SEt	H	trace	58	<1/>99

a) All new compounds gave satisfactory ^{1}H and ^{13}C NMR and HRMS spectra. The reactions were monitored by TLC, and the minor adducts were carefully compared with authentic samples.

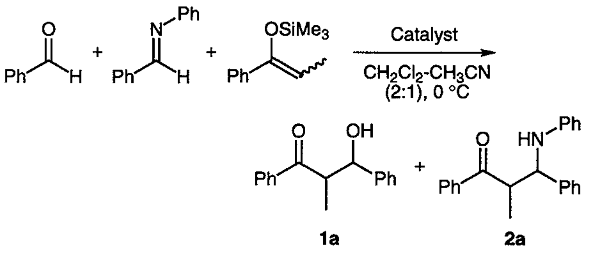
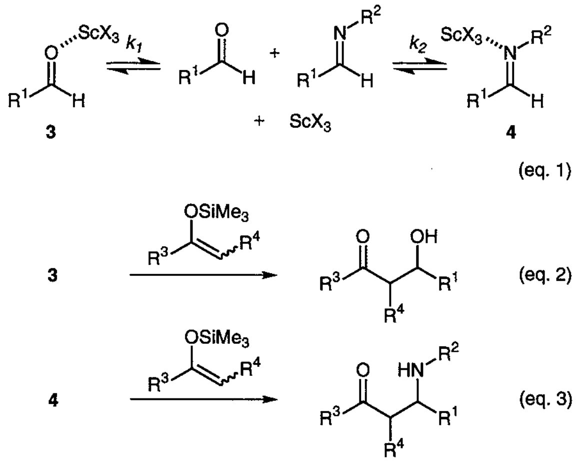


Table 3. Effect of Counter Anions of Scandium Salts

Catalyst	Yield (%) 1a	Yield (%) 2a	1a/2a
$Sc(OTf)_2(NTf_2)$	16	77	17/83
$Sc(NTf_2)_3$	45	45	50/50
$ScCl_3$	trace	51	<1/>99
$Sc(PF_6)_3$	trace	63	<1/>99
$Sc(SbF_6)_3$	1	55	2/98
$Sc(AsF_6)_3$	10	82	11/89
$Sc(ClO_4)_3$	1	61	2/98
$Sc(BPh_4)_3$	5	75	6/94
$\{[(3,5\text{-}CF_3)_2Ph]_4B\}_3Sc$	1	87	1/99

of scandium compounds, and the **1**/**2** ratios shown in Table 3 could depend on the stability of the complexes influenced by the counter anions. On the other hand, when the polymer-supported scandium catalyst (PA-Sc-TAD) was used, the catalyst also coordinates aldimines first. In this case, however, the aldimine-polymer-supported catalyst complexes are more stable than aldimine-*nonpolymer* Lewis acid complexes due to *the polymer effect*. Hence, the aldimines activated by the polymer-supported catalyst reacted with silyl enolates to afford aldimine-adducts exclusively.



In summary, we have developed aldimine-selective reactions in the coexistence of aldehydes using a polymer-supported scandium catalyst. These unique chemoselectivities can be explained by the stability of the aldimine-polymer-supported catalyst complexes. It is noteworthy that this paper shows a remarkable example of the polymer effect on catalysts to increase selectivity. Because of the usefulness of polymer-supported catalysts, these aldimine-selective reactions will be applied to other nucleophilic addition reactions in organic chemistry.

A typical experimental procedure is described for the competition reaction between an aldehyde and an aldimine with a silyl enolate using PA-Sc-TAD: To a mixture of PA-Sc-TAD (56.0 mg), an aldehyde (0.4 mmol), and an aldimine (0.4 mmol) in CH_2Cl_2-CH_3CN (2:1, 1.6 ml) was added a silyl enolate (0.4 mmol) in CH_2Cl_2-CH_3CN (2:1, 0.8 ml), and the mixture was stirred for 16 h at 0 °C. After hexane (20 ml) was added to the reaction mixture, the catalyst was filtered (the catalyst was recovered quantitatively and reused). The filtrate was concentrated *in vacuo* to afford a crude adduct, which was treated with THF-1N HCl (10:1) for 30 min at 0 °C. After a usual work-up, the crude product was chromatographed on silica gel to afford the corresponding aldimine-adduct.

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References and Notes

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(5) We have already found that $Sc(OTf)_3$ is an excellent catalyst in the aldol reactions of aldehydes with silyl enolates and in the imino-aldol reactions of aldimines with silyl enolates. (a) Kobayashi, S.; Hachiya, I.; Ishitani, H.; Araki, M. *Synlett* **1993**, 472. (b) Kobayashi, S.; Araki, M.; Ishitani, H.; Nagayama, S.; Hachiya, I. *Synlett* **1995**, 233. (c) Kobayashi, S. *Synlett* **1994**, 689.

(6) PA-Sc-TAD = Polyallylscandium trifylamide ditriflate. As for the reactions using PA-Sc-TAD, see (a) Kobayashi, S.; Nagayama, S. *J. Am. Chem. Soc.* **1996**, *118*, 8977. (b) Kobayashi, S.; Nagayama, S.; Busujima, T. *Tetrahedron Lett.* **1996**, *37*, 9221.