Azidolysis of α,*β*-Epoxycarboxylic Acids. A Water-Promoted Process Efficiently Catalyzed by Indium Trichloride at pH 4.0

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The catalytic efficiency of $InCl_3$, $Yb(OTf)_3$, and $Sc(OTf)_3$ in the azidolysis of α,*β*-epoxycarboxylic acids has been studied in water and in organic solvents, for comparison using NaN_3 and Me_3SiN_3 as the source of the azido group. In water, the catalytic effectiveness of these metal salts strongly depends on the pH of the aqueous medium and on the type of Lewis acid catalyst. In water their catalytic activity is mostly due to the corresponding aqua ion species, the concentration of which becomes significant when the pH of the aqueous medium is below the corresponding $pK_{1,1}$ hydrolysis constant. The process is more efficient in water than in organic solvents. At pH 4.0, $InCl_3$ is a far better catalyst than $Yb(OTf)_3$ or $Sc(OTf)_3$ and allows the highly regio- and diasteroselective preparation of *β*-azido-α-hydroxycarboxylic acids, which can be isolated in pure form in very high yields.

Introduction

In recent years water has become an intriguing reaction medium, especially for metal salt catalyzed organic transformations.[1] In many cases the catalyst and/or the aqueous medium can be recovered and reused, thereby reducing the environmental impact of these processes.[2,3] For several years we have been studying organic reactions performed in water as reaction medium,[2−7] and currently we are interested to the synthesis of *β*-amino-α-hydroxycarboxylic acids. The planned strategy is based on the oxirane ring opening of α,*β*-epoxycarboxylic acids, or their methyl esters, by azido ion and the subsequent reduction of the resulting azido-hydroxycarboxylic acids. Both processes are catalyzed by metal salts under pH-controlled conditions. In view of a practical application for this project, we are attempting to develop a process that (i) is performed in water only in a *one-pot* procedure under mild and metal salt catalyzed reaction conditions, (ii) occurs in high yield and high regio- and diasteroselectivity, and (iii) allows reuse of a metal salt catalyst. Since an efficient azidolysis of α,*β*-epoxycarboxylic acids, or their corresponding esters, is fundamental for the success of our strategy, we have carefully investigated this step. This paper reports the results that were obtained by using $InCl_3$, $Yb(OTf)_3$, and $Sc(OTf)_3$ as catalysts, NaN_3 or Me_3SiN_3 as nucleophile, and water or organic solvents as reaction medium.

In the realm of Lewis acids, $InCl_3$, $Yb(OTf)_3$, and $Sc(OTf)_3$ are mild catalysts that have been receiving a lot of attention, and their effectiveness in many organic reactions has been proven.[8−10] $InCl_3$ has been largely used in organic solvents, more rarely in pure water,[8−10] and never as catalyst for epoxide ring opening by nucleophiles.[11]

Although the azidolysis of methyl and ethyl α,*β*-epoxycarboxylates has been extensively investigated,[13−17] to our knowledge, only two papers have reported the azidolysis of α,*β*-epoxycarboxylic acids.[2,13] In 1985 Sharpless et al. carried out the considered reaction using LiN_3 (3 mol/equiv) in EtOH at room temperature in the presence of an excess of $Ti(O\text{-}i\text{Pr})_4$ (150 mol %) as catalyst.[13] Fifteen years later we performed the reaction using NaN_3 (5 mol/equiv) in pure water at 30 °C and pH 4.0, catalyzed by $Cu(NO_3)_2$ (10 mol %).[2] Here we report that $InCl_3$ in aqueous medium is an efficient catalyst.

Results and Discussion

To indicate that $InCl_3$, $Yb(OTf)_3$, and $Sc(OTf)_3$ are stable in water, they are classified as *water-tolerant*

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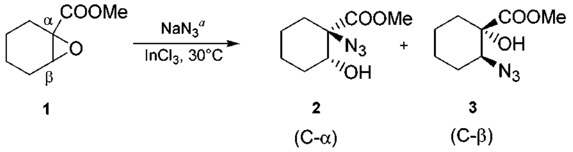
Table 1. $InCl_3$-Catalyzed Azidolysis of Methyl α,β-Epoxycyclohexanecarboxylate (1)



entry	medium	pH[b]	$InCl_3$ (mol %)	t (h)	C[c] (%)	C-β (%)	C-α (%)
1	MeCN		none	8	0		
2	MeCN		30	8	0		
3	H_2O	7.0	none	8	>99	90	10
4	H_2O	7.0	30	8	>99	90	10
5	H_2O	4.0	none	24	25	90	10
6	H_2O	4.0	30	2	>99	>99[d]	<1

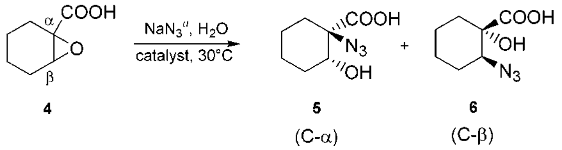
[a] 5 mol/equiv. [b] Held constant for the entire reaction time.[20] [c] Reaction conversion. The percentage of **2** and **3** were determined by GC analyses. [d] The regioisomer **3** was isolated in pure form in 95% yield, and its structure was proven as reported.[2]

Lewis acids.[8] In this medium they actually dissociate quickly and hydrolyz,e thereby generating the corresponding aqua ion ($M(H_2O)_6^{3+}$, where M = In, Yb, and Sc) and a number of mononuclear and polynuclear species. At a fixed temperature, the distribution is a function of the pH of the medium and the metal and the nucleophile concentration.[18,19] The highest efficiency of a metal salt as catalyst in water must be attributed to the corresponding aqua ion. In water this species is the most abundant, among all the others, as long as the pH value goes below the related aqua ion $pK_{1,1}$ hydrolysis constant.[18,19] On this basis, we have shown that $AlCl_3$, believed to be unstable in water, is on the contrary a very efficient catalyst for the azidolysis of α,β-epoxycarboxylic acids at pH 4.0.[3b]

First, we examined the effectiveness of $InCl_3$ on the azidolysis in water and MeCN of the methyl α,β-epoxycyclohexanecarboxylate (**1**) by using 5 mol/equiv of NaN_3 (Table 1). Considering that the $pK_{1,1}$ of $InCl_3$ is 4.0,[18,19] the experiments were performed at pH 4.0 and at 7.0 to verify the relationship between the catalytic efficiency of this metal salt and the pH with respect to the $pK_{1,1}$ hydrolysis constant. In each case the chosen pH values of the aqueous medium were held constant for the entire reaction time and for all the azidolysis reactions carried out in water. We considered pH 4.0 to be the lowest pH value at which a significant concentration of azido ion would be present (considering that the pK_a of HN_3 = 4.70, under our experimental conditions (5 mol/equiv of NaN_3 in 2 mL/mmol of water) at pH 4.0 the concentration of azido ion would be ~0.4 M).[6]

In MeCN at 30 °C (Table 1, entries 1 and 2) the reaction did not work even with 30 mol % of catalyst. In water the process stereo- and regioselectively affords product **3** as a result of an anti attack of azido ion at C-β (**3**/**2** = 9:1). The aqueous medium alone, particularly at pH 7.0, shows a relevant beneficial effect (Table 1, entries 3 and 5 vs entry 1). In aqueous medium at pH 7.0, the $InCl_3$ is inoperative even if a large amount is used (Table 1, entry 3 vs 4). A fairly good catalytic effect of this metal salt was observed when working at pH 4.0, as can be noted by comparing the azidolyses performed in the presence and in the absence of $InCl_3$ at the same hydrogenionic concentration (Table 1, entry 5 vs 6). Because of the large amount of catalyst needed to obtain the desired results, this protocol is not acceptable for our goal, so we began to investigate the azidolysis of α,β-epoxycarboxylic acids.

Table 2. Azidolysis in Pure Water of α,β-Epoxycyclohexanecarboxylic Acid (4) Catalyzed by Various Salts; Reactions Stopped after 1.5 h



entry	catalyst[b]	pH[c]	C[d] (%)	C-β (%)	C-α (%)
1	none	7.0	15	80	20
2	$InCl_3$	7.0	25	>99	<1
3	$Yb(OTf)_3$	7.0	32	>99	<1
4	$Sc(OTf)_3$	7.0	17	>99	<1
5	none	4.0	10	>99	<1
6	$InCl_3$	4.0	>99	>99[e]	<1
7	$Yb(OTf)_3$	4.0	32	>99	<1
8	$Sc(OTf)_3$	4.0	30	>99	<1

[a] 5 mol/equiv. [b] 1 mol %. [c] Held constant for the entire reaction time.[20] [d] Reaction conversion. The percentage of **5** and **6** were determined by GC analyses of their methyl ester derivatives. [e] The regioisomer **6** was isolated in pure form in 95% yield, and its structure was proven as reported.[2,16]

The α,β-epoxycyclohexanecarboxylic acid (**4**) was taken as a model. We carefully examined the efficiency of various catalysts and the beneficial effect of the aqueous medium at different pH values, in comparison with MeCN, which is the most commonly used organic solvent in these transformations. All azidolyses were performed at 30 °C and using 5 mol/equiv of NaN_3.[20] The effectiveness using 1 mol % of $InCl_3$, $Sc(OTf)_3$, and $Yb(OTf)_3$ for the reactions performed in water at pH 7.0 and 4.0 are reported in Table 2. The reaction conversions were measured after 1.5 h. In the presence of the mentioned metal salts the *trans*-β-azido-α-hydroxycyclohexanecarboxylic acid (**6**) was always the sole reaction product. $Yb(OTf)_3$ and $Sc(OTf)_3$ had a slight influence on the process at either pH 7.0 or pH 4.0 (Table 2, entries 3, 4 vs 1 and 7, 8 vs 5). $InCl_3$ is barely active under neutral conditions (Table 2, entry 2 vs 1), whereas at pH 4.0, it efficiently catalyzes the azidolysis reaction, as proven by comparing the results with the azidolysis performed in the absence of $InCl_3$ at the same hydrogenionic concentration (Table 2, entry 6 vs 5).

The results of further investigations of the azidolysis of α,β-epoxycyclohexanecarboxylic acid (**4**) in the presence and absence of $InCl_3$ in MeCN and in pure water are illustrated in Table 3. In MeCN as reaction medium, the azidolysis did not work in the absence of $InCl_3$ (Table 3, entry 1), while with 1 mol % of the Lewis acid, the conversion of **4** is total after 8 h and only the *trans*-(C-β)-azido compound **6** was detected (Table 3, entry 2). With 30 mol % of $InCl_3$ the azidolysis was complete after 30 min (Table 3, entry 3). As for the azidolysis of methyl ester **1**, water per se has a beneficial effect for the epoxide

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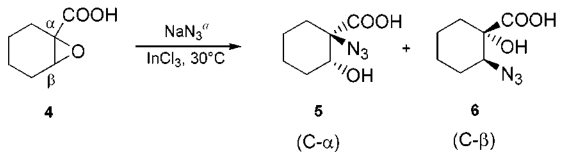
(20) The pH of a 2.5 M aqueous solution of NaN_3 (5 mol/equiv) containing the α,β-epoxyacid **4** (1 eq) is 4.5 and becomes 5.0 in the presence (0.01 mol/equiv) of $InCl_3$; the pH was then fixed at 4.0 or 7.0 by adding a 50% H_2SO_4 aqueous solution or a 5 M NaOH aqueous solution by a pH-stat (see Experimental Section). The same procedure was used for the epoxycarboxylic ester **1**.

Table 3. $InCl_3$-Catalyzed Azidolysis of α,*β*-Epoxycyclohexanecarboxylic Acid (4)



4 **5** (C-α) **6** (C-β)

entry	medium	pH[b]	$InCl_3$ (mol %)	*t* (h)	*C*[c] (%)	C-*β* (%)	C-α (%)
1	MeCN		none	8	7	>99	<1
2	MeCN		1	8	>99	>99	<1
3	MeCN		30	0.5	>99	>99	<1
4	H_2O	7.0	none	8	50	80	20
5	H_2O	7.0	1	8	89	>99	<1
6	H_2O	7.0	30	0.5	>99	98	2
7	H_2O	4.0	none	1.5	10	>99	<1
8	H_2O	4.0	none	8	38	>99	<1
9	H_2O	4.0	none	75	>99	>99	<1
10	H_2O	4.0	1	1.5	>99	>99	<1
11	H_2O	4.0	10	1/60	>99	>99	<1

[a] 5 mol/equiv. [b] Held constant for the entire reaction time.[20] [c] Reaction conversion. The percentage of **5** and **6** were determined by GC analyses of their methyl ester derivative; under catalytic conditions the product **6** was isolated with 95% yield. [d] After 8 h $C = 38\%$ and after 75 h $C > 99$.

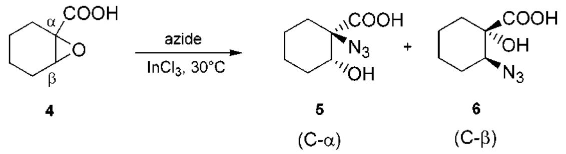
ring opening of **4**. After 8 h the reaction conversions in MeCN and in water at pH 7.0 and 4.0 were 7%, 50%, and 38%, respectively (Table 3, entries 1, 4, and 8).

The catalytic effect of $InCl_3$, quantified by comparing the reaction conversions of the $InCl_3$-catalyzed and uncatalyzed reactions in the same solvent after the same reaction time, was higher when the reaction was carried out in MeCN rather than in water under neutral conditions (Table 3, entries 1 vs 2, and 4 vs 5). This is due to the fact that water is a hard base and therefore hinders the complexation of an α,*β*-epoxyacid by the Lewis acid more than an organic solvent. This result is similar to that observed by Engberts et al. in the Diels–Alder cycloaddition in water of bidentate dienophile 3-phenyl-1-(2-pyridyl)-2-propen-1-one with cyclopentadiene catalyzed by $Cu(NO_3)_2$.[21, 22]

The above results show that the highest efficiency of $InCl_3$ was found when the azidolysis of **4** and its methyl ester **1** was performed in water at pH 4.0, but in the case of **4** far less catalyst was needed. When 1 mol % of $InCl_3$ was used, the reaction was complete in 1.5 h, and with 10 mol % the reaction was practically instantaneous (Table 3, entries 10 and 11), making this process much more intriguing for synthetic applications.

To exhaustively compare the efficiencies of the water/NaN_3 system and the organic system, azidolysis reactions were also performed in some representative organic solvents using NaN_3 or Me_3SiN_3 as the nucleophile source. $InCl_3$ (1 mol %)-catalyzed azidolysis of α,*β*-epoxycyclohexanecarboxylic acid (**4**) was carried out in different organic solvents under dry conditions and using the organic azide Me_3SiN_3. The results, compared with those obtained in water and MeCN, are reported in Table 4. In all cases the aqueous medium promotes the process much more efficiently than the organic solvents.

Table 4. $InCl_3$-Catalyzed (1 mol %) Azidolysis of α,*β*-Epoxycyclohexanecarboxylic Acid (4) with NaN_3 and Me_3SiN_3 in Various Solvents; Reactions Were Stopped after 1.5 h

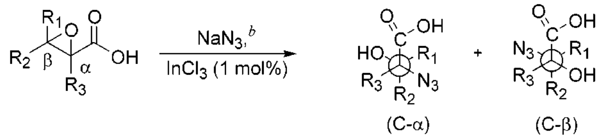


4 **5** (C-α) **6** (C-β)

entry	medium	azide[a]	C[b] (%)
1	H_2O[c]	NaN_3	>99
2	MeCN	NaN_3	40
3	CH_2Cl_2[d]	Me_3SiN_3	20
4	THF[d]	Me_3SiN_3	10
5	Et_2O[d]	Me_3SiN_3	3

[a] 5 mol/equiv. [b] Reaction conversion was determined by GC analysis of their methyl ester derivative; only the C-*β* regioisomer was detected. [c] At pH 4.0. [d] Dry conditions.

Table 5. $InCl_3$-Catalyzed Azidolysis in Water of the α,*β*-Epoxycarboxylic Acids at pH 4.0[a]



(C-α) (C-β)

entry	epoxide R₁	R₂	R₃	$InCl_3$ (mol %)	*T* (°C)	*t* (h)	*C*[c] (%)	C-*β* (%)	C-α (%)
1	H	Me	H	none	30	16	25	50	50
2	H	Me	H	1	30	10	>99	>99	<1
3	H	*n*-Pr	H	none	65	24	82	44	56
4	H	*n*-Pr	H	1	65	2	>99	>99	<1
5	H	Ph	H	none	30	1.5	12	>99	<1
6	H	Ph	H	10[d]	30	1 min	>99	>99	<1
7	H	Et	Me	none	30	8	20	>99	<1
8	H	Et	Me	1	30	8	>99	>99	<1
9	H	Ph	Me	none	65	20	>99	>99	<1
10	H	Ph	Me	1	65	2	>99	>99	<1
11	H	$-(CH_2)_4-$		none	30	75	>99	>99	<1
12	H	$-(CH_2)_4-$		1	30	1.5	>99	>99	<1
13	Me	Me	H	none	30	1.2	4	>99	<1
14	Me	Me	H	1	30	1.2	>99	>99	<1

[a] Held constant for the entire reaction time. [b] 5 mol/equiv. [c] Reaction conversion. The percentage of C-*β* and C-α products were determined by GC analyses of their methyl ester derivative; under catalytic conditions the products were isolated in 93–95% yield. [d] By using 1 mol % of catalyst the reaction time increases and decarboxylation of the α,*β*-epoxycarboxylic acid occurs.

The best reaction conditions (aqueous medium, 1 mol % $InCl_3$, 5 mol/equiv NaN_3, pH 4.0) (Table 2, entry 6) were then extended to the azidolysis of a variety of α- and *β*-substituted α,*β*-epoxycarboxylic acids. Table 5 illustrates the results obtained at 30 and 65 °C in the presence and absence of $InCl_3$. The $InCl_3$-catalyzed azidolyses are highly regio- and stereoselective and pure *anti*- or *trans*-(C-*β*)-adducts were easily isolated in 93–95% yield. The Brønsted acid catalysis was always negligible. The presence of a phenyl ring in the *trans* *β*-position of the oxirane ring (Table 5, entries 6 and 10) increases the substrate reactivity by favoring the decarboxylation of the starting α,*β*-epoxycarboxylic acid. To avoid this side reaction, the azidolysis of *trans*-cinnamic acid was carried out in the presence of 10 mol % of $InCl_3$ (entry 6).

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The data collected during this study show that $InCl_3$ is a particularly good catalyst for the azidolysis of α,β-epoxycarboxylic acids when the reaction is performed in water at pH 4.0. Under the same hydrogenionic concentration but in the absence of $InCl_3$, the process is slower and sometimes not regioselective. The catalytic efficiency of $InCl_3$ in water at pH 4.0 can be explained considering that the $pK_{1,1}$ of the hydrolysis reaction of the aqua ion $In(H_2O)_6^{3+}$ is 4.0.[18,19] At this pH value, the aqua ion species is prevalent, and we hypothesize that in water $In(H_2O)_6^{3+}$ can easily coordinate the α,β-epoxycarboxylic acid and the azide ion, forming a reactive complex. The azido ion is then transferred with high regio- and stereoselectivity to C-β of the oxirane ring via an internal delivery.

The catalytic efficiencies of $Yb(OTf)_3$ ($pK_{1,1} = 7.7$)[18,19] and $Sc(OTf)_3$ ($pK_{1,1} = 4.5-4.8$)[18,19] at either pH 4.0 or pH 7.0 are about the same for the azidolysis of α,β-epoxycarboxylic acid **4** (Table 2, entries 3 and 4 vs 1, and 7 and 8 vs 5).

This fact seems to be in contrast to a relationship between the aqueous medium pH and catalytic efficiency of metal salts such as Lewis acids. In fact, the catalytic efficiency of Lewis acid salts in water depends on two factors: (i) the pH of the reaction medium that must be equal to or below the $pK_{1,1}$ hydrolysis constant of the corresponding aqua ion (presence of the aqua ion) and (ii) the ability of the aqua ion to give an active complex with the reagents (affinity of the aqua ion). Thus $Yb(OTf)_3$ and $Sc(OTf)_3$ at pH 4.0, generate a high concentration of the aqua ion. At pH 4.0, the azido ion concentration is smaller than at pH 7.0, and the activity of these salts increases on going from neutral to acidic pH values (Table 2). However, the lack of reaction specificity considerably reduces their catalytic efficiency.

We also investigated the possibility to reusing the mother liquors from the workup of the reaction mixture, which contain the $InCl_3$. At the end of the reaction the final mixture must be acidified to pH 2.0 in order to efficiently remove the azido-hydroxycarboxylic acid. After extracting the reaction product the mother liquors can be reused after the pH is adjusted (see Experimental Section). The mother liquors were reused four times without loss of the reaction yield or selectivity.

Conclusions

Different Lewis acid catalysts, reaction media, and azides were used for the azidolysis of a variety α,β-epoxycarboxylic acids. The best protocol found uses an aqueous solution at pH 4.0 as the reaction medium, NaN_3 as the source of the azido group, and 1 mol % of $InCl_3$ as catalyst. Under these reaction conditions, *anti*-β-azido-α-hydroxycarboxylic acids with high regio- and diastereoselectivity (>99%) are obtained and can be easily isolated in pure form and with high yields (93−95%).

The best efficiency of $InCl_3$ as a catalyst in water is closely related to the $pK_{1,1}$ hydrolysis constant of the corresponding aqua ion ($pK_{1,1}$ $In(H_2O)_6^{3+} = 4.0$[6]) and in the azidolysis reactions is found at pH 4.0. The aqueous solution of $InCl_3$ after the workup can be recycled and reused and maintains its effectiveness for at least four transformations.

Experimental Section

General Procedures. CAUTION: *Azides can be very explosive compounds and should be handled with great care. During our study we encountered no problems.*[23] All chemicals were purchased and used without any further purification. Organic solvents were dried by conventional methods with the exception of MeCN, which was used without drying. GC analyses were performed with an SPB-5 fused silica capillary column (30 m, 0.25 mm diameter), an "on column" injector system, an FID detector, and hydrogen as the carrier gas. GC−MS analyses were carried out with 70 eV electron energy. The reaction products from the azidolysis of α,β-epoxycarboxylic acids were analyzed by GC as methyl ester derivatives obtained by treating them with an ether solution of CH_2N_2. ^1H and ^{13}C NMR spectra were recorded at 400 and 100.6 MHz, respectively, in $CDCl_3$ as solvent with TMS as internal standard. Reactions were carried out at a controlled pH value using a pH-stat apparatus with a combined refillable pH electrode. The β-azido-α-hydroxycarboxylic acids and their methyl ester derivatives are all known in the literature[2,16] with the exception of *anti*-3-azido-2-hydroxy-2-methyl-3-phenylpropionic acid, which is a new compound and is described below.

Azidolysis of α,β-Epoxycyclohexanecarboxylic Acid (4) Catalyzed by $InCl_3$ (1 mol %) in Water at pH 4.0 (Table 2, entry 6). α,β-Epoxycyclohexanecarboxylic acid (**4**) (1.0 mmol) was dissolved in water (2 mL) in a flask thermostated at 30 °C, equipped with a magnetic stirrer and with a pH-stat apparatus, and under stirring powdered NaN_3 (5.0 mmol) was added to the mixture. An aqueous 0.5 M solution of $InCl_3$ (0.01 mmol in 20 μL of water) was added, and the resulting pH was adjusted to 4.0 with 100 μL of a 50% H_2SO_4 aqueous solution. During the reaction, the pH was kept constant by the pH-stat by adding a 50% H_2SO_4 aqueous solution (100 μL). After 1.5 h the reaction mixture was cooled to 0 °C, acidified to pH 2.0 by adding some drops of a 50% H_2SO_4 aqueous solution, and extracted with Et_2O (×3). The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure to give the pure *trans*-β-azido,α-hydroxycyclohexanecarboxylic acid **6**,[2] which was isolated in 95% yield.

Azidolysis of α,β-Epoxycyclohexanecarboxylic Acid (4) Catalyzed by $InCl_3$ (30 mol %) in MeCN (Table 3, entry 3). α,β-Epoxycyclohexanecarboxylic acid (**4**) (1.0 mmol) was dissolved in MeCN (2 mL) in a flask thermostated at 30 °C, equipped with a magnetic stirrer, and under stirring powdered NaN_3 (5.0 mmol) was added. Next, 0.3 mmol of powdered $InCl_3$ was added to the resulting mixture. After 30 min the reaction mixture was cooled to 0 °C, 2 mL of water was added, and the mixture was acidified to pH 2.0 by adding a few drops of 50% H_2SO_4 aqueous solution and then extracted with Et_2O (×3). The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure to give the pure *trans*-β-azido-α-hydroxycyclohexanecarboxylic acid **6**, which was isolated in 95% yield.

Azidolysis of α,β-Epoxycyclohexanecarboxylic Acid (4) Catalyzed by $InCl_3$ (1 mol %) in Organic Solvents (Table 4, entries 3−5). Under nitrogen atmosphere, α,β-epoxycyclohexanecarboxylic acid (**4**) (1.0 mmol) and 0.01 mmol of powdered $InCl_3$ were dissolved in a dry organic solvent (CH_2Cl_2, THF, or Et_2O) (2 mL) in a flask thermostated at 30 °C, equipped with a magnetic stirrer, and under stirring Me_3SiN_3 (5.0 mmol) was added. After 1. 5 h the reaction mixture was cooled to 0 °C, 2 mL of water was added, and the mixture was acidified to pH 2.0 by adding a few drops of 50% H_2SO_4 aqueous solution and then extracted with Et_2O (×3). The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure to give a mixture of **4** and **6** as reported in Table 4.

***anti*-3-Azido-2-hydroxy-2-methyl-3-phenylpropionic Acid.** Prepared in 95% yield, at pH 4.0 (Table 5, entry 10) by using 1 mol % of $InCl_3$ according to the procedure described for **4**: mp = 122−123 °C from CH_2Cl_2/*n*-hexane 5:95; IR (CCl_4) ν = 3066, 3022, 2928, 2943, 2621, 2108, 1714, 1491, 1451, 1161, 964; ^1H NMR δ 1.59 (*s*, 3H, Me), 4.76 (*s*, 1H, C-3), 7.31−7.51 (*m*, 5H, Ar); ^{13}C NMR δ 23.1, 70.9, 77.9, 128.8, 129.2, 129.8, 136.7, 175.6; MS (EI, 70 eV) *m*/*z* 221 (M^+, 5), 220 (15), 194 (100), 165 (20), 116 (23), 89 (40), 77 (18). Anal. Calcd for $C_{10}H_{11}N_3O_3$: C 54.29, H 5.01, N 19.00. Found: C 54.27, H 5.05, N 18.97.

Reuse of the Catalyst (1 mol %). Powdered NaN_3 (5 mmol) was added to the remaining mother liquors (ca. 2 mL) after extraction of β-azido-α-hydroxycarboxylic acid. α,β-Epoxycarboxylic acid (1 mmol) was then added, and the pH of the reaction medium was adjusted to 4.0 by 50% H_2SO_4 aqueous solution (ca. 100 μL). The resulting mixture was stirred at the temperature for the time indicated in Table 5, and the pH was kept at the 4.0 value by using a pH-stat. The final mixture was then worked up as indicated in the typical procedure. The mother liquors were reused four times without loss of reactivity and selectivity.

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