Preparation, Characterization, and Synthetic Uses of Lanthanide(III) Catalysts Supported on Ion Exchange Resins

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Received October 15, 1996[⊗]

Lanthanide(III) catalysts supported on ion exchange resins (Ln-resins) were prepared from Dowex, Amberlite, Amberlyst, and other cation exchange resins. The amount of lanthanides on resin supports was measured through EDTA titration. The results indicated that the lanthanides in aqueous solution exchanged with almost all the cations (H^+ or Na^+) on the resins to form stable ionic complexes between the lanthanides(III) and the resins. The effects of resin types, resin sizes, and lanthanide salts were investigated with a reaction of indole and hexanal in aqueous solution and with an aldol reaction of benzaldehyde and silyl enol ether in organic solvents. The study found that among ion exchange resins tested Amberlyst XN-1010 and Amberlyst 15 complexed with lanthanides(III) were the most effective catalysts. In addition, the selective Ln-resins were utilized to catalyze acetalization of aldehydes, aldol reaction of formaldehyde or benzaldehyde in aqueous solution, nucleophilic addition to an imine, allylation of an aldehyde, an aza Diels−Alder (DA) reaction, and a ring-opening reaction of an epoxide. Furthermore, glycosylation of alcohol using glucosyl fluoride as a donor was also promoted with the Ln-resin. Thus, this work demonstrated potential uses of lanthanide(III) catalysts supported on ion exchange resins in routine organic reactions.

Introduction

Organic synthesis supported by inorganic or organic solid phases has been playing an important role in chemistry and biology. During the last 3 decades, the introduction of solid phase technology has made synthesis of complicated peptides[1] and nucleotides[2] possible. Applications of solid phases include three aspects: (a) solid-supported substrates, (b) supported reagents, (c) solid catalysts. As the interest in combinatorial chemistry[3] increases, a lot of efforts are currently being made to execute various organic reactions with the substrates on solid phases in order to build up a library of small molecules.[4] Development of reagents supported on solid phases has blossomed since the use of silver carbonate on Celite was reported by Fetizon and Golfier.[5] There are numerous potential advantages for immobilized reagents, but the most important are significant improvement in reactivity and selectivity and simplified operation and isolation.[6] Solid catalysts have been used routinely in chemical laboratories and industrial processes. Inorganic solid acids are widely utilized in petroleum industry as cheap and effective catalysts.[7] For example, clays and zeolites have been used to bring about catalytic cracking and related processes on a large scale. Polymeric organic supports are dominated by functionalized cross-linked polystyrene in various forms.[8] The supported species include common chemical catalysts and biocatalysts such as immobilized enzymes. Under the increasing pressure of environmental problems caused by the chemical industry, solid phase catalysis is recognized to play a leading part in the development of green chemistry. The main advantages to exploit solid phase catalysts in organic synthesis are to adjust reactivity, improve selectivity, simplify separation, recycle the catalysts, and eventually reduce hazardous pollution to achieve environmentally friendly processes.

Lanthanides have been extensively used in organic synthesis because lanthanide-mediated reactions display high chemical and stereoselectivities.[9] Tetravalent lanthanides such as cerium(IV) are effective and mild one-electron oxidants of alcohols and electron-rich aromatic compounds.[10] Cerium(IV) was complexed to Nafion 511 to make a solid oxidation catalyst for transformation of a secondary alcohol to a ketone with $NaBrO_3$ as co-oxidant.[11] Trivalent lanthanides can serve as hard Lewis acids to promote reactions of carbonyl compounds.[9b] For example, Ce(III)-mediated selective 1, 2-addition of $NaBH_4$

[⊗] Abstract published in *Advance ACS Abstracts,* May 15, 1997.

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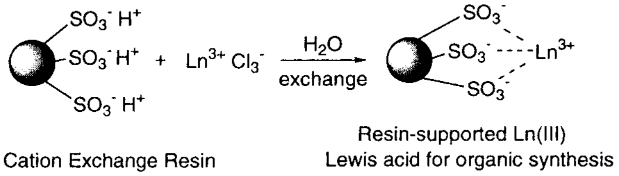
S0022-3263(96)01933-0 CCC: $14.00

Table 1. Yb-Resins Prepared from Ytterbium Sulfate and Different Resins

entry	Ln-resin	ion exchange resin used[a]	H^+ exchange capacity (mmol/g)	Yb content (mmol/g)[b]	exchange percentage[c] (%)
1	Yb-Dowex	Dowex 50X-8, SA, gel, 20−50 mesh	5.1	1.57	92
2	Yb-XN1010	Amberlyst XN-1010, macroreticular, high-specific surface	2.58	0.76	92
3	Yb-Amberlyst 15	Amberlyst 15, SA, macroreticular	4.85	1.52	94
4	Yb-Amberlyst 15(w)	Amberlyst 15(wet), SA, macroporous	4.80	1.60	100
5	Yb-CG50	Amberlite CG-50, WA, gel, 100−200 mesh	9.32	0.42	14
6	Yb-IRP	Amberlite IRP-64, 100−400 mesh	9.69	0.42	13
7	Yb-Nafion	Nafion NR-50	0.89	0.30	100
8	Yb-IR118	Amberlite IR-118	4.85	1.62	100
9	Yb-IR120	Amberlite IR-120	4.88	1.53	94
10	Yb-Sephadex	SP-Sephadex SP-C25-120, 40−120 μm	2.32	0.76	98
11	Yb-Cellulose	sulfoxyethyl cellulose fast flow, fibrous form	2.33	0.77	99

[a] Entries 5 and 6, carboxylic acids; others, sulfonic acids. [b] Yb content calculated according to the formula in the text. [c] Exchange percentage (EP) calculated as: EP = 3 × Yb content/H^+ exchange capacity.

Scheme 1. Preparation of Ln-Resins



to unsaturated ketones has become a standard method in organic synthesis.[12] Divalent lanthanides, particularly SmI_2, are versatile reducing agents which initiate radical reactions between a halide and unsaturated functionalities and have been used in the synthesis of natural products.[13] Recently, researchers have found that lanthanide triflates are water tolerable and recyclable Lewis acids which catalyze a variety of important organic reactions in mild conditions under organic or protic solvents.[9b,14]

Due to the versatility of lanthanide catalysts in organic synthesis, we envisioned that lanthanides(III) supported on ion exchange resins would afford a novel type of solid phase Lewis acids which take advantage of the merits of both lanthanides(III) and the solid phase (e.g., possessing catalytic properties of lanthanides and simplifying isolation of products (Scheme 1)). In fact, ion exchange resins have been exploited to separate rare earth metals. Relative binding strength (or affinity) among metal ions of different groups as well as varied charges have been measured.[15] For example, lanthanide(III) cations bind approximately 50−60 times more strongly than Li^+ to cation exchange resins. Reccently, Kobayashi[16] reported Sc(III) catalysts supported on solid phase. Herein we report our work on the use of lanthanide catalysts supported on organic polymers (Ln-resins).

Results and Discussion

Preparation and Characterization of the Lanthanides Supported on Resins. Table 1 lists the resins used in our experiments, which are commercially available in strong acid form or weak acid form. We first measured the proton capacity of the dry resins by acid base titration. Amberlite IRP-64 (100−400 mesh) contains the highest capacity of 9.69 mmol/g. Owing to the heavier atomic weight of fluorine, Nafion NR-50 has the lowest capacity of 0.89 mmol/g. Dowex and Amberlyst XN-1010 contain medium amounts of protons.

Table 2. Yb-Dowex Prepared from Dowex 50WX 8 (H^+ form, 20−50 mesh) and Different Ytterbium(III) Salts

	Yb salt			
	Cl^-	NO_3^-	SO_4^{2-}	OTf^-
Yb capacity[a] (mmol/g)	1.57	1.67	1.70	1.70
exchange percentage (%)[b]	92	98	100	100

[a] Yb content was calculated according to the formula in the text. [b] Exchange percentage (EP) calculated as: EP = 3 × Yb content/H^+ exchange capacity.

Considering the similar properties of the trivalent lanthanides(III), ytterbium(III) was chosen to study the effect of different ytterbium salts in the exchange process. Ytterbium(III) nitrate, chloride, sulfate, or triflate was exchanged with Dowex 50WX-8 (H^+ form). The exchange percentage on the resins was from 92% to 100% (Table 2). Long exchange times and higher concentrations of ytterbium salts helped complete the exchange. In terms of efficiency and cost, lanthanide sulfates are suitable sources of lanthanides for the preparation of Ln-resins.

The above data showed that more than 90% of the protons on the resins could be exchanged with lanthanides. In order to exclude possible influences of the unexchanged protons on Yb-resins in the reactions we planned to perform, the resins (H^+ form) were first transformed into the Na^+ form. The capacity of Yb(III) on different Yb-resins is summarized in Table 1 along with exchange percentage. It is noteworthy that we employed aqueous solution of lanthanides to perform the exchange between resins and lanthanides at room temperature, while Kobayashi[16a] used acetonitrile under reflux conditions to prepare Sc-Nafion. The Yb-Nafion we prepared contained 0.30 mmol/g ytterbium(III); in comparison, the Sc-Nafion was reported to contain 0.29 mmol/g scandium(III).[16] Our method appears convenient to prepare Ln-resins because it avoids heating and organic solvents.

In order to test the effect of different rare earth metals in the catalysis, we prepared Ln-resins (La, Pr, Nd, Gd, Dy, Er, Yb, and Sc) by the exchange of Amberlyst XN-1010 with lanthanide salts following the above method (Table 3). The content of lanthanides on these resins was around 0.75 mmol/g.

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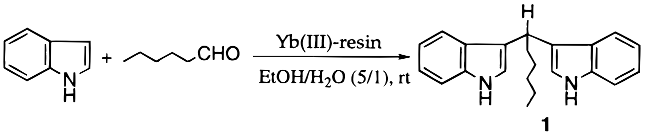
Table 3. Ln-Resins Prepared from Different Lanthanides

entry	Ln-resin	Ln used	content of Ln(III) on resin (mmol/g)[a]
1	La-XN1010	$LaCl_3$	0.72
2	Pr-XN1010	$Pr(OTf)_3$	0.78
3	Nd-XN1010	$Nd(OTf)_3$	0.75
4	Gd-XN1010	$Gd(OTf)_3$	0.70
5	Dy-XN1010	$Dy(OTf)_3$	0.74
6	Er-XN1010	$Er(OTf)_3$	0.77
7	Yb-XN1010	$YbCl_3$	0.79
8	Sc-XN1010	$Sc(OTf)_3$	0.74

[a] Yb content was calculated according to the formula in the text.

Scheme 2. Reaction of Indole with Hexanal Catalyzed by Yb(III)-Resins



Synthetic Applications of Ln-Resins. To evaluate how efficiently the lanthanides supported on ion exchange resins work as solid Lewis acid catalysts in organic synthesis, we studied two reactions with respect to yields, solvents, and recyclability: (i) a reaction of indole with hexanal and (ii) an aldol reaction of benzaldehyde with a silyl enol ether. Based on the results of these two reactions, we chose an optimal Ln-resin to catalyze a variety of other reactions.

(i) Reaction of Indole with Hexanal. Reactions[17] of indoles with aldehydes or ketones to give 2 + 1 coupling products are well known and have been catalyzed by protic acids[18] or Lewis acids[19] such as $BF_3{\cdot}OEt_2$. We recently found that the reactions of indoles with aldehydes or ketones can be catalyzed in an ethanol/water system by lanthanide triflates.[14b] Here we used several different Yb-resins to catalyze the reaction of indole with hexanal in an ethanol/water solvent system (Scheme 2). The results are summarized in Table 4. Amberlyst XN-1010 and Amberlyst 15 catalyzed the reaction most effectively. After 24 h the reaction gave more than 90% yield of product **1**. For CG-50 and IRP-60, which are weak acids (carboxylic aicds), the yields were around 20%. Although Yb-Sephadex and Yb-Cellulose bear sulfonated anions, only limited catalysis was observed. For Yb-Dowex and Yb-IR118, the reaction took a longer time (48 h) to achieve a yield of 90%.

To compare the catalytic effect of different rare earth ions, the reaction was run in the presence of the eight Ln-resins (Sc, La, Pr, Nd, Gd, Er, Dy, and Yb(III)), respectively. Similar to the results obtained with soluble lanthanide triflate salts,[14b] no obvious differences were observed for these resin-supported catalysts in terms of the reaction yields (Table 5).

Table 4. Yields of Reactions 1 and 2 Catalyzed by Yb-Resins[a]

		yields (%)	
entry	Yb-resin	reaction 1	reaction 2
1	Yb-Dowex-1	76	51
2	Yb-Dowex-2	84	47
3	Yb-XN1010	93	83
4	Yb-15	90	89
5	Yb-15(w)	89	86
6	Yb-CG50	18	7
7	Yb-IRP64	20	9
8	Yb-Nafion	30	30
9	Yb-IR118	34	49
10	Yb-IR120	16	46
11	Yb-Sephadex	15	33
12	Yb-Cellulose	10	42

[a] Reactions 1 and 2 are illustrated in Schemes 2 and 3, respectively.

Table 5. Results of Reactions 1 and 2 Catalyzed by Different Lanthanides over Amberlyst XN-1010[a]

		yields (%)	
entry	Ln-XN1010	reaction 1[a]	reaction **2**[a]
1	Sc	92	85
2	La	91	71
3	Pr	89	75
4	Nd	91	73
5	Gd	92	72
6	Dy	92	78
7	Er	88	81
8	Yb	92	83

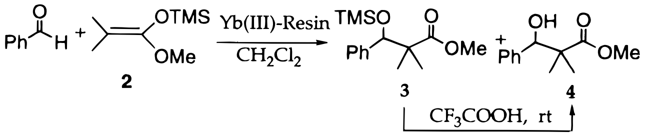
[a] Reaction 1 and 2 are illustrated in Schemes 2 and 3, respectively.

Table 6. Effect of Resin Size on the Reaction of Indole with Hexanal

entry	Ln-resin	resin size (mesh)	Yb content (mmol/g)[a]	yield (%)
1	Yb-Dowex 50X-8	20−50	1.57	76
2	Yb-Dowex 50X-8	100−200	1.44	84
3	Yb-Dowex 50X-8	400−200	1.57	86
4	Yb-Dowex 50X-2	400−200	1.43	30

[a] Yb content was calculated according to the formula in the text.

Scheme 3. Aldol Reaction Catalyzed by Yb(III)-Resins in Dichloromethane



The effect of particle size of the solid support was examined by performing the reaction in the presence of Yb-Dowex 50WX-8 of different sizes. The resin of smaller size gave a better yield of product **1** (Table 6). In addition, Yb-Dowex with a cross-linking degree of 2% was not effective to catalyze the reaction.

(ii) Aldol Reaction of Benzaldehyde and Silyl Enol Ether 2. Traditional Lewis acids used in aldol reaction are moisture sensitive so that the reaction must be done under water free conditions. Lanthanide complexes can serve as Lewis acids to promote the reaction of silyl enol ethers with aldehydes without the requirement of water free conditions.[20] We examined the catalytic effect of the Ln-resins on the reaction of benzaldehyde and silyl enol ether **2** (Scheme 3).

Firstly, the reaction was carried out overnight in dichloromethane in the presence of different resin sup-

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Table 7. Recyclability of Amberlyst XN1010-Yb(III) for Reaction 2[a]

run	1	2	3	4	5	6	7	8	9	10
yield (%)	83	76	73	79	80	71	79	78	80	79

[a] Reaction 2 is illustrated in Scheme 3.

ports with ytterbium as the lanthanide ion. Mixtures of silylated and unsilylated aldols **3** and **4** were formed, and **3** was desilylated to **4** when the filtrate was treated with TFA in dichloromethane. The reaction yields listed in Table 4 indicate that the supports have an important impact on the reaction. Weak acid resins exhibited very poor catalytic effects. Strong sulfonated resins exhibited moderate to excellent catalysis. Moreover, the surface area and pore size of the resin were crucial to the performance of catalysis. Amberlyst XN-1010 and Amberlyst 15, which were designed to have large surface areas, were found to be the best catalysts in this aldol reaction. Dowex resins, on the other hand, gave moderate yields. Sephadex and cellulose did not display satisfactory results.

Secondly, the reaction was carried out in the presence of different lanthanides(III) (Sc, La, Pr, Nd, Gd, Er, Dy, and Yb(III)) on Amberlyst XN-1010. The reaction yields were comparable (Table 5). Thirdly, we used the Yb-XN1010 catalyst 10 successive times for the aldol reaction and did not find any loss of catalytic activity (Table 7). Thus, ion exchange-supported lanthanide(III) catalysts can be recycled and reused.

Other Reactions Catalyzed by Ln-Resins. The above results showed that Amberlyst XN-1010 and Amberlyst 15, which have high cross-linking degrees and large surface areas, are suitable supports for lanthanide catalysts. Thus we employed Ln-resins Yb-XN1010 or Yb-Amberlyst 15 to catalyze the formation of acetals, aldol reactions in aqueous solution, nucleophilic addition to an imime, allylation of an aldehyde, aza DA reaction, ring-opening reaction of an epoxide, and glycosylation using glycosyl fluorides as a donor (Table 8).

Acetalization. Lanthanide salts have proven to be extraordinary catalysts for acetalization, providing essentially quantitative yields of desired acetals with minimal side effect[22] (i.e., rearrangement, epimerization, or racemization). In addition, previous examples have demonstrated the ability of lanthanide Lewis acids to chemoselectively acetalize aldehydes in the presence of ketones.[23] When Yb-XN1010 was used as a catalyst, *p*-bromobenzaldehyde was quantitatively transformed to an acetal in a mixture of dichloromethane and trimethyl orthoformate (5/1) (Table 8, entry 1). In a mixture of methanol and trimethyl orthoformate (5/1), Yb-Amberlyst 15 catalyzed acetalization of (*S*)-citronellal ((3*S*), 7-dimethyl-6-octenal) (Table 8, entry 2). Obviously, this process is a convenient operation because Ln-resin can be filtered off and, more importantly, products are not contaminated. Thus, the ion exchange resin-supported lanthanide(III) should be accepted as a general method of choice for acetalization of aldehydes.

Aldol Reactions in Aqueous Solution. The Mukaiyama reaction[24] of a silyl enol ether with aldehydes or ketones requires a catalyst such as $TiCl_4$ under strictly nonaqueous conditions. Kobayashi first reported the use of lanthanide(III) triflate as catalyst for the Mukaiyama reaction using a commercially available aqueous formaldehyde solution to make hydroxymethyl adducts.[25] We tested the Ln-resins in the reaction of (cyclohexenyloxy)-trimethylsilane with formaldehyde in aqueous THF (Table 8, entry 3). Yb-XN1010 and Yb-Amberlyst 15 displayed better catalytic effects than Yb-Nafion. However, only Yb-Nafion catalyzed the reaction of benzaldehyde with (cyclohexenyloxy)trimethylsilane to give products **8** and **9** (Table 8, entry 4).

Reaction of an Imine with Silyl Enol Ether 2. Lanthanide triflates were reported to catalyze the reaction of an imine and a silyl enol ether.[26] In our hands, Yb-XN1010 was found to catalyze the reaction of silyl enol ether **2** and an imine prepared by condensation of benzaldehyde and aniline (Table 8, entry 5).

Allylation of Hexanal with Tetraallyltin. Lanthanides were reported to catalyze the reaction of carbonyl compounds with tetraallyltin in an aqueous medium.[16a,27] Here Yb-XN1010 was also found to catalyze the reaction of hexanal and tetraallytin in a toluene/ethanol/H_2O solvent system (Table 8, entry 6). In this case, Yb-XN1010 was actually better than Yb-Nafion.

Aza Diels–Alder Reaction of Hexanal, Benzylamine Hydrochloride, and Cyclopentadiene. We recently reported that lanthanide(III) triflate can serve as an effective catalyst for aza DA reactions[28,29] in aqueous solution between inactivated iminium salts generated in situ from aldehydes and amine hydrochlorides under Mannich-like conditions with dienes. The reaction yields were improved significantly with the use of lanthanides, and many previously unreactive aldehydes could be used in the aza DA reaction.[14a] Therefore, Yb-Amberlyst 15 was implemented into the reaction of hexanal, benzylamine hydrochloride, and cyclopentadiene. We found that the resin increased reaction yield from 7% to 22%, but it was not so effective as ytterbium triflate in solution (Table 8, entry 7).

Ring-Opening Reaction of 1,2-Epoxyoctane in Methanol. Lanthanides are known to catalyze the ring

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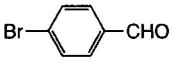
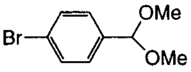
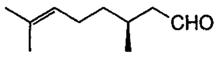
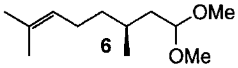
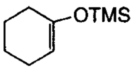
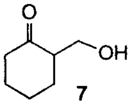
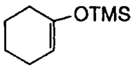
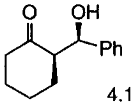
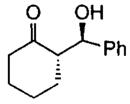
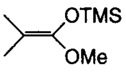
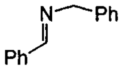
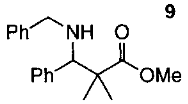
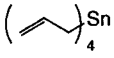
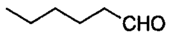
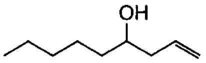
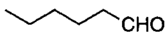
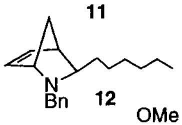
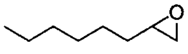
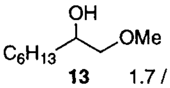
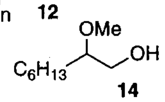
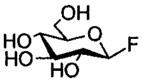
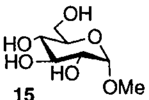
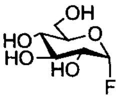
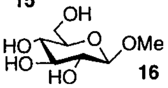
Table 8. Ln-Resin-Catalyzed Reactions

Entry	Reactents			Solvent	Catalysts	Products	Yield (%)
1		$CH(OMe)_3$		CH_2Cl_2	Yb-Amberlyst XN-1010	 5	100
2		$CH(OMe)_3$		MeOH	Yb-Amberlyst 15		95
3		CH_2O		THF/H_2O (4/1)	Yb-Amberlyst-15	 7	82
4		PhCHO		THF/H_2O (4/1)	Yb-Nafion NR-50	 4.1 / 1  8 9	34
5				CH_2Cl_2	Yb-Amberlyst XN-1010	 10	87
6				PhMe/EtOH/H_2O	Yb-Amberlyst-15	 11	91
7		$BnNH_3^+Cl^-$		H_2O	Yb-Amberlyst-15	 12	21 (*exo*)
8				MeOH	Yb-Amberlyst-15	 1.7 / 1  13 14	97
9				MeOH	Yb-Amberlyst-15	 15	85
10				MeOH	Yb-Amberlyst-15	 16	89

opening of oxiranes with many nucleophiles such as amine[30] and cyanide.[31] Here the use of resin-supported lanthanide(III) was demonstrated in the ring-opening reaction of 1, 2-epoxyoctane to result in two isomers (1.7/1) in methanol in the presence of Yb-Amberlyst 15 (Table 8, entry 8) with an excellent yield.

Glycosylation with Glucosyl Fluoride in Alcohols Promoted by Ln-Resins. Glycosyl fluorides have been extensively utilized in constructing complicated oligosaccharides, and accordingly, various Lewis acid promotors have been developed to activate 1-fluoroglycosides.[32] Most recently, lanthanides have been used as promotors by Shibasaki et al.[33] We found that Ln-resins, especially Yb-XN1010 and Yb-Amberlyst 15, promoted glycosylation of unprotected glucosyl fluoride in methanol (Table 8, entries 9 and 10). It is noticed that methyl glucosides are formed stereospecifically with complete inversion of the anomeric chiral center of the glucosyl fluoride. Lanthanide triflates can also promote this reaction, but removal of the soluble lanthanide is troublesome.

Conclusion

Lanthanides(III) supported on ion exchange resin are a novel type of solid acid catalyst that combine the Lewis acid properties of the lanthanide and the advantages of solid phase. The preparation of the resin-supported catalysts is straightforward, and the resultant catalysts are stable and active under common conditions (acidic conditions and room temperature) in organic synthesis. The catalysts have been demonstrated to be effective in a number of important organic transformations. Among a number of ion exchange resins tested, Amberlyst XN-1010 and Amberlyst 15 complexed with lanthanides(III) were the most effective catalysts. The simplification in workup and separation of products and the recyclability of the catalysts make the use of these novel catalysts a promising alternative both in research laboratories and in industrial processes.

Experimental Section

General Remarks. All unspecified reagents were from commercial resources. Thin-layer chromatography was conducted on EM silica gel 60 Si_{254F} TLC plates with fluorescent indicator. Column chromatography was conducted with silica gel, grade 62, 60–200 mesh, 150 Å. All the products were identified by ^1H NMR and compared with literature data.

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Determination of the Proton Exchange Capacity of Resins. Dowex 50X-8 resins (100 g) were washed sequentially with MeOH (200 mL), deionized water (200 mL), and HCl (1 M, 100 mL) with a flow rate of 2 mL/min in a column. Then it was washed with water to neutral followed by drying overnight *in vacuo* at 65 °C in the presence of P_2O_5. The dry resins (W g) were stirred with an excessive standard solution of NaOH (a mL, b M) in 20 mL of water for 4 h at 20 °C. The NaOH remaining in solution was titrated with standard HCl solution (c M). It consumed a volume (d mL) of HCl. The acidic exchange capacity of the resins (EC) was calculated according to the following formula:

$$\mathrm{EC} = (ab - cd)/W\ (\mathrm{mmol/g})$$

Preparation of Na-Resins from H-Resins. Ion exchange resin was packed in a column and washed with methanol and water. Then the resin was washed with a saturated Na_2SO_4 solution until the eluent was neutral followed by three washings with water. The resin was dried overnight *in vacuo* at 65 °C in the presence of P_2O_5.

Preparation and Determination of Lanthanide Content of Ln-Resins. The resin (W_1 g) was placed into an Erlenmeyer flask containing a solution of $Ln_2(SO_4)_3$ (W_1 mmol) in water. Then the resulting mixture was stirred overnight. The resin was filtered and washed with water three times. The combined aqueous solution was transferred into a 100 mL volumetric flask. The resin was washed with ethanol and dried overnight *in vacuo* at 65 °C in the presence of P_2O_5. The weight of the Ln resin was W_2 g. The remaining amount of lanthanide in the solution was determined by titration using EDTA (0.0100 M) as a standard solution with xylenol orange (sodium salt) as an indicator. From the above volumetric flask, V_1 mL of the solution was taken out and put into a 100 mL Erlenmeyer containing a buffer of 20% hexamethylenetetraamine. Then the solution was titrated with an EDTA solution with xylenol orange as indicator. The titration ended as soon as the red color turned into yellow. It consumed V_2 mL of the EDTA solution. The lanthanide content on the resin was calculated as follows:

$$\mathrm{Ln\ content} = (2W_1 - V_2 \times 0.01/V_1 \times 100)/W_2\ (\mathrm{mmol/g})$$

Reaction of Indole with Hexanal. A mixture (1 mL) of ethanol and water (5/1, v/v), Ln-resin (200 mg), hexanal (100 mg, 1.0 mmol), and indole (235 mg, 2.0 mmol) was added to a 7 mL vial. The mixture was shaken for 12 h. The resin was filtered and washed with ethanol three times. The combined filtrate was concentrated *in vacuo* to give a residue, which was purified via column chromatography eluting with ethyl acetate and hexane (1/1, v/v) to give compound **1**:[14b] ^{1}H NMR ($CDCl_3$) δ 0.84 (3 H, t, J = 7.2 Hz), 1.22−1.44 (6 H, m), 2.19 (2 H, m), 4.45 (1 H, t, J = 7.6 Hz), 6.94 (2 H, d, J = 2.4 Hz), 7.02 (2 H, t, J = 7.6 Hz), 7.13 (2 H, t, J = 7.6 Hz), 7.28 (2 H, d, J = 8.0 Hz), 7.58 (2 H, d, J = 7.6 Hz), 7.84 (2 H, br, 2 NH); MS *m/e* 316 (M^+).

Aldol Reaction of Benzaldehyde and Silyl Ether 2 in Dichloromethane. Ln-resin (200 mg), benzaldehyde (53 μL, 0.5 mmol), and **2** (121 μL, 0.6 mmol) were added to a 7 mL vial containing 1 mL of dichloromethane. The reaction mixture was shaken overnight. The resin was filtered and washed with dichloromethane three times. To the filtrate was added 0.1 mL of TFA, and the resulting solution was stirred at room temperature for 10 min. After removal of solvent *in vacuo* the residue was purified via column chromatography eluting with ethyl acetate and hexane (1/4, v/v) to give **4**:[20] ^{1}H NMR ($CDCl_3$) δ 1.09 (3 H, s), 1.13 (3 H, s), 3.70 (3 H, s), 4.88 (1 H, s), 7.29 (5 H, m); MS (*m/e*) 208 (M^+).

Acetalization of *p*-Bromobenzaldehyde. Yb-XN1010 (100 mg), dichloromethane (1 mL), trimethyl orthoformate (0.2 mL), and *p*-bromobenzaldehyde (100 mg) were added to a 7 mL vial. The mixture was shaken overnight. The resin was filtered off and washed with dichloromethane (2 mL × 3). The combined organic solvents were removed *in vacuo* to give *p*-bromobenzaldehyde acetal (**5**) (124 mg) in a quantitative yield:[34] ^{1}H NMR ($CDCl_3$) δ 3.31 (6 H, s), 5.36 (1 H, s), 7.33 (1 H, d, J = 8.4 Hz), 7.50 (1 H, d, J = 8.4 Hz).

Acetalization of (*S*)-(−)-Citronellal. Yb-Amberlyst 15 (100 mg), methanol (1 mL), trimethyl orthoformate (0.2 mL), and (*S*)-(−)-citronellal (155 mg) were added to a 7 mL vial. The mixture was shaken overnight. The resin was filtered off and washed with methanol (2 mL × 3). The combined organic solvents were removed *in vacuo* to give a residue, which was purified to give (*S*)-(−)-citronellal acetal (**6**) (191 mg, 95% yield), eluting with hexane and ethyl acetate (9/1, v/v):[35] ^{1}H NMR ($CDCl_3$) δ 0.92 (3 H, d, J = 6.4 Hz), 1.19 (1 H, m), 1.36 (1 H, m), 1.60 (3 H, s), 1.68 (3 H, s), 1.98 (1 H, m), 3.30 (3 H, s), 3.31 (3 H, s), 4.46 (1 H, t, J = 6.6 Hz), 5.10 (1 H, t, J = 6.8 Hz).

Aldol Reaction in Aqueous Solution: (i) Reaction of (1-Cyclohexenyloxy)trimethylsilane with Formaldehyde. (Cyclohexenyloxy)trimethylsilane (85 mg) was added to a suspension of Yb-Amberlyst 15 (200 mg) in a mixture (2 mL) of THF (1.5 mL) and 37% aqueous formaldehyde (0.5 mL). The reaction mixture was stirred at room temperature overnight. The resin was filtered and washed with THF and water (4/1, v/v). Water (10 mL) was added to the combined filtrate followed by extraction with ethyl acetate three times. The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. The solvents were removed, and the residue was purified via column chromatography eluting with hexane and ethyl acetate (1/4, v/v) to give product **7** (61 mg) in 81% yield:[25c] ^{1}H NMR ($CDCl_3$) δ 1.40−2.16 (m, 6 H), 2.25−2.67 (m, 3 H), 3.55−3.63 (m, 1 H), 3.73 (dd, J = 11.4, 7.2 Hz, 1 H).

Reaction of (1-Cyclohexenyloxy)trimethylsilane with Benzaldehyde. Benzaldehyde (53 μL, 0.5 mmol) and cyclohexenyltrimethylsilane (130 μL, 0.6) were added to a suspension of Yb-Nafion NR-50 (300 mg) in a mixture (1 mL) of THF and water (4/1, v/v). The reaction mixture was stirred at rt for 2 days. The resin was filtered and washed with THF. Water (10 mL) was added to the combined filtrate followed by extraction with ethyl acetate three times. The combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. The solvents were removed, and the residue was purified through column chromatography. Two products **8**, and **9**, were collected together in a combined 43% yield. The ratio (*threo*-**8**:*erythreo*-**9**, 4:1) was determined by proton NMR analysis:[25c] ^{1}H NMR ($CDCl_3$) δ 5.39 (1 H, d, J = 2.4 Hz, CHOH) for **8**, 4.89 (1 H, J = 8.4 Hz, C*H*OH) for **9**.

Reaction of an Imine with Silyl Enol Ether 2. Silyl ether **2** (0.7 mmol) and the imine (0.5 mmol) prepared from aniline and benzaldehyde were added to a suspension of Yb-XN1010 (200 mg) in dichloromethane. The reaction mixture was stirred for 5 h. The resin was filtered and washed with dichloromethane. The filtrate was concentrated *in vacuo* to give a residue, which was purified through column chromatography eluting with hexane and ethyl acetate (1/1, v/v) to afford product **10** (129 mg) in 87% yield:[26] ^{1}H NMR ($CDCl_3$) δ 1.20 (3 H, s), 1.30 (3 H, s), 3.66 (3 H, s), 4.56 (1 H, s), 4.88 (1 H, br, NH), 6.53 (2 H, m), 6.63 (1 H, t, J = 8.4 Hz), 7.06 (2 H, m), 7.30 (5 H, m); MS *m/e* 297 (M^+).

Allylation of Hexanal with Tetraallyltin. Hexanal (125 μL, 1.0 mmol) and tetraallyltin (240 μL, 1.0 mmol) in water/ethanol/toluene (1.2 mL, 1/7/4, v/v/v) was added to a solution of Yb-Amberlyst 15 resin (250 mg). The suspension was shaken at rt for 24 h in a sealed vial. The resin was filtered and washed with ethanol (3 mL × 3). The filtrate was mixed with 0.5 mL of 0.5 M HCl and stirred for 10 min. The solution was extracted with ethyl acetate, and the organic phase was washed with brine and dried over anhydrous $MgSO_4$. After removal of solvents, the residue was purified through column chromatography eluting with hexane and ethyl acetate (8/2, v/v) to give alcohol **11** (129 mg) in 91% yield.[27a] (NMR spectrum is identical to that of the sample from Sigma): ^{1}H NMR ($CDCl_3$) δ 0.91 (3 H, t, J = 6.8 Hz), 1.32 (4 H, m), 1.46 (2 H, m), 1.71 (1 H, br, OH), 2.14 (2 H, m), 2.30 (2 H, m), 2.30 (2 H,

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m), 3.64 (1 H, m), 5.11 (1 H, m), 5.15 (1 H, s), 5.84 (1 H, m); MS *m*/*e* 142 (M^+).

Aza Diels−Alder Reaction of Hexanal, Benzylamine Hydrochloride, and Cyclopentadiene. Yb-Amberlyst 15 (200 mg), water (1 mL), benzylamine hydrochloride (144 mg), hexanal (100 mg), and cyclopentadiene (200 mg) were added to a 7 mL vial. The mixture was shaken for 2 days. The resin was filtered and washed with water. The combined solution was extracted with ethyl acetate (5 mL × 3). The combined organic phase was neutralized with ammonia. The solvent was removed, and the residue was purified to give *exo* product **12** in 35% yield:[14a] ^{1}H NMR ($CDCl_3$) δ 0.86 (t, J = 6.4 Hz, 3 H), 1.28 (m, 8 H), 1.42 (m, 1 H), 1.61 (d, J = 8.4 Hz, 1 H), 1.69 (d, J = 8.4 Hz, 1 H), 2.61 (s, 1 H), 3.30 (d, J = 12.4 Hz, 1 H), 3.43 (d, J = 12.4 Hz, 1 H), 3.65 (s, 1 H), 6.08 (m, 1 H), 6.42 (m, 1 H), 7.29 (m, 5 H).

Ring-Opening Reaction of 1,2-Epoxyoctane in Methanol. A 7 mL vial containing methanol (1 mL) was added to Yb-Amberlyst 15 and 1,2-epoxyoctane (128 mg). The reaction mixture was shaken for 20 h. The resin was filtered off, and the filtrate was condensed *in vacuo* to give a residue. Two isomers, **13** and **14,** were isolated through column chromatography. The ratio of 1-methoxy-2-octanol (**13**) to 2-methoxy-1-octanol (**14**) was 1.7:1 with a combined yield of 97%. **13**: ^{1}H NMR ($CDCl_3$) δ 0.89 (3 H, t, J = 7.5 Hz), 1.31 (m, 8 H), 1.46 (1 H, m), 1.58 (1 H, m), 3.26 (1 H, m), 3.41 (3 H, s), 3.46 (1 H, m), 3.68 (m, 1 H). **14**: ^{1}H ($CDCl_3$) δ 0.88 (3 H, t, J = 7.2 Hz), 1.29 (m, 8 H), 1.44 (2 H, m), 3.23 (1 H, dd, J = 9.2, 8.0 Hz), 3.39 (s, 3 H), 3.41 (m, 1 H), 3.77 (1 H, m).

Glycosylation of Glucosyl Fluoride in Alcohol. The Yb-resin (200 mg) was immersed in 1 mL of methanol, and α−glucosyl fluoride (50 mg) was added. The mixture was stirred at rt until the starting material disappeared by TLC monitoring. The resin was filtered and washed with methanol. The filtrate was concentrated *in vacuo* to give a residue, which was chromatographed eluting with ethyl acetate and ethanol (5/2) to give methyl β−glucoside (**16**) (48 mg) in 89% yield:[36] ^{1}H NMR (CD_3OD) δ 3.15 (1 H, dd, J = 9.2, 8.0 Hz), 3.28 (1 H, m), 3.38 (2 H, m), 3.47 (3 H, s), 3.61 (1 H, dd, J = 12.4, 6.0 Hz), 3.82 (1 H, dd, J = 12.4, 2.4 Hz), 4.27 (1 H, d, J = 8.4 Hz).

α−Glucosyl fluoride was replaced with β−glucosyl fluoride and the same procedure was followed. The reaction gave methyl α−glucoside (**15**) (46 mg) in 85% yield: [36] ^{1}H NMR (CD_3OD) δ 3.28 (1 H, m), 3.30 (3 H, s), 3.43 (1 H, dd, J = 10.0, 4.0 Hz), 3.53 (2 H, m), 3.63 (1 H, dd, J = 12.0, 4.0 Hz), 3.74 (1 H, s), 3.77 (1 H, m), 4.75 (1 H, m).

Acknowledgment. The authors thank Hercules Inc. for financial support of this work. We are also grateful to Drs. H.-N. Cheng, Robert G. Nickol, and Brian J. Swetlin for helpful discussions.

JO961933+

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