Supporting Information

Design, Synthesis, and Application of Fluorine-Labeled Taxoids as ^{19}F NMR Probes for the Metabolic Stability Assessment of Tumor-Targeted Drug Delivery Systems

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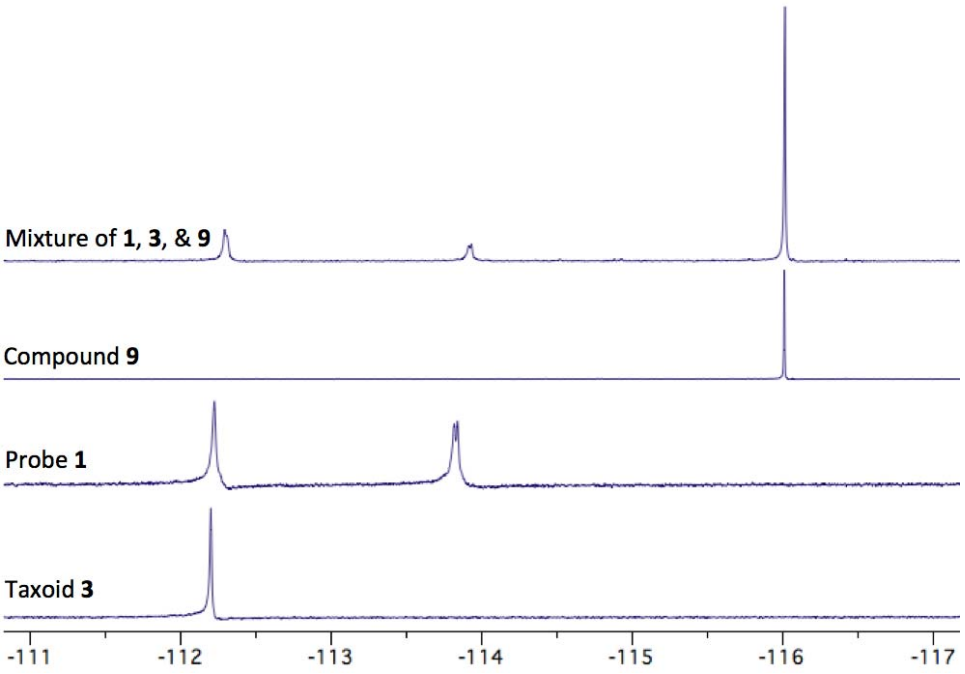

Figure S1. ^{19}F NMR spectra showing individual chemical shifts of probe **1**, taxoid **3**, thiolactone **9**, and a mixture of **1**, **3**, and **9** in D_2O-DMSO (70:30).

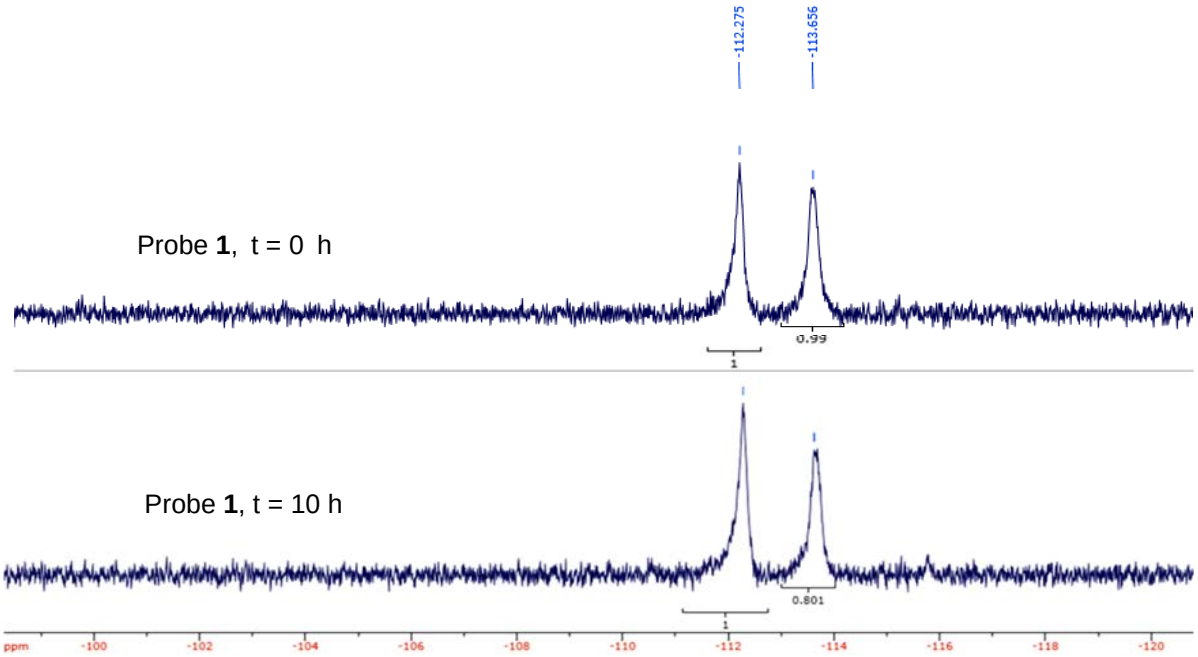

Figure S2. ^{19}F NMR spectra of **1** (2.5 mM) formulated in 5% solutol, 5% ethanol, 70% saline, 20% D_2O before (top) and after (10 h) (bottom) the addition of 6 equiv. of GSH. Integration of the signals clearly depicts ~20% cleavage of the disulfide bond.

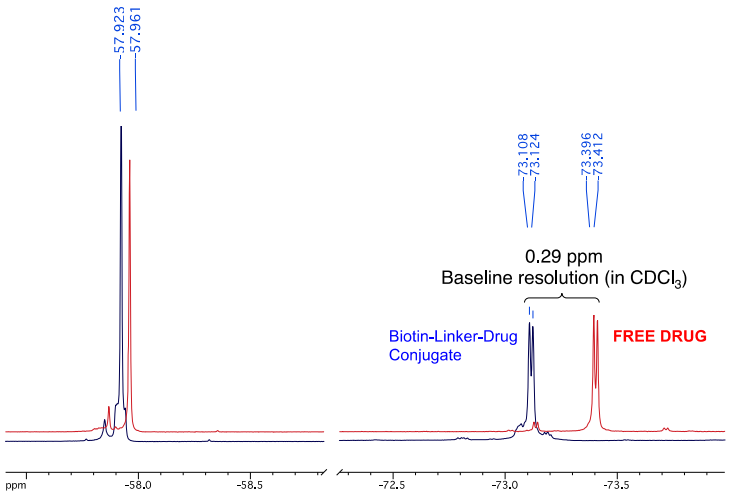

Figure S3. ^{19}F NMR spectral overlay showing individual chemical shifts of probe **2** (blue) and taxoid **4** (red) in $CDCl_3$ (Table 1, Entry 1).

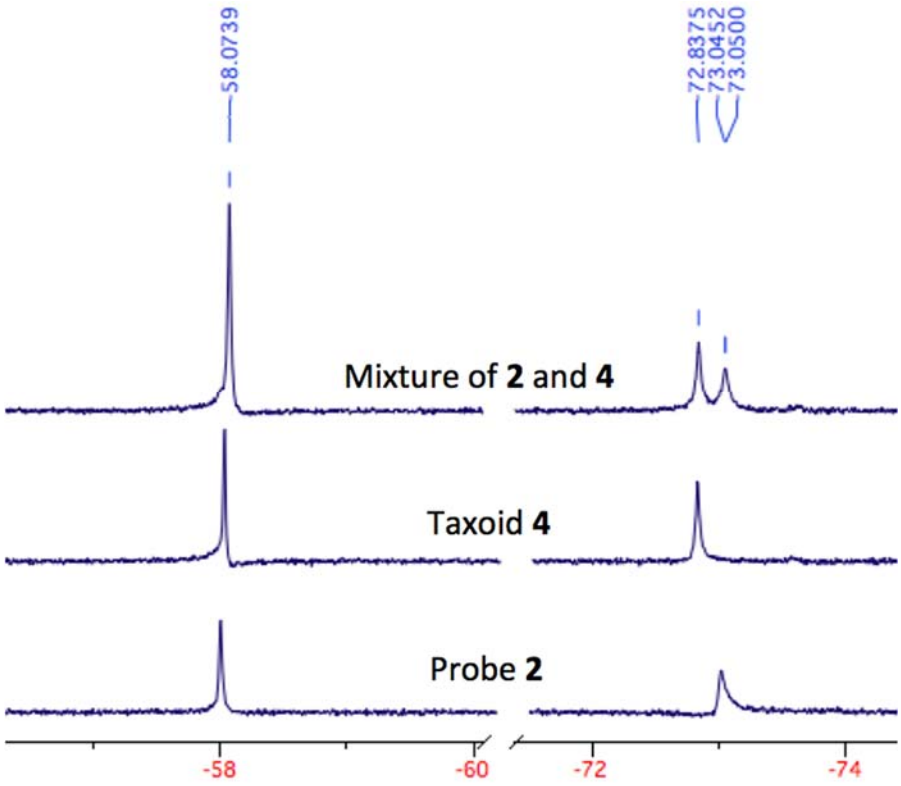

Figure S4. ^{19}F NMR spectra (1024 scans) showing individual chemical shifts of 200 μM solutions of **2** and **4** in blood plasma-D_2O-ethanol-polysorbate 80 (86:10:2:2), and a 1:1 mixture of **2** and **4** in blood plasma-D_2O-ethanol-polysorbate 80 (84:10:4:2) (Table 1, Entry 2).

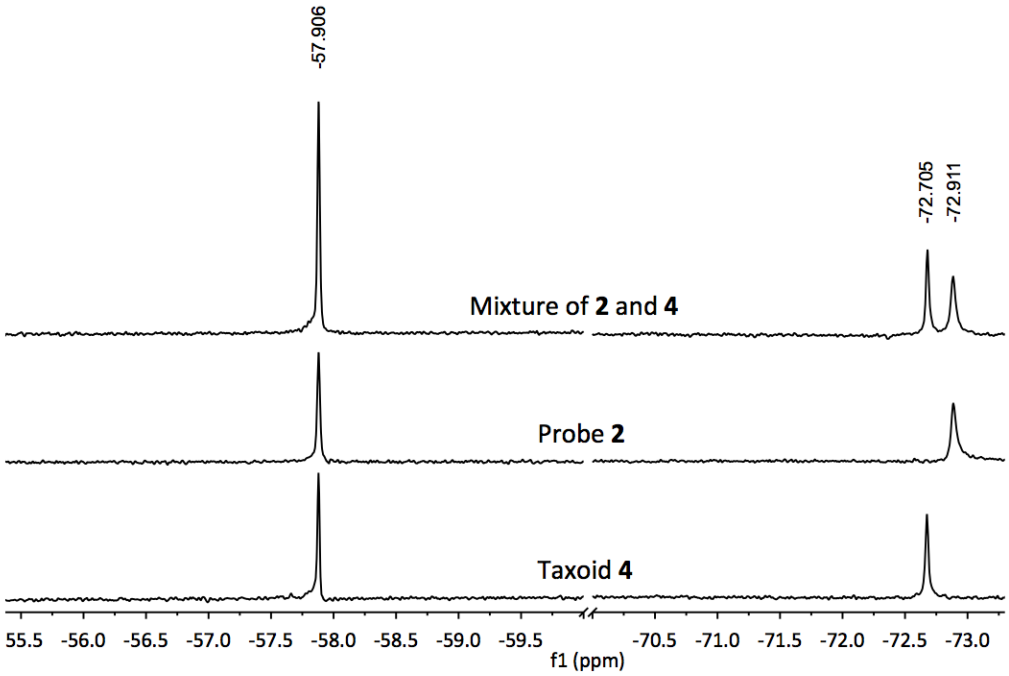

Figure S5. ^{19}F NMR spectra (512 scans) showing individual chemical shifts of 200 μM solutions of **2** and **4** in RPMI 1640-D_2O-ethanol-polysorbate 80 (86:10:2:2), and a 1:1 mixture of **2** and **4** in RPMI 1640-D_2O-ethanol-polysorbate 80 (84:10:4:2) (Table 1, Entry 3).

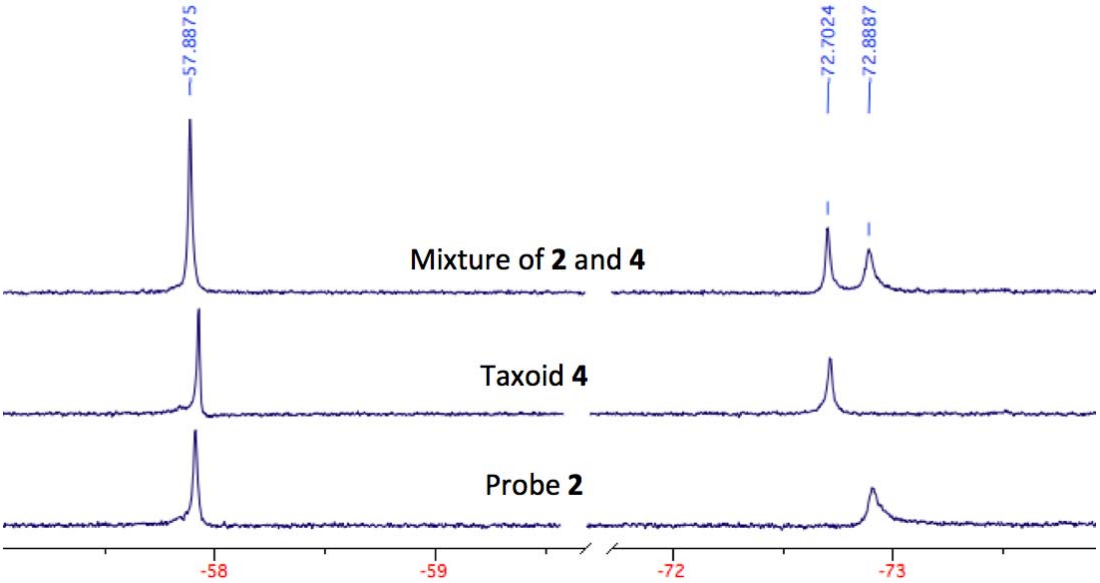

Figure S6. ^{19}F NMR spectra (512 scans) showing individual chemical shifts of 200 μM solutions of **2** and **4** in D_2O-ethanol-polysorbate 80 (96:2:2), and a 1:1 mixture of **2** and **4** in D_2O-ethanol-polysorbate 80 (94:4:2) (Table 1, Entry 4).

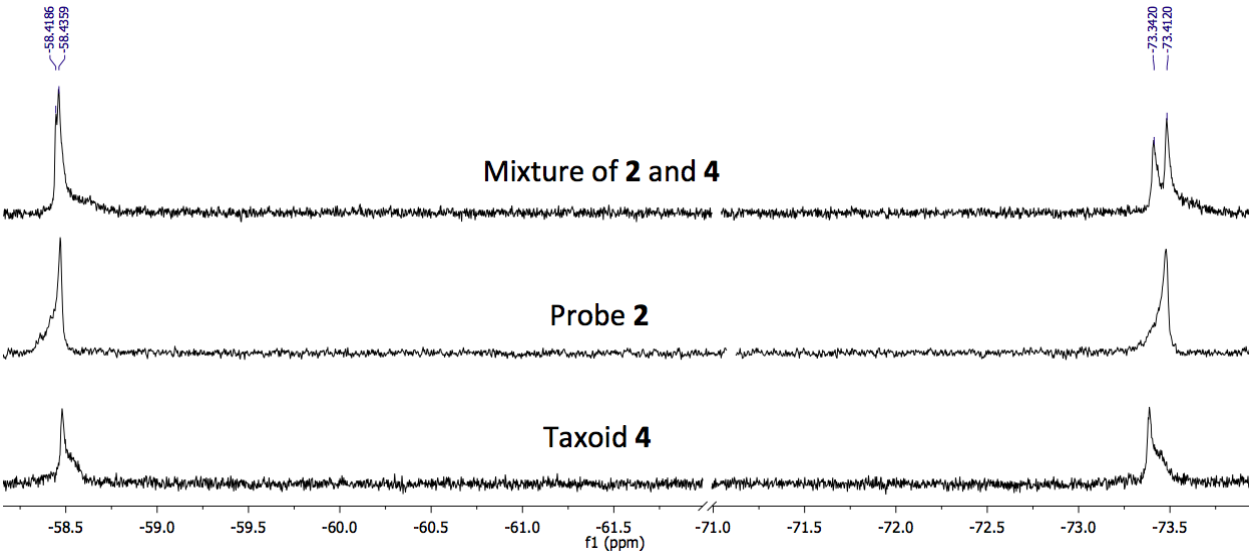

Figure S7. ^{19}F NMR spectra (220 scans) showing individual chemical shifts of 200 μM solutions of **2** and **4**, and a 1:1 mixture of **2** and **4** in saline-D_2O-ethanol (50:40:10) (Table 1, Entry 5).

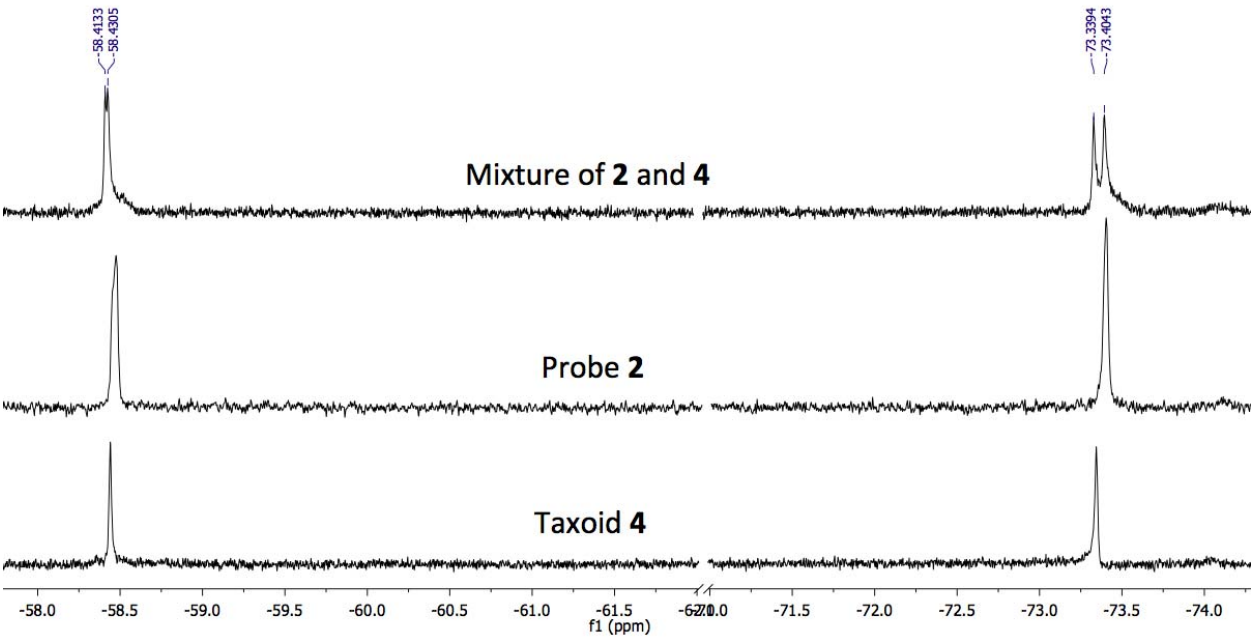

Figure S8. ^{19}F NMR spectra (220 scans) showing individual chemical shifts of 200 μM solutions of **2** and **4**, and a 1:1 mixture of **2** and **4** in PBS-D_2O-ethanol (50:40:10) (Table 1, Entry 6).

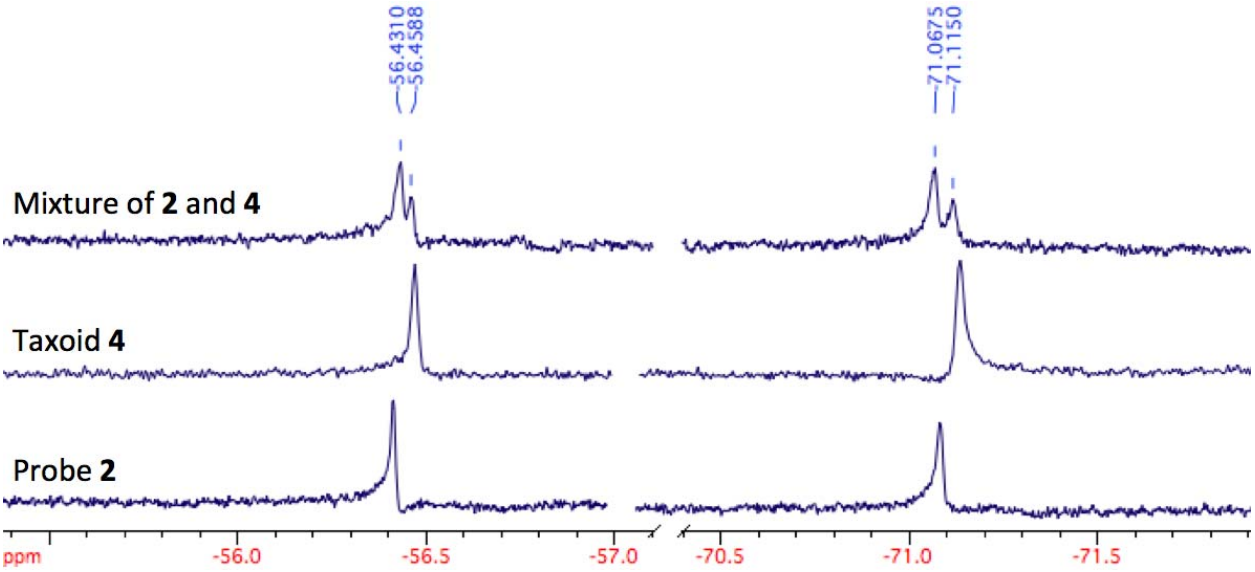

Figure S9. ^{19}F NMR spectra (1024 scans) showing individual chemical shifts of 200 μM solutions of **2**, **4**, and a 1:1 mixture of **2** and **4** in DMSO-D_2O (70:30) (Table 1, Entry 7).

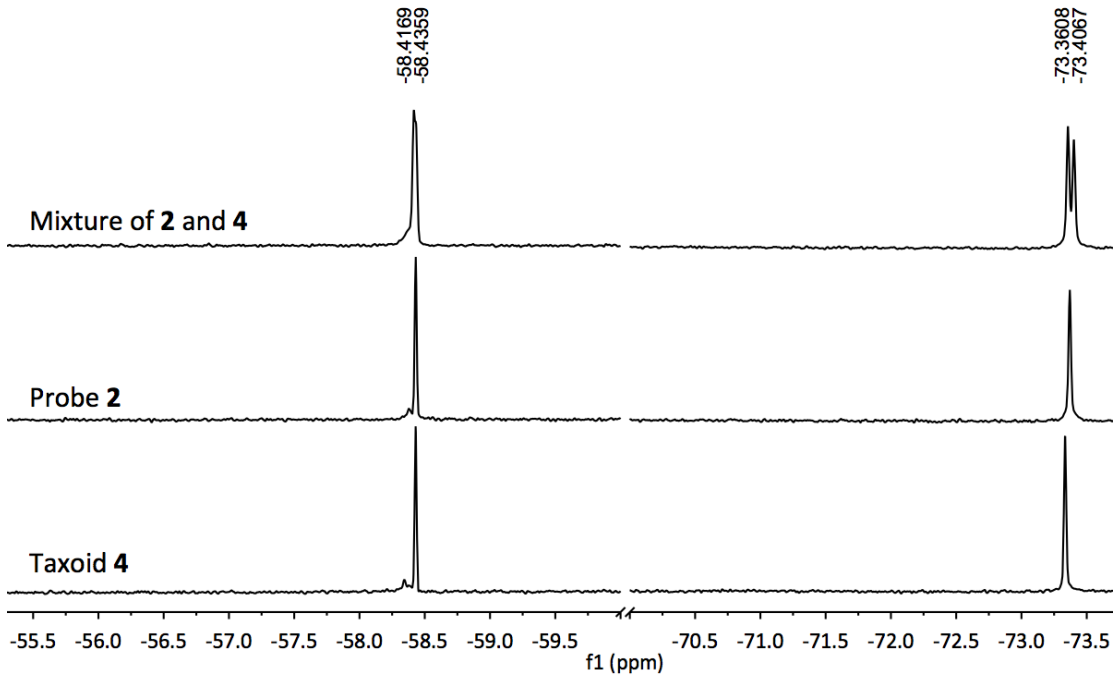

Figure S10. ^{19}F NMR spectra (512 scans) showing individual chemical shifts of 200 μM solutions of **2**, **4**, and a 1:1 mixture of **2** and **4** in D_2O-ethanol (60:40) (Table 1, Entry 8).

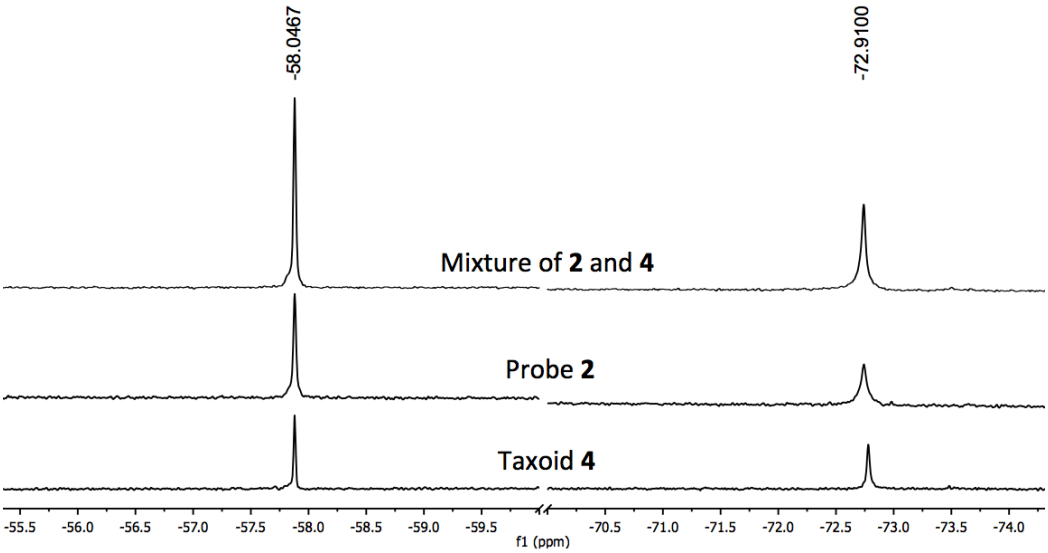

Figure S11. ^{19}F NMR spectra (>268 scans) showing individual chemical shifts of 200 μM solutions of **2**, **4**, and a 1:1 mixture of **2** and **4** in D_2O-ethanol-solutol HS15 (84:8:8) (Table 1, Entry 9).

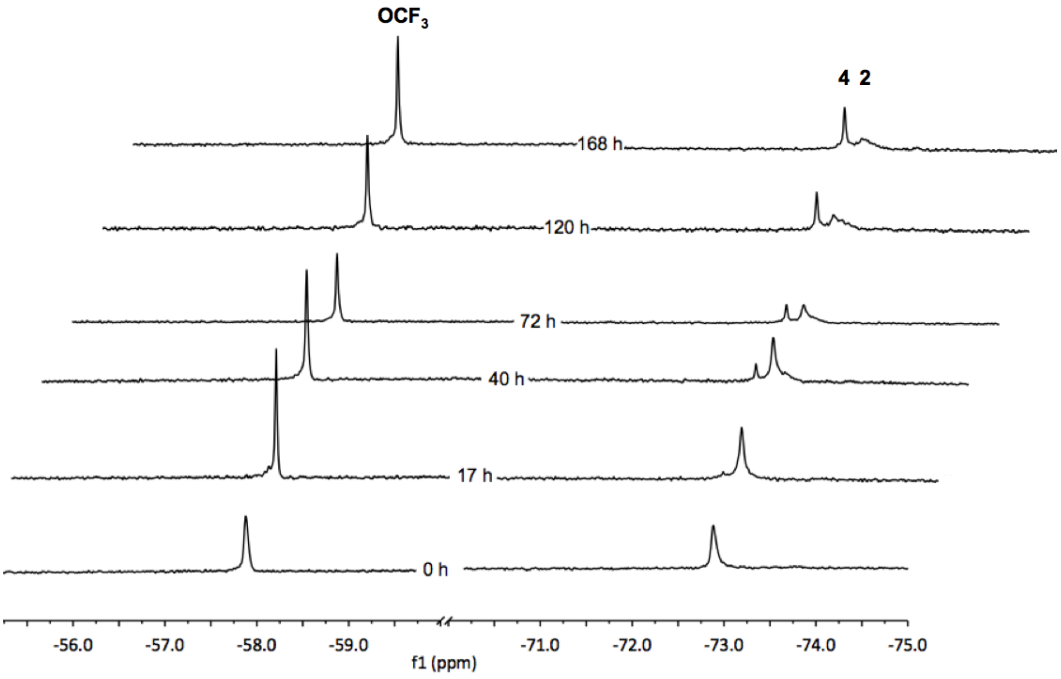

Figure S12. ^{19}F NMR spectra (>512 scans) showing chemical shifts of a 200 μM solution of **2** and released taxoid **4** with 100 equivalents of GSH in D_2O-ethanol-polysorbate 80 (96:2:2) at 0, 17, 40, 72, 120, and 168 h, indicating a $t_{1/2}$ of approximately 4 d.

Table S1.

Experimental data and normalized values for the drug release study of probe **4**, shown in Figure 7.

time (h)	Normalized Integration for **2**	Normalized Integration for **4**
0	1	0
1	0.841018667	0.158981333
2	0.658950264	0.341049736
3	0.500068503	0.499931497
4	0.37350062	0.62649938
5	0.23476298	0.76523702
6	0.152388797	0.847611203
7	0.110911486	0.889088514
8	0.094353851	0.905646149
9	0.054218871	0.945781129
10	0.028866218	0.971133782
11	0.019893467	0.980106533
12	0.020392911	0.979607089
13	0.014137708	0.985862292

time (h)	Experimental Integration for **2**	Experimental Integration for **4**
0	1	0
1	0.6803	0.1286
2	0.575	0.2976
3	0.365	0.3649
4	0.2709	0.4544
5	0.1976	0.6441
6	0.1295	0.7203
7	0.0926	0.7423
8	0.1001	0.9608
9	0.0489	0.853
10	0.0249	0.8377
11	0.0183	0.9016
12	0.0191	0.9175
13	0.0131	0.9135