Supporting Information for:

# Synthesis of fluorescent ring-fused 2-pyridone peptidomimetics

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**Table of Contents**:

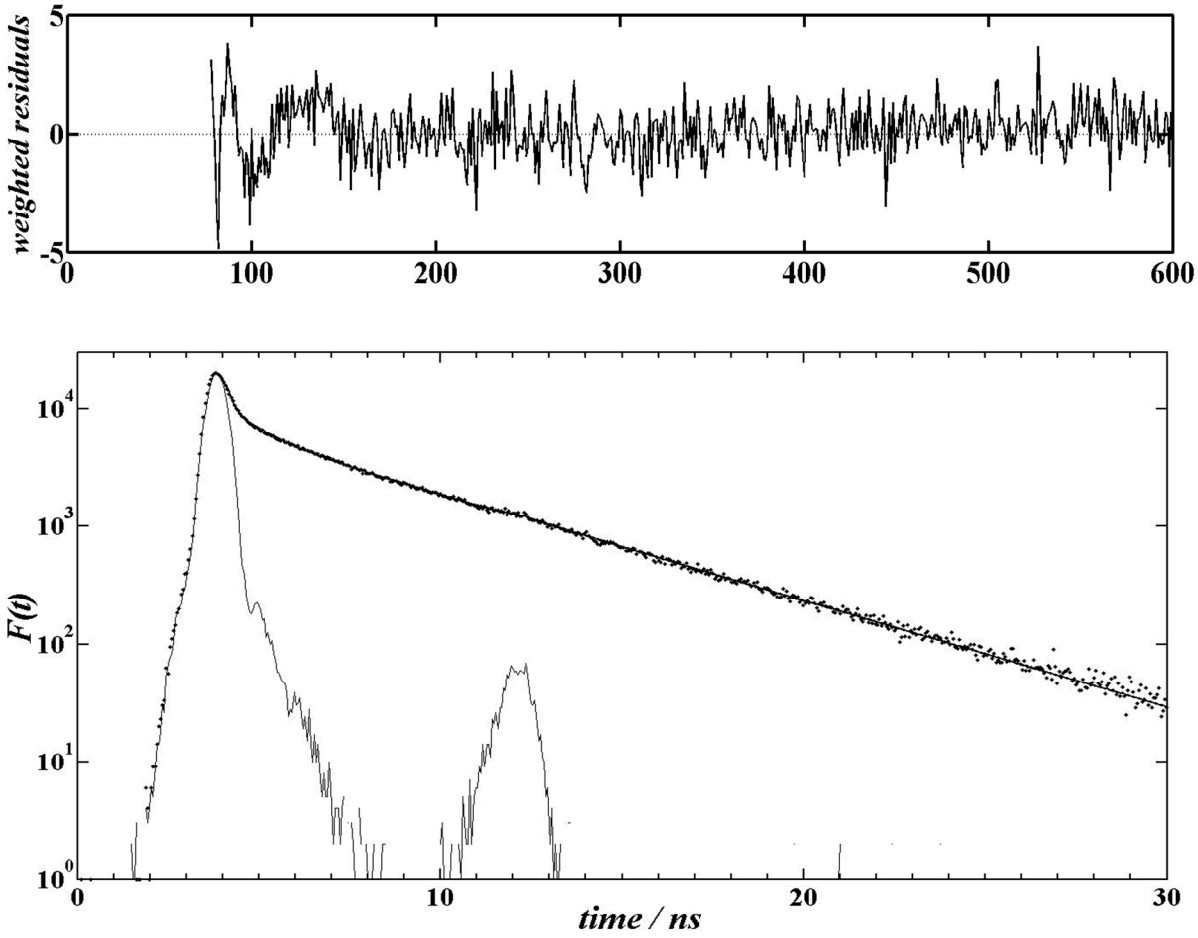
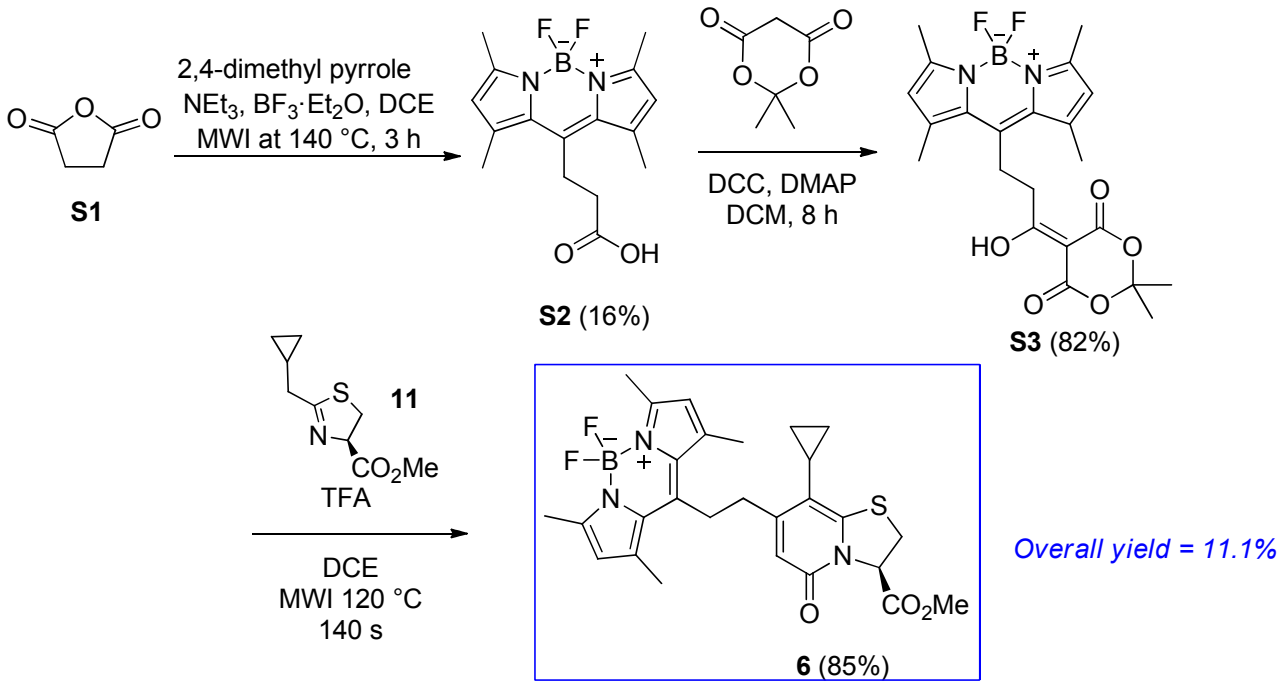



**FIGURE S1** - Time-resolved fluorescence decay of **19c** dissolved in DMSO at 25 °C [$F(t)$, *i.e.* the number of counted photons *vs*. time]. In the lower graph, the upper curve reveals biphasic fluorescence decay, while the lower curve displays the instrumental response function. The upper graph shows the weighted residual obtained by fitting the decay to a sum of exponential functions.

**SCHEME S1** – Original route towards BODIPY containing thiazolino 2-pyridones.[1]




**SCHEME S2** – Revised route towards BODIPY-containing thiazolino 2-pyridones.

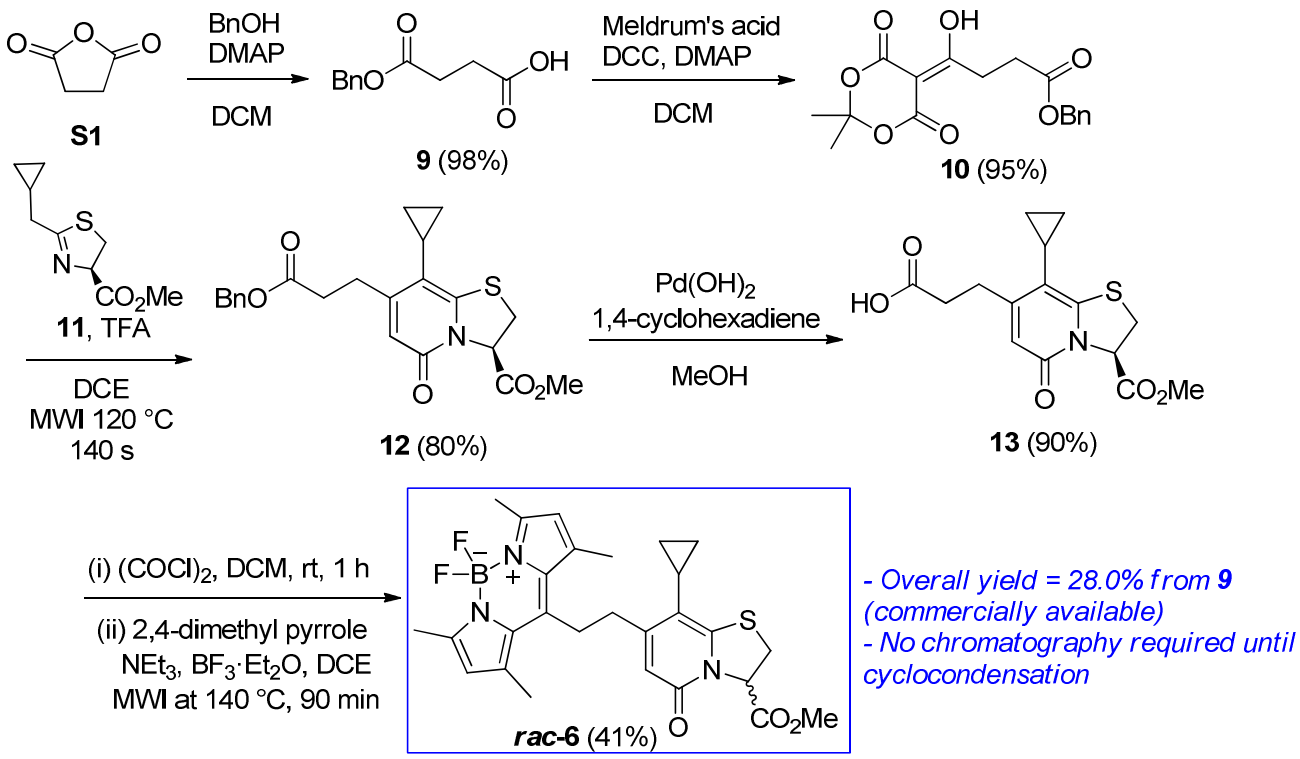
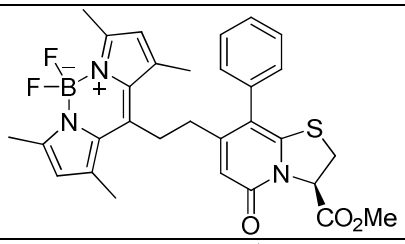
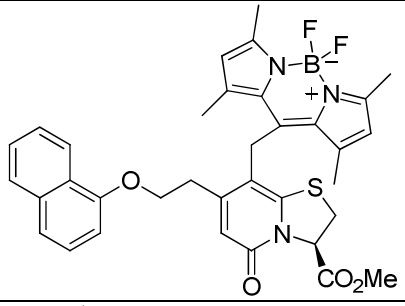
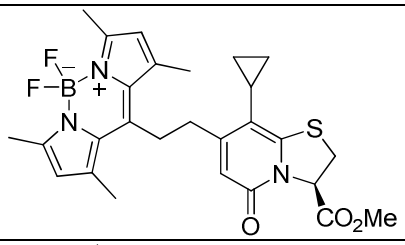
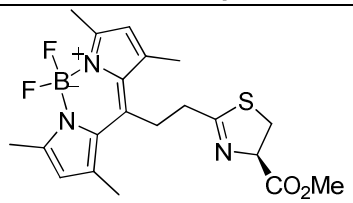
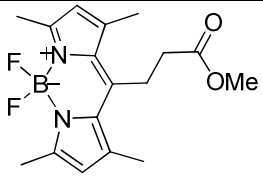
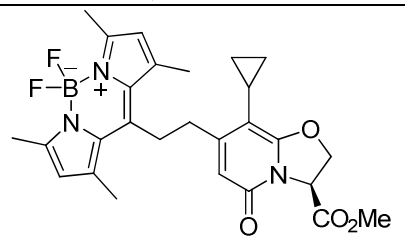


**TABLE S1** - Screened hydrolysis conditions for BODIPY methyl ester **17a**.

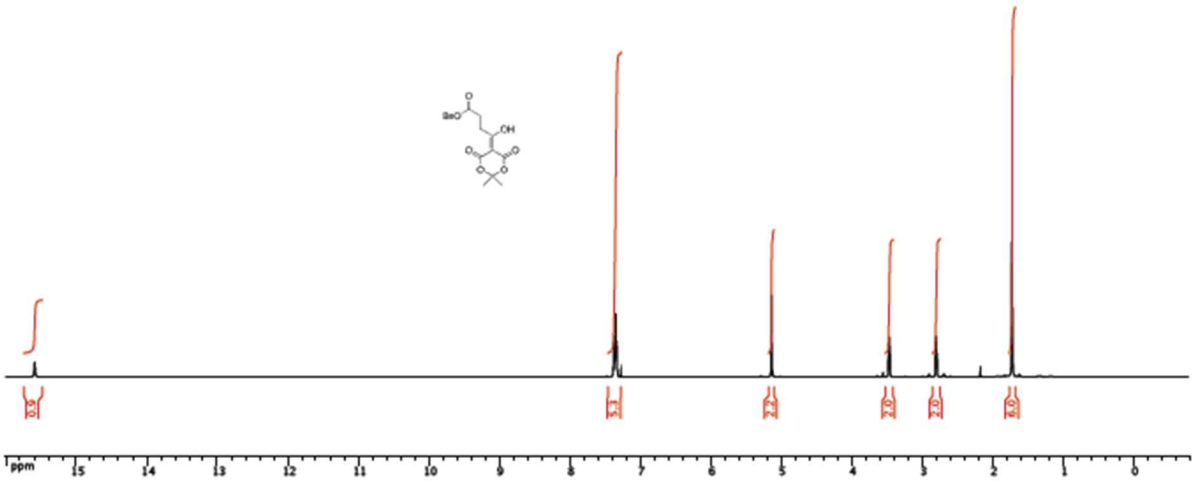
| Entry | Hydrolysis method | Solvent | Temp (°C) | Time | LCMS conversion (isolated yield) | Notes/Reference |
|---|---|---|---|---|---|---|
| **1** | LiOH | THF/MeOH | rt | 2 h | - | [1] |
| **2** | LiOH | Dioxane | rt | 16 h | - | |
| **3** | NaOH | THF/MeOH | rt | 30 min | - | Decomposition.[2] |
| **4** | KOH | THF/MeOH | rt | 30 min | - | Decomposition.[3] |
| **5** | $K_2CO_3$ | DMF | rt | 6 h | - | |
| **6** | TMSI | $CCl_4/CDCl_3$ | rt | 6 h | - | [4] |
| **7** | TMSI, MWI | $CCl_4/CDCl_3$, | 60-90 | 20 min | - | [4] |
| **8** | $Me_3SnOH$ | DCE | rt | 6 h | - | [5] |
| **9** | $Me_3SnOH$, MWI | DCE | 80-110 | 30 min | - | [5] |
| **10** | *Mucor javanicus* | Acetone /phosphate buffer | 38 | 6 h | - | |
| **11** | *Candida antartica lipase* B | THF/phosphate buffer | 38 | 6 h | - | |
| **12** | $Et_3N$ (20 eq.), LiBr (20 eq.) | MeCN/$H_2O$ (98/2) | rt | 24 h | <16% | [6] |
| **13** | $Et_3N$ (20 eq.), LiBr (20 eq.) | THF/$H_2O$ (98/2) | rt | 24 h | - | [6] |
| **14** | $Et_3N$ (20 eq.), LiBr (20 eq.) | MeOH/$H_2O$ (98/2) | rt | 24 h | - | [6] |
| **15** | $Et_3N$ (20 eq.), KBr (20 eq.) | MeCN/$H_2O$ (98/2) | rt | 24 h | - | |
| **16** | $Et_3N$ (20 eq.), LiBr (20 eq.) | MeCN/$H_2O$ (98/2) | 40 | 5 h | 16% | Complex mixture of products.[6] |
| **17** | DABCO (20 eq.), LiBr (20 eq.) | MeCN/$H_2O$ (98/2) | 40 | 5 h | - | [6] |
| **18** | DBU (20 eq.), LiBr (20 eq.) | MeCN/$H_2O$ (98/2) | 40 | 5 h | - | Decomposition.[6] |
| **19** | DMAP (20 eq.), LiBr (20 eq.) | MeCN/$H_2O$ (98/2) | 40 | 5 h | - | [6] |
| **20** | LiCl (15 eq.), MWI | DMF | 80 | 15 min | - | [7] |
| **21** | LiBr (15 eq.), MWI | DMF | 80 | 15 min | Trace | |
| **22** | LiBr (15 eq.) | DMF | rt | 16 h | - | |
| **23** | LiBr (15 eq.) | DMF | 60 | 4 h | - | |
| **24** | LiBr (10 eq.), MWI | DMF | 90 | 2 h | 16% | |
| **25** | LiBr (10 eq.), MWI | DMF/$H_2O$ (90/10) | 90 | 2 h | 20% | |
| **26** | LiBr (50 eq.), MWI | DMF | 90 | 70 min | 75% (65%) | |

**TABLE S2** - LiI halogenolysis in DMF of BODIPY methyl esters.

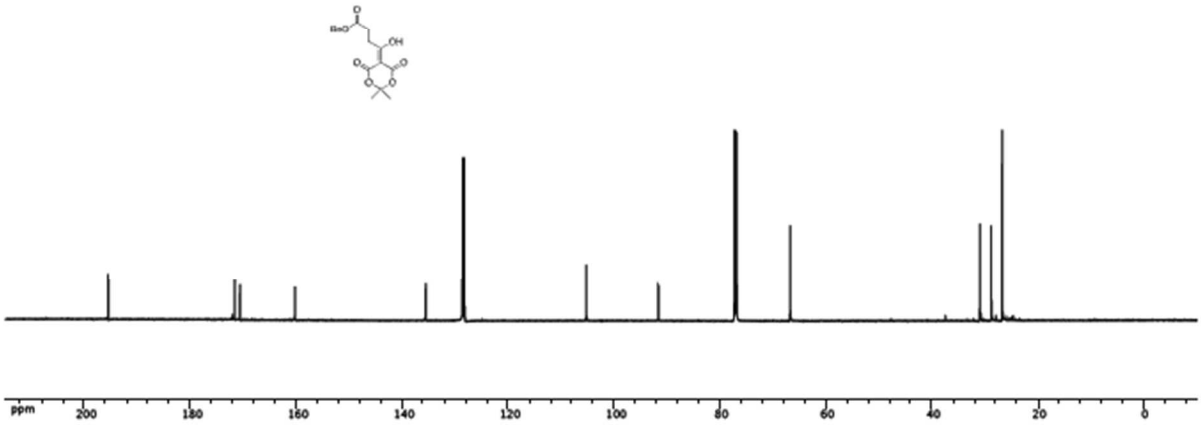
| Compound | Structure | Conditions | Conversion | Lit. Yield | Lit. Conditions |
|---|---|---|---|---|---|
| **S4** |  | MWI, 110 °C, 30 min | 70%[a] | 88% | (i) 0.1 M LiOH (aq), THF/MeOH (4:1) 2 h; (ii) AcOH.[1] |
| **S5** |  | MWI, 140 °C, 10 min | Trace | 29%[b] | (i) LiI, pyridine, MWI, 140 °C, 15 min; (ii) $BF_3{\cdot}Et_2O$, DCE, 80 °C, 15 min.[1] |
| **6** |  | MWI, 140 °C, 12 min | 100%[a] | n/a | - |
| **S6** |  | MWI, 100 °C, 1 h | 40%[a] | n/a | - |
| **S7** |  | MWI, 120 °C, 1 h | 50%[a] | n/a | - |
| **S8** |  | MWI, 110 °C, 20 min | 80%[a] | 88% | (i) LiBr, $NEt_3$, MeCN (2 *v/v*% $H_2O$), 3h (ii) AcOH.[1] |

**Notes: a = LC-MS conversion; b = removal of $BF_2$ observed. n/a = not available.**

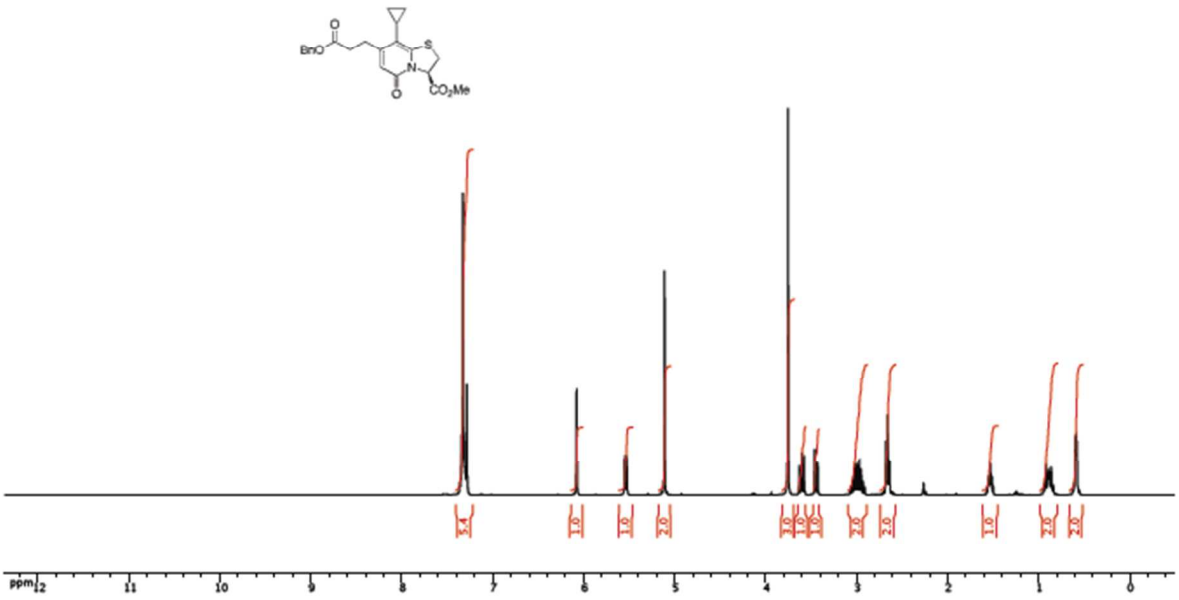
$^{1}$H NMR spectra of **10** ($CDCl_3$)



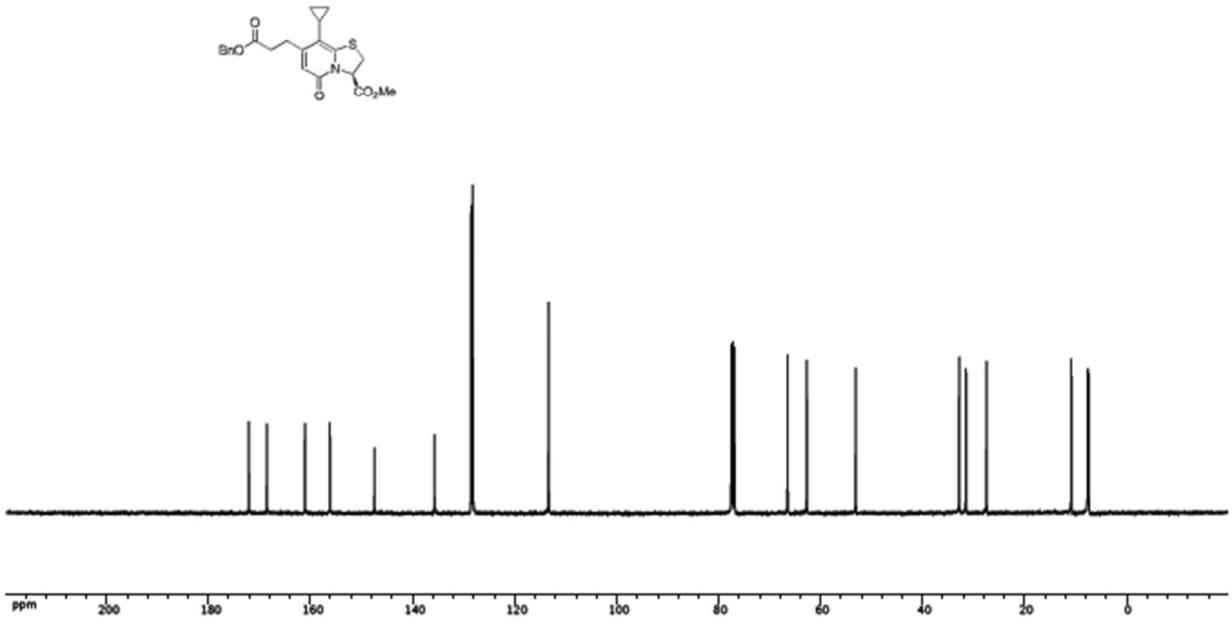

$^{13}$C NMR spectra of **10** ($CDCl_3$)



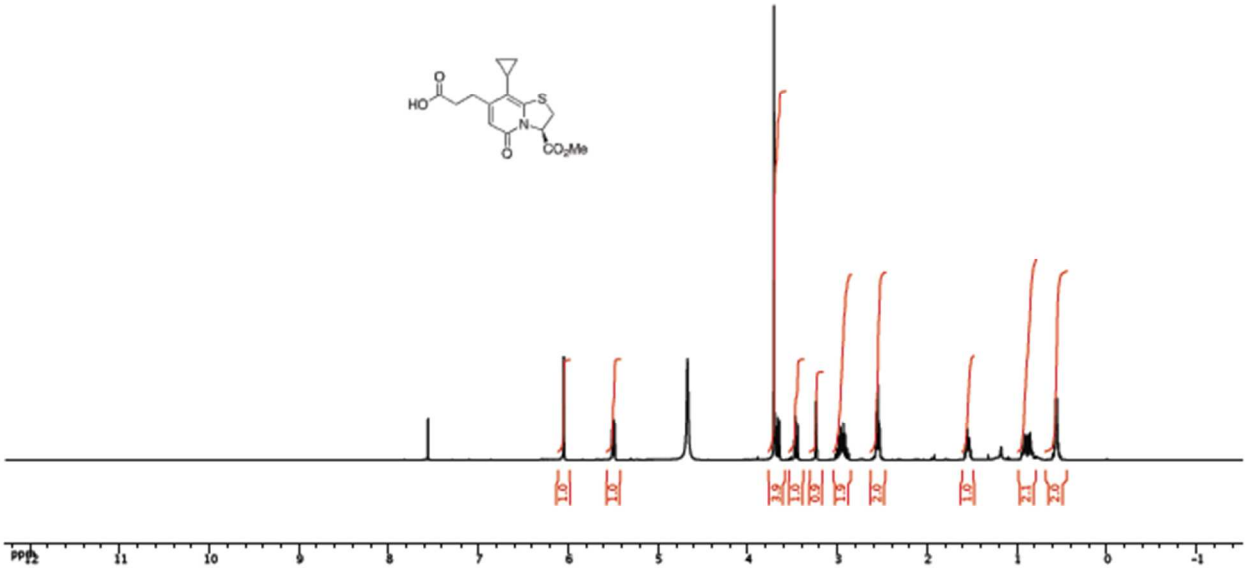
H NMR spectra of **12** ($CDCl_3$)



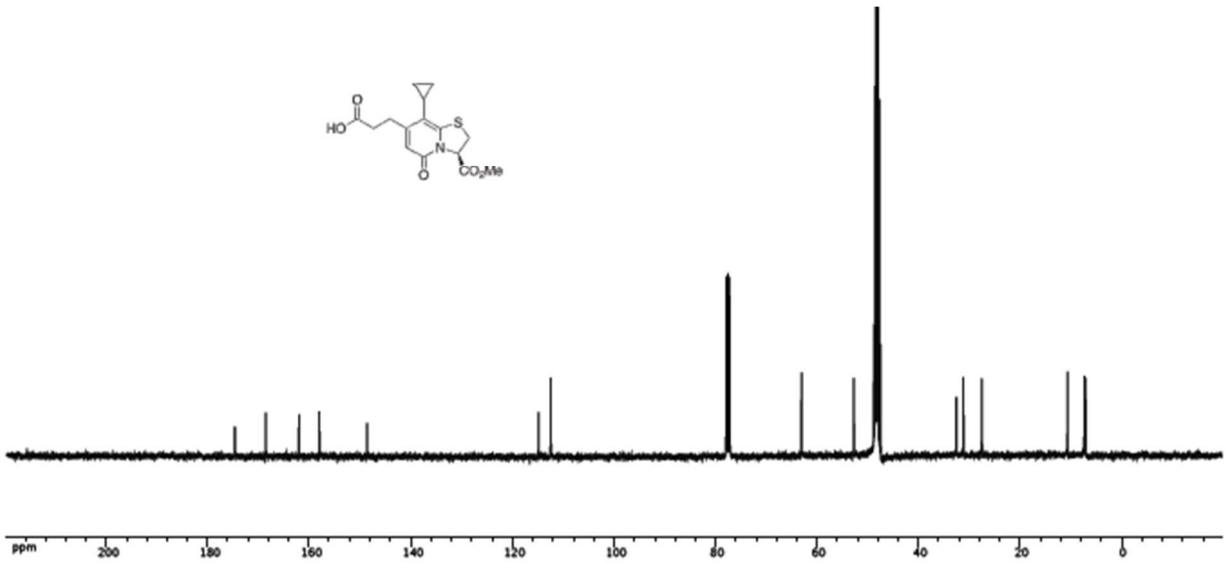
$^{13}C$ NMR spectra of **12** ($CDCl_3$)



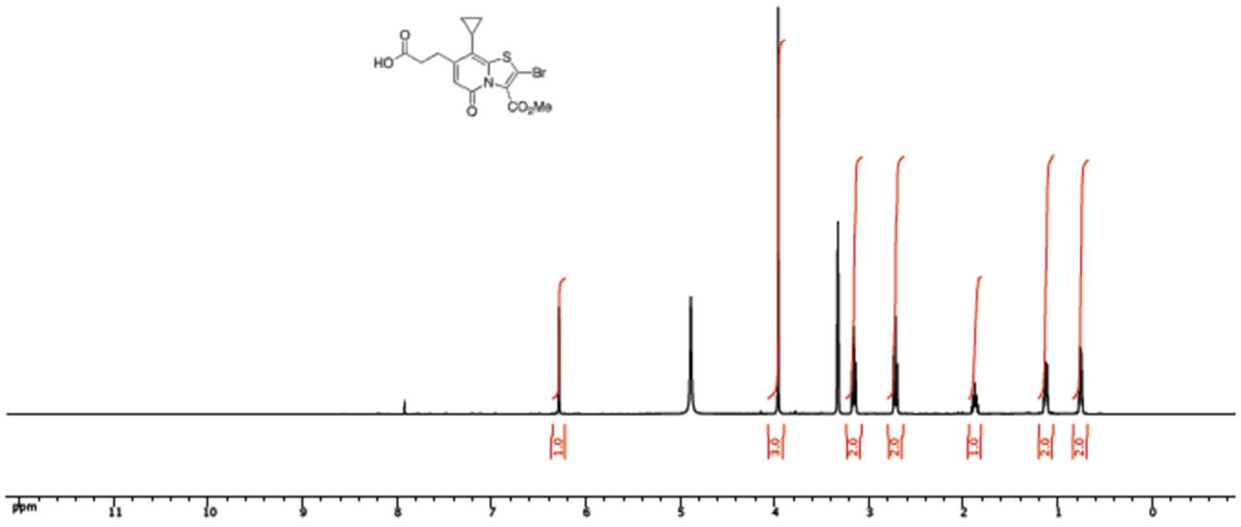
$^{1}$H NMR spectra of **13** (MeOD + $CDCl_3$)



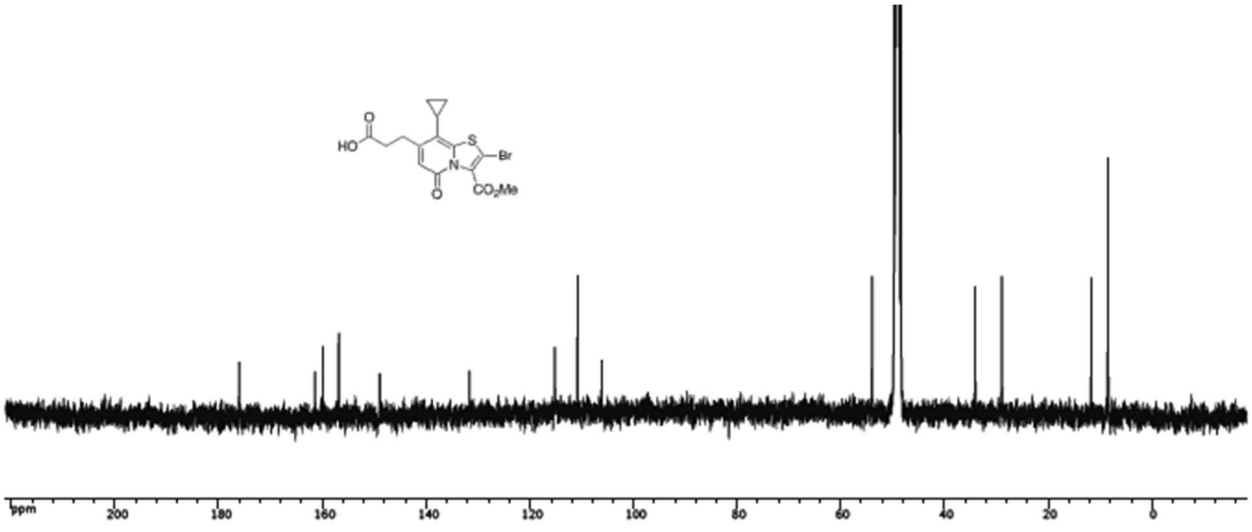

$^{13}$C NMR spectra of **13** (MeOD + $CDCl_3$)



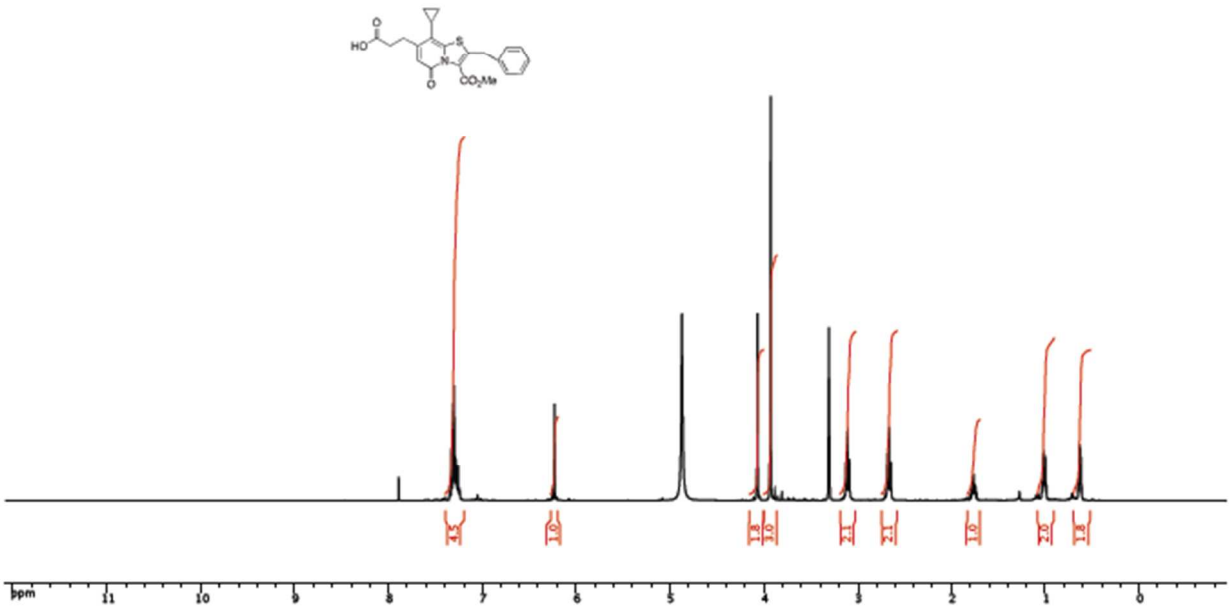
$^{1}$H NMR spectra of **8** (MeOD)



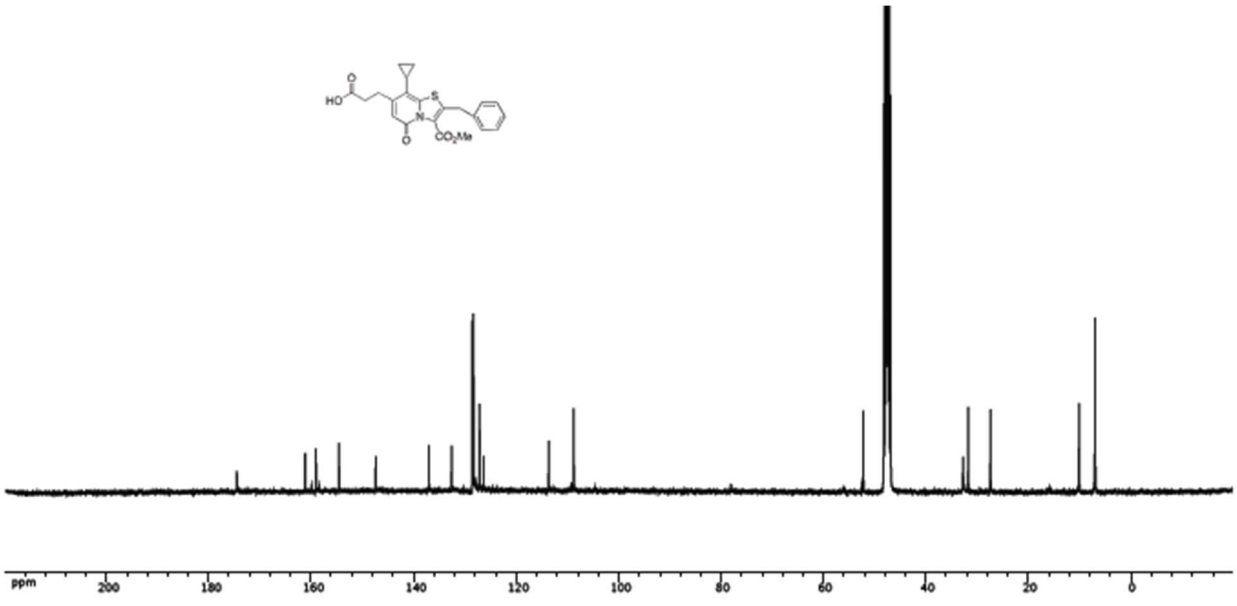

$^{13}$C NMR spectra of **8** (MeOD)



$^{1}$H NMR spectra of **14a** (MeOD)



$^{13}$C NMR spectra of **14a** (MeOD)



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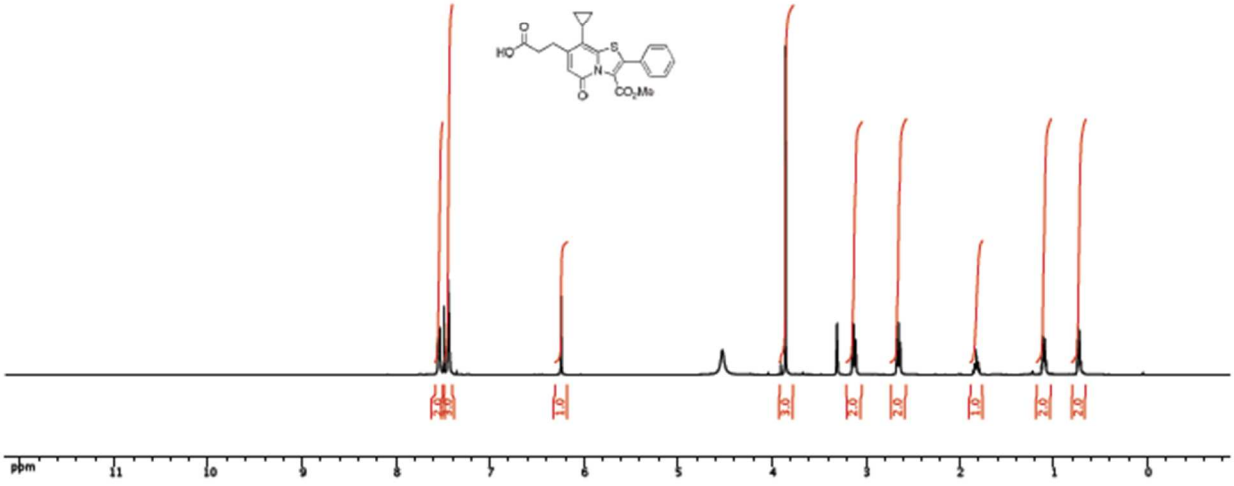
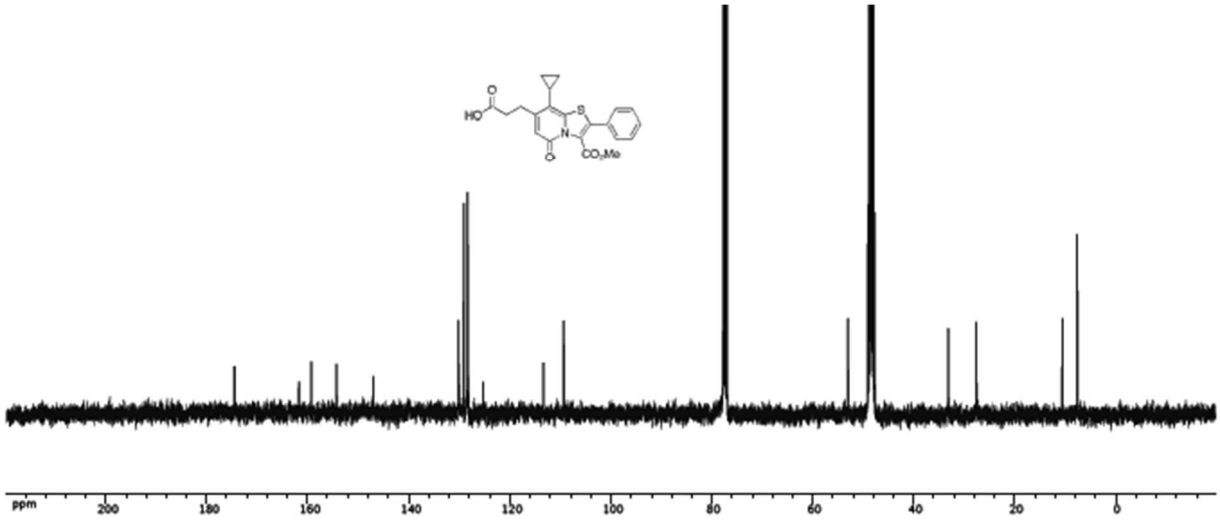
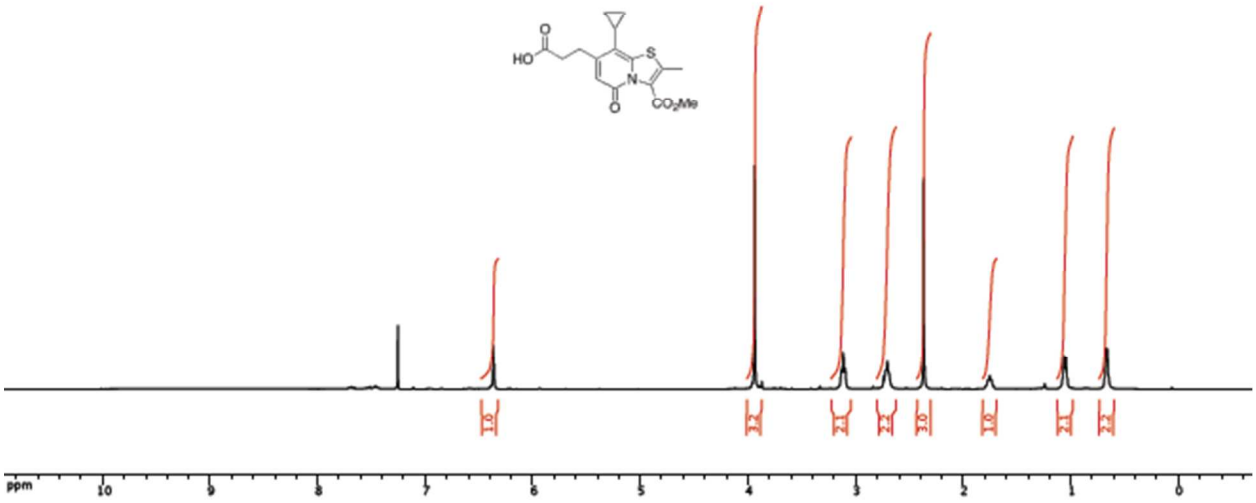


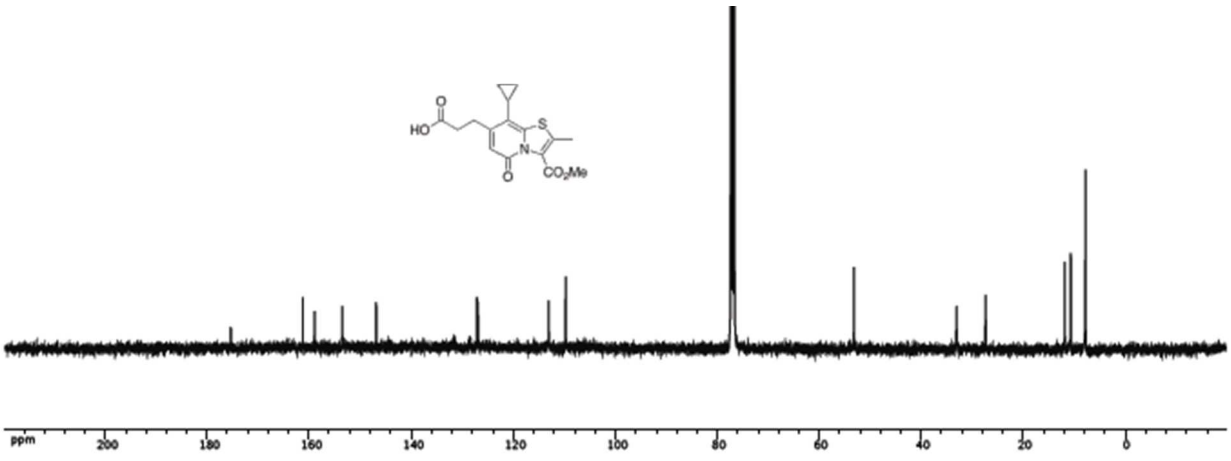
$^{13}$C NMR spectra of **14b** (MeOD + $CDCl_3$)



$^{1}$H NMR spectra of **14c** ($CDCl_3$)




$^{13}$C NMR spectra of **14c** ($CDCl_3$)



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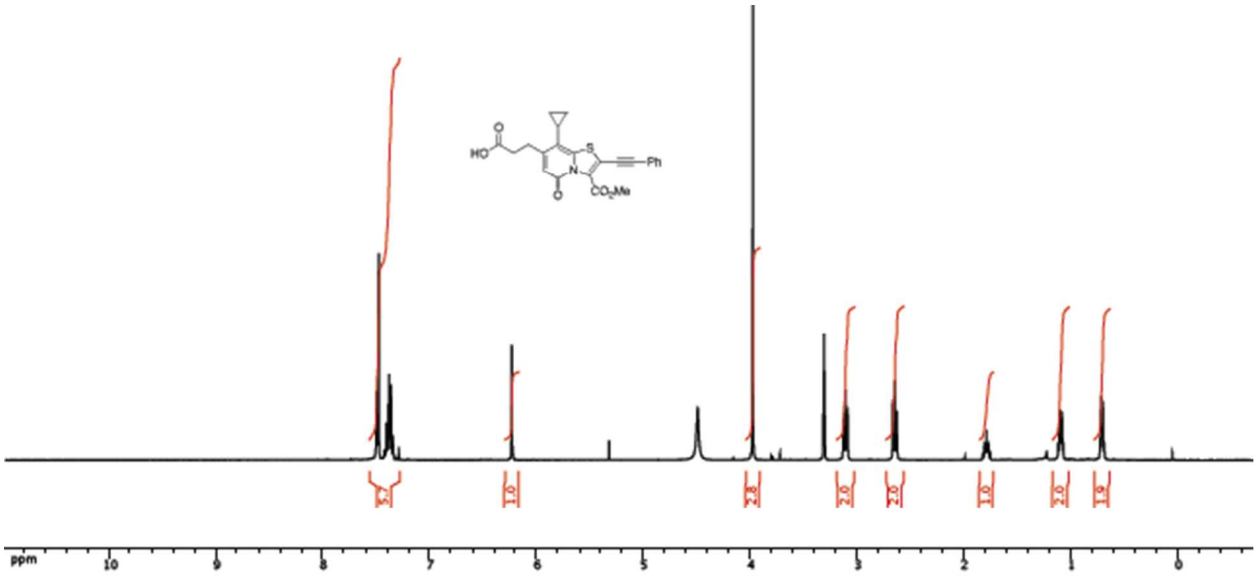
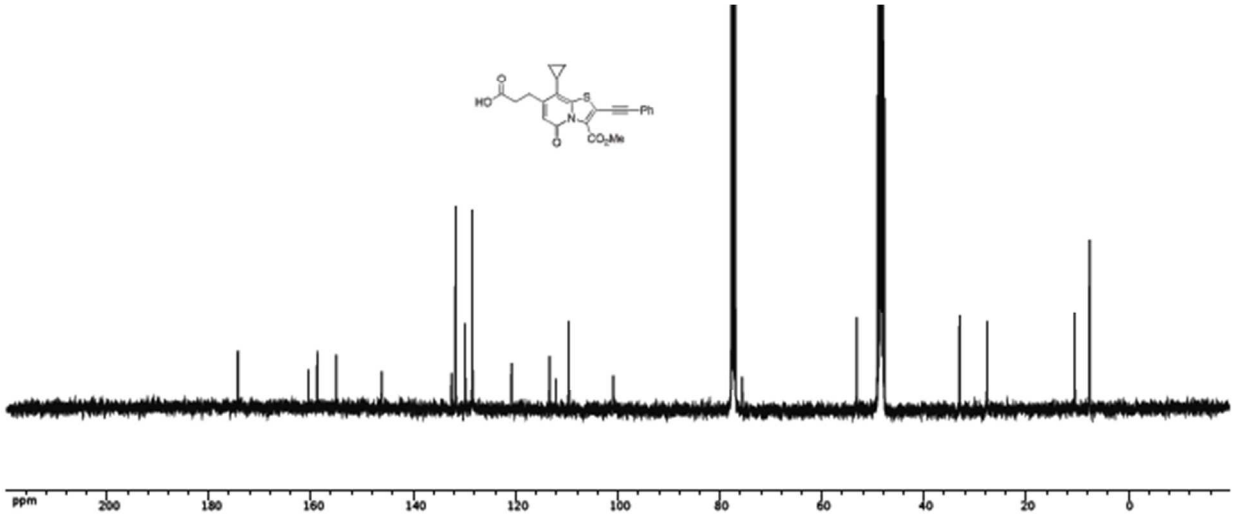



$^{13}$C NMR spectra of **15** (MeOD + $CDCl_3$)



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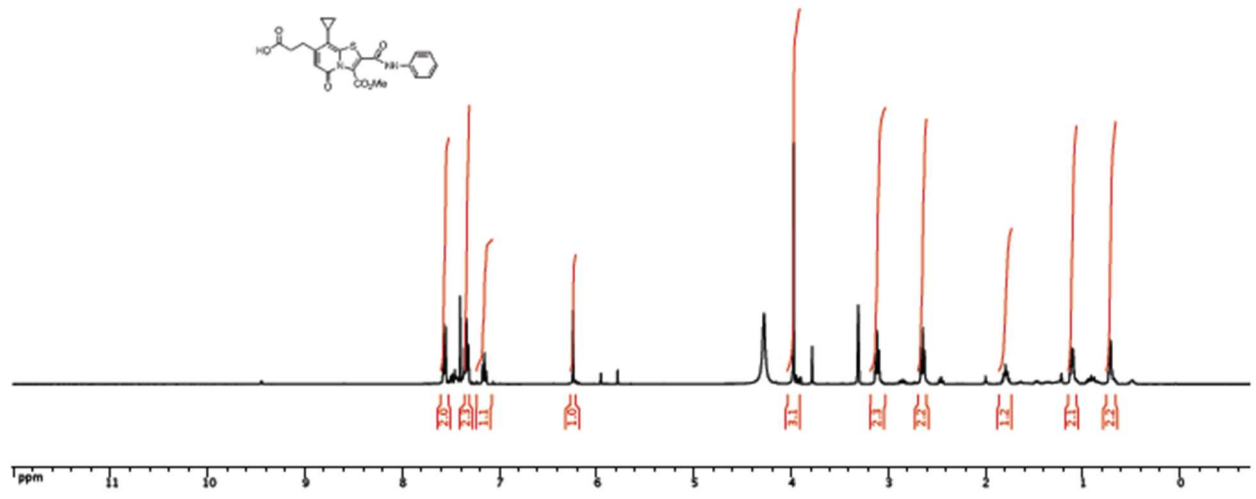
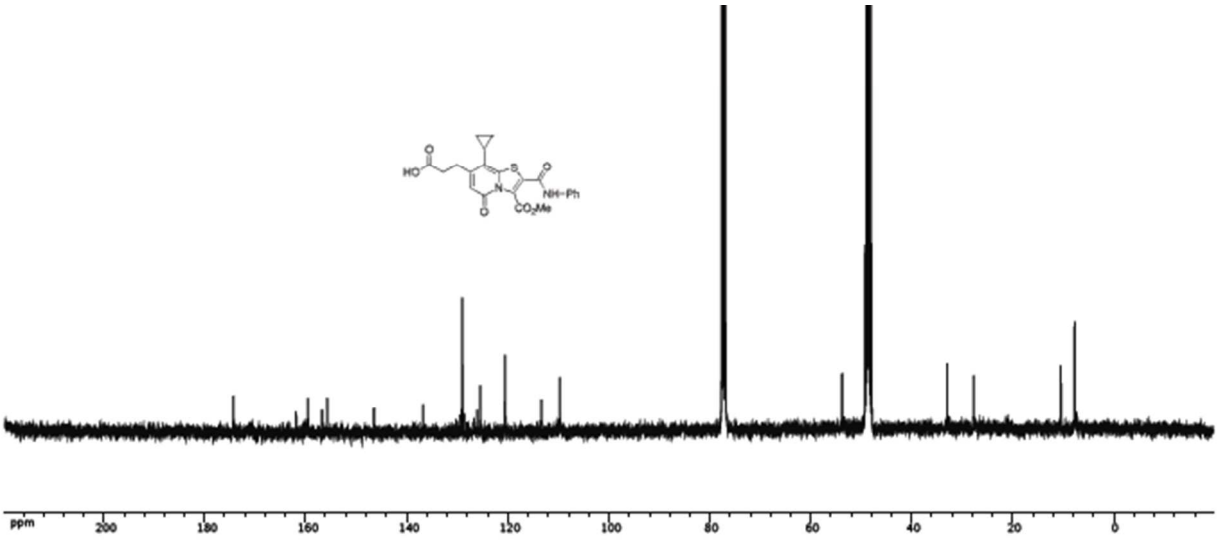
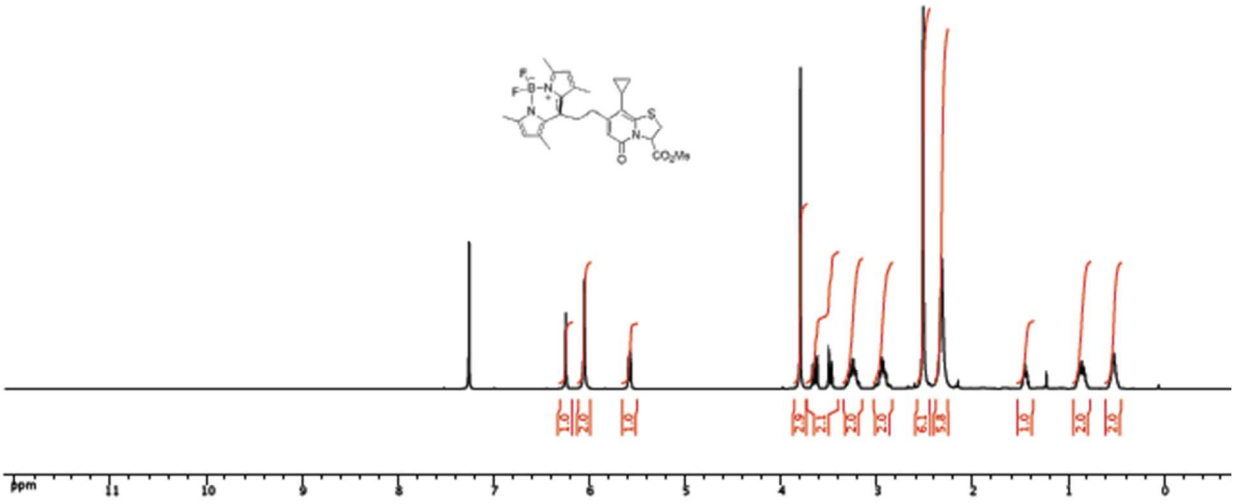



$^{13}$C NMR spectra of **16** (MeOD + $CDCl_3$)



$^{1}$H NMR spectra of **6** ($CDCl_3$)



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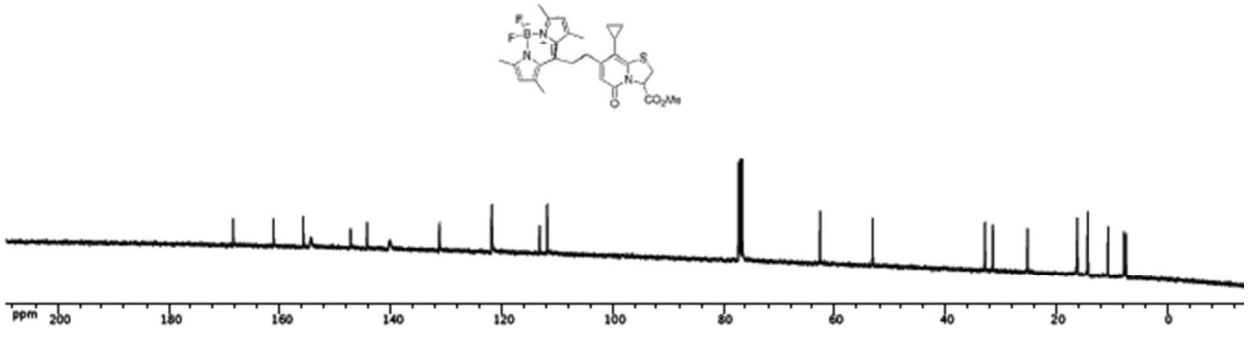
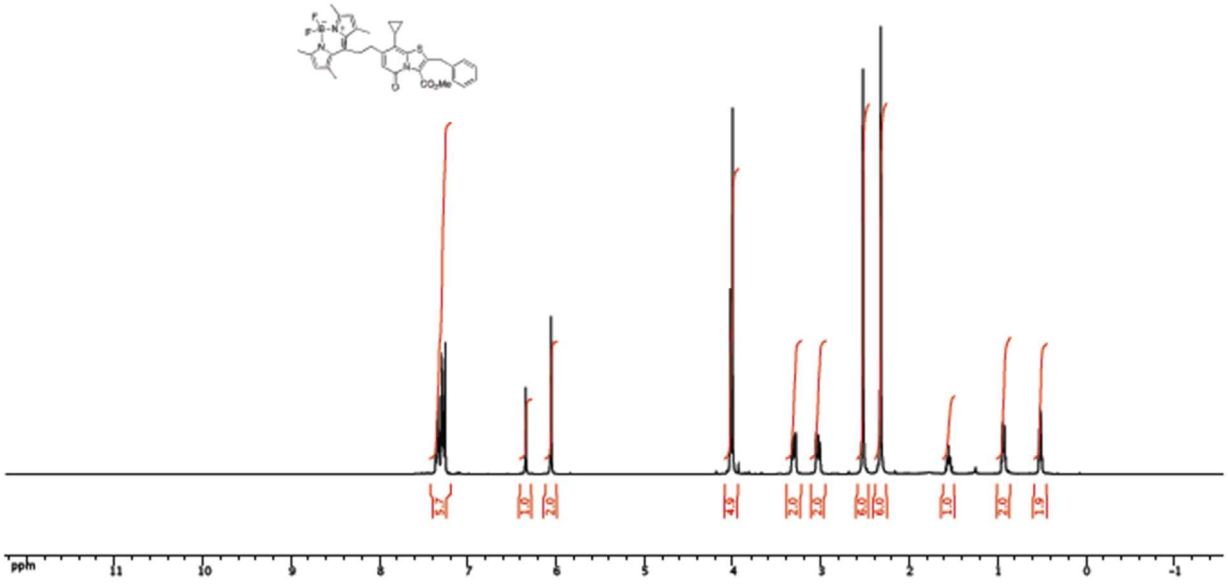
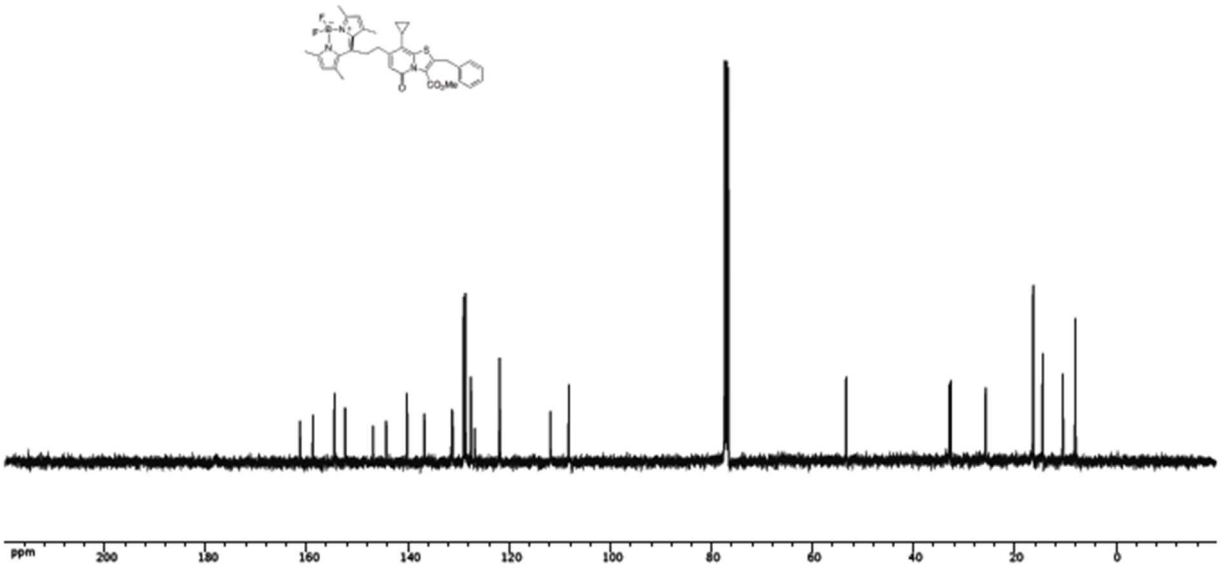


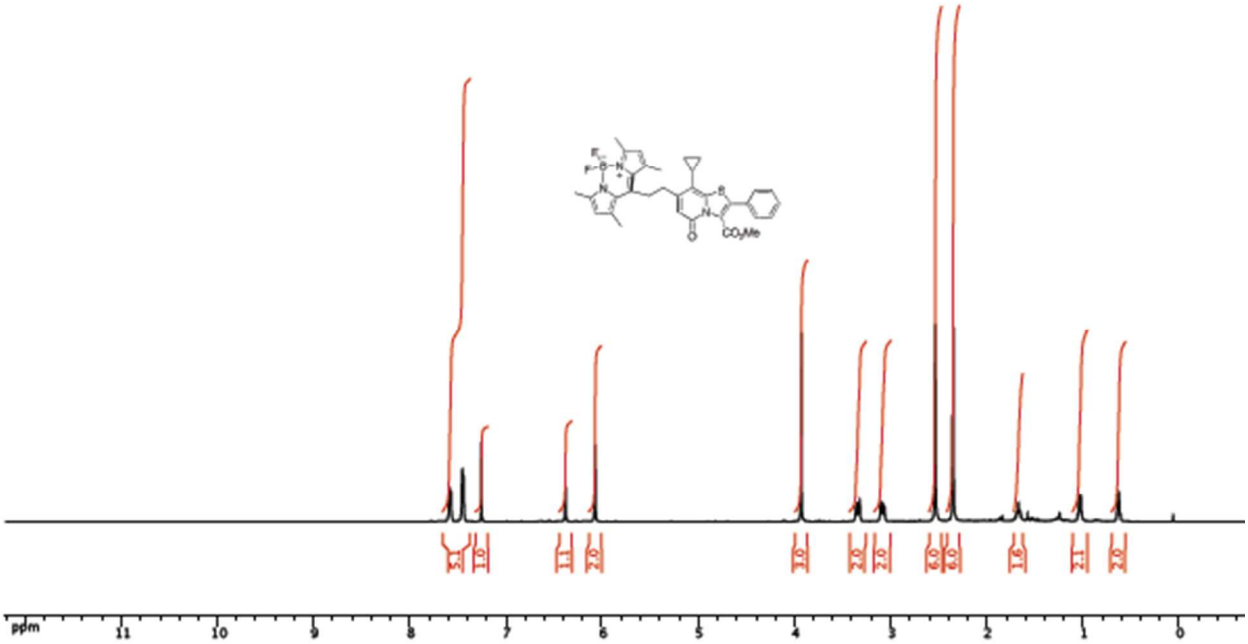
$^{1}$H NMR spectra of **17a** ($CDCl_3$)




$^{13}$C NMR spectra of **17a** ($CDCl_3$)



$^{1}$H NMR spectra of **17b** ($CDCl_3$)

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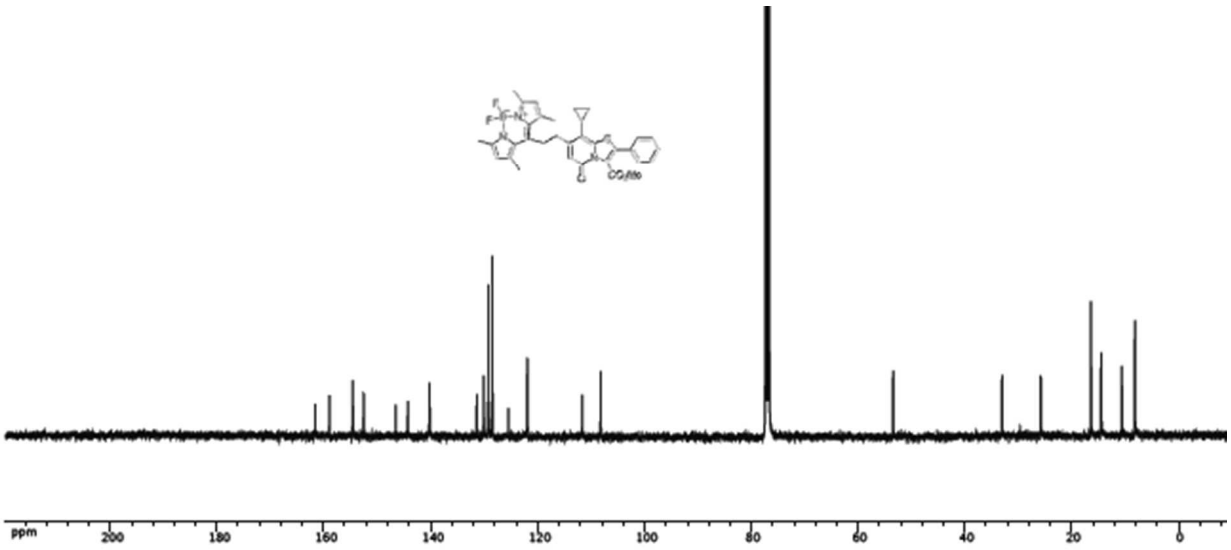
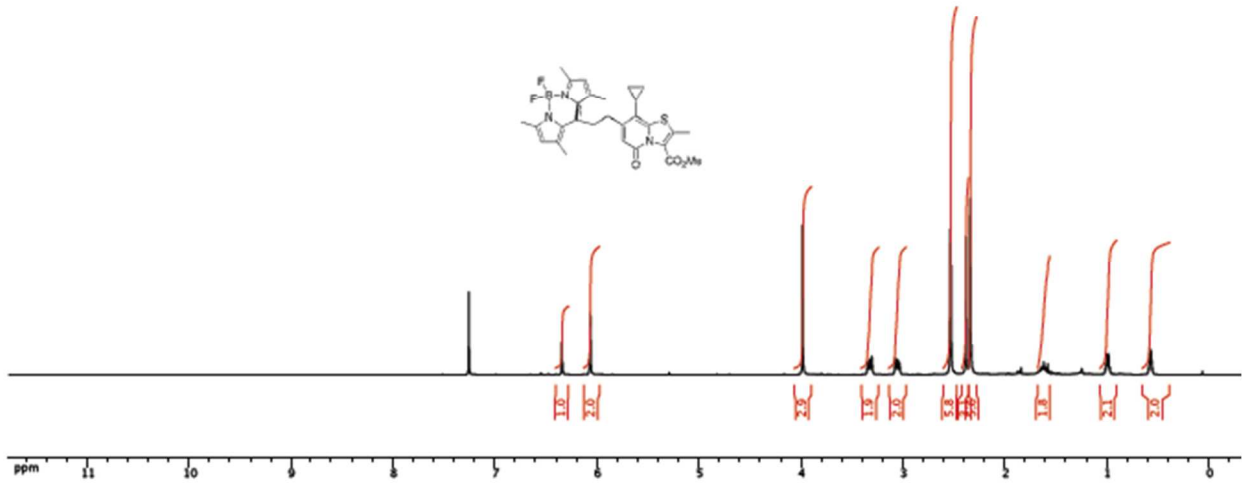
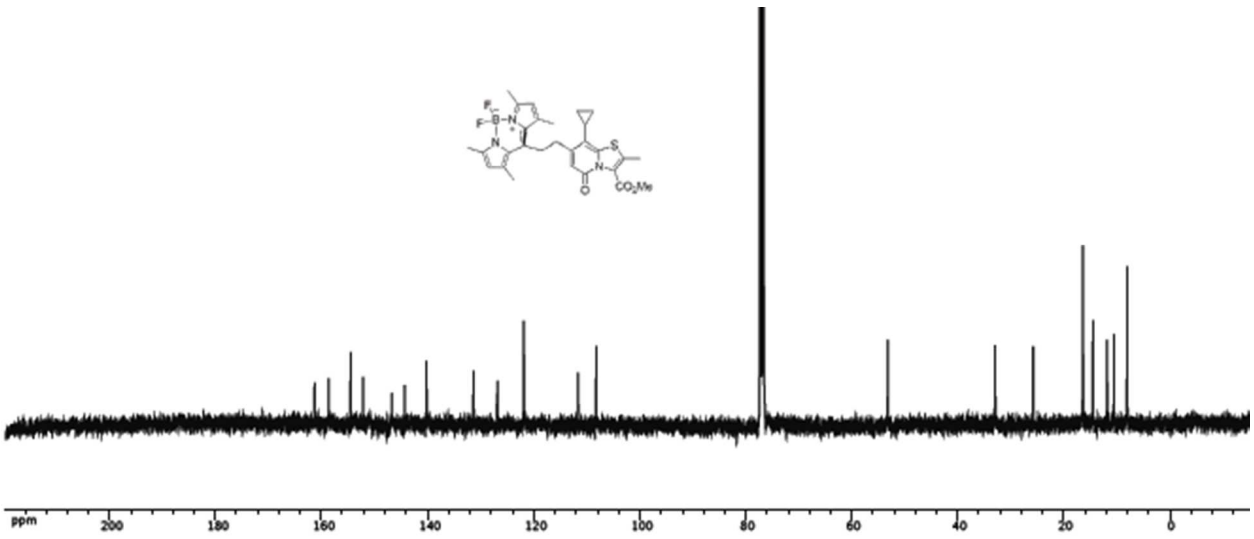


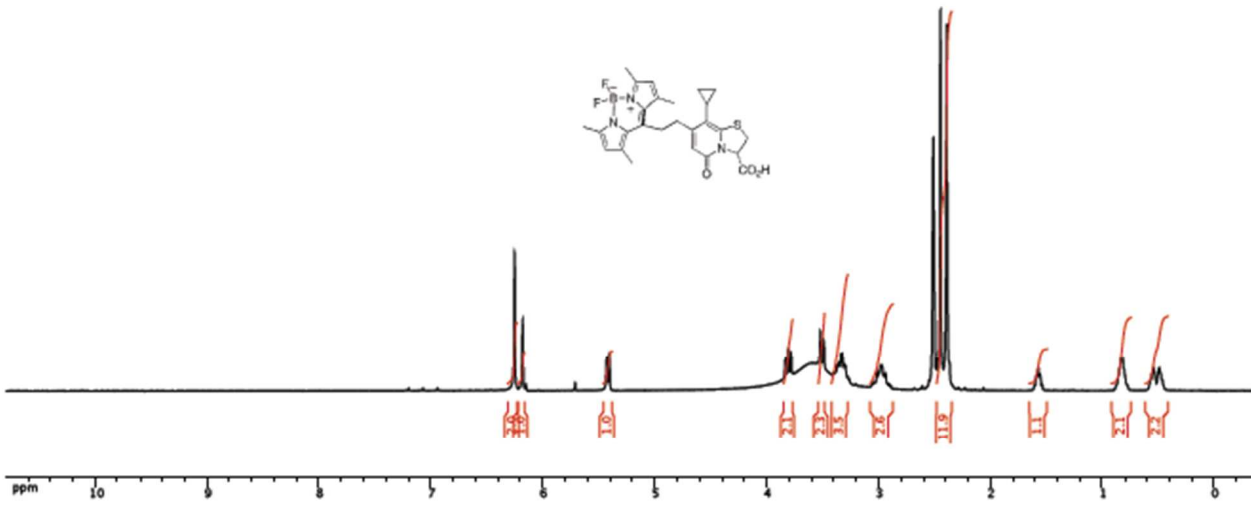
$^{1}$H NMR spectra of **17c** ($CDCl_3$)



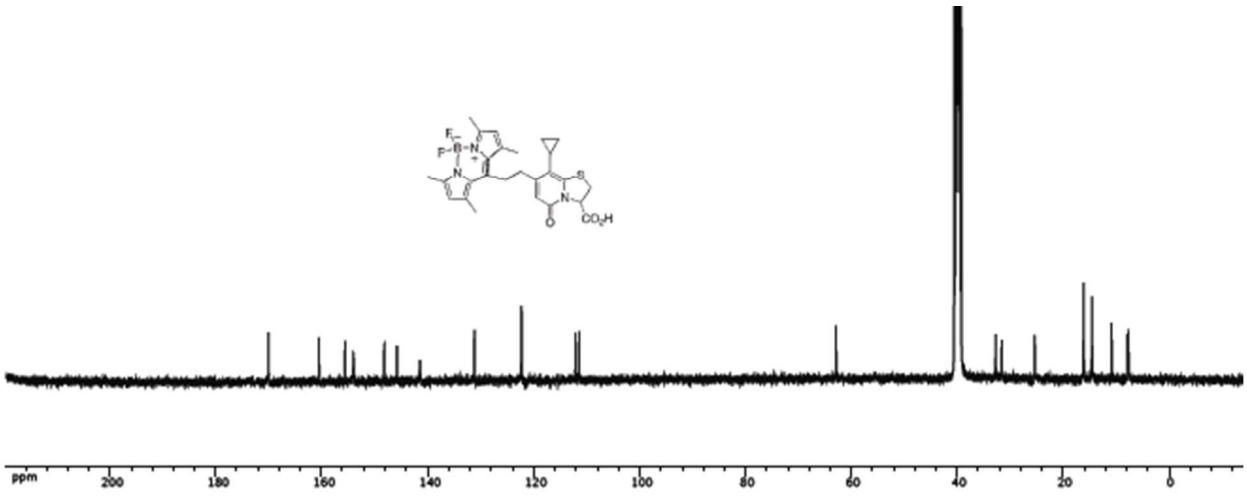

$^{13}$C NMR spectra of **17c** ($CDCl_3$)



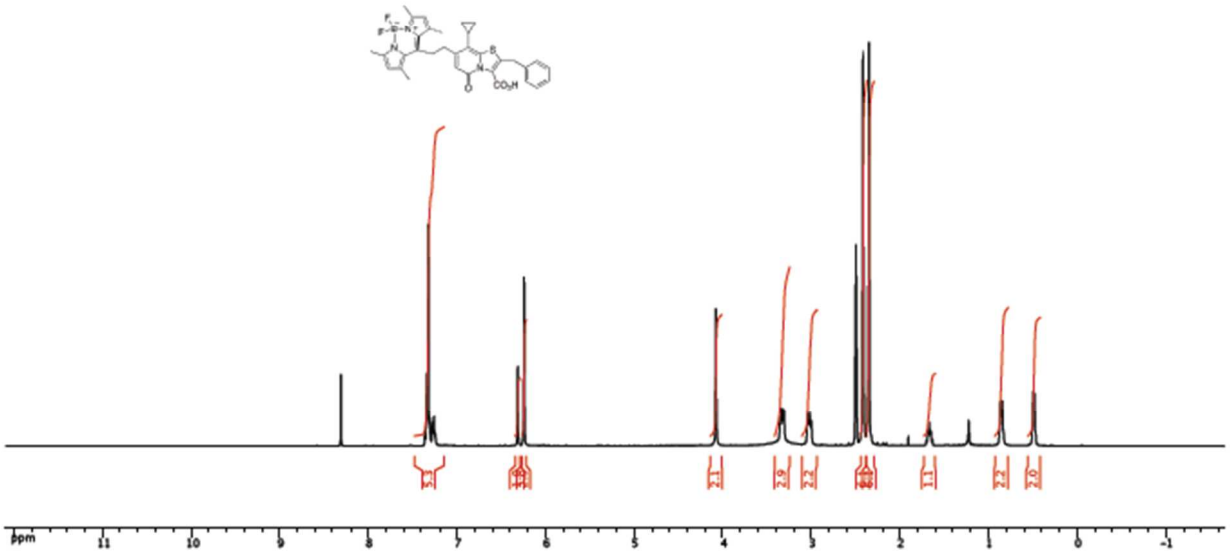
$^{1}$H NMR spectra of **18** (DMSO-$d_6$)



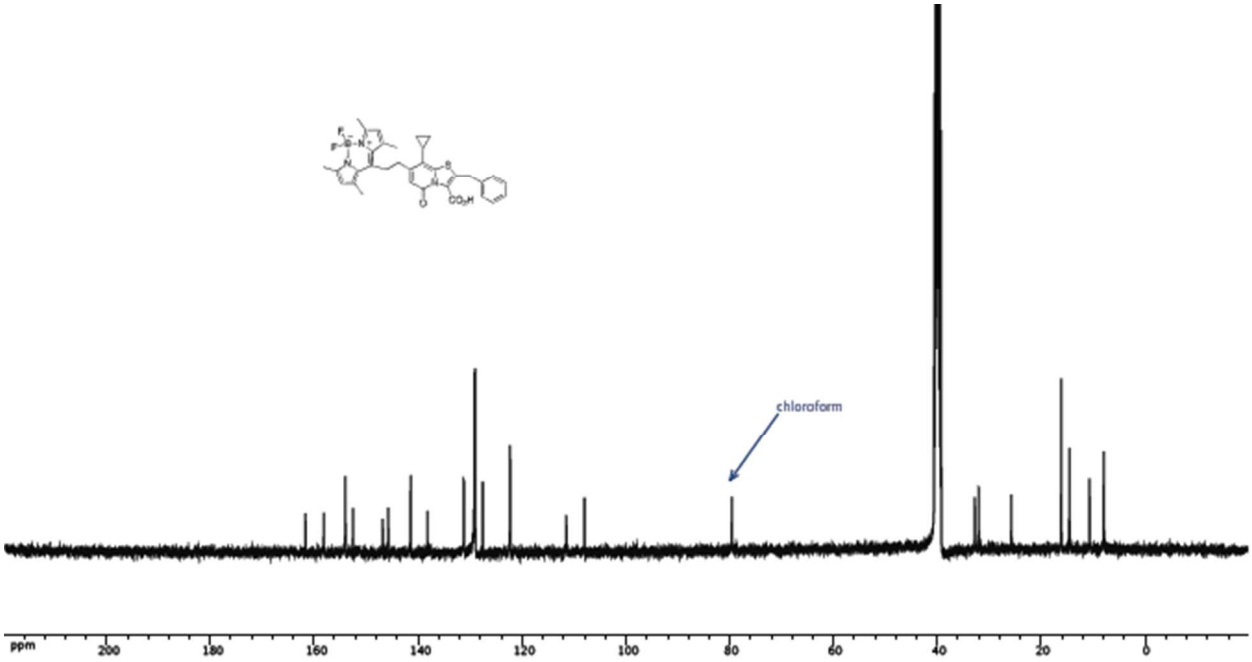

$^{13}$C NMR spectra of **18** (DMSO-$D_6$)



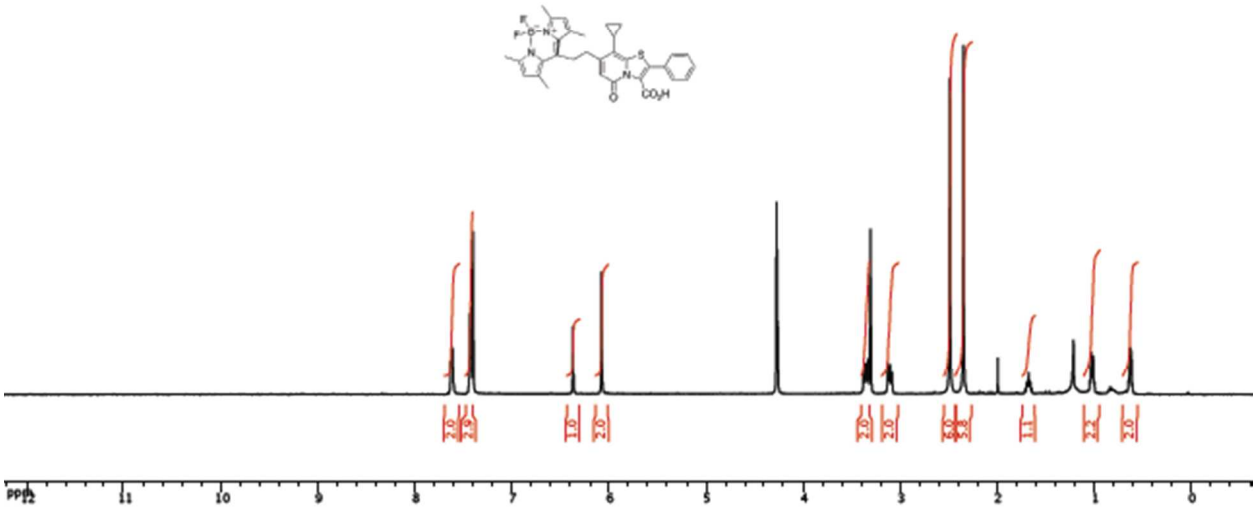
$^{1}$H NMR spectra of **19a** (DMSO-$D_6$)



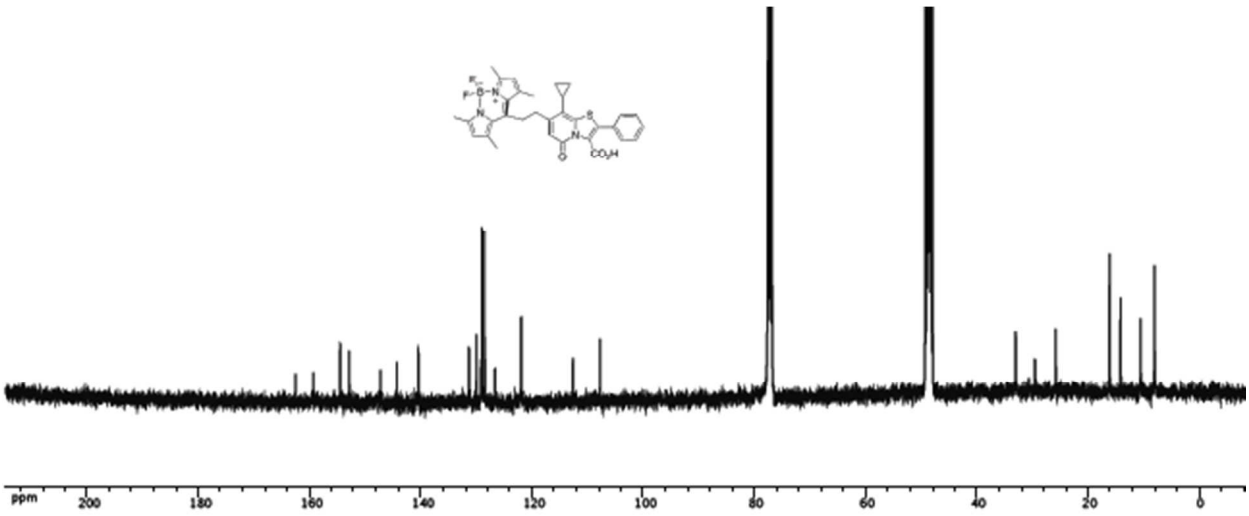

$^{13}$C NMR spectra of **19a** (DMSO-$D_6$)



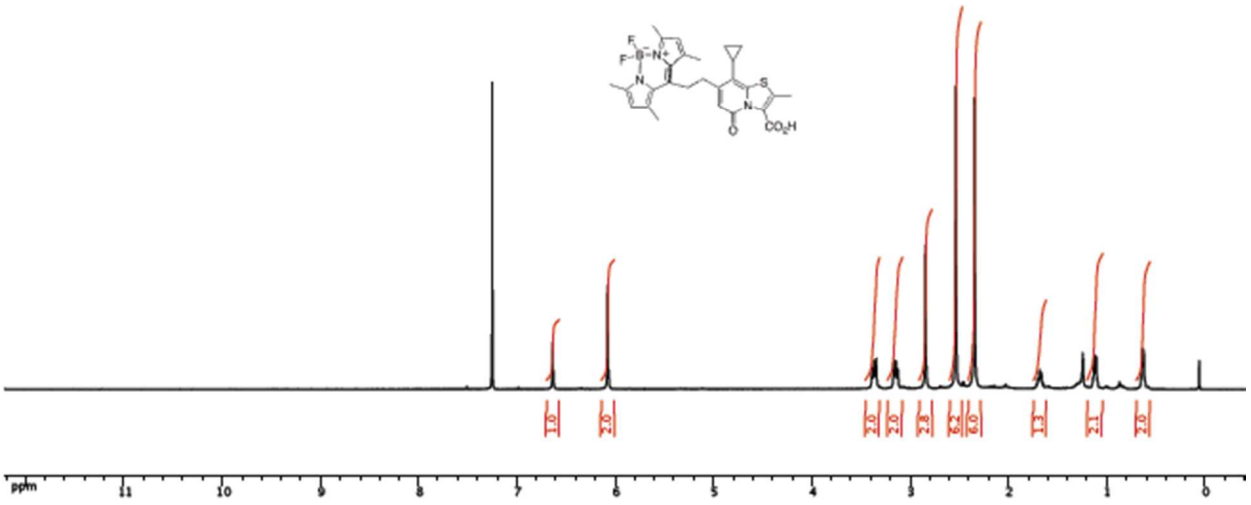
$^{1}$H NMR spectra of **19b** (MeOD + $CDCl_3$)



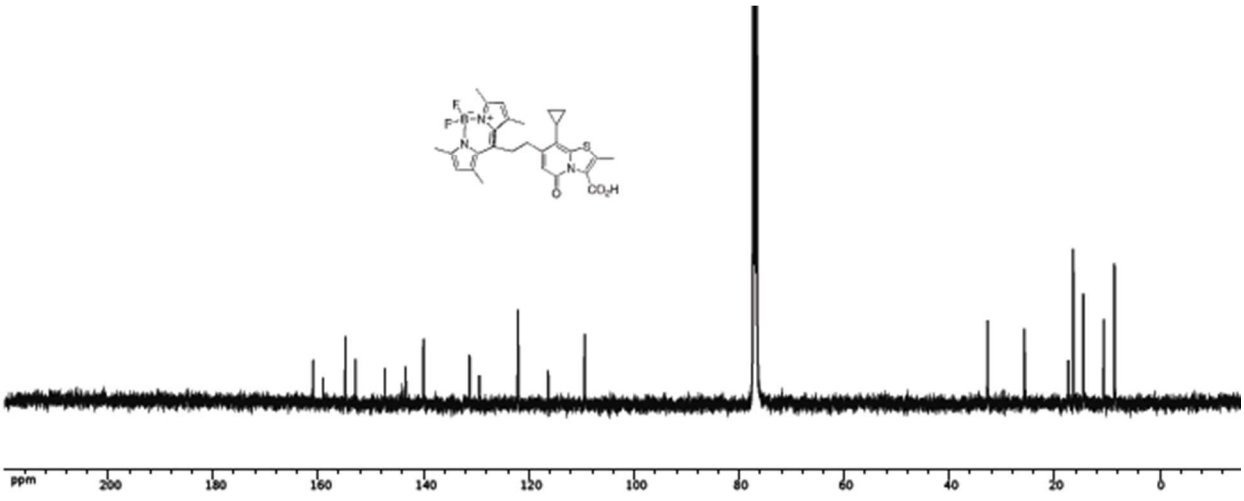
$^{13}$C NMR spectra of **19b** (MeOD + $CDCl_3$)



$^{1}$H NMR spectra of **19c** ($CDCl_3$)




$^{13}$C NMR spectra of **19c** ($CDCl_3$)



**Supplementary References**

(1) Chorell, E.; Pinkner, J. S.; Bengtsson, C.; Edvinsson, S.; Cusumano, C. K.; Rosenbaum, E.; Johansson, L. B. Å.; Hultgren, S. J.; Almqvist, F. *Chem. Eur. J.* **2012**, *18*, 4522.

(2) Boldyrev, I. A.; Zhai, X.; Momsen, M. M.; Brockman, H. L.; Brown, R. E.; Molotkovsky, J. G. *J. Lipid Res.* **2007**, *48*, 1518.

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