Supporting Information

Synthesis and pH-dependent hydrolysis profiles of mono- and dialkyl substituted maleamic acids

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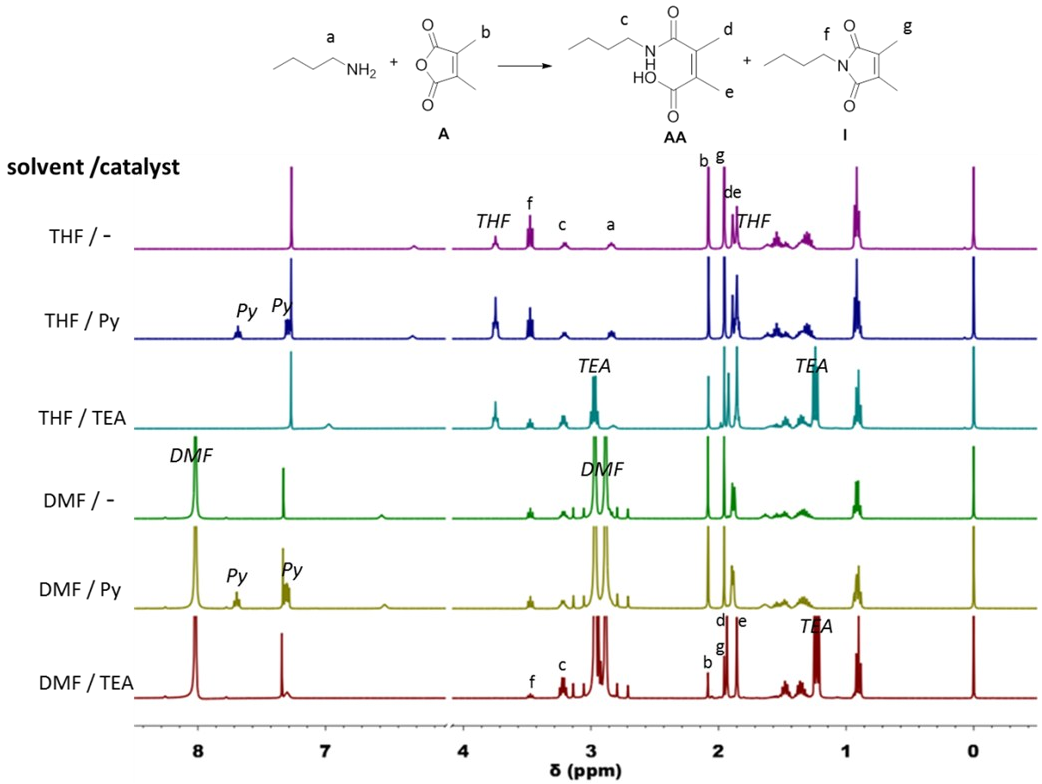


Fig. S1 ^{1}H NMR spectra of the reaction mixture of n-butyl amine and 2,3-dimethylmaleic anhydride under various conditions, 30 ^{o}C, 4 h. The percent content of the amidic acid, the imide and the anhydride was estimated by comparing the integrals of peak c, f and b.

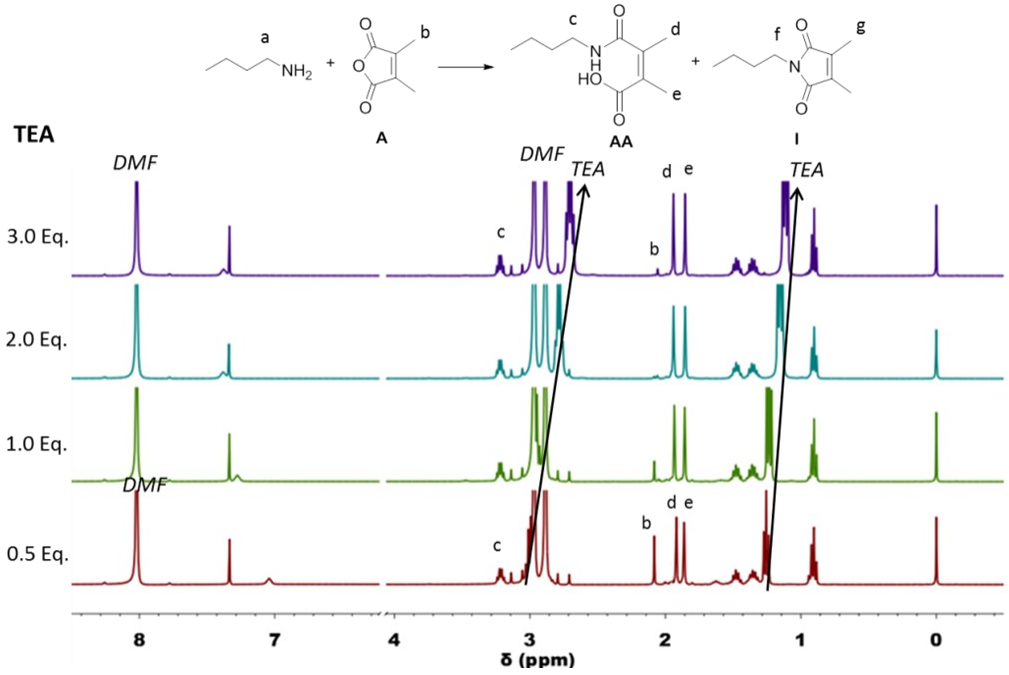
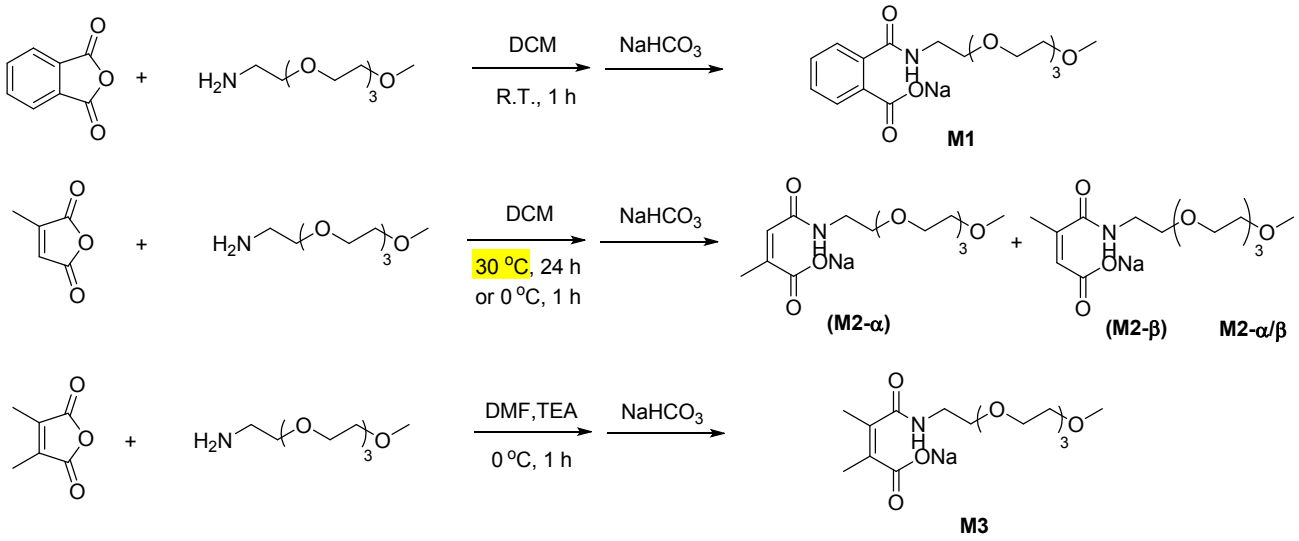


Fig. S2 ^{1}H NMR spectra of the reaction mixture of n-butyl amine and 2,3-dimethylmaleic anhydride with various TEA equivalents in DMF, 30 ^{o}C, 4 h.



Scheme S1 Synthesis of compounds **M1**, **M2-α/β**, and **M3**.

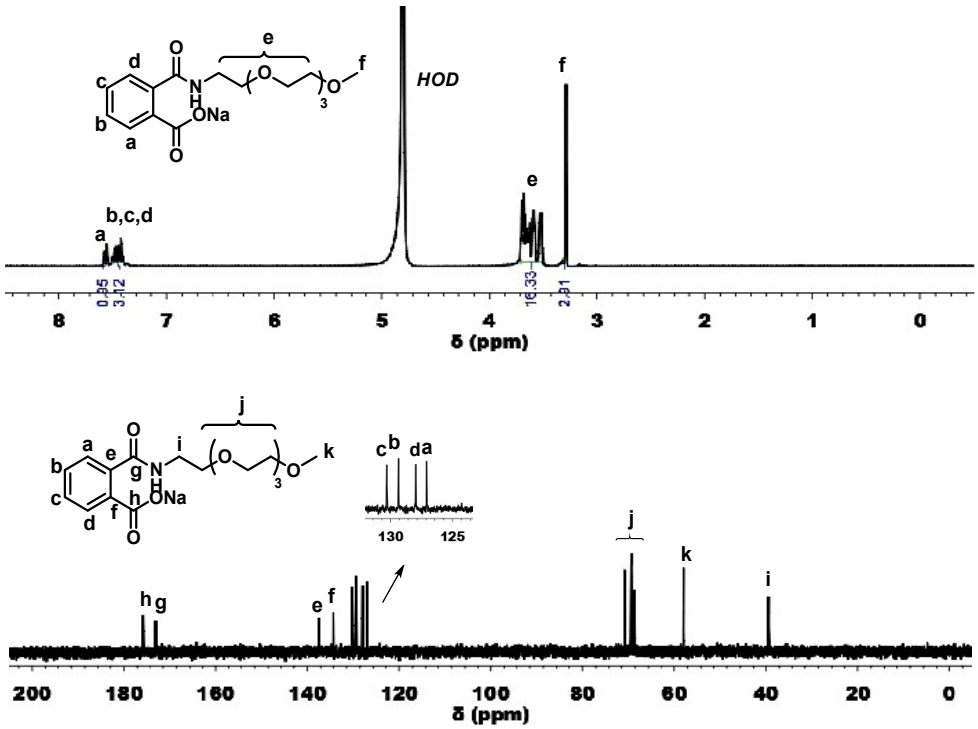


Fig. S3 ^{1}H NMR and ^{13}C NMR spectra of **M1**.

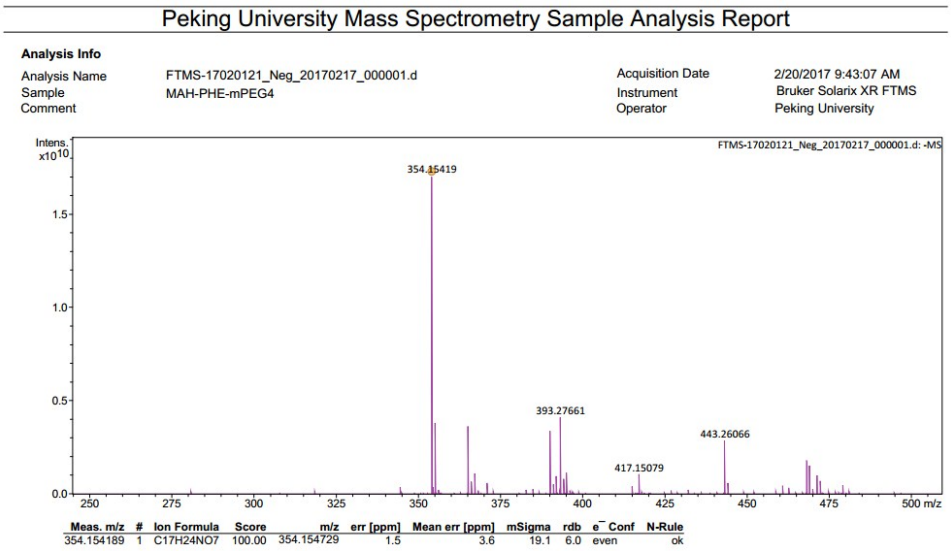


Fig. S4 ESI-MS spectrum of **M1**.

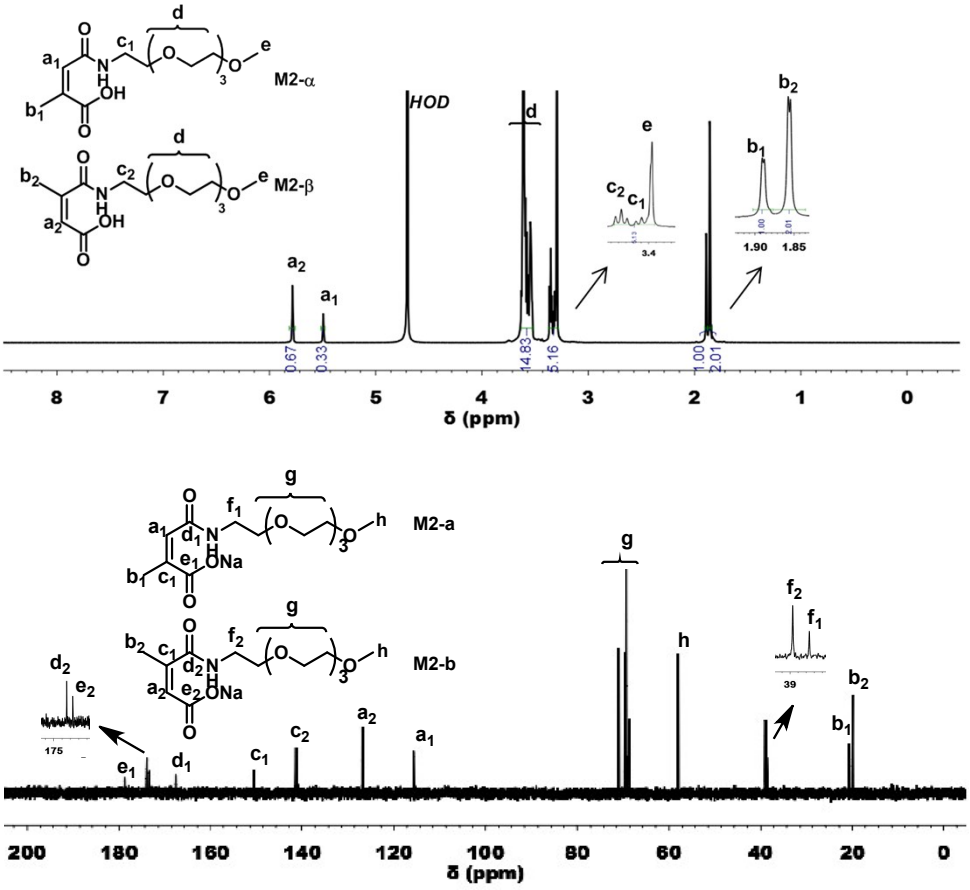


Fig. S5 ^{1}H NMR and ^{13}C NMR spectra of **M2-33/67**.

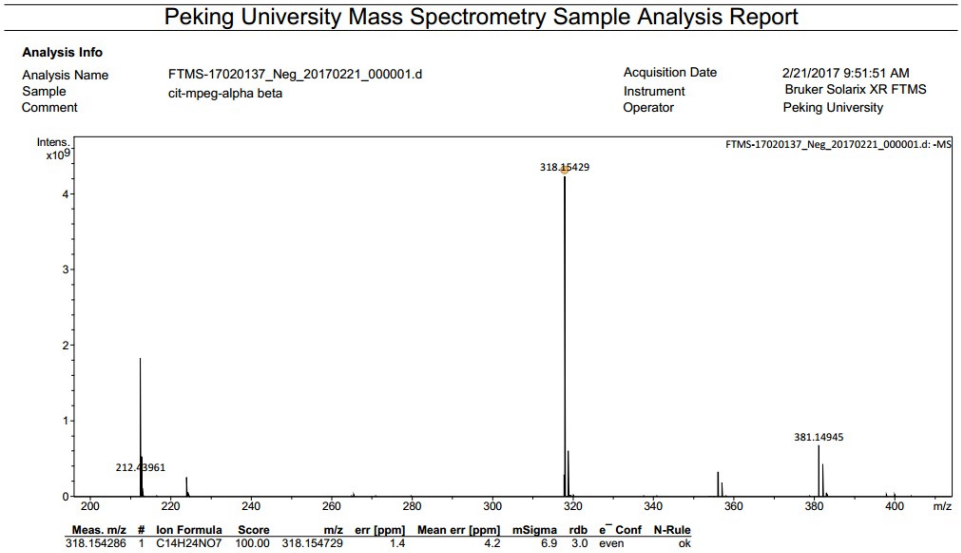


Fig. S6 ESI-MS spectrum of **M2-33/67**.

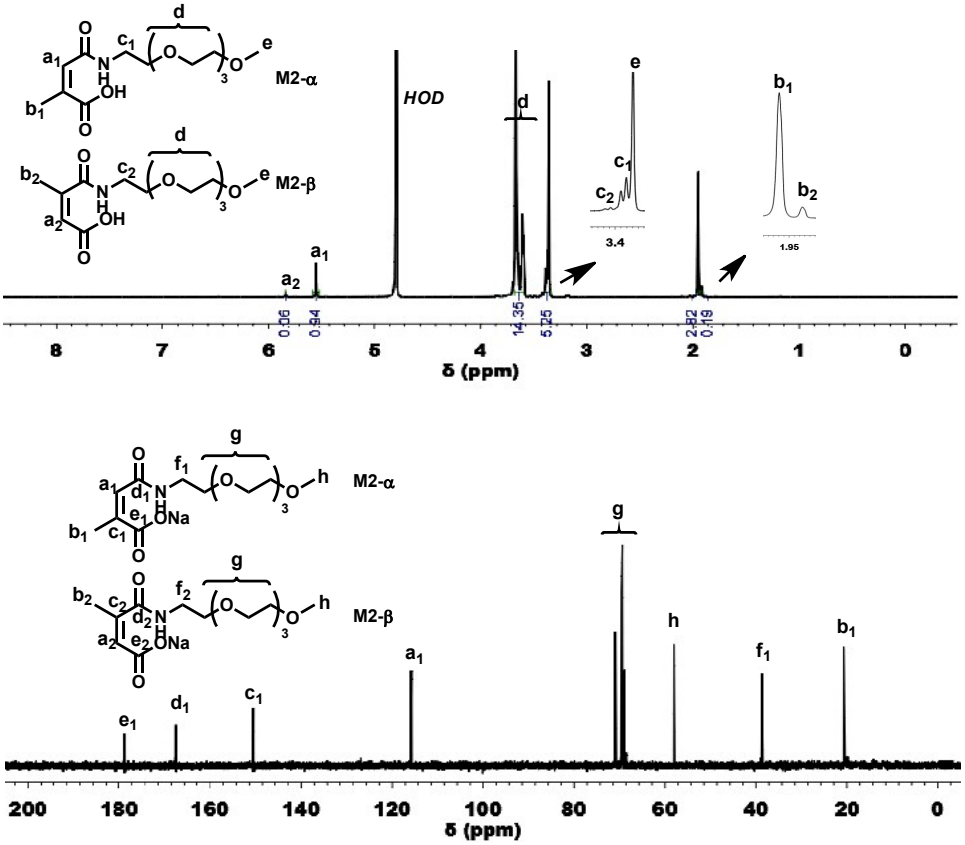


Fig. S7 ^{1}H NMR and ^{13}C NMR spectra of **M2-94/6**.

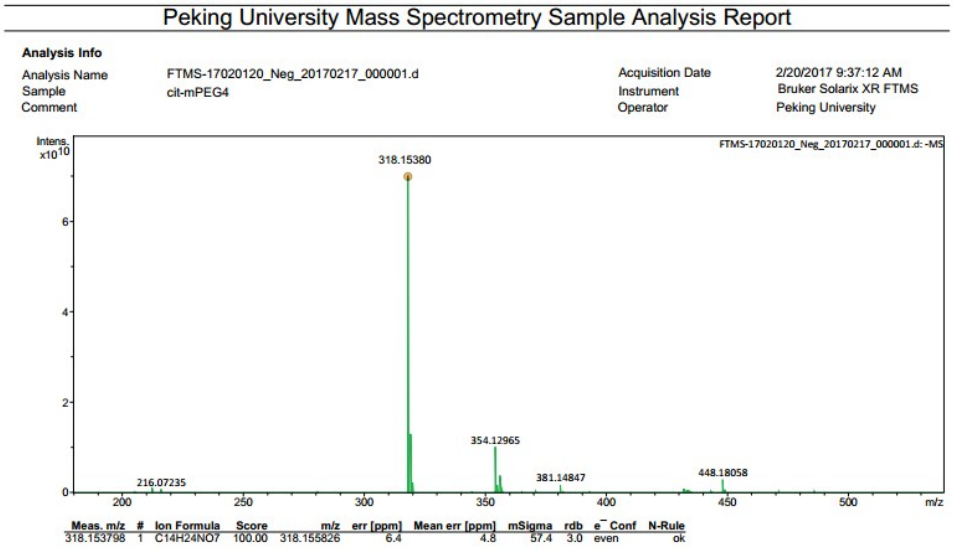


Fig. S8 ESI-MS spectrum of **M2-94/6**.

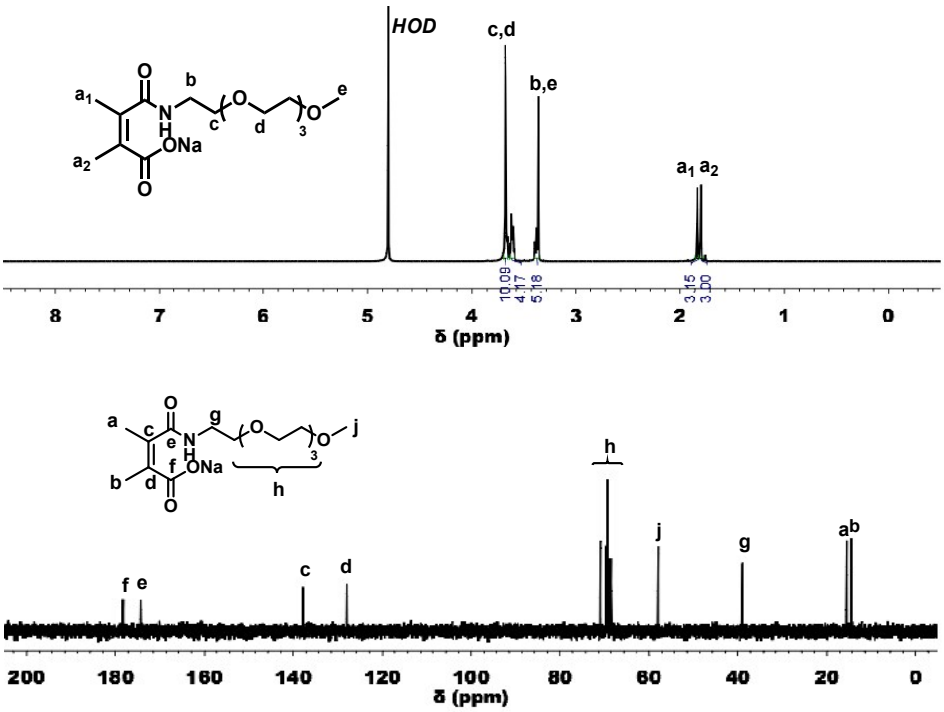


Fig. S9 ^{1}H NMR and ^{13}C NMR spectra of **M3**.

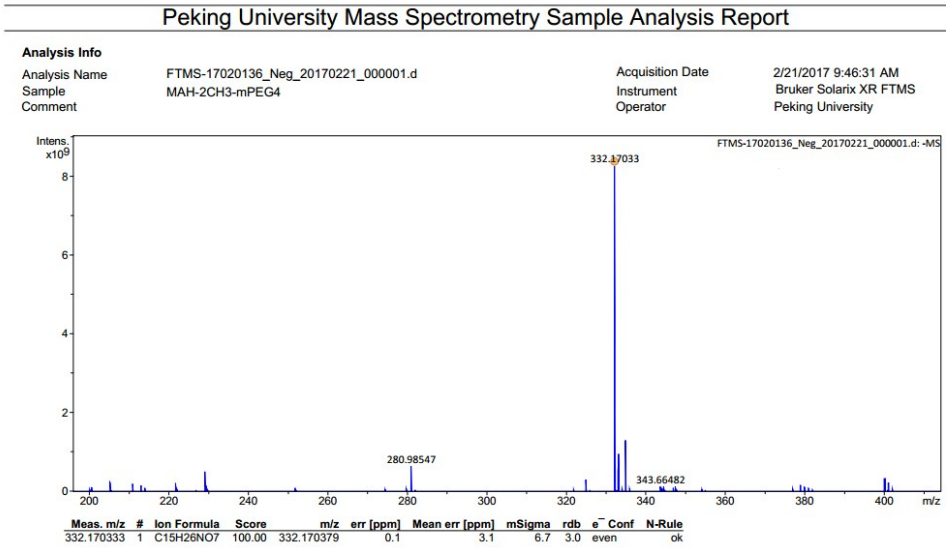


Fig. S10 ESI-MS spectrum of **M3**.

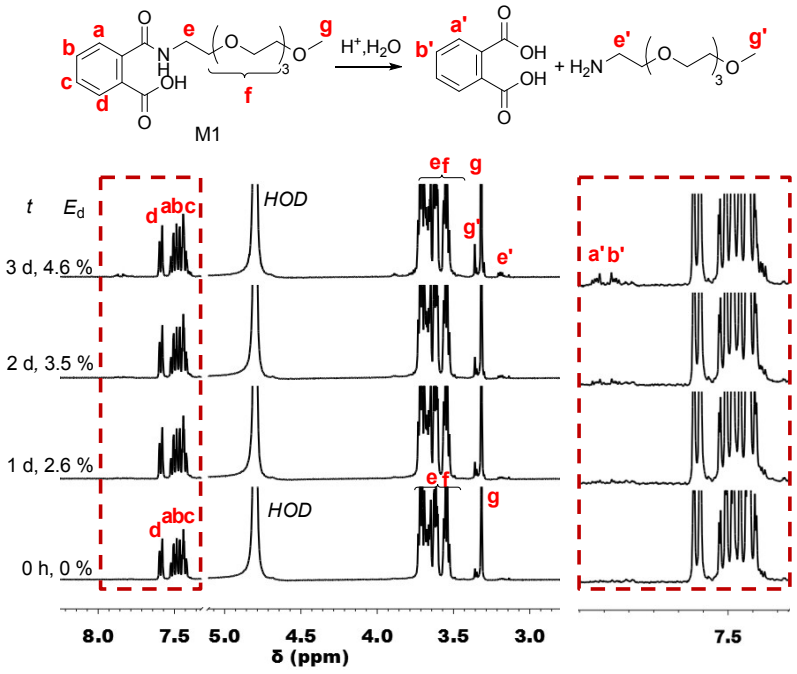


Fig. S11 ^{1}H NMR spectra of **M1** monitored during the hydrolysis process in deuterated phosphate buffer (PB) solution (pH 5.5) at 37 °C. The extent of hydrolysis (E_d) of **M1** was estimated by comparing the integrals of peaks a + b + c + d and a'+b' ($E_d = I_{a'+b'}/(I_{a+b+c+d} + I_{a'+b'})$).

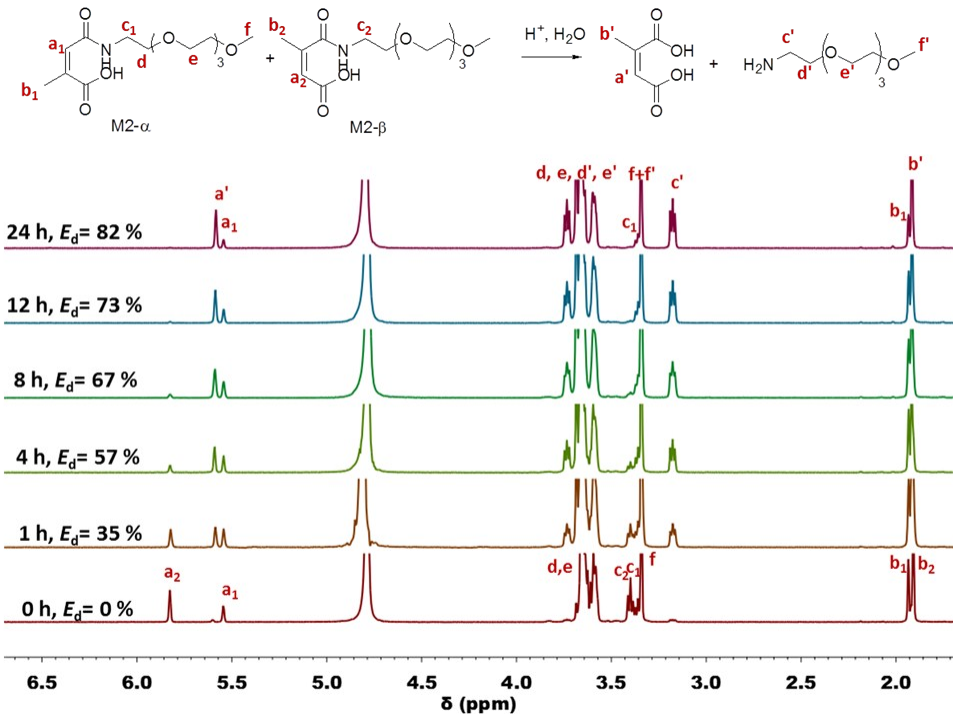


Fig. S12 The detailed ^{1}H NMR spectra of **M2-33/67** monitored during the hydrolysis process in buffered D_2O (pH 5.5) at 37 °C. The E_d of **M2** was estimated by comparing the integrals of peaks a_1, a_2 and a' ($E_d = I_{a'}/(I_{a'} + I_{a1} + I_{a2})$).

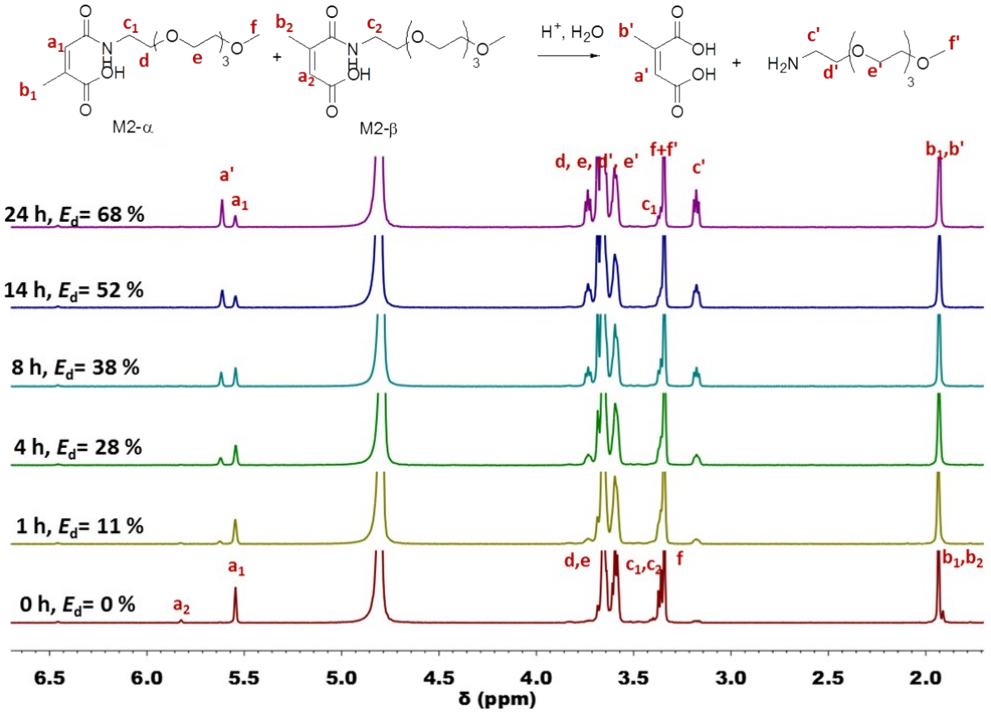


Fig. S13 ^{1}H NMR spectra of **M2-94/6** monitored during the hydrolysis process in buffered D_2O (pH 5.5) at 37 °C.

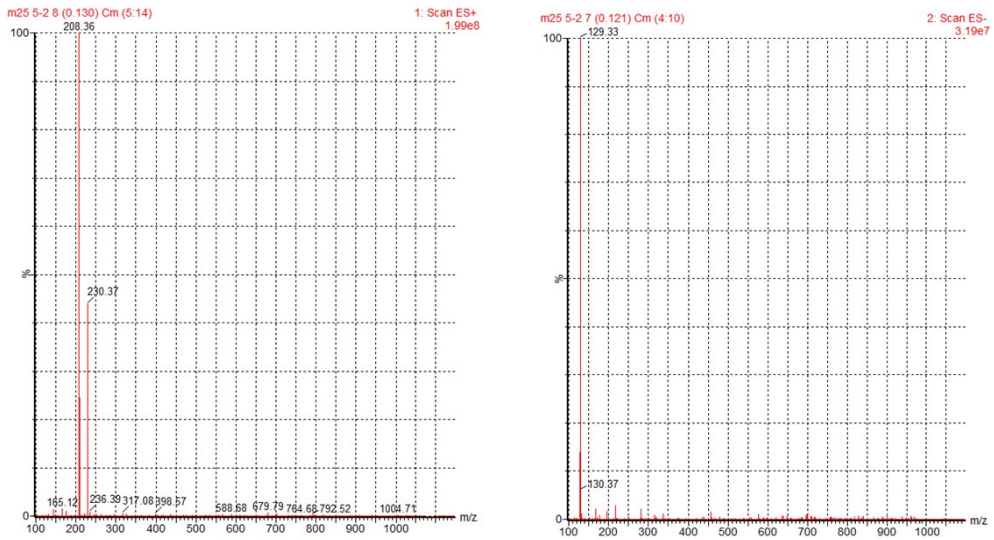


Fig. S14 MS spectra of the hydrolysis products of the mixture **M2-33/67** in buffered D_2O (pH 5.5). Positive ion mode (left): $mPEG_4\text{-}NH_2$ ($C_9H_{21}NO_4$ + H^+), calcd: 208.15; found: 208.36. ($C_9H_{21}NO_4$ + Na^+), calcd: 230.14; found: 230.37. Negative ion mode (right): citraconic acid ($C_5H_5O_4^-$), calcd: 129.02; found: 129.33.

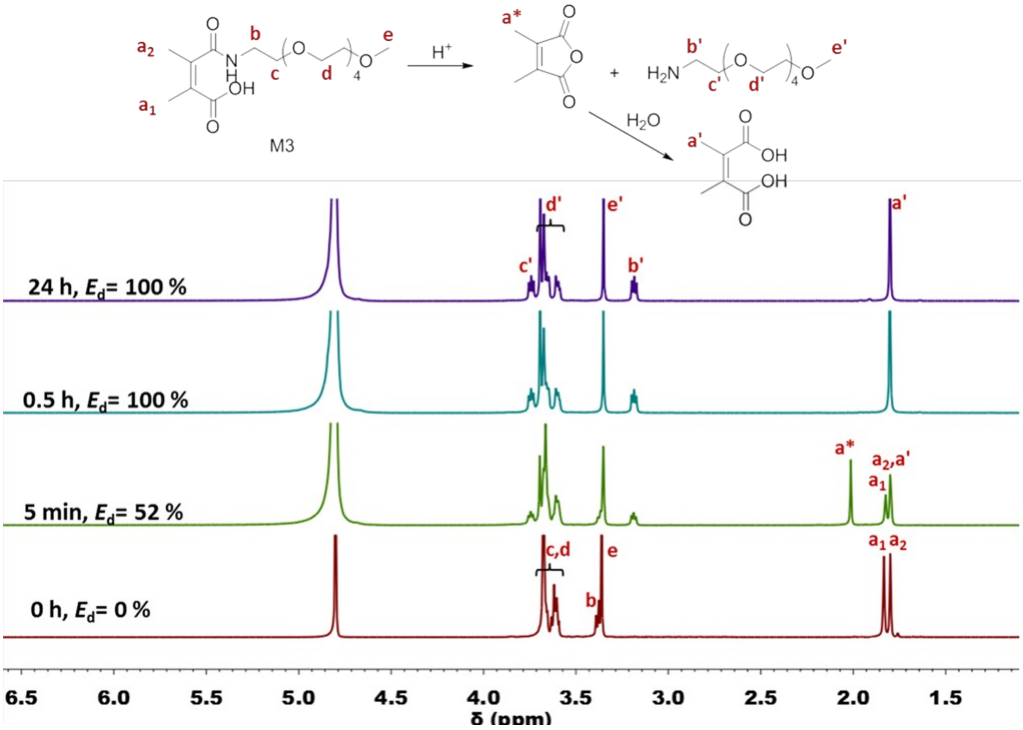


Fig. S15 ^{1}H NMR spectra of **M3** monitored during the hydrolysis process in buffered D_2O (pH 5.5) at 37 °C. The E_d of **M3** was estimated by comparing the integrals of peaks a_1, a_2 and a' (a*) ($E_d = (I_{a'} + I_{a*})/(I_{a'} + I_{a1+a2} + I_{a*})$).

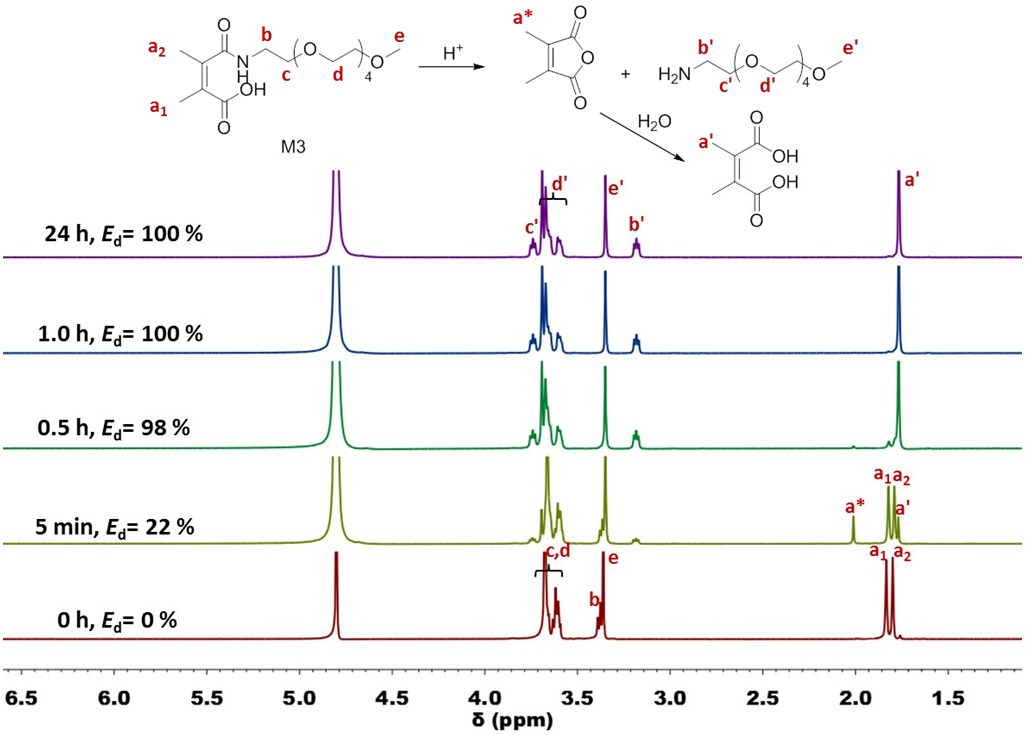


Fig. S16 ^{1}H NMR spectra of **M3** monitored during the hydrolysis process in buffered D_2O (pH 6.5) at 37 °C.

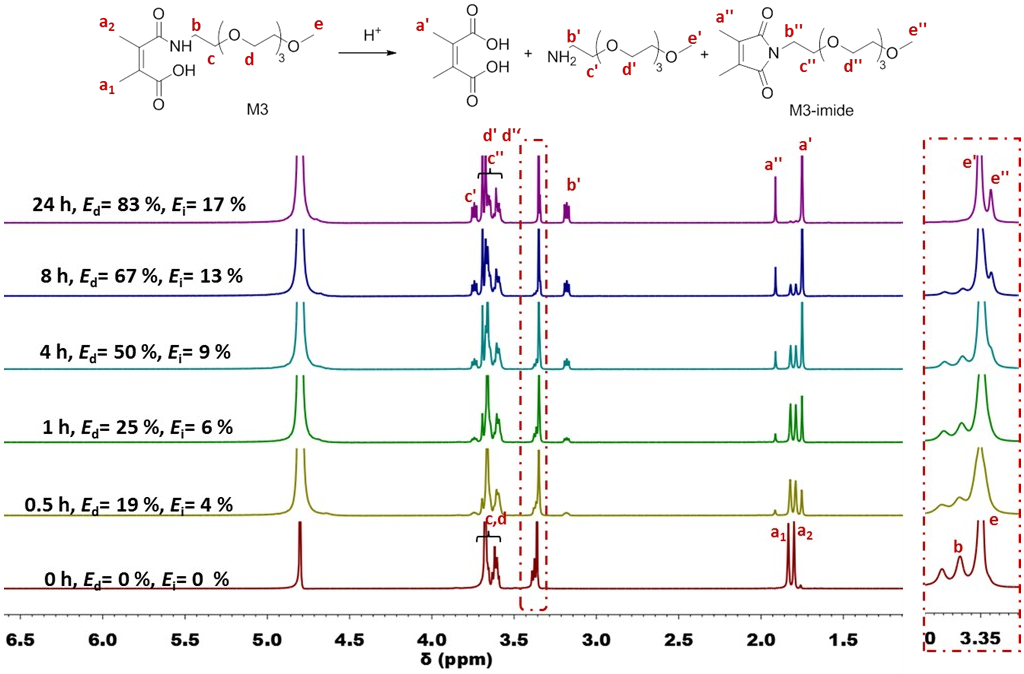


Fig. S17 The detailed ^{1}H NMR spectra of **M3** monitored during the hydrolysis process in buffered D_2O (pH 7.4) at 37 °C, E_i is the percent content of **M3-imide**. The E_d and E_i of **M3** were estimated by comparing the integrals of peaks a_1, a_2, a' and a'' ($E_d = I_{a'}/(I_{a'} + I_{a''} + I_{a1+a2})$; $E_i = I_{a''}/(I_{a'} + I_{a''} + I_{a1+a2})$).

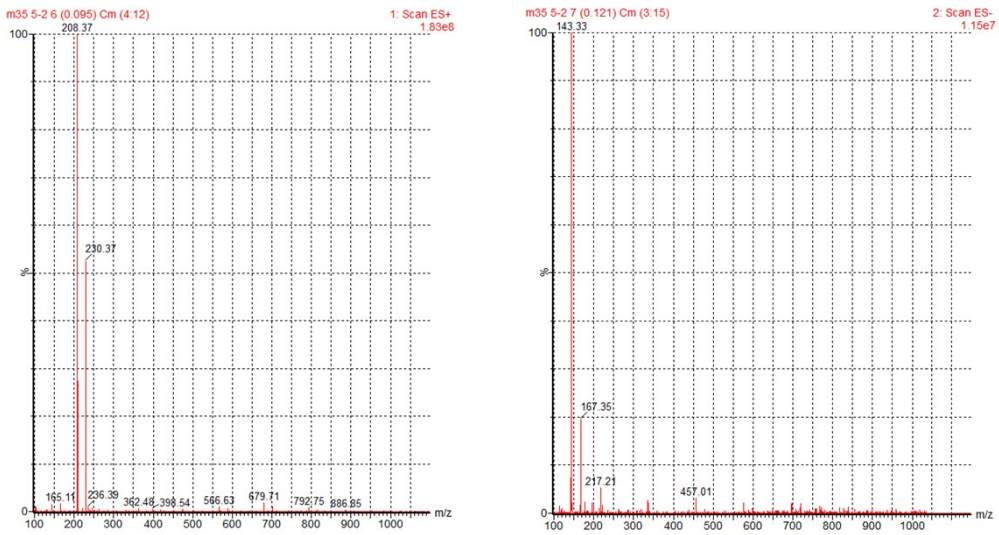


Fig. S18 MS spectra of the hydrolysis products of compound **M3** in buffered D_2O (pH 5.5). Positive ion mode (left): mPEG$_4$-NH$_2$ ($C_9H_{21}NO_4 + H^+$), calcd: 208.15; found: 208.37. ($C_9H_{21}NO_4 + Na^+$), calcd: 230.14; found: 230.37. Negative ion mode (right): 2,3-dimethyl maleic acid ($C_6H_7O_4^-$), calcd: 143.03; found: 143.33.

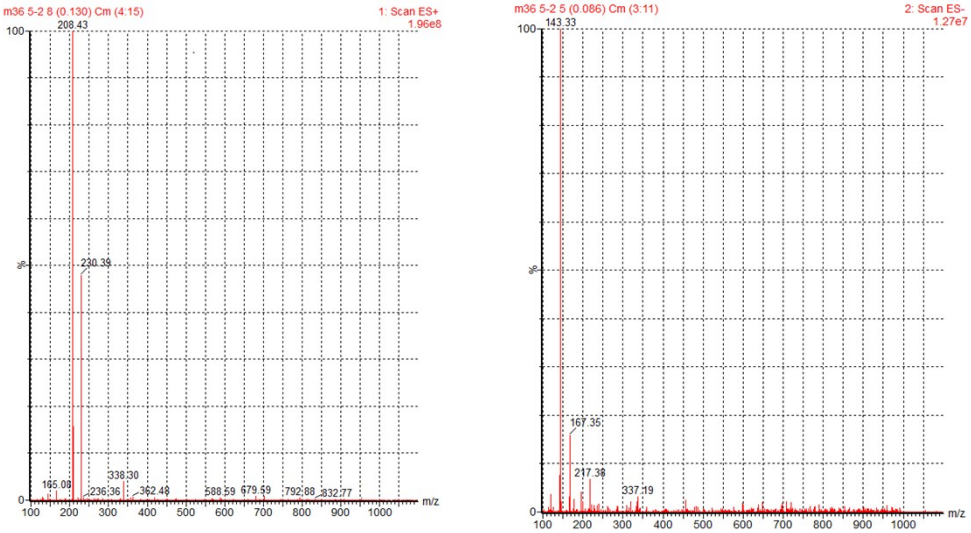


Fig. S19 MS spectra of the hydrolysis products of compound **M3** in buffered D_2O (pH 6.5). Positive ion mode (left): mPEG$_4$-NH$_2$ ($C_9H_{21}NO_4 + H^+$), calcd: 208.15; found: 208.43. ($C_9H_{21}NO_4 + Na^+$), calcd: 230.14; found: 230.39. Negative ion mode (right): 2,3-dimethyl maleic acid ($C_6H_7O_4^-$), calcd: 143.03; found: 143.33.

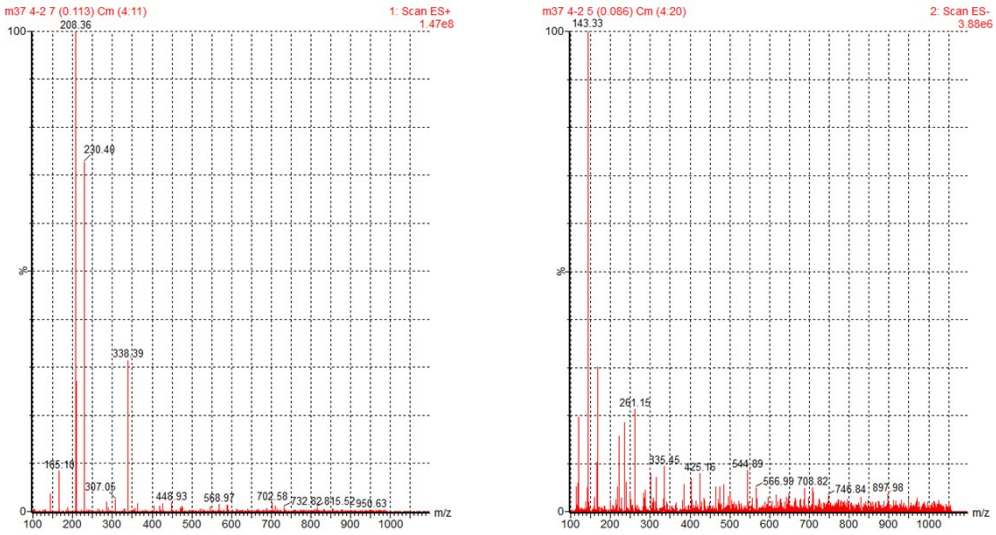


Fig. S20 MS spectra of the hydrolysis products of compound **M3** in buffered D_2O (pH 7.4). Positive ion mode (left): $mPEG_4$-NH_2 ($C_9H_{21}NO_4$ + H^+), calcd: 208.15; found: 208.36. ($C_9H_{21}NO_4$ + Na^+), calcd: 230.14; found: 230.40. **M3**-imide ($C_{15}H_{25}NO_6$ + Na^+), calcd: 338.16; found: 338.39. Negative ion mode (right): 2,3-dimethylmaleic acid ($C_6H_7O_4^-$), calcd: 143.03; found: 143.33.