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ARTICLE

Free-solvent Michael addition of glycerol to acrylic compounds

Frédéric Nadeau[a], Michèle Sindt[a] and Nicolas Oget*[a]

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In this paper, we report the study of the free-solvent nucleophilic addition of alcohols and glycerol to acrylic compounds, in presence of catalytic bases. With acrylates, Michael addition and transesterification are in competition: only PTC reaction with t-butyl acrylate gave trifonctionalizated glycerol. With acrylonitrile, the cyanoethylation of glycerol varies with catalyst, temperature, time reaction and amount of acrylonitrile. Mono fonctionalisation of glycerol can be obtained in 28% yield. The optimization of the free-solvent Michael addition of glycerol to acrylonitrile (3.4 quiv., 4 mol% NaOH, 5h) leads to TCEG (tricyanoethylglycerol, 88% yield, 99% purity) without HCl neutralisation, chlorinated solvent or purification (chromatography or distilation). TCEG can be used as prochiral core of dendrimer: G0.5 has been synthesized.

Introduction

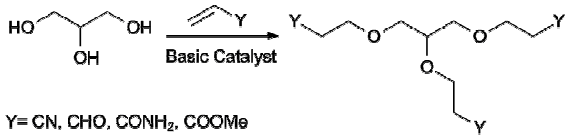
Michael addition is a widely reaction used in organic chemistry. In recent years, many studies have focused on the nucleophilic addition of heteroatoms [1], such as nitrogen compounds, thiol, alcohol or phosphorus with unsaturated carbonyl compounds (hetero-Michael reaction) and particularly in asymmetric synthesis. Thia-, aza- or phospha-Michael reactions are generally catalyzed by base, Lewis acid or metallic catalyst [2-4]. In the context of green chemistry, some reactions are performed in aqueous media [5-7], with ionic liquids as solvent or catalyst [8-10], assisted by ultrasonic irradiation [11], or without solvent [12,13]. The Michael addition of alcohol to conjugated reagents is less studied compared to nucleophilic additions of other heteroatoms [14] because of the low nucleophilicity of the alcohol function on the one hand, and the reversibility of the step of addition of the alcohol [14] on the other hand. Most oxa-Michael additions are catalyzed by strong bases, acids, transition metals or by ionic liquids (basic, chiral or even acidic ones) [15]. Recently, Guo et al. have used sodium carbonate to promote Michael addition of alcohols to activated olefins [15].

Whereas the acrylic compounds offer a wide field of investigation due to the high reactivity of the acrylic function (polymerization, reduction of double bonds C=C or C=O, 1,2 or 1,4-additions), there are few Michael additions of alcohol to acrylic derivatives. Nevertheless, all reactions are catalyzed. The 10 mol% triphenylphosphine Michael addition of primary alcohols to acrylates and acrylonitrile (AN) led to 22-79% yields after 2-24h reaction time [16]. The 5 mol% DBU catalysis between methanol and AN (or methyl methacrylate) gave respectively 62% and 79% yields, and with iPrOH and AN 86% after 70h reaction time [17]. 10 mol% $CuCl_2$ catalyzed Michael addition in presence of bases promoted the addition of primary alcohols to acrylamide derivatives [18]. Copper alkoxyde imidazole complex catalyzed hydroxyalkoxylation of AN and methyl methacrylate [19]. Oxa Michael addition on acrolein was developed using acidic ionic liquid [NMP] H_2PO_4 [20]. Jenner et al. showed that high pressure may promote the nucleophilic addition of alcohols on hindered acrylics [21] or AN [22]. Moreover, very few examples of nucleophilic addition of polyol to acrylic derivatives are presented: tetraalkylation of pentaerythritol was accomplished using AN in presence of NaOH [23] or KOH [24] as a catalyst, or more recently using *t*-butyl acrylate with phase transfer catalyst [25]. To our knowledge, only two publications focus on the addition of glycerol to acrylic derivatives: Bruson [26,27] in 1943 carried out the reaction between polyol and AN in the presence of 2-4% sodium methylate or 5-7% by weight of aqueous 40% potassium hydroxide solution to yield after 6-18h 70-95% of polycyanoethylation products (74% of tricyanoethylglycerol TCEG was obtained after HCl neutralization and ethylene dichloride extraction [27]). More recently, Trinadh et al. [28] used Amberlyst A21 resin as a catalyst and TCEG was obtained with 8% yield. Probably, the low solubility of glycerol in common organic solvents, and the presence of both primary and secondary alcohol functions can explain these only two examples. For all that, the major biobased byproduct from manufacturing biodiesel, glycerol, is an intermediate in the synthesis of a large number of compounds used in industry and its transformations into other valuable products are in number, some of them by sustainable production [29-35].

In the present paper, we investigate the reactivity of the nucleophilic addition of glycerol to acrylic compounds (AN, acrolein, acrylamide and alkyl acrylates) in the presence of several basic catalysts (Scheme 1).

[a] LCP-A2MC, Université de Lorraine, Institut Jean Barriol, 1, Boulevard Arago, 57078 Metz, France.

‡ Electronic supplementary information (ESI) available: Kinetic monitoring of reaction, Identification of Product



Scheme 1 Michael addition of glycerol to acrylic compounds

Also, 1- and 4- heptanol have been used to understand the reactivity of primary and secondary alcohol functions of glycerol, before optimizing the free-solvent nucleophilic addition of glycerol to acrylonitrile and the workup without HCl or chlorinated solvent.

Results and discussion

Preliminary tests

Nucleophilic addition of glycerol to AN, acrolein, acrylamide and methyl acrylate (MA) was performed without solvent in presence of basic catalysts (4 mol%) (Table 1) and under phase transfer catalysis conditions (PTC) (entry 10). Without catalyst (entry 1) no reaction was detected. Neither was it for the reaction between glycerol and acrylamide whatever the catalyst used. Polymerization of acrolein has been observed and, even in the presence of monomethylether hydroquinone (MEHQ) as inhibitor, no addition product was obtained. With AN, the best reactivity was obtained using MeONa, hydroxides and DBU (entries 2-5): this is coherent with Bruson's results [26]. In contrast, we have observed a low reactivity with Triton B and t-BuOK (entries 7-8) and a lack of reactivity for Na_2CO_3 or by PTC (entries 9-10).

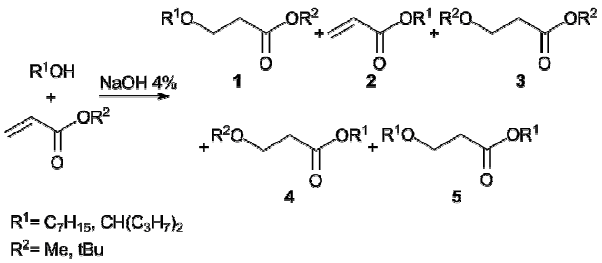
In the case of MA, only a little amount of a complex mixture was obtained and products of addition reaction have been detected (*vide infra*). The difference of reactivity between acrylic compounds is in accordance with electroattractive effect of groups [36] and the reactivity of acrylic Michael acceptor: CHO > CN > CO_2Me > $CONH_2$.

Table 1 Conversion of glycerol by Michael addition of glycerol to acrylic compounds CH_2=CH-Y

		CH_2=CH-Y (%) [c]			
Entry	Catalyst	CN	CHO	$CONH_2$ [a]	COOMe
1	/	0	0	0	0
2	MeONa	>50	0	0	<10
3	NaOH	>50	0	0	10-50
4	KOH	>50	0	0	<10
5	DBU	>50	0	0	10-50
6	PPh_3	<10	0	0	<10
7	Triton B	10-50	0	0	10-50
8	tBuOK	10-50	0	0	<10
9	Na_2CO_3	0	0	0	0
10	TBAB [b]	0	0	0	0

Experimental conditions: 12.5 mmol glycerol (1 equiv.), 37.5 mmol acrylic compounds (3 equiv.), 0.5 mmol catalyst (4 mol%), 25 ºC, 6h

[a] 5ml MeOH was used. [b] PTC : 20 mmol glycerol (1 equiv.), 62 mmol methyl acrylate (3.1 equiv.), 10 mmol TBAB (0.5equiv.), 16 mL NaOH 40%, 25 ºC, 18H. [c]The conversion of glycerol was determined by GC or NMR analysis.



Scheme 2 Reaction of heptanols with MA and tBA

Study of the reactivity of glycerol and alcohols to acrylates

Considering the complexity of the mixture obtained between glycerol and MA, 1-heptanol and 4-heptanol used as respectively primary and secondary alcohol functions of glycerol, have been added to MA and t-butyl acrylate (tBA) (Scheme 2). The conversion of alcohols and proportions of addition and/or by transesterification products are given in Table 2. Reaction of 1-heptanol and MA (entry 1) led to the formation of five compounds, and transesterification products **2**, **4**, **5** were mainly obtained (91%). The median selectivity in favor of **2** and the presence of **4** and **5** in higher a percentage (respectively 21% and 12%) than **1** (6%) suggest that the transesterification is much faster than the addition reaction. For 4-heptanol (entry 2), the conversion was extremely low (1%). To prevent transesterification and hydrolysis in basic media, nucleophilic addition of heptanol to tBA was performed. In this case, 64% and 34% conversion of respectively 1-heptanol and 4-heptanol were observed (entries 3-4). Moreover, a good selectivity in favor of addition products **1** was obtained for both primary and secondary alcohols, respectively 85% and 98%.

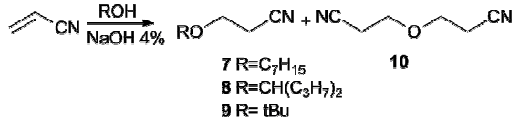
These results provide insight into the complex mixture obtained for the reaction between MA and glycerol. The addition reaction of glycerol (3 alcohol functions) to AM and the possible intra- or inter-molecular transesterifications lead to a large number of products and oligomers, whose separation is not possible.

Table 2 Addition of 1-heptanol and 4-heptanol to MA and tBA

Entry	Alcohol R^1	Acrylic R^2	R^1OH Conv. [a] (%)	Products [a] (%)				
				1	**2**	**3**	**4**	**5**
1	C_7H_{15}	Me	77	6	58	3	21	12
2	$CH(C_3H_7)_2$	Me	1	0	100	0	0	0
3	C_7H_{15}	*t*-Bu	64	85	2	0	0	13
4	$CH(C_3H_7)_2$	*t*-Bu	34	98	2	0	0	0

Experimental conditions: 10 mmol glycerol (1 equiv.), 10 mmol AN (1 equiv.), 0.5 mmol NaOH (4 mol%), 25 ºC, 6h.

[a] conversion and proportion determined by GCMS and GC analysis

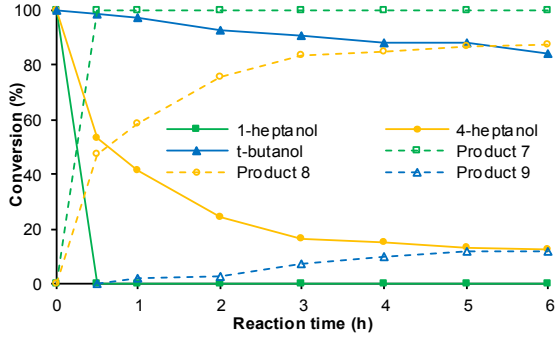


Scheme 3 Reaction of alcohols with acrylonitrile

Also, other reactions of glycerol to butyl acrylate or tBA in the presence of NaOH, KOH, DBU and MeONa (4% mol) led to an unexploitable complex mixture. In contrast, only the PTC reaction between glycerol and large excess of tBA under Landeros conditions (0.5 equiv. tetrabutylammonium bromide, NaOH 50%) [25] achieved a rich mixture of addition products. After purification, 1,2,3-tri-(t-butoxycarbonylethyl)glycerol **6** was obtained with only 12% yield. Under the same PTC condition MA and butyl acrylate were hydrolyzed by aqueous phase NaOH 40%.

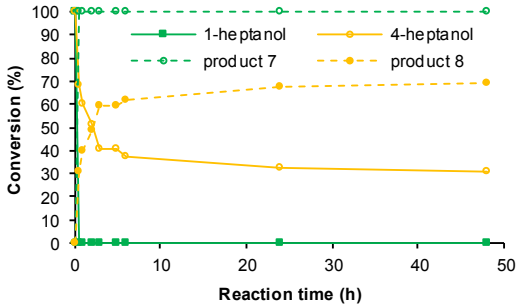
Reactivity of acrylonitrile with primary, secondary and tertiary alcohols

Unlike acrylate compounds, the addition of 1-heptanol to AN in presence of NaOH 4% was fast and quantitative after 30 min (Figure 1). Logically, we observed a slower reactivity with the secondary alcohol 4-heptanol, and the tertiary alcohol t-BuOH reacted even more slowly. Besides, a secondary product was observed, 2-cyanoethyl ether **10** (Scheme 3), resulting of the direct addition of hydroxide to AN, more particularly with higher amounts of NaOH and a long reaction time. After 48h, the conversion of 4-heptanol reached a plateau at 70% of **8** (Figure 2), which is a lower value than in Figure 1. This is according to the ratio AN/alcohol due to the very low reactivity of t-butanol, the ratio AN/4-heptanol in Figure 1 (three alcohols mixture) is higher than the one of the two alcohols mixture (Figure 2). So, more the ratio AN/4-heptanol increases, the faster addition reaction is, the higher the plateau value is (Figure SI1‡).



Experimental conditions: 10 mmol 1-heptanol, 10 mmol 4-heptanol, 10 mmol t-butanol, 30 mmol AN, 1.2 mmol NaOH (4 mol%), 25 °C

Figure 1 Kinetic monitoring of the addition of equimolar mixture (1-heptanol, 4-heptanol and t-butanol) to AN with 4 mol% NaOH



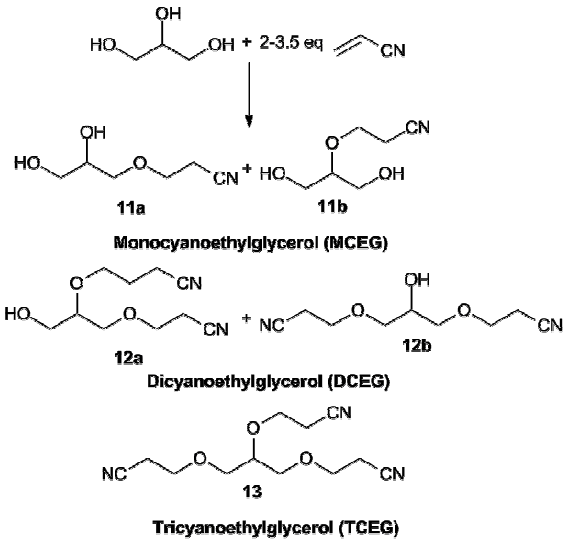
Experimental conditions: 10 mmol 1-heptanol, 10 mmol 4-heptanol, 20 mmol AN, 0.8 mmol NaOH (4 mol%), 25 °C

Figure 2 Kinetic monitoring of the addition of the equimolar mixture (1-heptanol, 4-heptanol) to AN with 4 mol% NaOH

However, even after 5 equiv. of AN, conversion of 4-heptanol was limited to 95%. Other reactions, with excess of AN (1-10 equiv.) and/or higher catalyst amounts (4-10 mol % NaOH) did not result in higher conversion[§]. It consenquently seems difficult to consider the quantitative tricyanoethylation of glycerol.

Cyanoethylation of glycerol

The addition reaction of glycerol to acrylonitrile can produce five products (Scheme 4): two monocyanoethyl glycerol (MCEG) **11a**, **11b**, two dicyanoethyl glycerol (DCEG) **12a**, **12b** and tricyanoethylglycerol (TCEG) **13**. The general procedure was as follows: 1 equiv. of glycerol reacted with 3 equiv. of AN in presence of catalyst, without solvent; after the reaction, the mixture was solubilized in dichloromethane and washed with distilled water, and the organic phase was dried, concentrated, and the crude product analyzed by ^{1}H NMR and GC. By this treatment, only TCEG and DCEG were obtained (MCEG and glycerol stay in aqueous phase).



Scheme 4 Product of the cyanoethylation of the glycerol

Table 3 Cyanoethylation of glycerol with basic catalyst

Entry	Catalyst (4%)	Time (h)	Ratio [a] TCEG:DCEG of isolated products	Yield of TCEG
1	/	6	-	0 %
2	MeONa	6	88 :12	66 %
3	NaOH	6	88 :12	67 %
4	KOH	6	84 :16	68 %
5	tBuOK	6	92 :8	51 %
6	DBU	6	88 :12	68 %
7	Triton B	6	80 :20	51 %
8	PPh_3	6	-	0 %
9	Na_2CO_3	6	-	0 %
10	K_2CO_3	6	-	0 %
11	Cs_2CO_3	6	-	0 %
12	NaOH	18	92:8	71 %
13	NaOH	24	94:6	73 %
14	MeONa	18	89:11	68 %
15	KOH	18	88:12	69 %
16	DBU	18	91:9	71 %

Experimental conditions: 12.5 mmol glycerol (1 equiv.), 37.5 mmol AN (3 equiv.), 0,5 mmol catalyst (4 mol%), 25°C

[a] determined by RMN ^{1}H or GC analysis

Without catalyst (Table 3, entry 1) or in presence of 4 mol% phosphine or carbonate catalysts (entries 8-11), TCEG and DCEG were not detected after 6h at 25°C. With stronger bases (hydroxyde or alcoholate, entries 2-7), the crude product was a mixture of TCEG:DGEG where TCEG was the major product (>80%). The best yields of TCEG were obtained with four catalysts : MeONa, NaOH, KOH and DBU, and in these cases, a longer reaction time, 18h or 24h (entries 12-16), led to a very slight increase of ratio TCEG:DGEG and of TCEG yield.

Table 4 Effect of the amount of catalysts and the temperature on the reaction

Entry	Catalyst	Catalyst (mol%)	Tempe rature	Time (h)	Ratio [a] TCEG :DCEG	Yield of TCEG
1	NaOH	10 %	25ºC	6	95:5	71 %
2	KOH	10 %	25ºC	6	89:11	63 %
3	NaOH	10 %	50°C	6	12 :88	68%
4	Na_2CO_3	10 %	25ºC	6	-	0 %
5	K_2CO_3	10 %	25ºC	6	-	0 %
6	Cs_2CO_3	10 %	25ºC	6	-	0 %
7	Cs_2CO_3	10 %	25ºC	168	93:7	63 %
8	DBU	30 %	25ºC	72	88:12	73 %
9	PPh_3	30 %	50ºC	24	-	0 %
10	$CuCl_2$ 30 %, MeONa in MeOH	30 %	reflux	18	-	0 %

Experimental conditions: 12.5 mmol glycerol (1 equiv.), 37.5 mmol AN (3 equiv.)

[a] Ratio TCEG:DCEG of isolated products determined by ^{1}H NMR or GC analysis

An increasing amount of catalyst to 10-30 % had no significant effect (Table 4). After 6h, neither DCEG nor TCEG were detected with 10 mol% carbonate catalyst (entries 4-6) and only a little increase of ratio TCEG:DGEG was observed with KOH or NaOH (entries 1-2). With 10% $CsCO_3$ only a reaction time of one week, led to 63% of TCEG (entry 7). Compared to the initial conditions (6h, 4 mol% catalyst), 30 mol% DBU did not improve even after 3 days of reaction (entry 8), neither 30 mol% PPh_3 over 24h (entry 9), nor copper catalysis (entry 10) according to Wang et al. conditions [18]. Furthermore, the increase of both temperature (25°C to 50°C) and amount of catalyst NaOH (4 to 10 mol%) (entry 3), led to the same result as with 25°C and 4 mol% NaOH and a lower TCEG : DCEG ratio than this one obtained for only NaOH was up to 10 mol% (entry 1). So, this result suggests that the increase in temperature is not favorable to the formation of TCEG. As already observed for 4-heptanol, the cyanoethylation of glycerol also depends, on the ratio of AN:alcohol (Table 5). The ratio TCEG:DCEG 99:1 was obtained in 6h at 25°C with 4 mol% NaOH and 3.4 equiv. of AN.

Figure 3 shows the kinetic of the cyanoethylation of glycerol (3.4 equiv AN, 25°C, 6h): the proportions of MCEG, DCEG and TCEG were determined by GC analysis, after silylation of the products[§§]. Whatever the catalysts (NaOH, KOH, MeONa) and the amounts used, (4 mol% or 5 mol%), MCEG was produced rapidly, and its proportion decreased to benefit DCEG and TCEG, which is consistent with the difference in reactivity of primary and secondary alcohols. 4 mol% KOH had a low catalytic effect compared to MeONa and NaOH. With 5 mol% NaOH, the cyanoethylation of MCEG was faster (Figure 3d) but the optimum ratio TCEG:DCEG (Table 6) was obtained for 4 mol% NaOH after 5h.

Table 5 Effect of the AN amounts on the reaction of cyanoethylation of glycerol

AN equiv.	Product distribution [a]			Ratio TCEG:DCEG	Yield of TCEG [b]
	TCEG	DCEG	Ether		
1	68%	32%	<1%	32:68	4%
2	46 %	54%	<1%	44:56	33%
3	87%	11%	1%	88:12	67%
3.1	93%	7%	<1%	93:7	74%
3.2	94%	5%	1%	94 :6	74%
3.3	96%	4%	1%	97 :3	80%
3.4	97%	2%	<1%	99:1	86%
3.5	94%	2%	4%	98 :2	83 %
4	88%	2%	10%	98:2	76%

[a] glycerol, MCEG and acrylonitrile were not observed

Experimental conditions: 12.5 mmol glycerol, x mmol AN, 0.5 mmol NaOH (4 mol%), 25ºC, 6h

[b] determined by ^{1}H NMR or GC analysis

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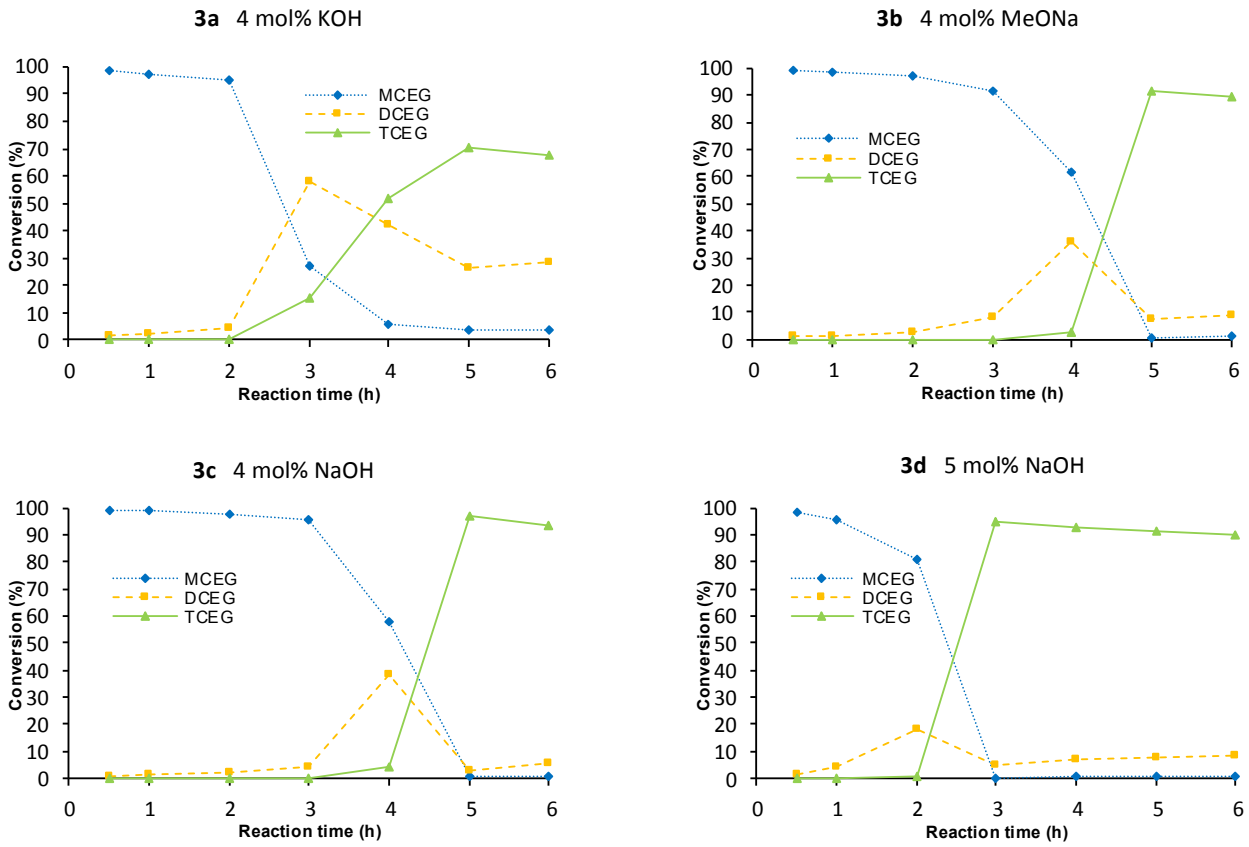


Experimental conditions: 12.5 mmol glycerol, 42.5 mmol acrylonitrile, x mmol catalyst, 25 °C, 6h

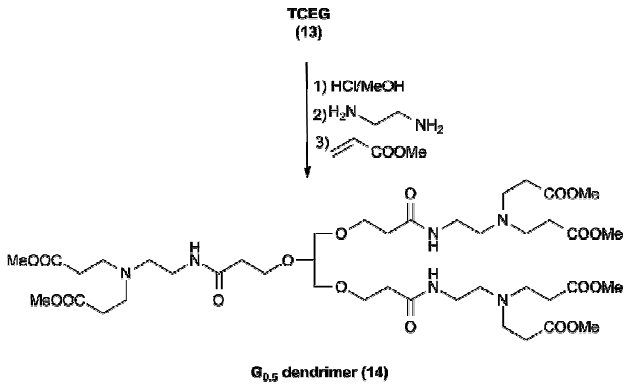
Figure 3 Product distribution of the cyanoethylation of glycerol

Indeed, whatever catalyst was used, figure 3 shows an optimum proportion of TCEG at 5h for an amount of catalyst of 4 mol% (respectively at 3h with 5 mol% NaOH) and then, the proportion of TCEG decreases. Unlike compounds **7** and **8**, when a pure sample TCEG was mixed with 4 mol% NaOH (Figure SI2‡), the decyanoethylation of TCGE to DCEG was observed over time. Moreover, Figure 3c shows that the main product MCEG **11a** was obtained after 3 hours with 4 mol% NaOH. This compound could be precursor of glycerol mono-functionalized derivatives used for their emulsifying properties in the industry [29,37]. The 3h reaction of 1 equiv. of glycerol and 1 equiv. of AN, in presence of 4 mol% NaOH, led to **11a** with 28% yield.

The workup was modified to reduce the amount of solvent and to substitute dichloromethane. The optimum conditions were as follows: after 5 h of reaction between 12.5 mmol glycerol and 42.5 mmol AN, at 25 °C in presence of 4 mol% NaOH, 20mL of ethyl acetate was added to the mixture and washed with 20mL of water. After drying the organic phase, evaporation yielded 88% TCEG (GC purity ≈99%, 1% DCEG).

Table 6 Optimum of ratio TCEG:DCEG

Catalyst	Optimum	Ratio TCEG :DCEG
NaOH 4 mol%	5h	97:3
NaOH 5 mol%	3h	92:8
MeONa 4 mol%	5h	92:8
KOH 4 mol%	5h	73:27



Scheme 5 Synthesis $G_{0.5}$ dendrimer

Nevertheless, pure TCEG was obtained: after reaction, 20mL of ethyl acetate was added to the mixture and flash chromatography (silica gel, ethyl acetate) gave a 80 % yield (purity GC >99.9%).

Pure TCEG is an interesting molecule to access dendritic structures. Because of the ether function, this new core resists the HCl hydrolysis condition and ethylenediamine treatment. The Scheme 5 shows the synthetic route to the $G_{0.5}$ generation of PAMAM type dendrimer **14** (75% yield).

Conclusions

To conclude, we have shown that the nucleophile addition of glycerol on acrylates leads to complex mixtures, because the transesterification reaction is in competition with Michael addition. In Phase transfer catalyst conditions, (40 %mol NaOH), trifunctionalized glycerol was obtained (12% yield) with t-butyl acrylate. Optimal conditions to obtain tricyanoethylglycerol (88 % yield, 99% purity) have been determined, without purification methods for the workup (chromatography column, distillation), HCl neutralization or chlorinated solvents. The methanolysis of tricyanoethylglycerol is an alternative route to the 1,2,3-trimethoxycarbonyl ethylglycerol that cannot be obtained from the direct reaction between methyl acrylate and glycerol. At present, we are investigating on the one hand, the mono-functionalization of glycerol *via* the monocyanoethylation reaction and on the other hand, the synthesis of new dendrimers from the prochiral tricyanoethylglycerol core.

Experimental section

Materials and Instruments

All reagents were commercially purchased and were used as received for the reactions. GC were performed on a PERKIN-ELMER Clarus 500 system equipped with a capillary column separation (Elite-5MS: Length: 30 m, I.D: 0.25 mm, Film Thickness: 0.25 µm) and an FID detector or MS detector (EI/70eV). Two temperature programmes were used: initial temperature at 60°C for 2.5 min, then 10 °C/min to 300°C, hold for 2.5min and initial temperature at 100°C for 1 min, then 20 °C/min to 300°C, hold for 3min. NMR spectra were recorded on a Bruker Advance 400 spectrometer 400 MHz. FT-IR spectra were run on PERKIN-ELMER Spectrum one spectrometer serial 73028. Thin-layer chromatography (TLC) was conducted with pre-coated TLC sheets ALUGRAM SIL G/UV254 (silica gel 60 with fluorescent indicator UV254, 0.2 mm thickness) and visualized under UV or by potassium permanganate. Column chromatography was performed using silica gel 60 with distilled solvents. High-resolution mass spectral analysis (HRMS) was performed with a Varian/IonSpec QFT-9 FTICR mass spectrometer equipped with a superconducting 9.4 Tesla magnet and ESI ion source.

General procedure for the Michael addition of glycerol to acrylic compounds

A 50 mL single-neck round-botton flask was charged with a magnetic stir bar, 0.04 mmol of catalyst and 12.5 mmol of glycerol at 65 °C, then the mixture was cooled at room temperature. The necessary mmol of acrylic reagent was added dropwise (5 min) and the mixture was stirred for 6h at 25 °C. 50 mL dichloromethane were added to the mixture and the organic layer was washed twice with 50 mL distilled water, dried ($MgSO_4$) and concentrated to give the additional and/or transesterification product(s).

Optimal procedure for the Michael addition of glycerol to acrylonitrile

A 50 mL single-neck round-botton flask was charged with a magnetic stir bar, 0.04 mmol of catalyst and 12.5 mmol of glycerol at 65 °C, then the mixture was cooled at room temperature. 42.5 mmol of acrylonitrile were added dropwise (5 min) and the mixture was stirred for 5h at 25 °C. 20 mL AcOEt was added of mixture. Two workups can be used to obtain TCEG. (i) The organic layer was washed with 20 mL distilled water, dried ($MgSO_4$) and concentrated to give 88% yield TCEG (99% GC purity, 1% DCEG). (ii) A flash chromatography (silica gel 60, AcOEt) of the organic layer was performed. The AcOEt solution was dried ($MgSO_4$) and concentrated to give 80% yield purified TCEG (99.9% CG purity).

Procedure for phase transfer catalysis

A 100 mL single-neck round-botton flask was charged with a magnetic stir bar, 20 mmol of glycerol and 16mL NaOH solution (40% w). The flask was purged and under N_2 atmosphere, the mixture were vigorously stirred at room temperature for 1 h. 10 mmol of tetra-n-butylammonium bromide (TBAB) in 8 mL distilled water was added. The mixture was cooled down to 0°C, 62 mmol of t-butyl acrylate was added dropwise and the reaction was maintained at room temperature for 18 h. The reaction was quenched by adding 20 mL cold water and the solution was extracted with diethyl ether (3*25 mL). The combined organic extracts were successively washed with 50 mL saturated $NaHCO_3$ solution and 50 mL brine solution, dried ($MgSO_4$) and concentrated.

The resulting material was purified by column chromatography (silica gel 60, Hexane:AcOEt 3:1) to give 12% yield.

Procedure for synthesis of the $G_{0.5}$ dendrimers

A 100 mL single-neck round-botton flask was charged with a magnetic stir bar, 5 mmol of TCEG dissolved in 2 mL methanol. 10 mL HCl 37% were added dropwise and the mixture was stirred at 65 °C for 6 hours. Then, 10 mL methanol was added and the solution was stirred at 35 °C for 5 hours. The products were extracted with dichloromethane (3*10mL) and the combined organic layer were washed with 20 mL brine solution and 20 mL distilled water. The organic layer was dried ($MgSO_4$) and concentrated. A 250 mL single-neck round-botton flask was charged with a magnetic stir bar, 1 mol of ethylenediamine dissolved in 25 mL methanol. The solution was cooled in dry ice and the flask was purged under N_2 atmosphere. The triester in 5 mL methanol was added dropwise and the mixture was stirred at room temperature for 7 days. The excess of EDA and methanol was distilled off as an azeotrope with n-butanol to give G_0. A 100 mL single-neck round-botton flask was charged with a magnetic stir bar, G_0 dendrimer and 18mL methanol. The solution was cooled in dry ice and the flask was purged under N_2 atmosphere. 33 mmol of methyl acrylate was added dropwise and the mixture was stirred for 5 days at room temperature. The excess of methyl acrylate and solvent were removed under vacuum at a temperature below 50°C. The resulting product was purified by column chromatography (silica gel 60, CH_2Cl_2:MeOH 10:1) to give 75% yield of amber-colored syrup.

Identification of Product

Data of compounds 1-10 are in ESI‡.

3-(2,3-dihydroxypropoxy)-propanenitrile (**11a**). GC-MS (EI, 70eV): t_R= 13.05 min, m/z (%): 114(12), 86(30), 85(45), 72(20), 54(100), 43(55), 31(37)

3-[2-hydroxy-1-(hydroxymethyl)ethoxy]-propanenitrile (**11b**). GC-MS (EI, 70eV): t_R= 13.40 min, m/z (%): 114(12), 97(25), 86(30), 73(10), 54(100), 43(55), 31(40)

1,3-di(cyanoethoxy)propan-2-ol (**12a**). GC-MS (EI, 70eV): t_R= 17.56 min, m/z (%): 114(22), 86(45), 54(100), 31(20)

1,2-di(cyanoethoxy)propan-3-ol (**12b**). GC-MS (EI, 70eV): t_R= 17.82 min, m/z (%): 167(10), 114(15), 97(30), 86(20), 54(100), 31(20)

1,2,3-tri(cyanoethoxy)propane TCEG (**13**). Colorless oil (m= 2.76g; Yield= 88%). IR (neat) ν=2882, 2250, 1106 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ= 2.63 (6H, t), 3.60 (4H, m), 3.70 (1H, m), 3.72 (4H, t), 3.88 (2H, t); ^{13}C NMR ($CDCl_3$, 100 MHz) δ= 18.8, 19.4, 65.6, 66.3, 71.0, 78.8, 117.5, 118.0; GC-MS (EI, 70eV): t_R= 21.83 min, m/z (%):167 (30%), 113 (20%), 84 (30%), 57 (10%), 54 (100%), 31 (20%); HRMS (ESI) for $C_{12}H_{17}N_3O_3$ (M + H)+: calculated 252.1343; Found, 252.1343.

$G_{0.5}$ dendrimer (**14**). Amber-colored syrup (m= 4.51g Yield= 75%) IR (neat) ν= 3366, 1728, 1645, 1197 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ= 2.45 (18H, t), 2.56 (6H, t), 2.77 (12H, t), 3.31 (6H, m), 3.51 (4H, t), 3.62 (1H, m), 3.68 (18H, s), 3.72 (4H, t), 3.74 (2H, t), 6.86 (2H, s), 6.92 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ= 32.6, 36.9, 37, 37.2, 49.3, 51.7, 52.9, 53.0, 66.5, 67.6, 70.6, 77.9, 171, 171.2, 173.0; HRMS (ESI) for $C_{42}H_{74}N_6O_{18}$ $(M+H)^+$: calculated 951.5132; found, 951.5134.

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§ The degradation of compounds **7** and **8** has not been observed neither along the time nor on GC column.

§§ Silylation of glycerol remains difficult and does not lead to reproducible results in GC analysis. Only TCEG and the silylation products of MCEG and DCGE are given in Figure 4 (products distribution).

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Functionalization of biobased glycerol by acrylic compounds was optimized and the tricyanoethylglycerol can be used as prochiral core of dendrimer.