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Zeo-Click Chemistry: Copper(I)–Zeolite-Catalyzed Cascade Reaction; One-Pot Epoxide Ring-Opening and Cycloaddition

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Dedicated to Professor Gregorio Asensio on his 60th birthday

Keywords: Alkynes / Copper / Click chemistry / Multicomponent reactions / Regioselectivity / Zeolites

Copper(I)-modified zeolites, especially Cu^{I}–USY, proved to be very efficient catalysts in multi-component reactions of epoxides with sodium azide and terminal alkynes. Such catalysts allow highly regio- and stereoselective syntheses of hydroxymethylated triazoles. These heterogeneous, modified zeolites can easily be recovered and reused. Moreover, the cascade reaction was best performed in water at room temperature, rendering all the processes truly green. Detailed investigations revealed the role the Cu^{I}-modified zeolites play both during the epoxide ring-opening and cycloaddition steps.

Introduction

The construction of complex architectures through an intermolecular union of simple starting materials in a one-pot operation still represents significant synthetic challenges. Such transformations, in which a product is assembled through a cascade of elementary chemical reactions, are called multi-component reactions (MCRs) and have been the focus of many interesting achievements in recent years.[1] MCRs are inherently "green" since they are convergent, exhibit economy of steps and are usually atom-economic, most of the incoming atoms being linked together in a single product. If such reactions could be run in innocuous solvents and be promoted by catalysts that can be recycled, such as heterogeneous catalysts, they would thus comply with most of the Green Chemistry principles.[2]

Within this Green Chemistry context, we are currently exploring the scope and limitations of metal-doped zeolites as catalysts for organic synthesis. We recently demonstrated that cycloadditions, such as the Huisgen and the Dorn reactions leading to triazoles and pyrazolines, respectively, could be catalyzed by Cu^{I}–zeolites in a very efficient way, with the catalysts being recyclable several times (Figure 1a and b).[3,4] We also demonstrated that Cu^{I}–zeolites can catalyze a number of coupling reactions, such as the homocoupling of terminal alkynes (Figure 1c).[5] This set of reactions led us to propose the new "zeo-click" concept (Figure 1),[6] in analogy to the "click chemistry" principles developed by Sharpless.[7]

We are now merging both domains, looking for the first zeo-click MCR. Very recently, we showed that Cu^{I}–zeolites are excellent catalysts for the three-component synthesis of propargylamines (Figure 1d).[8] Now, we report that Cu^{I}–zeolites catalyze another cascade reaction, starting from epoxides. The latter react with terminal alkynes and sodium azide in the presence of catalytic amounts of Cu^{I}–zeolites, leading to hydroxymethylated 1,4-disubstituted 1,2,3-triazoles in a one-pot, two-step, three-component process (Figure 1e). The functionalized heterocycles thus produced are useful compounds that can be used to selectively open calcium channels in cells,[9] to inhibit enzymes,[10] and to regulate plant growth.[11] They have also been used as peptide mimics[12] and as key components in materials, such as conducting or energetic polymers,[13,14] or spin-based materials.[15]

Sodium azide ring-opening of epoxides is a well-known reaction that usually leads to mixtures of β-hydroxy azides,[16] which are usually further converted into 1,2-amino alcohols or α-amino acids.[17] Various approaches have been developed to achieve high regioselectivity under mild conditions, especially through the use of Lewis acids (Scheme 1),[18] although water alone also promotes this ring-opening, depending on temperature and pH.[19]

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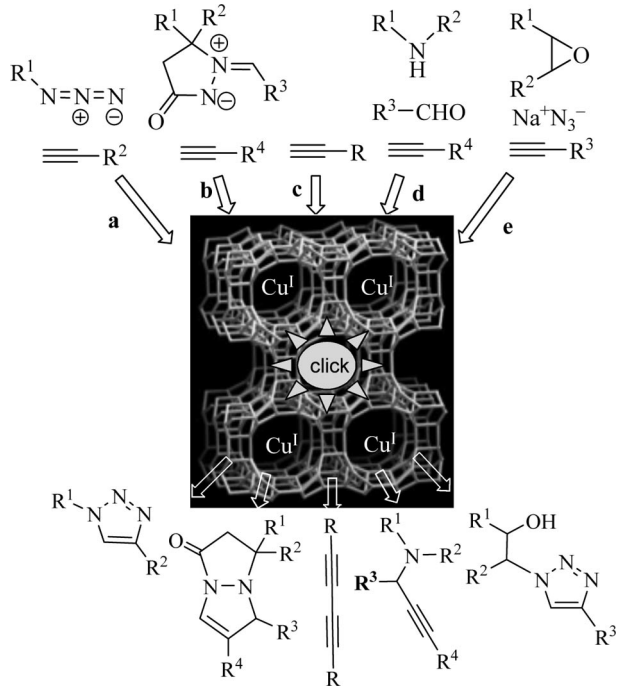
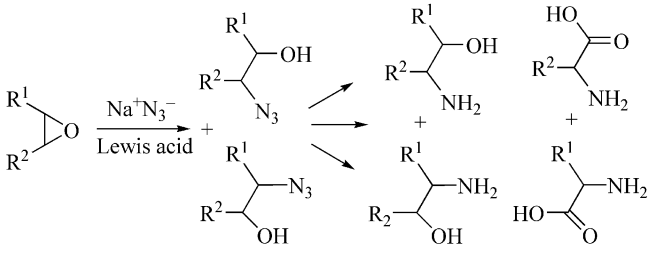


Figure 1. The zeo-click concept, with Cu^{I}–zeolites as catalyst.



Scheme 1. Sodium azide mediated opening of epoxides and synthesis of 1,2-amino alcohols or α-amino acids.

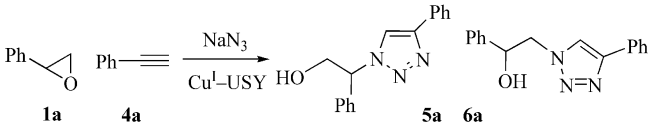
Although never previously explored, Cu^{I}–zeolites should catalyze such ring-opening reactions, with the copper(I) loaded into the zeolite acting as a Lewis acid. Because we demonstrated that Cu^{I}–zeolites can catalyze the cycloaddition of azides with terminal alkynes,[3] we reasoned that a one-pot cascade reaction should be accessible that would convert epoxides into functionalized triazoles under the action of this type of heterogeneous catalyst (Scheme 2).[20] Moreover, the discriminatory properties of zeolites would be beneficial to this reaction. The different sizes and shapes of the zeolite frameworks would alter the regioselectivity of the ring-opening step, either enhancing or reversing it, depending on the zeolite used. It is worth noting that this Cu^{I}–zeolite-catalyzed cascade reaction would be the first to be promoted by a heterogeneous catalyst.[21]

Results and Discussion

Conditions

To explore the feasibility of this zeo-click MCR for epoxides, we first selected styrene oxide as the starting material, because this reaction is the literature benchmark for epoxide ring-opening. Because most of the preceding reactions with Cu^{I}–zeolites were best performed with Cu^{I}–USY, we first used this modified zeolite to screen the reaction conditions. The behavior of styrene oxide was thus examined in the presence of phenylacetylene, sodium azide, and Cu^{I}–USY in various polar solvents, which were selected to minimize solubility problems and favor epoxide ring-opening (Table 1).

Table 1. Establishing optimal conditions.[a]

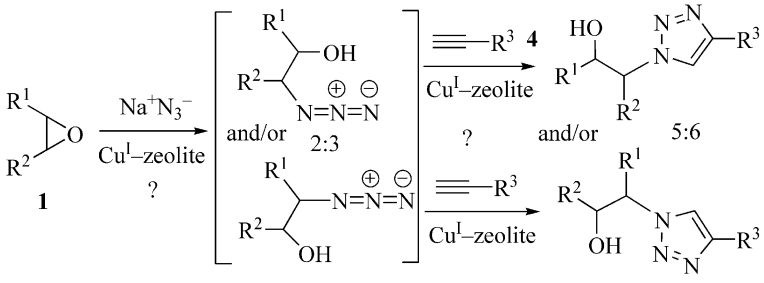


1a 4a 5a 6a

Entry	Solvent	Temp. [°C]	Time [h]	Ratio	Yield [%][b,c]
1	THF	20	20	–	0
2	THF	66	20	–	traces
3	DMF	20	20	–	0
4	DMF	100	20	–	traces
5	MeOH	20	20	–	traces
6	MeOH	78	20	86:14	52
7	H_2O	20	20	94:6	77
8	H_2O	90	2	96:4	83

[a] Reaction performed on 1 mmol of each component with a zeolite loading of 20 mg.[22] [b] Yields of products purified by chromatography. [c] The ring-opening product was also recovered.

In solvents of medium polarity, such as tetrahydrofuran (THF), no transformation took place regardless of the temperature (Table 1, Entries 1 and 2). Surprisingly, highly polar but aprotic solvents, such as *N*,*N*-dimethylformamide (DMF), led to the same lack of reaction. In sharp contrast, protic solvents were able to promote the expected cascade



Scheme 2. One-pot Cu^{I}–zeolite-catalyzed ring-opening of epoxides and subsequent cycloaddition.

reaction, leading to a mixture of regioisomeric hydroxymethylated 1,4-disubstituted triazoles in medium to high yields (Table 1, Entries 5–8). Methanol required heating to give a mixture of isomers in reasonable yield (Table 1, Entry 6 vs. 5). Water proved to be the best choice; in this solvent, good yield and very high regioselectivity were achieved even at room temperature (Table 1, Entry 7). Heating improved both the regioselectivity and the yield, while dramatically accelerating the reaction (Table 1, Entry 8 vs. 7).

The major regioisomer resulted from epoxide ring-opening at the benzylic position, as revealed by the NMR shifts of the corresponding proton signal compared with that of the alternative isomer (δ = 5.67 vs. 5.23 ppm). It is worth noting that the regioselectivity achieved under such conditions (95:5 on average; Table 1, Entries 7–8) is better than the 85:15 regioselectivity observed for the ring-opening of styrene oxide promoted by PEG,[20a] suggesting a role for the Cu^I–zeolite in the ring-opening step of the present cascade reaction.

Catalysts

Water was thus selected as the reaction medium, and reactions were performed at room temperature to save energy and to create the mild conditions required to better comply with established "green principles". Under these conditions, the influence of the internal structure of the zeolite was then investigated with a series of Cu^I–zeolites, which were screened and compared as catalysts for the same reaction (Table 2).

Control experiments showed that no product was formed without catalyst or with copper(I) chloride alone, even after prolonged reaction times (Table 2, Entries 1 and 2). In contrast, every zeolite examined proved to be efficient as catalyst, although variations in efficiency and selectivity were observed (Table 2, Entries 3–7). Cage-type zeolites, having the largest pore size, were better catalysts than the smaller channel-type zeolites (Table 2, Entries 3 and 4 vs. 6 and 7).

Size discrimination was nevertheless not the sole factor, because Cu^I–mordenite, which exhibits small pores in one of its channel systems, proved to be almost as effective as Cu^I–USY in terms of both efficiency and regioselectivity (Table 2, Entry 5 vs. 3). However, the Si/Al ratio of the zeolites also seems critical (Figure 2). A high ratio was clearly deleterious, whereas a very low ratio also diminished the catalyst efficiency; an optimum was found to exist for USY.

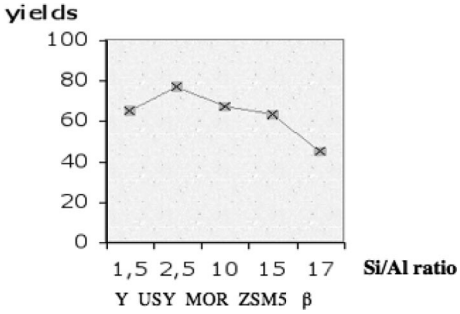


Figure 2. Correlation between Cu^I–zeolite acidities and yields.

In terms of regioselectivity, it seems that the most active zeolite catalysts were also the most selective ones (Table 2, Entries 3 and 5 vs. 4 and 6–7). Again, the Si/Al ratio clearly showed an optimum in the 3–10 range, corresponding to the USY and MOR zeolites (Figure 3).

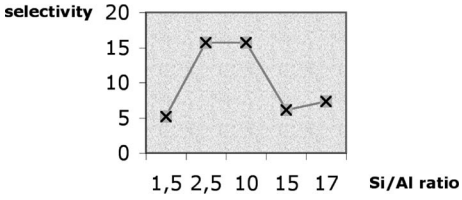
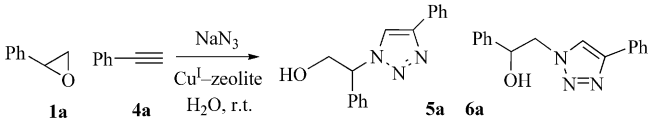


Figure 3. Correlation between Cu^I–zeolite acidities and regioselectivities.

Table 2. Optimizing the zeolite catalysts.[a]



Entry	Catalyst	Topology	Pore size [Å]	Number of acidic sites [mmol/g][b]	Time	Ratio **5a/6a**	Yield[c] [%]
1	none	–	–	–	3 d	–	0[d]
2	CuCl	–	–	–	3 d	–	traces[d]
3	Cu^I–USY	cage-type	7.4 × 7.4	4.39	22 h	94:6	77
4	Cu^I–Y	cage-type	7.4 × 7.4	6.67	22 h	84:16	65
5	Cu^I–MOR	channel-type	7.6 × 6.4 5.5 × 5.5	1.48	22 h	94:6	67
6	Cu^I–ZSM5	channel-type	5.1 × 5.5 5.3 × 5.6	1.04	22 h	86:14	63
7	Cu^I-β	channel-type	6.5 × 7.0 3.4 × 3.8	0.90–1.23	22 h	88:12	45[d]

[a] Reaction was performed with styrene oxide (1 mmol), phenylacetylene (1 mmol), NaN_3 (1.2 mmol), 20 h, with a zeolite loading[22] of 20 mg (ca. 0.08 mmol Cu^I). [b] For the corresponding acid zeolite. [c] Yields of products purified by chromatography. [d] The ring-opened product was also recovered.

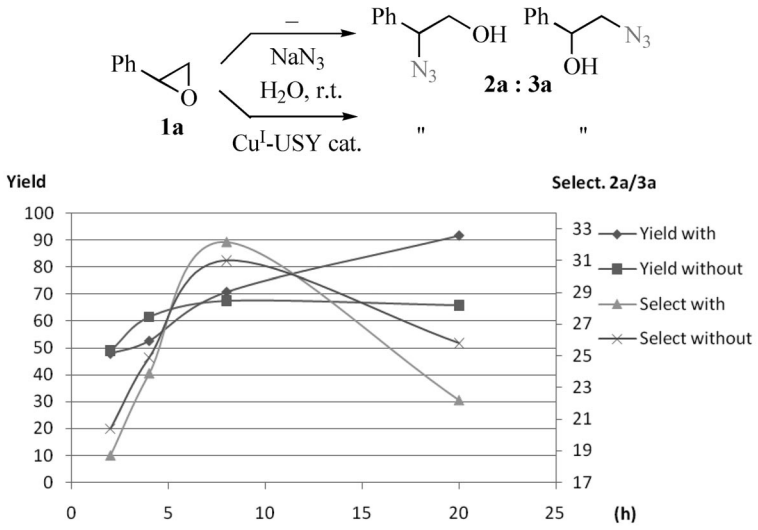


Figure 4. Role of Cu^{I}–zeolite in epoxide ring-opening: Yield and regioselectivity (select) in styrene oxide ring-opening by sodium azide in the absence or presence of Cu^{I}–USY.

Further control experiments conducted without alkyne revealed that the epoxide ring-opening reaction took several hours and that Cu^{I}–zeolites clearly improved this reaction (Figure 4). Indeed, without catalyst, the ring-opening reaction of styrene oxide stopped at 60% conversion after 5 h, whereas a classical evolution occurred in the presence of Cu^{I}–USY as catalyst, reaching complete conversion after 20 h. However, the regioselectivity did not dramatically change with or without catalyst.

These results confirmed that Cu^{I}–zeolites indeed play a role in the epoxide ring-opening step of the cascade reaction they catalyzed.

Recycling

As expected, Cu^{I}–zeolites were easily separated by simple filtration through a Nylon membrane. A simple wash allowed the organic materials and the zeolite to be recovered.

The same reaction with styrene oxide was then performed several times by using the same batch of Cu^{I}–USY as catalyst. After each run, the catalyst was recovered by filtration and reused in the next run with or without regeneration by heating before being reused. As shown in Figure 5, the Cu^{I}–USY catalyst could be recycled five times without dramatic changes when the catalyst was regenerated; a net decrease in efficiency was observed after three runs without regeneration. The regioselectivity was not affected in these successive reactions.

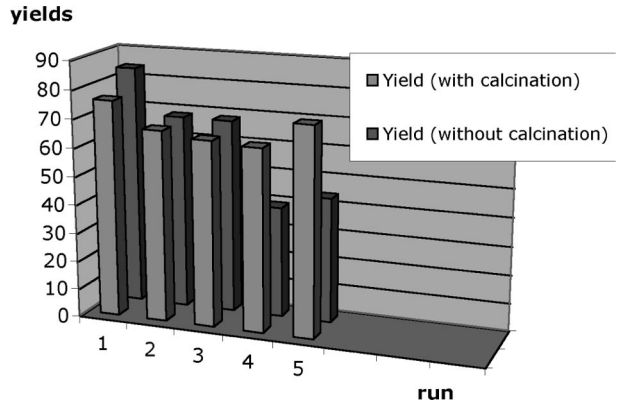


Figure 5. Recycling of Cu^{I}–USY with (front row) and without (back row) heating before each run. The reactions were performed with styrene oxide and phenylacetylene under the conditions described above.

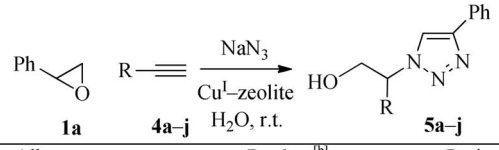
Scope and Limitations

With the optimized conditions in hand, we examined the scope and limitations of this zeo-click MCR starting from epoxides. Various alkynes were allowed to react with styrene oxide in the presence of Cu^{I}–USY as catalyst in water at room temperature (Table 3). Under these conditions, tolylacetylene gave the same regioselectivity as phenylacetylene but with higher yield (Table 3, Entry 2 vs. 1), suggesting some electronic influence of the electron-donating methyl group. However, the corresponding electron-deficient (trifluorophenyl)acetylene gave an even better yield as well as displaying a better regioselectivity (Table 3, Entry 3 vs. 1), thus ruling out electronic effects in such a cascade reaction. Indeed, aliphatic alkynes reacted in a manner similar to phenylacetylene, giving the corresponding hydroxymethylated triazoles with mostly the same yields and selectivities (Table 3, Entries 4 and 5 vs. 1). Interestingly, aliphatic diynes could be fully converted into the corresponding bis-(hydroxymethyl)triazole, with a high overall yield taking into account the four steps involved in this cascade (Table 3, Entry 6). No monotriazole intermediate could be detected in this reaction.

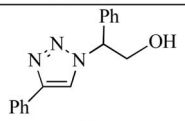
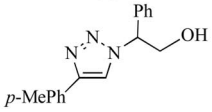
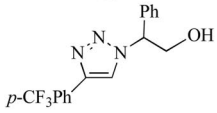
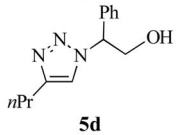
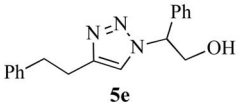
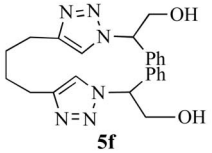
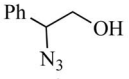
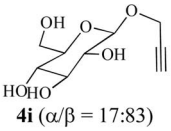
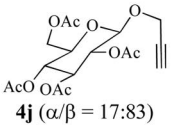
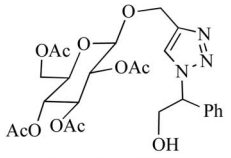
As expected from our earlier zeo-click studies,[3] neither alkynes carrying a free acid function nor disubstituted alkynes reacted, and only the epoxide ring-opening products were recovered (Table 3, Entries 7 and 8, respectively).

Although fully soluble in the aqueous reaction medium, propargylated, unprotected carbohydrates did not react significantly regardless of the temperature, which is again in

Table 3. Scope of the cascade reaction catalyzed by Cu^I–USY.[a]



1a 4a–j 5a–j

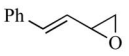
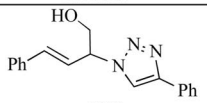
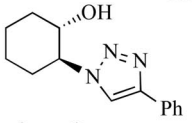
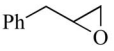
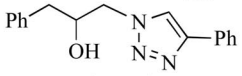
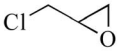
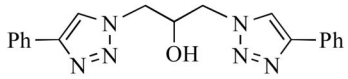
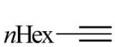
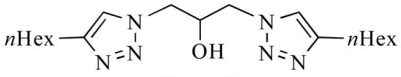
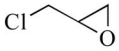
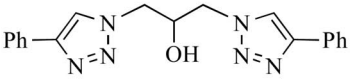
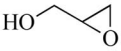
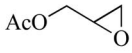
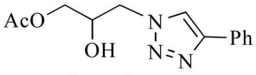
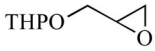
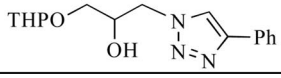
Entry	Alkyne	Product[b]	Ratio	Yield (%)[c]
1	Ph— **4a**	 **5a**	94:6	77
2	*p*-MePh— **4b**	 **5b**	94:6	88
3	*p*-CF_3Ph— **4c**	 **5c**	98:2	92
4	*n*Pr— **4d**	 **5d**	96:4	79
5	Ph **4e**	 **5e**	93:7	84
6	**4f**	 **5f**	93:7	57
7	HOOC **4g**	 **2a**	–	98
8	Ph—CONHPh **4h**	**2a**	–	98
9	 **4i** (α/β = 17:83)	–	–	traces
10		–	–	traces[d]
11	 **4j** (α/β = 17:83)	 **5g** (α/β = 17:83)	94:6	94[e]

[a] Reaction performed with styrene oxide (1 mmol), alkyne (1 mmol), and NaN_3 (1.2 mmol), 20 h, with a zeolite loading[22] of 20 mg (ca. 0.08 mmol Cu^I). [b] Only the major regioisomer is represented. [c] Yields of isolated products after chromatography; the intermediate ring-opening product (**2a**) accounted for the mass balance. [d] Performed at 95 °C. [e] A co-solvent (toluene) was required.

agreement with our earlier studies (Table 3, Entries 9 and 10). The corresponding protected carbohydrates only reacted when a co-solvent was added to the reaction mixture for solubility reasons, and high yield and regioselectivity were thus achieved (Table 3, Entry 11). It is worth noting that no epimerization occurred at the anomeric center under such conditions.

The reactivities of various epoxides were then examined by submitting them to the reaction with phenylacetylene under the same conditions (Table 4). Vinylepoxides reacted

Table 4. Scope of the cascade reaction catalyzed by Cu^{I}–USY.[a]

Entry	Epoxide		Alkyne		Product[b]		Ratio	Yield (%)[c]
1		**1b**		**4a**		**5h**	100:0	59
2		**1c**		**4a**		**5i**	–	65[d]
3		**1d**		**4a**		**5j**	0:100	58
4		**1e**		**4a**		**9a**	–	48[e]
5				**4k**		**9b**	–	40[e]
6		**1e**		**4a**		**9a**	–	67[f]
7		**1f**		**4a**	–	–	–	traces[g]
8				**4k**	–	–	–	traces[g]
9		**1g**		**4a**		**5k**	0:100	70
10		**1h**		**4a**		**5l**	0:100	34[h]

[a] Reaction performed with epoxide (1 mmol), alkyne (1 mmol), and NaN_3 (1.2 mmol), 20 h, with a zeolite loading[22] of 20 mg (ca. 0.08 mmol Cu^{I}). [b] Only the major isomer is represented. [c] Yields of isolated products after chromatography; the intermediate ring-opening product accounted for the mass balance. [d] Prolonged reaction time (60 h) was required. [e] See text. [f] NaN_3 (3 equiv.) and alkyne (3 equiv.) were used. [g] Without or with various co-solvents (dichloromethane, toluene). [h] An unidentified oligomeric by-product was also formed.

similarly to styrene oxide, except that the reaction was even more regioselective. From (*E*)-4-phenyl-1,2-epoxybut-3-ene (**1b**), a single regioisomer was produced. Comparison of the NMR spectroscopic data with those of known compounds[23] revealed that the ring-opening step only occurred at the allylic position (Table 4, Entry 1). This result is in sharp contrast with conventional aminolysis of vinyl epoxides, which yield the other regioisomer, i.e., the amino allylic alcohol.[24]

Nonconjugated epoxides were also converted into the corresponding hydroxymethylated triazoles, although in variable yields, depending on the epoxide structures (Table 4, Entries 2–10). 1,2-Epoxycyclohexane (**1c**) smoothly gave the ring-opened and click-cyclized product **5i**. The latter was obtained with high *trans* selectivity, suggesting the occurrence of an S_N2 pathway for the epoxide ring-opening step, as expected (Table 4, Entry 2). Similarly, 3-phenyl-1,2-epoxypropane (**1d**) gave a single regioisomer corresponding to opening at the terminal epoxide carbon atom, in agreement with a pure S_N2 pathway (Table 4, Entry 3). Compared to conjugated epoxides, the regioselectivity was reversed in favor of the less hindered isomer, probably for electronic as well as steric reasons.

Epichlorohydrin (**1e**) also reacted well, both with aromatic and aliphatic alkynes, the latter being less reactive than the former. Surprisingly, the reaction proved to be more complex than anticipated, and control experiments without alkyne were performed to gain a better understanding of this reaction.

When styrene oxide and sodium azide (1:1.2 molar ratio) were mixed at room temperature in deuterated water in the presence of Cu^{I}–USY, NMR spectroscopic analysis revealed that three new compounds were produced. However, solubility differences between these compounds did not allow accurate quantification. Thus, a series of experiments were performed under the same conditions and stopped by

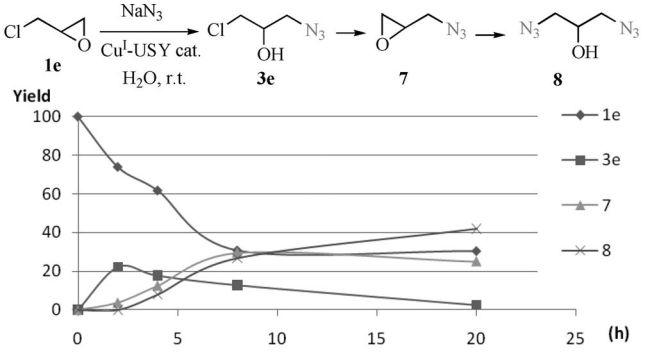
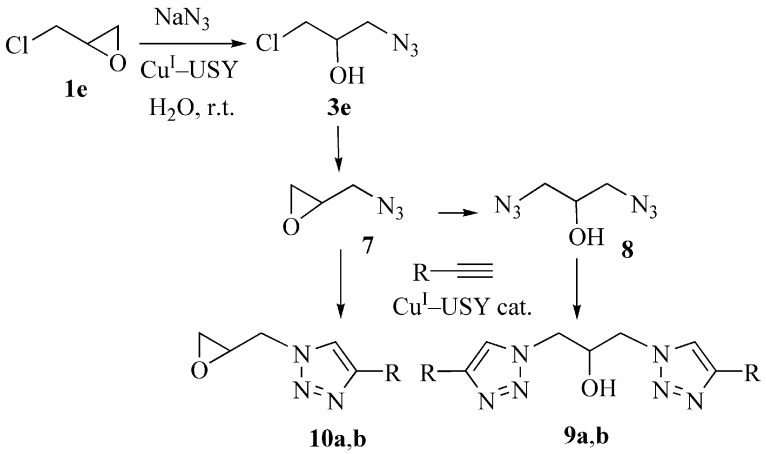


Figure 6. Reaction of epichlorohydrin without alkyne in the presence of sodium azide and Cu^{I}–USY as catalyst; evolution of the mixture.



Scheme 3. Cu^I–zeolite-catalyzed cascade reaction observed upon epichlorohydrin treatment with sodium azide, alkyne, and Cu^I–USY as catalyst.

extraction at different times; the products were then quantified by NMR spectroscopic analysis of the crude material and of the pure material after purification (Figure 6). The product **3e**, resulting from the expected ring-opening at the less substituted epoxide end, was initially formed but, soon after, the formation of a new epoxide **7**, corresponding to ring-closing of the chlorohydrin **3e**, was observed. After 2 h, the ring-opening product of this new epoxide, the diazide **8**, was also formed. Due to the ratio of styrene oxide and sodium azide used, the reaction stopped at approximately 60% conversion.

Under the same conditions, but in the presence of aromatic or aliphatic alkyne, a mixture of compounds was produced, with the bis(triazoles) **9a** and **9b** formed as the major products (Table 4, Entries 4 and 5). Nevertheless, the diazido alcohol **8** and the new epoxytriazole **10** could also be isolated as minor products in approximately 15 and 7% yield, respectively (Scheme 3). The bis(triazoles) **9a** and **9b** clearly arose from reaction with the intermediate diazido alcohol **8**, whereas the epoxytriazole **10** came from the azido epoxide **7**, which is the precursor of **8**. Such a complex cascade seemed unprecedented, although epichlorohydrin ring-opening has been reported.[18,20] This behavior further illustrates the role of Cu^I–zeolites in the cascade reaction.

With higher molar ratios of sodium azide, alkyne, and epichlorhydrin, the formation of the double ring-opening and double click product **9a** was favored, and this significantly improved the yield of isolated product (Table 4, Entry 6).

The more water-soluble 2,3-epoxypropan-1-ol surprisingly proved to be poorly reactive, giving only traces of adducts regardless of the nature of the alkyne, even in the presence of co-solvents (Table 4, Entries 7 and 8). This is reminiscent of the results observed with unprotected carbohydrate (see Table 3, Entries 9 and 10). In contrast, the corresponding acetylated derivative reacted well and with a very high regioselectivity (Table 4, Entry 9), revealing the importance of electronic effects in this series. The corresponding tetrahydropyranyl derivative also gave the expected product, again with very high regioselectivity, but with modest yield due to the formation of oligomeric species (Table 4, Entry 10).

Conclusions

Cu-modified zeolites, especially Cu^I–USY, proved to be very efficient catalysts for the one-pot synthesis of hydroxymethylated 1,4-substituted triazoles from epoxides, alkynes, and sodium azide.

Such heterogeneous catalysts can easily be recovered and reused up to five times without severe loss in efficiency, provided the catalyst is activated between each run. This Cu^I–zeolite-catalyzed cascade reaction proved to be highly regio- and stereoselective and tolerated a wide range of functional groups.

Performed in water and at room temperature with Cu^I–zeolites as heterogeneous catalysts, the present multi-component reaction of epoxides with sodium azide and terminal alkynes complies with most "Green Chemistry" principles.

Detailed investigations revealed the role that Cu^I-modified zeolites played both during the epoxide ring-opening and the cycloaddition steps.

Experimental Section

General: All starting materials were commercially available and were used as received. The reactions were monitored by thin-layer chromatography (TLC), carried out on silica plates (silica gel 60 F_{254}, Merck) by using UV light and *p*-anisaldehyde for visualization. Column chromatography was performed on silica gel 60 (0.040–0.063 mm, Merck) by using mixtures of ethyl acetate and cyclohexane as eluents. Evaporation of solvents were conducted under reduced pressure at temperatures below 30 °C unless otherwise noted. Melting points were measured in open capillary tubes. ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance 300 spectrometer at 300 and 75 MHz, respectively. Chemical shifts (δ) and coupling constants (J) are given in ppm and Hz, respectively. Chemical shifts are reported relative to residual solvent as an in-

ternal standard ($CDCl_3$: δ = 7.24 ppm for ^1H and δ = 77.23 ppm for ^{13}C). Carbon multiplicities were determined by DEPT 135 experiments. Electron impact (EI) and electrospray (ESIMS) low/high-resolution mass spectra were obtained from the Mass Spectrometry Department of the Institut de Chimie, Strasbourg.

Preparation of Cu^I-USY:[25] Commercial NH_4–USY was placed in an oven and heated at 550 °C for 4 h to give H–USY. Subsequently, H–USY (1 g) and CuCl (475 mg, 1.1 equiv.) were mixed by using a mortar and charged in a closed reactor. The mixture of powders was heated at 350 °C for 3 d under a nitrogen flow, quantitatively yielding Cu^I–USY.

General Procedure for the Cu^I–Zeolite-Catalyzed, One-Pot Reaction of Epoxides and Terminal Alkynes: To a suspension of Cu^I–USY (20 mg, 0.07 equiv.) in H_2O (3 mL) were successively added epoxide **1** (1.0 mmol, 1.0 equiv.), sodium azide (1.2 mmol, 1.2 equiv.), and then alkyne **4** (1.2 mmol, 1.2 equiv.). After 20 h of stirring at 20 °C, the mixture was diluted with ethyl acetate (5 mL), the catalyst was removed by filtration, and the solvent was evaporated to provide the crude product (usually ca. 95% purity as judged by NMR spectroscopic analysis). Column chromatography was then performed.

Some of the adducts are known compounds, and triazoles **5a**,[20] **6a**,[21] **5b**,[20,21] **5i**,[3b] **9a**,**b**,[26] and **10**[27] have been reported, as have intermediates **7**[28] and **8**.[29]

Preparation of 2-(Oxiran-2-ylmethoxy)tetrahydro-2*H*-pyran (1i): In a 50 mL round-bottom flask were dissolved *m*-chloroperbenzoic acid (1.45 g, 8.45 mmol, 1.2 equiv.) and sodium hydrogen carbonate (0.72 g, 8.5 mmol, 1.21 equiv.) in $CHCl_3$ (20 mL), and the resulting solution was cooled to 0 °C in an ice bath. To this cold solution was added 2-(allyloxy)tetrahydro-2*H*-pyran (1 g, 7.04 mmol), and the reaction mixture was stirred at 0 °C for 16 h. The reaction mixture was then transferred to a separatory funnel and washed with aqueous NaOH (10%, 2 × 20 mL) and with distilled water. The organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuum. The product was purified by column chromatography (*c*Hex/Et_2O, 80:20 with 1% of Et_3N) to give pure **1i** as a colorless liquid. Yield: 403 mg (36%). NMR spectroscopic analysis of the product showed the presence of two diastereoisomers in a 1:1 ratio. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.63 (ddd, $^3J_{H,H}$ = 7, $^3J_{H,H}$ = 4, $^4J_{H,H}$ = 3 Hz, 1 H), 3.92 (dd, $^3J_{H,H}$ = 12, $^3J_{H,H}$ = 3 Hz, 0.5 H), 3.88–3.79 (m, 1 H), 3.74–3.63 (m, 1 H), 3.52–3.45 (m, 1 H), 3.37 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 6 Hz, 0.5 H), 3.19–3.13 (m, 1 H), 2.78 (ddd, $^2J_{H,H}$ = 5, $^3J_{H,H}$ = 4, $^4J_{H,H}$ = 2 Hz, 1 H), 2.66 (dd, $^2J_{H,H}$ = 5, $^3J_{H,H}$ = 3 Hz, 0.5 H), 2.57 (dd, $^2J_{H,H}$ = 5, $^3J_{H,H}$ = 3 Hz, 0.5 H), 1.84–1.47 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 99.1 (CH), 98.9 (CH), 68.7 (CH_2), 67.5 (CH_2), 62.4 (CH_2), 62.2 (CH_2), 51.1 (CH), 50.8 (CH), 44.8 (CH_2), 44.7 (CH_2), 30.7 (CH_2), 30.6 (CH_2), 25.6 (CH_2), 19.5 (CH_2), 19.4 (CH_2) ppm. HRMS: calcd. for $C_8H_{14}O_2Na^+$ 165.089; found 165.086.

2-Phenyl-2-{4-[4-(trifluoromethyl)phenyl]-1*H*-1,2,3-triazol-1-yl}ethanol (5c): Isolated yield: 302 mg (92%); white solid; m.p. 108 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.87 (s, 1 H), 7.72 (d, $^3J_{H,H}$ = 8 Hz, 1 H), 7.52 (d, $^3J_{H,H}$ = 8 Hz, 2 H), 7.35–7.26 (m, 5 H), 5.73 (dd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 4 Hz, 1 H), 4.61 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 8 Hz, 1 H), 4.36 (br. s, 1 H), 4.23 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 146.0 (C), 135.9 (C), 133.6 (C), 130.2 (q, $^1J_{C,F}$ = 33 Hz, 1 C), 129.2 (2 CH), 129.1 (2 CH), 127.3 (2 CH), 125.8 (CH), 125.7 (2 CH), 122.4 (C), 121.6 (CH), 67.7 (CH_2), 64.8 (CH) ppm. HRMS: calcd. for $C_{17}H_{14}F_3N_3ONa^+$ 356.099; found 356.093.

2-Phenyl-2-(4-propyl-1*H*-1,2,3-triazol-1-yl)ethanol (5d): Isolated yield: 183 mg (79%); colorless oil. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.36–7.31 (m, 3 H), 7.21–7.16 (m, 3 H), 5.56 (dd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 4 Hz, 1 H), 4.54 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 8 Hz, 1 H), 4.14 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 4 Hz, 1 H), 2.79 (br. s, 1 H), 2.64 (t, $^3J_{H,H}$ = 7 Hz, 2 H), 1.64 (qt, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 7 Hz, 2 H), 0.92 (t, $^3J_{H,H}$ = 7 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 148.5 (C), 136.5 (C), 129.3 (2 CH), 129.0 (CH), 127.2 (2 CH), 121.8 (CH), 67.2 (CH), 65.4 (CH_2), 27.8 (CH_2), 22.7 (CH_2), 14.0 (CH_3) ppm. HRMS: calcd. for $C_{13}H_{17}N_3ONa^+$ 254.127; found 254.147.

2-(4-Phenethyl-1*H*-1,2,3-triazol-1-yl)-2-phenylethanol (5e): Isolated yield: 246 mg (84%); white solid; m.p. 64 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.33–7.31 (m, 3 H), 7.26–7.10 (m, 8 H), 5.66 (dd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 4 Hz, 1 H), 4.48 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 8 Hz, 1 H), 4.17 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 4 Hz, 1 H), 2.92–2.89 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 147.7 (C), 141.2 (C), 136.4 (C), 129.2 (2 CH), 129.0 (CH), 128.6 (2 CH), 128.5 (2 CH), 127.2 (2 CH), 126.3 (CH), 121.1 (CH), 67.1 (CH), 65.2 (CH_2), 35.6 (CH_2), 27.7 (CH_2) ppm. HRMS: calcd. for $C_{18}H_{20}N_3O^+$ 294.160; found 294.158.

1,4-Bis[1-(2-hydroxy-1-phenylethyl)-1*H*-1,2,3-triazol-4-yl]butane (5f): Isolated yield: 246 mg (57%); white solid; m.p. 182 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.32–7.26 (m, 8 H), 7.22–7.18 (m, 4 H), 5.60 (dd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 4 Hz, 2 H), 4.49 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 8 Hz, 2 H), 4.12 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 4 Hz, 2 H), 2.59 (t, $^3J_{H,H}$ = 6 Hz, 4 H), 1.63–1.58 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 147.7 (2 C), 136.5 (2 C), 129.1 (4CH), 128.9 (2 CH), 127.3 (4CH), 122.0 (2 CH), 67.2 (2 CH), 65.0 (2 CH_2), 28.4 (2 CH_2), 25.2 (2 CH_2) ppm. HRMS: calcd. for $C_{24}H_{29}N_6O_2^+$ 433.235; found 433.229.

[1-(2-Hydroxy-1-phenylethyl)-1*H*-1,2,3-triazol-4-yl]methyl β-D-2,3,4,6-*O*-Tetracetylglucoside (5g): Isolated yield: 689 mg (94%); white solid; m.p. 46 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.47 (d, $^3J_{H,H}$ = 7 Hz, 1 H), 7.26–7.11 (m, 5 H), 5.58 (ddd, $^3J_{H,H}$ = 11, $^3J_{H,H}$ = 8, $^4J_{H,H}$ = 3 Hz), 5.34 (t, $^3J_{H,H}$ = 9 Hz, 1 H), 5.08 (t, $^3J_{H,H}$ = 4 Hz, 1 H), 4.94 (t, $^3J_{H,H}$ = 10 Hz, 1 H), 4.71–4.65 (m, 2 H), 4.56 (d, $^3J_{H,H}$ = 12 Hz, 1 H), 4.50–4.41 (m, 1 H), 4.13–4.03 (m, 2 H), 4.01–3.92 (m, 2 H), 3.10 (br. s, 1 H), 1.97–1.82 (m, 12 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.8 (C), 170.5 (C), 170.2 (C), 169.7 (C), 143.5 (C), 136.0 (C), 129.3 (2 CH), 127.4 (CH), 124.1 (2 CH), 123.8 (CH), 94.9 (CH), 71.0 (CH), 70.1 (CH), 68.5 (CH), 67.6 (CH), 67.2 (CH), 64.9 (CH_2), 61.8 (CH_2), 61.3 (CH_2), 20.9 (CH_3), 20.8 (CH_3), 20.7 (CH_3) ppm. HRMS: calcd. for $C_{25}H_{31}N_3O_{11}Na^+$ 572.186; found 572.180.

(*E*)-4-Phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)but-3-en-1-ol (5h): Isolated yield: 172 mg (59%); white solid; m.p. 85 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.81 (s, 1 H), 7.66–7.62 (m, 2 H), 7.37–7.22 (m, 8 H), 6.62 (d, $^3J_{H,H}$ = 16 Hz, 1 H), 6.45 (dd, $^3J_{H,H}$ = 16, $^3J_{H,H}$ = 8 Hz, 1 H), 5.25 (ddd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 7, $^3J_{H,H}$ = 4 Hz, 1 H), 4.59 (br. s, 1 H), 4.29 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 7 Hz, 1 H), 4.19 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 147.2 (C), 135.6 (C), 135.3 (2 CH), 130.2 (C), 128.9 (2 CH), 128.8 (2 CH), 128.7 (CH), 128.3 (CH), 126.9 (2 CH), 125.7 (2 CH), 123.1 (CH), 120.2 (CH), 65.8 (CH_2), 64.7 (CH) ppm. HRMS: calcd. for $C_{18}H_{18}N_3O^+$ 292.145; found 292.142.

1-Phenyl-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)propan-2-ol (5j): Isolated yield: 162 mg (58%); white solid; m.p. 140 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.80 (s, 1 H), 7.70–7.67 (m, 2 H), 7.38–7.21 (m, 8 H), 4.48 (dd, $^2J_{H,H}$ = 13, $^3J_{H,H}$ = 3 Hz, 1 H), 4.34 (tdd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 6, $^3J_{H,H}$ = 3 Hz, 1 H), 4.24 (dd, $^2J_{H,H}$ = 13, $^3J_{H,H}$ = 8 Hz, 1 H), 3.24 (br. s, 1 H), 2.88 (dd, $^2J_{H,H}$ = 14, $^3J_{H,H}$ = 6 Hz, 1 H), 2.81 (dd, $^2J_{H,H}$ = 13, $^3J_{H,H}$ = 7 Hz, 1 H) ppm. ^{13}C NMR

(75 MHz, $CDCl_3$, 25 °C): δ = 147.5 (C), 136.8 (C), 130.7 (C), 129.6 (2 CH), 129.1 (2 CH), 129.1 (2 CH), 128.4 (CH), 127.3 (CH), 125.9 (2 CH), 121.4 (CH), 71.6 (CH), 53.4 (CH_2), 41.2 (CH_2) ppm. HRMS: calcd. for $C_{17}H_{18}N_3O^+$ 280.145; found 280.145.

2-Hydroxy-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)propyl Acetate (5k): Isolated yield: 183 mg (70%); white solid; m.p. 90 °C. ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.86 (s, 1 H), 7.77 (d, $^3J_{H,H}$ = 8 Hz, 2 H), 7.39 (dd, $^3J_{H,H}$ = 8, $^3J_{H,H}$ = 7 Hz, 2 H), 7.32 (t, $^3J_{H,H}$ = 7 Hz, 1 H), 4.58 (dd, $^2J_{H,H}$ = 14, $^3J_{H,H}$ = 3 Hz, 1 H), 4.41 (dd, $^2J_{H,H}$ = 14, $^3J_{H,H}$ = 7 Hz, 1 H), 4.37 (dtd, $^3J_{H,H}$ = 7, $^3J_{H,H}$ = 6, $^3J_{H,H}$ = 3 Hz, 1 H), 4.23 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 4 Hz, 1 H), 4.14 (dd, $^2J_{H,H}$ = 12, $^3J_{H,H}$ = 6 Hz, 1 H), 2.10 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 171.2 (C), 147.7 (C), 130.2 (C), 129.0 (2 CH), 128.5 (CH, 1 C), 125.7 (2 CH), 121.5 (CH), 68.7 (CH_2), 65.8 (CH), 53.4 (CH_2), 21.0 (CH_3) ppm. HRMS: calcd. for $C_{13}H_{16}N_3O_3H^+$ 262.119; found 262.121.

1-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-3-(tetrahydro-2*H*-pyran-2-yloxy)-propan-2-ol (5l): Isolated yield: 103 mg (34%) as a 1:1 mixture of diastereoisomers. White waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.84 (s, 1 H), 7.68–7.64 (m, 2 H), 7.31–7.18 (m, 3 H), 4.54–4.11 (m, 5 H), 3.85–3.75 (m, 1 H), 3.7 (dd, $^2J_{H,H}$ = 11, $^3J_{H,H}$ = 4, 0.5 Hz), 3.58 (d, $^3J_{H,H}$ = 5 Hz, 1 H), 3.53 (dd, $^2J_{H,H}$ = 11, $^3J_{H,H}$ = 5, 0.5 Hz), 3.46–3.38 (m, 1 H), 1.76–1.62 (m, 2 H), 1.39–1.51 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 147.6 (C), 130.7 (C), 128.9 (2 CH), 128.2 (CH), 125.8 (2 CH), 121.5 (CH), 121.4 (CH), 101.0 (CH), 100.6 (CH), 70.7 (CH), 70.5 (CH), 69.6 (CH_2), 69.5 (CH_2), 64.1 (CH_2), 63.6 (CH_2), 53.5 (CH_2), 53.2 (CH_2), 30.9 (CH_2), 30.8 (CH_2), 25.3 (CH_2), 25.2 (CH_2), 20.5 (CH_2), 20.1 (CH_2) ppm. HRMS: calcd. for $C_{16}H_{21}N_3O_3Na^+$ 326.148; found 326.147.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of the new compounds described in the Experimental Section.

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[1] For recent reviews, see: a) J. Zhu, H. Bienaymé, *Multicomponent Reactions*, Wiley-VCH, Weinheim, **2005**; b) I. Marek, *Tetrahedron* **2005**, *61*, 11309–11519; c) A. de Meijere, P. von Zezschwitz, S. Brase, *Acc. Chem. Res.* **2005**, *38*, 413–422; d) J. C. Wasilke, S. J. Obrey, R. T. Baker, G. C. Bazan, *Chem. Rev.* **2005**, *105*, 1000–1020; e) A. Ajamian, J. L. Gleason, *Angew. Chem. Int. Ed.* **2004**, *43*, 3754–3760; f) J. M. Lee, Y. Na, H. Han, S. Chang, *Chem. Soc. Rev.* **2004**, *33*, 302–342; g) A. Dömling, I. Ugi, *Angew. Chem. Int. Ed.* **2000**, *39*, 3168–3210; h) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136.

[2] a) P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, **1998**; b) P. T. Anastas, T. C. Williamson, *Green Chemistry: Frontiers in Benign Synthesis and Practices*, Oxford University Press, Oxford, **1998**; c) P. Tundo, P. T. Anastas, *Green Chemistry: Challenging Perspectives*, Oxford Science, Oxford, **1999**.

[3] a) S. Chassaing, M. Kumarraja, A. Sani Souna Sido, P. Pale, J. Sommer, *Org. Lett.* **2007**, *9*, 883–886; b) S. Chassaing, A. Sani Souna Sido, A. Alix, M. Kumarraja, P. Pale, J. Sommer, *Chem. Eur. J.* **2008**, *14*, 6713–6721; c) A. Alix, S. Chassaing, P. Pale, J. Sommer, *Tetrahedron* **2008**, *64*, 8922–8929.

[4] M. Keller, A. Sani Souna Sido, P. Pale, J. Sommer, *Chem. Eur. J.* **2009**, *15*, 2810–2817.

[5] a) P. Kuhn, A. Alix, M. Kumarraja, B. Louis, P. Pale, J. Sommer, *Eur. J. Org. Chem.* **2009**, 423–429; b) P. Kuhn, P. Pale, J. Sommer, B. Louis, *J. Phys. Chem. C* **2009**, *113*, 2903–2910.

[6] S. Chassaing, A. Alix, A. Sani Souna Sido, M. Keller, P. Kuhn, B. Louis, P. Pale, J. Sommer, *Synthesis* **2010**, 1557–1567.

[7] H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021.

[8] M. K. Patil, M. Keller, M. B. Reddy, P. Pale, J. Sommer, *Eur. J. Org. Chem.* **2008**, 4440–4445.

[9] V. Calderone, I. Giorgi, O. Livi, E. Martinotti, E. Mantuano, A. Martelli, A. Nardi, *Eur. J. Med. Chem.* **2005**, *40*, 521–528.

[10] U. Nilsson, PCT Int. Appl., WO 2009139719 A1 20091119, **2009**.

[11] J. M. Beck, R. K. Mann, Eli-Lilly, US Pat. 4931083, June **1990**.

[12] a) K. Burgess, U. S. Pat. Appl., US 2009264315 A1 20091022, **2009**; b) A. Brik, J. Alexandratos, Y.-C. Lin, J. H. Elder, A. JOlson, A. Wlodawer, D. S. Goodsell, C. H. Wong, *ChemBioChem* **2005**, *6*, 1167–1169.

[13] S. Martwiset, R. C. Woudenberg, S. Granados-Ficii, O. Yavuzcetin, M. T. Tuominen, E. B. Coughlin, *Solid State Ionics* **2007**, *178*, 1398–1403.

[14] R. Reed Jr., US Pat. 6103029, June **1997**.

[15] Y. Garcia, V. Ksenofontov, P. Gütlich, *Hyperfine Interact.* **2002**, *139–140*, 543–551.

[16] a) D. J. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.* **1996**, *96*, 835–876; b) S. C. Bergmeier, *Tetrahedron* **2000**, *56*, 2561–2576.

[17] For a review on epoxide ring-opening by nitrogen nucleophiles, see: L. I. Kas'yan, S. I. Okovityi, A. O. Kas'yan, *Russ. J. Org. Chem.* **2004**, *40*, 1–34.

[18] For reactions promoted by LiOTf, see: a) M. Chini, P. Crotti, F. Macchia, *Tetrahedron Lett.* **1990**, *31*, 5641–5644; for reactions promoted by $Mg(ClO_4)_2$, see: b) M. Meguro, N. Asao, Y. Yamamoto, *J. Chem. Soc., Chem. Commun.* **1995**, 1021–1022; for Al-catalyzed reactions, see: c) K. I. Sutowardoyo, D. Sinou, *Bull. Soc. Chim. Fr.* **1991**, 387–392; d) K. I. Sutowardoyo, M. Emziane, P. Lhoste, D. Sinou, *Tetrahedron* **1991**, *47*, 1435–1446; e) Y. S. Youn, I. S. Cho, B. Y. Chung, *Tetrahedron Lett.* **1998**, *39*, 4337–4338; for Ti-catalyzed reaction, see: f) M. Caron, P. R. Carlier, K. B. Sharpless, *J. Org. Chem.* **1988**, *53*, 5185–5187; for Bi-catalyzed reaction, see: g) H. Gaspard-Houghmane, C. Le Roux, *Eur. J. Org. Chem.* **2004**, 2517–2532; for Sn-catalyzed reaction, see: h) S. Saito, S. Yamashita, T. Nishikawa, Y. Yokoyama, M. Inaba, T. Moriwake, *Tetrahedron Lett.* **1989**, *30*, 4153–4156; i) S. Saito, T. Nishikawa, Y. Yokoyama, T. Moriwake, *Tetrahedron Lett.* **1990**, *31*, 221–224; for Sm-catalyzed reaction, see: j) P. Van de Weghe, J. Collin, *Tetrahedron Lett.* **1995**, *36*, 1649–1652; k) K. Bhaumik, U. W. Mali, K. G. Akamanchi, *Synth. Commun.* **2003**, *33*, 1603–1610; for Cr-catalyzed reaction, see: l) W.-H. Leung, E. K. F. Chow, M.-C. Wu, P. W. Y. Kum, L.-L. Yeun, *Tetrahedron Lett.* **1995**, *36*, 107–108; m) L. E. Martinez, J. L. Leighton, D. H. Carsten, E. N. Jacobsen, *J. Am. Chem. Soc.* **1995**, *117*, 5897–5898; for Ga-catalyzed reaction, see: n) X. Chen, H. Wu, R. Xu, M. Liu, J. Ding, W. Su, *Synth. Commun.* **2008**, *38*, 1855–1865.

[19] F. Fringuelli, O. Piermatti, F. Pizzo, L. Vaccaro, *J. Org. Chem.* **1999**, *64*, 6094–6096.

[20] For related one-pot reactions, see: a) G. Kumaraswamy, K. Andamma, A. Pitchaiah, *J. Org. Chem.* **2007**, *72*, 9822–9825; b) J. S. Yadav, B. V. S. Reddy, G. M. Reddy, D. N. Chary, *Tetrahedron Lett.* **2007**, *48*, 8773–8776; c) L. S. Campbell-Verduyn, W. Szymaski, C. P. Postema, R. A. Dierckx, P. H. Elsinga, D. B. Janssen, B. L. Feringa, *Chem. Commun.* **2010**, *46*, 898–900.

[21] While completing this work, another heterogeneous version was published that describes a surprising inverted regioselectivity of the epoxide ring-opening, see: H. Sharghi, M. H. Beyzavi, A. Safavi, M. M. Doroodmand, R. Khalifeh, *Adv. Synth. Catal.* **2009**, *351*, 2391–2410.

[22] 10 mol-% catalyst corresponds to 10 mol-% Cu^{I} species, based on the theoretical number of native acidic sites in the corresponding H–zeolite. For recent methods for determining Brønsted acid sites in zeolites, see: B. Louis, S. Walspurger, J. Sommer, *Catal. Lett.* **2004**, *93*, 81–84; S. Walspurger, B. Louis, *Appl. Catal. A Gen.* **2007**, *336*, 109–115.
[23] R. R. Hung, J. A. Straub, G. M. Whitesides, *J. Org. Chem.* **1991**, *56*, 3849–3855.
[24] N. Zenker, L. S. Hubbard, J. Wright, *J. Nat. Prod.* **1988**, *51*, 862–865.
[25] Z. Li, K. Xie, R. C. T. Slade, *Appl. Catal. A* **2001**, *209*, 107–115.
[26] T. R. Chan, R. Hilgraf, K. B. Sharpless, V. V. Fokin, *Org. Lett.* **2004**, *6*, 2853–2855.
[27] A. V. Maksikova, E. S. Serebryakova, V. V. Shcherbakov, G. A. Gareev, L. I. Vereshchagin, *Zh. Org. Khim.* **1989**, *25*, 1519–1523.
[28] J. H. L. Spelberg, L. Tang, R. M. Kellog, D. B. Janssen, *Tetrahedron: Asymmetry* **2004**, *15*, 1095–1102.
[29] B. Tamani, H. Malavi, *Tetrahedron Lett.* **2001**, *42*, 8721–8724.

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