Ring-Opening of γ-Valerolactone with Amino Compounds

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ABSTRACT: Diols obtained by the ring-opening of biomass-based γ-valerolactone (GVL) are potentially valuable building blocks that can be used as precursors in the manufacture of green polymers and resins. We report here a study on the ring-opening of GVL through adding amine compounds. The reactivity of the applied amine compounds in this ring-opening was tested by varying the structure of the amine compounds. Both mono-amines (ammonium, 2-aminoethanol, 2-phenylethylamine, and morpholine) and di-amines (1,2-diaminoethane, 1,2-diaminopropane, and piperazine) were used. The study showed that steric hindrance at the reacting amine-function plays a more prominent role than local point charge. To optimize the yield of the desired di-functional monomers, the ring-opening of GVL with 1,2-diaminoethane (1,2-DE) was studied in more detail. Reaction temperature (25–100°C), reaction time, and molar ratio of the reactants appeared to be the determining processing parameters. These were found to be more important than the use of catalysts (triphenylphosphine, Tin(II)-2-ethylhexanoate, Ytterbium(III)trifuoromethanesulfonate, $AlCl_3$, and $SnCl_2$) and solvent polarity (methanol, DMA, DMSO, and water). © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 123: 3556–3564, 2012

Key words: polyurethanes; monomers; polyamides

INTRODUCTION

The production of platform chemicals by the conversion of lignocellulosic biomass has received increasing attention in the past decade.[1] Ethanol and glycerol derivatives are produced at commercial scale and other chemicals are being explored as precursors for different applications such as fuel additives and bio-based polymers. Levulinic acid (LA) and γ-valerolactone (GVL), obtained by hydrogenation of LA, are examples of base-chemicals that can be obtained from biomass.[2–5] Both chemicals have been studied as intermediates to methylfuran, pentanediol, or alkanes,[1,6] and to precursors for the synthesis of biodegradable polymers.[7] GVL, in particular, has been studied as a potential source for the manufacture of biodegradable polyesters[8] through controlled ring-opening polymerization.[8–11] However, in contrast to δ-valerolactone and ε-caprolactone, GVL has a very low reactivity due to its low ring strain and direct polymerization resulting in relatively low molecular weight products.[12–14]

Therefore, other chemistry leading to more reactive intermediates from LA directly or indirectly by the ring-opening of GVL is desired to develop a new versatile route to produce polymers with high molecular weights. Potential routes have been reported for caprolactone[15] and butyrolactone.[16] Burba and Volland have synthesized an amino-amide containing a free hydroxyl-group via the addition of diamine compounds to caprolactone, while Nelson et al. reported that bond cleavage on β-butyrolactone can be accomplished by nucleophilic reagents. For the latter ring-opening, "hard" nucleophilic compounds were found to add to the carbonyl function, whereas "soft" ones attack the γ-carbon of the lactone.

This observed regio-selective addition suggests that the nucleophilic nature of amino compounds can be applied to open GVL into γ-hydroxy(amino)amide compounds under mild conditions. As such, the novel pathway is expected to deliver co-monomers that are useful in the synthesis of polymers such as polyurethanes, polyesters, and polyethers.

The aim of this work is to study the reactivity of amino compounds for the ring-opening of GVL and to develop an optimized pathway for the synthesis of GVL-based polymer precursors. Both mono- and di-amino compounds were reacted with GVL under different reaction conditions and the effect of process variables on the conversion and adduct-selectivity was studied. Process variables such as the presence of a catalyst, solvent polarity, temperature, and mole ratio of lactone to amine were studied to gain insight in and to optimize the reactivity for this ring-opening of GVL.

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EXPERIMENTAL

Materials

All chemicals used in this study were of analytical grade and used without purification. GVL (**1**), 2-aminoethanol (**3**), 1,2-diaminoethane, (1,2-DE) (**6**), and 1,2-propanediamine (**8**), were purchased from Sigma Aldrich, Germany. *N*,*N*-dimethylacetamide (DMA) was purchased from Sigma, Germany. Ytterbium (III)-trifuoromethanesulfonate (YFMS) was purchased from Aldrich, Germany. Triphenylhosphine (TP), Tin(II)-2-ethylhexanoate (TEH), 2-phenylethylamine (**4**), and piparazine (**7**) were purchased from Fluka, Germany. Aluminum(III)trichloride ($AlCl_3$) and ammonium (**2**) were purchased from Merck, Germany. $SnCl_2.2H_2O$ and morpholine (**5**) were, respectively, provided by Riedel-de Haen and Janssen Chemica, The Netherlands. Dimethylsulfoxide (DMSO) was provided by ACROS, Germany. Diethyl ether, methanol, and *n*-hexane were obtained from Lab Scan, The Netherlands. Silica gel Davisil®, grade 633 with pore size 60 Å and 200–425 mesh was purchased from Aldrich, Germany.

Analyses and characterizations

^{1}H- and ^{13}C-NMR spectra were recorded on a 400 MHz NMR (Varian AMS 100) spectrometer using D_2O d-2 as the solvent with tetramethylsilane (TMS) as internal reference. Multiplicities of proton resonance were designated as single (s), triplet (t), and multiplet (m). FTIR spectra were recorded on a Perkin-Elmer FTIR spectrometer (Spectrum 2000 series, resolution 2.0 cm^{-1}, 100 scans). Spectra of solids were recorded using KBr pellets. Vibrational transition frequencies are reported in wave number (cm^{-1}). Band intensities are assigned as weak (w), medium (m), shoulder (sh), strong (s), and broad (br). Elemental analyses were carried out using an Elemental Analyzer (Flash EA 1112, CE Instruments).

Procedure for GVL (1) ring-opening with amines

An amount of (**1**) was mixed with an amount of an amine compound without solvent, and the mixture was stirred at given temperatures and reaction times (see Table I for details). Samples were withdrawn from the reaction mixture at the end of the reaction and directly characterized by ^{1}H-NMR analysis to determine the conversion of the mono-amine and the conversion and selectivity towards the mono- and di-adduct for the di-amine. For di-amine additions, calculation of both parameters was performed by assuming that the proton integration values (I) of the di-amine ($I_{\text{di-amine}}$), the mono-adduct ($I_{\text{mono-adduct}}$), and the di-adduct ($I_{\text{di-adduct}}$) are equivalent to their molar amount (n). Therefore, the conversion of di-amine ($X_{\text{di-amine}}$) and the selectivity of both mono-adduct ($S_{\text{mono-adduct}}$) and the di-adduct ($S_{\text{mono-adduct}}$) can be calculated by using eqs. (1)–(3), respectively:

TABLE I
Experimental Conditions for Ring Opening of Valerolactone (1) with Amines

Exp.	Amines	Amount (mmol)	(1) amount (mmol)	Temp. (°C)	Time (h)
1	(2)	16.25	20.75	25	5
2	(3)	16.25	20.75	25	5
3	(4)	16.25	20.75	25	5
4	(5)	16.25	20.75	25	5
5	(6)	8.13	20.75	50	3
6	(7)	8.13	20.75	50	3
7	(8)	8.13	20.75	50	3

$$X_{\text{di-amine}} = \frac{I_{\text{mono-adduct}} + I_{\text{di-adduct}}}{I_{\text{di-amine}} + I_{\text{mono-adduct}} + I_{\text{di-adduct}}} \quad (1)$$

$$S_{\text{mono-adduct}} = \frac{I_{\text{mono-adduct}}}{I_{\text{mono-adduct}} + I_{\text{di-adduct}}} \quad (2)$$

$$S_{\text{di-adduct}} = \frac{I_{\text{di-adduct}}}{I_{\text{mono-adduct}} + I_{\text{di-adduct}}} \quad (3)$$

The separation of the final product from the remaining reactants and the intermediate product, and the characterization of the final product were conducted by adding a mixture of *n*-hexane and diethyl ether (1/1 v/v) and stirring. This is to precipitate the product and dissolve the remaining reactants in the solvent mixture. The precipitate was decanted and then washed three times using the same solvent mixture. Finally, the precipitate was dried under vacuum for about 5 h at 70°C to remove the remaining solvents. The weight of products was determined to calculate the yield of the reactions. The products were characterized by the ^{1}H- and ^{13}C-NMR analysis, FTIR, and elemental analysis. The product of (**1**) and (**7**) reaction was further separated from the mixture by chromatography using silica gel (200–425 mesh) with methanol and water mixture (1/1 v/v) as the eluent.

Optimization procedure of GVL (1) ring-opening with 1,2-DE (6)

In a typical procedure as shown in Table II, (**1**) was mixed with (**6**) (dissolved in a solvent), and the mixture (the solution) was stirred at given temperatures and reaction times. Samples were withdrawn from the reaction mixture at the end of the reaction, and directly characterized by ^{1}H-NMR analysis to calculate the conversion and selectivity of di-amine addition according eqs. (1)–(3).

Molecular modeling calculation

Steric hindrance at and around the nitrogen atom and electron densities (DelRe's method) at the

TABLE II
Experimental Conditions for Optimization of (1) Ring-Opening with (6)

Exp.	(1) (mmol)	(6) (mmol)	Catalyst[a]	Solvent[a]	Temp. (°C)	Time (h)
8	20.75	8.13	–	–	50	0.5
9	20.75	8.13	TEH	–	50	0.5
10	20.75	8.13	TP	–	50	0.5
11	20.75	8.13	$AlCl_3$	–	50	0.5
12	20.75	8.13	$SnCl_2$	–	50	0.5
13	20.75	8.13	YFMS	–	50	0.5
14	20.75	8.13	–	DMA	50	3.0
15	20.75	8.13	–	DMSO	50	3.0
16	20.75	8.13	–	Methanol	50	3.0
17	20.75	8.13	–	Water	50	3.0
18	20.75	8.13	–	–	25	3.0
19	20.75	8.13	–	–	50	3.0
20	20.75	8.13	–	–	75	3.0
21	20.75	8.13	–	–	100	3.0
22	40.65	8.13	–	–	50	3.0
23	56.91	8.13	–	–	50	3.0
24	73.17	8.13	–	–	50	3.0

[a] Amounts of catalyst and solvent were 0.08 mmol (1.0%-mole of 1,2-DE) and 12 mL, respectively.

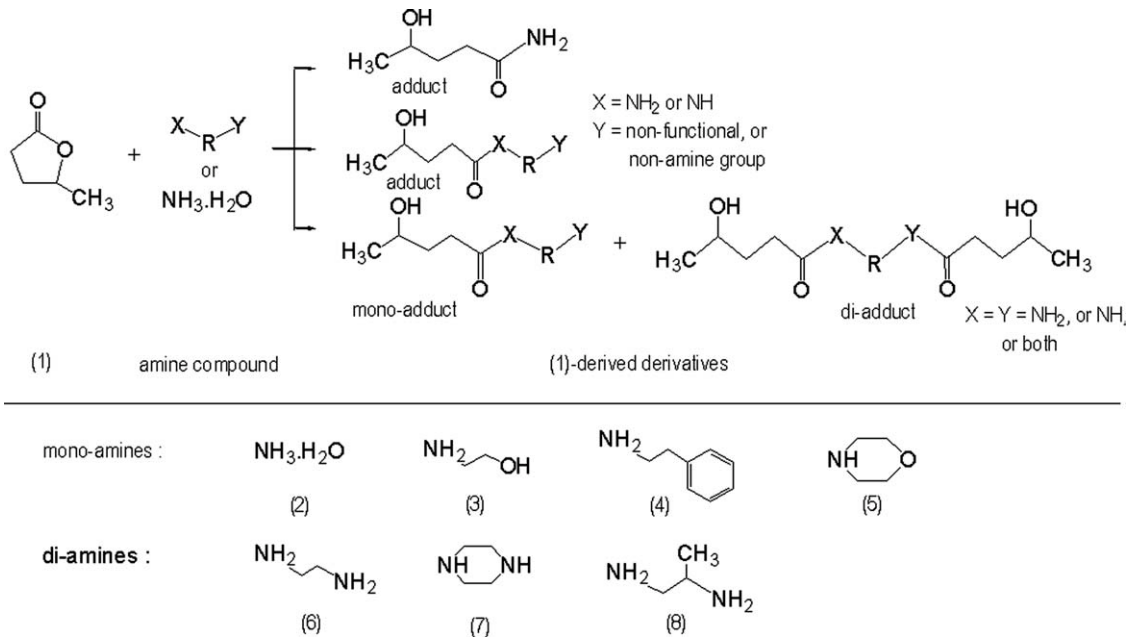
nitrogen atom in the selected mono- and di-amines were calculated using Molecular Modeling Pro Plus Software for Windows released by ChemSW, Inc.

RESULTS AND DISCUSSIONS

GVL (1) ring-opening with amines

The (**1**)-ringopening reactions resulted in γ-hydroxy-amides (see Scheme 1). Referring to the structure of the products, methyne, amide, and methyl functions become the typical groups in the adducts. Characterization of the structures, particularly the typical groups was carried out by ^{1}H- and ^{13}C-NMR, FTIR, and elemental analysis. The representative ^{1}H- and ^{13}C-NMR spectra for adduct obtained from (**1**) and (**4**) are shown in Figure 1(a,b) as an example.

In the ^{1}H-NMR spectra, the chemical shifts of the typical methyl [1 in Fig. 1(a)] and methyne group [6 in Fig. 1(a)] appear at δ 0.96 and δ 3.47 ppm, respectively. In the ^{13}C-NMR Spectra, the chemical shifts of the typical methyl [1 in Fig. 1(b)], methyne group [6 in Fig. 1(b)], and C=O [11 in Fig. 1(b)] of the amide group resulted from (**1**) and (**4**) appear at δ 21.79, δ 67.02, and δ 176.26 ppm, respectively.



Scheme 1 γ-Valerolactone ring-opening through varying the structure of the amine compounds.

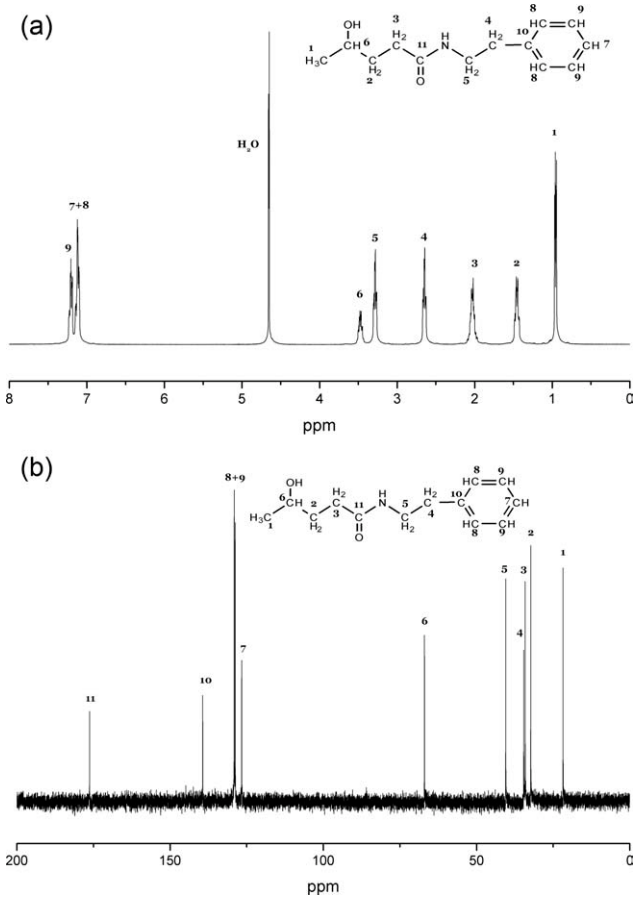


Figure 1 (a) ^{1}H- and (b) ^{13}C-NMR spectra of (**1**) and (**4**) reaction product in D_2O-d_2 at 25°C.

The structural assignments are confirmed by the FTIR spectrum. The v_{NH} (the amine bonds) appear at 2929–3311 cm^{-1}, while the v_{CONH} (the amide groups) appear at 1633 cm^{-1}. Elemental analysis further supports the composition of the compound. The detailed analytical data for the ring-opening products obtained for the others are shown in Tables III and IV.

Reactivity of amines in GVL (1) ring-opening

The experiments of the (**1**)-ring-opening with mono-amines show that at the applied reaction conditions yields were found as a sequence: (**2**)—95% > (**3**)—62% > (**4**)—54% > (**5**)—22%. Referring to Scheme 1 and the analytical support for the structures summarized in Table V, nucleophilicity of the amines appears to play an important role in the ring-opening of (**1**). The amines act as hard nucleophiles as they only add to the lactone carbonyl. This elicit ring-opening via an addition–elimination pathway.[16] This conclusion is confirmed by NMR analysis which indicates no further adduct formation through a second addition of the newly formed amide function formed upon the reaction of (**1**) and (**2**). This absence of further reaction by the amide can be explained by the soft nucleophilic nature of the amide. Beside that, NMR spectra of the reaction mixture before and after purification also do not indicate a reaction product resulting from the amine attack at the γ-position of the lactone. This behavior implies that the mono-amines behave as "hard" nucleophiles, as reported by Pearson.[17] A mechanism is proposed to depict nucleophilic addition for this ring-opening (see Scheme 2).

The sequence for the observed yield and the mode of ring opening shown in Scheme 2 suggests that steric hindrance and charge density at the nitrogen atom, i.e., the level of hardness, become the dominating factors to influence the reactivity of the amines.

Based on calculation, the sequence for the increase of the steric hindrance at and around the nitrogen atom is (**2**) < (**3**) ≈ (**4**) < (**5**). And electron densities (DelRe's method) at the nitrogen atom in the selected mono-amines lead to the following ranking: (**2**) > (**3**) > (**4**) > (**5**). Values of both parameters are represented in Table V.

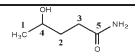
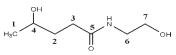
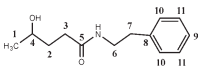
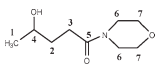
Comparison of the yields obtained for this set of (**1**) ring-opening reactions suggests that both the charge density and the steric hindrance at and around the N-atom (or a combination of the two) can be correlated with yield. However, from these data it is difficult to conclude which of the two parameters plays a dominant role.

To gain insight in and understanding of the influence of the both steric hindrance and charge density on the amine reactivity, additional experiments were conducted by mixing (**1**) with some selected di-amines ((**6**), (**7**), and (**8**)) (see Scheme 1). The amines in this study were selected such that steric hindrance and charge density at the nitrogen atom were varied in a controlled manner.

Figure 2 summarizes the data showing a sequence of 1.00; 0.90; and 0.57 for the conversion of (**6**), (**7**), and (**8**), respectively, and 0.70; 0.60; and 0.50 for the selectivity to di-adducts obtained from the (**1**)-ring-opening with (**6**), (**7**), and (**8**), respectively. It is important to note that 4-hydroxy-*N*-(1-methyl-2-amino-ethyl)-pentanamide, i.e., the mono-addition product obtained by the reaction of the sterically hindered amine in (**8**), was not observed by NMR measurement before and after purification of the reaction mixture. The conversion data to di-adduct show a decrease for the di-amine reactivity according the sequence: (**6**) > (**7**) > (**8**).

Comparing the conversion data (Fig. 2) and the molecular parameters calculated for the di-amines (**6**) and (**8**) (Table VI) clearly indicates that the steric hindrance has a stronger effect than charge density on the reactivity of the evaluated di-amino compounds.

TABLE III
Yield, Appearance, Elemental Analysis, ^{1}H−, ^{13}C-NMR chemical shifts at 25°C in D_2O-d_2 and FTIR for Products of (1) with Mono-Amines

Product	Chemical structure appearance and elemental analysis	^{1}H-Chemical Shift (ppm)	^{13}C-Chemical Shift (ppm)	FTIR (cm^{-1})
(1) + (2) reaction, 95% (yield)		(H-1) 1.02	(C-1) 21.83	3346 (free N—H, br)
	4-hydroxy-pentanamide			
	$C_5H_{11}NO_2$, white waxy solid;	(H-2) 1.58	(C-2) 31.54	2969–2953 (H-bonded
	Calcd: C, 51.3; H, 9.5; N 11.9%	(H-3) 2.17	(C-3) 33.93	N—H, m)
	Found: C, 50.9; H, 9.6; N, 11.9%	(H-4) 3.67	(C-4) 67.16	1663 (C=O in amide, s)
			(C-5) 179.77	1563 (stretched C—N & bended N—H, s)
(1) + (3) reaction, 62% (yield)		(H-1) 1.03	(C-1) 24.50	3286 (free N—H, br)
	4-hydroxy-N-(2-hydroxyethyl)-pentanamide			
	$C_7H_{15}NO_3$, brownish viscous liquid;	(H-2) 1.57	(C-2) 34.90	2873–2965
	Calcd.: C, 52.2; H 9.4; N, 8.7%			(H-bonded N—H, m)
	Found: C, 51.9; H, 9.5; N, 8.5%	(H-3) 2.16	(C-3) 36.70	1633 (C=O in amide, s)
		(H-4) 3.64	(C-4) 44.14	1548 (stretched C—N & bended N—H, s)
		(H-6) 3.17	(C-5) 179.46	
		(H-7) 3.49	(C-6) 62.65	
			(C-7) 69.77	
(1)+(4) reaction, 54% (yield)		(H-1) 0.96	(C-1) 21.79	3311 (free N—H, br)
	4-hydroxy-N-(2-phenylethyl)-pentanamide			
	$C_{13}H_{19}NO_2$, brownish waxy solid;	(H-2) 1.45	(C-2) 32.32	3065–2929
	Calcd: C, 70.6; H, 8.7; N, 6.3%;			(H-bonded N—H, m)
	Found: C, 70.3; H, 8.7; N, 6.3%	(H-3) 2.03	(C-3) 34.18	1633 (C=O in amide, s)
		(H-4) 3.47	(C-4) 67.02	1543 (stretched C—N & bended N—H, s)
		(H-6) 3.28	(C-5) 176.26	
		(H-7) 2.65	(C-6) 40.49	
		(H-9 &10) 7.12	(C-7) 34.64	
		(H-11) 7.21	(C-8)	
			(C-9) 67.02	
			(C-10) 128.75	
			(C-11) 129.07	
(1)+(5) reaction, 4% (yield)		(H-1) 1.05	(C-1) 21.96	3383 (free N—H, br)
	4-hydroxy-N,N-(diethylenoxide)-pentanamide			
	$C_9H_{17}NO_3$, brownish viscous liquid;	(H-2) 1.58	(C-2) 29.08	2854–2970
	Calcd: C, 57.7; H, 9.2; N, 7.5%;			(H-bonded N—H, m)
	Found: C, 57.6; H, 9.2; N, 7.6%.	(H-3) 2.36	(C-3) 33.93	1633 (C=O in amide, s)
		(H-4) 3.69	(C-4) 67.21	1435 (stretched C—N & bended N—H, s)
		(H-6) 3.45	(C-5) 174.74	
		(H-7) 3.59	(C-6) 44.31	
			(C-7) 66.46	

Optimization study of GVL (1) ring-opening with 1,2-DE (6)

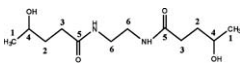
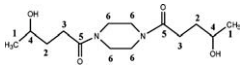
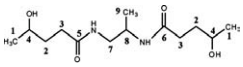
Formation of the mono- and the di-adduct during the reaction of (**6**) and (**1**) was monitored by measuring the ^{1}H-NMR spectra at regular time intervals. Based on these spectra, the reaction profile can be constructed by calculating the ratio of prominent peak integrations.

Figure 3 depicts that the reaction of (**1**) and (**6**) occurred through two steps, i.e., initial formation of the mono-adduct followed by the formation of the di-adduct. Rates of the reactions can be expressed as,

$$1.\ \text{ring} - \text{opening rate of } (6) : \frac{d[1]}{dt} = -k_1[6]^a[1]^b \quad (4)$$

$$2.\ \text{formation rate of mono} - \text{adduct} : \frac{d[\text{mono} - \text{adduct}]}{dt} = k_1[6]^a[1]^b - k_2[\text{mono} - \text{adduct}]^c[1]^d) \quad (5)$$

TABLE IV
Yield, Appearance, Elemental Analysis, ^{1}H−, ^{13}C-NMR Chemical Shifts at 25°C in D_2O-d_2 & FTIR for Products of (1) with Di-Amines

Product	Chemical structure appearance and elemental analysis	^{1}H-Chemical Shift (ppm)	^{13}C-Chemical Shift (ppm)	FTIR (cm^{-1})
(1)+(6) reaction, 88% (yield)		(H-1) 1.03	(C-1) 21.85	3276 (free N—H, br)
	N,N′-1,2-ethanediylbis-(4-hydroxy-pentanamide)			
	$C_{12}H_{24}N_2O_4$,, white powder;	(H-2) 1.58	(C-2) 32.37	2907–2964 (H-bonded N—H, m)
	Calcd: C, 55.4; H, 9.3; N, 10.8%;			
	Found: C, 55.4; H, 9.3; N, 10.7%	(H-3) 2.15	(C-3) 34.16	1639 (C=O in amide, s)
		(H-4) 3.65	(C-4) 67.19	1555 (stretched C—N & bended N—H, s)
		(H-6) 3.17	(C-5) 176.89	
			(C-6) 38.72	
(1) + (7) reaction, 16% (yield)		(H-1) 1.02	(C-1) 21.93	3384 (free N—H, br)
	N,N′-1,2-diethanediylbis-(4-hydroxy-pentanamide)			
	$C_{14}H_{26}N_2O_4$, brownish viscous liquid;	(H-2) 1.54	(C-2) 29.25	2970–2926 (H-bonded N—H, m)
	Calcd: C, 58.7; H, 9.2; N, 9.8%;			
	Found: C, 57.4; H, 9.1; N, 9.1%	(H-3) 2.36	(C-3) 33.62	1614 (C=O in amide, s)
		(H-4) 3.60	(C-4) 67.20	1423 (stretched C—N & bended N—H, s)
		(H-6) 3.47	(C-5) 174.93	
			(C-6) 41.62	
(1) + (8) reaction, 44% (yield)		(H-1) 1.01	(C-1) 21.92	3274 (free N—H, br)
	N,N′-1,2-propanediylbis-(4-hydroxy-pentanamide)			
	$C_{13}H_{26}N_2O_4$, yellowish viscous liquid;	(H-2) 1.54	(C-2) 32.45	2970–2927 (H-bonded N—H, m)
	Calcd: 56.9% C; 9.6% H; 10.2% N.;			
	Found: 56.2% C; 9.7% H; 10.3% N	(H-3) 2.12	(C-3) 34.50	1633 (C=O in amide, s)
		(H-4) 3.67	(C-4) 67.16	1539 (stretched C—N & bended N—H, s)
		(H-7) 3.02	(C-5) 176.73	
		(H-8) 4.87	(C-6) 176.03	
		(H-9) 0.96	(C-7) 45.29	
			(C-8) 43.99	
			(C-9) 17.15	

3. formation rate of the di−adduct : $\frac{d[\text{di}-\text{adduct}]}{dt} = k_2[\text{mono}-\text{adduct}]^c[1]^d \quad (6)$

Assuming first order for the reaction orders (*a–d*), simplifying the kinetics to pseudo-first order by taking sufficient access (**1**) and referring to derivations for the rate equations, as given in literature,[18] values of k_1' and k_2' were determined by iterating the experimental data shown in Figure 3. These iterations, which were performed by using *Mathcad* software, results in values of k_1' and k_2' as 0.0108 mmol/min and 0.0026 mmol/min, respectively. Even though the applied molar ratio of (**1**)/(**6**) does not represent true pseudo first-order conditions, comparison of both rate constants shows that the first addition step is somewhat faster than the di-adduct formation.

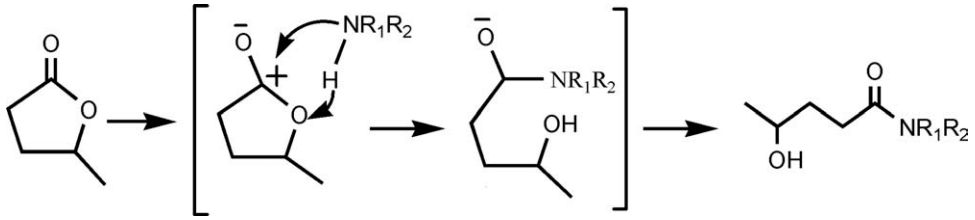
As the di-adduct is the desired product, an investigation to enhance its formation rate appeared justified and a number of experiments were conducted to investigate the effect of process variables on the yield and rate of the reaction between (**1**) and (**6**).

TABLE V
Calculated Charge Density and Steric Hindrance at the N Atom

No.	Amine compound	Charge density	Steric hindrance[a] (%)	Yield[b] (%)
1	(**2**)	−0.8772	35	95
2	(**3**)	−0.6519	38	62
3	(**4**)	−0.6527	38	54
4	(**5**)	−0.4407	41	22

[a] For reference: replacing the N-H proton in dimethylamine by methyl, ethyl, *i*-propyl and *t*-butyl increases the steric hindrance at the N-atom from 37.2 to 39.5, 41.9, 43.4 and 45.4, respectively.

[b] For experimental conditions: see Table I for experiment numbers 1–4.



Scheme 2 Addition mechanism of ammonia, and the aliphatic primary and secondary amines to valerolactone (**1**).

Effect of solvent

The reaction mechanism shown for the opening of lactones (Scheme 2) indicates a polar intermediate upon the addition of the amine to the carbonyl function of the lactone. This suggests that the use of solvents which stabilize polar transition states and polar intermediates should have a positive effect on the rates of the reaction. The solvent effect on the reaction was studied by comparing various polar solvents as diluents for the ring-opening of (**1**). As selected solvents methanol, DMA, DMSO, and water were investigated and the observed results are presented in Figure 4.

Comparing the results for the reactions in solvent shows that they have a significant positive effect on the conversion, a slight negative—but desired—effect on the formation of the mono-adduct and a limited positive effect on the second reaction which delivers the di-adduct. These effects can be explained as mentioned above, i.e. the solvents play a role in determining the rate and, possibly, the selectivity of a chemical process as they can stabilize or destabilize the intermediates and transition states that are formed in the reaction paths that take place.[19] This implies that for the reactions with these polar intermediates the effects of the solvents should be correlated to the polarity of the solvents. Considering the data shown in Figure 4 and the solubility parameters (the Hildebrand parameter, δ) for the solvents in Table VII, the improvements in the conversion can be understood.

The conversion and the ratio mono-adduct to di-adduct seems to be correlated with the polarity of the solvent. In addition, it seems fair to state that the higher conversion in methanol and water compared with DMA and DMSO may be related to the hydrogen bonding capability of the first two solvents.

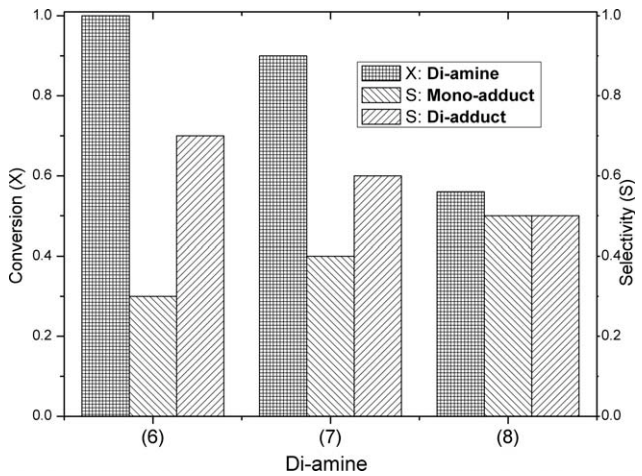


Figure 2 Comparison of the (**1**) ring-opening through adding structurally different di-amines. (See experimental number 5–7 in Table I for the experimental conditions).

Effect of catalyst

Different catalysts were investigated to find a suitable system to enhance the reaction performance, i.e., yield and rate of the (**1**) ring-opening reaction. Saiyasombat et al. reported that ring-opening of β-butyrolactone can be catalyzed by using Lewis acid catalysts.[8] Considering that a similar reactivity may be expected for GVL, this study was carried out with a set of catalysts that are reported in literature as suitable systems for carbonyl activation, such as $AlCl_3$, $SnCl_2.2H_2O$, triphenylphosphine (TP), Ytterbium (III)trifuoromethanesulfonate (YFMS), and Tin (II)-2-ethylhexanoate (TEH).

Figure 5 shows that at the same reaction conditions the addition of the catalysts enhances the conversion from 0.23 to at least 0.79. Although a slight

TABLE VI
Calculated Charge Density and Steric Hindrance at the N Atoms

No.	Amine compound	Chemical structure	Partial charge		Steric hindrance (%)	
			N_a	N_b	N_a	N_b
1	(6)		−0.6527	−0.6527	38	38
2	(7)		−0.4421	−0.4421	41	41
3	(8)		−0.6529	−0.6544	39	53

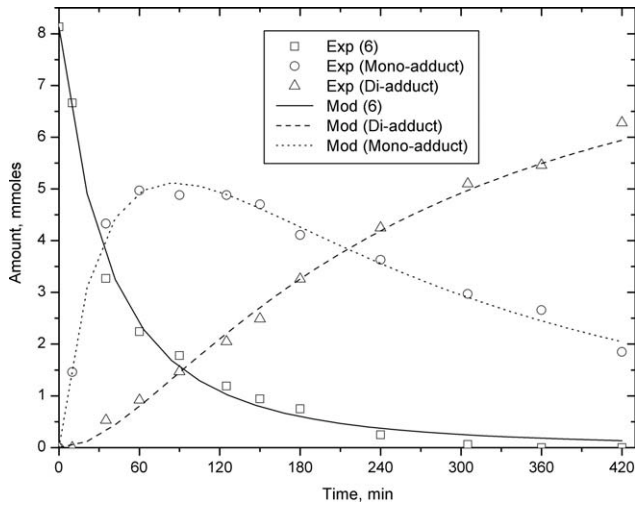


Figure 3 The reaction profile of (**6**) (8.125 mmol) and (**1**) (41.5 mmol) in bulk mixture at 25°C.

improvement in the selectivity for the formation of the di-adduct selectivity can be observed, the results are disappointing and it can be concluded that the systems that catalyze the ring-opening of β-butyrolactone are not very effective for the conversion of (**1**) with (**6**).

On the basis of the conversion level for $SnCl_2$ or YFMS experiments (50°C for 0.5 h) and taking the bulk experiment in Figure 5 (50°C for 3 h) as a reference at the same conditions, illustrates that the positive effect of the catalyst amounts to about 2–2.5 h of reduction in reaction time.

Effect of temperature

From a reaction engineering point of view, the addition of (**1**) to (**6**) to produce its mono-adduct and di-adduct, should be considered as multiple order reactions with rates that can be affected by temperature and reactant concentration. In this section, some experiments will be described in which the reaction of (**6**) with (**1**) was carried out at various temperatures. The conversion of (**6**) and the selectivity to the mono- and the di-adduct are shown in Figure 6.

As expected, the experiments show that temperature has a significant effect on the rate of the reaction. For di-amine (**6**), the data show that high

TABLE VII
Solubility Parameters (the Hildebrand) of the Solvents[20]

Solvent	Solubility parameters ($MPa^{1/2}$)
DMA	22.7
DMSO	26.6
Methanol	29.7
Water	47.9

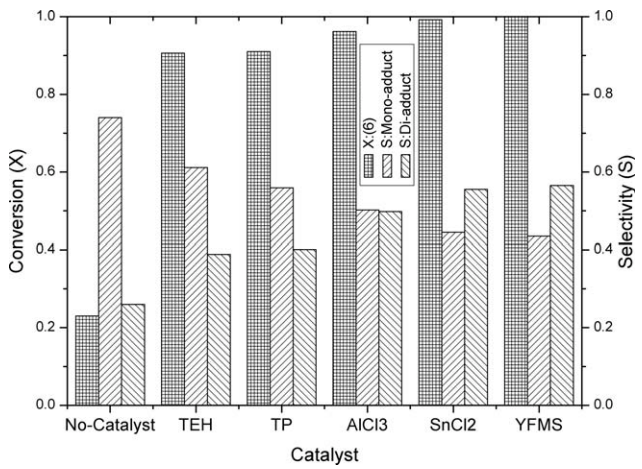


Figure 5 The effect of various Lewis acids on the reaction of (**1**) with (**6**). (See experimental number 8–13 in Table II for the experimental conditions).

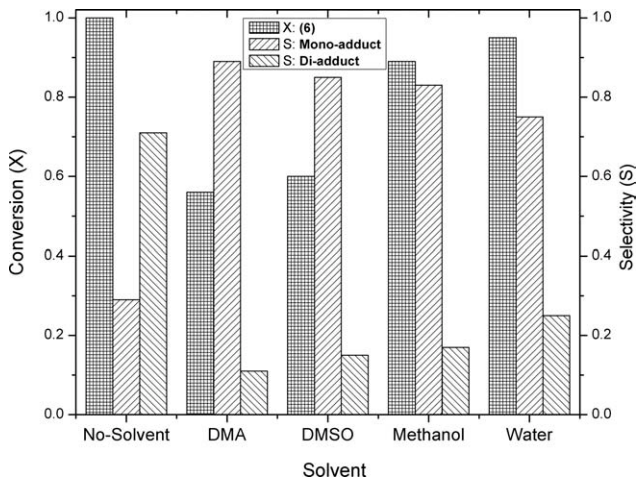


Figure 4 The effect of the various solvents on the reaction of (**1**) with (**6**). (See experimental number 14–17 and 19 in Table II for the experimental conditions).

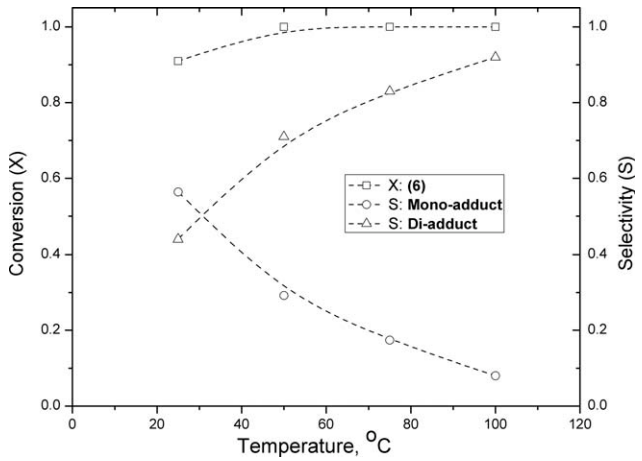


Figure 6 The temperature effect on the reaction of (**1**) and (**6**). (See experimental number 18 -21 in Table II for the experimental conditions).

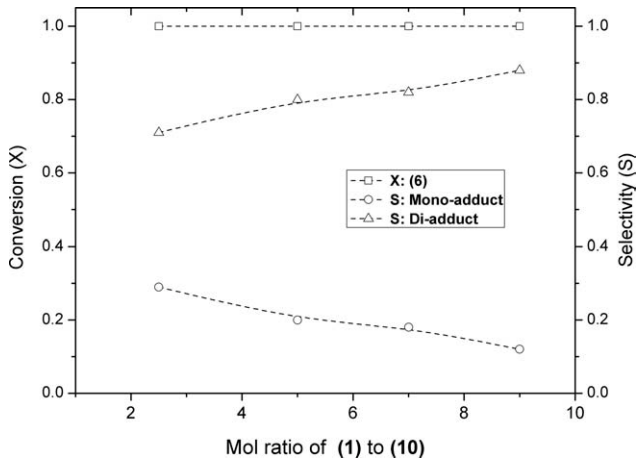


Figure 7 The effect of mole ratio of (**1**)–(**6**) on the reaction of (**1**) and (**6**). (See experimental number 19, 22–24 in Table II for the experimental conditions).

conversions can be obtained at temperatures slightly above room temperature (50–60°C) and that a further increase in temperature to around 100°C enables almost full conversion to the di-adduct. The graphs in Figure 6 clearly suggest that a slightly longer reaction time and a temperature just above 100°C should be sufficient to achieve full conversion of (**1**) and (**6**) to the desired di-adduct.

Effect of mole ratio of GVL (1) to 1,2-DE (6)

On the basis of the results described above, it is expected that an increase in mole ratio of (**1**) to (**6**) will have a positive effect on the conversion and selectivity of the reaction. This parameter was studied by performing some reactions at different amounts of (**1**) on a fixed amount of (**6**). The conversion and the selectivities for reactions carried out at 50°C for 3 h are shown in Figure 7.

The data indeed show that an increase in the amount of (**1**) at a fixed amount of (**6**) has a significant effect on the selectivity. At the applied reaction conditions, a mole ratio of (**1**) to (**6**) of 2 is sufficient to achieve full conversion of the di-amine (**6**) while the selectivity for the di-adduct steadily increases with an increase in mole ratio.

CONCLUSIONS

GVL (**1**) undergoes ring-opening at mild conditions into γ-hydroxy-amides. Through adding amines such as mono- or di-functional aliphatic primary or secondary amines, the ring opens via the nucleophilic addition of the "hard" amine to the lactone carbonyl and results in the formation of an amide and cleavage of the cyclic ester.

To gain more insight in the amine-lactone reactivity, model compounds representing mono- and di-amines were added to GVL (**1**) and the dominating factors for the reactivity of the amines were determined. Steric hindrance around the nucleophilic nitrogen centre was found to be more important than charge density at the nitrogen atom.

The ring-opening of GVL (**1**) by 1,2-diaminoethane (**6**) was studied in more detail to optimize the yield of the desired difunctional monomers. Of the processing parameters studied, the reaction temperature, reaction time, and molar ratio of the reactants appeared to be the determining factors. These parameters were found to be more important than the use of catalysts and solvent polarity. Although the latter improved the reactivity of the amines, the selectivity to the desired products remained below expectation.

In conclusion, it may be stated that the GVL ring-opening by amines is a promising novel pathway to di-functional monomers suitable for polymer synthesis. Through the proper selection of the amine structure, such as backbone composition and presence of secondary functional groups, a promising polymer engineering pathway has been uncovered.

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