

## Supporting Information

### Crystallization of Lipidated Dexamethasone Prodrugs: The Linker Matters

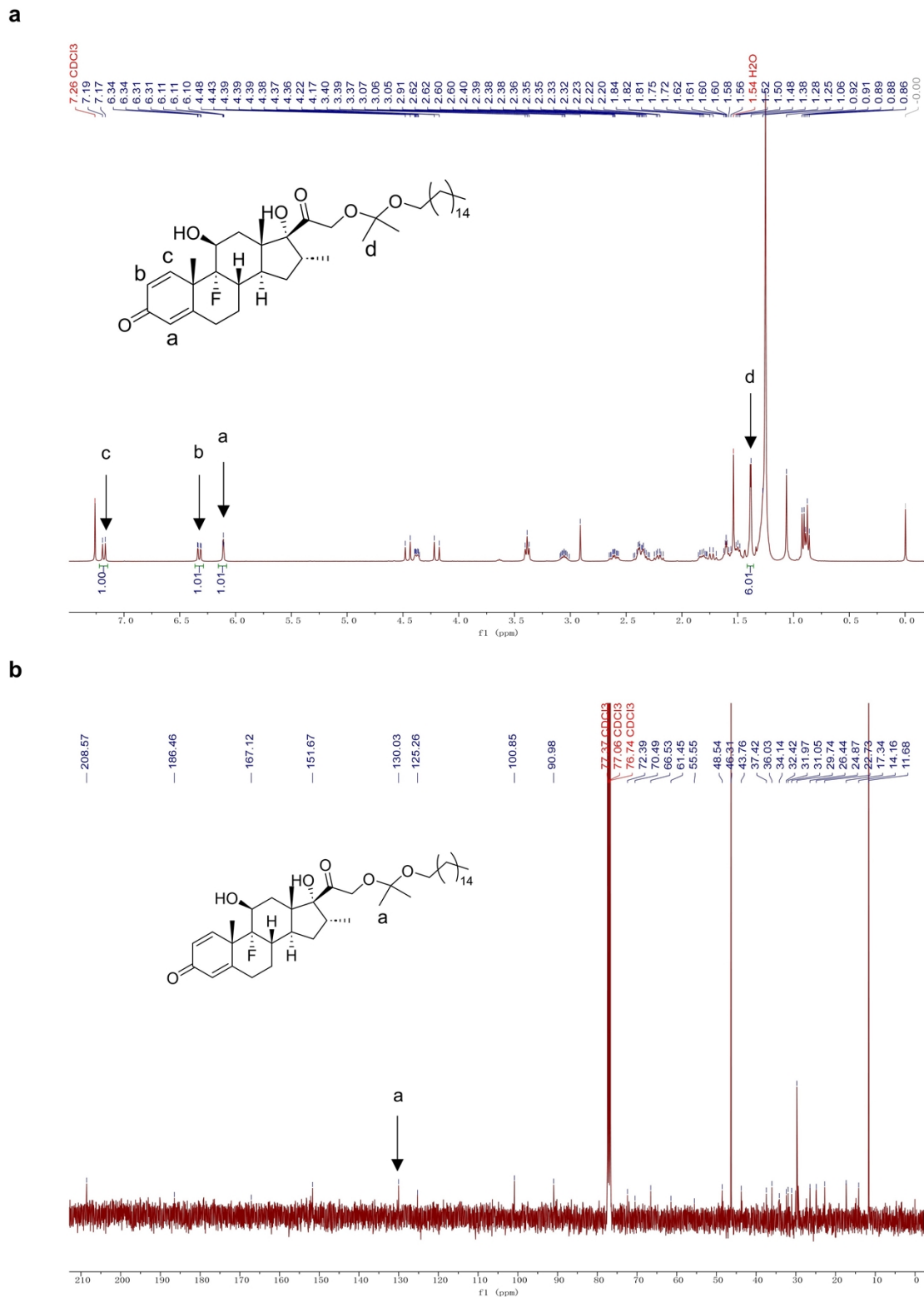
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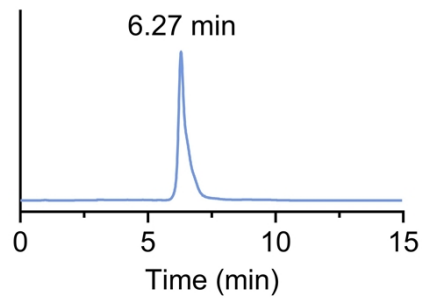
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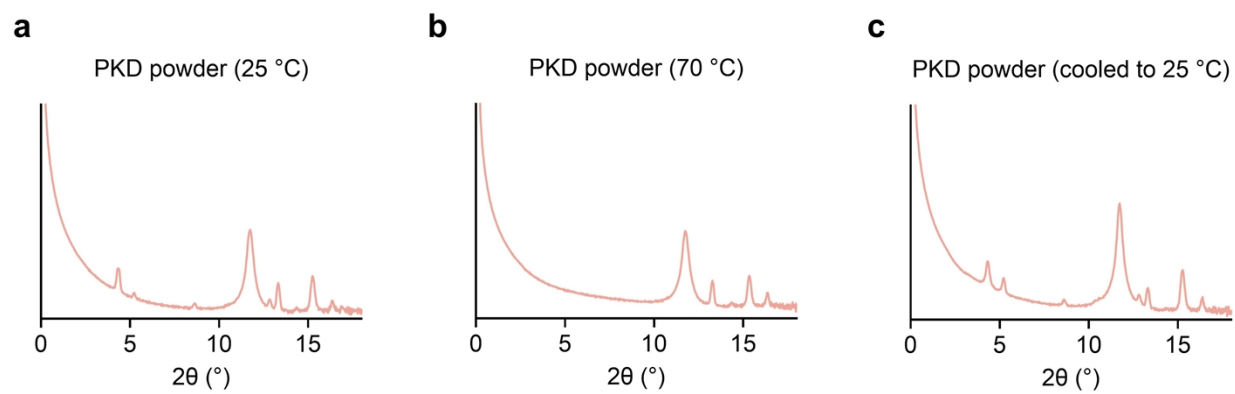
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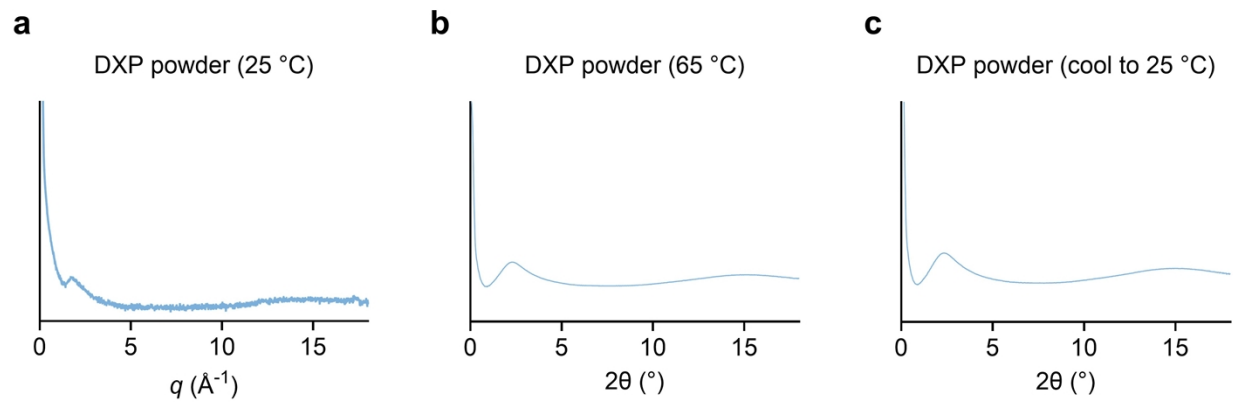
**Fig. S1** Characterization of PKD. (a)  $^1\text{H}$  NMR spectrum of PKD; (b)  $^{13}\text{C}$  NMR spectrum of PKD.



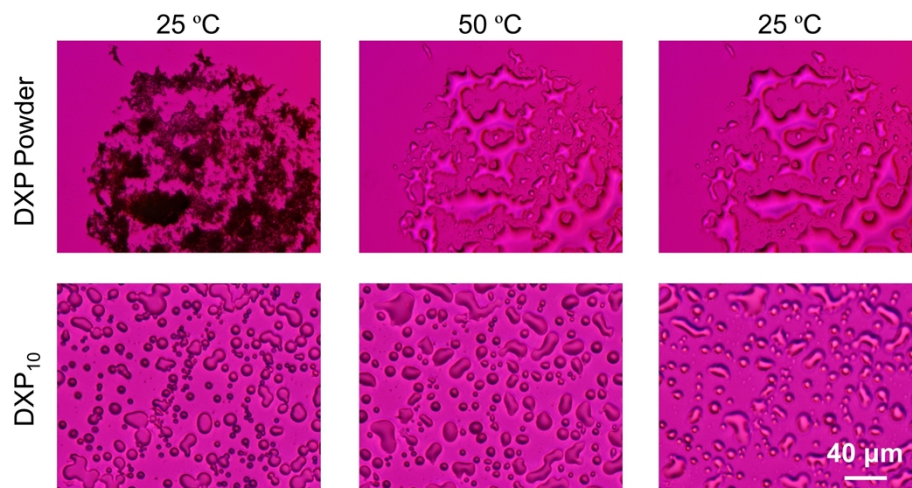
**Fig. S2** HPLC chromatograms of PKD (retention time: 6.27 min).



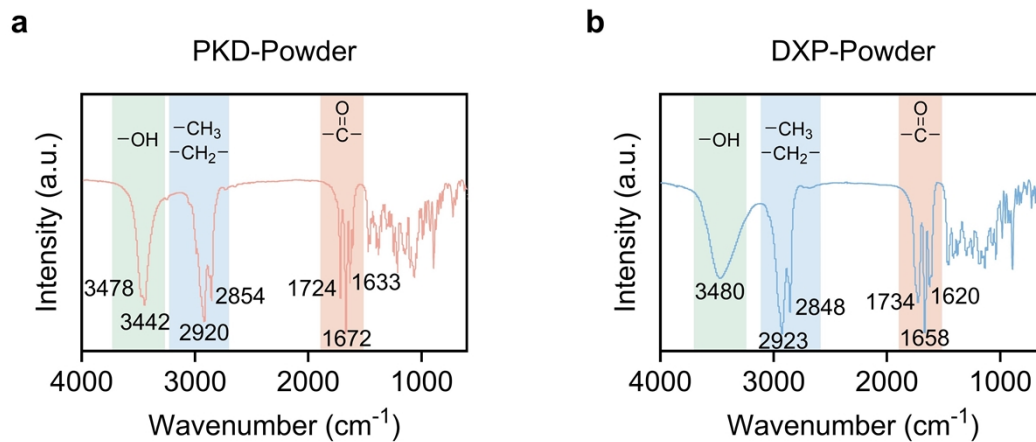
**Fig. S3** LAXS profiles of PKD powder at 25 °C (a), 70 °C (b), and after cooling back to 25 °C (c).



**Fig. S4** LAXS profiles of DXP powder at 25 °C (a), 65 °C (b), and after cooling back to 25 °C (c).



**Fig. S5** Temperature-dependent polarized optical microscopy images of DXP powder and DXP<sub>10</sub> aggregates, prepared from ethanolic solutions (10 mg/mL) at a solvent-to-antisolvent volume ratio of 1:2 (v/v), recorded at room temperature, at 50 °C, and after cooling back to room temperature.



**Fig. S6** FT-IR spectra of PKD (a) and DXP (b) powder.

**Table. S1** Detailed parameters for the antisolvent treatment of PKD and DXP.

	Initial concentration (mg/mL)	Solvent-to-antisolvent ratio (v/v)
PKD <sub>50</sub>	50	1:2
PKD <sub>25</sub>	25	1:2
PKD <sub>10</sub>	10	1:2
PKD <sub>1:2</sub>	10	1:2
PKD <sub>1:5</sub>	10	1:5
PKD <sub>1:10</sub>	10	1:10
DXP <sub>50</sub>	50	1:2
DXP <sub>25</sub>	25	1:2
DXP <sub>10</sub>	10	1:2
DXP <sub>1:2</sub>	10	1:2
DXP <sub>1:5</sub>	10	1:5
DXP <sub>1:10</sub>	10	1:10

**Table. S2** Parameter of PKD crystal measured via SCXRD.

Parameter	
Formula, FW	C <sub>41</sub> H <sub>67</sub> FO <sub>6</sub> , 674.94
Crystal system, space group	P2111, monoclinic
	a = 19.06416 (17) Å
	b = 7.98111 (10) Å
	c = 25.6022 (3) Å
	β = 98.4211° (8)
Z, Z'	4, 2
R	0.03