Electronic Supplementary Material (ESI) for Green Chemistry.

Synthesis of Highly Functional Carbamates through Ring-Opening of Cyclic Carbonates with Unprotected α-Amino Acids in Water

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SUPPORTING INFORMATION

Experimental

1,5-Hexadiene-3,4-diol, mixture of (±) and meso. The applied synthetic procedure was inspired by the reductive coupling developed by Hekmatshoar[6] and applied by Trost et al.[7] for the synthesis of 1,5-Hexadiene-3,4-diol, mixture of (±) and meso with some alterations. Acrolein (45 ml, 0.674 mol) was dissolved in 400 ml THF, followed by addition of acetic acid (50 ml, 0.841 mol). The solution was stirred for 5 minutes followed by rapid addition of granulated Zink(0) (50g, 0.765) ,the solution was left to stir over night (18 h). The crude reaction mixture was filtered the and the solute was concentrated followed by distillation to yield 33.1 g (77 %) of the desired product at a purity of 90 % as determined from ^{1}H NMR. The target compound was used without any further purification. ^{1}H (400 MHz, CDCl3): δ 5.94-5.84 (m, 2H), 5.42-5.24 (m, 4H), 4.25-4.00 (m,2H)

Cis-1,2-divinylethylene carbonate and trans-1,2-divinylethylene carbonate (DVC). The synthesis of 1,2-divinylethylene carbonate was performed in accordance with the procedure developed by Braun with some alterations.[8] 1,5-Hexadien-3,4-diol (8 g, 70 mmol) was dissolved in Diethyl carbonate (17 ml, 140 mmol) together with 10 mol% of NaH, 60% in a mineral oil dispersion (0.29 g, 7mmol in a 50 ml round bottom flask and equipped with a reflux-condenser. The reaction mixture was left at 100 ^{o}C over-night followed by distillation yielding 9.1 g (76 %) of DVC at a purity 95 % as determined via ^{1}H NMR. ^{1}H (400 MHz, CDCl3): δ 5.81-5.70 (m, 2H), 5.47 (d,2H), 5.42 (d, 2H), 5.19-5.13 (m 2H).

Ring opening of cyclic carbonates with glycine

In a typical reaction; desired amount of glycine (210 mg, 2.8 mmol) was dissolved in 1 ml H_2O in a 5 ml vial equipped with a magnetic stirrer. After 5 minute TEA (0.2 ml, 1.4 mmol) was added to the solution and let to stir for 10 minutes. The stirring rate was increases and the desired carbonate (0.7 mmol) was added in one shot at ambient temperature. The reaction was let to proceed for 2h, followed by direct precipitation in 20 ml a THF:MeOH 3:1 mixture. The solute was collected and concentrated giving the desired carbamate as a TEA-adduct. In order to remove the TEA the product was passed through a silica-plug, EtOAc:AcOH 20:1, giving the carbamate

Cis and Trans (((4-hydroxyhexa-1,5-dien-3-yl)oxy)carbonyl)glycine. Procedure according to above, TEA-adduct (0.63:1) 152 mg (yield 95% as a yellow oil), after silica-plug 100 mg (yield 81 % as a yellow oil) ^{1}H NMR. ^{1}H (400 MHz, D_2O): δ 5.97-5.85 (m, 2H), 5.40-5.29 (m, 4H), 5.17-5.11 (m, 1H), 5.39-5.31 (m, 1H), 3.93 (d, 2H). ^{13}C NMR (100 MHz, MeOD-d4): 172.4, 157.3, 136.8, 133.7, 132.4, 117.2, 117.1, 116.1, 78.2, 77.9, 74.1, 73.9, 42.0 HRMS (ESI): calculated for C9H13NO5Na: 238.0691; found 238.0686

(((1-hydroxybut-3-en-2-yl)oxy)carbonyl)glycine [1], (((2-hydroxybut-3-en-1-yl)oxy)carbonyl)glycine [2]Procedure according to above, TEA-adduct (0.44:1) 150 mg (yield 91% as a light yellow oil), after silica-plug 100 mg (yield 75 % as a light yellow oil) the product ration was determined via ^{1}H NMR as **[1]** 36 % and **[2]** 64 %. ^{1}H (400 MHz, D_2O): δ 5.89-5.75 (m, 1H), 5.33-5.19 (m, 2H), 5.09-5.07 (m, 0.36 H), 4.34-4.32 (m, 0.64 H), 4.11 (dd, 0.64 H), 3.97 (dd, 0.64 H), 3.85 (d, 2H), 3.69 (dd, 0.36 H), 3.60 (dd, 0.36H) ^{13}C NMR

(100 MHz, MeOD-d4): 173.6, 159.0, 158.5, 138.3, 135.2, 117.7, 116.7, 77.5, 71.8, 69.5, 64.8, 43.1 HRMS (ESI) calculated for C7H11NO5Na: 212.0535; found 212.0529

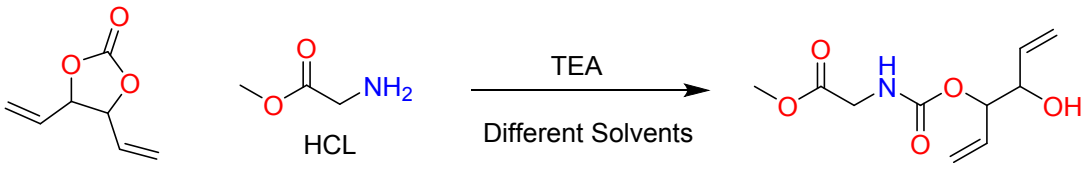
(((1-hydroxypropan-2-yl)oxy)carbonyl)glycine [3], ((2-hydroxypropoxy)carbonyl)glycine [4] Procedure according to above, TEA-adduct (0.53:1) 160 mg (yield 96% as a transparent oil), after silica-plug 105mg (yield 83 % as a transparent oil) the product ratio was determined via ^{1}H NMR as **[1]** 60 % and **[2]** 40 %. ^{1}H (400 MHz, 1:1 D_2O:MeOD mixture): δ 4.77 (td, 0.89 H), 3.95 (m, 1.23 H), 3.82 (d, 2 H), 3.55 (d, 1.23 H), 1.21 (d, 1.87 H), 1.20 (m, 1.20 H) ^{13}C NMR (100 MHz, MeOD-d4): 173.7, 173.6, 159.1, 158.9, 73.6, 71.0, 66.7, 65.8, 43.1, 19.5, 16.8 HRMS (ESI): calculated for C6H11NO5Na: 200.0535; found 200.0535

((2-hydroxyethoxy)carbonyl)glycine Procedure according to above, TEA-adduct (0.40:1) 149 mg (yield 95 % as a transparent oil), after silica-plug 97 mg (yield 83 % as a transparent oil) after purification through the silica plug it was observed the formation of a side product constituting of the condensation reaction between the carboxylic acid and the primary alcohol ^{1}H (400 MHz, 1:1 D_2O:MeOD mixture): δ 4.12 (t, 2H), 3.82 (s, 2 H), 3.71 (t, 2 H), ^{13}C NMR (100 MHz, MeOD-d4): 173.7, 159.2, 67.7, 61.4, 43.1 HRMS (ESI): calculated for C5H9NO5Na: 186.0378; found 186.0375

Kinetic evaluation

General procedure: Desired amount of Glycine(GLY) and triethylamine (TEA) was dissolved in 1 ml of D_2O followed by rapid addition of the desired amount of 1,5-Hexadiene-3,4-diol, mixture of (±) and meso (DVC). At specified time periods aliquot of specified times aliquots of 50 µL was withdrawn and the reaction kinetics was quenched with addition of 5 ekv. AcOH in respect to TEA, subsequent followed by analysis by ^{1}H NMR.

Kinetic data not included in the manuscript.



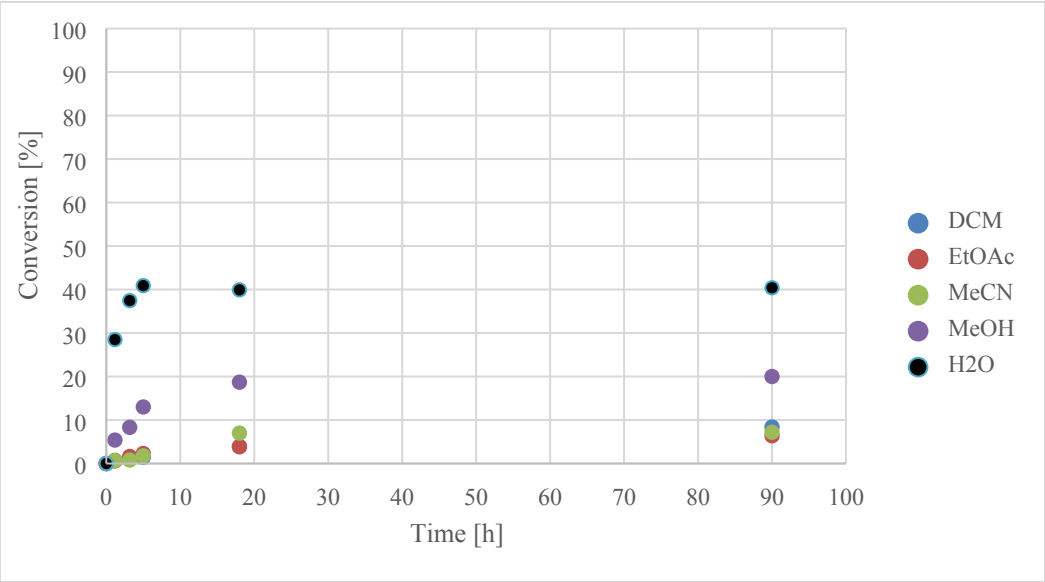


Figure S1. Initial evaluation of the ring-opening behavior of DVC with the methylester of glycine in different solvent with a reaction ratio of [GLY-OMe]:[DVC]:[TEA] = 1:1:1

Only the formation of other products beside hydrolysis was evaluated. It was observed that these reaction conditions produced a mixture of products arising from the nucleophilic action of the free amine and methyl ester within the system.

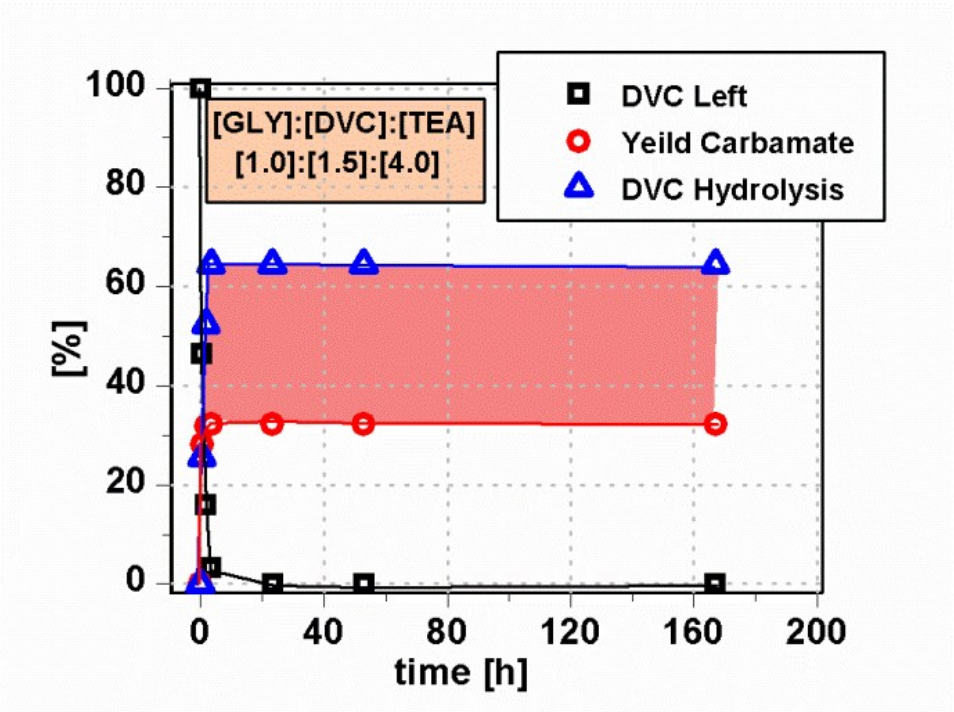


Figure S2. Ring-Opening behavior with increased amount of TEA in relation to GLY and DVC

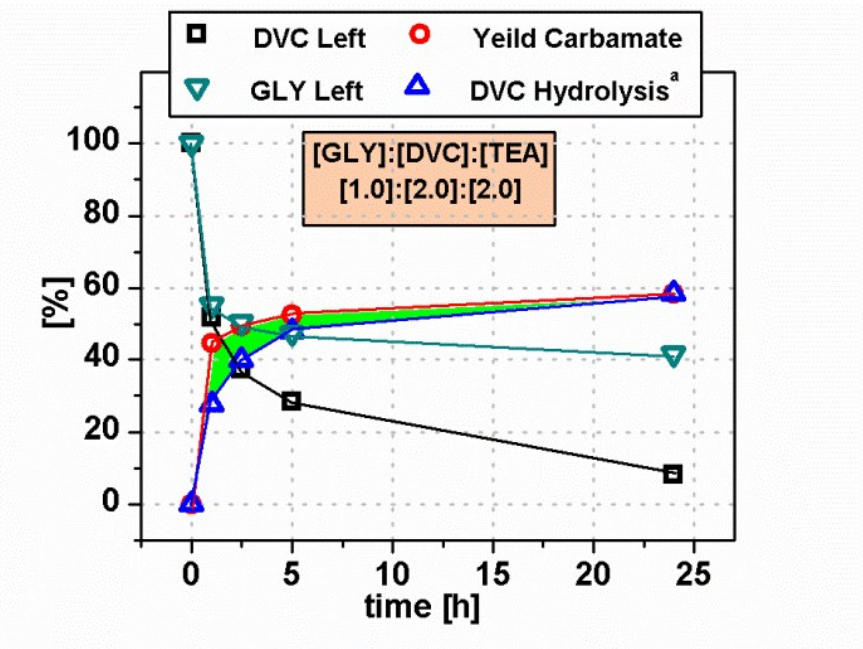


Figure S3. Ring-Opening behavior at different equivalents

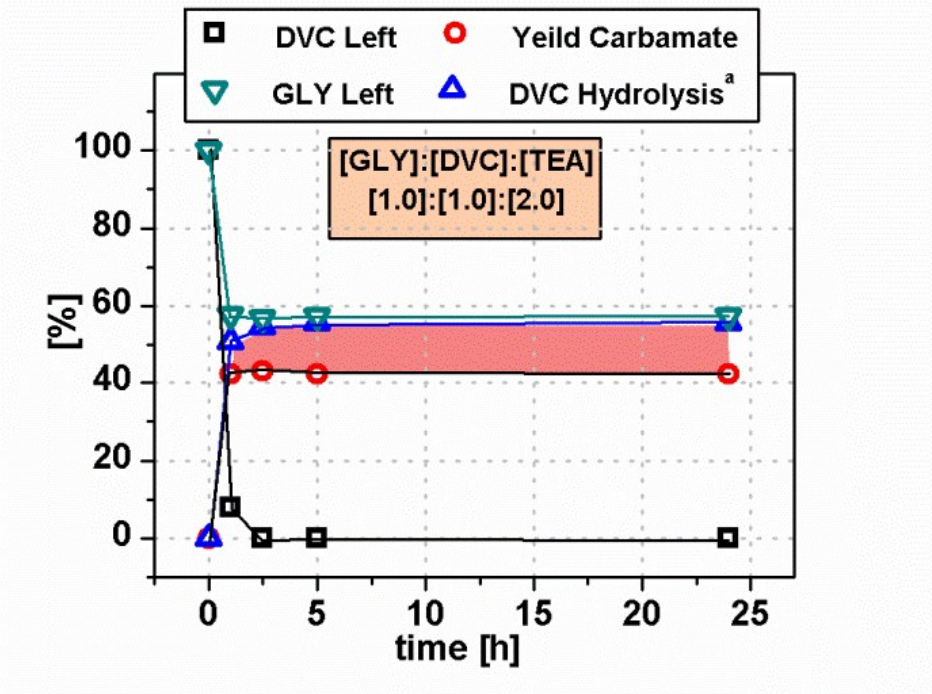


Figure S4. Ring-Opening behavior at different equivalents

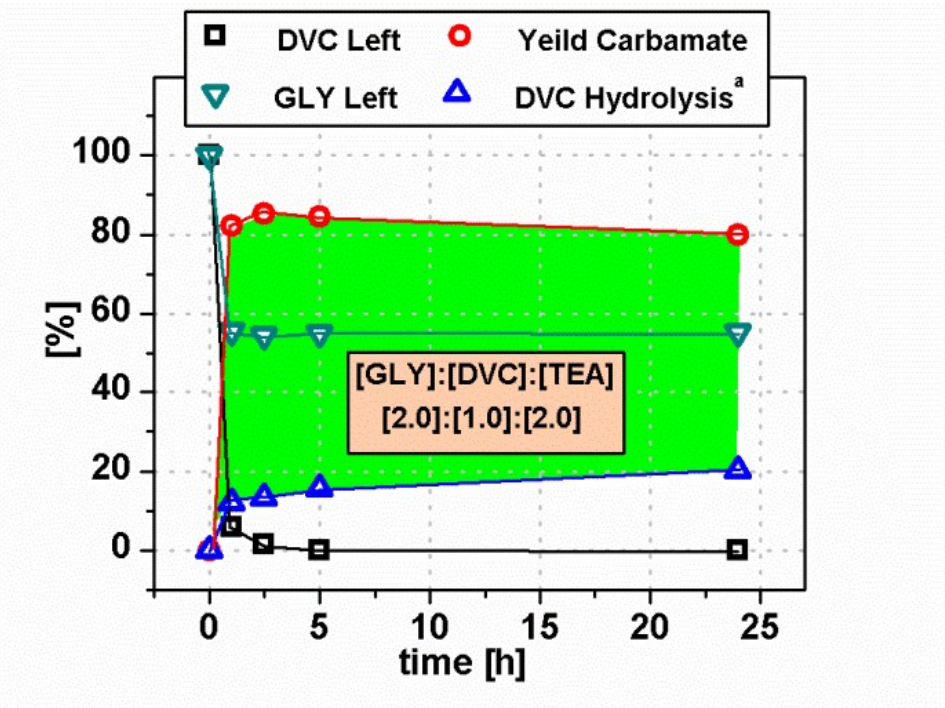


Figure S5. Ring-Opening behavior at different equivalents

Different substrates

[EC]:[GLY]:[TEA] = 1:4:2

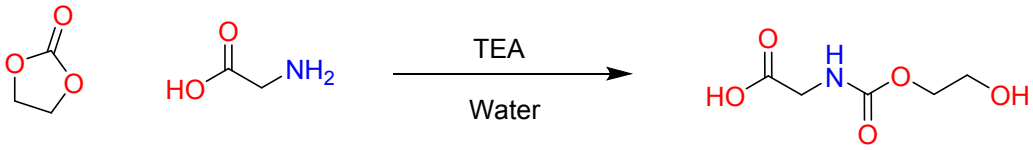


Illustration of the synthetic protocol during the synthesis of ((2hydroxyethoxy)carbonyl)glycine

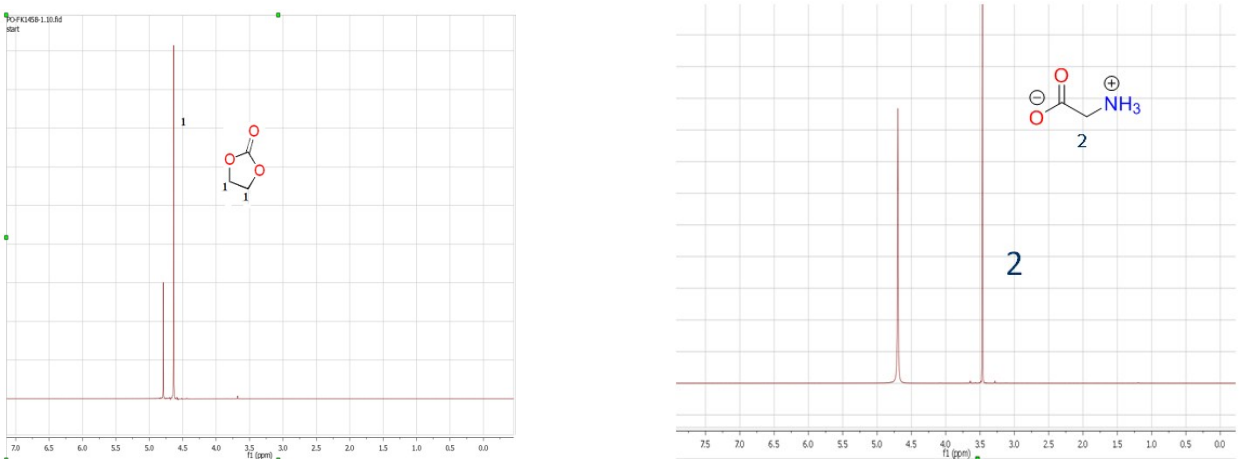


Figure S6. [1]HNMR on the starting compounds for the ring-opening reaction

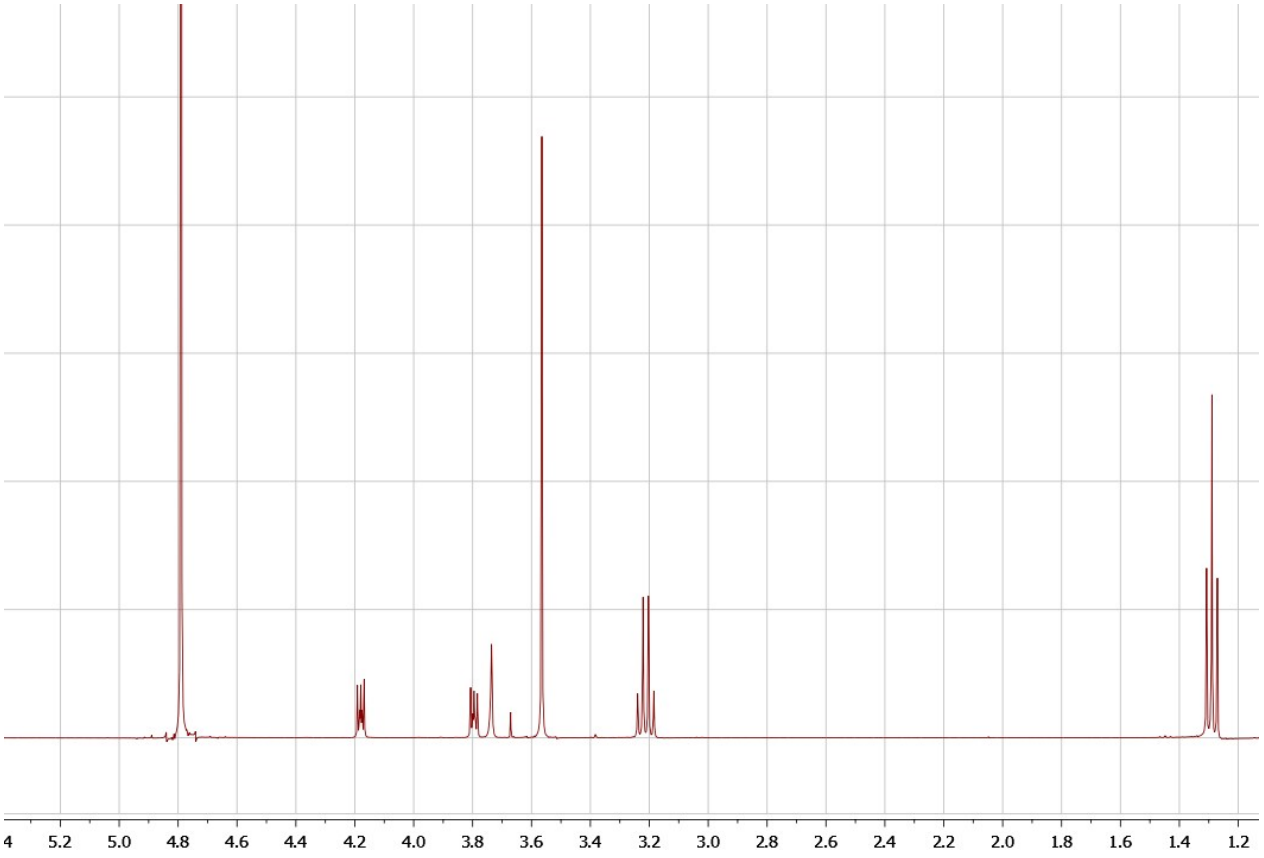


Figure S7. [1]HNMR on the crude reaction mixture

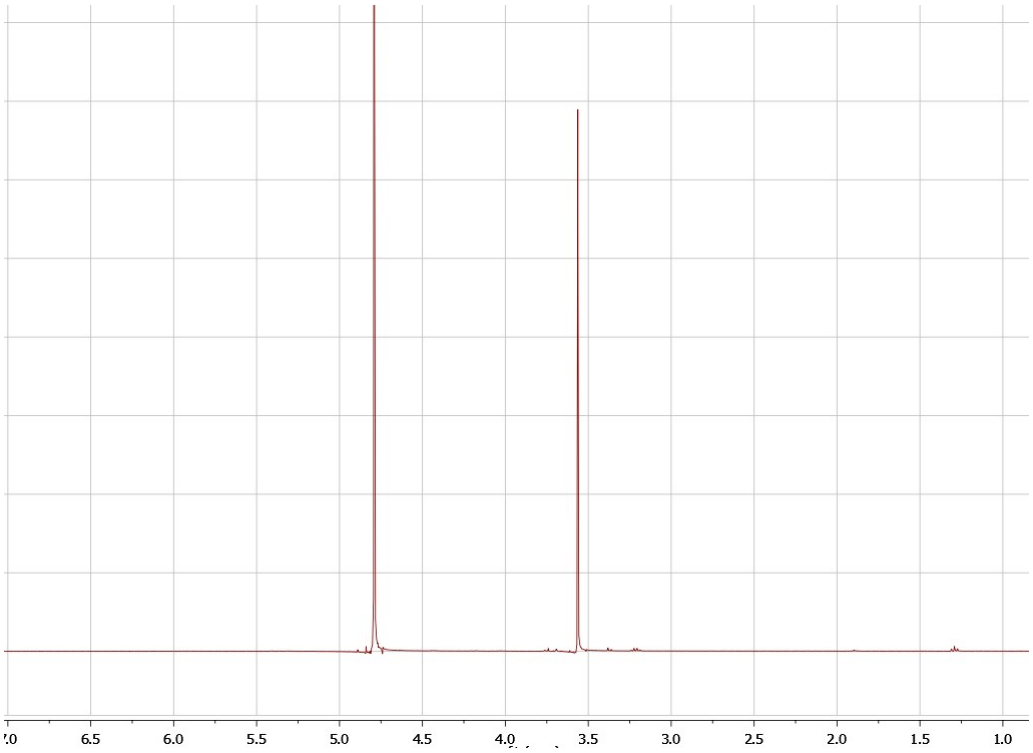


Figure S8. [1]HNMR on the precipitate, containing only unreacted glycine

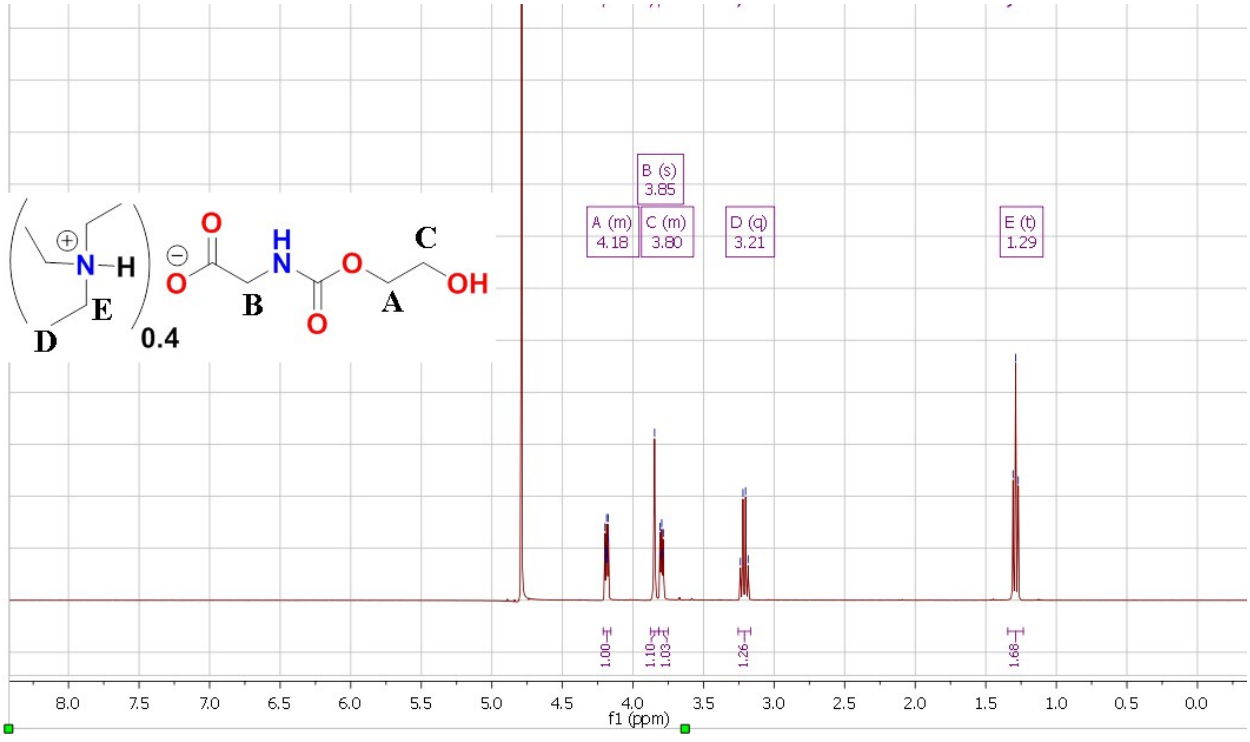


Figure S9. [1]HNMR on the concentrated solute after the precipitation

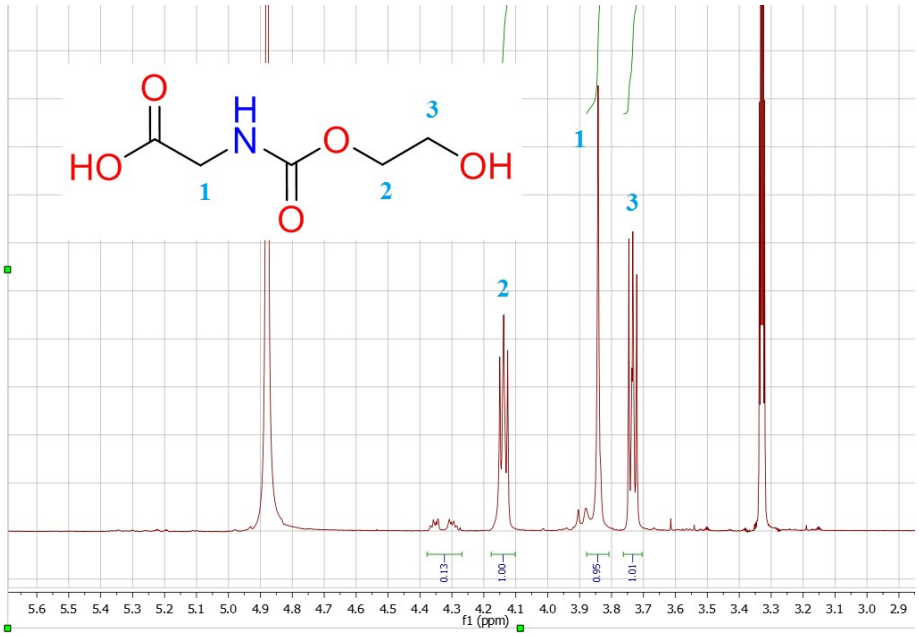


Figure S10. [1]HNMR on the obtained product after silica-plug, showing appearance of a side product belied to arise from the condensation of the free carboxylic acid and the alcohol during solvent evaporation.

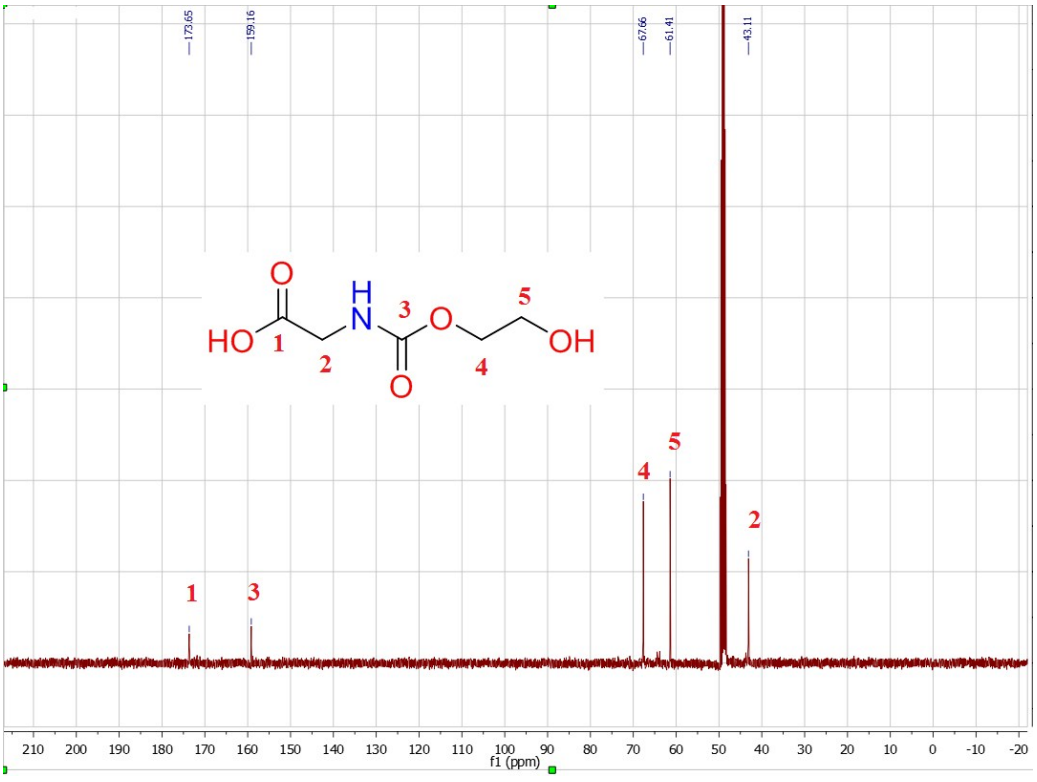


Figure S11. [13]CNMR on the obtained product after silica plug

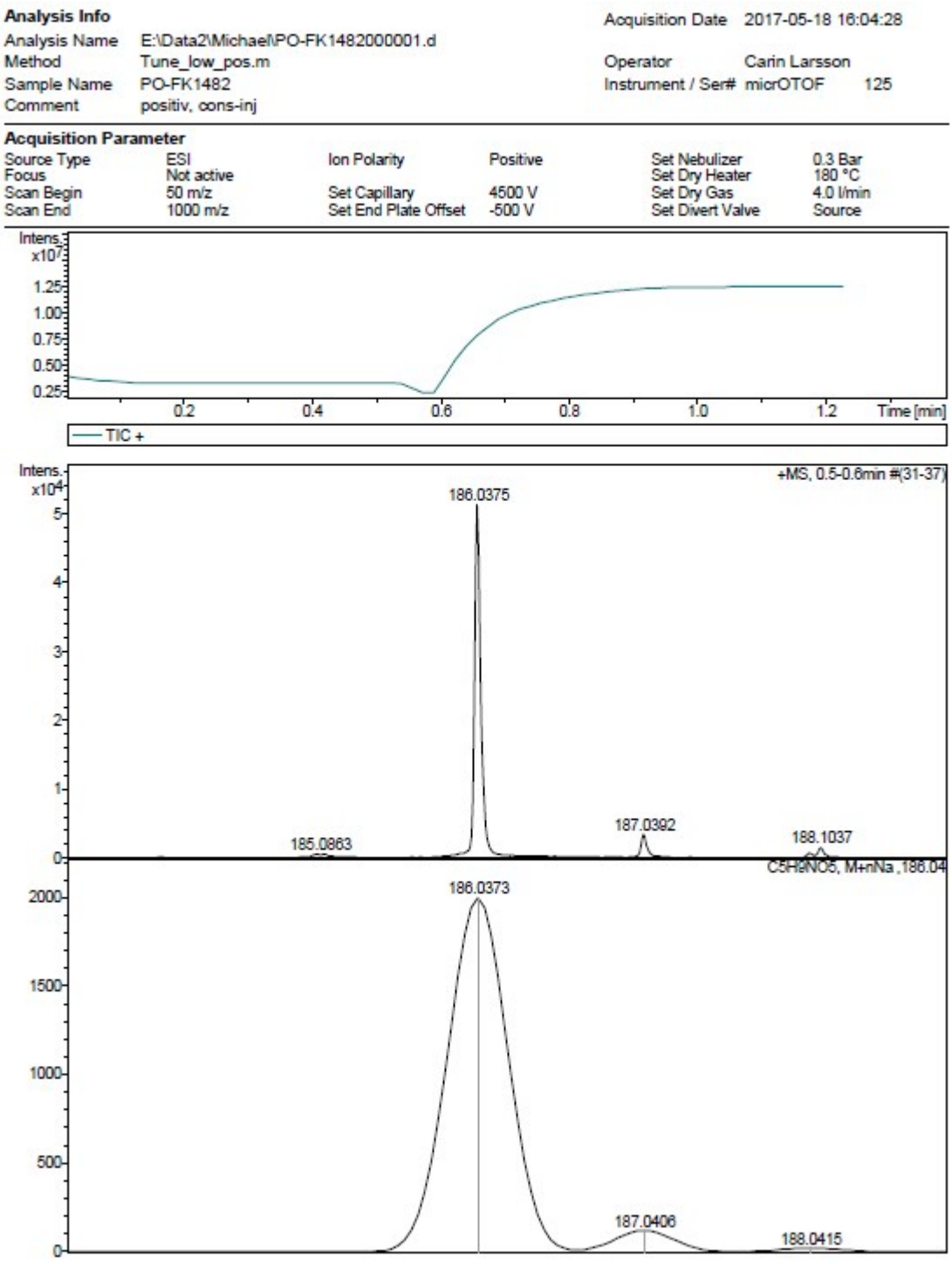
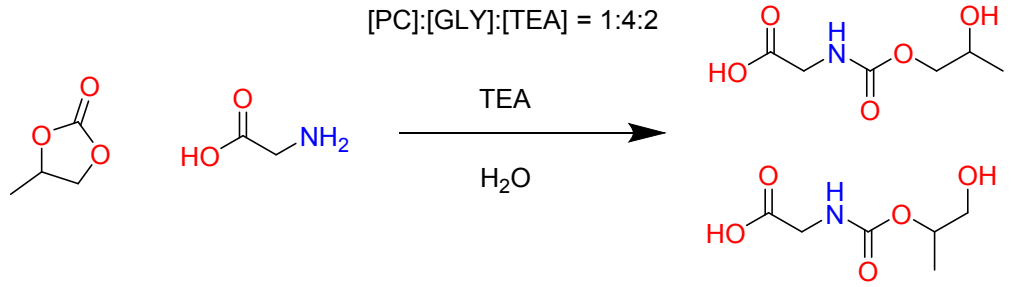


Figure S12. HRMS (ESI) calculated for C5H9NO5Na: 186.0378; found 186.0375

Synthesis of (((1-hydroxypropan-2-yl)oxy)carbonyl)glycine and ((2-hydroxypropoxy)carbonyl)glycine



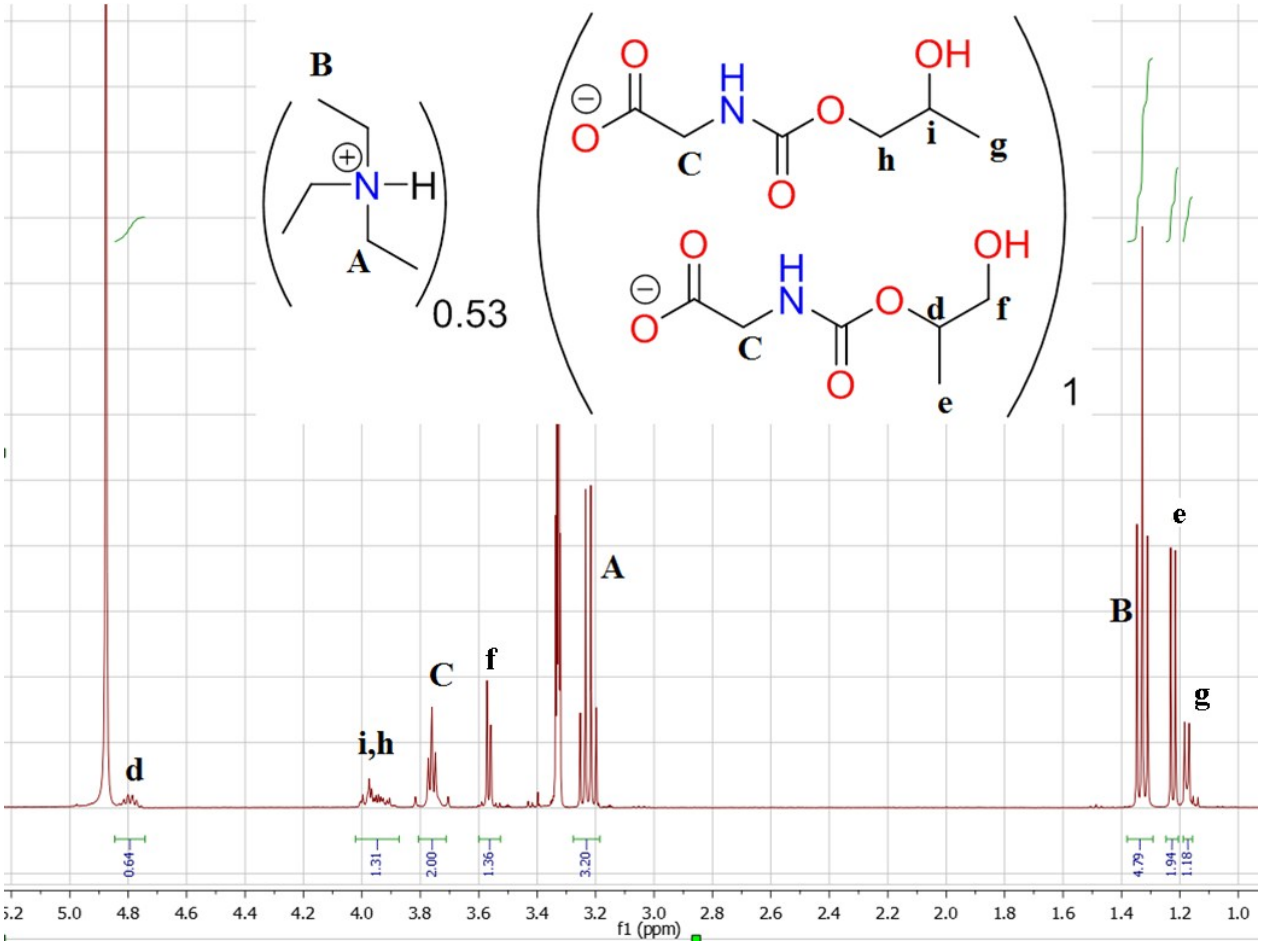


Figure S13. ^{1}H NMR on the concentrated solute after the precipitation

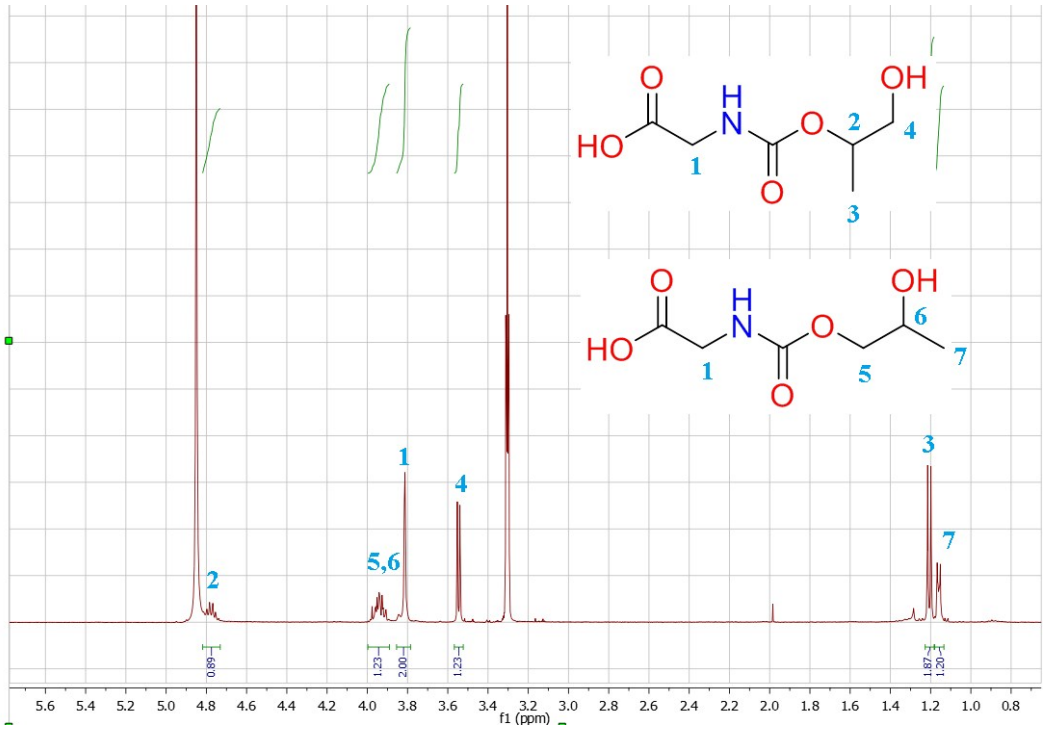


Figure S14. ^{1}HNMR on the obtained product after silica-plug

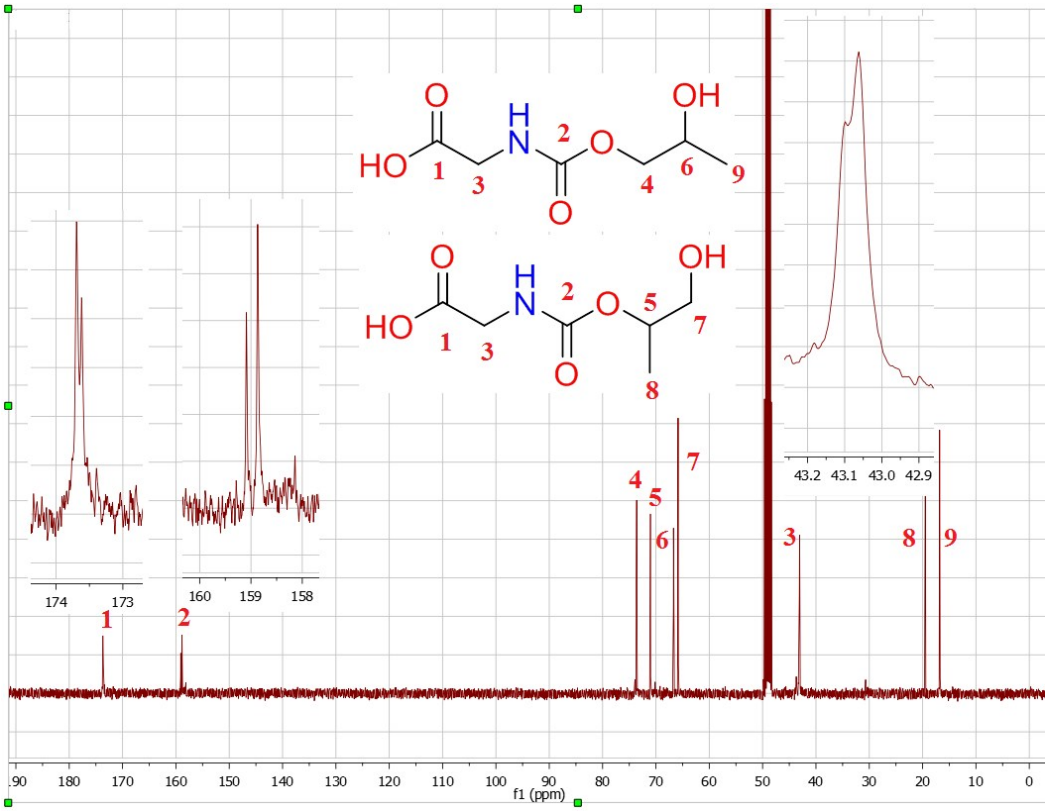


Figure S15. ^{13}CNMR on the obtained product after silica plug

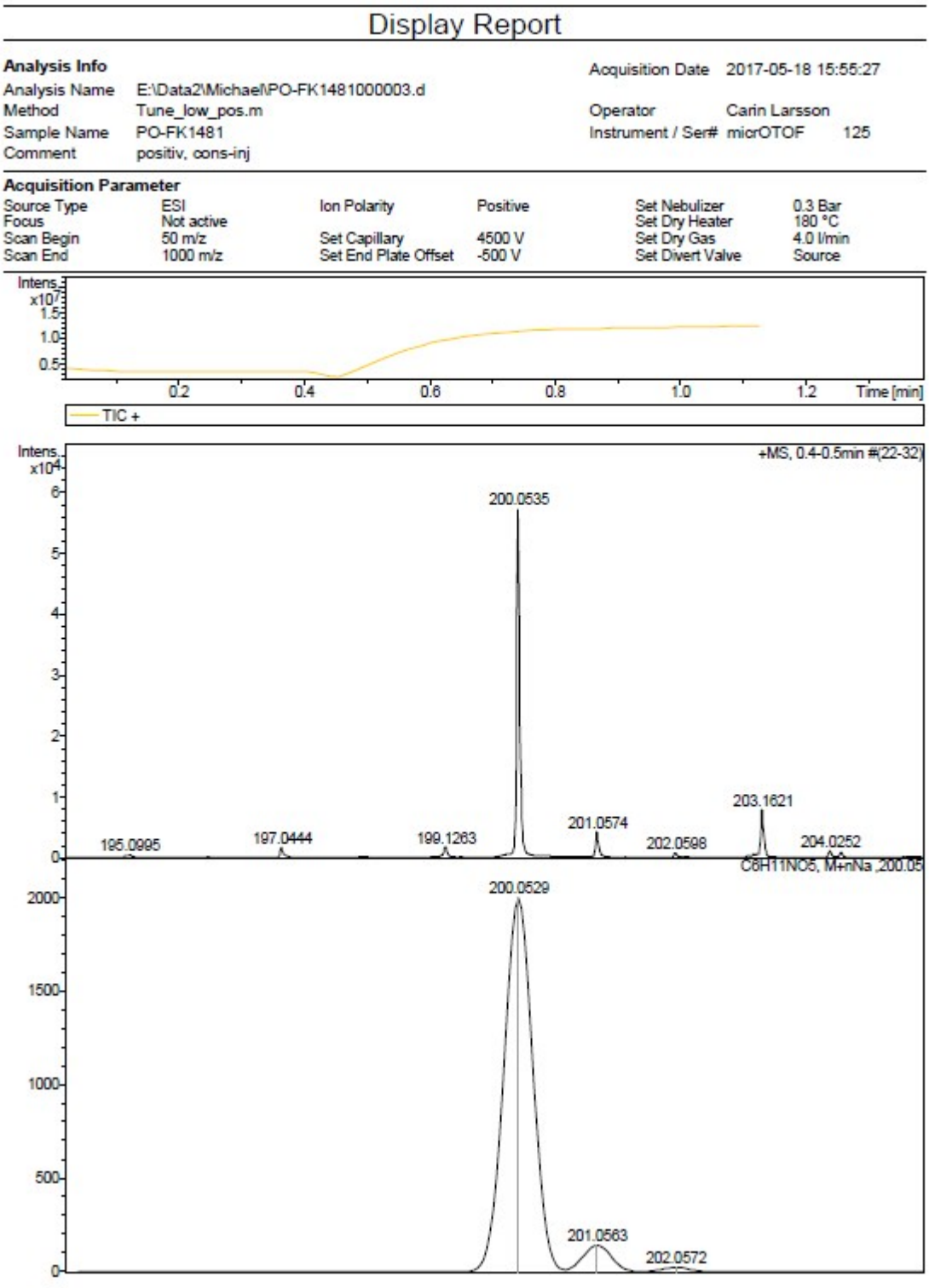
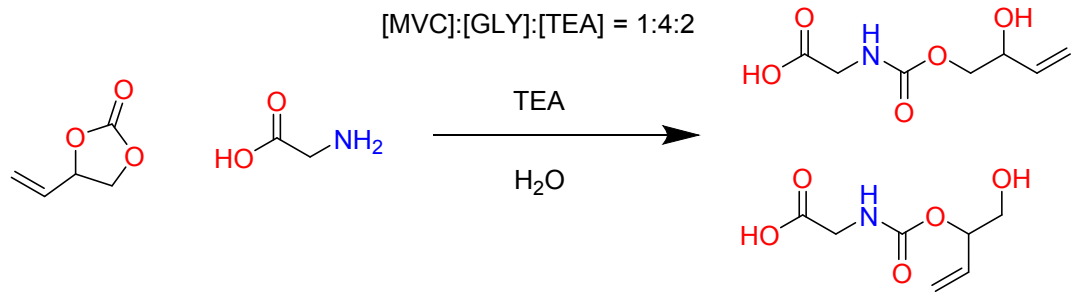


Figure S16. HRMS (ESI) calculated for C6H11NO5Na: 200.0535; found 200.0535

Synthesis of (((1-hydroxybut-3-en-2-yl)oxy)carbonyl)glycine and (((2-hydroxybut-3-en-1-yl)oxy)carbonyl)glycine



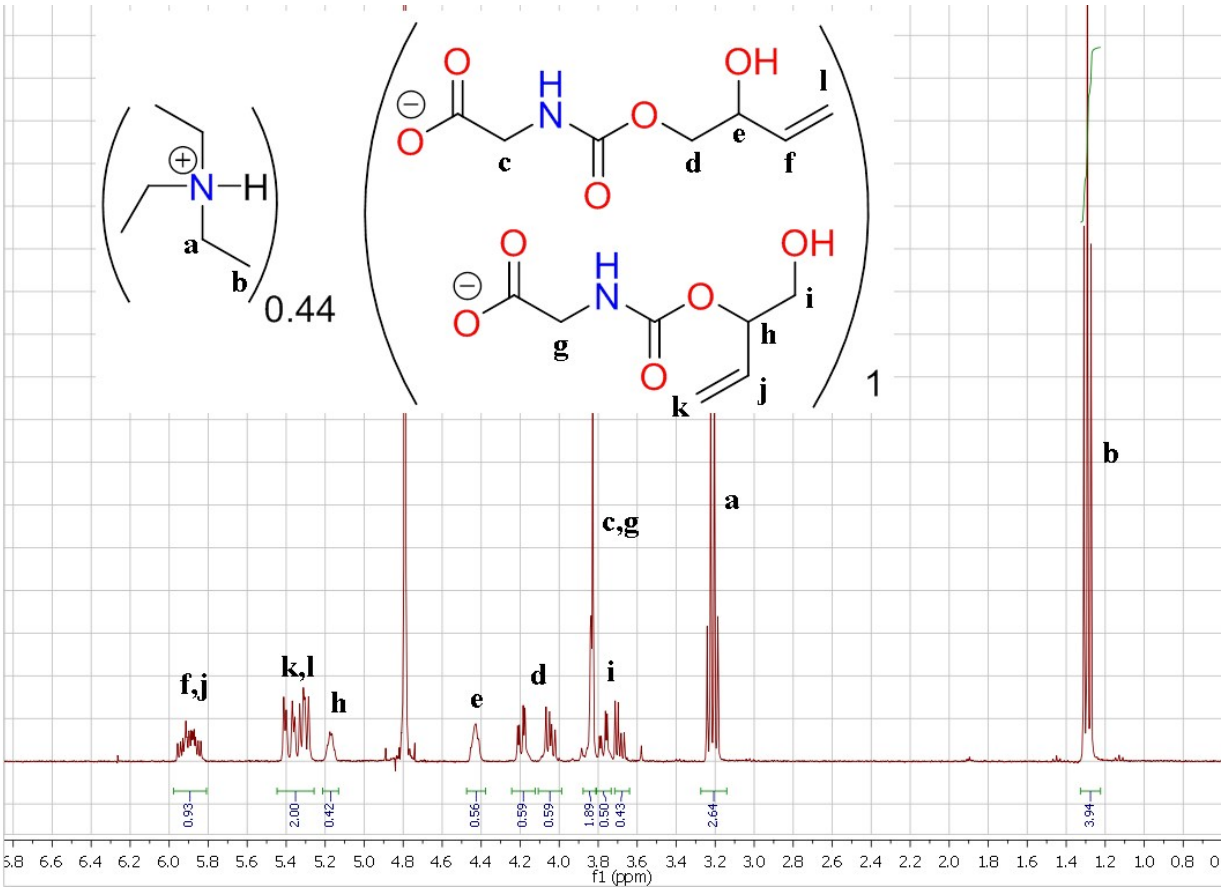


Figure S17. [1]HNMR on the concentrated solute after the precipitation

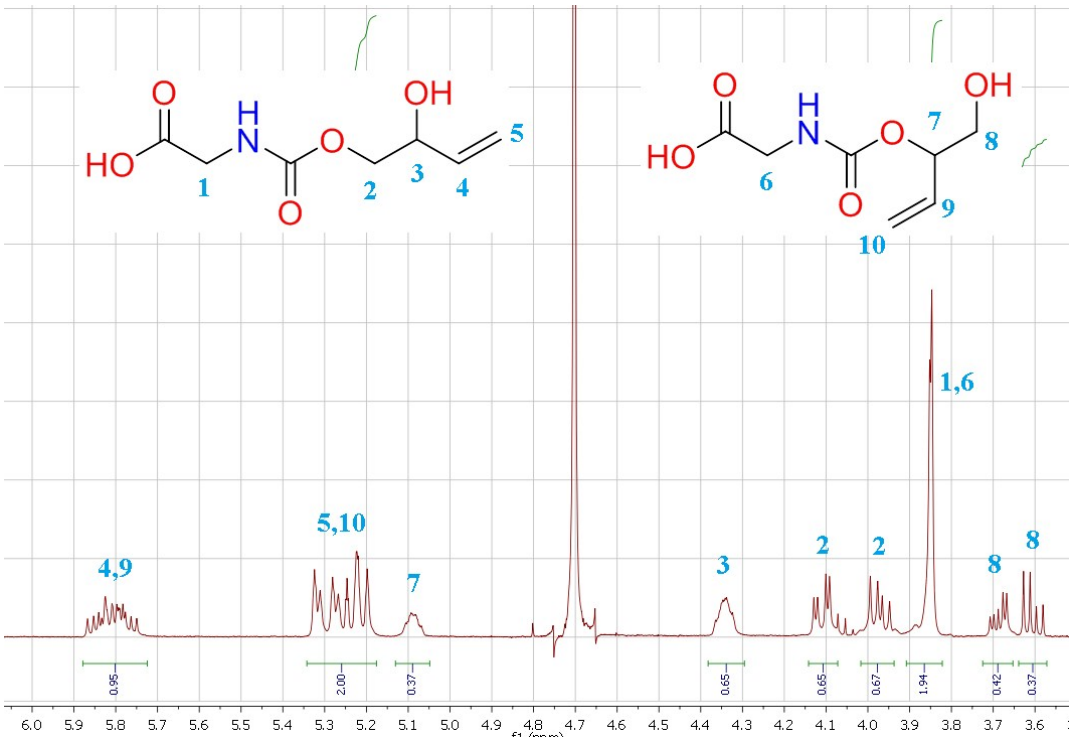


Figure S18. [1]HNMR on the obtained product after silica-plug

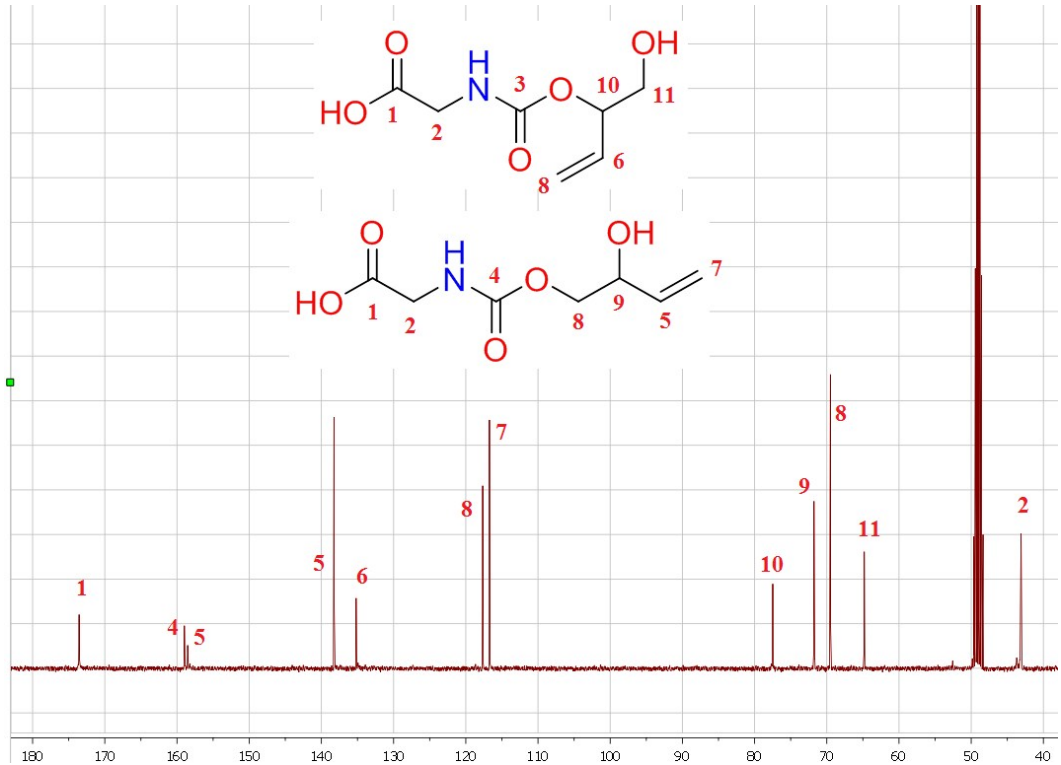


Figure S19. [13]CNMR on the obtained product after silica plug

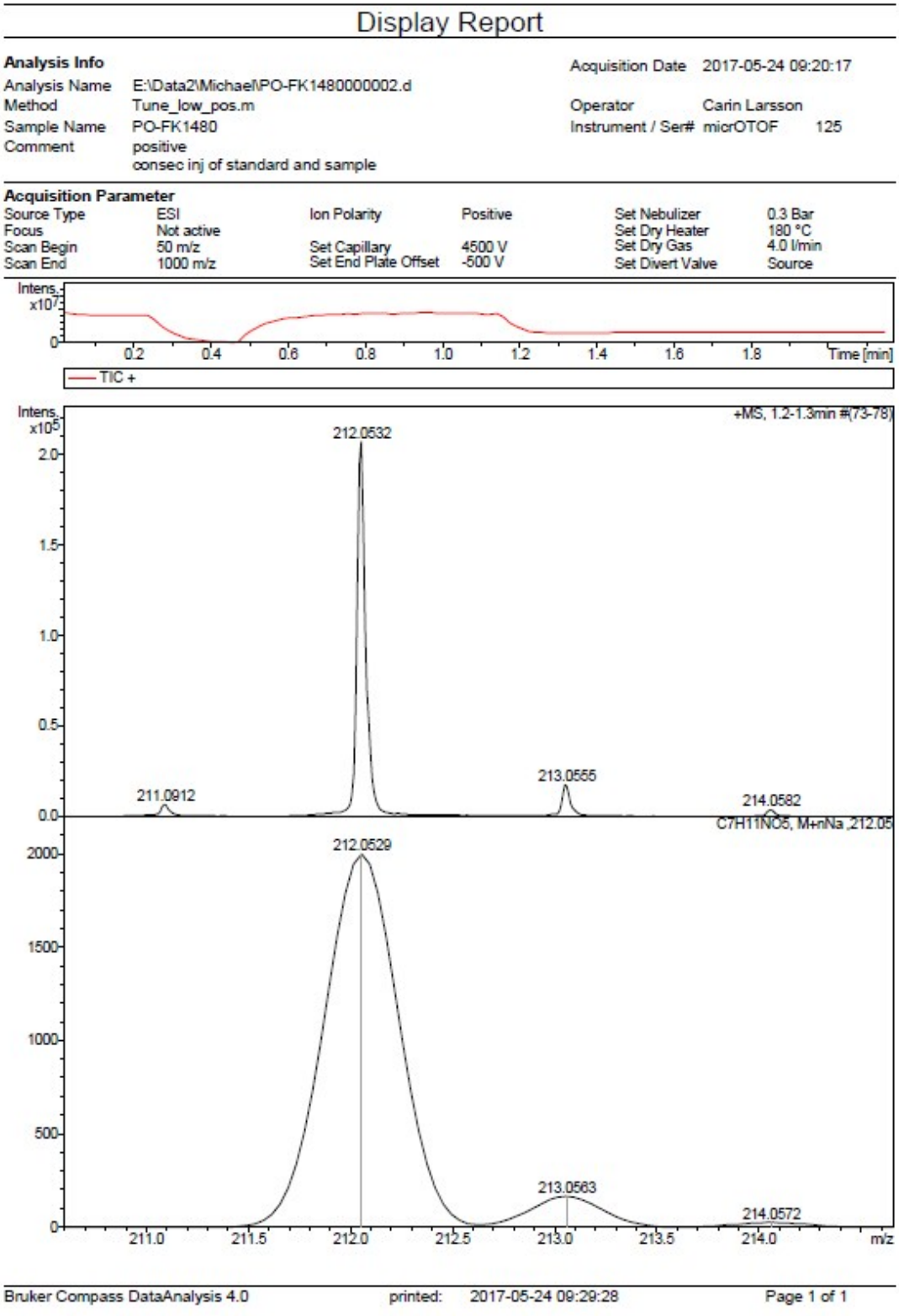


Figure S20. HRMS (ESI) calculated for C7H11NO5Na: 212.0535; found 212.0529

Synthesis of Cis and Trans (((4-hydroxyhexa-1,5-dien-3-yl)oxy)carbonyl)glycine

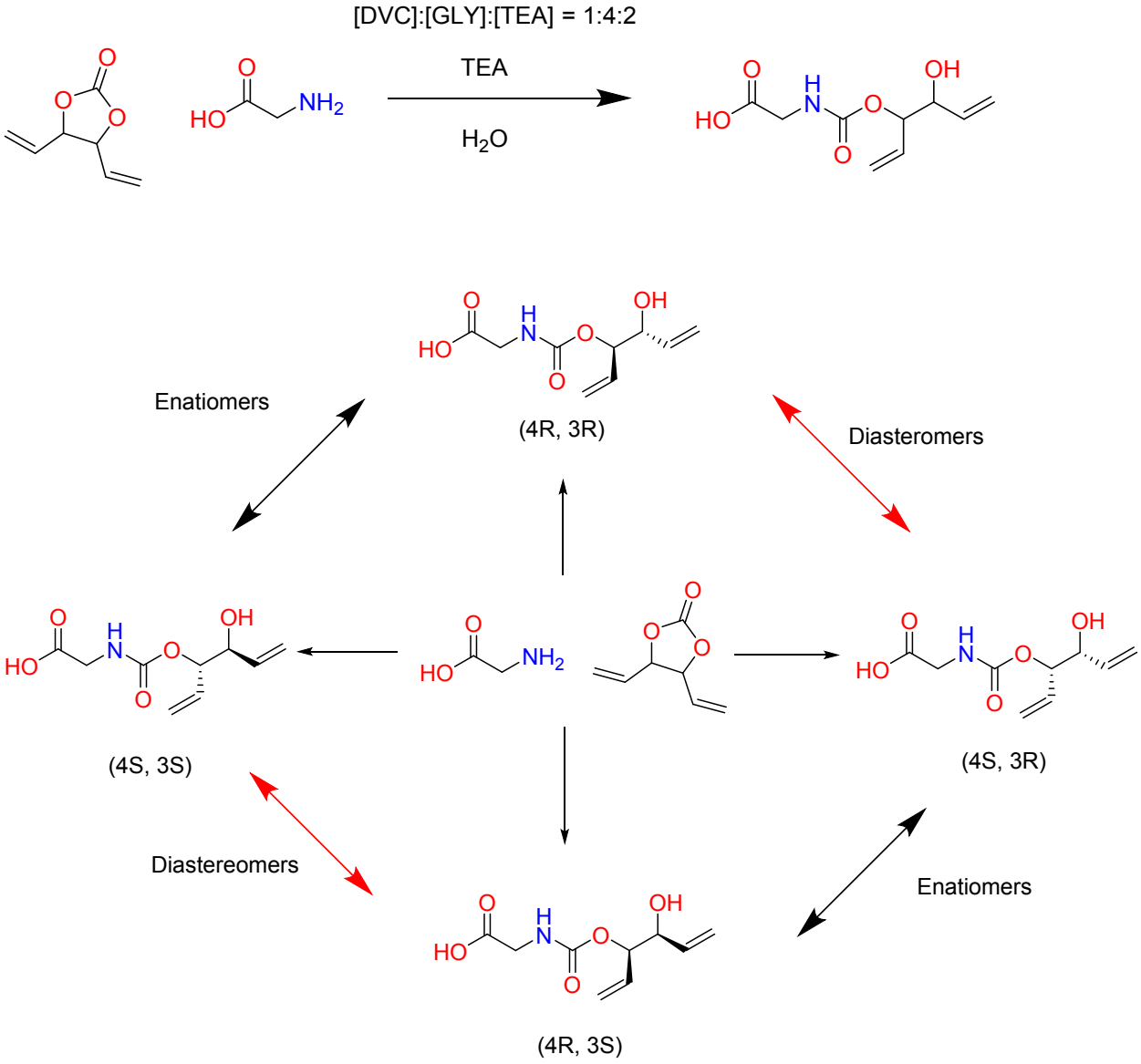


Figure S21 Possible product outcome from the ring opening behavior of DVC and GLY

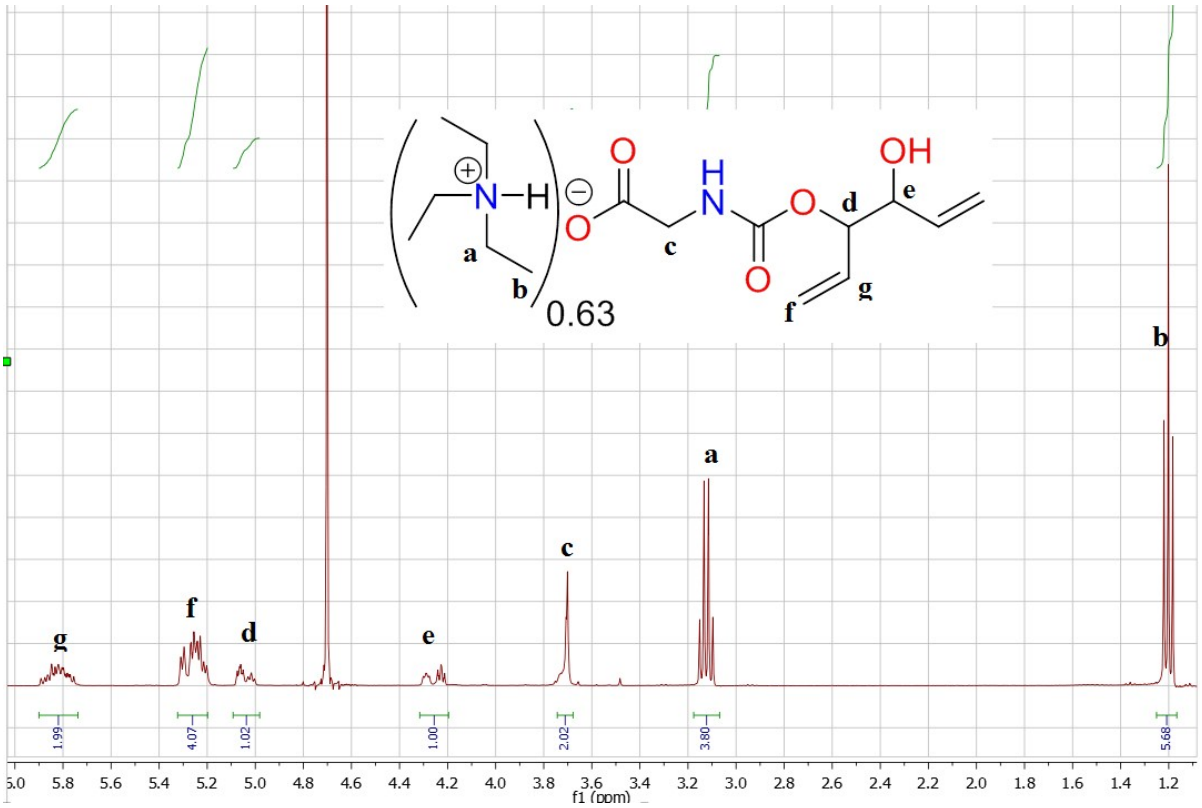


Figure S22. ^{1}H NMR on the concentrated solute after the precipitation

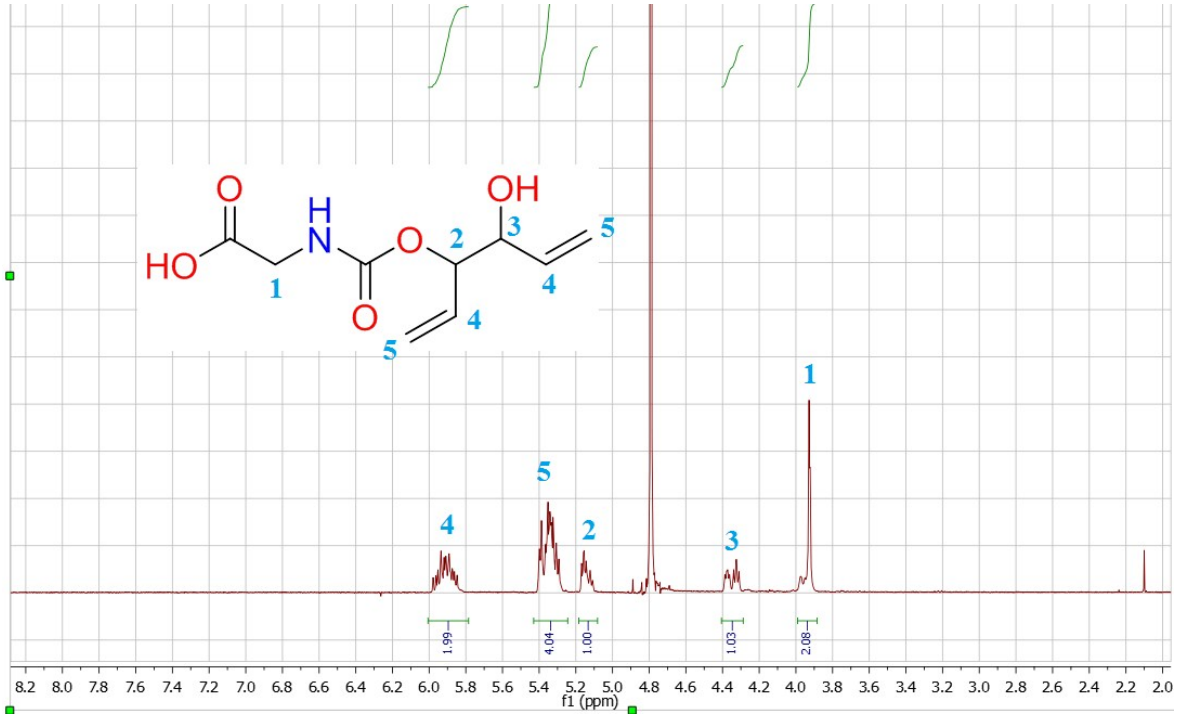


Figure S23. ^{1}H NMR on the obtained product after silica plug

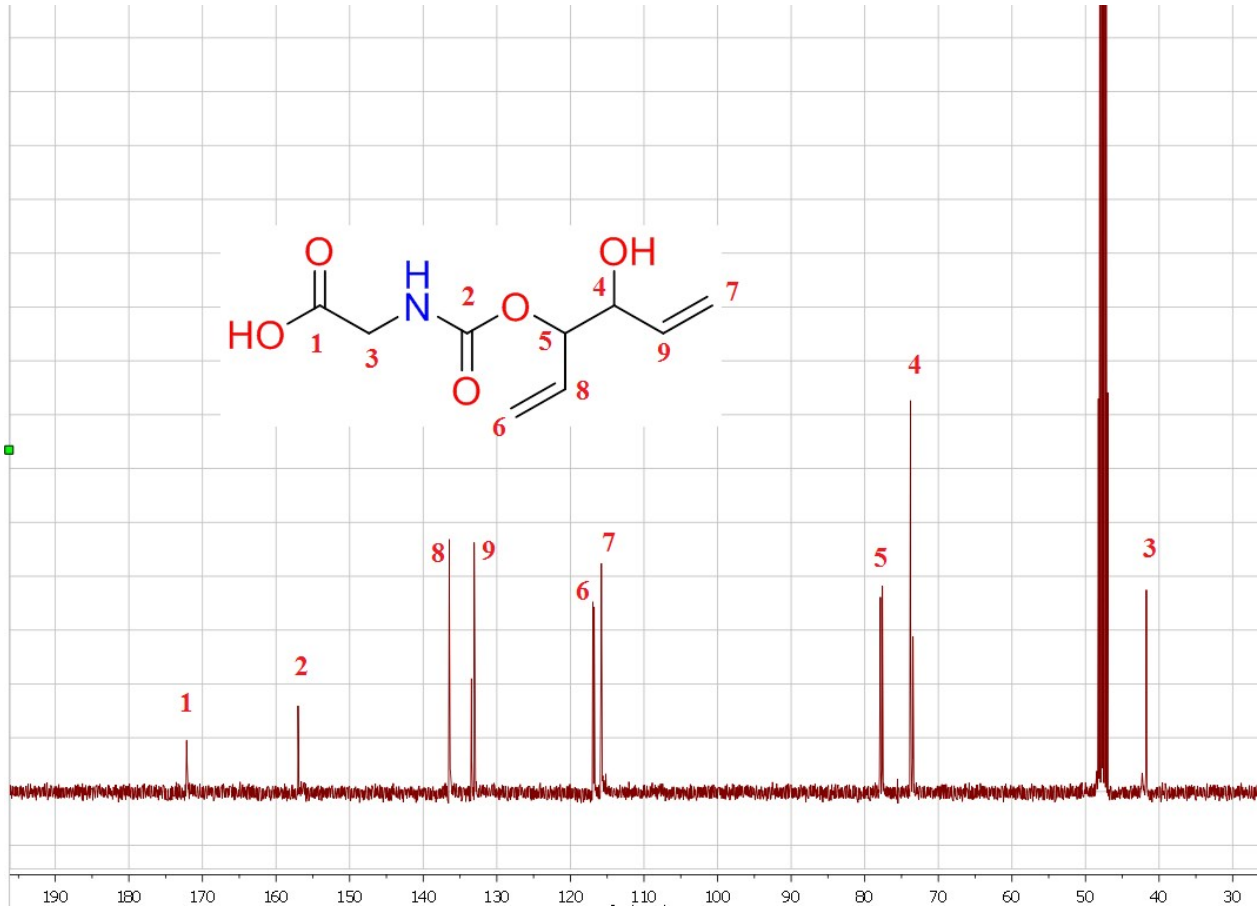


Figure S24. ^{13}CNMR on the obtained product after silica plug

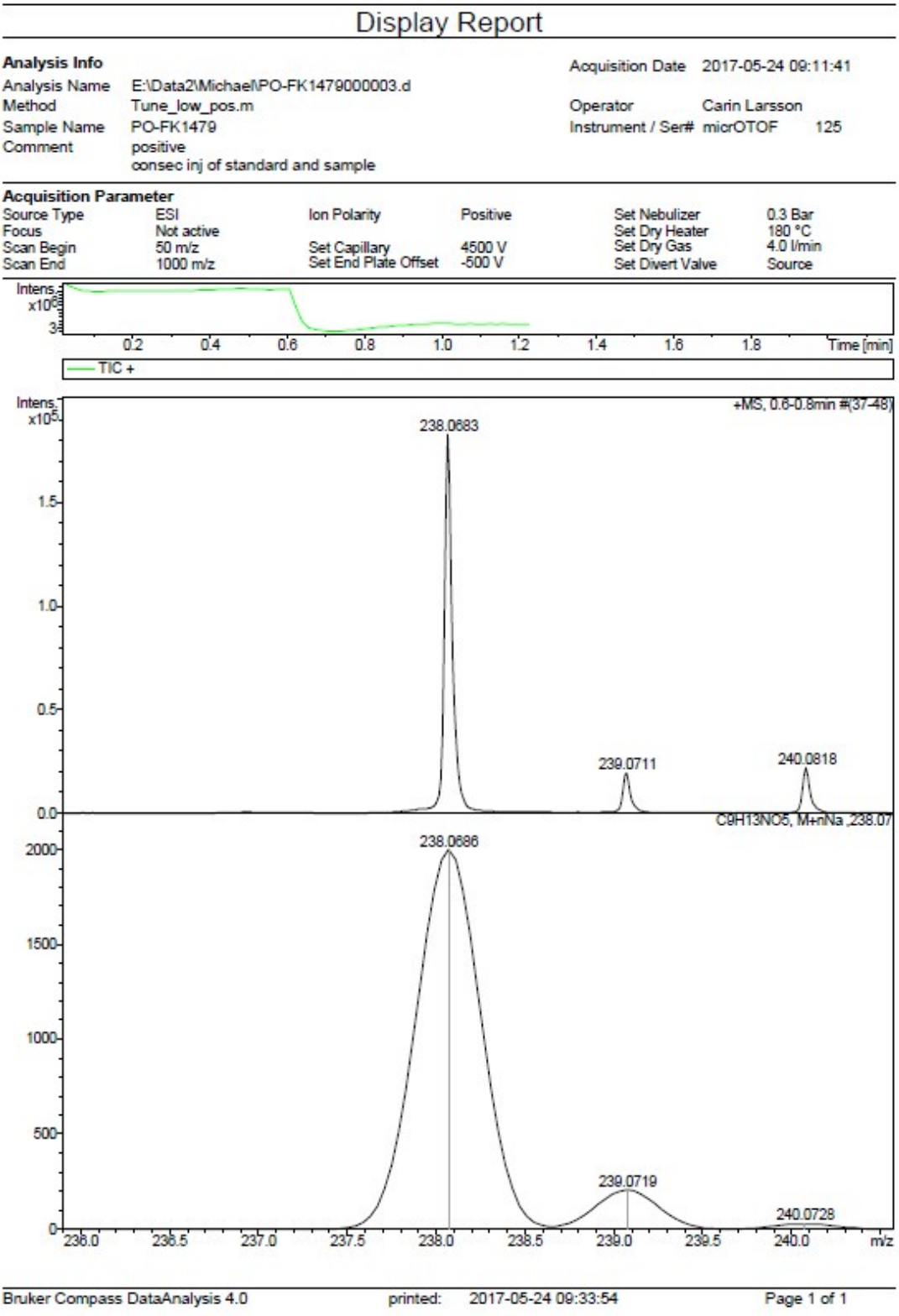


Figure S25. HRMS (ESI) calculated for C9H13NO5Na: 238.0691; found 238.0686

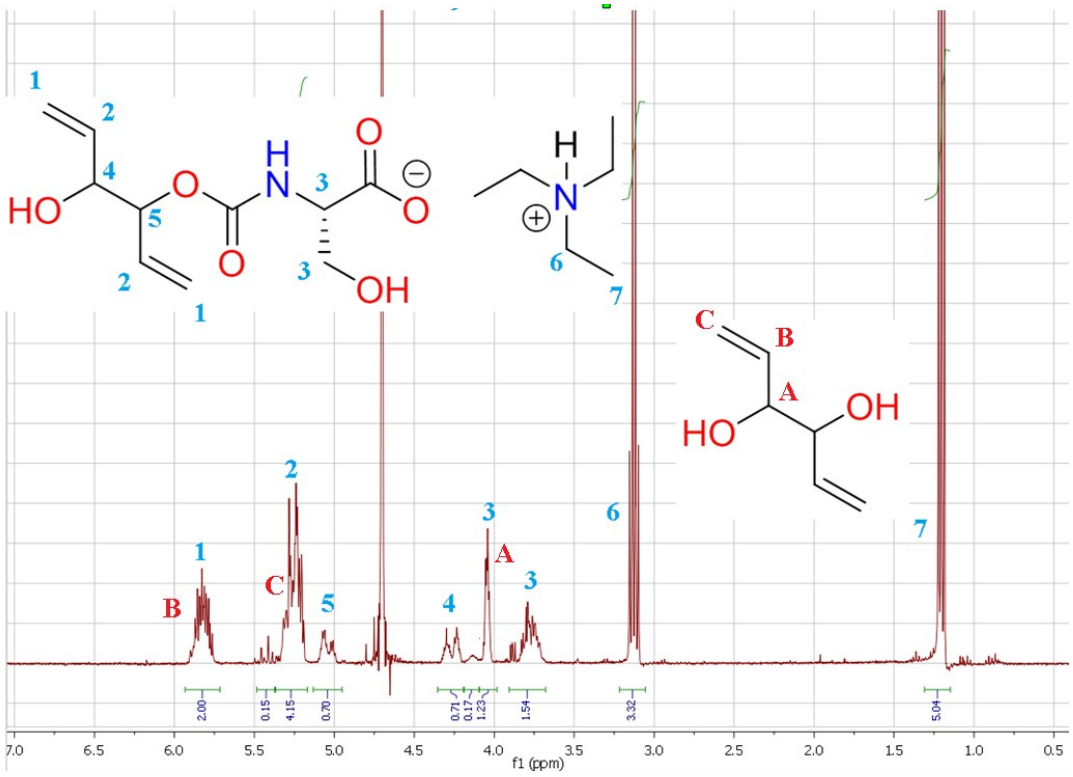


Figure S26 ^{1}HNMR on the obtained product after silica-plug

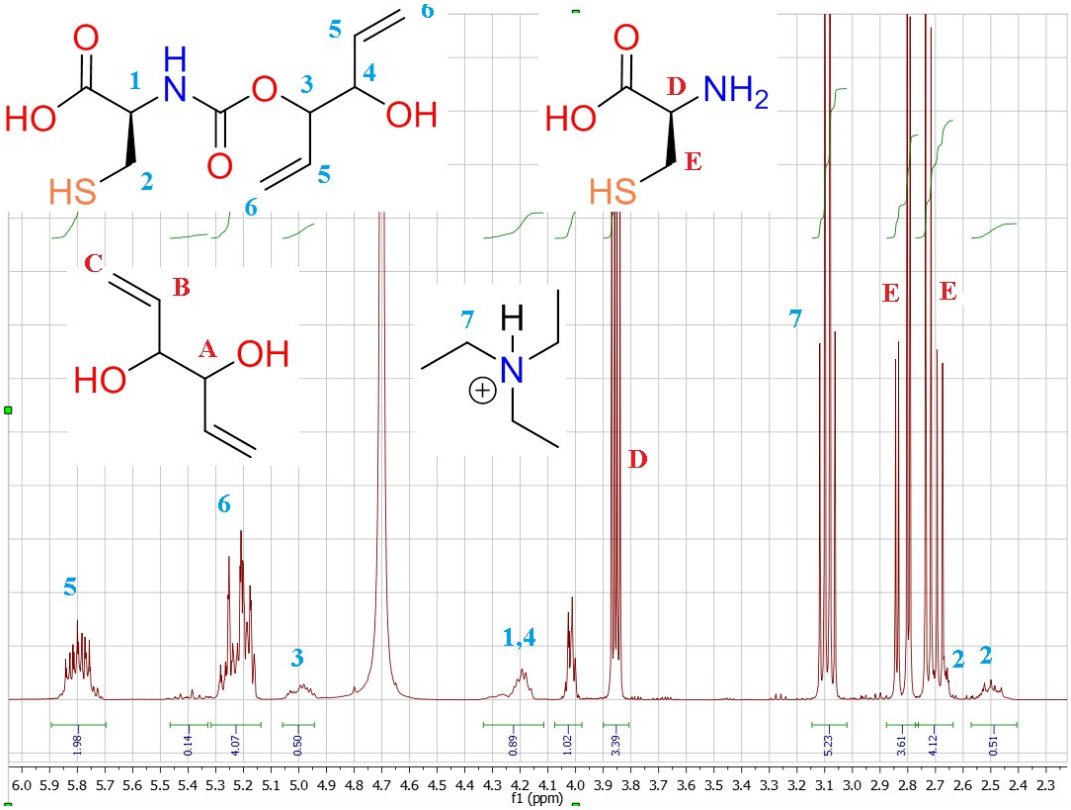


Figure S27 ^{1}HNMR on the on the crude product

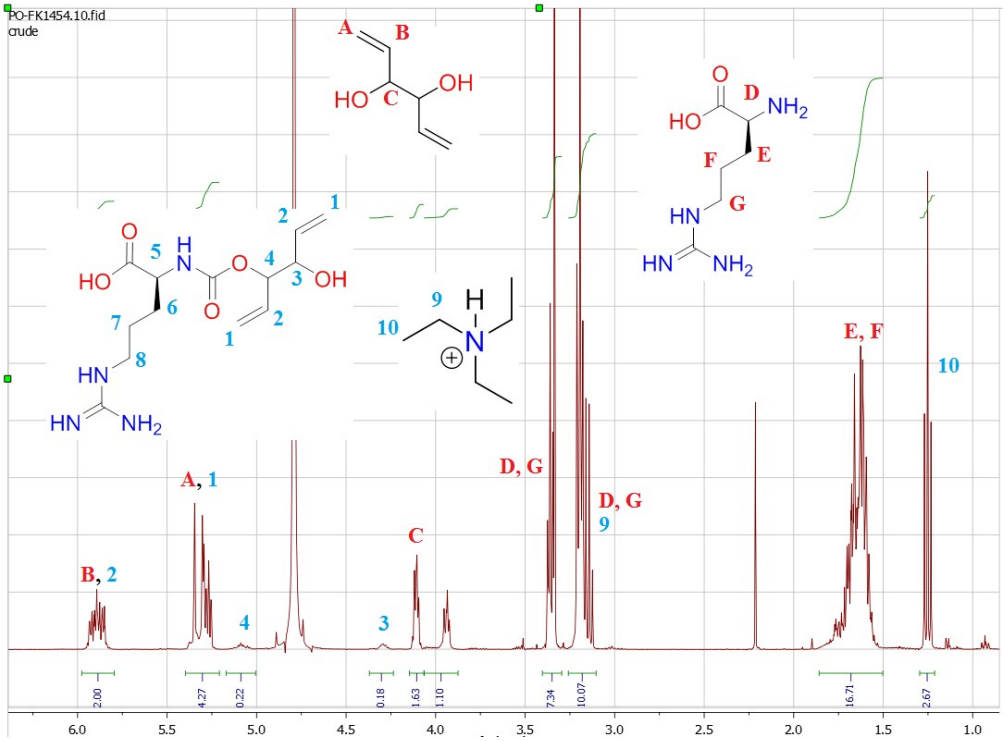


Figure S28 [1]HNMR on the on the crude product

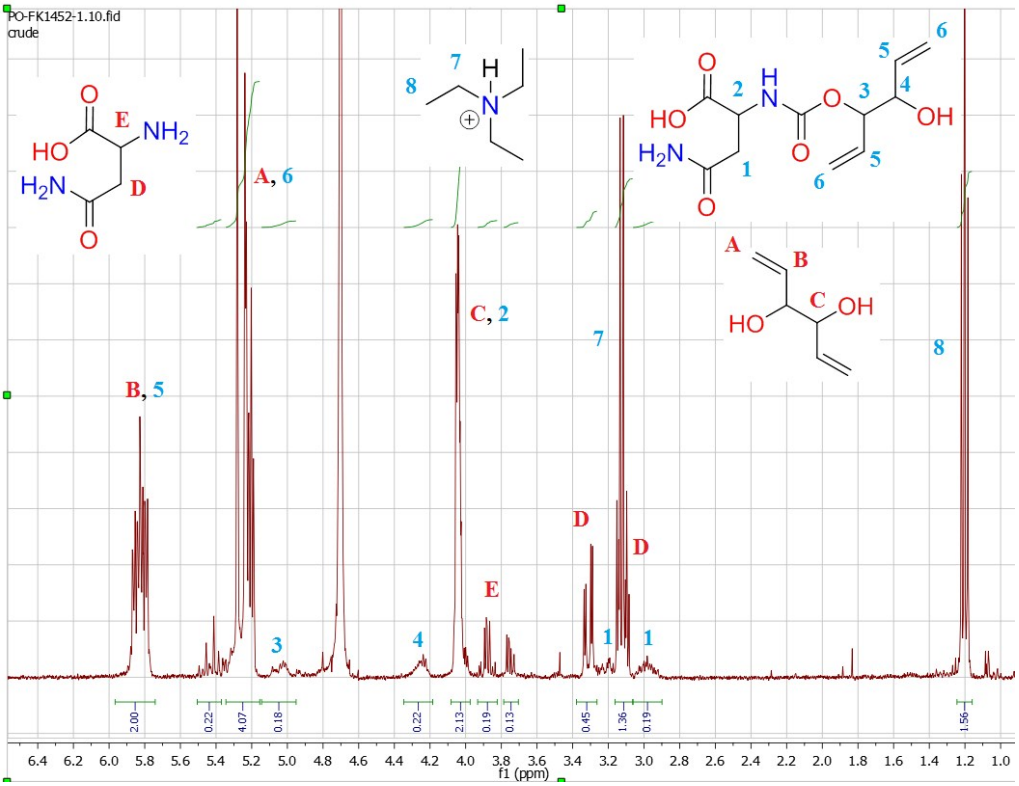


Figure S29 [1]HNMR on the on the crude product

Carbonyl activation

The carbonyl activation was studied on the change in chemical shift for the carbons related to the ethylene carbonate at different equivalents of glycine with acetonitrile as an internal standard, figure

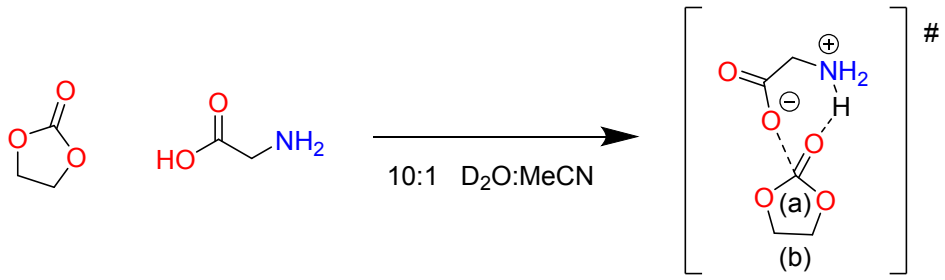


Figure S30. Displaying the envisioned activation of the carbonyl carbon with the zwitterionic glycine substrate.

Glycine to Ethylene carbonate ratio 1.1

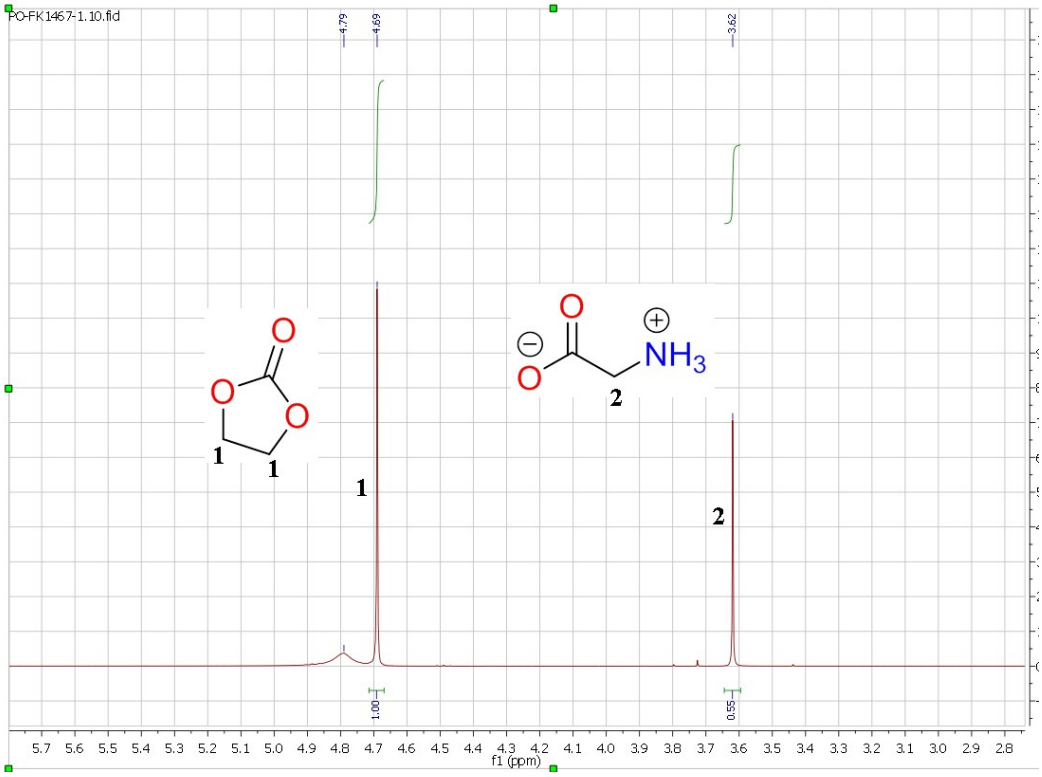


Figure S31. ^{1}H NMR example of ratio determination between GLY and EC

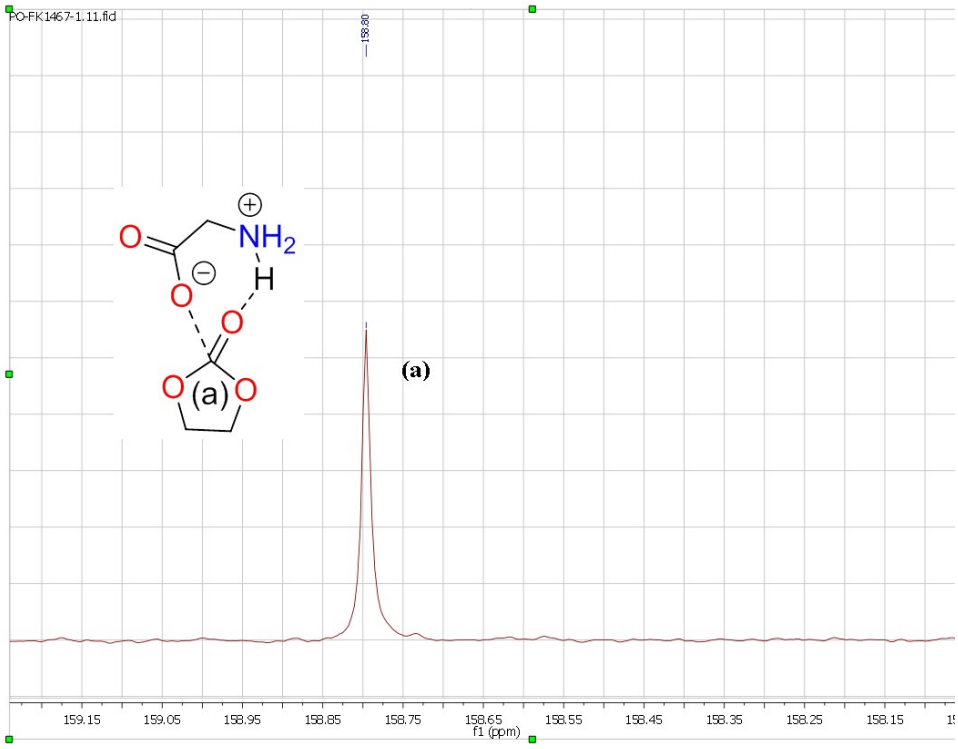


Figure S32. ^{13}C NMR shift of the ethylene carbon

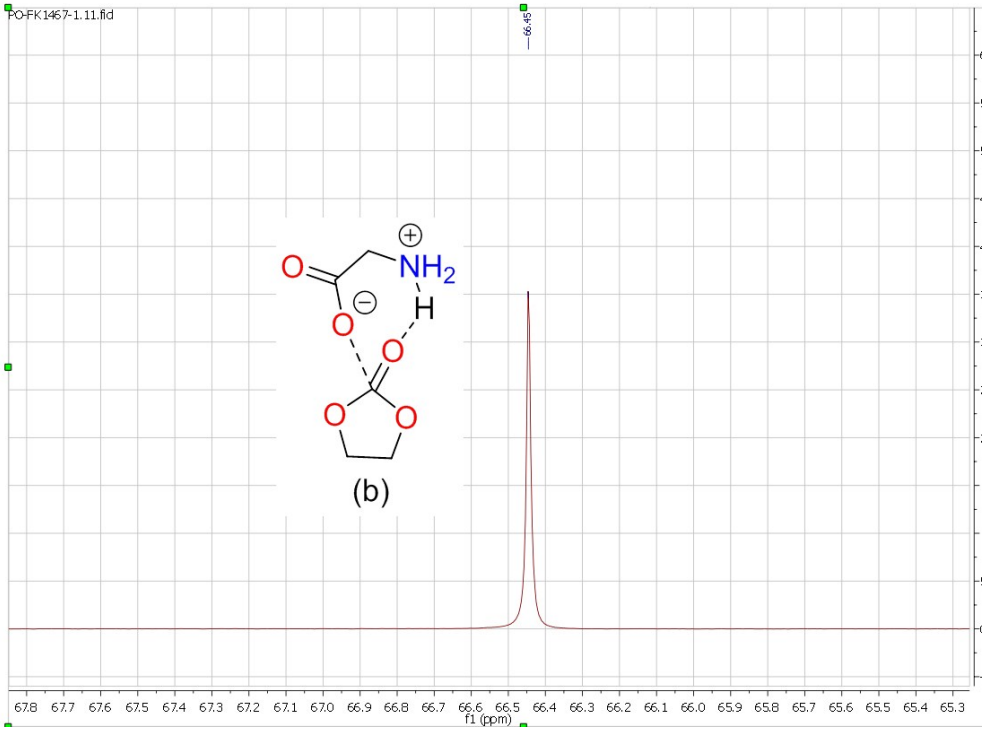


Figure S33. ^{13}C NMR shift of the carbonyl carbon

Table S1 Change in chemical shift for EC in the presence of GLY

Sample	Ratio	(a) ppm	(b) ppm
1	1.1	158.80	66.45
2	0.54	158.86	66.48
3	1.9	158.75	66.41
4	0.25	158.90	66.50
5	4.0	158.78	66.42
6	0	158.94	66.53

Table S2 Change in chemical shift for EC in the presence of GLY-OMe

Sample	Ratio	(a) ppm	(b) ppm
1	1.28	158.85	66.21
2	0.60	158.87	66.51
3	2.54	158.69	66.46
4	0.30	159.02	66.57
5	3.57	158.59	66.43
6	0	158.94	66.53