Supporting Information

Concatenated batch and continuous flow procedures for the upgrading of glycerol-derived aminodiols via N-acetylation and acetalization reactions

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N-(2,3-dihydroxypropyl)acetamide, ***1a***

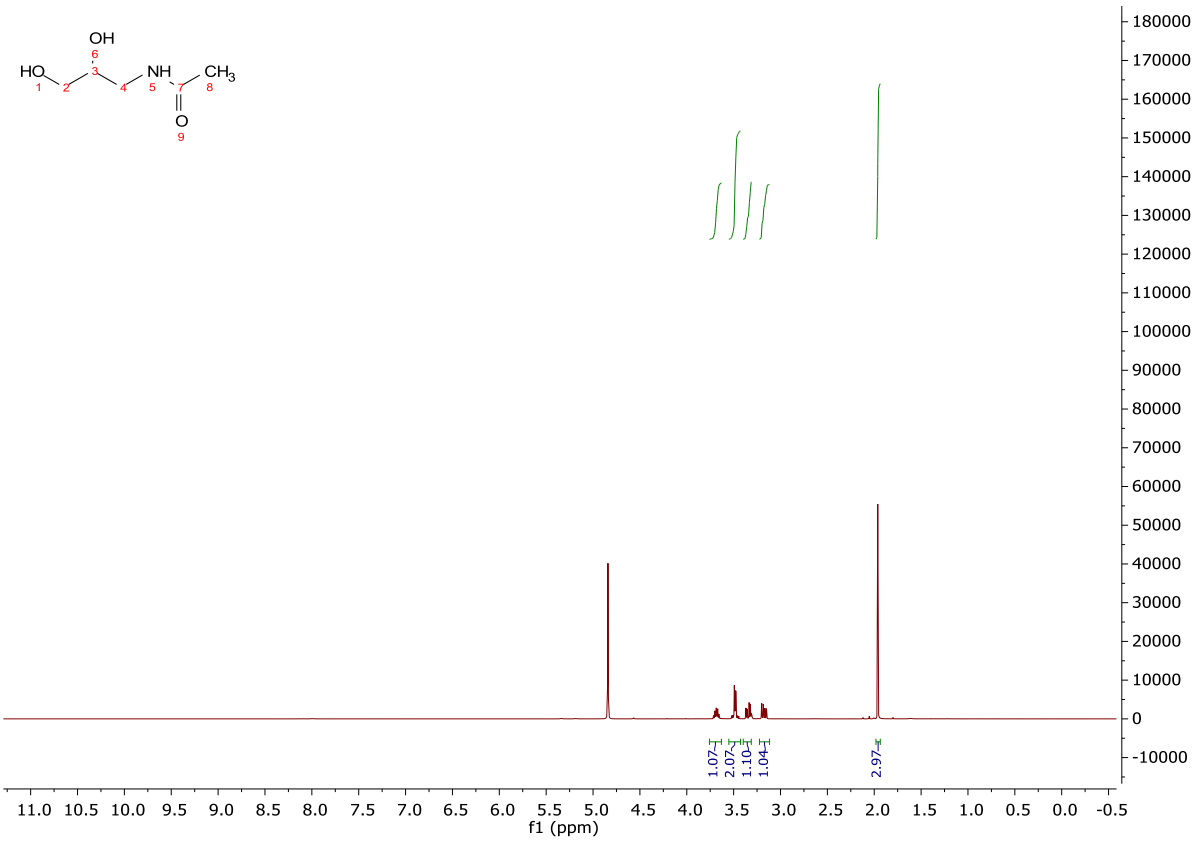


Figure S1. ^{1}H NMR of compound **1a** in CD_3OD.

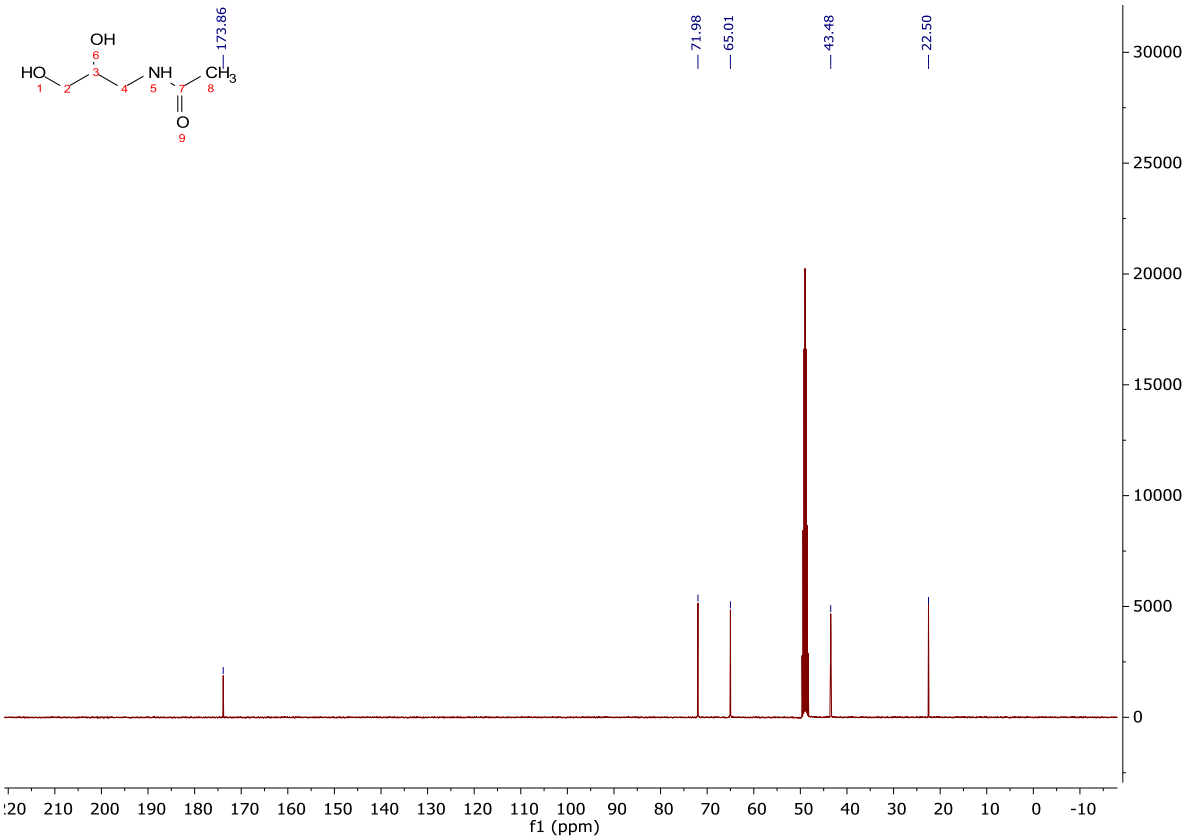


Figure S2. ^{13}C NMR of compound **1a** in CD_3OD.

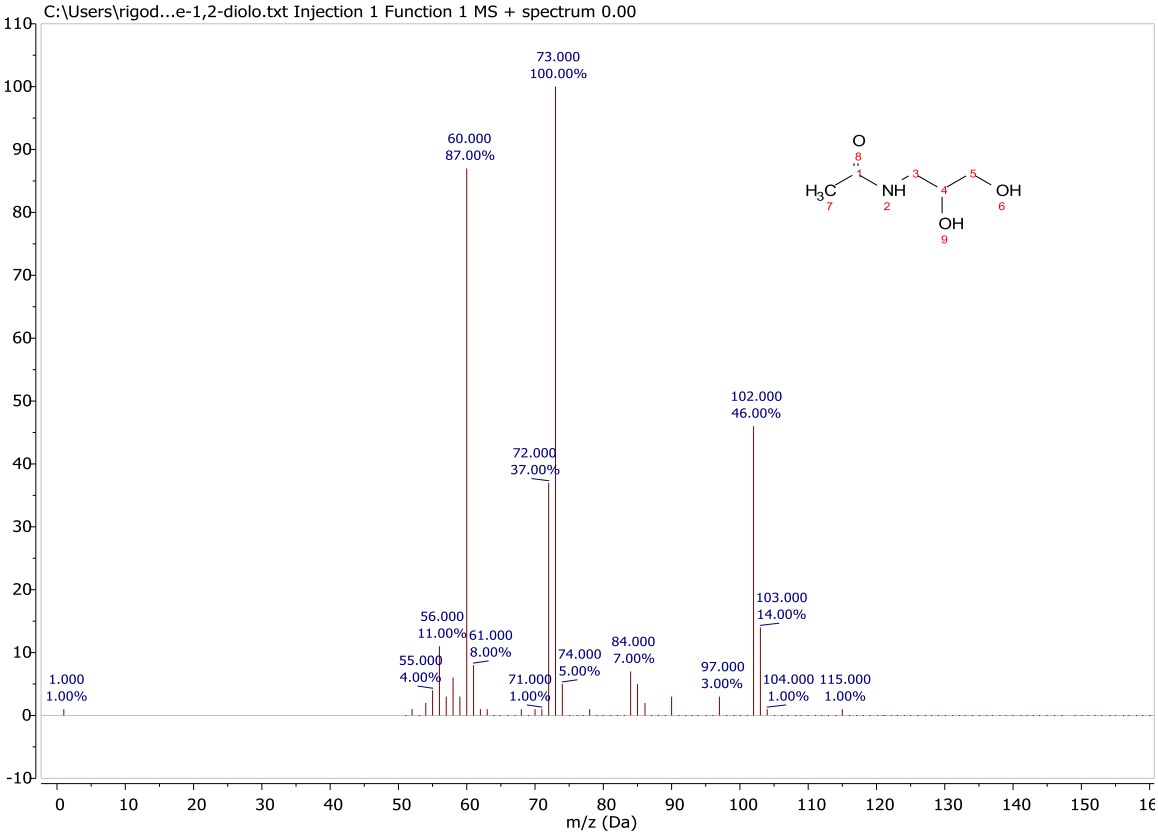


Figure S3. MS spectrum (70eV) of compound **1a**.

N-(1,3-dihydroxypropan-2-yl)acetamide, ***2a***

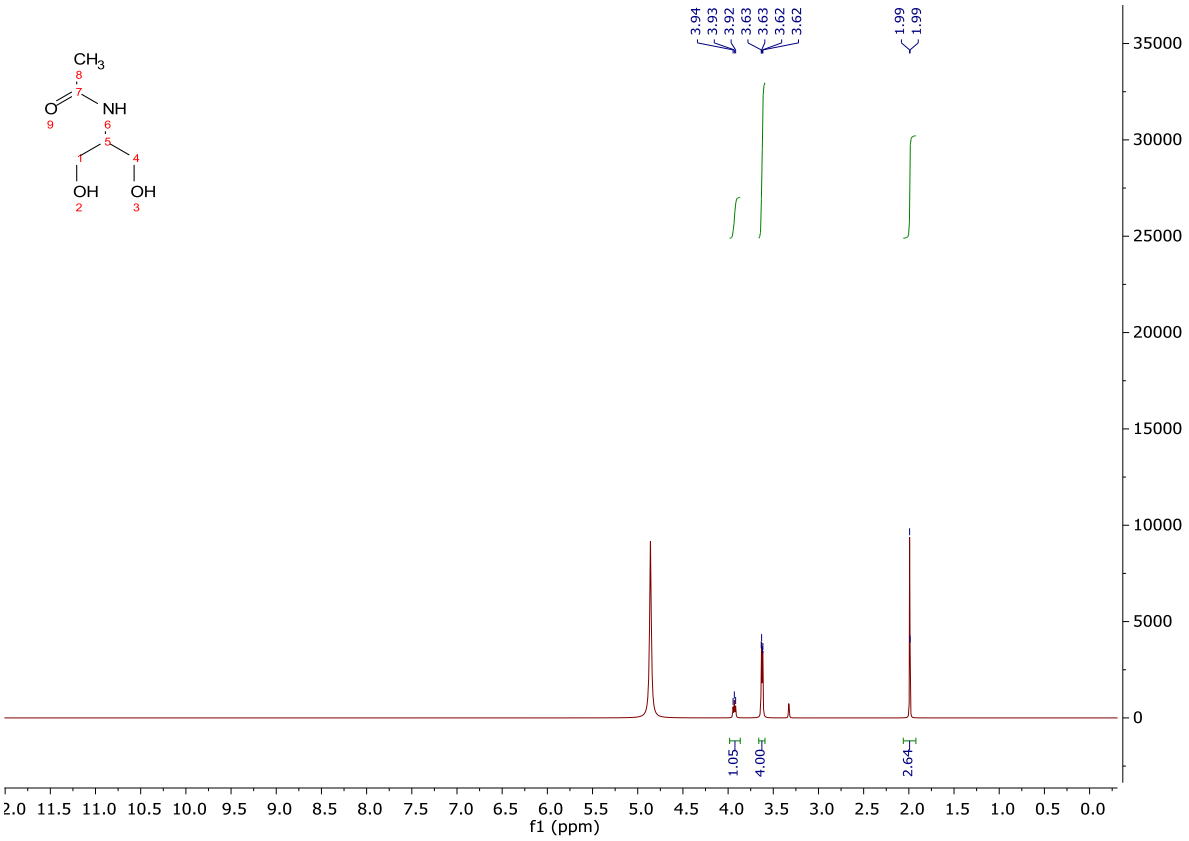


Figure S4. ^{1}H NMR of compound **2a** in CD_3OD.

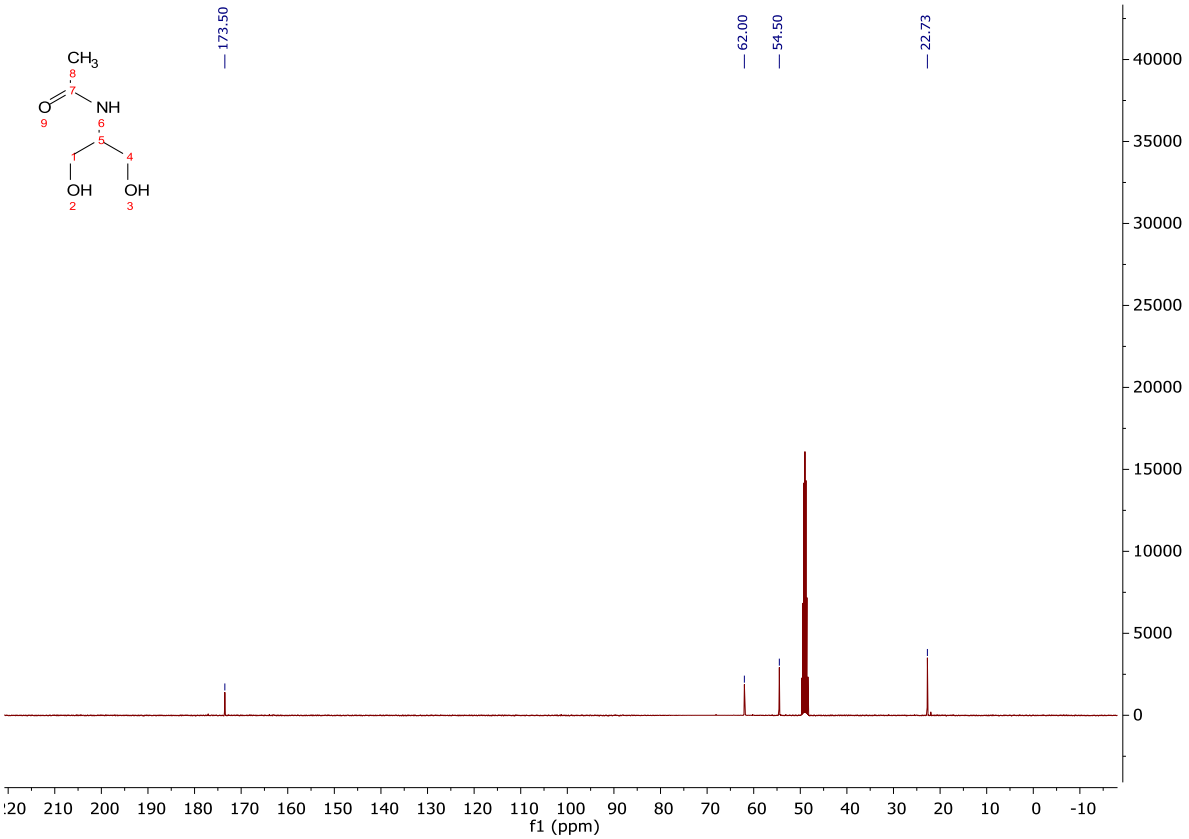


Figure S5. ^{13}C NMR of compound **2a** in CD_3OD.

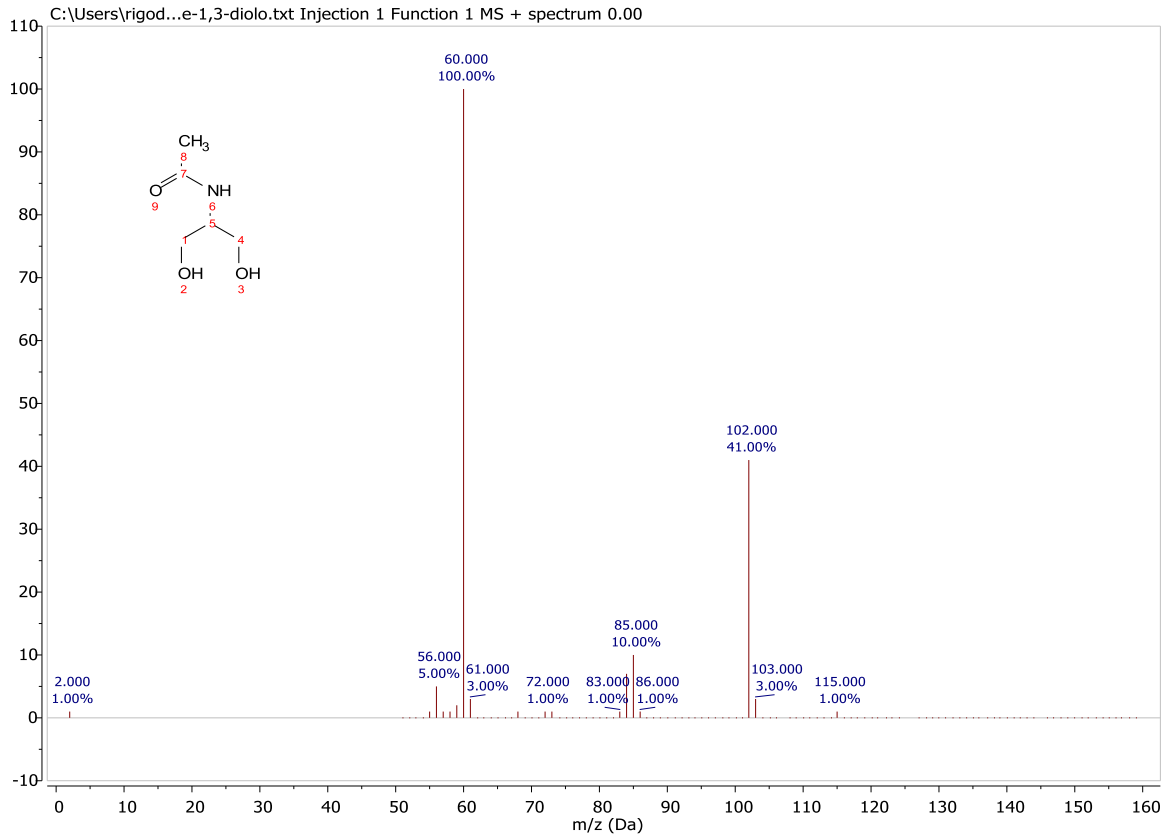


Figure S6. MS spectrum (70eV) of compound **2a**.

The continuous-flow apparatus

A schematic chart of the experimental setup used for continuous-flow (CF) reactions is represented in Figure S7.

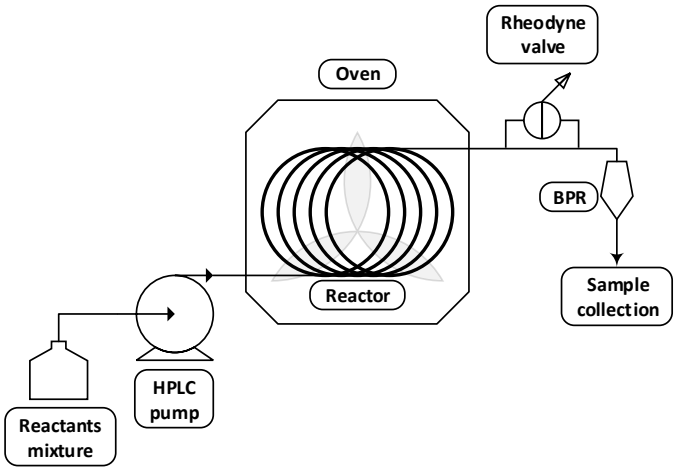


Figure S7. Experimental setup used for continuous-flow reactions

The apparatus was in-house assembled. An HPLC pump was used to send the reactants solution (diol, enol ester, and the solvent) to a stainless-steel tubular reactor (l = 12 cm, i.d. = 6 mm, inner volume = 1.4 mL) filled with the solid catalyst. The reactor was heated at the desired temperature by a fan oven. At the outlet of the reactor, a manual Swagelok KPB1N0G412 back pressure regulator (BPR), equipped with an electronic pressure sensor, was used to control the system pressure. Reactions were all carried out at a pressure slightly above ambient conditions to overcome the

pressure drop within the continuous-flow system. Placed between the reactor and the BPR, a Rheodyne valve (7725i) with a 100 µL loop was used to sample the reaction mixture.

N-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)acetamide, ***1b***

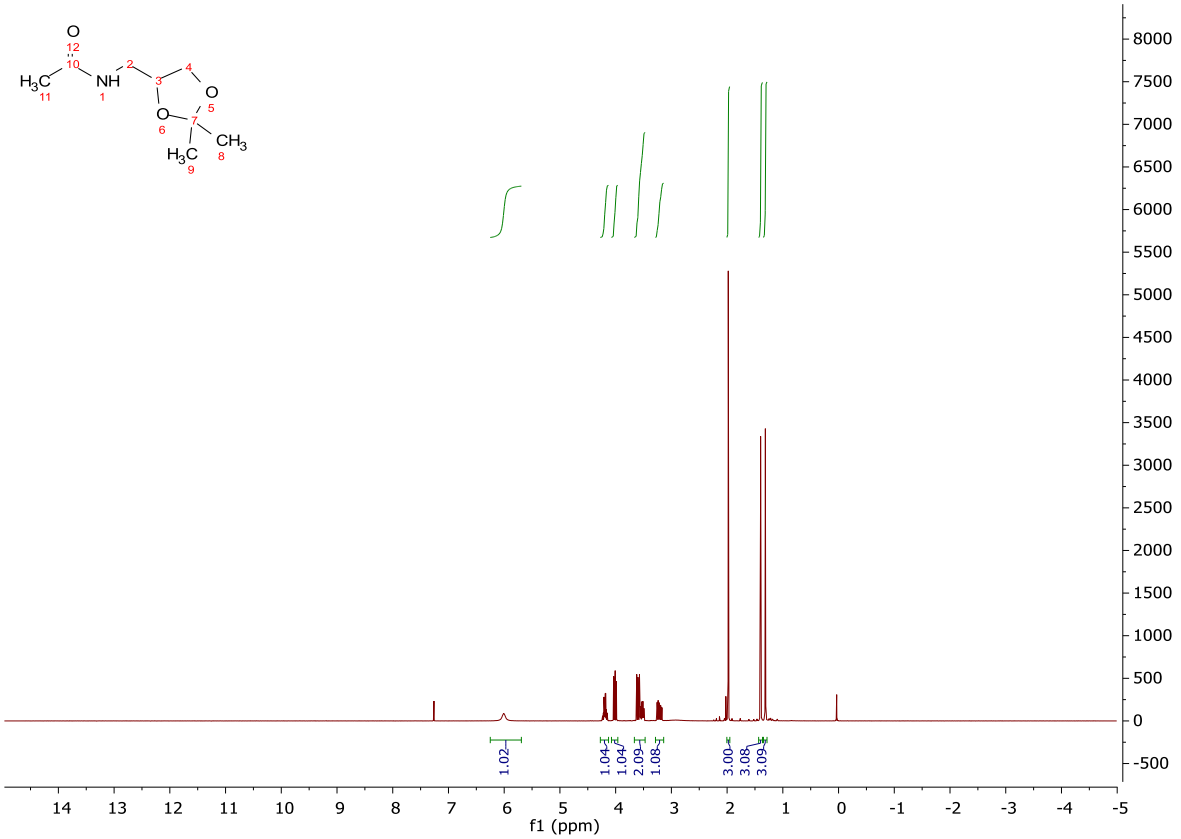


Figure S8. ^{1}H NMR of compound **1b** in CD_3OD

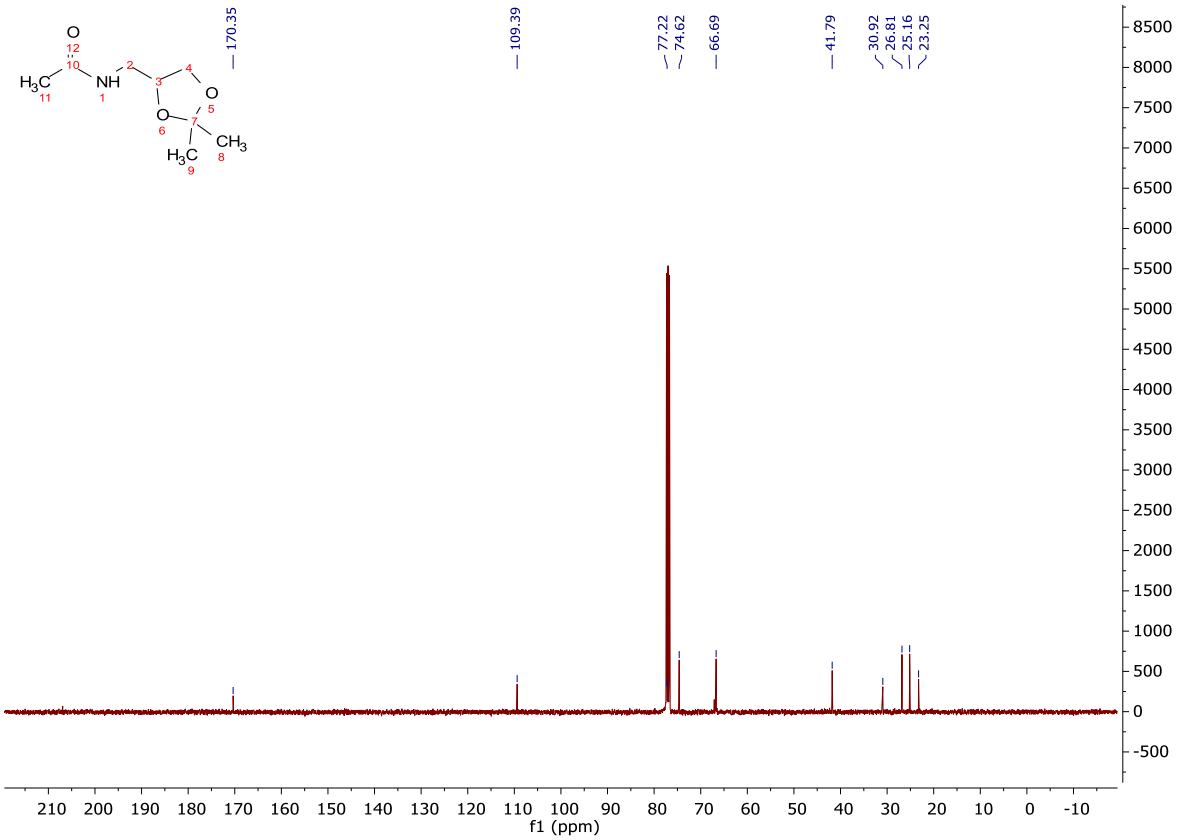


Figure S9. ^{13}C NMR of compound **1b** in $CDCl_3$.

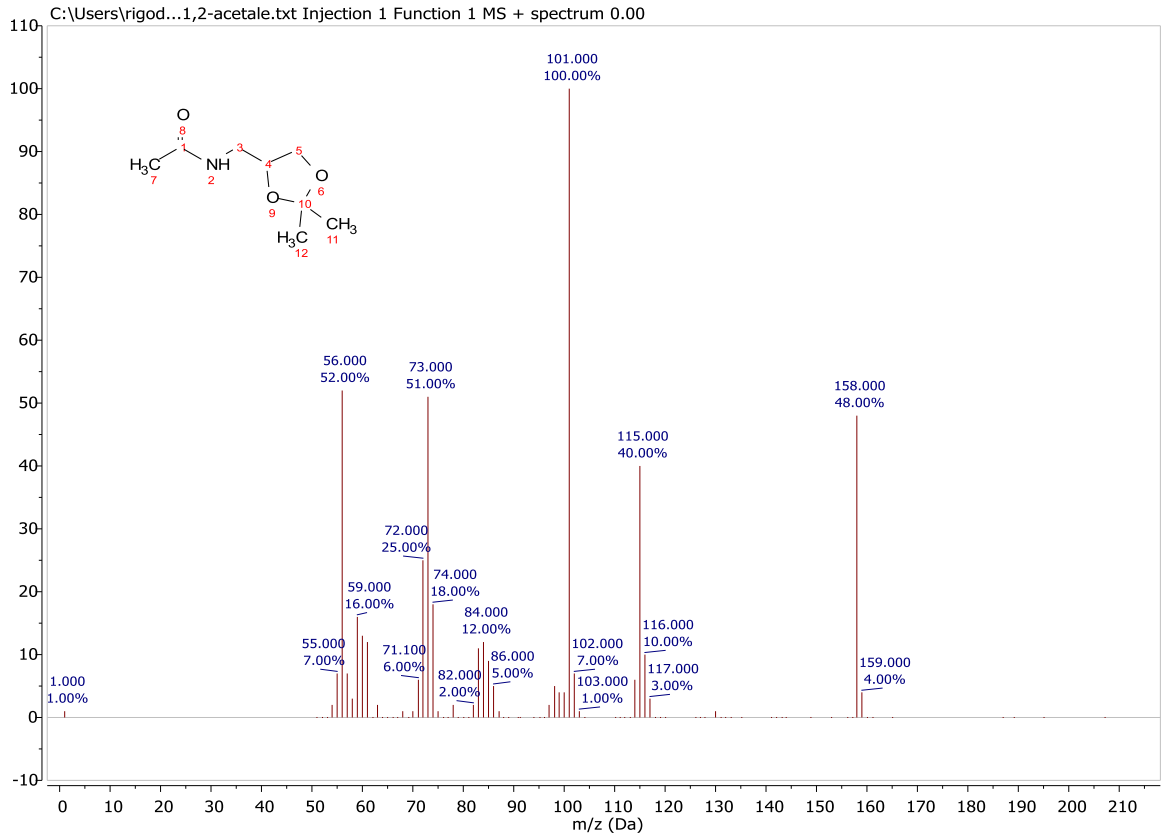
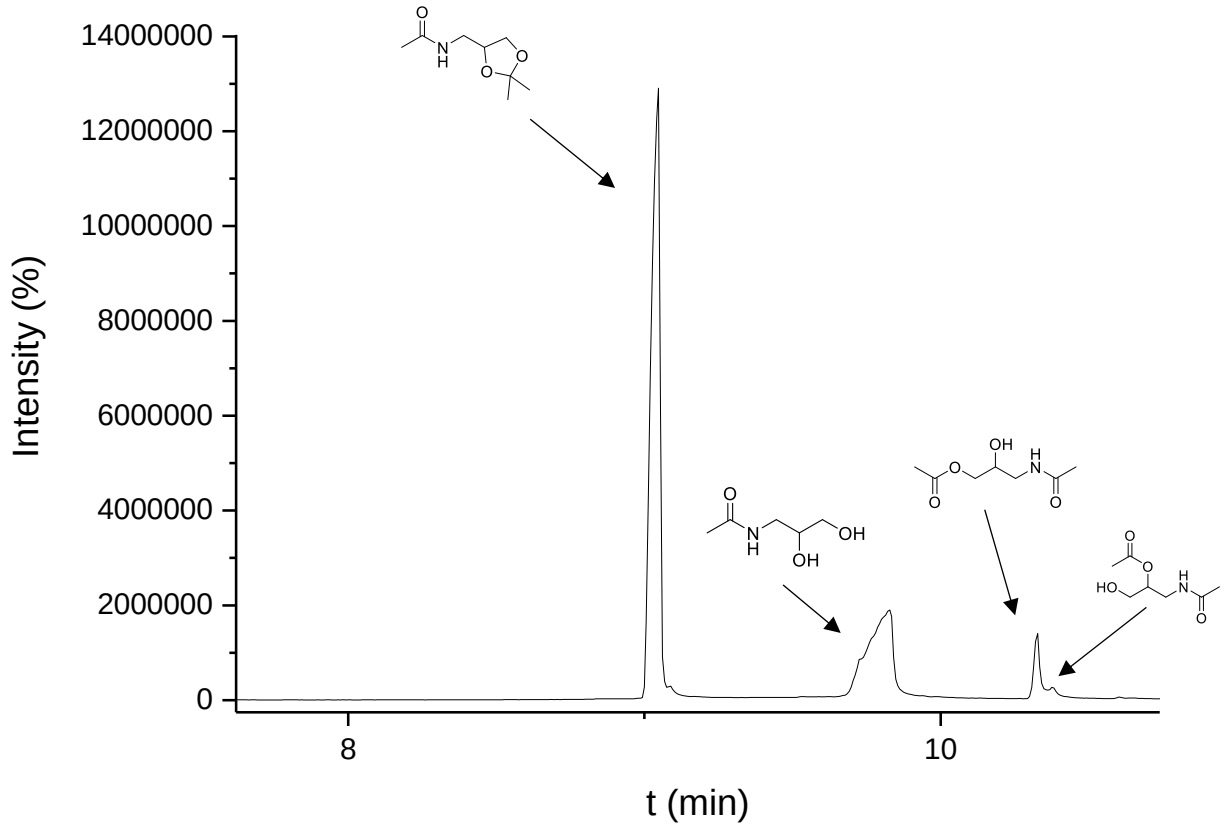


Figure S10. MS spectrum (70eV) of compound **1b**.

*Acetate esters of amide **1a**: 3-acetamido-2-hydroxypropyl acetate and 1-acetamido-3-hydroxypropan-2-yl acetate*. The GC/MS analysis could not resolve the two regioisomers products deriving from the transesterification of the primary and the secondary OH group of amide **1a**. The GC-peaks of these compounds appeared largely overlapped (Figure S11, top). The reported MS-spectrum was acquired in a median position of the total GC-signal (Figure S11, bottom). The heaviest ion fragment was observed at m/z=157 corresponding to the loss of water from the molecular ion ($[M^{+\cdot}]–H_2O$ = 175-18= 157). Other relevant fragments were 132, 115 and 102, consistent with the loss of CH_3CO (43), CH_3COO + H (59-1=60), and CH_3COOCH_2 (73) from the molecular ion. The most abundant fragment (100%) was detected at m/z=73 consistent with $[CH_3COOCH_2]^+$ ion.



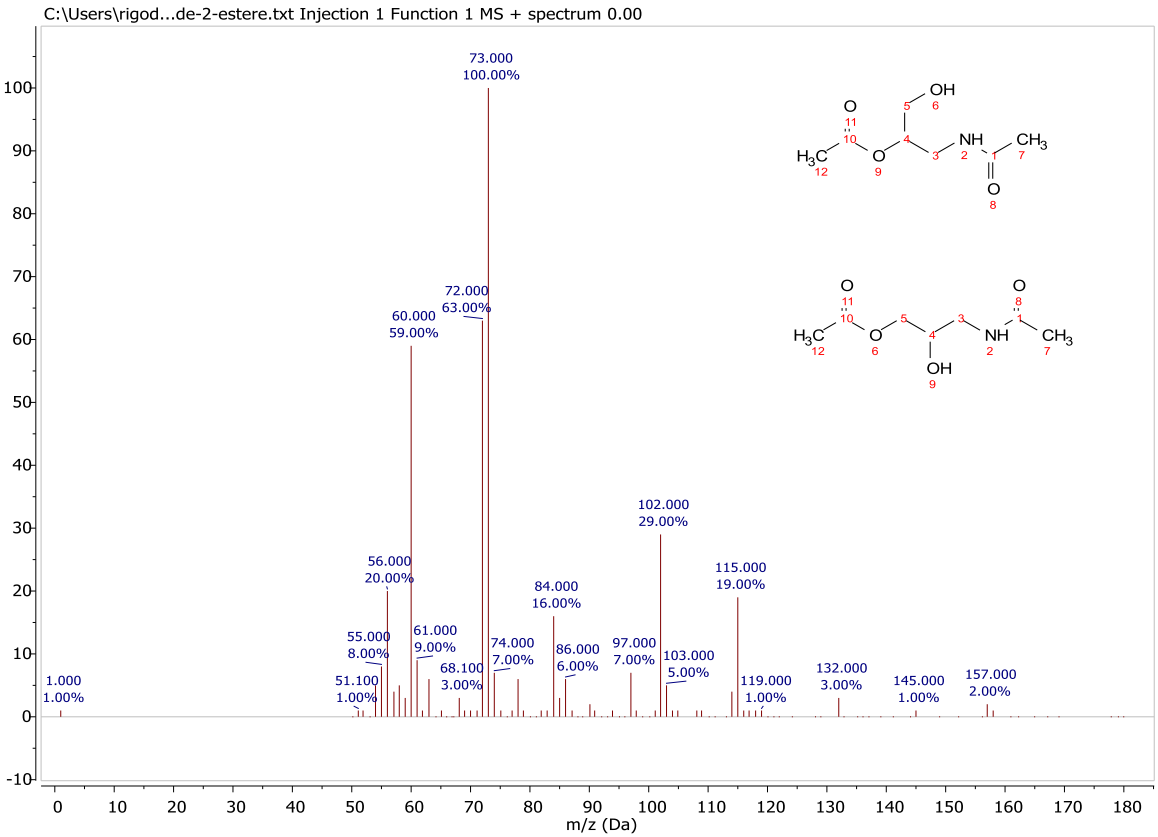


Figure S11. Top: GC/MS chromatogram of the mixture from the concatenated reaction of compound **1a** in 1,4-dioxane (onditions: 0.2 M mixture of **1a** in 1,4-dioxane, 40 equivs. of acetone, T = 50 °C, *p* = 1 bar, F = 0.1 mL/min). Bottom: MS spectrum (70 eV) of monoacetate esters of amide **1a**.

N-(2,2-dimethyl-1,3-dioxan-5-yl)acetamide, ***2b***

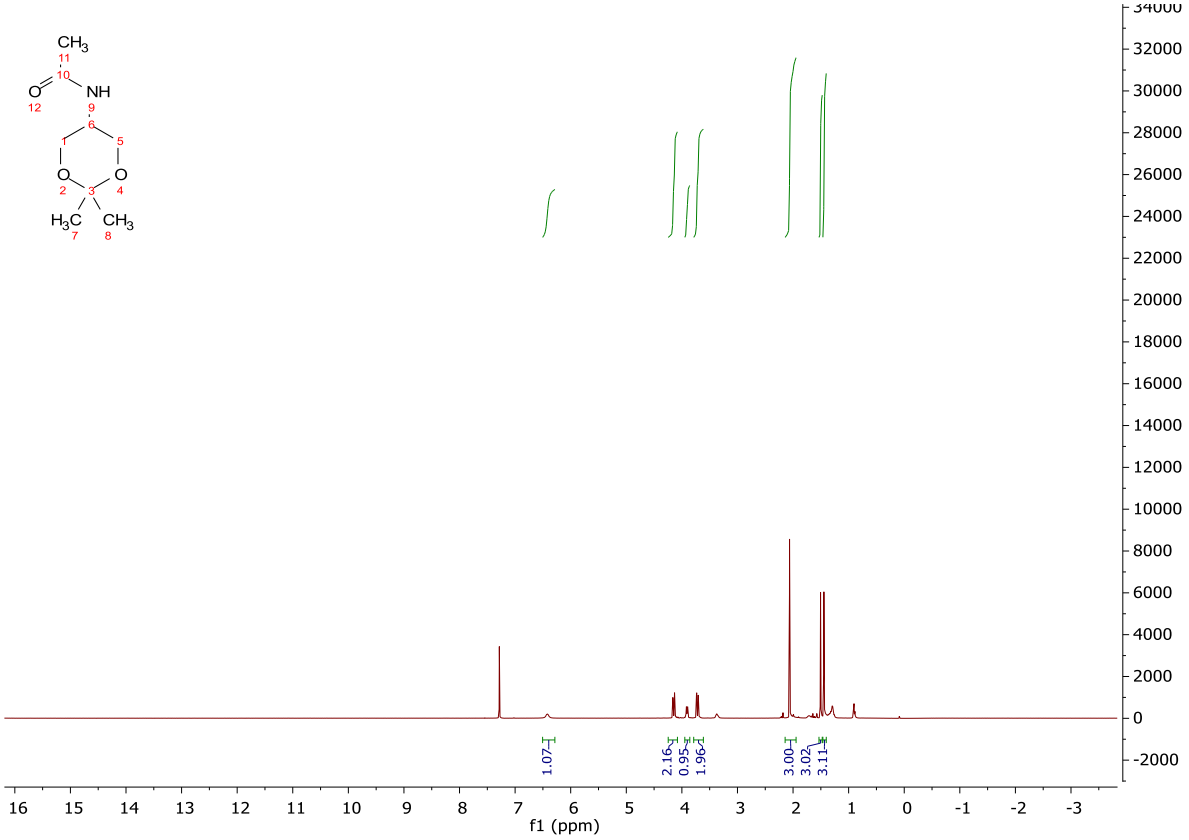


Figure S12. ^{1}H NMR of compound **2b** in $CDCl_3$.

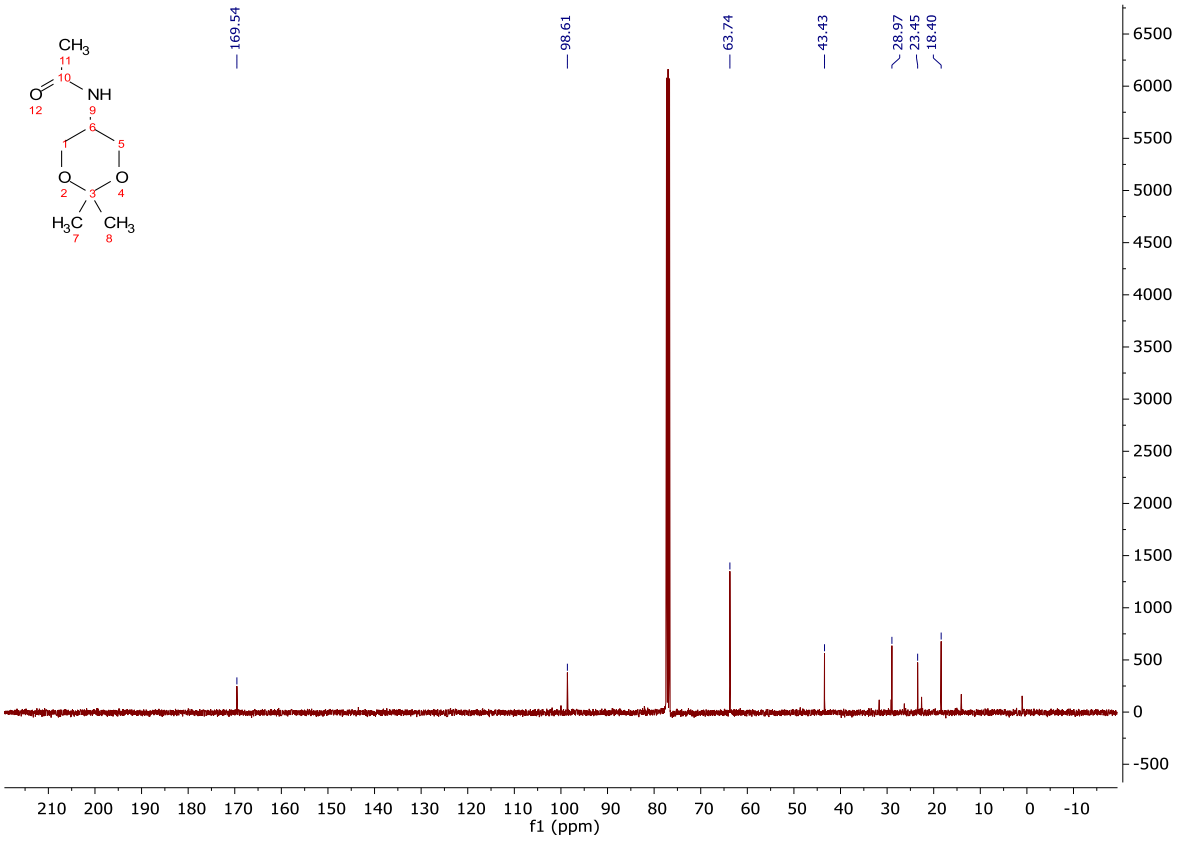


Figure S13. ^{13}C NMR of compound **2b** in $CDCl_3$.

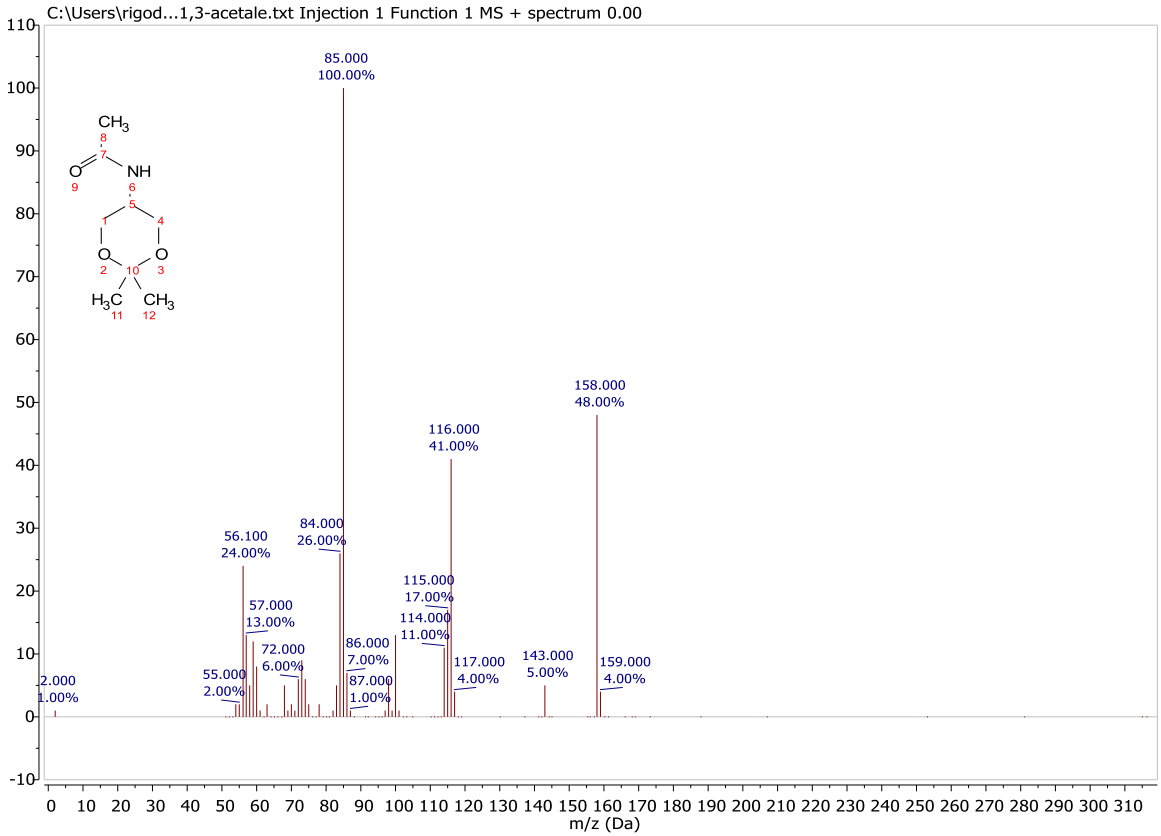


Figure S14. MS spectrum (70eV) of compound **2b**.

*Acetate esters of amide **2a**: 2-acetamido-3-hydroxypropyl acetate and 2-acetamidopropane-1,3-diyl diacetate.*

Figure S15 reports the GC/MS chromatogram of the mixture from the concatenated reaction of compound **2a** in 1,4-dioxane, where the signals of both the mono-acetate ester (2-acetamido-3-hydroxypropyl acetate) and the diacetate ester are shown.

The MS spectrum of monoacetate ester (2-acetamido-3-hydroxypropyl acetate, Figure S16, top) showed both analogies and differences to that of the corresponding isomer derived from amide **1a** (compare figure S11). Analogies: i) the heaviest ion fragment was observed at m/z=157 corresponding to the loss of water from the molecular ion ($[M^{+\cdot}]–H_2O$ = 175-18= 157); ii) other relevant fragments were at 115 and 102, consistent with the loss of CH_3CO (43), and CH_3COOCH_2 (73) from the molecular ion. Differences: i) the most abundant fragment (100%) was detected at m/z=60 consistent with $[CH_3COOCH_2]^+$ ion; ii) another relevant fragment were at m/z=84 consistent with the loss of $[CH_3COOCH_2+H_2O]$ from the molecular ion.

The MS spectrum of diacetate ester (2-acetamidopropane-1,3-diyl diacetate) is reported in Figure S16, bottom.

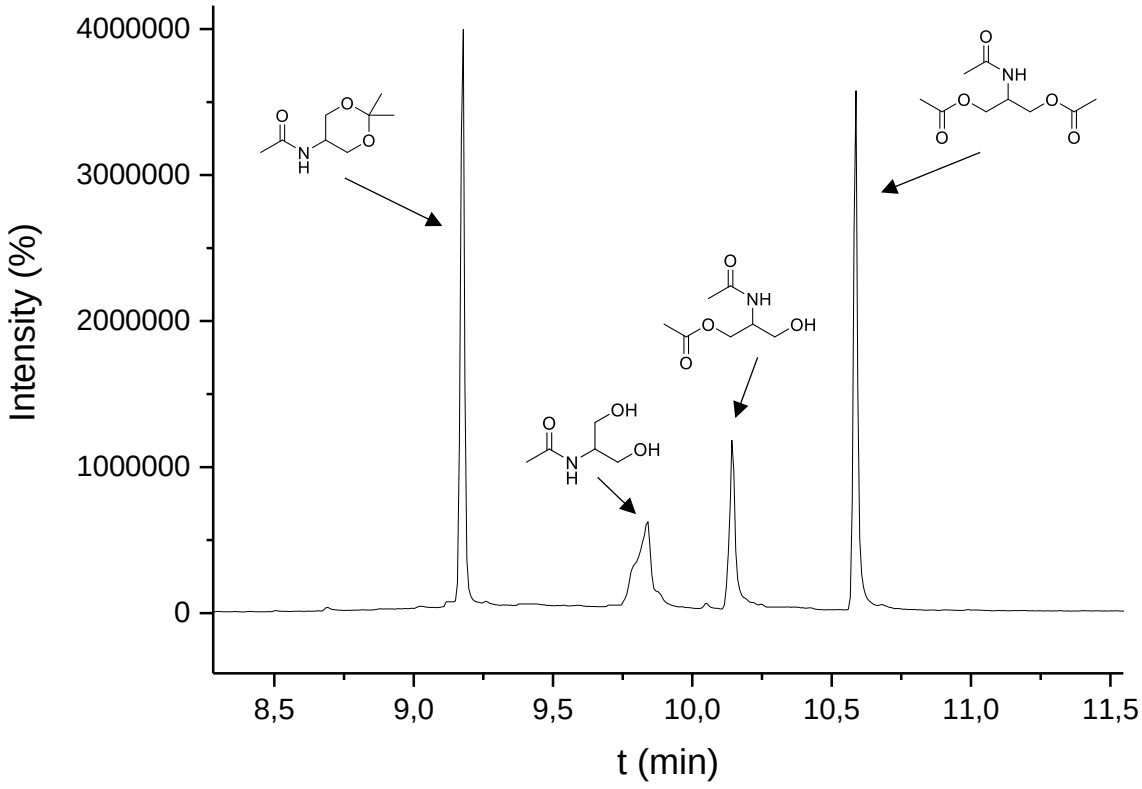


Figure S15. GC/MS chromatogram of the mixture from the concatenated reaction of compound **2a** in 1,4-dioxane (Conditions: 0.2 M mixture of **2a** in 1,4-dioxane, 40 equivs. of acetone, T = 100°C, *p* = 10 bar, F = 0.3 mL/min)

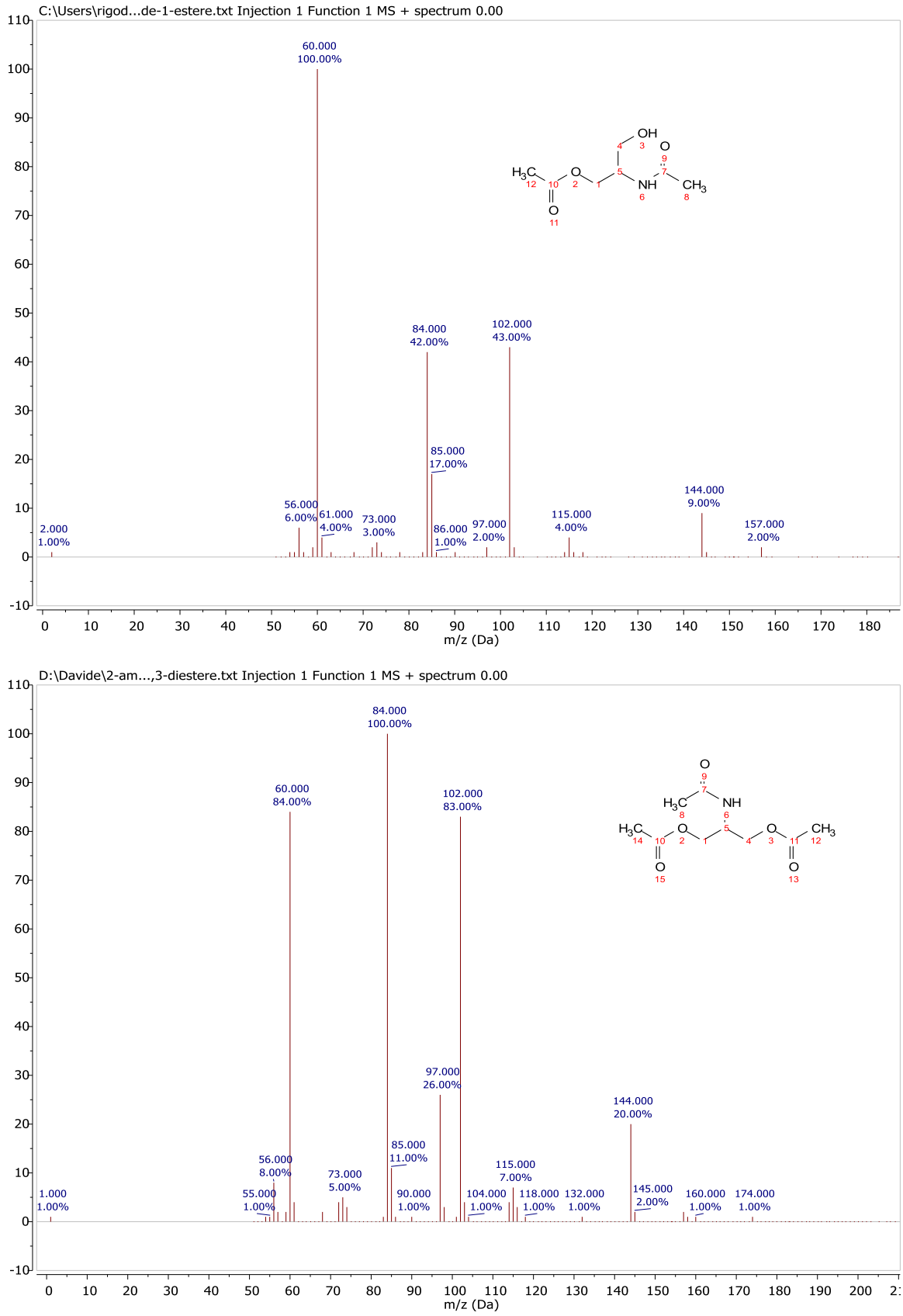


Figure S16. Top: MS spectrum (70 eV) of the monoacetate ester of amide **2a.** Bottom: MS spectrum (70 eV) of the diacetate ester of amide **2a.**