

Tianeptine Esters Derivatives: A Study of Protein-Drug Interaction Performed by Fluorescence Quenching and Molecular Docking

Franciela A. Soares,^a Marco A. Ceschi,^b Daniel B. Franceschini,^a Vanessa P. do Canto,^a
Paulo A. Netz^{*c} and Leandra F. Campo^{id *b}

^aPrograma de Pós-Graduação em Química, Instituto de Química,
Universidade Federal do Rio Grande do Sul, 91501-970 Porto Alegre-RS, Brazil

^bDepartamento de Química Orgânica, Instituto de Química,
Universidade Federal do Rio Grande do Sul, 91501-970 Porto Alegre-RS, Brazil

^cDepartamento de Físico-Química, Instituto de Química,
Universidade Federal do Rio Grande do Sul, 91501-970 Porto Alegre-RS, Brazil

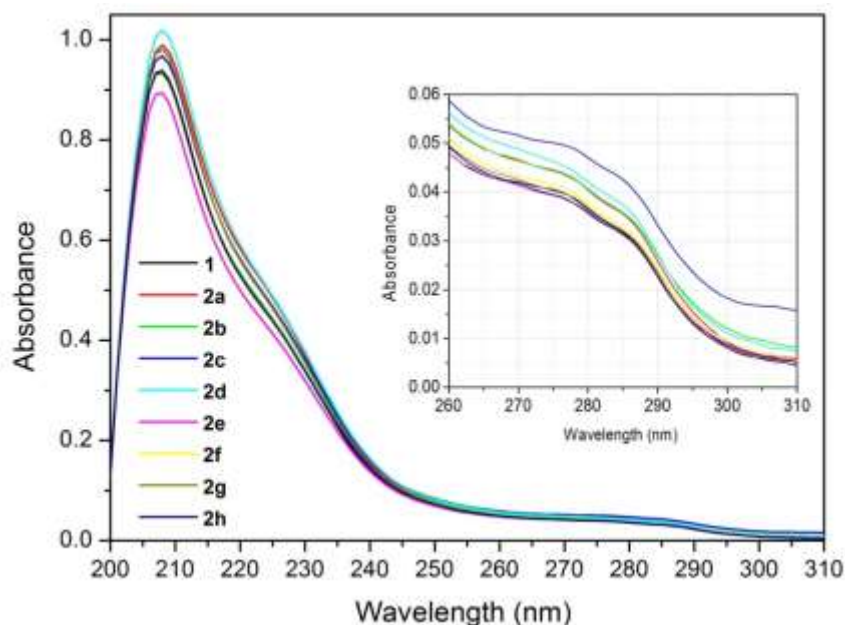


Figure S1. UV-Vis absorption spectra of tianeptine **1** and its esters **2a-h** in MeOH at 30 μM.

*e-mail: paulo.netz@gmail.com; leandra.campo@ufrgs.br

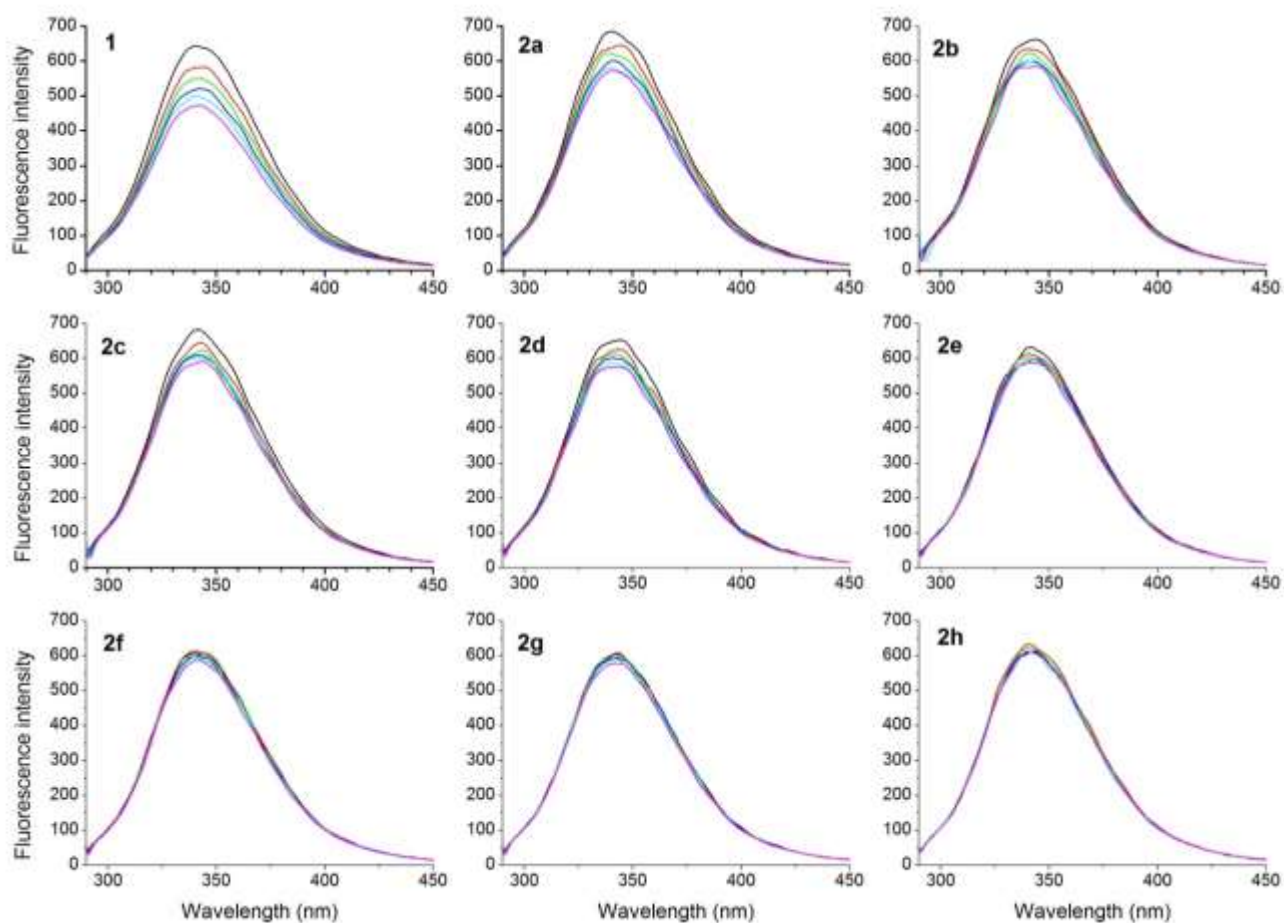


Figure S2. The effects of tianeptine **1** and esters **2a-h** on the fluorescence spectra of BSA at 303 K. $\lambda_{\text{ex}} = 280 \text{ nm}$; $[\text{BSA}] = 5 \mu\text{mol L}^{-1}$; $[\mathbf{1}, \mathbf{2a-h}] (\mu\text{mol L}^{-1})$ (a-f) = 0, 5, 10, 15, 20 and 25, respectively.

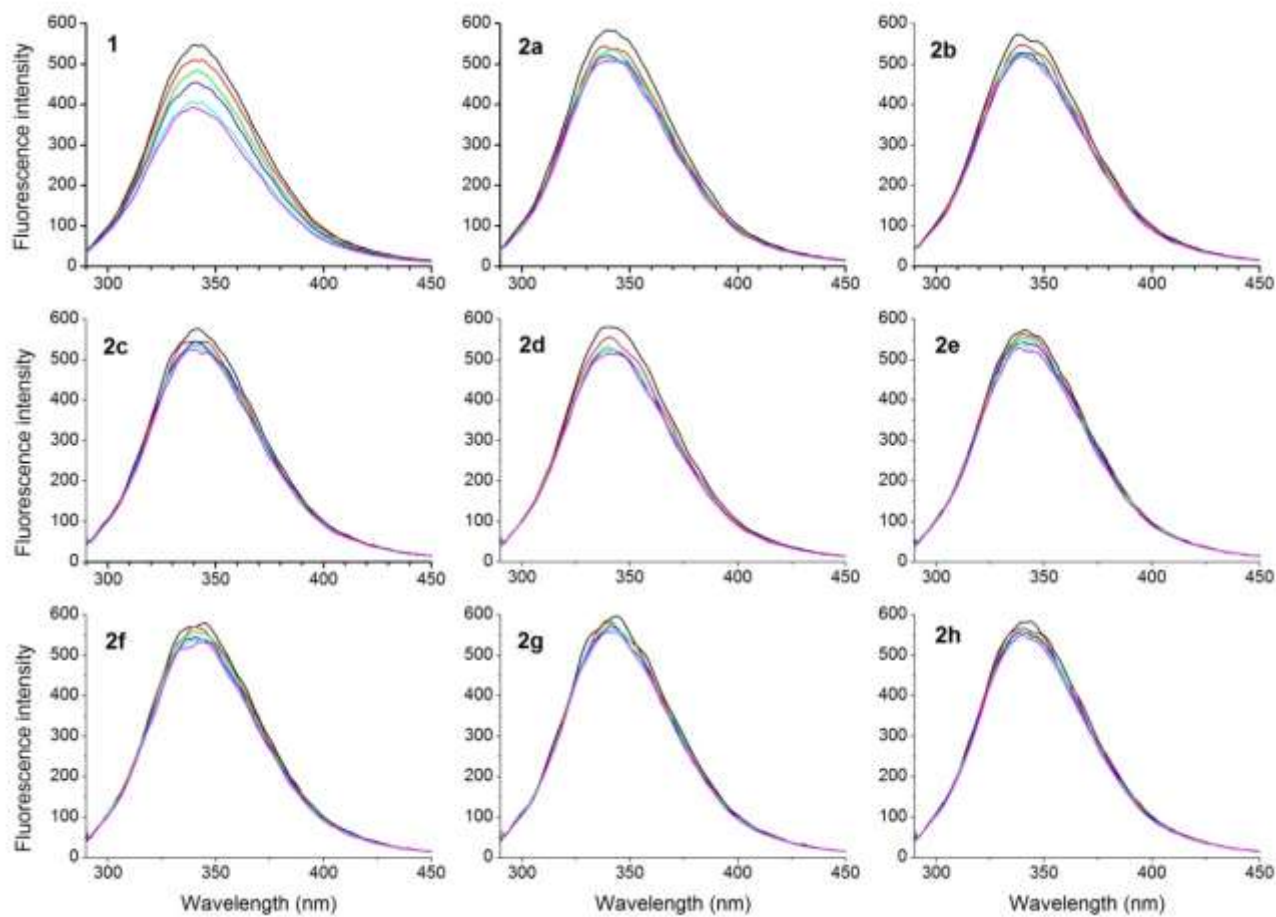


Figure S3. The effects of tianeptine **1** and esters **2a-h** on the fluorescence spectra of BSA at 313 K. $\lambda_{\text{ex}} = 280 \text{ nm}$; $[\text{BSA}] = 5 \mu\text{mol L}^{-1}$; $[\mathbf{1}, \mathbf{2a-h}] (\mu\text{mol L}^{-1})$ (a-f) = 0, 5, 10, 15, 20 and 25, respectively.

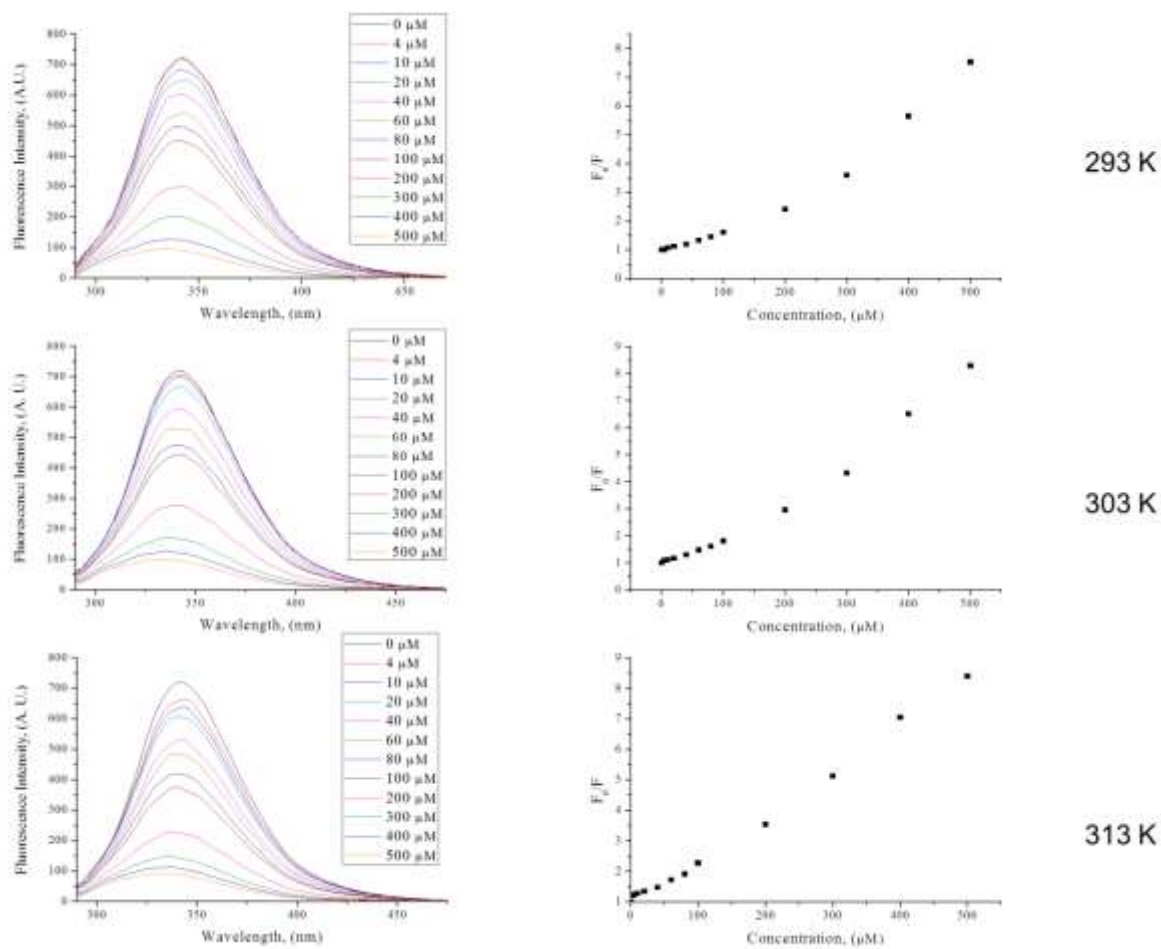


Figure S4. The effects of tianeptine 1 on the fluorescence spectra of BSA at three temperatures. $\lambda_{\text{ex}} = 280 \text{ nm}$; $[\text{BSA}] = 5 \mu\text{mol L}^{-1}$; Stern-Volmer non-linear plots at same three temperatures.

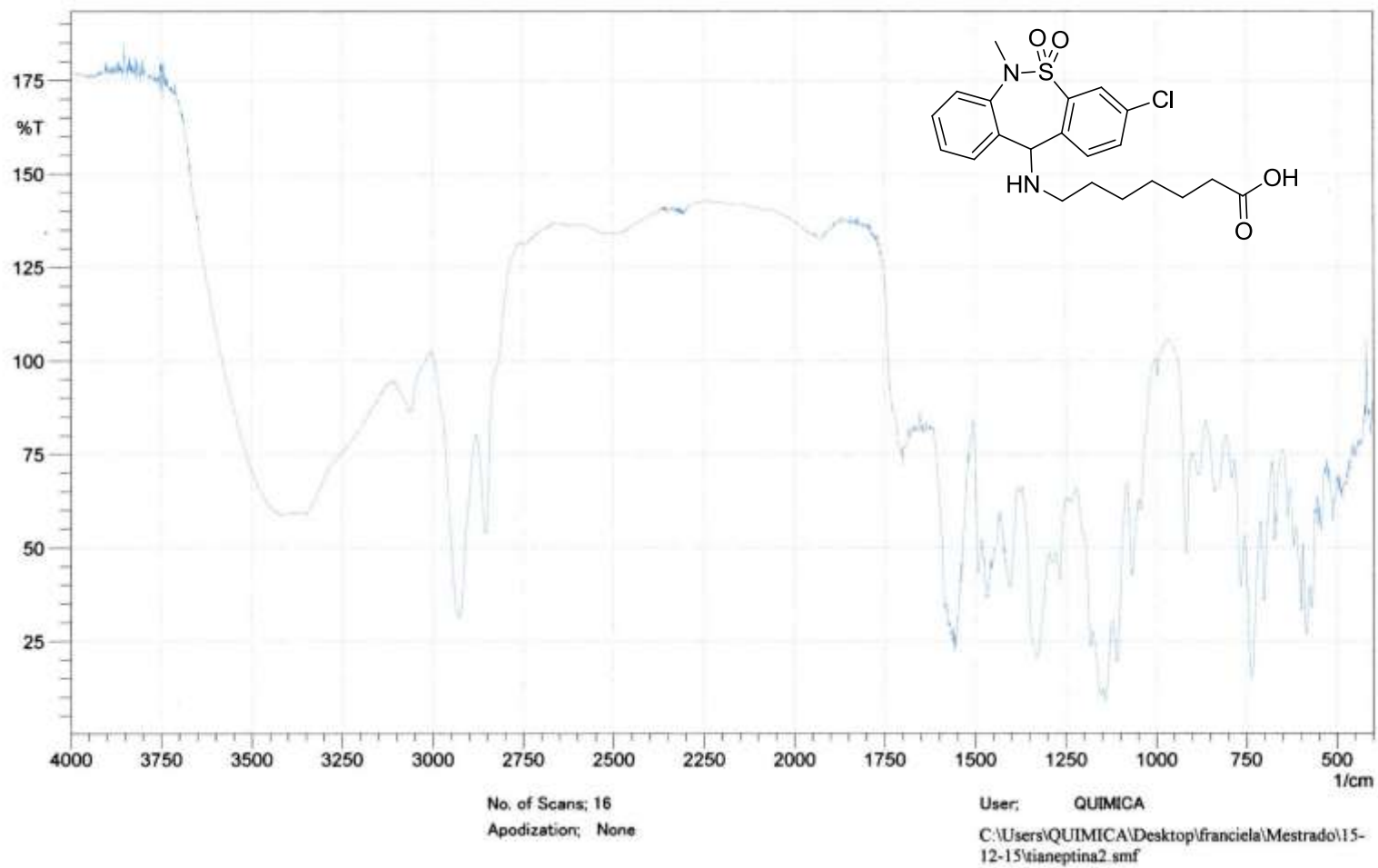


Figure S5. IR spectrum (KBr) of tianeptine 1.

| | | | | | |
|------------------------|----------------------|-------------------|---|------------------------|----------------------|
| Acquisition Time (sec) | 3.9715 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 17 Jun 2015 17:39:28 |
| Date Stamp | 17 Jun 2015 17:39:28 | File Name | C:\USERS\FRANCIELA\DROPBOX\MESTRADO 2\RMN\TIANEPTINA-1H\1\FID | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 16 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 71.80 | SW(cyclical) (Hz) | 8250.83 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 2462.4312 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8250.57 |
| | | | | Temperature (degree C) | 25.000 |

TIANEPTINA-1H.001.esp

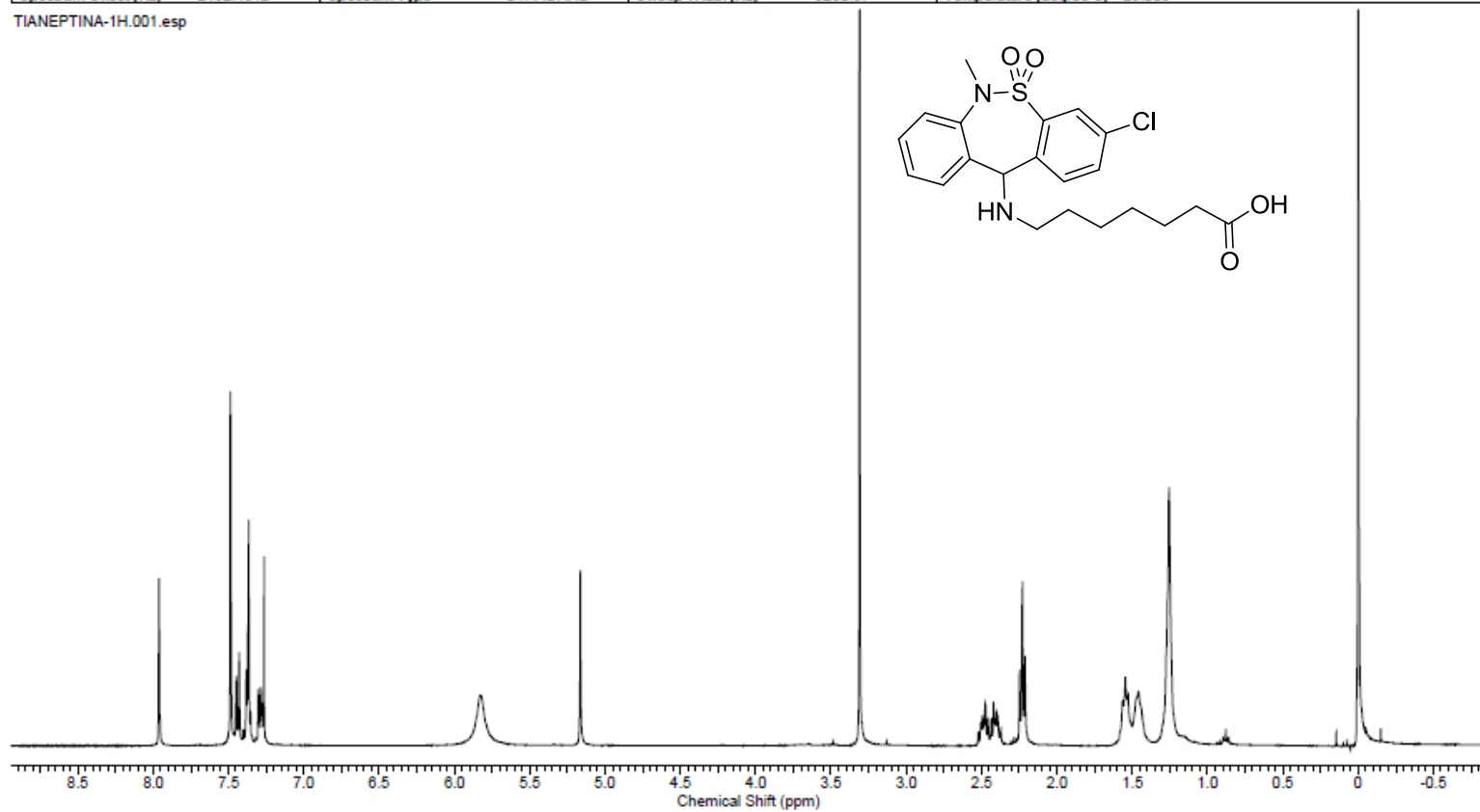


Figure S6. ^1H NMR spectrum (400.1 MHz, CDCl_3) of tianeptine **1**.

| | | | | | |
|------------------------|----------------------|-------------------|--|------------------------|----------------------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 18 Jun 2015 05:21:20 |
| Date Stamp | 18 Jun 2015 05:21:20 | File Name | C:\Users\Franciela\Dropbox\Mestrado 2\RMN\Tianeptina-13C\2\fid | | |
| Frequency (MHz) | 100.61 | Nucleus | 13C | Number of Transients | 12288 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 11585.20 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 10056.9092 | Spectrum Type | APT | Sweep Width (Hz) | 24037.73 |
| | | | | Temperature (degree C) | 24.900 |

Tianeptina-13C.002.esp

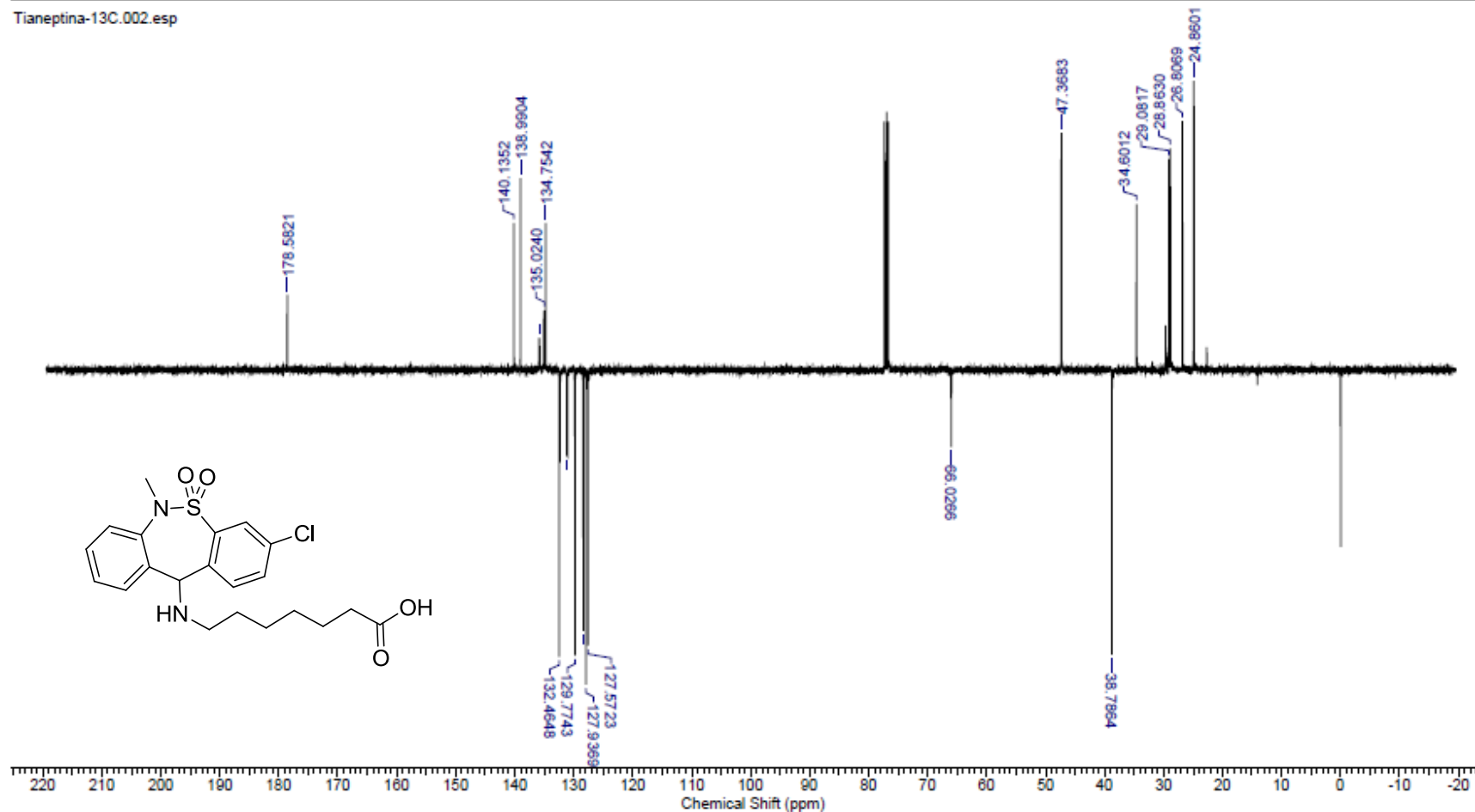


Figure S7. ¹³C NMR APT spectrum (100.6 MHz, CDCl₃) of tianeptine 1.

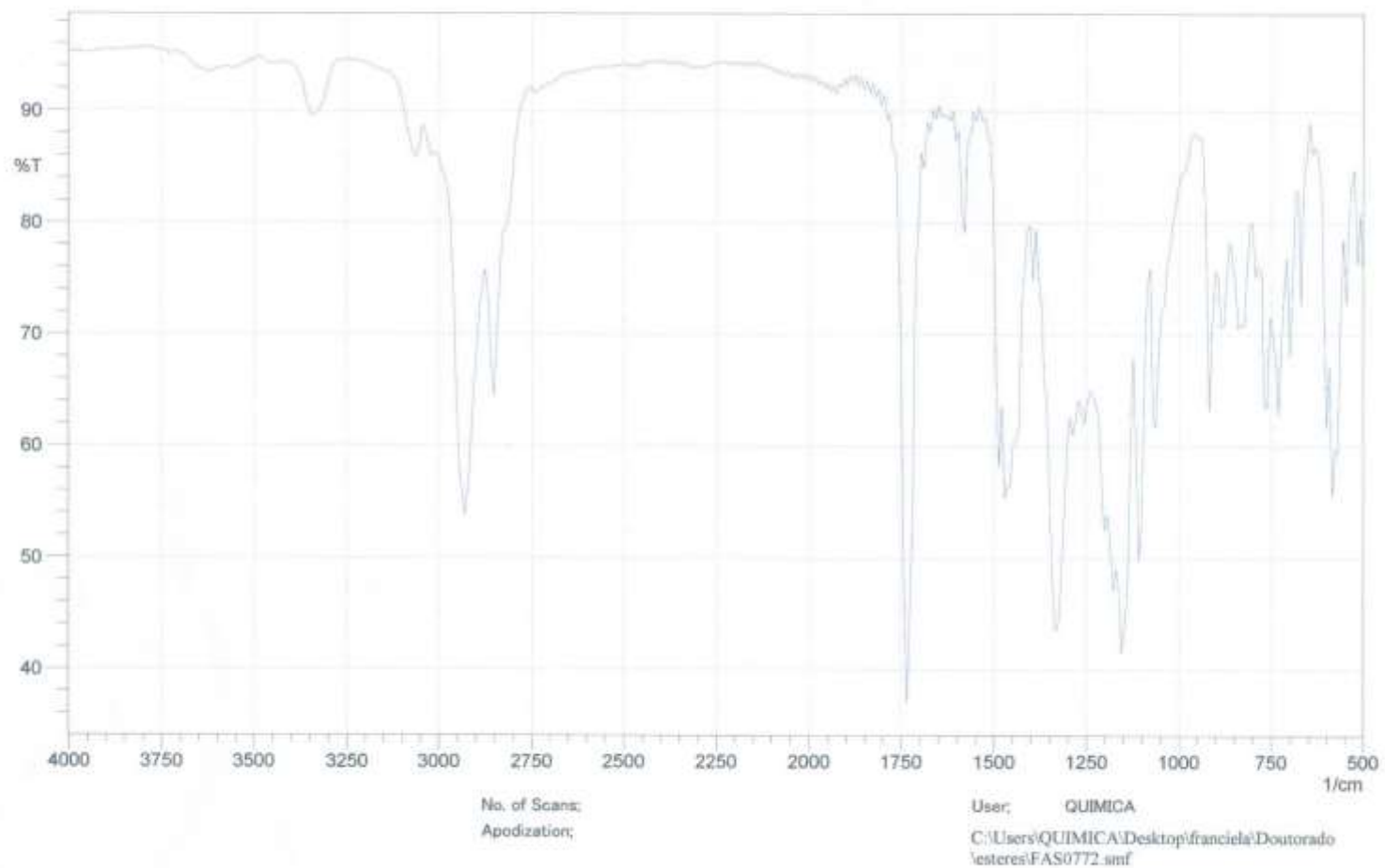
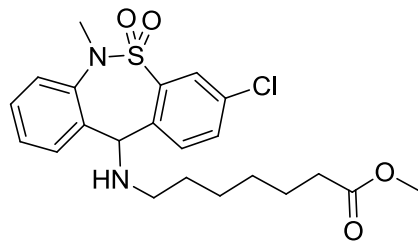


Figure S8. IR spectrum (KBr) of ester **2a**.

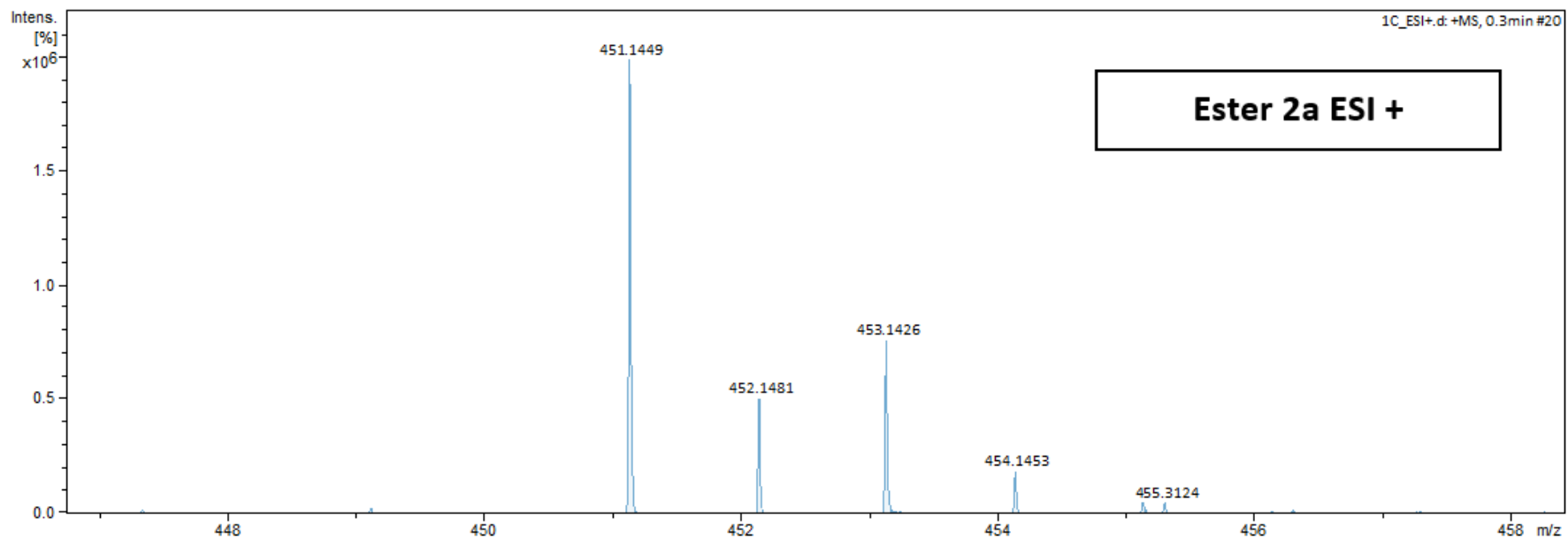


Figure S9. Mass spectrum of ester **2a**, calcd. for $C_{22}H_{27}ClN_2O_4S$ $[M]^+$: 451.1458, found: 451.1449.

| | | | | | |
|------------------------|----------------------|-------------------|---|------------------------|----------------------|
| Acquisition Time (sec) | 3.9715 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 09 Nov 2016 12:15:28 |
| Date Stamp | 09 Nov 2016 12:15:28 | File Name | C:\Users\Franciela\Dropbox\Doc\Estereis\RMN\Leandra-Franciela2895-FAS-077\11fid | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 32 |
| Original Points Count | 32788 | Owner | User | Points Count | 32788 |
| Receiver Gain | 181.00 | SW(cyclical) (Hz) | 8250.83 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 2486.1633 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8250.57 |
| | | | | Temperature (degree C) | 24.900 |

Leandra-Franciela2895-FAS-077.001.esp

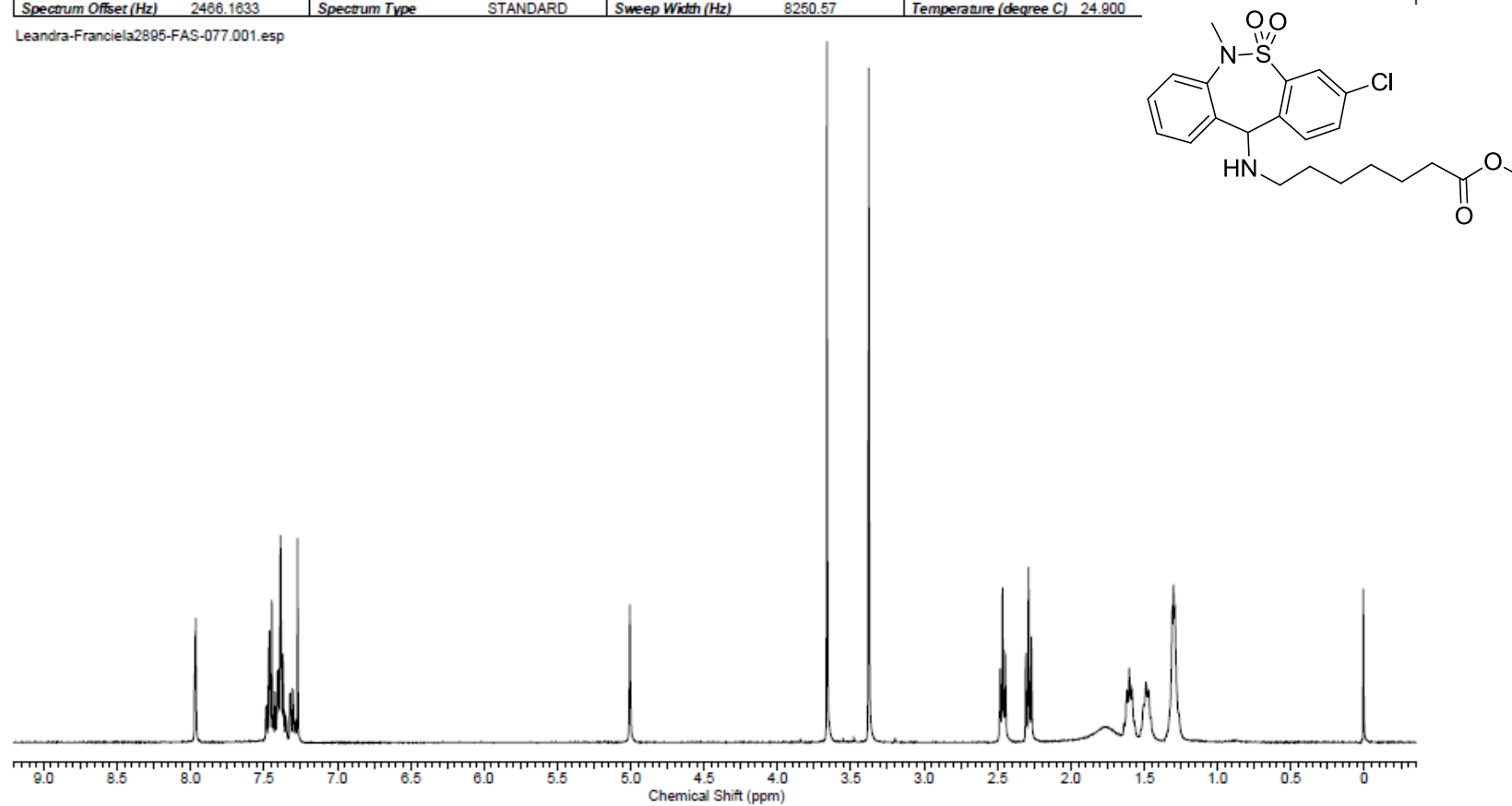


Figure S10. ^1H NMR spectrum (400.1 MHz, CDCl_3) of **2a**.

| | | | | | | | |
|------------------------|----------------------|-------------------|--|----------------------|--------------|------------------------|--------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | | Date | 04 Dec 2016 21:06:40 | |
| Date Stamp | 04 Dec 2016 21:06:40 | File Name | F:\Leandra-Franciela3087-FAS-077-APT\1\fid | | | | |
| Frequency (MHz) | 100.61 | Nucleus | 13C | Number of Transients | 3600 | Origin | spect |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 | Pulse Sequence | jmod |
| Receiver Gain | 16384.00 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d | | |
| Spectrum Offset (Hz) | 10055.4414 | Spectrum Type | APT | Sweep Width (Hz) | 24037.73 | Temperature (degree C) | 21.400 |

Leandra-Franciela3087-FAS-077-APT.001.esp

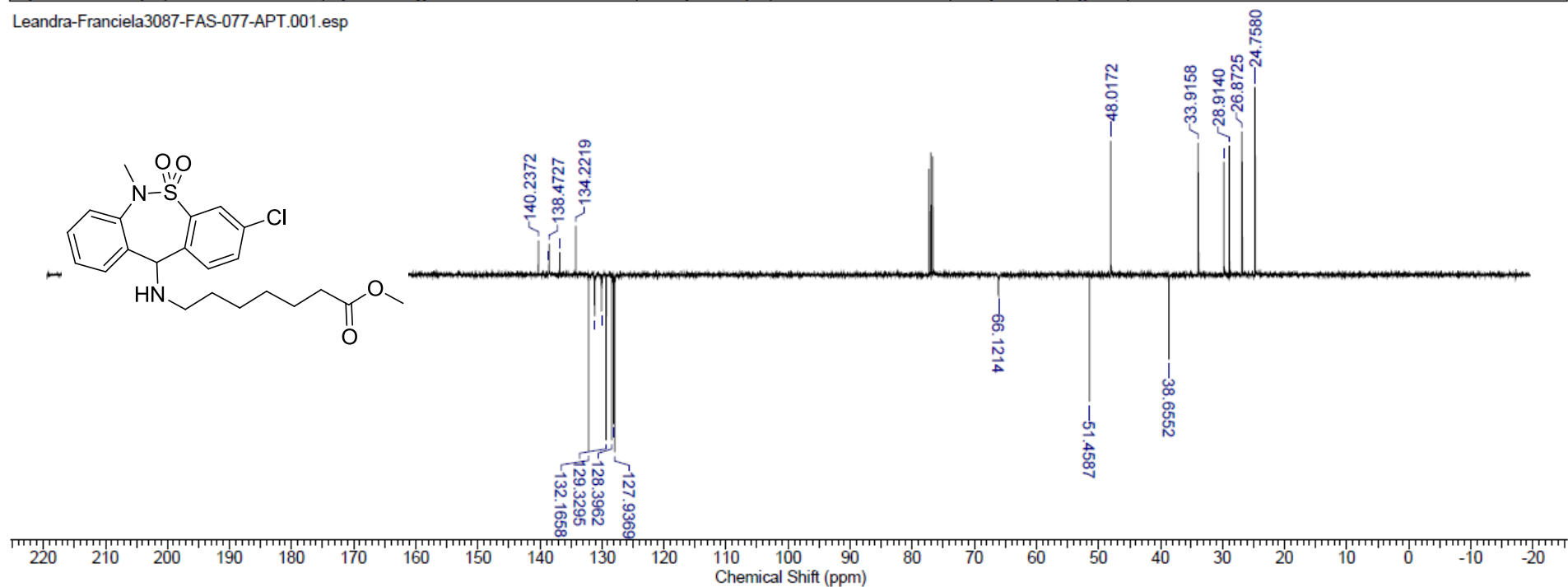


Figure S11. ^{13}C NMR APT spectrum (100.6 MHz, CDCl_3) of ester **2a**.

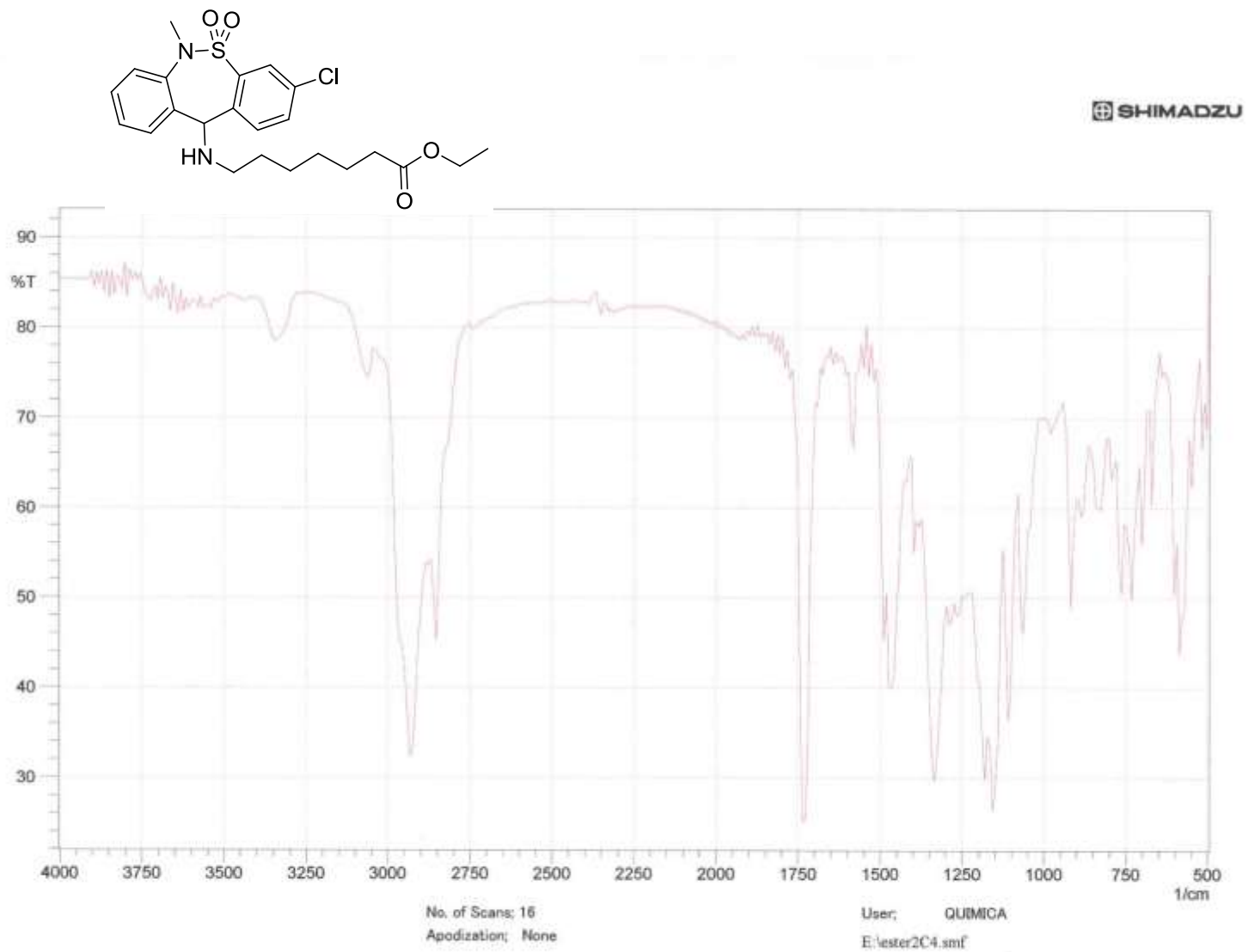


Figure S12. IR spectrum (KBr) of ester **2b**.

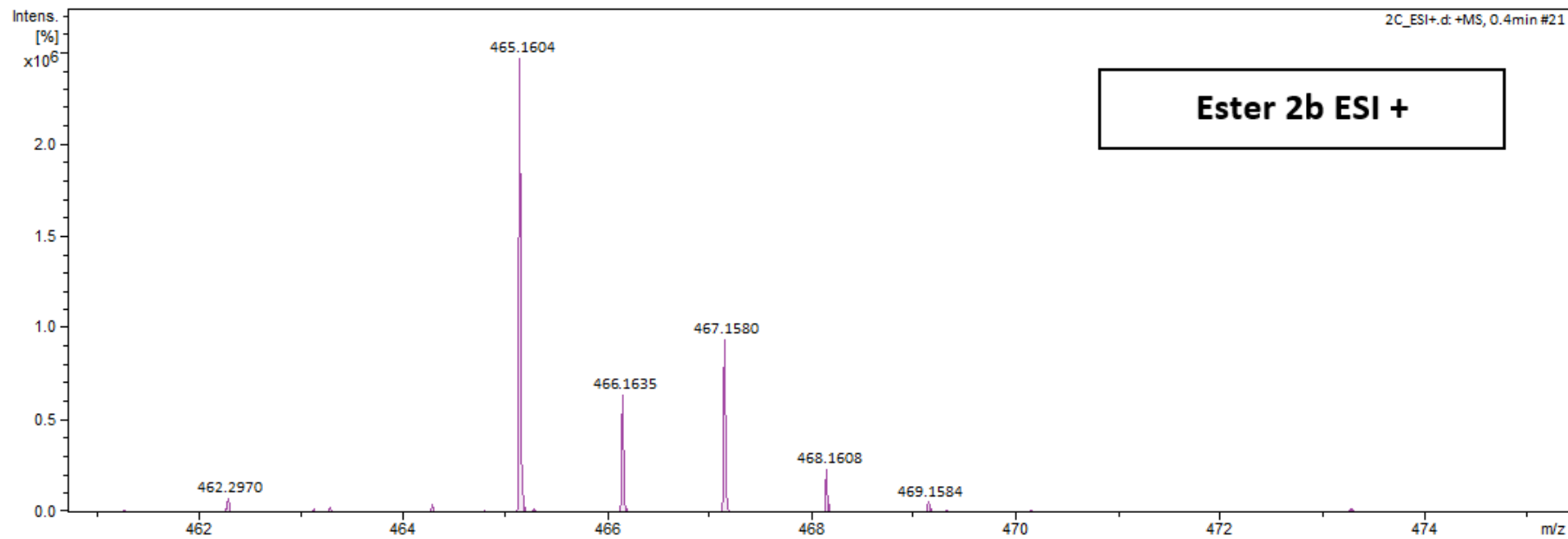


Figure S13. Mass spectrum of ester **2b**, calcd. for $C_{23}H_{29}ClN_2O_4S$ $[M]^+$: 465.1614, found: 465.1604.

| | | | | | |
|------------------------|----------------------|-------------------|---|------------------------|----------------------|
| Acquisition Time (sec) | 3.9715 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 11 Dec 2016 15:04:00 |
| Date Stamp | 11 Dec 2016 15:04:00 | File Name | C:\Users\Franciela\Dropbox\Doc\Esteres\RMN\Leandra-Franciela3229-FAS082-1H\1fid | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 32 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 64.00 | SW(cyclical) (Hz) | 8250.83 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 2465.2009 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8250.57 |
| | | | | Temperature (degree C) | 24.900 |

Leandra-Franciela3229-FAS082-1H.001.esp

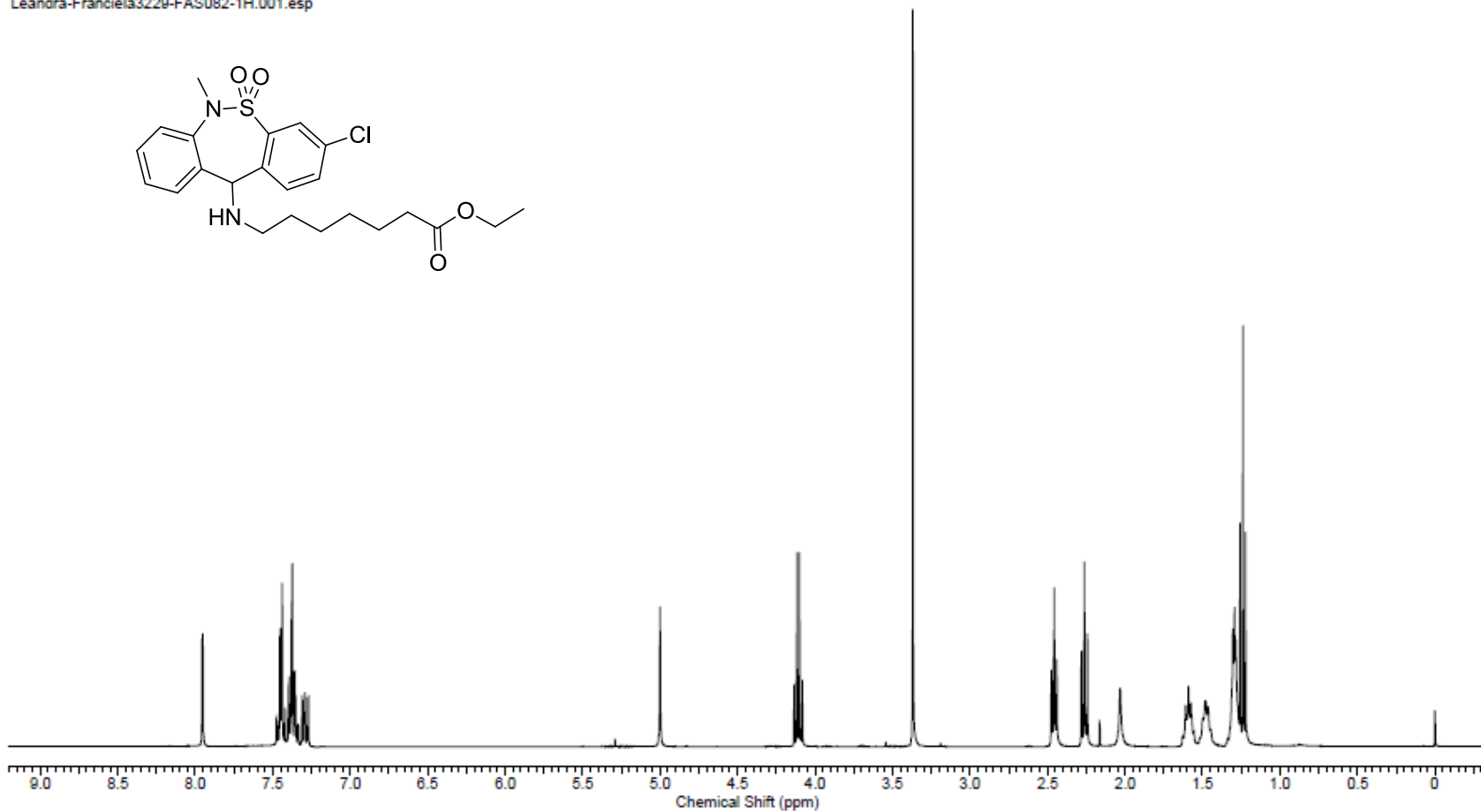


Figure S14. ¹H NMR spectrum (400.1 MHz, CDCl₃) of ester **2b**.

| | | | | | | | |
|------------------------|----------------------|-------------------|---|----------------------|--------------|------------------------|--------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | | Date | 11 Dec 2016 16:33:36 | |
| Date Stamp | 11 Dec 2016 16:33:36 | File Name | F:\Leandra-Franciela3229-FAS082-13C\2\fid | | | | |
| Frequency (MHz) | 100.61 | Nucleus | 13C | Number of Transients | 1536 | Origin | spect |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 | Pulse Sequence | jmod |
| Receiver Gain | 16384.00 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d | | |
| Spectrum Offset (Hz) | 10053.2402 | Spectrum Type | APT | Sweep Width (Hz) | 24037.73 | Temperature (degree C) | 24.900 |

Leandra-Franciela3229-FAS082-13C.002.esp

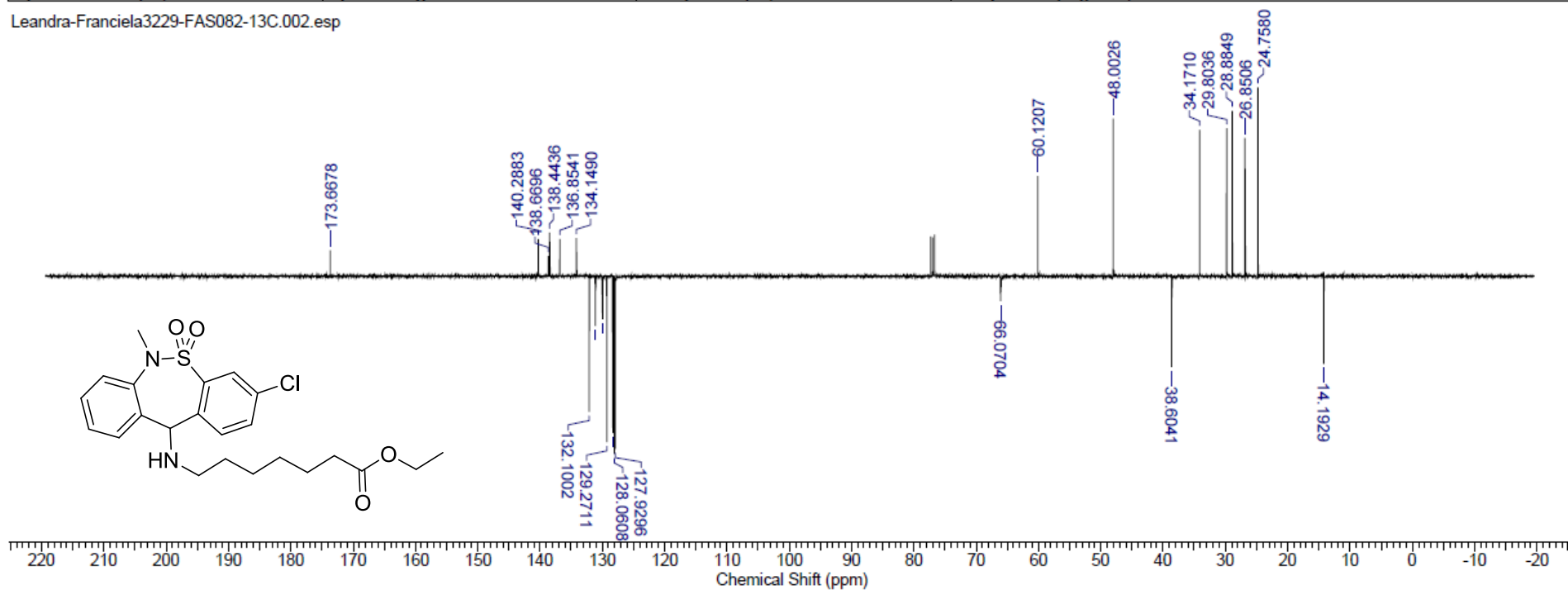
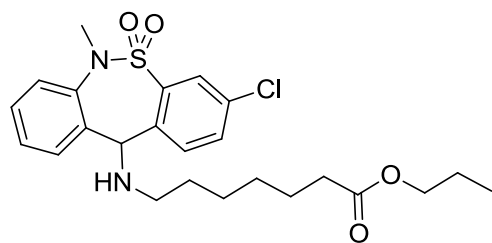


Figure S15. ^{13}C NMR APT spectrum (100.6 MHz, CDCl_3) of ester **2b**.



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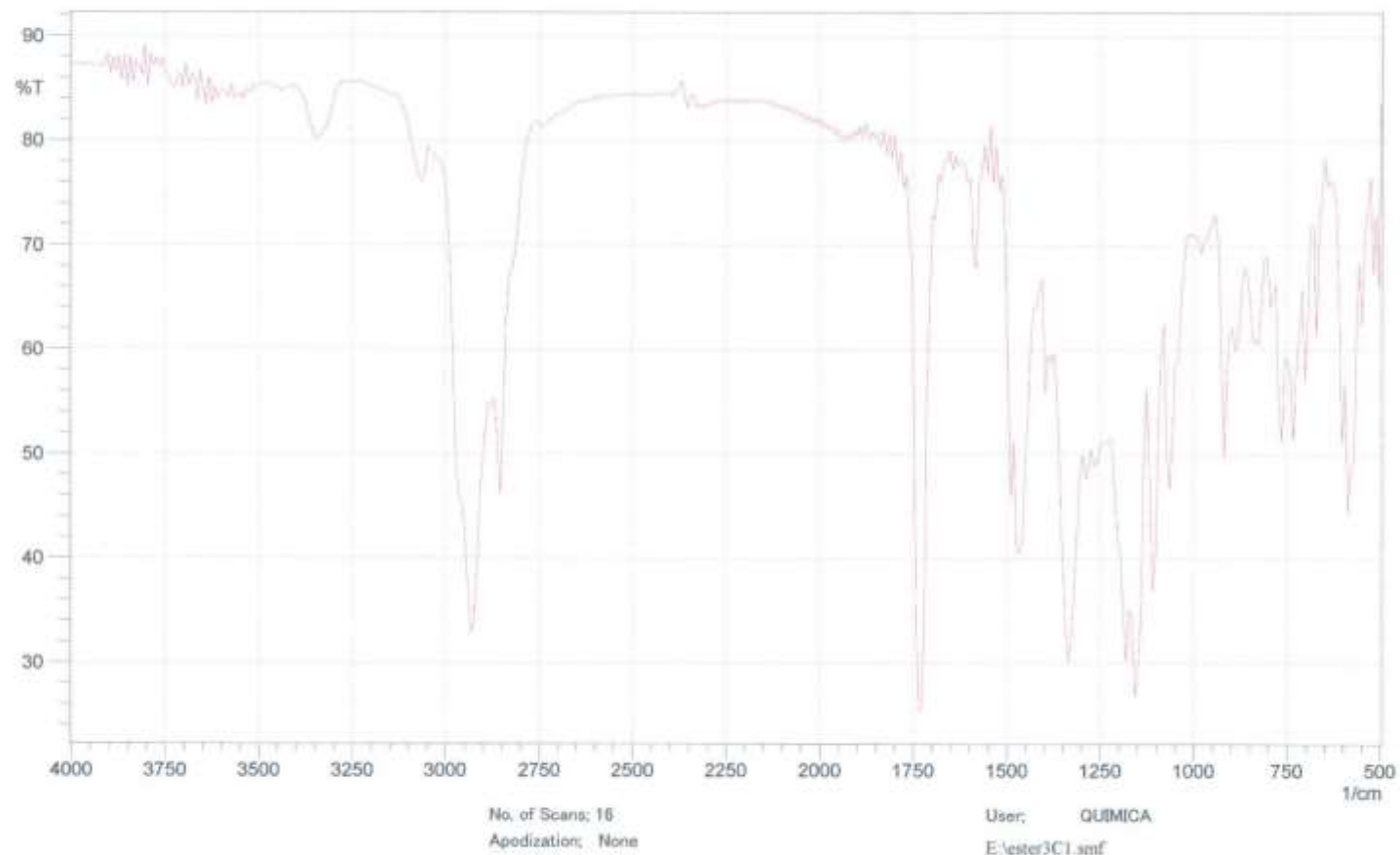


Figure S16. IR spectrum (KBr) of ester 2c.

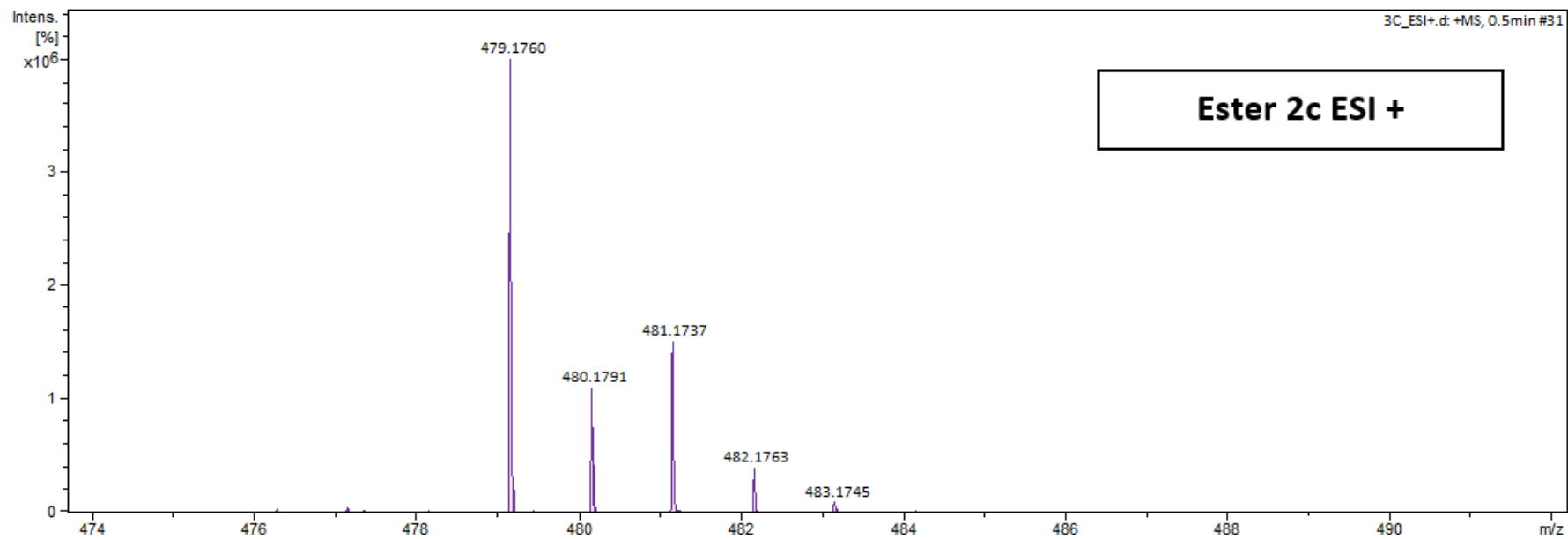


Figure S17. Mass spectrum of ester **2c**, calcd. for $C_{24}H_{31}ClN_2O_4S$ $[M]^+$: 479.1771, found: 479.1760.

| | | | | | |
|------------------------|----------------------|-------------------|--|------------------------|----------------------|
| Acquisition Time (sec) | 3.9715 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 09 Nov 2016 12:32:32 |
| Date Stamp | 09 Nov 2016 12:32:32 | File Name | C:\Users\Franciela\Dropbox\Doc\Esteres\RMN\Leandra-Franciela2897-FAS-079\1\fid | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 32 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 181.00 | SW(cyclical) (Hz) | 8250.83 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 2466.1633 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8250.57 |
| | | | | Temperature (degree C) | 25.000 |

Leandra-Franciela2897-FAS-079.001.esp

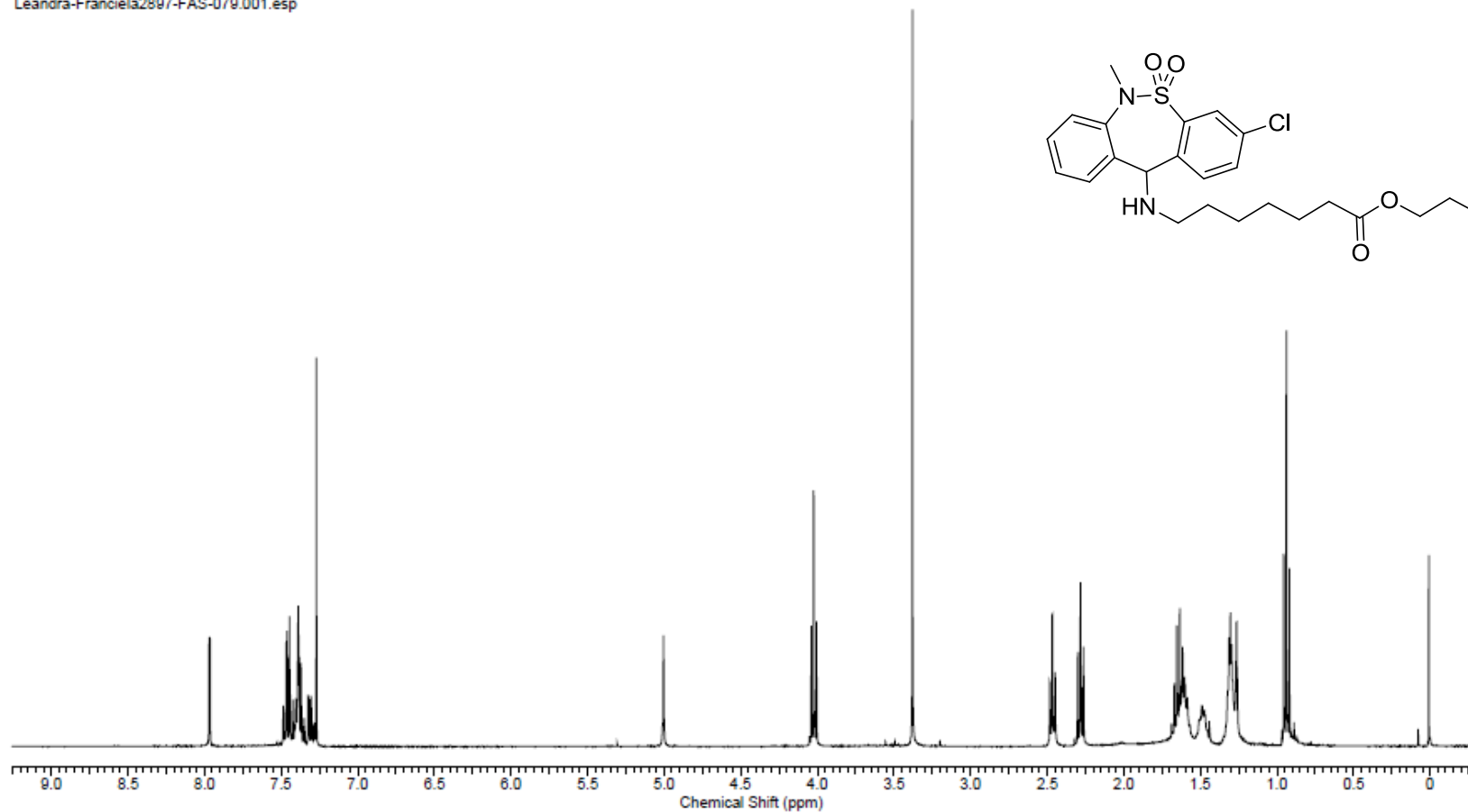


Figure S18. ^1H NMR spectrum (400.1 MHz, CDCl_3) of ester **2c**.

| | | | | | | | |
|------------------------|----------------------|-------------------|---|----------------------|--------------|------------------------|--------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | | Date | 08 Dec 2016 18:35:12 | |
| Date Stamp | 08 Dec 2016 18:35:12 | File Name | F:\LEANDRA-FRANCIELA3206-FAS079-13C\1\FID | | | | |
| Frequency (MHz) | 100.61 | Nucleus | 13C | Number of Transients | 1600 | Origin | spect |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 | Pulse Sequence | jmod |
| Receiver Gain | 16384.00 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d | | |
| Spectrum Offset (Hz) | 10053.9746 | Spectrum Type | APT | Sweep Width (Hz) | 24037.73 | Temperature (degree C) | 29.900 |

LEANDRA-FRANCIELA3206-FAS079-13C.001.esp

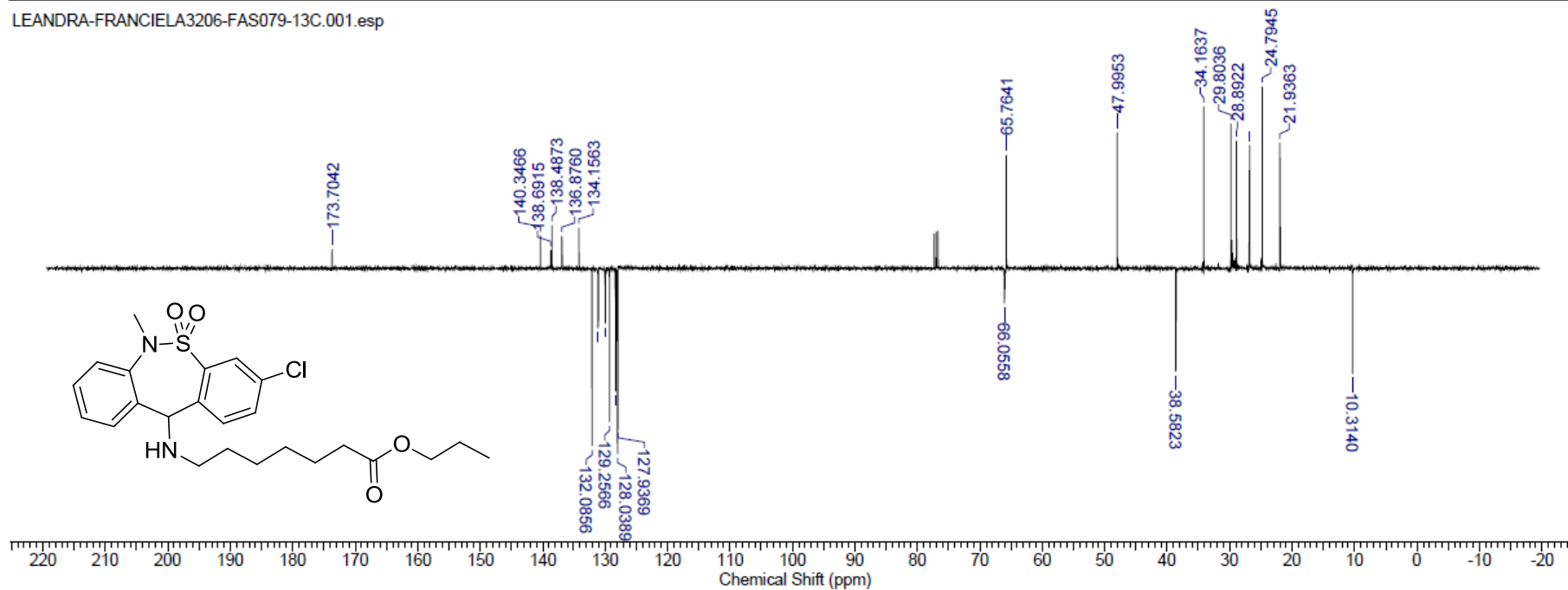
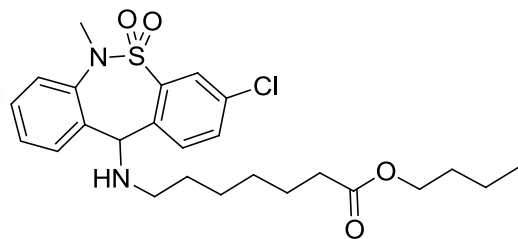


Figure S19. ^{13}C NMR APT spectrum (100.6 MHz, CDCl_3) of ester **2c**.



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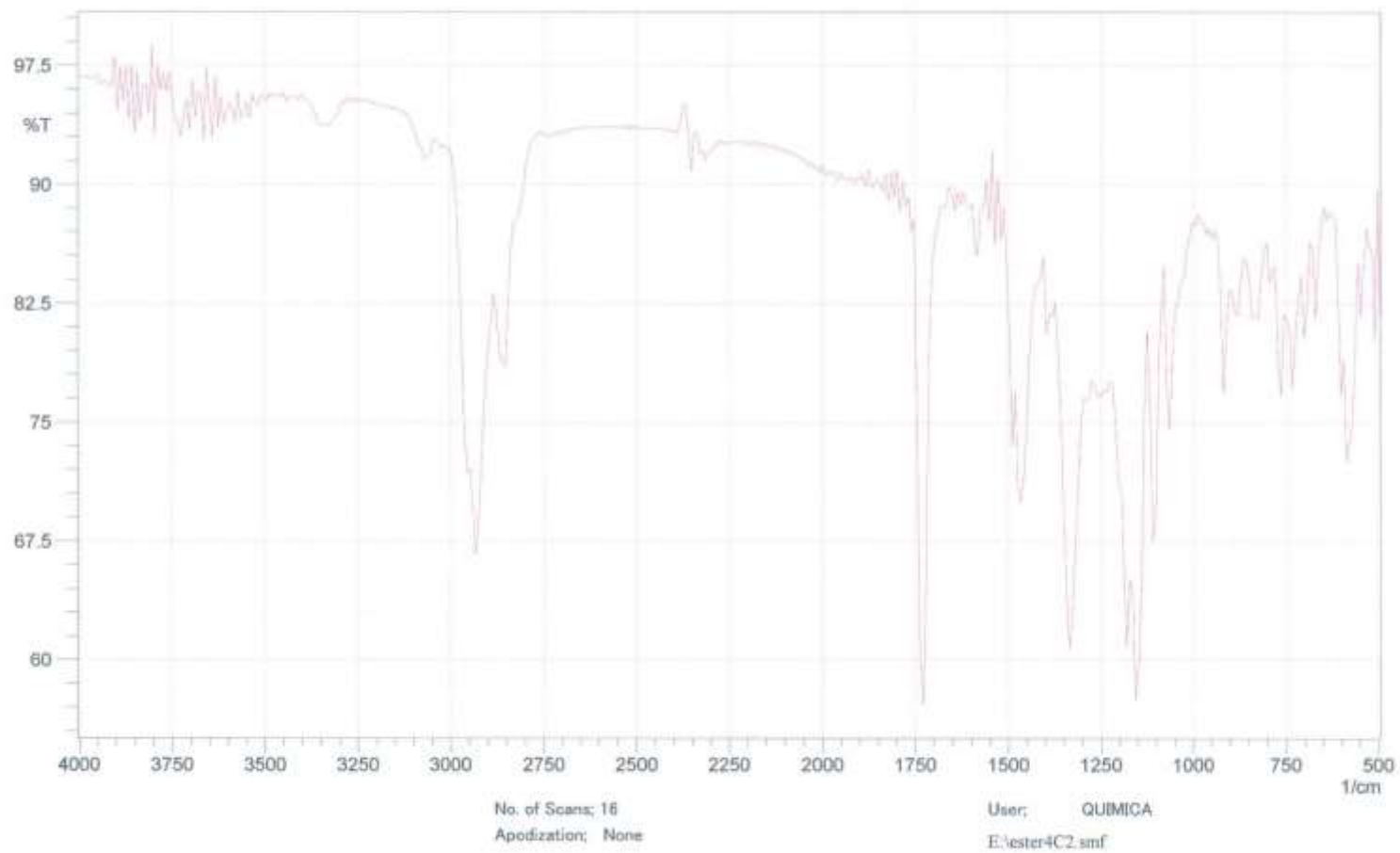


Figure S20. IR spectrum (KBr) of ester **2d**.

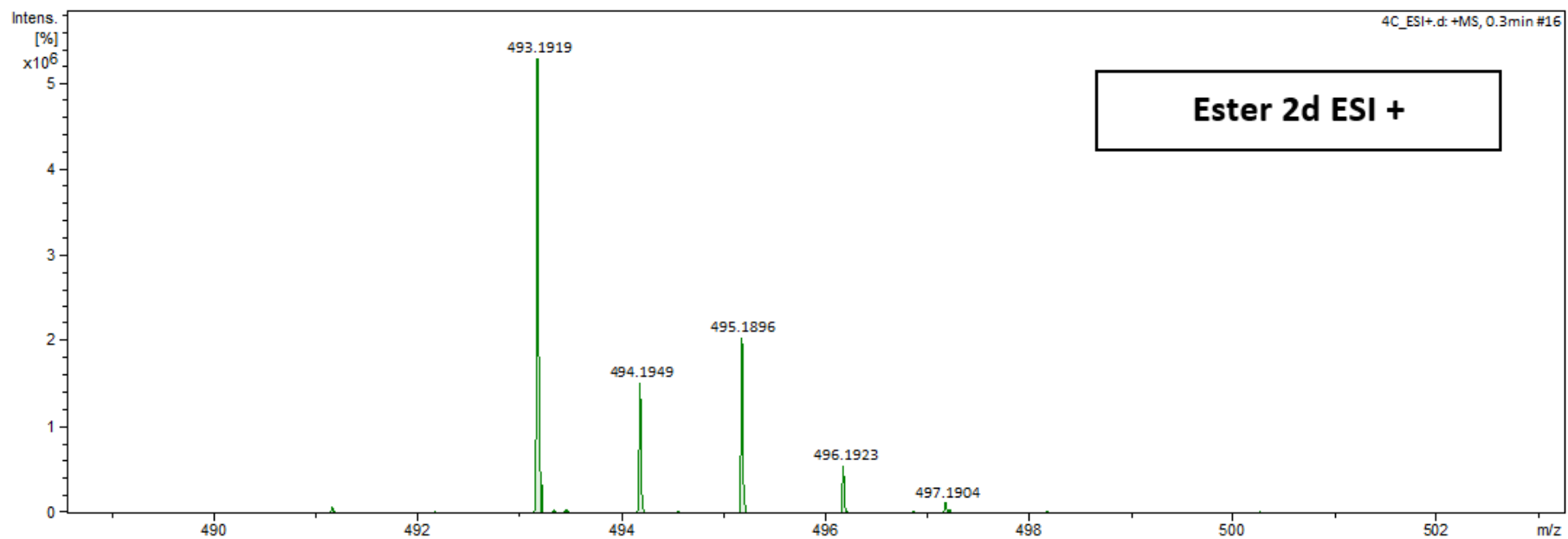


Figure S21. Mass spectrum of ester **2d**, calcd. for $C_{25}H_{33}ClN_2O_4S$ $[M]^+$: 493.1928, found: 493.1919.

| | | | | | | | |
|------------------------|----------------------|-------------------|---|----------------------|--------------|------------------------|--------|
| Acquisition Time (sec) | 2.0447 | Comment | 5 mm PABBO BB/19F-1H/D Z-GRD Z116098/0308 | | Date | 13 Dec 2016 15:08:16 | |
| Date Stamp | 13 Dec 2016 15:08:16 | File Name | C:\Users\Franciela\Dropbox\Doc\Esteres\RMN\Leandra-Franciela3230-FAS-073-1H\1\fid | | | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 32 | Origin | spect |
| Original Points Count | 16384 | Owner | nmr | Points Count | 16384 | Pulse Sequence | zg30 |
| Receiver Gain | 62.94 | SW(cyclical) (Hz) | 8012.82 | Solvent | CHLOROFORM-d | | |
| Spectrum Offset (Hz) | 2463.1694 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8012.33 | Temperature (degree C) | 25.002 |

Leandra-Franciela3230-FAS-073-1H.001.esp

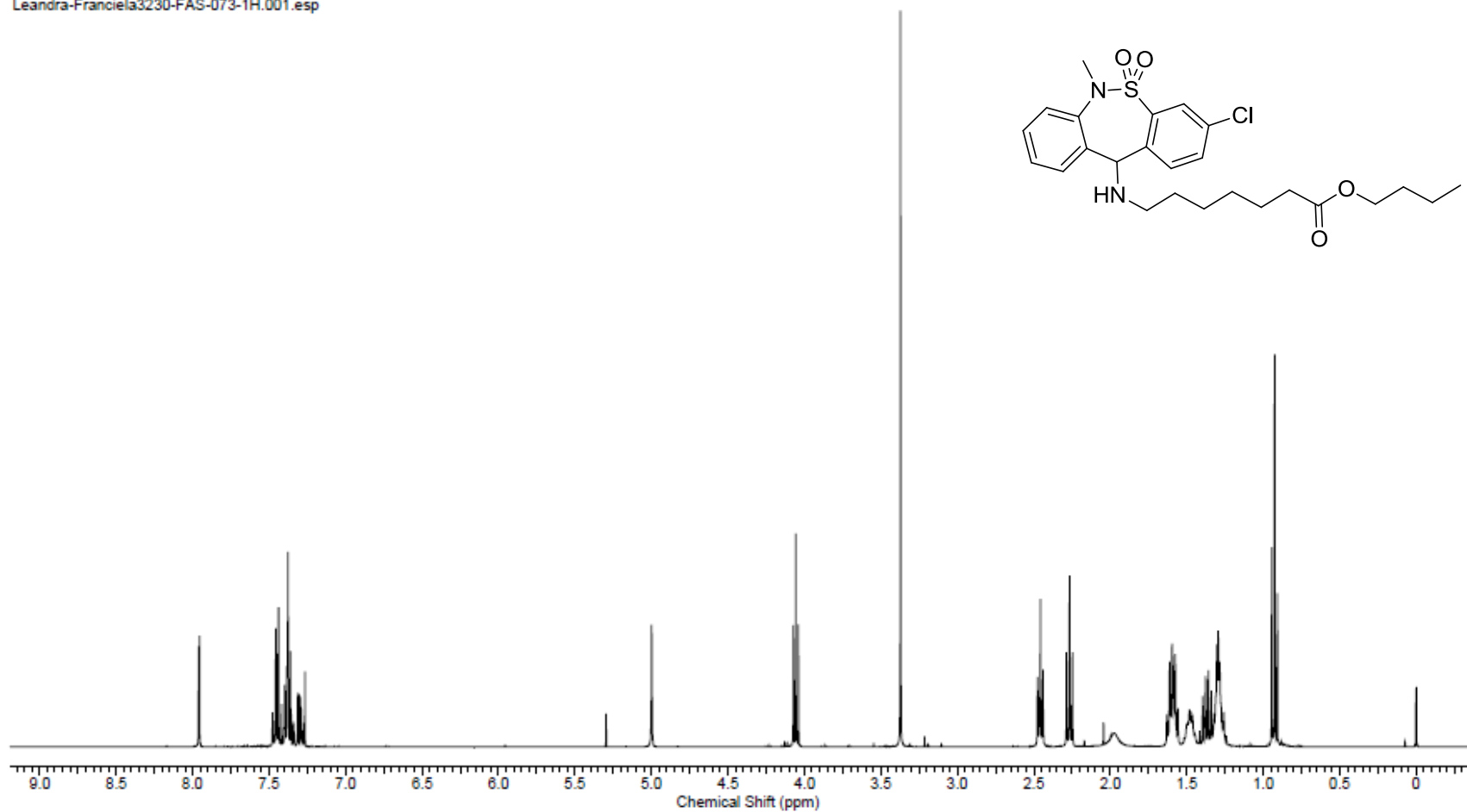


Figure S22. ¹H NMR spectrum (400.1 MHz, CDCl₃) of ester **2d**.

| | | | | | | | |
|------------------------|----------------------|-------------------|---|----------------------|--------------|------------------------|--------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB/19F-1H/D Z-GRD Z116098/0308 | | Date | 13 Dec 2016 15:21:04 | |
| Date Stamp | 13 Dec 2016 15:21:04 | File Name | F:\Leandra-Franciela3230-FAS-073-APT2\fid | | | | |
| Frequency (MHz) | 100.61 | Nucleus | 13C | Number of Transients | 2008 | Origin | spect |
| Original Points Count | 32768 | Owner | nmr | Points Count | 32768 | Pulse Sequence | jmod |
| Receiver Gain | 195.04 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d | | |
| Spectrum Offset (Hz) | 10055.4414 | Spectrum Type | APT | Sweep Width (Hz) | 24037.73 | Temperature (degree C) | 25.002 |

Leandra-Franciela3230-FAS-073-APT.002.esp

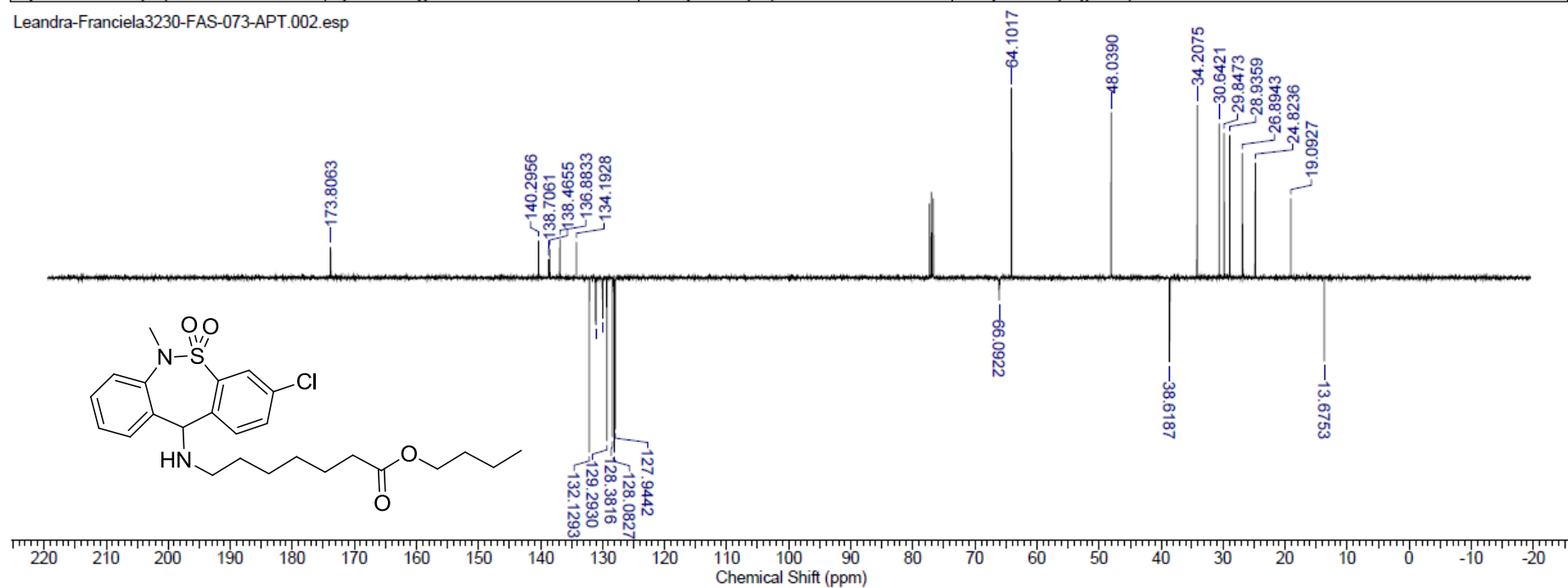
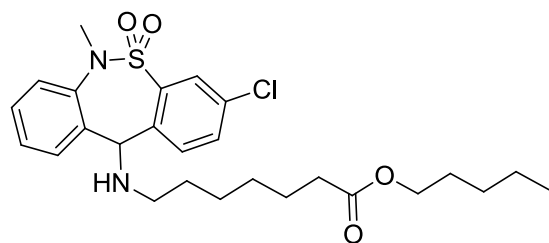


Figure S23. ¹³C NMR APT spectrum (100.6 MHz, CDCl₃) of ester 2d.



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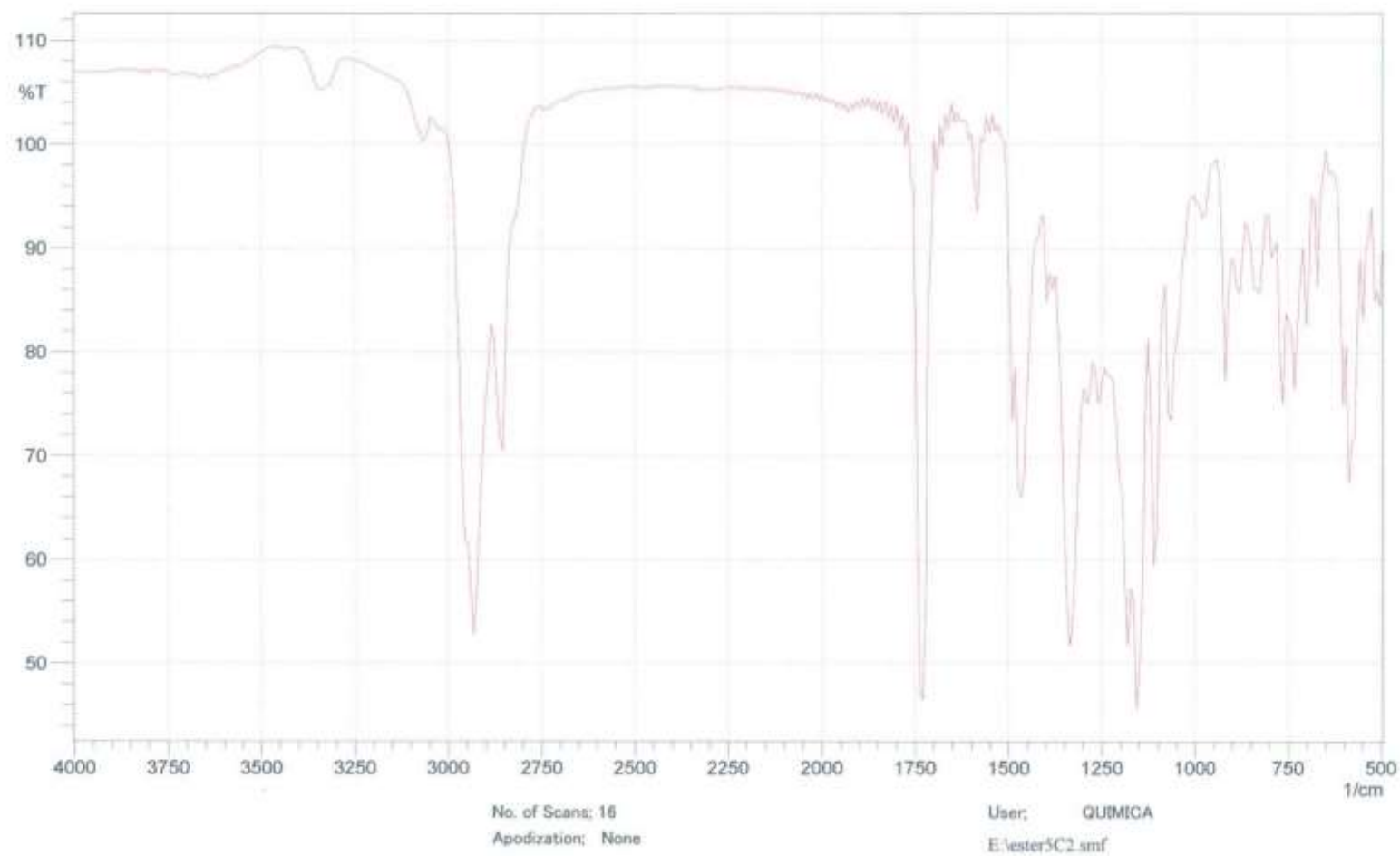


Figure S24. IR spectrum (KBr) of ester **2e**.

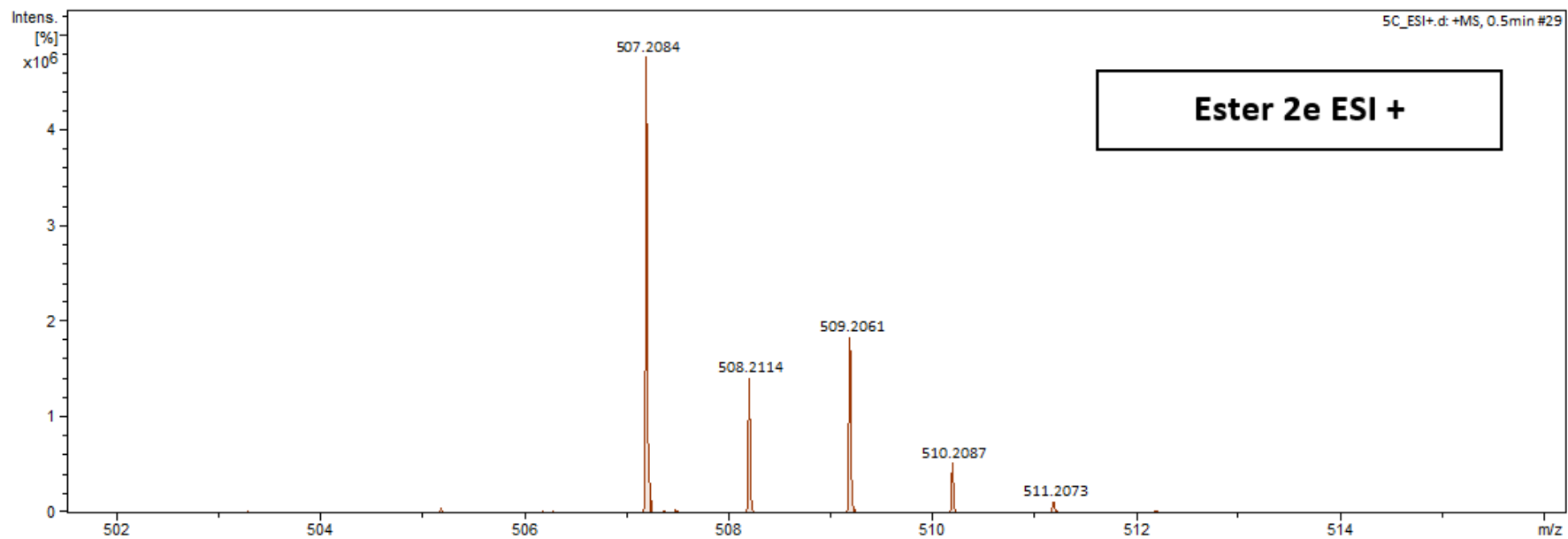


Figure S25. Mass spectrum of ester **2e**, calcd. for $C_{26}H_{35}ClN_2O_4S$ $[M]^+$: 507.2084, found: 507.2084.

| | | | | | |
|------------------------|----------------------|-------------------|--|------------------------|----------------------|
| Acquisition Time (sec) | 3.9715 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 09 Nov 2016 12:38:56 |
| Date Stamp | 09 Nov 2016 12:38:56 | File Name | C:\Users\Franciela\Dropbox\Doc\Esteres\RMN\Leandra-Franciela2898-FAS-080\1\fid | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 32 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 128.00 | SW(cyclical) (Hz) | 8250.83 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 2466.1633 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8250.57 |
| | | | | Temperature (degree C) | 25.000 |

Leandra-Franciela2898-FAS-080.001.esp

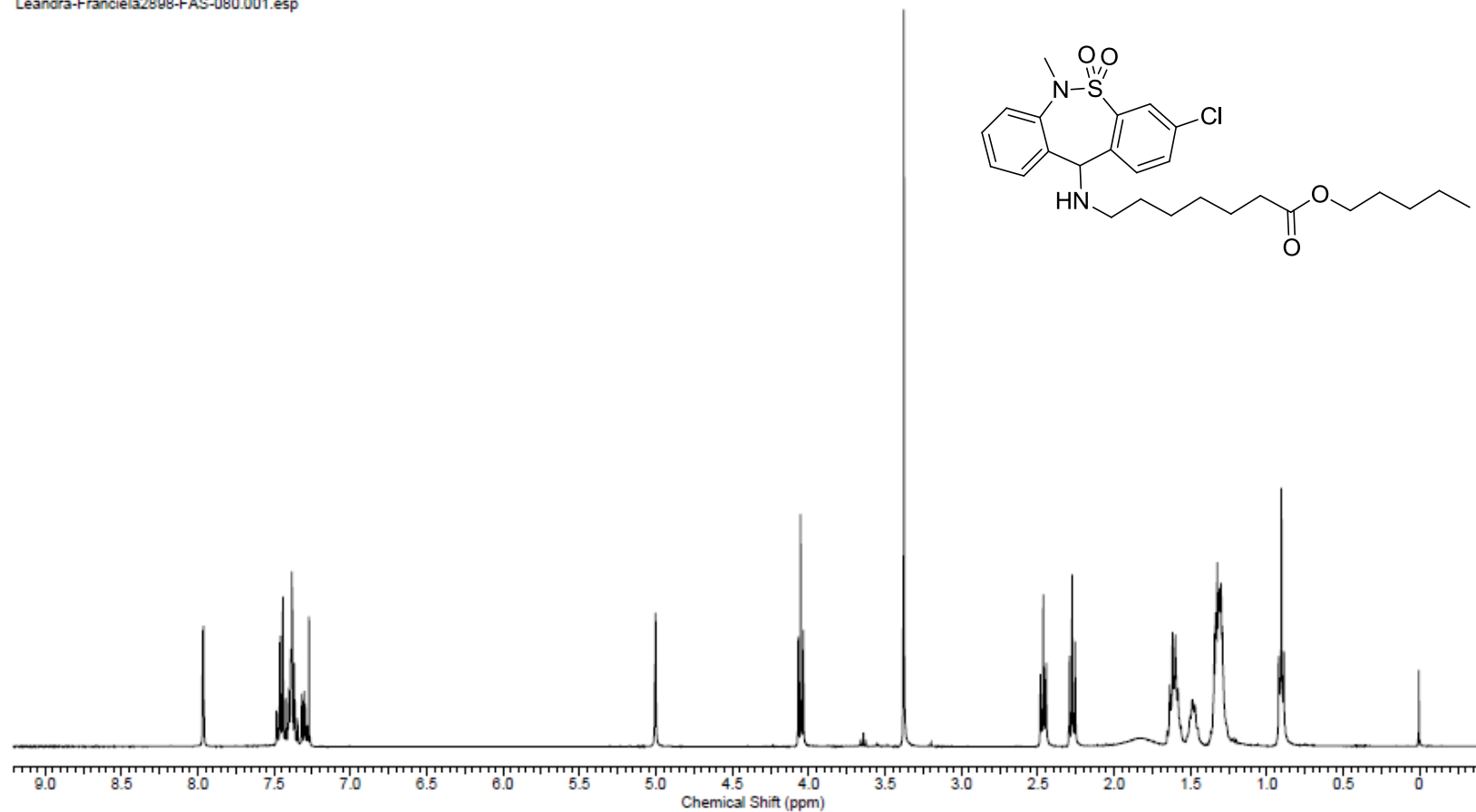


Figure S26. ¹H NMR spectrum (400.1 MHz, CDCl₃) of ester **2e**.

| | | | | | |
|------------------------|----------------------|-------------------|--|------------------------|----------------------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 05 Dec 2016 00:33:36 |
| Date Stamp | 05 Dec 2016 00:33:36 | File Name | F:\Leandra-Franciela3088-FAS-080-APT\1\fid | | |
| Frequency (MHz) | 100.61 | Nucleus | ¹³ C | Number of Transients | 3600 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 16384.00 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 10053.9746 | Spectrum Type | APT | Sweep Width (Hz) | 24037.73 |
| | | | | Temperature (degree C) | 21.600 |

Leandra-Franciela3088-FAS-080-APT.001.esp

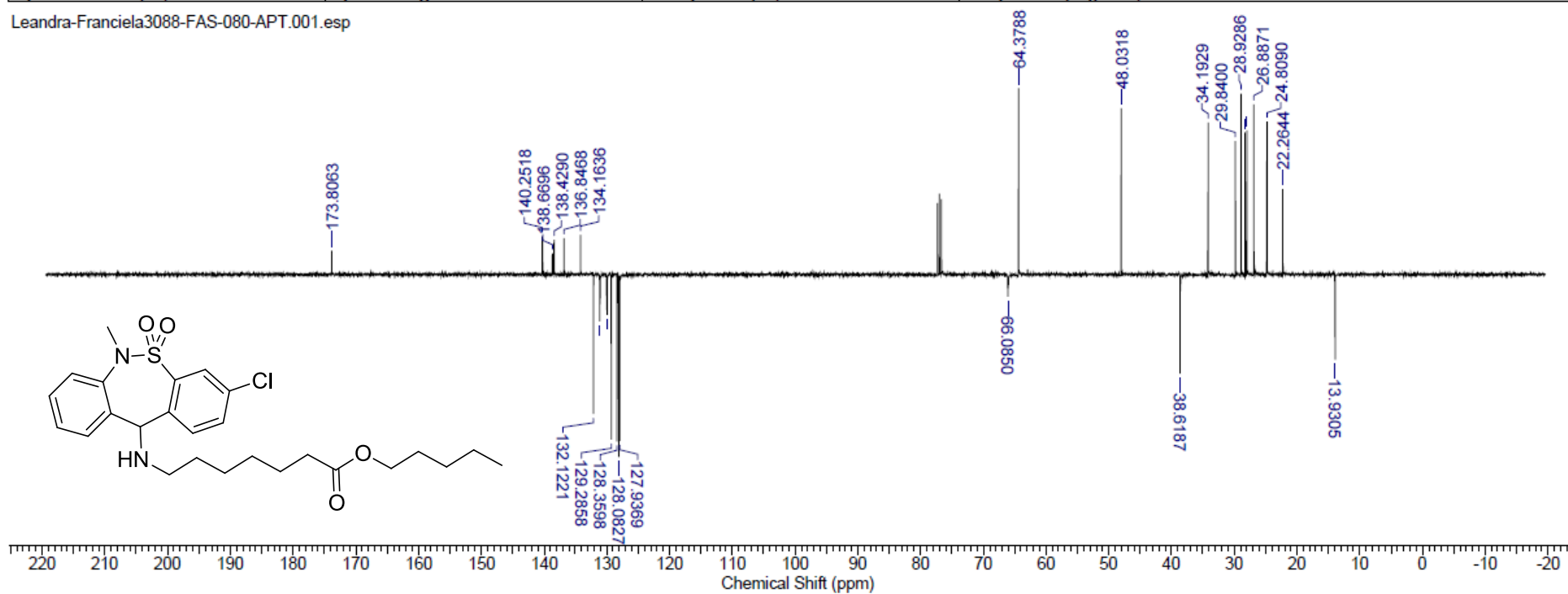
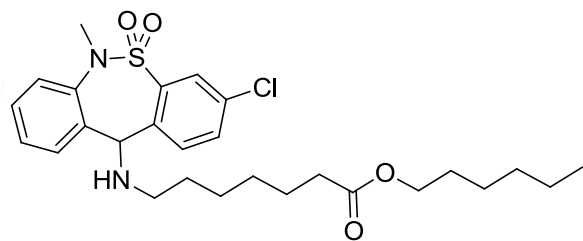


Figure S27. ¹³C NMR APT spectrum (100.6 MHz, CDCl₃) of ester **2e**.



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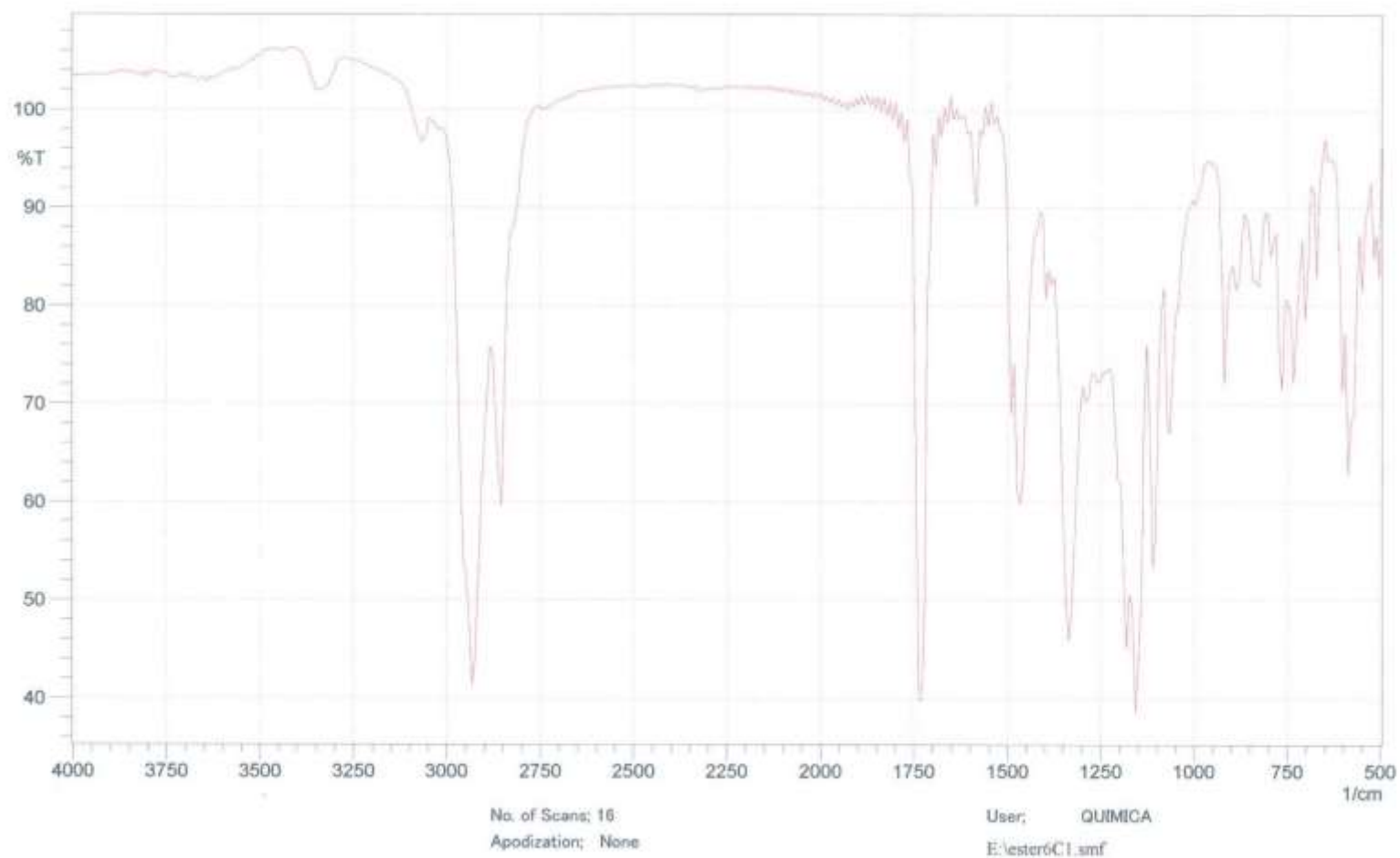


Figure S28. IR spectrum (KBr) of ester **2f**.

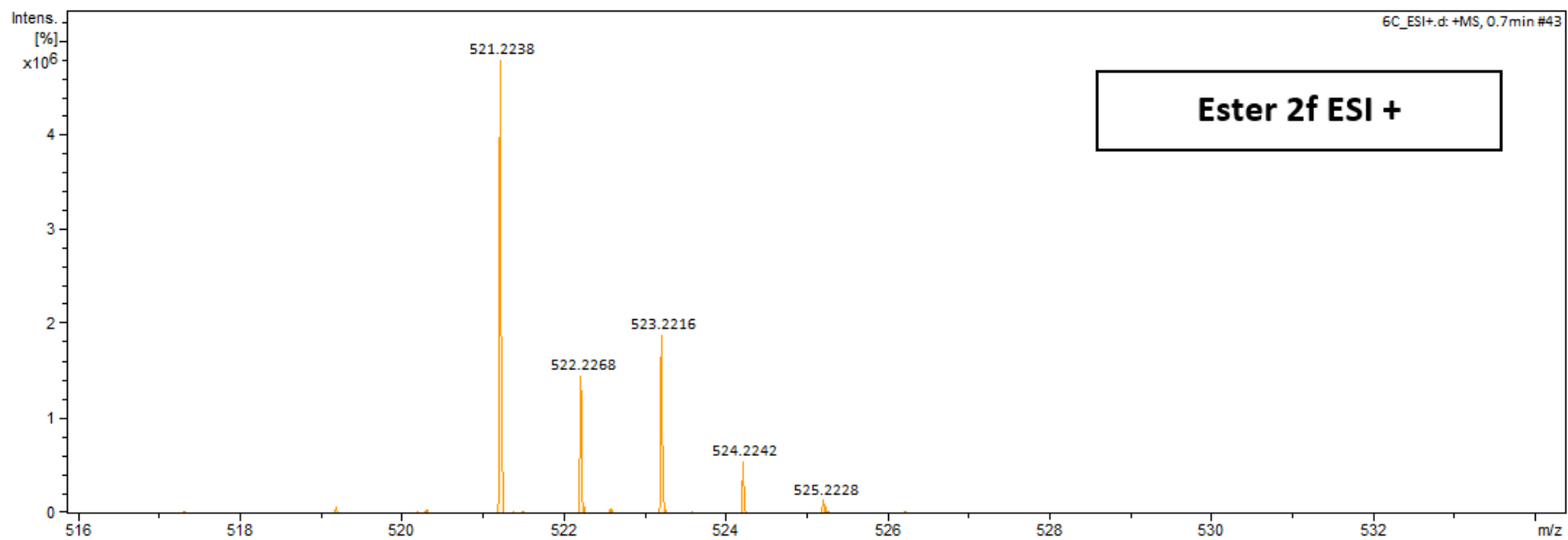


Figure S29. Mass spectrum of ester **2f**, calcd. for $C_{27}H_{37}ClN_2O_4S$ $[M]^+$: 521.2241, found: 521.2238.

| | | | | | |
|------------------------|----------------------|-------------------|--|------------------------|----------------------|
| Acquisition Time (sec) | 3.9715 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 09 Nov 2016 15:06:08 |
| Date Stamp | 09 Nov 2016 15:06:08 | File Name | C:\Users\Franciela\Dropbox\Doc\Esteres\RMN\Leandra-Franciela2907-FAS74\1.fid | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 32 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 71.80 | SW(cyclical) (Hz) | 8250.83 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 2466.1633 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8250.57 |
| | | | | Temperature (degree C) | 21.300 |

Leandra-Franciela2907-FAS74.001.esp

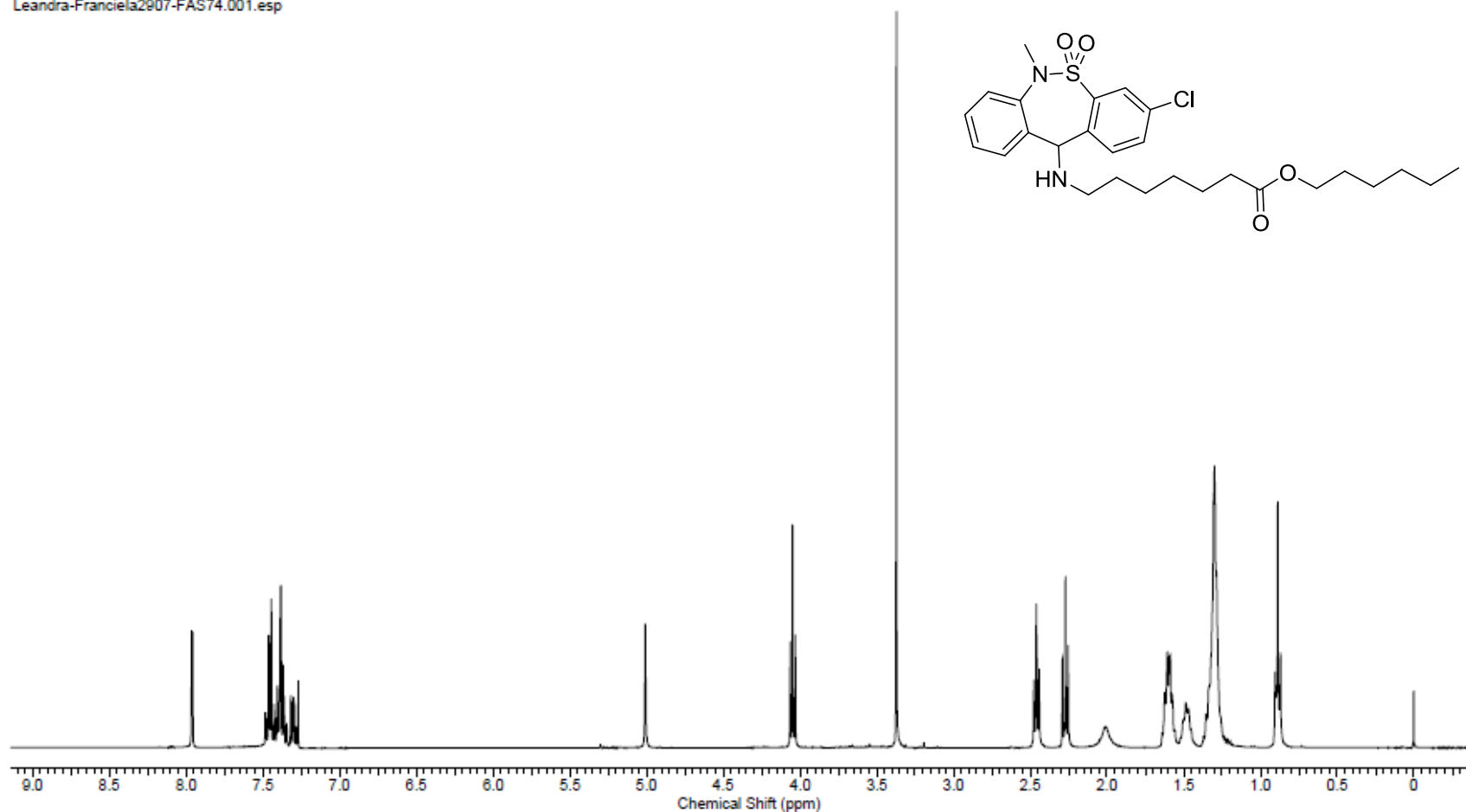


Figure S30. ¹H NMR spectrum (400.1 MHz, CDCl₃) of ester **2f**.

| | | | | | | | |
|------------------------|----------------------|-------------------|---|----------------------|--------------|------------------------|--------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | | Date | 08 Dec 2016 20:09:04 | |
| Date Stamp | 08 Dec 2016 20:09:04 | File Name | F:\Leandra-Franciela3207-FAS074-APT\1.fid | | | | |
| Frequency (MHz) | 100.61 | Nucleus | 13C | Number of Transients | 1600 | Origin | spect |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 | Pulse Sequence | jmod |
| Receiver Gain | 16384.00 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d | | |
| Spectrum Offset (Hz) | 10052.5078 | Spectrum Type | APT | Sweep Width (Hz) | 24037.73 | Temperature (degree C) | 30.100 |

Leandra-Franciela3207-FAS074-APT.001.esp

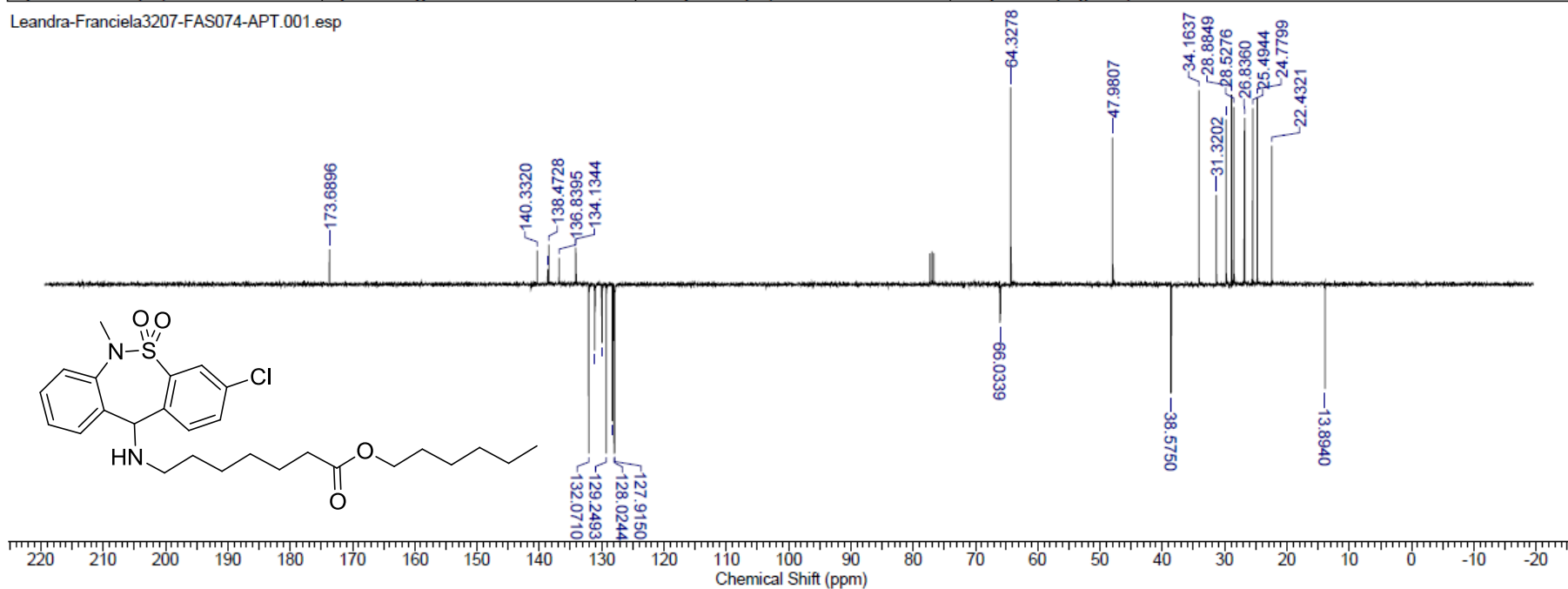
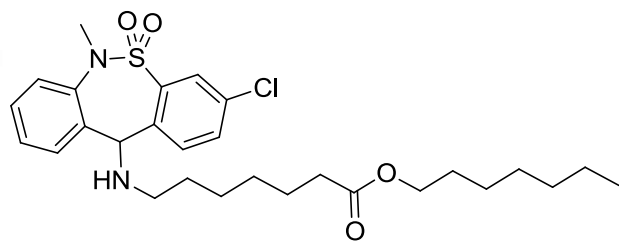


Figure S31. ^{13}C NMR APT spectrum (100.6 MHz, CDCl_3) of ester **2f**.



SHIMADZU

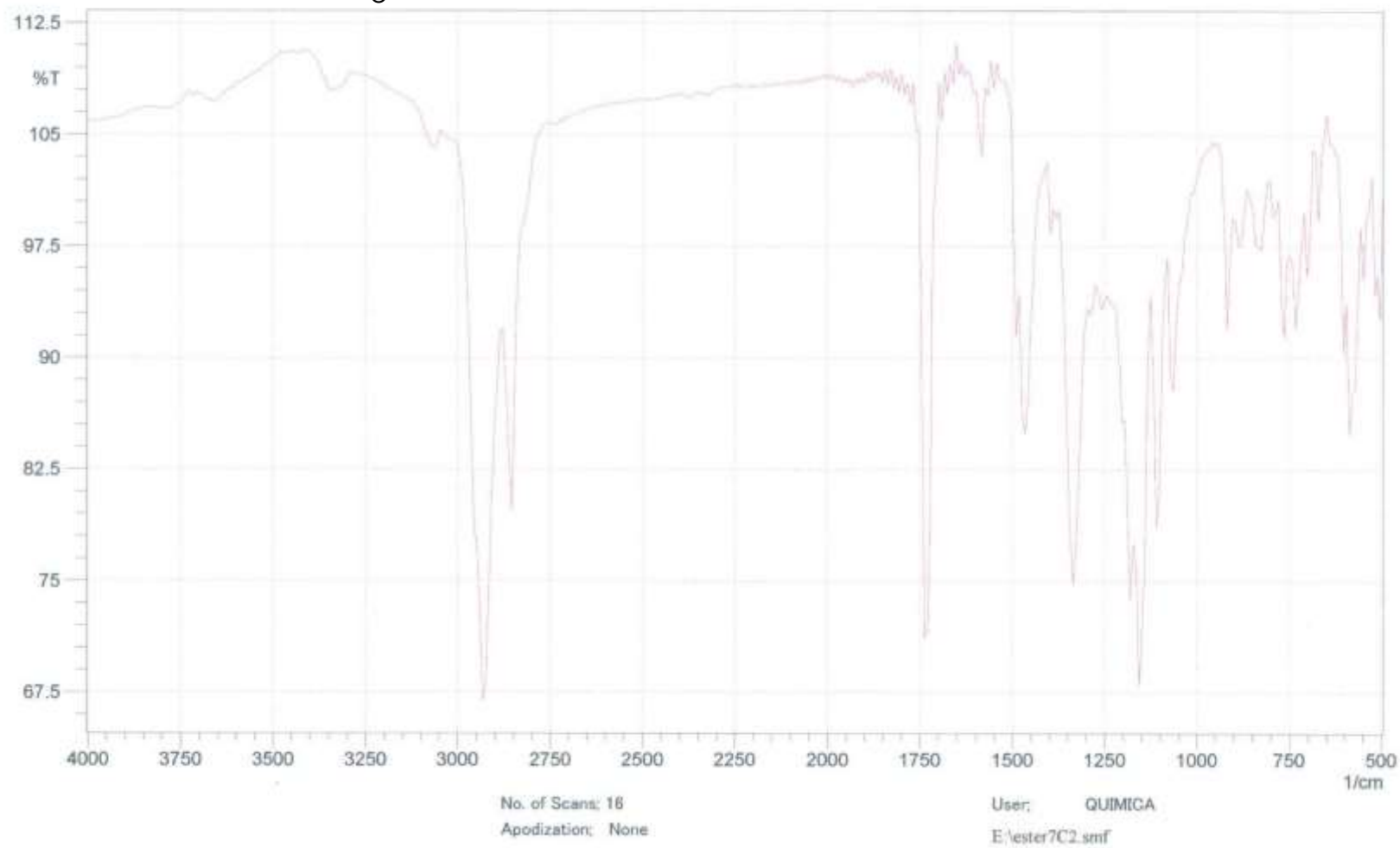


Figure S32. IR spectrum (KBr) of ester 2g.

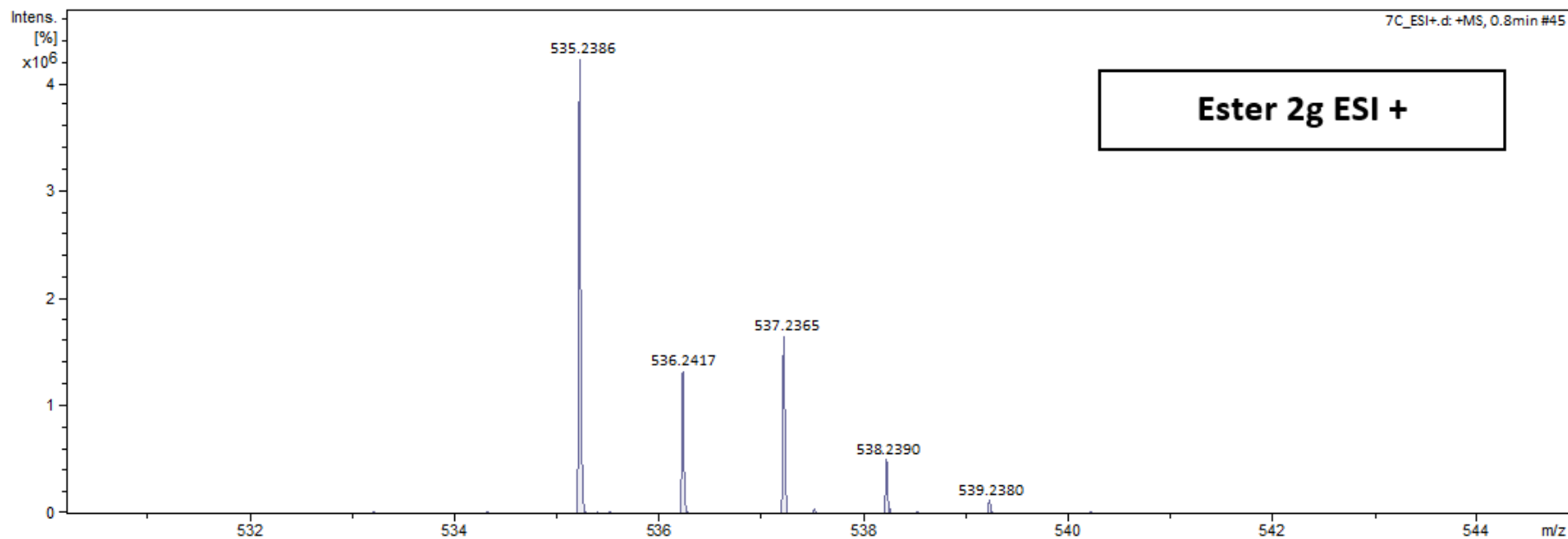


Figure S33. Mass spectrum of ester **2g**, calcd. for $C_{28}H_{39}ClN_2O_4S$ $[M]^+$: 535.2397, found: 535.2386.

| | | | | | |
|------------------------|----------------------|-------------------|---|------------------------|----------------------|
| Acquisition Time (sec) | 3.9715 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 09 Nov 2016 14:59:44 |
| Date Stamp | 09 Nov 2016 14:59:44 | File Name | C:\Users\Franciela\Dropbox\Doc\Esteres\RMN\Leandra-Franciela2906-FAS811\fid | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 32 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 90.50 | SW(cyclical) (Hz) | 8250.83 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 2466.1633 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8250.57 |
| | | | | Temperature (degree C) | 21.100 |

Leandra-Franciela2906-FAS81.001.esp

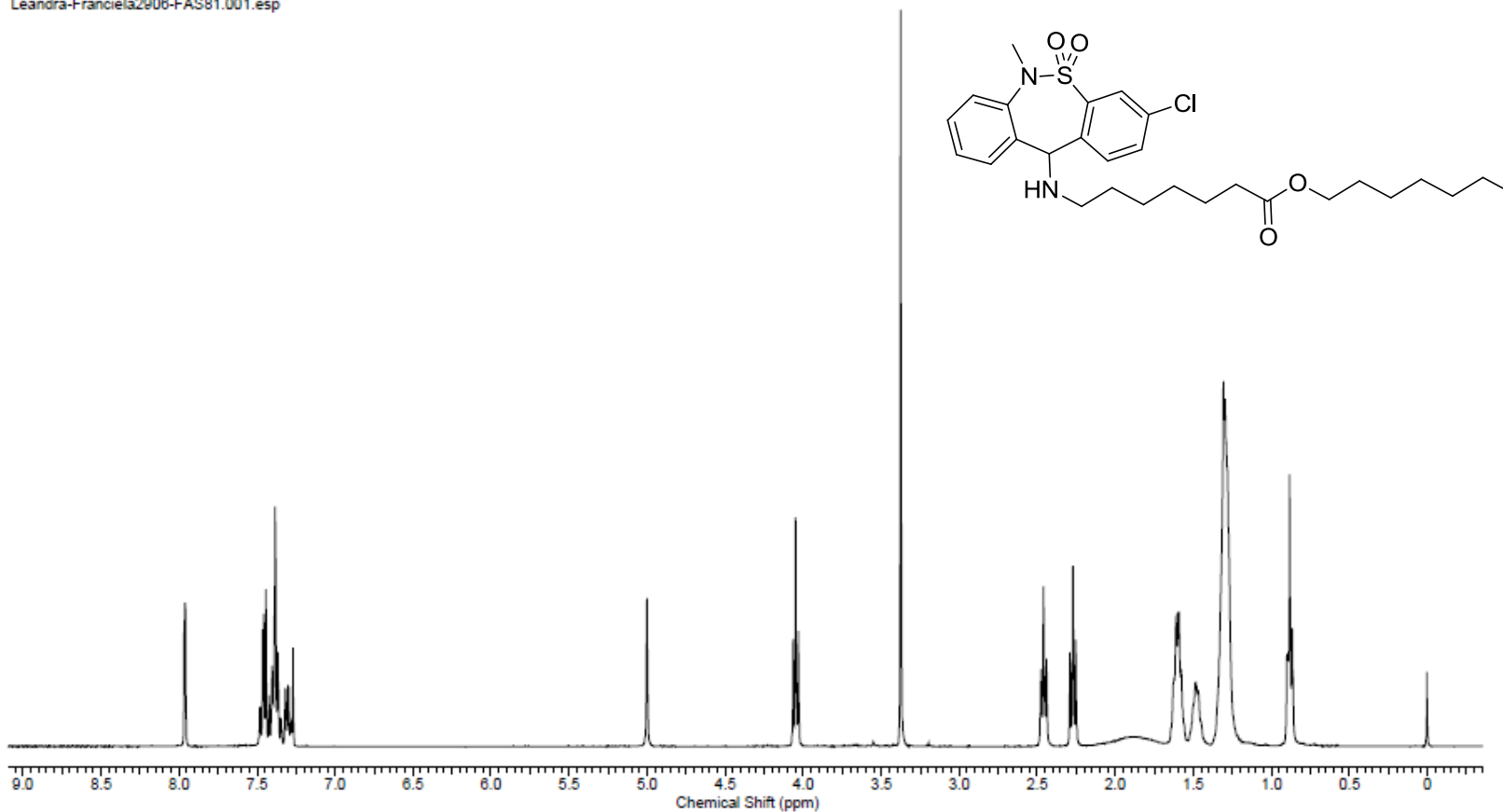


Figure S34. ^1H NMR spectrum (400.1 MHz, CDCl_3) of ester **2g**.

| | | | | | | | |
|------------------------|----------------------|-------------------|---|----------------------|--------------|------------------------|--------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | | Date | 08 Dec 2016 21:42:56 | |
| Date Stamp | 08 Dec 2016 21:42:56 | File Name | F:\Leandra-Franciela3208-FAS081-APT\1\fid | | | | |
| Frequency (MHz) | 100.61 | Nucleus | 13C | Number of Transients | 1600 | Origin | spect |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 | Pulse Sequence | jmod |
| Receiver Gain | 16384.00 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d | | |
| Spectrum Offset (Hz) | 10053.2402 | Spectrum Type | APT | Sweep Width (Hz) | 24037.73 | Temperature (degree C) | 30.100 |

Leandra-Franciela3208-FAS081-APT.001.esp

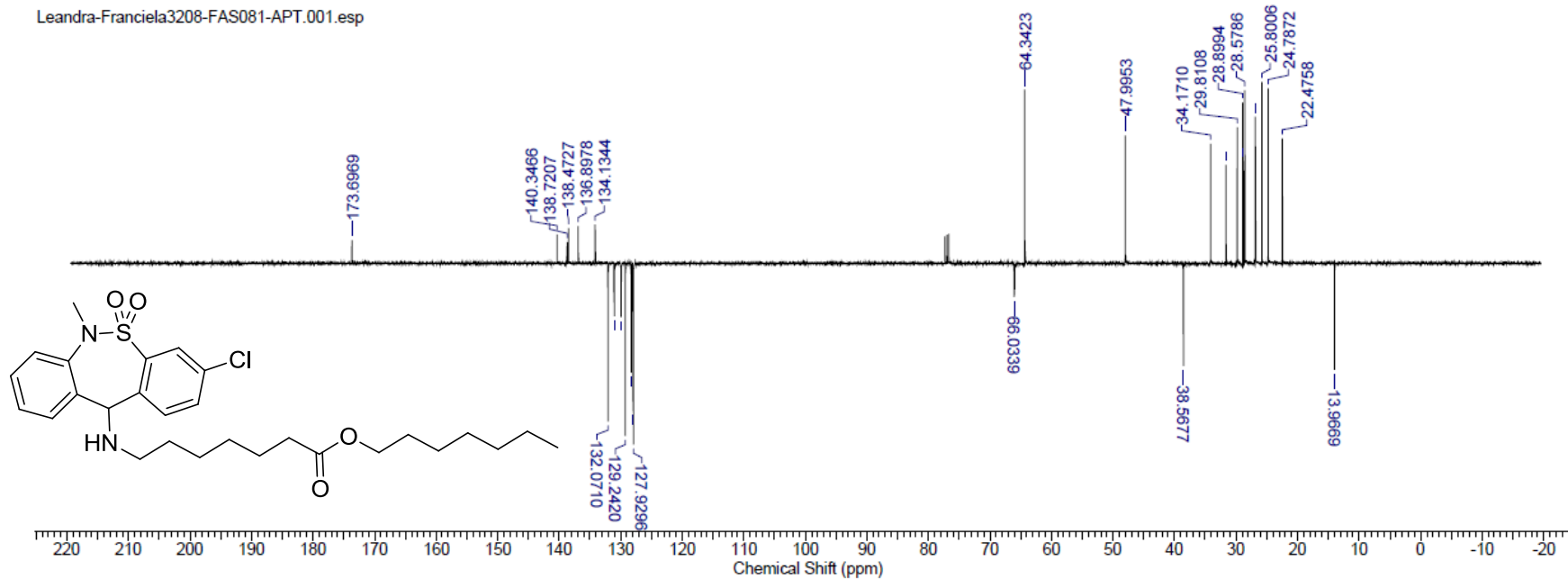
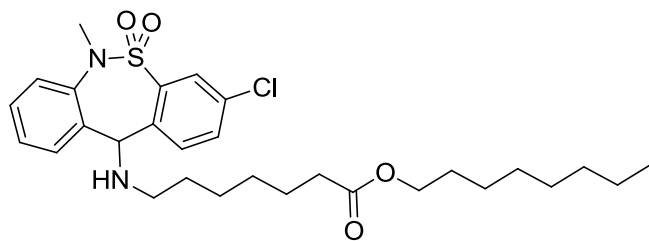


Figure S35. ¹³C NMR APT spectrum (100.6 MHz, CDCl₃) of ester **2g**.



SHIMADZU

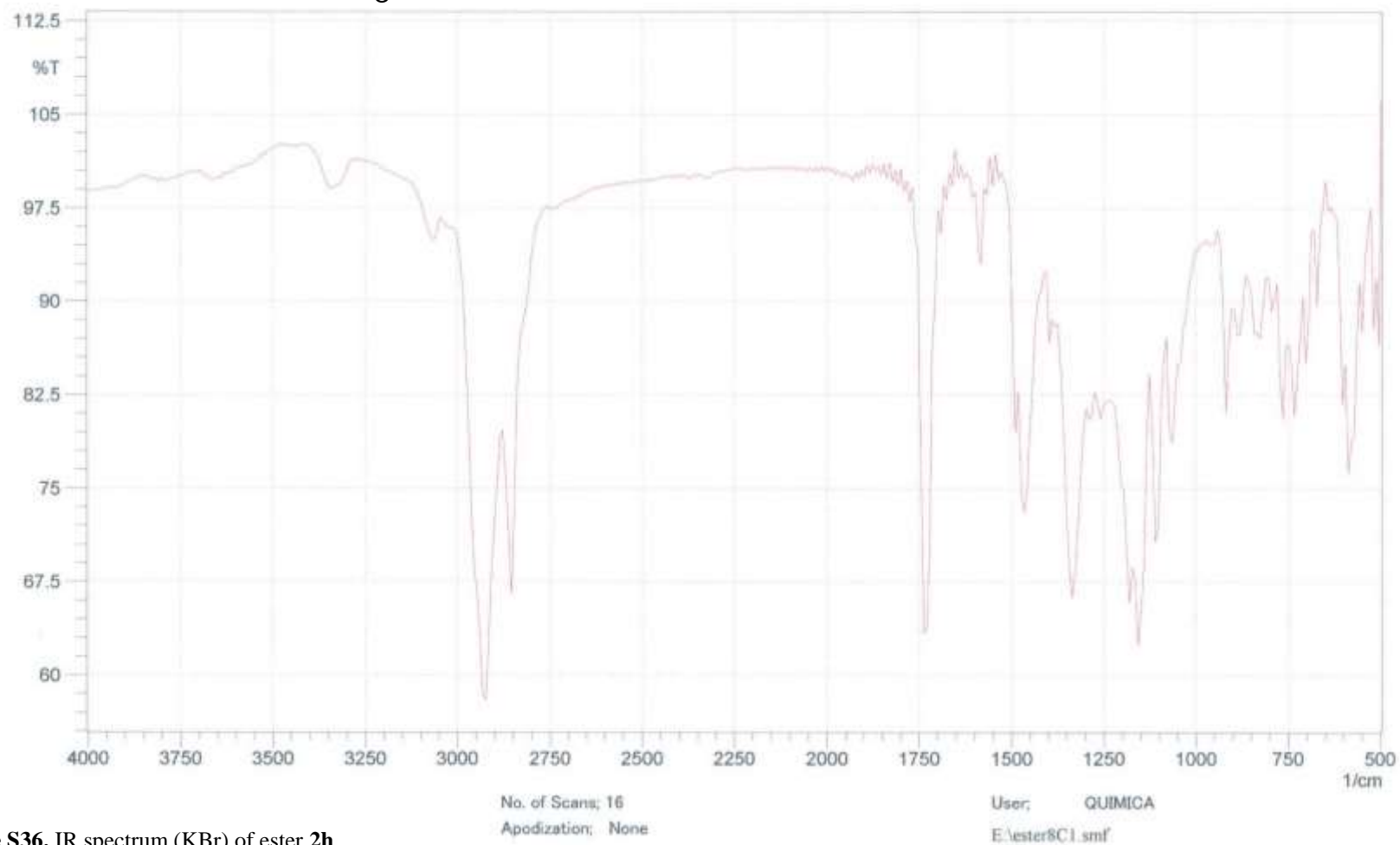


Figure S36. IR spectrum (KBr) of ester 2h.

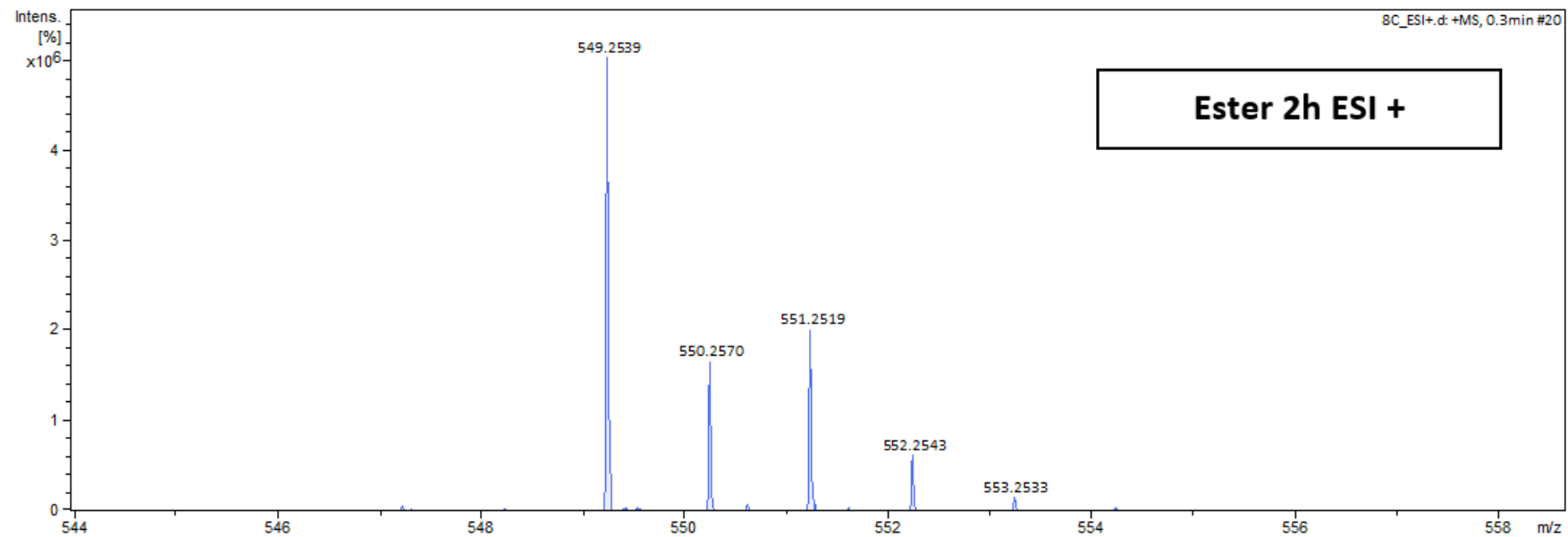


Figure S37. Mass spectrum of ester **2h**, calcd. for $C_{29}H_{41}ClN_2O_4S [M]^+$: 549.2554, found: 549.2539.

| | | | | | | | |
|------------------------|----------------------|-------------------|--|----------------------|--------------|------------------------|--------|
| Acquisition Time (sec) | 3.9715 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | | Date | 09 Nov 2016 15:12:32 | |
| Date Stamp | 09 Nov 2016 15:12:32 | File Name | C:\Users\Franciela\Dropbox\Doc\Esteres\RMN\Leandra-Franciela2908-FAS76\1\fid | | | | |
| Frequency (MHz) | 400.13 | Nucleus | 1H | Number of Transients | 32 | Origin | spect |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 | Pulse Sequence | zg30 |
| Receiver Gain | 71.80 | SW(cyclical) (Hz) | 8250.83 | Solvent | CHLOROFORM-d | | |
| Spectrum Offset (Hz) | 2465.2009 | Spectrum Type | STANDARD | Sweep Width (Hz) | 8250.57 | Temperature (degree C) | 21.400 |

Leandra-Franciela2908-FAS76.001.esp

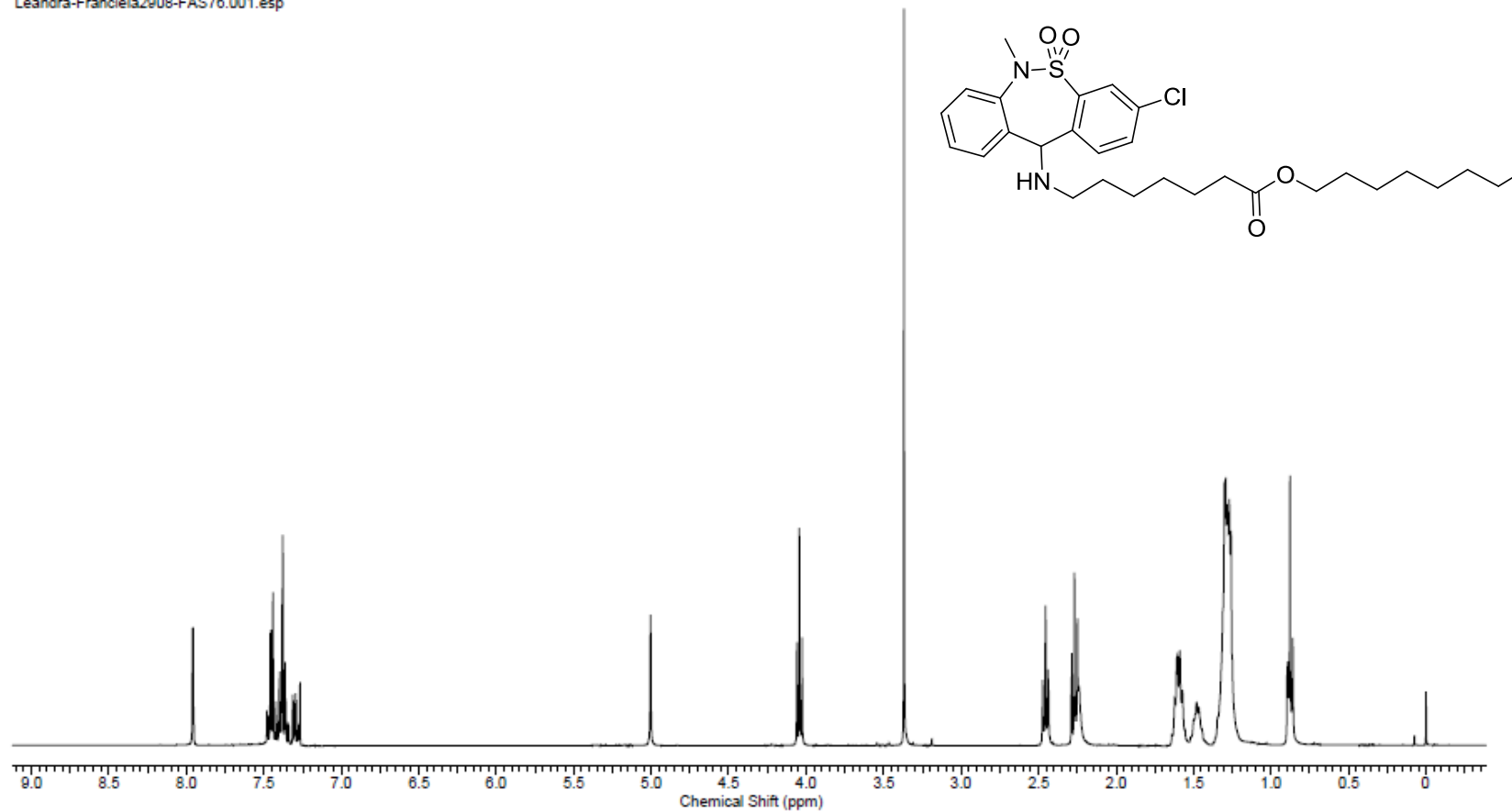


Figure S38. ^1H NMR spectrum (400.1 MHz, CDCl_3) of ester **2h**.

| | | | | | |
|------------------------|----------------------|-------------------|--|------------------------|----------------------|
| Acquisition Time (sec) | 1.3631 | Comment | 5 mm PABBO BB-1H/D Z-GRD Z108618/0521 | Date | 13 Dec 2016 11:22:08 |
| Date Stamp | 13 Dec 2016 11:22:08 | File Name | F:\Leandra-Franciela3228-FAS-076-13C\5\fid | | |
| Frequency (MHz) | 100.61 | Nucleus | 13C | Number of Transients | 3600 |
| Original Points Count | 32768 | Owner | User | Points Count | 32768 |
| Receiver Gain | 23170.50 | SW(cyclical) (Hz) | 24038.46 | Solvent | CHLOROFORM-d |
| Spectrum Offset (Hz) | 10053.9746 | Spectrum Type | STANDARD | Sweep Width (Hz) | 24037.73 |
| | | | | Temperature (degree C) | 25.100 |

Leandra-Franciela3228-FAS-076-13C.005.esp

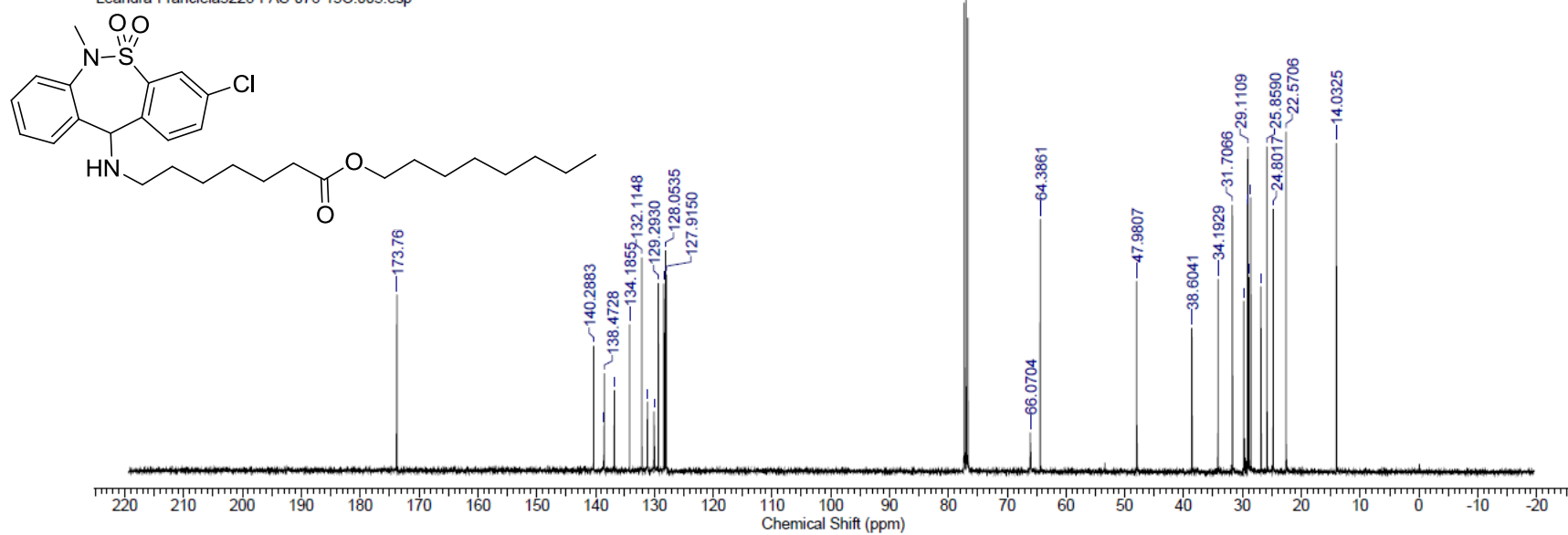


Figure S39. ^{13}C NMR APT spectrum (100.6 MHz, CDCl_3) of ester **2h**.

Table S1. Interactions with the most negative score poses with BSA 4OR0 residues in the region of Trp-213 and Trp-134

| Ligand deprotonated | No. docking Trp-134 (pose 1) | Score / (kJ mol ⁻¹) | Interaction | No. docking Trp-213 (pose 1) | Score / (kJ mol ⁻¹) | Interaction |
|---------------------|------------------------------|---------------------------------|--|------------------------------|---------------------------------|---|
| 1 | 1 | -7.9 | PRO117, TYR160, LYS136, TYR137, LEU115, ILE141, ARG185, LYS114, LEU159 | 1 | -8.6 | GLU152, ALA290, ARG256, ARG194, LYS221, TYR149, ASP450, ARG217, ARG198, HIS241, ^a LEU237, LEU218, TRP213 |
| 2a | 1 ou 3 | -7.9 | LEU189, ARG185, TYR160, ILE141, TYR137, LYS114, LEU115, PRO117, GLU140, PHE133 | 3 | -8.5 | GLU152, ALA290, ARG194, ARG256, LYS221, TYR149, ARG217, ARG198, HIS241, ^a TRP213, LEU237, LEU218 |
| 2b | 1 ou 2 no overlap | -7.2 | ARG185, TYR160, TYR137, ARG144, LEU115, LYS114, PRO117, LYS116, LYS136, PHE133, ILE181, LEU122, GLU125 | 2 | -8.6 | SER343, LYS221, VAL342, LEU346, ARG217, ALA290, ARG194, LEU454, LEU218, TRP213, LEU197, ARG198, LEU237, GLU152, HIS241, ^a ARG256, TYR149 |
| 2c | 1 | -8.0 | PHE133, LEU122, PRO117, LYS136, TYR160, TYR137, GLU140, ILE141, LEU115, ARG185, LYS114, LEU189 | 2 ou 3 | -8.6 | ARG256, GLU152, TYR149, ALA290, HIS241, ARG194, ARG198, ARG217, TRP213, LEU197, VAL342, LYS221, LEU237, LEU218, LEU454 |
| 2d | 3 | -7.4 | LEU122, PRO117, LYS114, LEU115, ARG185, TYR160, GLU140, TYR137, ARG144, ILE141 | 2 | -8.7 | ARG194, ALA290, LYS221, GLU152, ARG217, LEU197, VAL342, ARG198, ARG256, TYR149, TRP213, LEU480, VAL481, HIS241, ^a LEU218, LEU237, LEU346 |
| 2e | 1 | -8.1 | LYS114, LEU122, PRO117, LEU115, LYS136, PHE133, GLU140, ARG185, TYR137, ILE141, TYR160, LEU189 | 2 | -8.9 | LYS221, ALA290, LEU237, ARG217, LEU346, VAL342, TRP213, ARG256, HIS241, ^a VAL481, ARG198, ARG194, GLU152, TYR149, LEU480, LEU197, LEU454, SER343 |
| 2f | 1 | -7.8 | LEU189, TYR160, ILE141, TYR137, ARG185, GLU140, PHE133, LYS136, LEU115, PRO117, LEU122, LYS114 | 2 ou 3 | -8.7 | LYS221, ALA290, LEU218, ARG217, VAL342, LEU346, SER343, VAL481, ARG194, LEU454, TRP213, LEU237, ARG198, LEU197, LEU480, GLU152, HIS241, ^a ARG256, TYR149, SER201 |
| 2g | 2 | -7.6 | ASP118, PRO117, LEU115, TYR 160, TYR137, GLU140, LYS114, ILE141, ARG185, LEU189 | 2 | -8.1 | PHE222, GLU291, ALA290, ^a ARG219, LEU218, LEU259, TRP213, LEU237, ARG194, ARG198, TYR190, SER191, ARG256, TYR149, ^a HIS241 |
| 2h | 1, 2 or 3 | -7.7 | LEU189, ARG185, ILE141, TYR160, TYR137, GLU140, LEU115, LYS114, PRO117, LYS136, PHE133, LEU122 | 3 | -8.6 | LEU237, HIS241, ^a LEU218, ARG256, TRP213, TYR149, LEU346, LEU480, ARG198, GLU152, VAL481, VAL342, LEU197, ARG217, LYS221, ALA290, ARG194, LEU454 |

^aHydrogen bond.

Table S2. Interactions with the most negative score poses with BSA 4OR0 residues protonated in the region of Trp-213 and Trp-134

| Ligand protonated | No. docking Trp-134 (pose 1) | Score / (kJ mol ⁻¹) | Interaction (Trp-134) | No. docking Trp-213 (pose 1) | Score / (kJ mol ⁻¹) | Interaction (Trp-213) |
|-------------------|------------------------------|---------------------------------|---|------------------------------|---------------------------------|--|
| 1 | 1 | -6.9 | TRP134, LYS131, LYS132, GLY135, LYS20, PHE36, LEU24, VAL43, VAL40, ASN44, ASP37 | 1 | -8.6 | ARG458, ILE455, LEU454, TYR451, LYS431, THR190, LEU189, HID145, ALA193, ARG435 ^a |
| 2a | 2 | -6.9 | LYS132, PHE36, VAL40, ASN44, VAL43, LEU24, GLY135, LYS20, GLY21, TRP134 | 3 | -9.0 | THR190, LEU189, HID145, PRO146, TYR147, ARG435, LEU454, ALA193, ARG196, LYS431, SER428, ILE455, ARG458 |
| 2b | 1 | -7.9 | LYS114, LEU115, PRO117, ILE141, ARG185, LEU189, TYR137, ILE 181, TYR160 | 1 | -8.5 | GLU152, ILE289, ARG256, TYR149, SER191, ALA290, LEU259, ARG194, LYS221, PHE222, LEU218, ARG217, TRP213, HID241, ARG198 ^a |
| 2c | 1 | -8.0 | LEU189, ARG185, ILE181, TYR160, TYR137, ILE141, LEU122, LYS 114, LEU115 ^a | 3 | -8.3 | HID241, TYR149, ARG198, LEU237, LEU480, LEU197, TRP213, LEU346, ARG217, ARG194, ALA290, GLU291 |
| 2d | 3 | -7.2 | LEU189, ARG185, ILE181, LYS114, ARG144, LEU115, ILE141, TYR137 | 1 | -8.4 | LEU346, TRP213, ARG217, LEU237, ALA290, GLU291, HID241, ARG194, TYR149, LEU480, LEU197, ARG198 ^a |
| 2e | 3 | -7.9 | ILE181, ARG185, LEU189, TYR160, PRO117, TYR137, ILE141, PHE133, LYS114, GLU140, LYS136, LEU115 ^a | 2 | -8.5 | ARG194, LEU197, TYR149, HID241, TRP213, GLU291, ALA290, LEU237, VAL342, LEU346, ARG198 ^a |
| 2f | 3 | -7.1 | TYR137, LYS136, GLU140, ILE181, ARG185, PRO117, LEU122, PRO113, ASP118, LYS116, LEU115 ^a | 2 | -8.4 | GLU152, TYR149, ARG194, LEU197, SER453, ARG256, ALA290, HID241, LEU480, LEU237, ARG217, TRP213, VAL342, SER343, VAL481, LYS221, LEU346 |
| 2g | 1 | -8.0 | LEU189, ARG185, VAL188, HID145, TYR160, ILE141, TYR137, LYS114, ARG144, LEU115, GLU140 | 3 | -8.4 | TYR149, ARG194, LEU197, LEU480, GLU291, ALA290, LEU237, RG217, TRP213, HID241, VAL342, ALA209, LEU346, ARG198 ^a |
| 2h | 1 | -7.8 | LEU189, ARG185, ILE181, VAL188, TYR160, LYS114, ARG144, LEU115, GLU140, ILE141, LYR137, PHE133 | 2 | -8.7 | ARG194, LEU197, LEU180, TYR149, GLU291, ALA290, ARG217, LEU237, TRP213, VAL342, LEU346, ALA209, ARG198 ^a |

^aHydrogen bond.

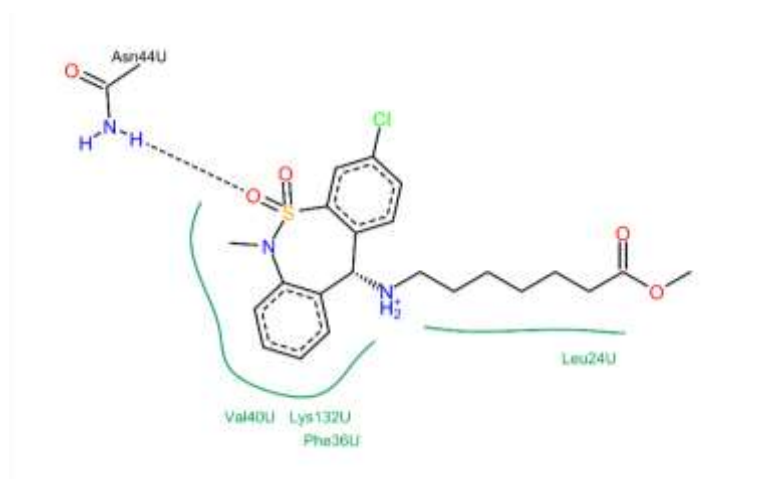


Figure 40. Interactions with BSA amino acids residues near to Trp-134 for protonated ligand **2a**.

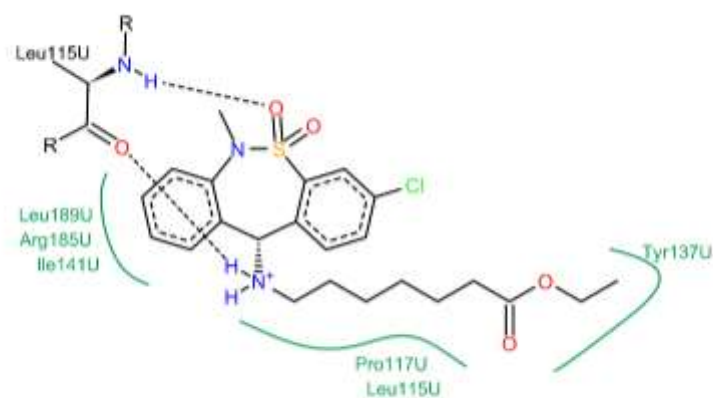


Figure 41. Interactions with BSA amino acids residues near to Trp-134 for protonated ligand **2b**.

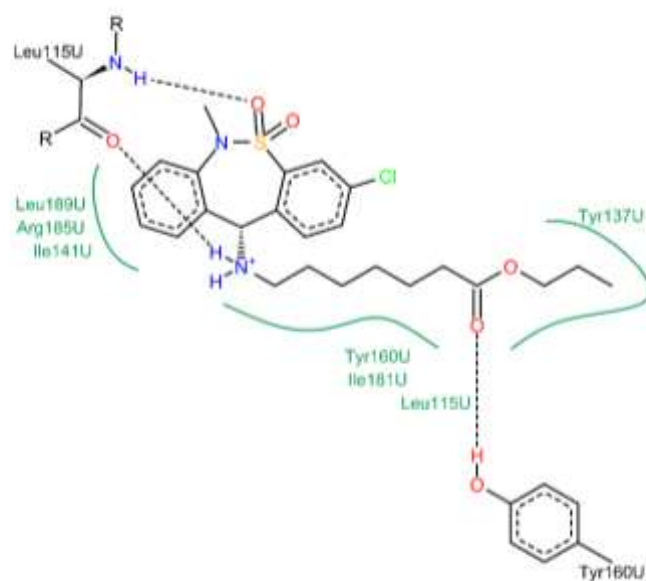


Figure 42. Interactions with BSA amino acids residues near to Trp-134 for protonated ligand **2c**.

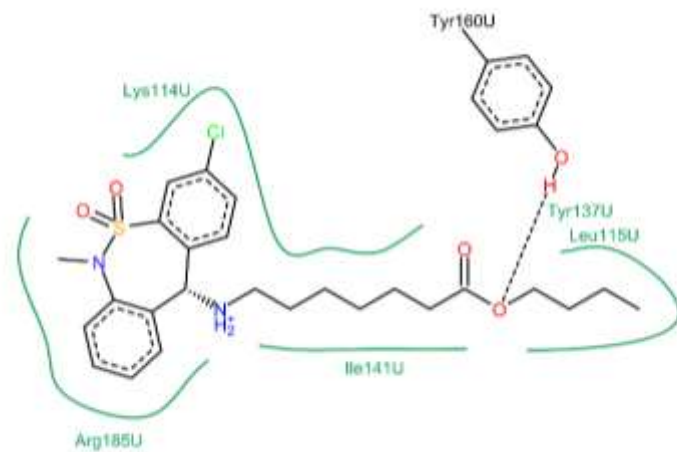


Figure 43. Interactions with BSA amino acids residues near to Trp-134 for protonated ligand **2d**.

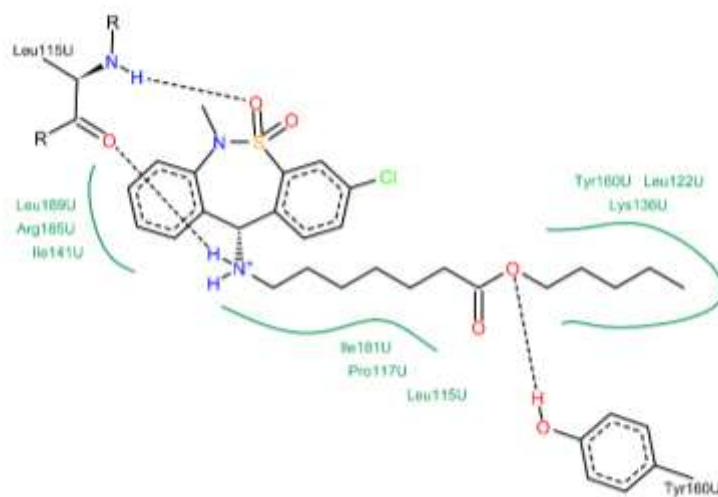


Figure 44. Interactions with BSA amino acids residues near to Trp-134 for protonated ligand **2e**.

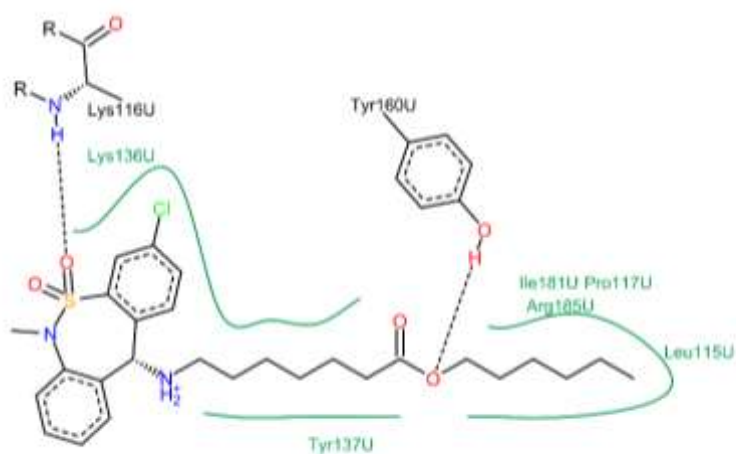


Figure 45. Interactions with BSA amino acids residues near to Trp-134 for protonated ligand **2f**.

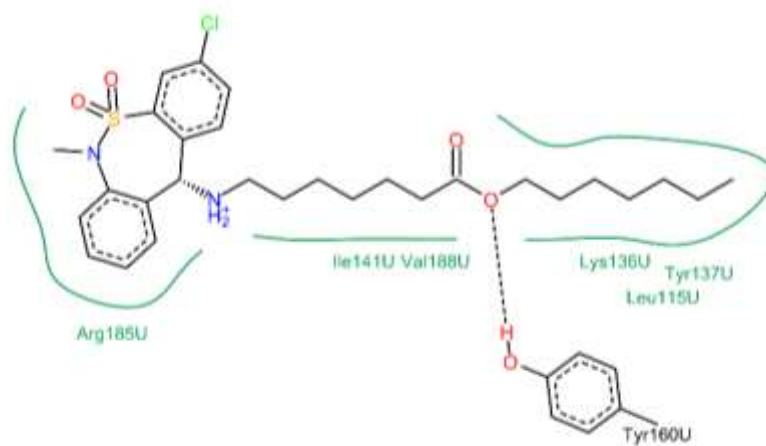


Figure 46. Interactions with BSA amino acids residues near to Trp-134 for protonated ligand **2g**.

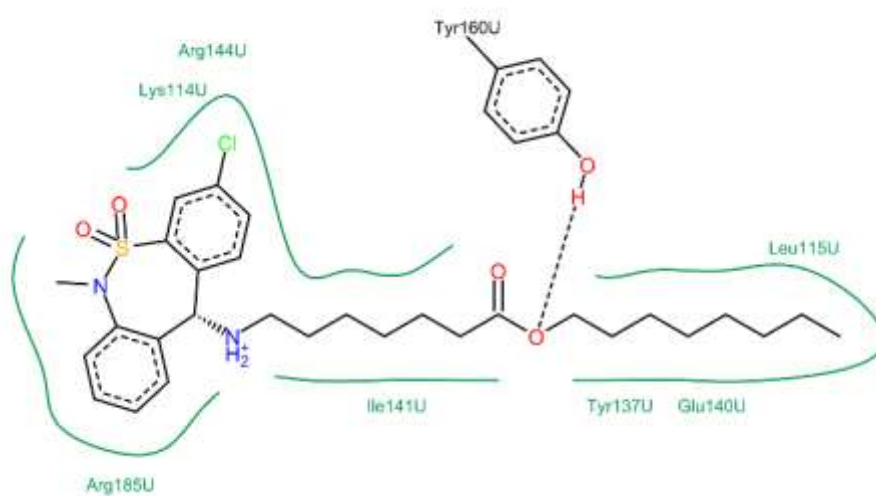


Figure 47. Interactions with BSA amino acids residues near to Trp-134 for protonated ligand **2h**.

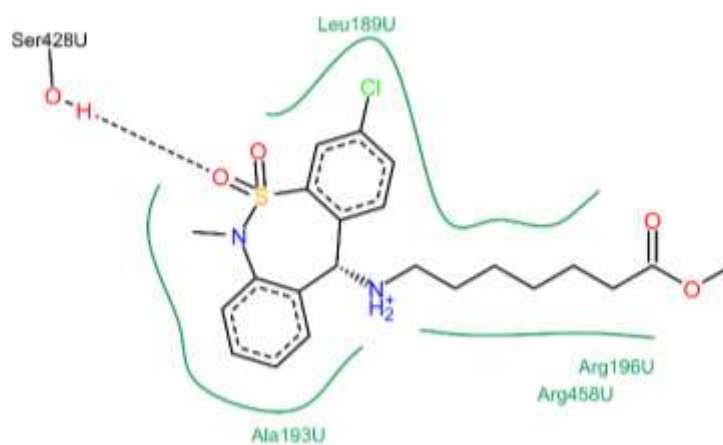


Figure 48. Interactions with BSA amino acids residues near to Trp-213 for protonated ligand **2a**.

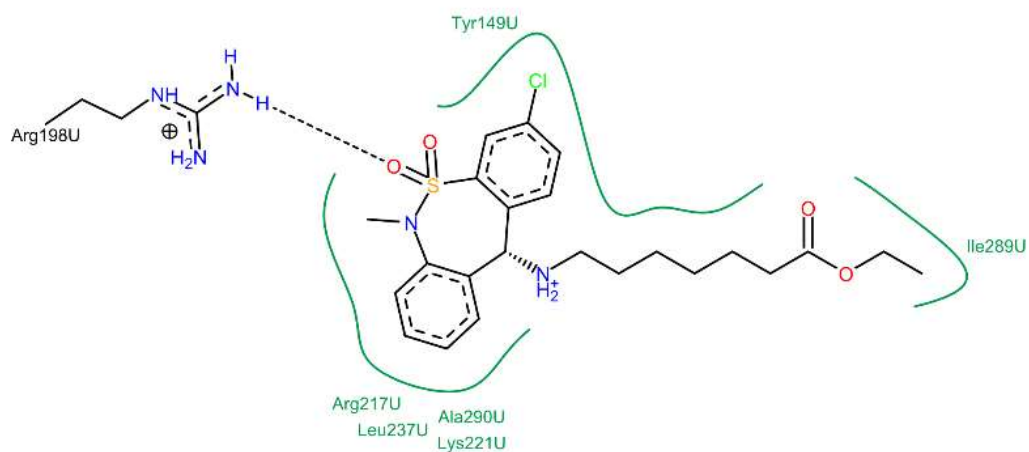


Figure 49. Interactions with BSA amino acids residues near to Trp-213 for protonated ligand **2b**.

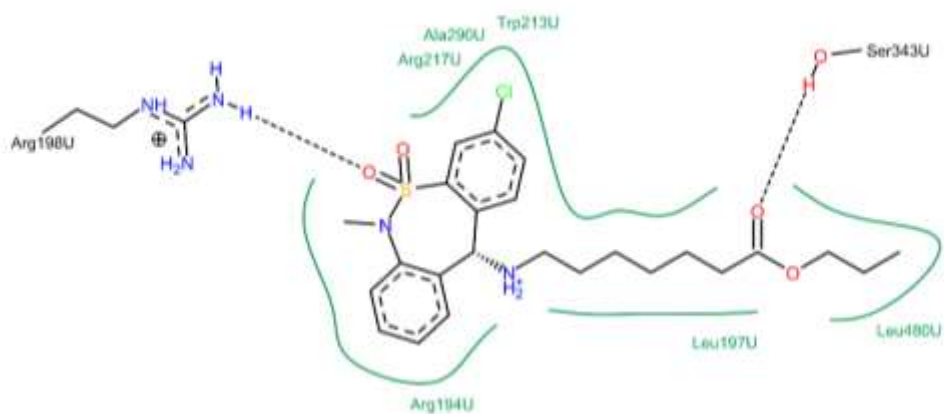


Figure 50. Interactions with BSA amino acids residues near to Trp-213 for protonated ligand **2c**.

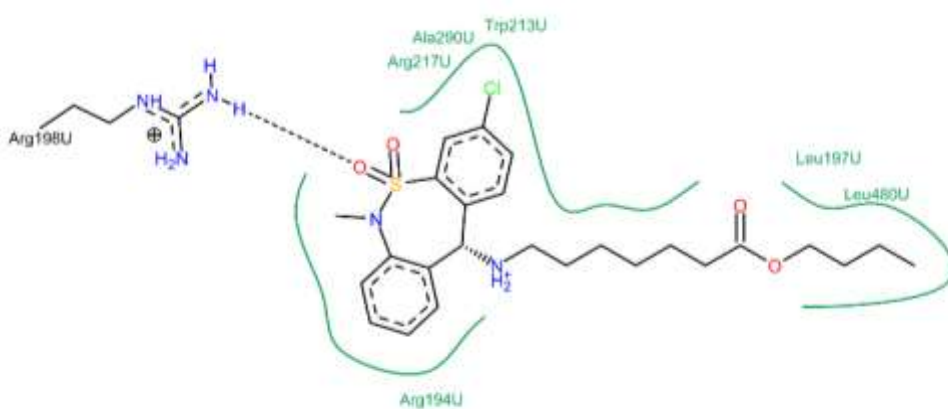


Figure 51. Interactions with BSA amino acids residues near to Trp-213 for protonated ligand **2d**.

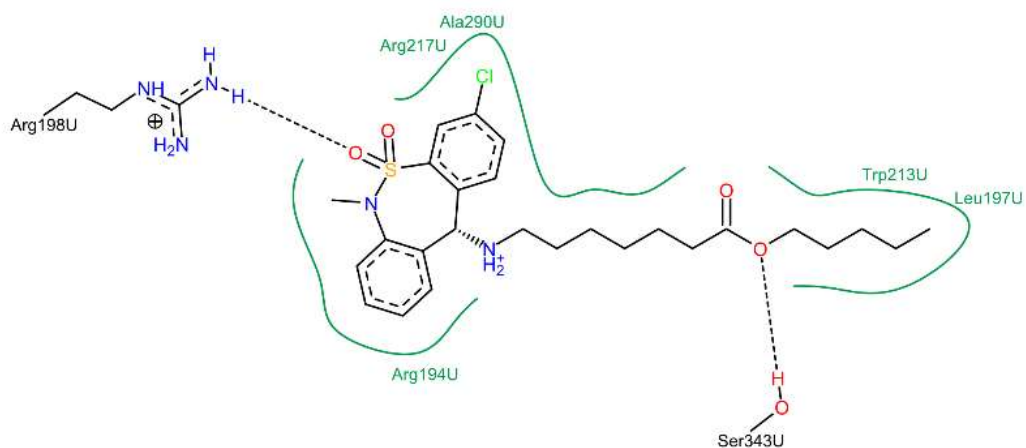


Figure 52. Interactions with BSA amino acids residues near to Trp-213 for protonated ligand 2e.

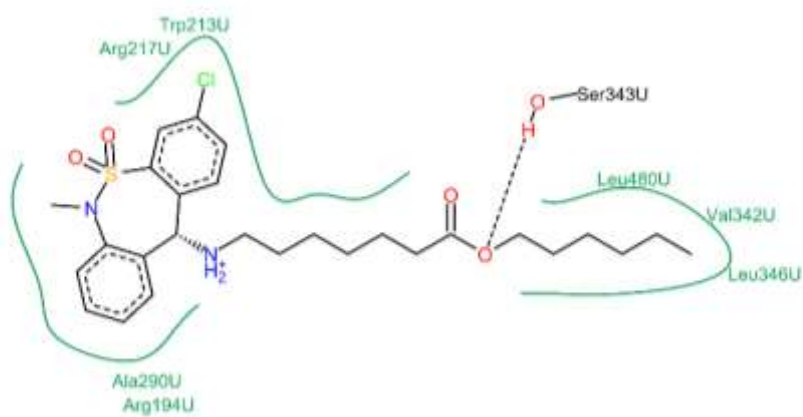


Figure 53. Interactions with BSA amino acids residues near to Trp-213 for protonated ligand 2f.

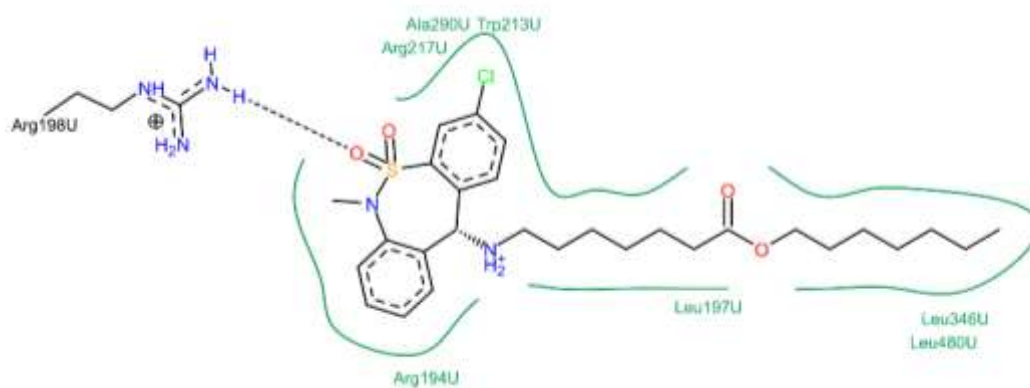


Figure 54. Interactions with amino acids residues near Trp-213 for protonated ligand 2g.

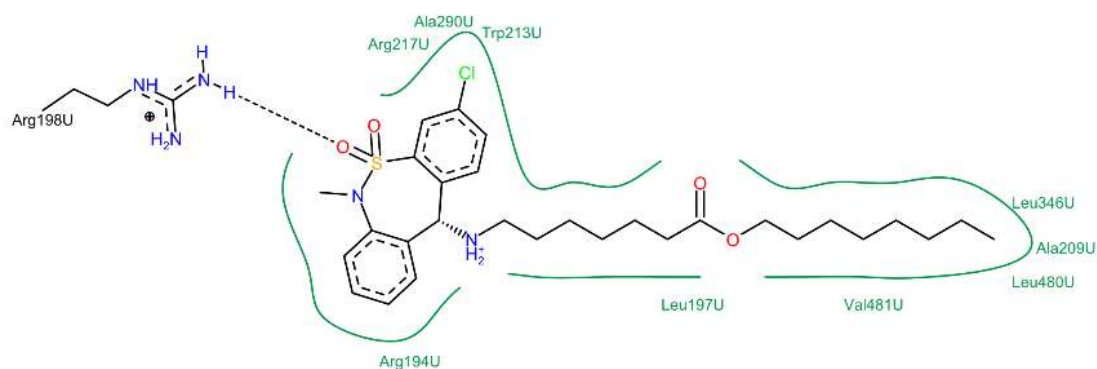


Figure 55. Interactions with amino acids residues near Trp-213 for protonated ligand **2h**.

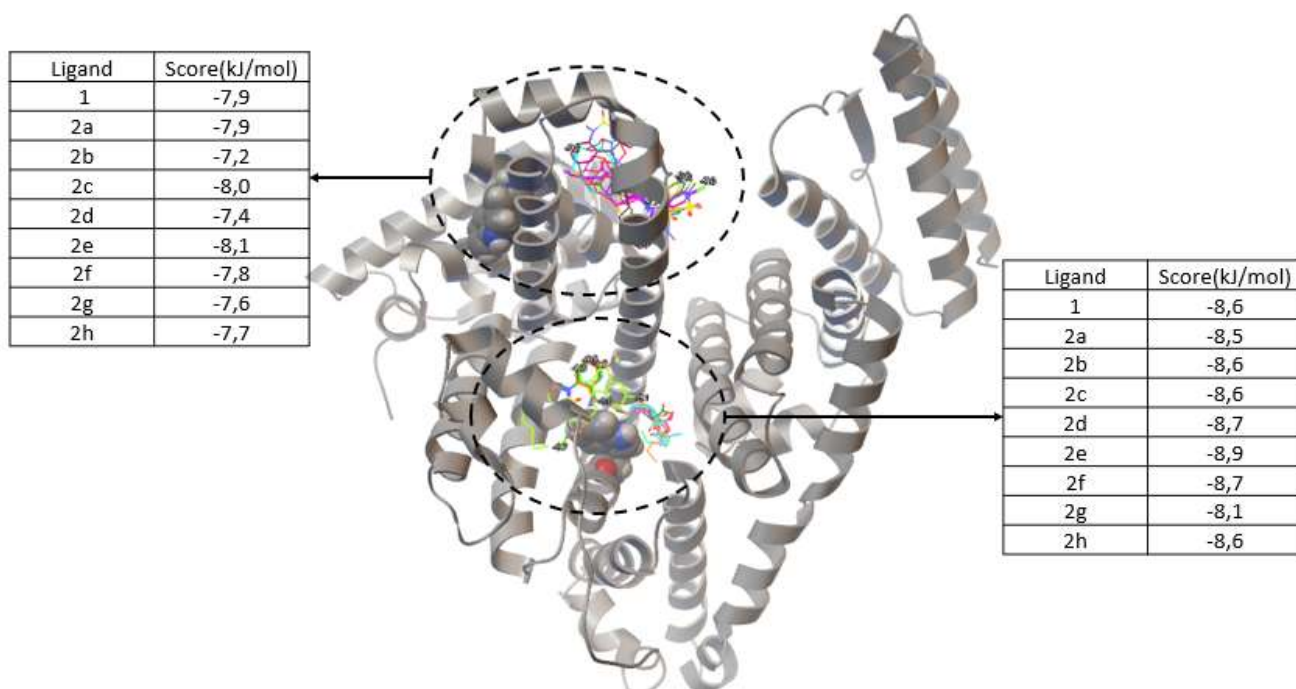


Figure 56. Best ranked docked poses for all molecules in the BSA binding site IB (above) and IIA (below). This figure shows the superposition of all ligand conformations (unprotonated) in their best ranked poses.