Supporting information

Drug-Mediated, Controlled Ring-Opening Polymerization for the Synthesis of Polymer-Drug Conjugates

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Table S1. Ptxl / (BDI-II)ZnN(TMS)$_2$-mediated ROP of LA[a]

Entry	[LA]/[Ptxl]	Conv. (%)	M_{exp}(× 10^3 g/mol)	M_n (× 10^3 g/mol)	MWD (M_w/M_n)
1	50	>99%	8.1	7.8	1.04
2	75	>99%	11.7	9.6	1.09
3	100	>99%	15.3	12.7	1.03
4	200	>99%	29.7	28.1	1.02
5	300	>99%	44.1	35.2	1.03

[a]All reactions were performed in anhydrous THF with $[LA]_0$ = 0.69 M. Abbreviations: Conv. = conversion; M_{exp}, expected MW; MWD = molecular weight distribution; Ptxl = paclitaxel. LA conversion was measured by FT-IR. Incorporation efficiency was determined by reversed-phase HPLC analysis of unreacted Ptxl. M_n and MWD were determined by GPC.

Table S2. Dtxl / (BDI-II)ZnN(TMS)$_2$-mediated ROP of LA[a]

Entry	[LA]/[Dtxl]	Conv. (%)	M_{exp}(× 10^3 g/mol)	M_n (× 10^3 g/mol)	MWD (M_w/M_n)[c]
1	75	>99%	11.6	8.9	1.05
2	100	>99%	15.2	13.6	1.04
3	200	>99%	29.6	25.2	1.03
4	300	>99%	44.0	47.1	1.04
5	400	>99%	58.4	55.3	1.13

[a]All reactions were performed in anhydrous THF with $[LA]_0$ = 0.69 M. Abbreviations: Conv. = conversion; M_{exp}, expected MW; MWD = molecular weight distribution; Dtxl = docetaxel. LA conversion was measured by FT-IR. Incorporation efficiency was determined by reversed-phase HPLC analysis of unreacted Dtxl. M_n and MWD were determined by GPC.

Table S3. Ptxl (or Dtxl) / (BDI-II)ZnN(TMS)$_2$-mediated ROP of VL, TMC, and CL[a]

Entry	Initiator (R)	Monomer	[M]/[R]	Catalyst ligand	Time (h)	Temp. (^{o}C)	Conv. (%)	Incop eff. (%)	M_n / M_{exp} (× 10^3 g/mol)	MWD (M_w/M_n)
1	Ptxl	CL	100	BDI-II	10	r.t.	>99	>99	11.9 / 12.3	1.14
2	Ptxl	CL	200	BDI-II	10	r.t.	>99	>99	20.3 / 23.7	1.07
3	Ptxl	CL	300	BDI-II	10	r.t.	>99	>99	27.5 / 35.1	1.15
4	Ptxl	CL	100	BDI-IICN	10	r.t.	>99	>99	13.0 / 12/3	1.10
5	Ptxl	CL	200	BDI-IICN	10	r.t.	>99	>99	26.2 / 23.7	1.07
6	Dtxl	CL	100	BDI-II	10	r.t.	>99	>99	11.2 / 12.2	1.05
7	Dtxl	CL	200	BDI-II	10	r.t.	>99	>99	20.9 / 23.6	1.15
8	Dtxl	CL	300	BDI-II	10	r.t.	>99	>99	38.4 / 35.0	1.13
9	Ptxl	VL	100	BDI-II	12	r.t.	>99	>99	15.1 / 10.8	1.17
10	Ptxl	VL	200	BDI-II	12	r.t.	>99	>99	23.1 / 20.8	1.18
11	Ptxl	VL	300	BDI-II	12	r.t.	>99	>99	31.2 / 30.8	1.18
12	Dtxl	VL	100	BDI-II	12	r.t.	>99	>99	14.2 / 10.7	1.15
13	Dtxl	VL	100	BDI-IICN	12	r.t.	>99	>99	12.6 / 10.7	1.13
14	Ptxl	TMC	100	BDI-II	6	50	>99	>99	14.7 / 11.1	1.10
15	Ptxl	TMC	200	BDI-II	6	50	>99	>99	27.6 / 21.3	1.21
16	Ptxl	TMC	300	BDI-II	6	50	>99	>99	49.2 / 31.5	1.21
17	Ptxl	TMC	100	BDI-IICN	6	50	>99	>99	18.1 /11.1	1.10
18	Dtxl	TMC	100	BDI-II	6	50	>99	>99	12.6 / 11.0	1.23
19	Dtxl	TMC	200	BDI-II	6	50	>99	>99	25.9 / 21.3	1.19

[a]All reactions were performed in anhydrous THF with $[monomer]_0$ = 0.69 M. Abbreviations: Conv. = conversion; Dtxl = docetaxel; Incorp. eff. = incorporation efficiency; M_{exp}, expected MW; MWD = molecular weight distribution; Ptxl = paclitaxel. Monomer conversion was measured by FT-IR. Incorporation efficiency was determined by reversed-phase HPLC analysis of unreacted Ptxl (or Dtxl). M_n and MWD were determined by GPC.

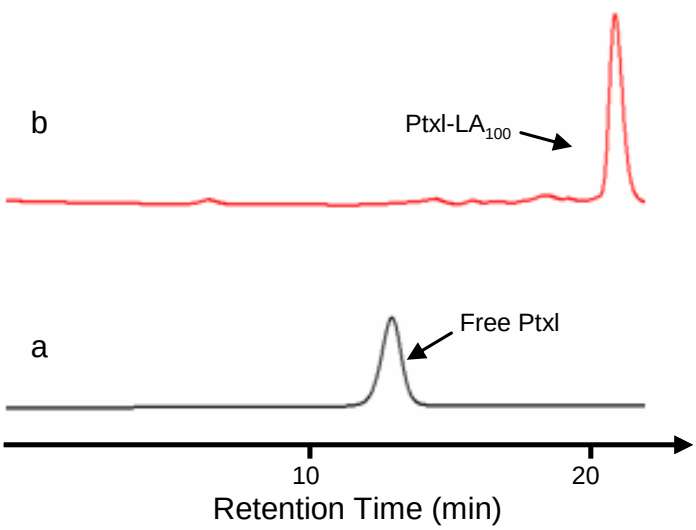
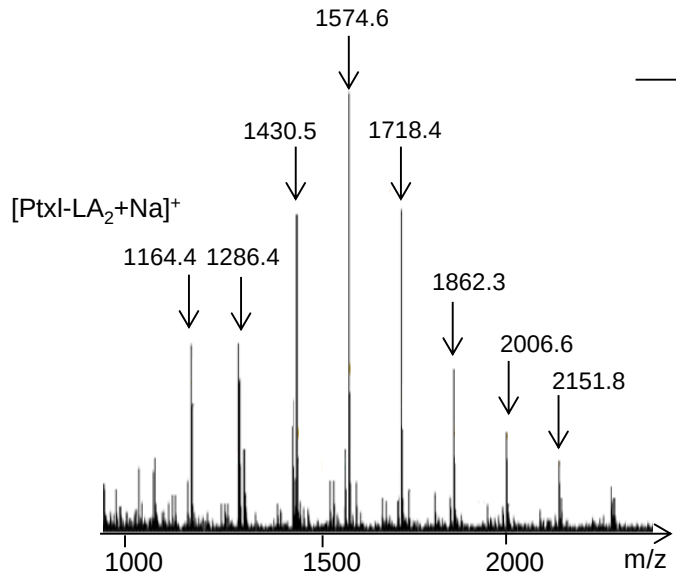


Figure S1. HPLC spectrum of (a) free Ptxl and (b) the solution of Ptxl / (BDI-II)ZnN(TMS)$_2$-mediated LA polymerization at a LA/Ptxl ratio of 100. An aliquot (30-50 μL) of polymerization solution was injected into HPLC equipped with analytical RP-HPLC column (Curosil-PFP, 4.6 × 250 mm, 5μ, Phenomenex, Torrance, CA). Mobile phase was acetonitrile/water with 0.1% TFA (50/50 (v/v)); the flow rate was set at 1.0 mL/min.



n	[Ptxl-LA$_n$+H]$^+$
2	1142.4
3	1286.5
4	1430.5
5	1574.5
6	1718.6
7	1862.6
8	2006.7
9	2151.7

Figure S2. ESI-MS analysis of Ptxl-LA$_5$. Ptxl-LA$_5$ was prepared by Ptxl/(BDI-II)ZnN(TMS)$_2$ (1/1 molar ratio).

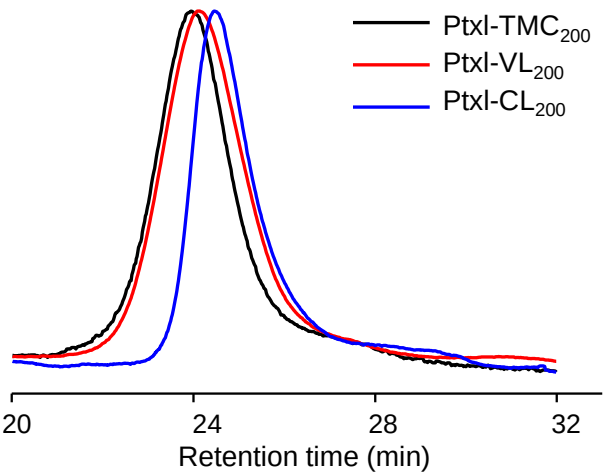


Figure S3. Overlay of GPC chromatogram of Ptxl-TMC_{200}, Ptxl-VL_{200} and Ptxl-CL_{200}. All reactions were mediated by Ptxl/(BDI-II)ZnN$(TMS)_2$

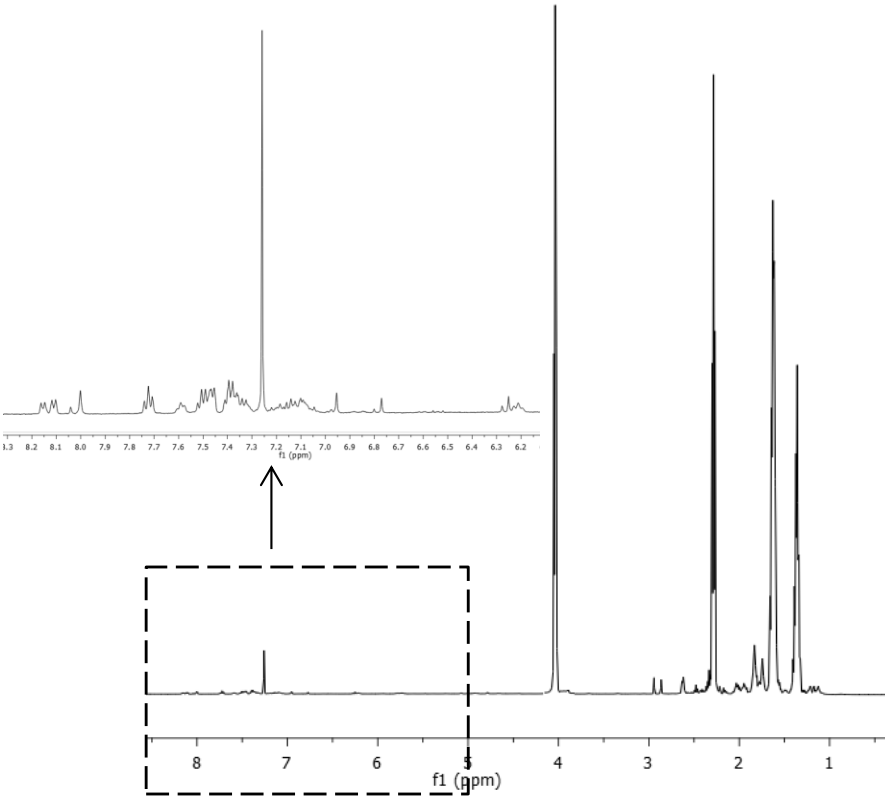


Figure S4. ^{1}H-NMR spectrum of Ptxl-CL_{100}. Inset: magnified spectrum. The small peaks indicated the Ptxl conjugated onto the polymer.

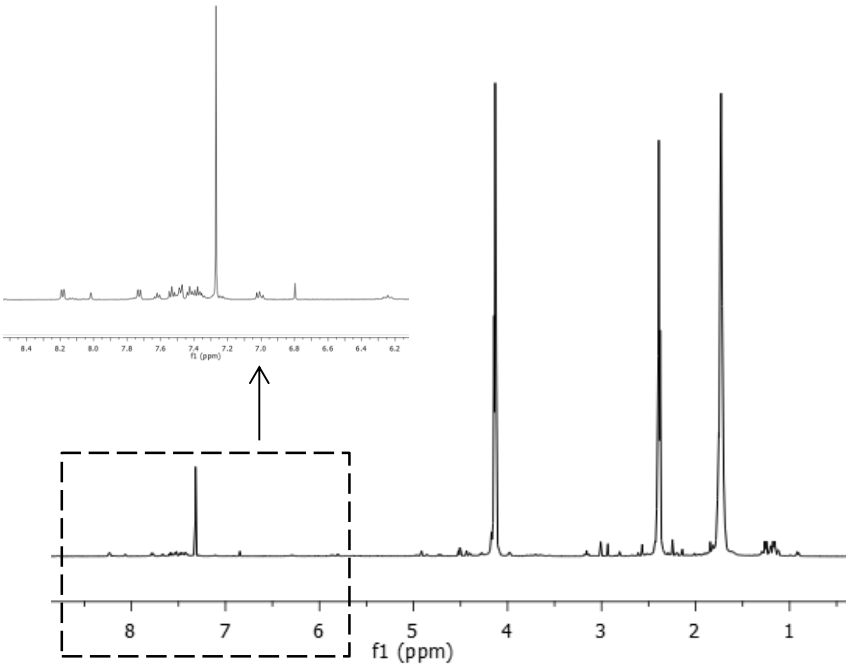


Figure S5. ^{1}H-NMR spectrum of Ptxl-VL_{100}. Inset: magnified spectrum. The small peaks indicated the Ptxl conjugated onto the polymer.

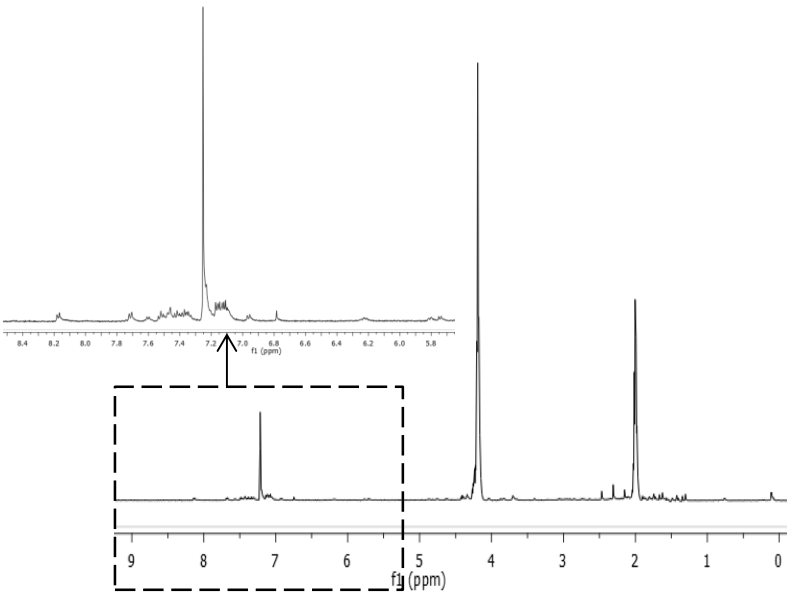


Figure S6. ^{1}H-NMR spectrum of Ptxl-TMC_{100}. Inset: magnified spectrum. The small peaks indicated the Ptxl conjugated onto the polymer.