

Supporting Information

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

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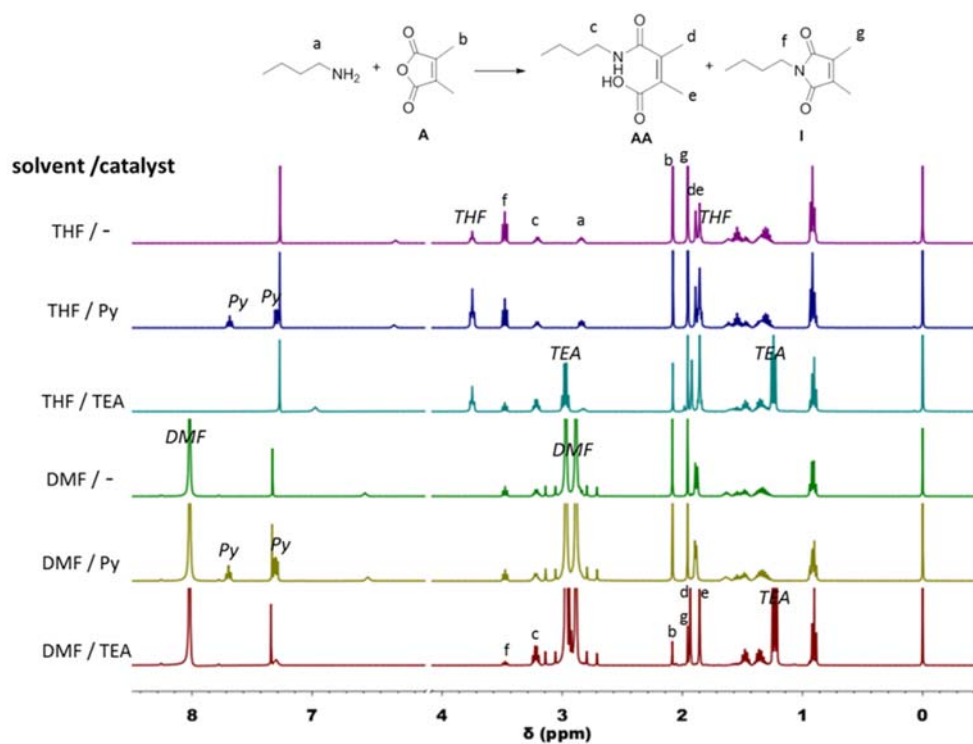


Fig. S1 ^1H NMR spectra of the reaction mixture of n-butyl amine and 2,3-dimethylmaleic anhydride under various conditions, 30 °C, 4 h. The percent content of the amidic acid, the imide and the anhydride was estimated by comparing the integrals of peak c, f and b.

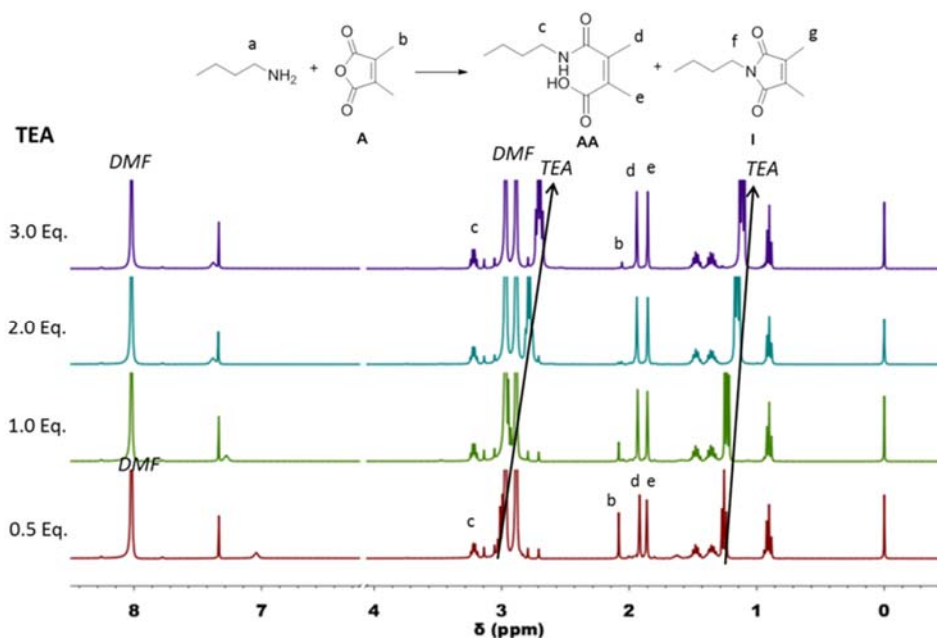
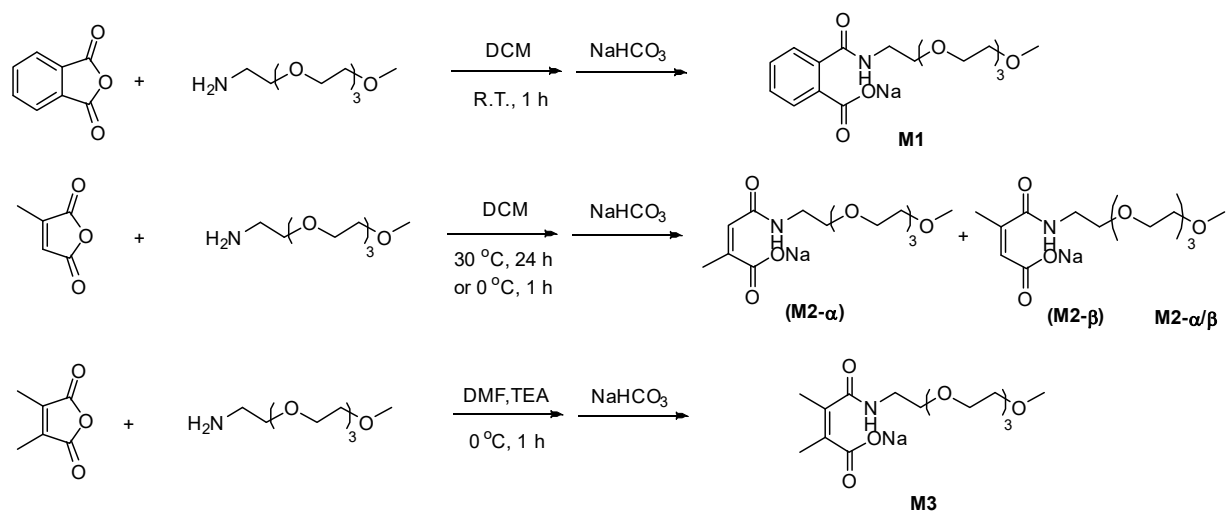


Fig. S2 ^1H NMR spectra of the reaction mixture of n-butyl amine and 2,3-dimethylmaleic anhydride with various TEA equivalents in DMF, 30 °C, 4 h.



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

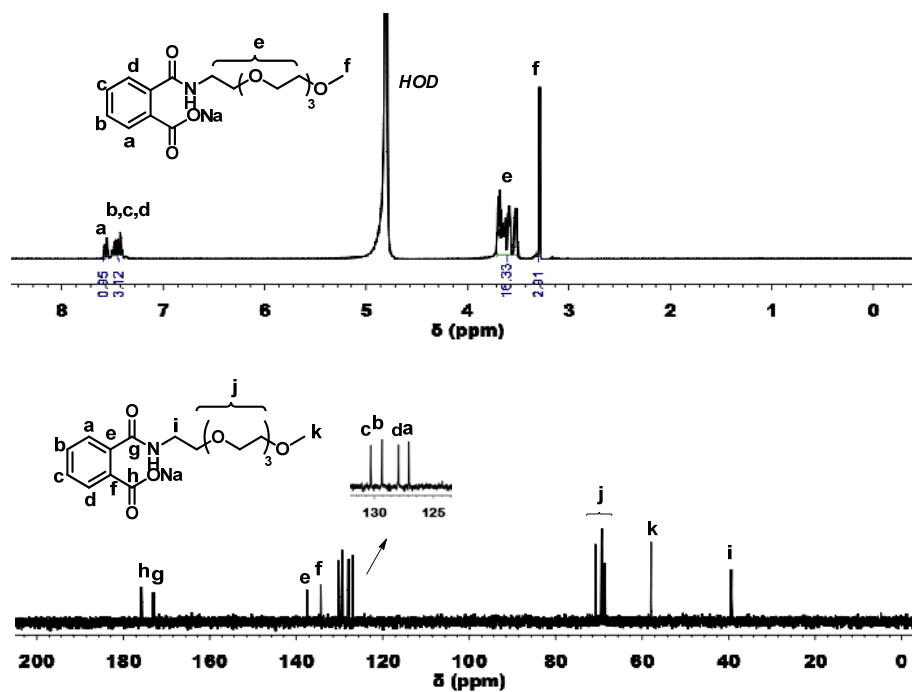


Fig. S3 ^1H NMR and ^{13}C NMR spectra of **M1**.

Peking University Mass Spectrometry Sample Analysis Report

Analysis Info

Analysis Name FTMS-17020121_Neg_20170217_000001.d
Sample MAH-PHE-mPEG4
Comment

Acquisition Date 2/20/2017 9:43:07 AM
Instrument Bruker Solarix XR FTMS
Operator Peking University

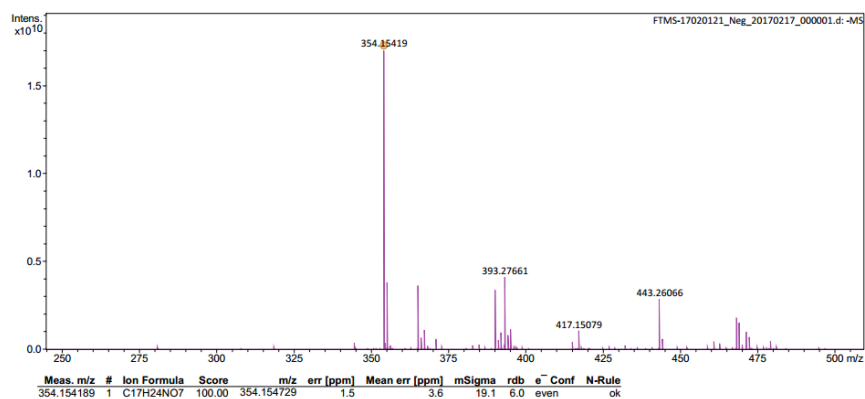


Fig. S4 ESI-MS spectrum of M1.

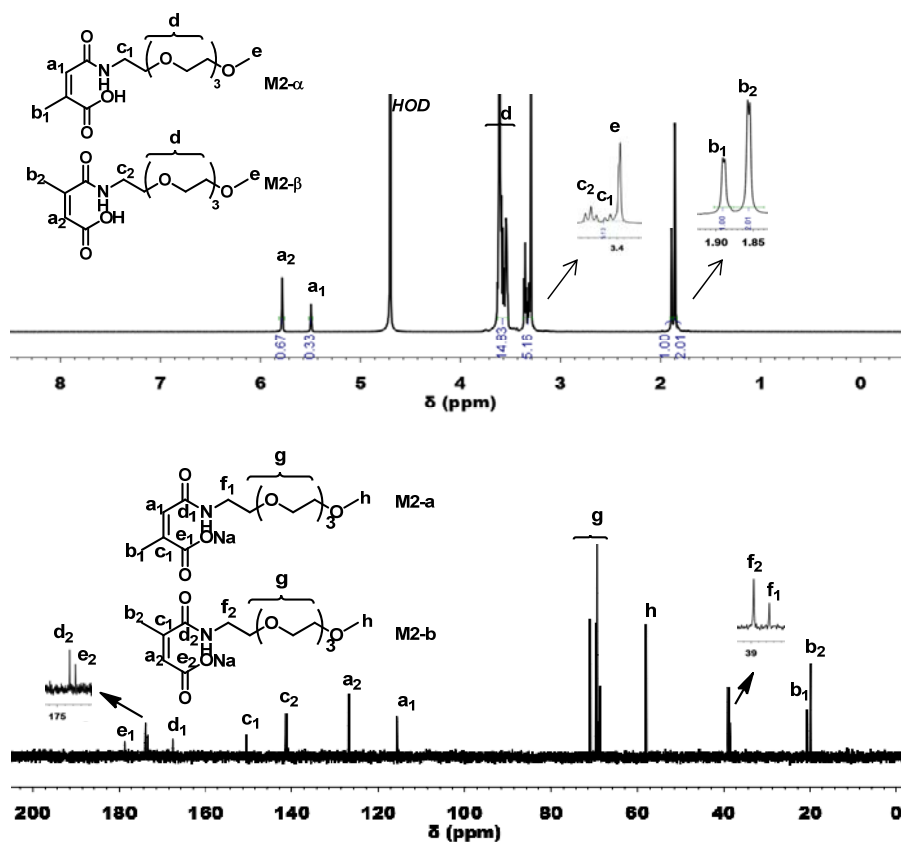


Fig. S5 ¹H NMR and ¹³C NMR spectra of M2-33/67.

Peking University Mass Spectrometry Sample Analysis Report

Analysis Info

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Sample cit-mpeg-alpha beta
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Instrument Bruker Solarix XR FTMS
Operator Peking University

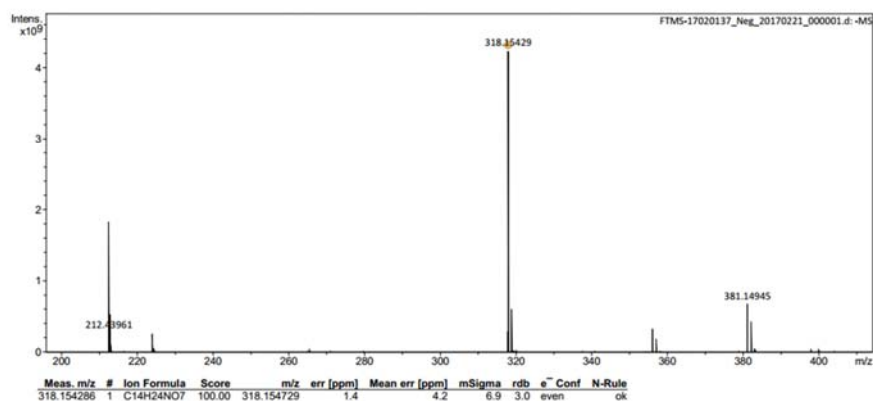


Fig. S6 ESI-MS spectrum of M2-33/67.

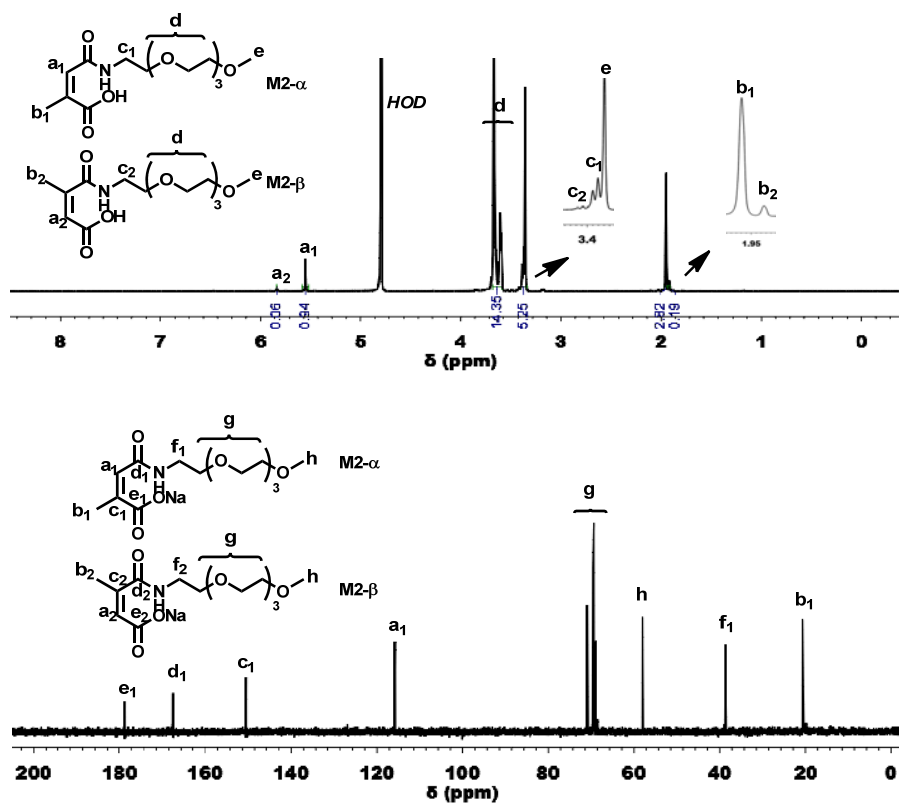


Fig. S7 ¹H NMR and ¹³C NMR spectra of M2-94/6.

Peking University Mass Spectrometry Sample Analysis Report

Analysis Info

Analysis Name FTMS-17020120_Neg_20170217_000001.d
Sample cit-mPEG4
Comment

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Instrument Bruker Solarix XR FTMS
Operator Peking University

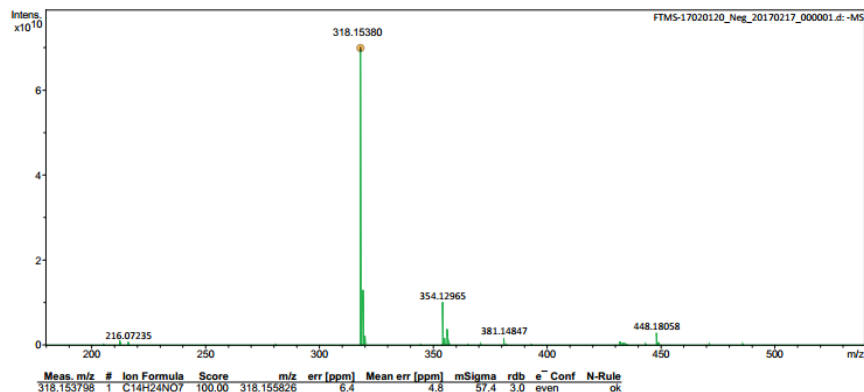


Fig. S8 ESI-MS spectrum of M2-94/6.

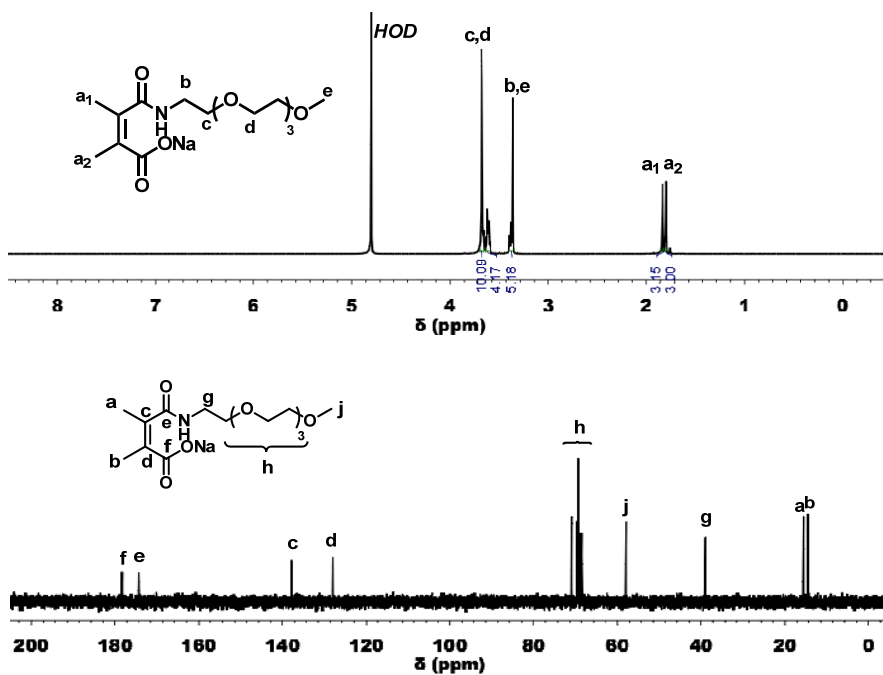


Fig. S9 ¹H NMR and ¹³C NMR spectra of M3.

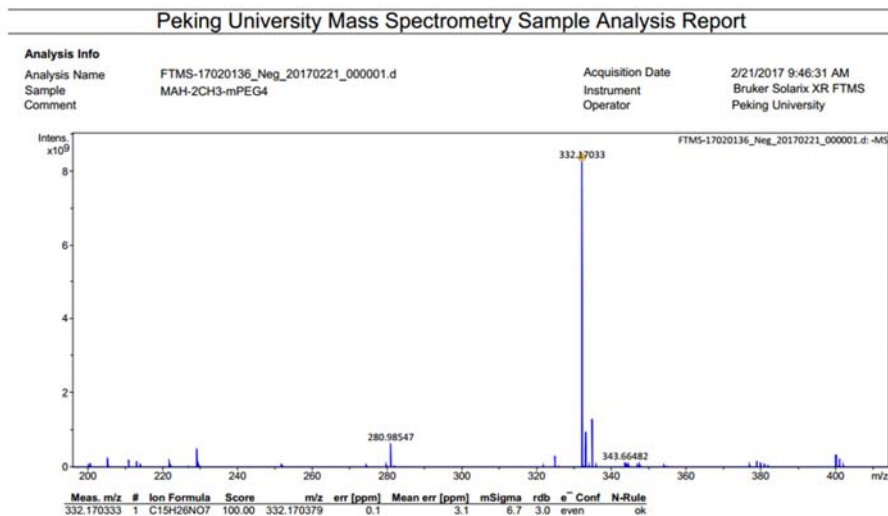


Fig. S10 ESI-MS spectrum of **M3**.

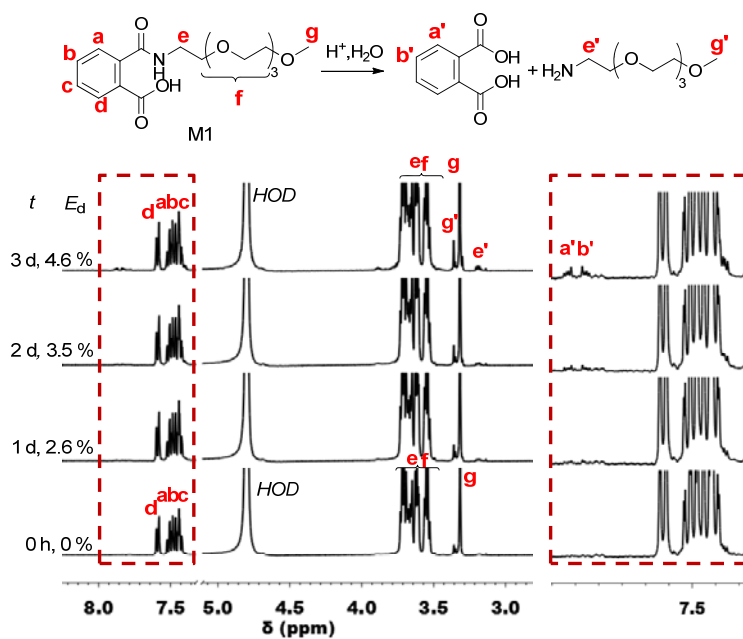


Fig. S11 1H NMR spectra of **M1** monitored during the hydrolysis process in deuterated phosphate buffer (PB) solution (pH 5.5) at 37 °C. The extent of hydrolysis (E_d) of **M1** was estimated by comparing the integrals of peaks a + b + c + d and a'+b' ($E_d = I_{a'+b'} / (I_{a+b+c+d} + I_{a'+b'})$).

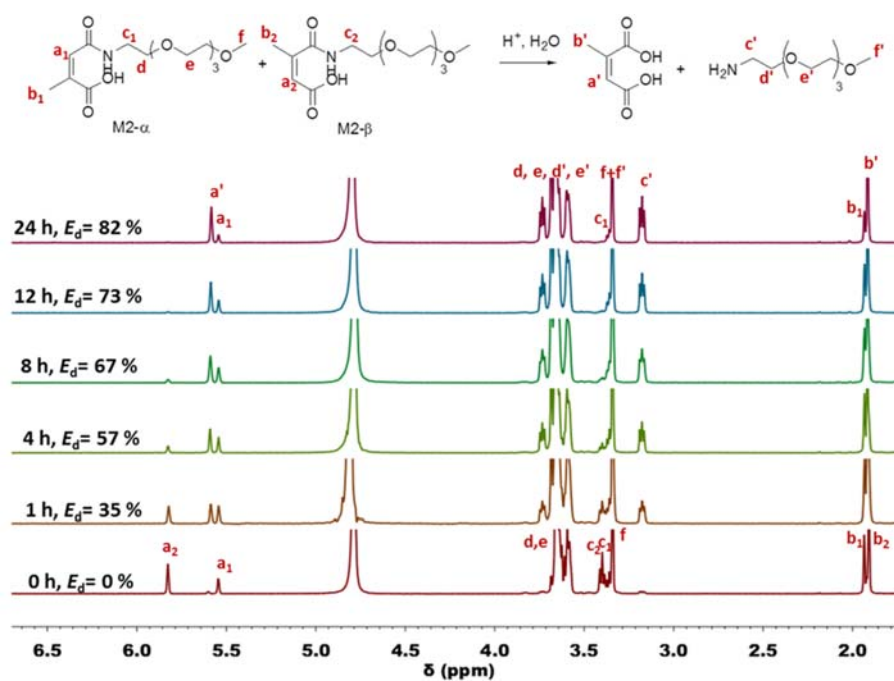


Fig. S12 The detailed 1H NMR spectra of **M2-33/67** monitored during the hydrolysis process in buffered D_2O (pH 5.5) at 37 °C. The E_d of **M2** was estimated by comparing the integrals of peaks a_1 , a_2 and a' ($E_d = I_{a'}/(I_{a'} + I_{a_1} + I_{a_2})$).

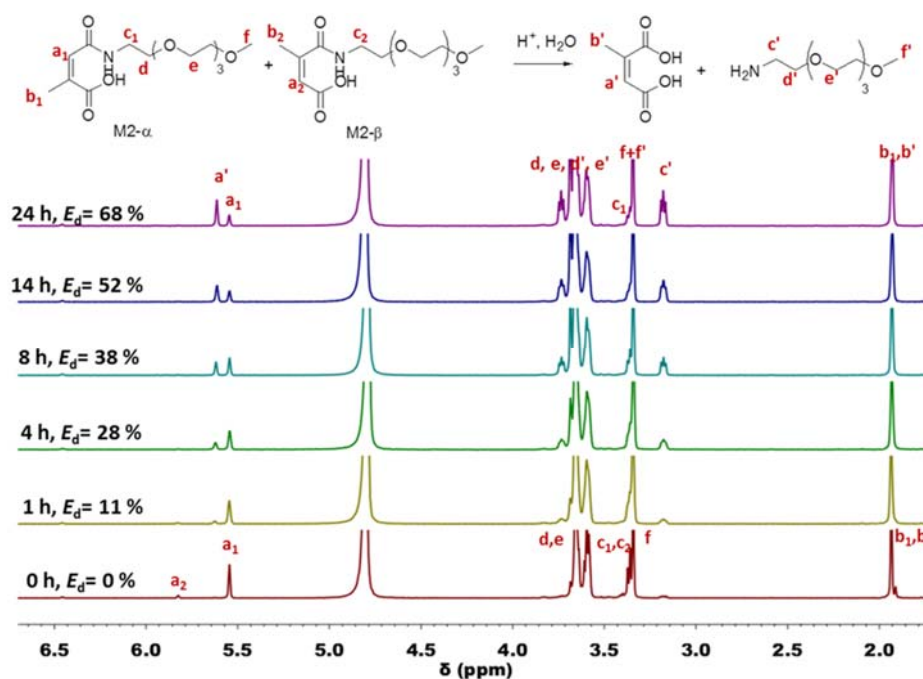


Fig. S13 1H NMR spectra of **M2-94/6** monitored during the hydrolysis process in buffered D_2O (pH 5.5) at 37 °C.

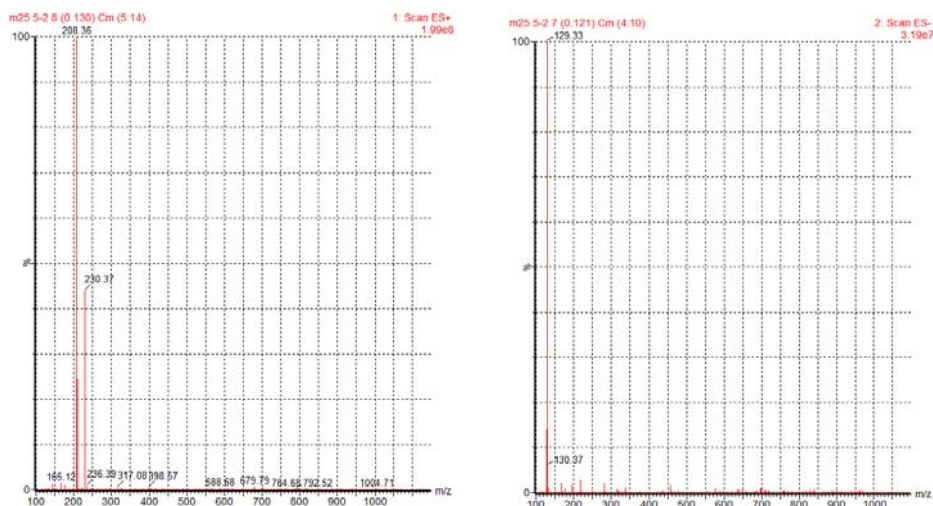


Fig. S14 MS spectra of the hydrolysis products of the mixture **M2-33/67** in buffered D₂O (pH 5.5). Positive ion mode (left): mPEG₄-NH₂ (C₉H₂₁NO₄ + H⁺), calcd: 208.15; found: 208.36. (C₉H₂₁NO₄ + Na⁺), calcd: 230.14; found: 230.37. Negative ion mode (right): citraconic acid (C₅H₅O₄⁻), calcd: 129.02; found: 129.33.

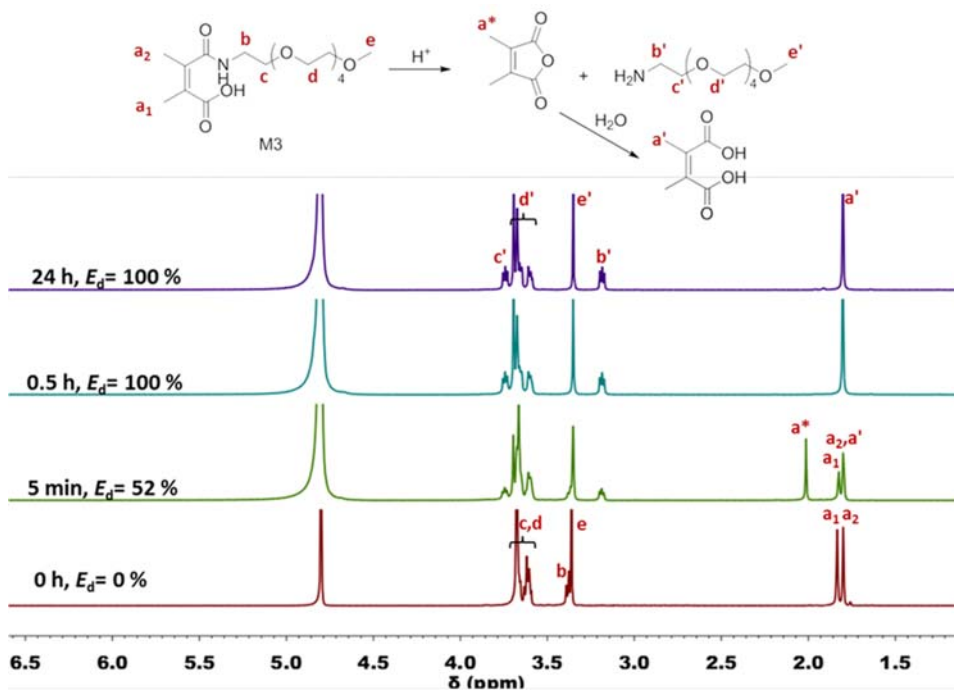


Fig. S15 ¹H NMR spectra of **M3** monitored during the hydrolysis process in buffered D₂O (pH 5.5) at 37 °C. The E_d of **M3** was estimated by comparing the integrals of peaks a_1 , a_2 and a' (a^*) ($E_d = (I_{a'} + I_{a^*}) / (I_{a'} + I_{a_1} + I_{a_2} + I_{a^*})$).

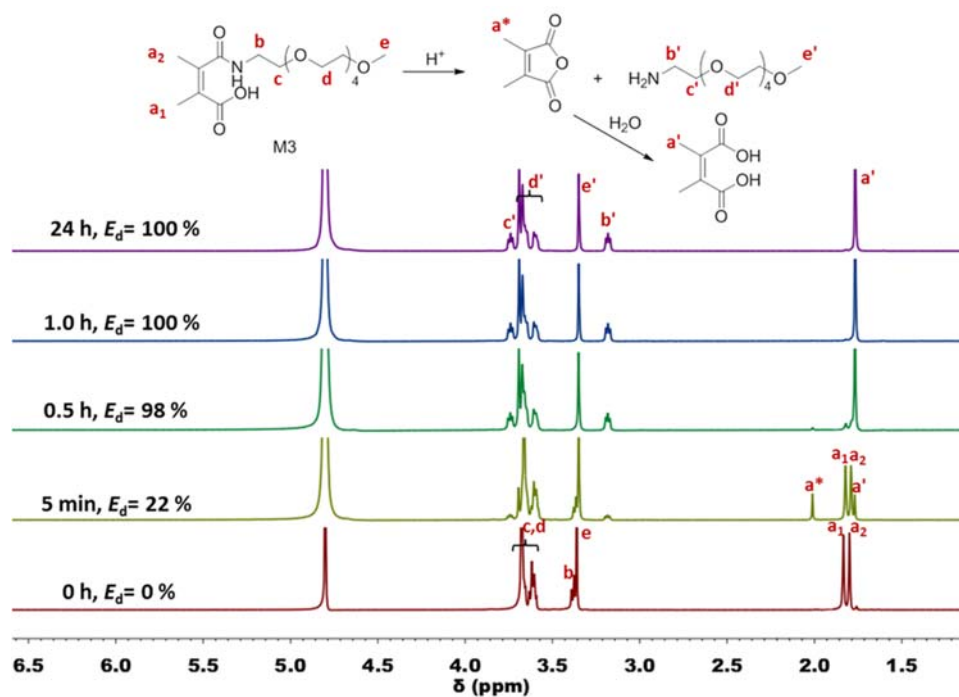


Fig. S16 ^1H NMR spectra of **M3** monitored during the hydrolysis process in buffered D_2O (pH 6.5) at 37°C .

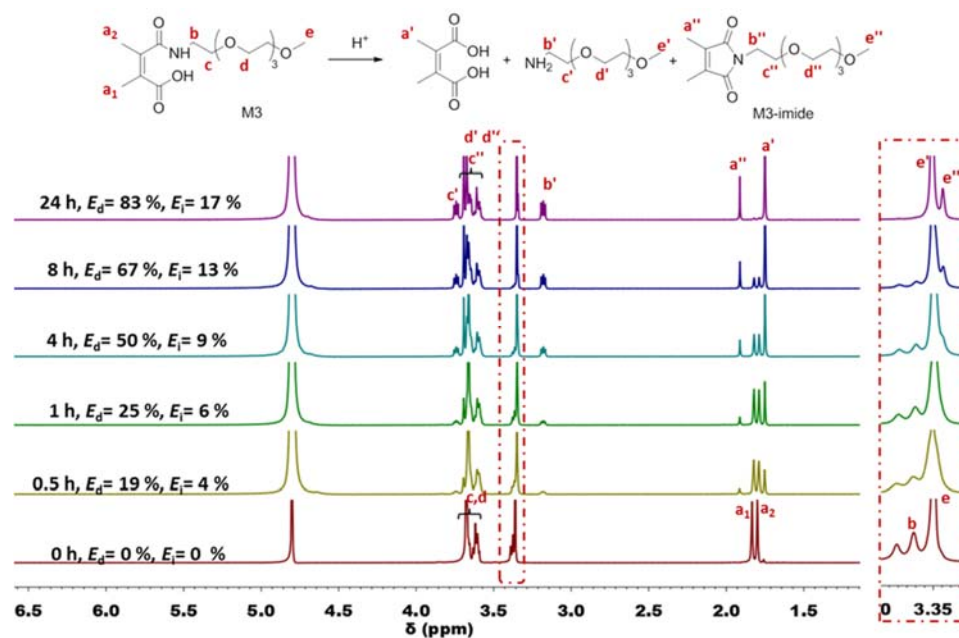


Fig. S17 The detailed ^1H NMR spectra of **M3** monitored during the hydrolysis process in buffered D_2O (pH 7.4) at 37°C , E_i is the percent content of **M3-imide**. The E_d and E_i of **M3** were estimated by comparing the integrals of peaks a_1 , a_2 , a' and a'' ($E_d = I_{a'}/(I_{a'} + I_{a''}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

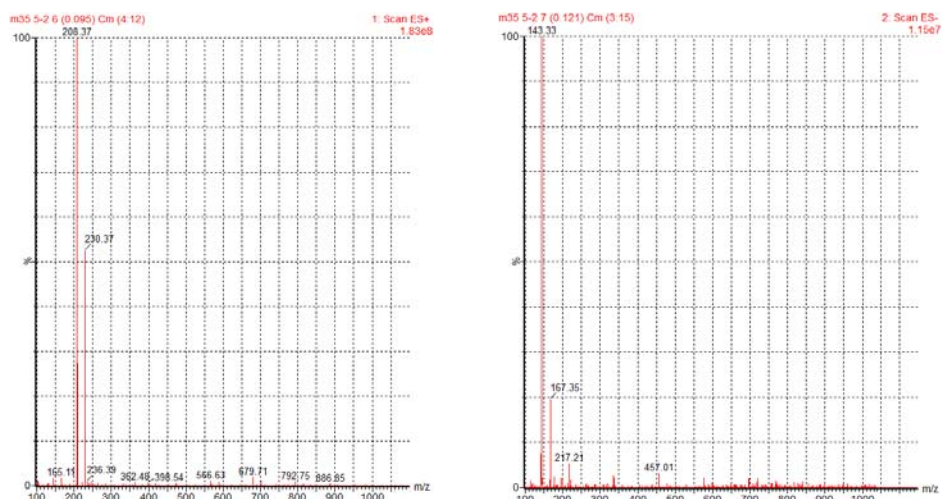


Fig. S18 MS spectra of the hydrolysis products of compound **M3** in buffered D₂O (pH 5.5). Positive ion mode (left): mPEG₄-NH₂ (C₉H₂₁NO₄ + H⁺), calcd: 208.15; found: 208.37. (C₉H₂₁NO₄ + Na⁺), calcd: 230.14; found: 230.37. Negative ion mode (right): 2,3-dimethyl maleic acid (C₆H₇O₄⁻), calcd: 143.03; found: 143.33.

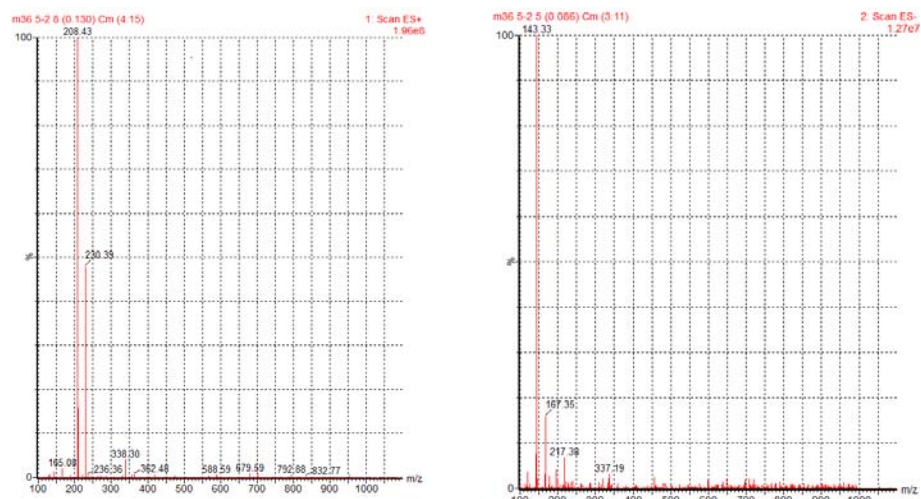


Fig. S19 MS spectra of the hydrolysis products of compound **M3** in buffered D₂O (pH 6.5). Positive ion mode (left): mPEG₄-NH₂ (C₉H₂₁NO₄ + H⁺), calcd: 208.15; found: 208.43. (C₉H₂₁NO₄ + Na⁺), calcd: 230.14; found: 230.39. Negative ion mode (right): 2,3-dimethyl maleic acid (C₆H₇O₄⁻), calcd: 143.03; found: 143.33.

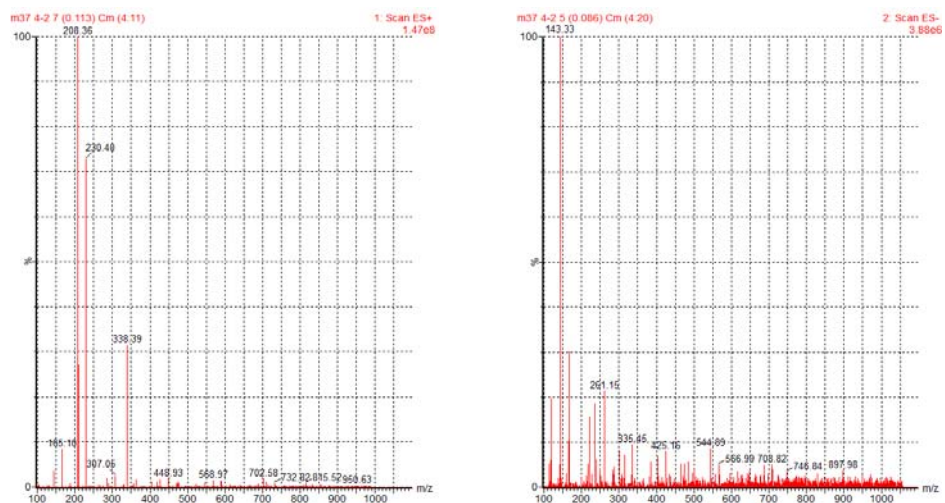


Fig. S20 MS spectra of the hydrolysis products of compound **M3** in buffered D₂O (pH 7.4). Positive ion mode (left): mPEG₄-NH₂ (C₉H₂₁NO₄ + H⁺), calcd: 208.15; found: 208.36. (C₉H₂₁NO₄ + Na⁺), calcd: 230.14; found: 230.40. **M3**-imide (C₁₅H₂₅NO₆ + Na⁺), calcd: 338.16; found: 338.39. Negative ion mode (right): 2,3-dimethylmaleic acid (C₆H₇O₄⁻), calcd: 143.03; found: 143.33.