Supplementary Material

Synthesis of Florbetapir aza-analogues using chemistry of pyridinium *N*-aminides

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1. Table S1. Optimization of the alkylation of aminides 3 and synthesis of acetamides 4

Table S1. Optimization of the alkylation of aminides **3** and synthesis of acetamides **4**

Entry	Alkylating agent	n	Temp.	Time (min)	% (^{1}H-NMR estimated)			Catalyst	% 4 (two steps)
					3	**8**	**9**		
1	**7a**	2	90 °C	60	54	30	16		
2				90	16	60	24		
3				120	0	69	31	→ Pt/C 5 wt. %	28
4			110 °C	30	*	*	*		
5	**7b**	3	90 °C	60	67	20	13		
6			110 °C	10	75	17	8		
7				20	20	53	27		
8				30	0	64	36	→ Pt/C 1 wt. %	21
9			150 °C	20	*	*	*		

*Carbonization of the mixture

2. Numbering employed in NMR analysis

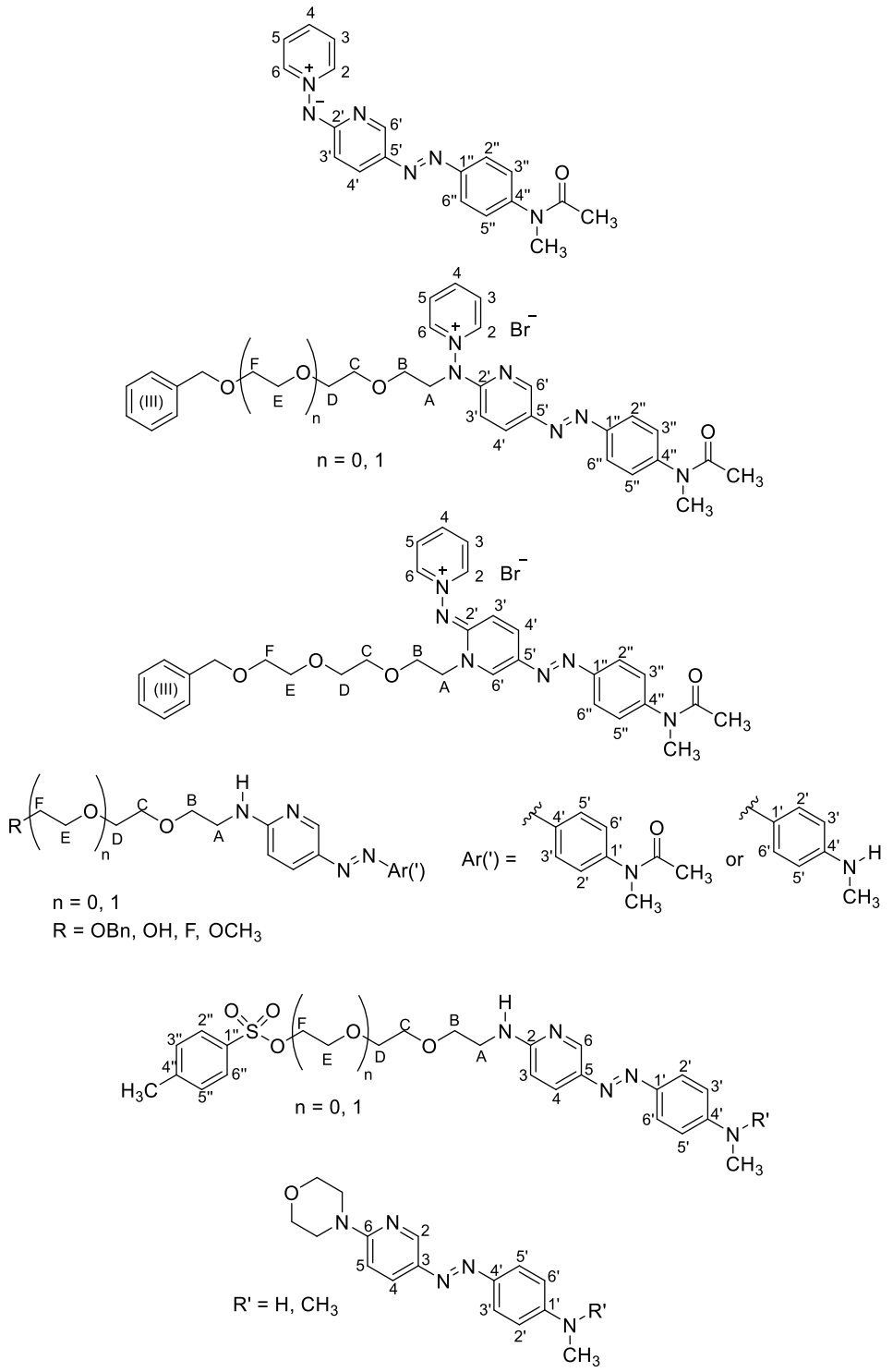

Figure S1. Numbering employed in NMR analysis.

3. Synthesis of alkylating agents

2-{2-[2-(Benzyloxy)ethoxy]ethoxy}ethanol (20)[1]

Procedure. Benzyl bromide (6.5 mL, 55 mmol) was added dropwise to a solution of triethylene glycol (7.51 g, 50 mmol) and freshly prepared Ag_2O (17.4 g, 75 mmol) in CH_2Cl_2 (20 mL) at room temperature. The suspension was stirred for 24 h then filtered through Celite. The filtrate was evaporated and the resulting residue was purified by flash chromatography (hexane/ethyl acetate 1:1), to give 2-{2-[2-(Benzyloxy)ethoxy]ethoxy}ethanol **20** (10.5 g, 88 %, 44 mmol) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34-7.26 (5H, m, Ar*H*), 4.56 (2H, s, C*H*$_2$Ar), 3.72-3.58 (12H, m, C*H*$_2$O), 2.50 (1H, br s, O*H*) ppm.

1,12-diphenyl-2,5,8,11-tetraoxadodecane 21 was obtained as a secondary product. Colourless oil (0.82 g, 5 %, 2.5 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.25 (10H, m, Ar*H*), 4.57 (4H, s, C*H*$_2$Ar), 3.69-3.63 (12H, m, C*H*$_2$O) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.3 (*C*1), 128.3 (*C*3(5)), 127.7 (*C*2(6)), 127.6 (*C*4), 73.2 (*C*H$_2$Ph), 70.7 (2*C*H$_2$O), 69.4 (4*C*H$_2$O) ppm.

Tosylation of poly (ethylene glycol) derivatives

General procedure. Tosyl chloride (10.5 g, 55 mmol) in dry CH_2Cl_2 (50 mL) was added to a solution of the corresponding monobenzylated polyethylene glycol derivative (50 mmol), Et_3N (7.5 mL, 54 mmol) and DMAP (12.2 g, 100 mmol) in dry CH_2Cl_2 (250 mL) at 0 °C, and the mixture was stirred for 2 h at room temperature. After washing with 1 M HCl, then with a saturated aqueous solution of $NaHCO_3$ and finally with brine, the organic layer was dried (Na_2SO_4) and the solvent evaporated to dryness, to obtain the desired product, which was used in the next step without further purification. Experimental data were consistent with previously reported literature values.

2-[2-(Benzyloxy)ethoxy]ethyl-4-methylbenzenesulfonate (22a). Tosylate **22a** was obtained as an yellow oil (14.9 g, 85 %, 42.5 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (2H, d, *J* 8.4, *H*2(6)), 7.29 (7H, m, *H*3(5) and Ar*H*), 4.53 (2H, s, C*H*$_2$-Ar), 4.17 (2H, t, *J* 4.2 Hz, C*H*$_2$A), 3.67-3.56 (6H, m, C*H*$_2$B, C*H*$_2$C and C*H*$_2$D), 2.40 (3H, s, C*H*$_3$) ppm.

2-{2-[2-(Benzyloxy)ethoxy]ethoxy}ethyl-4-methylbenzenesulfonate (22b). Tosylate **22b** was obtained as an yellow oil (12.0 g, 72 %, 36 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (2H, d, *J* 8.4, *H*2(6)), 7.33-7.26 (7H, m, *H*3(5) and Ar*H*), 4.54 (2H, s, C*H*$_2$-Ph), 4.14 (2H, m, C*H*$_2$A), 3.67 (2H, m, C*H*$_2$B), 3.62-3.57 (8H, m, C*H*$_2$C, C*H*$_2$D, C*H*$_2$E and C*H*$_2$F), 2.41 (3H, s, C*H*$_3$) ppm.

Obtaining of the polyethylene glycol bromides

General procedure. LiBr (24.5 g, 280 mmol) was added to a solution of the corresponding tosylate **22** (28 mmol) in acetone (80 mL) and the mixture refluxed for 6 h. The solution was then cooled and the solvent removed. The resulting residue was suspended in H_2O (80 mL), extracted four times with CH_2Cl_2 (4 x 80 mL) and the layers separated. The combined organic extracts were then dried (Na_2SO_4), filtered and the solvent evaporated to obtain the desired product **7**. Experimental data were consistent with previously reported literature values.

[2-(2-Bromoethoxy)ethoxy]methylbenzene (7a). Derivative **7a** was obtained as a yellow liquid (6.89 g, 95 %, 26.6 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (5H, m, Ar*H*), 4.55 (2H, s, C*H*$_2$Ar), 3.78 (2H, t, *J* 6.3 Hz, C*H*$_2$B), 3.66 (2H, m, C*H*$_2$C or C*H*$_2$D), 3.60 (2H, m, C*H*$_2$D or C*H*$_2$C), 3.45 (2H, t, *J* 6.3 Hz, C*H*$_2$A) ppm.

{2-[2-(2-Bromoethoxy)ethoxy]ethoxy}methylbenzene (7b). Derivative **7b** was obtained as a yellow liquid (7.89 g, 93 %, 26.0 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.26 (5H, m, Ar*H*), 4.57 (2H, s, C*H*$_2$Ar), 3.81 (2H, t, *J* 7.0 Hz, C*H*$_2$B), 3.70-3.63 (8H, m, C*H*$_2$C, C*H*$_2$D, C*H*$_2$E and C*H*$_2$F), 3.46 (2H, t, *J* 7.0 Hz, C*H*$_2$A) ppm.

[1] Bouzide, A.; Sauvé, G. *Tetrahedron Lett.* **1997**, *38*, 5945-5948.

4. ^{1}H, ^{13}C and ^{19}F NMR of new compounds synthesized.

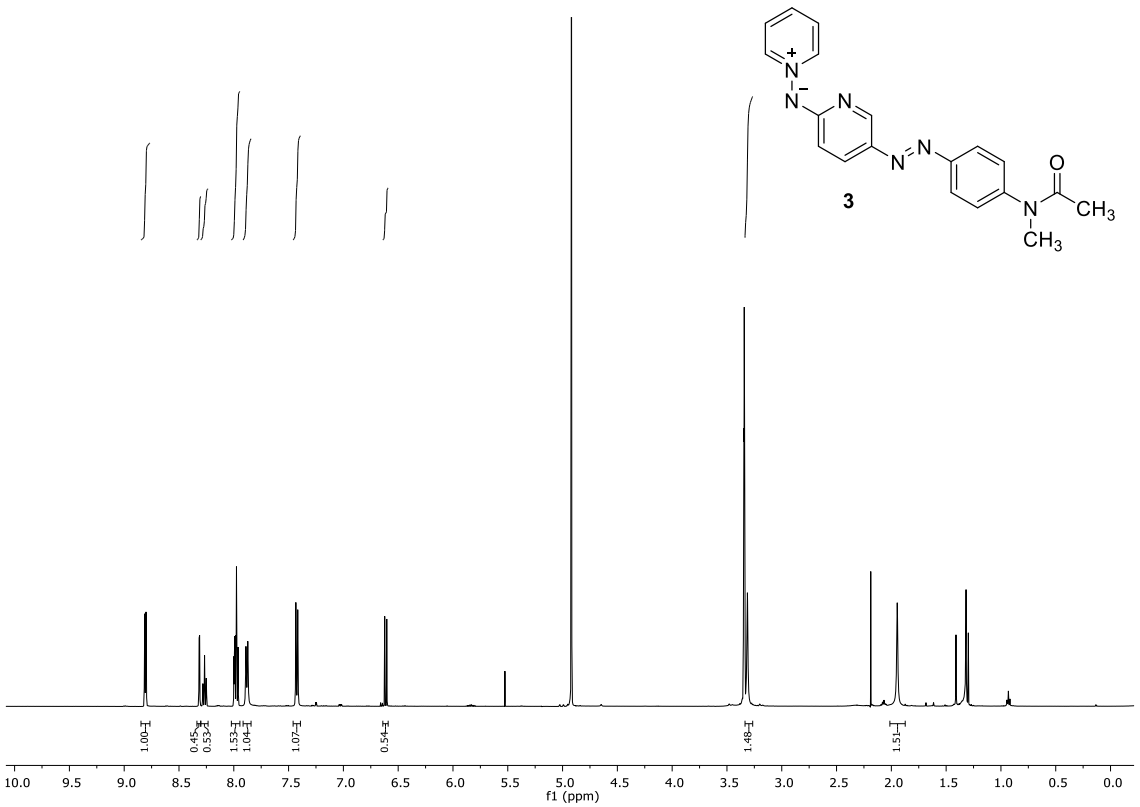

Figure S2. ^{1}H-NMR of product **3**.

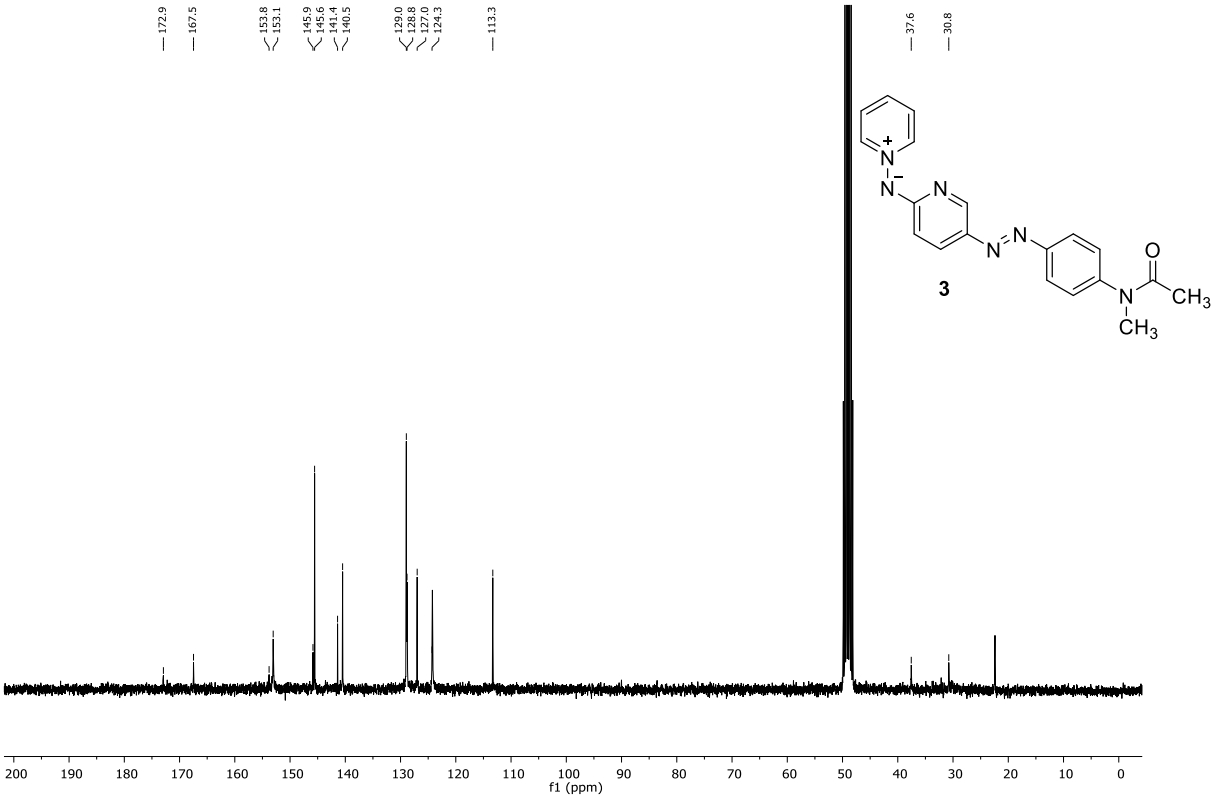

Figure S3. ^{13}C-NMR of product **3**.

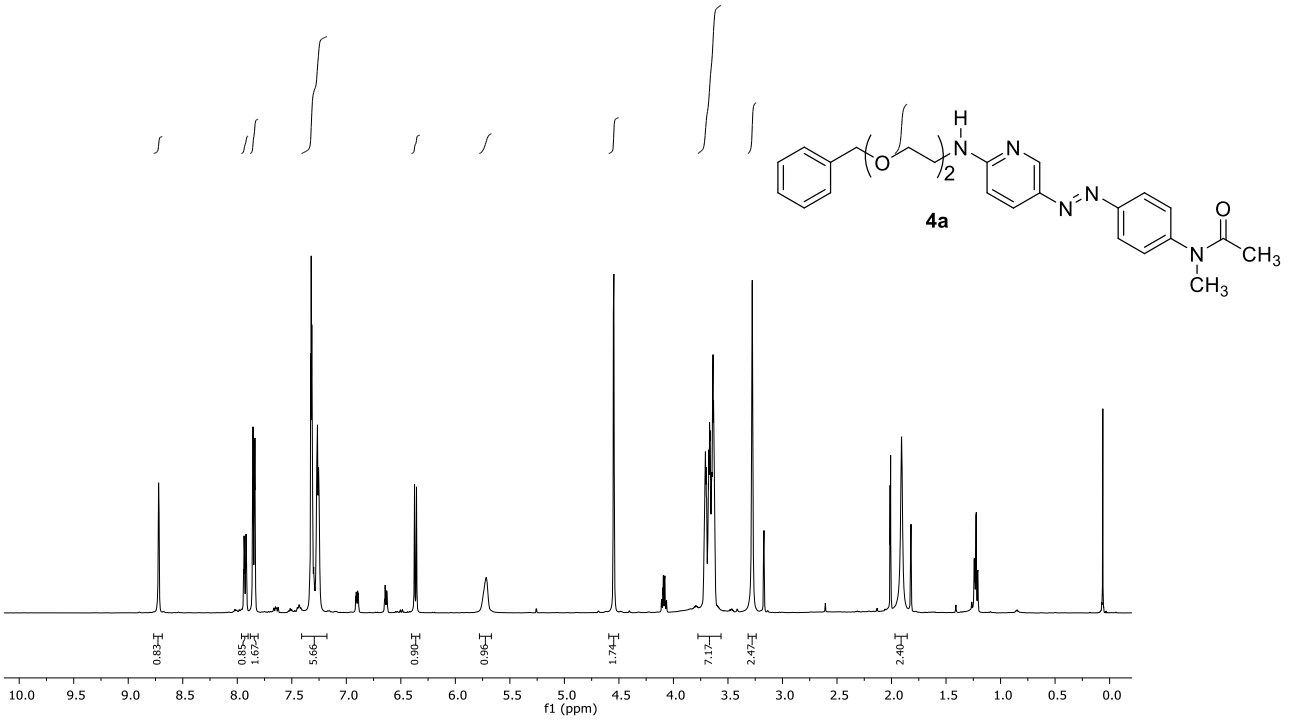

Figure S4. [1]H-NMR of product **4a**.

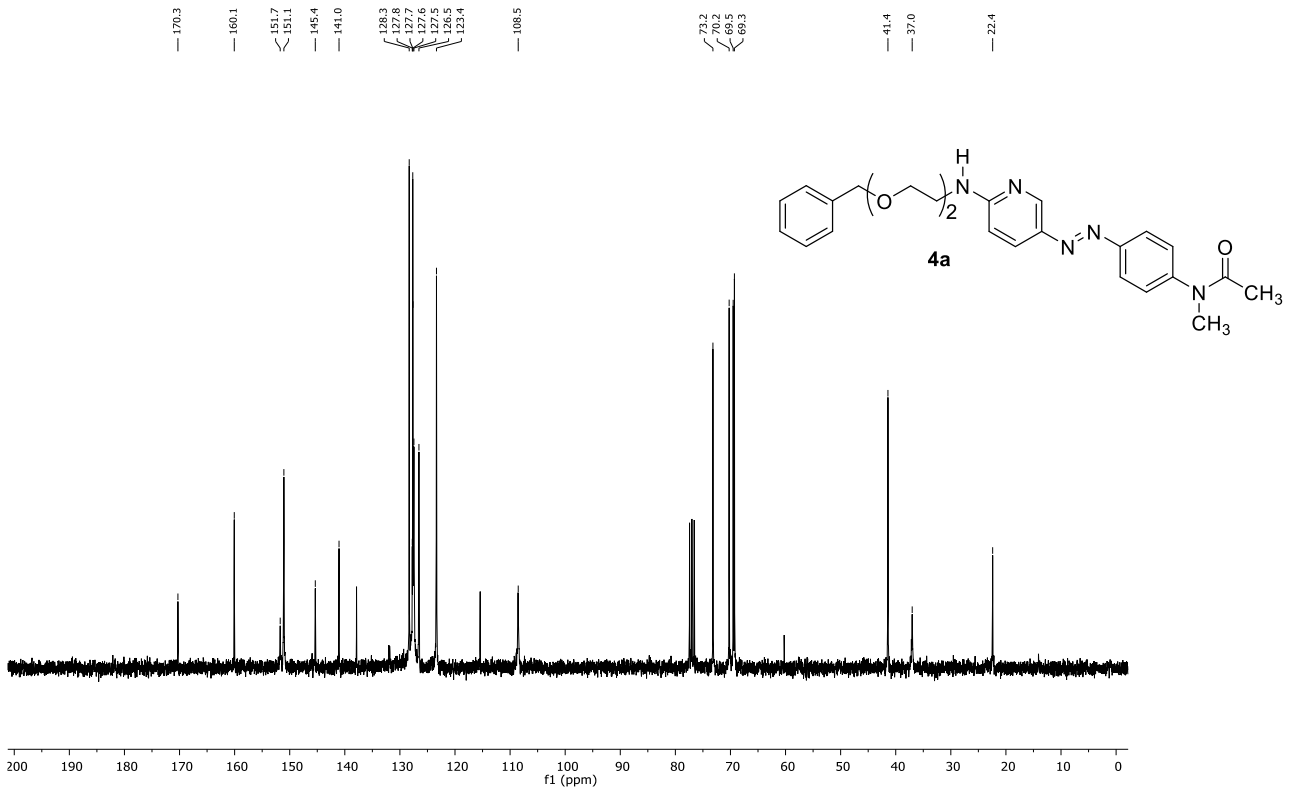

Figure S5. [13]C-NMR of product **4a**.

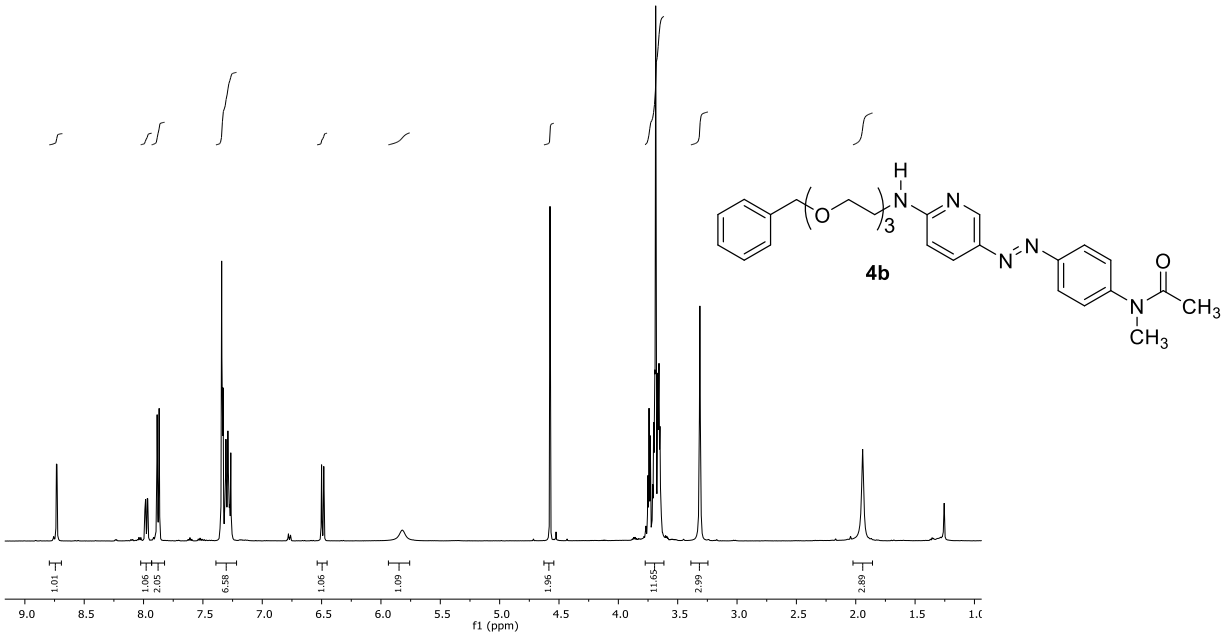

Figure S6. ^{1}H-NMR of product **4b**.

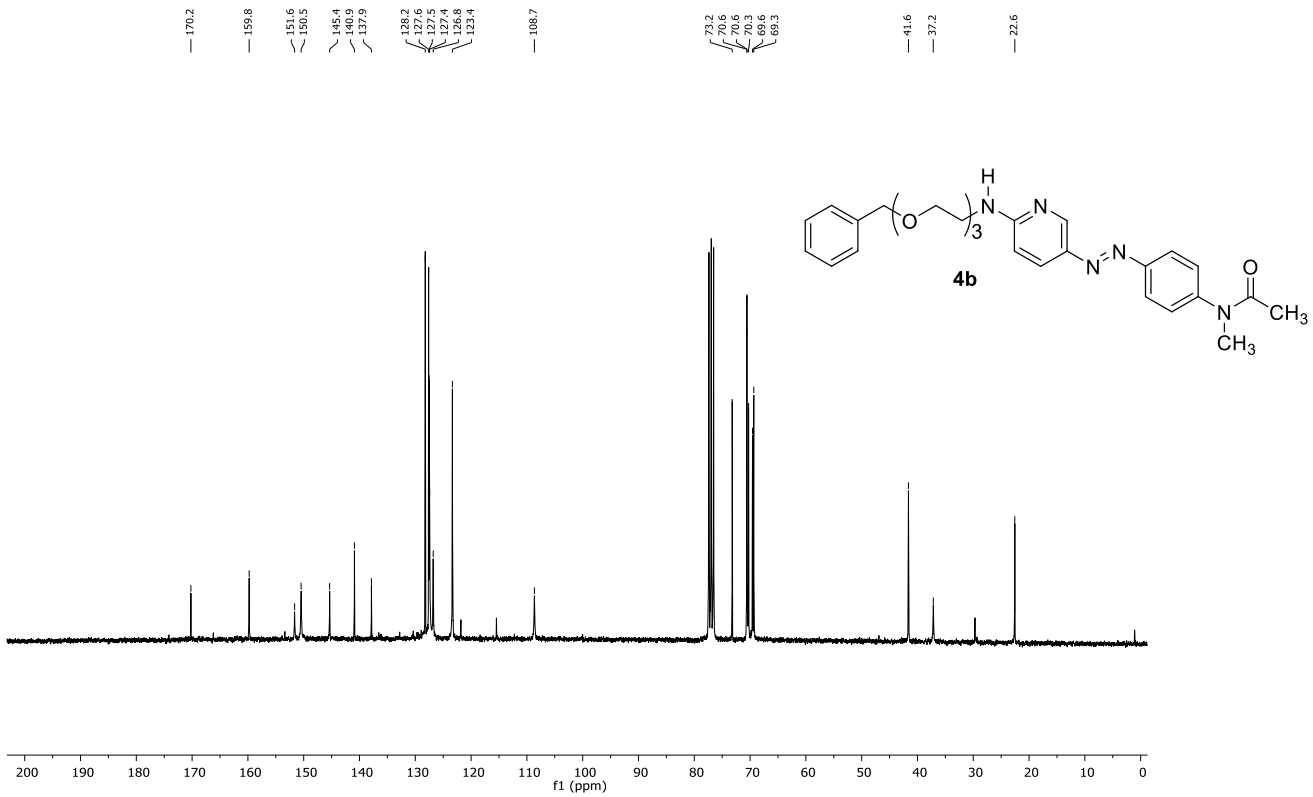

Figure S7. ^{13}C-NMR of product **4b**.

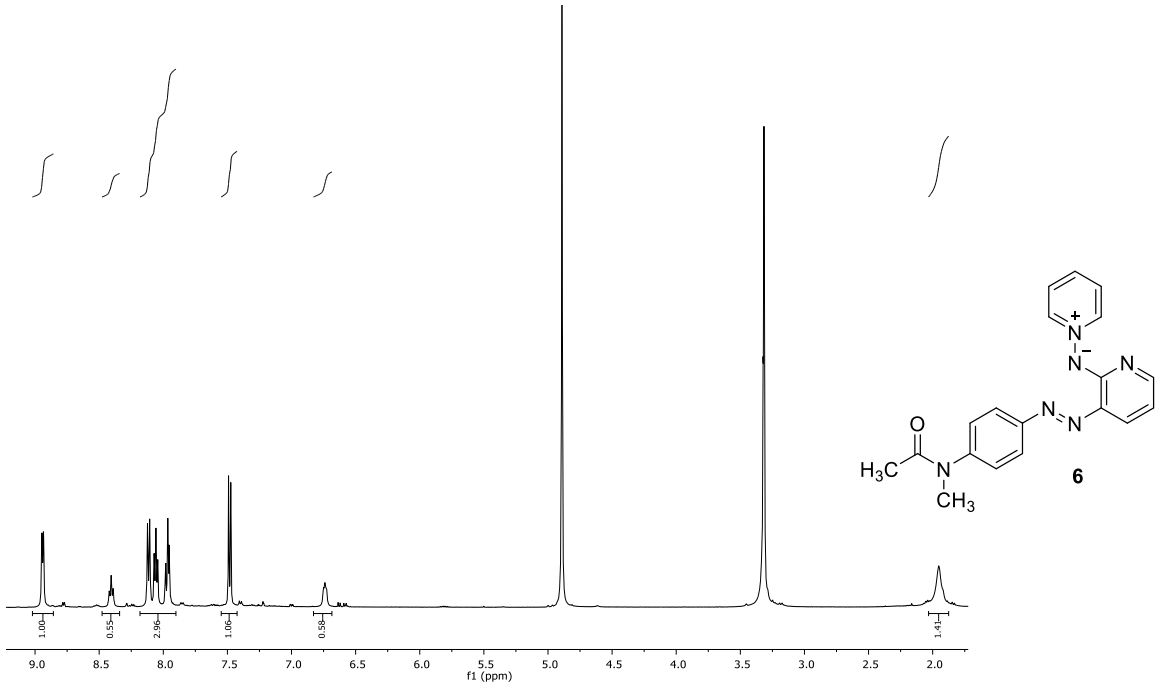

Figure S8. ^{1}H-NMR of product **6**.

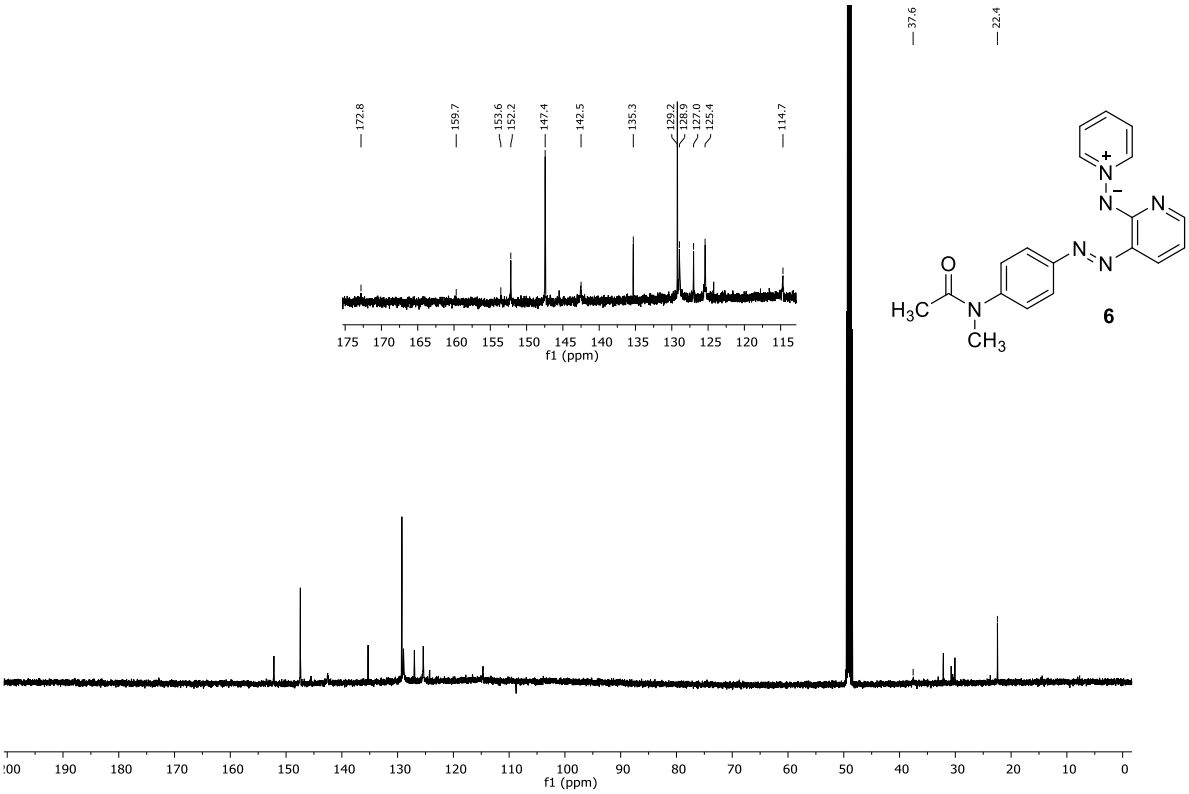

Figure S9. ^{13}C-NMR of product **6**.

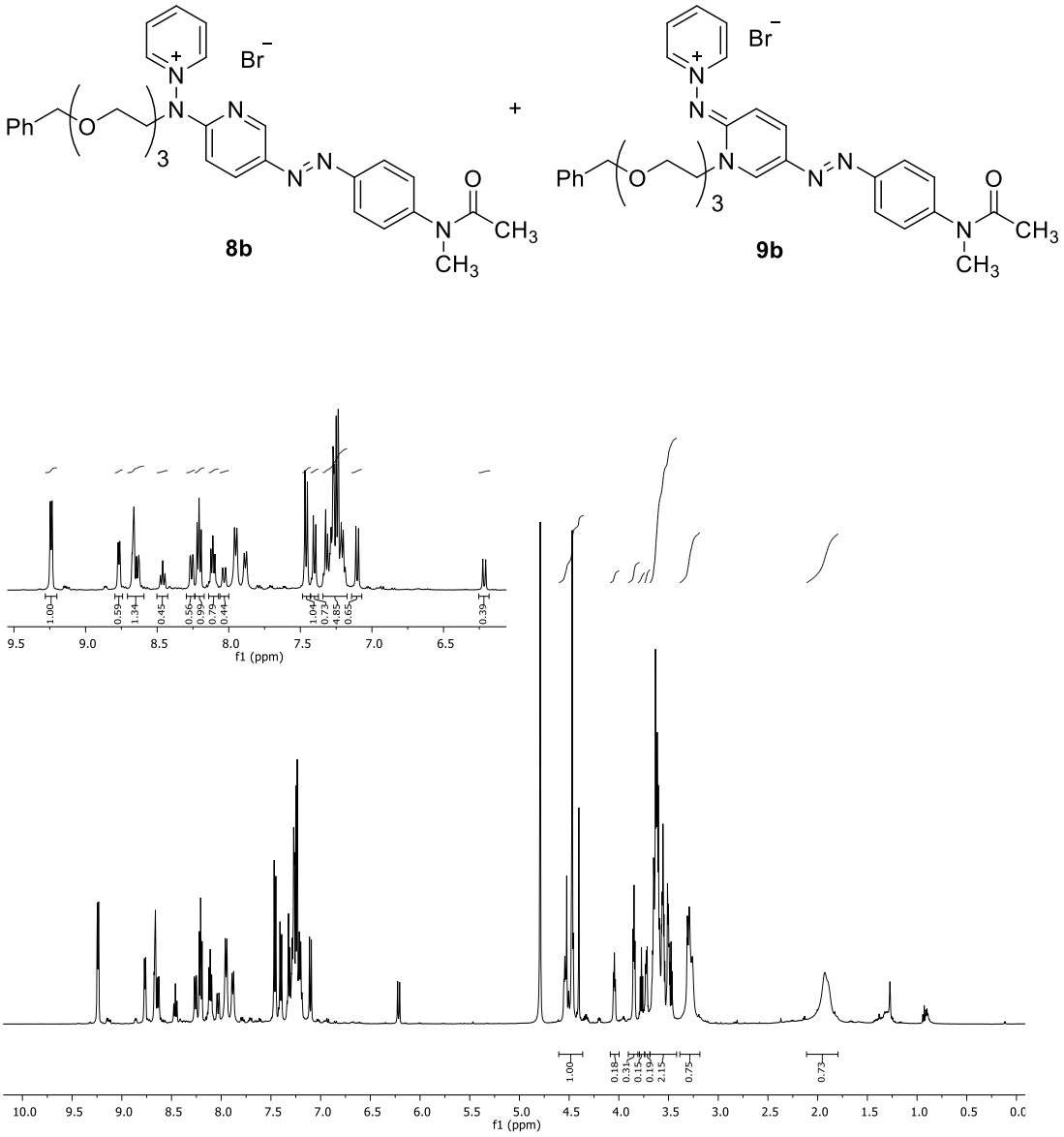

Figure S10. ^{1}H-NMR of mixture of salts **8b** and **9b**.

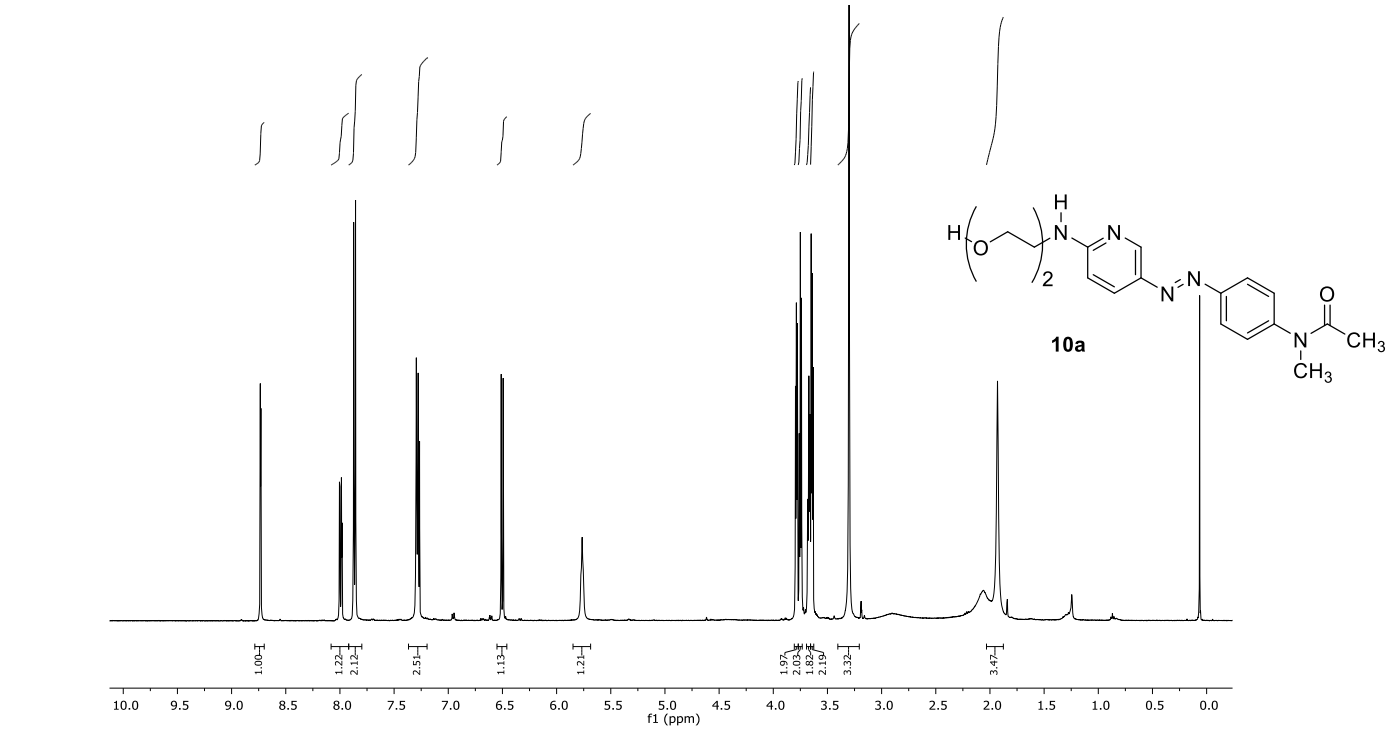

Figure S11. ^{1}H-NMR of product **10a**.

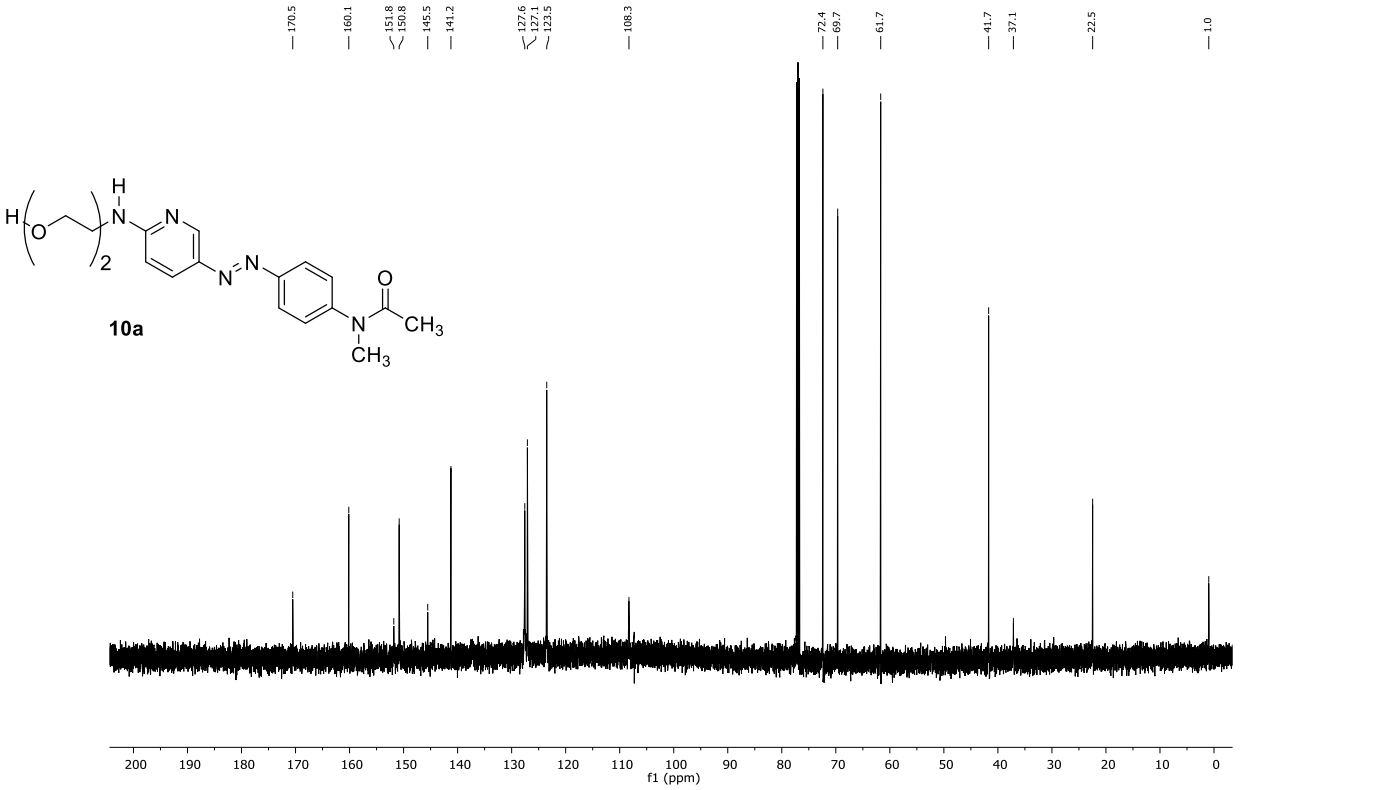

Figure S12. ^{13}C-NMR of product **10a**.

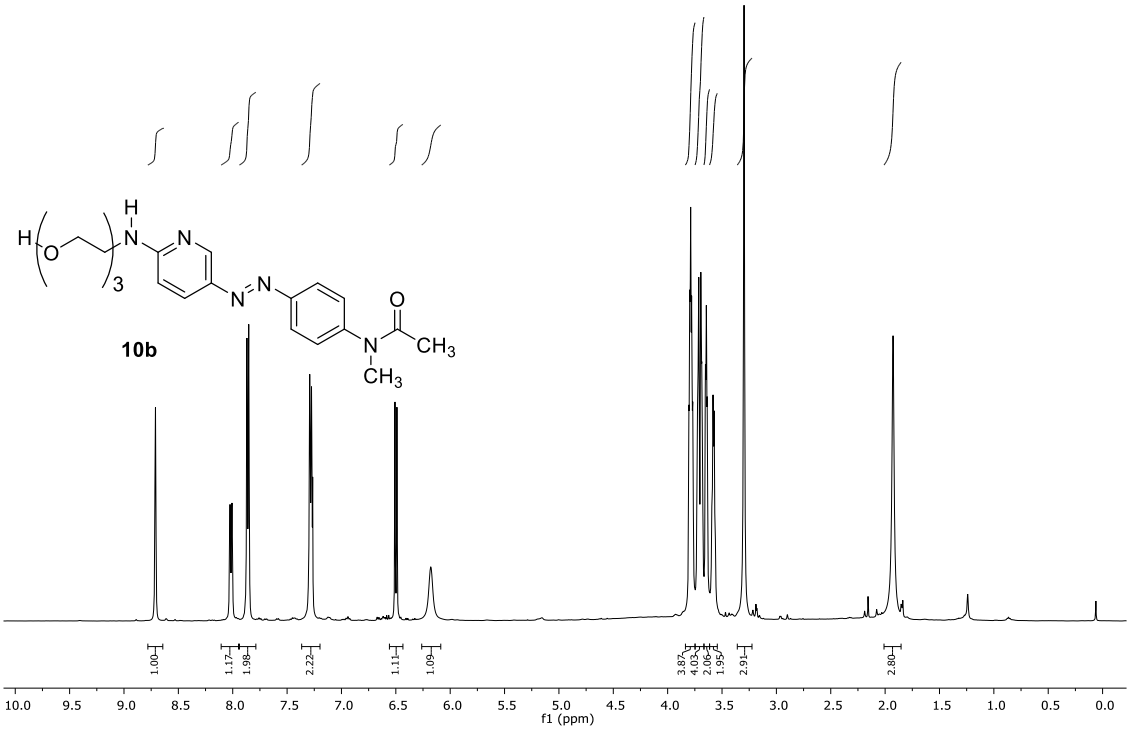

Figure S13. ^{1}H-NMR of product **10b**.

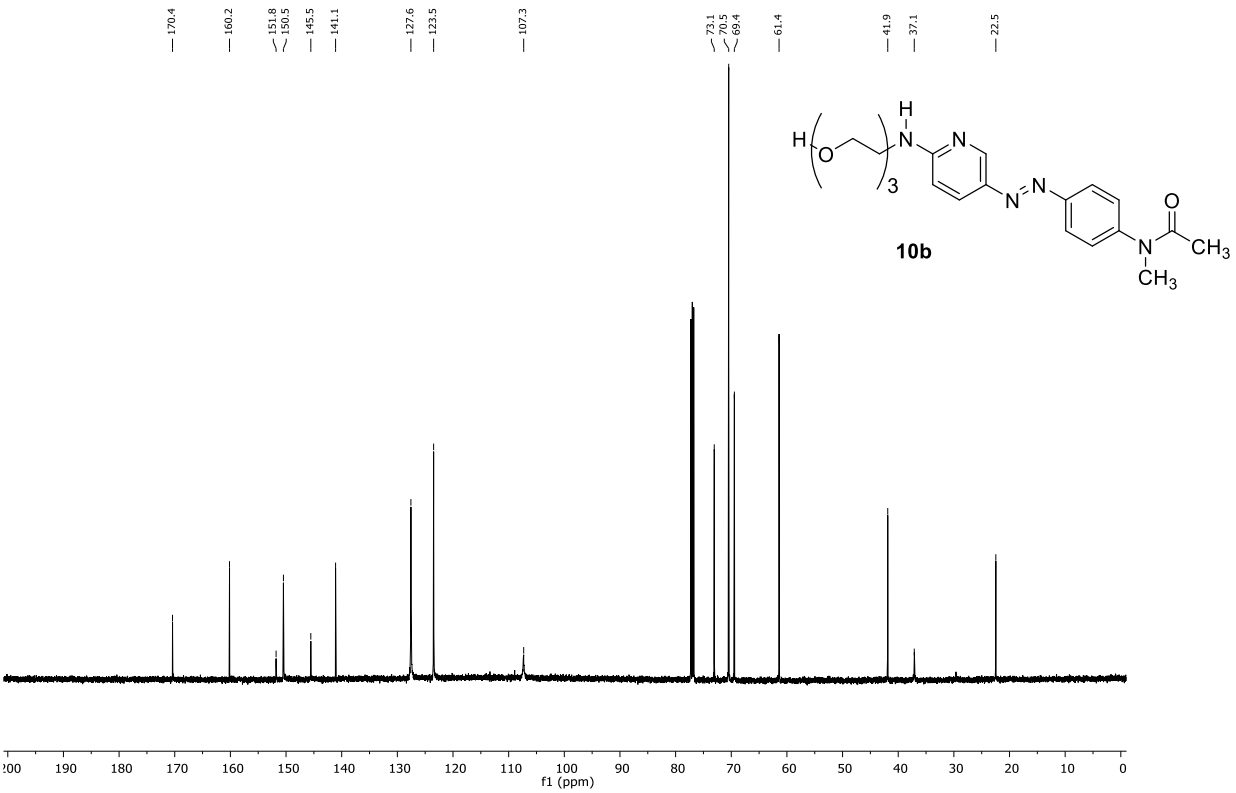

Figure S14. ^{13}C-NMR of product **10b**.

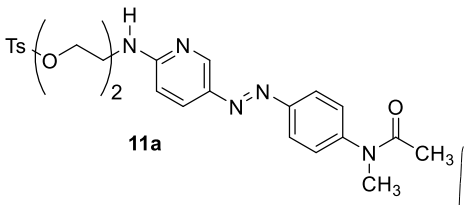

Figure S15. ^{1}H-NMR of product **11a**.

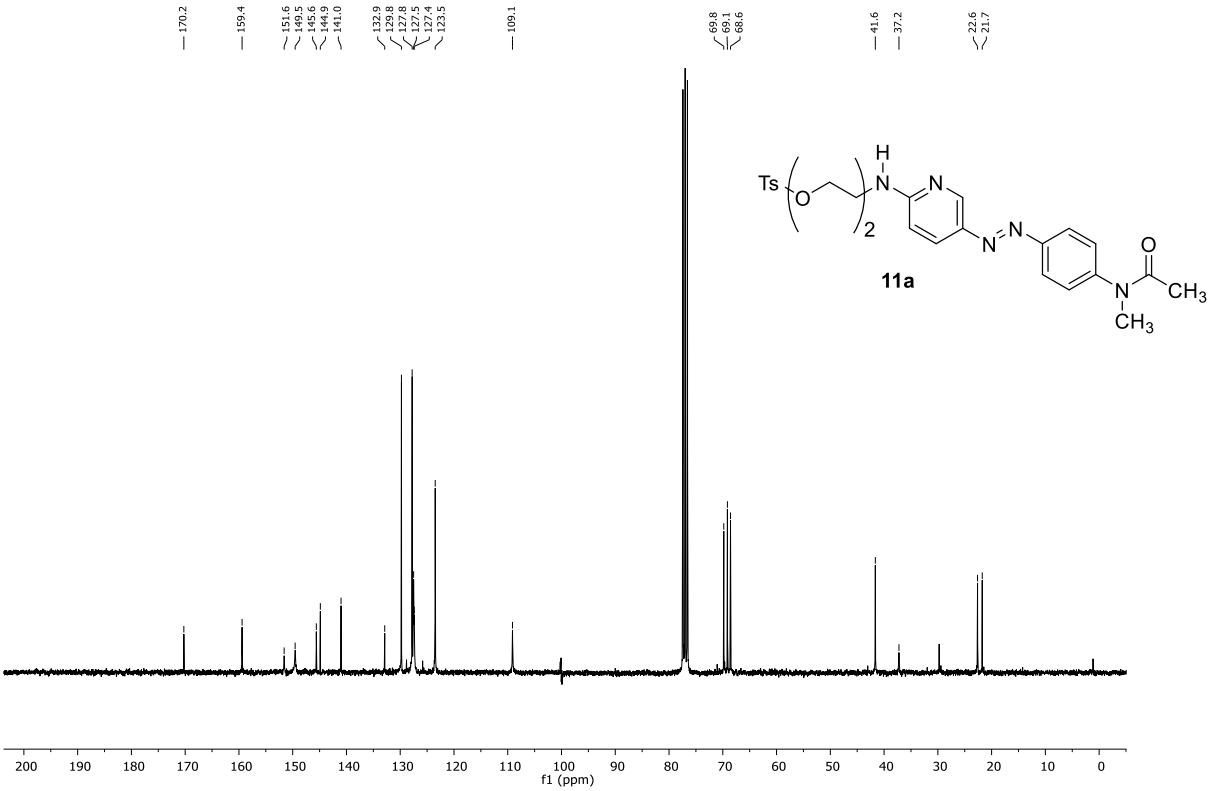

Figure S16. ^{13}C-NMR of product **11a**.

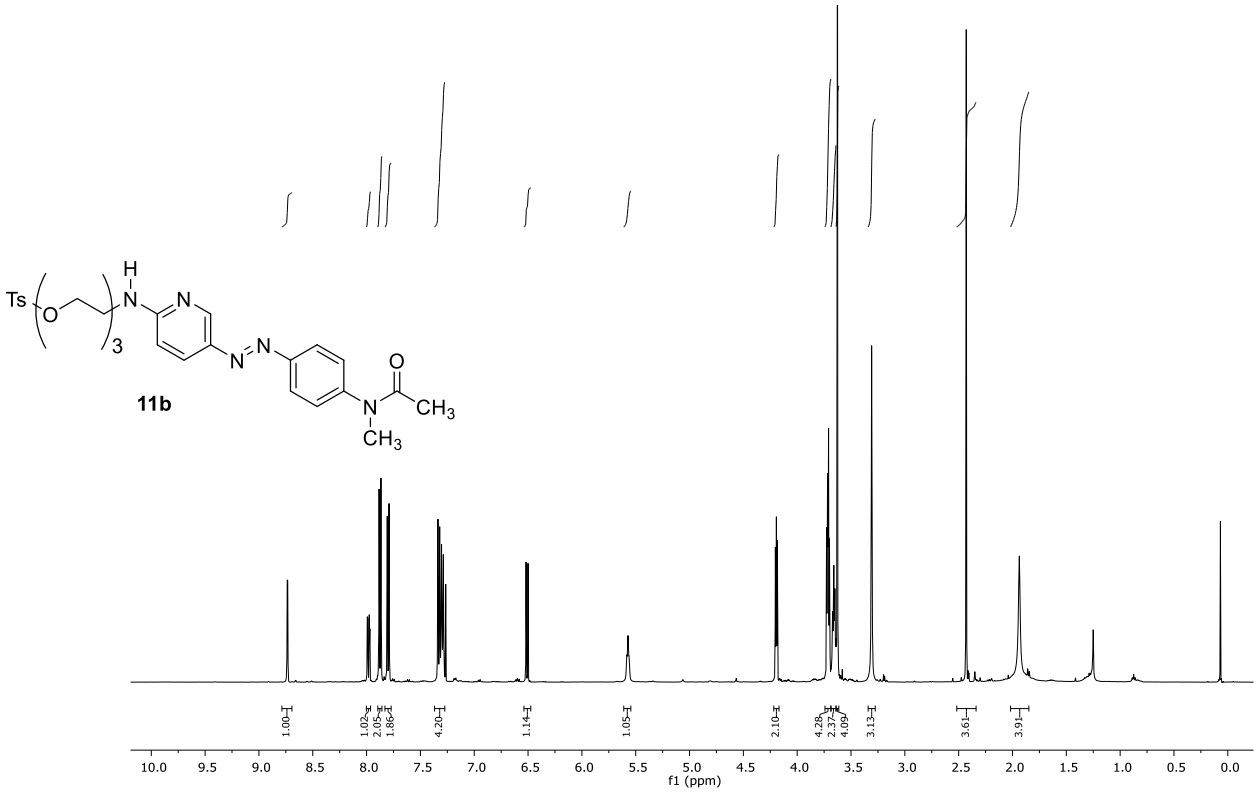

Figure S17. ^{1}H-NMR of product **11b**.

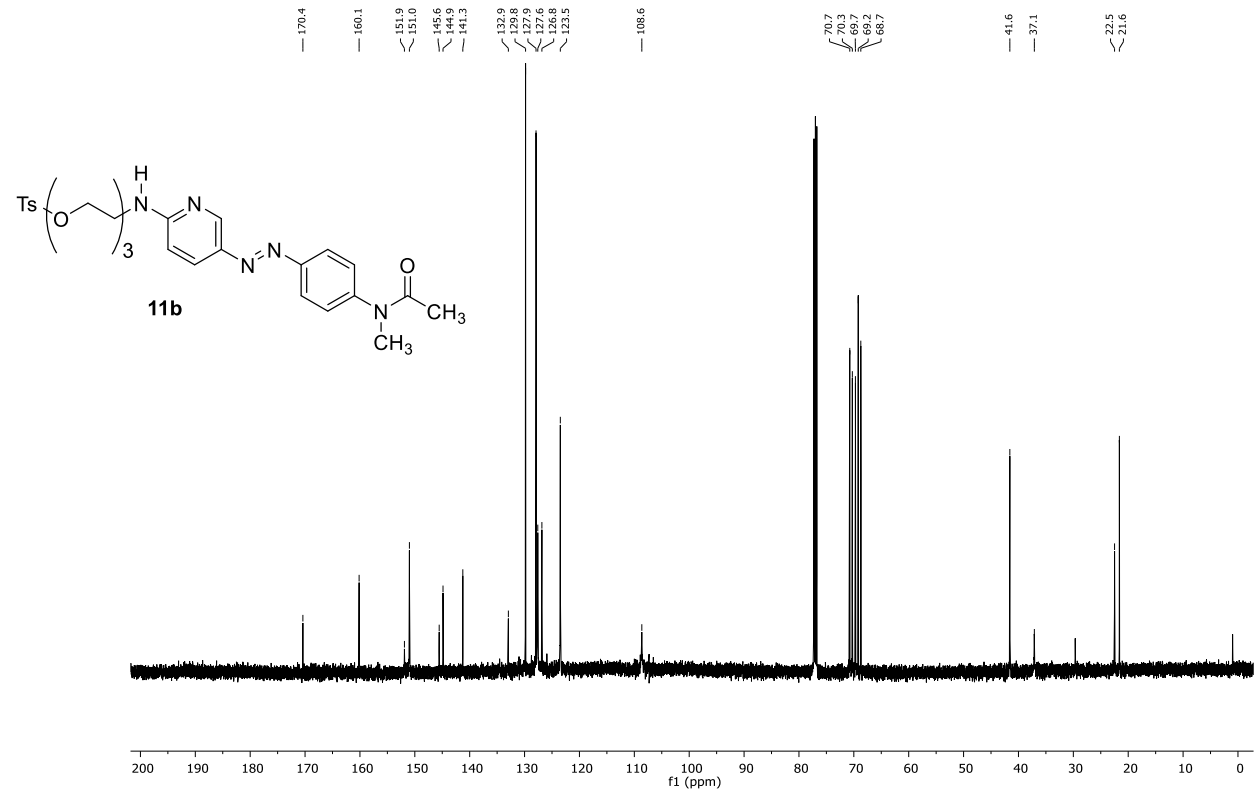

Figure S18. ^{13}C-NMR of product **11b**.

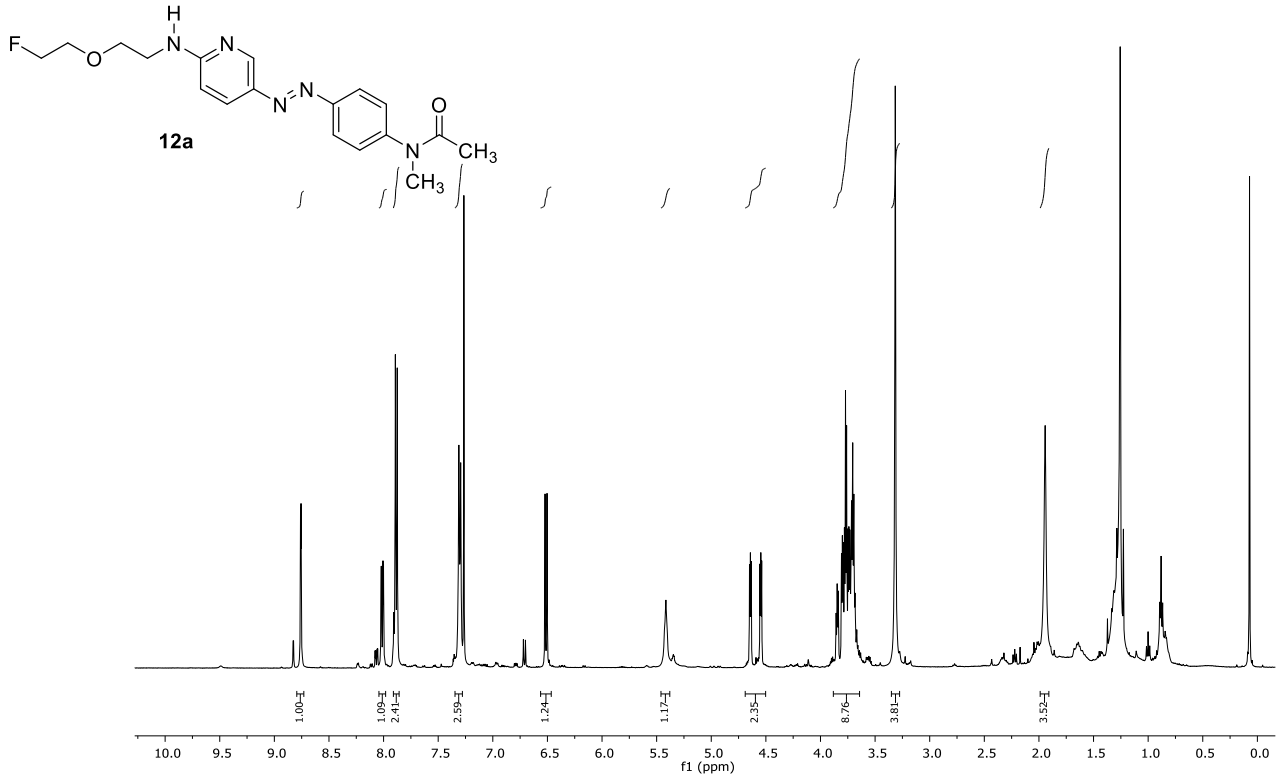

Figure S19. ^{1}H-NMR of product **12a**.

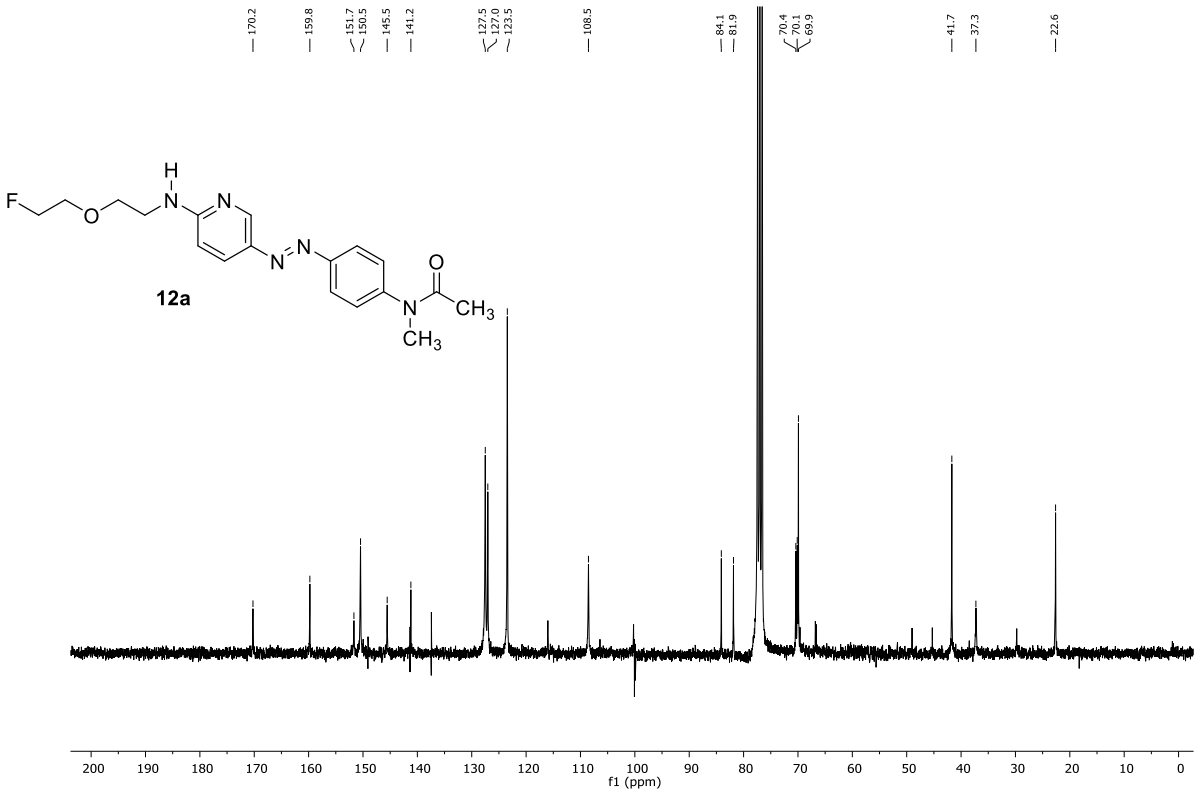

Figure S20. ^{13}C-NMR of product **12a**.

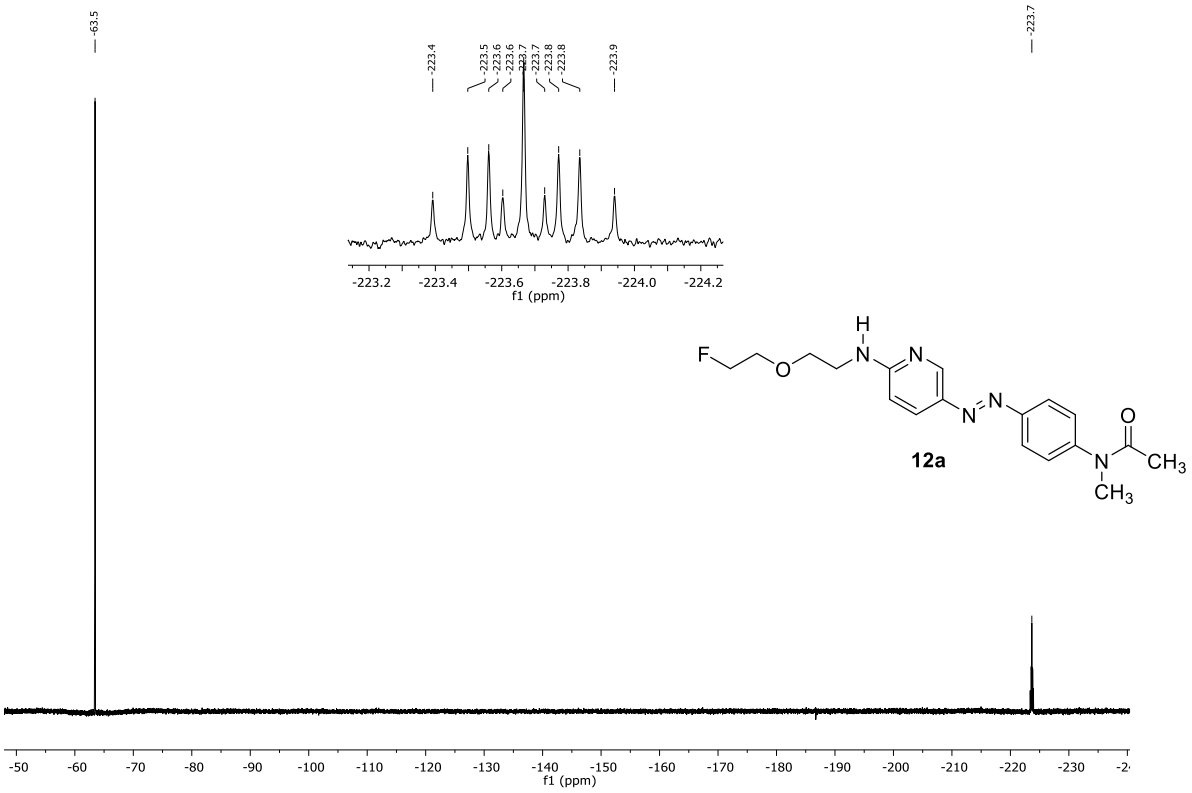

Figure S21. ^{19}F-NMR of product **12a**.

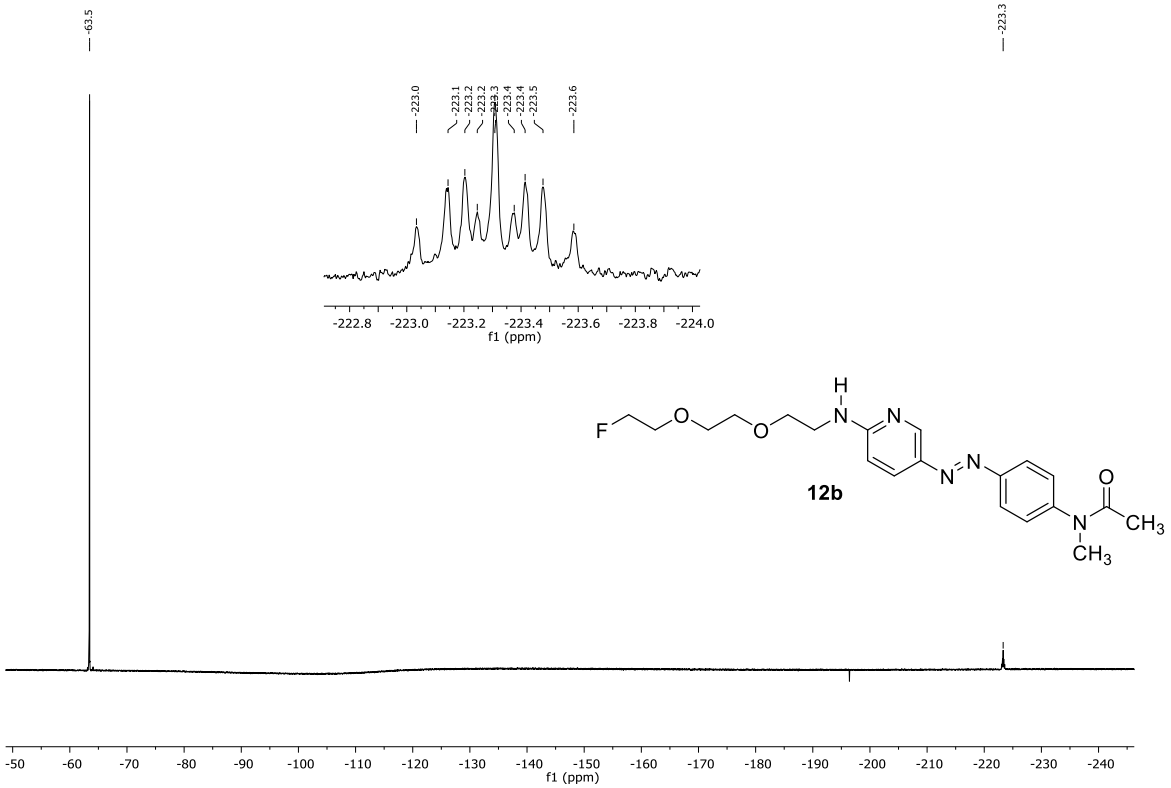

Figure S22. ^{19}F-NMR of product **12b**.

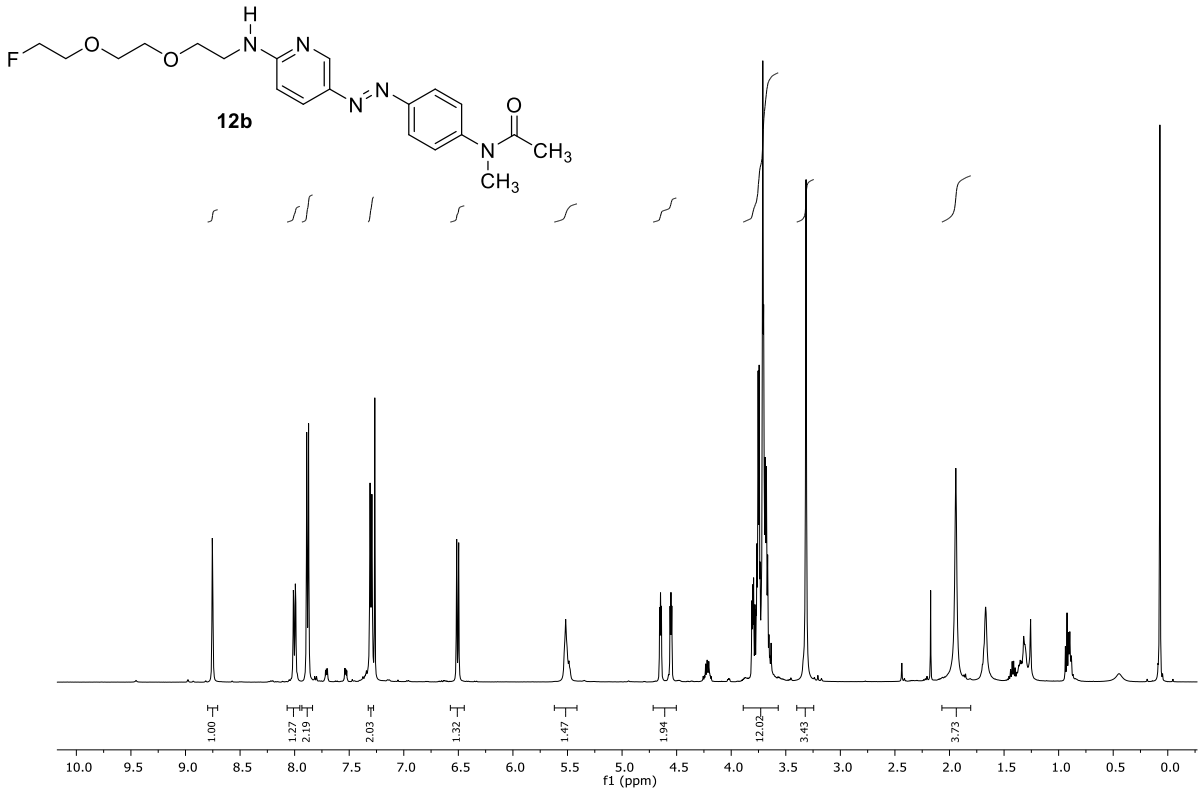

Figure S23. ^{1}H-NMR of product **12b**.

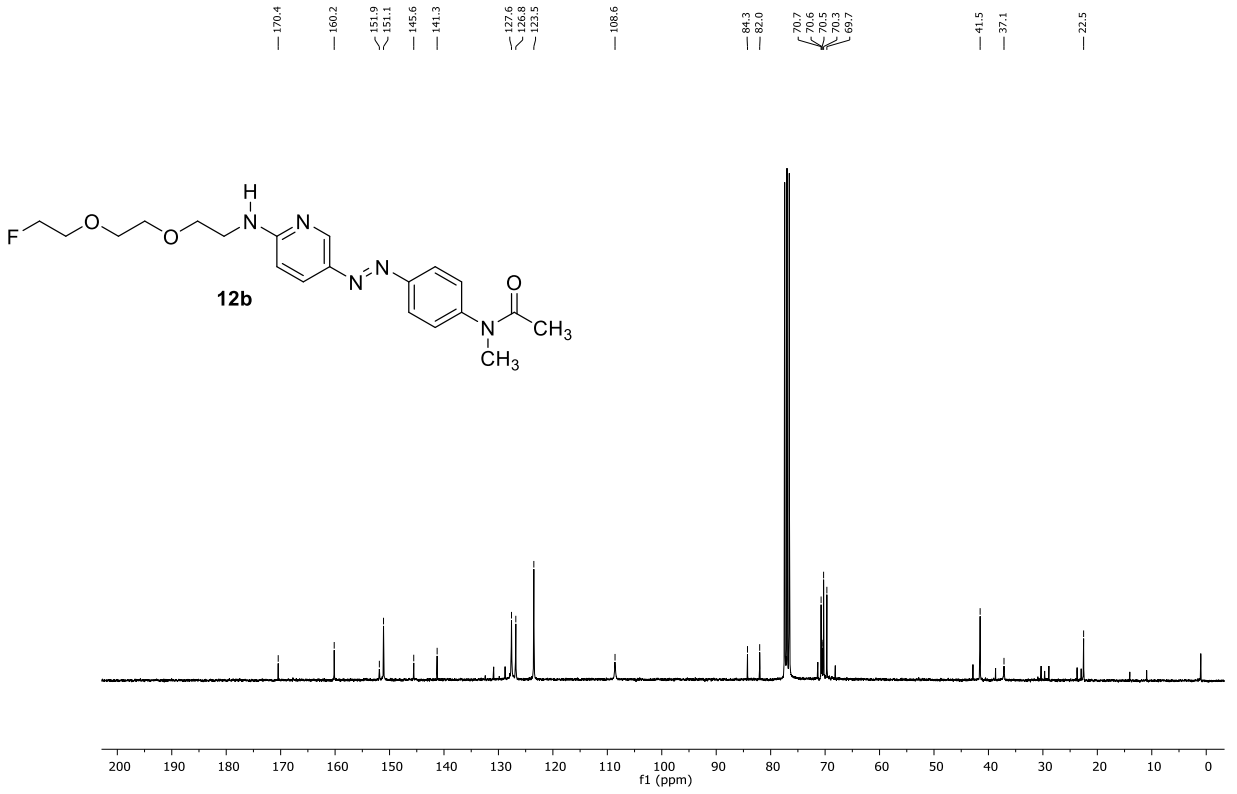

Figure S24. ^{13}C-NMR of product **12b**.

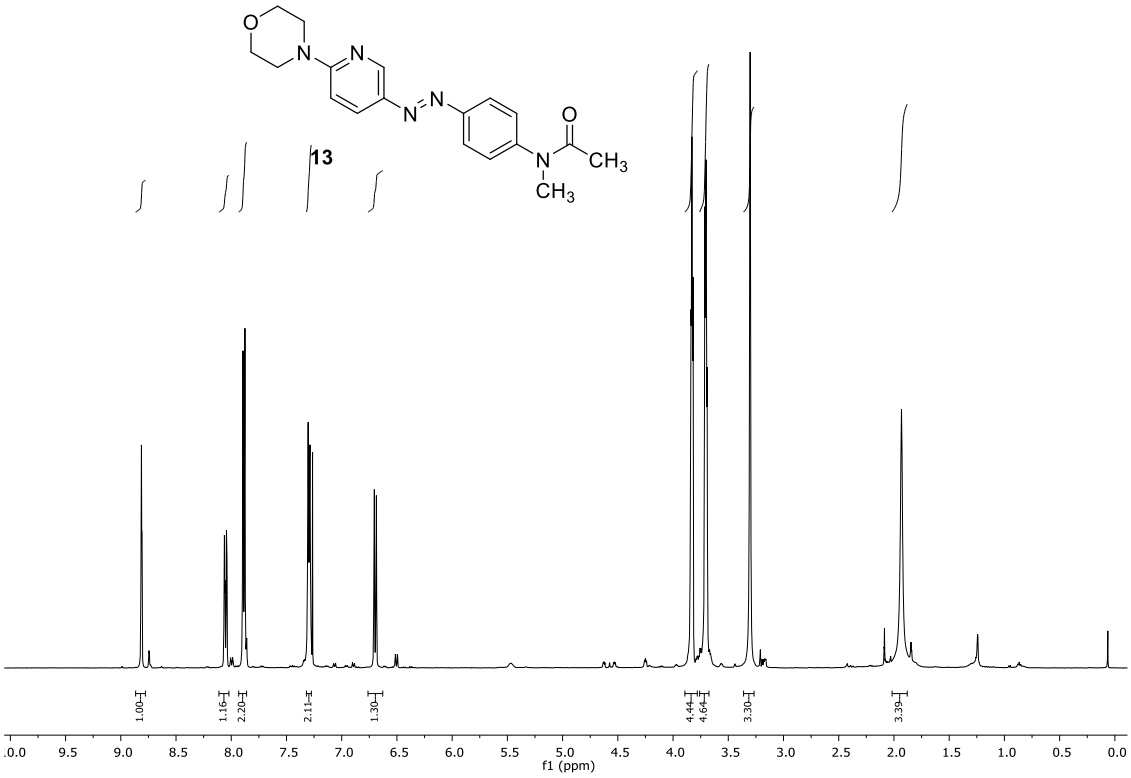

Figure S25. ^{1}H-NMR of product **13**.

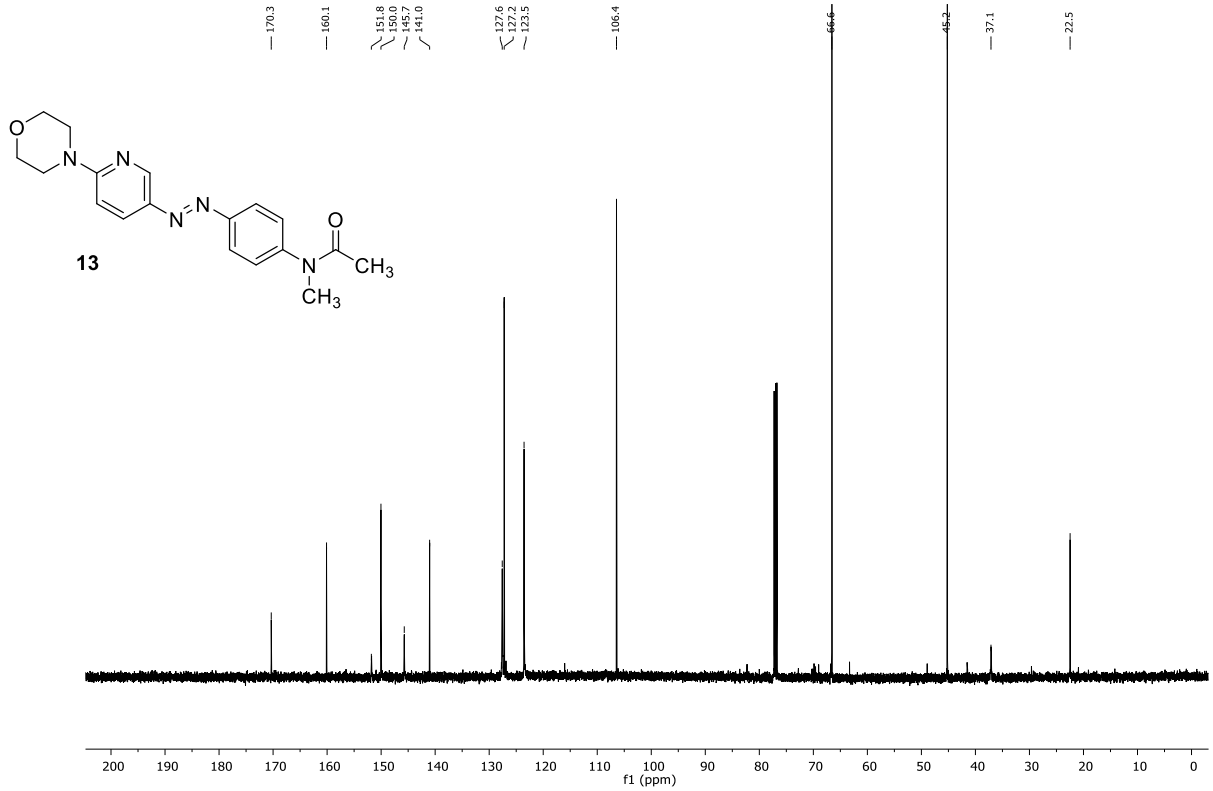

Figure S26. ^{13}C-NMR of product **13**.

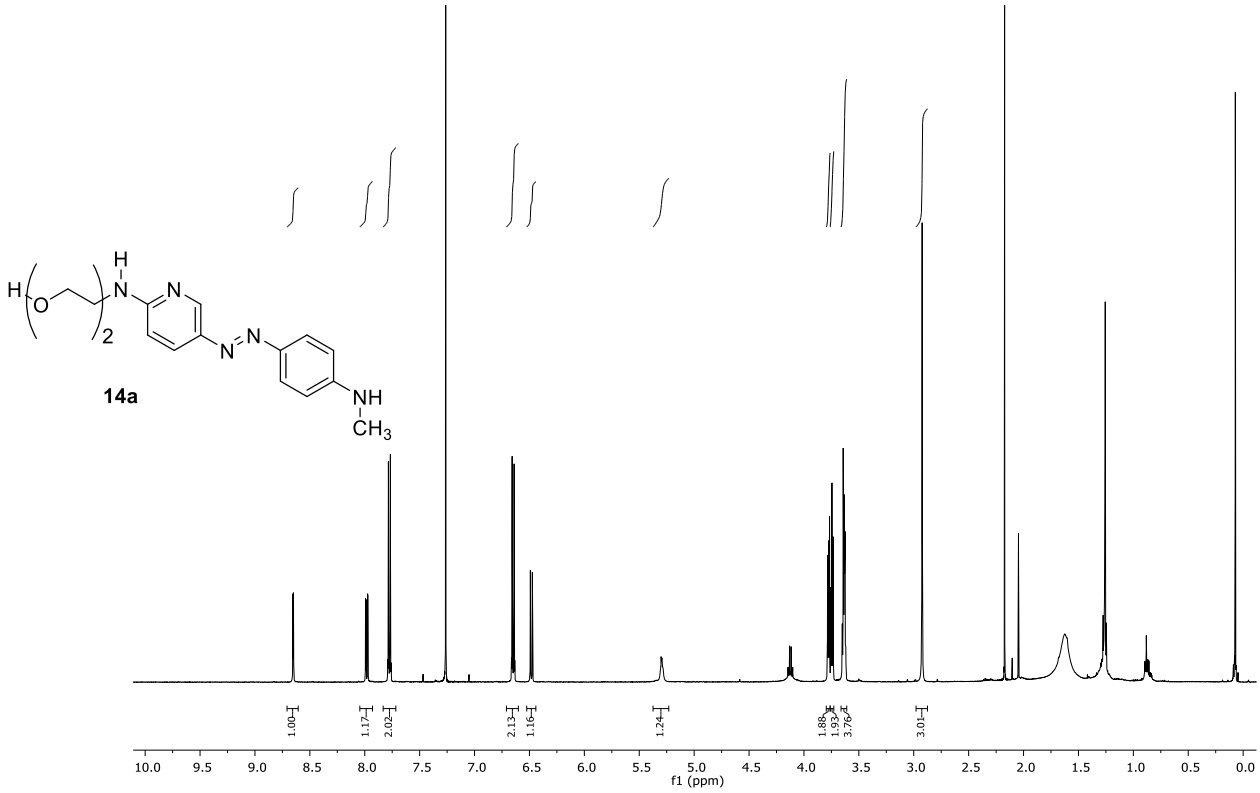

Figure S27. ^{1}H-NMR of product **14a**.

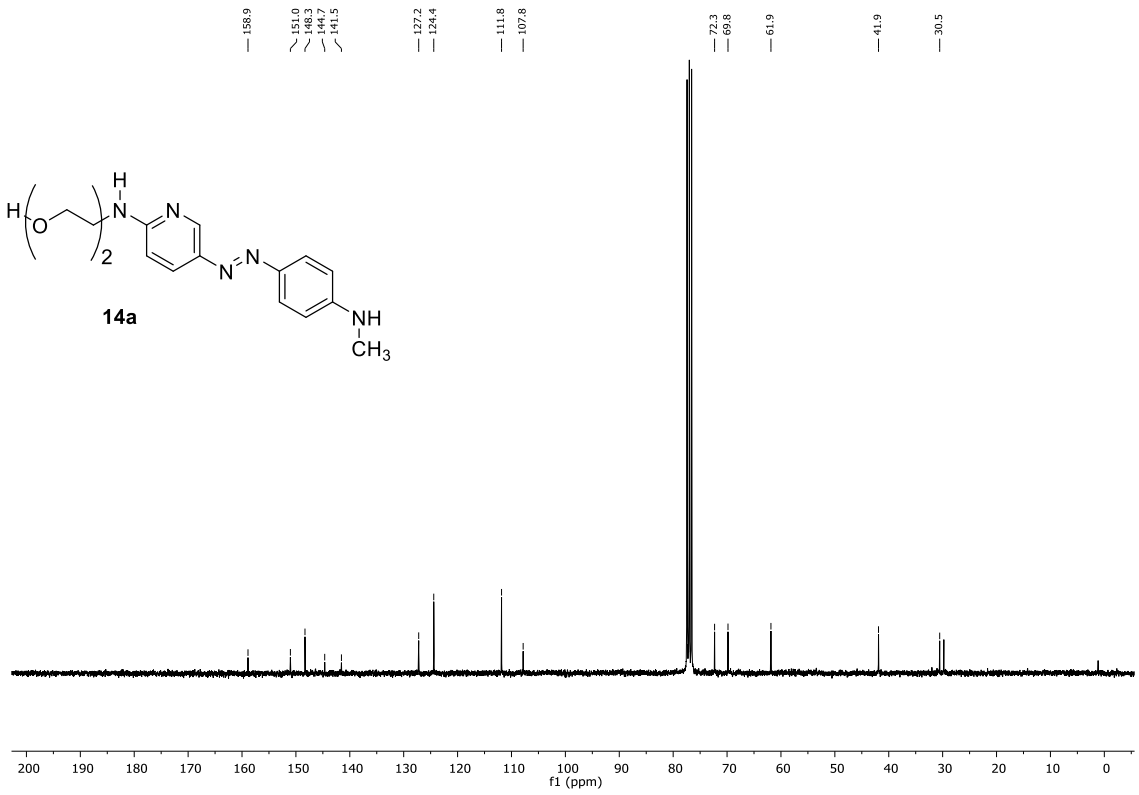

Figure S28. ^{13}C-NMR of product **14a**.

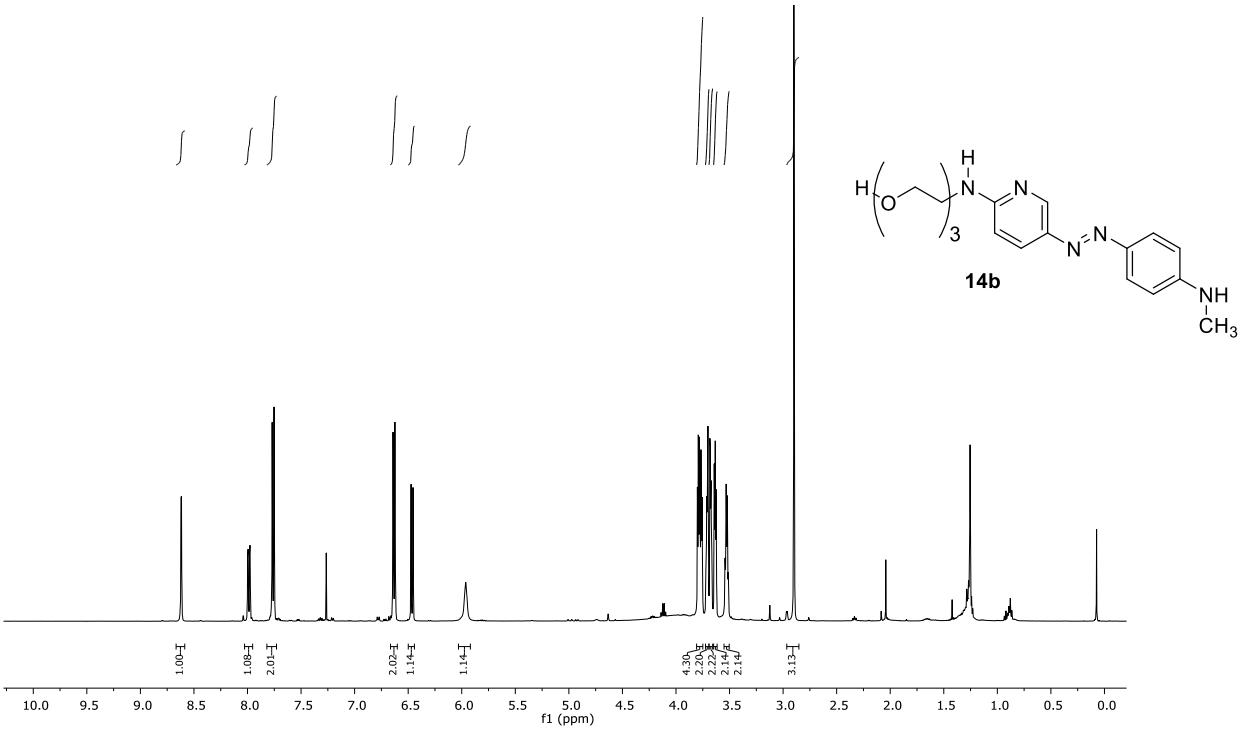

Figure S29. ^{1}H-NMR of product **14b**.

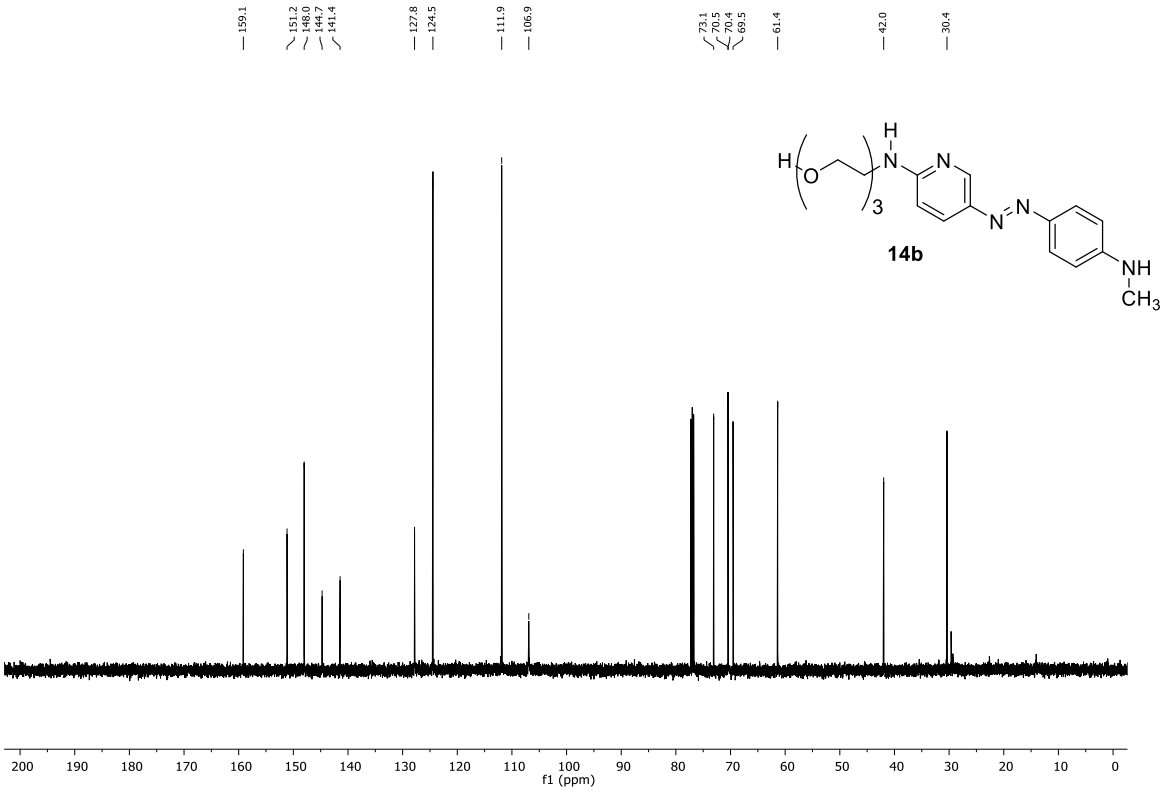

Figure S30. ^{13}C-NMR of product **14b**.

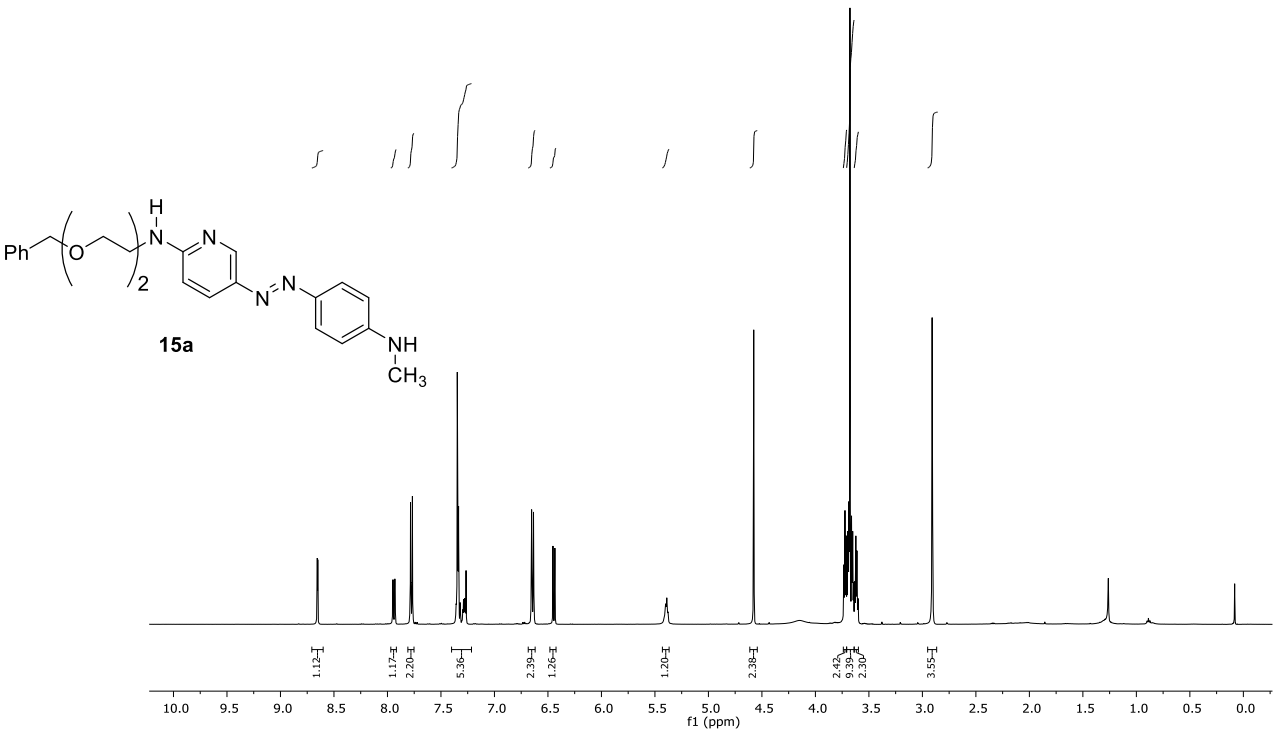

Figure S31. ^{1}H-NMR of product **15a**.

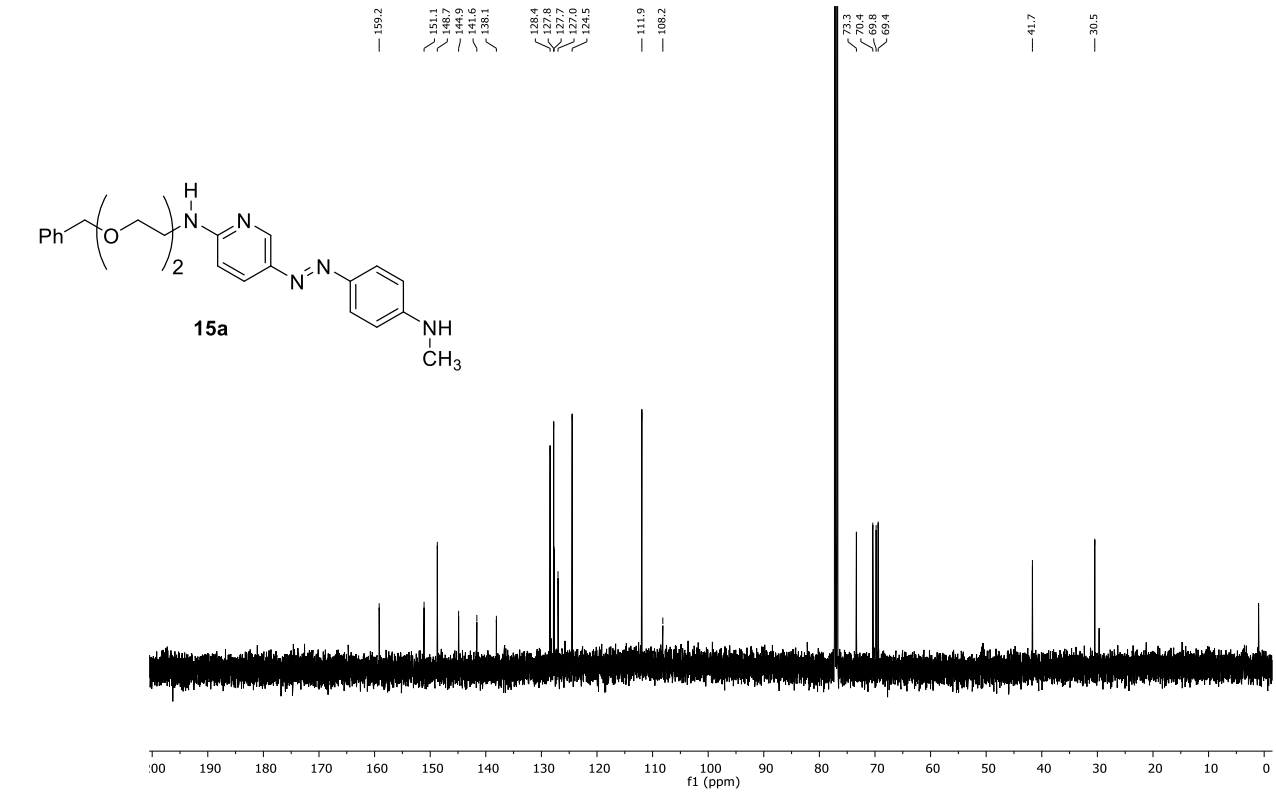

Figure S32. ^{13}C-NMR of product **15a**.

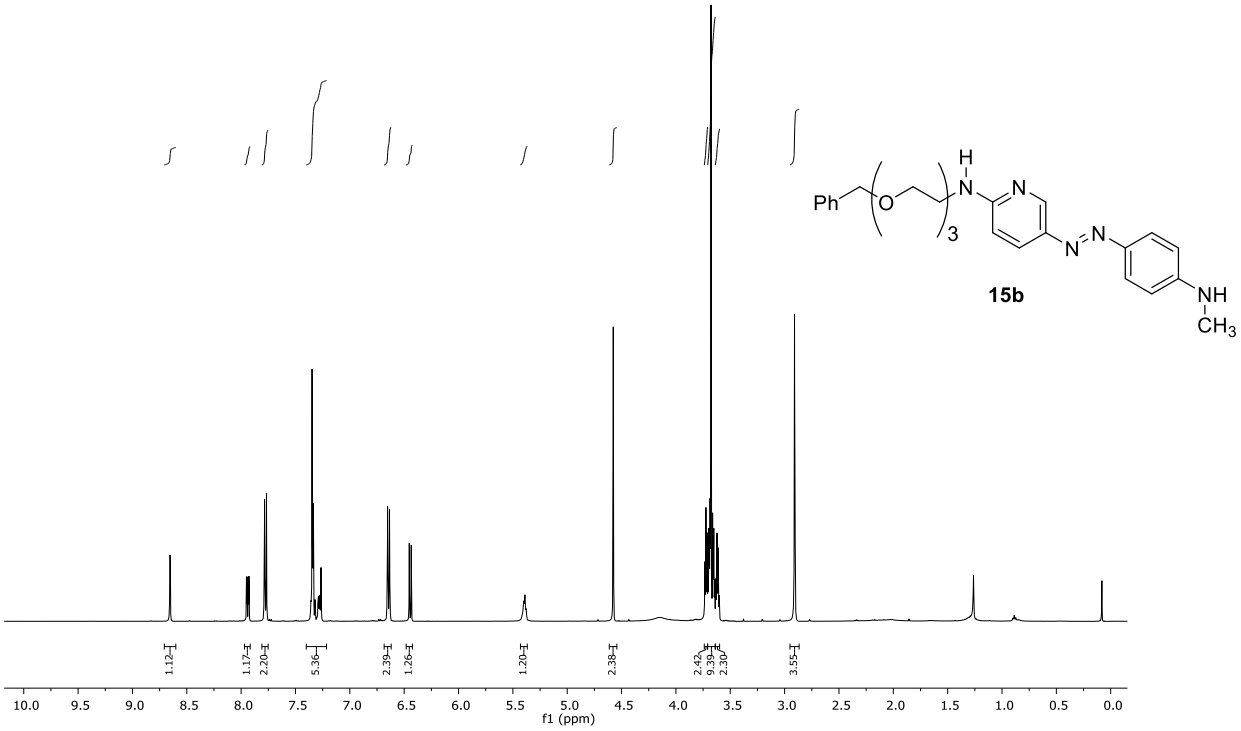

Figure S33. ^{1}H-NMR of product **15b**.

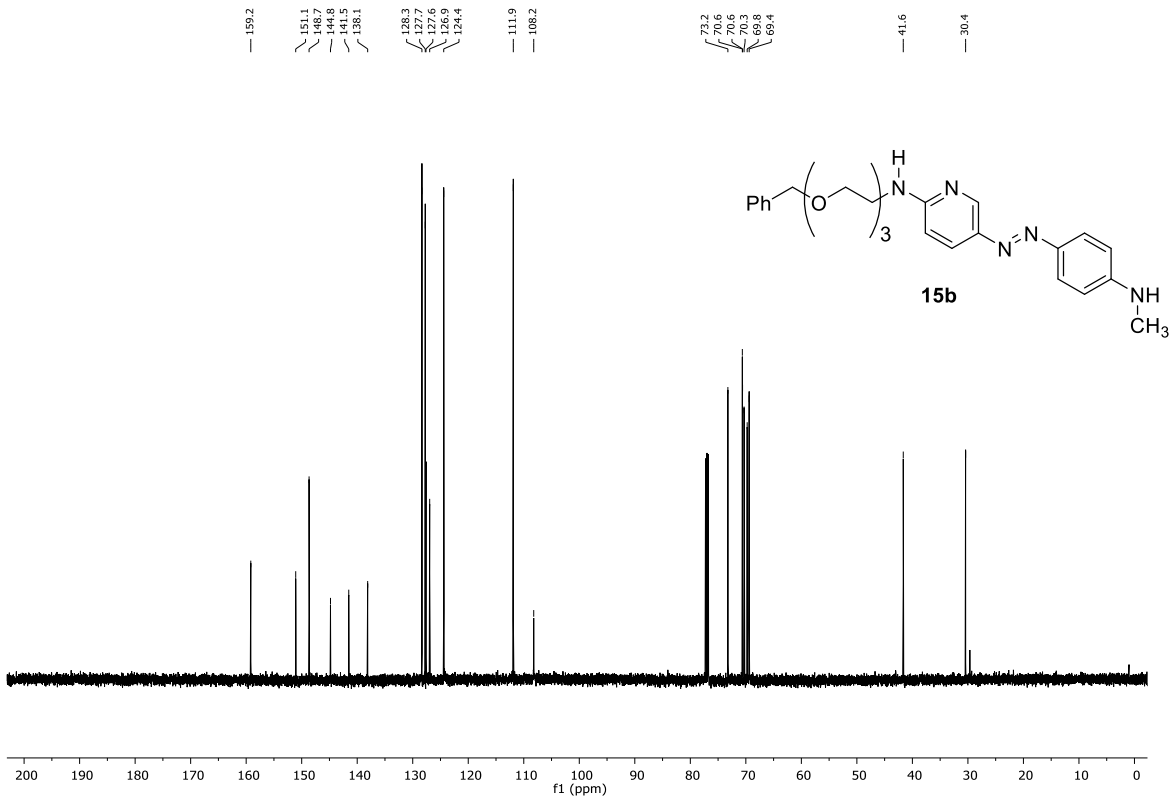

Figure S34. ^{13}C-NMR of product **15b**.

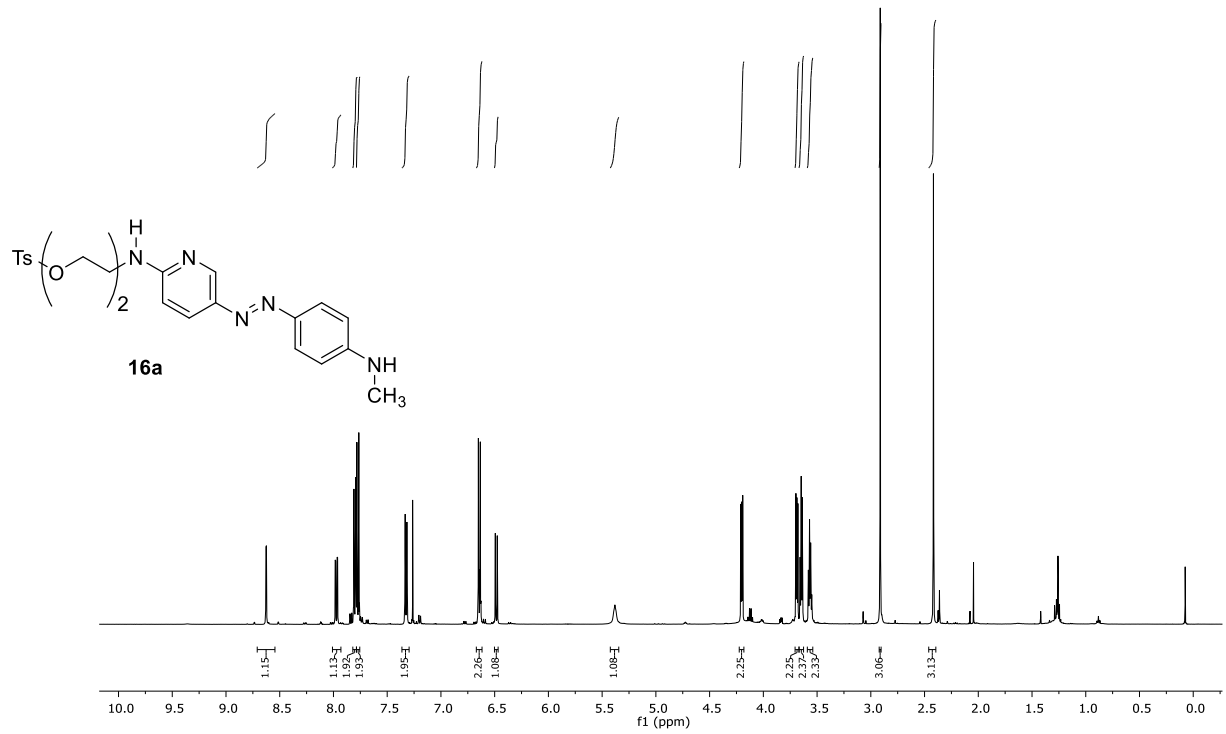

Figure S35. ^{1}H-NMR of product **16a**.

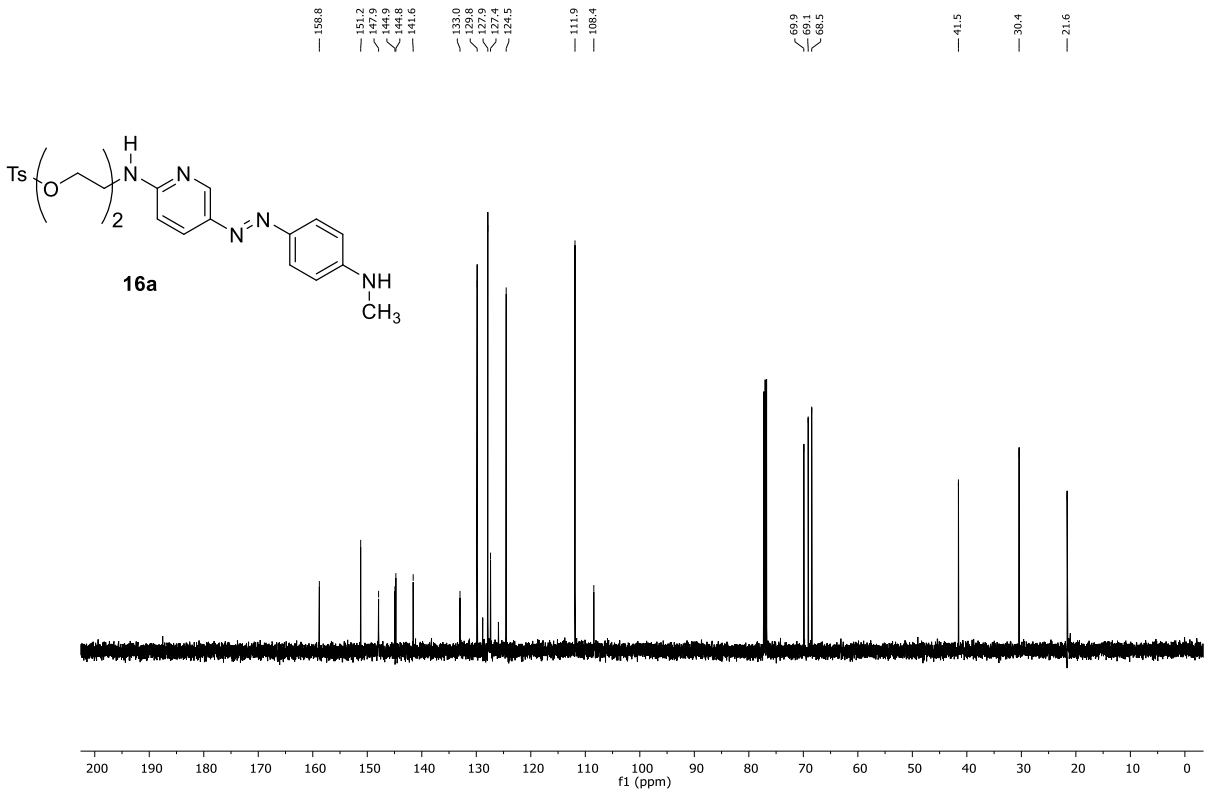

Figure S36. ^{13}C-NMR of product **16a**.

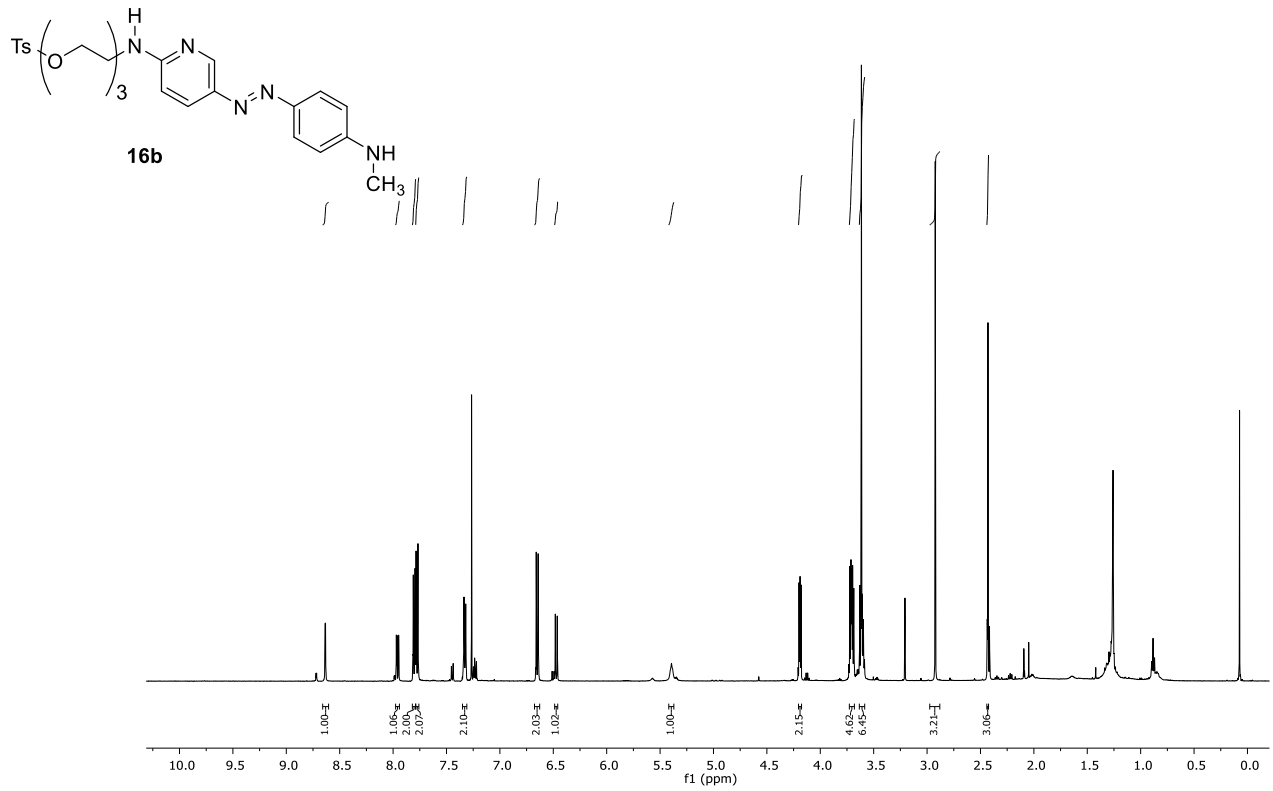

Figure S37. ^{1}H-NMR of product **16b**.

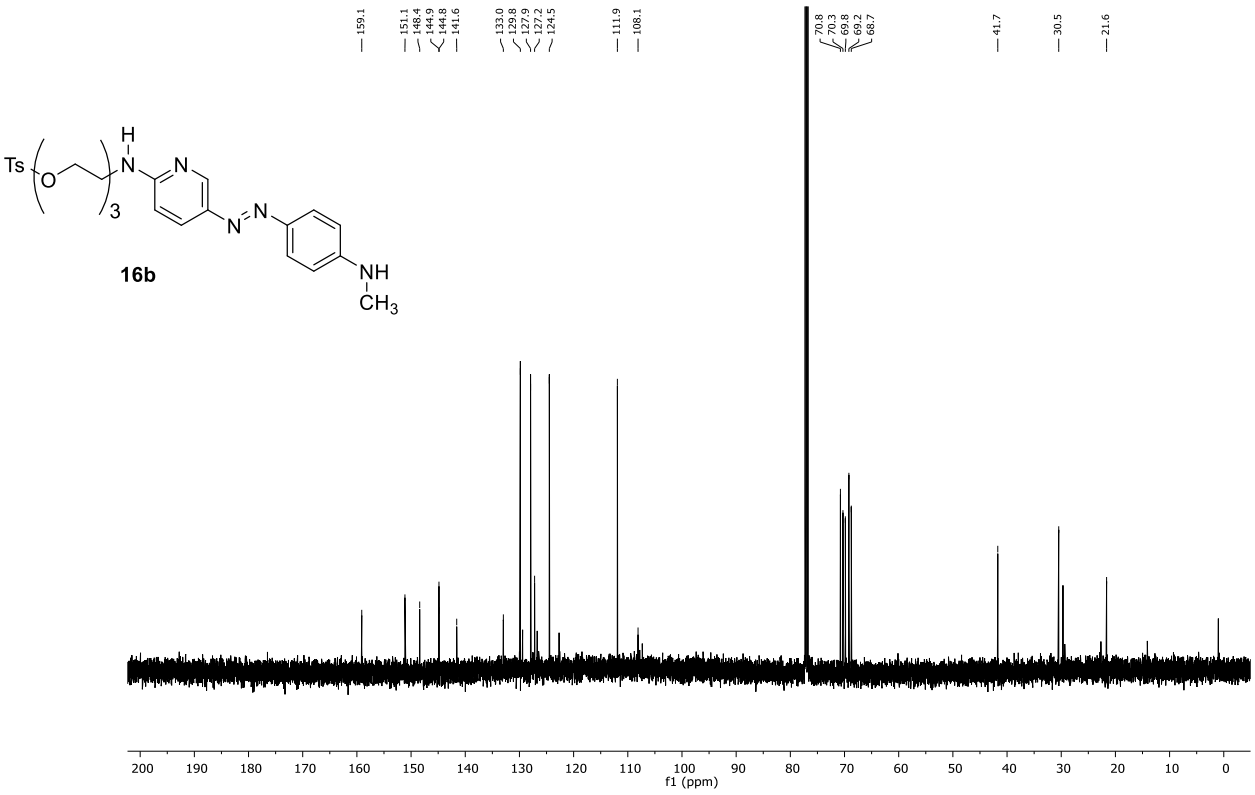

Figure S38. ^{13}C-NMR of product **16b**.

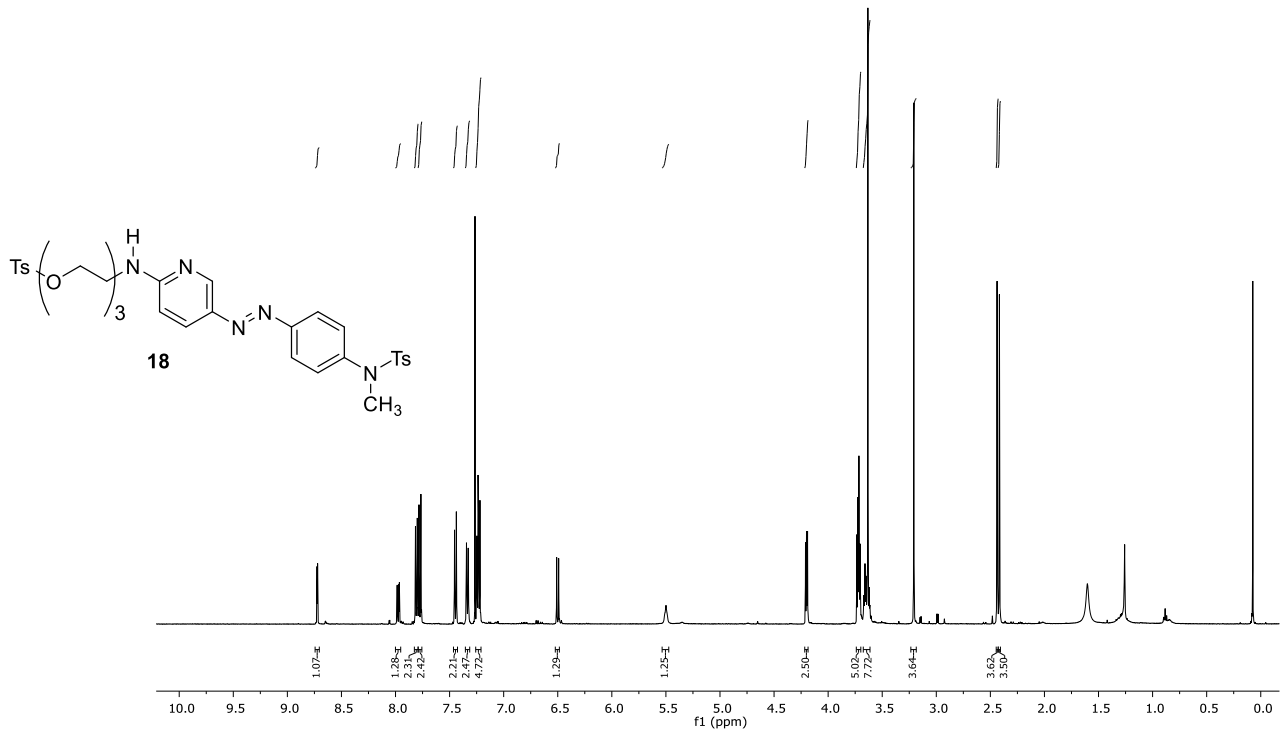

Figure S39. ^{1}H-NMR of product **18**.

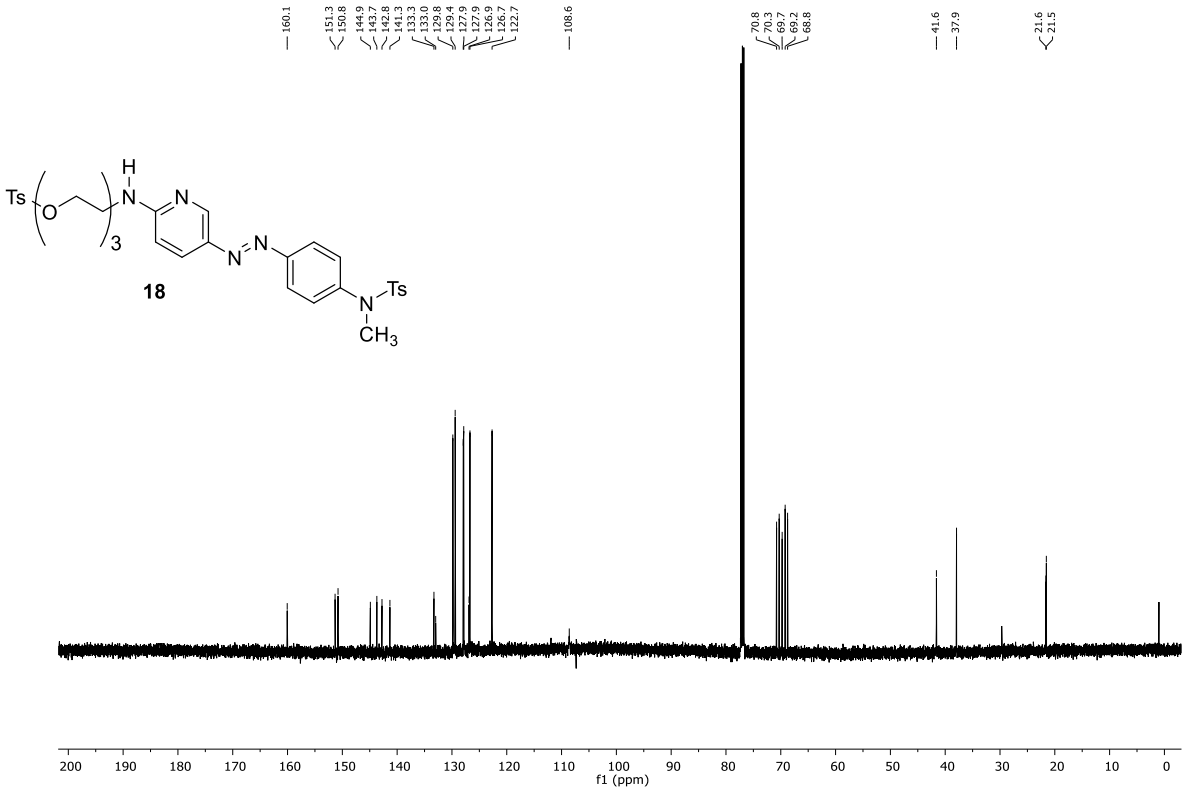

Figure S40. ^{13}C-NMR of product **16b**.

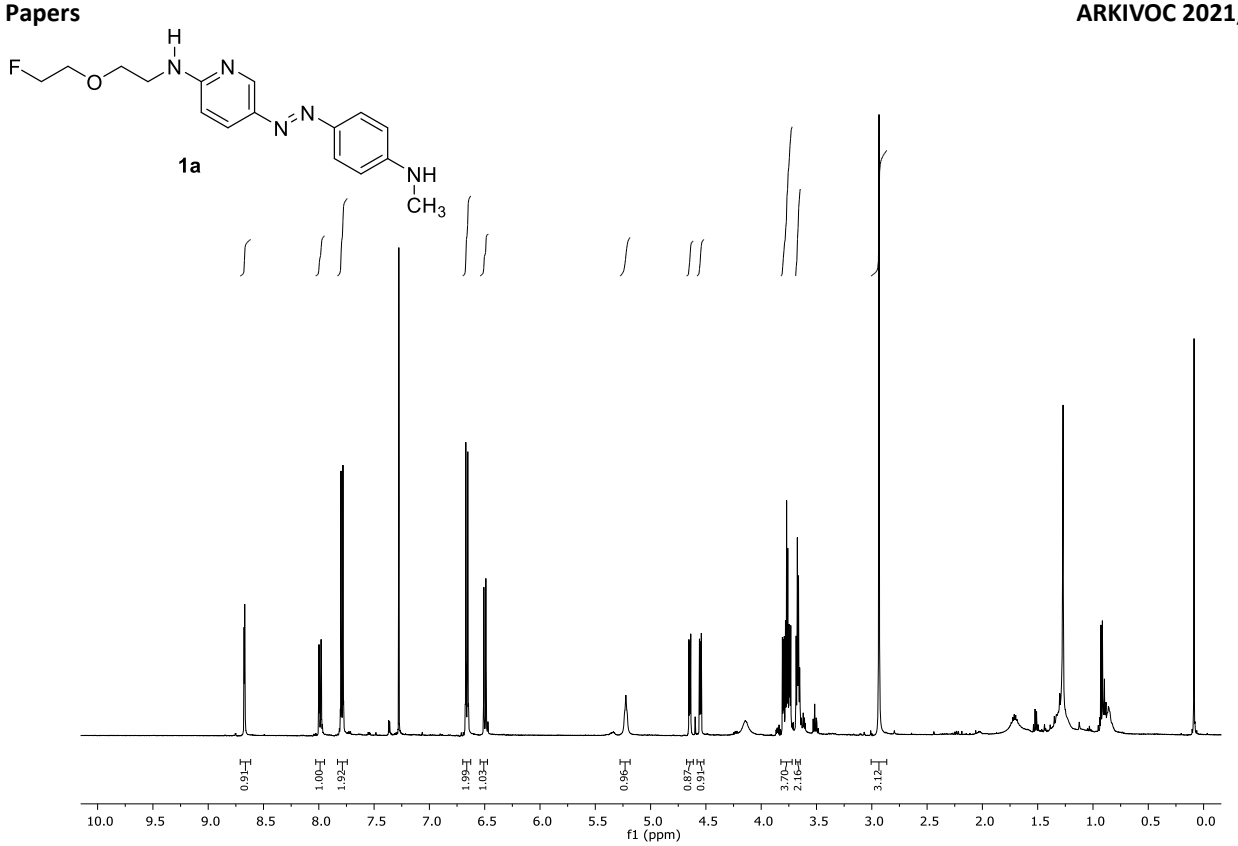

Figure S41. ^{1}H-NMR of product **1a**.

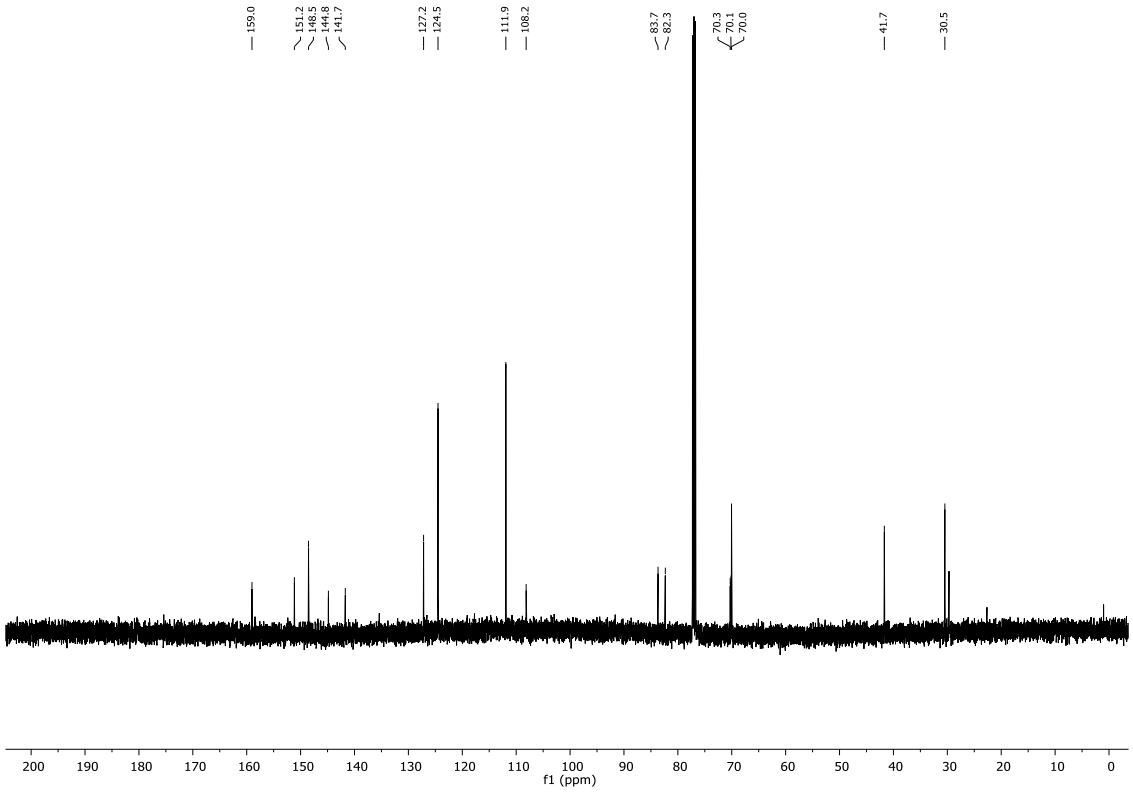

Figure S42. ^{13}C-NMR of product **1a**.

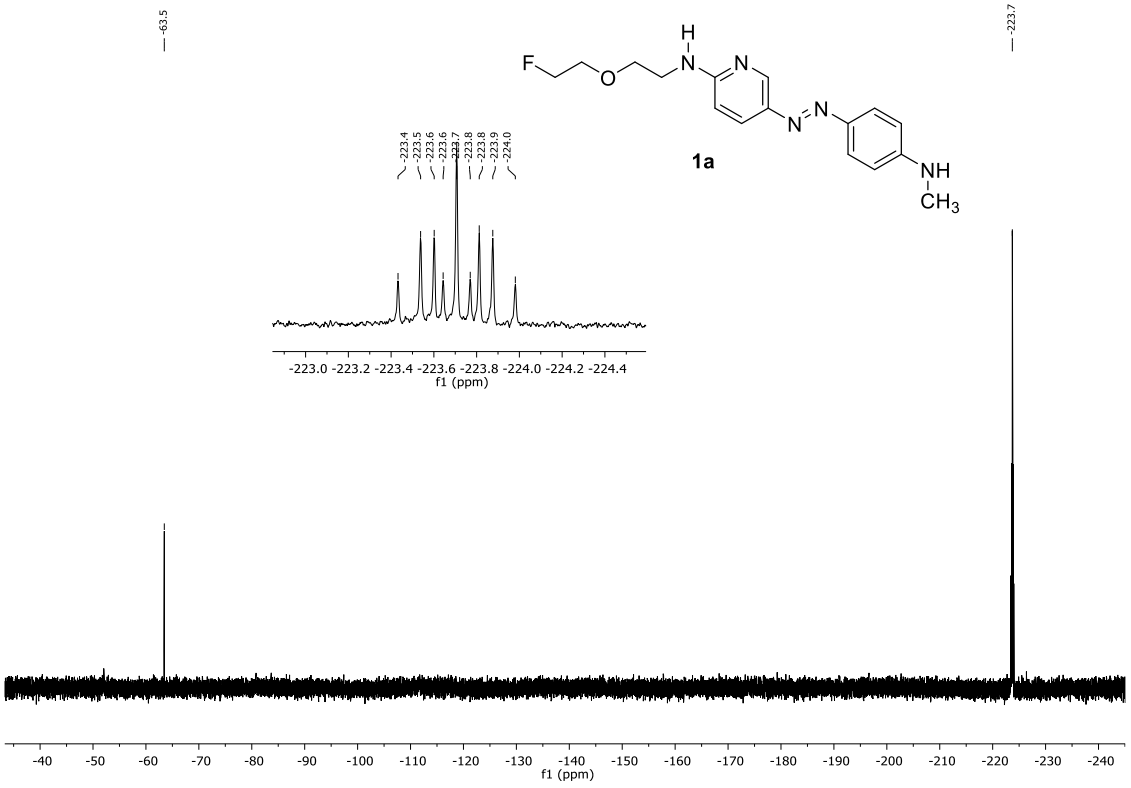

Figure S43. ^{19}F-NMR of product **1a**.

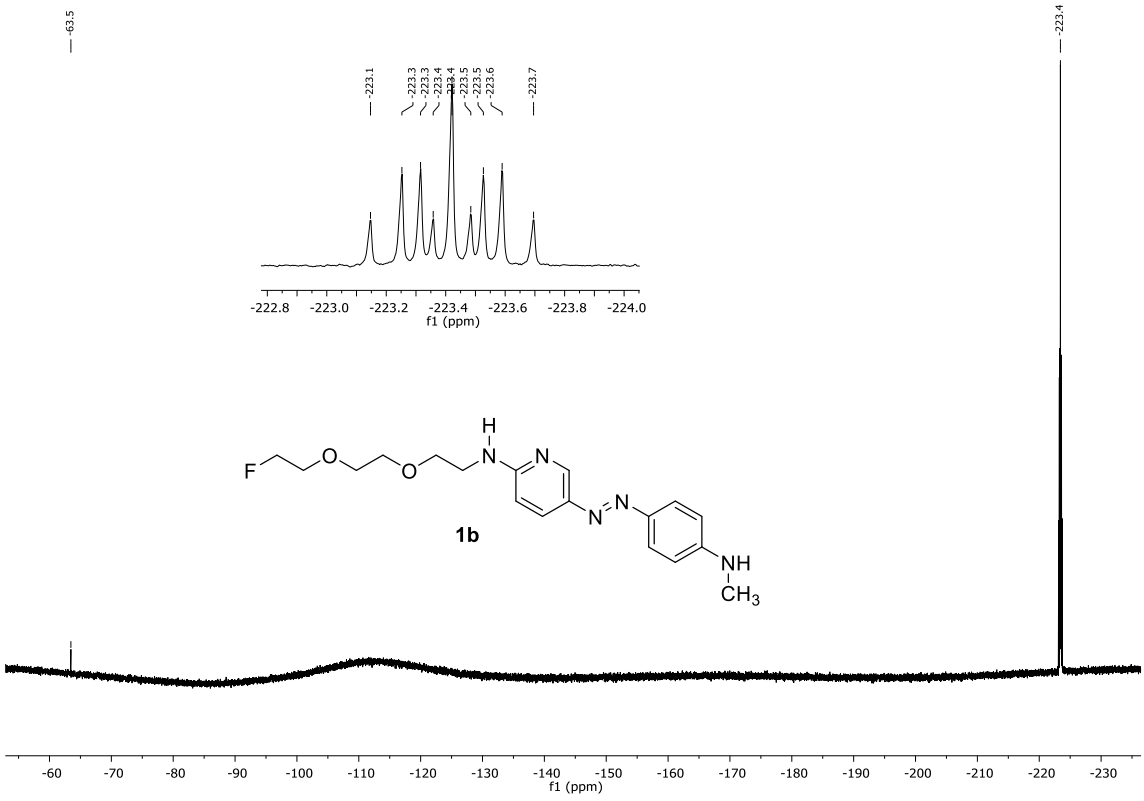

Figure S44. ^{19}F-NMR of product **1b**.

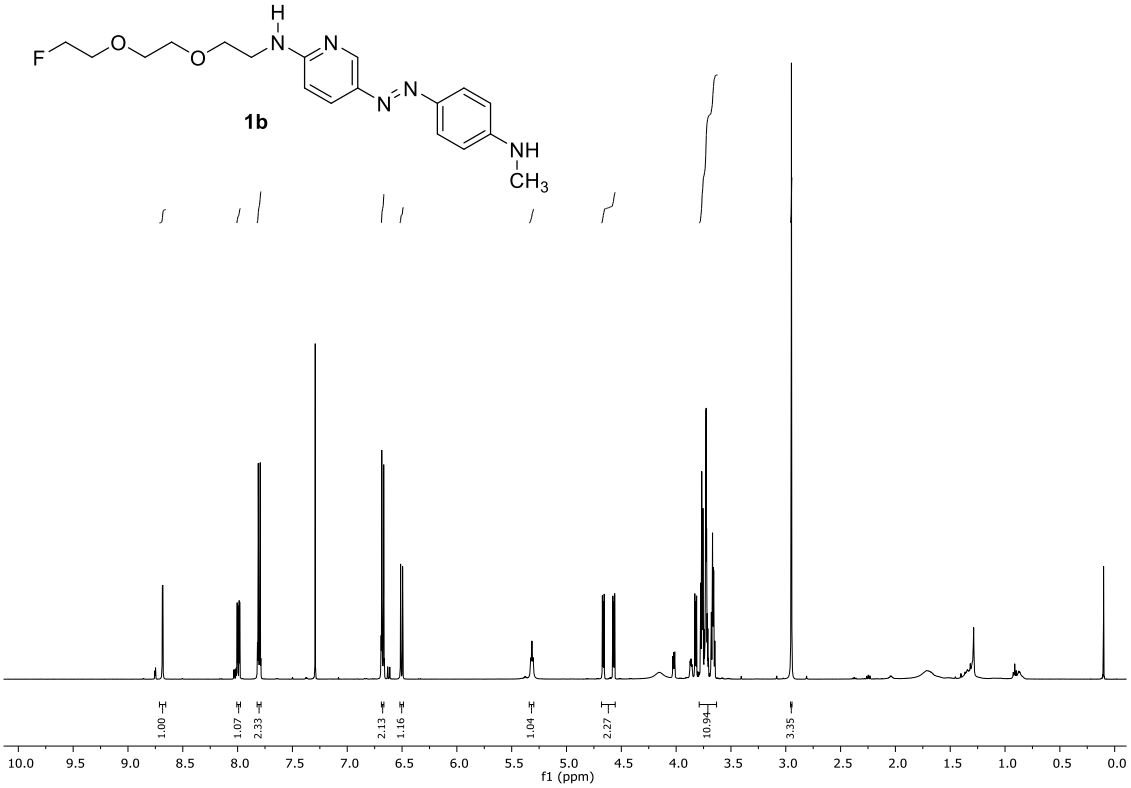

Figure S45. ^{1}H-NMR of product **1b**.

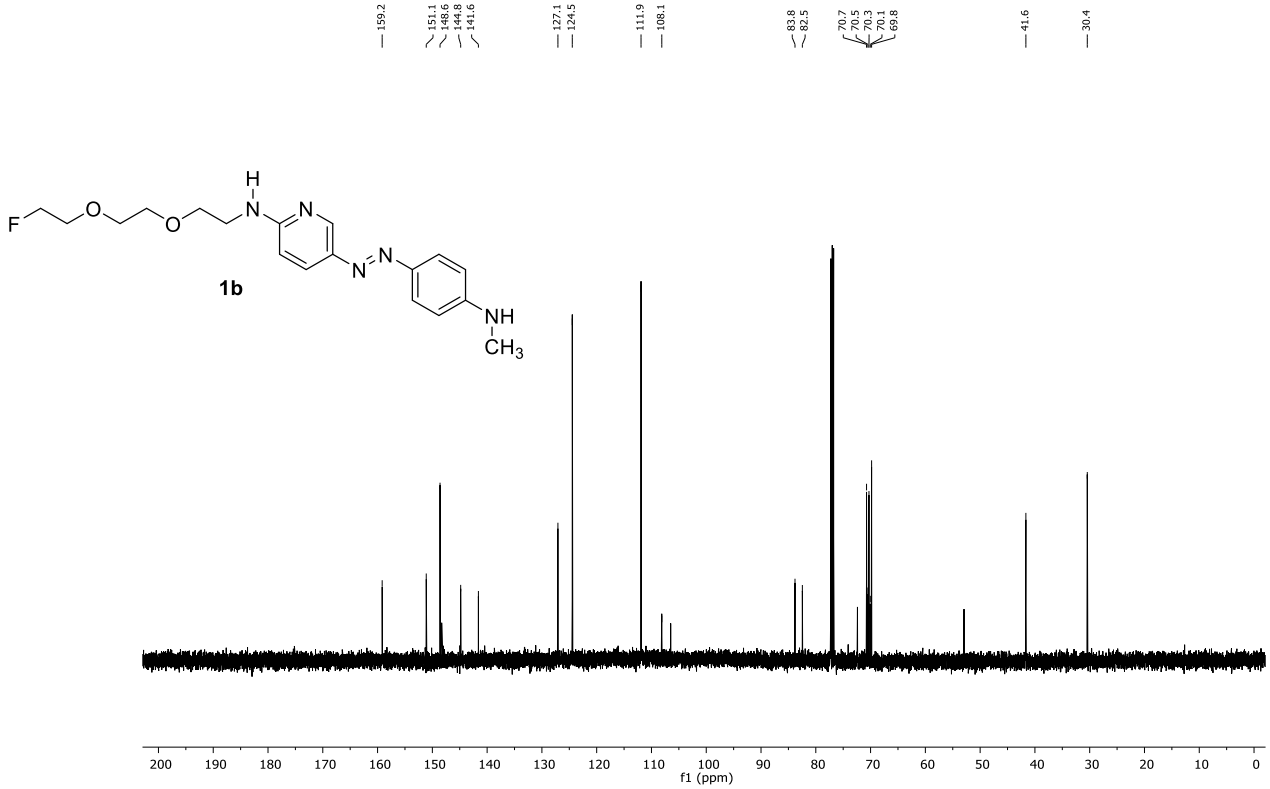

Figure S46. ^{13}C-NMR of product **1a**.

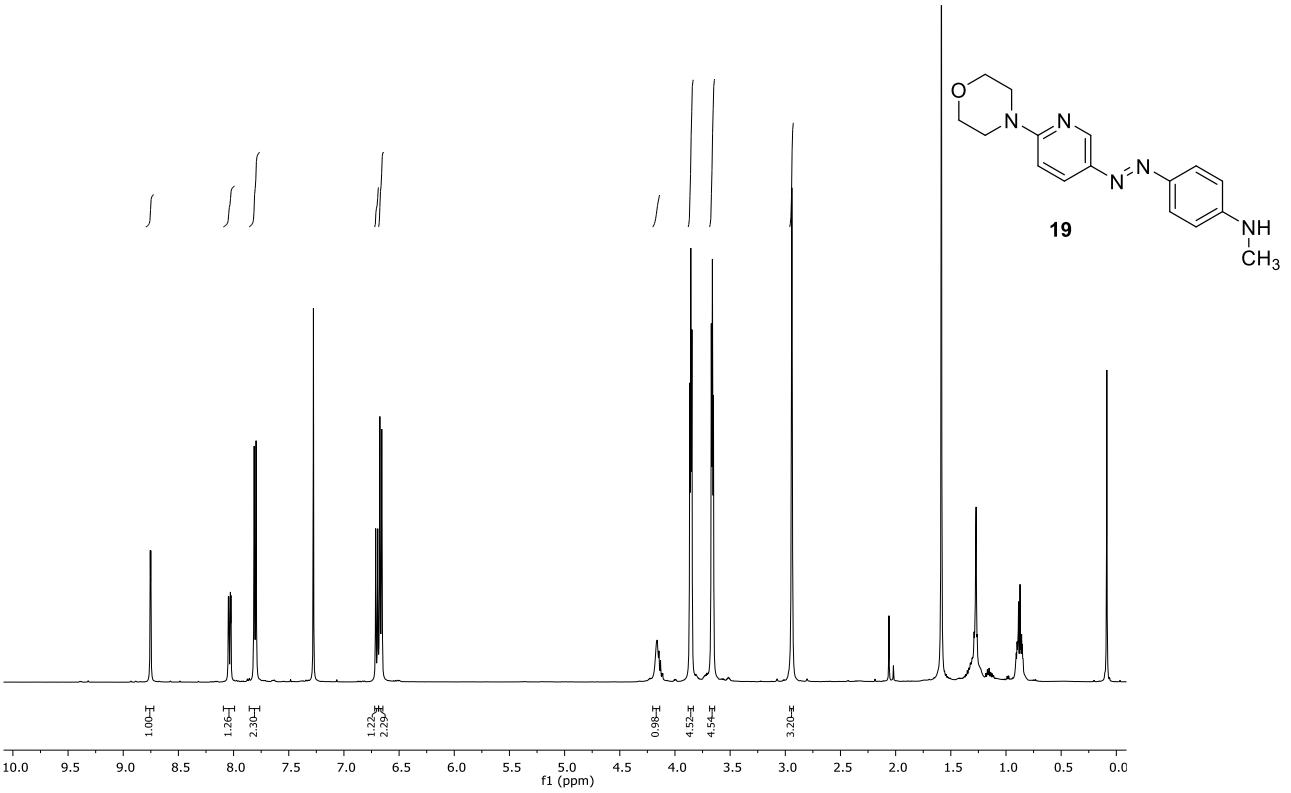

Figure S47. ^{1}H-NMR of product **19**.

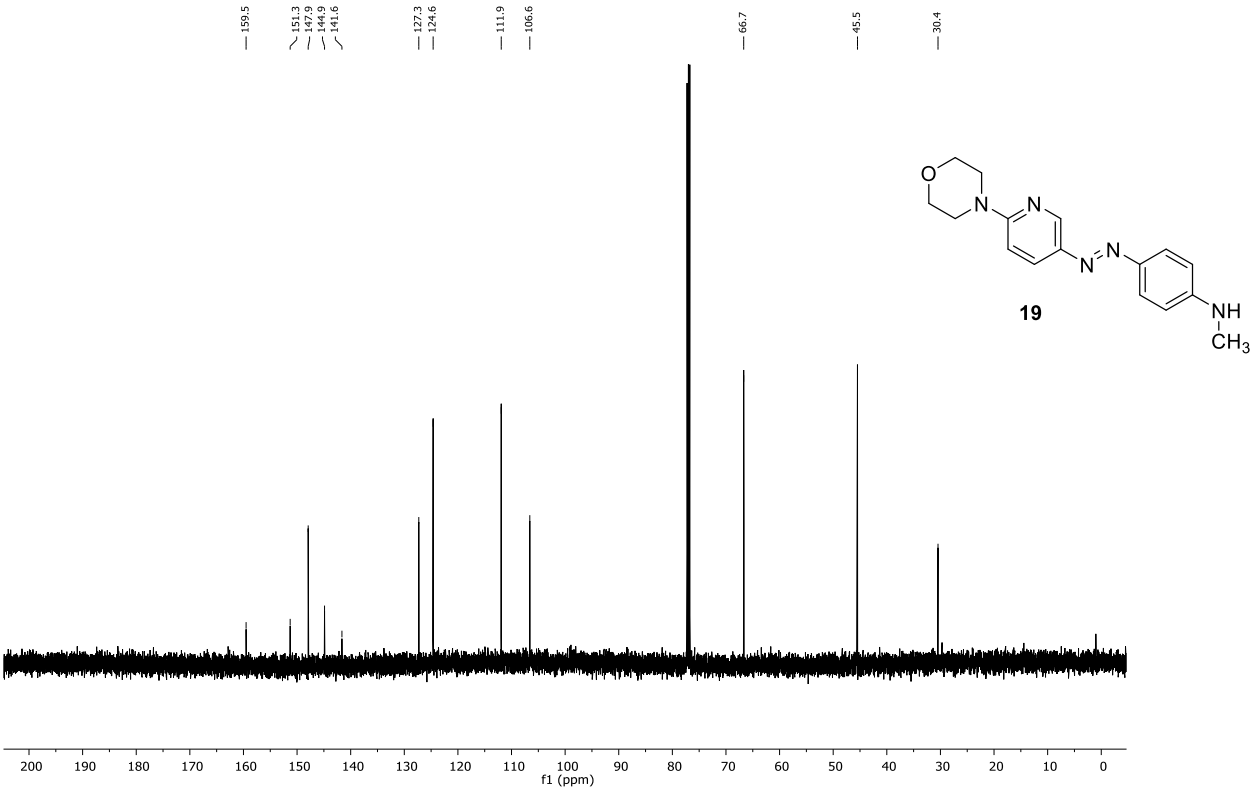

Figure S48. ^{13}C-NMR of product **19**.