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A convenient method for producing mono- and dichlorohydrins from glycerol

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A new method for the transformation of glycerol into mono- and dichlorohydrins has been studied. With trimethylchlorosilane as chlorinating agent and acetic acid as catalyst, mono- and dichlorohydrins have been obtained in high yields and selectivity. In fact, under different reaction conditions, the synthesis of α-monochlorohydrin (3-chloropropan-1,2-diol) or α,γ-dichlorohydrin (1,3-dichloropropan-2-ol) as predominant product has been achieved. This process was also exploited for the valorisation of the crude mixture of glycerol and monochlorohydrin (glyceric mixture), a by-product from an earlier BioDiesel production. A reaction mechanism has been proposed based on investigations on the chlorination of different alcohols.

1. Introduction

Glycerol is a nontoxic renewable commodity, with many industrial applications in different domains (foods, beverages, cosmetics, paper, textiles, tobacco, *etc.*).[1] Industrially, glycerol is obtained as a by-product by the saponification, hydrolysis or transesterification of triglycerides (animal fats and vegetable oils) during BioDiesel (BD) production. From these sources glycerol is recovered (*ca.* 10% by weight of the initial mass) in a crude state, and needs to be purified by distillation or ion exchange treatments. Other important pathways to produce glycerol are the synthesis from propene or by fermentation.[1] Nowadays, the growing production of BD makes glycerol a cheap raw material for several derived products like ethers, esters, organic acids, acrolein and chlorohydrins.[2–7] The chlorohydrins, in particular dichlorohydrins, are precursors of epichlorohydrin, an important intermediate in the production of epoxide resins and several fine chemicals.[8–10]

For decades chlorohydrins have been made by hypochlorination of allyl chloride or by chlorination of allyl alcohol, but both these synthetic routes start from propene.[8] Thus, chlorination of glycerol represents an interesting alternative, in particular starting from a renewable raw material originated from biomass.

The chlorination reaction of glycerol was already known at the beginning of the twentieth century. It was performed mixing glycerol with phosphorus trichloride or phosphorus pentachloride,[11] by heating glycerol in the presence of disulfur chloride (S_2Cl_2)[12,13] or thionyl chloride ($SOCl_2$),[14] or by hydrochloric acid (HCl) in the presence of small amounts of an organic acid (RCOOH).[2,15–25] In the first three methods the stoichiometry of the reaction must be precisely controlled to avoid over-chlorination, while the last method gave high selectivity towards 3-chloropropan-1,2-diol (1-MCH or α-monochlorohydrin) and 1,3-dichloropropan-2-ol (1,3-DCH or α,γ-dichlorohydrin) with low production of 1,2,3-trichloropropane and other undesirable chlorinated ethers and oligomers.

The chlorination of glycerol with HCl/RCOOH system has been widely studied. Many different reaction conditions have been tested, including aqueous or anhydrous conditions, low or high pressure, use of pure or crude glycerol. Acetic acid has been the first applied catalyst[15–19] and today it is still the cheaper one. However, a large number of other organic acids (as propionic, adipic, glutaric or malonic acid),[2,20–25] their derivatives (like esters, amides, lactones, lactames)[21] and even polymers (like polyacrylamide and polyacrylic acid)[26] have been tested as catalysts. On the other hand, the chlorinating agent has been always hydrochloric acid (HCl), in water solution or in gas form. The optimization of the conversion and the selectivity of the reaction led to maximize the production of monochlorohydrin[17,19,23] and, even more interestingly, to obtain dichlorohydrins, in particular 1,3-dichloropropan-2-ol in high yields.[16,20–22] Many efforts have been performed also to propose a reaction mechanism.[2,22,24,25,27,28]

Since glycerol is a polyalcohol, a chlorinating agent selective for primary alcohol groups like (chloro-phenylthio-methylene) dimethylammonium chloride[29] could be used to obtain 1-MCH and 1,3-DCH. However, in this case the price of the reactant is a limiting factor. Also trimethylchlorosilane (TMSCl) was found to be a good chlorinating agent for primary and tertiary alcohols.[30] This last reaction occurs at room temperature if catalysed by dimethylsulfoxide (DMSO).

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In literature, TMSCl has been also used as silylating agent of glycerol to obtain 1-trimethylsililoxypropan-2,3-diol[31] and as chlorinating agent on epichlorohydrin for the synthesis of 1,3-DCH.[32]

In the present work we report on the use of TMSCl, in addition with a catalytic amount of acetic acid, to produce α,γ-dichlorohydrin or α-monochlorohydrin in good yields and selectivity, starting from glycerol. The application of TMSCl to the transesterification of tryglycerides[33,34] for BioDiesel (BD) production has been recently studied in our laboratory. In this reaction two easily separable phases were obtained: the upper one consisted of fatty acid methyl esters useful for BD, while the other was a mixture of glycerol and α-monochlorohydrin in about equimolar ratio. In order to demonstrate the usefulness of the transesterification process in producing either BD or valuable derivatives of glycerol, the chlorination reaction in the present research has been performed also on this mixture of glycerol and α-monochlorohydrin.

Moreover hexamethyldisiloxane (HMDSO), the by-product coming from TMSCl, can be easily recovered from the reaction mixture and converted back into trimethylchlorosilane[35] with HCl and zinc chloride, lowering the price of the process.

2. Experimental

All reactants have been used as purchased. Only trimethylchlorosilane has been distilled before use and purity (93% w/w) has been checked by ^{1}H-NMR analysis. ^{13}C-NMR spectroscopy has been used as semi-quantitative method to determine the molar ratio of the chlorinated products and the residual glycerol. NMR spectra have been recorded with Varian Mercury plus 400 and Varian VXR 200 instruments.

2.1 Chlorination of glycerol

2.1.1 General procedure. In a typical experiment a mixture of 0.92 g of glycerol (10 mmol), 3.5 ml of TMSCl (3 g, 27 mmol) and 3 drops of AcOH (*ca.* 0.030 g, 0.5 mmol) were placed in a 15 ml screw-cap Sovirel©. The resulting biphasic mixture was allowed to react under continuous stirring at the desired temperature and for the desired time (see Table 1). At the end of the reaction the two phases were left to separate at room temperature. The upper one, containing unreacted TMSCl and hexamethyldisiloxane (HMDSO), was removed and the lower one was dried at room temperature under vacuum (10 mmHg) for 1 hour. A sample of the final liquid was analysed *via* ^{13}C-NMR to determine the content in glycerol and chloroderivatives.

2.1.2 Synthesis of α-monochlorohydrin from glycerol. Glycerol (2.69 g, 29 mmol), TMSCl (8.46 g, 10 ml, 72 mmol) and acetic acid (0.055 g, 0.9 mmol) were poured in a 25 ml screw-cap Sovirel©. The resulting biphasic mixture was allowed to react for 12 hours at 60 °C under continuous stirring. At the end of the reaction the upper phase was removed and the lower phase was distilled under vacuum (1 mmHg). The fraction collected at 63 °C (1.32 g, 41% w/w) was α-monochlorohydrin (99% purity). ^{1}H-NMR (400 MHz, DMSO-d_6) δ 4.68 (br, 2H), 3.66–3.60 (m, 2H), 3.49 (dd, 1H), 3.42–3.32 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 72.4 (d), 62.6 (t), 47.1 (t). Other two phases were collected: below 45 °C (0.45 g, 14% w/w) 1,3-DCH (99% purity); between 45 °C and 63 °C (0.58 g, 18% w/w) mixture of 1-MCH and 1,3-DCH (respectively 89% and 11%). The residue of distillation (0.61 g, 19% w/w) contained glycerol (41%) and 1-MCH (59%).

2.1.3 Synthesis of α,γ-dichlorohydrin from glycerol. Glycerol (2.78 g, 30 mmol), TMSCl (8.75 g, 10.5 ml, 75 mmol) and acetic acid (0.054 g, 0.9 mmol) were poured in a 25 ml screw-cap Sovirel©. The resulting biphasic mixture was allowed to react for 12 hours at 100 °C under continuous stirring. At the end of the reaction the upper phase was removed and the lower one was distilled under vacuum (18 mmHg). The fraction collected between 40 and 77 °C (3.14 g, 79% w/w) was α,γ-dichlorohydrin (99% purity). ^{1}H-NMR (400 MHz, DMSO-d_6) δ 5.16–4.82 (br, 1H), 3.90 (m, 1H), 3.63 (m, 4H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 69.9 (d), 46.3 (t).

2.1.4 Reaction of glycerol and TMSCl with DMSO as catalyst. Glycerol (0.92 g, 9.9 mmol), TMSCl (3.22 g, 3.8 ml, 29 mmol) and dimethylsulfoxide (0.363 g, 4.6 mmol) were poured in a 15 ml screw-cap Sovirel©. The resulting biphasic mixture was allowed to react for 18 hours at 100 °C under continuous stirring. At the end of the reaction the two phases were left to separate at room temperature. The upper phase was removed and the lower one was dried at room temperature under vacuum (10 mmHg) for 1 hour to eliminate water. ^{13}C-NMR analysis of the final liquid gives: 81% α-monochlorohydrin and 19% of unreacted glycerol.

2.2 Chlorination of the mixture of glycerol and monochlorohydrin (glyceric mixture) from BD production

Sunflower oil [19.0 g, 21.6 mmol for MW = 879 g mol^{-1}], TMSCl (5.48 g, 6.5 ml, 46.9 mmol) and methanol (3.15 g, 4 ml, 98.0 mmol) were poured in a 50 ml flask. After heating for 8 hours at 60 °C under continuous stirring, the mixture has been left to separate in two phases. The upper one (fatty acid methyl esters for BD) was removed and the second phase was washed with petroleum ether and dried at room temperature under vacuum (10 mmHg) for 1 hour to eliminate the volatile compounds. The resulting mixture consisted in glycerol and α-monochlorohydrin (1.92 g, 10% w/w, molar ratio 52 : 48 by ^{13}C-NMR).

2.2.1 Synthesis of α-monochlorohydrin from the glyceric mixture. TMSCl (1.28 g, 1.5 ml, 11.1 mmol) and a few drops of AcOH (0.018 g, 0.3 mmol) were added to 0.88 g of the glyceric mixture in a 15 ml screw-cap Sovirel©. The resulting biphasic mixture was allowed to react under continuous stirring at 60 °C for 9 hours. At the end of the reaction the upper phase was removed and the lower phase was dried at room temperature under vacuum (10 mmHg) for 1 hour to eliminate volatile by-products. The resulting mixture (0.99 g) was analysed *via* ^{13}C-NMR (Table 2, entry 3) showing 68% of α-monochlorohydrin, 30% of α,γ-dichlorohydrin and 2% of unreacted glycerol.

Table 1 Reactions performed with glycerol as starting material

Entry	TMSCl ratio[a]	AcOH ratio[a]	Temperature	Time	Distribution of products (molar ratio) by ^{13}C-NMR		
					1 (Gly)	**2** (1-MCH)	**3** (1,3-DCH)
1	2.9	no	100 °C	24 h	0.40	0.57	0.03
2	2.5	0.03	100 °C	2 h	—	0.63	0.37
3	2.9	0.04	100 °C	6 h	—	0.14	0.86
4	2.8	0.03	100 °C	8 h	—	0.12	0.88
5	2.8	0.03	100 °C	12 h	—	0.04	0.96
6	2.9	0.03	100 °C	18 h	—	0.01	0.99
7	2.5	0.04	60 °C	6 h	0.22	0.74	0.04
8	2.2	0.05	60 °C	12 h	0.05	0.77	0.18
9	2.5	0.04	60 °C	18 h	—	0.75	0.25
10	2.5	0.04	30 °C	65 h	0.29	0.68	0.03
11	1.1	0.03	100 °C	18 h	0.14	0.78	0.08
12	1.2	0.04	60 °C	18 h	0.16	0.78	0.05
13	1.9	0.04	60 °C	12 h	0.05	0.76	0.18
14	1.8	0.06	60 °C	18 h	—	0.68	0.32
15	2.5	(0.08)[b]	100 °C	5 h	—	0.47	0.53
16	3.0	(0.47)[c]	100 °C	18 h	0.19	0.81	—

[a] Ratio between the moles of reagent and the moles of glycerol. [b] Catalyst: tartaric acid (see ref. 23). [c] Catalyst: DMSO (see ref. 30).

Table 2 Reactions performed on a glycerol/1-MCH mixture originating from BD production[33,34]

Entry	TMSCl ratio[a]	AcOH ratio[a]	Temperature	Time	Distribution of products (molar ratio) by ^{13}C-NMR		
					1 (Gly)	**2** (1-MCH)	**3** (1,3-DCH)
A[b]					0.48	0.52	
1	2.7	0.05	100 °C	12 h	—	0.04	0.96
2	2.4	0.09	60 °C	18 h	—	0.29	0.71
3	2.7	0.07	60 °C	9 h	0.02	0.68	0.30

[a] Ratio between the moles of reagent and the moles of hydroxy groups involved in each reaction. [b] Composition of the starting material.

2.2.2 Synthesis of α,γ-dichlorohydrin starting from the glyceric mixture. TMSCl (2.40 g, 2.8 ml, 20.5 mmol) and a few drops of AcOH (0.033 g, 0.6 mmol) were added to 0.76 g of the glyceric mixture in a 15 ml screw-cap Sovirel©. The resulting biphasic mixture was allowed to react under continuous stirring at 100 °C for 12 hours. At the end of the reaction the upper phase was removed and the lower phase was dried at room temperature under vacuum (10 mmHg) for 1 hour to eliminate volatile by-products. The resulting mixture (0.89 g) was analysed *via* ^{13}C-NMR (Table 2, entry 1): 4% of α-monochlorohydrin, and 96% of α,γ-dichlorohydrin were detected.

2.3 TMSCl chlorination of different alcohols and diols

2.3.1 General procedure. The reaction was performed on benzyl alcohol, *n*-propyl alcohol, cyclohexanol, *t*-butyl alcohol, 1,2-propanediol and ethylene glycol. In a typical experiment a mixture of alcohol, TMSCl and catalyst, in the molar ratio reported in Table 3, was placed in a 15 ml screw-cap Sovirel©. The mixture was allowed to react at the temperature and for the time reported in Table 3 under continuous stirring. At the end of the reaction different work-up were performed as follows.

2.3.2 Benzyl alcohol. Operating at 60 °C two phases were observed and the upper one was dried at room temperature under vacuum (10 mmHg) for one hour. ^{1}H and ^{13}C-NMR analyses in $CDCl_3$ indicated a complete conversion of the alcohol and the formation of a mixture of benzyl chloride and benzyl acetate (Table 3). ^{1}H and ^{13}C-NMR in D_2O of the lower phase showed the presence of acetic acid.

2.3.3 *n*-Propyl alcohol. Working at 60 °C only one phase was observed. ^{1}H-NMR analysis in $CDCl_3$ indicated the presence of a mixture of the alcohol and the acetate, together with traces of 1-chloropropane. Heating at 100 °C, two phases were formed and ^{1}H and ^{13}C-NMR analyses in $CDCl_3$ of the upper one indicated the presence of a mixture of propyl chloride, propyl acetate, and traces of dipropyl ether (Table 3). Nevertheless ^{1}H and ^{13}C-NMR analyses in D_2O of the lower phase evidenced a residual presence of the unreacted alcohol.

Table 3 Chlorination on different alcohols and diols

Entry	Alcohol	TMSCl ratio[a]	AcOH ratio[a]	Temperature	Time	Final molar ratio (^{1}H-NMR or ^{13}C-NMR)[b] R–OH	R–Cl	R–OAc
1	Benzyl alcohol	1.1	0.98	60 °C	9 h	—	0.62	0.38
2	Benzyl alcohol	1.2	0.29	60 °C	9 h	—	0.85	0.15
3	Benzyl alcohol	1.2	0.06	60 °C	12 h	—	0.96	0.04
4	*n*-Propyl alcohol	1.2	0.28	60 °C	9 h	0.73	—	0.26
5	*n*-Propyl alcohol	1.2	0.06	60 °C	12 h	0.91	0.03	0.06
6	*n*-Propyl alcohol	1.2	0.06	100 °C	15 h	—	0.94	0.06[c]
7	Cyclohexanol	1.3	0.27	60 °C	9 h	0.71	—	0.29
8	Cyclohexanol	1.2	0.27	100 °C	15 h	—	0.84	0.14[c]
9	Cyclohexanol	1.2	0.06	100 °C	15 h	0.03	0.84	0.09[c]
10	*t*-Butyl alcohol	1.2	0.27	60 °C	9 h	—	0.99	—
11	*t*-Butyl alcohol	1.2	0.07	60 °C	12 h	—	0.99	—
12	1,2-Propanediol	2.3	0.06	60 °C	12 h	0.13	0.87[d]	—
13	Ethylene glycol	2.2	0.06	60 °C	12 h	—	0.98	0.02

[a] Ratio between the moles of reagent and the moles of alcohol. [b] Determined by comparison with literature data. [c] Traces of the ether derivative. [d] Mixture of 1-Cl-2-propanol (90%) and 2-Cl-1-propanol (10%).

2.3.4 Cyclohexanol. Working at 60 °C, only one phase was observed. ^{1}H-NMR analysis in $CDCl_3$ indicated no conversion of the alcohol into the chloro derivative and only a slight formation of the acetate was found. In the experiments at 100 °C two phases were observed. The upper one was dried at 50 °C under vacuum (10 mmHg) for one hour, and ^{1}H and ^{13}C-NMR analyses in $CDCl_3$ indicated a mixture of chlorocyclohexane, cyclohexyl acetate and traces of dicyclohexyl ether and unreacted alcohol (Table 3). ^{1}H and ^{13}C-NMR spectra in D_2O of the lower phase indicated the presence of acetic acid and traces of unreacted alcohol.

2.3.5 *t*-Butyl alcohol. At 60 °C two phases were observed and ^{1}H and ^{13}C-NMR analyses in $CDCl_3$ of the upper one indicated a complete conversion of the alcohol into 2-chloro-2-methyl-propane (Table 3). ^{1}H and ^{13}C-NMR spectra in D_2O of the lower phase indicated only the presence of acetic acid.

2.3.6 1,2-Propanediol. At 60 °C two phases were observed and ^{1}H and ^{13}C-NMR analyses in DMSO of the lower one indicated a partial conversion of the reagent into 1-chloro-2-propanol (**14**) together with a minor amount of 2-chloropropanol (see Table 3). ^{1}H and ^{13}C-NMR spectra in $CDCl_3$ of the upper phase indicated the presence of HMDSO and residual TMSCl.

2.3.7 Ethylene glycol. At 60 °C two phases were observed and ^{1}H and ^{13}C-NMR analyses in DMSO of the lower one indicated a complete conversion of the reagent into 2-chloroethanol (**15**) with traces of 2-chloroethyl acetate (see Table 3). ^{1}H and ^{13}C-NMR spectra in $CDCl_3$ of the upper phase indicated the presence of HMDSO and residual TMSCl.

3. Results and discussion

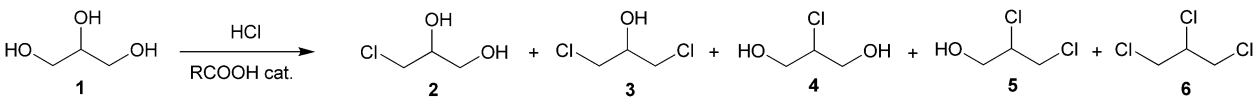
The chlorination of glycerol (**1**) with hydrochloric acid, catalysed by an organic acid, is reported in Scheme 1. Depending on the reaction conditions (temperature, time, catalyst and quantity of HCl) monochlorination or polychlorination can be obtained.

As pointed out in previous works,[2,20,21] the chlorination afforded predominantly 1-MCH (**2**) and 1,3-DCH (**3**) according with the higher reactivity and lower steric hindrance of primary alcohol groups with respect to secondary ones. Nevertheless small amount of 2-MCH (**4**), 1,2-DCH (**5**) and 1,2,3-trichloropropane (**6**) have been found, depending on the quantity of HCl used, temperature and reaction time. Moreover, the formation of minor chlorinated ethers and oligomers was also reported.[20,21]

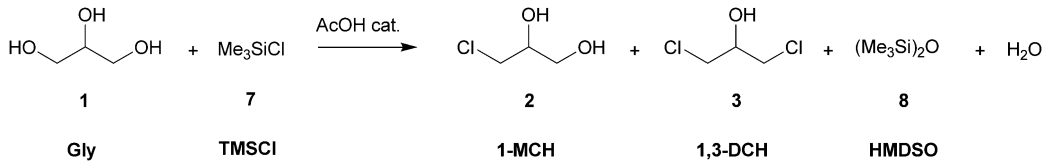
The chlorination of glycerol with TMSCl is reported in Scheme 2. Surprisingly, among the 5 possible chloroderivatives of glycerol, only compounds **2** and **3** were obtained, also in the absence of catalyst (Table 1, entry 1).

The reaction was monitored by ^{13}C-NMR spectroscopy as semiquantitative analysis technique. In fact, three CH signals, one for each molecule (glycerol, 3-chloropropan-1,2-diol and 1,3-dichloropropan-2-ol), are easily recognizable in the spectra (Fig. 1).

Several trials of chlorination of glycerol are reported in Table 1, performed by changing temperature and reaction times, and varying the amount of TMSCl and catalyst.



Scheme 1 Chlorination of glycerol with HCl.



Scheme 2 Chlorination of glycerol with TMSCl.

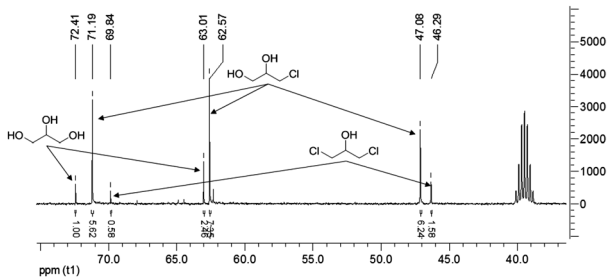


Fig. 1 Typical analysis: estimation of glycerol and chloroderivatives content by ^{13}C-NMR spectroscopy in DMSO-d_6 as solvent.

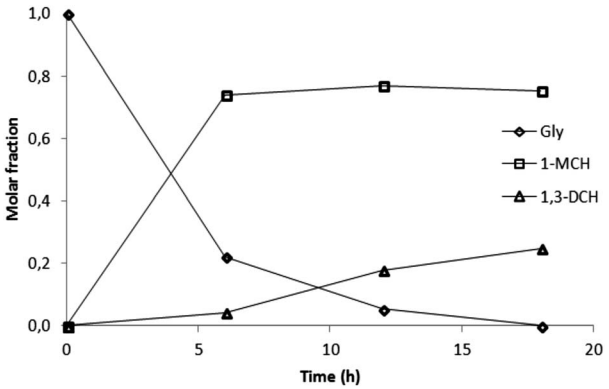


Fig. 3 Experiments at 60 °C (Table 1, entries 7–9).

The presence of acetic acid was essential for the complete conversion of glycerol. In fact, without catalyst, after 24 hours at 100 °C glycerol was still present in the reaction mixture (Table 1, entry 1) while the conversion was complete with acetic acid (entry 2), in less than two hours at the same temperature.

By comparison of the experiments carried out at 100 °C (TMSCl/glycerol molar ratio range 2.5–2.9) (Table 1, entries 2–6, and Fig. 2) it can be observed that glycerol was totally converted in the first two hours of reaction in a 1.7 : 1 mixture of 1-MCH (**2**) and 1,3-DCH (**3**) (entry 2). As the chlorination proceeded, after six hours **3** is the main product (1 : 6 ratio, entry 3) and a conversion greater than 95% is reached after 12 hours (Table 1, entry 5).

As regards the experiments carried out at 60 °C (TMSCl/glycerol molar ratio in the range 2.2–2.5) (Table 1, entries 7–9, and Fig. 3), it can be observed that 1-MCH (**2**) was the main product with a predominance close to 80%. A similar 1-MCH (**2**) formation was also achieved by lowering the temperature to 30 °C and increasing the reaction time to 65 hours (Table 1, entry 10) or by reducing the amount of TMSCl (Table 1, entries 11–14). However, in these cases, if the molar ratio of TMSCl was slightly higher than 1 the glycerol conversion was not complete (entries 11 and 12) while, if the quantity of TMSCl was between 1.8 and 2.5, the conversion depended only on the time of reaction (compare entries 13 with 8 and 14 with 9).

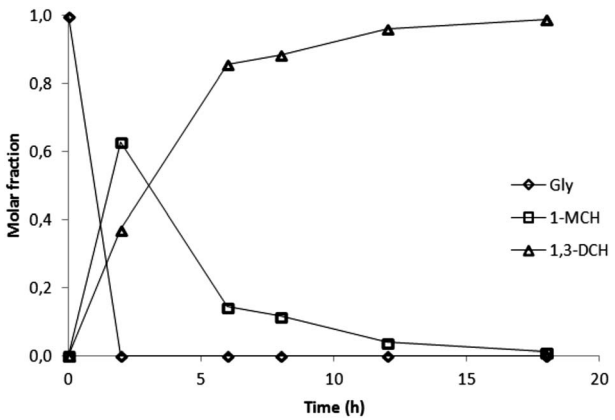
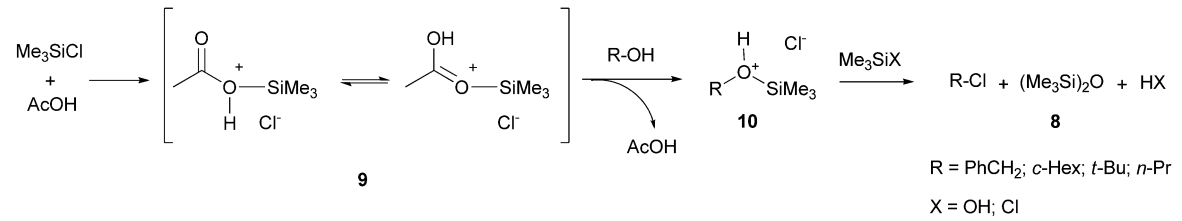


Fig. 2 Experiments performed at 100 °C (Table 1, entries 2–6).

Santacesaria and co-workers[2,22–25] found a relation between the pK_a of the organic acid used as catalyst and the degree of chlorination when HCl was used: acidic catalysts having p$K_a \geq 4$ were normally selective towards dichlorohydrin, while catalysts with pK_a values in the range 1.2–3 were more selective for monochlorohydrins. In fact, also in the present chlorination procedure, we found a higher amount of 1-MCH (**2**) using tartaric acid (first pK_a = 3.03) instead of acetic acid (pK_a = 4.75) (Table 1, entries 3 and 15). However, the system TMSCl/tartaric acid resulted poorly selective (**2** and **3** were obtained in almost equimolar ratio).

As final consideration, even if DMSO was reported[30] as a good catalyst for chlorination of primary alcohols with TMSCl, in the case of glycerol the best results were obtained under AcOH catalysis (compare entries 6 and 16, Table 1).

The best reaction conditions to obtain selectively α-monochlorohydrin (**2**) or α,γ-dichlorohydrin (**3**) found in the experiments carried out on pure glycerol, were also used with the mixture of glycerol and α-monochlorohydrin, deriving from the transesterification of sunflower oil with TMSCl, and the results are reported in Table 2. The amounts of TMSCl and AcOH were referred to the hydroxy groups involved in each reaction. In



Scheme 3 Proposed mechanism for monofunctional alcohol chlorination.

particular, the stoichiometric ratio to obtain α,γ-dichlorohydrin (**3**) was 2 with respect to glycerol and 1 with respect to 1-MCH (**2**). The stoichiometric ratio to obtain α-monochlorohydrin (**2**) was 1 with respect to glycerol.

The 1,3-DCH (**3**) was obtained with high selectivity operating at 100 °C for 12 hours (Table 2, entry 1).

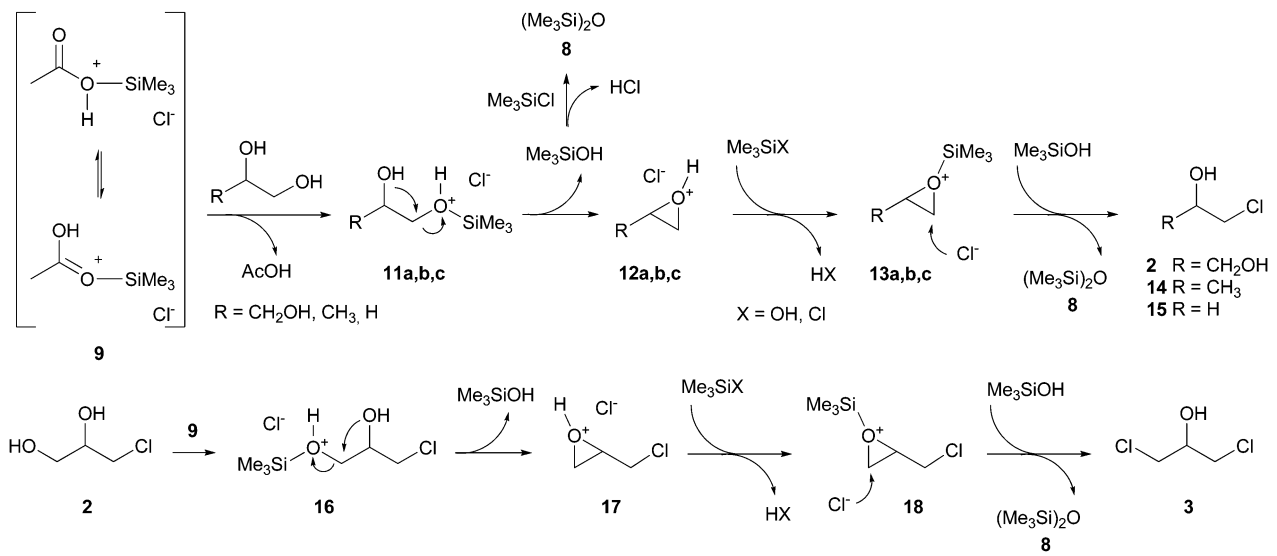
On the other hand, the formation of **2** as predominant product (**2**/**3** molar ratio 68 : 30) was achieved by heating the starting mixture at 60 °C for 9 hours (Table 2, entry 3). Longer reaction times or higher temperatures strongly favour dichlorination (Table 2, entries 1 and 2).

Finally, in order to understand the type of mechanism involved in the reaction, the chlorination system TMSCl/AcOH was applied to several alcohols (Table 3). A survey of the literature showed that TMSCl is a good chlorinating agent for primary and tertiary alcohols when the reaction is catalyzed by DMSO at room temperature.[30] The use of TMSCl with AcOH instead of DMSO, allows the chlorination of benzyl alcohol only by heating the reaction mixture at 60 °C. However, in our case the chlorination occurs also using a lower quantity of TMSCl, just above the stoichiometric ratio (1.2 equiv. *vs.* 2 equiv. used by Snyder[30]). It was found that, beside a complete conversion of the benzyl alcohol, the quantity of AcOH affects the selectivity of the reaction, because a side reaction affording benzyl acetate takes place (Table 3, entries 1–3). The best results were obtained with a molar ratio AcOH/ROH 0.06 by heating for 12 hours at 60 °C (Table 3, entry 3). A similar behaviour was also observed for *t*-butanol (Table 3, entries 10 and 11).

On the other hand *n*-propanol and cyclohexanol resulted much less reactive then benzyl alcohol and *t*-butanol in the same reaction conditions (Table 3, entries 4, 5 and 7). Only when heated at 100 °C for 15 hours they were converted into the corresponding chlorides (Table 3, entries 6, 8 and 9). It should be noted that secondary alcohols were found unreactive under the catalysis by DMSO.[30]

The reaction of 1,2-propanediol, using 2.3 equiv. of TMSCl, one equiv. for each hydroxyl group, showed a greater reactivity of this substrate with respect to the monofunctional alcohol (Table 3, entries 4–6 and 12), giving as main product 1-chloropropan-2-ol at lower temperature. Also ethylene glycol showed a great reactivity: in fact it was completely converted into the corresponding monochloro derivative.

The relevance of a possible generation of dry HCl by reaction of TMSCl with compounds having mobile protons (ROH or RCOOH) is, in our opinion, moderate. In analogy to Snyder,[30] we assume that the mechanism of the reaction on monohydroxy compounds could involve the attack of the acid catalyst on TMSCl leading to adduct **9** that is now activated for the nucleophilic attack of the alcohol, with the release of the catalyst. The last step is a nucleophilic substitution of the



Scheme 4 Proposed mechanism for chlorination of polyols.

chloride ion on the trimethylsilyl intermediate **10**, leading to the chloro derivative (Scheme 3).

On the other hand, the great difference of reactivity observed for *n*-propanol and 1,2-propanediol suggests a different reaction mechanism for the two substrates. While mono hydroxyl substrates react through simple nucleophilic substitution pathways (Scheme 3), for polyols (1,2-propanediol, ethylene glycol and glycerol) a two-step process involving the formation of epoxide intermediates **12a–c** and **13a–c** could be proposed, according with some literature data†.[2,22–25] In particular, the intermediate **13a** (R = CH_2OH) evolves into 1-MCH (**2**) by a nucleophilic attack of the chloride ion on the less hindered carbon atom (Scheme 4). The formation of the intermediates **12a–c** from activated polyols **11a–c** through intramolecular nucleophilic substitution can be described as an example of *symphoria* impossible for *n*-propanol and responsible for the higher reaction rate observed for 1,2-propanediol, ethylene glycol and glycerol. Furthermore, the presence of a 1,2-diol system on the α-monochlorohydrin (**2**) allows a second chlorination to give α,γ-dichlorohydrin (**3**).

4. Conclusions

A new method for glycerol chlorination has been carried out using trimethylchlorosilane as chlorinating agent and AcOH as catalyst. The process has shown, under optimized conditions, a very high selectivity towards α,γ-dichlorohydrin (**3**), an useful starting material for the production of epichlorohydrin. By controlling the reaction conditions is also possible to drive the conversion of glycerol towards α-monochlorohydrin (**2**). Hexamethyldisiloxane (HMDSO) is formed as by-product of the reaction, that can be quantitatively recovered by distillation and conveniently transformed back to TMSCl,[35] for recycling in the process. Moreover the present methodology could be easily integrated in the process for the transesterification of triglycerides with TMSCl,[33,34] for the conversion of the mixture glycerol/monochlorohydrin, by-product of the BD production, into valuable α,γ-dichlorohydrin (**3**).

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