

Efficient and Regioselective Ring-Opening of Epoxides with Alcohols and Sodium Azide by using Catalytic Amounts of GaCl₃/Polyvinylpyrrolidone

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A new polymeric catalyst was prepared by supporting GaCl₃ on cross-linked polyvinylpyrrolidone (GaCl₃/PVP). This catalyst was employed for efficient and regioselective ring-opening reaction of epoxides by various alcohols under solvent-free conditions at room temperature. In our procedure, this heterogeneous catalyst was used at neutral and mild reaction conditions to afford high yields of β-alkoxy alcohols. Also, regioselective conversion of epoxides to β-azidoalcohols was accomplished by sodium azide in MeOH in the presence of GaCl₃/PVP at room temperature. GaCl₃/PVP is a non-hygroscopic and recoverable catalyst and is easily separated from reaction mixture by a simple filtration and re-used repeatedly. Also, this catalyst has good handling and can be stored for long time without any reducing of its reactivity.

Key Words : Alcohol, Epoxide, Gallium trichloride, Ring-opening, Sodium azide

Introduction

While Lewis acid catalysts are widely used in organic synthesis as well as chemical industry, most of these catalysts are hygroscopic and decomposed upon reaction conditions in contact with small amounts of humidity.¹ Thus, storage, handling and using of these catalysts needs special conditions. Also, work-up of the Lewis acid-promoted reactions may yield many hazardous and pollutant acidic materials. Emerging these problems has restricted the use of Lewis acids in organic synthesis. Many investigations have developed to preparing new and non-hygroscopic green Lewis acids.² One solution may be using stable and non-hygroscopic polymer-supported catalysts with good handling and storage properties.³⁻⁵ Furthermore, using these catalysts can efficiently reduce the leaching of chemicals to reaction solvent or environment at work-up procedures such as extraction or chromatography. Cross-linked polymer supported catalysts are used for this purpose in the field of combinatorial chemistry and polymer assisted solution phase chemistry (PASP).⁶⁻⁸ On the other hand, these catalysts or reagents could be used under heterogeneous solvent-free conditions for conducting more environmentally benign reactions.⁹ These methods have simple work-up and diminished pollutant materials and also energy consumptions in comparison with conventional work-up of solution-phase reactions.

Gallium trichloride is a reactive Lewis acid.¹⁰ It was used as an efficient catalyst in many reactions.¹¹ Especially, in recent years valuable applications of this catalyst was reported in the literature.¹²⁻¹⁴ Although GaCl₃ is very useful catalyst, some of its properties such as hygroscopic nature and difficult handling were limited their generality. Due to solubility of GaCl₃ in water and many organic solvents, it is difficult to recovering and recycling the catalyst. These disadvantages can be overcome by supporting GaCl₃ on a

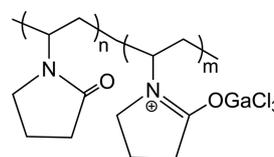
polymeric material and conducting the reactions under heterogeneous conditions.

In continuum of our previous studies in the field of polymer-supported reagents and catalysts,¹⁵⁻²¹ we have prepared a new polymeric catalyst by supporting GaCl₃ on cross-linked polyvinylpyrrolidone (GaCl₃/PVP). In this work, we report the catalytic effect of GaCl₃/PVP in the ring-opening reaction of epoxides by alcohols and azide as nucleophiles. This catalyst is a stable and recoverable catalyst and is easily separated from reaction mixture by a simple filtration and re-used repeatedly. Also, this catalyst has good handling and can be stored for long time without any reducing of its reactivity.

Results and Discussion

In this research, we first supported GaCl₃ on the cross-linked PVP (GaCl₃/PVP). The preparation of catalyst was done by adding cross-linked polyvinylpyrrolidone²¹ to a stirred solution of GaCl₃ in *n*-hexane. GaCl₃ can be form chelates with carbonyl groups of polyvinylpyrrolidone (Scheme 1). In FT-IR spectroscopy of GaCl₃/PVP, absorbance peak of carbonyl group is shifted to 1617 cm⁻¹, which is 37 cm⁻¹ lower than carbonyl group of PVP. GaCl₃/PVP is a non-hygroscopic catalyst that has good handling and can be stored for long time without any reducing of its reactivity.

Then, we investigated the catalytic effect of GaCl₃/PVP in the ring-opening reaction of epoxides by alcohols and azide as nucleophiles. For this purpose, styrene oxide was selected



Scheme 1. Structure of GaCl₃/PVP.

Table 1. Ring-opening of styrene oxide (1 mmol) with MeOH (1 mmol) in the presence of GaCl₃/PVP (0.2 g) in different solvents at room temperature

Entry	Solvent ^a	Reaction time (min.)	Conversion (%)
1	CH ₃ CN	120	85
2	CH ₂ Cl ₂	100	70
3	CHCl ₃	150	55
4	CCl ₄	120	45
5	<i>n</i> -Hexane	140	25
6	Ethyl acetate	150	20
7	MeOH	15	100

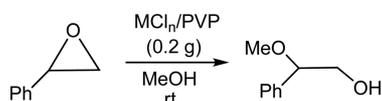
^a5 mL of each solvent was used.**Table 2.** Re-using of GaCl₃/PVP as catalyst in the ring-opening of styrene oxide (1 mmol) with MeOH (5 mL) at room temperature

Run	Reaction time (min.)	Conversion (%)
1	15	100
2	15	100
3	15	99
4	15	98
5	15	96
6	15	95
7	15	95
8	15	94

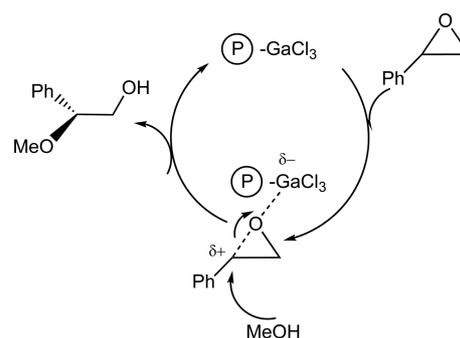
as a model compound and its reaction with MeOH was studied in the presence of GaCl₃/PVP (0.2 g) in different solvents at room temperature (Table 1). The results of Table 1 show that in MeOH as solvent after 15 min. the conversion of the reaction is 100%, and it is the best choice. This heterogeneous catalyst could be easily separated from reaction mixture by a simple filtration and re-used repeatedly. We used this catalyst 8 times in the reaction of styrene oxide with MeOH without considerable reducing of its activity (Table 2).

For comparing reactivity of GaCl₃/PVP with other polymer supported Lewis acids, we prepared BiCl₃/PVP, FeCl₃/PVP and ZrCl₄/PVP by same method and catalytic reactivity of these polymeric compounds were examined in the reaction of styrene oxide with methanol at room temperature (Scheme 2, Table 3). According to these results, GaCl₃/PVP is most reactive catalyst among all of these polymeric Lewis acids.

Styrene oxide is activated for a nucleophilic attack of MeOH by coordination with polymer supported GaCl₃. Then, regioselective attack of MeOH to phenyl substituted carbon affords 2-phenyl-2-methoxy ethanol. Phenyl group can stabilize carbocation and electrophilic character of attacked carbon. The proposed mechanism for the ring-

**Scheme 2.** Reaction of styrene oxide with MeOH in the presence of polymeric catalysts.**Table 3.** Ring-opening of styrene oxide (1 mmol) with MeOH (1 mmol) in the presence of different polymeric catalysts (0.2 g) in methanol at room temperature

Entry	Catalyst	$\Delta\nu^a$ (cm ⁻¹)	Reaction time (min.)	Conversion (%)
1	BiCl ₃ /PVP	38	120	100
2	FeCl ₃ /PVP	16	80	100
3	ZrCl ₄ /PVP	18	20	100
4	GaCl ₃ /PVP	37	15	100

^aThe shift of carbonyl group peak of catalyst with respect to PVP in FT-IR spectroscopy.**Scheme 3.** Proposed mechanism for ring-opening of styrene oxide with MeOH in the presence of GaCl₃/PVP.

opening of styrene oxide was shown in Scheme 3.

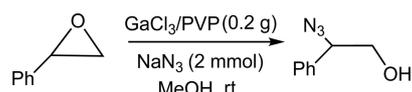
Structurally different epoxides efficiently and regioselectively react with alcohols in the presence of GaCl₃/PVP at room temperature under solvent-free conditions to produce β -alkoxy alcohols with high yields (Table 4). Ring-opening reactions of styrene oxide were efficiently completed in short times with respect to other epoxides (Table 4, entries 1-5). Also, these reactions were regioselectively proceeded through attack of alcohol as nucleophile on phenyl substituted carbon. This can be accounted by carbocation character of the electrophilic phenyl substituted carbon as described in Scheme 3. In the case of other epoxides *i.e.* phenoxyethyl- and chloromethyl- substituted oxirane rings, (Table 4, entries 6-10 and 16-20) attack of alcohol to unsubstituted carbon of epoxide ring was dominant and these reactions regioselectively yielded secondary alcohols.

The reaction of styrene oxide with NaN₃ was also studied in the presence of GaCl₃/PVP in different solvents at room temperature (Scheme 4, Table 5). The results of table 5 show that again in MeOH as solvent the reaction is completed after 15 min. while in other solvents conversions are 5-75%. Thus methanol is the best choice as solvent.

Results of Table 6 show that different epoxides efficiently and regioselectively react with sodium azide in the presence of catalytic amounts of GaCl₃/PVP at room temperature in MeOH to produce β -azidohydrines with good to high yields (75-95%). Styrene oxide was reacted with a similar mechanism as shown in Scheme 3. In this case, azide ion was attacked regioselectively to phenyl substituted carbon of oxirane ring (Table 6, entry 1) but the reactions of other one-substituted epoxides yielded secondary alcohols by attack of

Table 4. Regioselective ring opening of epoxides by various alcohols in the presence of GaCl₃/PVP at room temperature

Entry	Epoxide	Alcohol	Product	Reaction time (min.)	Isolated yield%
1		CH ₃ OH		15	96
2		C ₂ H ₅ OH		25	95
3		C ₃ H ₇ OH		6	80
4		C ₄ H ₉ OH		7	85
5		PhCH ₂ OH		10	90
6		CH ₃ OH		270	85
7		C ₂ H ₅ OH		275	85
8		C ₃ H ₇ OH		195	80
9		C ₄ H ₉ OH		205	90
10		PhCH ₂ OH		35	95
11		CH ₃ OH		120	95
12		C ₂ H ₅ OH		150	90
13		C ₃ H ₇ OH		170	87
14		C ₄ H ₉ OH		180	88
15		PhCH ₂ OH		100	85
16		CH ₃ OH		240	80
17		C ₂ H ₅ OH		260	80
18		C ₃ H ₇ OH		250	85
19		C ₄ H ₉ OH		300	88
20		PhCH ₂ OH		60	78

**Scheme 4.** Reaction of styrene oxide with NaN₃ in the presence of GaCl₃/PVP in MeOH.**Table 5.** Ring-opening of styrene oxide (1 mmol) with NaN₃ (2 mmol) in the presence of GaCl₃/PVP (0.2 g) in different solvents at room temperature

Entry	Solvent	Reaction time (min.)	Conversion (%)
1	CH ₃ OH	15	100
2	CH ₃ CN	30	75
3	CH ₂ Cl ₂	65	70
4	CHCl ₃	90	35
5	CCl ₄	120	25
6	<i>n</i> -Hexane	140	5
7	Ethyl acetate	150	60

Table 6. Regioselective ring opening of epoxides by sodium azide in the presence of GaCl₃/PVP at room temperature

Entry	Epoxide	Product	Reaction time (min.)	Isolated yield%
1			15	95
2			60	86
3			75	80
4			80	75
5			65	75

N₃⁻ to unsubstituted carbon (Table 6, entries 2-3).

Conclusion

GaCl₃/PVP was prepared by supporting GaCl₃ on cross-linked polyvinylpyrrolidone as a polymeric catalyst. This catalyst was employed for efficient and regioselective ring opening reaction of epoxides by various alcohols under heterogeneous and solvent-free conditions at room temperature. Also, regioselective conversion of epoxides to β-azidoalcohols was accomplished by sodium azide in MeOH in the presence of GaCl₃/PVP at room temperature. GaCl₃/PVP is a non-hygroscopic catalyst and is easily separated from reaction mixture by a simple filtration and re-used repeatedly. Also, this catalyst has good handling and can be stored for long time without any reducing of its reactivity. High yields, using neutral and mild reaction conditions are other advantages of our method.

Experimental

Instruments and Reagents. Chemicals were obtained from Merck and Fluka chemical companies. The progress of the reaction was monitored by thin-layer chromatography on commercial Merck precoated thin layer chromatography, TLC plates (silica gel 60 F₂₅₄) and GLC on a Varian CP-3800 instrument. All compounds were known and are identified by comparison of their physical and spectroscopic data with those of authentic samples. Melting points were determined in open capillary tubes with a Buchi 510 apparatus. FT-IR spectra were recorded on a Perkin Elmer RXI spectrometer. NMR spectra were recorded on a Bruker Avance DRX-500 instrument. Preparation of cross-linked polyvinylpyrrolidone was accomplished using PVP K-30, Fluka (Mw = 40,000) according to literature.²¹

Preparation of GaCl₃/PVP. To a solution of GaCl₃ (1.5 g) in *n*-hexane (100 mL) was added cross-linked polyvinylpyrrolidone (8 g). This mixture was stirred for 4 h at room temperature. After filtration, the solid catalyst was washed with 50 mL *n*-hexane and dried to afford 8.8 g GaCl₃/PVP.

Typical Procedure for Ring Opening of Epoxides. To a solution of styrene oxide (1 mmol, 0.120 g) in methanol (5 mL), was added GaCl₃/PVP (0.2 g). The mixture was stirred at room temperature and reaction progress was monitored until the reaction was completed. After 15 minutes, the mixture was filtered and the solid was washed with CH₂Cl₂ (3 × 5 mL). The organic phases was mixed and evaporated by rotary evaporator under reduced pressure. The obtained crude product was purified by short column chromatography using silica-gel with *n*-hexane and ethyl acetate (3:2 v/v) as eluent, then obtained 2-methoxy-2-phenyl ethanol (0.146 g, 96%).

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