

Electronic Supplementary Information for:

*Discovery of Hybrid Glypromate Conjugates with  
Neuroprotective Activity Against Paraquat-Induced Toxicity*

Sara C. Silva-Reis,<sup>a,b</sup> Vera M. Costa,<sup>b,c</sup> Daniela Correia da Silva,<sup>d</sup> David M. Pereira,<sup>d</sup> Xavier Cruz Correia,<sup>a</sup> Xerardo García-Mera,<sup>e</sup> José E. Rodríguez-Borges,<sup>a</sup> Ivo E. Sampaio-Dias<sup>a,\*</sup>

<sup>a</sup>LAQV/REQUIMTE, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Porto, 4169-007 Porto, Portugal.

<sup>b</sup>UCIBIO/REQUIMTE, Laboratory of Toxicology, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal.

<sup>c</sup>Associate Laboratory i4HB, Institute for Health and Bioeconomy, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal.

<sup>d</sup>LAQV/REQUIMTE, Laboratory of Pharmacognosy, Department of Chemistry, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal.

<sup>e</sup>Department of Organic Chemistry, Faculty of Pharmacy, University of Santiago de Compostela, E-15782 Santiago de Compostela, Spain.

\*E-mail: ivdias@fc.up.pt.

## Electronic Supplementary Information

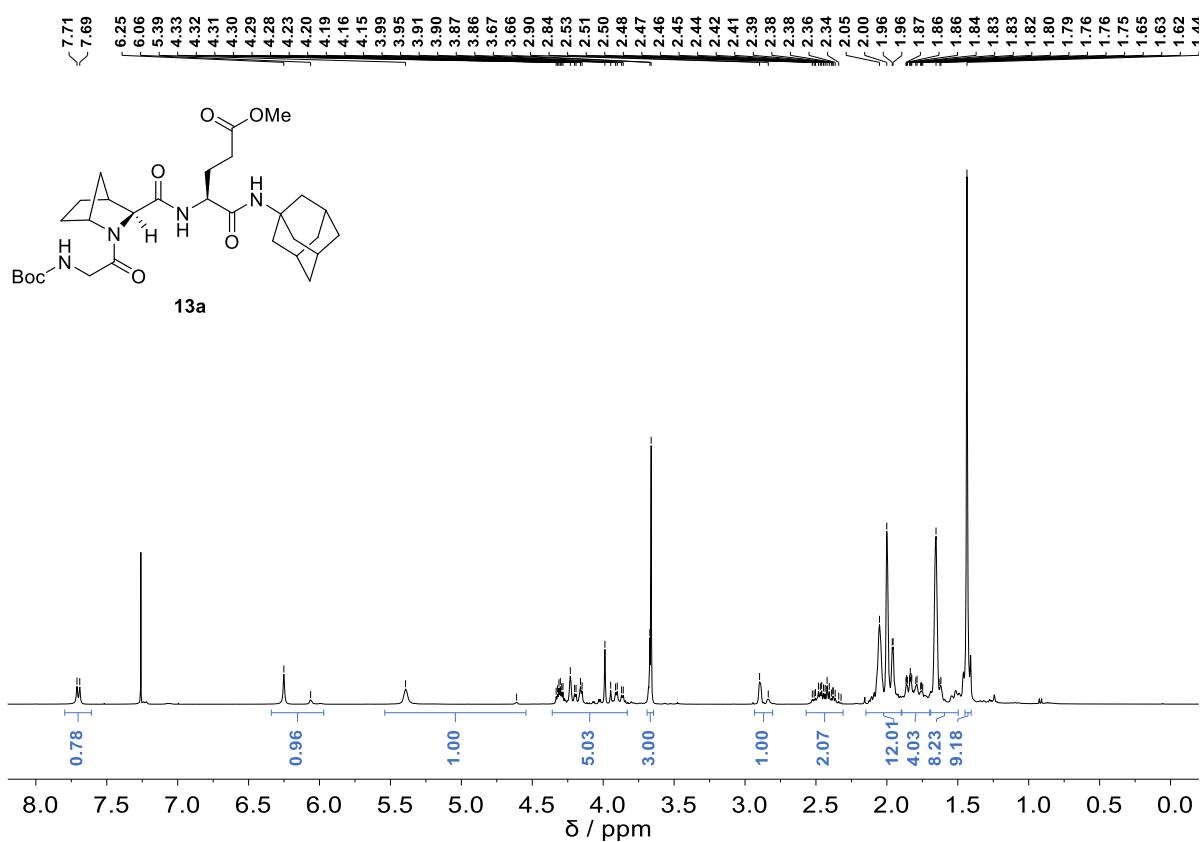
### Table of Contents

<b>Figure S1.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CDCl}_3$ ) of conjugate <b>13a</b> .	SI-3
<b>Figure S2.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CDCl}_3$ ) of conjugate <b>13a</b> .	SI-3
<b>Figure S3.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CDCl}_3$ ) of conjugate <b>13b</b> .	SI-4
<b>Figure S4.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CDCl}_3$ ) of conjugate <b>13b</b> .	SI-4
<b>Figure S5.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CDCl}_3$ ) of conjugate <b>13c</b> .	SI-5
<b>Figure S6.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CDCl}_3$ ) of conjugate <b>13c</b> .	SI-5
<b>Figure S7.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>14a</b> .	SI-6
<b>Figure S8.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>14a</b> .	SI-6
<b>Figure S9.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>14b</b> .	SI-7

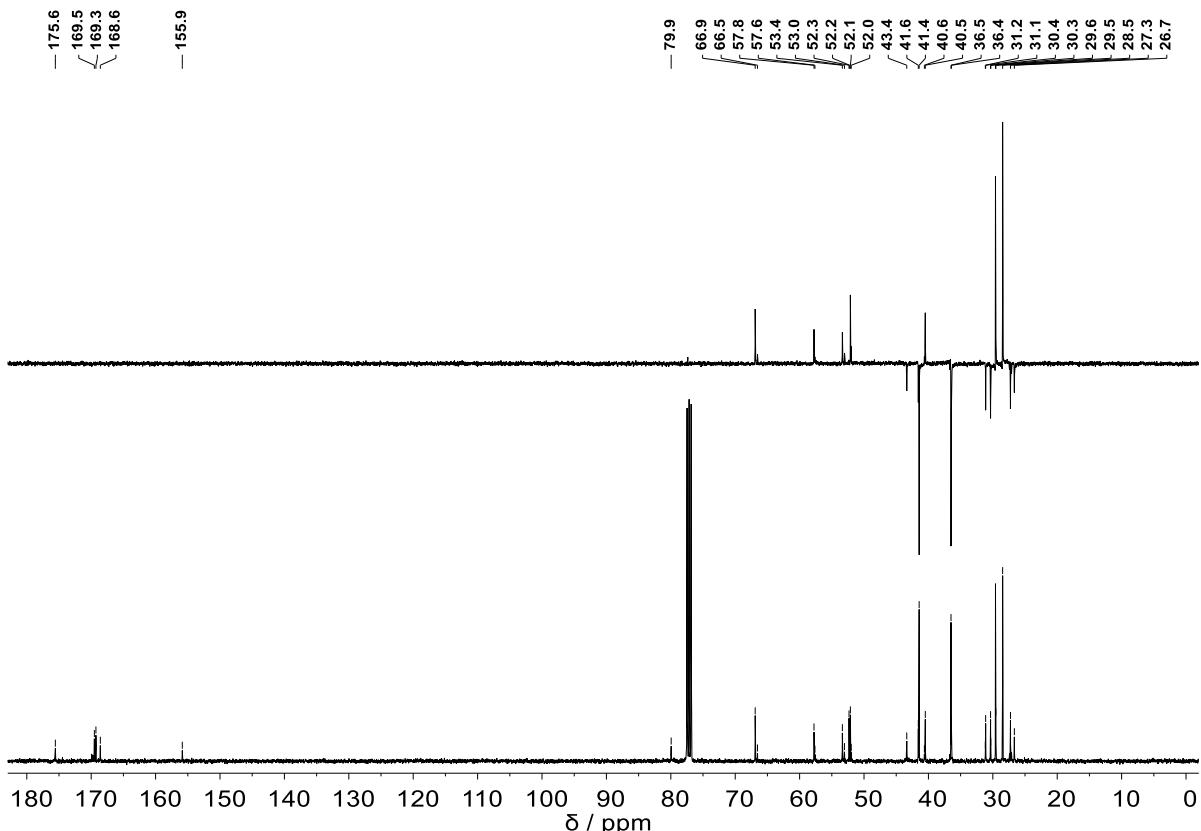
Electronic Supplementary Information

<b>Figure S10.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>14b</b> .	SI-7
<b>Figure S11.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>14c</b> .	SI-8
<b>Figure S12.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>14c</b> .	SI-8
<b>Figure S13.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>15a</b> .	SI-9
<b>Figure S14.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>15a</b> .	SI-9
<b>Figure S15.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>15b</b> .	SI-10
<b>Figure S16.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>15b</b> .	SI-10
<b>Figure S17.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>15c</b> .	SI-11
<b>Figure S18.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>15c</b> .	SI-11
<b>Figure S19.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CDCl}_3$ ) of conjugate <b>16a</b> .	SI-12
<b>Figure S20.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CDCl}_3$ ) of conjugate <b>16a</b> .	SI-12
<b>Figure S21.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CDCl}_3$ ) of conjugate <b>16b</b> .	SI-13
<b>Figure S22.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CDCl}_3$ ) of conjugate <b>16b</b> .	SI-13
<b>Figure S23.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CDCl}_3$ ) of conjugate <b>16c</b> .	SI-14
<b>Figure S24.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CDCl}_3$ ) of conjugate <b>16c</b> .	SI-14
<b>Figure S25.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>17a</b> .	SI-15
<b>Figure S26.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>17a</b> .	SI-15
<b>Figure S27.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>17b</b> .	SI-16
<b>Figure S28.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>17b</b> .	SI-16
<b>Figure S29.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>17c</b> .	SI-17
<b>Figure S30.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>17c</b> .	SI-17
<b>Figure S31.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>18a</b> .	SI-18
<b>Figure S32.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>18a</b> .	SI-18
<b>Figure S33.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>18b</b> .	SI-19
<b>Figure S34.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>18b</b> .	SI-19
<b>Figure S35.</b> $^1\text{H}$ -NMR spectrum (400 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>18c</b> .	SI-20
<b>Figure S36.</b> $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz, $\text{CD}_3\text{OD}$ ) of conjugate <b>18c</b> .	SI-20

Electronic Supplementary Information

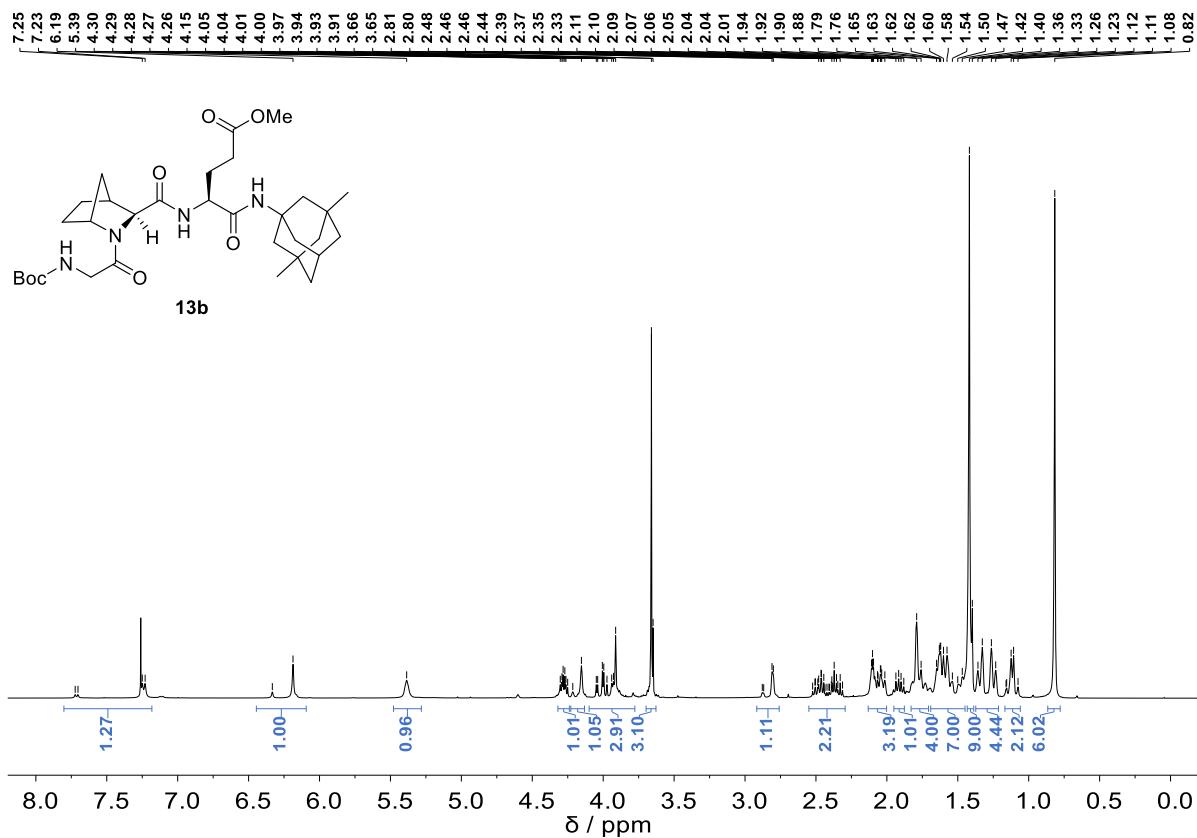


**Figure S1.** <sup>1</sup>H-NMR spectrum (400 MHz, CDCl<sub>3</sub>) of conjugate **13a**.

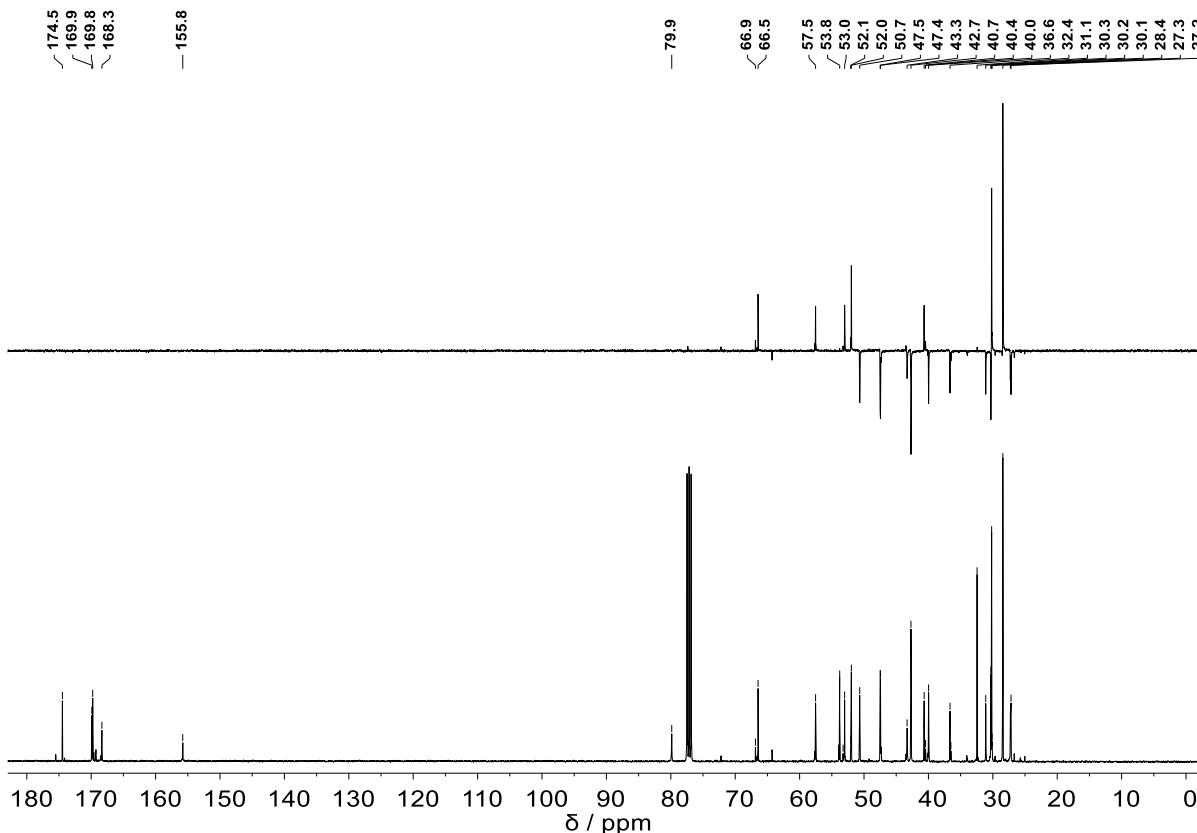


**Figure S2.** <sup>13</sup>C{<sup>1</sup>H}-NMR and DEPT-135 spectra (101 MHz, CDCl<sub>3</sub>) of conjugate **13a**.

Electronic Supplementary Information

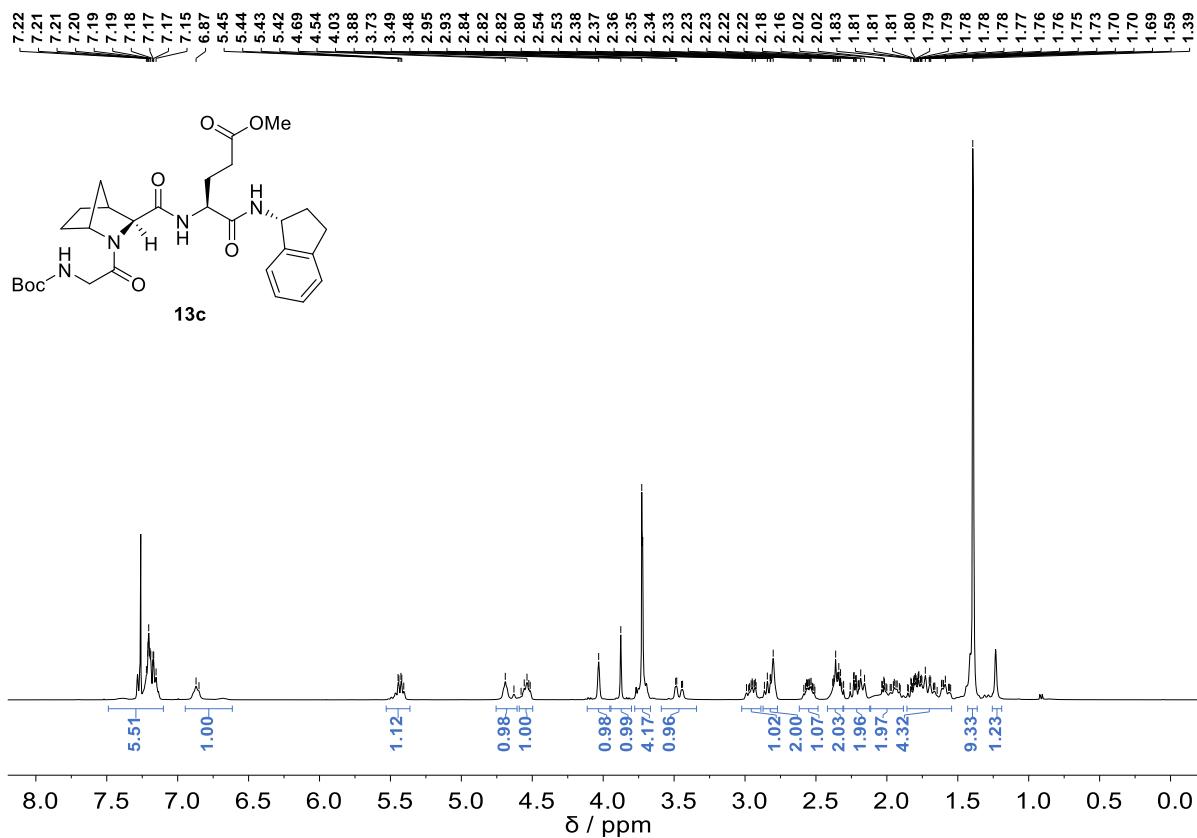


**Figure S3.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of conjugate **13b**.

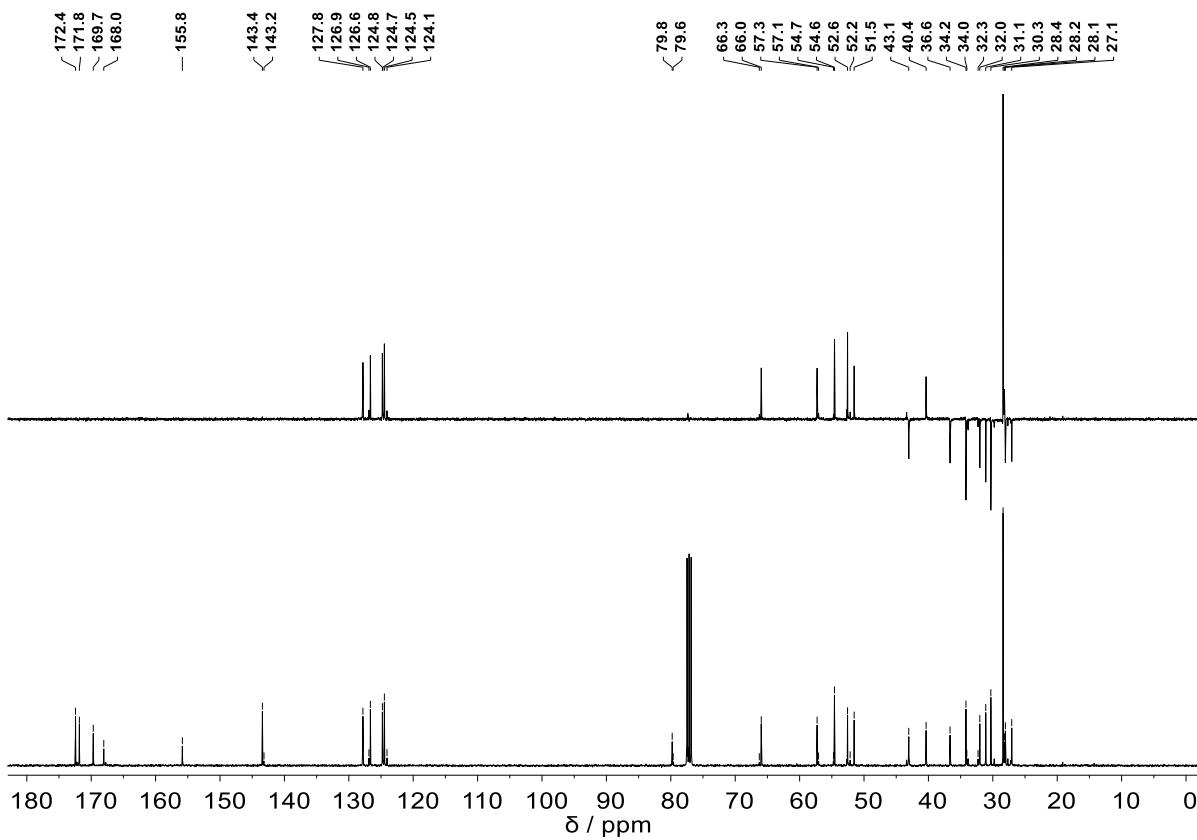


**Figure S4.**  $^{13}\text{C}\{^1\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CDCl}_3$ ) of conjugate **13b**.

## Electronic Supplementary Information

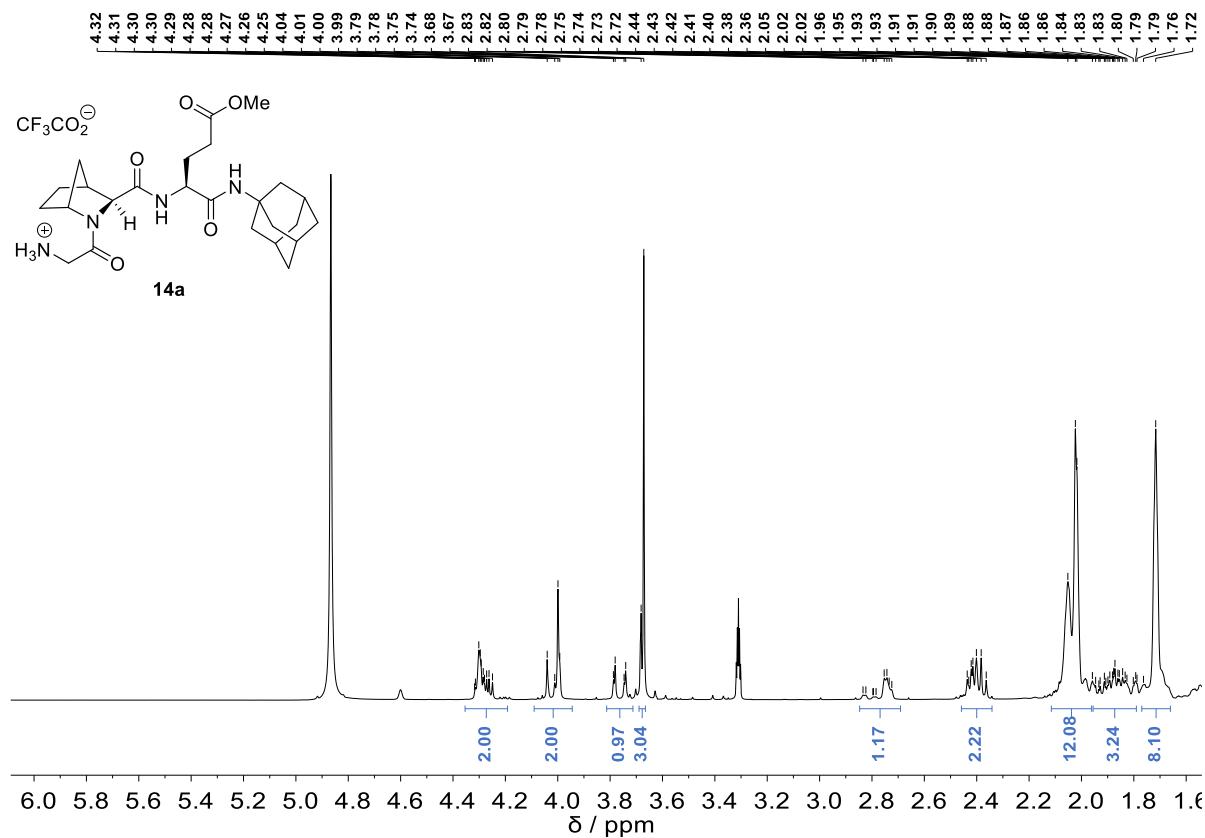


**Figure S5.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of conjugate **13c**.

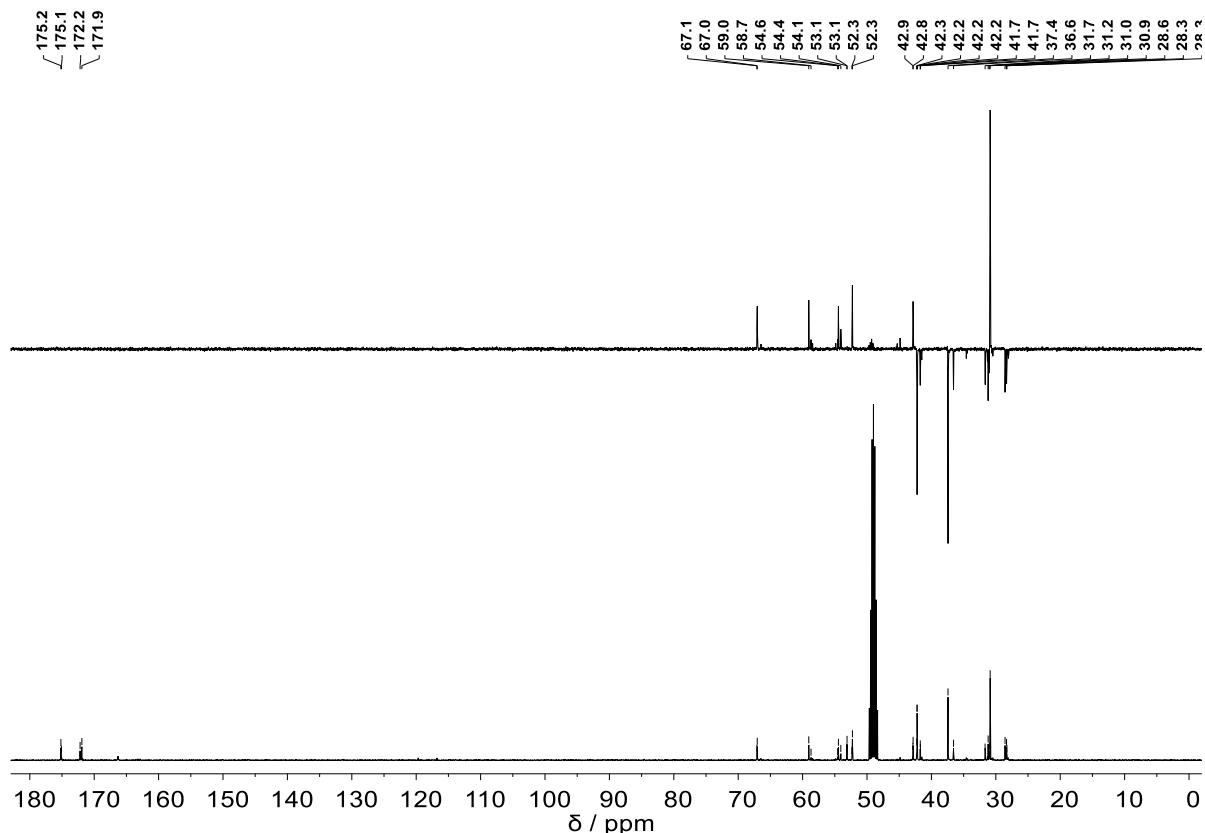


**Figure S6.**  $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CDCl}_3$ ) of conjugate **13c**.

Electronic Supplementary Information

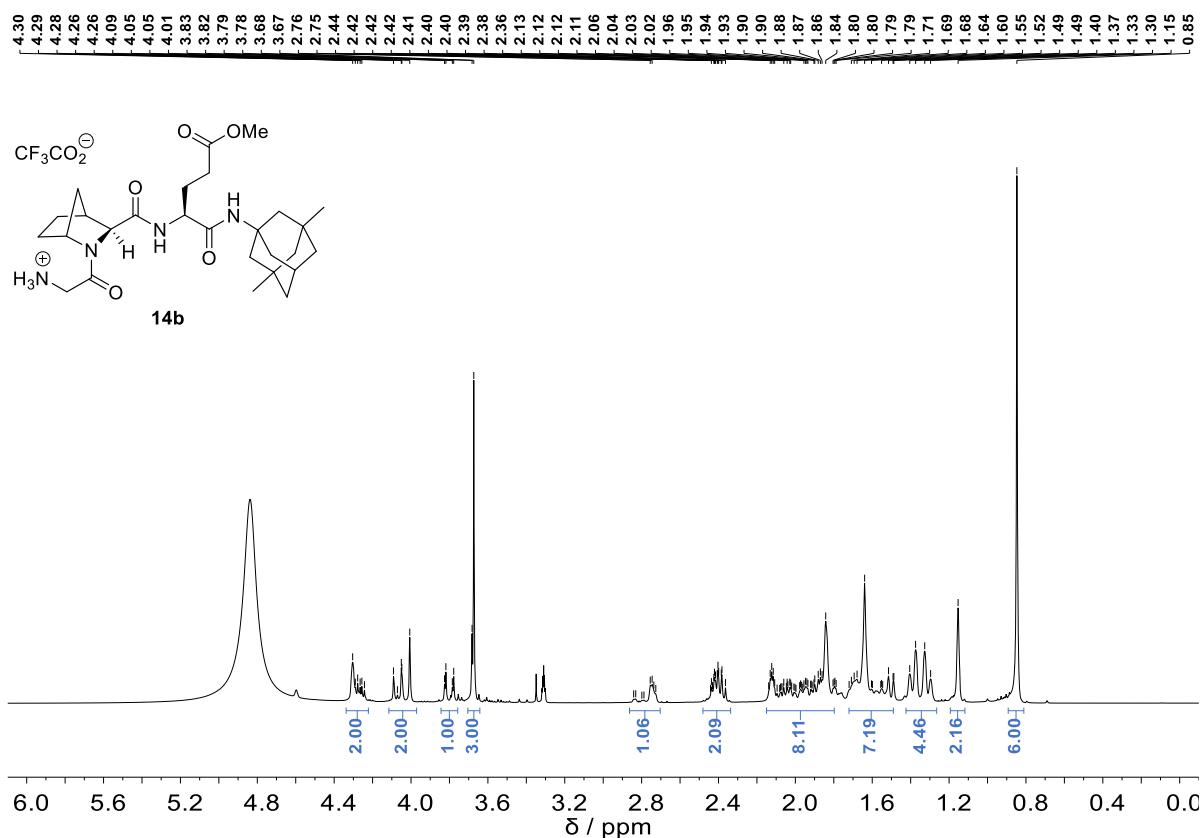


**Figure S7.** <sup>1</sup>H-NMR spectrum (400 MHz, CD<sub>3</sub>OD) of conjugate **14a**.

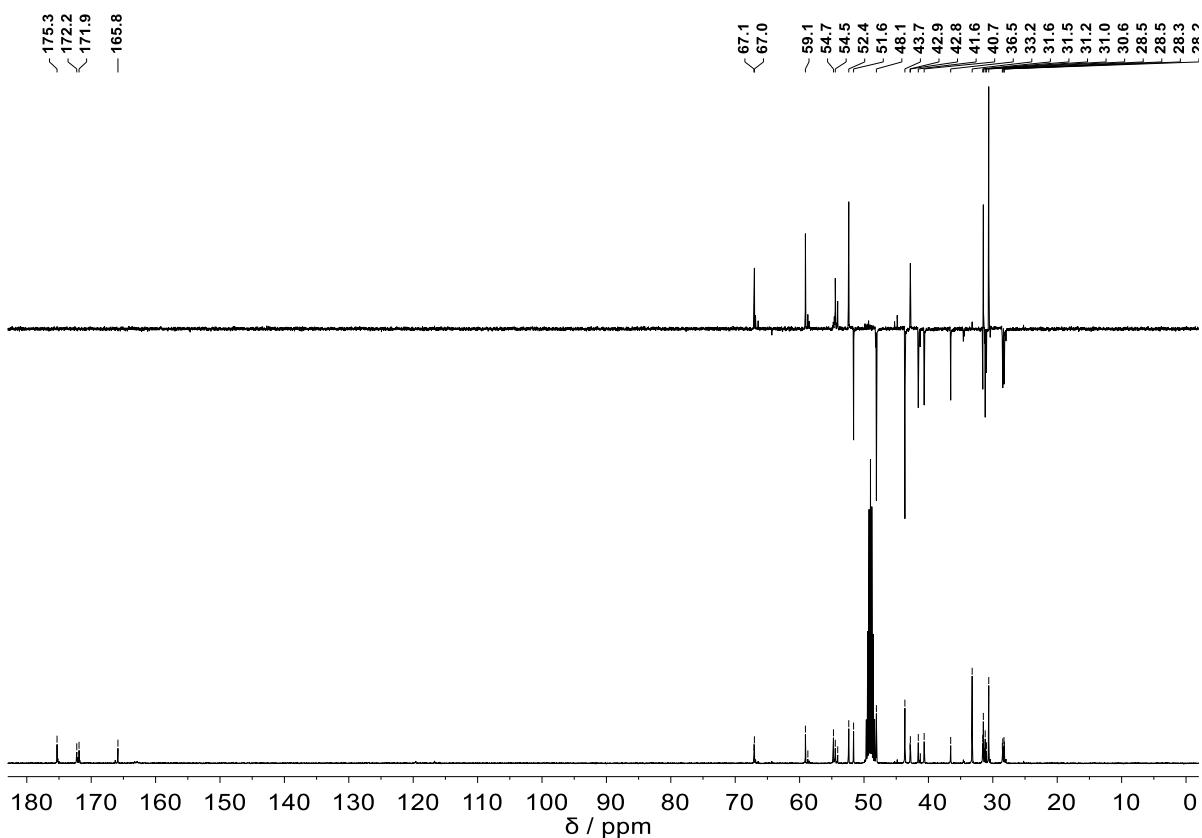


**Figure S8.** <sup>13</sup>C{<sup>1</sup>H}-NMR and DEPT-135 spectra (101 MHz, CD<sub>3</sub>OD) of conjugate **14a**.

## Electronic Supplementary Information

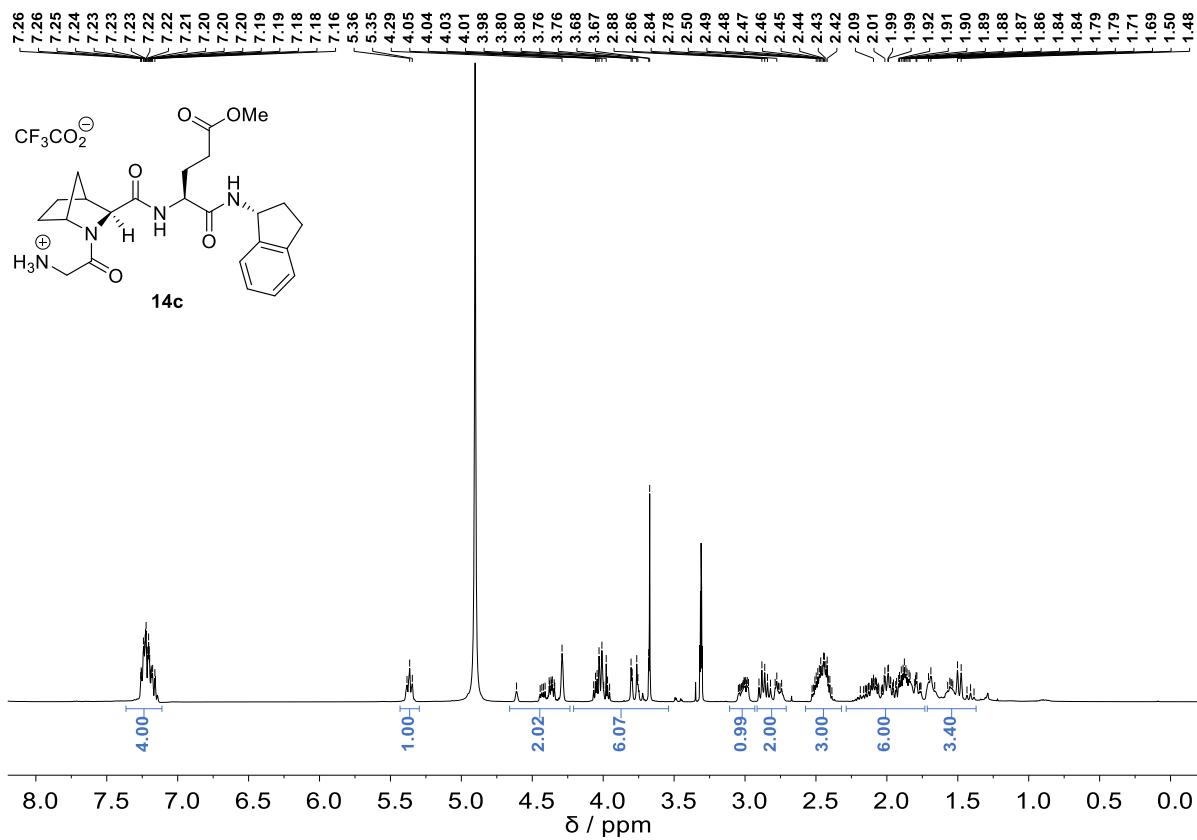


**Figure S9.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **14b**.

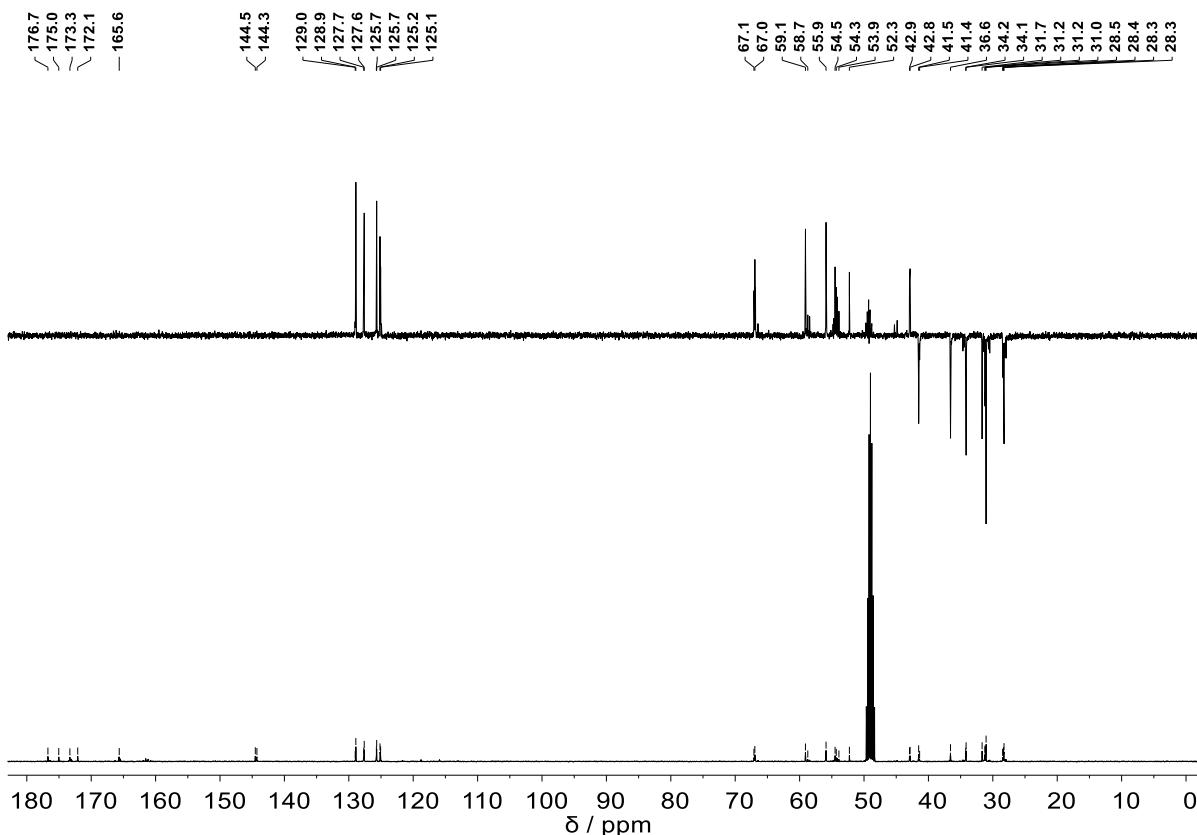


**Figure S10.**  $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **14b**.

## Electronic Supplementary Information

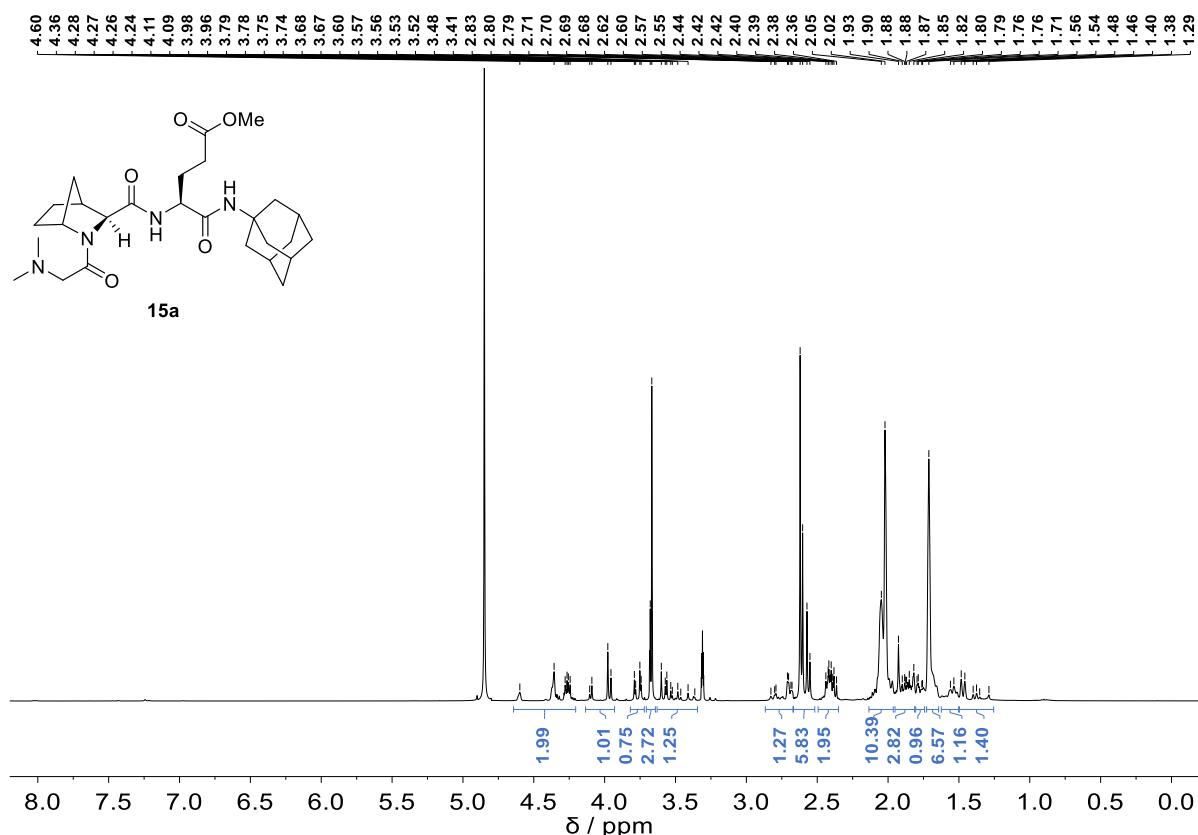


**Figure S11.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **14c**.

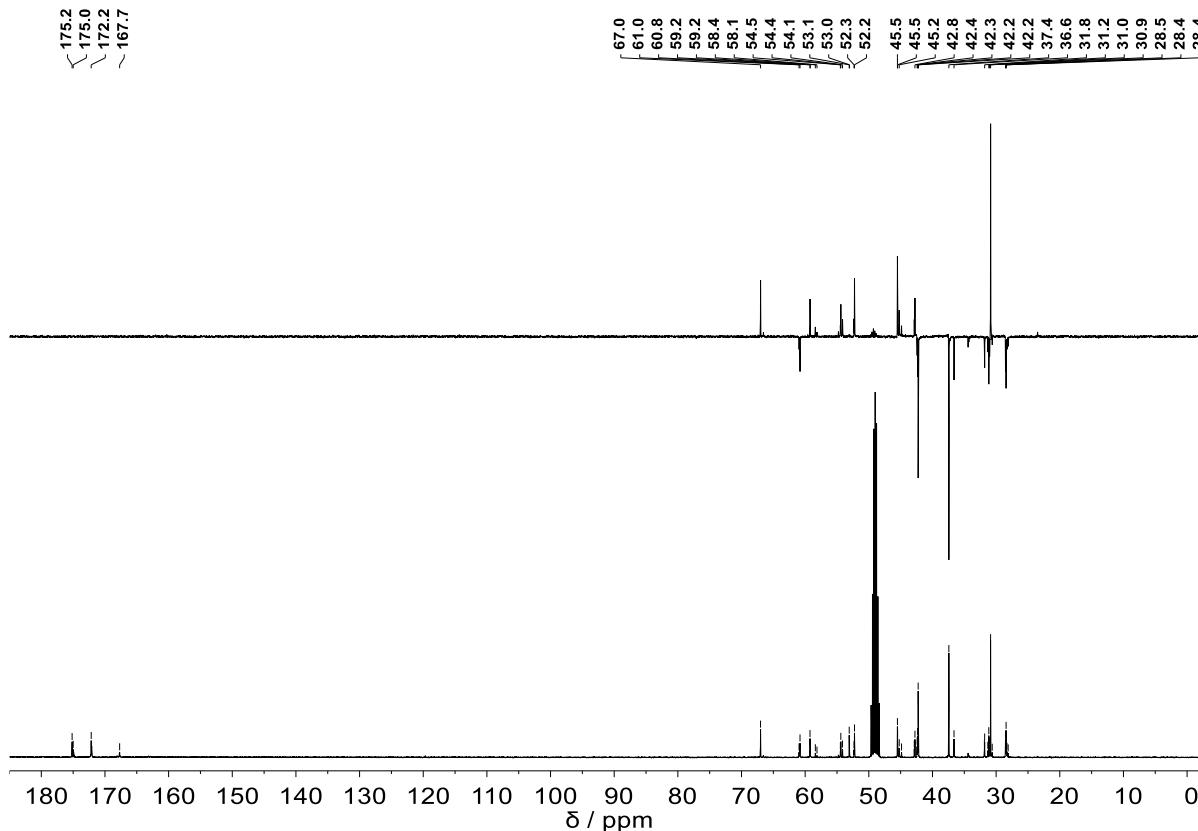


**Figure S12.**  $^{13}\text{C}\{^1\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **14c**.

Electronic Supplementary Information

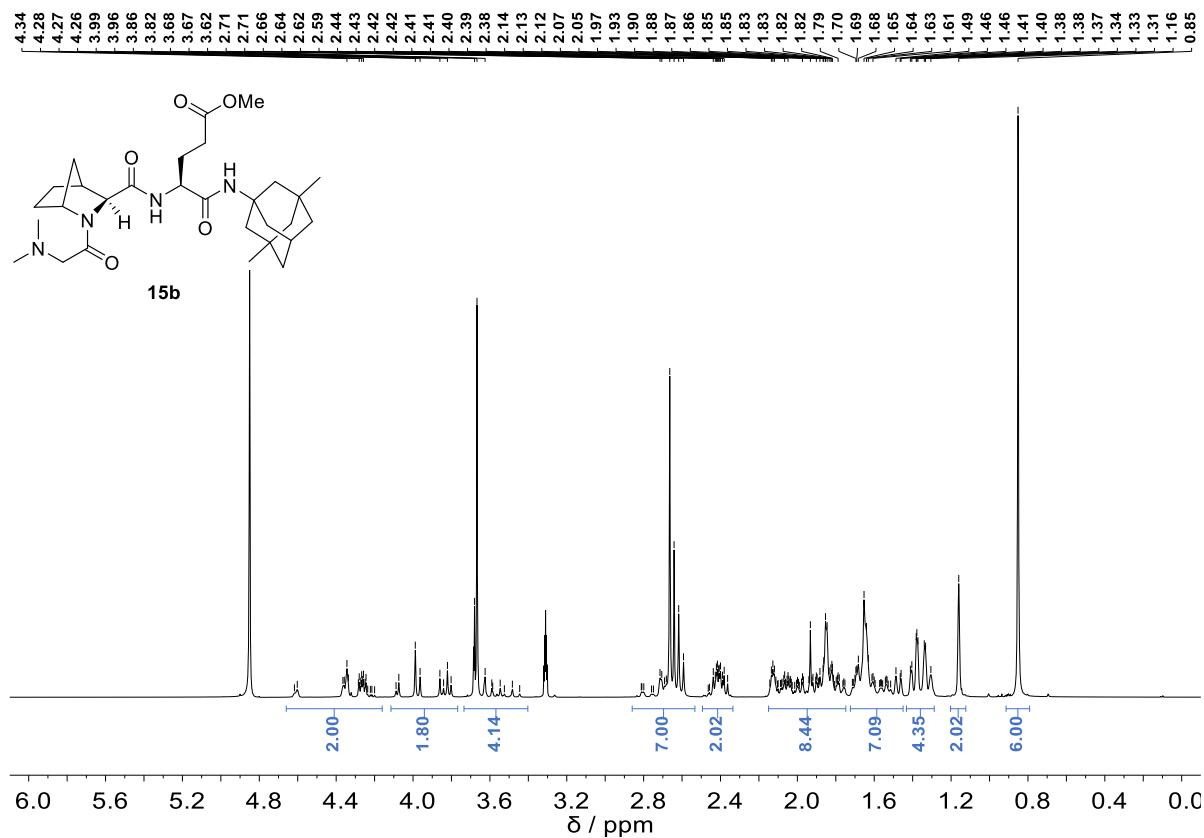


**Figure S13.** <sup>1</sup>H-NMR spectrum (400 MHz, CD<sub>3</sub>OD) of conjugate **15a**.

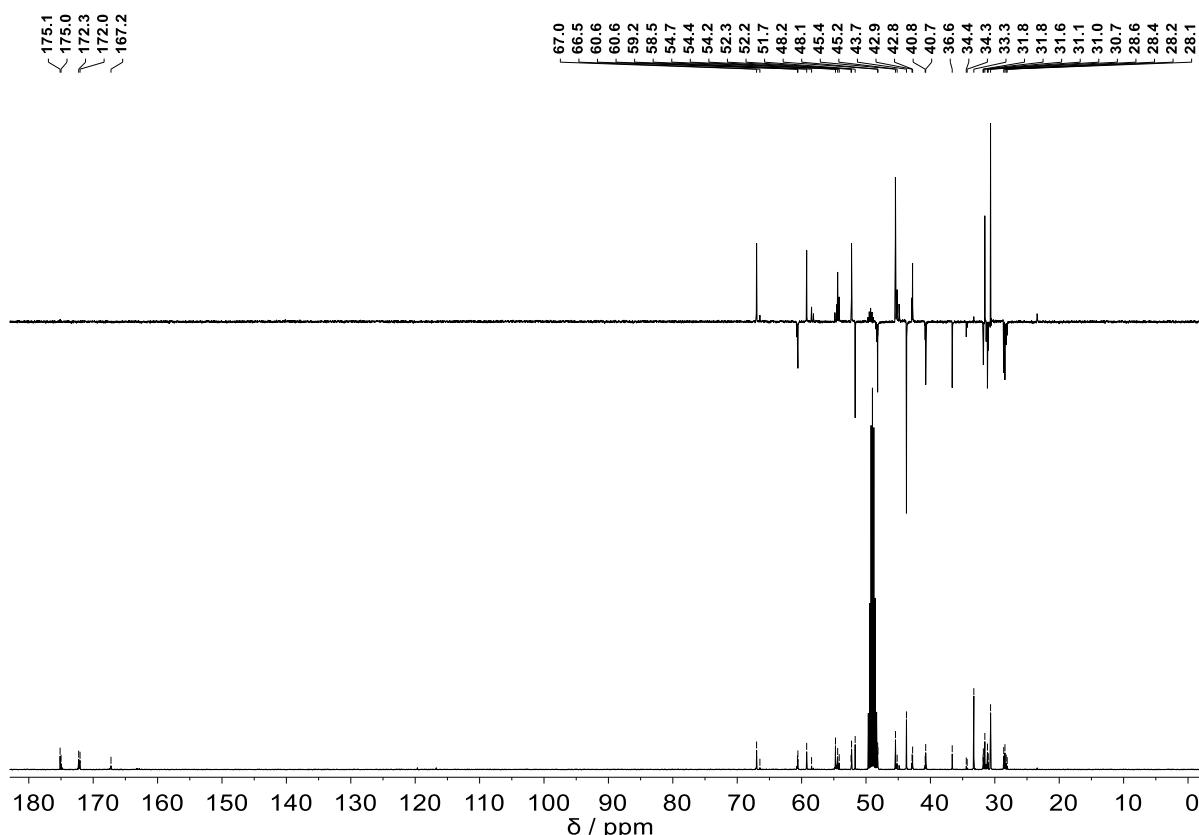


**Figure S14.** <sup>13</sup>C{<sup>1</sup>H}-NMR and DEPT-135 spectra (101 MHz, CD<sub>3</sub>OD) of conjugate **15a**.

## Electronic Supplementary Information

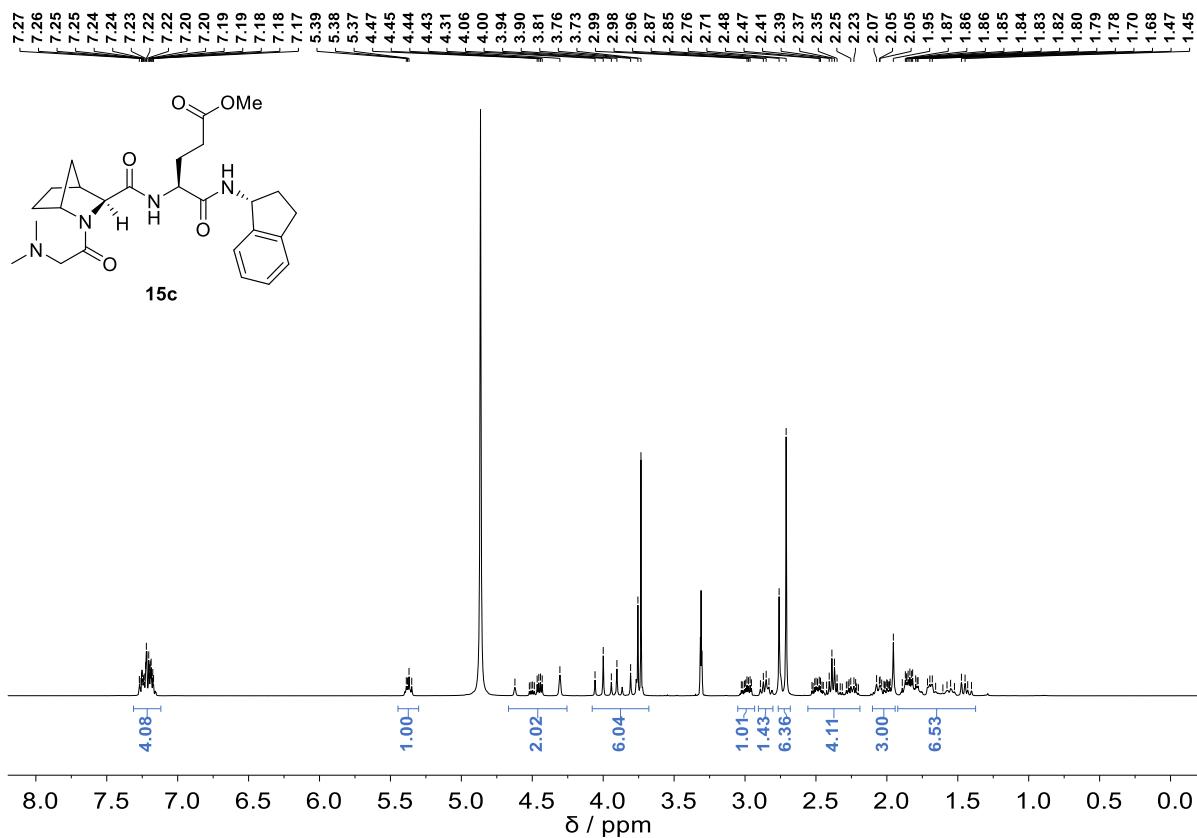


**Figure S15.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **15b**.

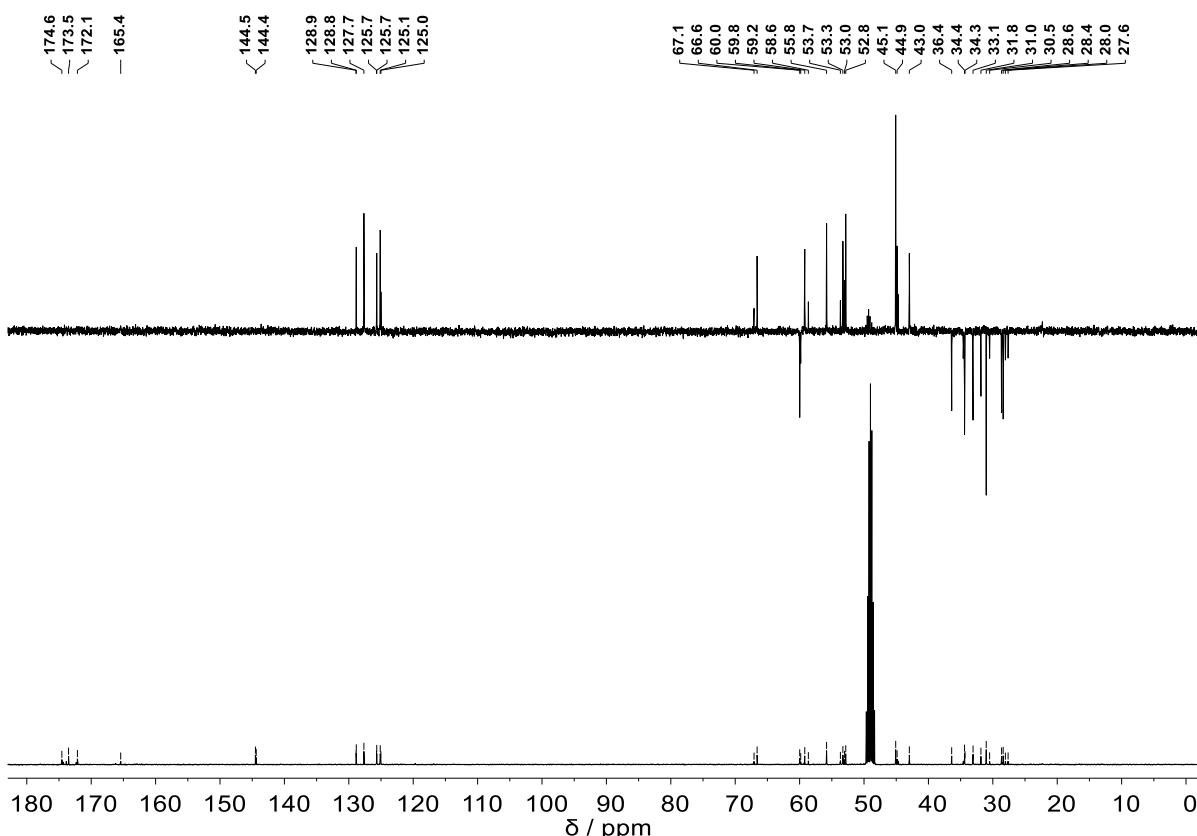


**Figure S16.**  $^{13}\text{C}\{^1\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **15b**.

Electronic Supplementary Information

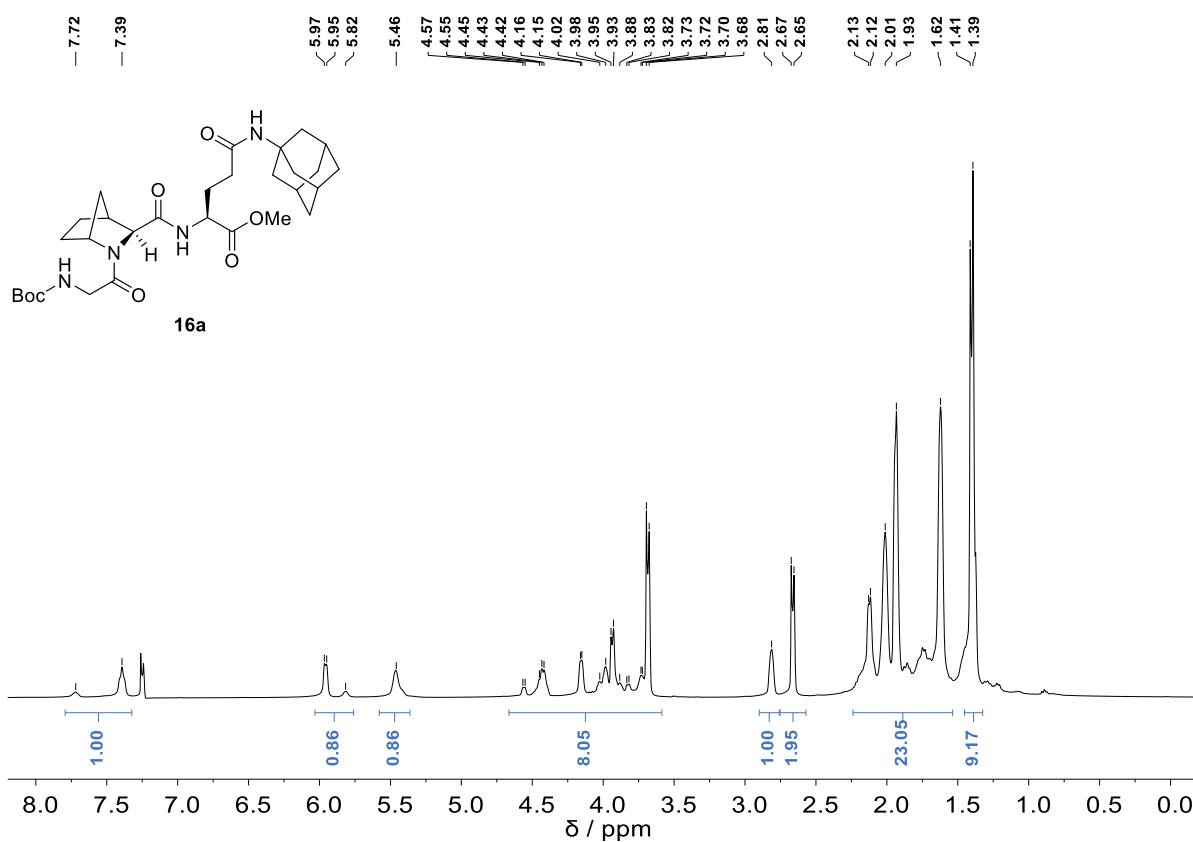


**Figure S17.** <sup>1</sup>H-NMR spectrum (400 MHz, CD<sub>3</sub>OD) of conjugate **15c**.

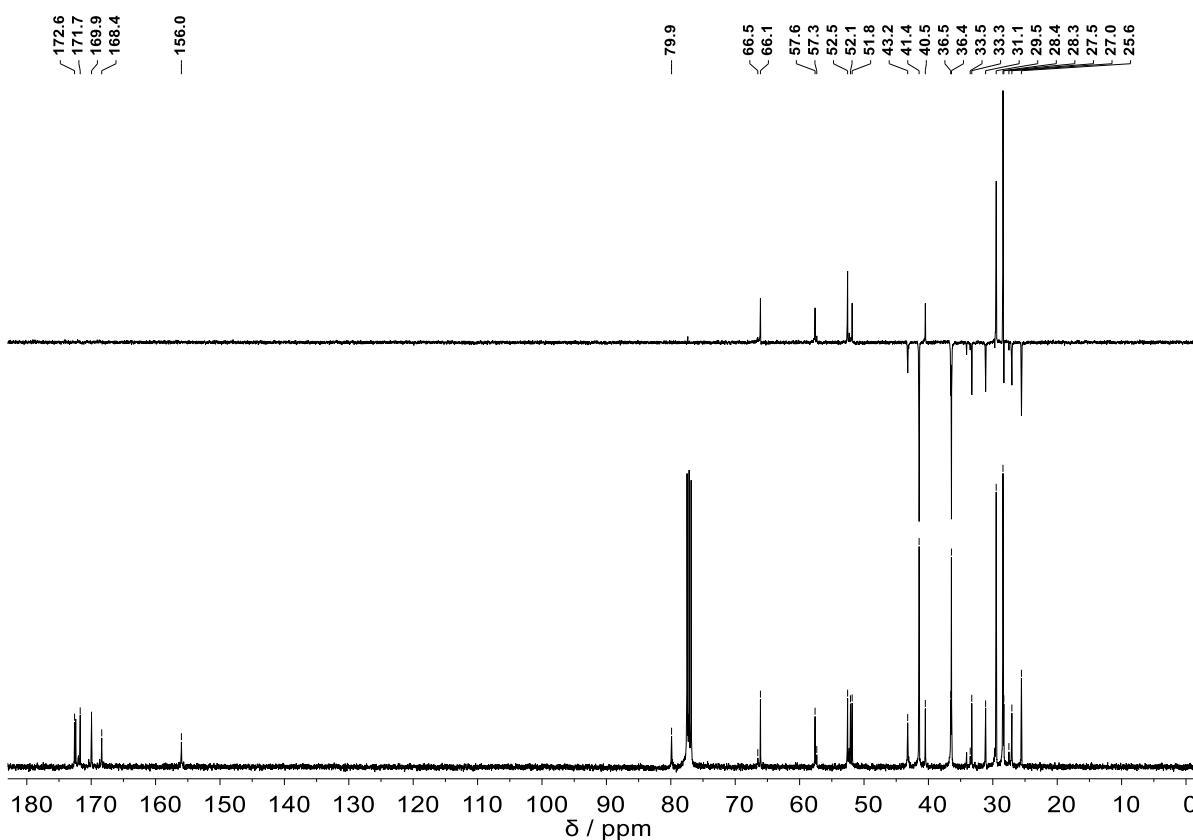


**Figure S18.** <sup>13</sup>C{<sup>1</sup>H}-NMR and DEPT-135 spectra (101 MHz, CD<sub>3</sub>OD) of conjugate **15c**.

Electronic Supplementary Information

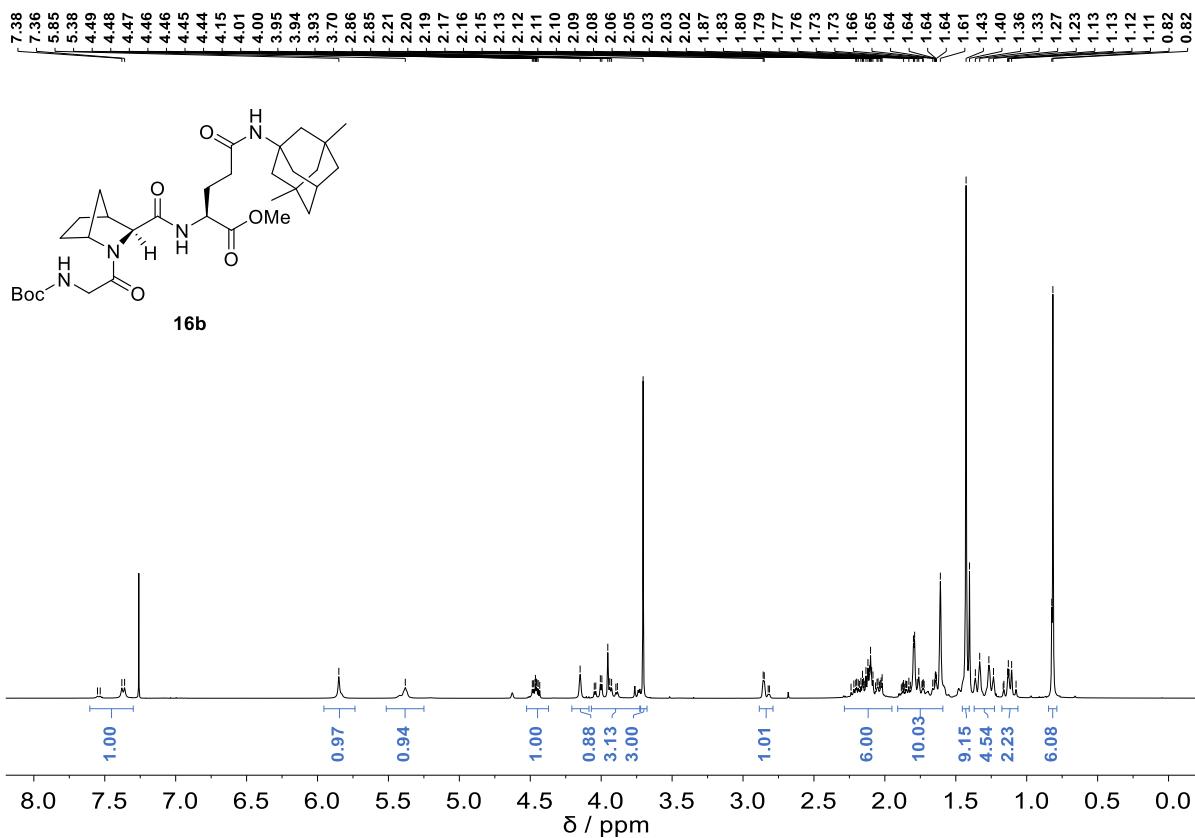


**Figure S19.** <sup>1</sup>H-NMR spectrum (400 MHz, CD<sub>3</sub>OD) of conjugate **16a**.

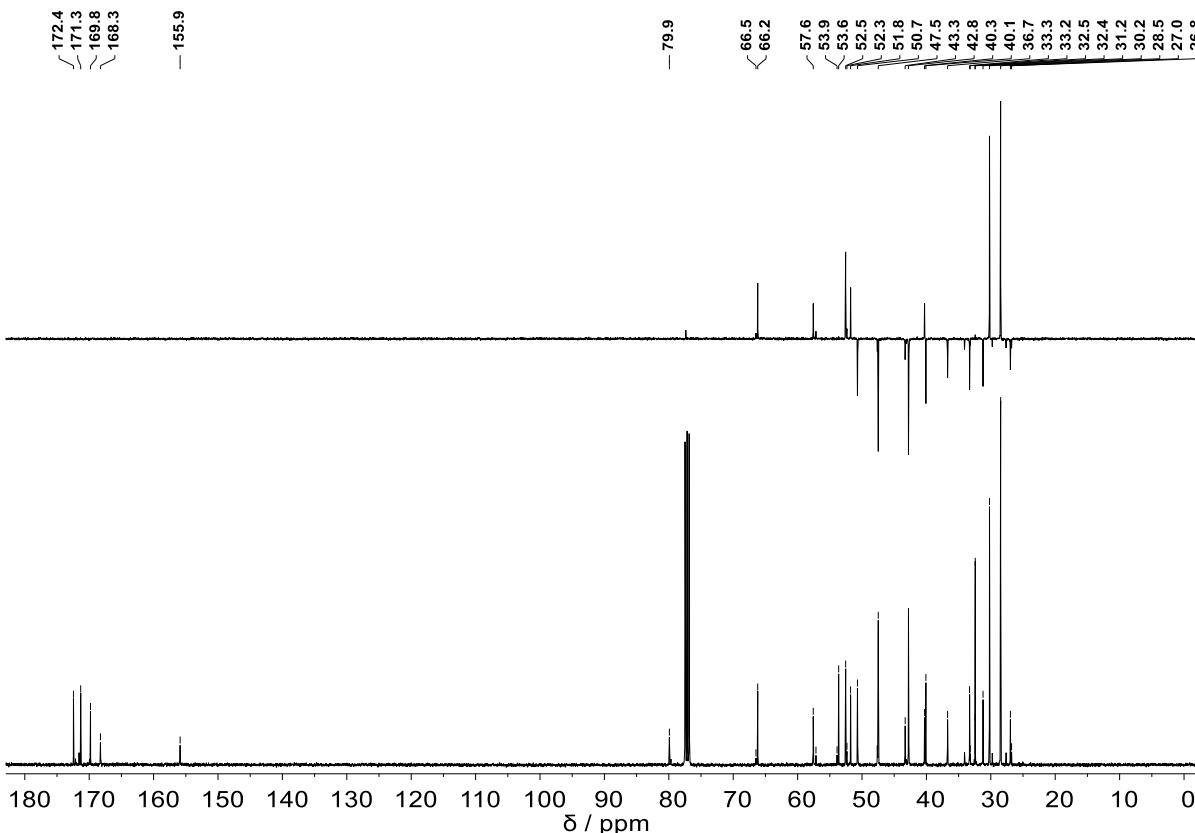


**Figure S20.** <sup>13</sup>C{<sup>1</sup>H}-NMR and DEPT-135 spectra (101 MHz, CD<sub>3</sub>OD) of conjugate **16a**.

Electronic Supplementary Information

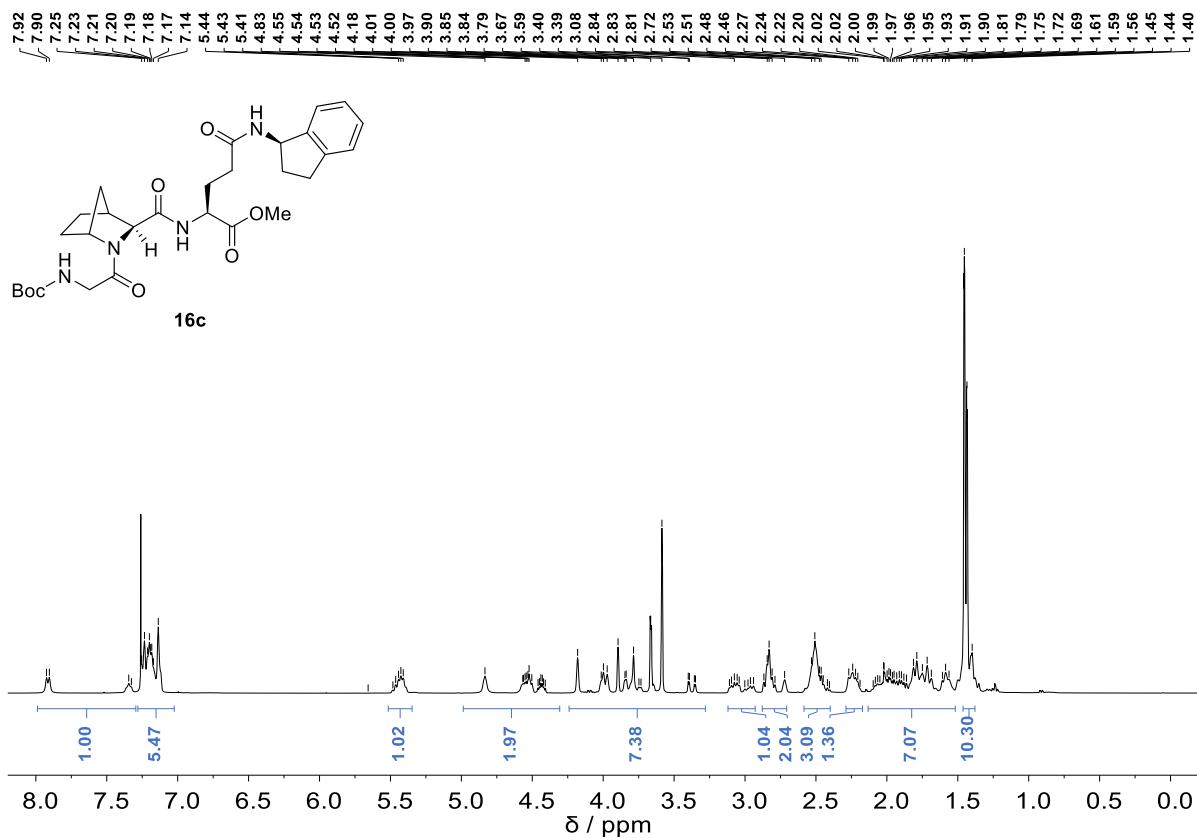


**Figure S21.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of conjugate **16b**.

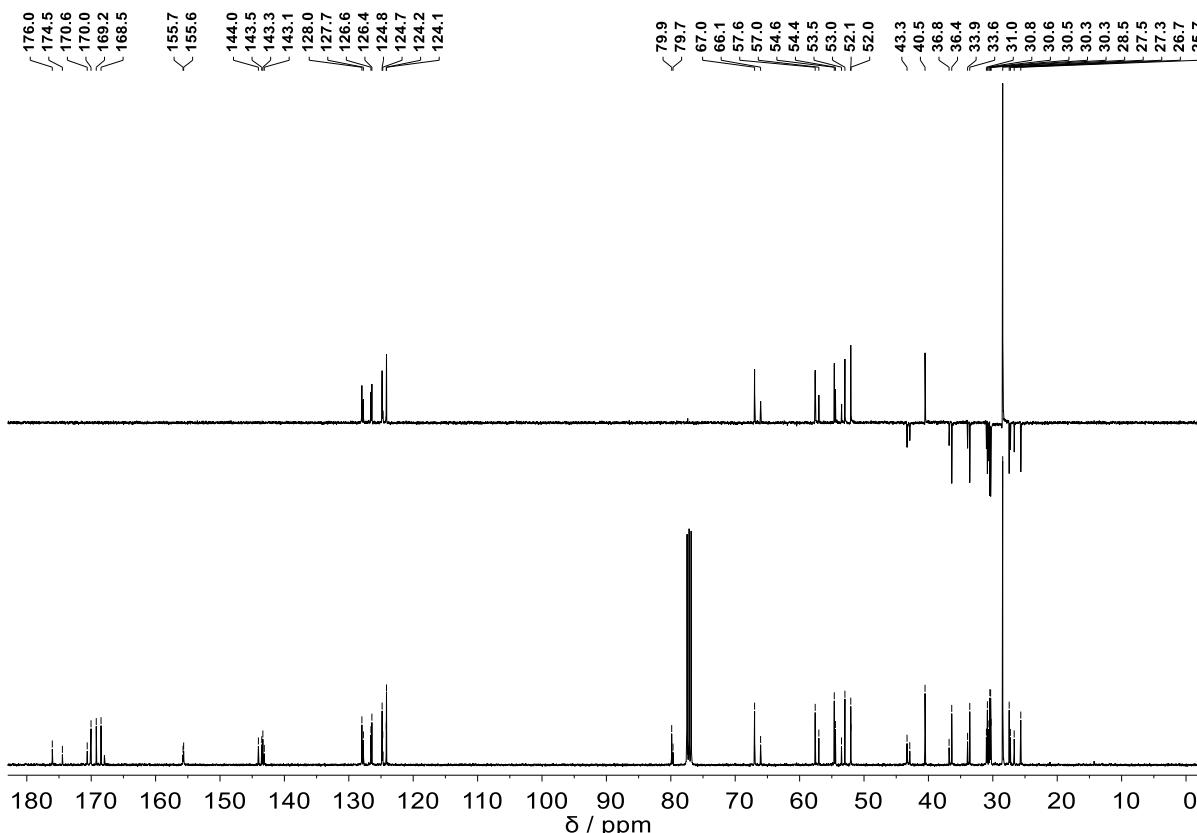


**Figure S22.**  $^{13}\text{C}\{^1\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CDCl}_3$ ) of conjugate **16b**.

Electronic Supplementary Information

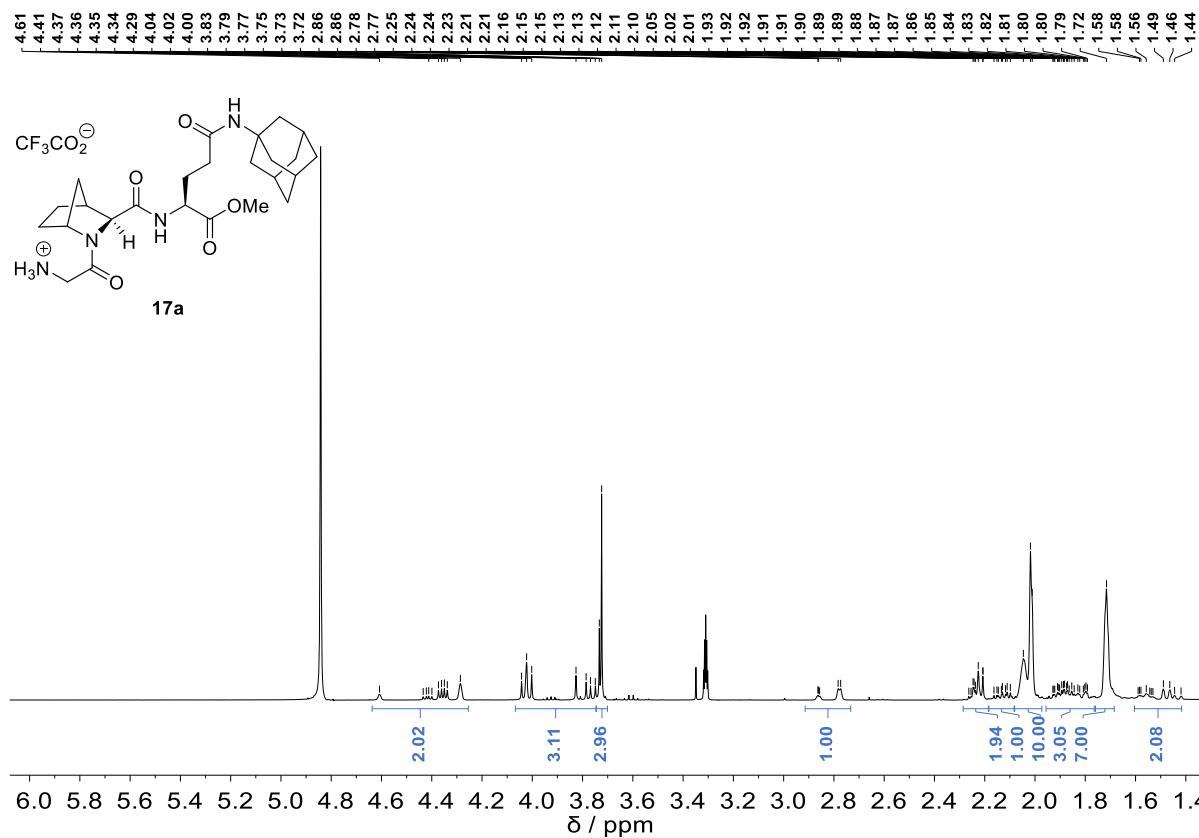


**Figure S23.** <sup>1</sup>H-NMR spectrum (400 MHz, CDCl<sub>3</sub>) of conjugate **16c**.

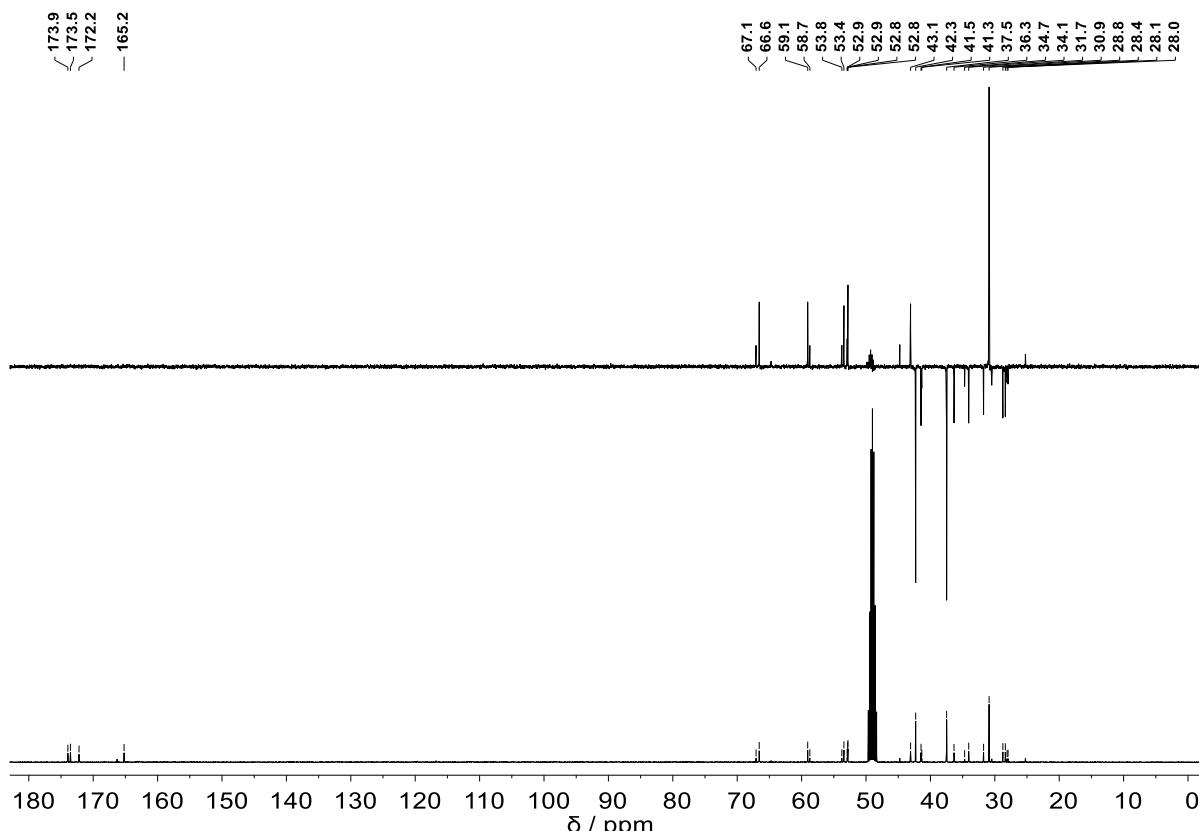


**Figure S24.** <sup>13</sup>C{<sup>1</sup>H}-NMR and DEPT-135 spectra (101 MHz, CDCl<sub>3</sub>) of conjugate **16c**.

Electronic Supplementary Information

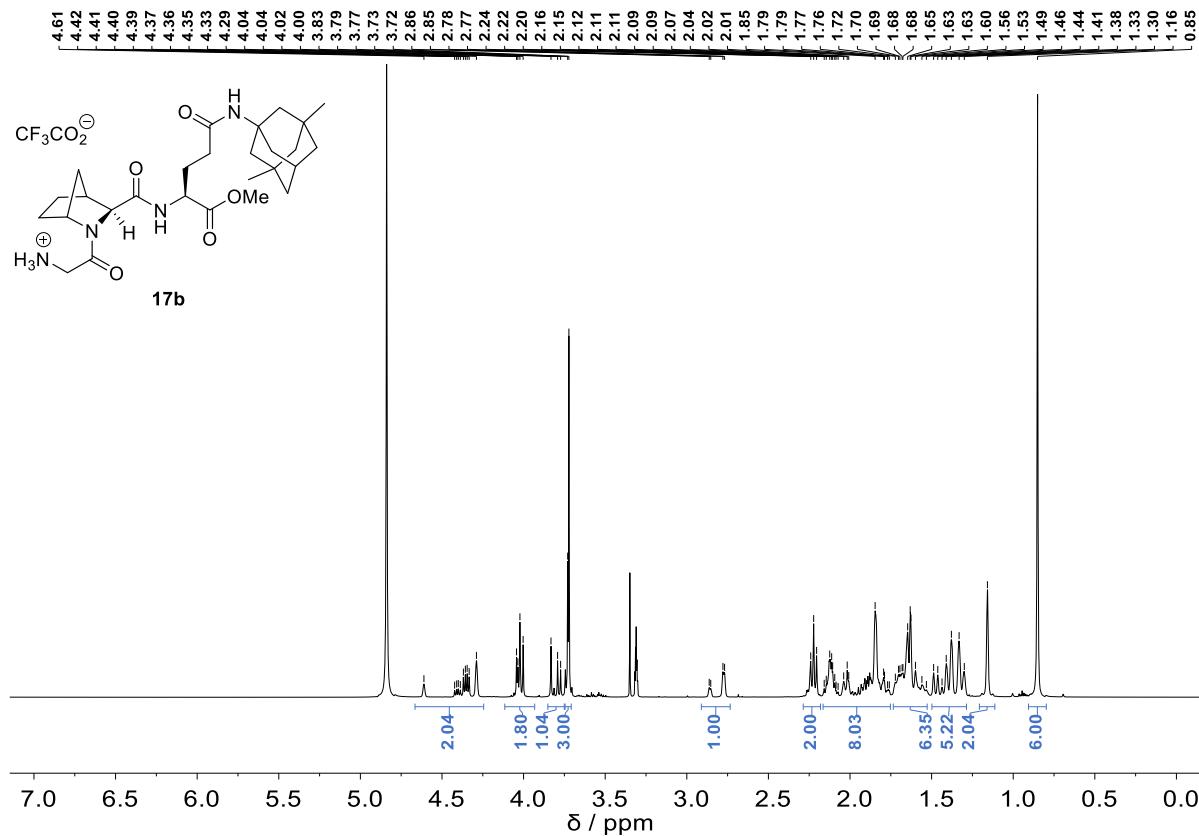


**Figure S25.** <sup>1</sup>H-NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **17a**.

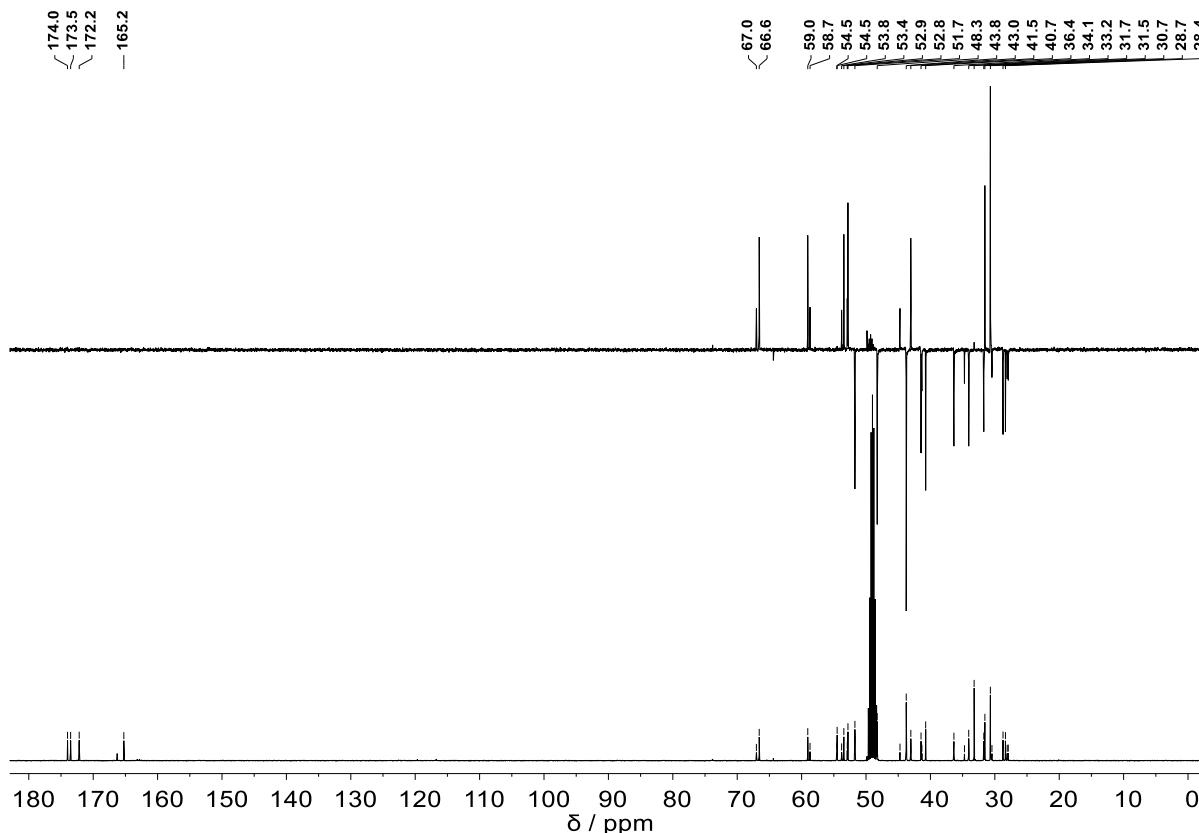


**Figure S26.** <sup>13</sup>C{<sup>1</sup>H}-NMR and DEPT-135 spectra (101 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **17a**.

Electronic Supplementary Information

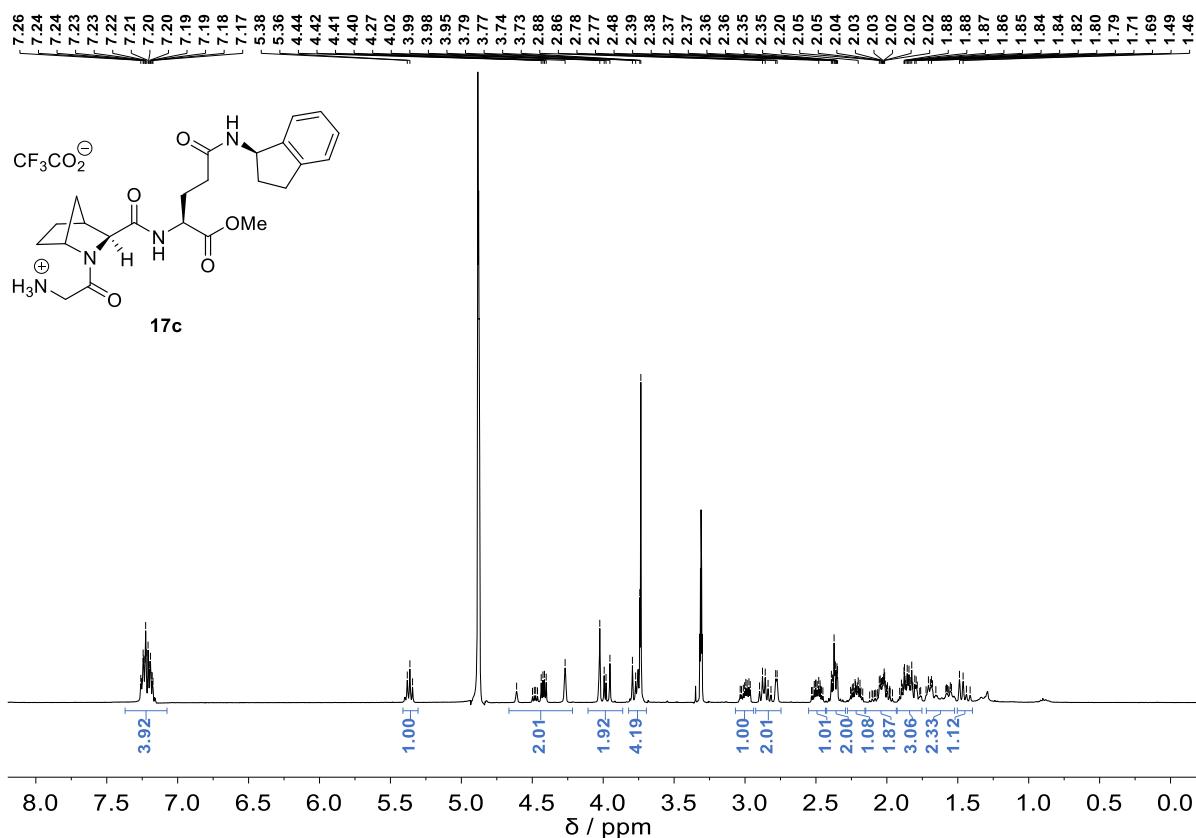


**Figure S27.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **17b**.

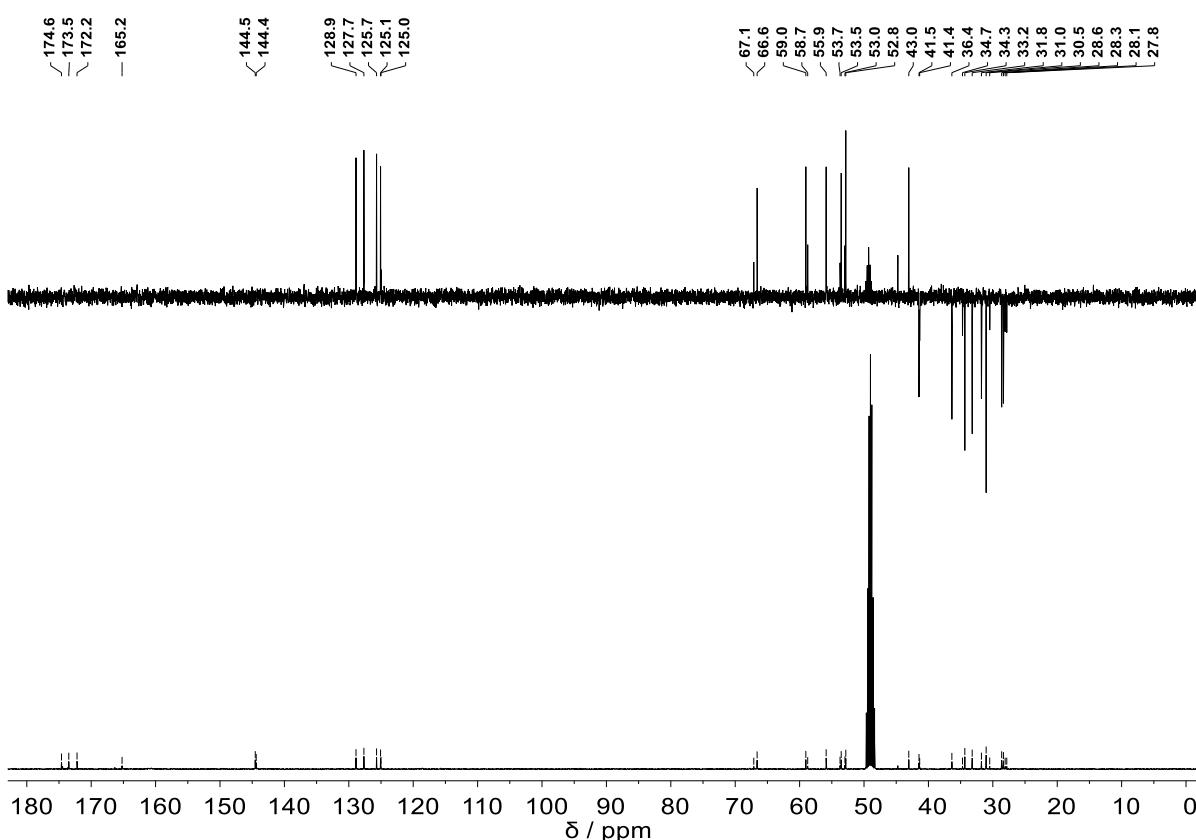


**Figure S28.**  $^{13}\text{C}\{^1\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **17b**.

## Electronic Supplementary Information

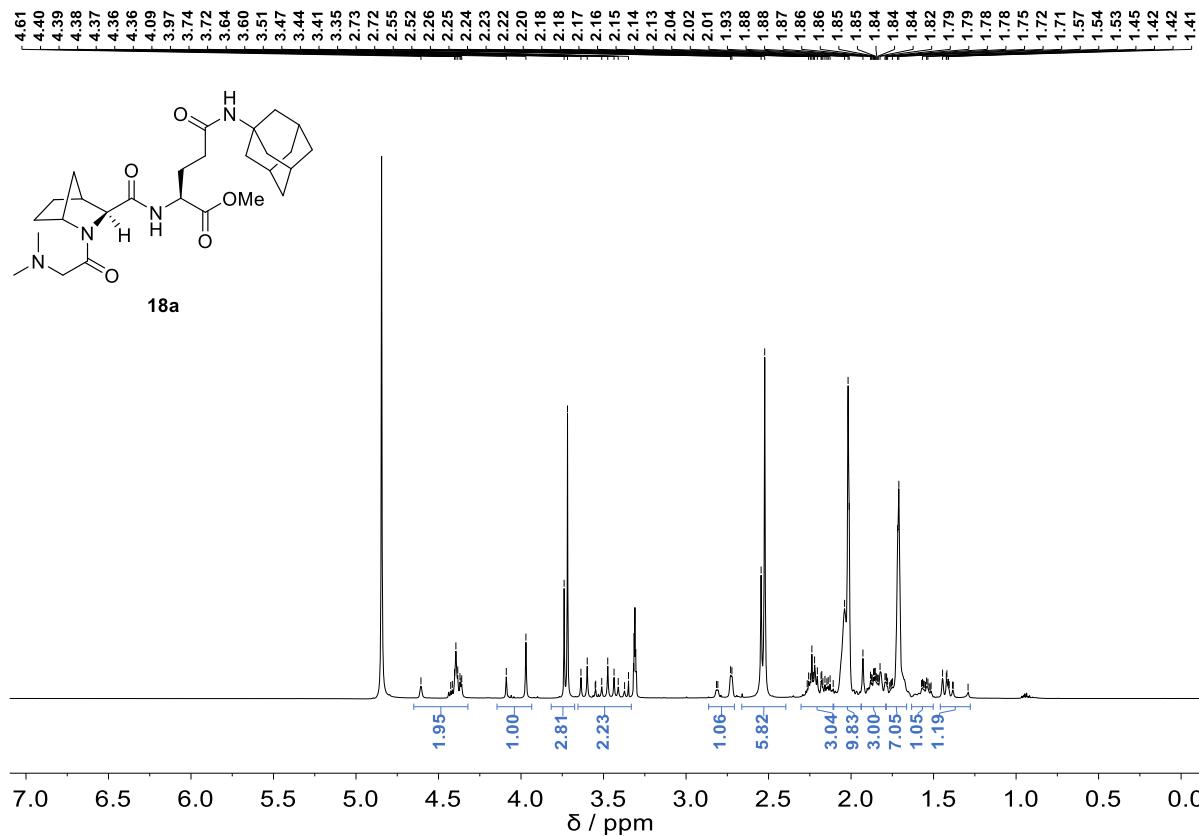


**Figure S29.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **17c**.

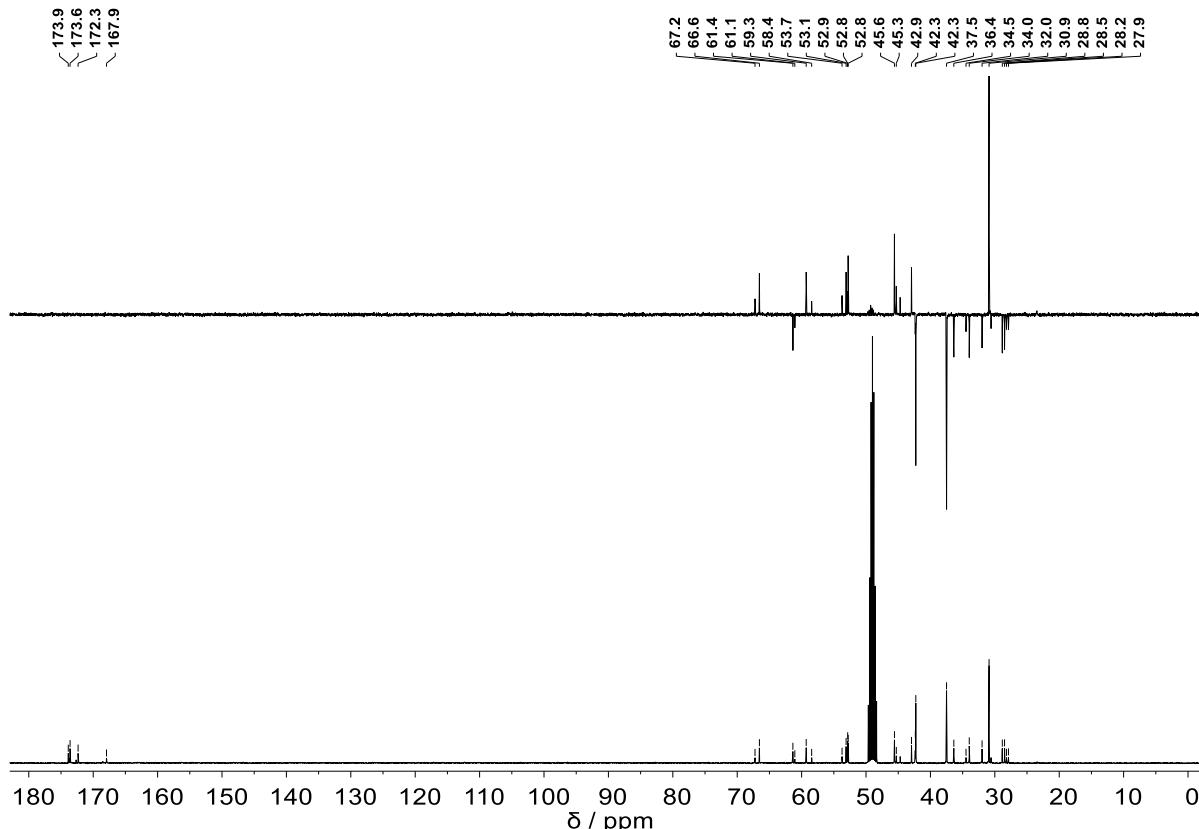


**Figure S30.**  $^{13}\text{C}\{\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **17c**.

Electronic Supplementary Information

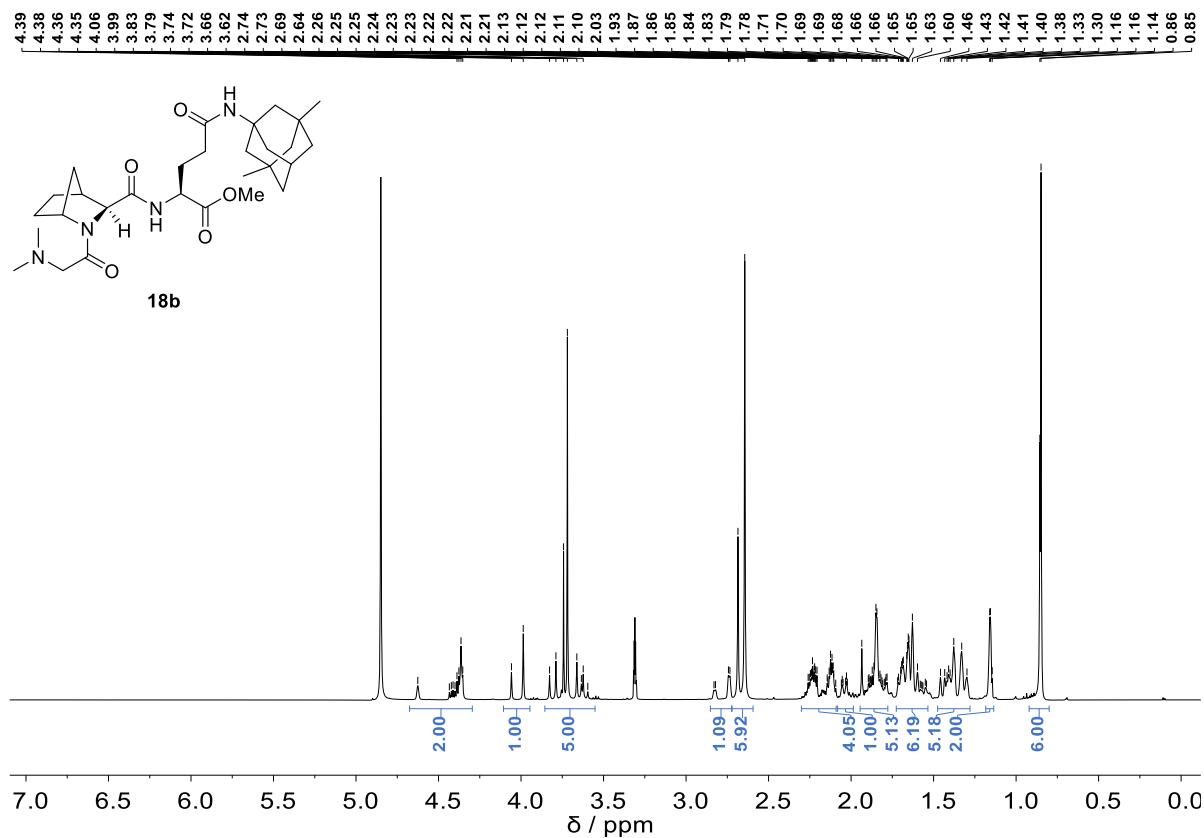


**Figure S31.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **18a**.

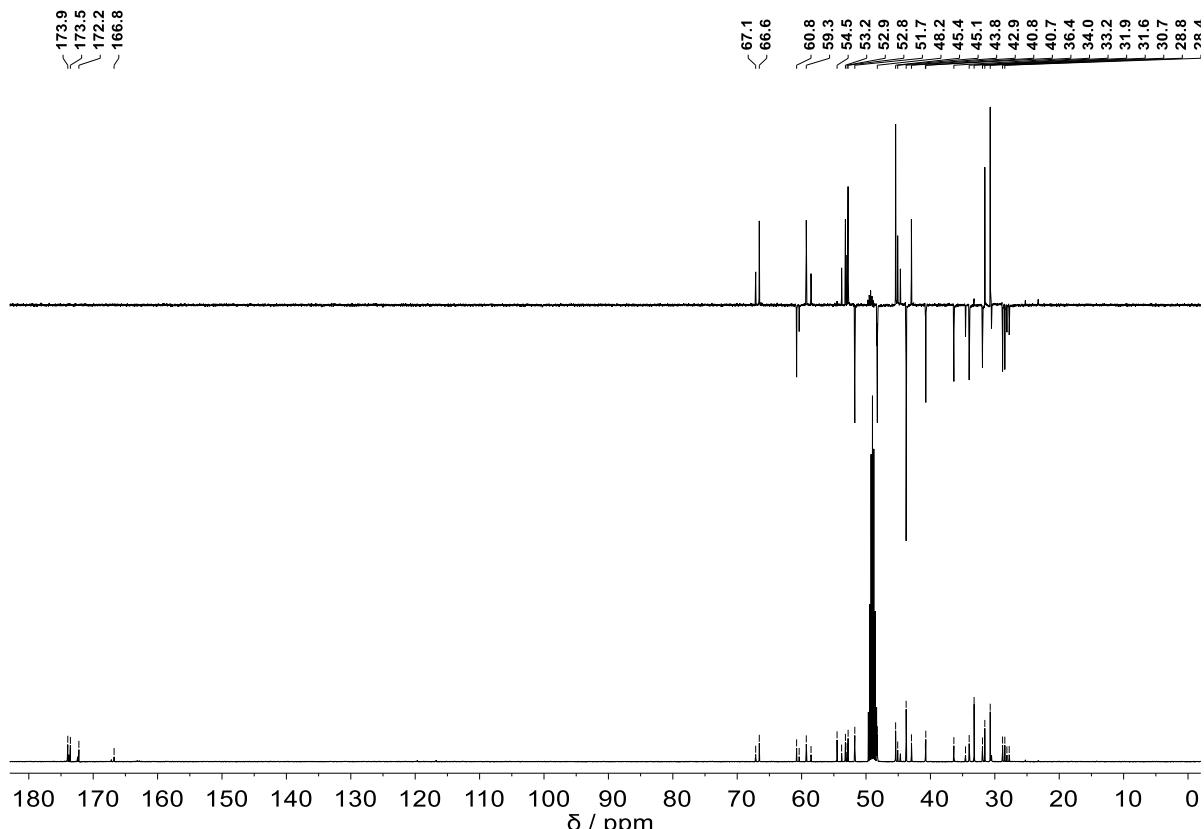


**Figure S32.**  $^{13}\text{C}\{^1\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CDCl}_3$ ) of conjugate **18a**.

Electronic Supplementary Information

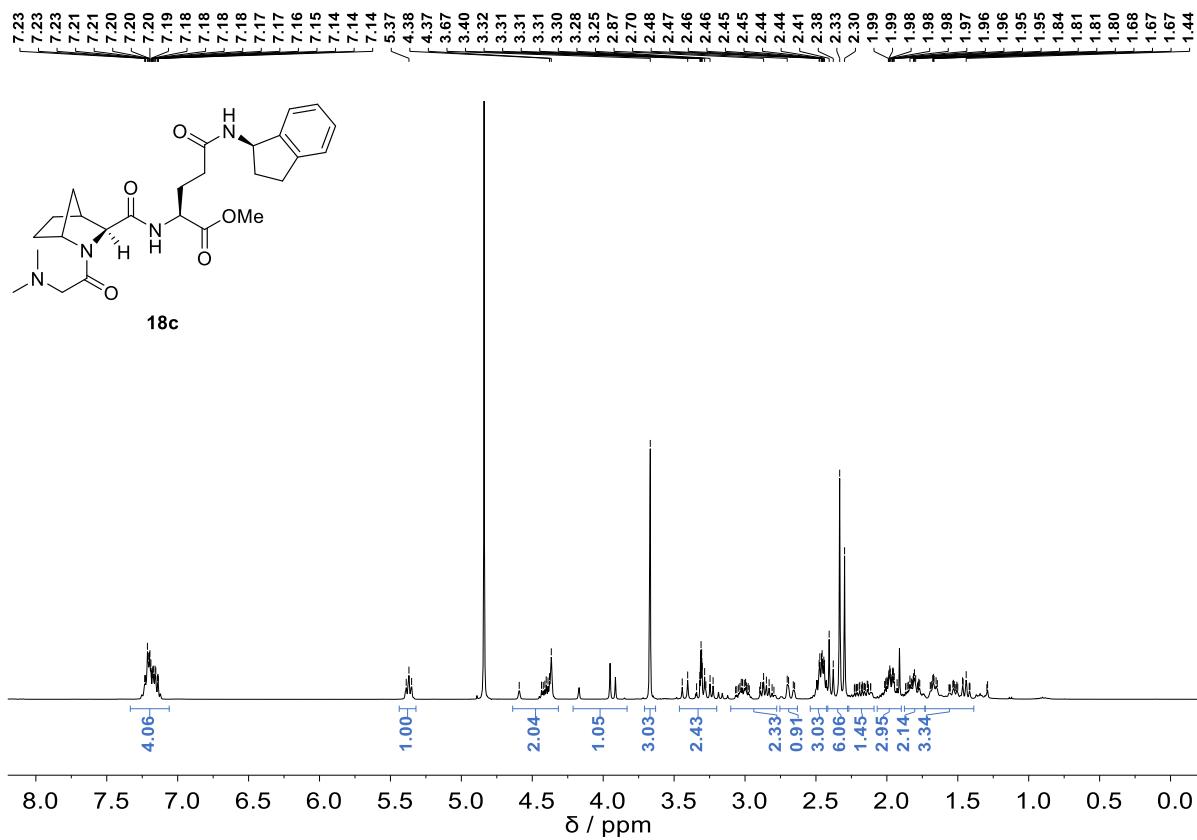


**Figure S33.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **18b**.

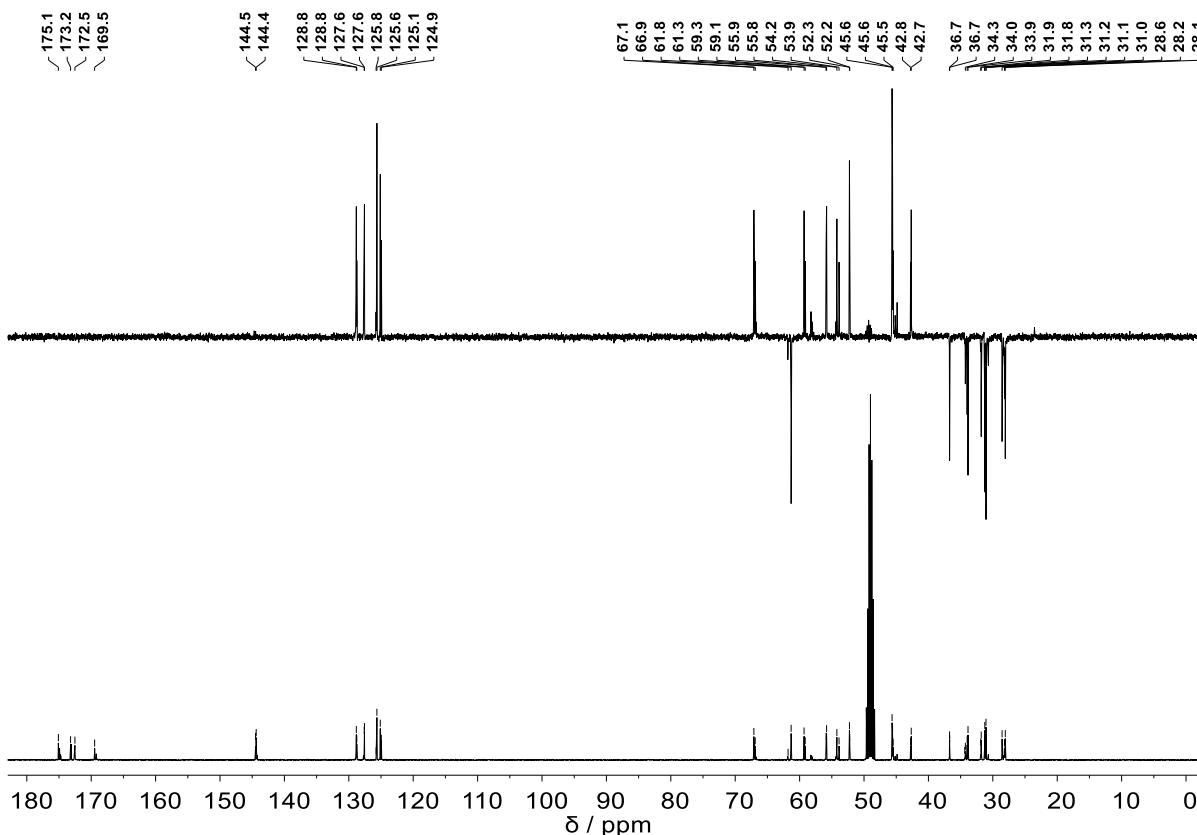


**Figure S34.**  $^{13}\text{C}\{^1\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **18b**.

## Electronic Supplementary Information



**Figure S35.**  $^1\text{H}$ -NMR spectrum (400 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **18c**.



**Figure S36.**  $^{13}\text{C}\{^1\text{H}\}$ -NMR and DEPT-135 spectra (101 MHz,  $\text{CD}_3\text{OD}$ ) of conjugate **18c**.