SUPPORTING INFORMATION:

Reversion of P-gp-mediated Drug Resistance in Ovarian Carcinoma Cells with PHPMA-Zosuquidar Conjugates

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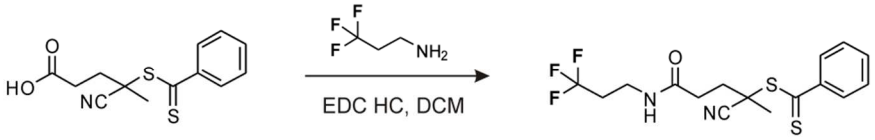
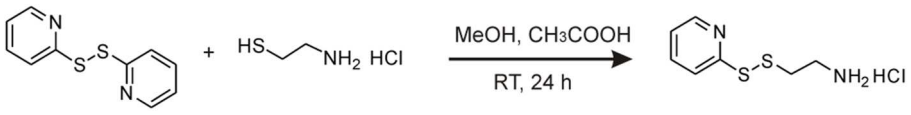
Synthesis of fluorinated CTA (F_3-CTA)



Scheme S1. Synthesis of F_3-CTA.

500.0 mg (1.79 mmol) 4-Cyano-4-(phenylcarbonothioylthio)pentanoic acid and 411.6 mg (2.15 mmol) EDC.HCl were dissolved in 8 mL dry DCM and the solution cooled down to 0 °C and stirred under nitrogen. In a second flask, 214.0 mg (1.43 mmol) 3,3,3-trifluoropropyl amine hydrochloride was dissolved in 8 mL dry DCM and 250 μL (1.43 mmol) triethylamine were added. After 10 minutes, the 3,3,3-trifluoropropyl amine solution was added dropwise to the first solution and the reaction was stirred at room temperature for 2 h. The solution was washed with 5 % $NaHCO_3$ and brine, dried over $MgSO_4$ and finally dried under vacuum. The crude product was purified by flash chromatography using ethyl acetate / hexane 4.5:5.5 to give the dark pink product (73 % yield). ^{1}H-NMR and ^{19}F-NMR spectra of the fluorinated CTA are included in **Figure S1** and **S2**.

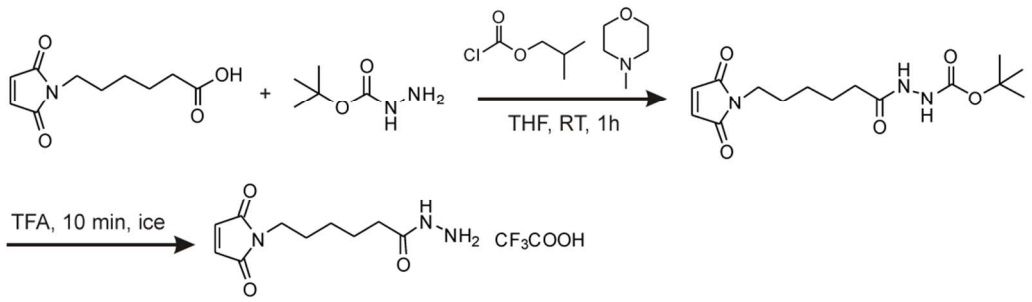
Synthesis of 2-(pyridyldithio)-ethylamine (PDA)



Scheme S2. Synthesis of 2-(pyridyldithio)-ethylamine (PDA).

2.20 mg (10 mmol) 2,2′-Dipyridyl disulphide were dissolved in 10 mL dry methanol and 400 µL acetic acid were added. Then, 5 mL of a methanol solution containing 568 mg (5 mmol) cystamine hydrochloride were added dropwise over a period of 30 min. After stirring the solution for 24 h, the solvent was removed by rotary evaporation and the product was isolated (75 % yield) by precipitation in diethyl ether followed by centrifugation (5 times). ^{1}H-NMR and ^{13}C-NMR spectra of PDA are included in **Figure S3** and **S4**.

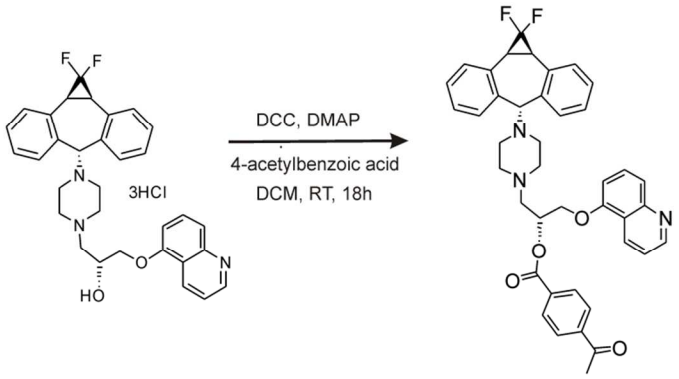
Synthesis of 6-maleimidocaproic acid hydrazide trifluoroacetic acid salt



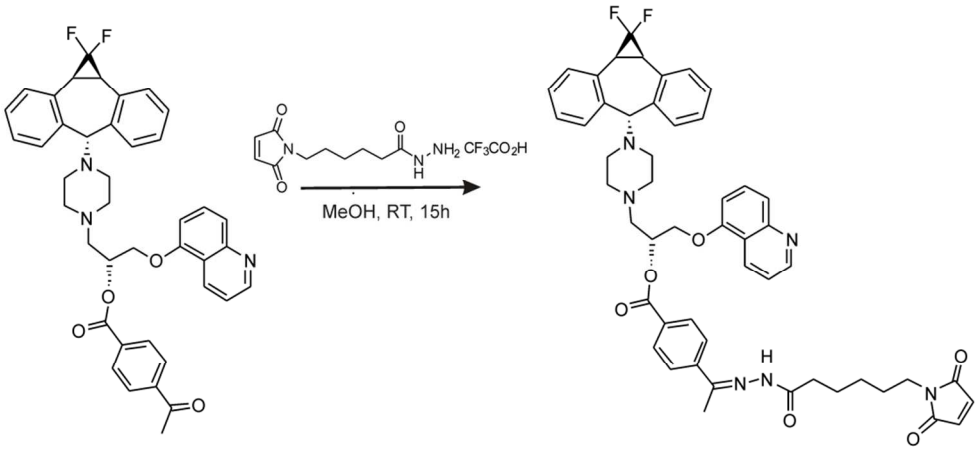
Scheme S3. Synthesis of 6-maleimidocaproic acid hydrazide trifluoroacetic acid salt.

6-Maleimidocaproic acid hydrazide trifluoroacetic acid salt was prepared as previously reported with few modifications.[1] Briefly, 400 mg (1.89 mmol) 6-maleimidocaproic acid were dissolved in 40 mL dry THF, the solution was cooled at 4 °C and 1 eq. (208 µL) *N*-methylmorpholine was added. Next, 1 eq. (257 mg) isobutyl chloroformate in 4 mL THF was added and after 5 min an additional 4 mL THF containing 1 eq. (250 mg) tert-butyl carbazate were added dropwise. The reaction mixture was kept at 4 °C for 30 min and subsequently stirred at room temperature for 1 h. The solvent was evaporated and the residue dissolved in ethyl acetate and washed with water before being dried over $MgSO_4$, filtered and dried under vacuum. The crude product was purified

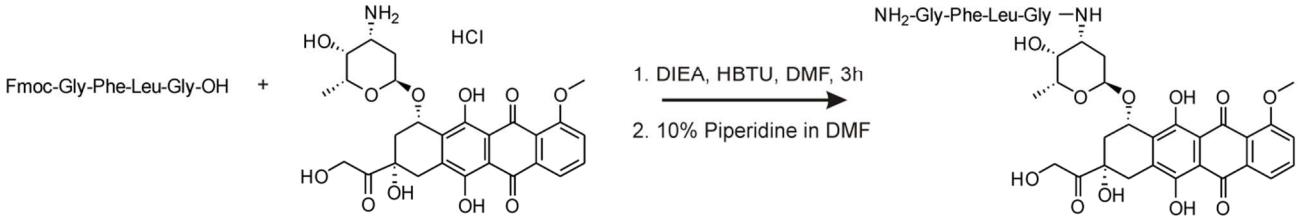
by flash chromatography using a gradient of DCM/MeOH from 100:1 to 100:2 (0.1 % acetic acid was added to the eluent). Boc deprotection was performed by stirring the product in 4 mL ice-cold trifluoroacetic acid for 8 minutes. The acid was removed by evaporation and the product was precipitated in diethyl ether (yield 66 %). ^{1}H-NMR and ^{13}C-NMR spectra are included in **Figure S5** and **S6**.



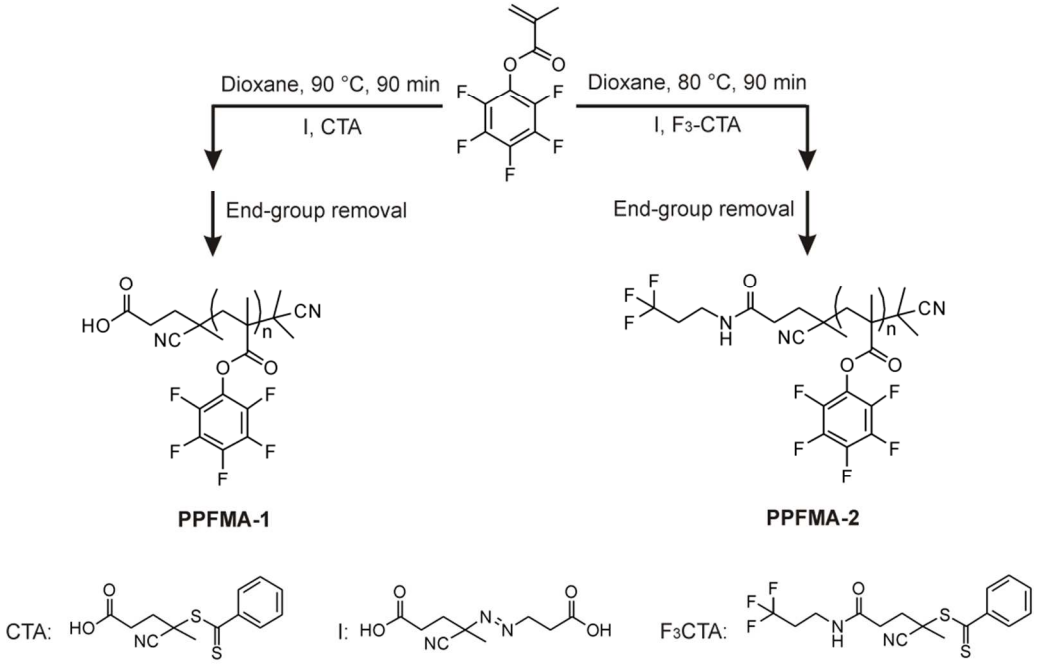
Scheme S4. Synthesis of Zos-Ket.



Scheme S5. Synthesis of Zos-Mal.



Scheme S6. Synthesis of NH_2-GFLG-Dox.



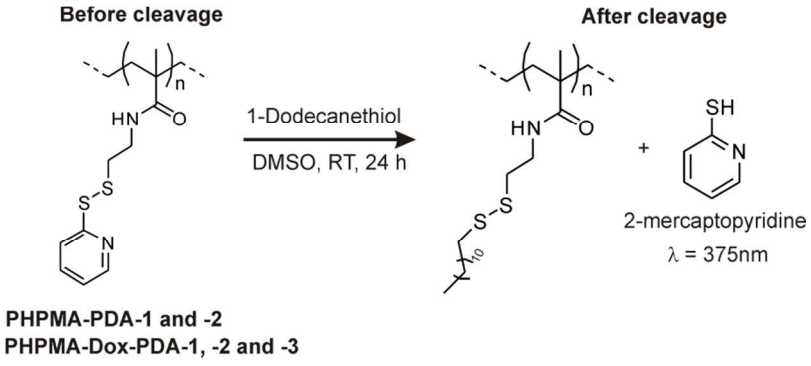
Scheme S7. Synthesis of poly(pentafluorophenyl methacrylate) precursors **PPFMA-1** and **PPFMA-2**. Chain transfer agent (CTA) = 4-cyano-4-(phenylcarbonothioylthio)pentanoic acid; initiator (I) = 4,4′-azobis(4-cyanovaleric acid).

Synthesis of PPFMA-1 and PPFMA-2

PPFMA-1 was prepared as previously reported by Gibson *et al*.[2] The following conditions were used: polymerization time of 90 minutes, [PFMA]:[CTA] = 200, [CTA]:[I] = 2 and [PFMA] = 2.30 M.

PPFMA-2 was obtained using the fluorinated RAFT agent F_3-CTA and the following conditions were used: [PFMA]:[CTA] = 200, [CTA]:[I] = 5 and [PFMA] = 2.5 M. In a typical experiment 5 g PFMA were added to a Schlenk tube together with 297 µL of a 0.33 M F_3-CTA stock solution and 277 µL of a 0.07 M initiator stock solution. 3.75 mL dioxane were added and the solution was degassed by four freeze-pump thaw cycles. The tube was filled with argon and the reaction was stirred at 80 °C for 90 minutes. The solution was immediately cooled down in an ice bath and the polymer was isolated by precipitation in ice-cold hexane followed by centrifugation (3 times). For both polymers the end-group removal was performed using an excess of 2,2′-azobis(2-methylpropionitrile) (AIBN) as previously reported.[3] **Figure S16** shows a ^{19}F-NMR spectrum of PPFMA-2. Molecular weights and polydispersity of PPFMA-1 and PPFMA-2 are summarized in **Table S1**.

Determination of mol % of Dox and PDA in the PHPMA conjugates by UV-Vis spectroscopy



The extent of PDA incorporation in the PHPMA conjugates was determined as follows: the PHPMA intermediates **PHPMA-PDA-1** and **PHPMA-PDA-2** were dissolved in DMSO and stirred with 30 eq. of 1-dodecanethiol for 24 hours in order to assure complete cleavage of the

linker. After 24 hours, the released 2-mercaptopyridine, which is directly proportional to the amount of PDA incorporated in the polymer was calculated form the UV absorption at 375 nm. The polymer conjugate bearing both the PDA linker and Dox (**PHPMA-Dox-PDA**) was first analyzed by UV in order to quantify the Dox content and the Dox-related absorbance at 375 nm. In a second step, the polymer solution was treated with 1-dodecanethiol for 24 h and the PDA content was determined by UV measurements. The PDA content of the **PHPMA-Dox-PDA** conjugate was calculated by subtracting the Dox related absorbance at 375 nm. Dox and PDA concentrations were estimated using the calibration curves reported in **Figure S17**. The measurements were repeated at least twice and the results were averaged. On example of UV spectra per each polymer conjugate is reported in **Figure S18**.

Table S1. Molecular weights and polydispersities of **PPFMA-1** and **PPFMA-2** and the corresponding PHPMA derivatives.

Precursor polymer	^{1}H-NMR[a]	^{19}F-NMR[a]	^{19}F-NMR[b]	SEC in THF[c]			PHPMA intermediates	SEC in DMF[d]	
	M_n^{TH} (g/mol)	M_n^{TH} (g/mol)	M_n (g/mol)	M_n (g/mol)	DP (-)	M_w/M_n (-)		M_n (g/mol)	M_w/M_n (-)
PPFMA-1	25200	-	-	17210	68	1.6	**PHPMA-PDA-1**	36830	1.9
PPFMA-2	21170	21670	28220	27630	110	1.4	**PHPMA-PDA-2**	45326	1.4
							PHPMA-Dox-PDA-1	-	-

[a] Theoretical number-average molecular weight (M_n^{TH}) calculated from the monomer conversion determined by ^{1}H- and ^{19}F-NMR.
[b] Number-average molecular weight (M_n) calculated from ^{19}F-NMR of the purified product.
[c] Conventional calibration using polystyrene (PS) standards.
[d] Conventional calibration using poly(methyl methacrylate) (PMMA) standards.

Table S2. Feed ratio and percentage of functionalization of the PHPMA intermediates and final conjugates.

Final conjugates	Zos content (mol %)		Dox content (mol %)		PHPMA intermediates	Feed ratio (eq.)			PDA content (mol %)		Dox content (mol %)	
	^{1}H-NMR[a]	^{19}F-NMR[b]	^{1}H-NMR[c]	UV[d]		HPA	PDA	Dox	^{1}H-NMR[e]	UV[f]	^{1}H-NMR[c]	UV[d]
PHPMA-Zos-1	2.2	-	-	-	**PHPMA-PDA-1**	1.7	0.3	-	2.4	2.3	-	-
PHPMA-Zos-2	4.3	4.6	-	-	**PHPMA-PDA-2**	1.6	0.4	-	4.7	4.3	-	-
PHPMA-Dox	-	-	2.4	2.5	**PHPMA-Dox**	1.8	-	0.2	-	-	2.4	2.5
PHPMA-Dox-Zos	0.2	0.4	2.9	2.9	**PHPMA-Dox-PDA**	1.9	0.1	0.15	0.2	0.4	2.6	2.9

[a] Determined by comparing the integrals of Zos signals with those of the polymer backbone and with the CH proton of the hydroxypropyl polymer side chains.
[b] Determined by comparing the integrals of fluorine signals of Zos with those of the polymer end group and taking into account the degree of polymerization (DP).
[c] Determined by comparing the integrals of the Dox signals with those of the polymer backbone and with the CH proton of the hydroxypropyl polymer side chains.
[d] Calculated from the absorbance peak at λ = 490 nm in DMSO (ε = 12049.6 cm^{-1} M^{-1}).
[e] Determined by comparing the integrals of the PDA aromatic signals with those of the polymer backbone and with the CH proton of the polymer hydroxypropyl side chains.
[f] Calculated from the absorbance peak at λ = 375 nm in DMSO (ε = 5898.6 cm^{-1} M^{-1}) after cleavage of the PDA linker with 1-dodecanethiol.

Table S3. Cytotoxicity of Dox and **PHPMA-Dox** in sensitive A2780 and resistant A2780ADR cells as determined by the MTT assay.

Compounds	Dox IC_{50} (μM)[a]	
	A2780	**A2780ADR**
Dox	0.013 ± 0.003	1.441 ± 0.362
PHPMA-Dox	~ 20	~ 100

[a] IC_{50} values (concentration of drug necessary to inhibit 50 % of the cells growth) were determined via MTT assay after 72 h incubation, the percentage viability was determined with respect to untreated cells. For free Dox, the IC_{50} values and standard errors were calculated using a sigmoidal dose-response curve fitting, in the case of **PHPMA-Dox** the IC_{50} values were only estimated from the viability profile shown in **Figure S31**.

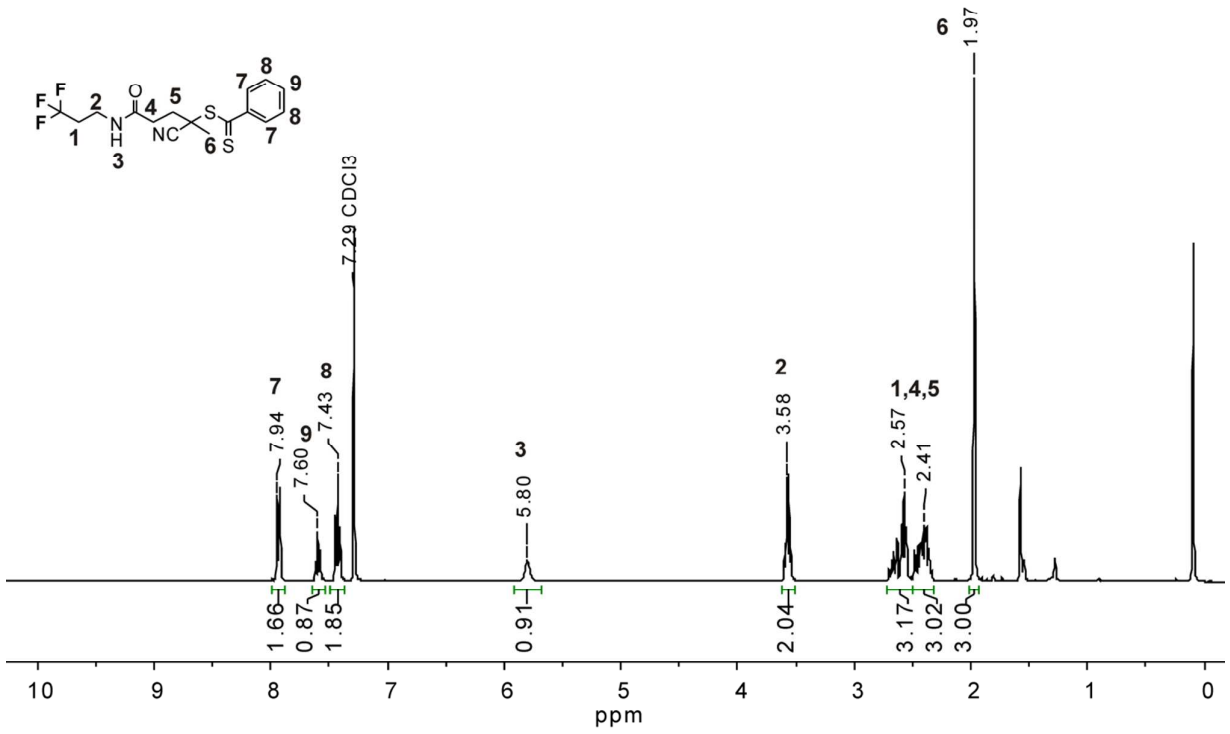


Figure S1. ^{1}H-NMR spectrum of F_3-CTA in $CDCl_3$.

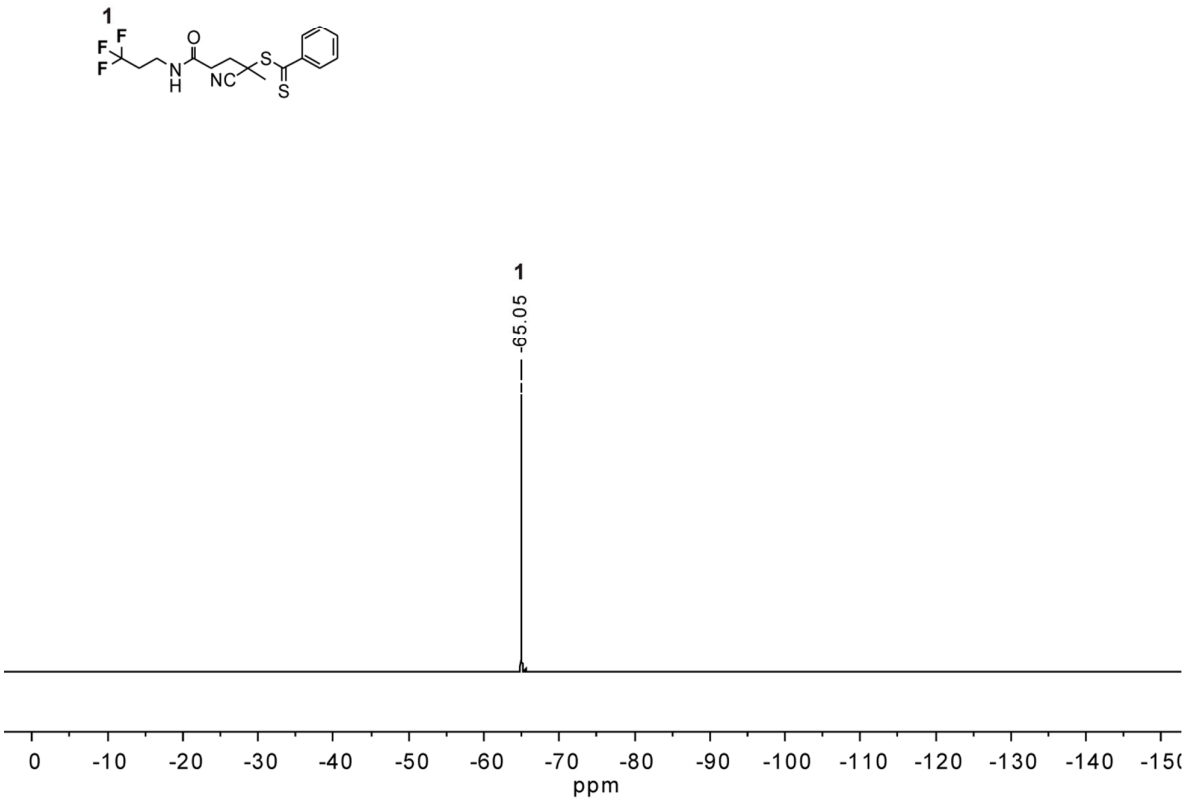


Figure S2. ^{19}F-NMR spectrum of F_3-CTA in $CDCl_3$.

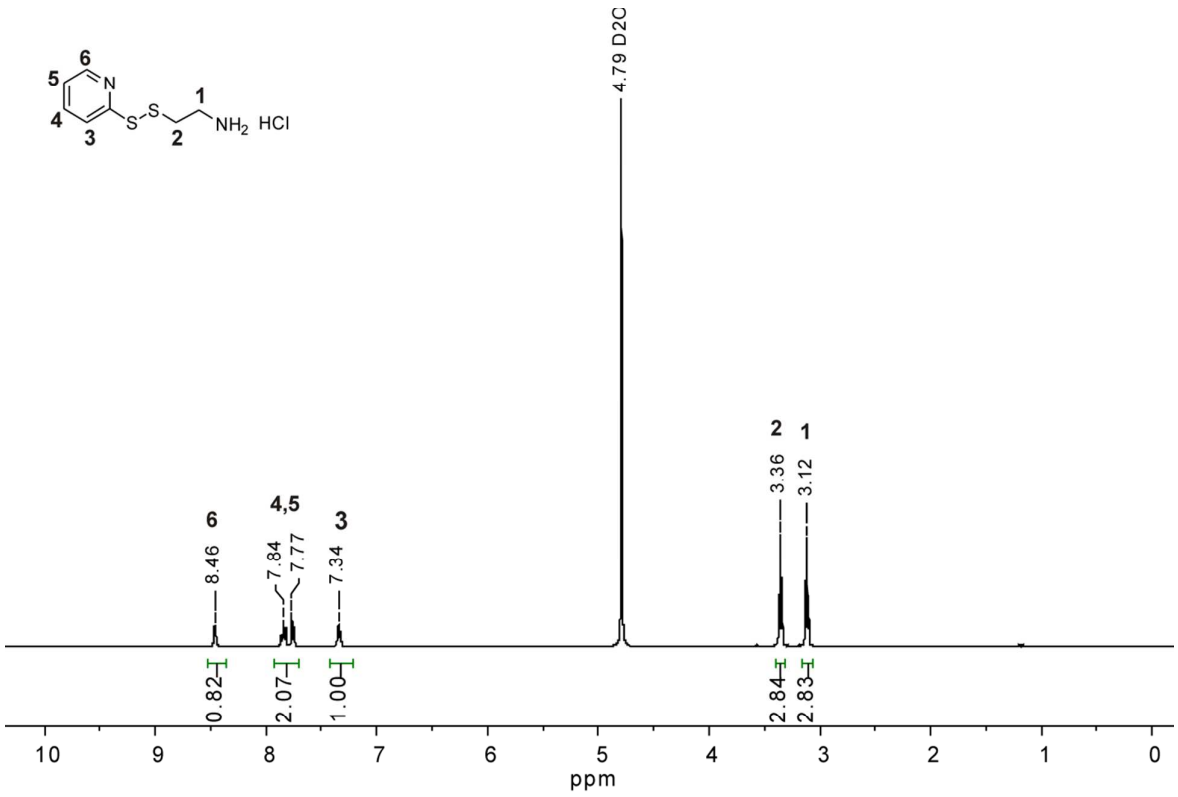


Figure S3. ^{1}H-NMR spectrum of 2-(pyridyldithio)-ethylamine (PDA) in D_2O.

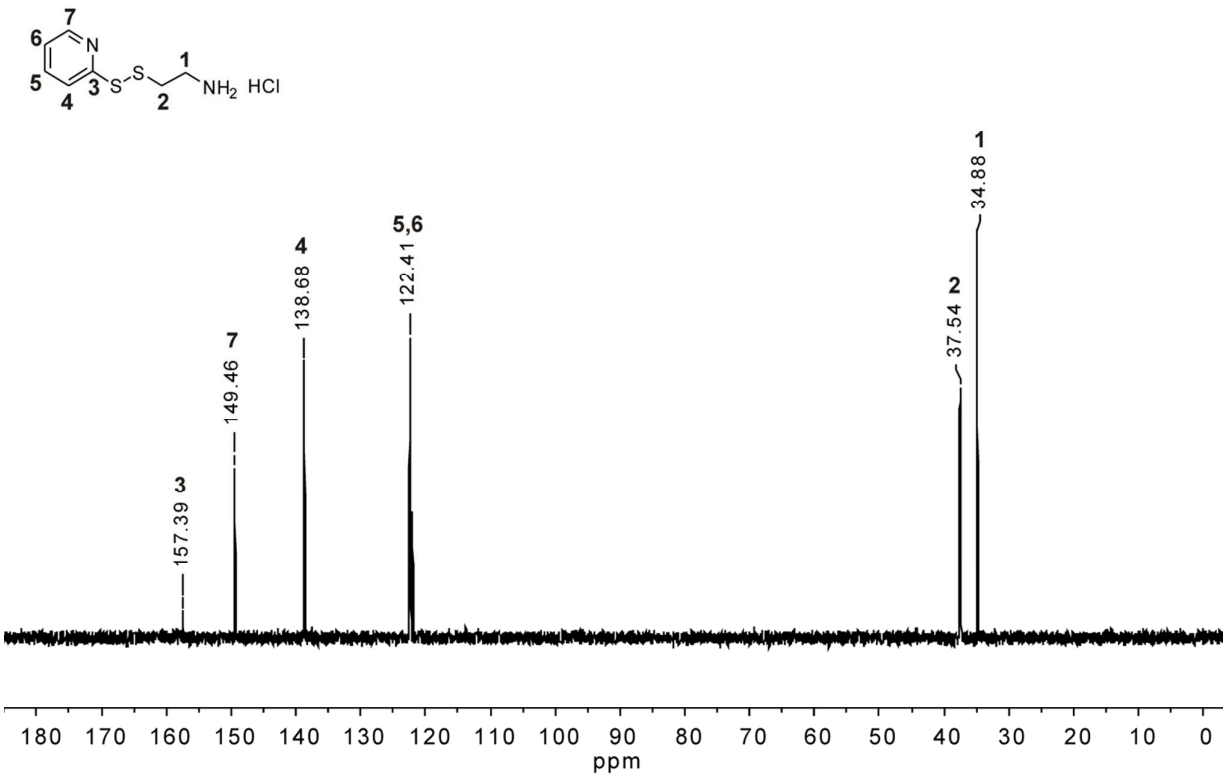


Figure S4. ^{13}C-NMR spectrum of 2-(pyridyldithio)-ethylamine (PDA) in D_2O.

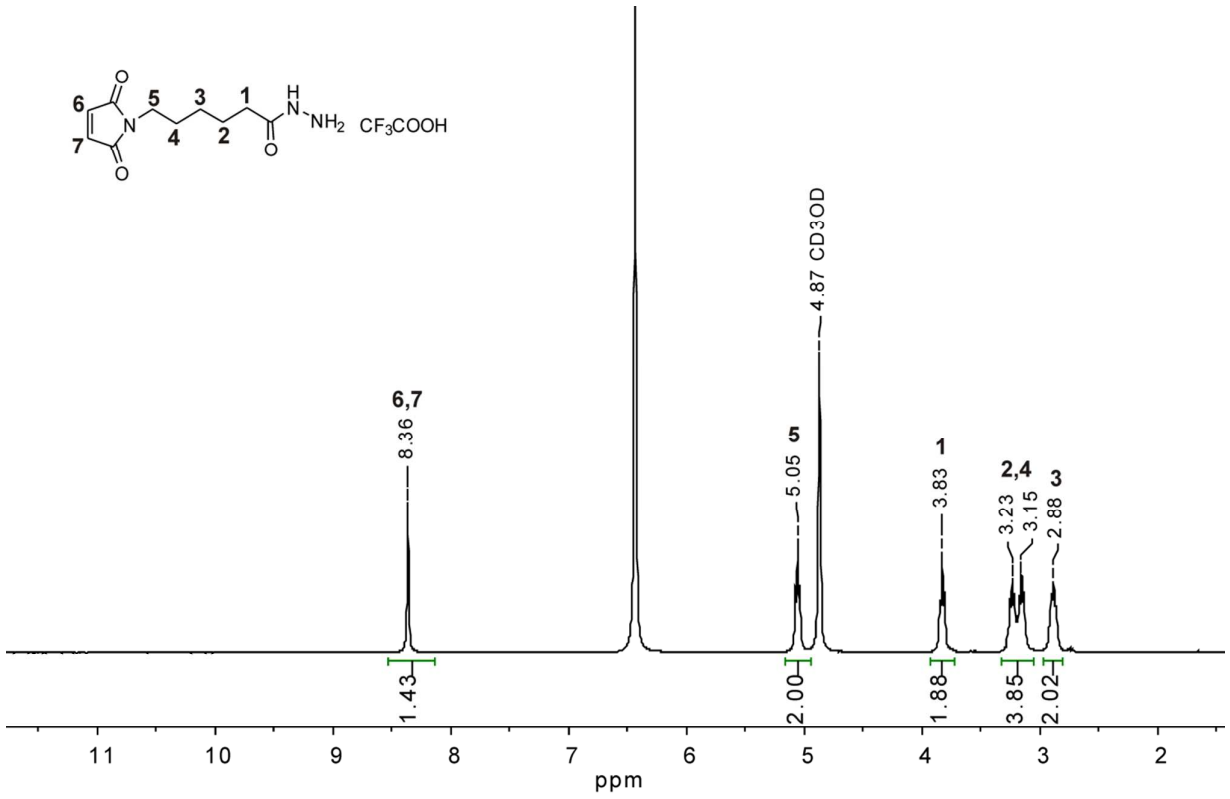


Figure S5. ^{1}H-NMR spectrum of 6-maleimidocaproic acid hydrazide trifluoroacetic acid salt in CD_3OD.

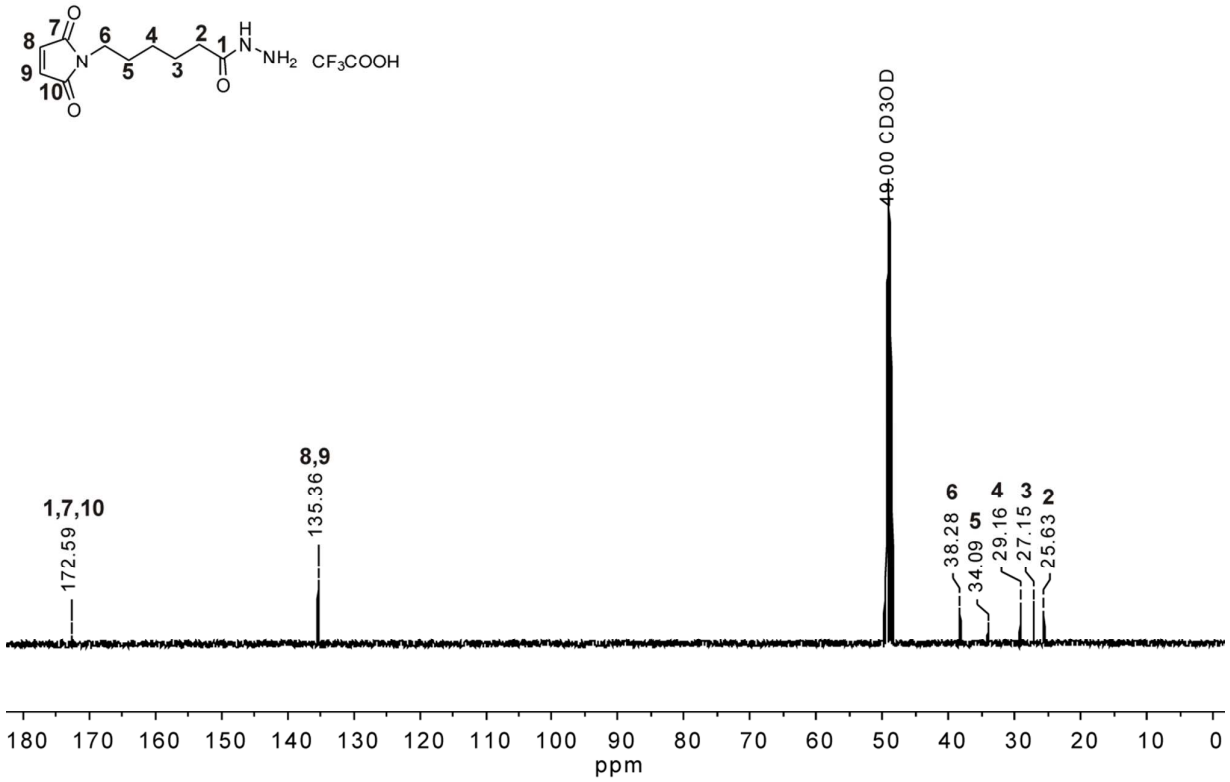


Figure S6. ^{13}C-NMR spectrum of 6-maleimidocaproic acid hydrazide trifluoroacetic acid salt in CD_3OD.

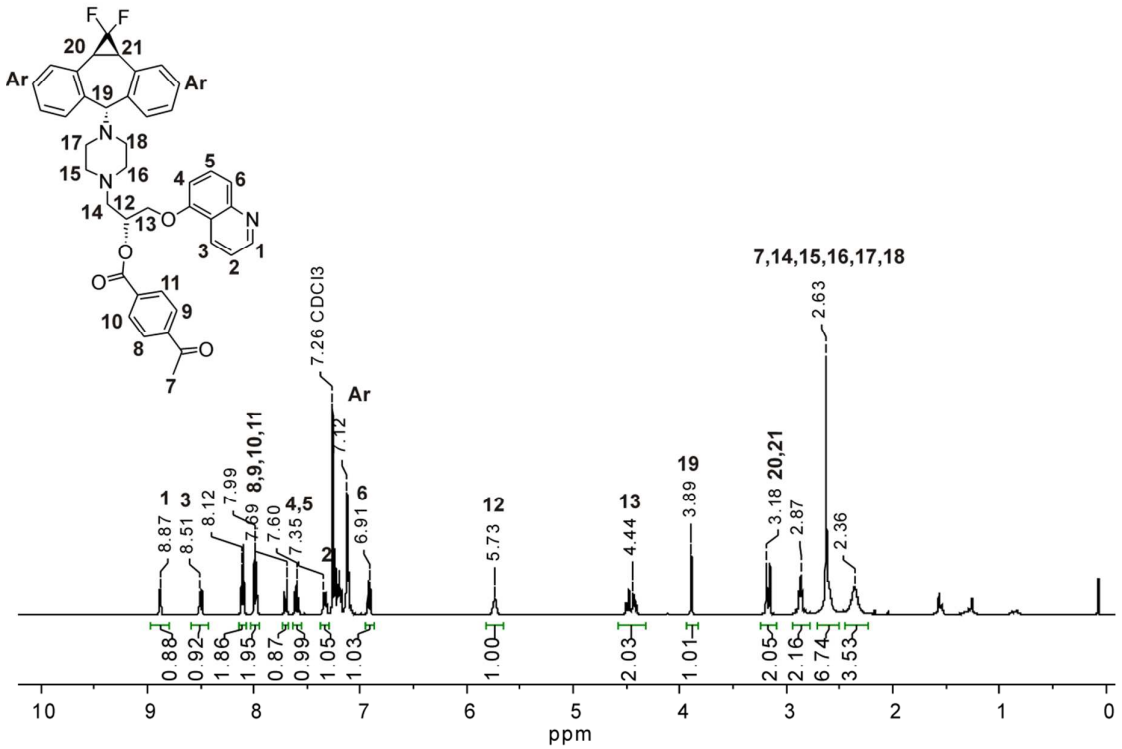


Figure S7. ^{1}H-NMR spectrum of Zos-Ket in $CDCl_3$.

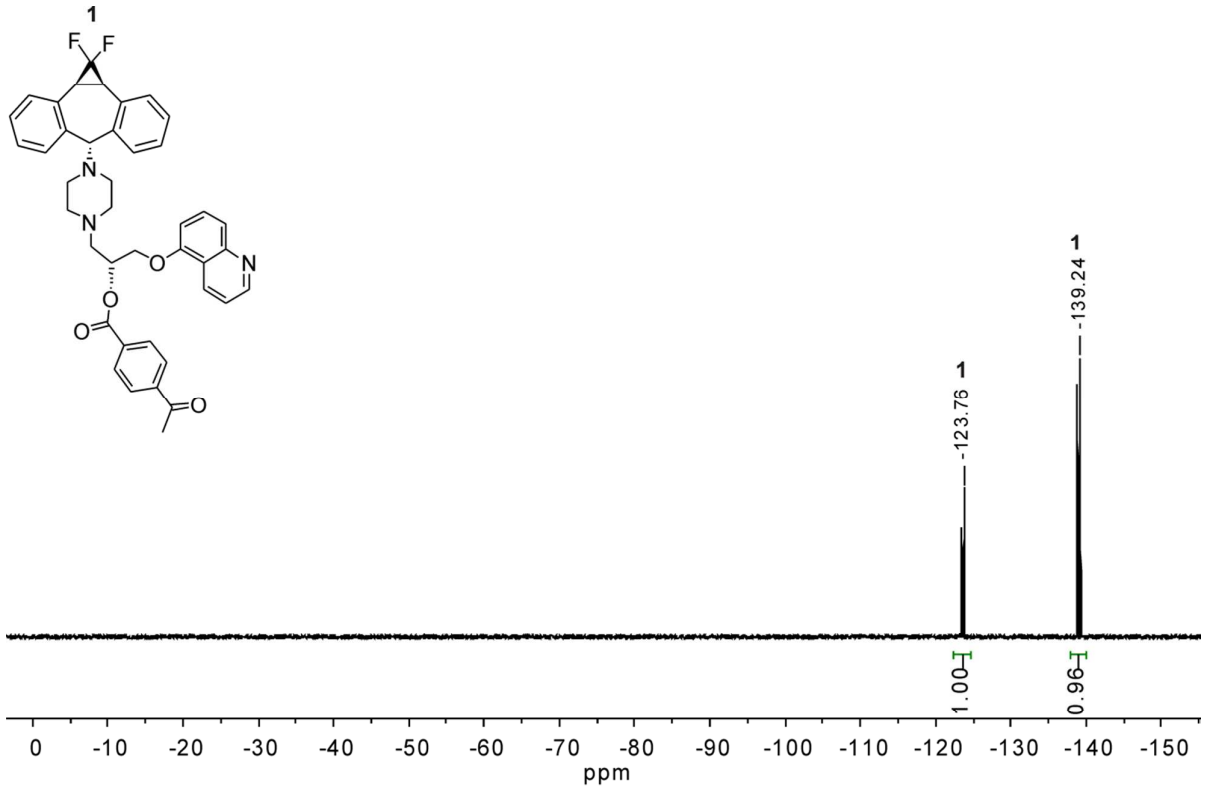


Figure S8. ^{19}F-NMR spectrum of Zos-Ket in $CDCl_3$.

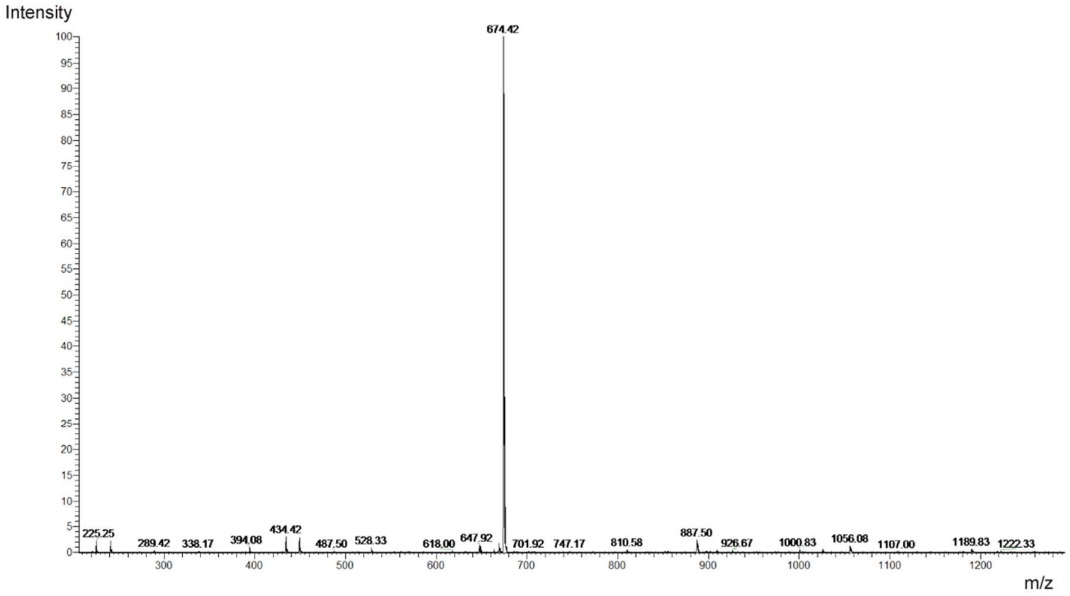


Figure S9. ESI-MS spectrum of Zos-Ket, exact mass [M] = 673.28, measured [M+H$^+$] = 674.72.

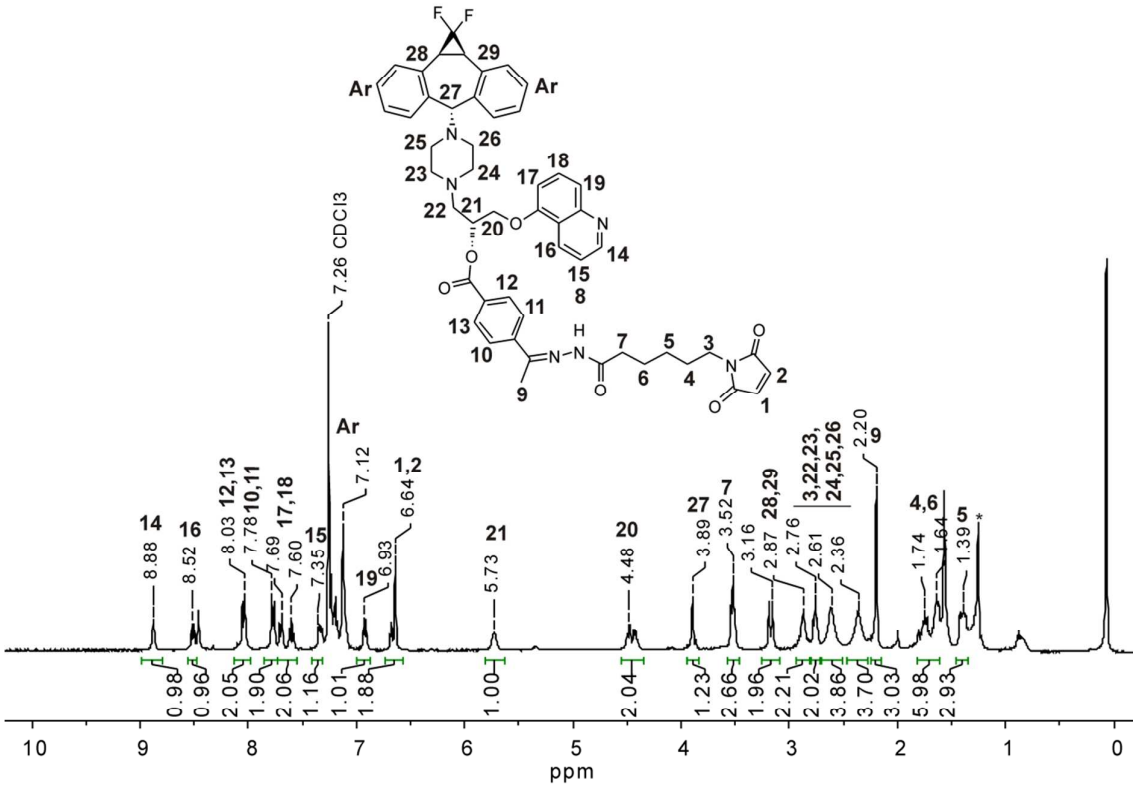


Figure S10. ^{1}H-NMR spectrum of Zos-Mal in $CDCl_3$. (* = Solvent impurity).

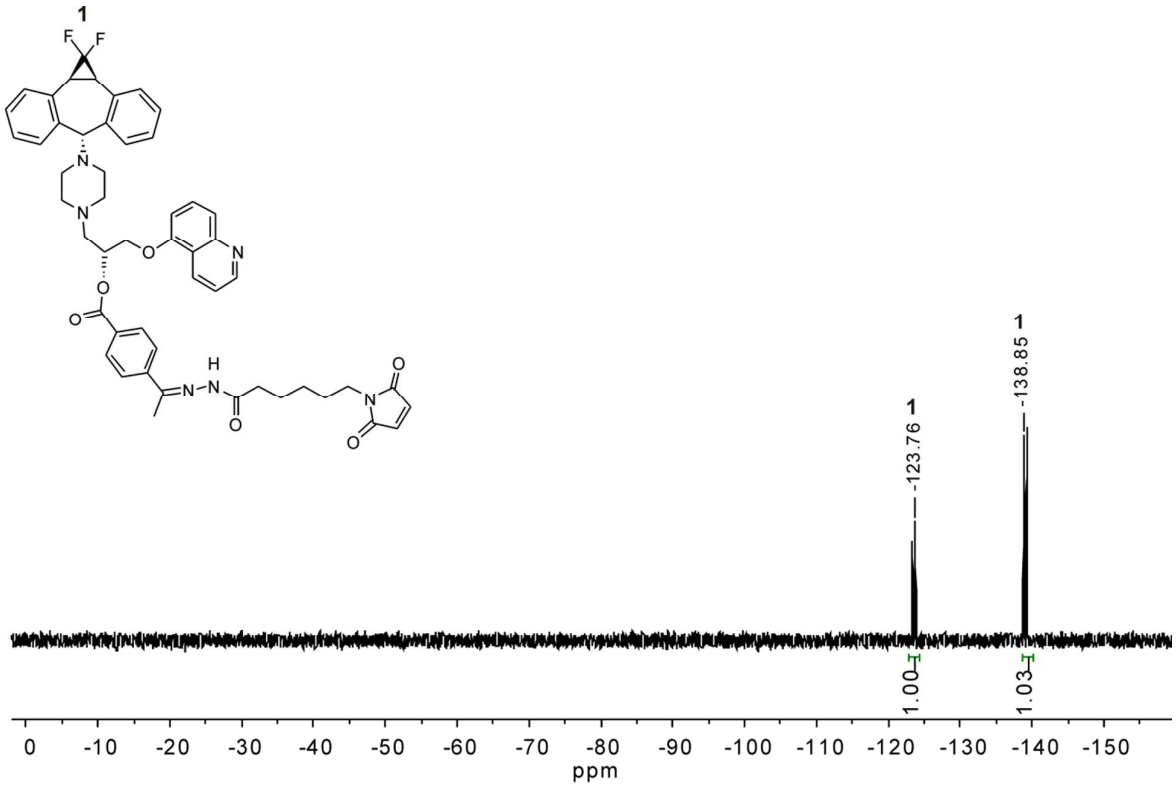


Figure S11. ^{19}F-NMR spectrum of Zos-Mal in $CDCl_3$.

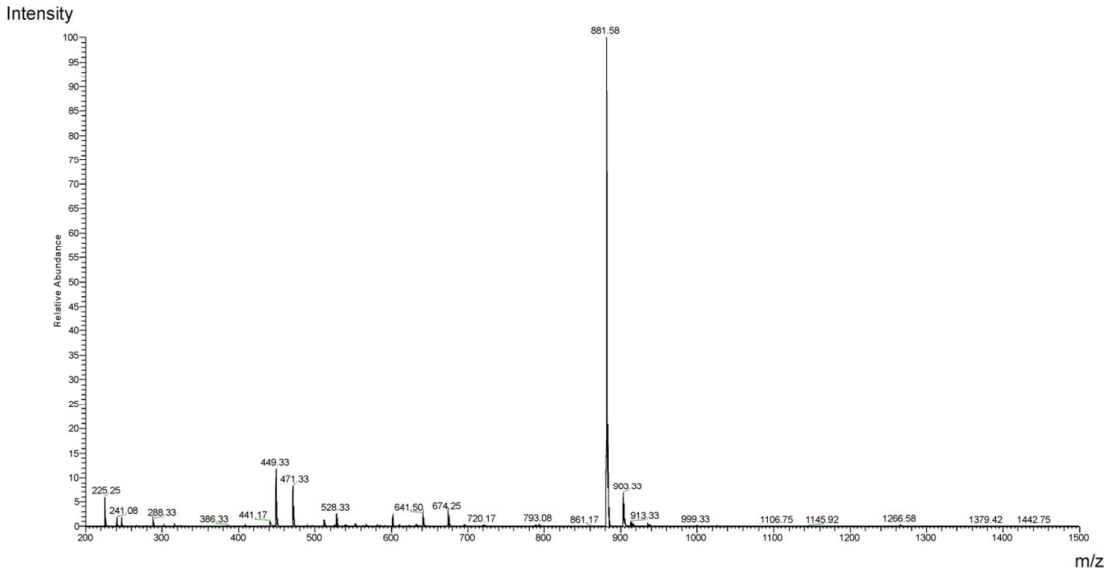


Figure S12. ESI-MS spectrum of Zos-Mal, exact mass [M] = 880.4, measured [$M+H^+$] = 881.6.

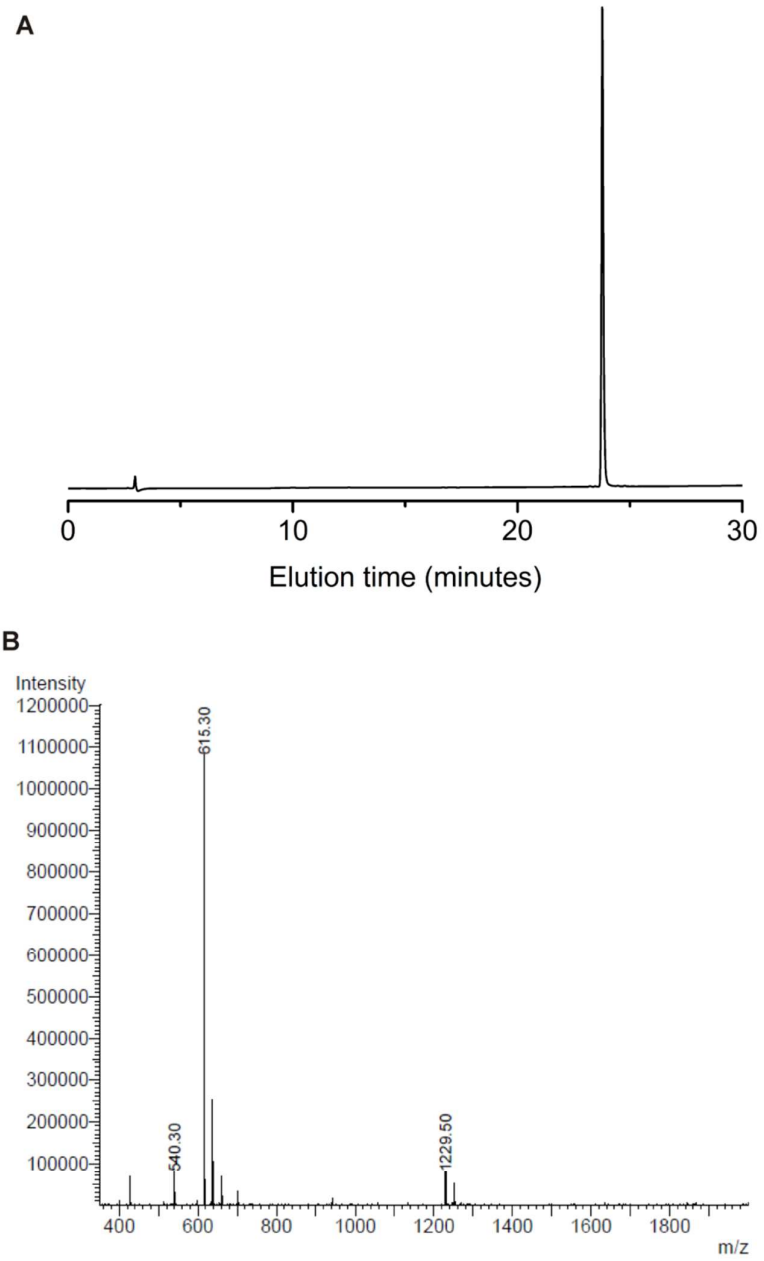


Figure S13. (A) RP-HPLC chromatogram and (B) ESI-MS spectrum of Fmoc-GFLG-OH, exact mass [M] = 614.3, measured [M+H$^+$] = 615.3, [M+Na$^+$] = 637.5.

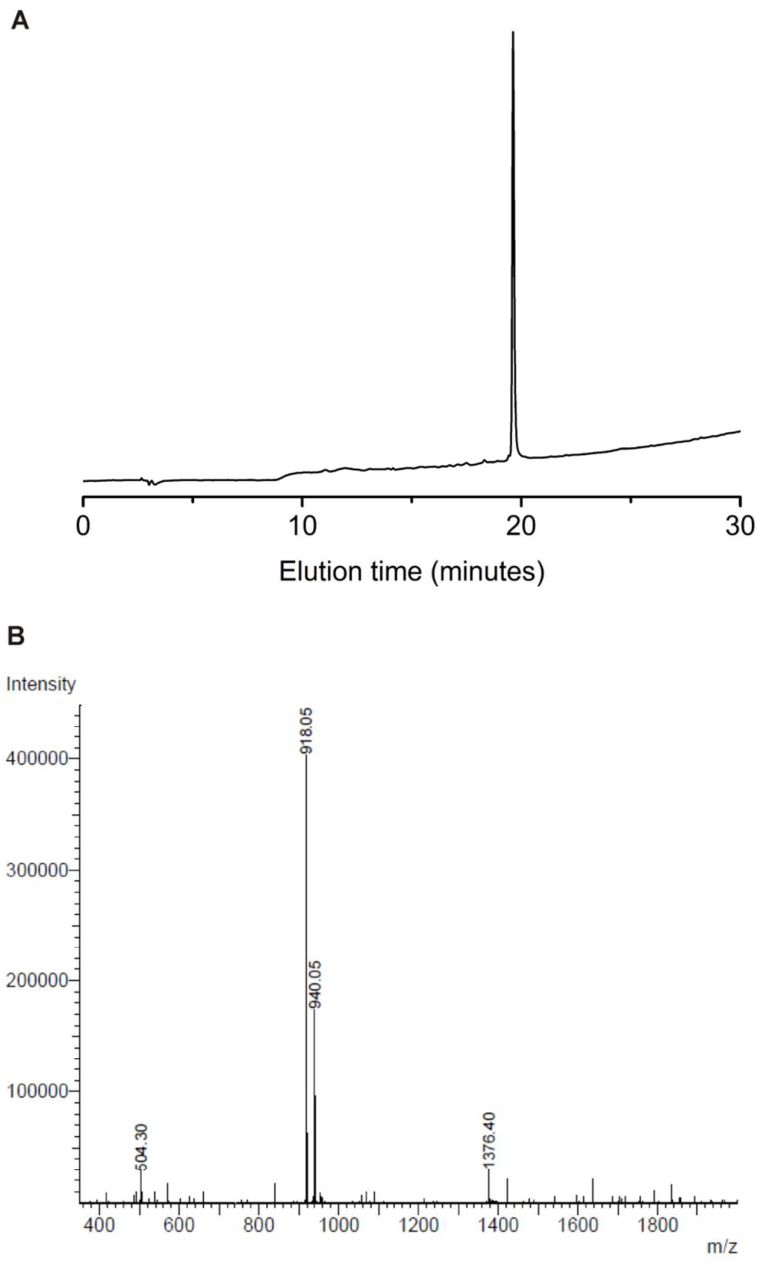


Figure S14. (A) RP-HPLC chromatogram and (B) ESI-MS spectrum of NH_2-GFLG-Dox, exact mass [M] = 917.4, measured [M+H^+] = 918.1, [M+Na^+] = 940.1.

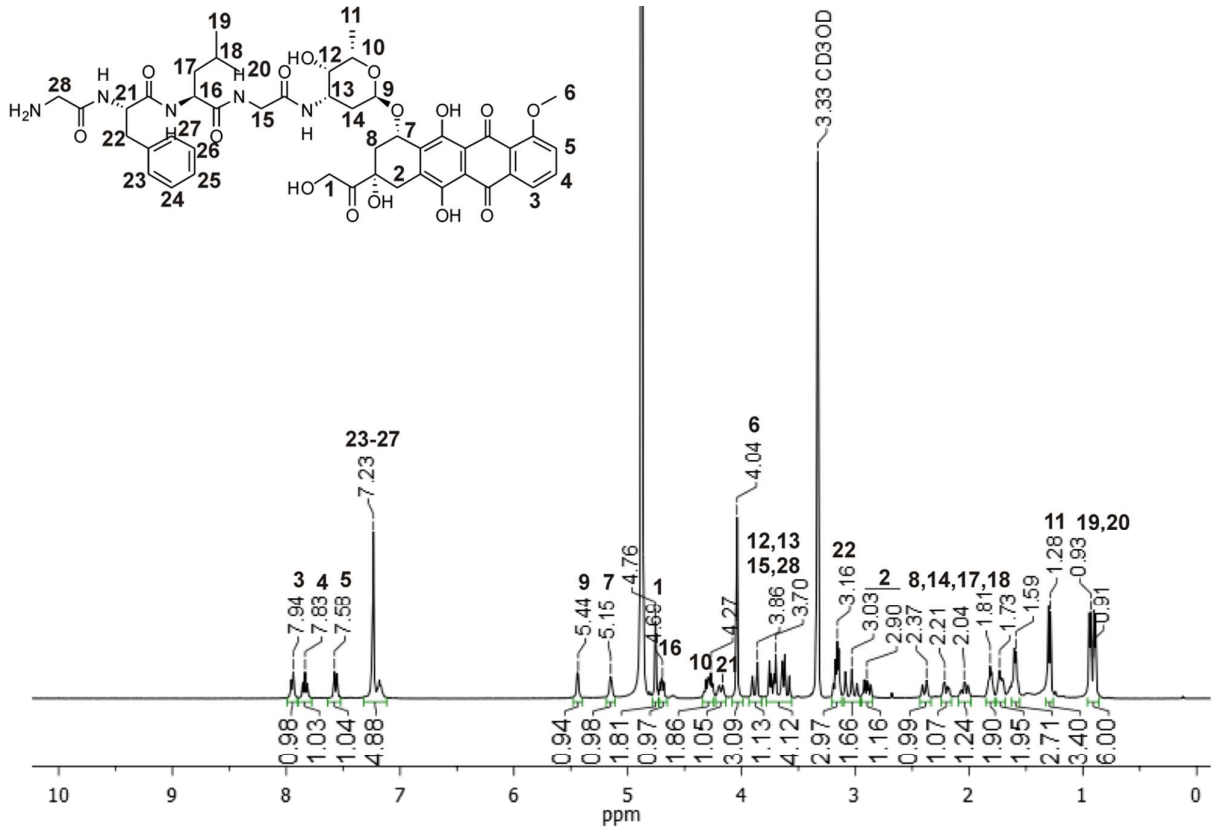


Figure S15. ^{1}H-NMR spectrum of NH_2-GFLG-Dox in MeOD.

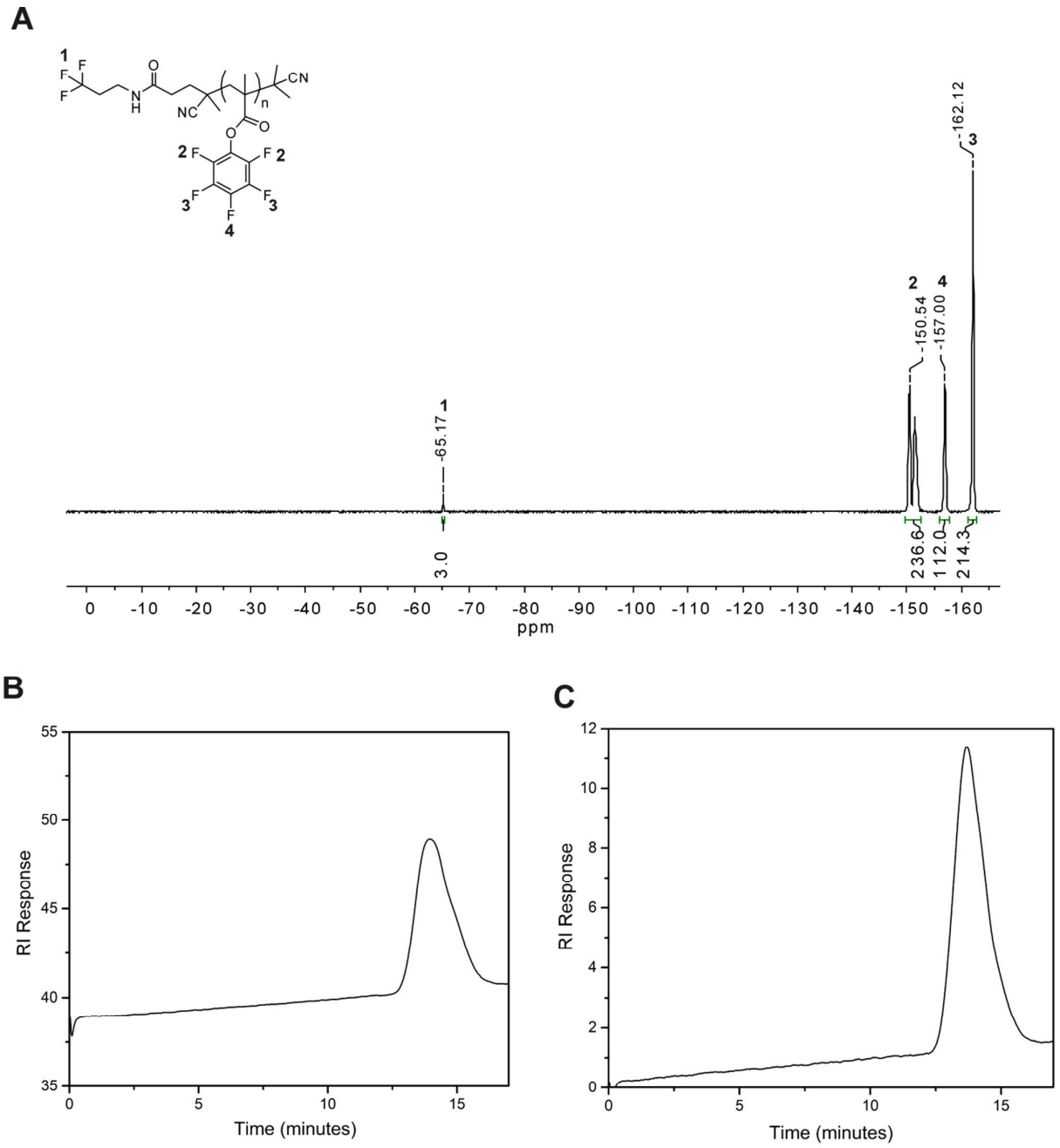


Figure S16. (A) ^{19}F-NMR spectrum of PPFMA-2 in $CDCl_3$. SEC plots of (B) PPFMA-1 and (C) PPFMA-2 in THF.

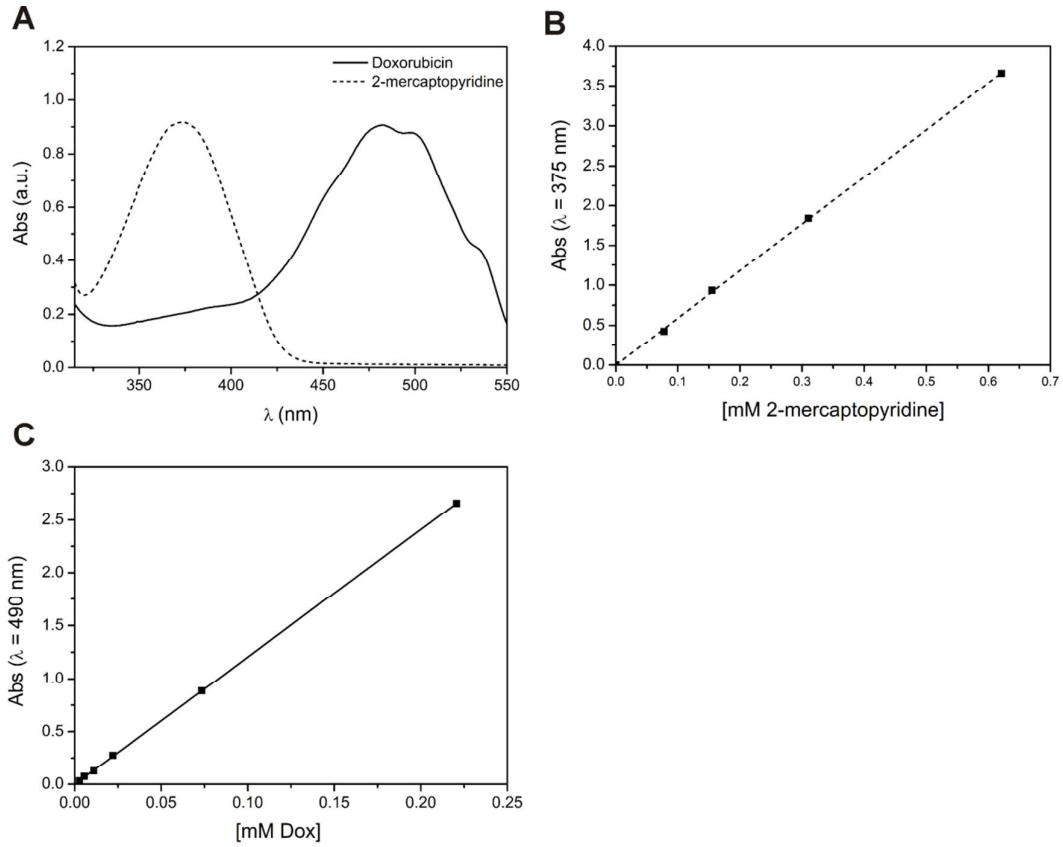


Figure S17. (A) UV spectra of a 0.15 mM solution of 2-mercaptopyridine and a 0.074 mM solution of Dox in DMSO; (B) calibration curve of 2-mercaptopyridine at λ_{max} = 375 nm in DMSO (ε = 5898.6 cm^{-1} M^{-1}); (C) calibration curve of Dox at λ_{max} = 490 nm in DMSO (ε = 12049.6 cm^{-1} M^{-1}) (optical length = 1 cm).

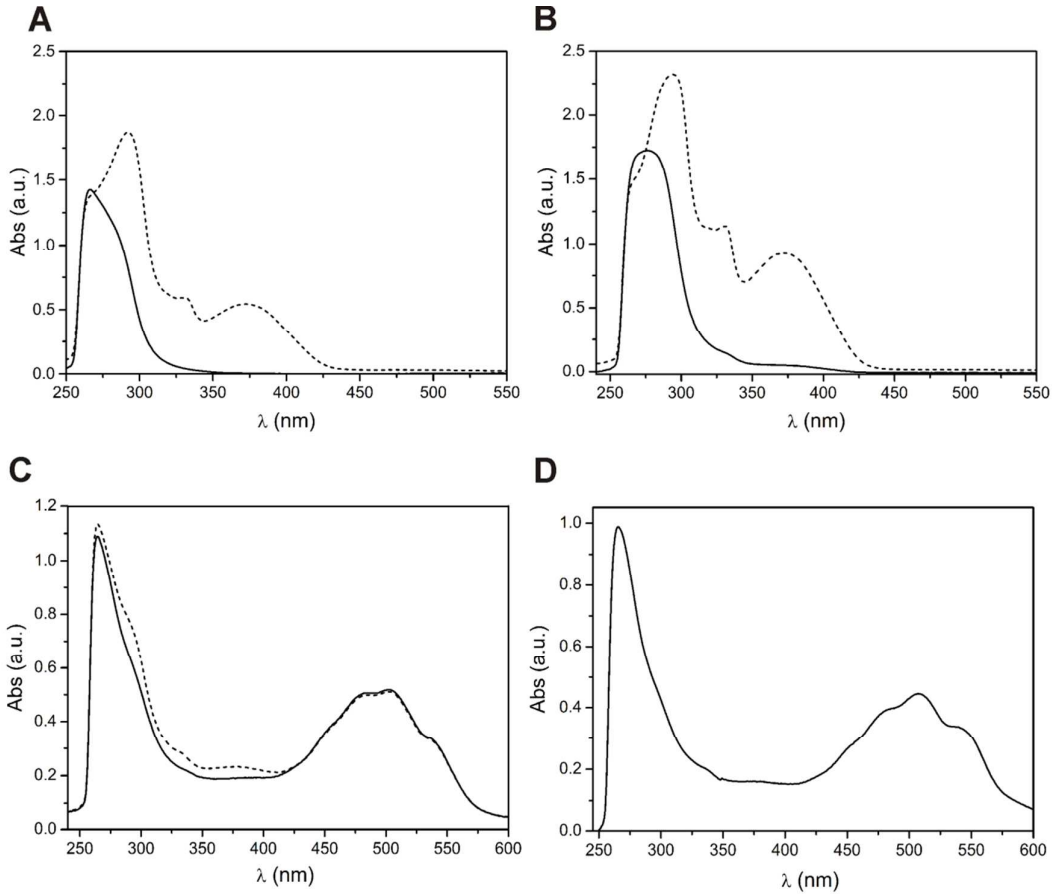


Figure S18. Examples of UV spectra of (A) 0.57 mg/mL **PHPMA-PDA-1**, (B) 0.53 mg/mL **PHPMA-PDA-2** and (C) 0.18 mg/mL **PHPMA-Dox-PDA** solutions in DMSO before (continuous lines) and after (dashed lines) PDA cleavage. (D) UV spectra of 0.2 mg/mL **PHPMA-Dox** solution in DMSO. The absorbance peak at λ= 375 nm is characteristic of the released 2-mercaptopyridine whereas the peak at λ = 490 nm is characteristic of Dox.

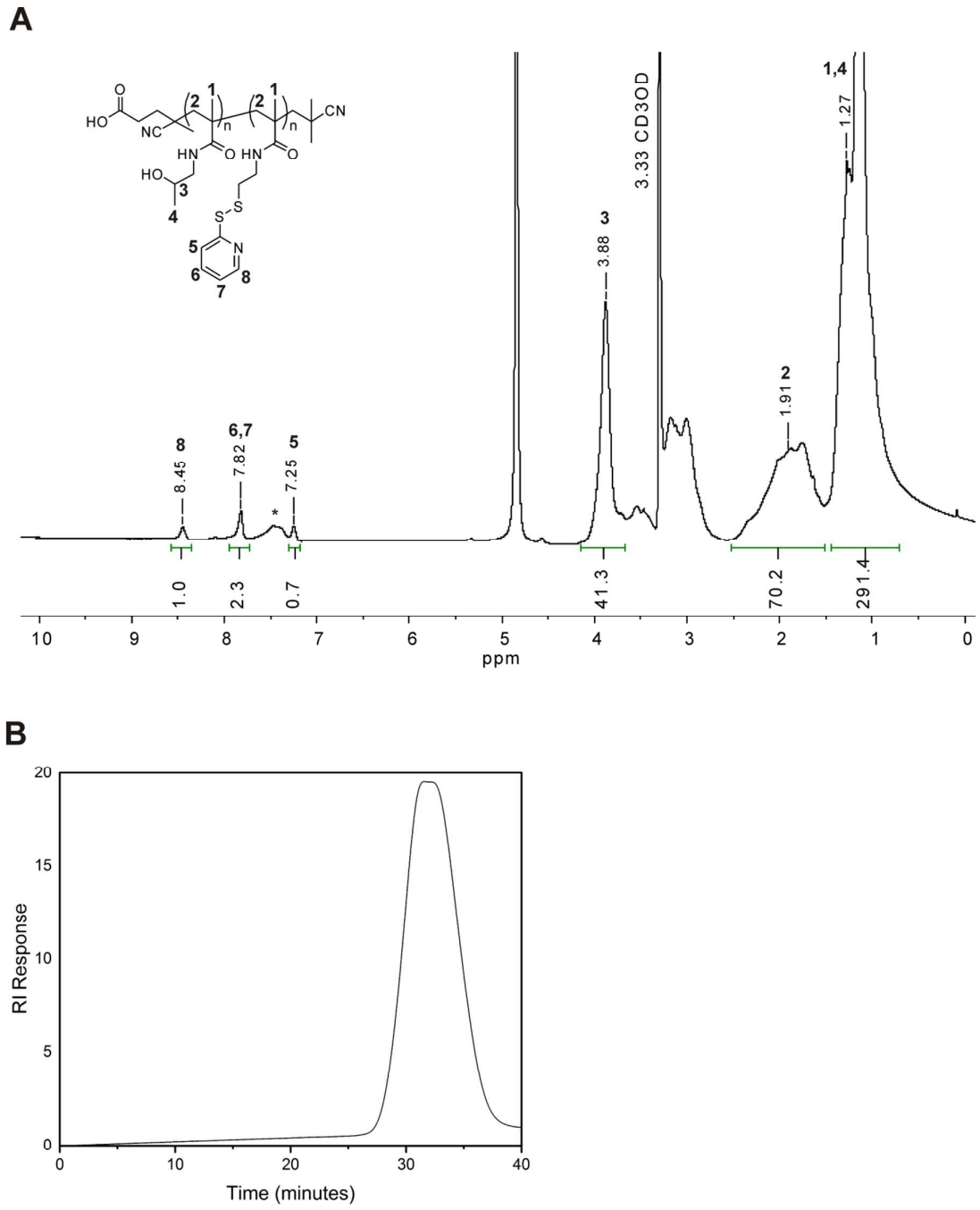


Figure S19. (A) ^{1}H-NMR spectrum of **PHPMA-PDA-1** in CD_3OD. To calculate the mol % of PDA incorporated in the polymer backbone the integrals of the PDA signals at 8.45 ppm (**8,** 1H**)**, at 7.82 ppm (**6,7**, 2H**)** and at 7.25 ppm (**5**, 1H) were averaged and compared to the integrals of the polymer signals at 3.88 ppm (**3**), at 1.91 ppm (**2**) and at 1.27 ppm (**1,4**). The result is reported as an average of the mol % obtained using the three different polymer signals. * = peaks associated with the amide protons of the polymer side chains. (B) SEC plot of **PHPMA-PDA-1** in DMF.

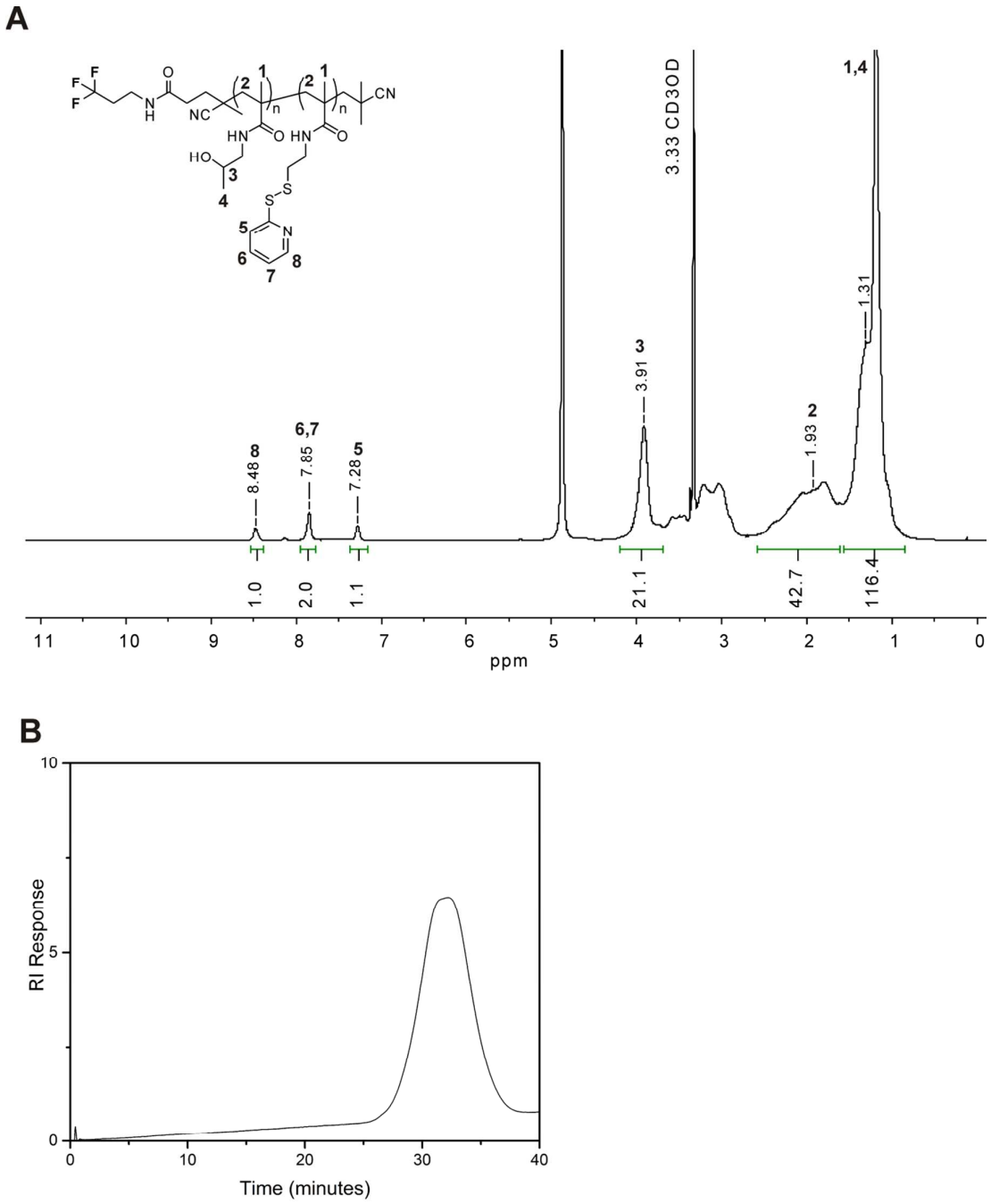


Figure S20. (A) ^{1}H-NMR spectrum of **PHPMA-PDA-2** in CD_3OD. To calculate the mol % of PDA incorporated in the polymer backbone the integrals of the PDA signals at 8.48 ppm (**8,** 1H**)**, at 7.85 ppm (**6,7**, 2H**)** and at 7.28 ppm (**5**, 1H) were averaged and compared to the integrals of the polymer signals at 3.91 ppm (**3**), at 1.93 ppm (**2**) and at 1.31 ppm (**1,4**). The result is reported as an average of the mol % obtained using the three different polymer signals. (B) SEC plot of **PHPMA-PDA-2** in DMF.

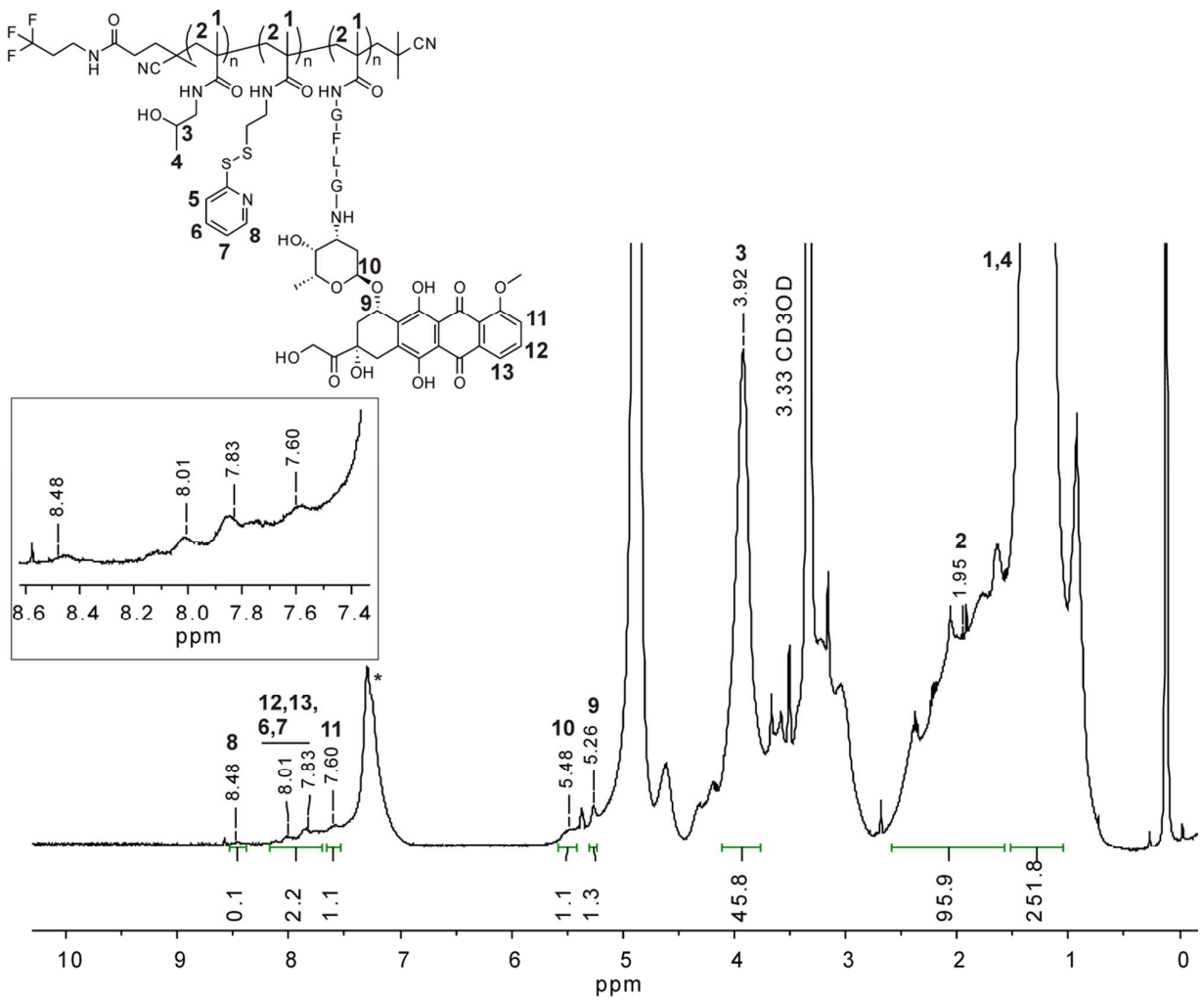


Figure S21. ^{1}H-NMR spectrum of **PHPMA-Dox-PDA** in CD_3OD. To calculate the mol % of PDA and Dox incorporated in the polymer backbone the integral of the PDA signal at 8.48 ppm (**8**, 1H**)**, and the average of the integrals of the Dox signals at 8.01-7.83 ppm (**12,13** 2H-Dox and **6,7** 2H-PDA), at 7.60 ppm (**11**, 1H), at 5.48 ppm (**10**, 1H**)** and at 5.26 ppm (**9**, 1H) were compared to the integrals of the polymer signals at 3.92 ppm (**3**), at 1.95 ppm (**2**) and at 1.27 ppm (**1,4**). The NH_2-GFLG-Dox-derived signals (**Figure S 15**) overlapping with that of the polymer were subtracted from the signals of the polymer (**3**, **2** and **1**,**4**) used for the calculation. The result is reported as an average of the mol % obtained using the three different polymer signals. * = peaks associated with the amide protons of the polymer side chains and with the amide and aromatic protons of the GFLG linker.

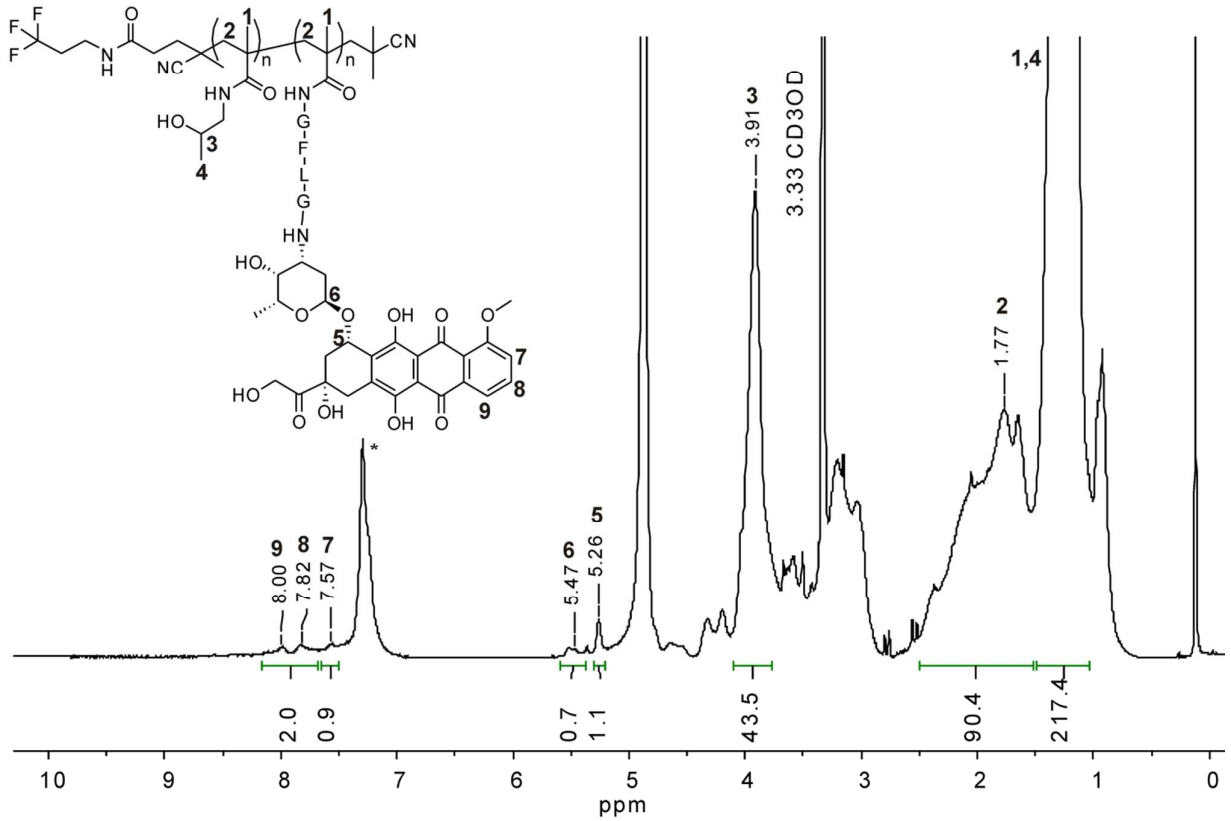


Figure S22. ^{1}H-NMR spectrum of **PHPMA-Dox** in CD_3OD. To calculate the mol % of Dox incorporated in the polymer backbone the integrals of the Dox signals at 8.00 ppm (**9**, 1H), at 7.82 ppm (**8**, 1H), 7.57 ppm (**7**, 1H), at 5.47 ppm (**6**, 1H) and at 5.26 ppm (**5**, 1H) were averaged and compared to the integrals of the polymer backbone signals at 3.91 ppm (**3**), at 1.77 ppm (**2**) and at 1.27 ppm (**1,4**). The NH_2-GFLG-Dox-derived signals (**Figure S15**) overlapping with that of the polymer were subtracted from the signals of the polymer (**3**, **2** and **1,4**) used for the calculation. The result is reported as an average of the mol % obtained using the three different polymer signals. * = peaks associated with the amide protons of the polymer side chains and with the amide and aromatic protons of the GFLG linker.

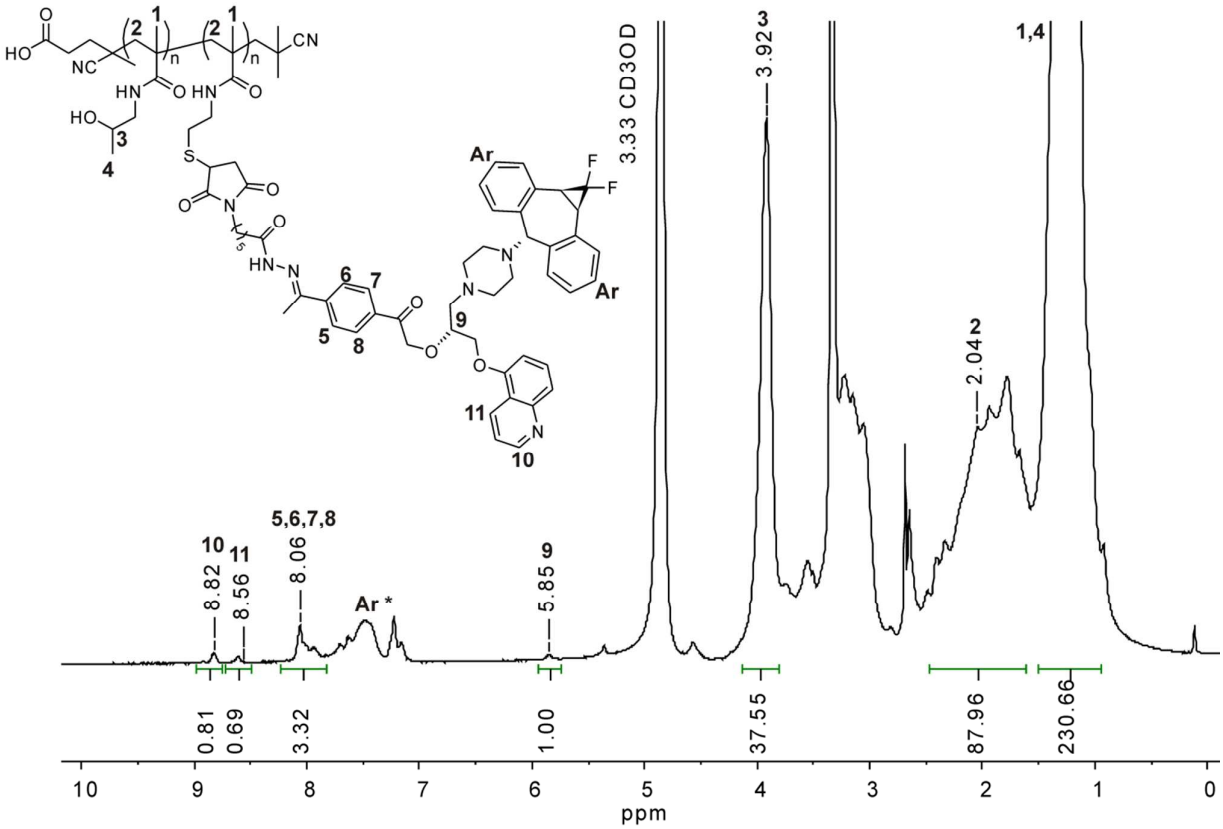


Figure S23. ^{1}H-NMR spectrum of **PHPMA-Zos-1** in CD_3OD. To calculate the mol % of Zos incorporated in the polymer backbone the integrals of the Zos signals at 8.81 ppm (**10**, 1H), 8.60 ppm (**12**, 1H), and at 5.84 ppm (**9**, 1H) were averaged and compared to the integrals of the polymer signals at 3.94 ppm (**3**), at 2.14 ppm (**2**) and at 1.31 ppm (**1,4**). The Zos Mal-derived signals (**Figure S10**) overlapping with that of the polymer backbone were subtracted from the signals of the polymer (**3, 2** and **1,4**) used for the calculation. The result is reported as an average of the mol % obtained using the three different polymer signals. * = peaks associated with the protons of the amide groups in the polymer side chains.

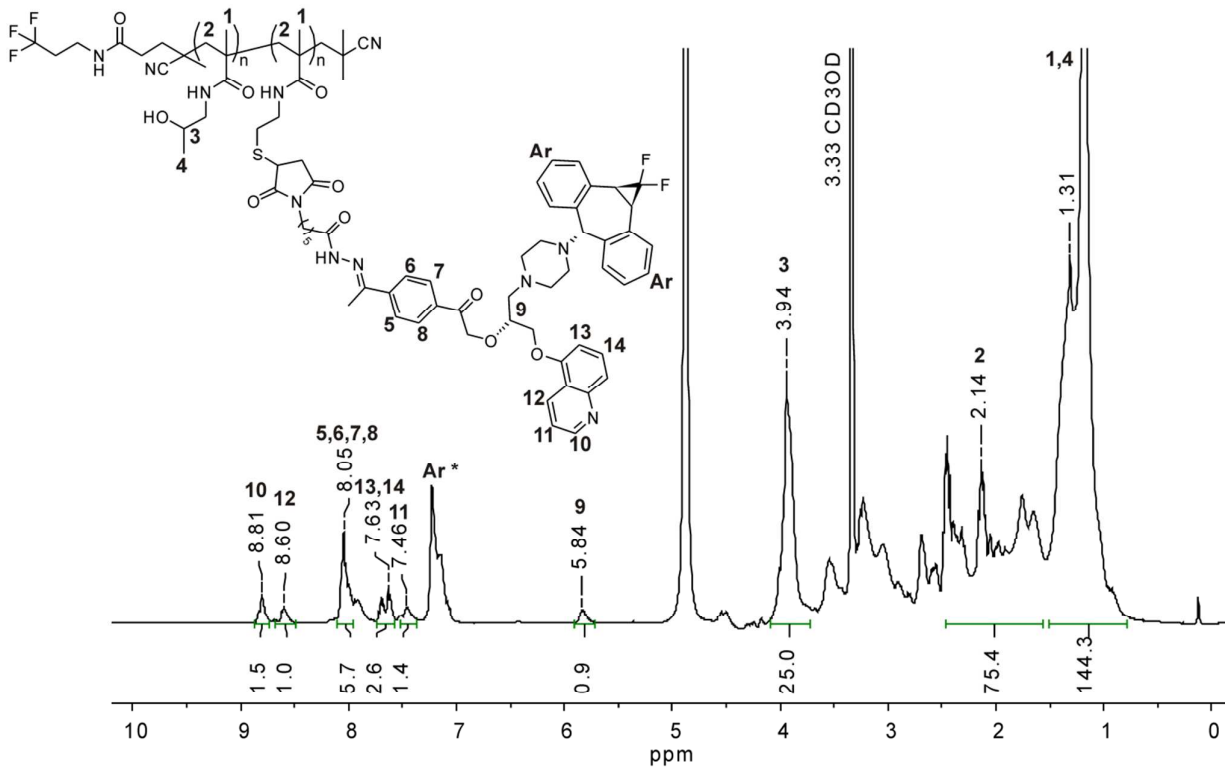


Figure S24. ^{1}H-NMR spectrum of **PHPMA-Zos-2** in CD_3OD. To calculate the mol % of Zos incorporated in the polymer backbone the integrals of the Zos signals at 8.82 ppm (**10**, 1H), at 8.56 ppm (**11**, 1H), and at 5.85 ppm (**9**, 1H) were averaged and compared to the integrals of the polymer signals at 3.92 ppm (**3**), at 2.04 ppm (**2**) and at 1.31 ppm (**1,4**). The Zos Mal-derived signals (**Figure S10**) overlapping with that of the polymer backbone were subtracted from the signals of the polymer (**3, 2** and **1,4**) used for the calculation. The result is reported as an average of the mol % obtained using the three different polymer signals. * = peaks associated with the protons of the amide groups in the polymer side chains.

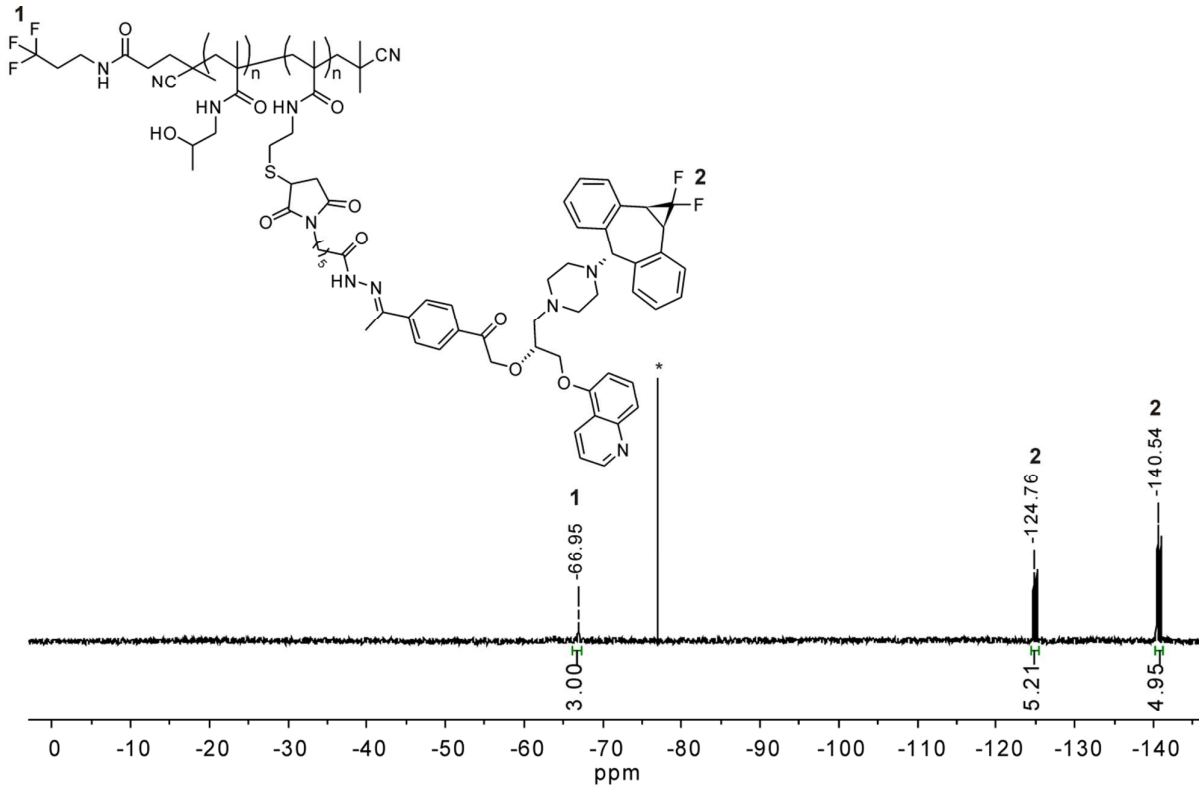


Figure S25. ^{19}F-NMR spectrum of **PHPMA-Zos-2** in CD_3OD (* = TFA). To calculate the mol % of Zos incorporated in the polymer backbone the integrals of the Zos signals at -124.76 ppm (**2**, 1F) and at -140.54 ppm (**2**, 1F) were compared to the integrals of the polymer end group signal at -66.95 ppm (**1**, 3F) and the result was related to the degree of polymerization (DP) determined by SEC of the **PPFMA-2** polymer precursor. The result is reported as an average of the mol % obtained using the two Zos signals.

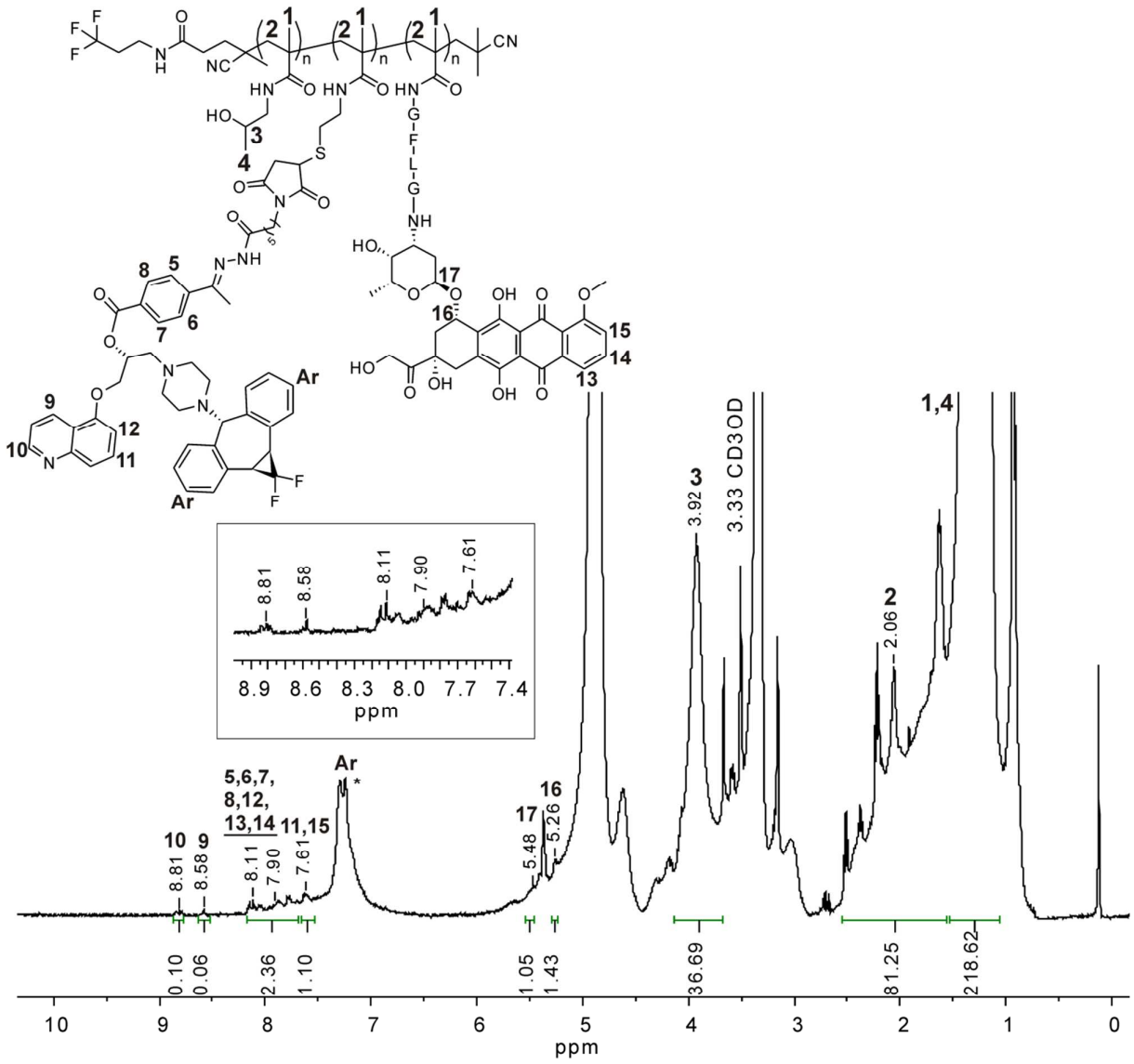


Figure S26. ^{1}H-NMR spectrum of **PHPMA-Dox-Zos** in CD_3OD. To calculate the mol % of Dox and Zos incorporated in the polymer backbone the integrals of the Dox signal at 7.61 ppm (**15**, 1H-Dox and **11**, 1H-Zos) and the average of the integrals of the Zos signals at 8.81 ppm (**10**, 1H**)** and at 8.85 ppm (**9**, 1H**)** were compared to the integrals of the polymer signals at 3.92 ppm (**3**), at 2.06 ppm (**2**) and at 1.27 ppm (**1,4**). The NH_2-GFLG-Dox-derived signal (**Figure S15**) and the Zos Mal-derived signals (**Figure S10**) overlapping with that of the polymer backbone were subtracted from the signal of the polymer (**3**, **2** and **1,4**) used for the calculation. The result is reported as an average of the mol % obtained using the three different polymer signals. * = peaks associated with the amide protons of the polymer side chains and with the amide and aromatic protons of the GFLG linker.

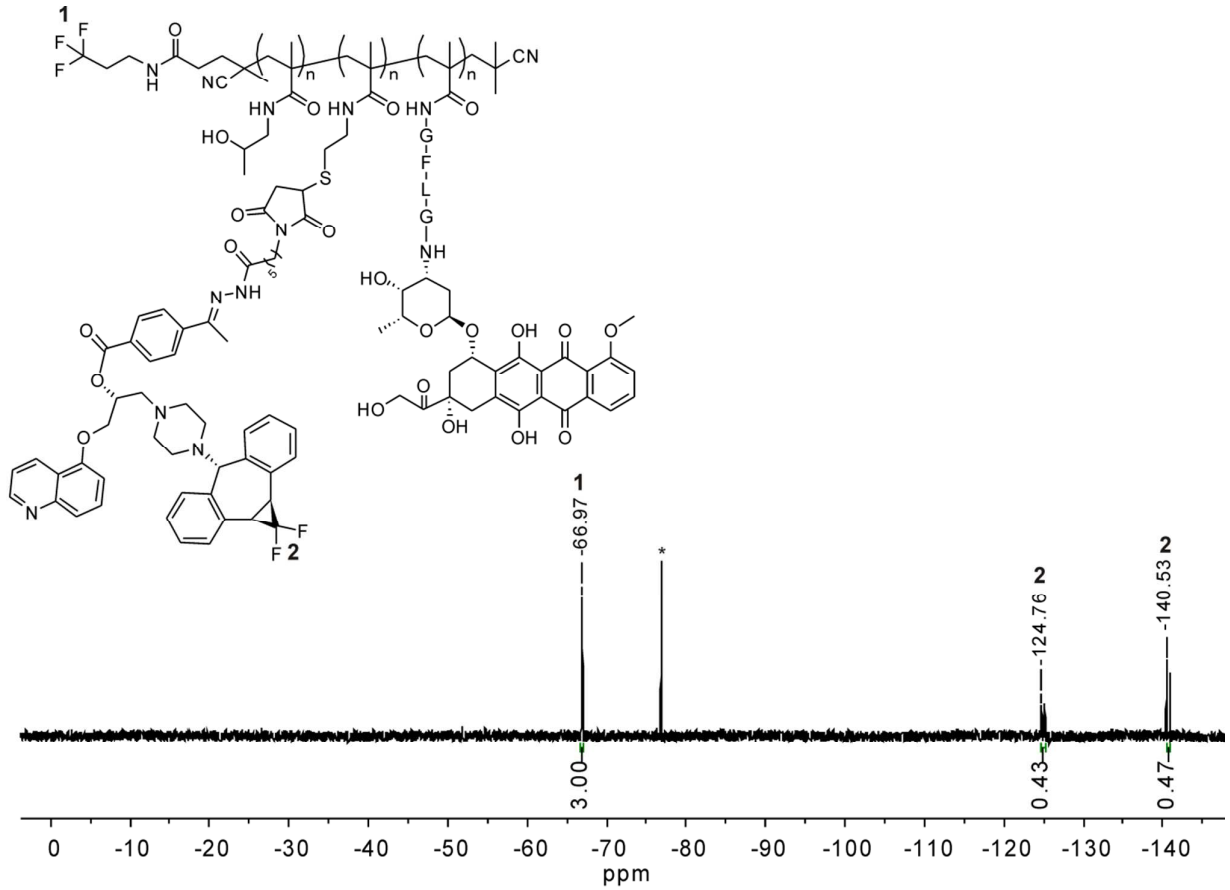


Figure S27. ^{19}F-NMR spectrum of **PHPMA-Dox-Zos** in CD_3OD (* = TFA). To calculate the mol % of Zos incorporated in the polymer backbone the integrals of the Zos signals at -124.76 ppm (**2**, 1F) and at -140.53 ppm (**2**, 1F) were compared to the integrals of the polymer end group signal at -66.97 ppm (**1**, 3F) and the result was related to the degree of polymerization of the PPFMA-2 polymer precursor determined by SEC. The result is reported as an average of the mol % obtained using the two Zos signals.

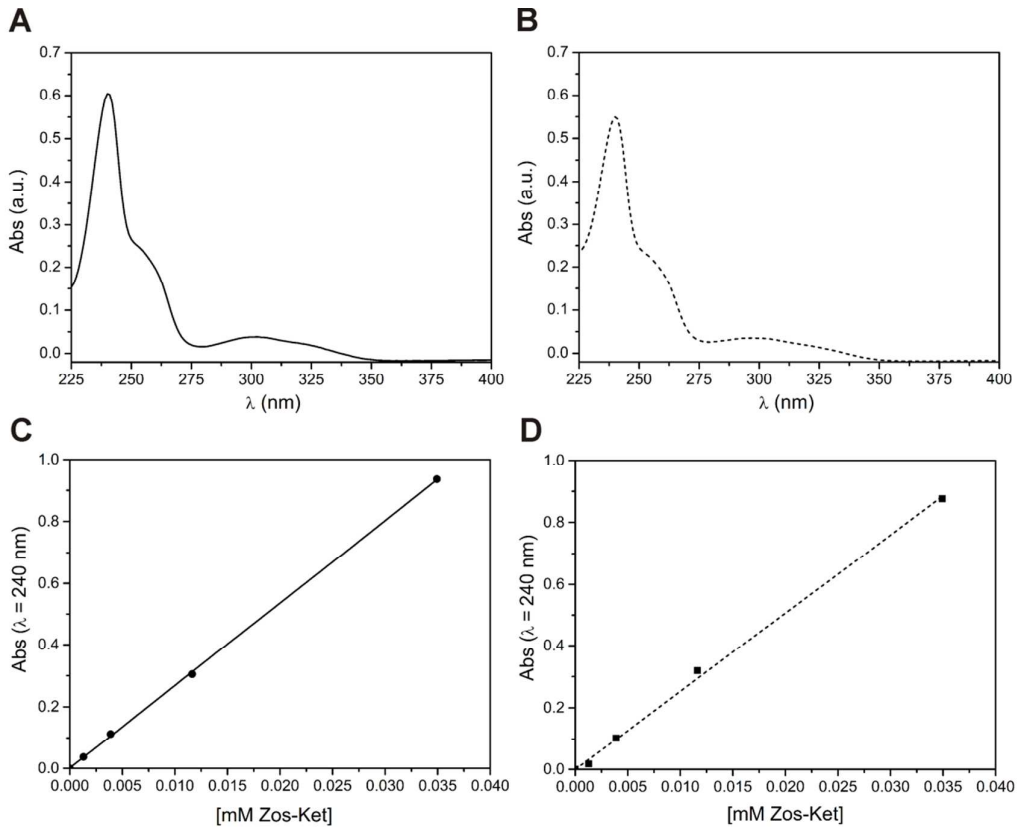


Figure S28. (A) UV spectra of a 0.22 mM solution of Zos-Ket in phosphate citrate buffer containing 30% ethanol at pH 7.4 and (B) 5.5 (optical path = 0.1 cm). (C) Calibration curves of Zos-Ket at λ_{max} = 240 nm in the same buffer solutions at pH 7.4 (ε = 26768 M^{-1} cm^{-1}) and (D) 5.5 (ε = 25313 M^{-1} cm^{-1}) (optical length = 1 cm).

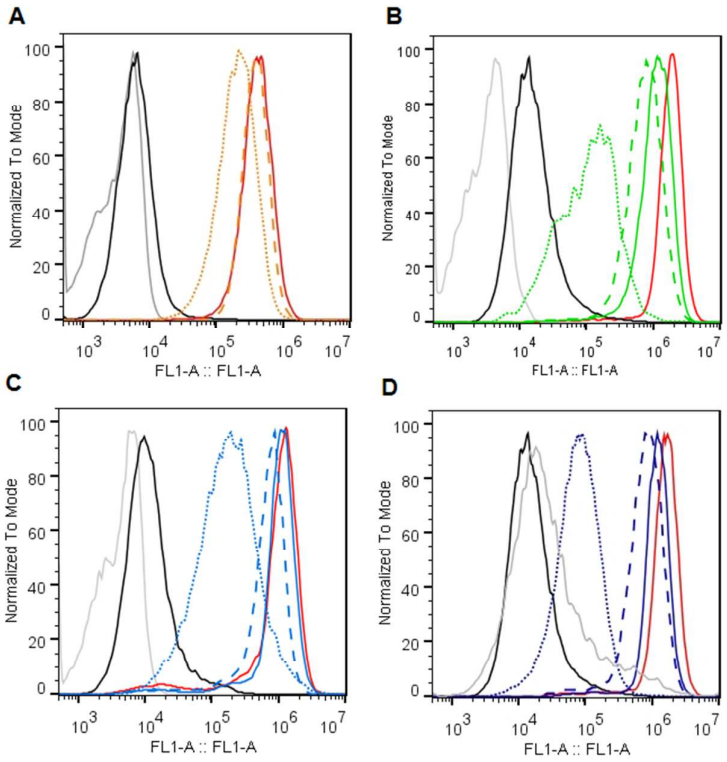


Figure S29. Flow cytometry analysis of ($DiOC_2(3)$) efflux inhibition from A2780ADR cells. CsA (red curve) was used as positive control and untreated cells (grey curves) were used as negative control. Black curves indicate the fluorescence of cells incubated at 37°C without inhibitors. (A) Incubation with Zos at 0.1 (dotted lines) and 1 (dashed lines) μM; (B) incubation with Zos-Ket at 0.1 (dotted lines), 1 (dashed lines) and 5 (continuous lines) μM. (C) Incubation with **PHPMA-Zos-1** and (D) **PHPMA-Zos-2** at 0.1 (dotted lines), 1 (dashed lines) and 5 (continuous lines) μM of polymer-bound drug.

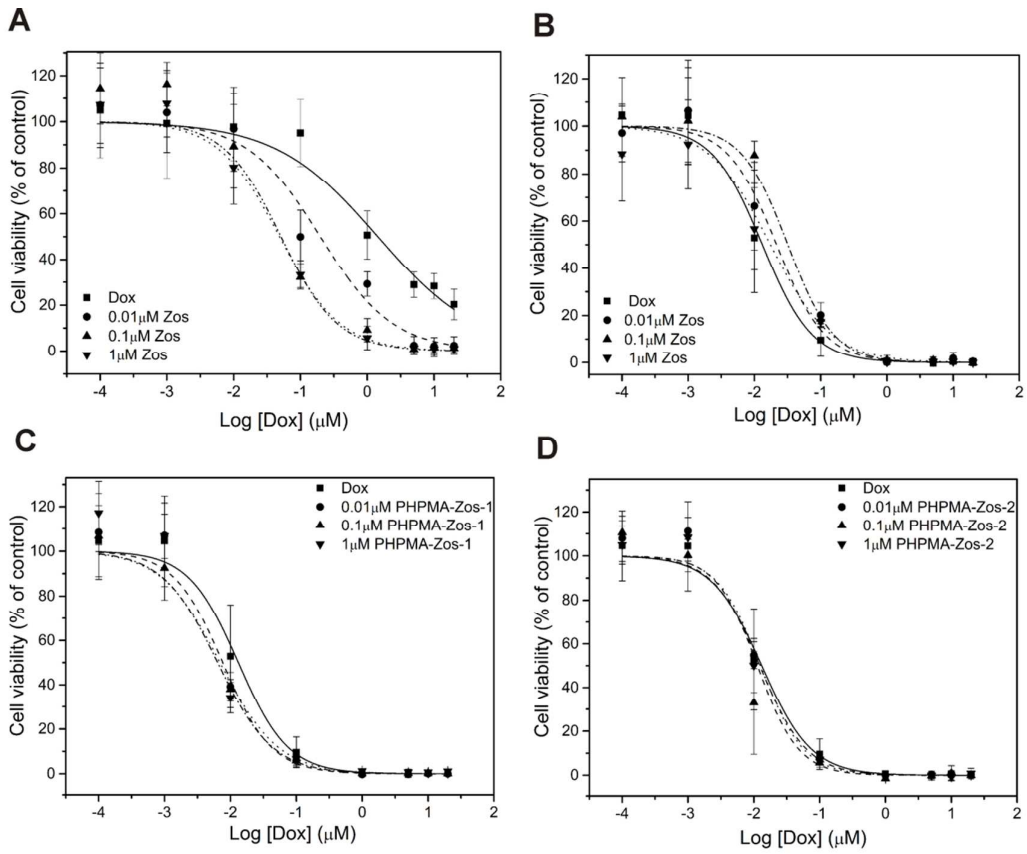


Figure S30. (A) Dox cytotoxicity alone and in combination with increasing concentrations of Zos in A2780ADR and (B) A2780 cells and with increasing concentrations of (C) **PHPMA-Zos-1** and (D) **PHPMA-Zos-2** in A2780 cells as determined by the MTT assay.

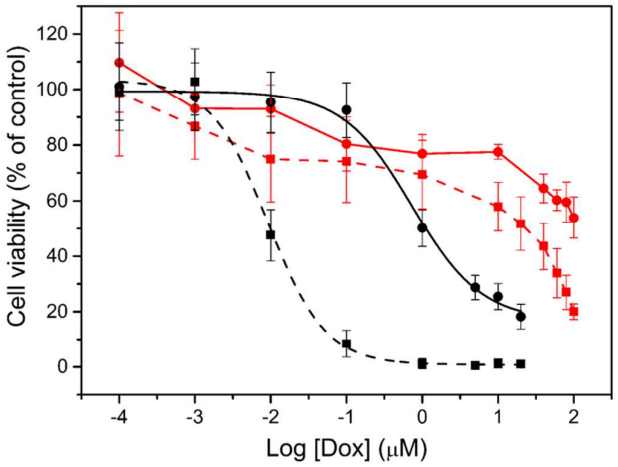


Figure S31. Comparison between the cytotoxicity of **PHPMA-Dox** (red) and free Dox (black) in sensitive A2780 (■) and in resistant A2780ADR (●) cells as determined by the MTT assay.

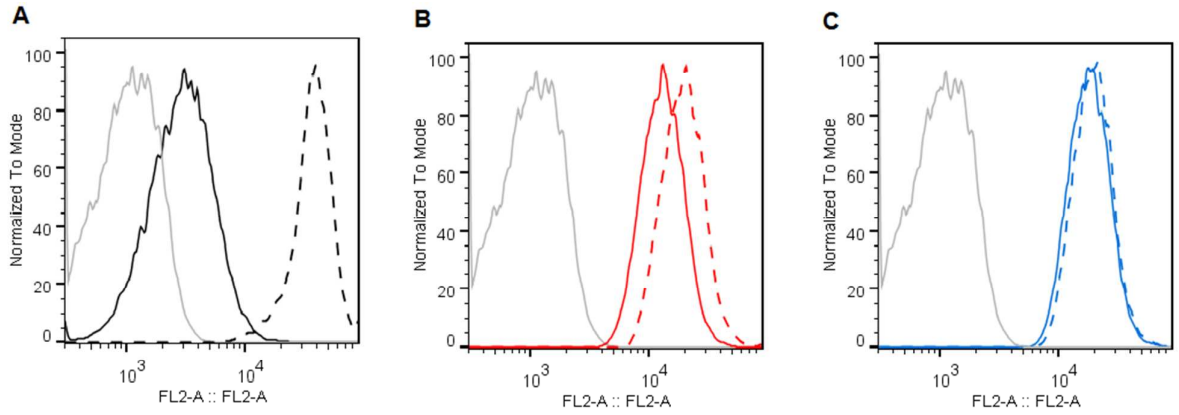


Figure S32. Example of Dox efflux from A2780ADR cells when administered as free drug (A) or delivered as (B) **PHPMA-Dox** or (C) **PHPMA-Dox-Zos** (continuous curves) as determined by flow cytometry. Control cells (gray curves) were used as negative control, cells treated with both Dox/Polymer-Dox conjugates and CsA (dashed lines) were used as positive control.

1. Willner, D.; Trail, P. A.; Hofstead, S. J.; King, H. D.; Lasch, S. J.; Braslawsky, G. R.; Greenfield, R. S.; Kaneko, T.; Firestone, R. A., (6-Maleimidocaproyl)Hydrazone of Doxorubicin - a New Derivative for the Preparation of Immunoconjugates of Doxorubicin. *Bioconjugate Chem.* **1993,** *4* (6), 521-527.

2. Gibson, M. I.; Frohlich, E.; Klok, H. A., Postpolymerization Modification of Poly(Pentafluorophenyl methacrylate): Synthesis of a Diverse Water-Soluble Polymer Library. *J. Polym. Sci., Part A: Polym. Chem.* **2009,** *47* (17), 4332-4345.

3. Perrier, S.; Takolpuckdee, P.; Mars, C. A., Reversible addition-fragmentation chain transfer polymerization: End group modification for functionalized polymers and chain transfer agent recovery. *Macromolecules* **2005,** *38* (6), 2033-2036.