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Selective Ring-Opening of ω-Epoxyalkyl (Meth)acrylates. An Efficient Access to Bifunctional Monomers.

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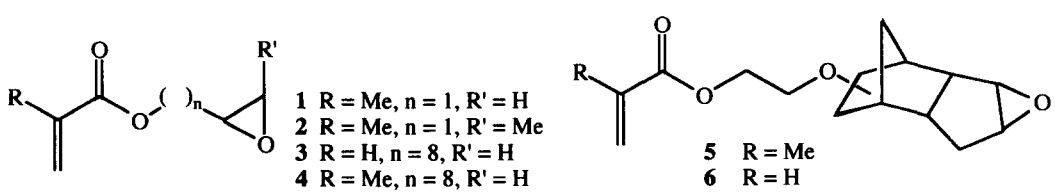
Abstract: It is shown that ω-epoxyalkyl (meth)acrylates constitute good precursors of bifunctional monomers by selective opening of the oxirane ring. © 1997 Elsevier Science Ltd.

The synthesis of functional (meth)acrylic monomers appears of high interest in order to obtain synthetic materials with widespread applications.[1] The classical way to obtain these monomers is the ester interchange of simple (meth)acrylates such as methyl methacrylate or ethyl acrylate.[2] This necessitates a catalyst and suffers from numerous drawbacks such as incompatibility with sensitive functional groups. In previous studies, we showed that the selective epoxidation of unsaturated methacrylic esters affords a good access to ω-epoxyalkyl methacrylates.[3] Given the versatility of reactivity of the oxirane ring,[4] these products could be valuable as precursors of (bi)functional monomers. If synthetic applications of oxiranes are extensively described,[5] little is reported in (meth)acrylic series. Indeed, we found only few reports dealing with the well known glycidyl methacrylate **1**.[6] On the other hand, the problem is to attack selectively the oxirane ring while leaving the sensitive (meth)acrylic unsaturation unchanged. For example, the attempted rearrangement of **1** or **2** into carbonyl derivatives using BF_3-Et_2O as an electrophilic reagent was not promising due to some polymerisation. In the same way, the use of $MgBr_2$ gave only bromhydrins in poor yields, and some degradation. Last but not least, the inertness of **1** versus lithium perchlorate-diethyl ether at 0°C was recently described,[7] showing the importance of the conditions used. In our ongoing interest in (meth)acrylic syntheses, we describe in this Letter some selective functionalisations of representative derivatives (Scheme 1), showing their potential synthetic usefulness.

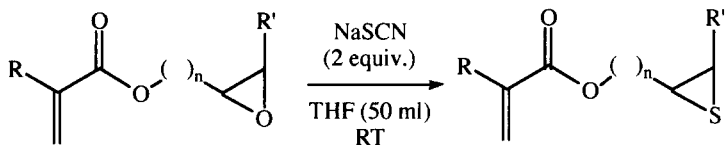


1 R = Me, n = 1, R' = H
2 R = Me, n = 1, R' = Me
3 R = H, n = 8, R' = H
4 R = Me, n = 8, R' = H

5 R = Me
6 R = H

Scheme 1

We first found that the reaction of **1-4** in THF at room temperature with a weak nucleophile such as the thiocyanate anion selectively led to the expected thiirane derivatives in high yields (Scheme 2). It must be underlined that this affords a good alternative to the classical route using thioacetamide, which only gave a 60 % yield under refluxing conditions.[8]



Substrate	Time (h)	Yield (%)
1 R = Me, n = 1, R' = H	6	87
2 R = Me, n = 1, R' = Me	60	80
3 R = H, n = 8, R' = H	12	83
4 R = Me, n = 8, R' = H	12	85

Scheme 2

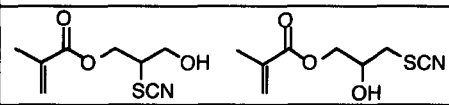
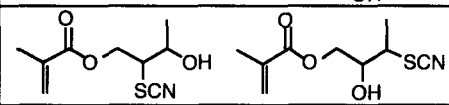
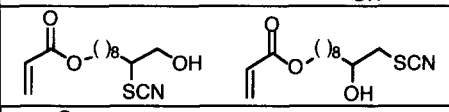
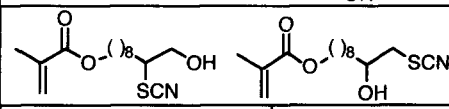
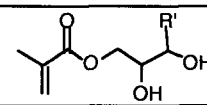
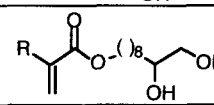
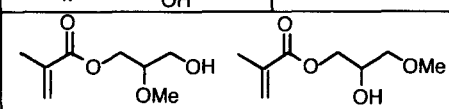
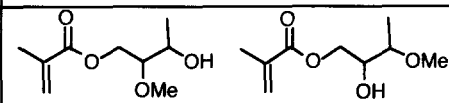
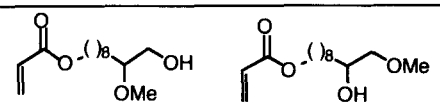
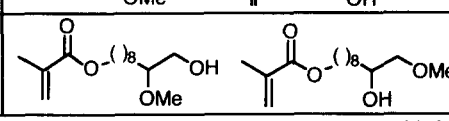
We next decided to perform these reactions under electrophilic assistance in order to shorten reaction times. Exploratory experiments showed that $TiCl_3$ and $ZnCl_2$ may efficiently activate the functionalization at room temperature, but the thiiranes were no longer observed. In fact, these conditions allowed the selective preparation of thiocyanato-alcohols in good yields. The best results were obtained with $TiCl_3$ in a 0.5 equiv. amount (Table 1, runs 1 to 4). It is worth noting that good isolated yields were obtained only after products were extracted with CH_2Cl_2.[9] As far as the regioselectivity is concerned, we observed a "normal opening" since the attack on the less substituted carbon predominated (up to 95 % for **1**,**3** or **4** and 65 % for **2**). This led us to conclude to the absence of participation of the ester part of the substrate during the reaction.

We then attempted to extend these selective functionalizations induced by a nucleophile-acid catalyst couple. Thus, the efficient formation of diols was obtained by reacting epoxides with sulfuric acid (0.5 equiv.) in a water-THF (5/1) mixture at RT (runs 5-8). These results contrast with the high stability of ω-epoxyalkyl (meth)acrylates during their preparation under phase transfer catalysis. [3] Lastly, this route favorably competes with the classical one consisting in hydrolysis of dioxolane derivatives.[10]

In the same way, the obtention of methoxy-alcohols required the use of BF_3-Et_2O (0.5 equiv.) as a Lewis acid in methanol as a reactive solvent (runs 9-12). At room temperature, yields reached from 80 to 95 % with a classical regioselectivity. Only few degradations were observed, showing the particular stability of the (meth)acrylic part in the conditions used. It must then be hypothesized that the polymerisations observed with BF_3-Et_2O in THF or Et_2O were initiated at the oxirane part of the monomers.

In contrast, we found that functionalizations by the AcONa/AcOH couple were not satisfactorily efficient (yields varying from 15 to 45%) due to transfunctionalisations and some degradations. This underlined the limitations of the selective functionalization of (meth)acrylic monomers.

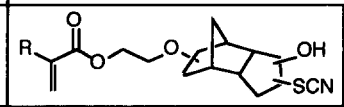
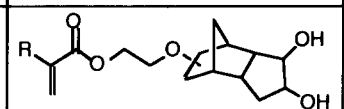
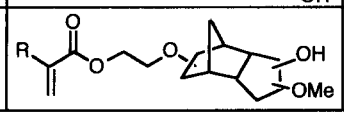
Table 1. Selective functionalizations of ω-epoxyalkyl (meth)acrylates.[a]

Run	Substrate	Reagent[b]	time (h)	Products	Yield (%)[c] Selectivity[d]
1	1	NaSCN $TiCl_3$	0.25		85 (5 / 95)
2	2	NaSCN $TiCl_3$	5		95 (35 / 65)
3	3	NaSCN $TiCl_3$	1		78 (5 / 95)
4	4	NaSCN $TiCl_3$	0.5		88 (2 / 98)
5	1	H_2O H_2SO_4	2		R' = H 88
6	2		4		R' = Me 90
7	3	H_2O H_2SO_4	2		R = H 87
8	4		4		R = Me 93
9	1	BF_3 MeOH	8		95 (20 / 80)
10	2	BF_3 MeOH	10		90 (40 / 60)
11	3	BF_3 MeOH	8		80 (5 / 95)
12	4	BF_3 MeOH	7		86 (5 / 95)

a) All reactions were performed on a 20 mmoles scale of ω-epoxyalkyl (meth)acrylates stabilized with 250 ppm EMHQ. b) Reactions were performed using 1.5 equiv. of NaSCN and 0.5 equiv. of $TiCl_3$ in 30 ml of THF at RT or a mixture of 10 ml of THF and 50 ml of 1N H_2SO_4 solution at RT or 0.5 equiv. of BF_3-Et_2O in 15 ml of MeOH at -30 °C during 1 h. then RT. c) Isolated yields after extraction with CH_2Cl_2 and flash chromatography. All the products were characterized on the basis of mass, IR, ^1H and ^{13}C NMR. d) Determined by ^1H NMR spectroscopy and confirmed by GC analyses.

Finally, we examined the reactivity of the industrial monomers **5** and **6** (also named globular (meth)acrylates). While **5** and **6** were surprisingly unreactive even at reflux, we found that bifunctional monomers can be efficiently obtained under electrophilic assistance (Table 2). The reaction temperature must reach 40°C or 60°C, depending on the agent of functionalization.

Table 2. Functionnalizations of epoxy globular (meth)acrylates.[a]

Run	Substrate	Reagent[b]	time (h)	T °C	Products		Yield (%)[c] Selectivity[d]
1	5	NaSCN $TiCl_3$	0.5	60		R = Me	82
2	6					R = H	80
1	5	H_2O H_2SO_4	48	40		R = Me	92
2	6					R = H	84
1	5	BF_3 MeOH	10	25		R = Me	90
2	6					R = H	85

a) All reactions were performed on a 20 mmoles scale of ω-epoxyalkyl (meth)acrylates stabilized with 150 ppm EMHQ. b) Reactions were performed using 1.5 equiv. of NaSCN and 0.5 equiv. of $TiCl_3$ in 30 ml of THF at 60 °C or a mixture of 10 ml of THF and 50 ml of 1N H_2SO_4 solution at 40 °C or 0.5 equiv. of BF_3-Et_2O in 15 ml of MeOH at -30 °C during 1 h. then RT. c) Isolated yields after extraction with CH_2Cl_2 and flash chromatography. All the compounds (isolated as a mixture of isomers) were characterized on the basis of mass, IR, ^1H and ^{13}C NMR. d) Determined by ^1H NMR spectroscopy and confirmed by GC analyses.

In conclusion, we showed that ω-epoxyalkyl methacrylates may be selectively functionalized, providing bifunctional monomers not easily obtained by classical ways. Studies are in progress in order to define the scope and limitations of these reactions.

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