Supporting information

Fabrication of Biocleavable Crosslinked Polyprodrug Vesicles via Reversible Donor-Acceptor Interactions for Enhanced Anticancer Drug Delivery

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1. Detailed calculation of PEG-*b*-P(CPTM-*co*-BEMA) and PEG-*b*-P(CPTM-*co*-CEMA) polyprodrug compositions

The ^{1}H NMR spectra were analyzed and used to determine the compositions of the synthesized polyprodrugs. Taking P1 as a typical example of PEG_{45}-*b*-P($CPTM_x$-*co*-$BEMA_y$) (Figure S7), the degrees of polymerization (DPs) of CPTM (x) and BEMA (y) units were determined respectively by comparing the ratio of the integrated intensity of peak *c* (-CH_2**C*H*$_3$ in the side chain of CPTM unit) or peak *d* (-C(C***H***$_3$)$_2$ in the side chain of BEMA unit) to that of peak *a* (-OC***H***$_2$C***H***$_2$- in the backbone of PEG) based on the following formulas,

$3x/(4\times45) = 36.8/180$,

$12y/(4\times45) = 85.8/180$,

x and y were calculated to be 12 and 7, respectively. P1 was thus denoted PEG_{45}-*b*-P($CPTM_{12}$-*co*-$BEMA_7$).

Similarly, the composition of PEG_{45}-*b*-P($CPTM_m$-*co*-$CEMA_n$) (P3) control polymer (Figure S8) was determined by comparing the ratio of the integrated intensity of peak *c* (-CH_2**C*H*$_3$ in the side chain of CPTM unit) or peak *b* (-OC***H***$_2$$C_6H_5$ in the side chain of CEMA unit) to that of peak *a* (-OC***H***$_2$C***H***$_2$- in the backbone of PEG) based on the following formulas,

$3m/(4\times45) = 37.6/180$,

$2n/(4\times45) = 17.8/180$,

m and n were calculated to be 12 and 9, respectively. P3 was thus denoted PEG_{45}-*b*-P($CPTM_{12}$-*co*-$BEMA_9$).

2. Captions of Figures and Scheme

Figure S1. ^{1}H NMR spectrum of CPTM in $CDCl_3$.

Figure S2. ^{13}C NMR spectrum of CPTM in $CDCl_3$

Figure S3. ^{1}H NMR spectrum of BEMA in $CDCl_3$.

Figure S4. ^{13}C NMR spectrum of BEMA in $CDCl_3$

Figure S5. ^{1}H NMR spectrum of CEMA in $CDCl_3$.

Figure S6. ^{13}C NMR spectrum of CEMA in $CDCl_3$

Figure S7. ^{1}H NMR spectrum of P1 in $CDCl_3$.

Figure S8. ^{1}H NMR spectrum of P3 in $CDCl_3$.

Figure S9. SEC elution traces of P1, P2, and P3 using DMF as an eluent.

Figure S10. ^{1}H NMR spectrum of P1 in $CDCl_3$ after deprotection.

Figure S11. ^{11}B NMR spectrum of phenylboronic acid before and after addition of 1,6-hexanediamine in DMSO-d_6/D_2O.

Figure S12. Stability of noncrosslinked P1 vesicles and CP1V upon dilution.

Figure S13. Average hydrodynamic size and size distribution of noncrosslinked P1 vesicles in water and PBS.

Figure S14. Average hydrodynamic size and size distribution of CP1V in water and PBS.

Figure S15. GSH (10 mM) and H_2O_2 (100 μM)-triggered size changes of CP1V monitored by DLS at 48h.

Scheme S1. The mechanism of reduction-triggered release of CPT via thiol group-mediated elimination reaction and H_2O_2-triggered degradation of BEMA toward

decrosslinking.

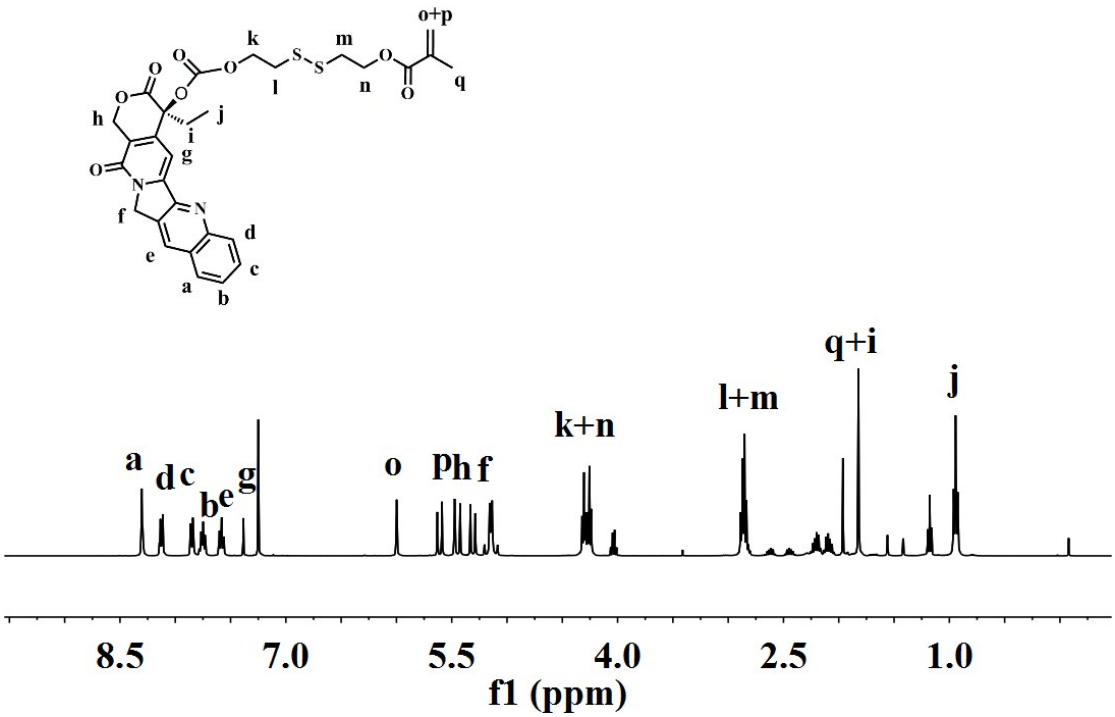


Figure S1. ^{1}H NMR spectrum of CPTM in $CDCl_3$.

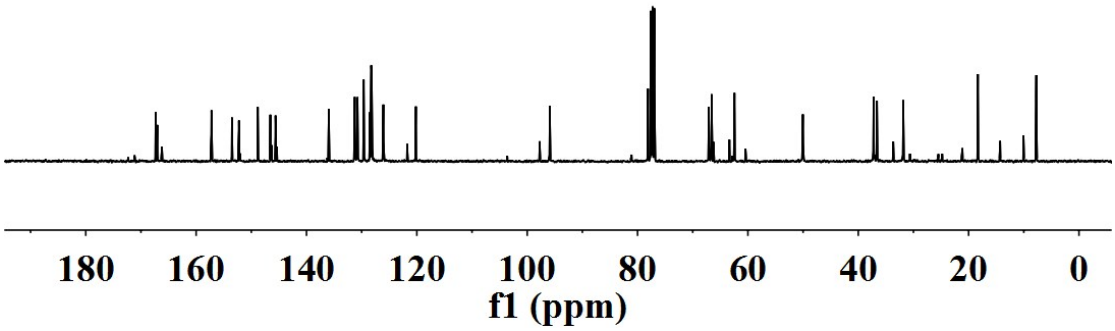


Figure S2. ^{13}C NMR spectrum of CPTM in $CDCl_3$.

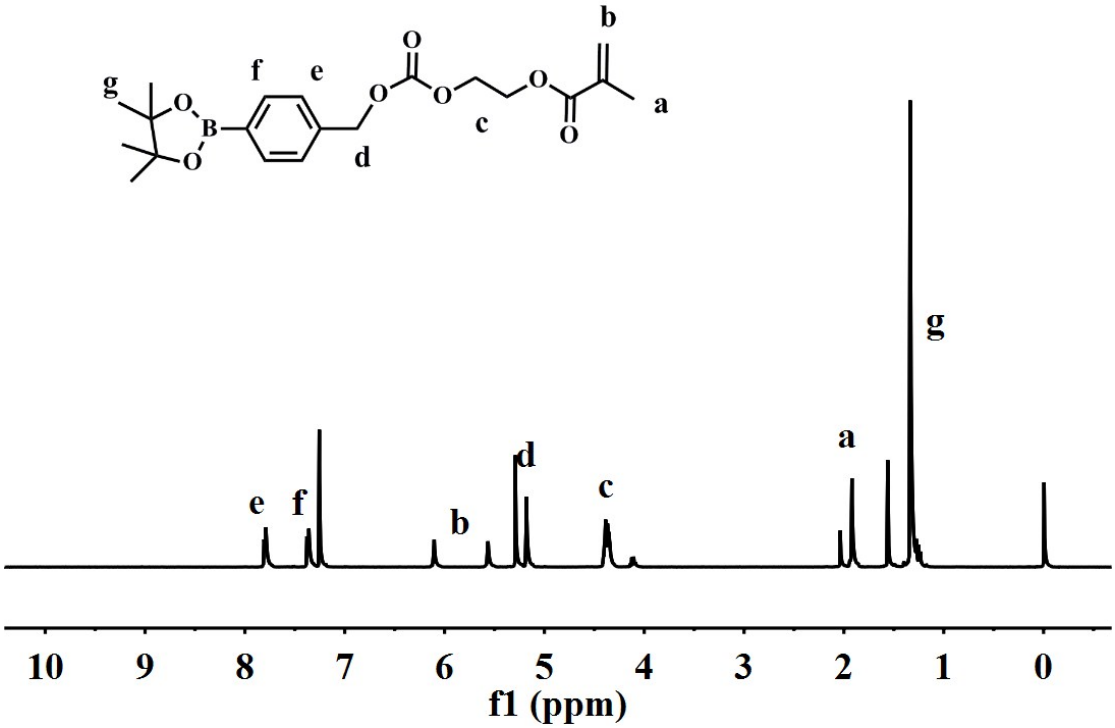


Figure S3. ^{1}H NMR spectrum of BEMA in $CDCl_3$.

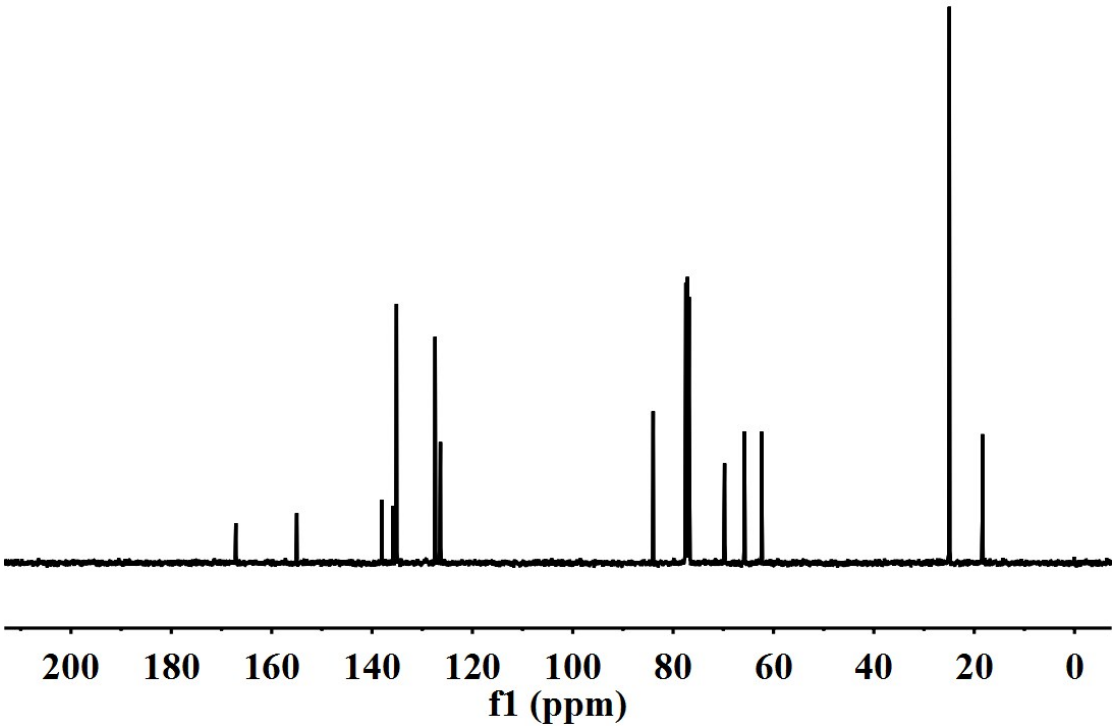


Figure S4. ^{13}C NMR spectrum of BEMA in $CDCl_3$.

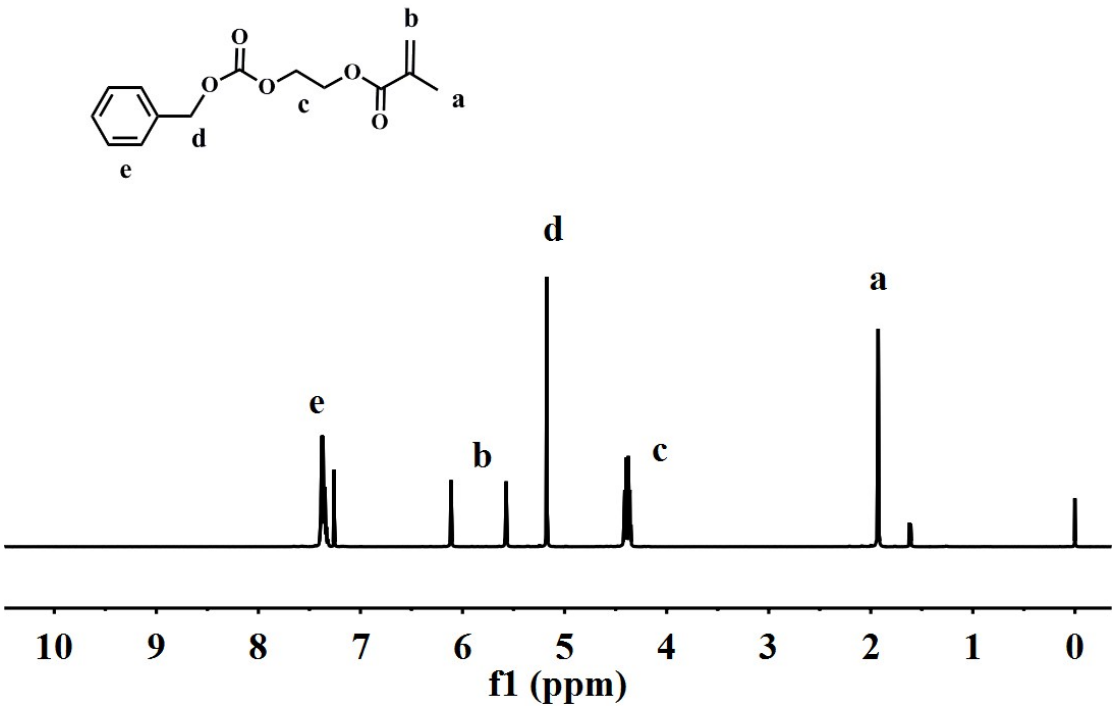


Figure S5. ^{1}H NMR spectrum of CEMA in $CDCl_3$.

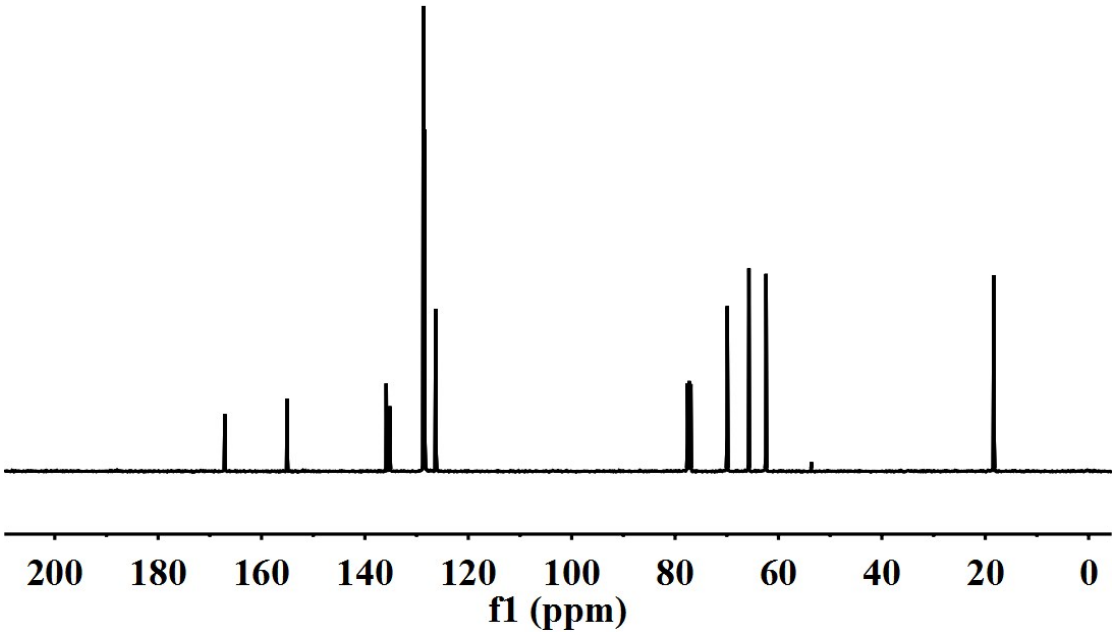


Figure S6. ^{13}C NMR spectrum of BEMA in $CDCl_3$.

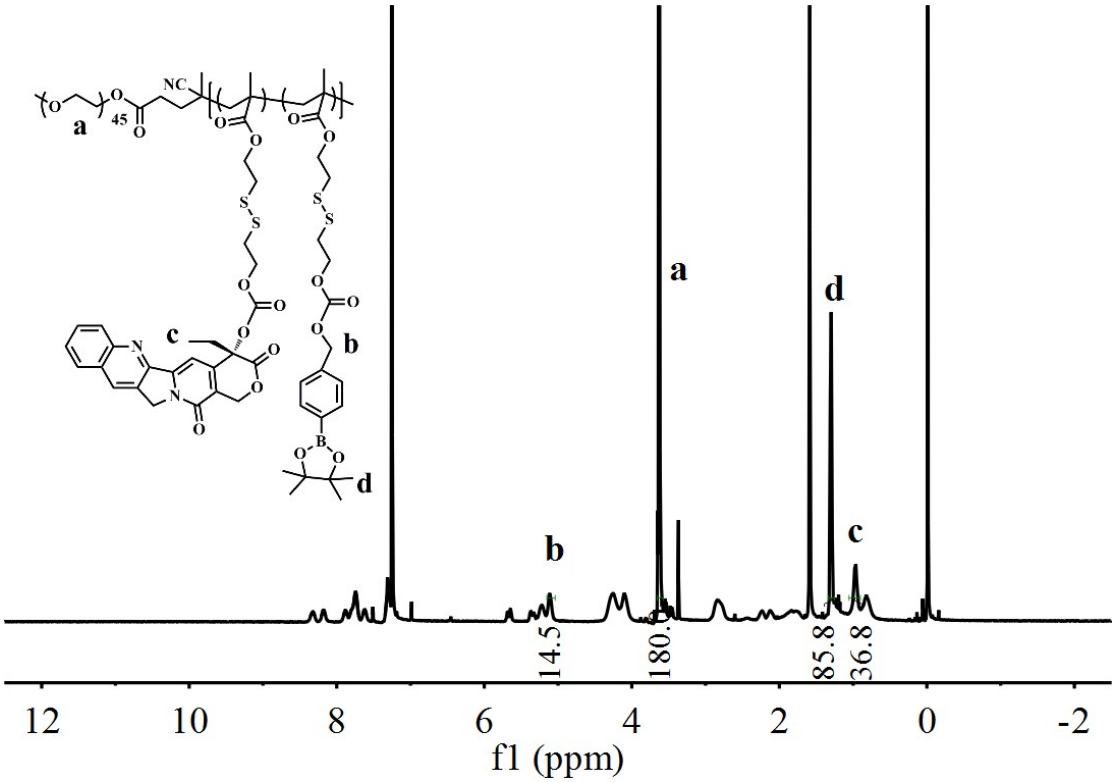


Figure S7. ^{1}H NMR spectrum of P1 in $CDCl_3$.

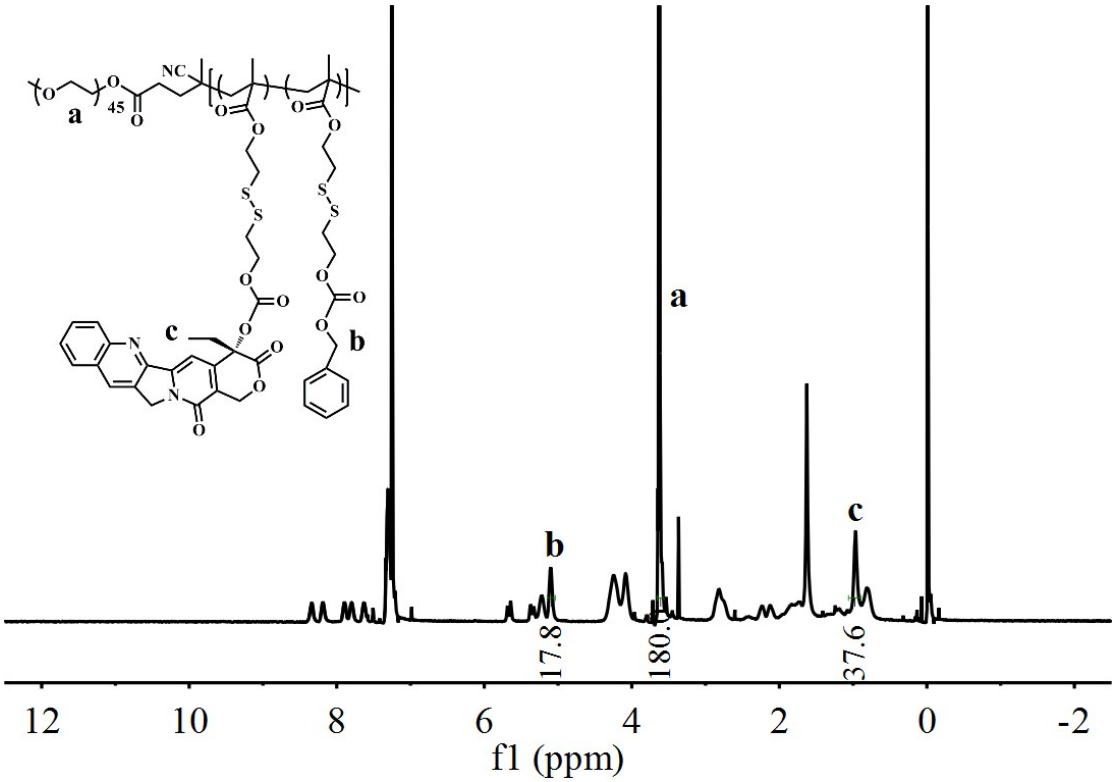


Figure S8. ^{1}H NMR spectrum of P3 in $CDCl_3$.

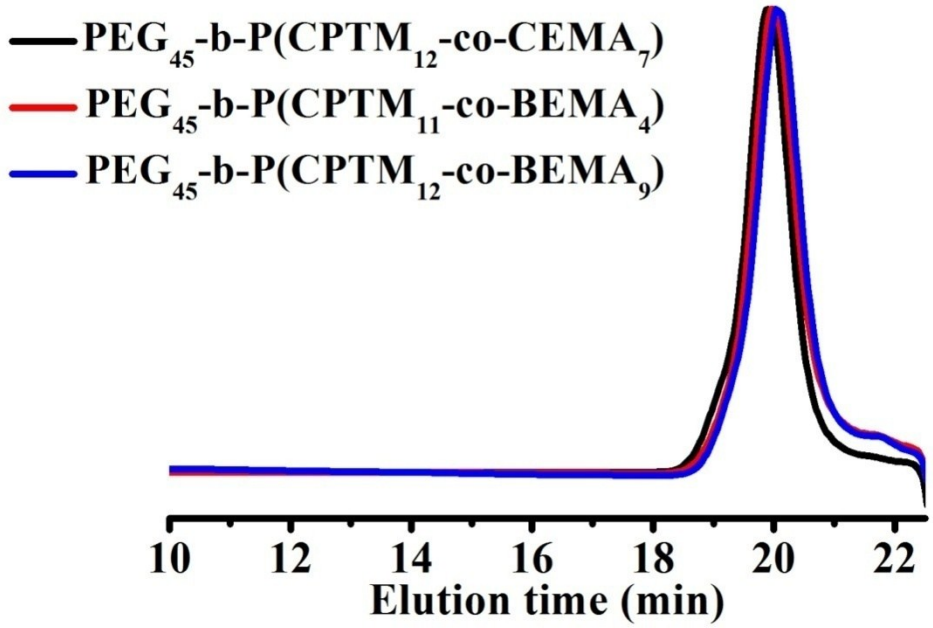


Figure S9. SEC elution traces of P1, P2, and P3 using DMF as an eluent.

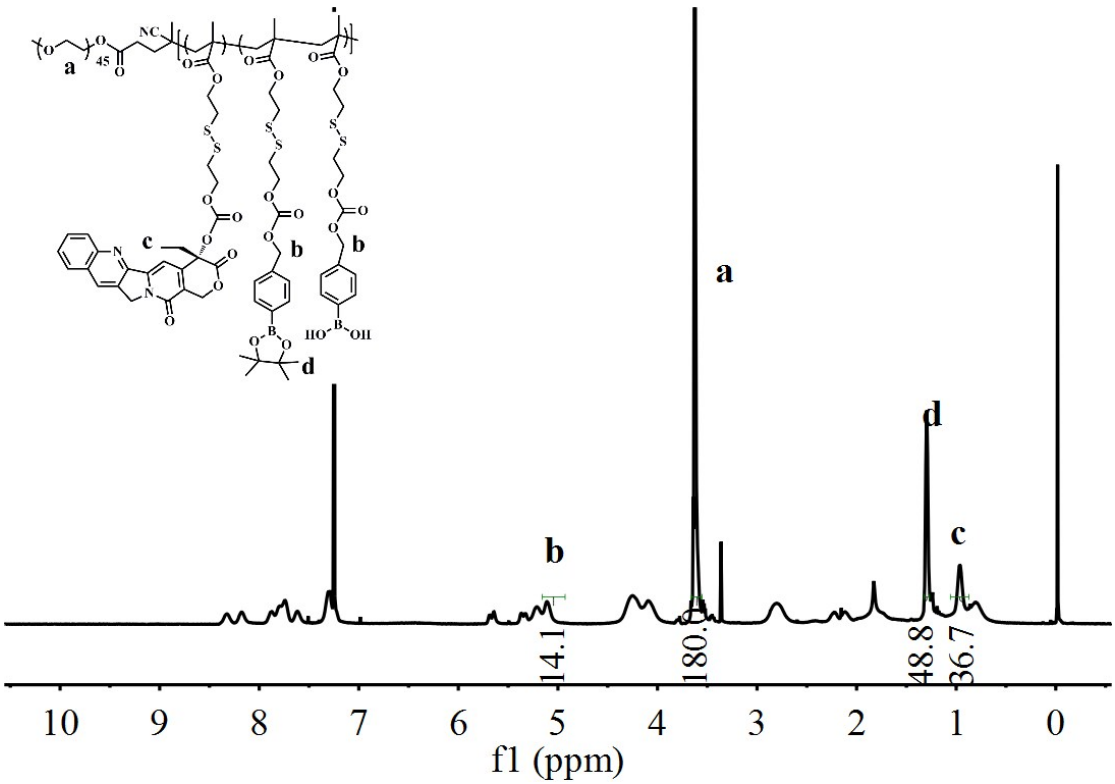
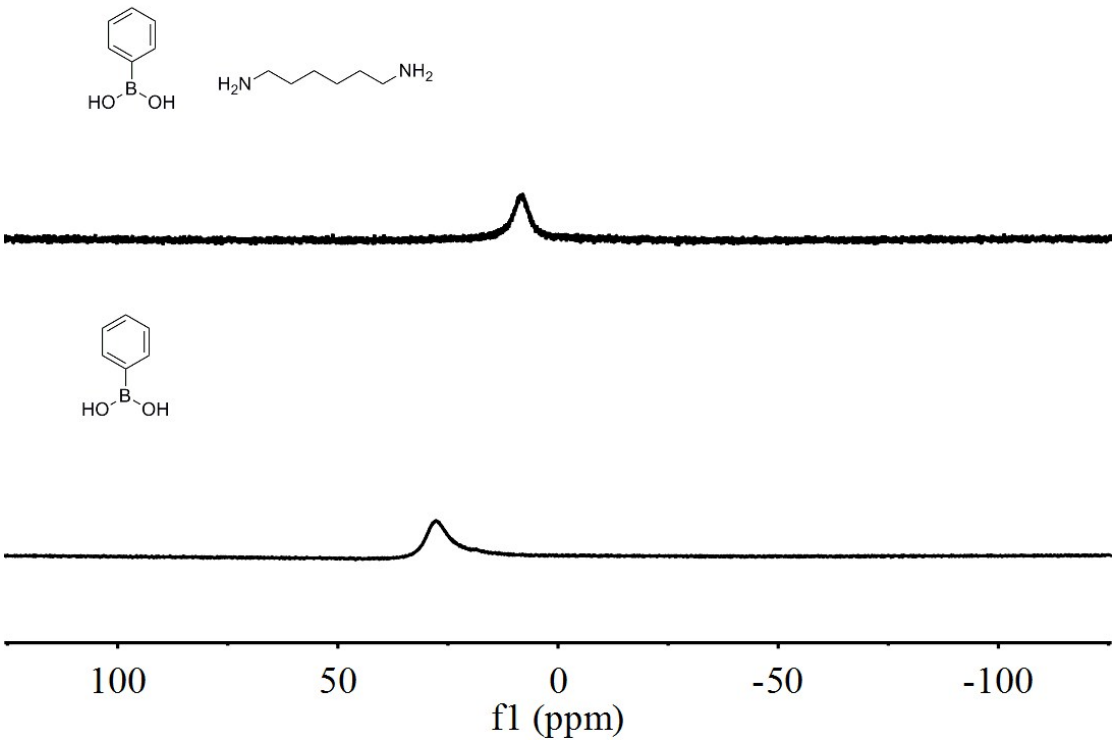


Figure S10. ^{1}H NMR spectrum of P1 in $CDCl_3$ after deprotection.



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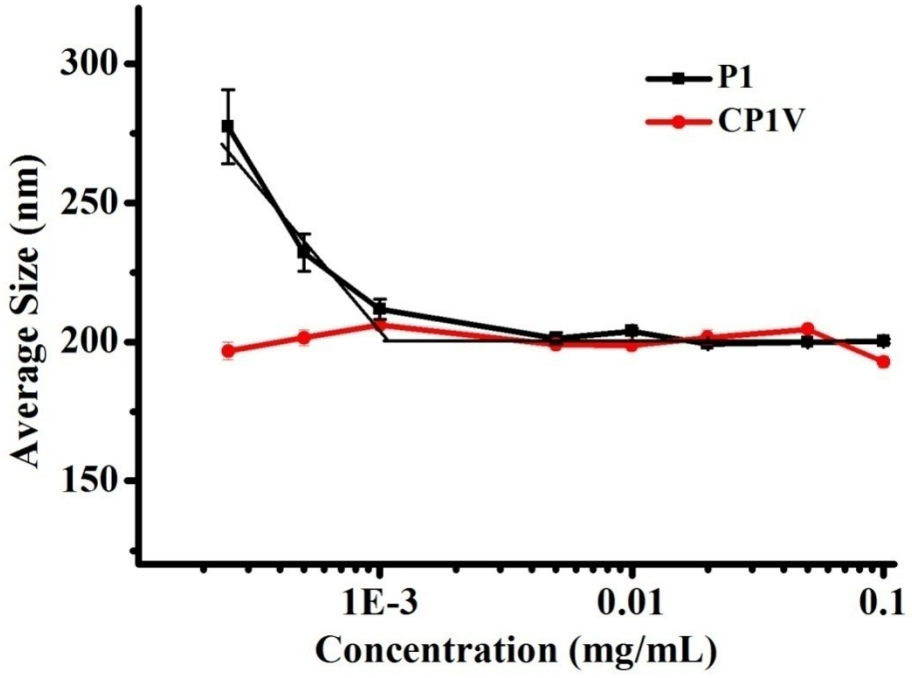


Figure S12. Stability of noncrosslinked P1 vesicles and CP1V upon dilution.

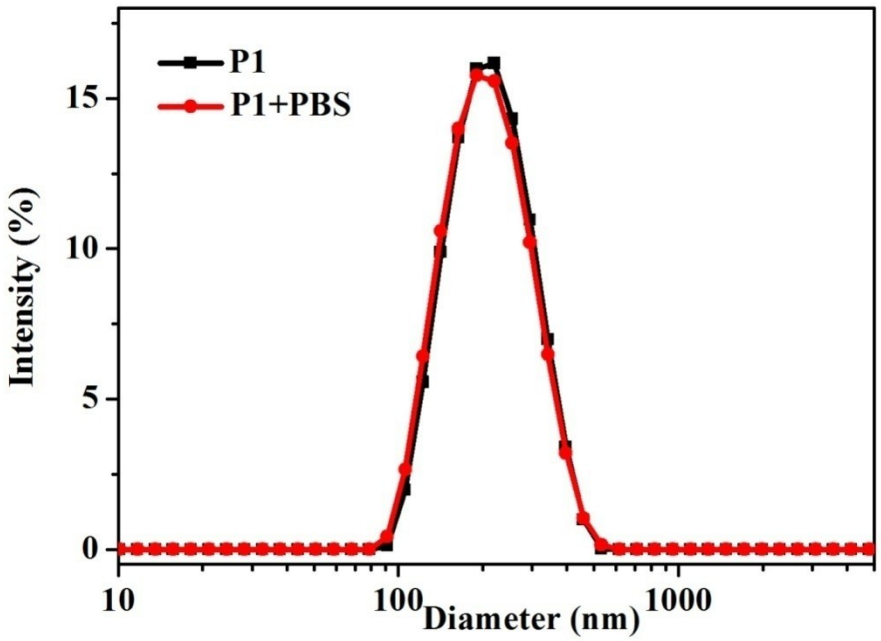


Figure S13. Average hydrodynamic size and size distribution of noncrosslinked P1 vesicles in water and PBS.

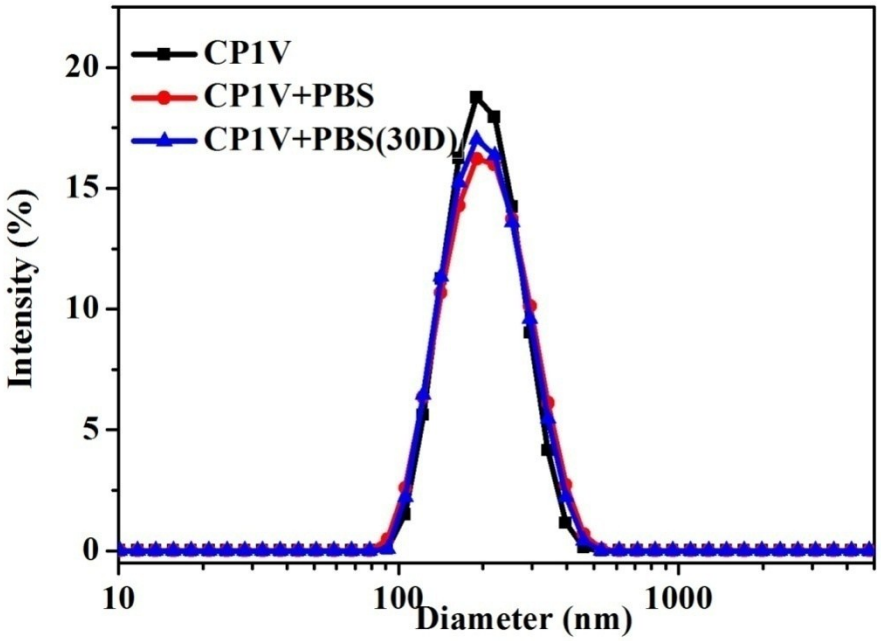
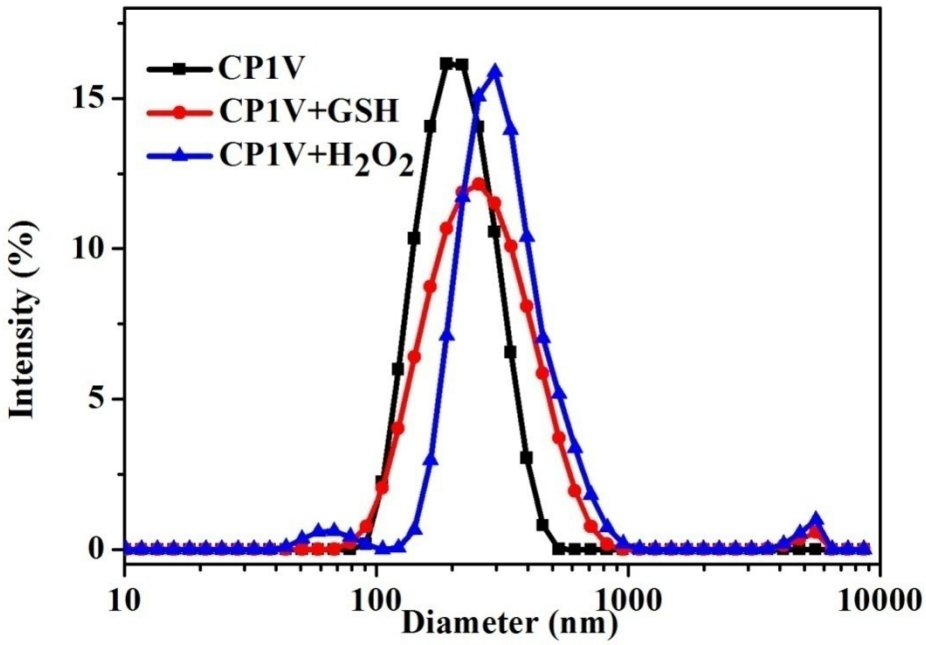


Figure S14. Average hydrodynamic size and size distribution of CP1V in water and PBS.



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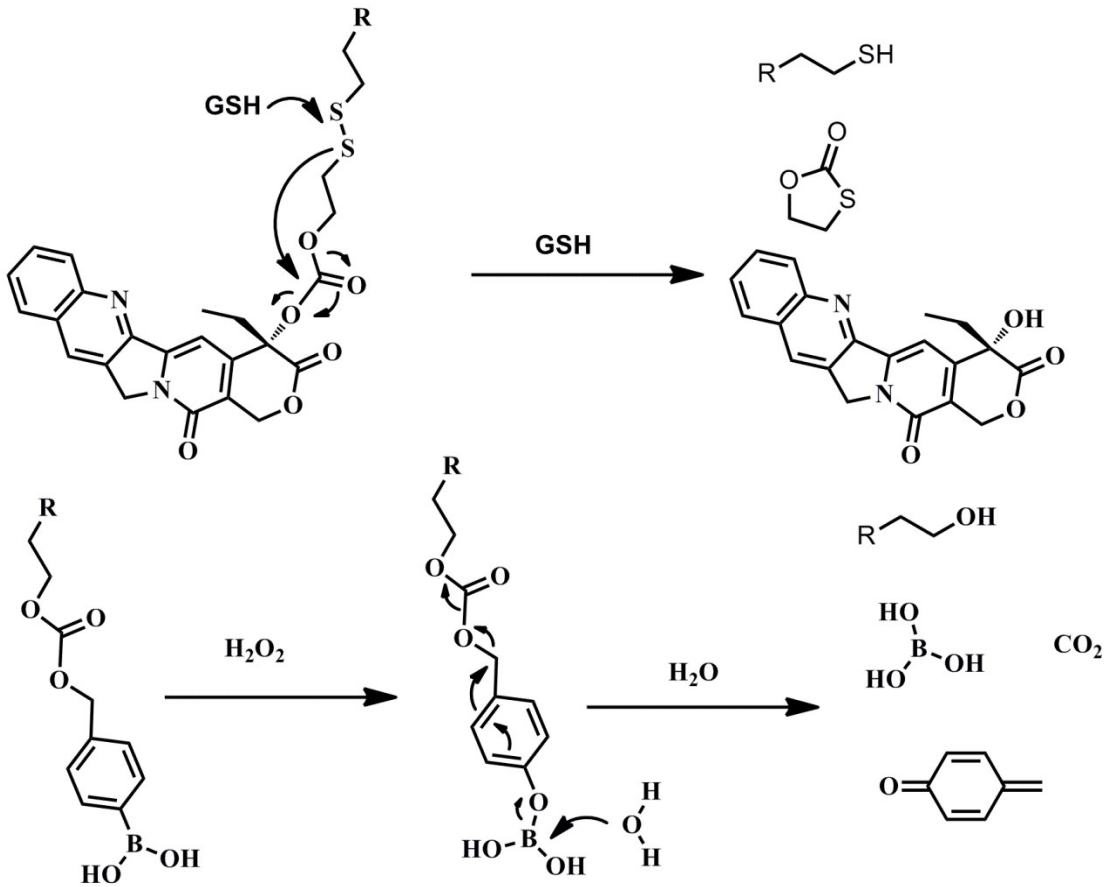

Scheme S1. The mechanism of reduction-triggered release of CPT via thiol group-mediated elimination reaction and H_2O_2-triggered degradation of BEMA toward decrosslinking.