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Aminolysis Reaction of Glycerol Carbonate in Organic and Hydroorganic Medium

**Bassam Nohra · Laure Candy · Jean-François Blanco ·
Yann Raoul · Zephirin Mouloungui**

Abstract Aminolysis reaction of glycerol carbonate with primary amine in organic and hydroorganic media leads to the formation of two hydroxyurethane isomers and a partial decomposition of glycerol carbonate into glycerol. Aminolysis with a secondary amine promotes the condensation reaction and limits the formation of glycerol. The ratio of α versus β was determined by zgig ^{13}C NMR. This technique permits computing the yield of α and β products in the medium. The quantity of glycerol was determined by GC analysis. The ratio of the isomers and the amount of glycerol depend on the amine and the solvent. Kinetic investigations reveal that, in hydroorganic medium, the more the alkyl chain of the amine increased, the less glycerol was formed. On the contrary, in organic medium, the alkyl chain of the amine does not play a major role in the formation of glycerol.

Keywords Aminolysis · Glycerol carbonate · Organic medium · Hydroorganic medium · Hydroxyurethane · Glycerol

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Introduction

Urethanes are useful compounds having a wide range of applications in the chemical industry, such as plastic materials and herbicides [1]. To produce urethanes, the most common reagent is isocyanate, which is toxic [2–4]. Alternatively, hydroxyurethanes are prepared according to non-isocyanate routes. Hydroxyurethanes are prepared in a reaction via ring-opening of cyclic carbonates. No volatile or non-volatile by-products are produced by this reaction [3].

Cyclic carbonates have been explored to develop various carbonyl compounds and polymers [5–14]. Glycerol carbonate is one of the glycerol derivatives that, at present, captures more academic and industrial attention. Glycerol carbonate is a green substitute for important petro-derivative compounds such as ethylene carbonate or propylene carbonate. It can be prepared using the reaction of glycerol with carbon dioxide [13, 14, 18], with urea [15] or carbonates such as dimethyl carbonate, ethylene carbonate and propylene carbonate [16, 17]. Cyclic carbonates undergo a number of reactions with various nucleophiles. The most explored reaction of cyclic carbonate has been that of aminolysis, which is the nucleophilic addition of an amine on the cyclocarbonate function. It provides a hydroxyurethane derivative having one hydroxyl group. In the case of glycerol carbonate, the aminolysis reaction gives rise to two hydroxyurethane isomers depending on the presence of the urethane function at the α or β position. Each hydroxyurethane isomer has two hydroxyl groups and a urethane unit on the skeleton of glycerol.

Some studies have focused on the effect of the substituent, the temperature and the solvent in the aminolysis of the cyclic carbonates. Several substituted cyclic carbonates were studied, and the reaction rate with amine was found to increase as the electron withdrawing character of

the substituent increased [6, 9]. This is in contradiction with the conclusions reached by Mikheev et al. [5, 12]. At low temperature, the aminolysis reaction results in hydroxyurethane, whereas at elevated temperatures (>100 °C), another amine molecule is able to react with the hydroxyurethane and yields a substituted urea [19]. In the presence of organic solvents, some authors indicated a somewhat higher ratio of β versus α hydroxyl [9, 20, 21]. However, the relative isomer ratio is insensitive to the reaction temperature and only slightly dependent on solvent polarity [9–11]. One study investigated the condensation reaction of glycerol carbonate with butylamine in the presence and absence of a solvent in stoichiometric amounts [22].

The kinetic features of the interaction of cyclocarbonates with amino groups were studied by Garipov et al. [23]. Studies of the kinetics of the reaction indicated that the rate of the reaction of cyclic carbonates with amines depends on the initial concentration of the amine [12, 24], but is independent of the substituent on the ring [12, 22]. When using water as a solvent, side reactions must be considered, such as hydrolysis, which decreases yields of products compared to those obtained when using organic solvents. Malkemus et al. [25] studied the reaction of ethylene carbonate with ammonia at 50 °C to form hydroxyalkylurethane; no formation of a secondary product has been classified. On the contrary, Ochiai et al. [26] described the aminolysis reaction of bicyclic carbonate. The polyaddition of a hydrophobic bifunctional cyclic carbonate and hexamethylenediamine effectively gives polyurethane with hydroxyl groups in aqueous media, although accompanied by hydrolysis of bicyclic carbonates into diols.

In this paper, we report the synthesis of hydroxyalkylurethanes by the reaction of glycerol carbonate with several primary (NH_2–C_nH_{2n+1}; $n = 0, 4, 6, 8, 12, 16$ or amine-terminated polypropylene glycol) and secondary amines (C_nH_{2n+1}–NH–C_4H_9, $n = 1$–2). α and β isomers were evaluated by the classical ^{13}C or ^{1}H NMR methods. We investigated the effects of the solvent, the length of the alkyl chain and the class of the amine (primary or secondary) on the selectivity of α versus β isomers. No studies have been yet reported in the literature describing the kinetics and the mechanism of the aminolysis reaction and the formation of glycerol as a by-product in organic and hydroorganic medium. We determined the kinetic constants of glycerol formation during the aminolysis of glycerol carbonate by different amines in organic and hydroorganic medium.

Materials and methods

Chemicals

Glycerol carbonate (Huntsman, 99.5%), ammonium hydroxide (Sigma Aldrich, 28% in water), butylamine (Sigma Aldrich, 99.5%), hexylamine (Sigma Aldrich, 99%), octylamine (Sigma Aldrich, 99%), dodecylamine (Fluka, 99%), hexadecylamine (Fluka, ≥92%), N-methyl-butylamine (Sigma, ≥96%), N-ethylbutylamine (Sigma, ≥98%) and O-(2-aminopropyl)-O'-(2-methoxyethyl) polypropylene glycol (jeffamine®, Aldrich, 99%, Mn = 600) were used as received. Methanol and acetonitrile (HPLC grade) were purchased from Merck (Germany).

Synthesis of 3a, a'

A solution of ammonium hydroxide (28%) was added at 50 °C to an equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). After 2 h under mechanical stirring, a homogeneous, clear and colorless solution resulted. The reaction mixture was then distilled under reduced pressure for ammonia and water removal. ^{1}H NMR (DMSO-d_6): δ in ppm = 4.13 (m, 1H, –CHOCO), 4.23 (m, 2H, –CH_2OCO), 3.90 (quint, 1H, –CHOH), 3.77 (m, 4H, –CH_2OH), 3.68 (m, 2H, –CH_2OH), ^{13}C NMR (DMSO-d_6): δ in ppm = 159.30 (α C=O), 159.26 (β C=O), 78.50 (–CHOCO), 74.10 (–CHOH), 67.40 (–CH_2OCO), 63.0 (–CH_2OH), 66.80 (–CH_2OH). IR (KBr): 3,342 cm^{-1} (υ-OH), 1,706 cm^{-1} (υ –OC(=O)NH–), 1,616 cm^{-1} (–OC=ONH–H). LRMS (CI): 136 (M + H$^+$), 153 (M + NH_4$^+$). HRMS (CI): found M + H$^+$, 136.0045. $C_4H_9NO_4$ requires 136.0042.

Synthesis of 3b, b'

N-butylamine (15.49 g, 0.2118 mol) was added at 50 °C to an equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). The reaction was kept at 50 °C under mechanical stirring for 2 h. ^{1}H NMR (DMSO-d_6): δ in ppm = 5.35–5.20 (m, 2H, –NH), 4.65 (m, 1H, –CHO), 4.1 (m, 2H, –CH_2OCO), 3.85 (quint, 1H, –CHOH), 3.70 (m, 4H, –CH_2OH), 3.60 (m, 2H, –CH_2OH), 3.10 (m, 4H, –CH_2N), 1.45 (m, 4H, –CH_2–CH_2–CH_3), 1.30 (m, 4H, –CH_2–CH_3), 1.3 (t, 6H, –CH_3). ^{13}C NMR (DMSO-d_6): δ in ppm = 157.0 (C=O), 79.2 (–CHOCO), 75.0 (–CHOH), 68.0 (–CH_2OCO), 65.0 (–CH_2OH), 45.0 (–CH_2N), 34.0 (–CH_2–CH_2–CH_3), 21.5 (–CH_2–CH_3), 14.2 (–CH_3). IR (KBr): 3,342 cm^{-1} (υ-OH), 1,697 cm^{-1} (υ –OC(=O)NH–), 1,543 cm^{-1} (–OC=ONH-R). LRMS (CI): 192 (M + H$^+$), 209 (M + NH_4$^+$). HRMS (CI): found M + H$^+$, 192.1228. $C_8H_{18}NO_4$ requires 192.1236.

Synthesis of 3c, c'

N-hexylamine (21.43 g, 0.2118 mol) was added at 50 °C to an equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). The reaction was kept at 50 °C under mechanical stirring for 2 h. ^{1}H NMR (MeOD): δ in ppm = 4.69 (m, 1H, –CHOCO), 4.06 (m, 2H,–CH_2OCO),

3.78 (quint, 1H, –CHOH), 3.66 (m, 4H, –CH$_2$OH), 3.54 (m, 2H, –CH$_2$OH), 3.08 (m, 4H, –CH$_2$NH), 1.48 (m, 4H, –CH$_2$–CH$_2$–CH$_3$), 1.3 (m, 12H, –CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 0.90 (t, 6H, –CH$_3$). **^{13}C NMR** (MeOD): δ in ppm = 159.18 (α C=O), 158.88 (β C=O), 77.06 (–CHOCO), 71.69 (–CHOH), 66.94 (–CH$_2$OCO), 62.12 (β, –CH$_2$OH), 64.21 (α, –CH$_2$OH), 41.96 (–CH$_2$NH), 33.10 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 30.58 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 31.03 (–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 23.84 (–CH$_2$–CH$_2$–CH$_3$), 14.54 (–CH$_3$). **IR** (KBr): 3,342 cm^{-1} (υ-OH), 1,697 cm^{-1} (υ –OC(=O)NH–), 1,543 cm^{-1} (–OC=ONH-R). **LRMS (CI):** 220 (M + H$^+$), 237 (M + NH$_4{}^+$). **HRMS (CI):** found M + H$^+$, 220.1707. C$_{10}$H$_{22}$NO$_4$ requires, 220. 1705.

Synthesis of 3d, d$'$

N-octylamine (27.40 g, 0.2118 mol) was added at 50 °C to an equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). The reaction was kept at 50 °C under mechanical stirring for 2 h. **^{1}H NMR** (MeOD): δ in ppm = 4.69 (m, 1H, –CHOCO), 4.06 (m, 2H, –CH$_2$OCO), 3.78 (quint, 1H, –CHOH), 3.66 (m, 4H, –CH$_2$OH), 3.54 (m, 2H, –CH$_2$OH), 3.08 (m, 4H, –CH$_2$NH), 1.48 (m, 4H, –CH$_2$–CH$_2$–CH$_3$), 1.30 (m, 20H, –CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 0.90 (t, 6H,–CH$_3$). **^{13}C NMR** (MeOD): δ in ppm = 159.18 (α C=O), 158.88 (β C=O), 77.06 (–CHOCO), 71.69 (–CHOH), 66.94 (–CH$_2$OCO), 64.21 (α, –CH$_2$OH), 62.12 (β, –CH$_2$OH), 41.96 (–CH$_2$NH), 33.15 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 28.02 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 30.58 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 30.55 (–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 31.07 (–CH$_2$–CH$_2$–CH$_3$), 23.87 (–CH$_2$–CH$_3$), 14.58 (–CH$_3$). **IR** (KBr): 3,342 cm^{-1} (υ-OH), 1,697 cm^{-1} (υ –OC(=O)NH–), 1,543 cm^{-1} (–OC=ONH-R). **LRMS (CI):** 248 (M + H$^+$), 265 (M + NH$_4{}^+$). **HRMS (CI):** found M + H$^+$, 248.1859. C$_{12}$H$_{26}$NO$_4$ requires, 248. 1862.

Synthesis of 3b, b$'$; 3c, c$'$ and 3d, d$'$ in water

A solution of butylamine, hexylamine or octylamine in water was added to glycerol carbonate in stoechiometric amount at 50 °C. The reaction was stirred for 2 h. Raw media were analyzed without purification.

Synthesis for the kinetic study

The kinetics synthesis followed the same protocol as the synthesis of **3a, a$'$**; **3b, b$'$** and **3d, d$'$**. The molar ratio was calculated by assuming that one mole of alkylamine consumes one mole of glycerol carbonate. Sampling was carried out every 15 min and was analyzed by GC.

Synthesis of 3e, e$'$

N-dodecylamine (39.25 g, 0.2118 mol) was added at 50 °C to an equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). The reaction was kept at 50 °C under mechanical stirring for 2 h. **^{1}H NMR** (DMSO-d$_6$): δ in ppm = 4.52 (m, 1H, –CHOCO), 3.93 (m, 2H,–CH$_2$OCO), 3.57 (quint, 1H,–CHOH), 3.45 (m,4H,–CH$_2$OH), 3.35 (m,2H, –CH$_2$OH), 2.93 (m, 4H,–CH$_2$NH), 1.23 (m,36H, –CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 1.36 (m, 4H, –CH$_2$–CH$_2$–CH$_3$), 0.85 (t, 6H,–CH$_3$). **^{13}C NMR** (DMSO-d$_6$): δ in ppm = 156.41 (α C=O), 156.16 (β C=O), 75.24 (–CHOCO), 69.83 (–CHOH), 65.49 (–CH$_2$OCO), 62.84 (α-CH$_2$OH), 60.14 (β-CH$_2$OH), 40.26 (–CH$_2$NH), 31.36 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 26.31 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 29.08 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 28.78 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 29.48 (–CH$_2$–CH$_2$–CH$_3$), 22.16 (–CH$_2$–CH$_3$), 14.01 (–CH$_3$). **IR** (KBr): 3,342 cm^{-1} (υ-OH), 1,697 cm^{-1} (υ –OC(=O)NH–), 1,543 cm^{-1} (–OC=ONH-R). **LRMS (CI):** 304 ($M + H^+$), 321 (M + NH$_4{}^+$). **HRMS (CI):** found M + H$^+$, 304.2483. C$_{16}$H$_{34}$NO$_4$ requires 304.2488.

Synthesis of 3f, f$'$

N-hexadecylamine (15.49 g, 0.2118 mol) was added at 50 °C to an equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). The reaction was kept at 50 °C under mechanical stirring for 2 h. **^{1}H NMR** (CDCl$_3$): δ in ppm = 4.91 (m, 1H, –CHOCO), 4.11 (m, 2H,–CH$_2$OCO), 3.87 (quint, 1H,–CHOH), 3.77 (m,4H,–CH$_2$OH), 3.65 (m,2H, –CH$_2$OH), 3.14 (m, 4H,–CH$_2$NH), 1.47 (m,4H,–CH$_2$–CH$_2$–CH$_3$), 1.23 (m, 52H,–CH$_2$ –CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$ –CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 0.86 (t, 6H,–CH$_3$). **^{13}C NMR** (CDCl$_3$): δ in ppm = 156.89 (α C=O), 156.92 (β C=O), 76.22 (–CHOCO), 70.88 (–CHOH), 65.95 (–CH$_2$OCO), 63.30 (α-CH$_2$OH), 62.99 (β-CH$_2$OH), 41.41 (–CH$_2$NH), 32.13 (–CH$_2$– CH$_2$–CH$_2$–NH), 26.96 (–CH$_2$– CH$_2$–CH$_2$–NH), 29.80 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 29.57 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 29.49 (–CH$_2$–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 30.04 (–CH$_2$–CH$_2$–CH$_2$–CH$_3$), 22.90 (–CH$_2$–CH$_2$–CH$_3$), 14.34 (–CH$_3$). **IR** (KBr): 3,342 cm^{-1} (υ-OH), 1,697 cm^{-1} (υ –OC(=O)NH–), 1,543 cm^{-1} (–OC=ONH-R). **LRMS (CI):** 360 (M + H$^+$), 377 (M + NH$_4{}^+$). **HRMS (CI):** found M + H$^+$, 360.3114. C$_{20}$H$_{42}$NO$_4$ requires, 360.3114.

Synthesis of 3g, g$'$

O-(2-aminopropyl)-O'-(2-methoxyethyl) polypropylene glycol (12.31 g, 0.106 mol) was added at 50 °C to an

equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). The reaction was kept at 50 °C under mechanical stirring for 4 h. **^{1}H NMR** MeOD): δ in ppm = 4.69 (m, 1H, –CHOCO), 3.60 (quint, 1H, –CHOH), 4.05 (m, 2H, –CH$_2$O), 3.76 (m, 4H, β, –CH$_2$OH), 3.36 (m, 2H, α, –CH$_2$OH), 3.20 (m, 4H, –NH–CH–CH$_2$), 7.90 (m, 2H, –NH–CH–CH$_3$), 1.03 (t, 6H, –NH–CH–CH$_3$), 3.47 (m, 4H*n, –O–CH$_2$–CH–CH$_3$), 3.62 (m, 2H*n, –O–CH$_2$–CH–CH$_3$), 1.13 (m, 6H*n, –O–CH$_2$–CH–CH$_3$), 3.60 (m, 8H, CH$_2$–CH$_2$–O–CH$_3$), 3.35 (t, 6H, –O–CH$_3$)..**^{13}C NMR** (MeOD) δ in ppm = 158.53 (α C=O), 158.17 (β C=O), 77.04 (–CHO), 71.65 (–CHOH), 69.86 (–CH$_2$O), 62.10 (β, –CH$_2$OH), 64.24 (α, –CH$_2$OH), 77.73 (–NH–CH–CH$_2$), 47.79 (–NH–CH–CH$_3$),19.28 (–NH–CH–CH$_3$), 74.51 (–O–CH$_2$–CH–CH$_3$), 76.80 (–O–CH$_2$–CH–CH$_3$), 17.77 (–O–CH$_2$–CH–CH$_3$), 72.25 (CH$_2$–CH$_2$–O–CH$_3$), 76.30 (CH$_2$–O–CH$_3$), 59.50 (–O–CH$_3$). **IR** (KBr): 3,342 cm^{-1} (υ-OH), 1,697 cm^{-1} (υ –OC(=O)NH–), 1,543 cm^{-1} (–OC=ONH-R). **Maldi-TOF:** Mn = 700, C$_7$H$_{14}$NO$_4$–(C$_3$H$_6$O)$_n$– C$_3$H$_7$O$_2$ with n = 7,72.

Synthesis of 3h, h′

N-methylbutylamine (18.46 g, 0.2118 mol) was added at 50 °C to an equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). The reaction was kept at 50 °C under mechanical stirring for 2 h. **^{1}H NMR** (DMSO-d$_6$): δ in ppm = 4.13 (m, 1H, –CHOCO), 4.23 (m, 2H,–CH$_2$OCO), 3.90 (quint, 1H,–CHOH), 3.77 (m,4H,–CH$_2$OH), 3.68 (m,2H, –CH$_2$OH), 2.90 (m, 6H,–CH$_3$N), 2.96 (m, 4H,–CH$_2$N), 1.55 (m,4H,–CH$_2$–CH$_2$–CH$_3$), 1.33 (m, 4H,–CH$_2$–CH$_3$), 0.96 (t, 6H,–CH$_3$).**^{13}C NMR** (DMSO-d$_6$): δ in ppm = 156.18 (α C=O), 156.39 (β C=O), 79.07 (–CHOCO), 68.00 (–CH$_2$OCO), 74.08 (–CHOH), 62.98 (–CH$_2$OH), 66.78 (–CH$_2$OH), 34.40 (–N–CH$_3$), 51.20 (–N–CH$_2$–), 31.30 (–CH$_2$–CH$_2$–CH$_3$), 20.50 (–CH$_2$–CH$_3$), 13.7 (–CH$_3$). **IR** (KBr): 3,401 cm^{-1} (υ-OH), 1,684 cm^{-1} (υ –OC(=O)N–). **LRMS (CI):** 206 ($M + H^+$), 223 (M + NH$_4^+$). **HRMS (CI):** found M + H$^+$, 206.1493. C$_9$H$_{20}$NO$_4$ requires 206.1501.

Synthesis of 3i, i′

N-ethylbutylamine (21.43 g, 0.2118 mol) was added at 50 °C to an equimolar quantity of glycerol carbonate (25 g, 0.2118 mol). The reaction was kept at 50 °C under mechanical stirring for 2 h. **^{1}H NMR** (DMSO-d$_6$): δ in ppm = 4.13 (m, 1H, –CHOCO), 4.23 (m, 2H,–CH$_2$OCO), 3.90 (quint, 1H,–CHOH), 3.77 (m,4H,–CH$_2$OH), 3.68 (m,2H, –CH$_2$OH), 3.00 (m, 4H, –N–CH$_2$–CH$_3$), 1.20 (m, 6H, –N–CH$_2$–CH$_3$), 2.96 (m, 4H,– N–CH$_2$–), 1.55 (m,4H,–CH$_2$–CH$_2$–CH$_3$), 1.33 (m, 4H,–CH$_2$–CH$_3$), 0.96 (t, 6H,–CH$_3$).**^{13}C NMR** (DMSO-d$_6$): δ in ppm = 156.19 (α C=O), 156.41 (β C=O), 79.10 (–CHOCO), 68.03 (–CH$_2$OCO), 74.10 (–CHOH), 63.00

(–CH$_2$OH), 66.80 (–CH$_2$OH), 42.10 (–N–CH$_2$–CH$_3$), 13.10 (–N–CH$_2$–CH$_3$), 48.70 (–N–CH$_2$–), 31.61 (–CH$_2$–CH$_2$–CH$_3$), 20.52 (–CH$_2$–CH$_3$), 13.70 (–CH$_3$). **IR** (KBr): 3,401 cm^{-1} (υ-OH), 1,684 cm^{-1} (υ –OC(=O)N–). **LRMS (CI):** 220 ($M + H^+$), 238 (M + NH$_4^+$). **HRMS (CI):** found M + H$^+$, 220.1545. C$_{10}$H$_{22}$NO$_4$ requires 220.1549.

Characterization

^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were achieved on a Bruker Avance® 300-MHz instrument using tetramethylsilane (TMS) as an internal standard and equipped with a QNP probe (^{1}H, ^{19}F, ^{31}P, ^{13}C). A preliminary study of ^{1}H (zg30), J-mod and dept135 signals completed with 2D studies (COSY, HSQC) led to the attribution of the NMR signals. The ratio of α/β isomers is determinated at 293.2 K, with the zgig ^{13}C pulse program. In the most recent experiments, the delay time D1 is greater than or equal to 30 s in order to permit the full relaxation of all nuclei concerned in the assay.

Fourier transform infrared (FT-IR) spectra were measured on a PerkinElmer Spectrum 65 spectrometer. Low resolution mass spectrometry analyses were performed on a triple quadruple instrument TSQ 700 (thermoquest). Mass calibration was conveniently carried out using the precursor ion NH$_4^+$ (m/z = 18). High-resolution mass spectrometry was obtained using the ionization method; CI refers to chemical ionization.

Gas chromatography (GC) analyses were performed with Varian 3900 using a BP20 (SGE) column (12 m × 0.53 mm × 1 μm) in a temperature range of 60–230 °C at 30 °C/min and 20 min at 230 °C, with methanol as the dilution solvent. The injector and FID detector temperatures were set at 250 °C. The injection volume was 1 μl. Chromatograms were treated by a Star Chromatography Workstation υ0.6.4. Software. O-(2-aminopropyl)-O′-(2-methoxyethyl) polypropylene glycolhydroxyurethane MALDI-TOF spectra were recorded on a MicroMX Waters MALDI apparatus equipped with a 337-nm nitrogen laser with 4-ns pulse duration. The samples were dissolved in MeOH and mixed with a solution of the MALDI-TOF matrix (2,5-dihydroxybenzoic acid, NaI).

Results and Discussion

Aminolysis reaction of glycerol carbonate in organic medium

Aminolysis reaction with primary amine

Aminolysis reaction of glycerol carbonate **1** with different amines **2** was carried out at 50 °C for 2 h to afford the

corresponding α and β hydroxyurethanes isomers **3** and the secondary product glycerol **4** (Fig 1). The reaction was conducted by infrared spectroscopy until the complete disappearance of the $\mu C=O$ bond of the carbonate function (1786 cm^{-1}) and the appearance of the $\mu(OC(=O)-NHR)$ bond of the urethane unit (1697 cm^{-1}). The urethane unit also gives two other bands. The high frequency at 1543 cm^{-1} corresponds to the ($-OC(=O)NH-R$), and the low frequency at 1250 cm^{-1} is attributed to $\mu(C(=O)-O-C)$ of the glycerol unit.

In the literature, the ratio of α versus β hydroxyurethanes is generally established in a post-reactional phase by spectroscopic methods more particularly by ^{1}H NMR [9, 10, 22]. The structures of the compounds and the ratio of α versus β hydroxyurethanes were determined by zgig ^{13}C NMR. Figure 2 depicts the zgig ^{13}C NMR of α and β N-octylhydroxyurethanes (**3d** and **3d'**) and shows the 65/35 ratio of the former and the latter. We verified the ratio of the selectivity on the signals assignable to the carbonyl carbon signals (**i** and **i'**) that appeared at 159.18 and 158.88 ppm, at the α-methine carbon signals (**k** and **k'**) at 71.69 and 77.06 ppm, but also at the β-methine carbon signals (**l** and **l'**) at 64.21 and 62.12 ppm of the glycerol skeleton. These results were confirmed by HPLC analysis.

With a 1:1 molar ratio (glycerol carbonate: amine) and a number of carbons of the alkyl chain of the amine less than or equal to 12, the conversion of glycerol carbonate and the yield of hydroxyurethanes was more than 87%. For longer alkyl chains, the conversion of glycerol carbonate was weaker and the yield of hydroxyurethanes decreased (runs
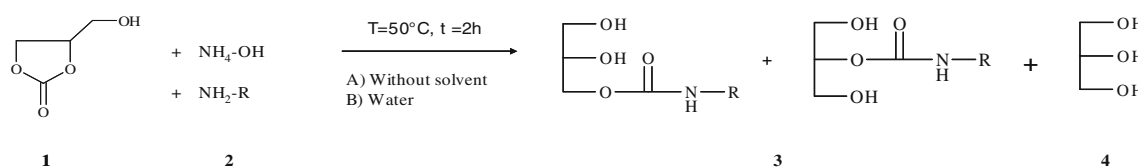
Fig. 1 Aminolysis reaction of glycerol carbonate (**3a** and **3a'**: α and β hydroxyurethane with R=H; **3b** and **3b'**: α and β N-butylhydroxyurethane with R=C$_4$H$_9$; **3c** and **3c'**: α and β N-hexylhydroxyurethane with R=C$_6$H$_{13}$; **3d** and **3d'**: α and β N-octylhydroxyurethane with R=C$_8$H$_{17}$; **3e** and **3e'**: α and β N-dodecylhydroxyurethane with R=C$_{12}$H$_{25}$; **3f** and **3f'**: α and β N-hexadecylhydroxyurethane R=C$_{16}$H$_{33}$; **3 g** and **3 g'**: α and β O-(2-aminopropyl)-O'-(2-methoxyethyl) polypropylene glycolhydroxyurethane with R=O-(2-aminopropyl)-O'-(2-methoxyethyl) polypropylene glycol
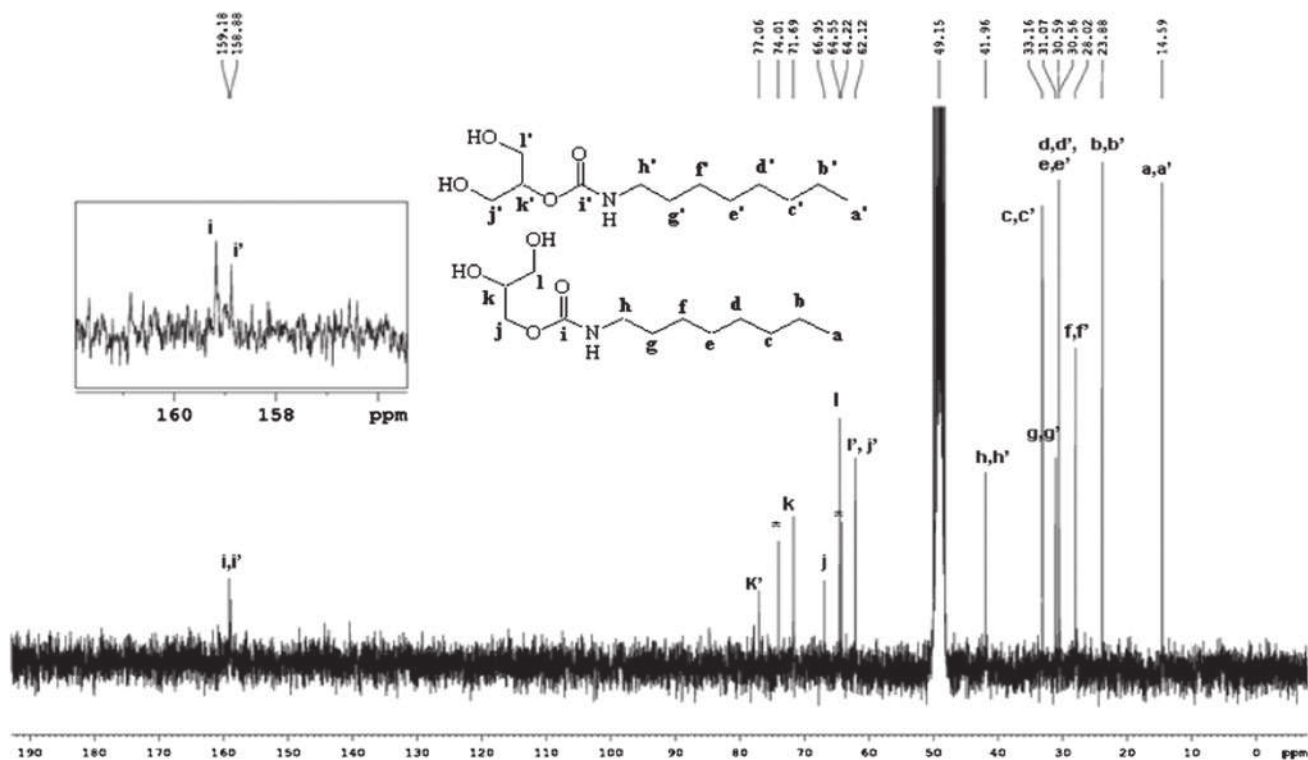
Fig. 2 Zgig ^{13}C NMR (300 MHz, MeOD) of α and β N-octylhydroxyurethanes (**3d** and **3d'**) obtained from glycerol carbonate and octylamine (*asterisk* indicates glycerol)

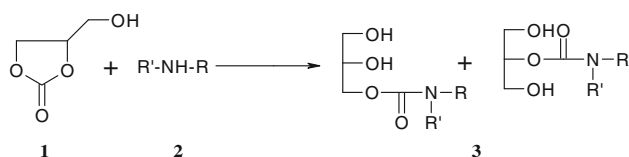long alkyl chain of the amine seems to be the main factor responsible for the modification of the rate constants of the ring-opening and so the modification of the selectivity of α versus β. The ratios of α and β isomers were almost dependent on amines as suggested by prior studies [11], but independent of the reaction temperature (runs **2–3**; **7** and **10**; **12–13**; **14–17**).

A surprising experimental fact is the presence of glycerol. This by-product derives from the aminolysis reaction of glycerol carbonate, more particularly in hydroorganic medium. The presence of glycerol in the medium was conducted by GC analysis. Gas chromatography is an analytical tool that affords simultaneous analysis of the conversion of glycerol carbonate, the formation of hydroxyurethanes and glycerol. Kinetic investigations of the aminolysis reaction were of value in order to evaluate the percentage of glycerol present in the reaction. This type of reaction is fast, and the formation of glycerol is significant. As shown in Table 1, in organic medium, the yield of glycerol was stable at around 10% whatever amine was

12, **14**). However, increasing the reaction temperature (runs **13**, **15**) and the amine ratio (runs **16–17**) favored the yield of the reaction. The conversion of glycerol carbonate and the yield of hydroxyurethanes were affected by the reaction temperature and the ratio of glycerol carbonate: amine.

The selectivity of the reaction favored the α isomer [7, 11, 12]. However, the length of the alkyl chain of the amine affects the regioselectivity of the ring-opening. Herewith, the more the alkyl chain increased, the more the ratio of the β isomer increased (Fig. 3). The steric hindrance due to the

Table 1 Aminolysis reaction of glycerol carbonate with amines

Run	T °C	t (h)	Solvent	Ratio[a]	Conversion[b]	α/β[c]	Yield[d] (%)	Yield of α[e]	Yield of β[f]	Yield of 4[g]	Compounds
1	50	2	water	1:1	100	95/5	69	65	3	31	**3a, a′**
2	25	2	–	1:1	78	75/25	73	55	18	5	**3b, b′**
3	50		–	1:1	100	75/25	91	68	23	9	
4	50		water			78/22	79	62	17	21	
5	50	2	–	1:1	100	71/29	90	64	26	9	**3c, c′**
6			water			75/25	86	65	22	14	
7	50	2	–	1:1	100	65/35	90	63	27	10	**3d, d′**
8	50		water		100	70/30	88	62	26	11	
9	50		DMSO		95	55/45	83	43	43	12	
10	60		–		100	65/35	89	63	27	11	
11	50	2	–	1:1	98	57/43	87	49	37	11	**3e, e′**
12	50	2	–	1:1	80	49/51	73	36	37	7	**3f, f′**
13	80	2			100		90	44	46	10	
14	50	2	–	1:1	20	51/49	18	9	9	2	**3g, g′**
15	80	2		1:1	44		42	21	21		
16	80	2		1:1.4	60		58	29	28		
17	90	4		1:1.4	100		98	50	48		
18	50	2	–	1:1	50	58/42	49	29	21	1	**3h, h′**
19	80	4		1:1.4	95		95	58	42		
21	50	2	–	1:1	30	52/46	29	15	13	1	**3i, i′**
22	80	4		1:1.4	70		69	36	32		
23	90	4		1:1.8	95		94	49	43		

[a] Molar ratio of glycerol carbonate versus amine

[b] Conversion of glycerol carbonate determined by GC analysis

[c] Selectivity of α versus β by zgig ¹³C NMR

[d] Yield of hydroxyurethanes

[e,f] Yield of α and β calculated

[g] Yield of glycerol determined by GC analysis

used (runs **3**, **5**, **7**, **11** and **13**). However, this yield decreases depending on the reactivity of the amine (runs **14–17**). A primary amine on a secondary carbon reacts faster than a primary amine on a tertiary carbon. The probable reason for this phenomenon is that the amine plays the roles of both catalyst and reagent, affording the ring-opening of the glycerol carbonate to form glycerol and hydroxyurethane isomers. Moreover, because of forming an intramolecular bond and blockage of carbonyl oxygen, it considerably lowers the susceptibility of the whole hydroxyalkylurethane group to hydrolysis.

Aminolysis reaction with secondary amine

The reaction of **1** with secondary amine **2** (Fig. 3) was carried out in the same conditions as for primary amines. The reaction was monitored by infrared spectroscopy until the complete disappearance of the μC=O bond of the carbonate function (1786 cm^{-1}) and the appearance of the μ(OC(=O)–N–) bond of the carbamoyle unit (1684 cm^{-1}). As summarized in Table 1, the conversion reached respectively 50% and 30% with N-methyl (run **18**) and N-ethylbutylamine (run **21**). The probable reason for this lower conversion of glycerol carbonate is the weaker nucleophilicity of the secondary amine and the hydrophobic character of the alkyl chain. The conversion of glycerol carbonate was improved by increasing either the reaction temperature or the reagent concentration. The reaction of glycerol carbonate with a secondary amine was dependent on the reaction temperature, the ratio of the reagents and the amine. Furthermore, the use of a secondary amine instead of a primary amine improved the selectivity toward the β isomer and limited the hydrolysis side reaction. This is probably due to the lower basicity (pK$_b$ butylamine = 3.55; pKb N-methylbutylamine = 3.1) and the higher steric hindrance of the secondary amine.

Aminolysis reaction of glycerol carbonate in hydroorganic medium

Aminolysis of the glycerol carbonate with several amines **2** in water at 50 °C affords hydroxyurethanes **3** and the by-product glycerol **4** (Fig. 1). The hydroorganic medium is initially made of glycerol carbonate, aliphatic amine and water, representing two competitive nucleophiles, the one being weaker than the other. Reagents are miscible with water to the extent that aliphatic amines have fewer than 12 carbon atoms. When using water as a solvent, side reactions must be considered, such as the decomposition of glycerol carbonate into glycerol that decreases yields of products. Glycerol carbonate is susceptible to glycerol and carbon dioxide formation at low temperature in the presence of 5% water under stirring. This decomposition is favored in the presence of bases [27]. The nucleophilic addition of the amine on the cyclocarbonate competes with the chemical instability of the reagent in the presence of aqueous amines.

As shown in Fig. 4, the more the alkyl chain increases, the less glycerol is formed. Moreover, the ratio in the β isomer increases with the number of carbon atoms. Indeed, the differing hydrophobicity of the amine is a probable reason for this clear difference. Octylamine containing a considerable degree of hydrophobic structure may have excluded water from the carbonate moieties to prevent its solvatation effect and then limited the decomposition of glycerol carbonate.

The formation of the by-product glycerol as a function of reaction time was investigated for different aminolysis reactions. Its formation was monitored by GC analysis. We have found some differences in the rate of the reaction and the formation of glycerol as a by-product between the different nitrogen nucleophiles. The reaction in the presence of ammonium hydroxide is very fast. It leads to a quick and total conversion of glycerol carbonate in about 15 min into glycerol along with the formation of short chain hydroxyurethane. At 5 min reaction time, glycerol was calculated to be 15%. After this time, the hydrolysis of urethane function takes place, and the percentage of glycerol increases progressively as a function of time. At 2 h, the hydrolysis product was 30%. For longer alkyl chain primary amines, it is readily apparent that the rate of formation of glycerol is slower. At 15 min reaction time, the decomposition of residual glycerol carbonate had started already, and the glycerol yield was calculated to be 6.5% for butylamine, 5.8% for hexylamine and 5.5% for octylamine. At the end of the reaction time, the glycerol yield was calculated to be 21% (run **4**), 14% (run **6**) and 11% (run **8**) for reactions with butylamine, hexylamine and octylamine, respectively. The reaction was complete after 2 h, leading to a total consumption of glycerol carbonate (Fig. 5). For short chain amines, the competition between aminolysis and decomposition of glycerol carbonate favored the decomposition as water easily reached the cyclocarbonate, which is not the case for longer hydrophobic amines. Even if the nucleophilic addition of amines remains the principal reaction, the presence of water in basic conditions enhances the parallel decomposition reaction of glycerol carbonate into glycerol.

In the progress of the aminolysis reaction of glycerol carbonate, the rates of the reaction were in the order of **2a > 2b > 2d,** indicating the lesser reactivity of **2d** and **2b** toward **2a**. Since the reactivity of **2a** was higher than that of **2b** and **2d**, we calculated the reaction rate constants *k* in order to evaluate the difference in reactivity. The kinetic disappearance of the amine and cyclic carbonate (i.e., glycerol carbonate) was studied by several authors [19, 22,
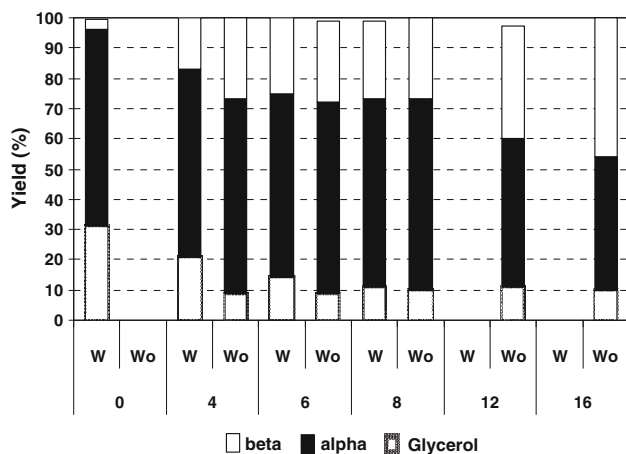
Fig. 4 Yield of α, β and glycerol in the function of the number of carbon atoms of the primary amine determined by GC analysis and ^{13}C NMR (W water, Wo without water)

28, 29]. However, the kinetic formation of glycerol as a by-product of the aminolysis reaction has never been demonstrated.

The reaction rates are expressed by Eq. (1).

$$-dC/dt = kC^2 (C : \text{ concentration of 1})$$ (1)

Equation (1) can be transformed to Eq. (2).

$$1/C - 1/C_0 = kt$$ (2)

Figure 6 illustrates the correlation between reaction time and $1/C-1/C_0$, where linear relationships through the origin can be observed, demonstrating the validity of the premise above. The slopes of the lines provided the reaction rate constants: $k_{2a} = 4.5035$ (g g min^{-1}), $k_{2b} = 1.054$ (g g min^{-1}) and $k_{2d} = 0.6223$ (g g min^{-1}), respectively. These results confirm the reactivity of every amine used in the aminolysis of glycerol carbonate. In conclusion, the use of water as a solvent enhances the by-product formation significantly, i.e., the decarboxylation of glycerol
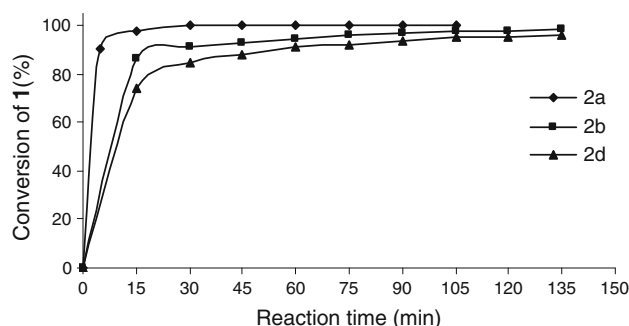
carbonate, and the rate of formation of glycerol is much faster.

Next, we studied the aminolysis reaction of glycerol carbonate with octylamine in solvent medium (runs 8 and 9) in order to study the effect of the solvent on the ratio of α versus β and the amount of glycerol formed. We found that the presence of glycerol is affected by the solvent polarity.

In the case of water, the selectivity of α versus β is affected by water presence (runs **4**, **6**, **8**). However, with organic solvents the selectivity of α versus β is slightly dependent on solvent polarity [11, 21, 22].

Conclusion

We have investigated the aminolysis reaction of glycerol carbonate in organic and hydroorganic media, giving two hydroxyurethane isomers and the by-product glycerol. We elucidated the ratio and the structures of α and β hydroxyalkylurethane isomers obtained by the reaction of **1** with amines. The conversion of glycerol carbonate and the yield of hydroxyurethanes were dependent on the reaction temperature and the ratio of the amine added. The ratio of the isomers was determined by zgig ^{13}C NMR, giving the same results as those determined by gas chromatography. The ratio in α hydroxyalkylurethane was higher than that of the β isomer using a primary amine and approximately the same with a secondary amine. Moreover, the selectivity of α versus β was independent of the reaction temperature, but dependent on the solvents and amines structures. We also demonstrated the non-negligible formation of glycerol as a by-product. The quantity of glycerol depends on the reactivity of the amine and the presence of water in the medium. The presence of water affects the formation of β isomer and increases the formation of glycerol. This effect is reduced with longer alkyl chains. Finally, the aminolysis reaction of glycerol carbonate with a secondary amine
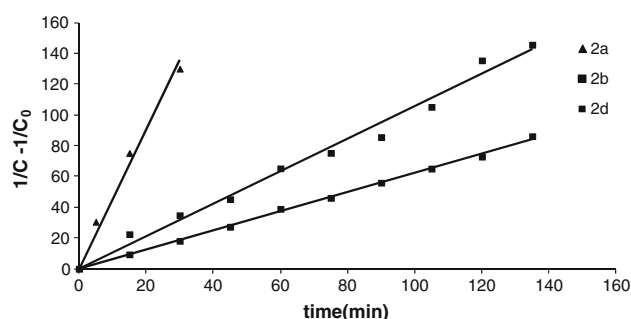

Fig. 5 Disappearance of glycerol carbonate in the aminolysis reaction of glycerol carbonate with ammonia (**2a**), butylamine (**2b**) and octylamine (**2d**) at 50 °C in water

Fig. 6 Time-(1/C-1/C_0) relationships in the aminolysis reaction of glycerol carbonate with ammonia (**2a**), butylamine (**2b**) and octylamine (**2d**) at 50 °C in water

promotes the condensation reaction and limits the formation of the hydrolysis product.

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