

Supporting information for:

### **Inhibitors of 15-Prostaglandin Dehydrogenase to Potentiate Tissue Repair**

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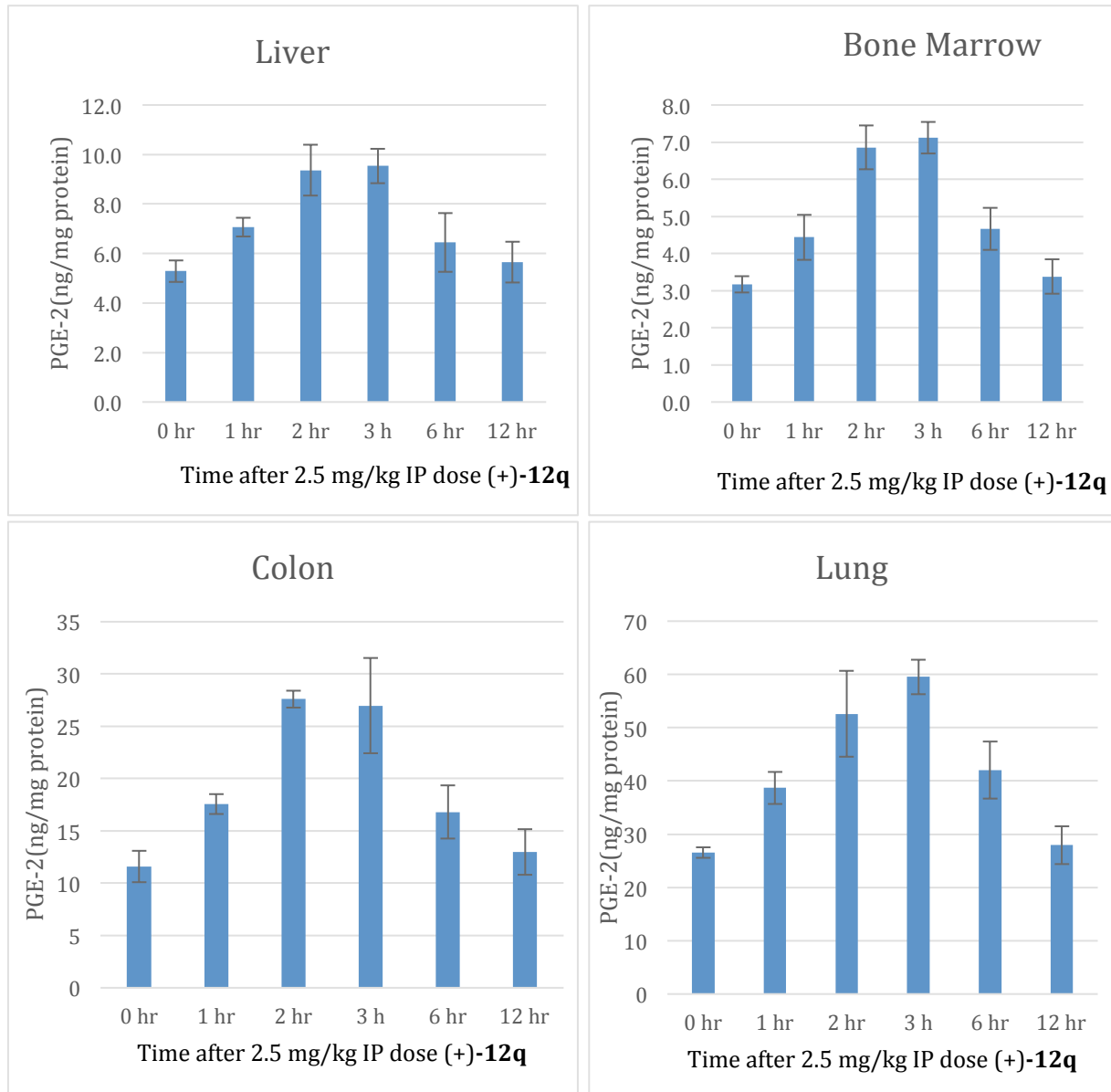
**Table S1. PGE2 induction in IL-1B treated A549 cells**

| Cmpd                                   | PGE 2<br>level, 2.5<br>uM | PGE 2<br>level, 20<br>nM | PGE2<br>level, 2.5<br>uM <b>1</b> | PGE2<br>level, 20<br>nM <b>1</b> | DMSO | + Compound                  |                            | + <b>1</b> (positive<br>control) |                            | adjusted<br>2.5 uM<br>induction | adjusted<br>20 nM<br>induction |
|--|---------------------------|--------------------------|-----------------------------------|----------------------------------|------|-----------------------------|----------------------------|----------------------------------|----------------------------|---------------------------------|--------------------------------|
|  |                           |                          |                                   |                                  |      | fold<br>induction<br>2.5 uM | fold<br>induction<br>20 nM | fold<br>induction<br>2.5 uM      | fold<br>induction<br>20 nM |                                 |                                |
| <b>1</b> (average from 12 experiments) |                           |                          |                                   |                                  |      |                             |                            |                                  |                            | 2.72                            | 1.9                            |
| From Table 1                           |                           |                          |                                   |                                  |      |                             |                            |                                  |                            |                                 |                                |
| <b>(R)-1</b>                           | 2634                      | 1622                     | 2483                              | 1562                             | 1175 | 2.24                        | 1.38                       | 2.11                             | 1.33                       | 2.885                           | 1.973                          |
| <b>(S)-1</b>                           | 1524                      | 1246                     | 2483                              | 1562                             | 1175 | 1.30                        | 1.06                       | 2.11                             | 1.33                       | 1.669                           | 1.516                          |
| <b>13a</b>                             | 1546                      | 716                      | 1980                              | 1442                             | 663  | 2.33                        | 1.08                       | 2.99                             | 2.17                       | 2.124                           | 0.943                          |
| <b>12b</b>                             | 1902                      | 1141                     | 1876                              | 1383                             | 823  | 2.31                        | 1.39                       | 2.28                             | 1.68                       | 2.758                           | 1.568                          |
| <b>12c</b>                             | 1689                      | 1256                     | 1876                              | 1383                             | 823  | 2.05                        | 1.53                       | 2.28                             | 1.68                       | 2.449                           | 1.726                          |
| <b>12f</b>                             | 1913                      | 1429                     | 1980                              | 1442                             | 663  | 2.89                        | 2.16                       | 2.99                             | 2.17                       | 2.628                           | 1.883                          |
| <b>16a</b>                             | 1059                      | 869                      | 1980                              | 1442                             | 663  | 1.60                        | 1.31                       | 2.99                             | 2.17                       | 1.455                           | 1.145                          |
| <b>16b</b>                             | 1772                      | 1467                     | 2268                              | 1555                             | 920  | 1.93                        | 1.59                       | 2.47                             | 1.69                       | 2.125                           | 1.792                          |
| <b>16c</b>                             | 1799                      | 1015                     | 2268                              | 1555                             | 920  | 1.96                        | 1.10                       | 2.47                             | 1.69                       | 2.158                           | 1.240                          |
| <b>16d</b>                             | 2268                      | 1355                     | 2268                              | 1555                             | 920  | 2.47                        | 1.47                       | 2.47                             | 1.69                       | 2.720                           | 1.656                          |
| From Table 2                           |                           |                          |                                   |                                  |      |                             |                            |                                  |                            |                                 |                                |
| <b>12g</b>                             | 1754                      | 1254                     | 1876                              | 1383                             | 823  | 2.13                        | 1.52                       | 2.28                             | 1.68                       | 2.543                           | 1.723                          |
| <b>12h</b>                             | 2068                      | 1888                     | 2370                              | 1910                             | 839  | 2.46                        | 2.25                       | 2.82                             | 2.28                       | 2.373                           | 1.878                          |
| <b>12i</b>                             | 3273                      | 1991                     | 3443                              | 2672                             | 951  | 3.44                        | 2.09                       | 3.62                             | 2.81                       | 2.586                           | 1.416                          |
| From Table 3                           |                           |                          |                                   |                                  |      |                             |                            |                                  |                            |                                 |                                |
| <b>21a</b>                             | 2061                      | 1653                     | 2603                              | 1862                             | 1220 | 1.69                        | 1.35                       | 2.13                             | 1.53                       | 2.154                           | 1.687                          |
| <b>21b</b>                             | 2086                      | 1576                     | 2603                              | 1862                             | 1220 | 1.71                        | 1.29                       | 2.13                             | 1.53                       | 2.180                           | 1.608                          |
| <b>22a</b>                             | 1963                      | 1781                     | 2603                              | 1862                             | 1220 | 1.61                        | 1.46                       | 2.13                             | 1.53                       | 2.051                           | 1.817                          |
| <b>23a</b>                             | 2665                      | 1658                     | 2609                              | 1406                             | 920  | 2.90                        | 1.80                       | 2.84                             | 1.53                       | 2.778                           | 2.241                          |
| <b>23b</b>                             | 1920                      | 1607                     | 1795                              | 1307                             | 971  | 1.98                        | 1.65                       | 1.85                             | 1.35                       | 2.909                           | 2.336                          |
| <b>23c</b>                             | 1651                      | 1107                     | 2268                              | 1555                             | 920  | 1.79                        | 1.20                       | 2.47                             | 1.69                       | 1.980                           | 1.353                          |
| <b>25</b>                              | 1525                      | 1320                     | 2296                              | 1527                             | 1062 | 1.44                        | 1.24                       | 2.16                             | 1.44                       | 1.807                           | 1.642                          |
| <b>26a</b>                             | 3224                      | 2141                     | 3443                              | 2672                             | 951  | 3.39                        | 2.25                       | 3.62                             | 2.81                       | 2.547                           | 1.522                          |
| <b>26b</b>                             | 1745                      | 1091                     | 2268                              | 1555                             | 920  | 1.90                        | 1.19                       | 2.47                             | 1.69                       | 2.093                           | 1.333                          |
| <b>27a</b>                             | 1282                      | 946                      | 1980                              | 1442                             | 663  | 1.93                        | 1.43                       | 2.99                             | 2.17                       | 1.761                           | 1.246                          |
| <b>28a</b>                             | 1303                      | 717                      | 1980                              | 1442                             | 663  | 1.97                        | 1.08                       | 2.99                             | 2.17                       | 1.790                           | 0.945                          |
| <b>28b</b>                             | 1650                      | 1007                     | 2268                              | 1555                             | 920  | 1.79                        | 1.09                       | 2.47                             | 1.69                       | 1.979                           | 1.230                          |
| <b>28c</b>                             | 1838                      | 1191                     | 1795                              | 1307                             | 971  | 1.89                        | 1.23                       | 1.85                             | 1.35                       | 2.785                           | 1.731                          |
| <b>30</b>                              | 1996                      | 1407                     | 2296                              | 1527                             | 1062 | 1.88                        | 1.32                       | 2.16                             | 1.44                       | 2.365                           | 1.751                          |
| <b>31</b>                              | 2223                      | 1598                     | 2603                              | 1862                             | 1220 | 1.82                        | 1.31                       | 2.13                             | 1.53                       | 2.323                           | 1.631                          |
| <b>(+)-32</b>                          | 1920                      | 1555                     | 1876                              | 1383                             | 823  | 2.33                        | 1.89                       | 2.28                             | 1.68                       | 2.784                           | 2.136                          |

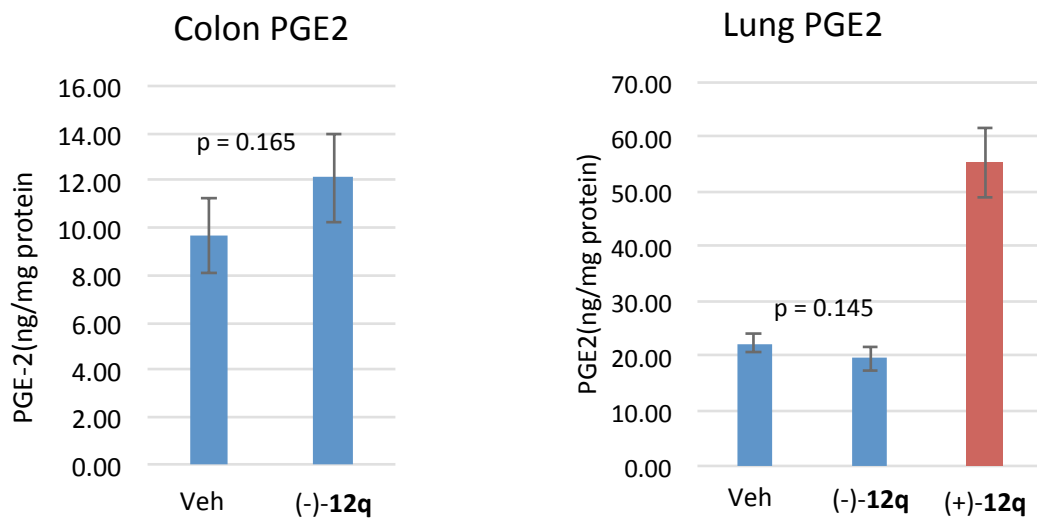
Table S1 continued.

| Cmpd                            | PGE 2<br>level, 2.5<br>uM | PGE 2<br>level, 20<br>nM | PGE2<br>level, 2.5<br>uM | PGE2<br>level, 20<br>nM | DMSO | + Compound                  |                            | + 1 (positive<br>control)   |                            | adjusted<br>2.5 uM<br>induction | adjusted<br>20 nM<br>induction |
|---------------------------------|---------------------------|--------------------------|--------------------------|-------------------------|------|-----------------------------|----------------------------|-----------------------------|----------------------------|---------------------------------|--------------------------------|
|                                 |                           |                          |                          |                         |      | fold<br>induction<br>2.5 uM | fold<br>induction<br>20 nM | fold<br>induction<br>2.5 uM | fold<br>induction<br>20 nM |                                 |                                |
| 1 (average from 12 experiments) |                           |                          |                          |                         |      |                             |                            |                             |                            | 2.72                            | 1.9                            |
| From Table 4                    |                           |                          |                          |                         |      |                             |                            |                             |                            |                                 |                                |
| <b>12j</b>                      | 1574                      | 1181                     | 1876                     | 1383                    | 823  | 1.91                        | 1.43                       | 2.28                        | 1.68                       | 2.282                           | 1.622                          |
| <b>38c</b>                      | 2667                      | 1917                     | 3895                     | 2408                    | 851  | 3.13                        | 2.25                       | 4.58                        | 2.83                       | 1.862                           | 1.513                          |
| <b>12k</b>                      | 3450                      | 2516                     | 3822                     | 3121                    | 1393 | 2.48                        | 1.81                       | 2.74                        | 2.24                       | 2.455                           | 1.532                          |
| <b>12m</b>                      | 1469                      | 583                      | 1980                     | 1442                    | 663  | 2.22                        | 0.88                       | 2.99                        | 2.17                       | 2.018                           | 0.768                          |
| <b>12n</b>                      | 4480                      | 3600                     | 3443                     | 2672                    | 951  | 4.71                        | 3.79                       | 3.62                        | 2.81                       | 3.539                           | 2.560                          |
| <b>12o</b>                      | 3591                      | 2777                     | 3822                     | 3121                    | 1393 | 2.58                        | 1.99                       | 2.74                        | 2.24                       | 2.556                           | 1.691                          |
| <b>12p</b>                      | 4059                      | 3609                     | 3443                     | 2672                    | 951  | 4.27                        | 3.79                       | 3.62                        | 2.81                       | 3.207                           | 2.566                          |
| <i>(R)</i> - <b>12q</b>         | 2584                      | 1726                     | 2483                     | 1562                    | 1175 | 2.20                        | 1.47                       | 2.11                        | 1.33                       | 2.831                           | 2.099                          |
| <i>(S)</i> - <b>12q</b>         | 1628                      | 1276                     | 2483                     | 1562                    | 1175 | 1.39                        | 1.09                       | 2.11                        | 1.33                       | 1.783                           | 1.552                          |
| <b>12r</b>                      | 1570                      | 1017                     | 1795                     | 1307                    | 971  | 1.62                        | 1.05                       | 1.85                        | 1.35                       | 2.379                           | 1.478                          |
| <i>(+)</i> - <b>12s</b>         | 1959                      | 1497                     | 1876                     | 1383                    | 823  | 2.38                        | 1.82                       | 2.28                        | 1.68                       | 2.840                           | 2.057                          |
| <b>12t</b>                      | 2302                      | 1413                     | 2603                     | 1862                    | 1220 | 1.89                        | 1.16                       | 2.13                        | 1.53                       | 2.405                           | 1.442                          |
| <b>12u</b>                      | 2112                      | 1018                     | 2609                     | 1406                    | 920  | 2.30                        | 1.11                       | 2.84                        | 1.53                       | 2.202                           | 1.376                          |
| From Table 5                    |                           |                          |                          |                         |      |                             |                            |                             |                            |                                 |                                |
| <b>44a</b>                      | 1702                      | 1295                     | 1876                     | 1383                    | 823  | 2.07                        | 1.57                       | 2.28                        | 1.68                       | 2.468                           | 1.779                          |
| <b>44c</b>                      | 2076                      | 1555                     | 1876                     | 1383                    | 823  | 2.52                        | 1.89                       | 2.28                        | 1.68                       | 3.010                           | 2.136                          |
| <b>44d</b>                      | 2116                      | 1654                     | 1980                     | 1442                    | 663  | 3.19                        | 2.49                       | 2.99                        | 2.17                       | 2.907                           | 2.179                          |
| <b>44e</b>                      | 1558                      | 1203                     | 1980                     | 1442                    | 663  | 2.35                        | 1.81                       | 2.99                        | 2.17                       | 2.140                           | 1.585                          |
| From Scheme 6                   |                           |                          |                          |                         |      |                             |                            |                             |                            |                                 |                                |
| <b>12v</b>                      | 2255                      | 1544                     | 2312                     | 1555                    | 1034 | 2.18                        | 1.49                       | 2.24                        | 1.50                       | 2.653                           | 1.887                          |
| <b>12w</b>                      | 1833                      | 1334                     | 1876                     | 1383                    | 823  | 2.23                        | 1.62                       | 2.28                        | 1.68                       | 2.658                           | 1.833                          |
| <b>12x</b>                      | 1889                      | 1388                     | 1795                     | 1307                    | 971  | 1.95                        | 1.43                       | 1.85                        | 1.35                       | 2.862                           | 2.018                          |

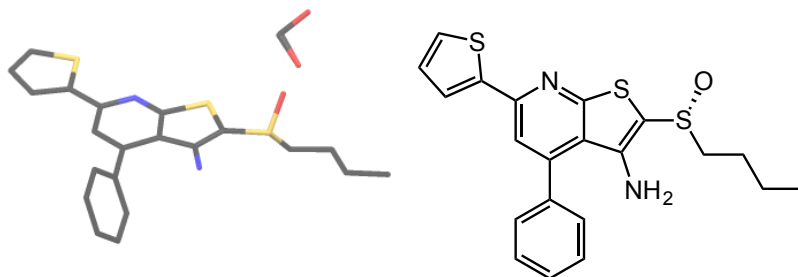
**Figure S1.** Elevation of PGE2 in four tissues following a single IP dose of 2.5 mg/kg body weight (+)-12q. C57BL/6J mice, n=3/time point.



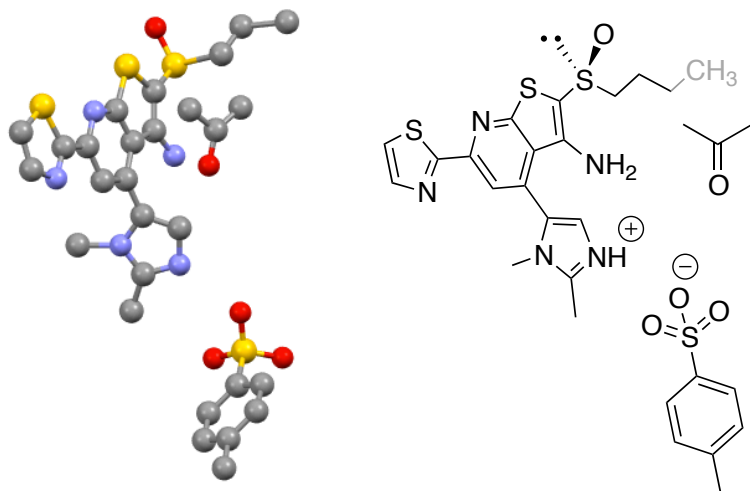
**Figure S2.** (-)-*S*-**12q** does not elevate PGE2 levels in vivo. PGE2 levels were evaluated 3 h after a single IP dose of 5 mg/kg body weight (+)- or (-)-**12q** or vehicle.

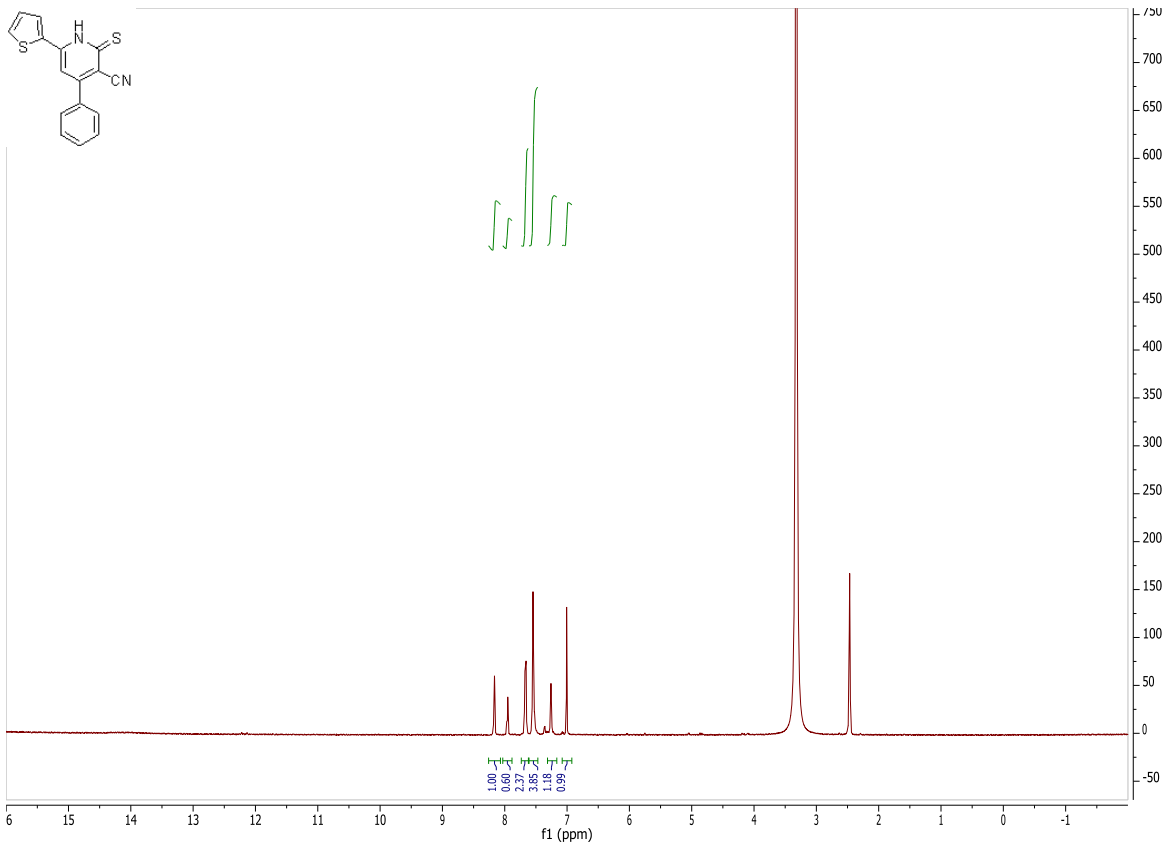
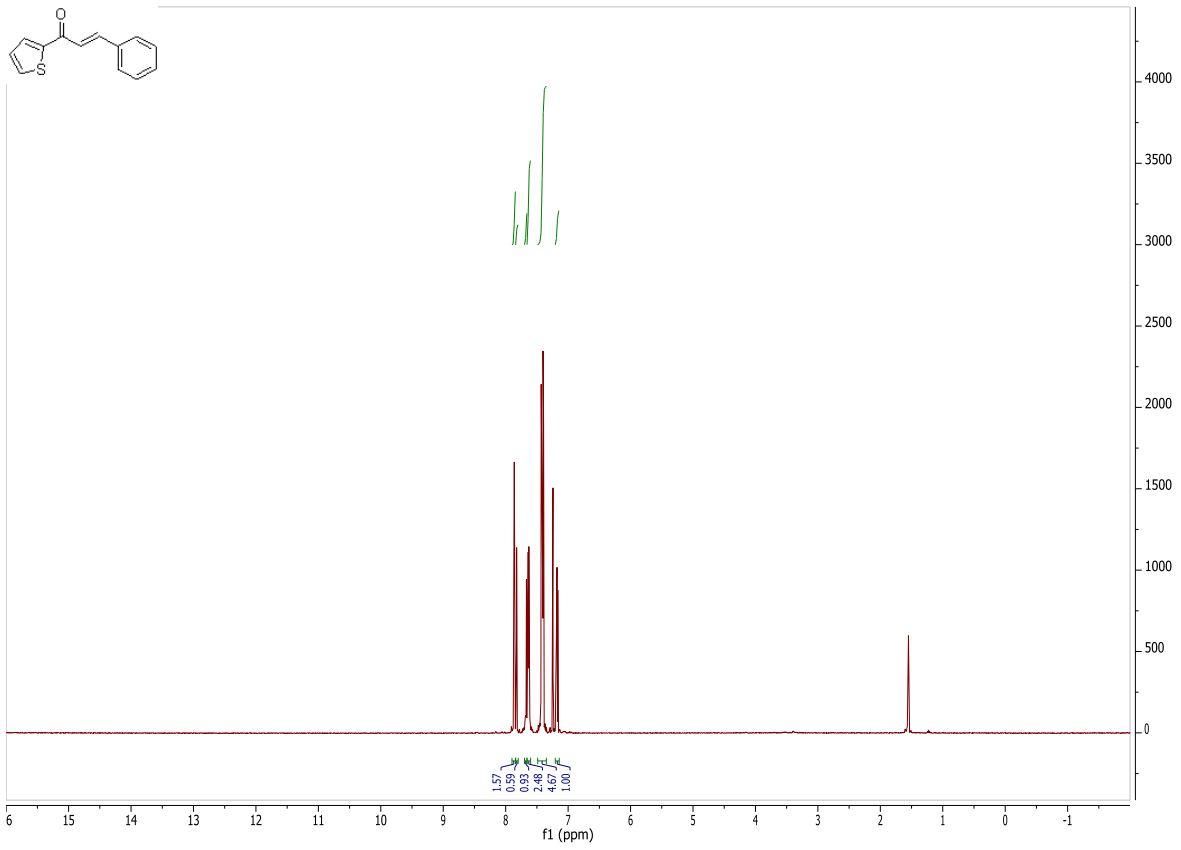


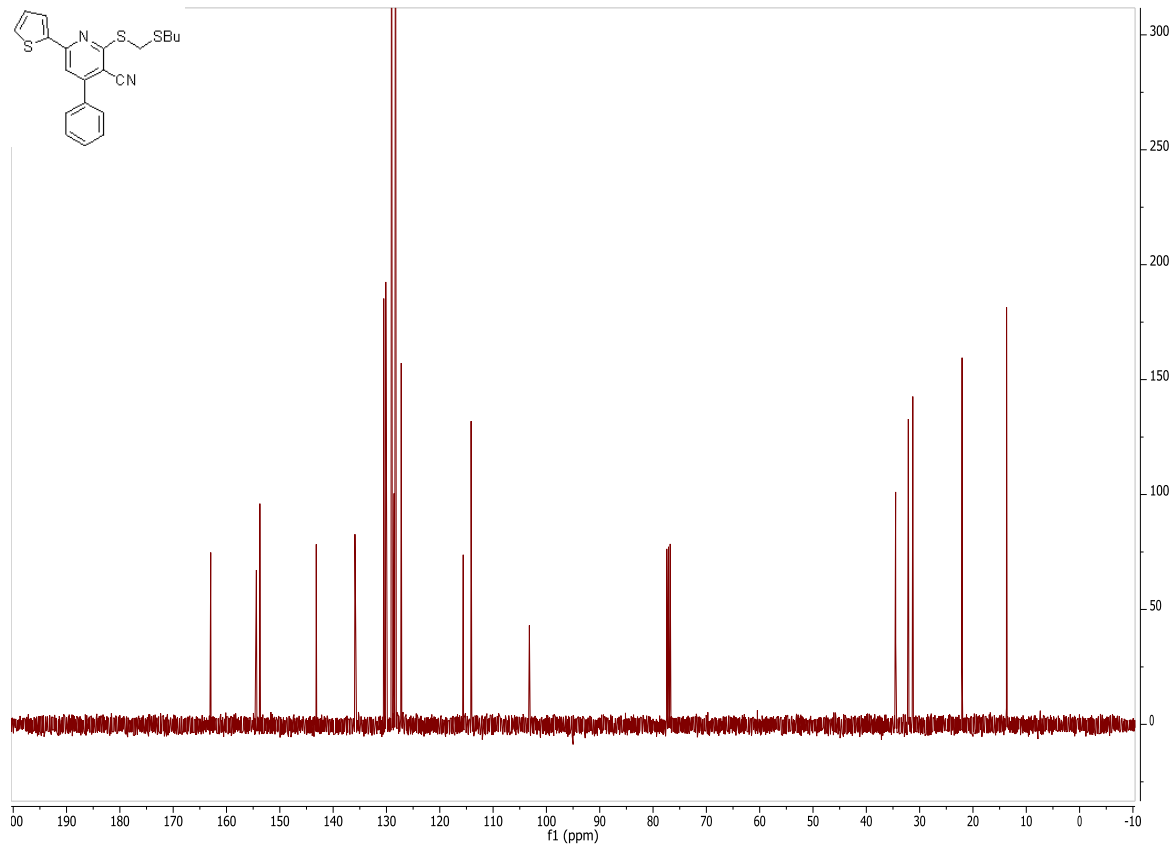
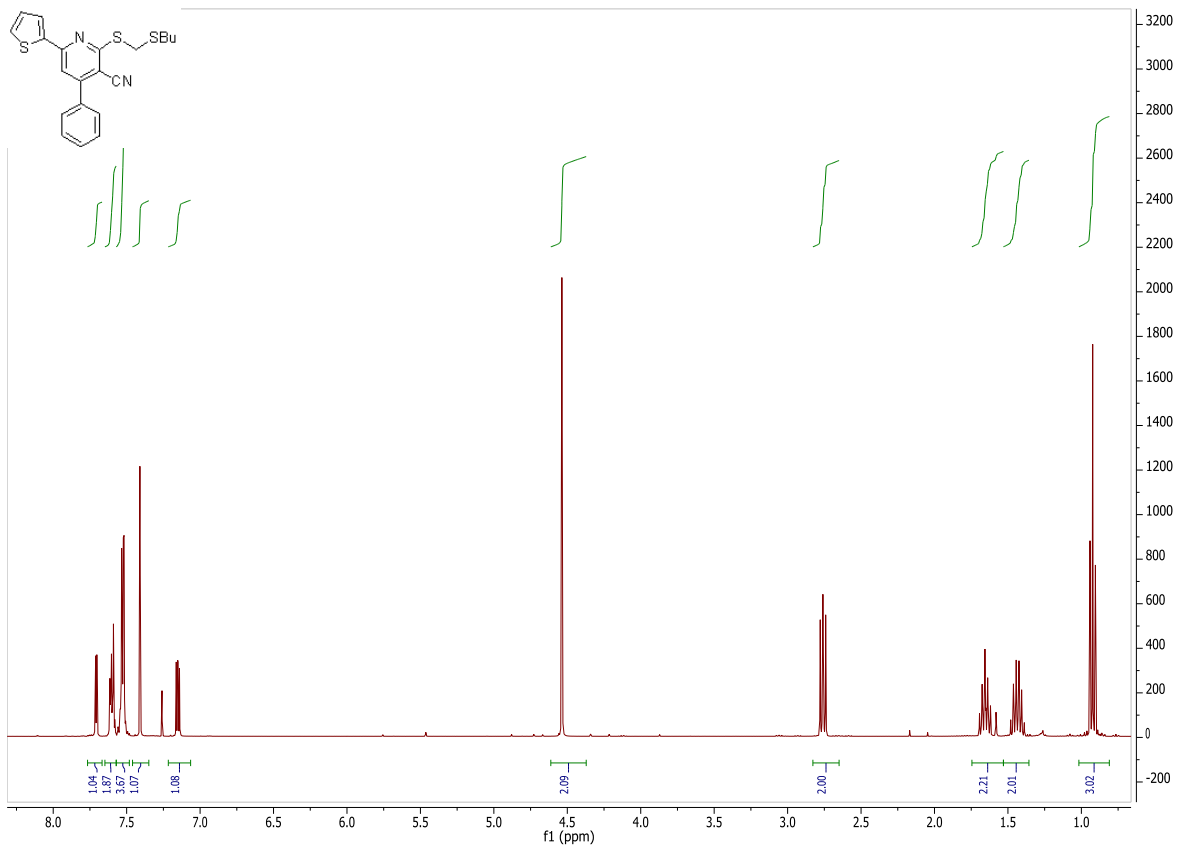
**Figure S3.** X-ray structure of (+)-**1**. A superposition of methanol in two orientations is observed in the unit cell.



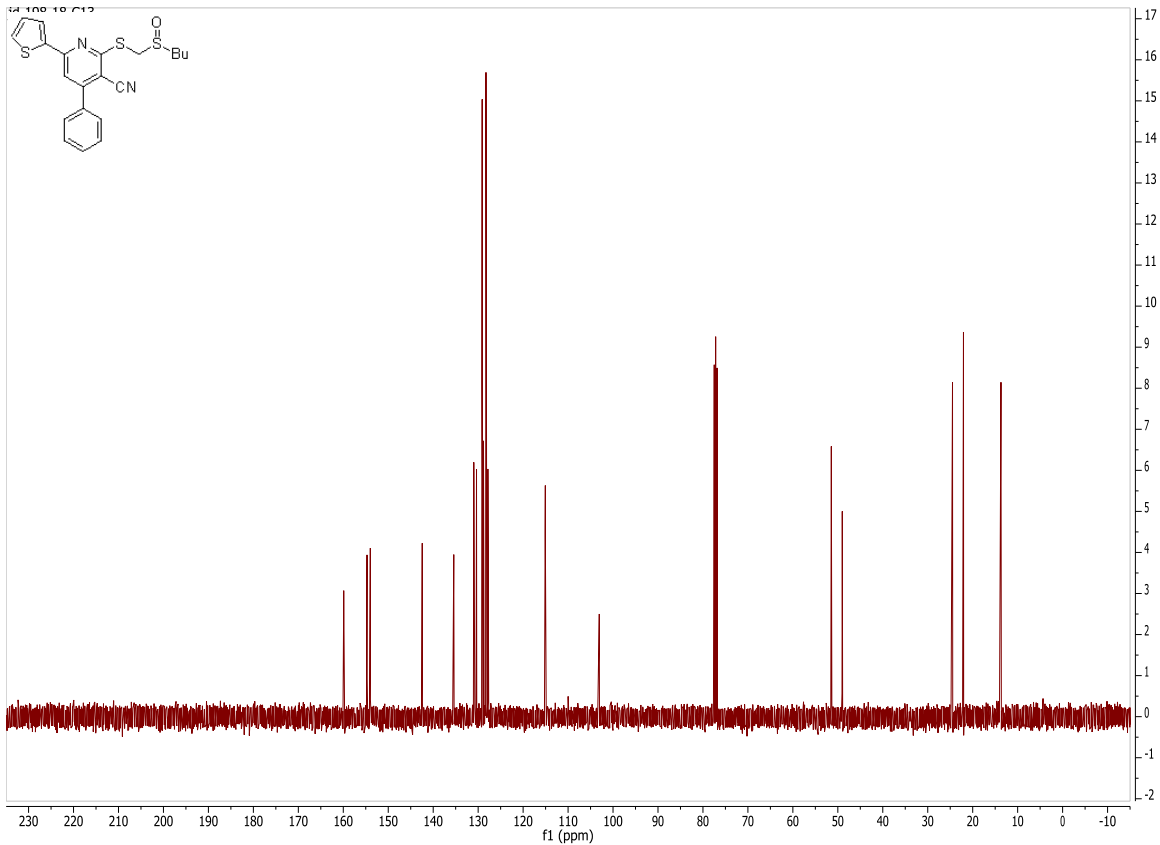
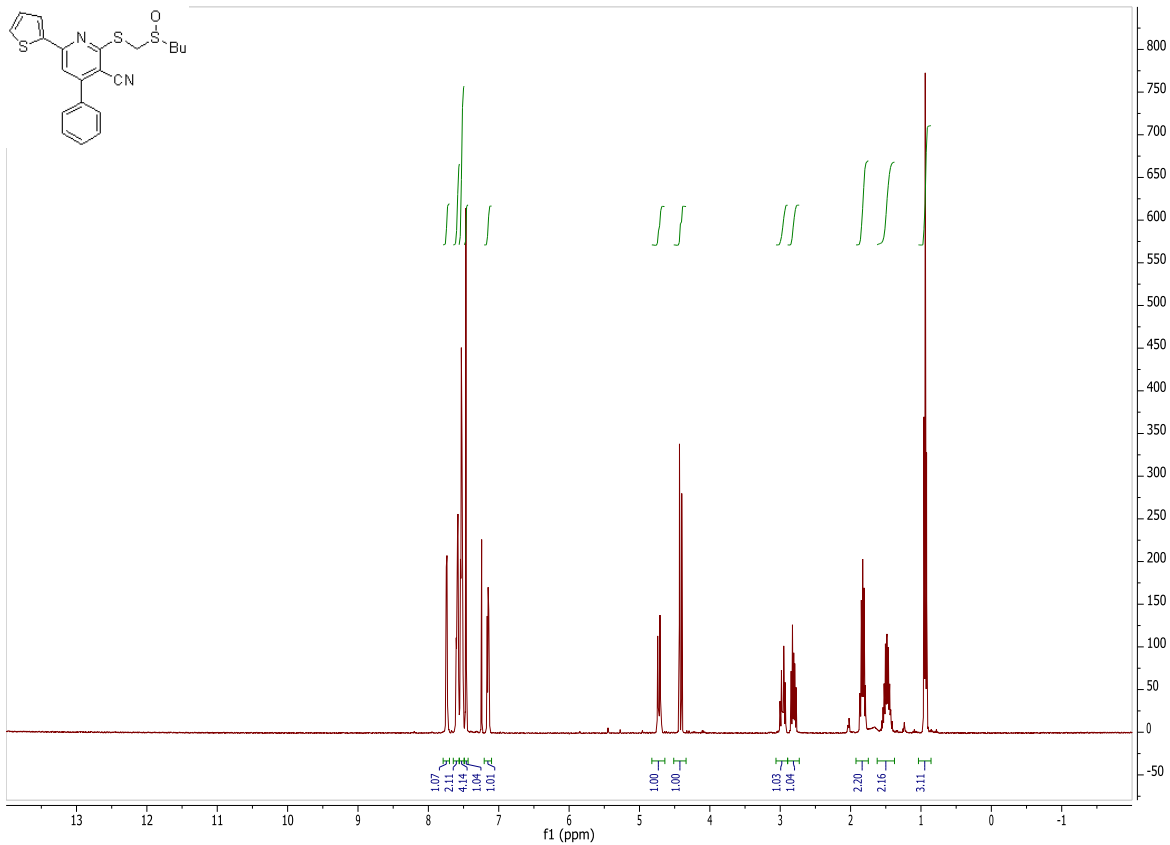
**Figure S4.** X-ray crystal structure of (-)-**12q**·OTs·acetone (less active enantiomer). Terminal carbon of butyl chain disordered.



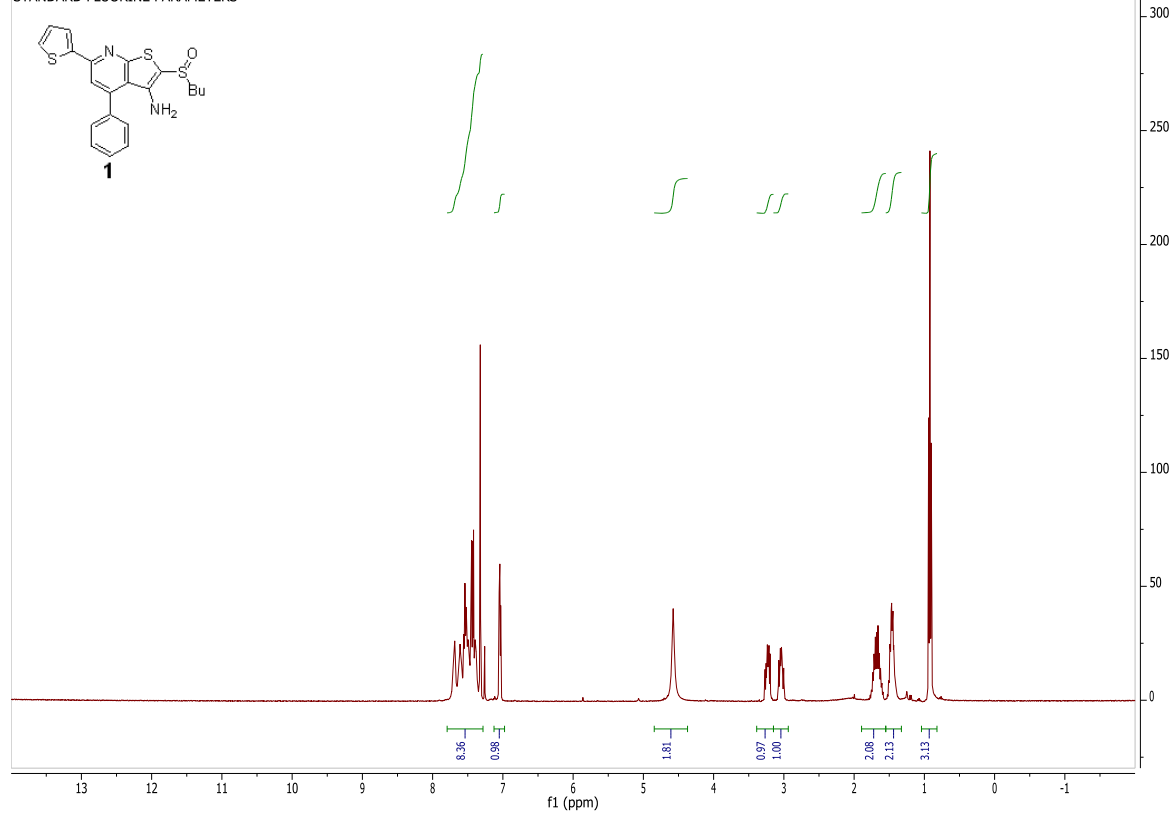




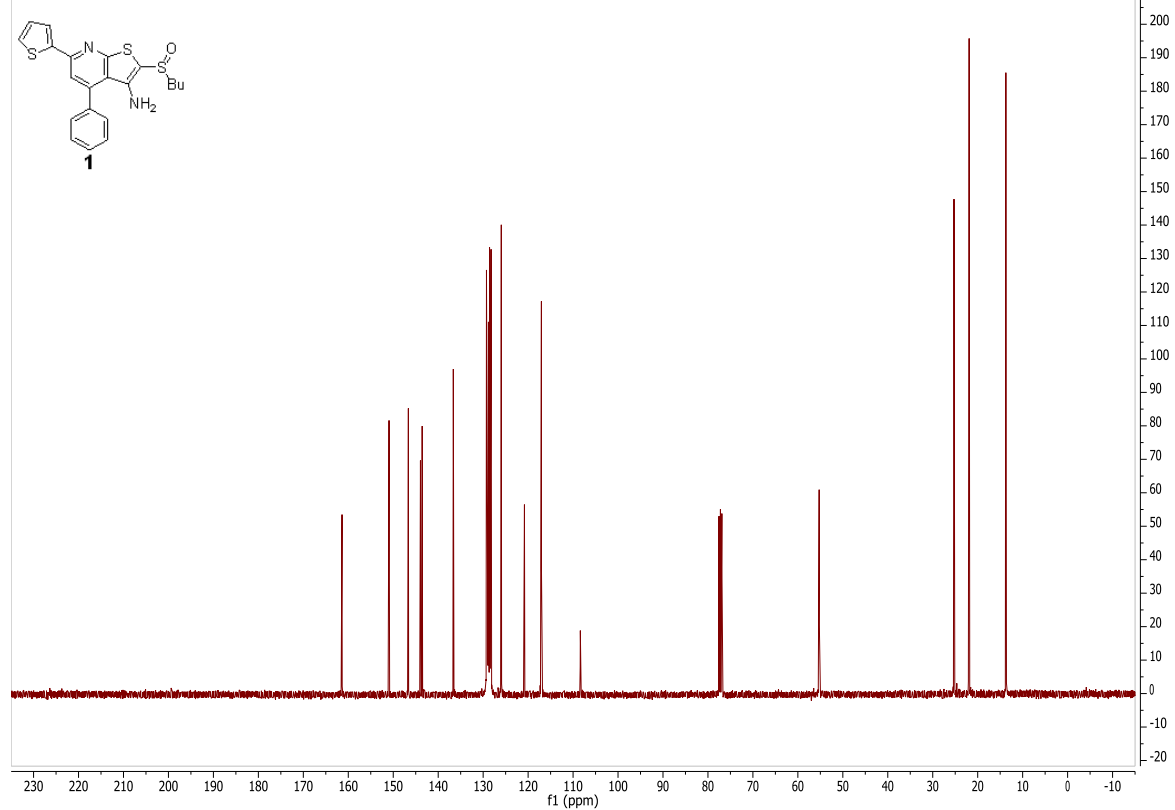


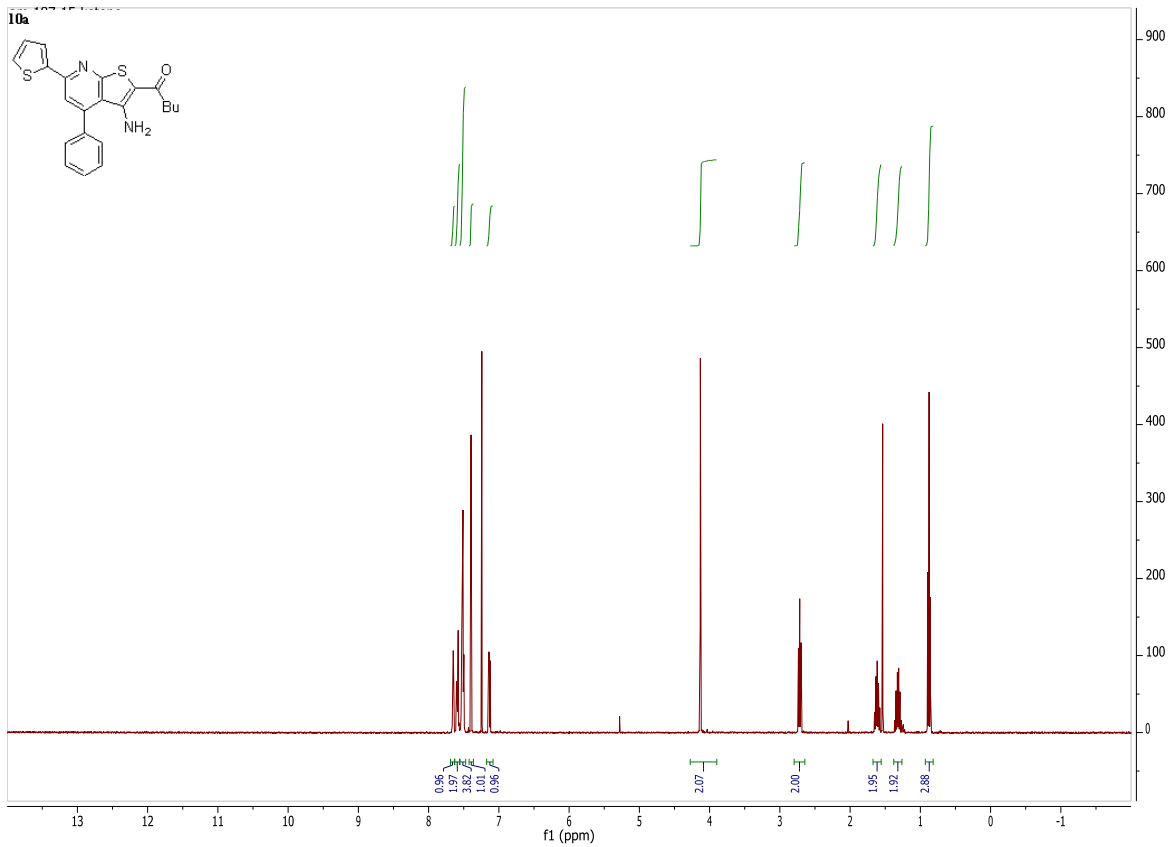
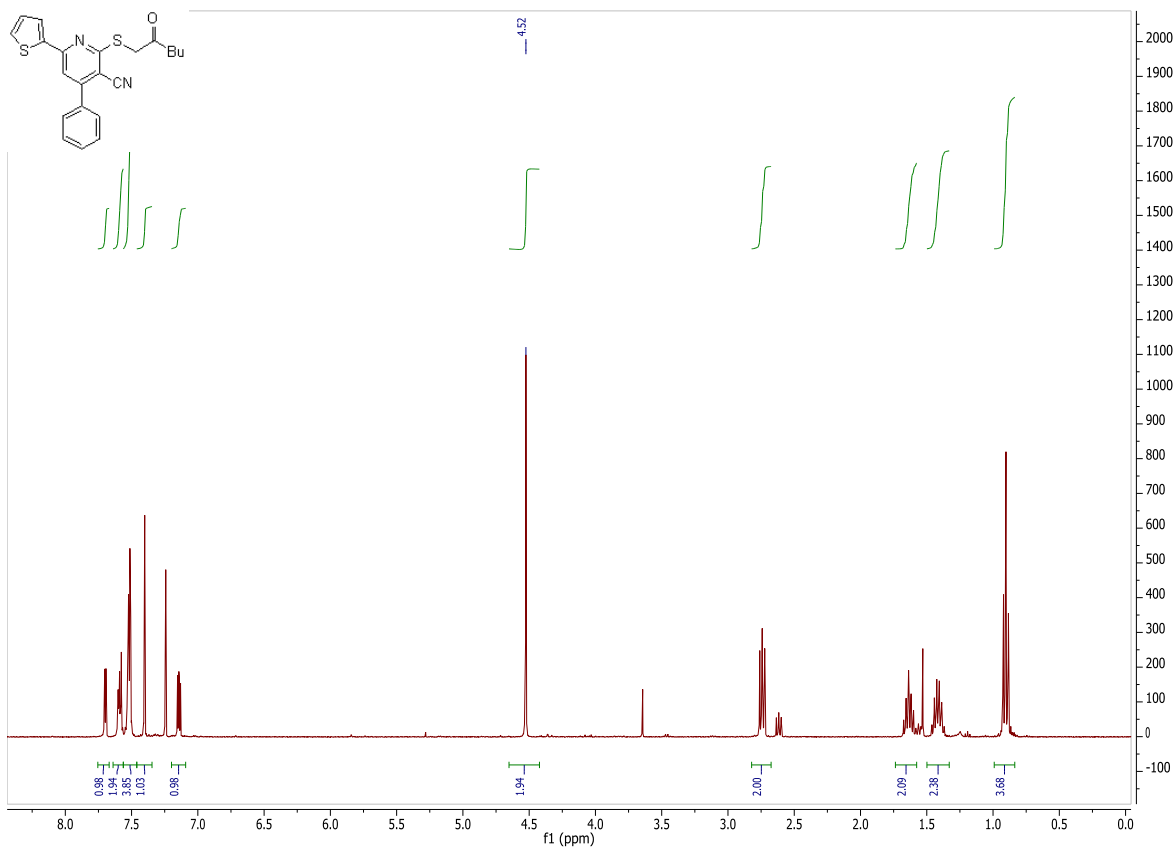


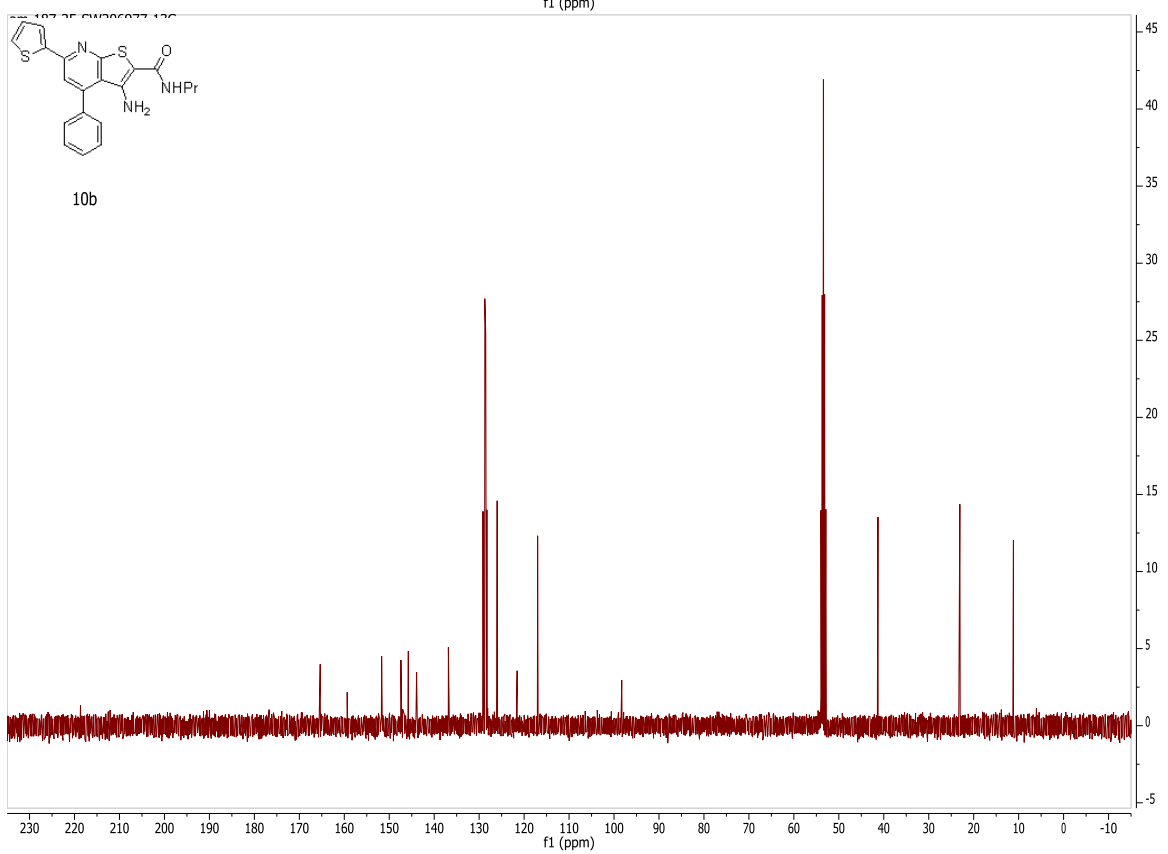
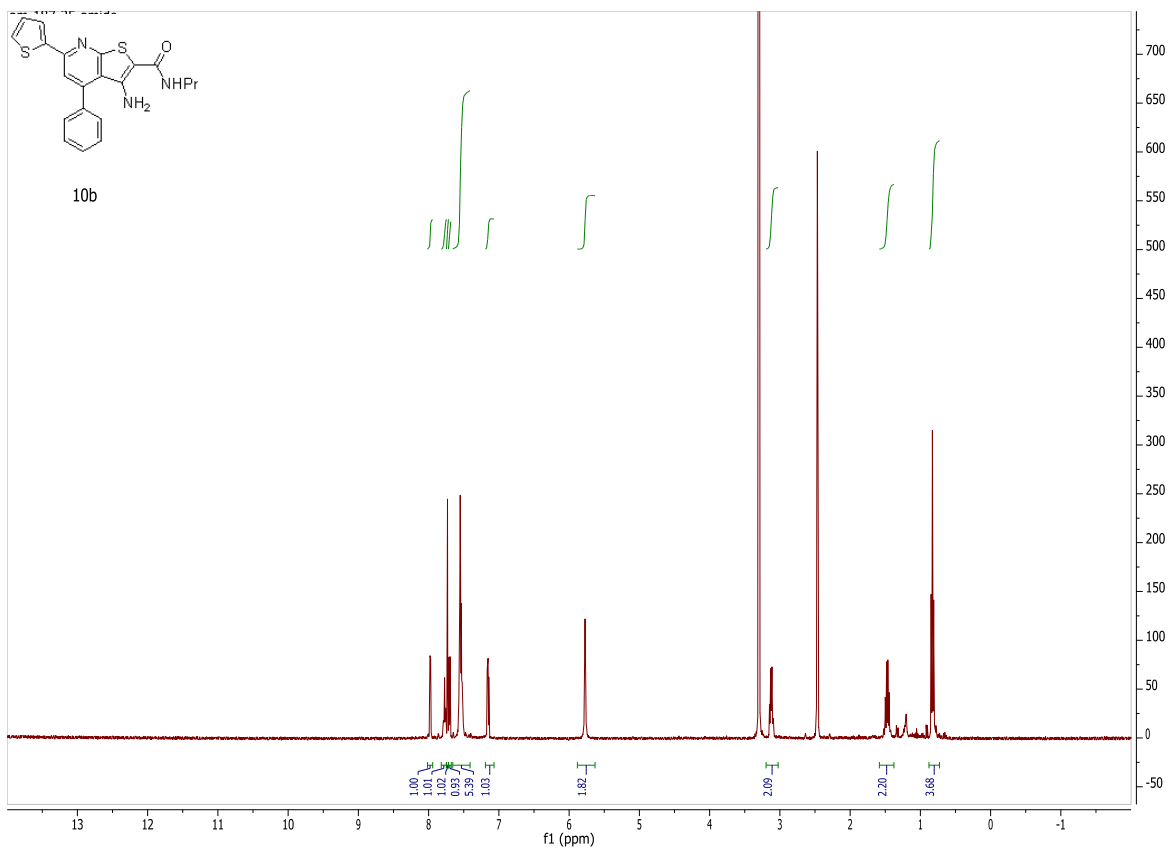
291-H1  
STANDARD FLUORINE PARAMETERS

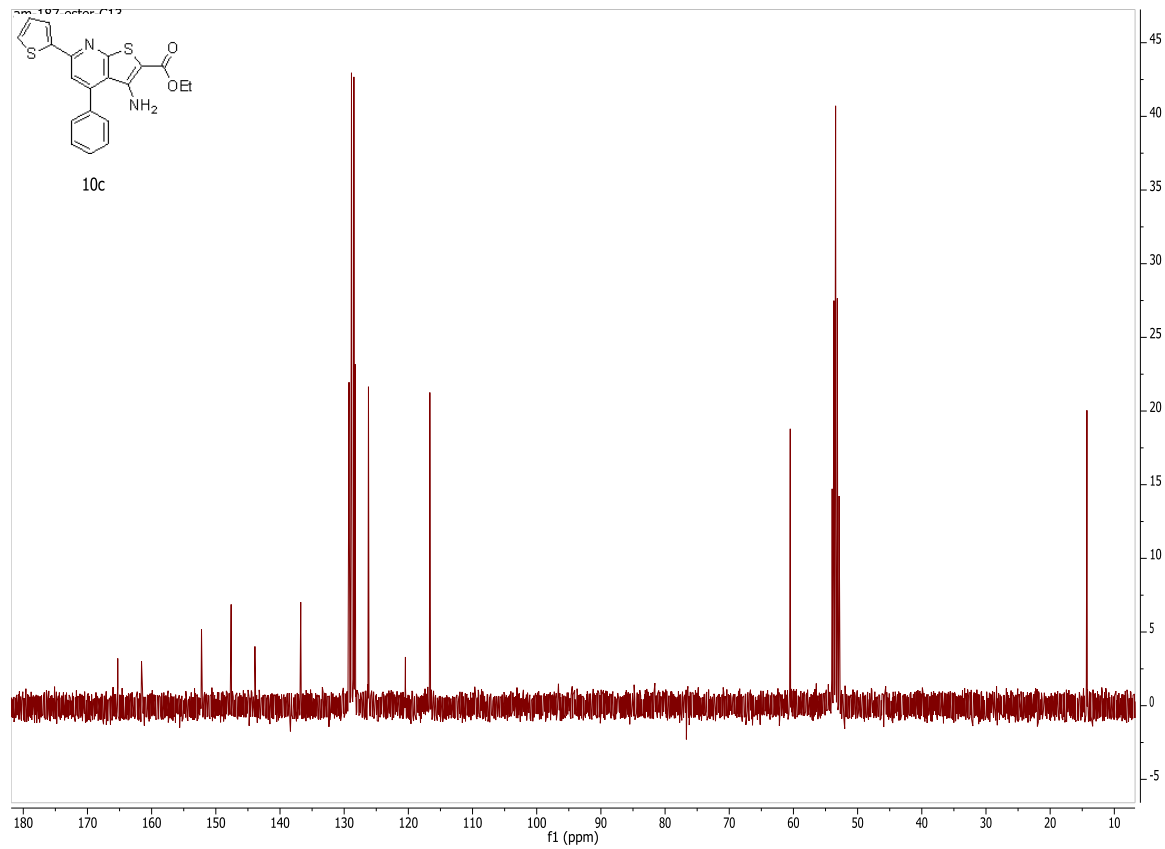
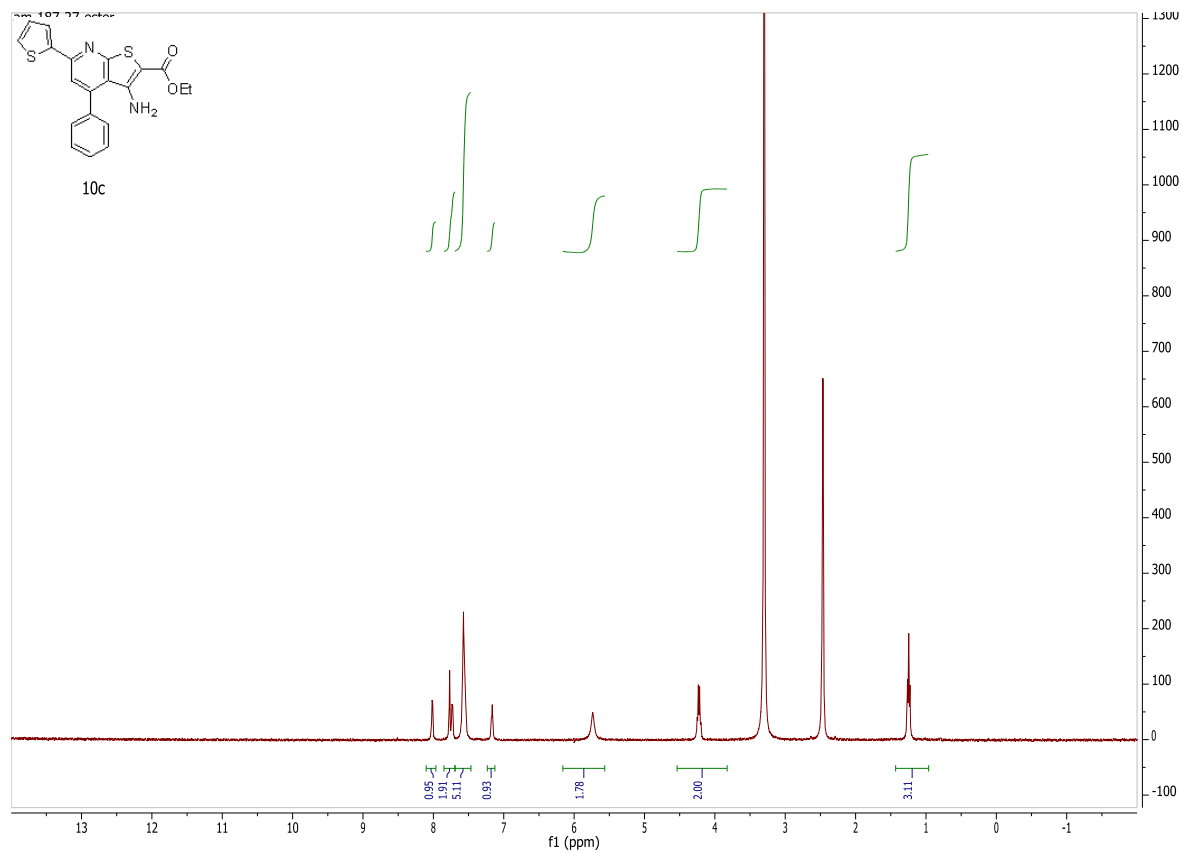


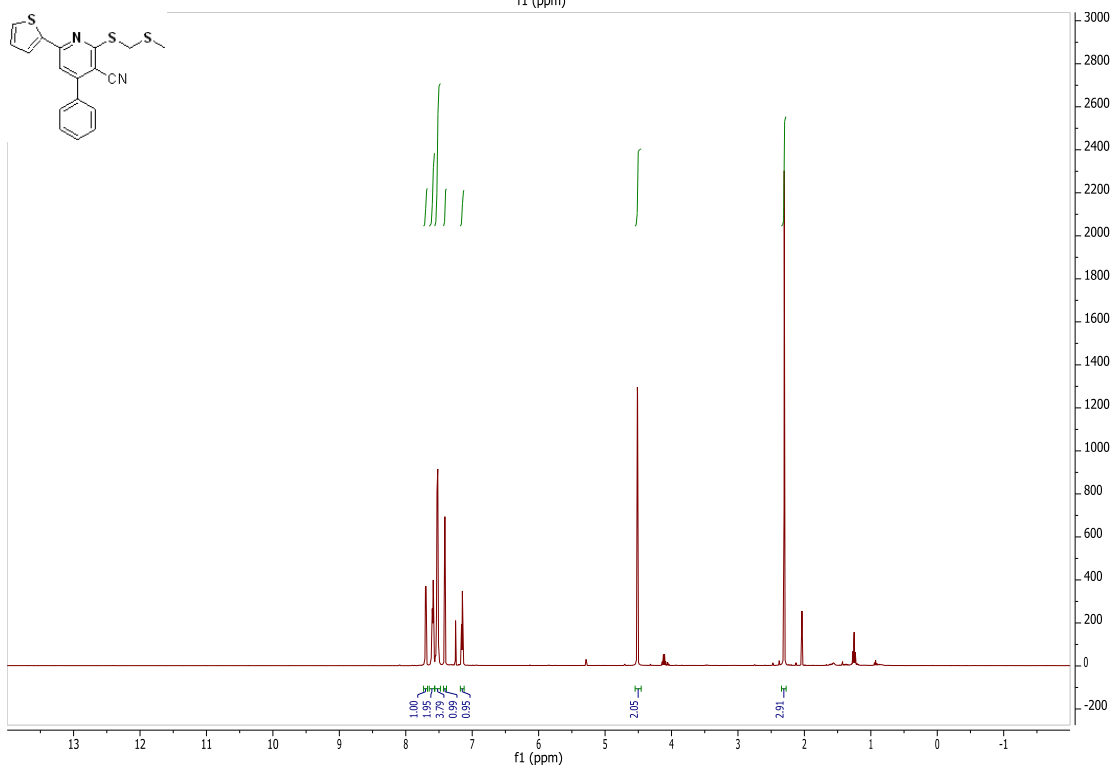
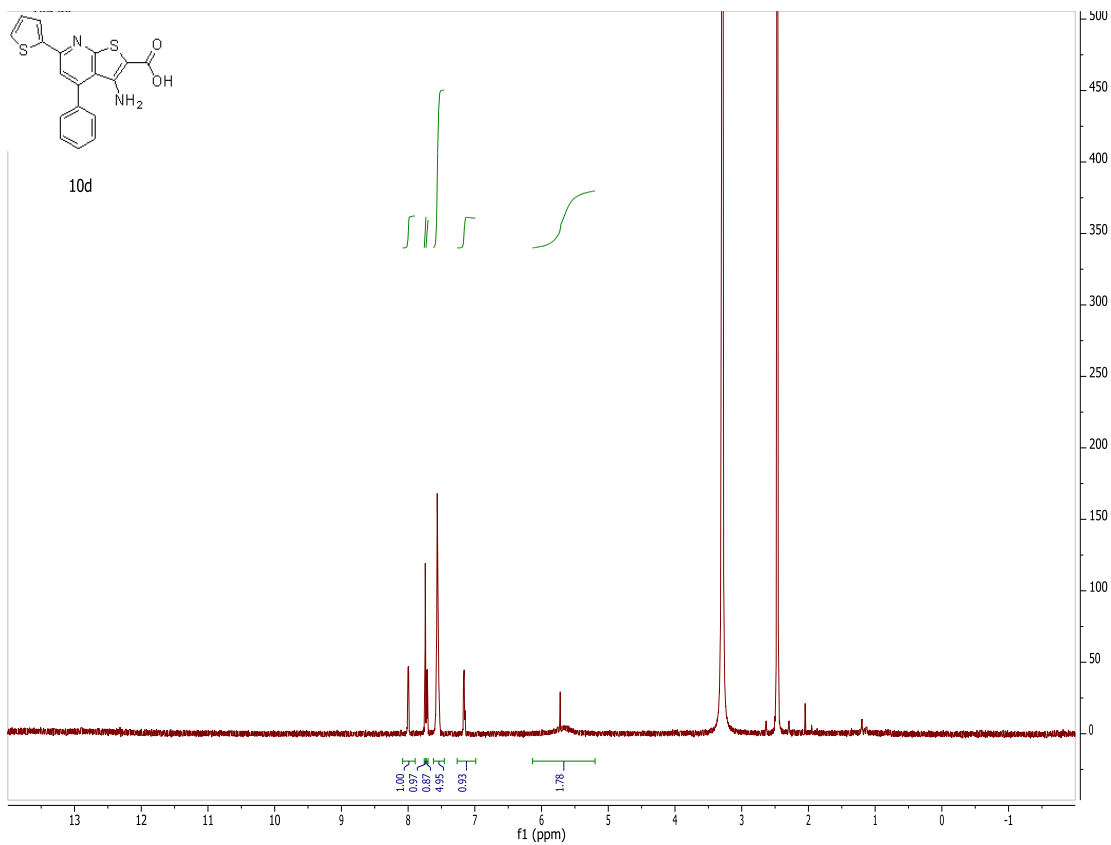
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STANDARD FLUORINE PARAMETERS

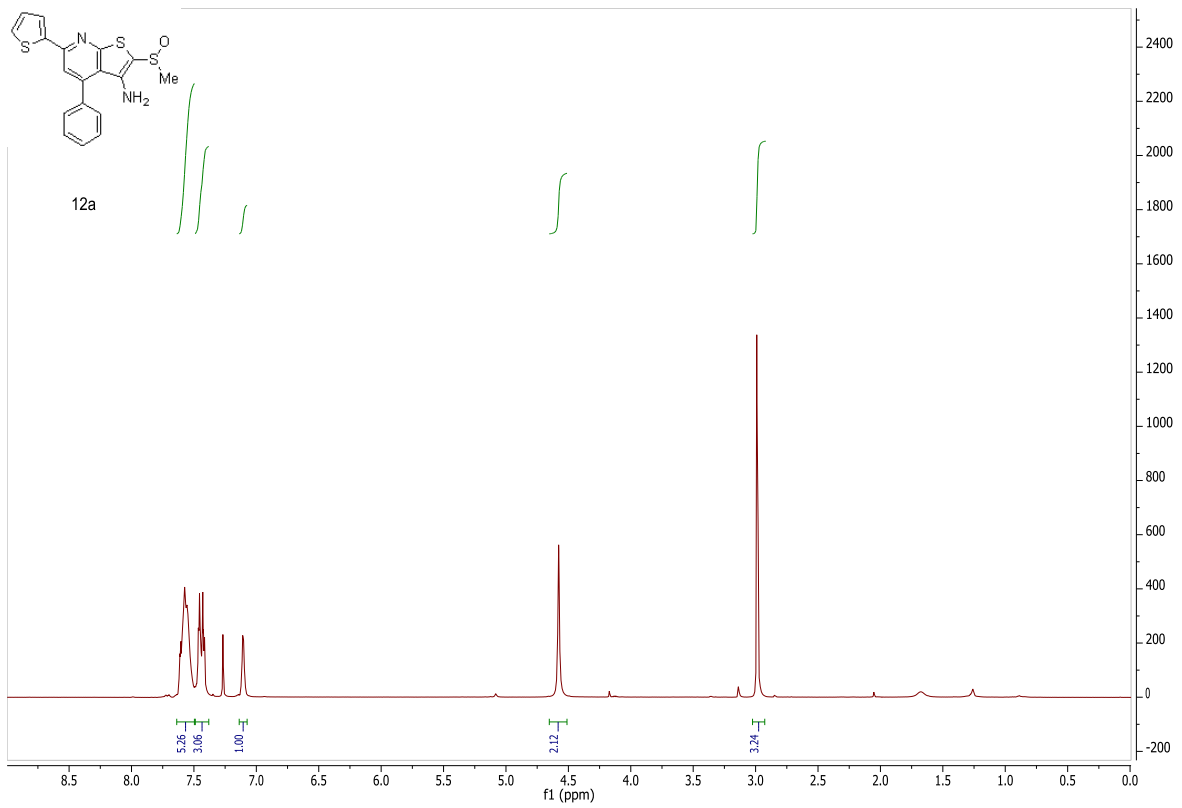
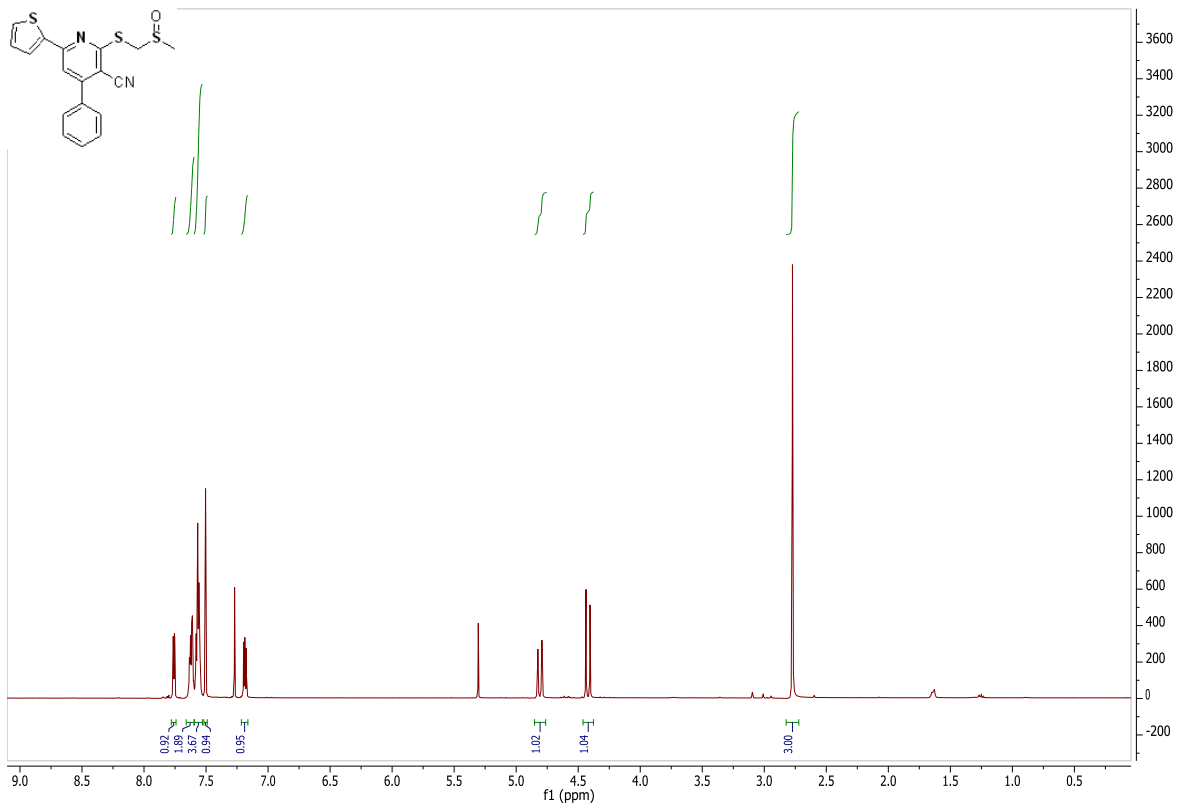


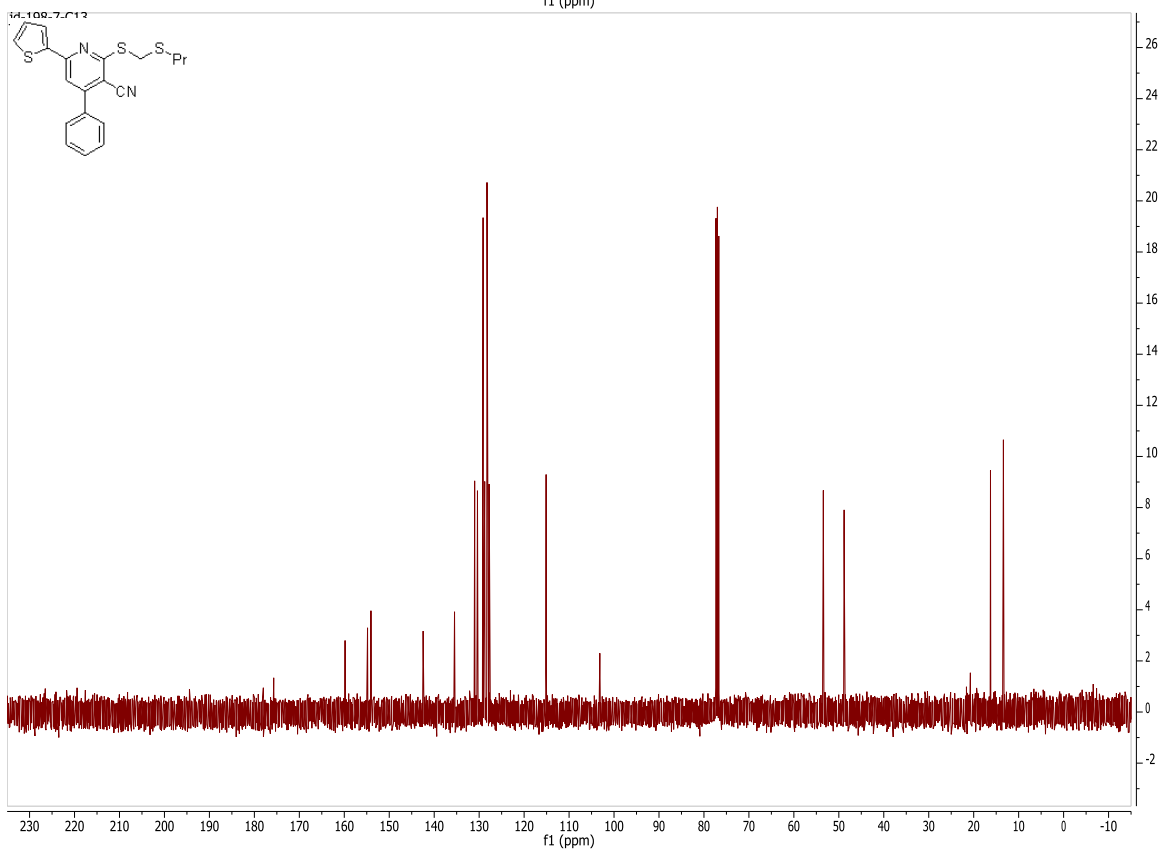
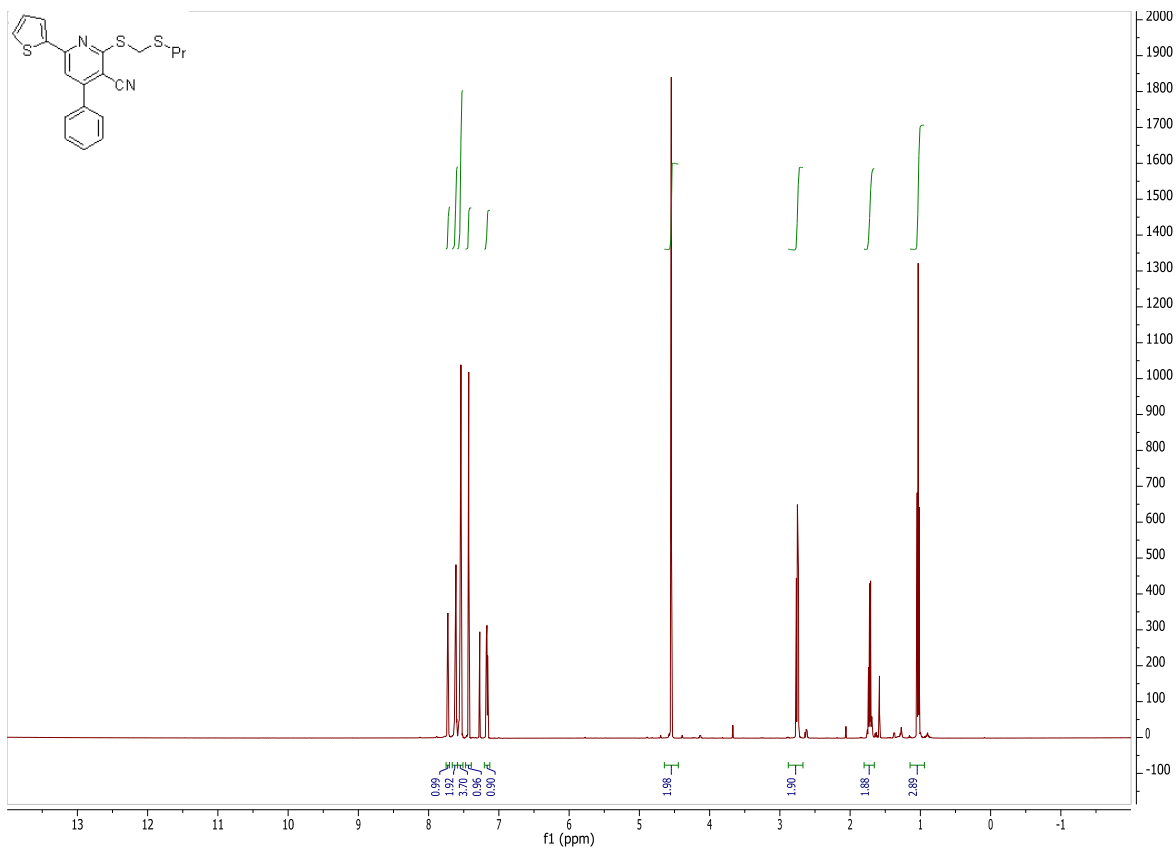




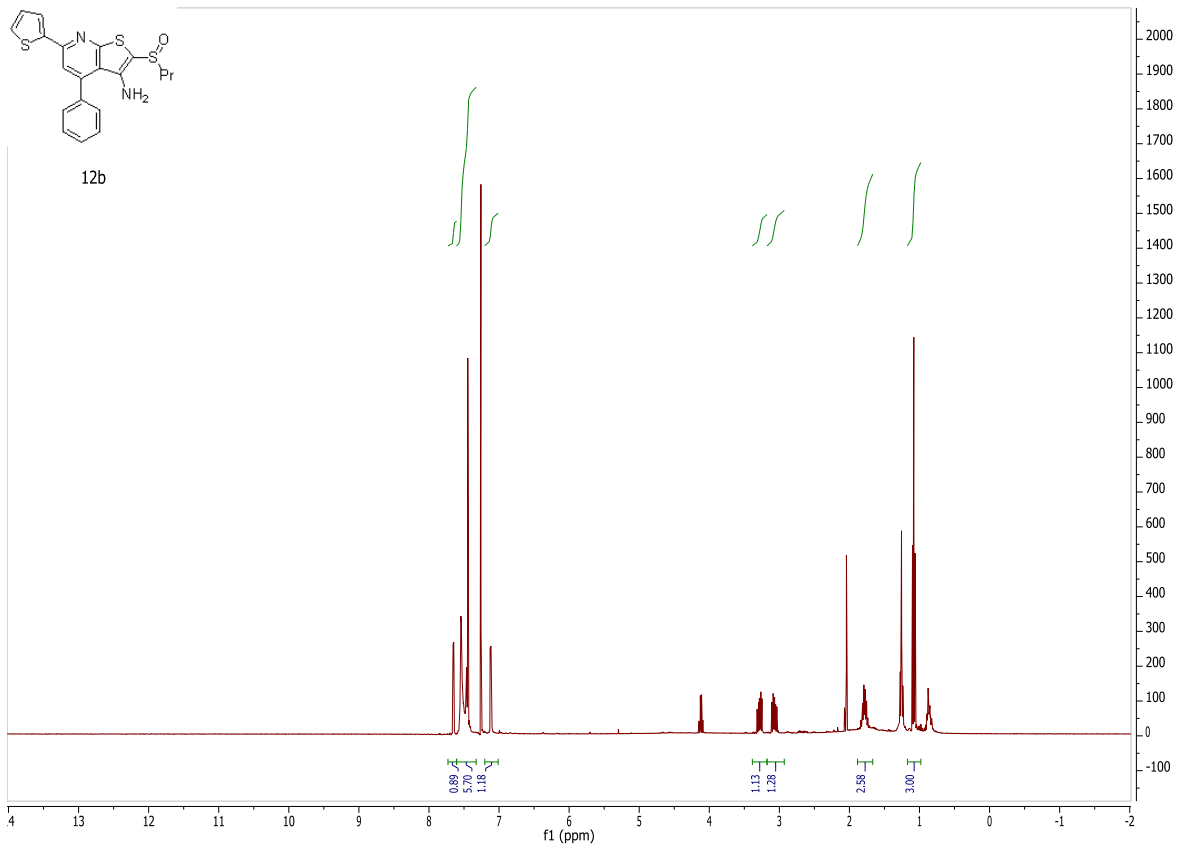
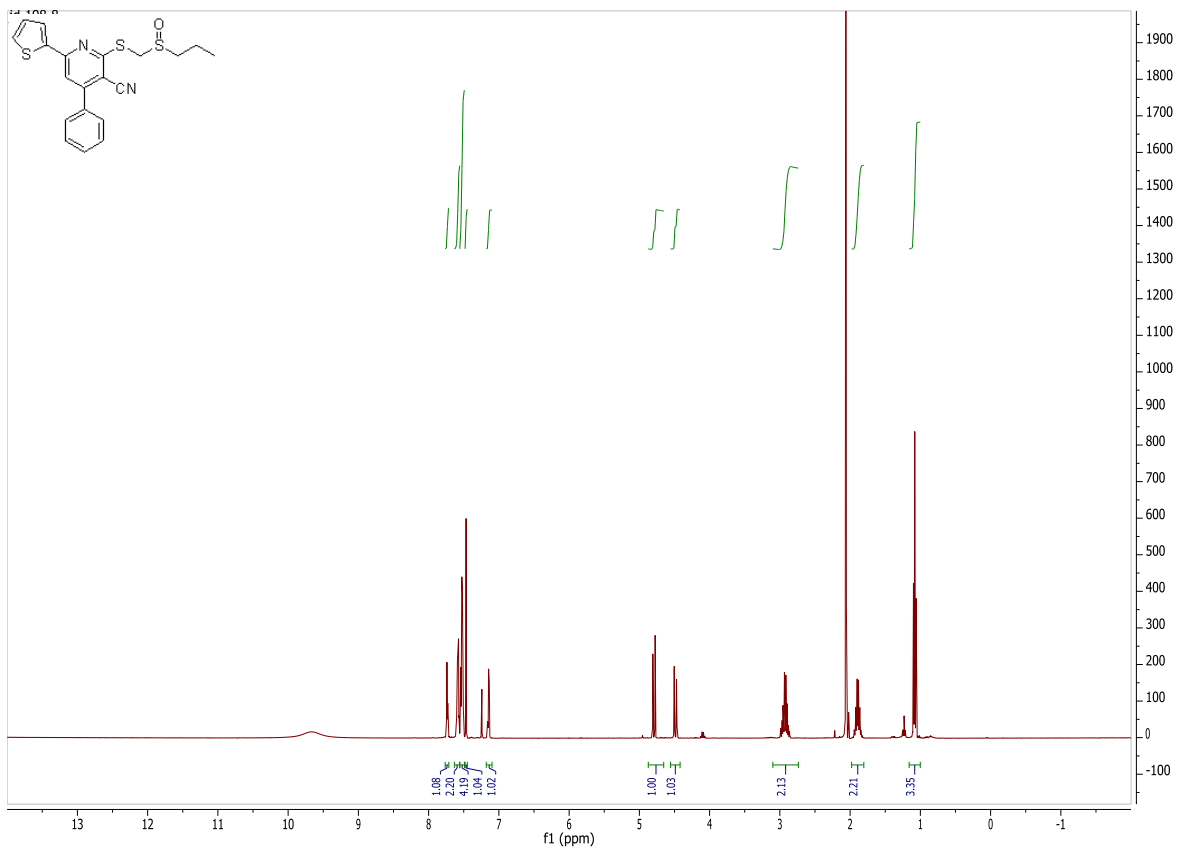


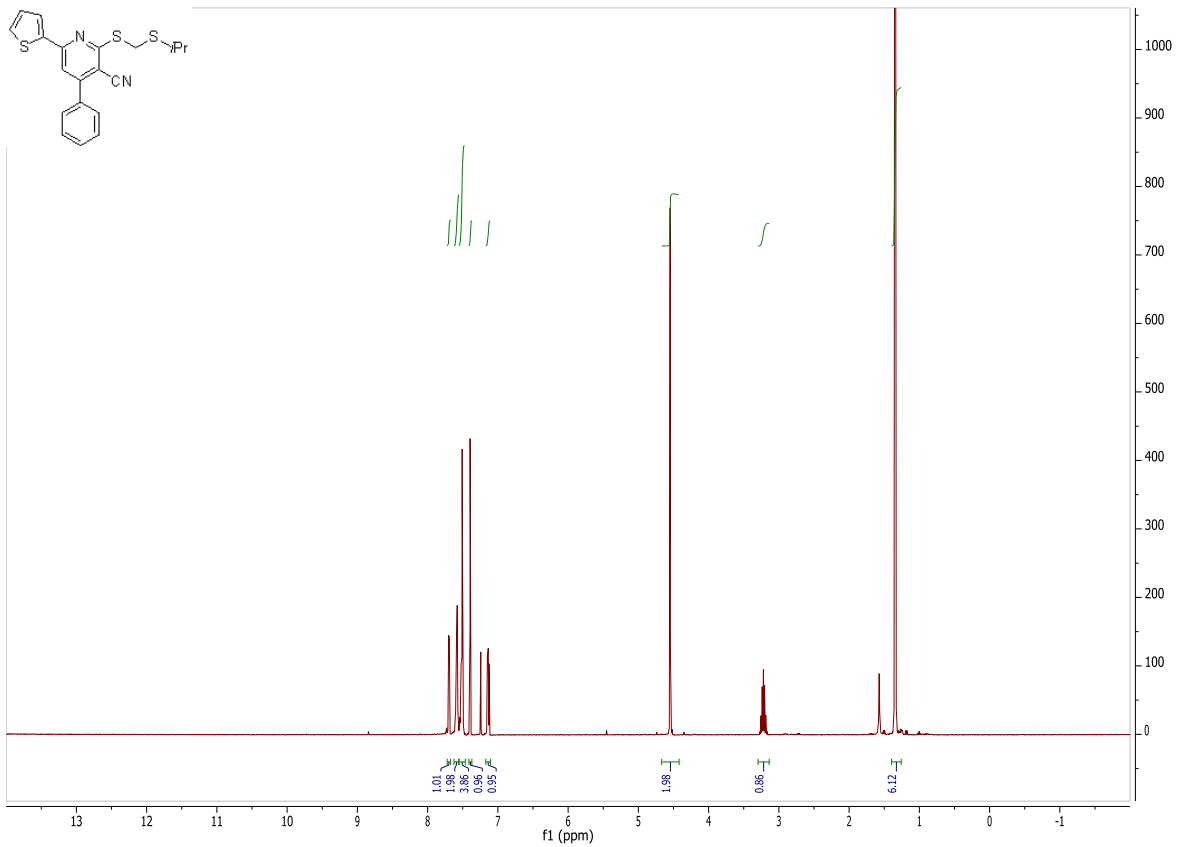
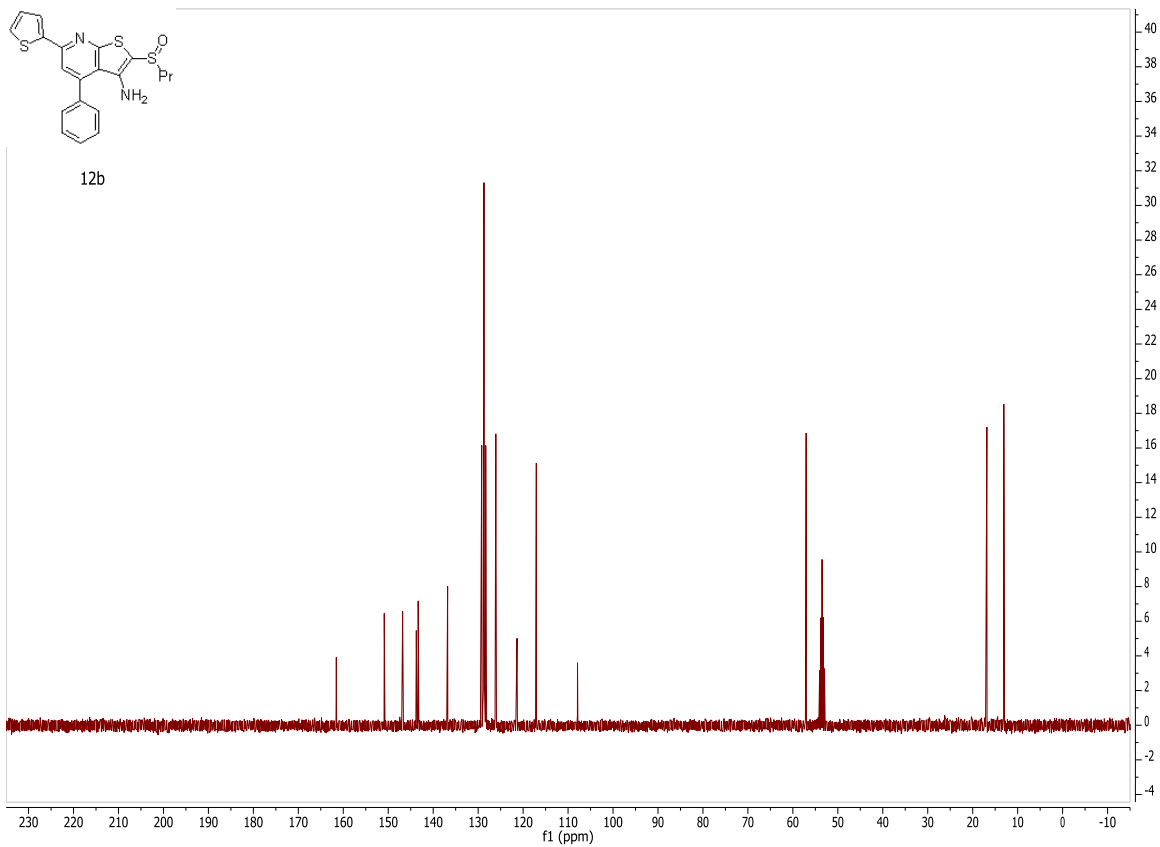


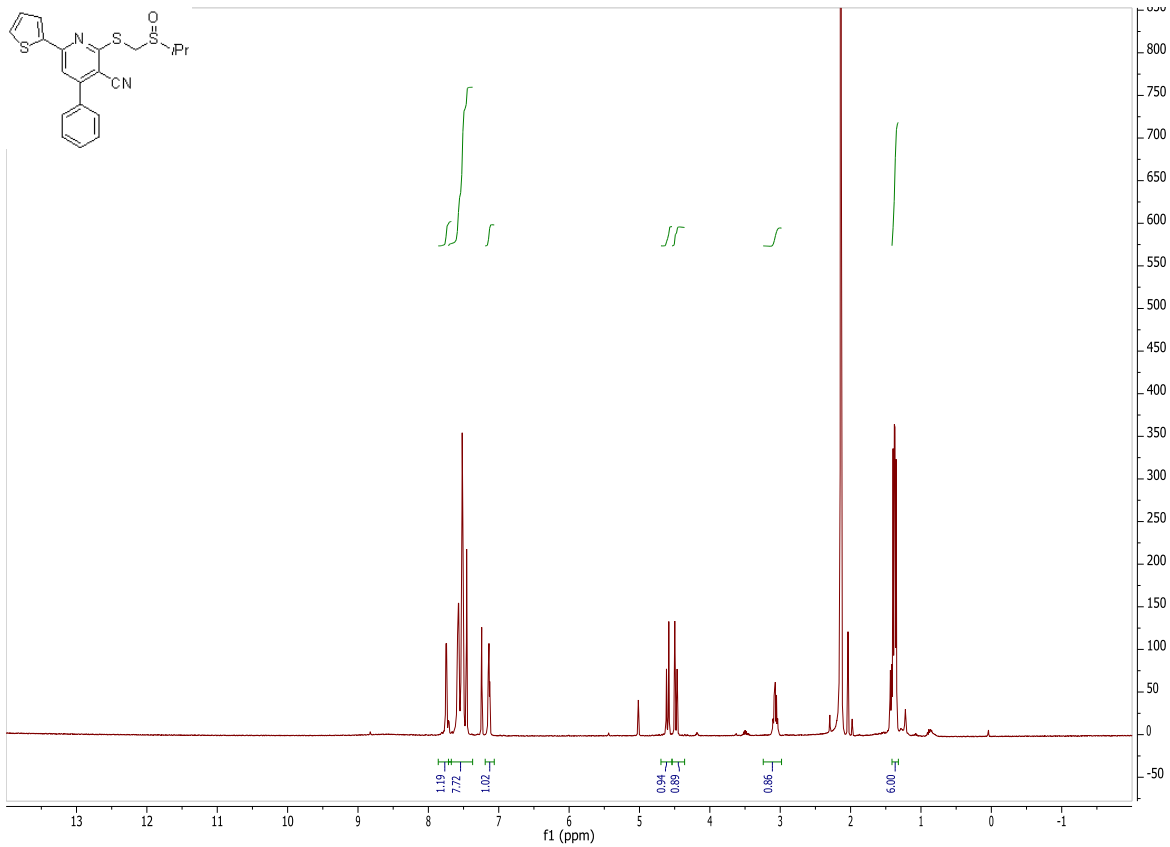
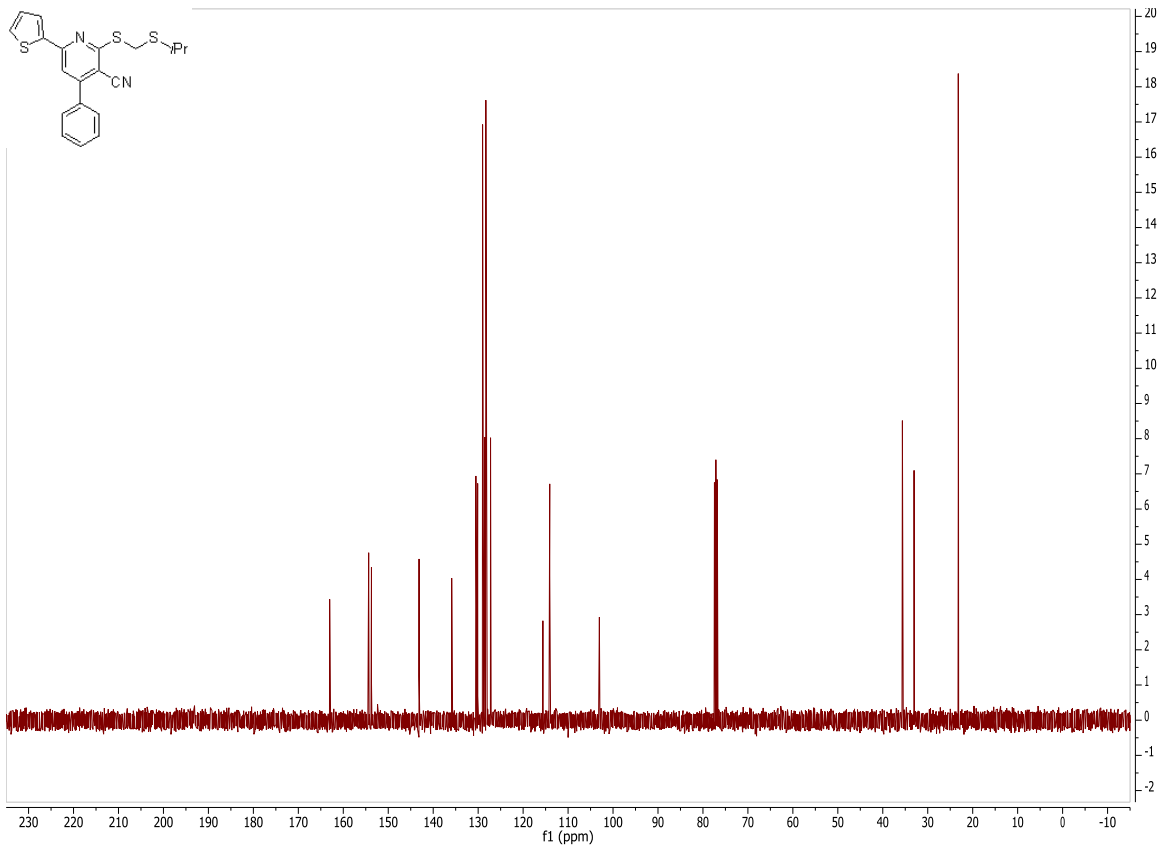


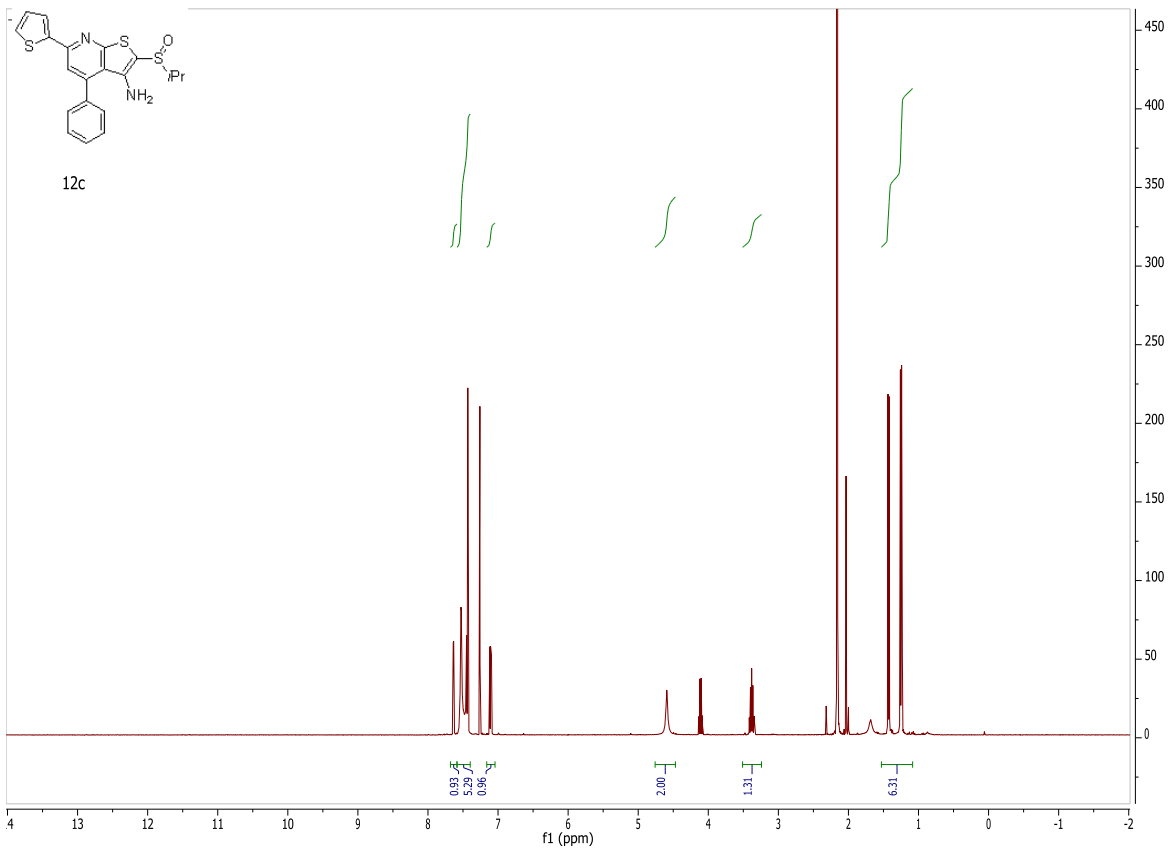
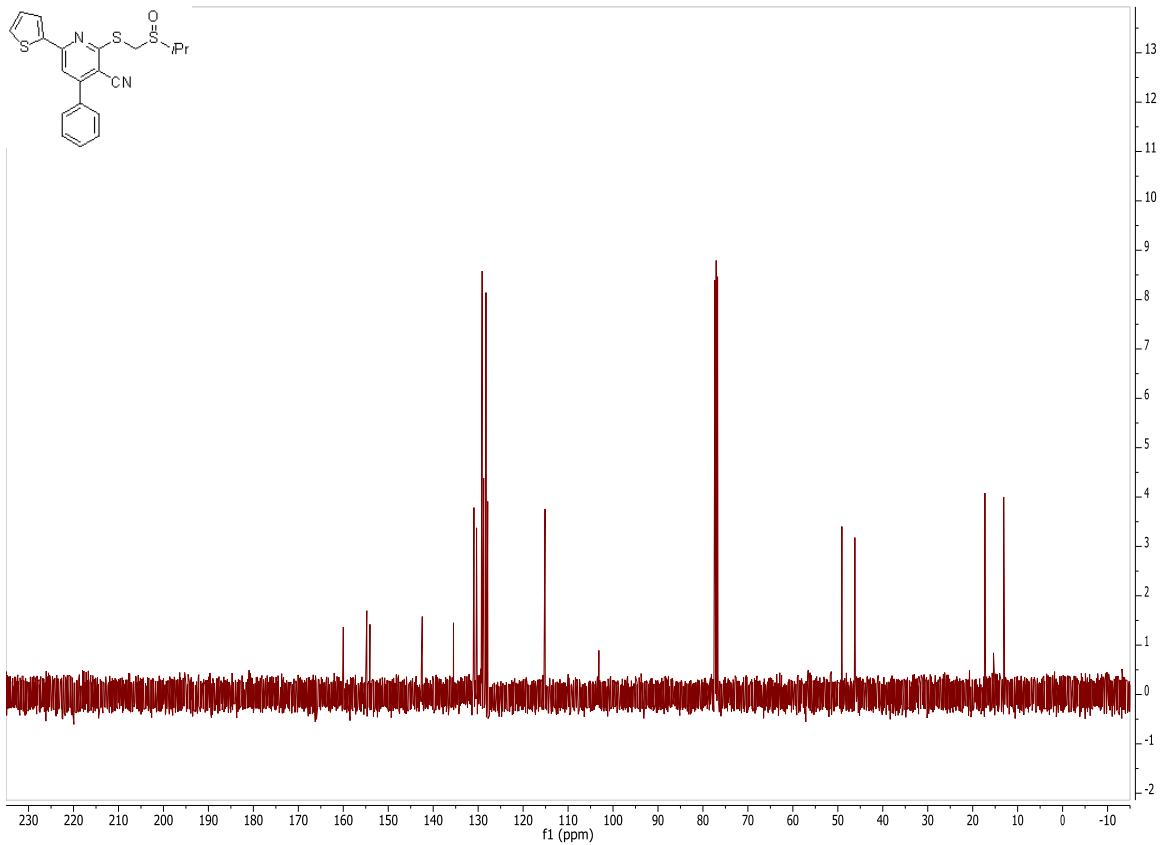


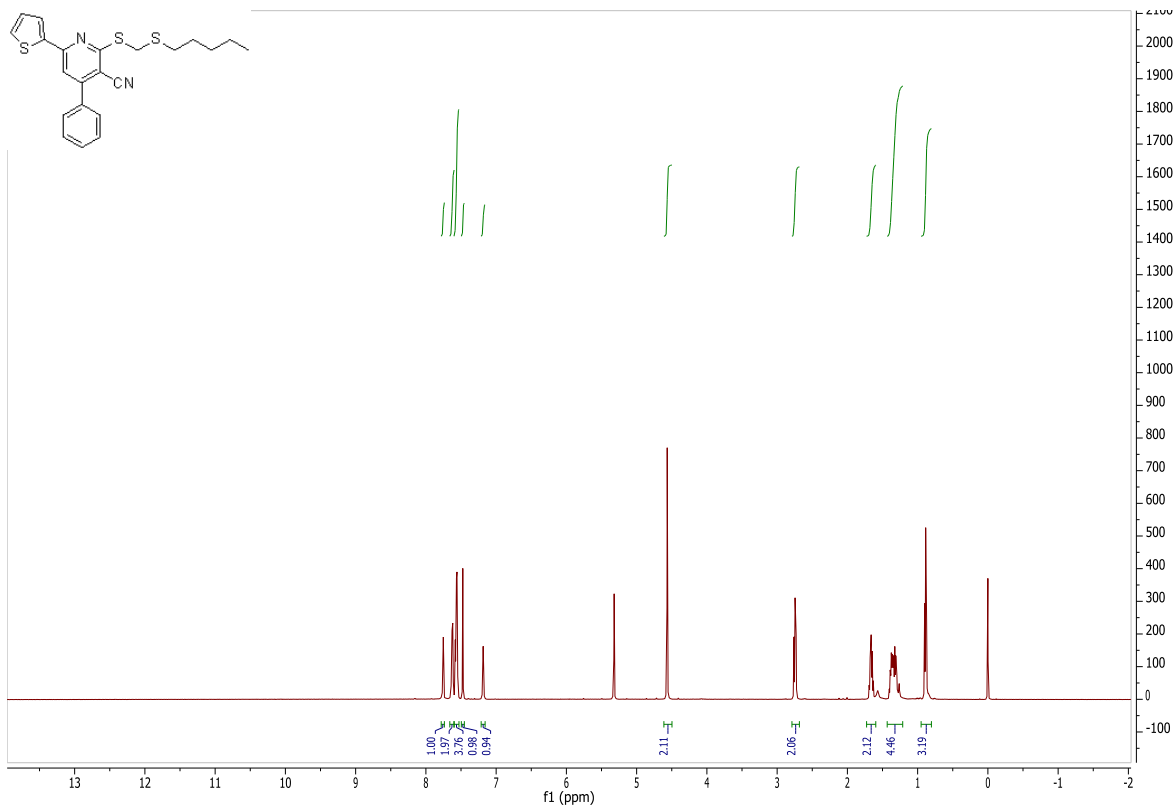
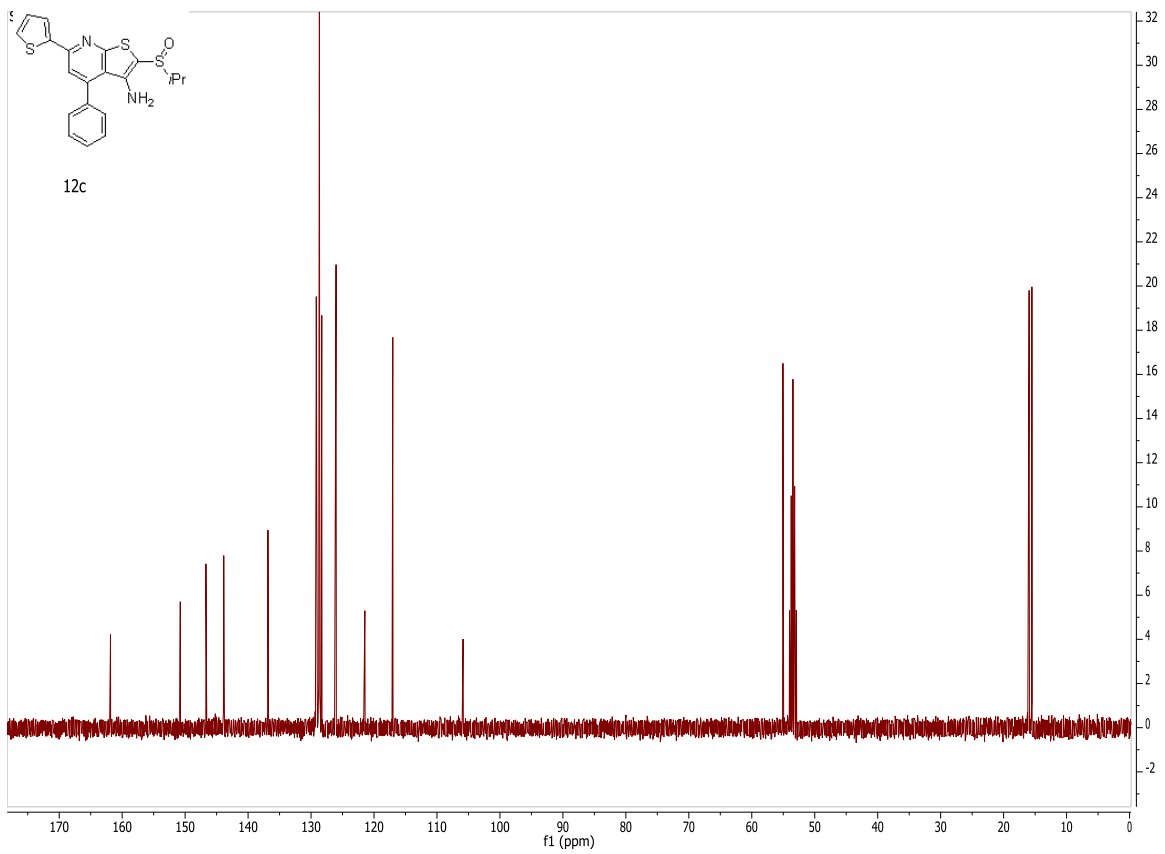


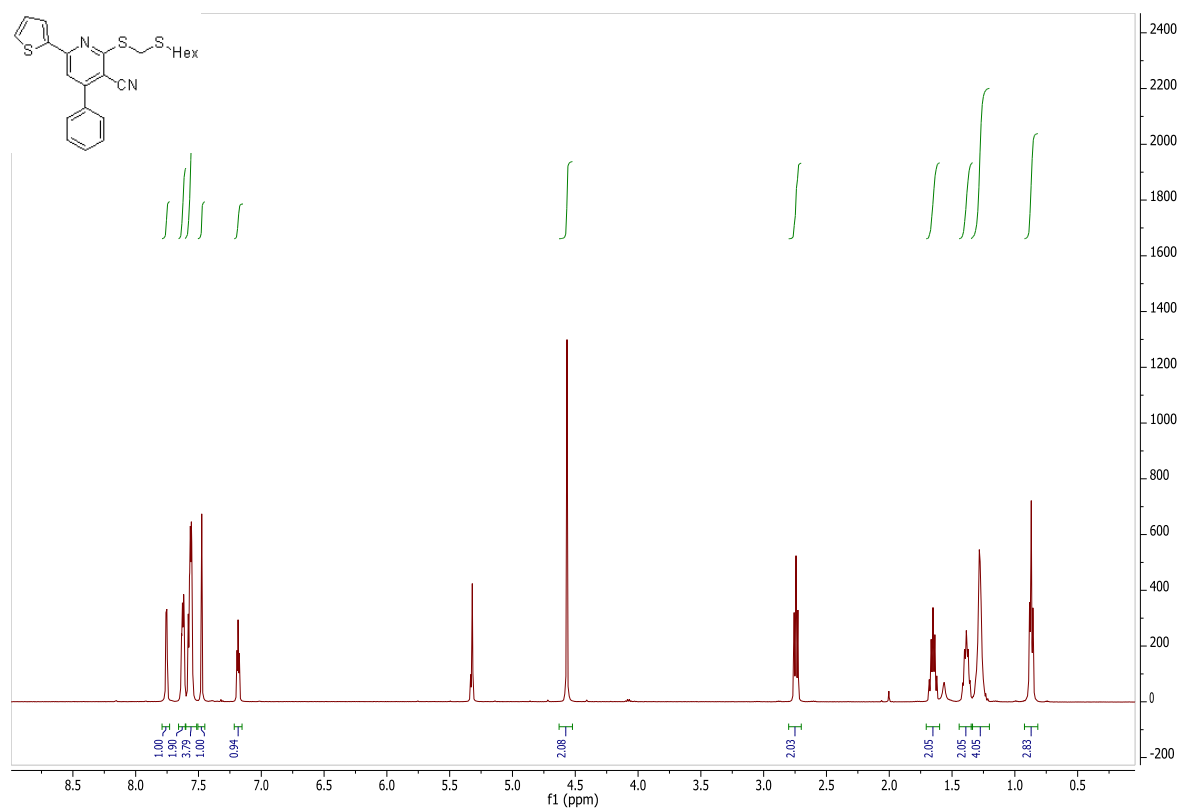
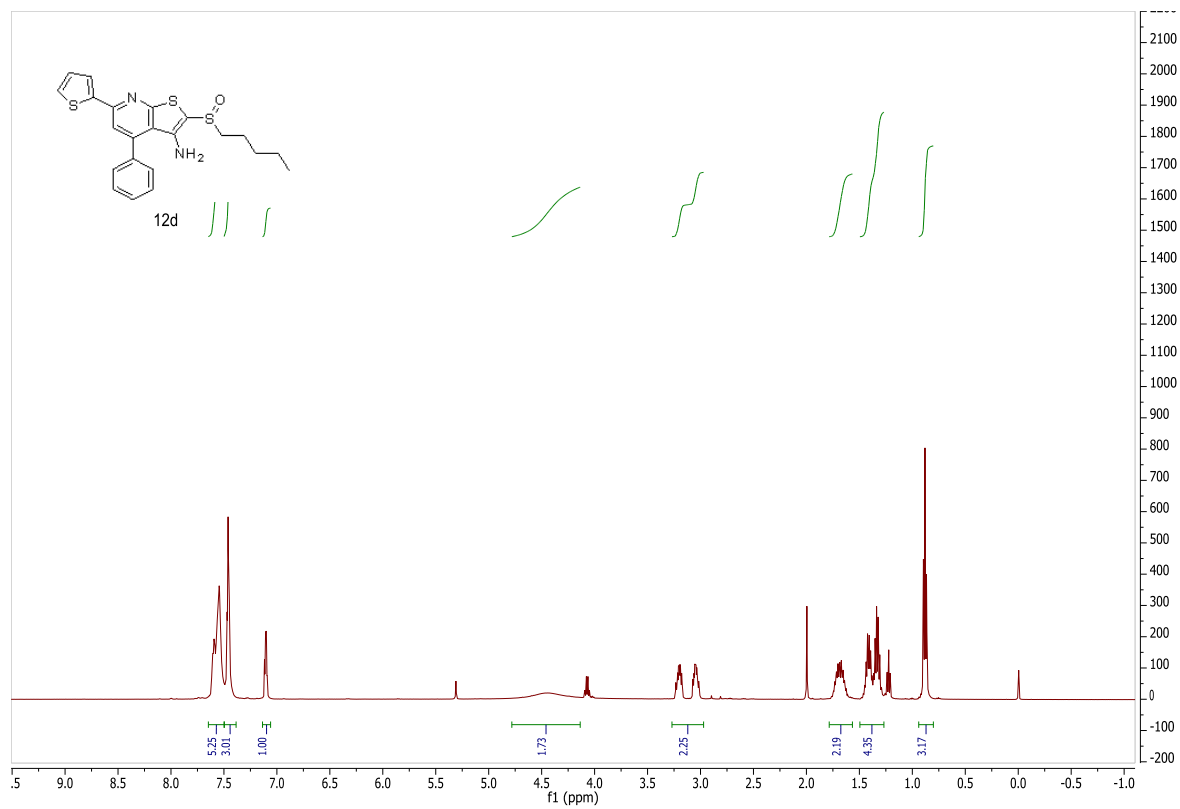


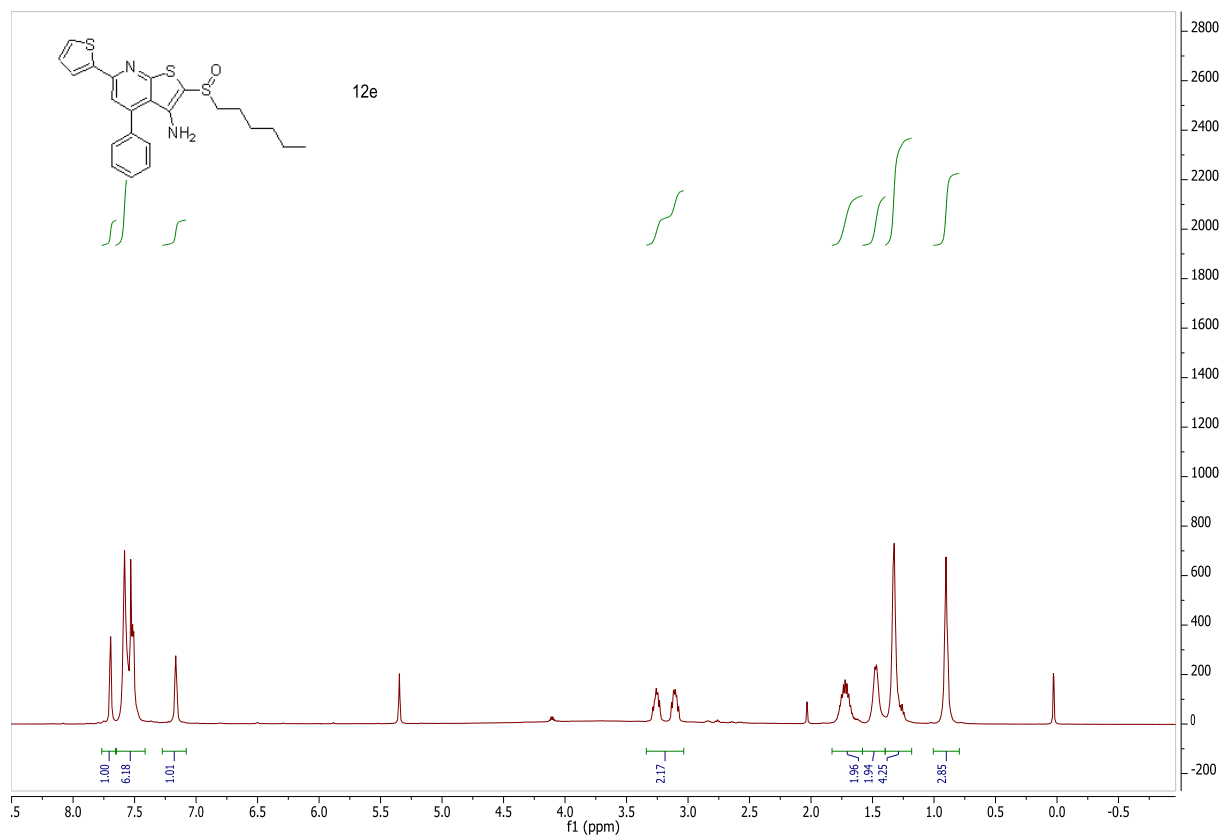
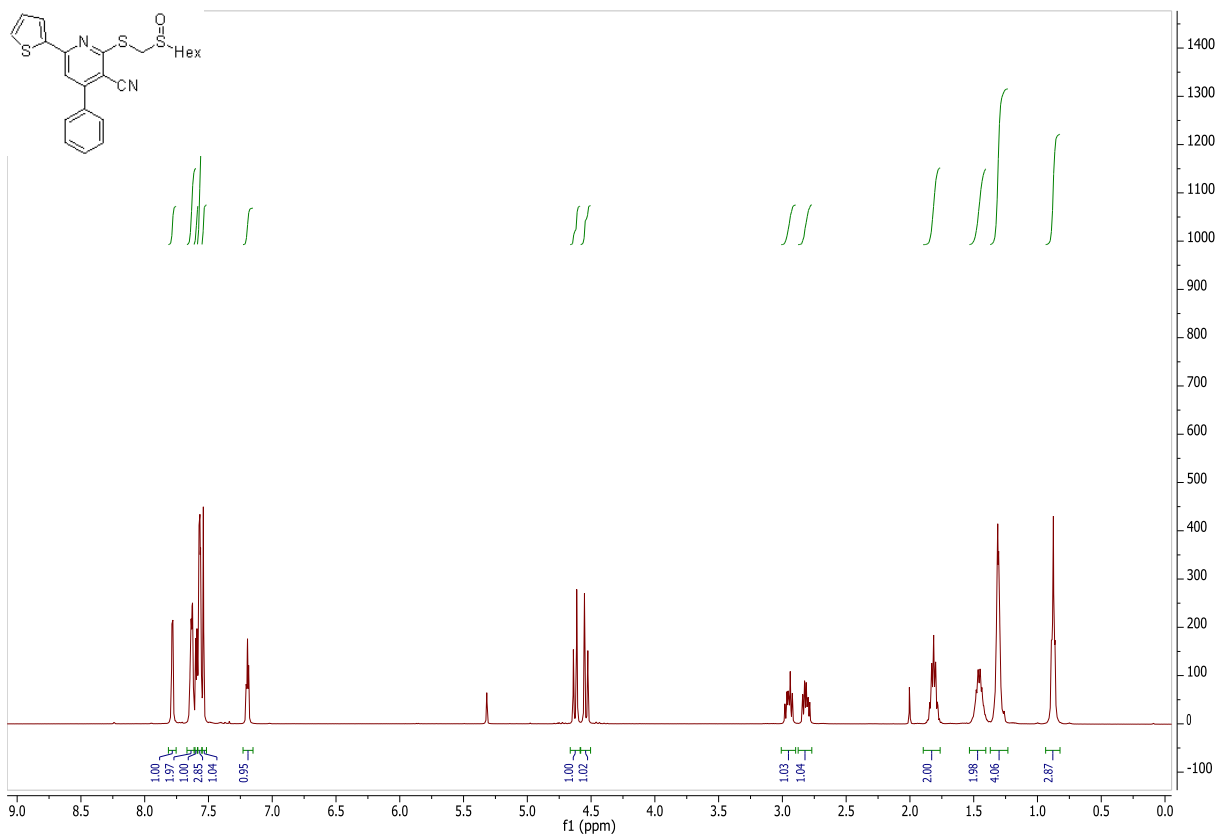


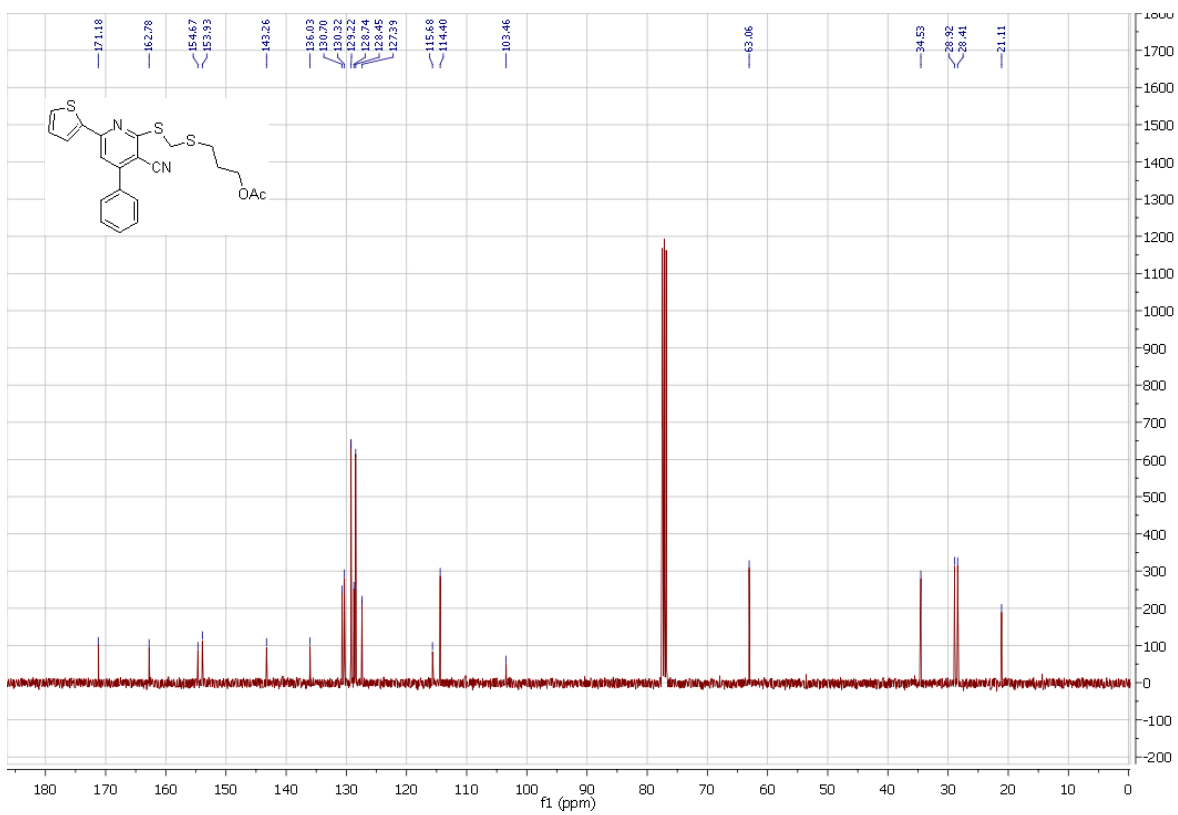
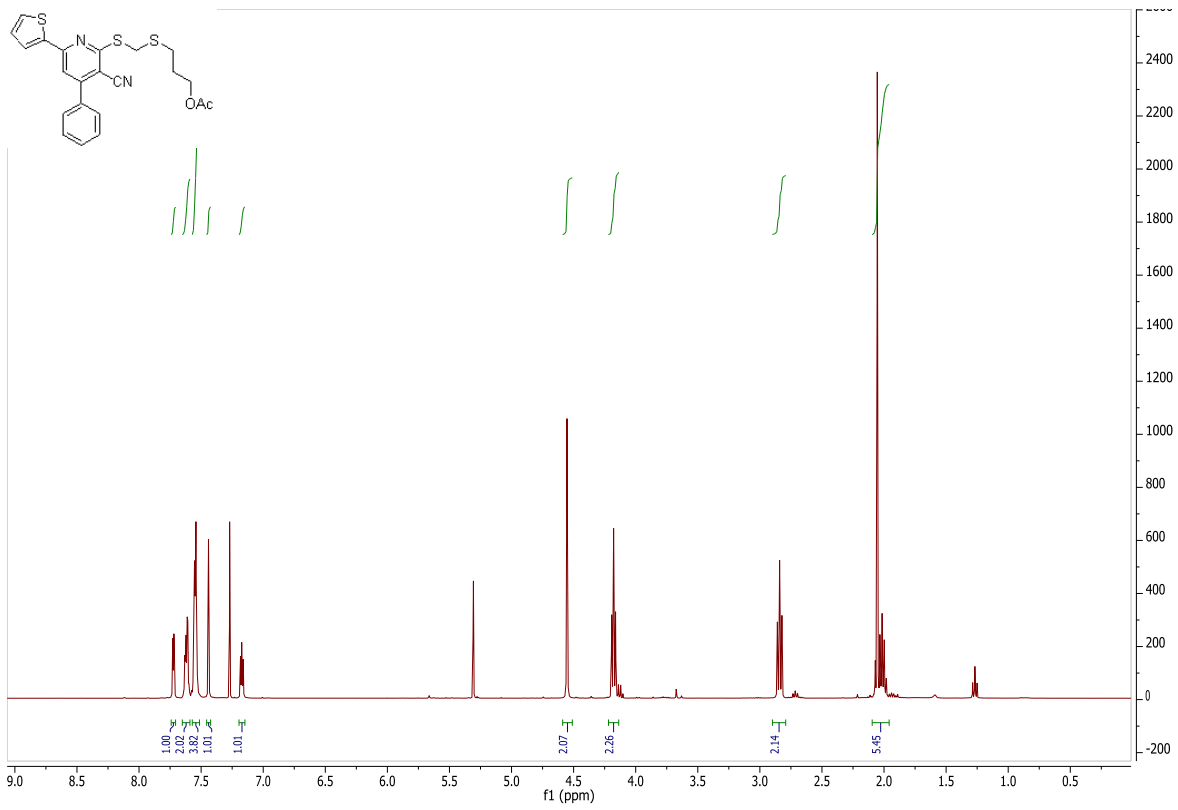




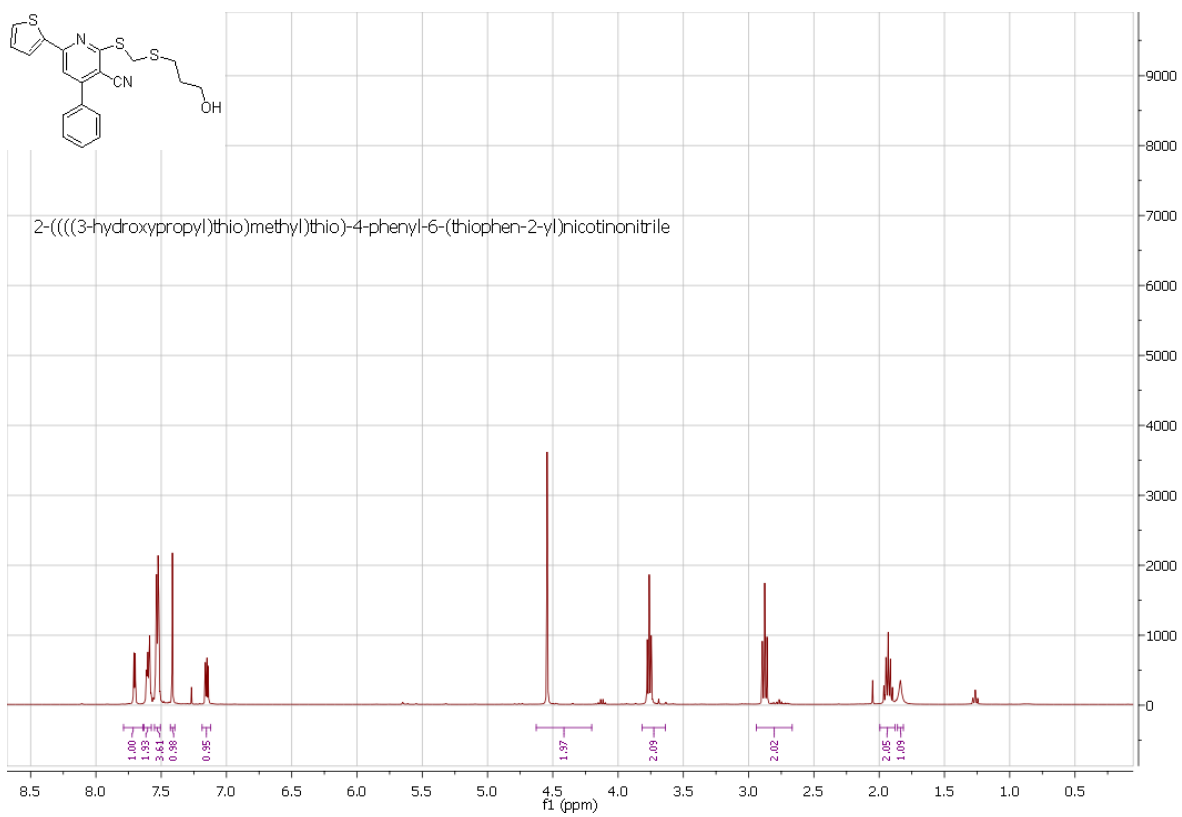
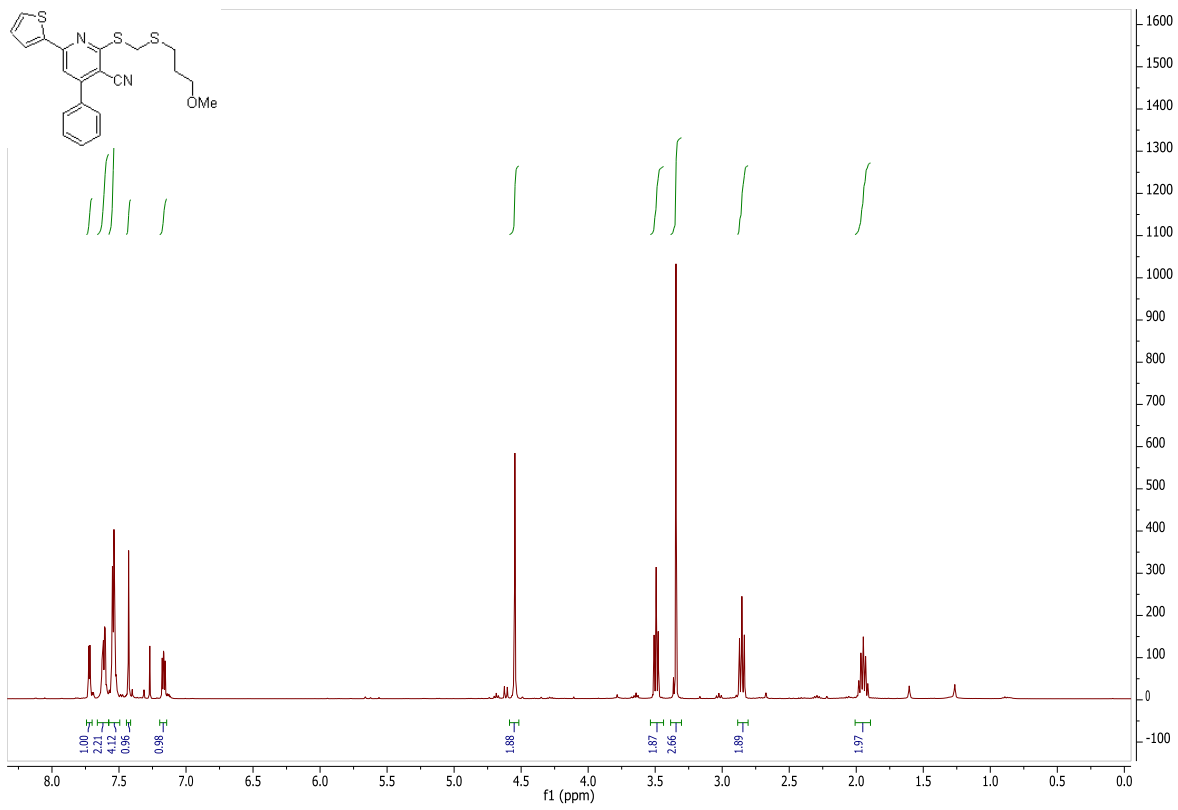


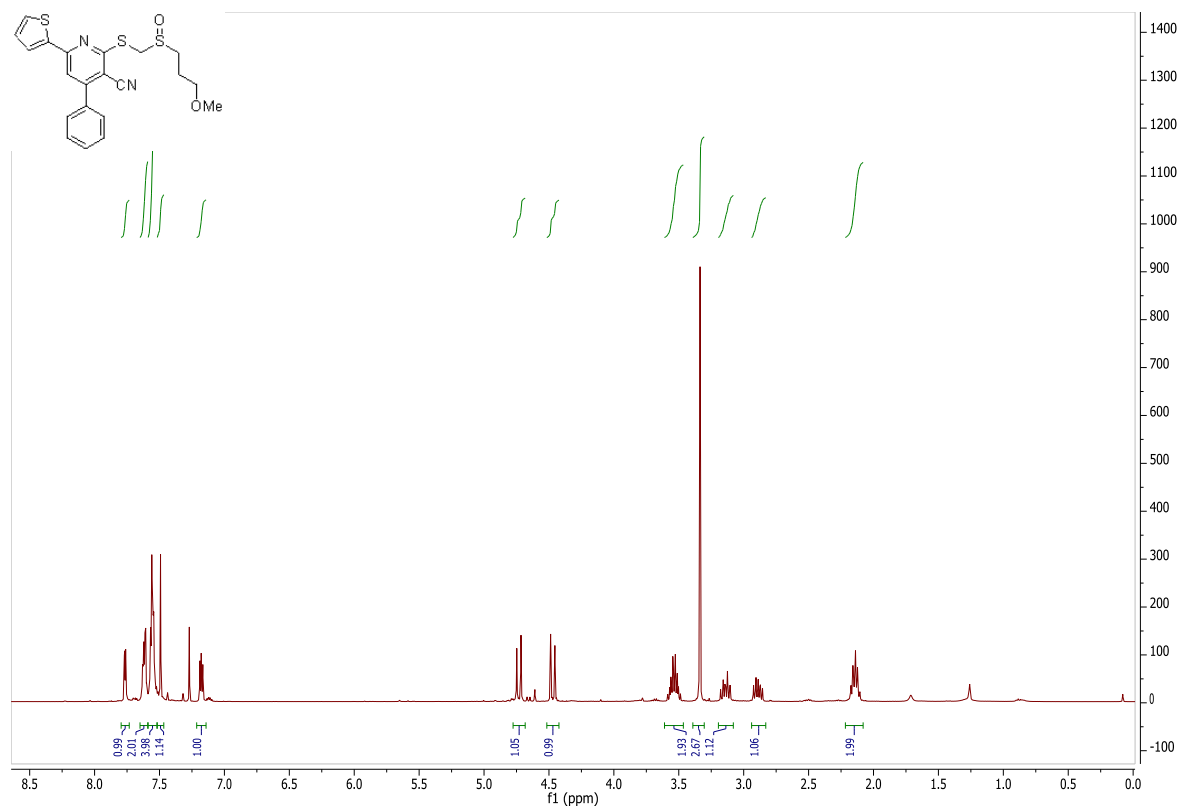
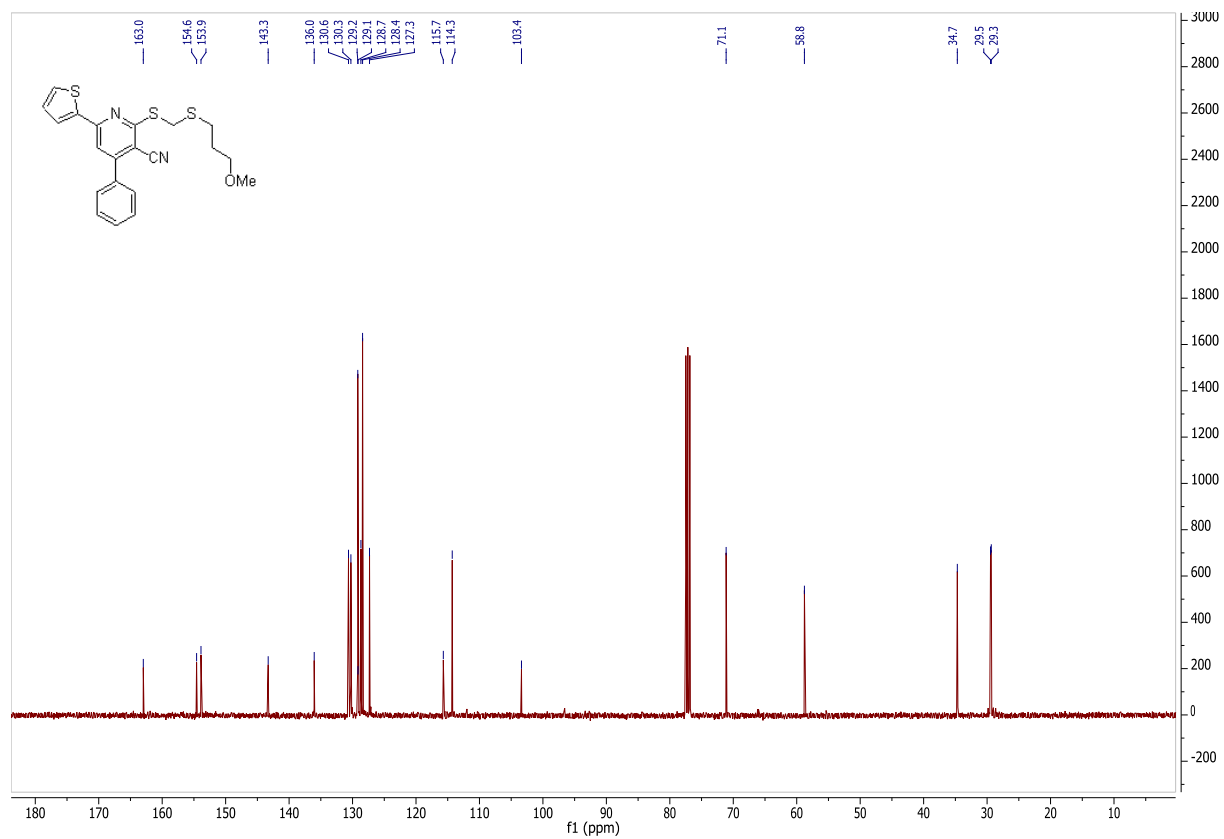


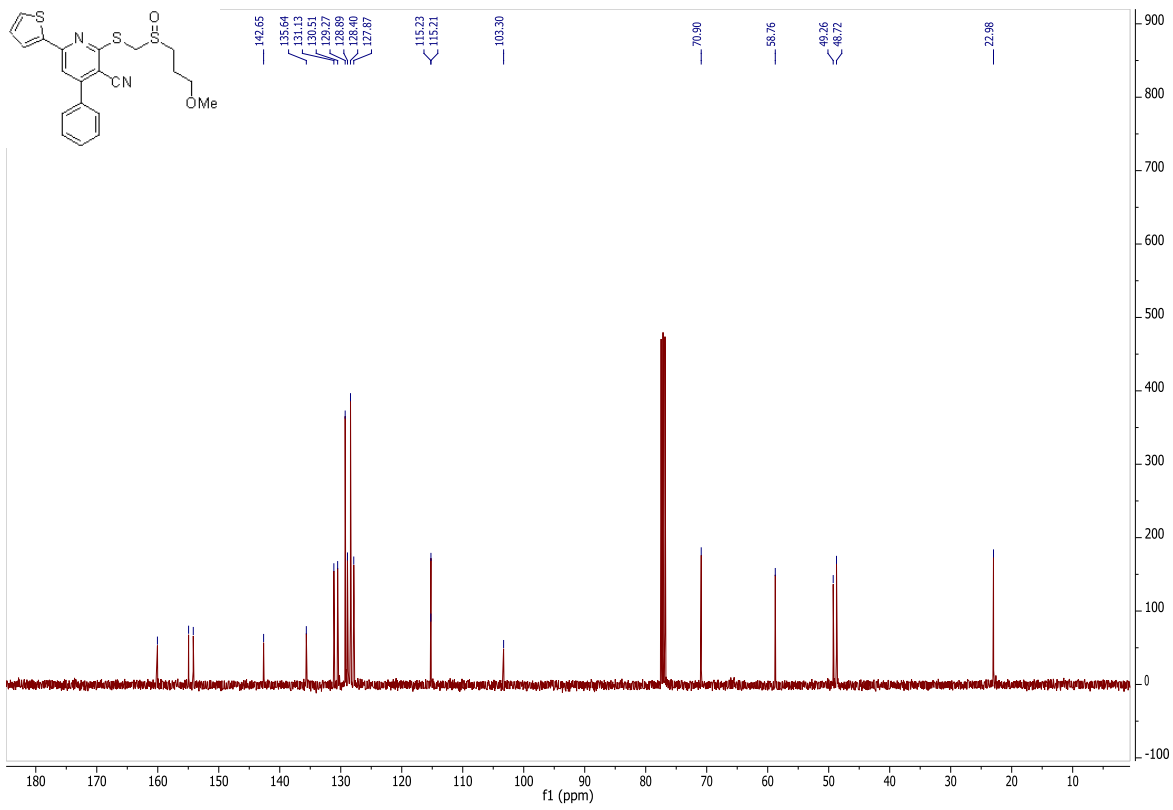


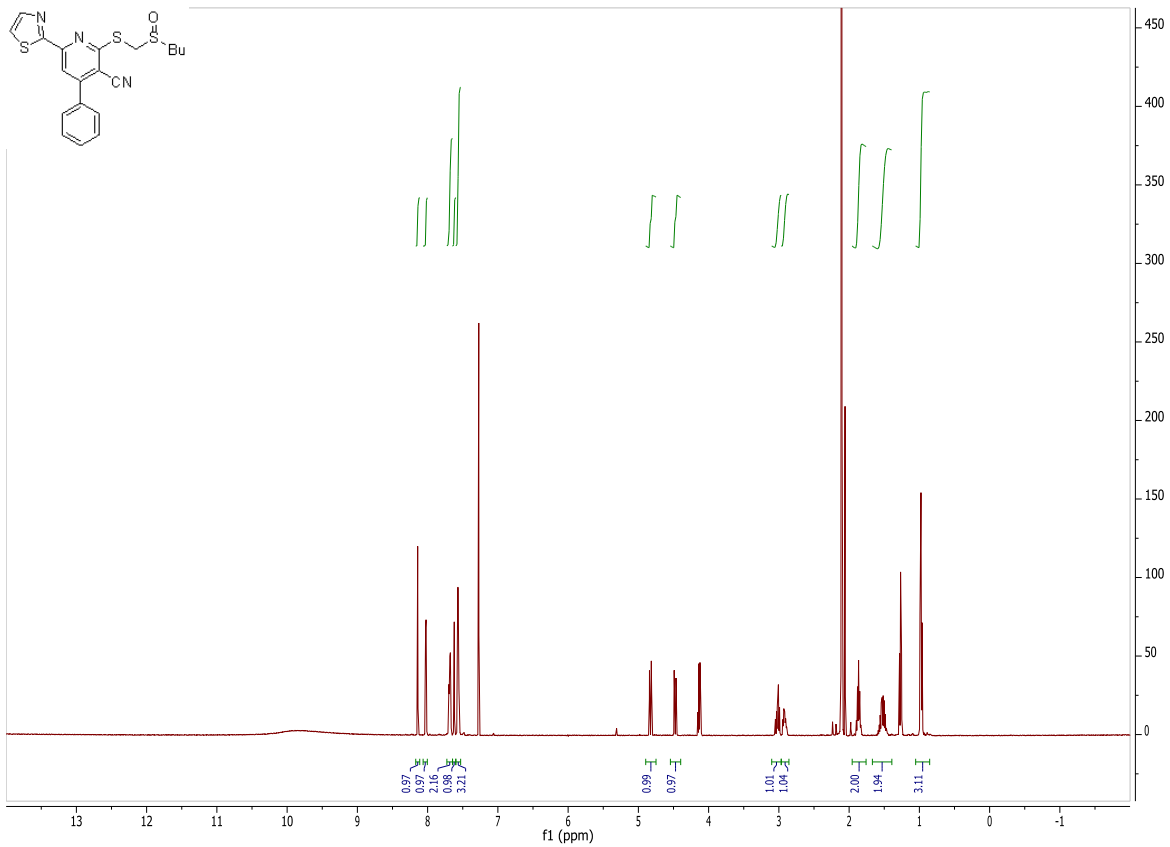
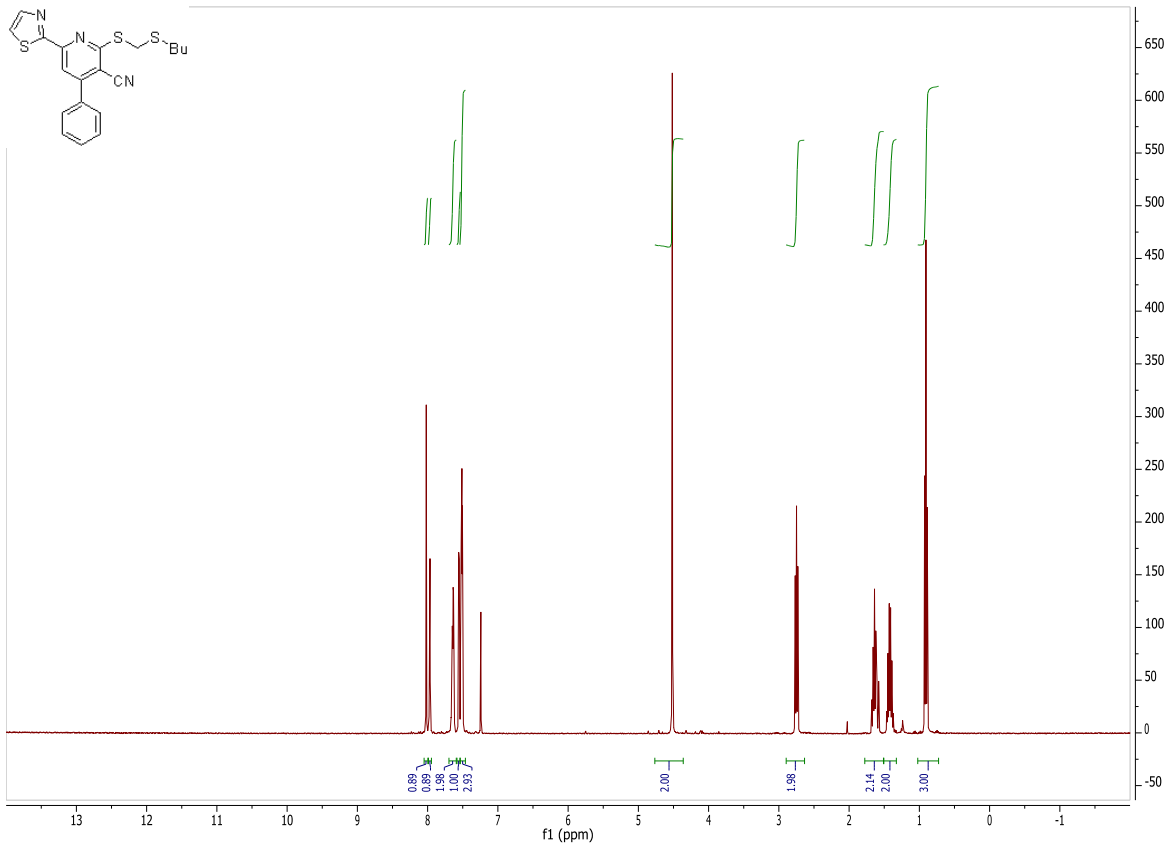


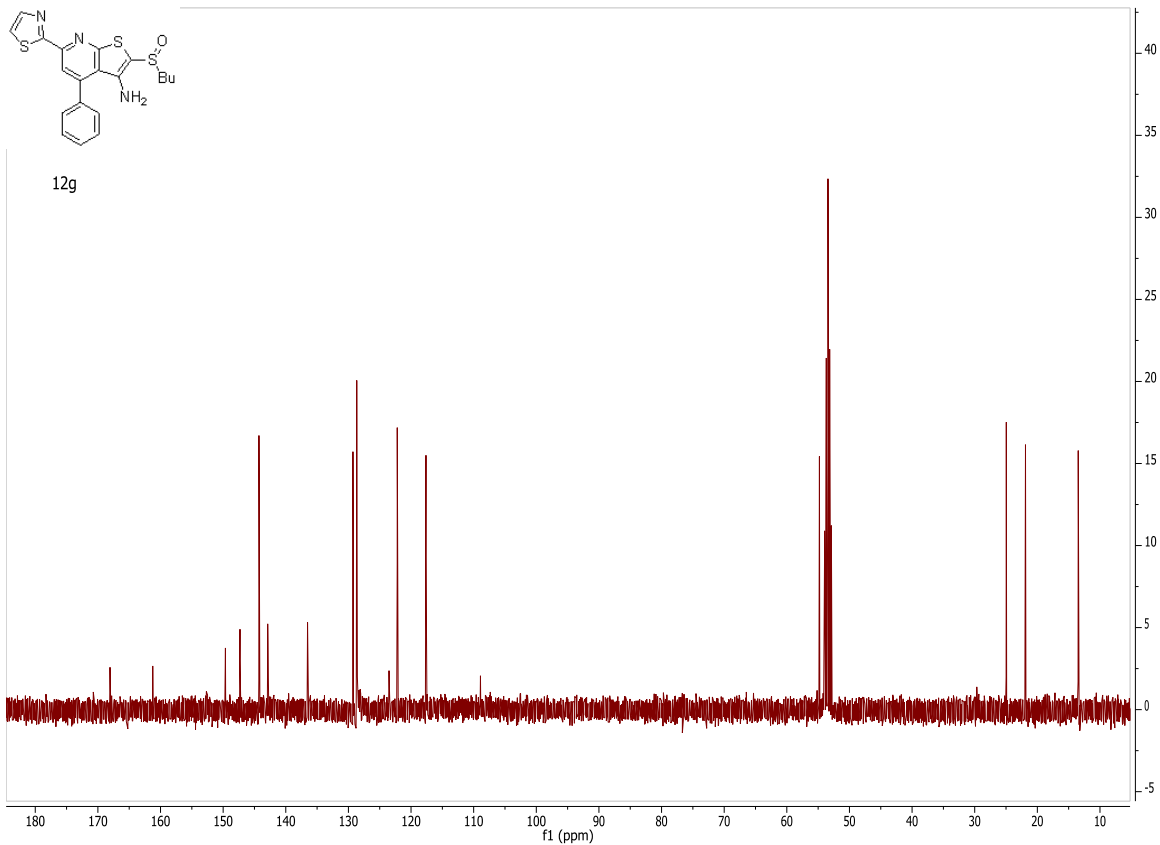
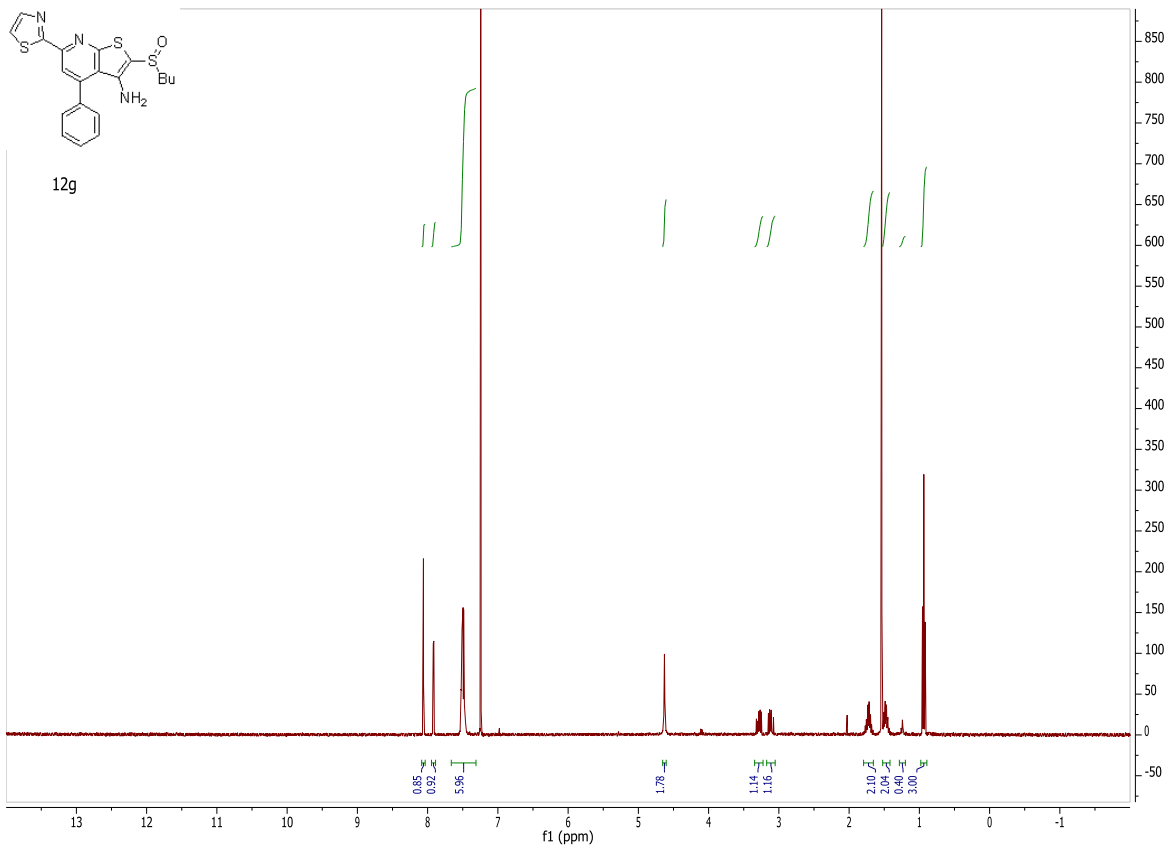


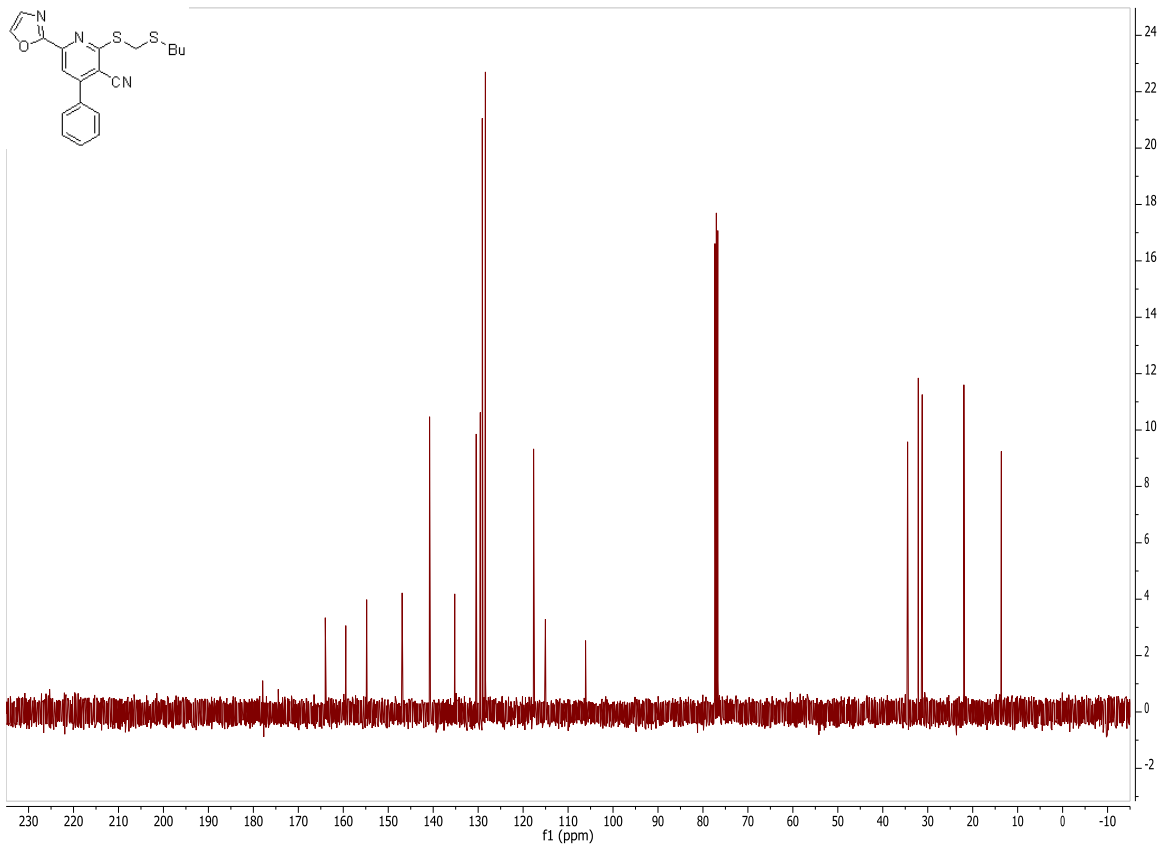
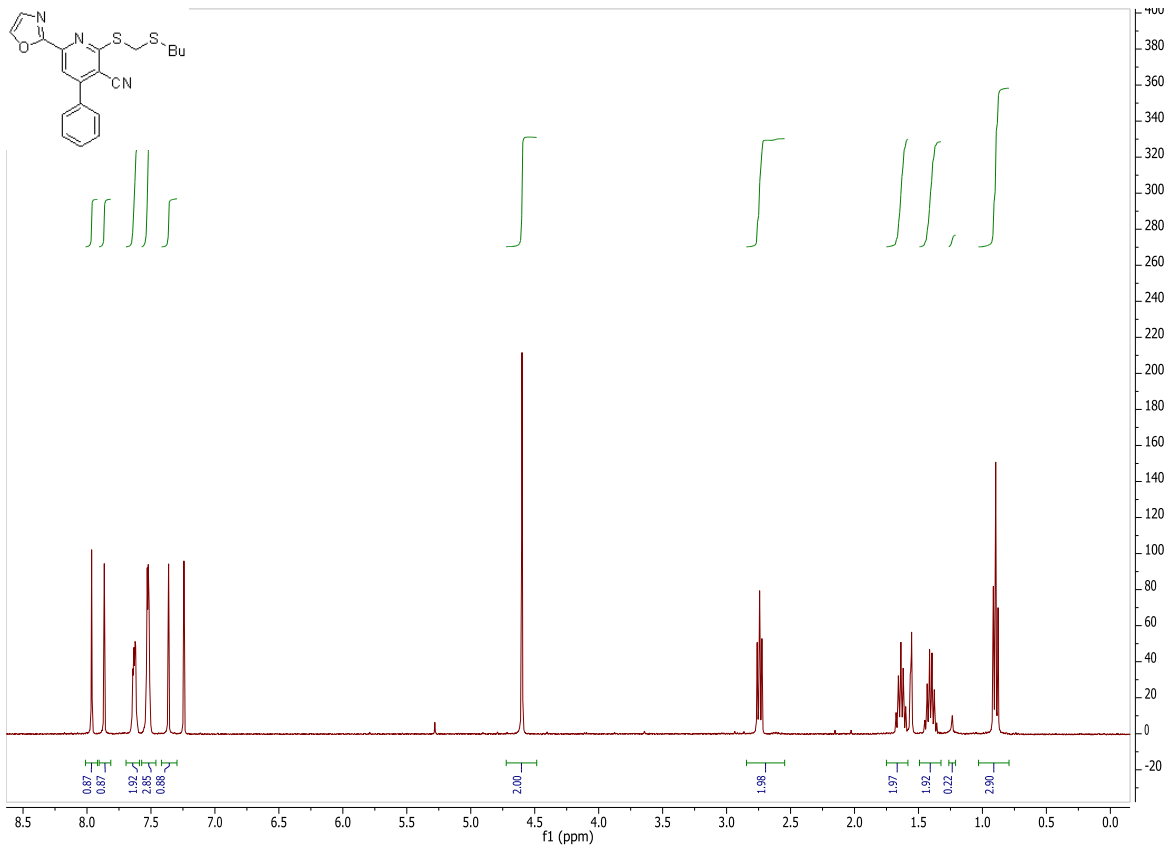


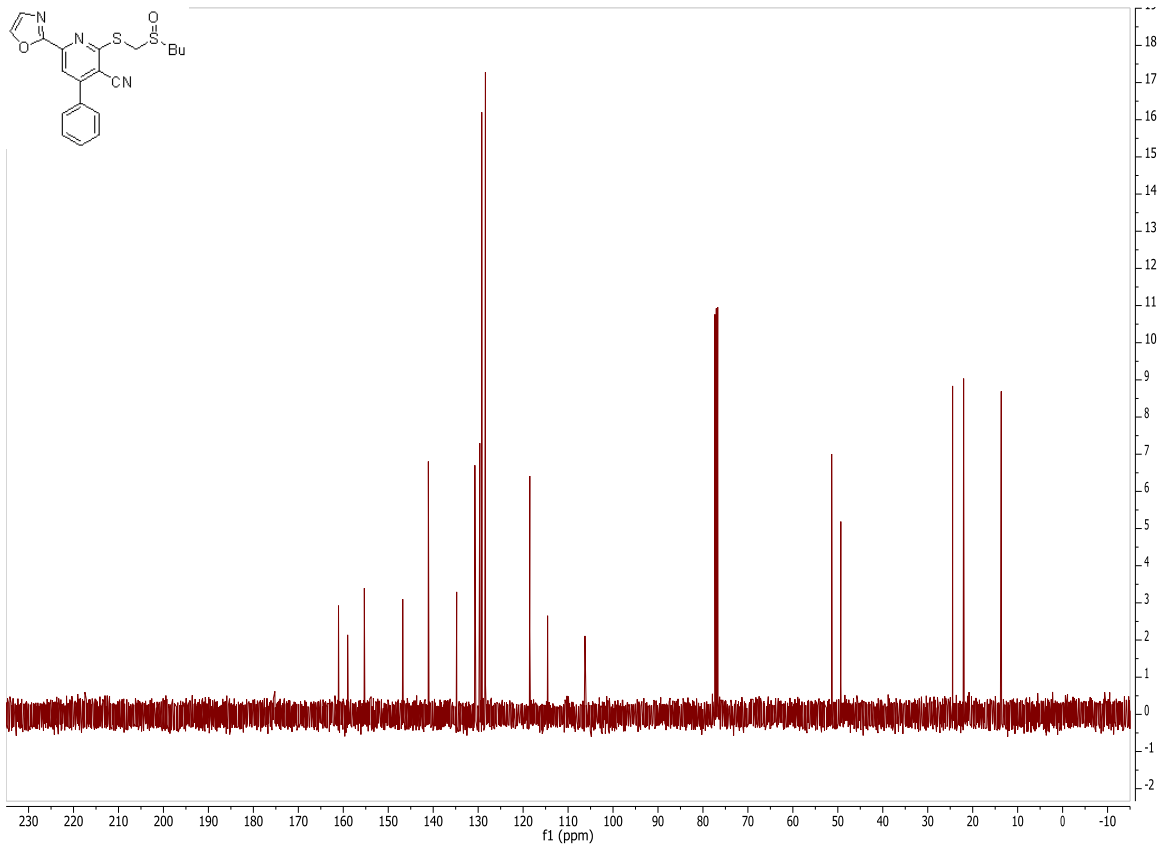
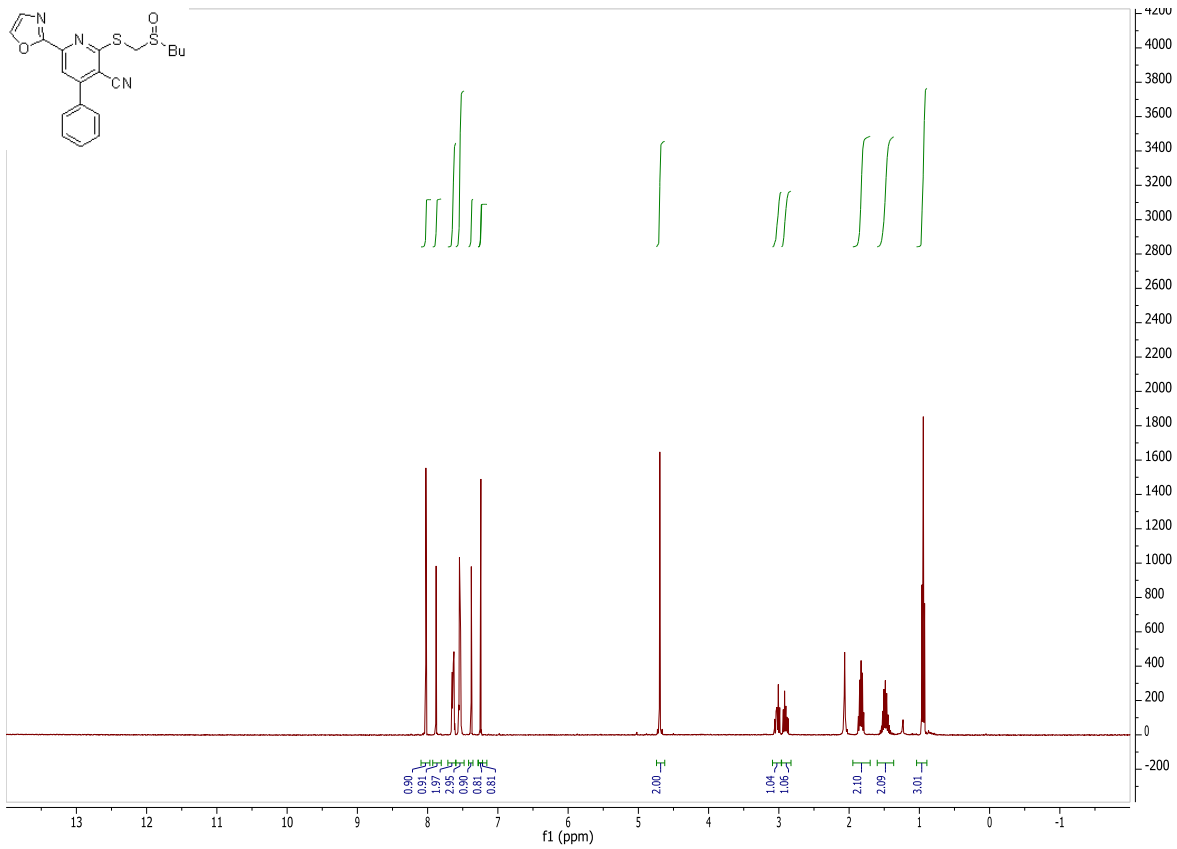


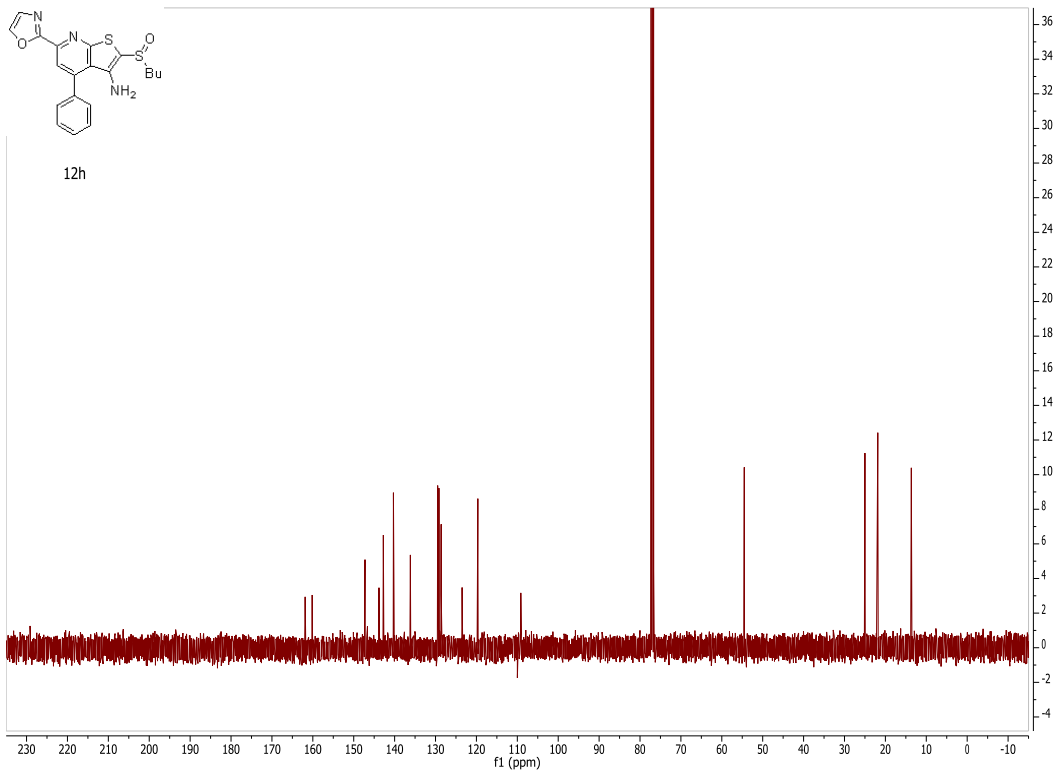
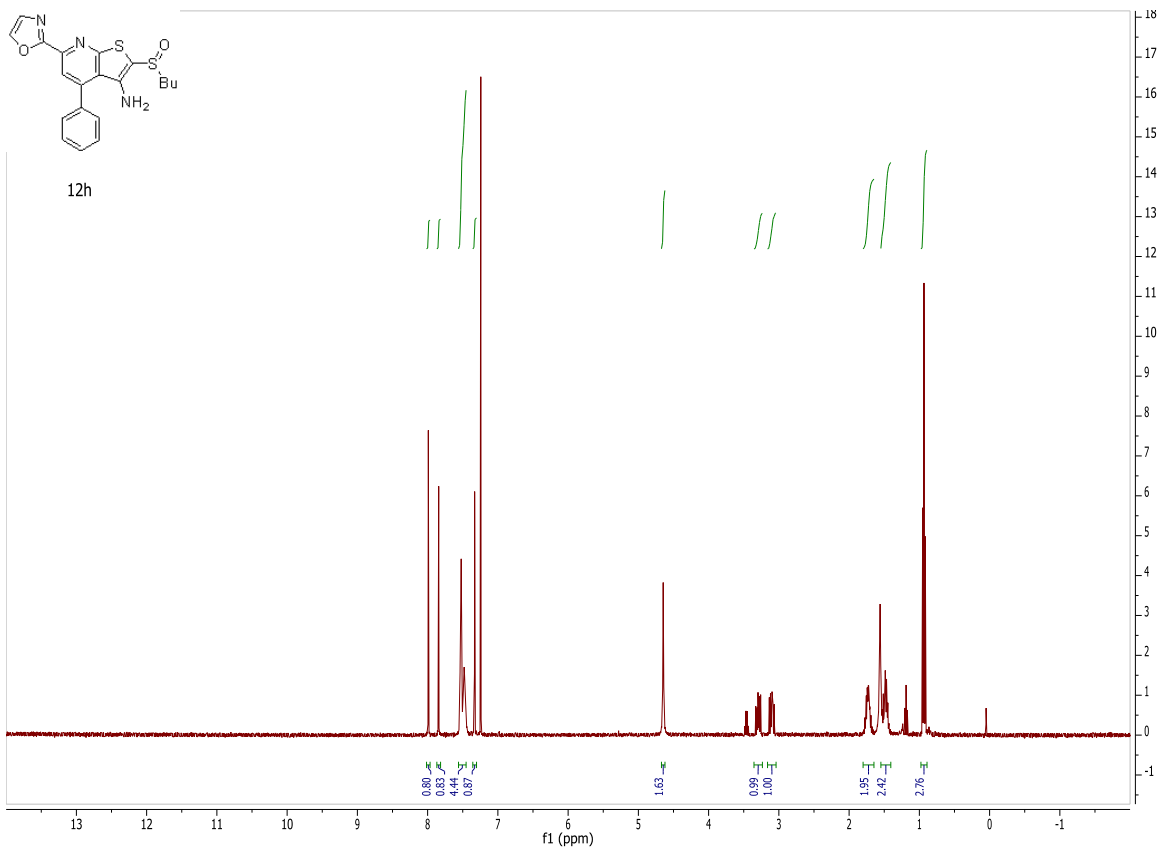




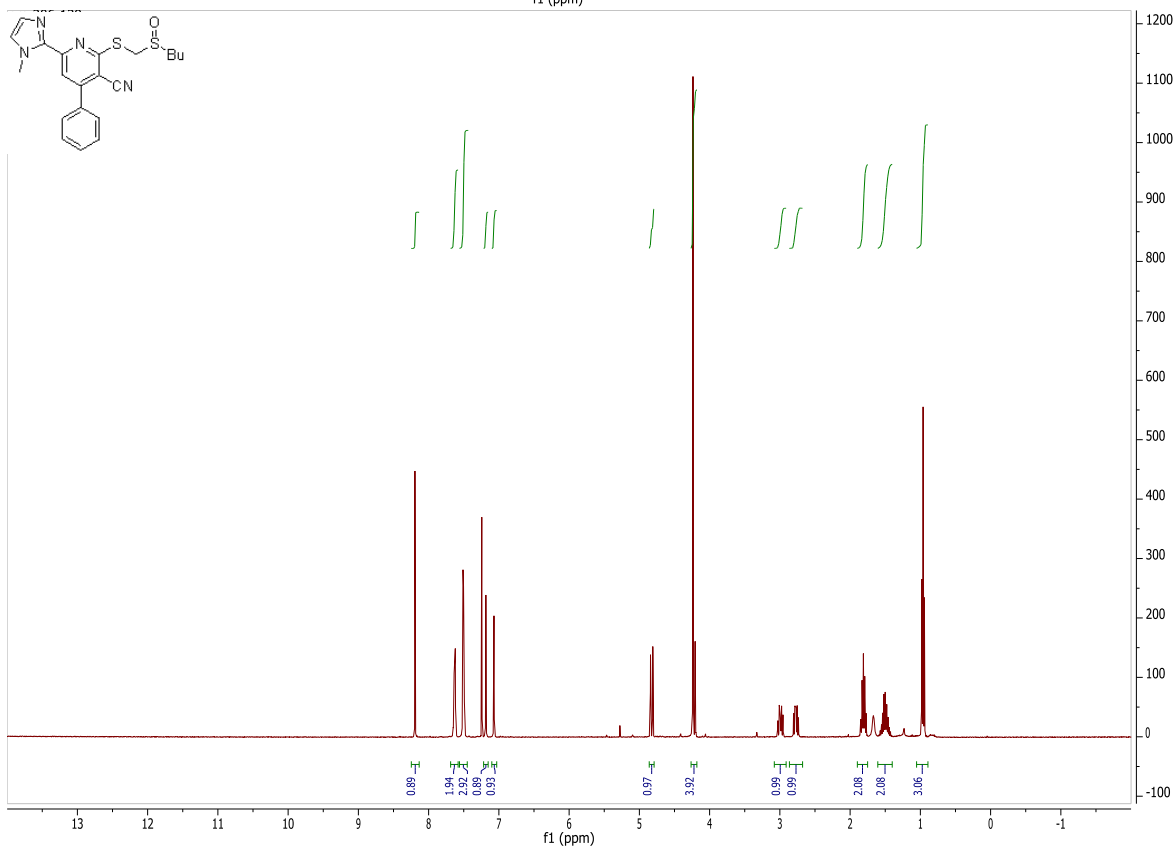
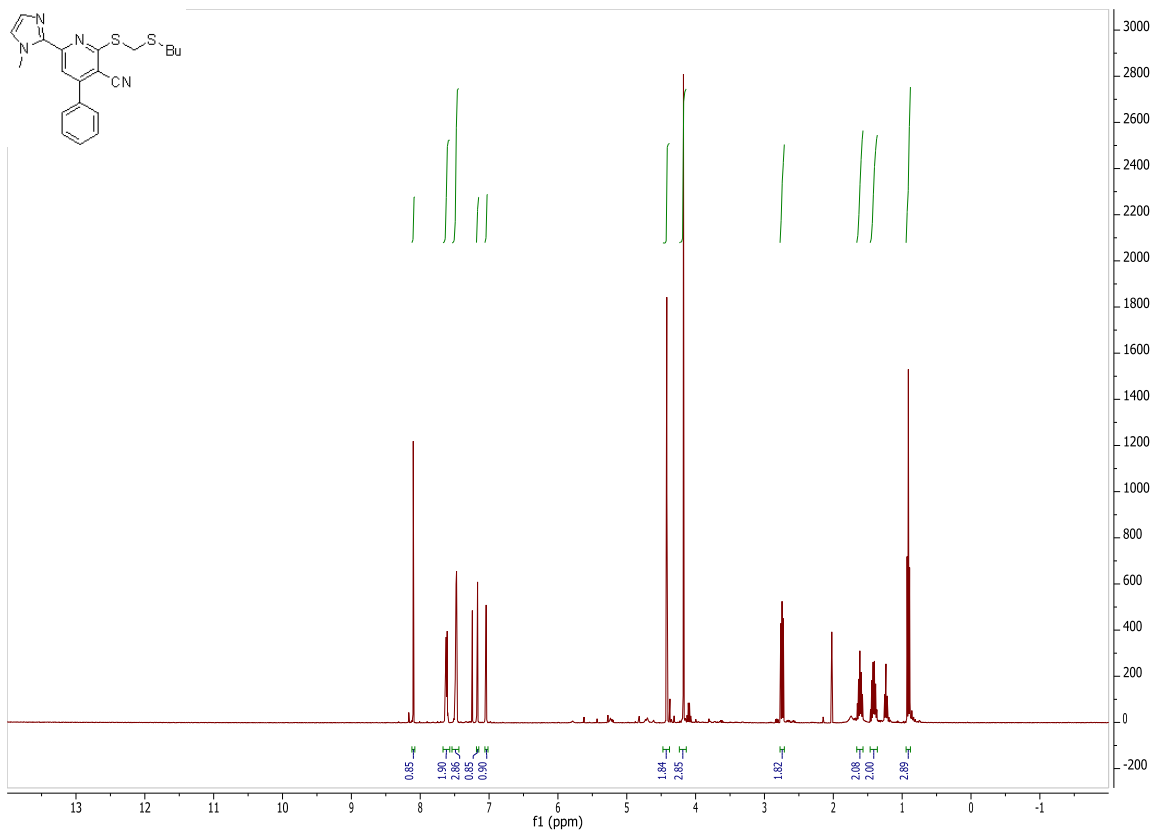


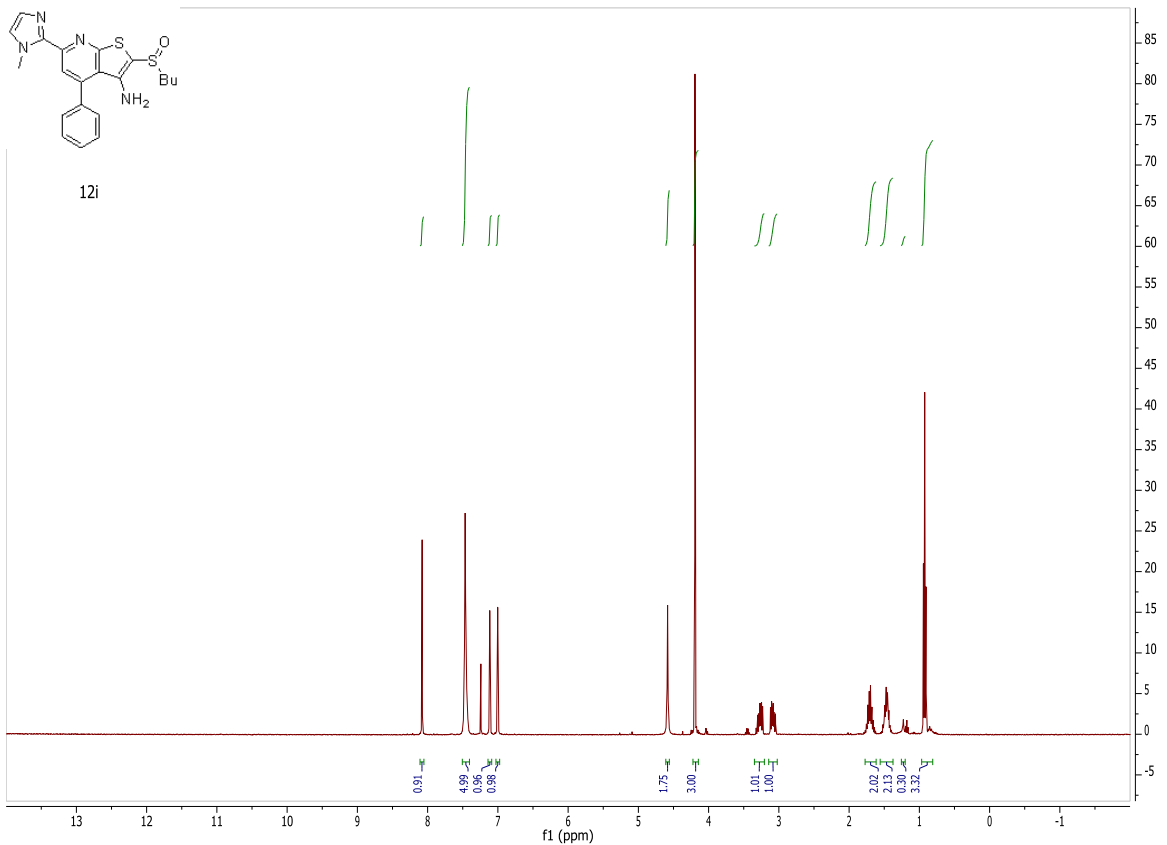
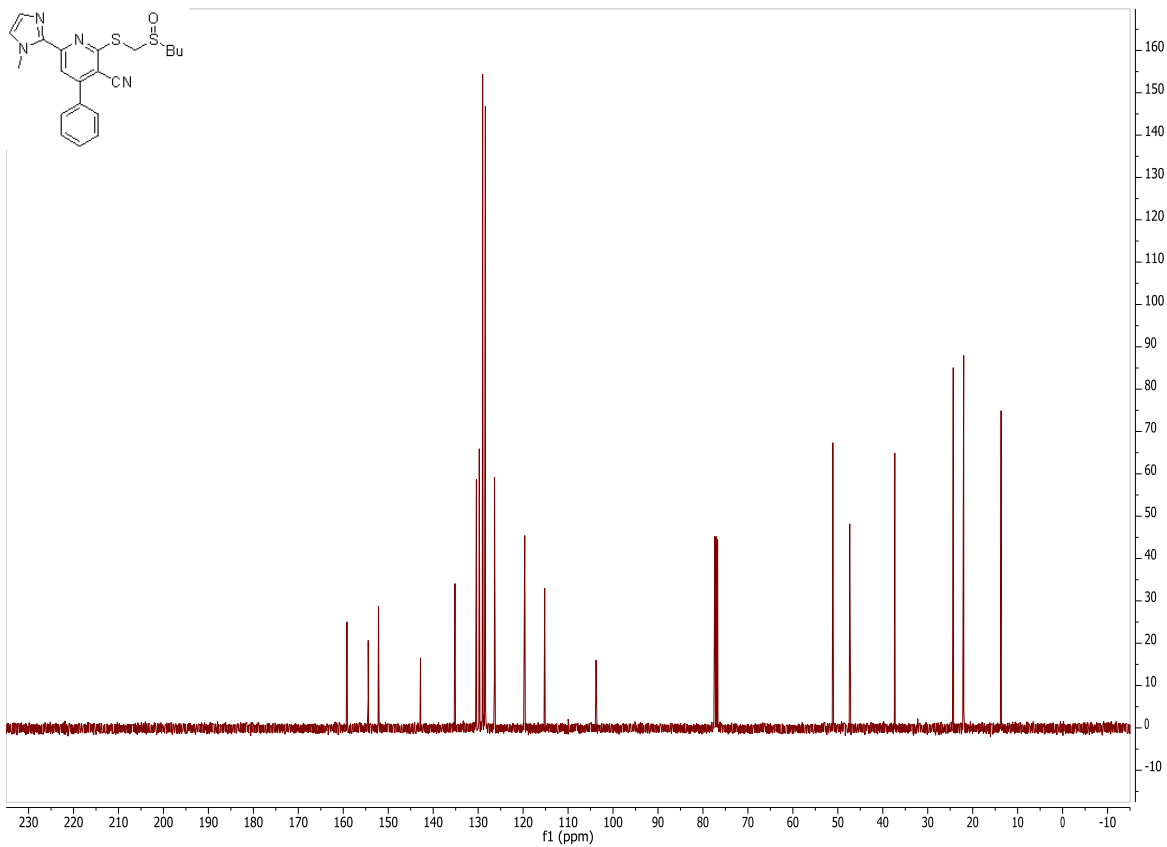


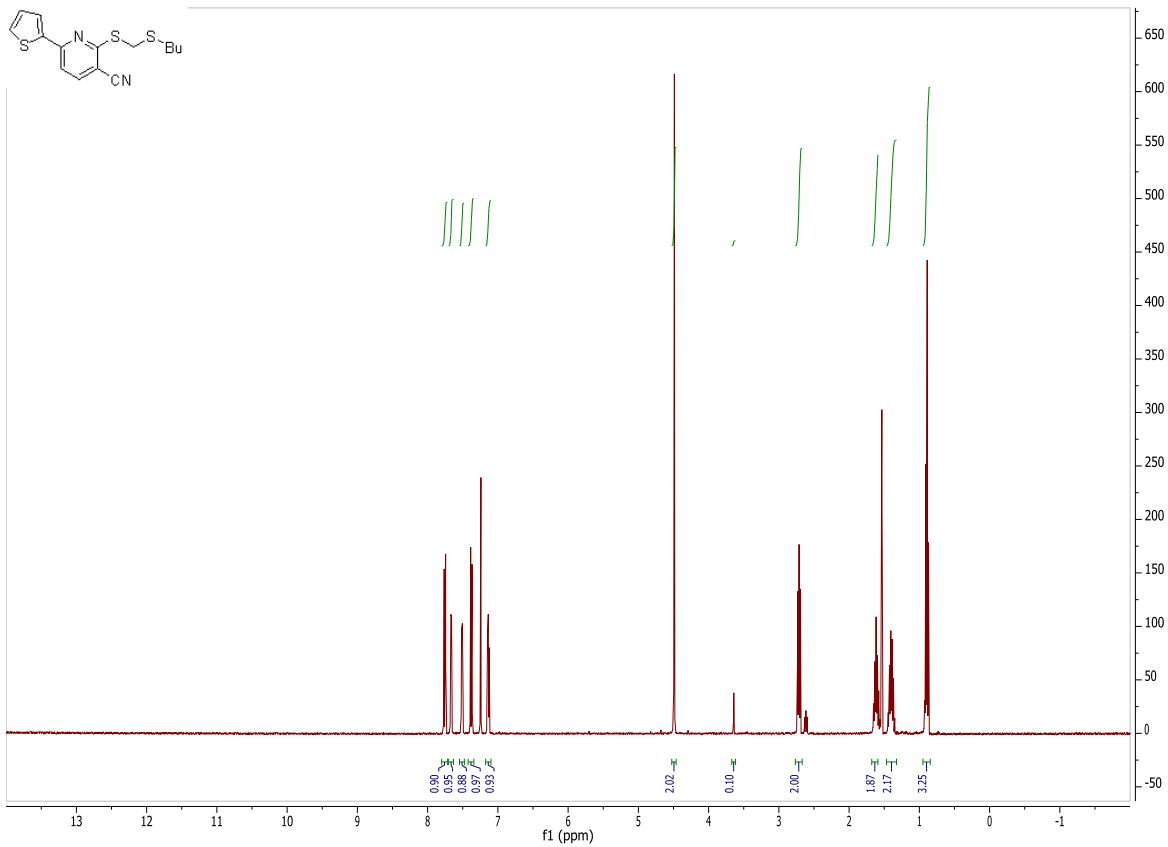
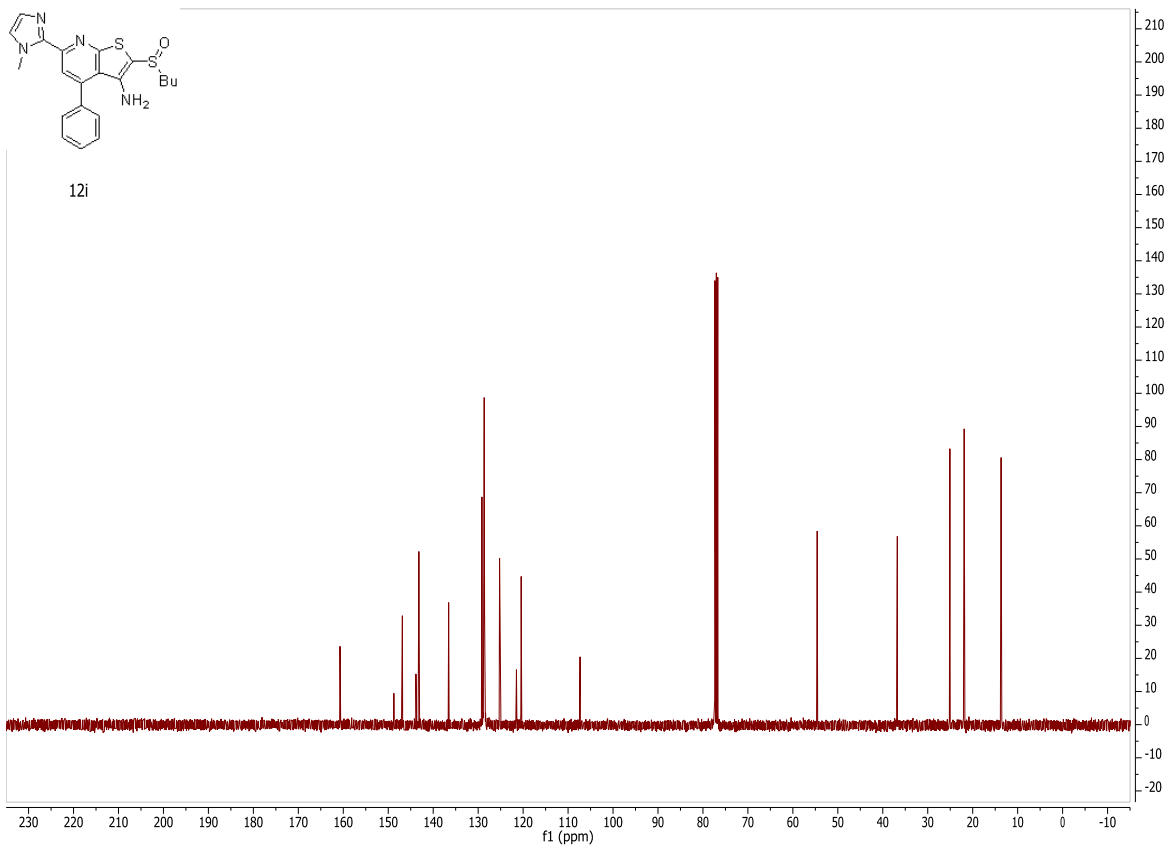


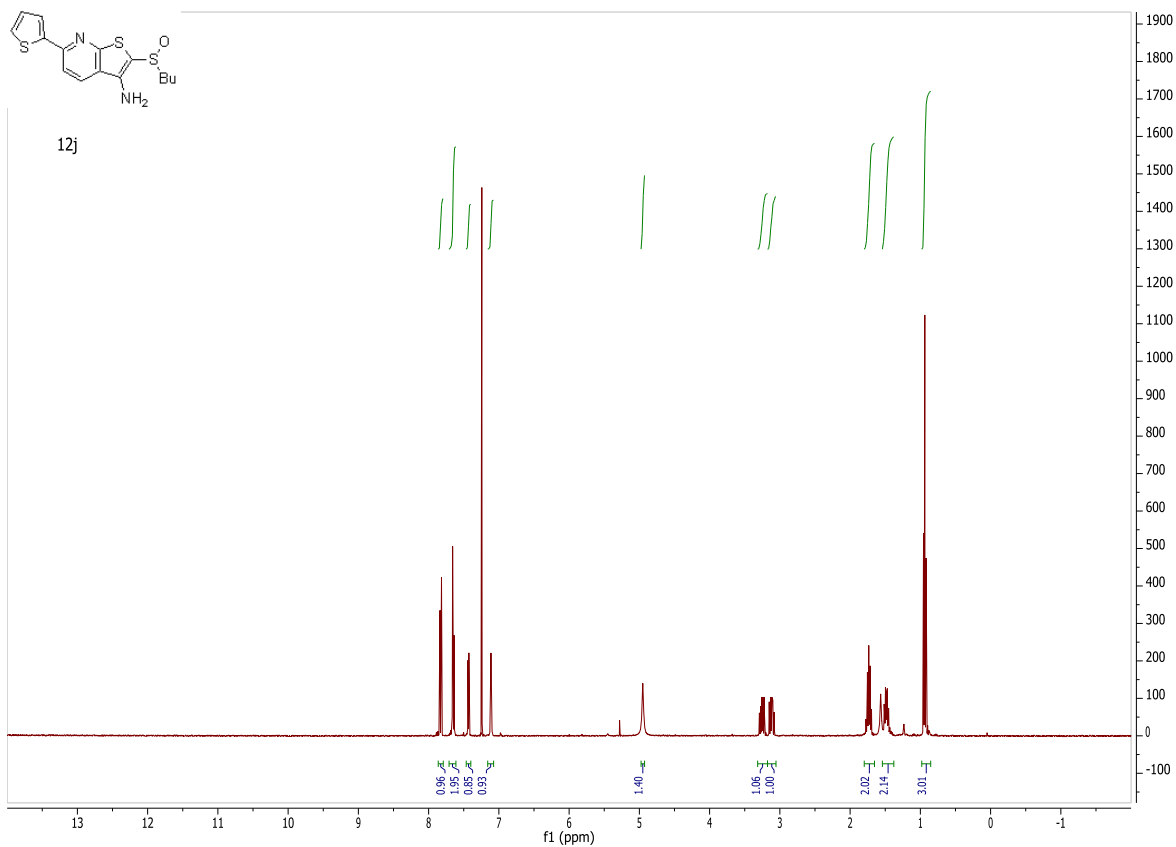
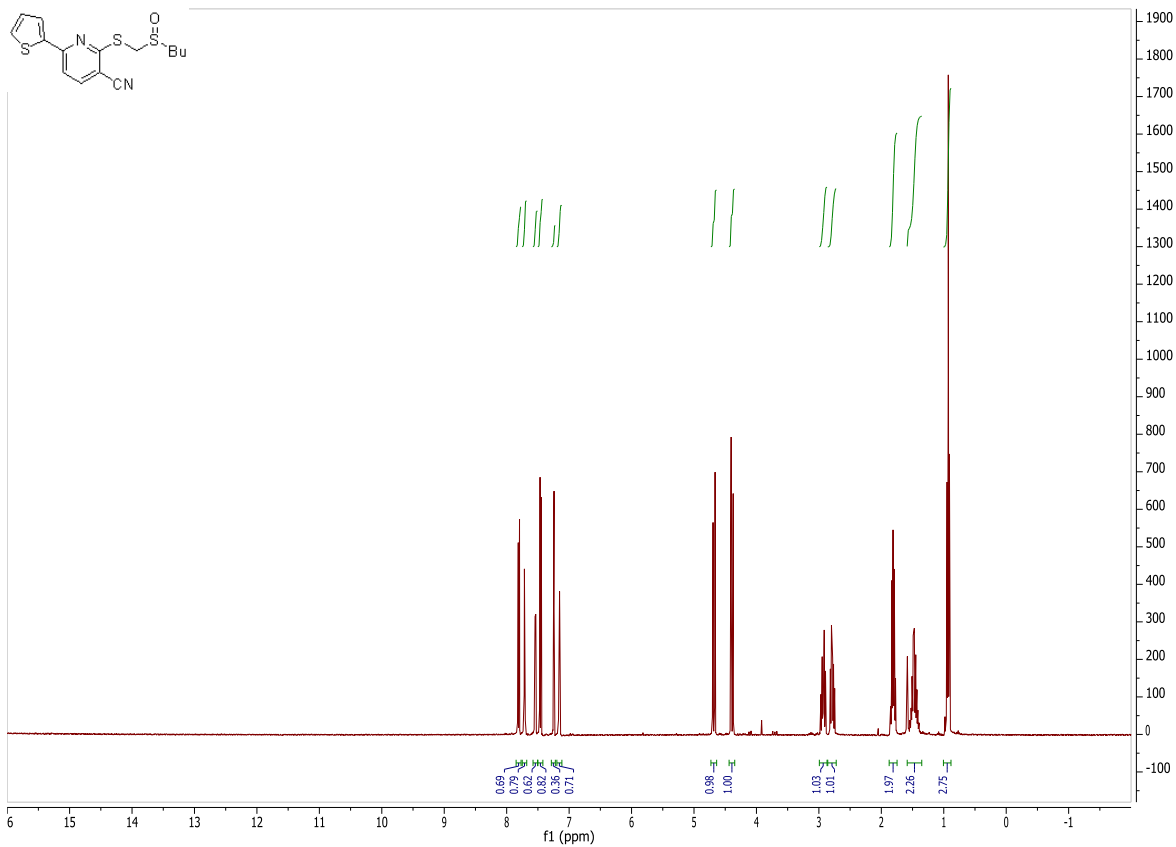


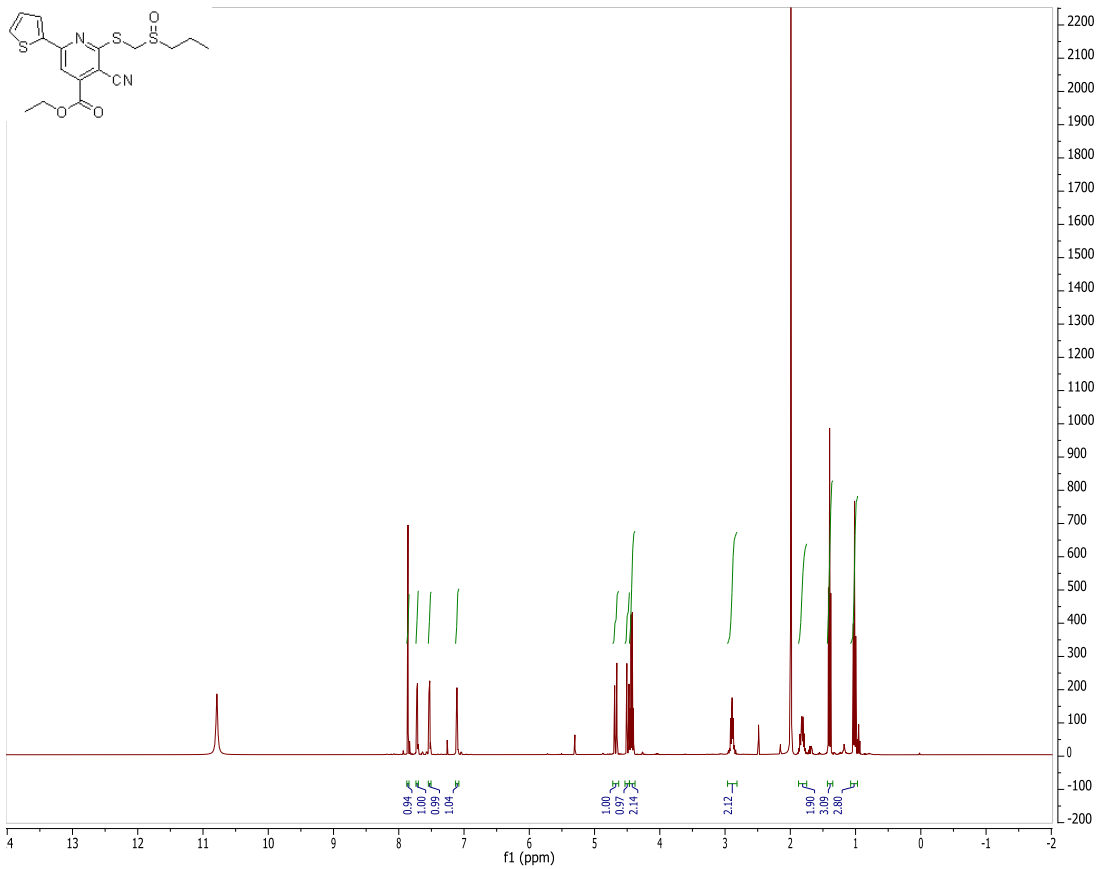
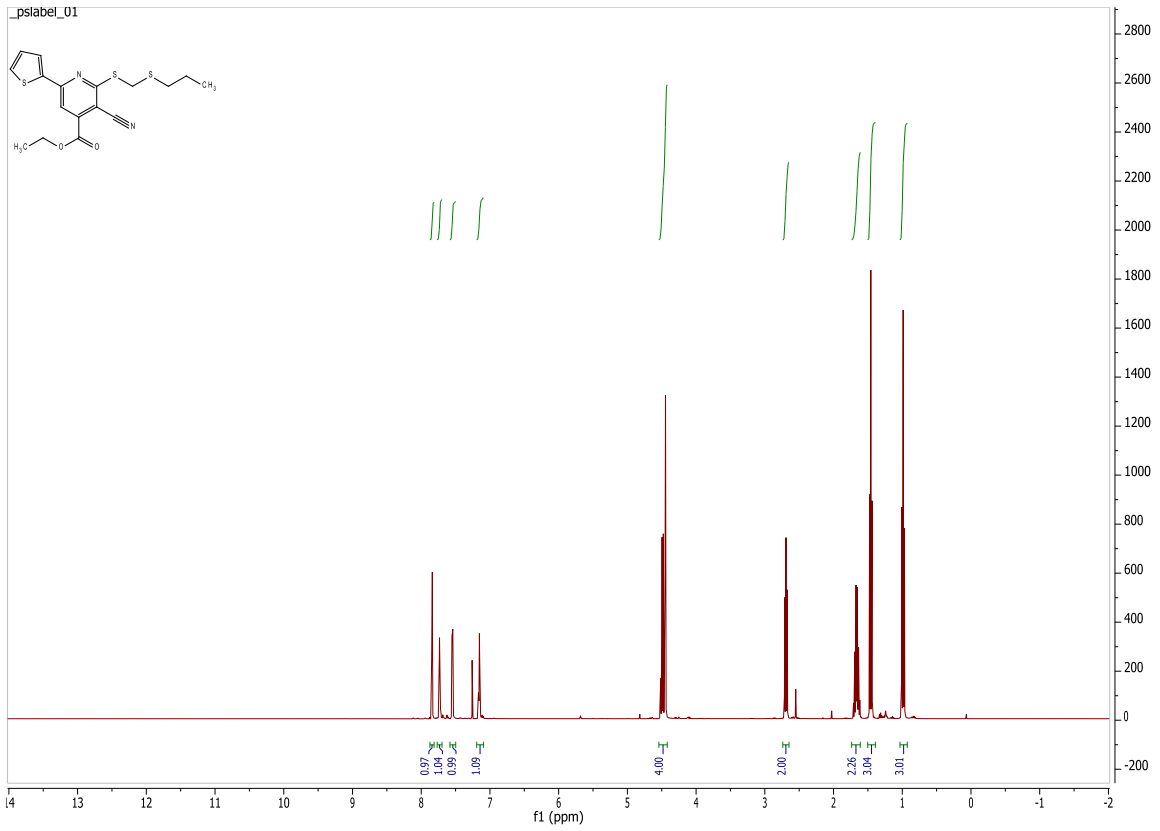


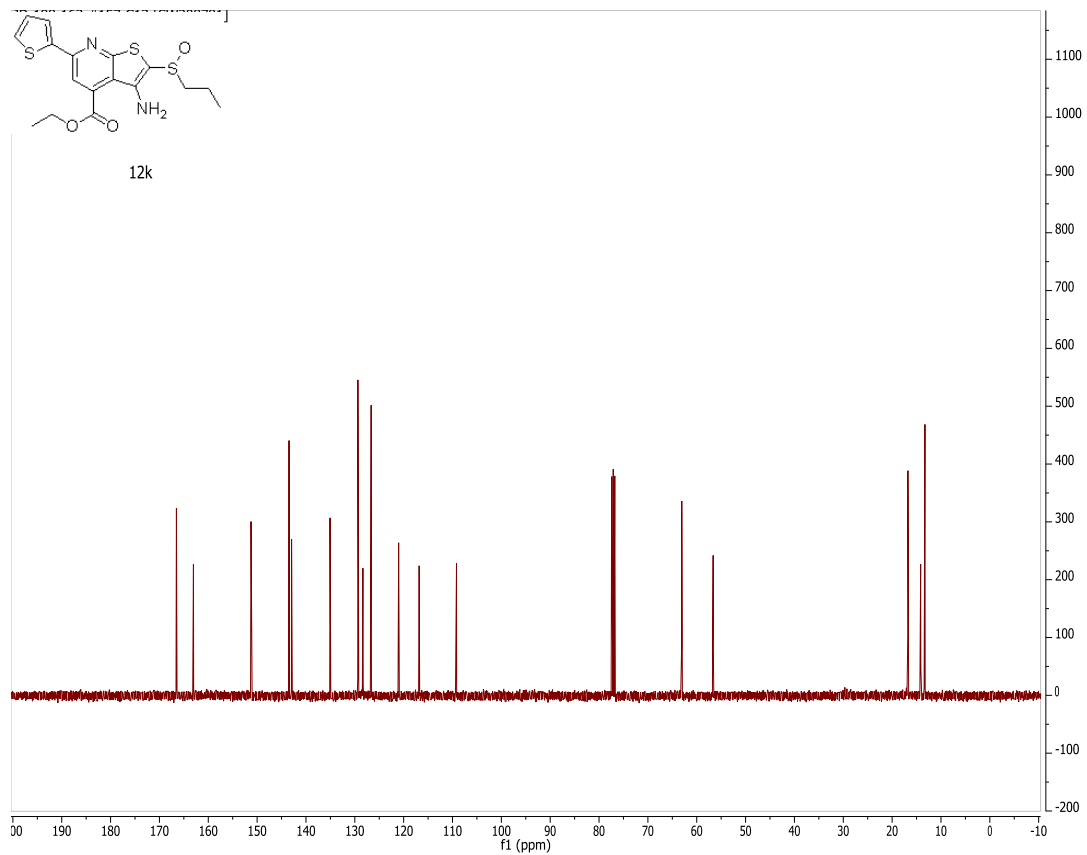
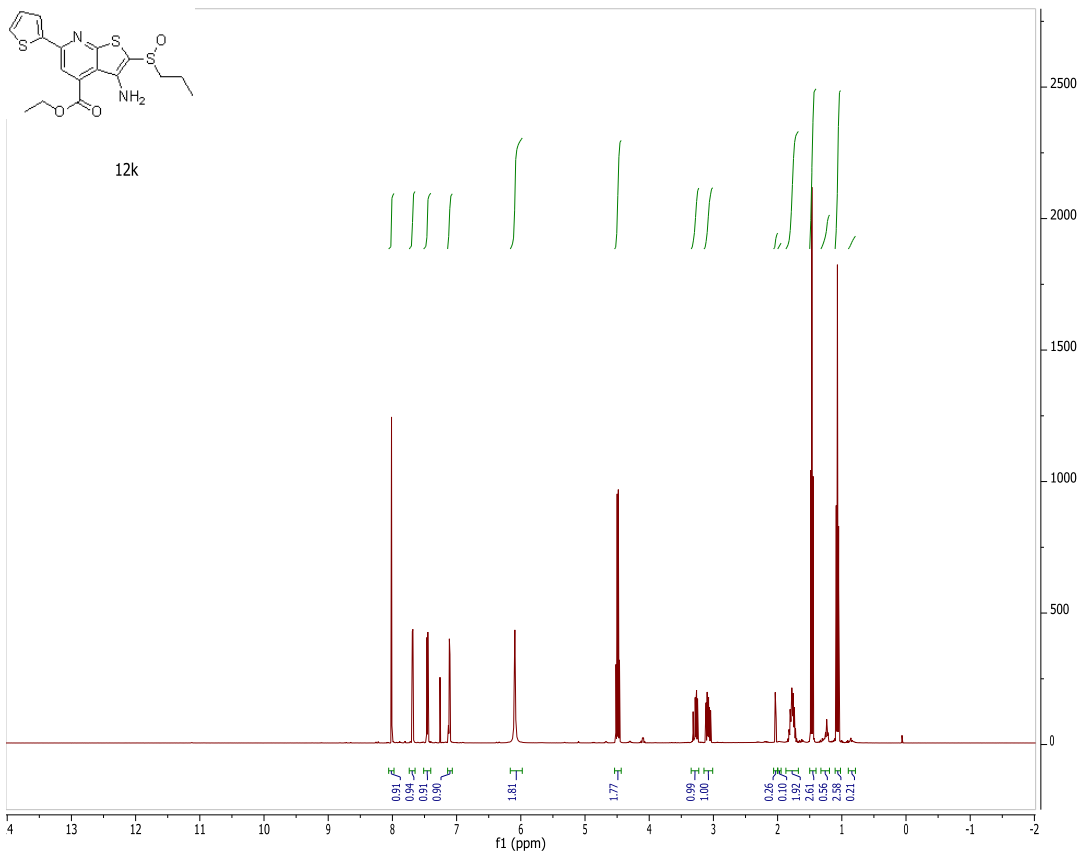


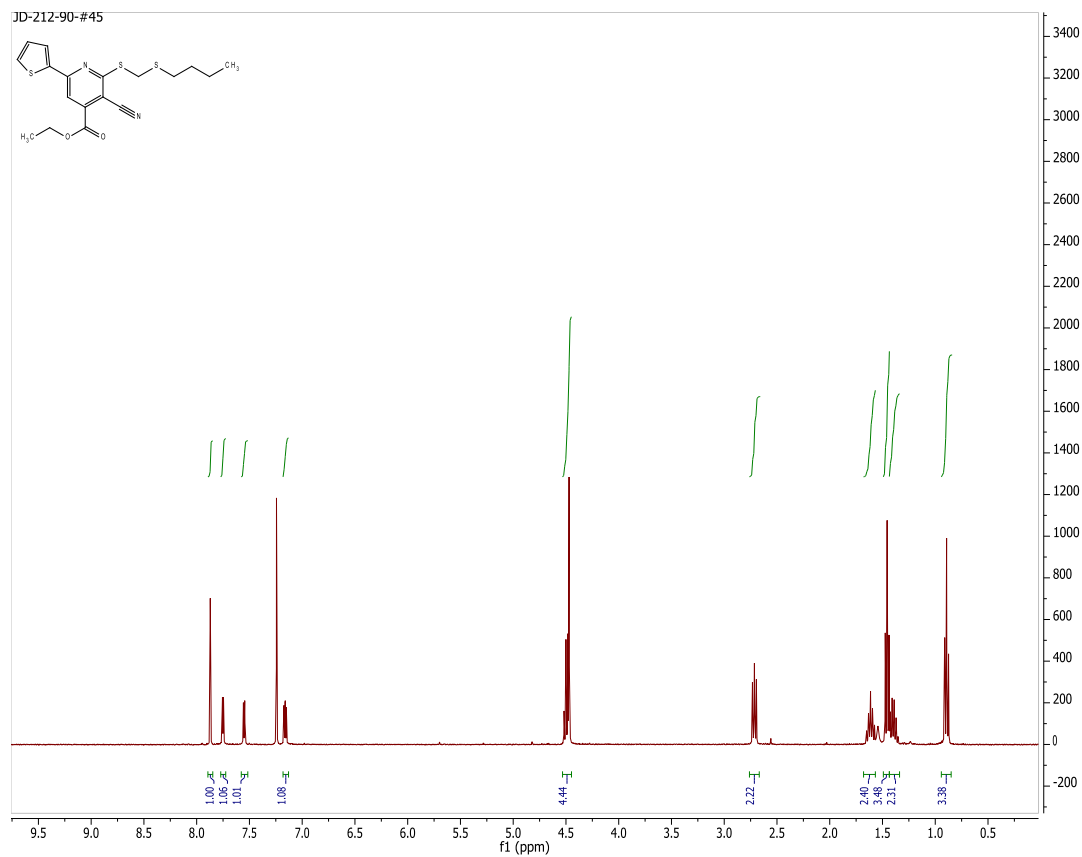
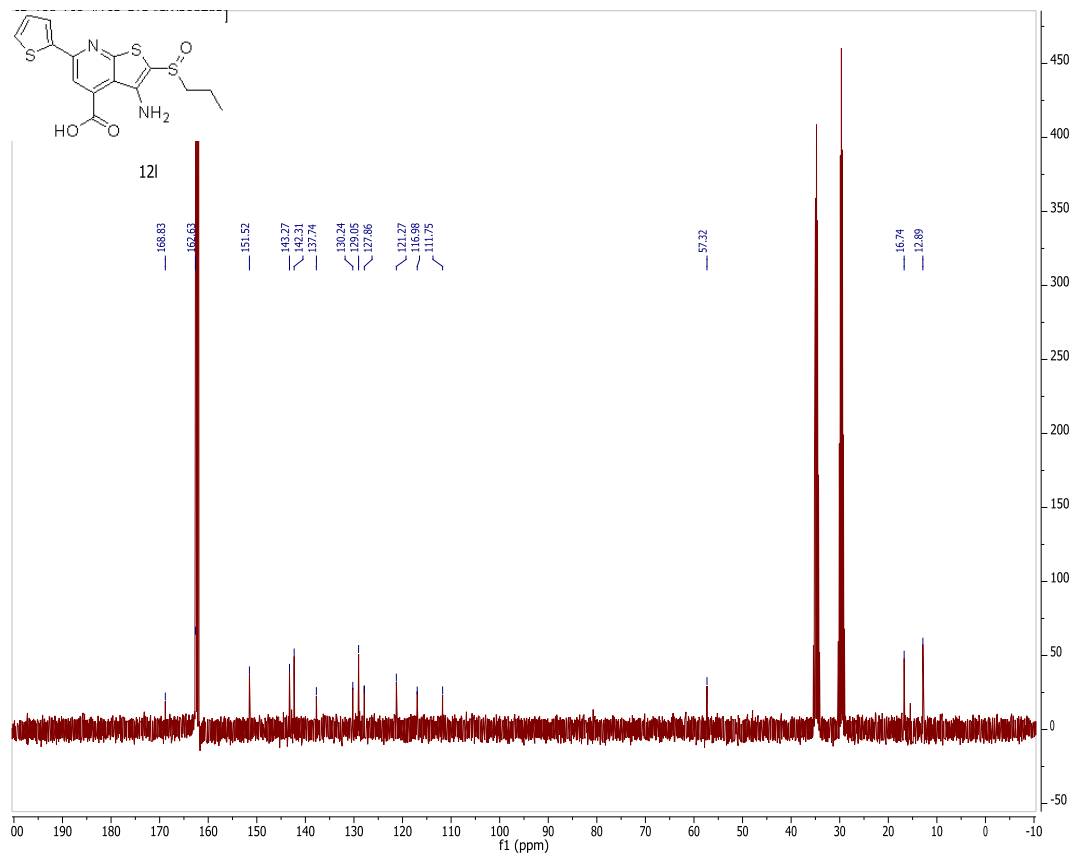




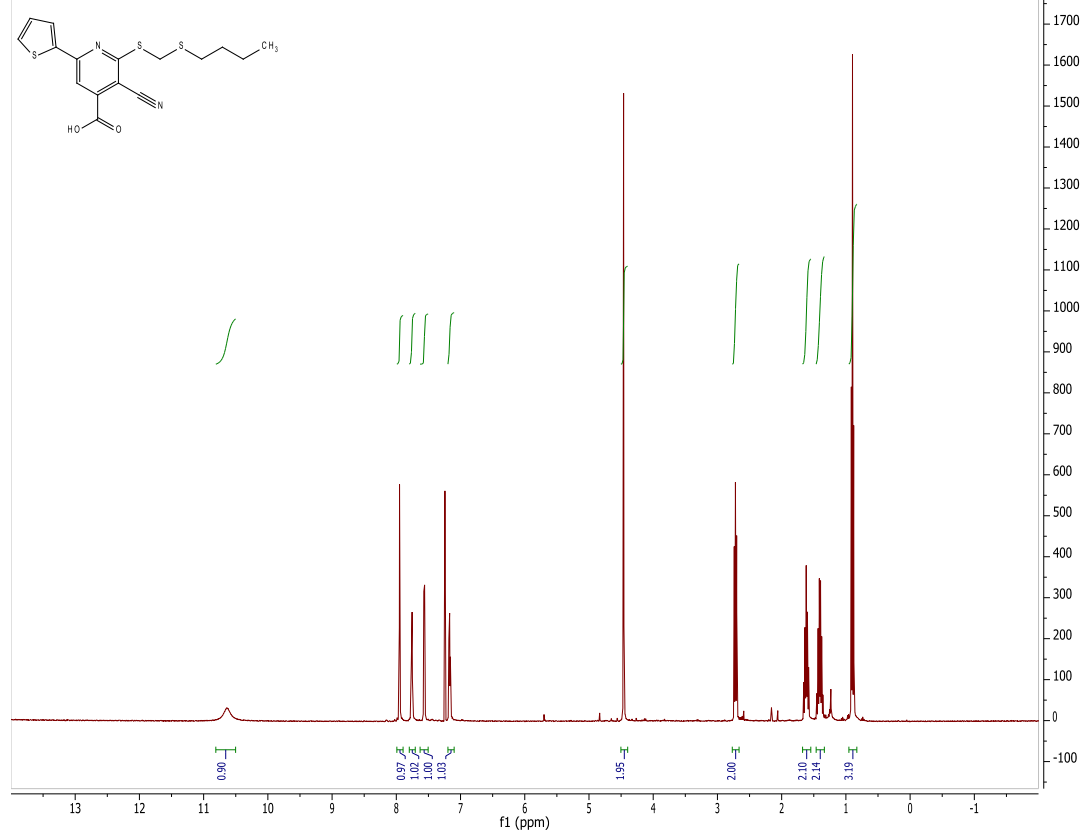




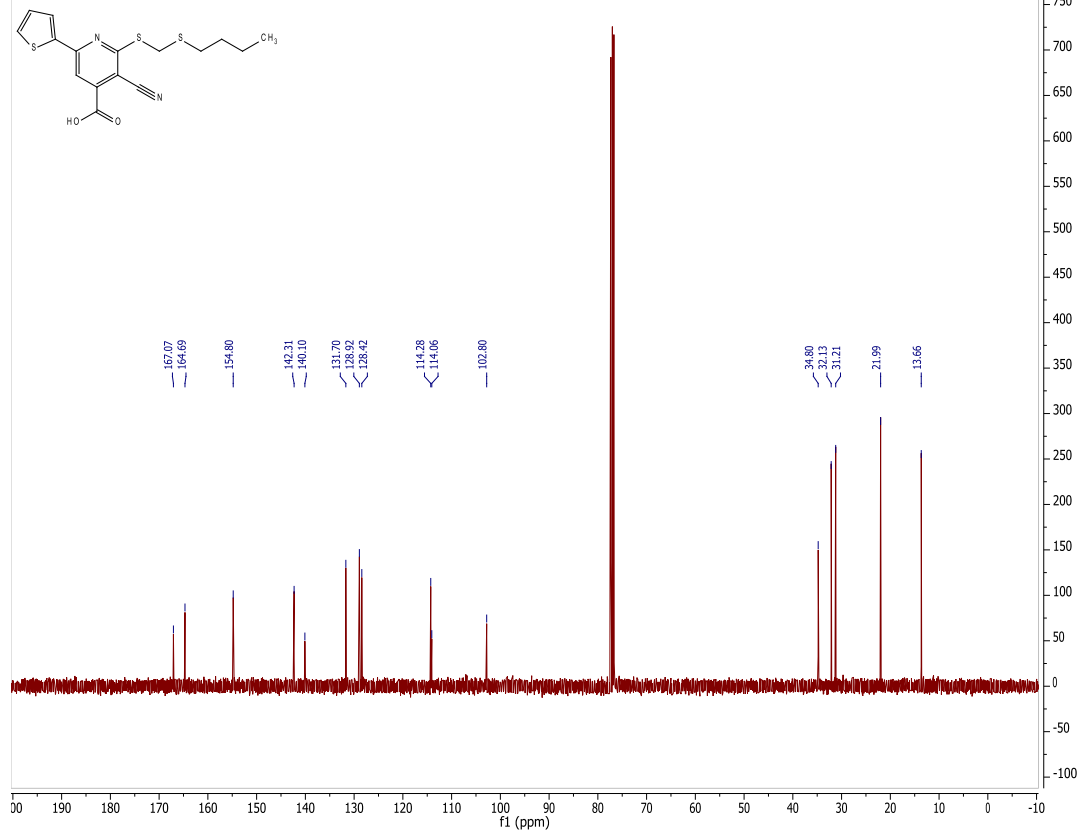




JD-212-94-#47

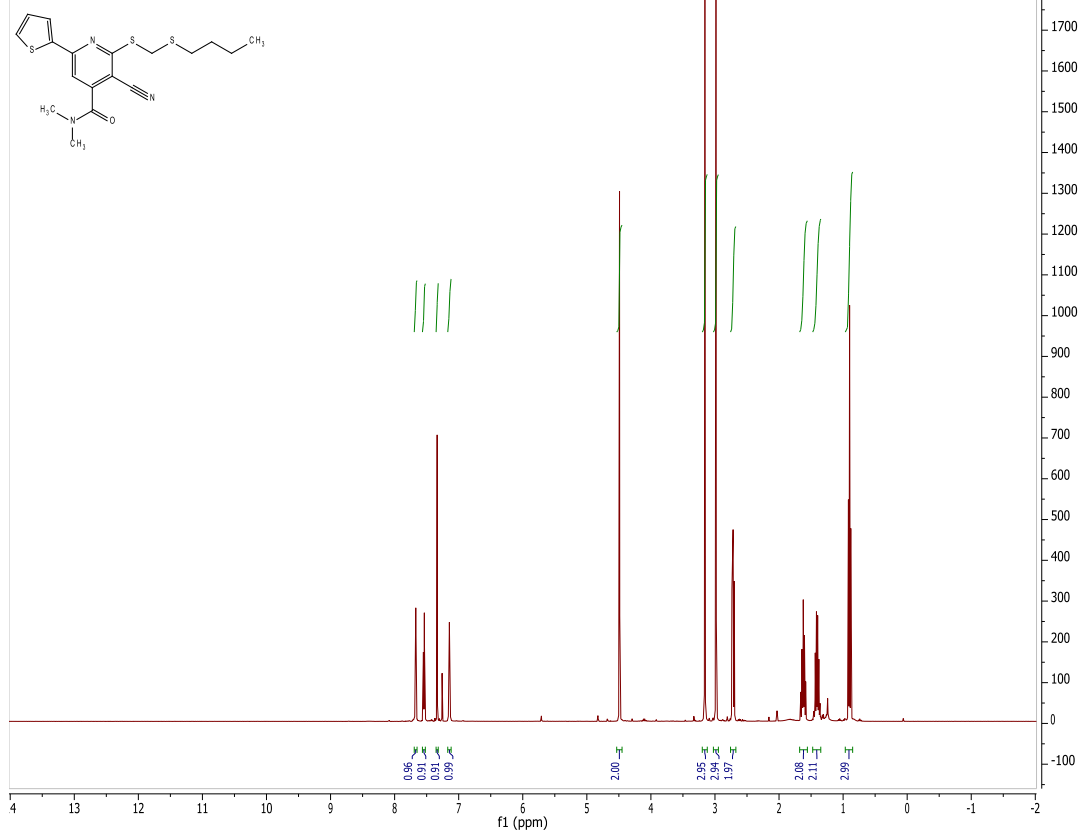


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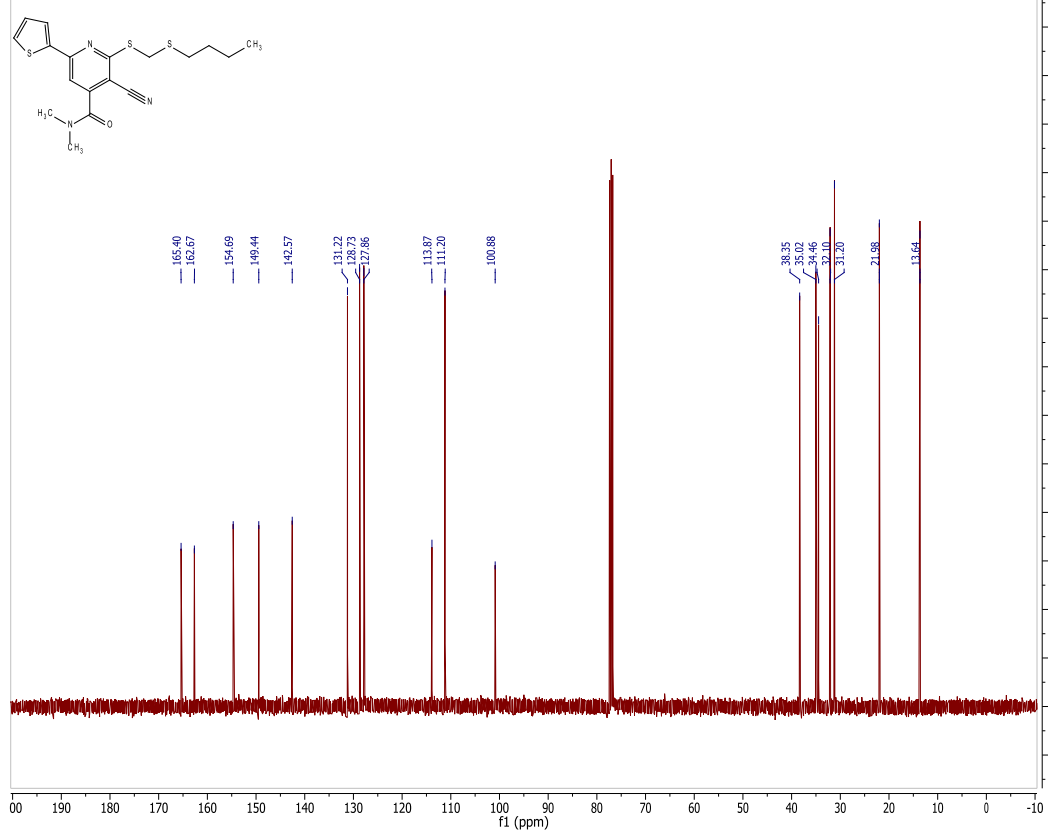




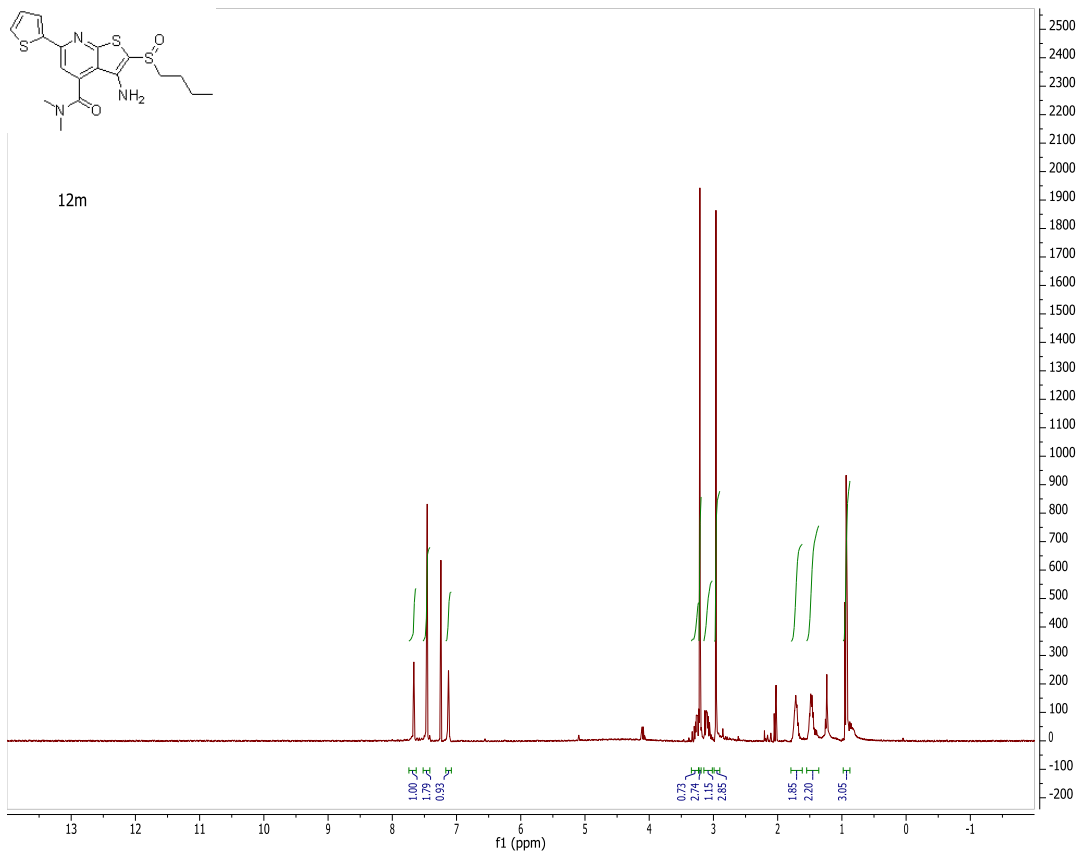
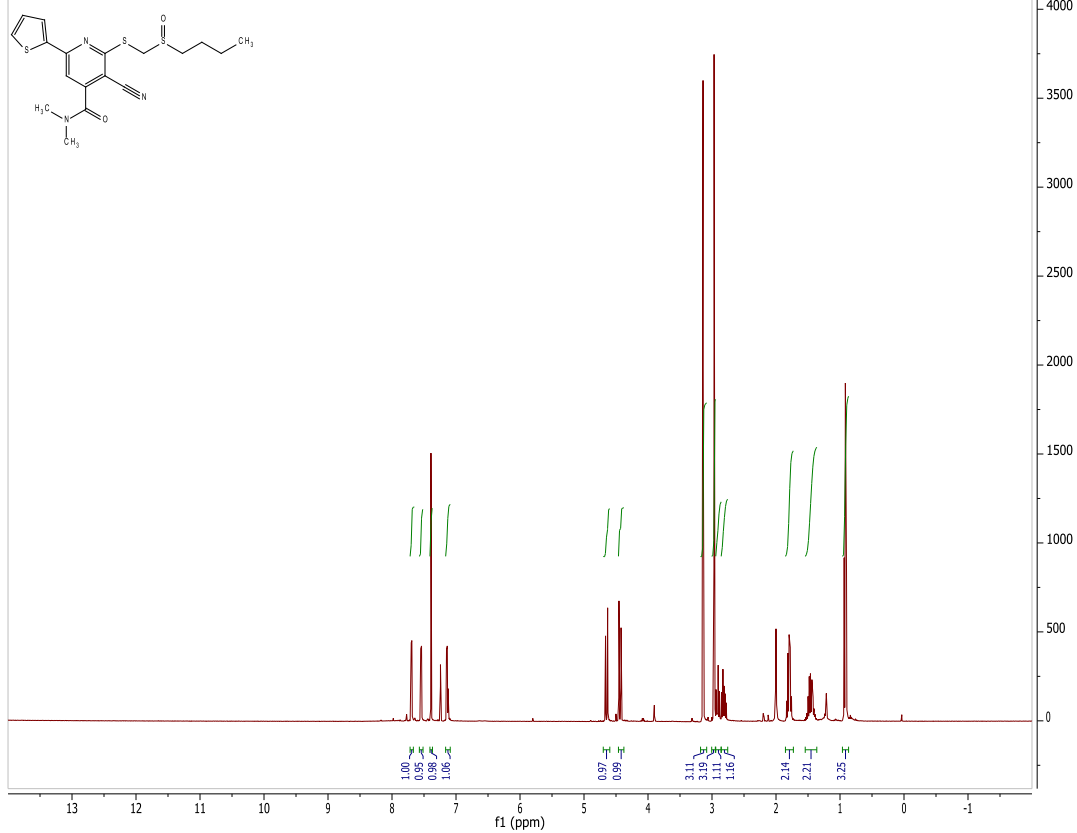
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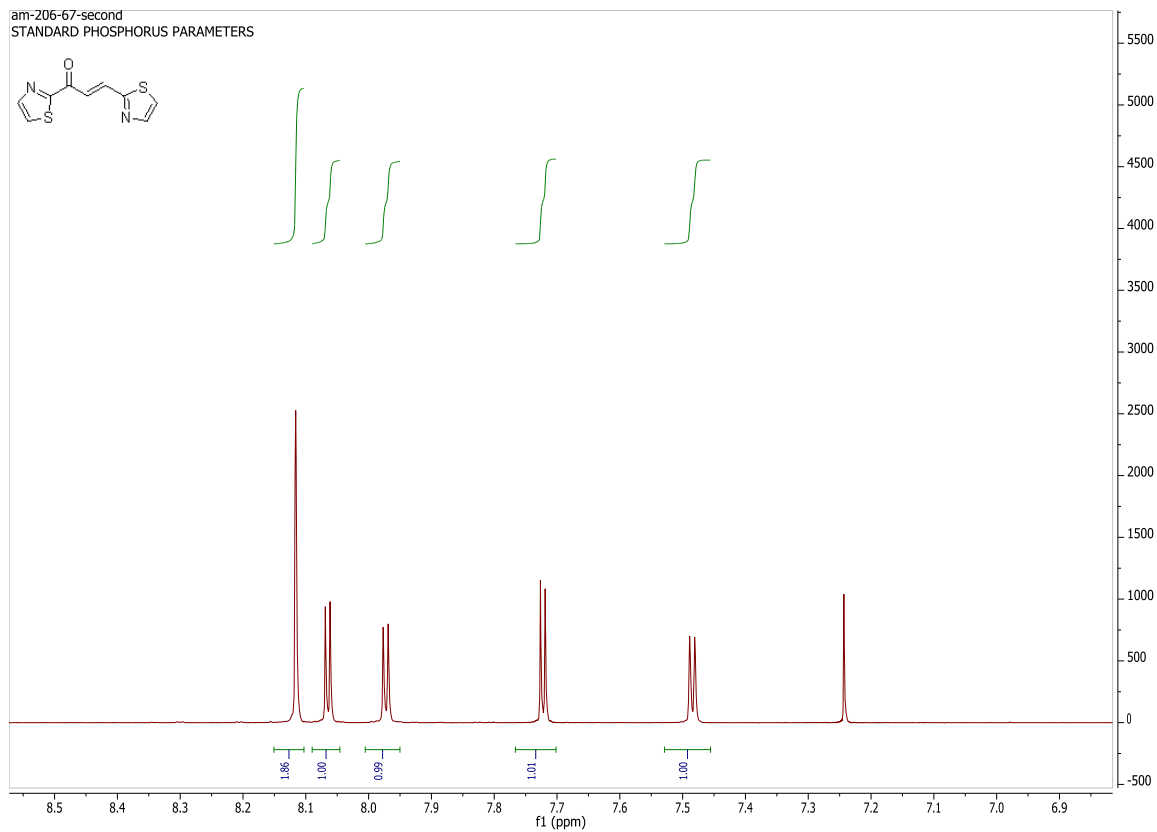
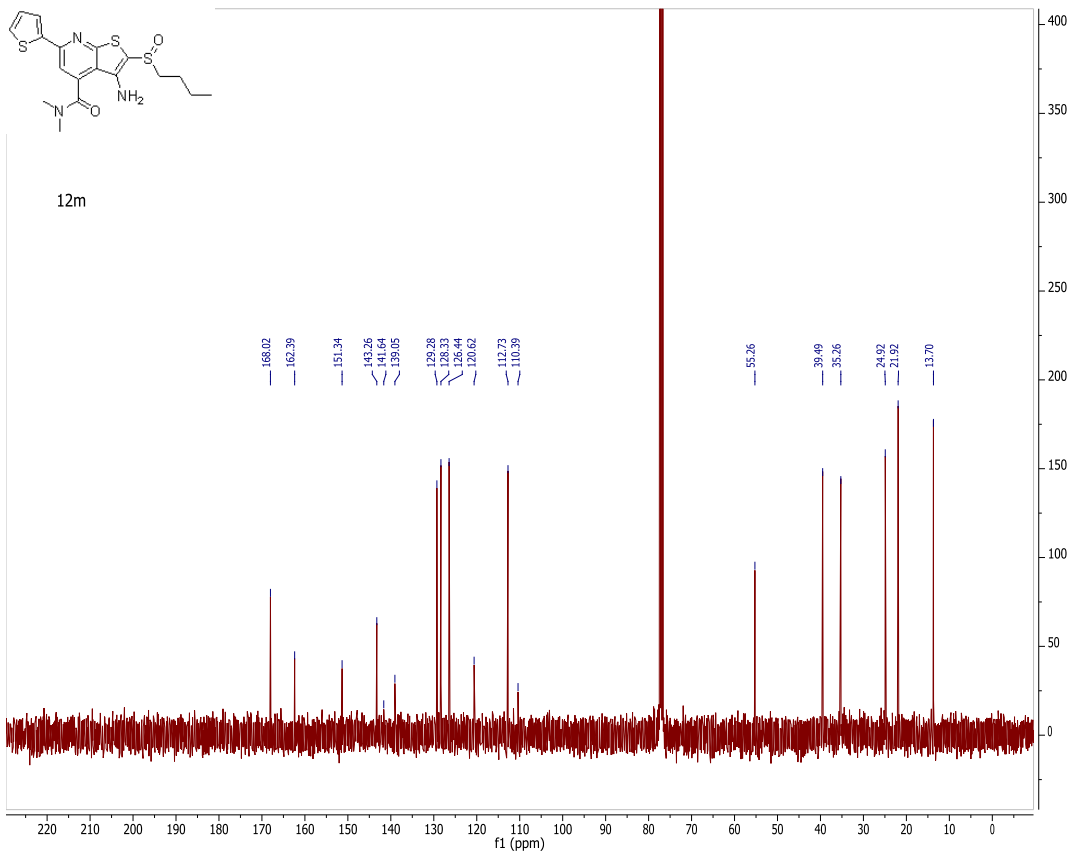


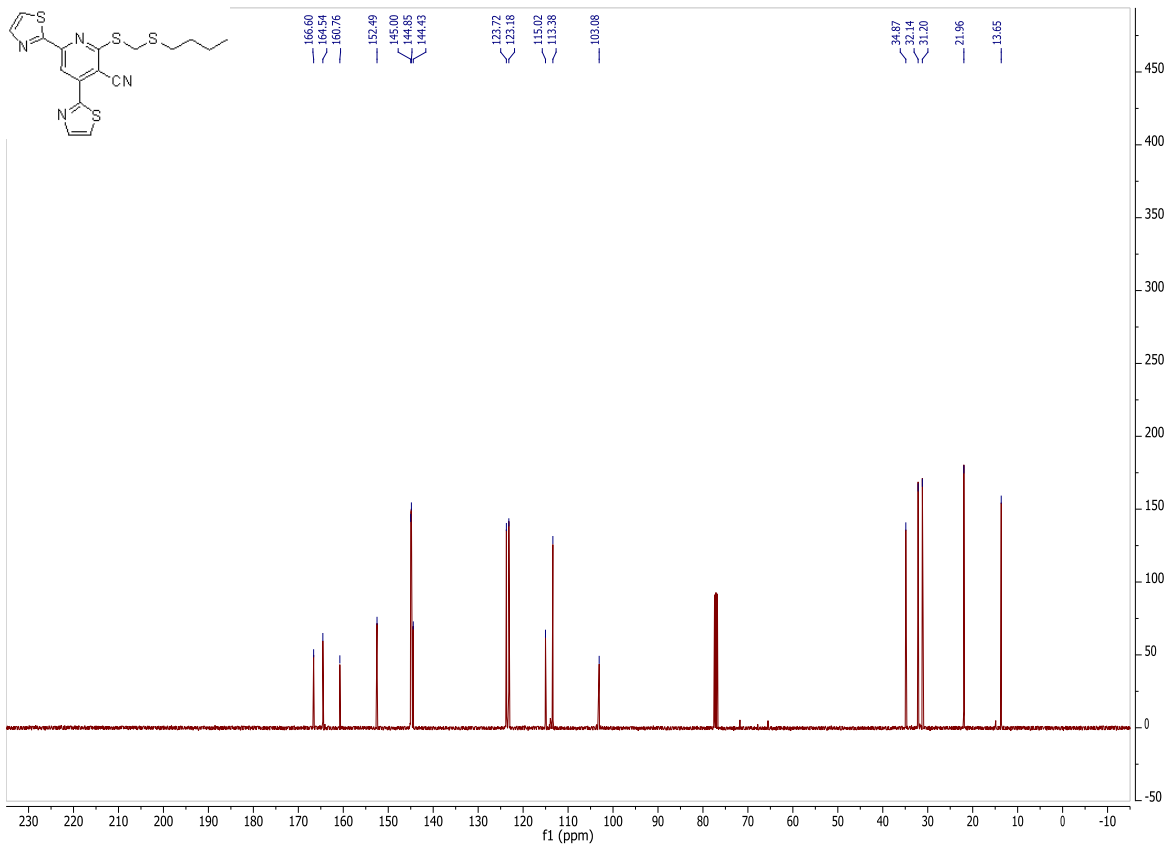
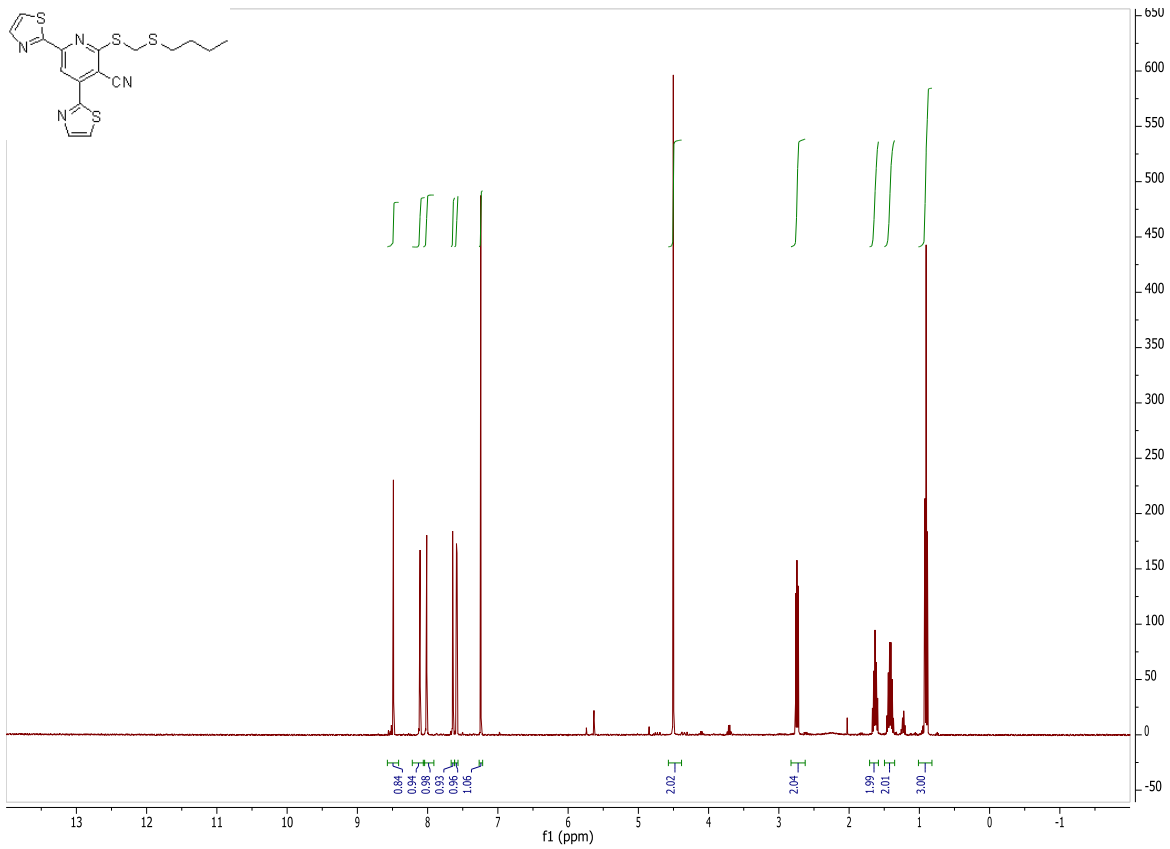
JD-212-106-#53-C13

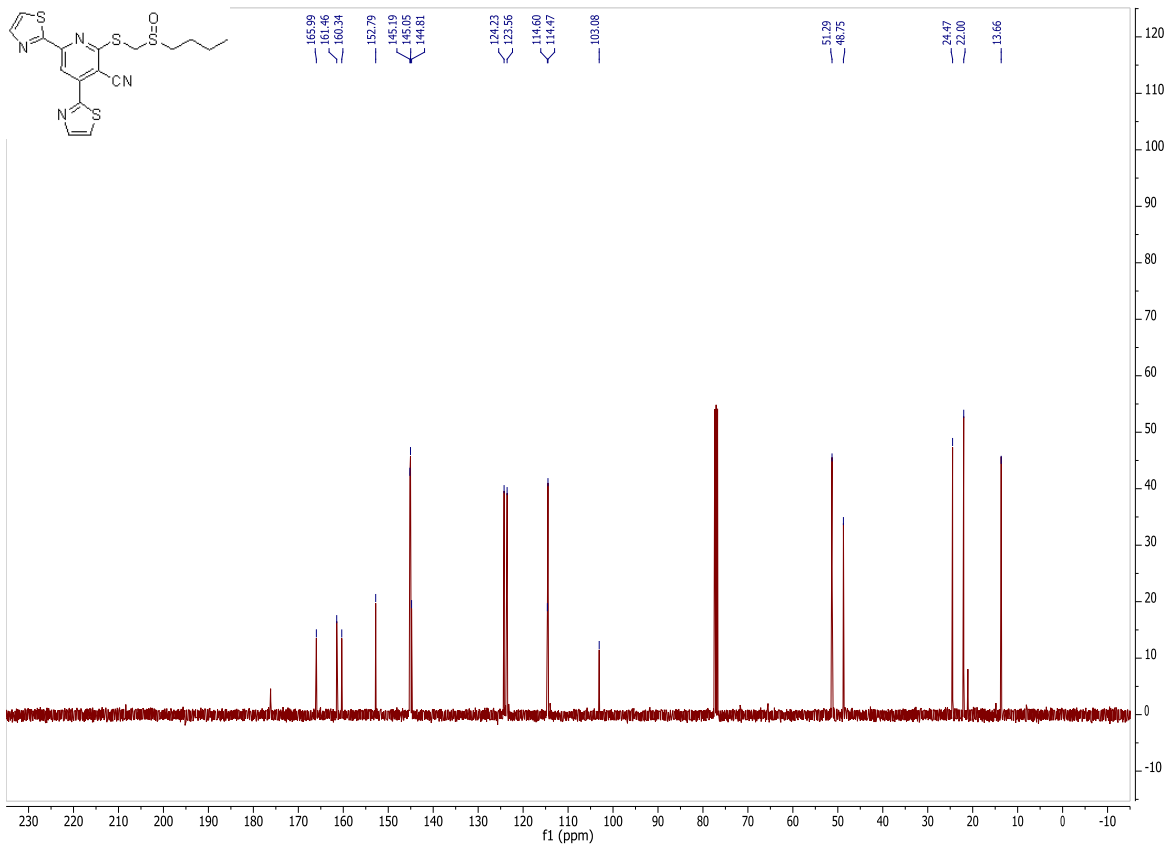
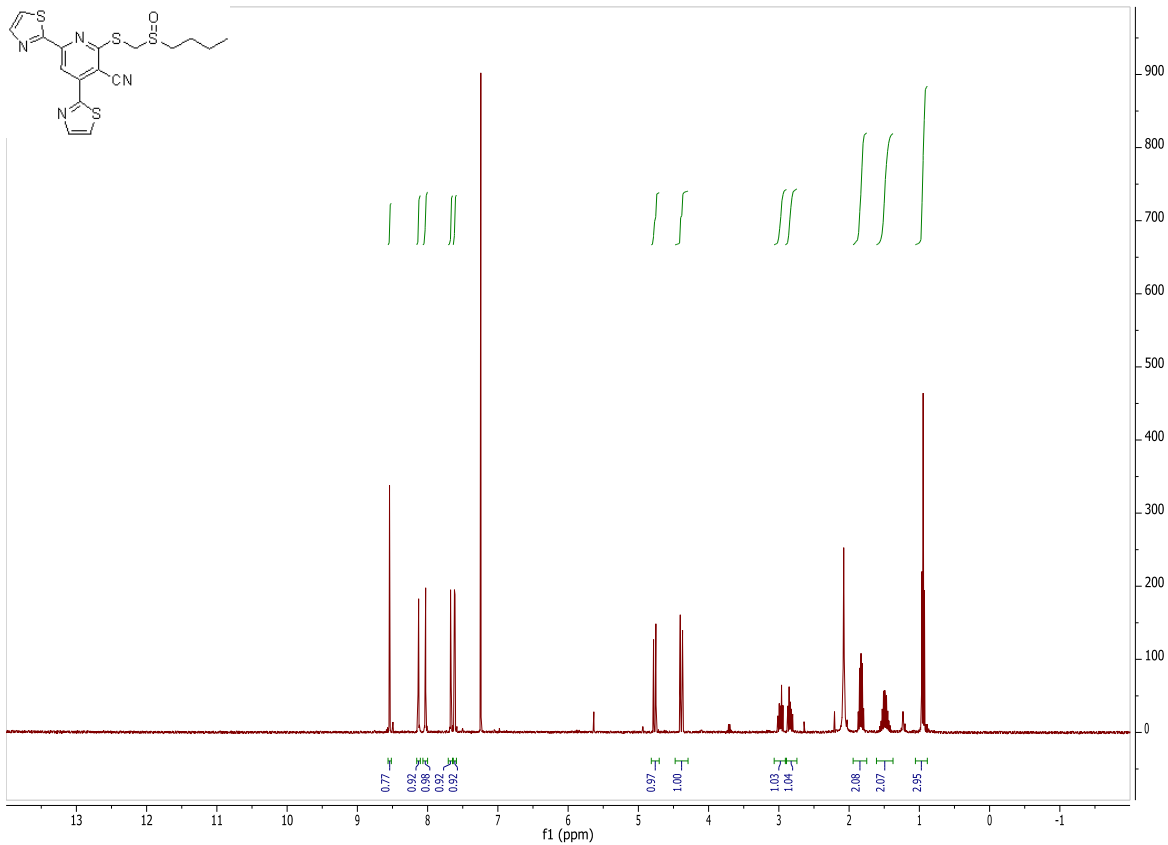


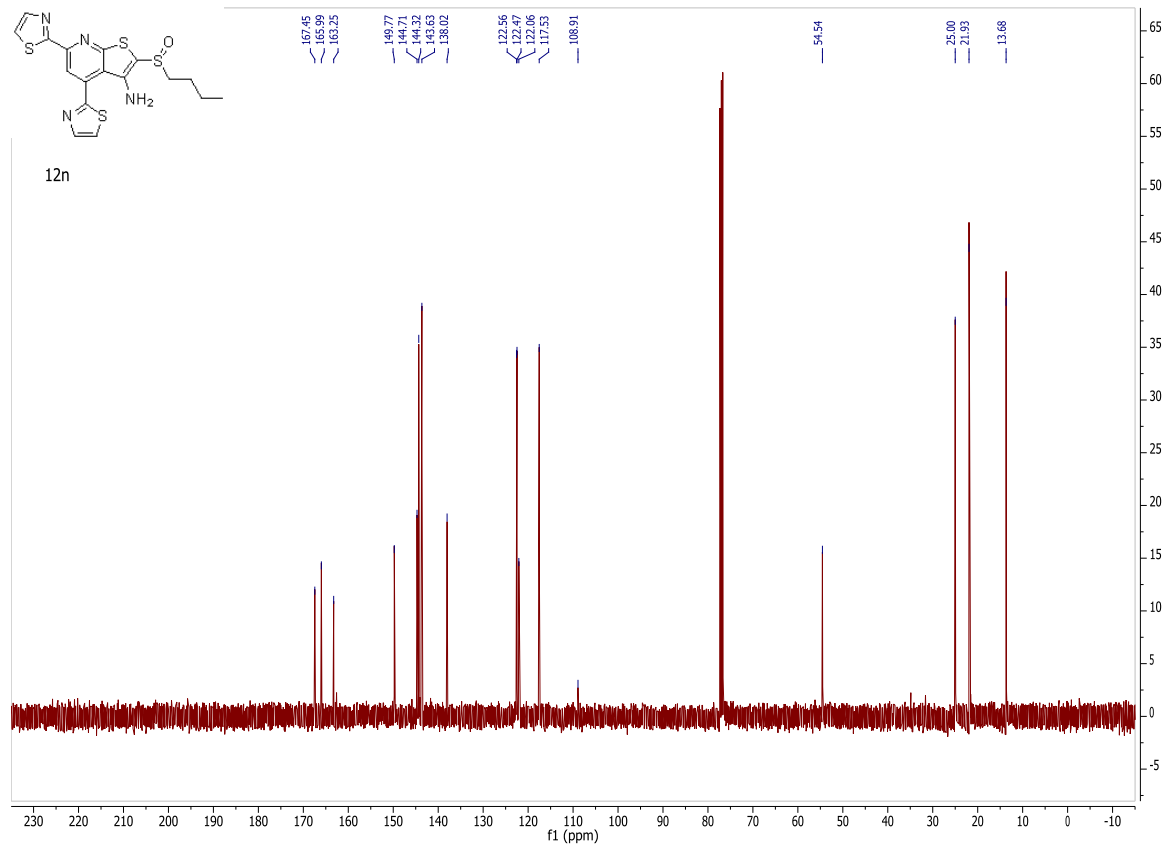
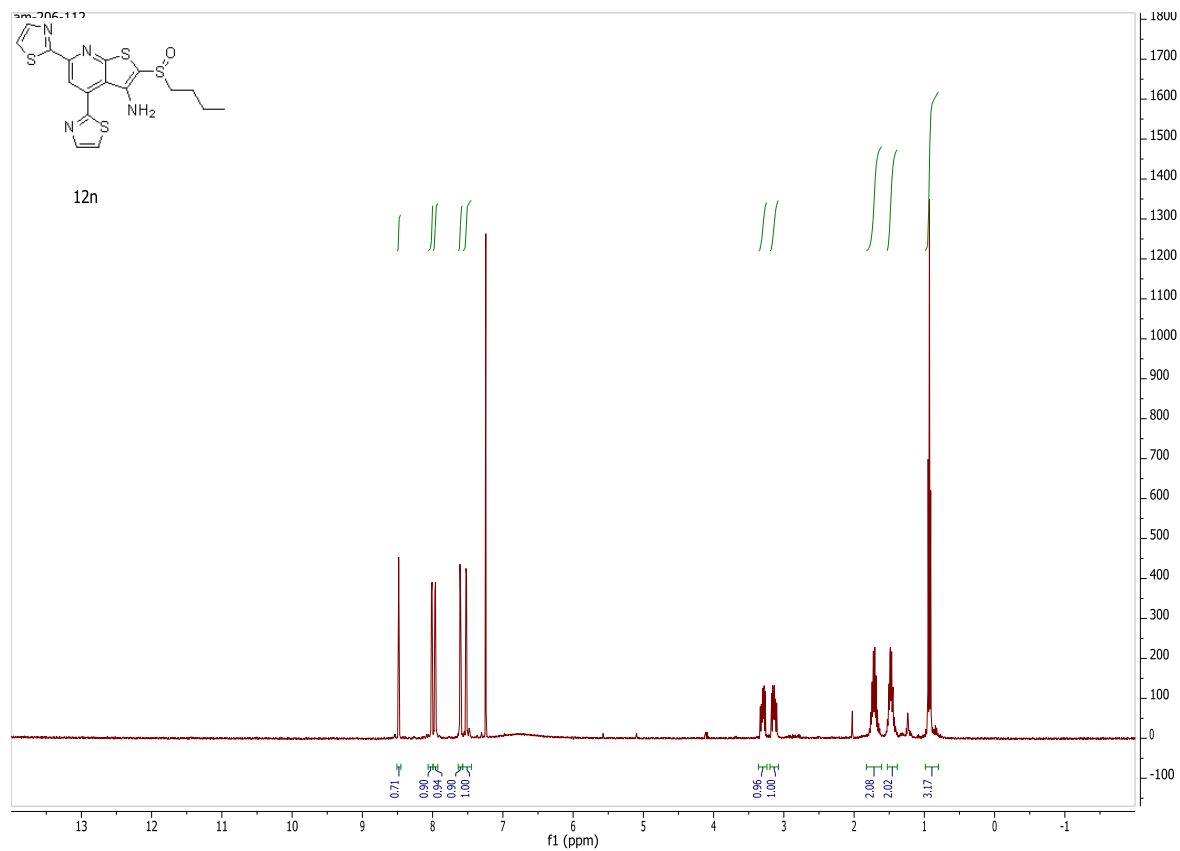
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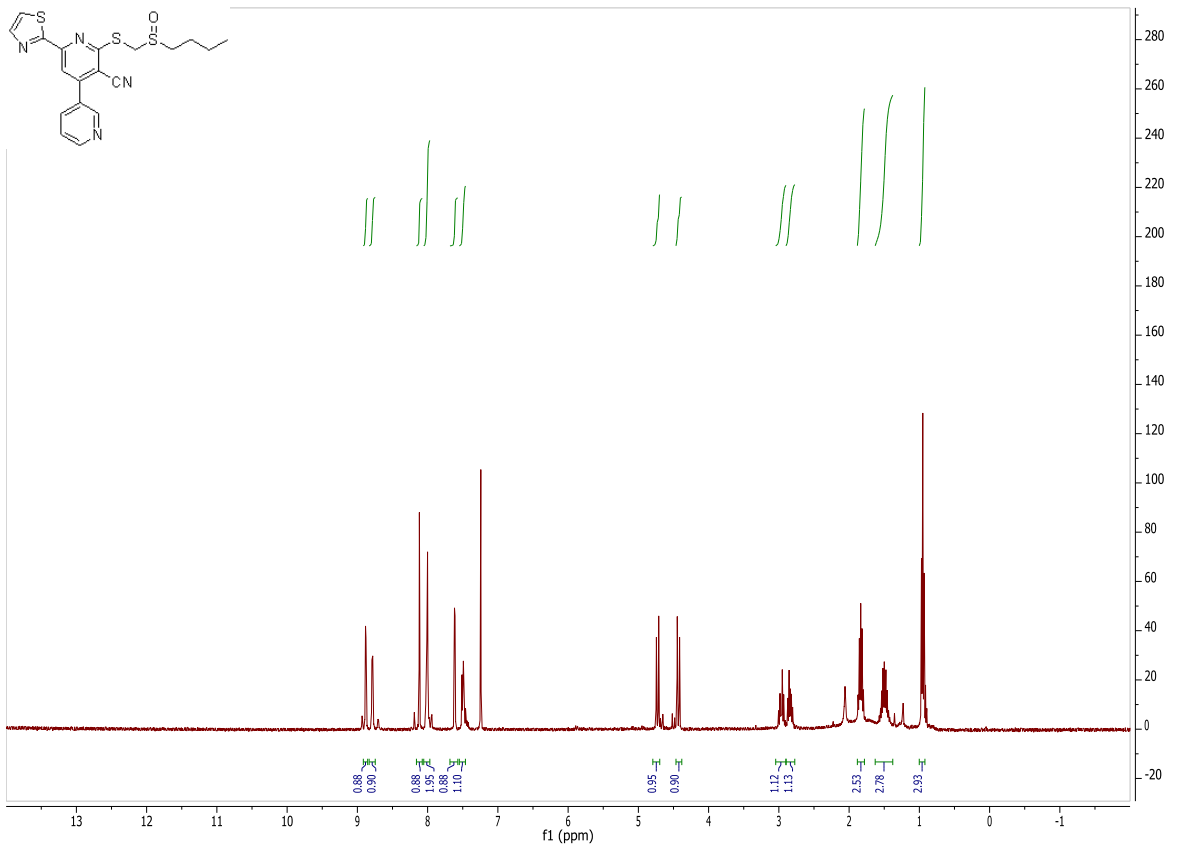
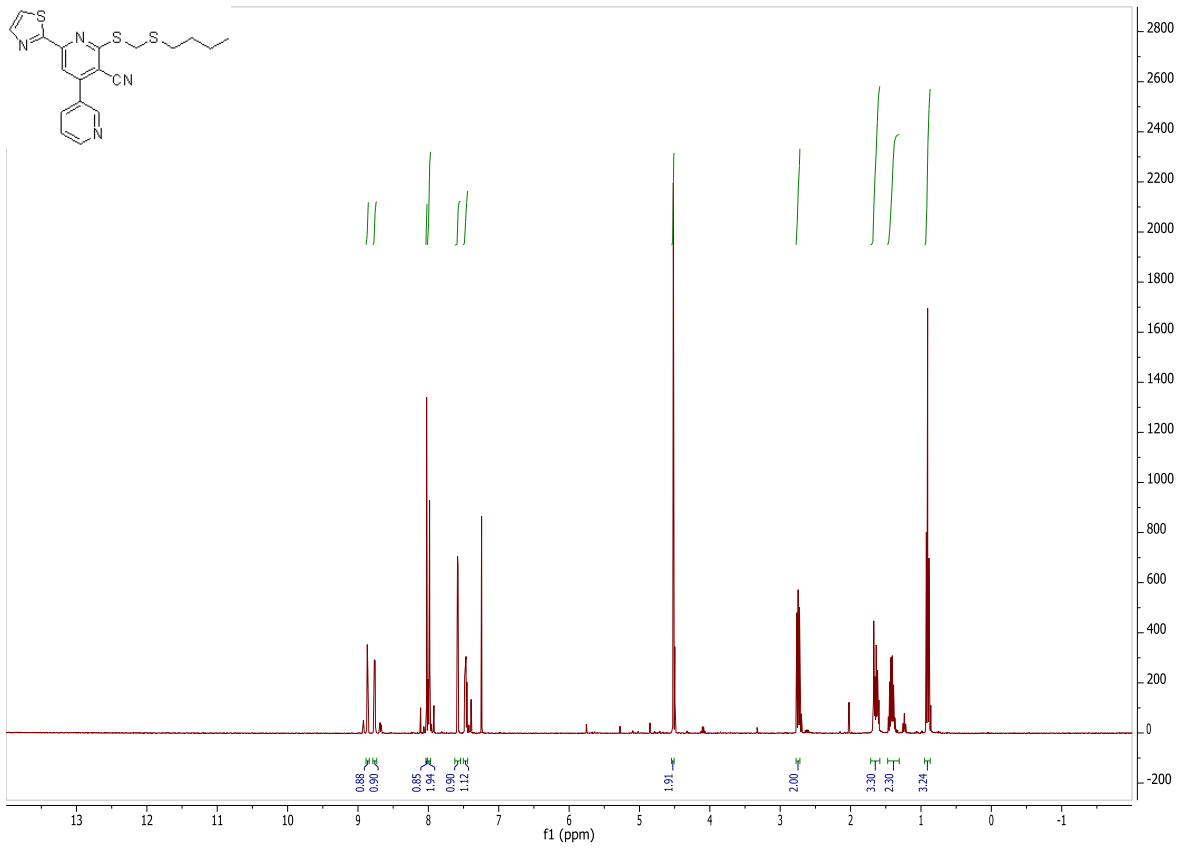


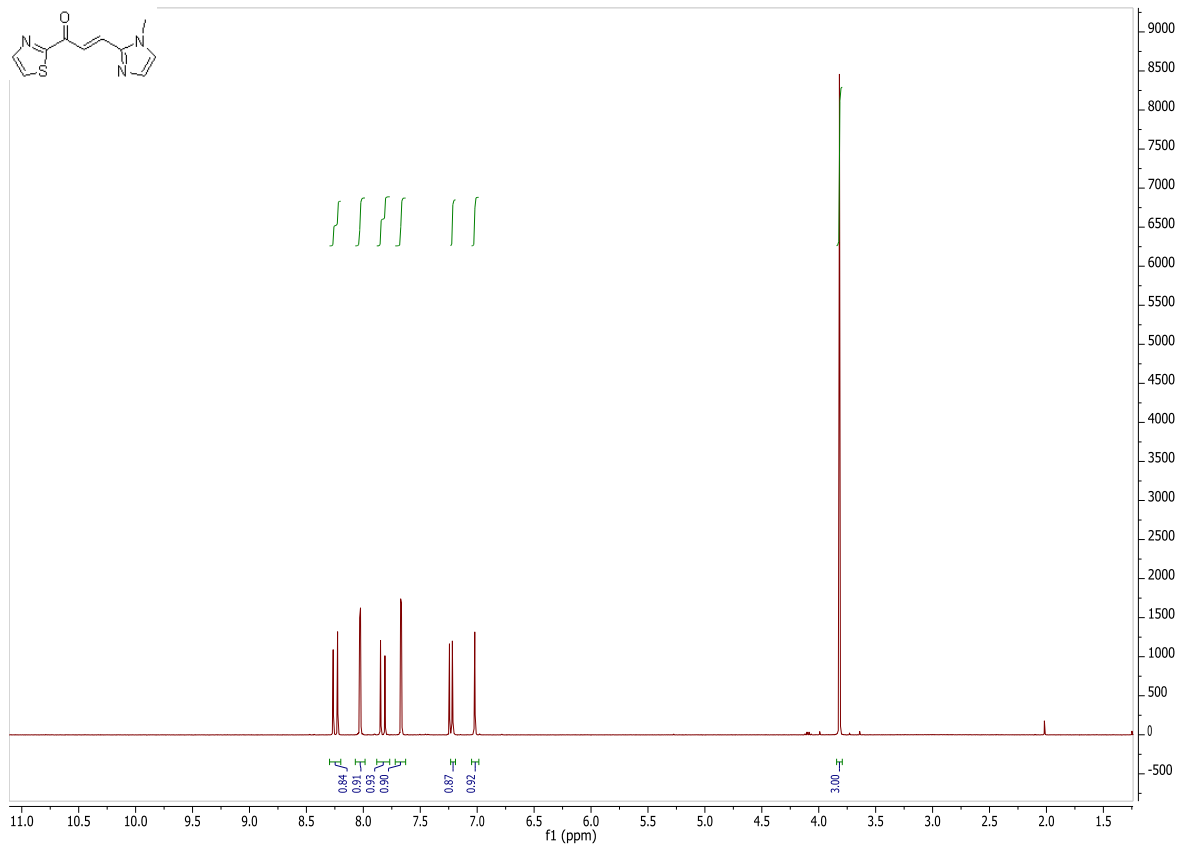
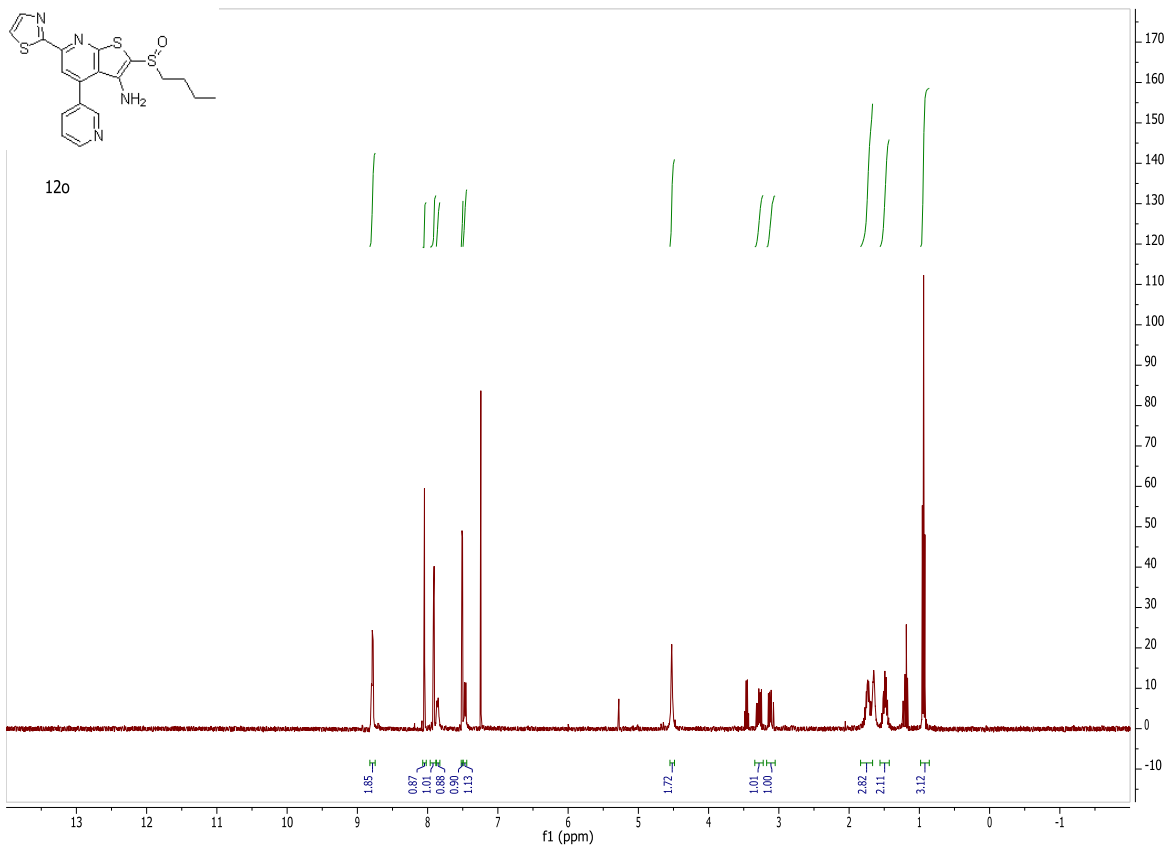




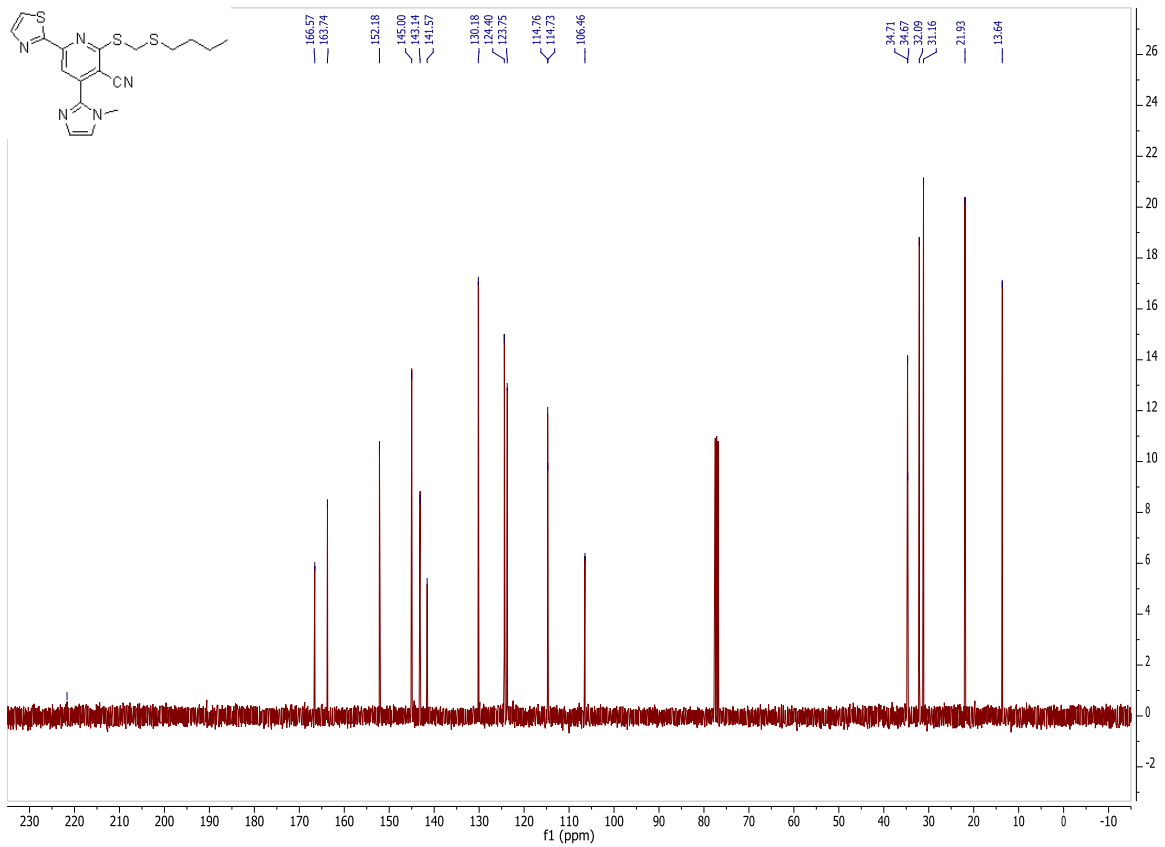
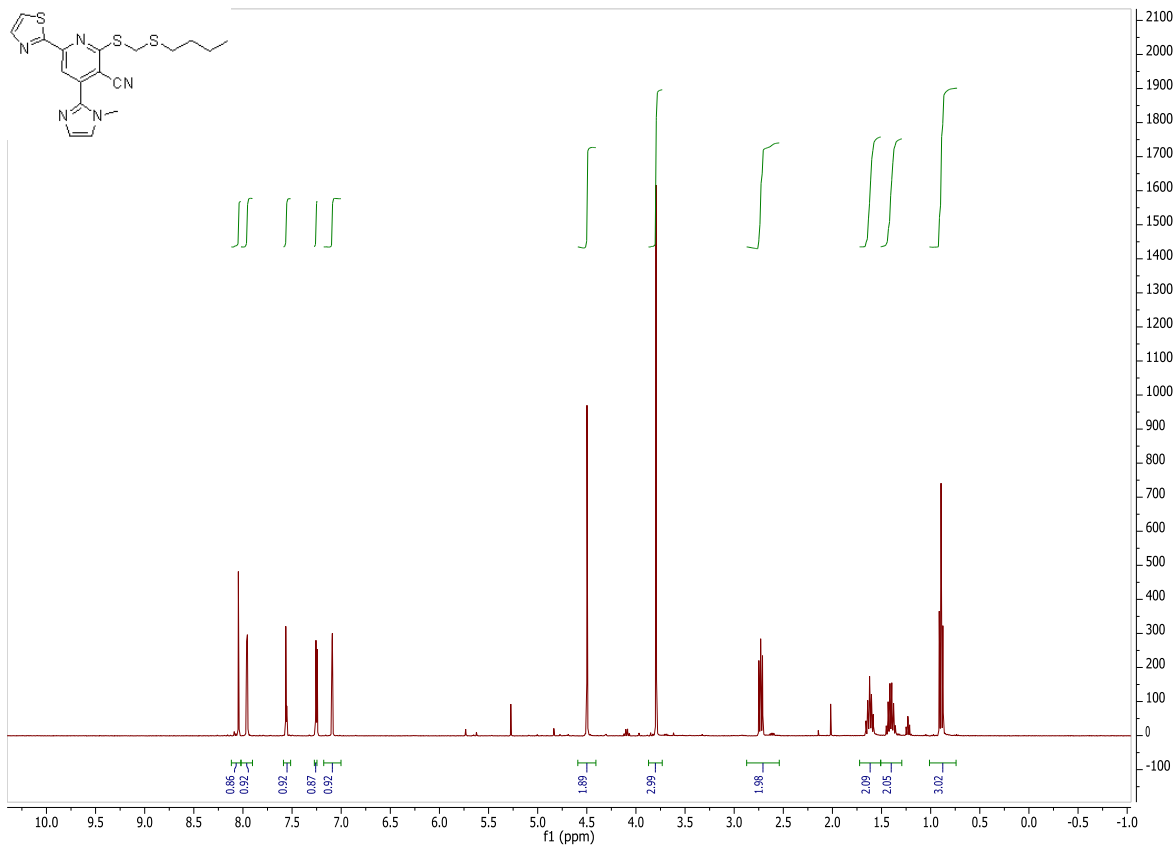


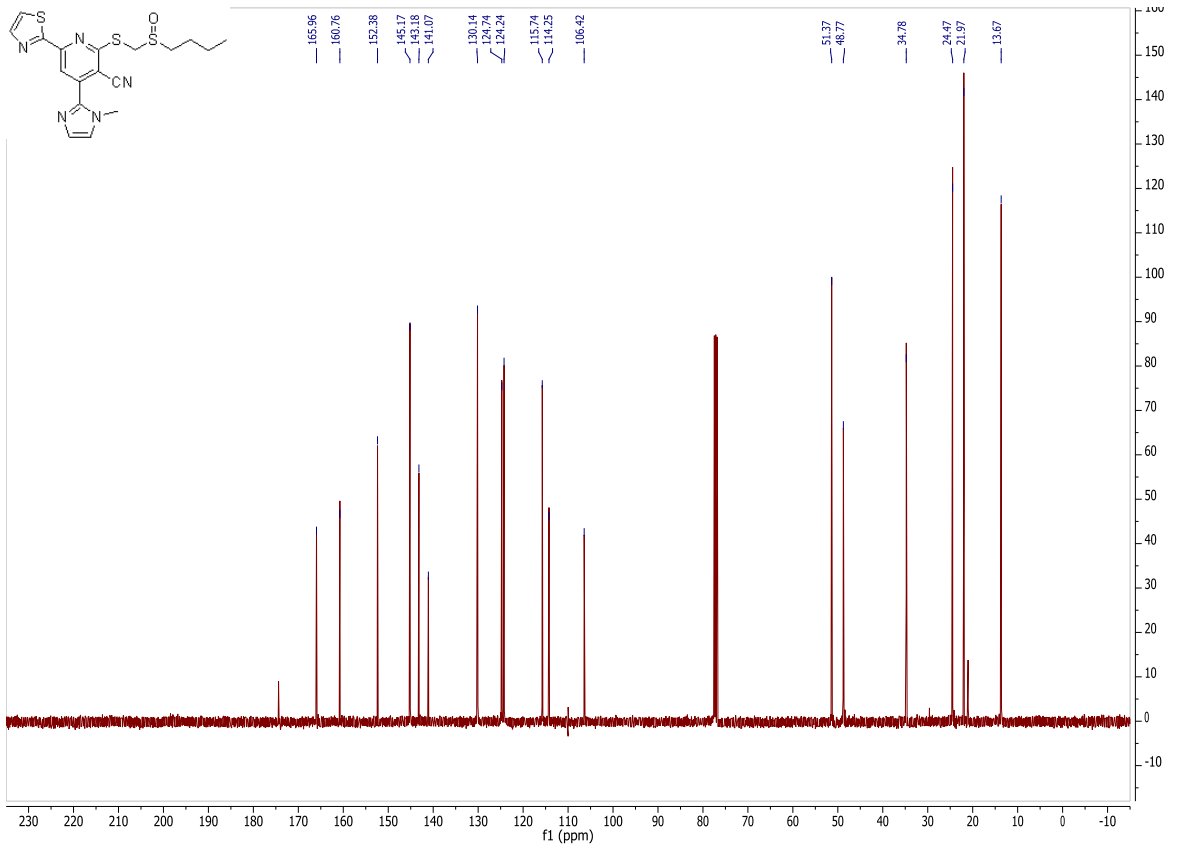
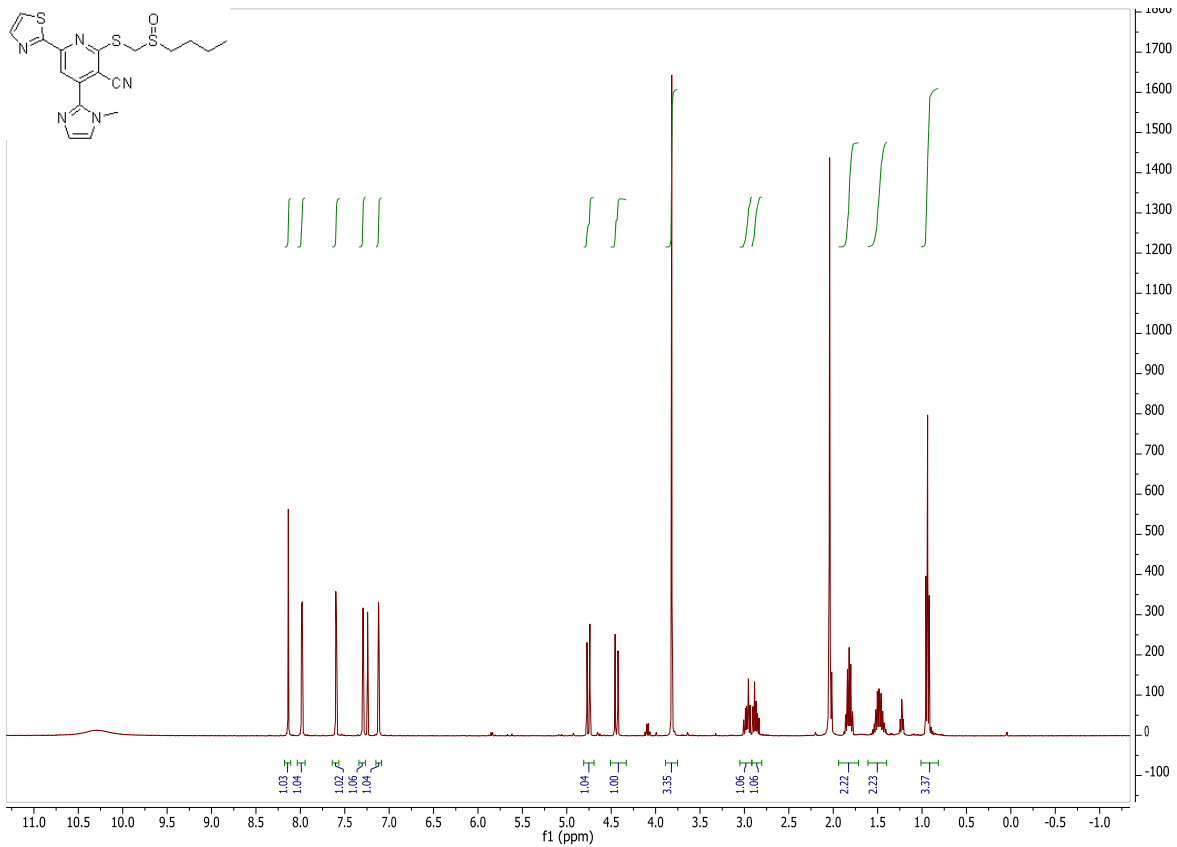


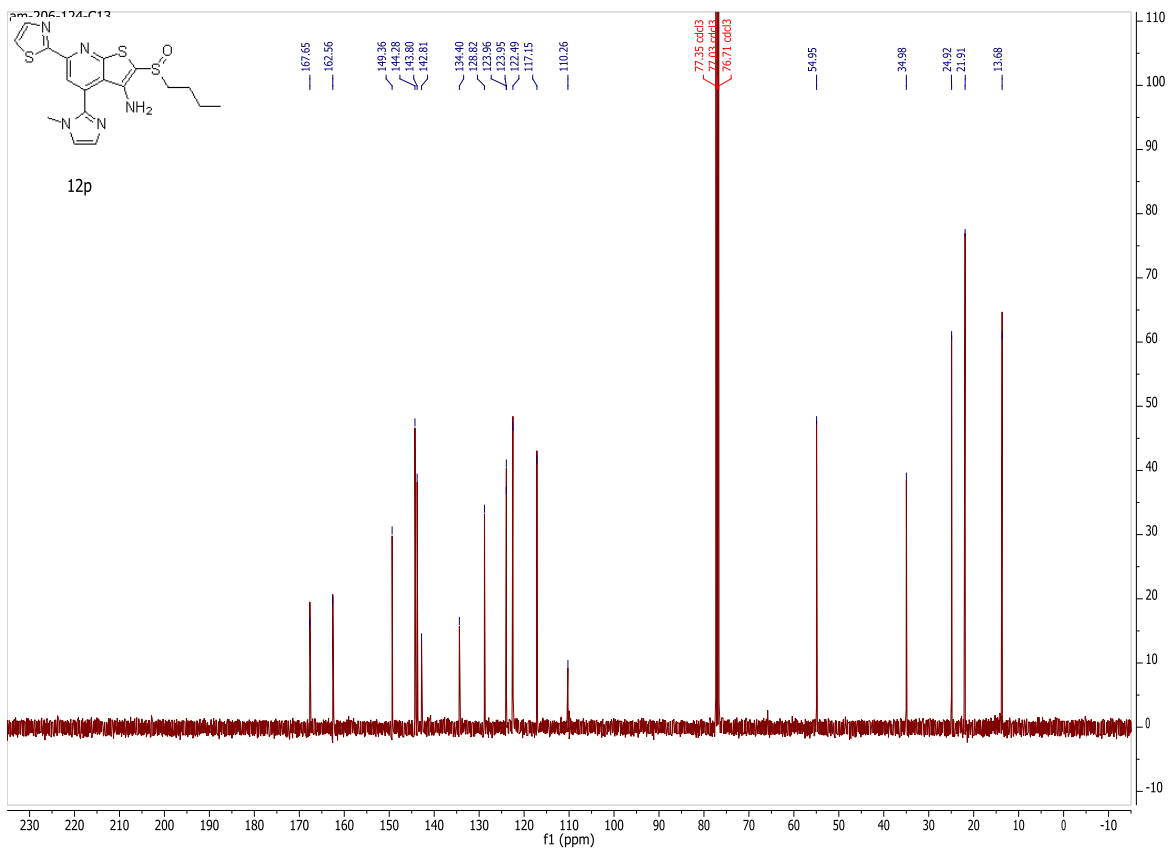
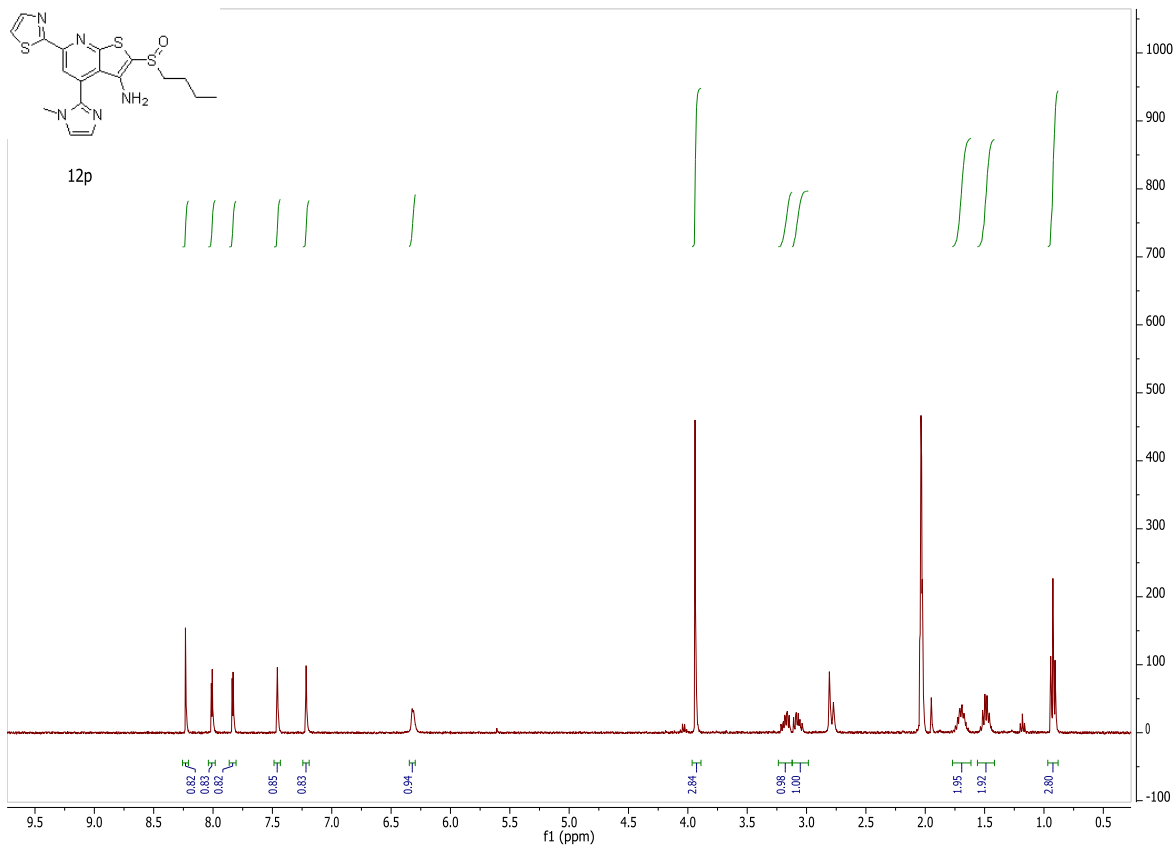


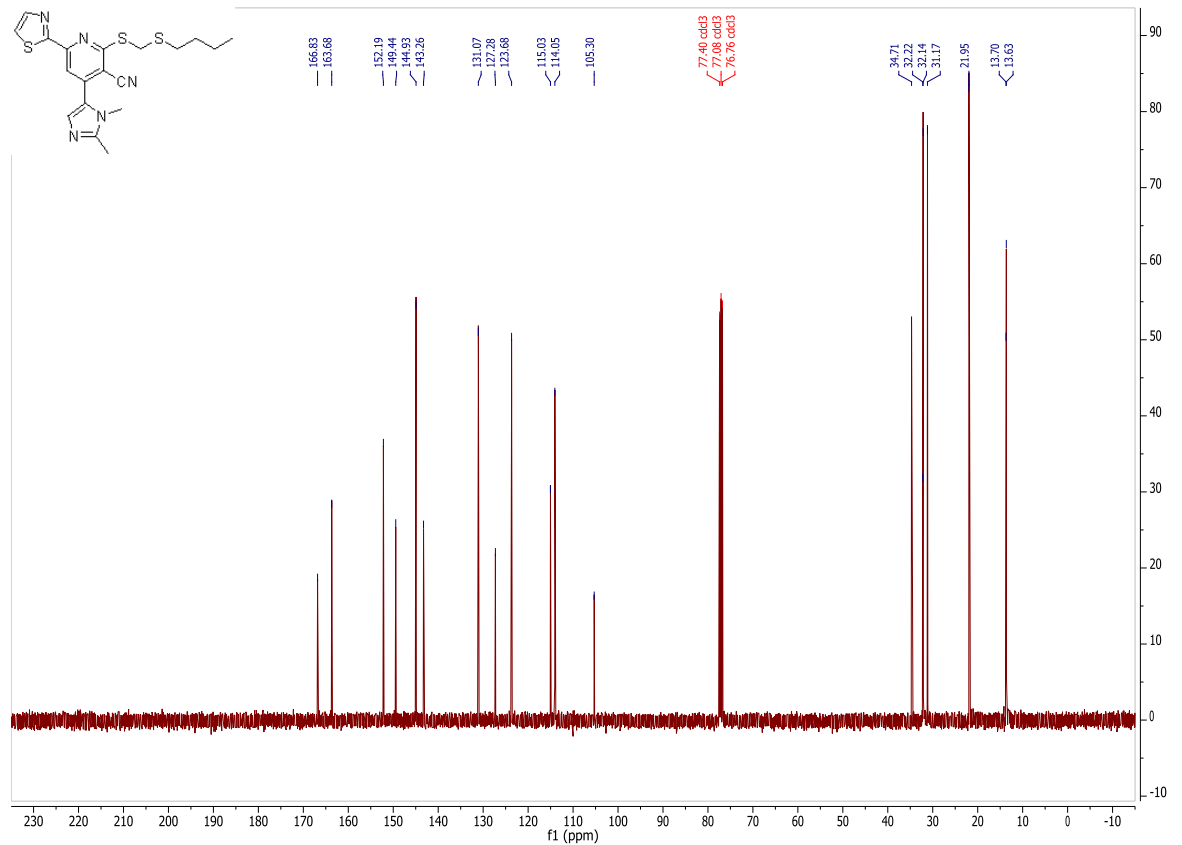
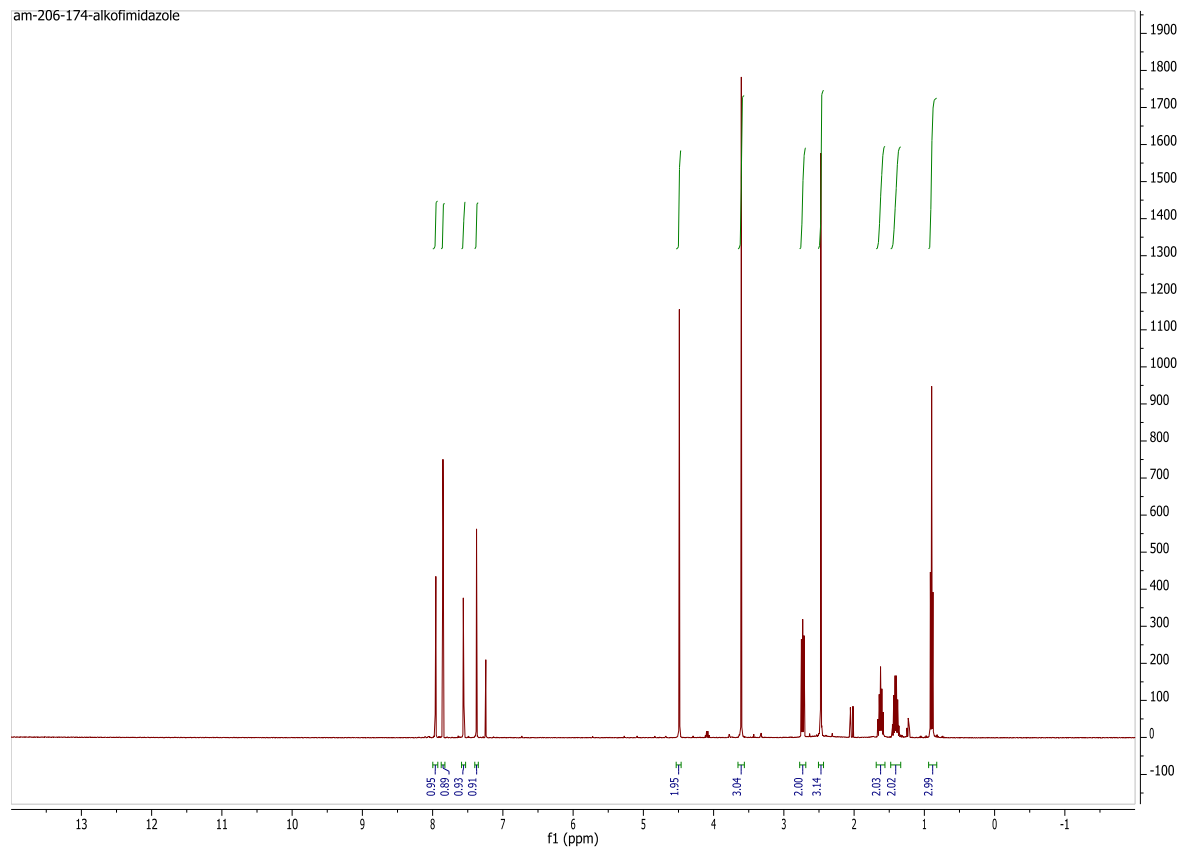


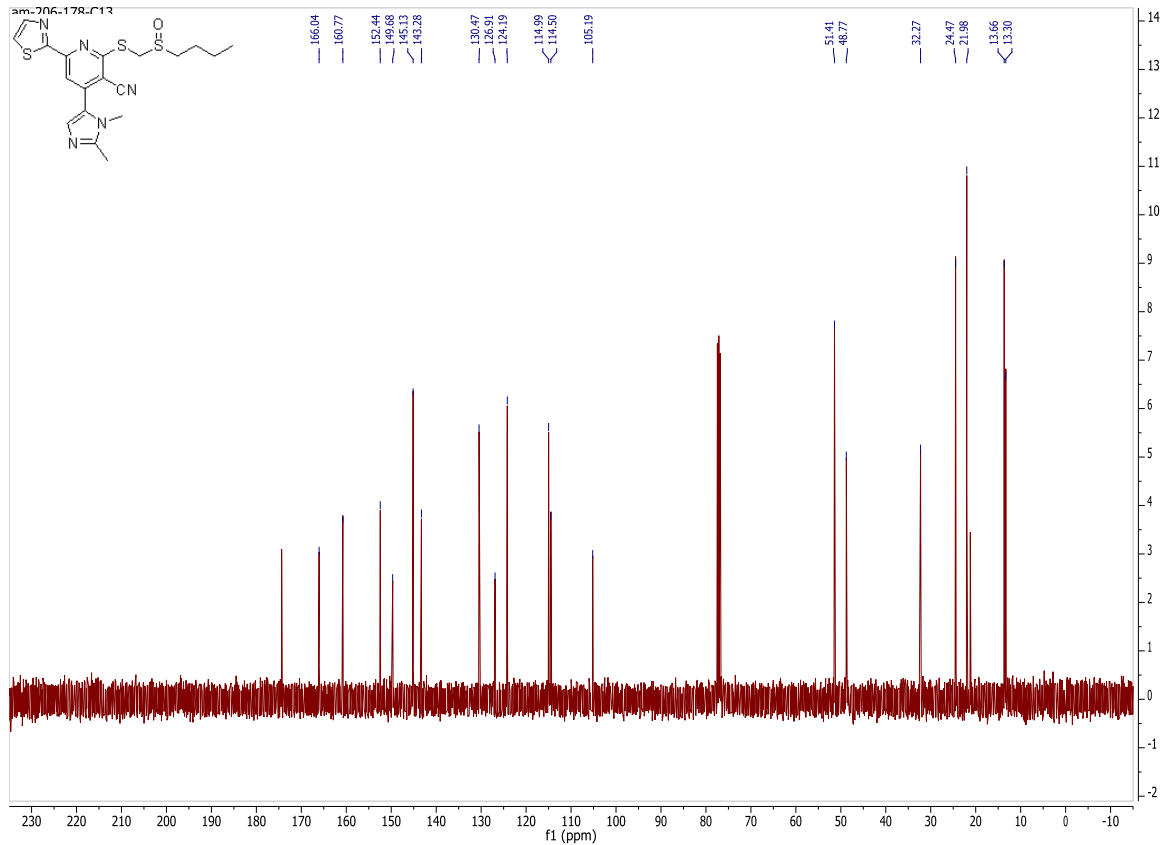
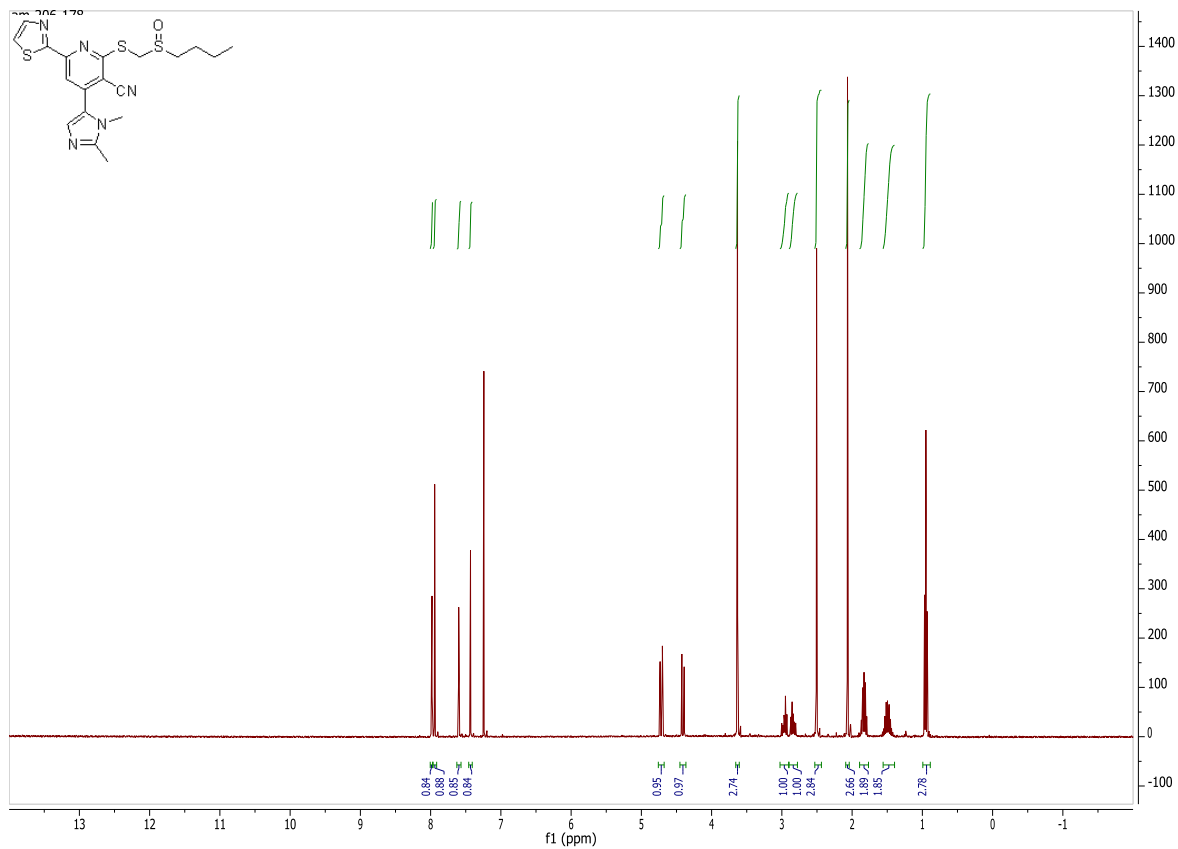


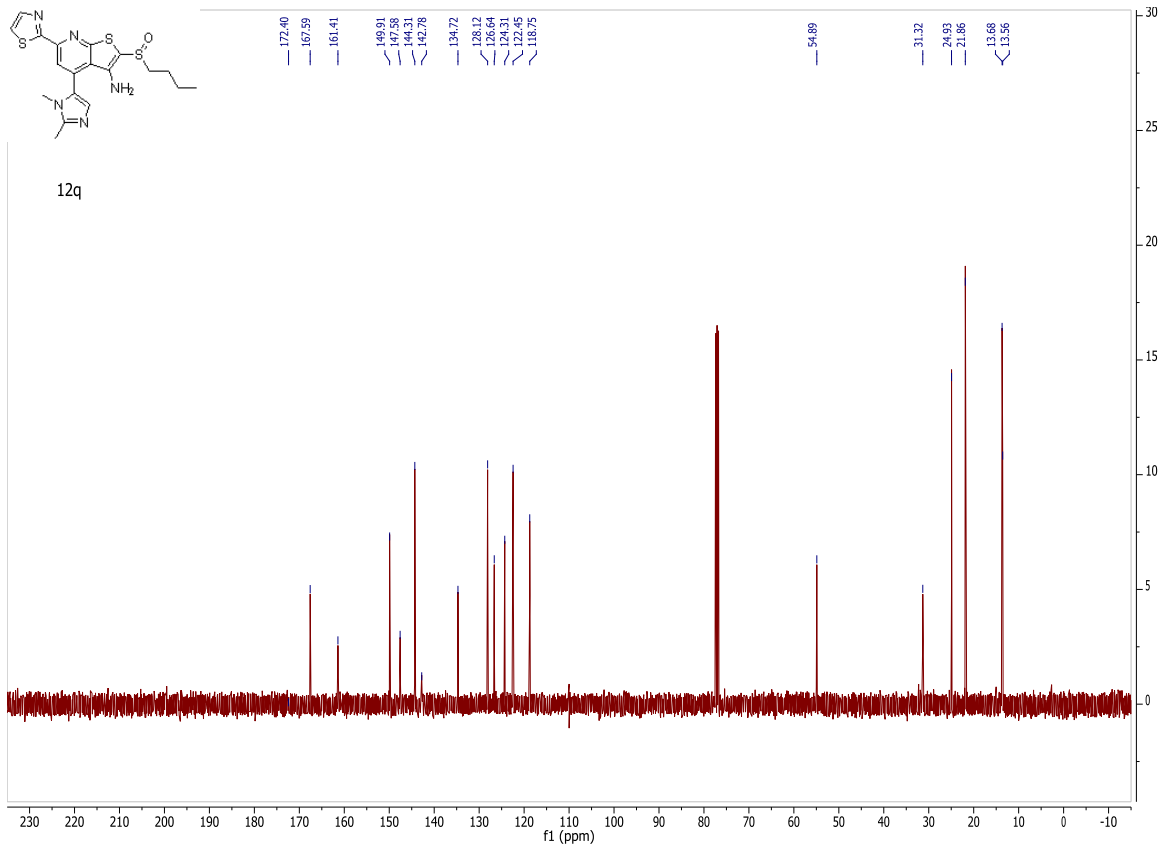
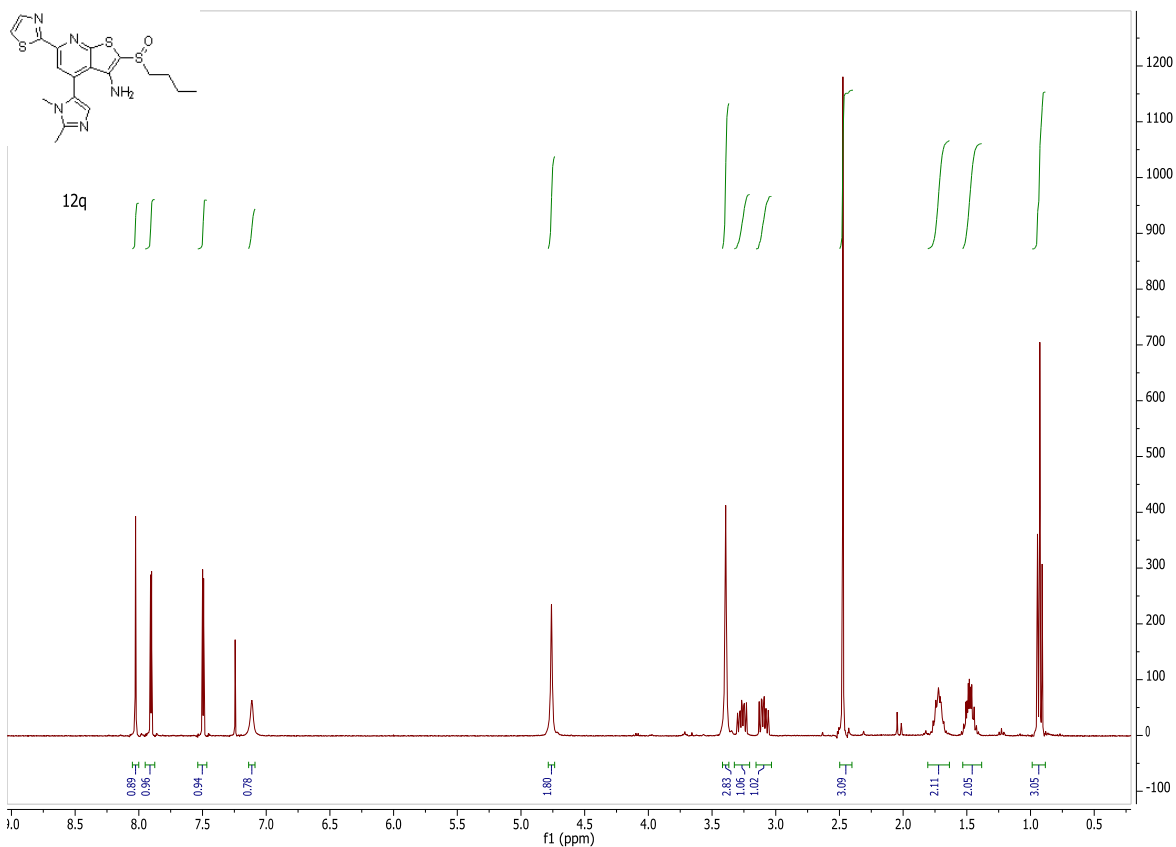


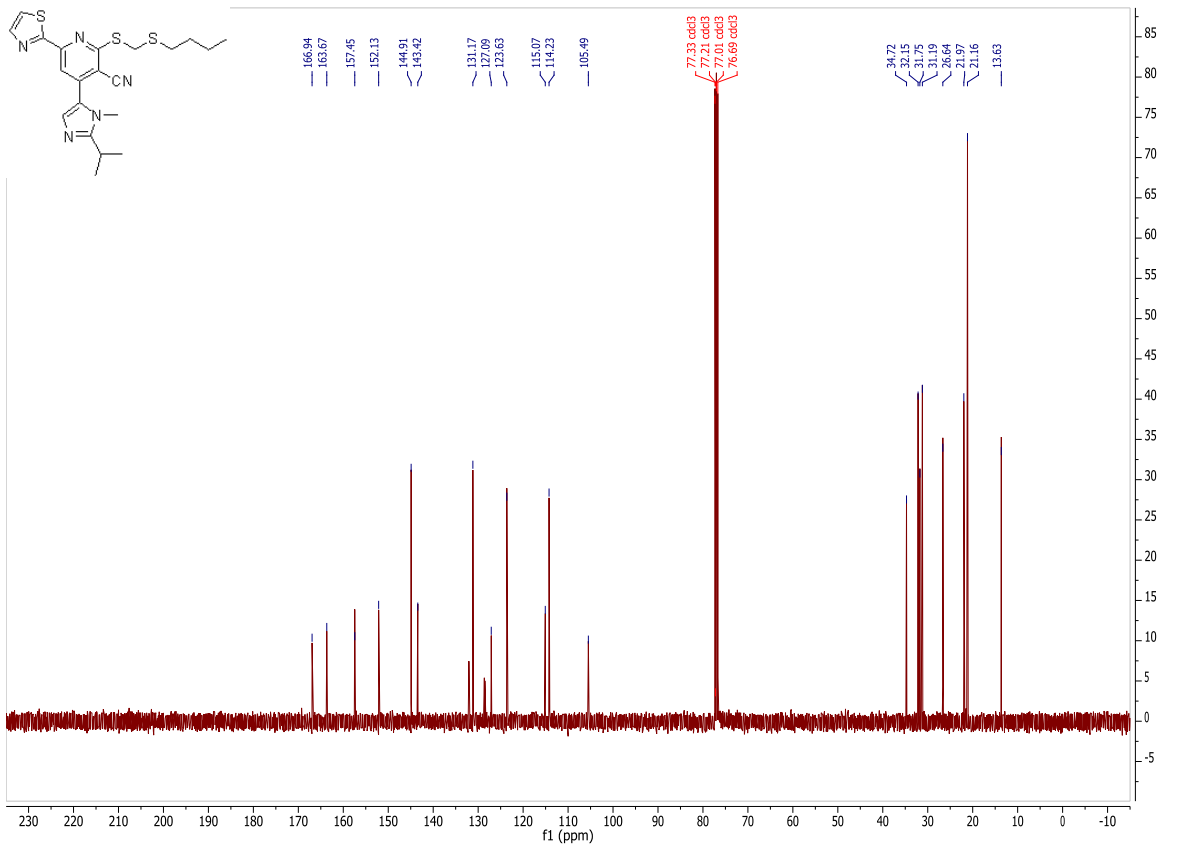
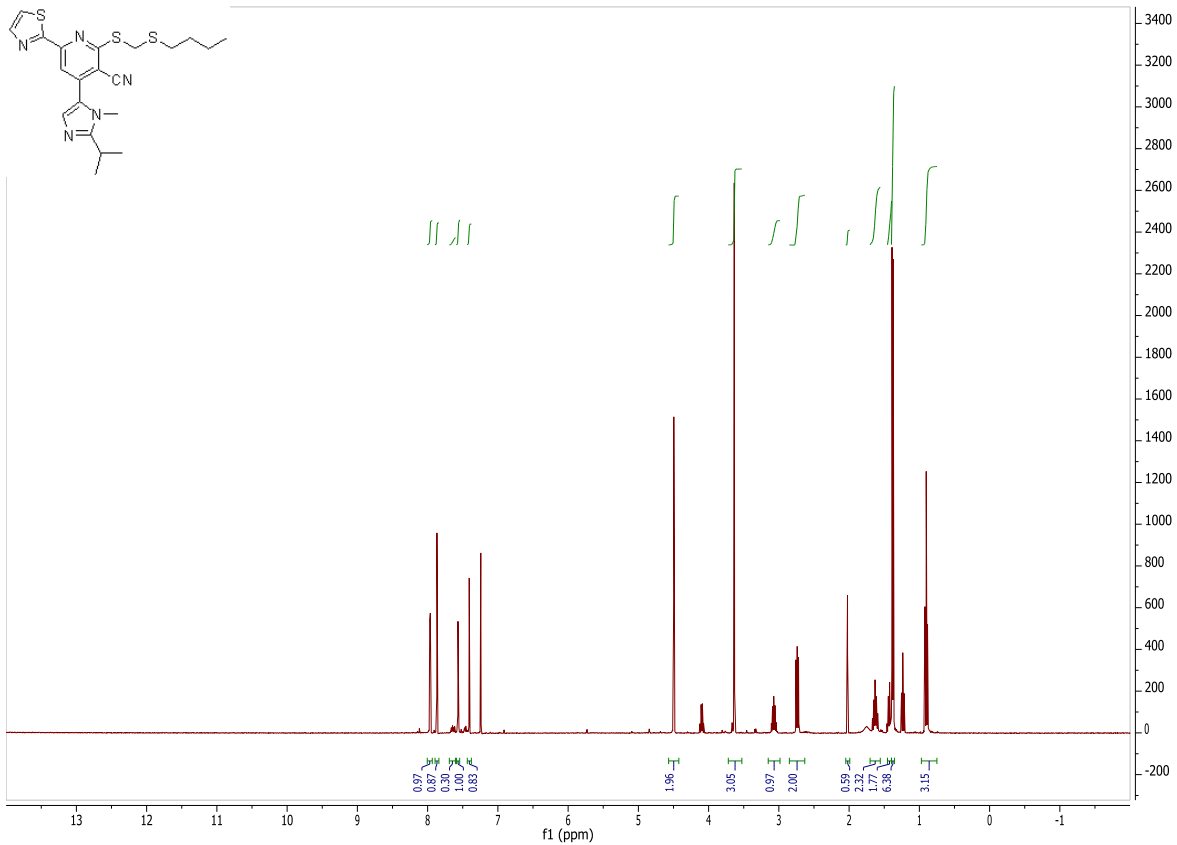


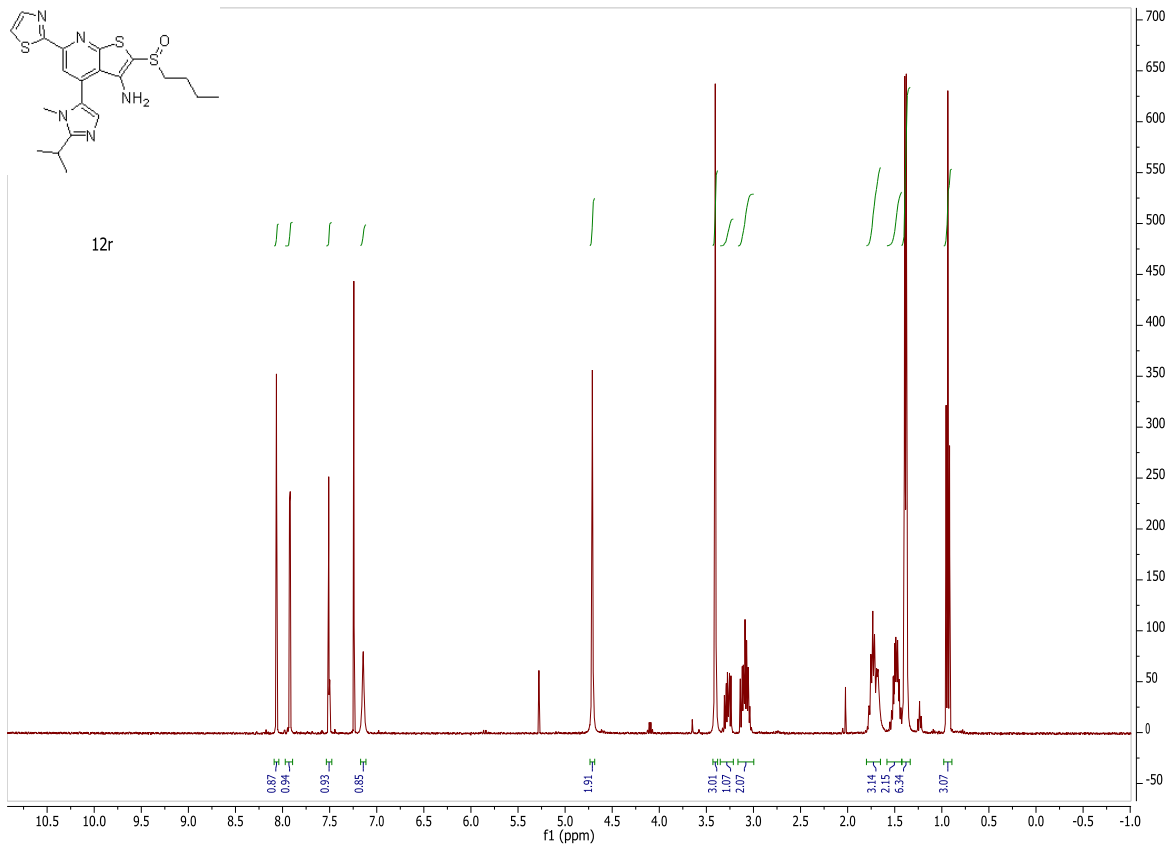
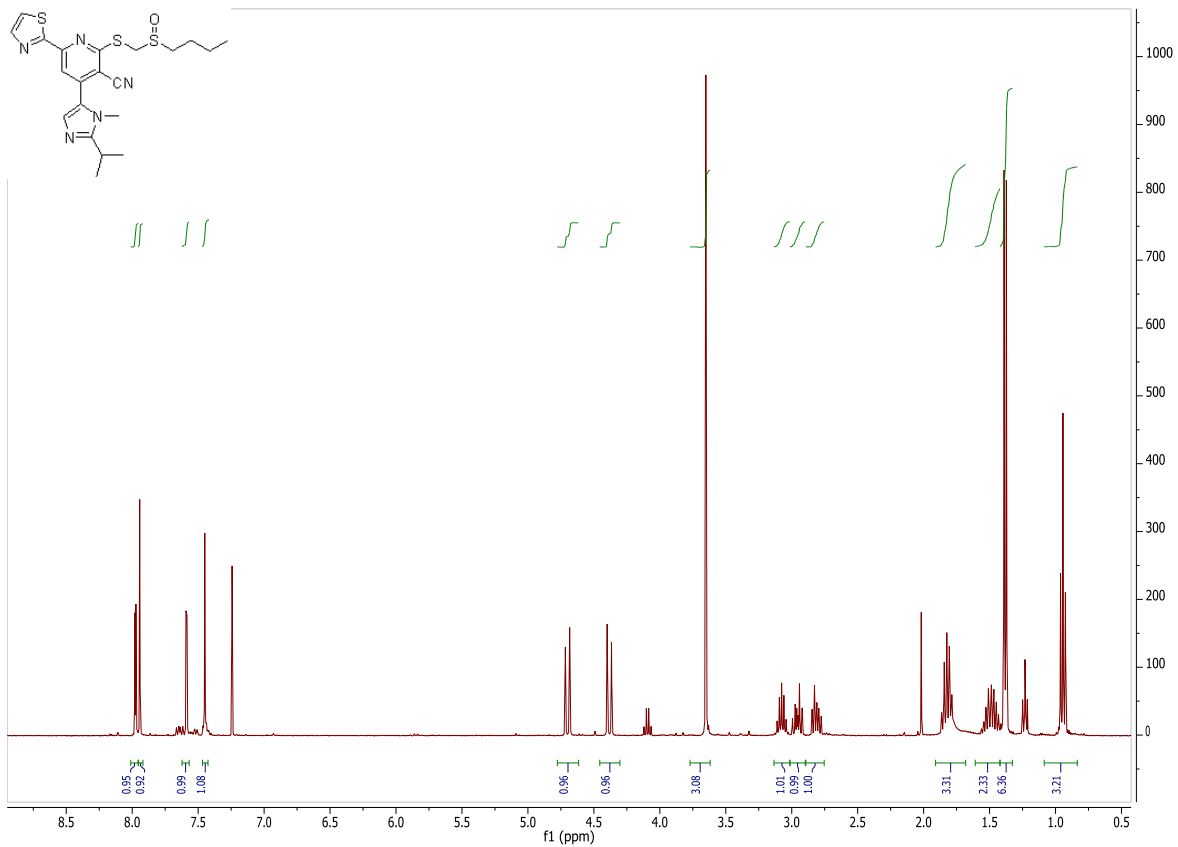




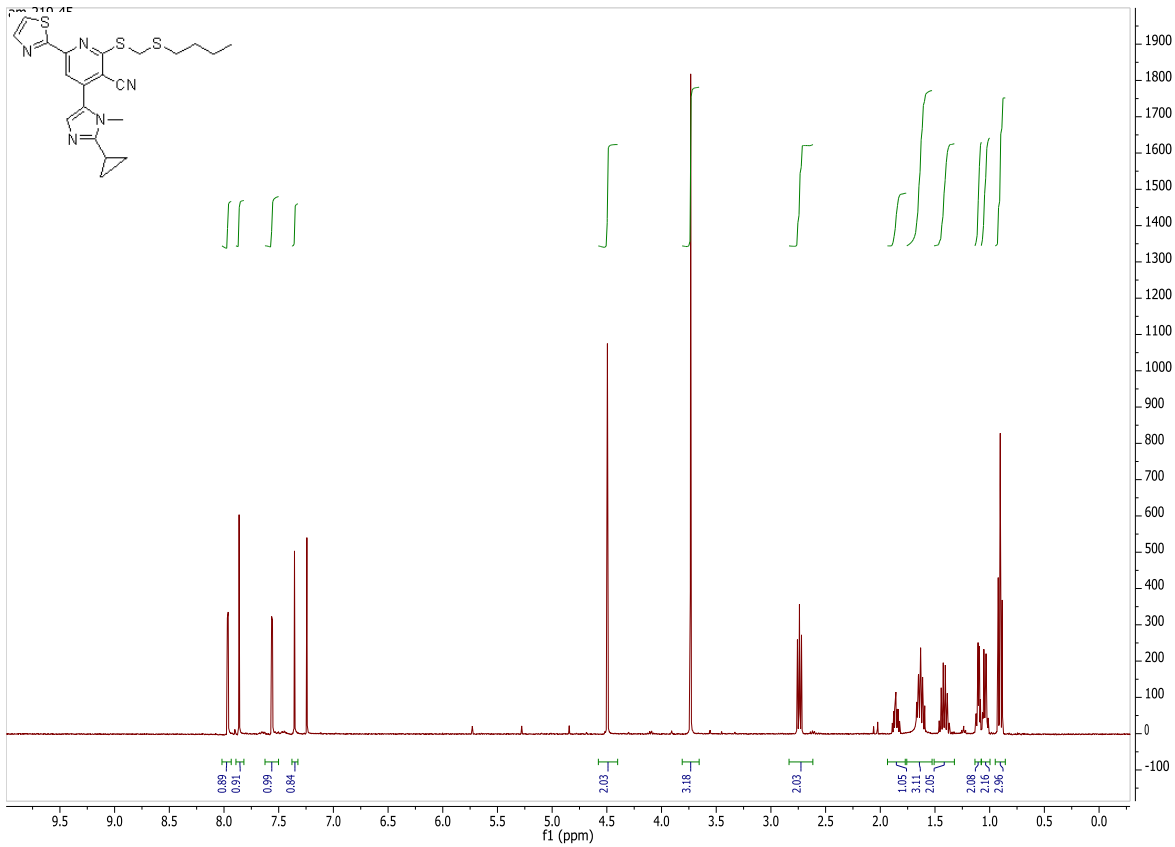
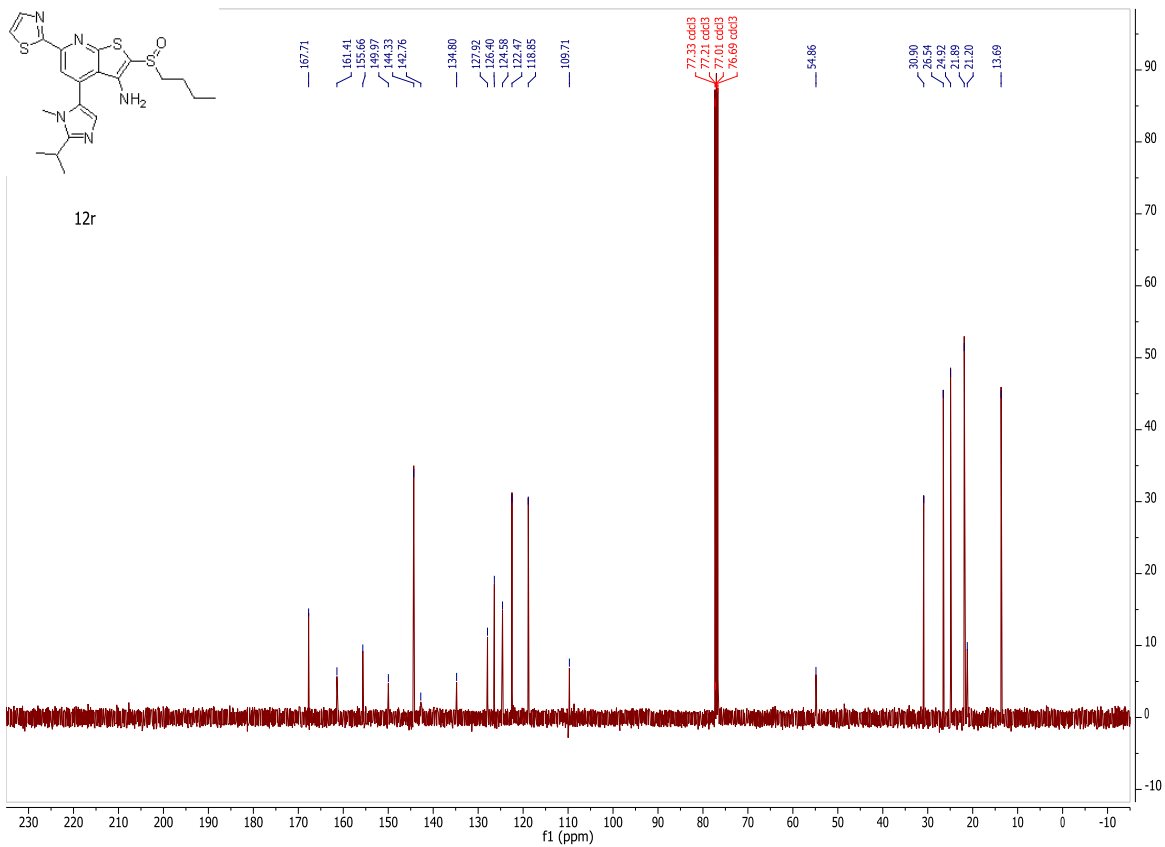


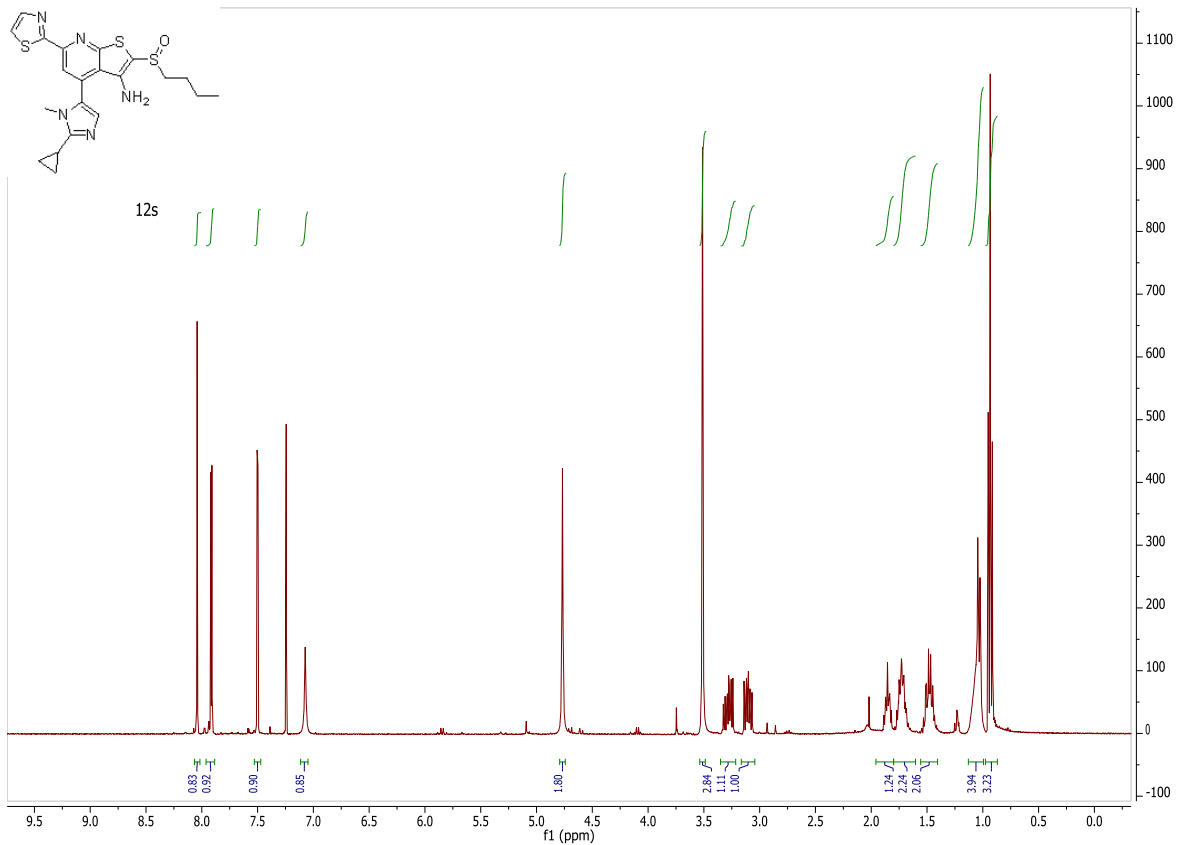
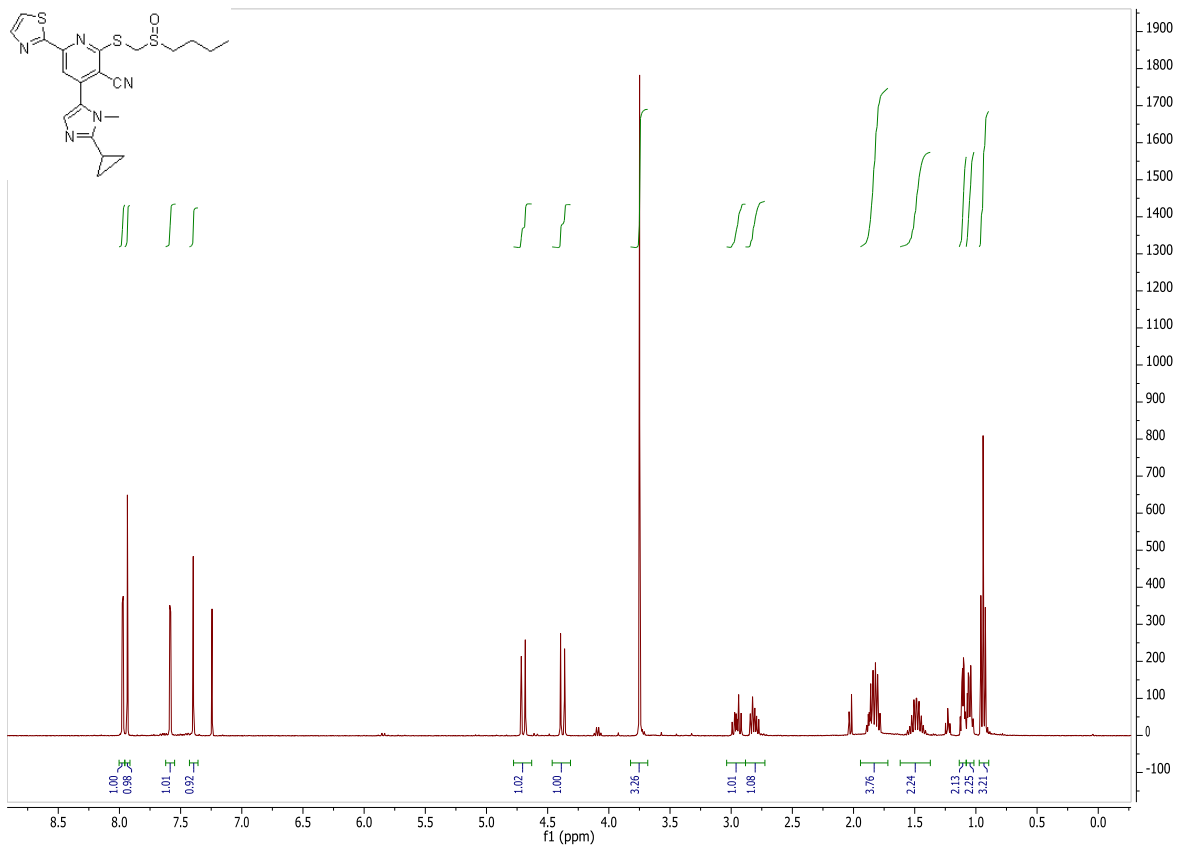


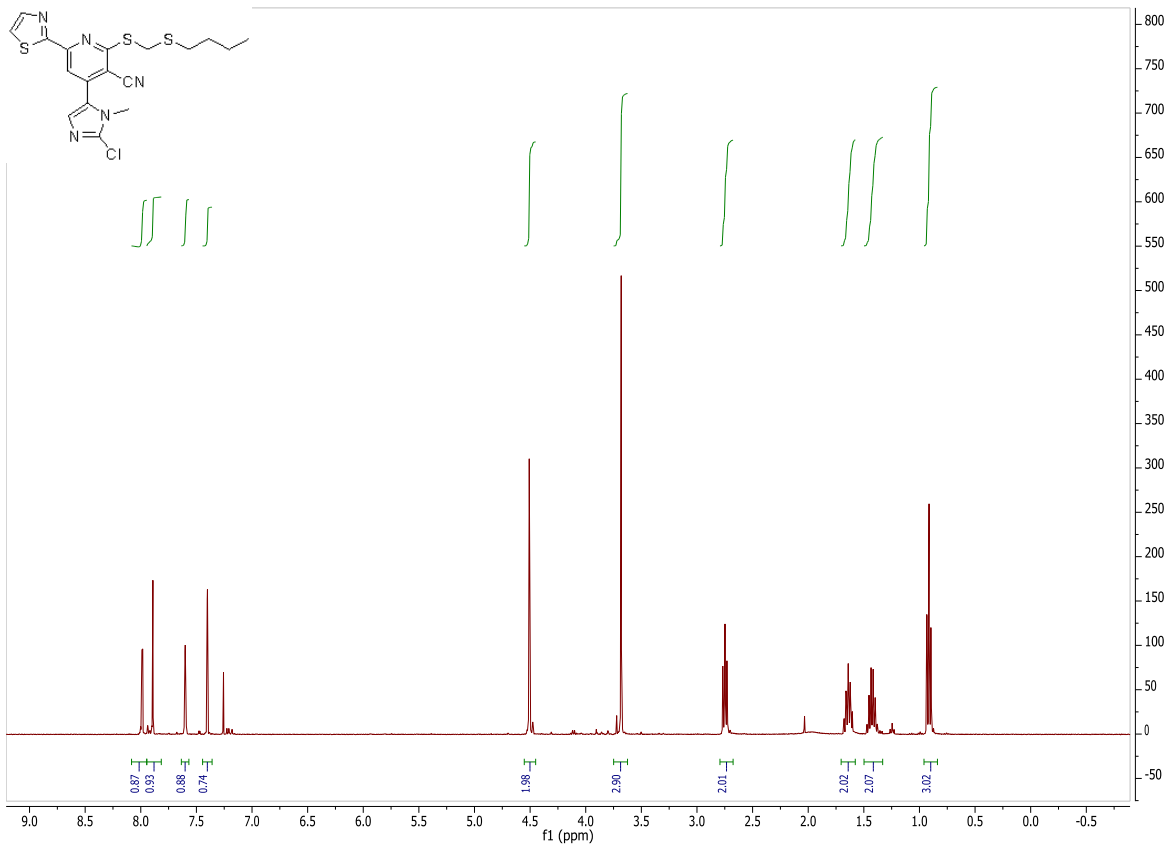
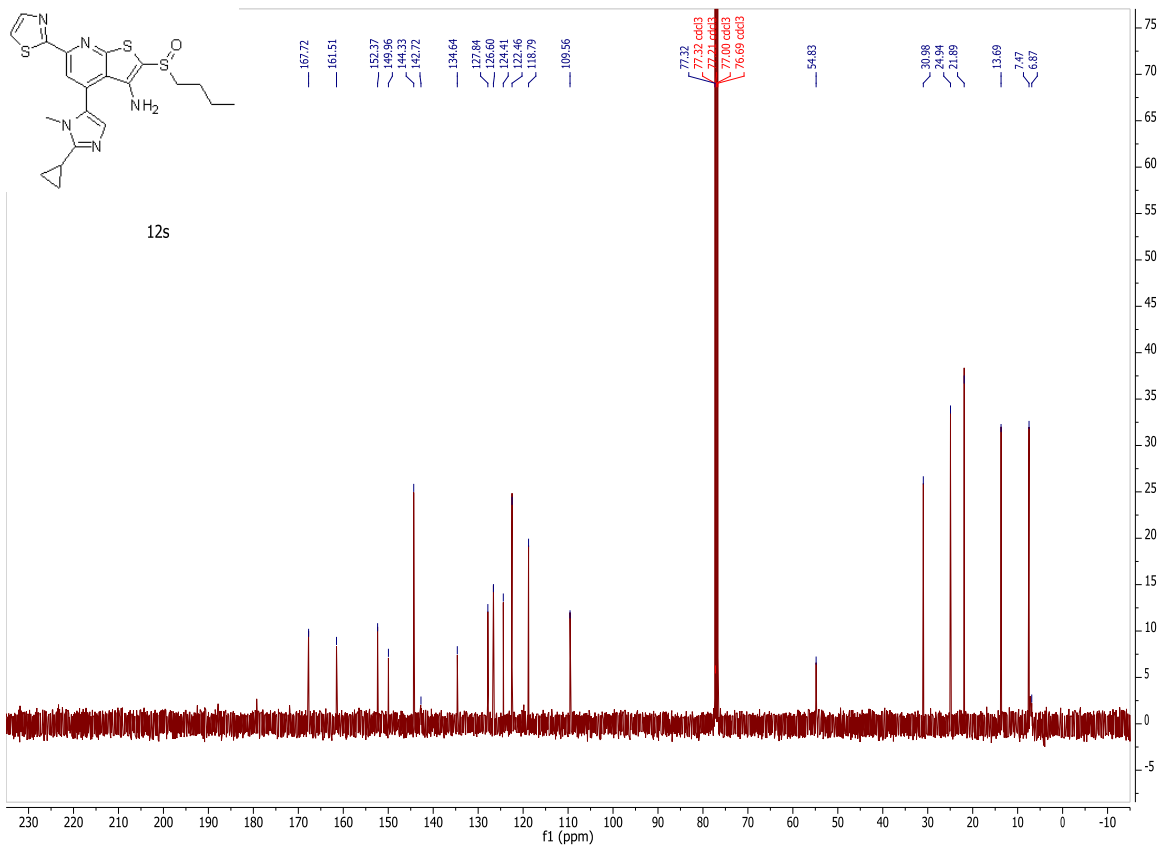


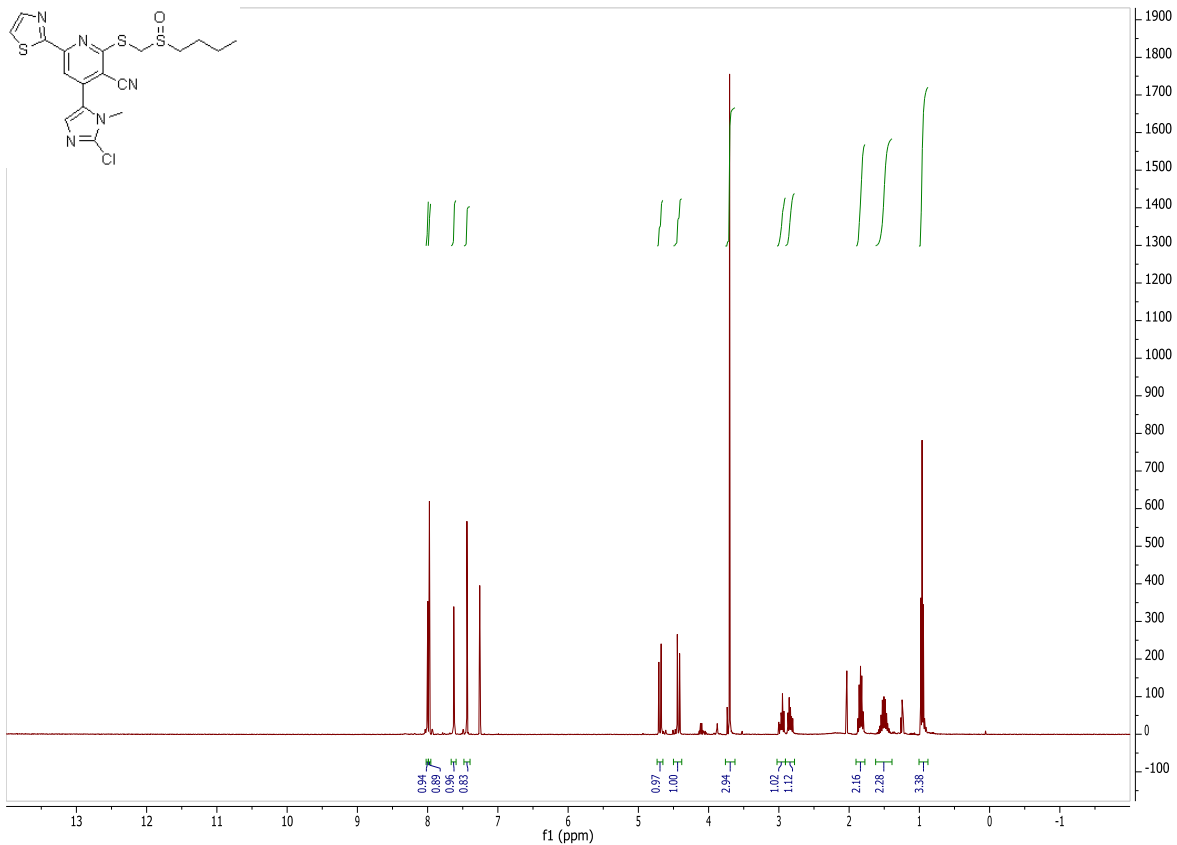
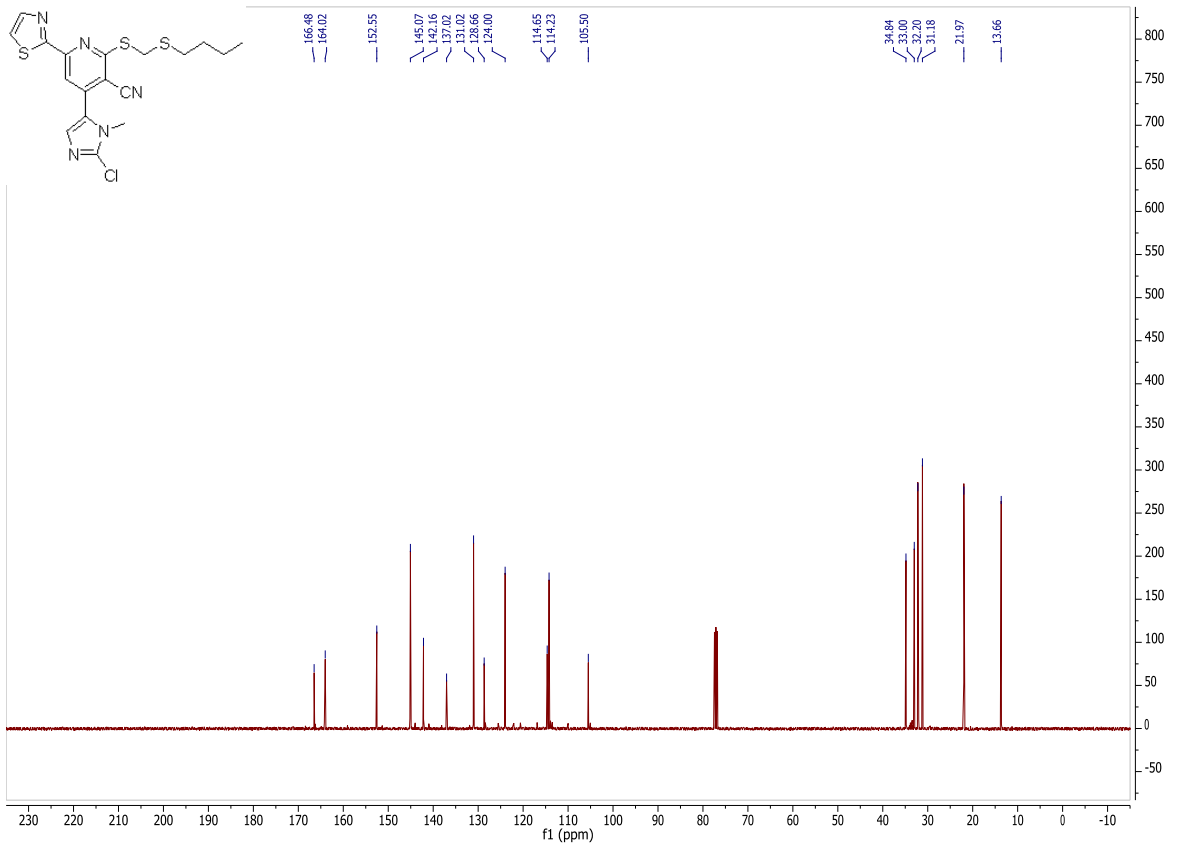




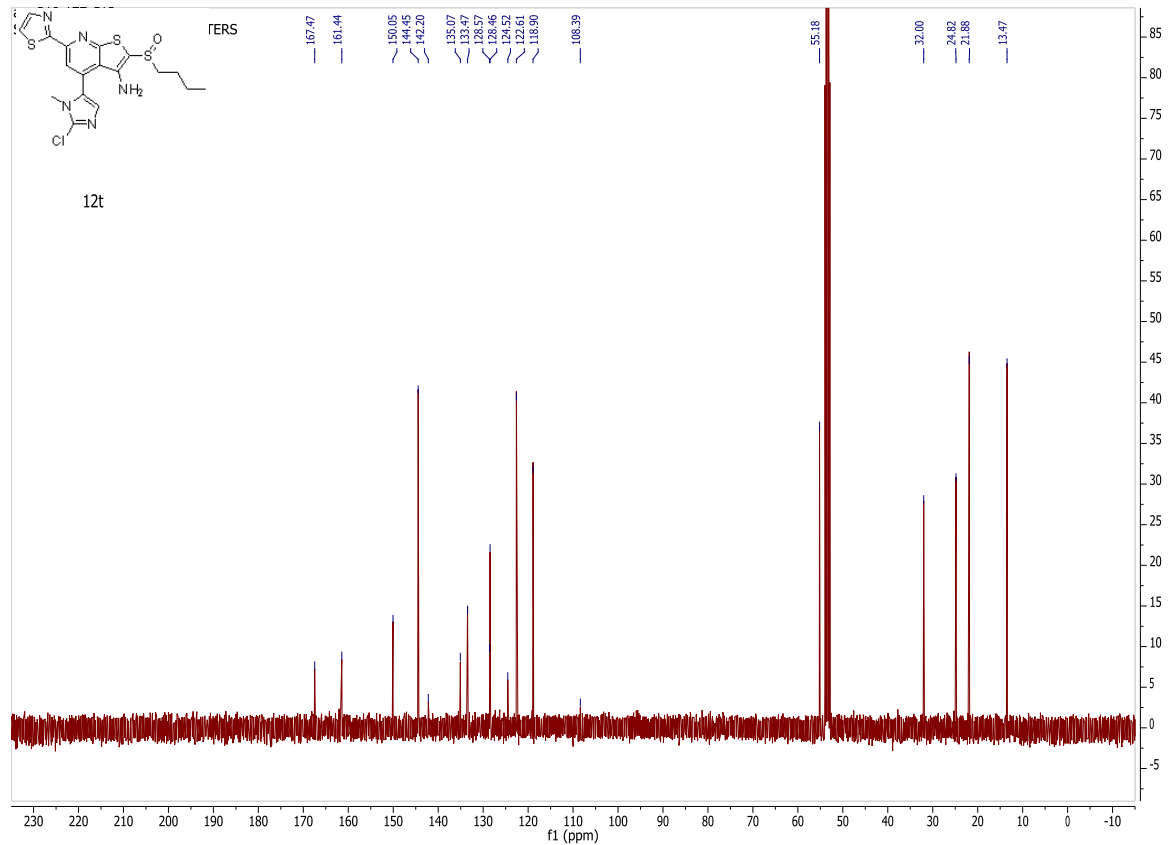
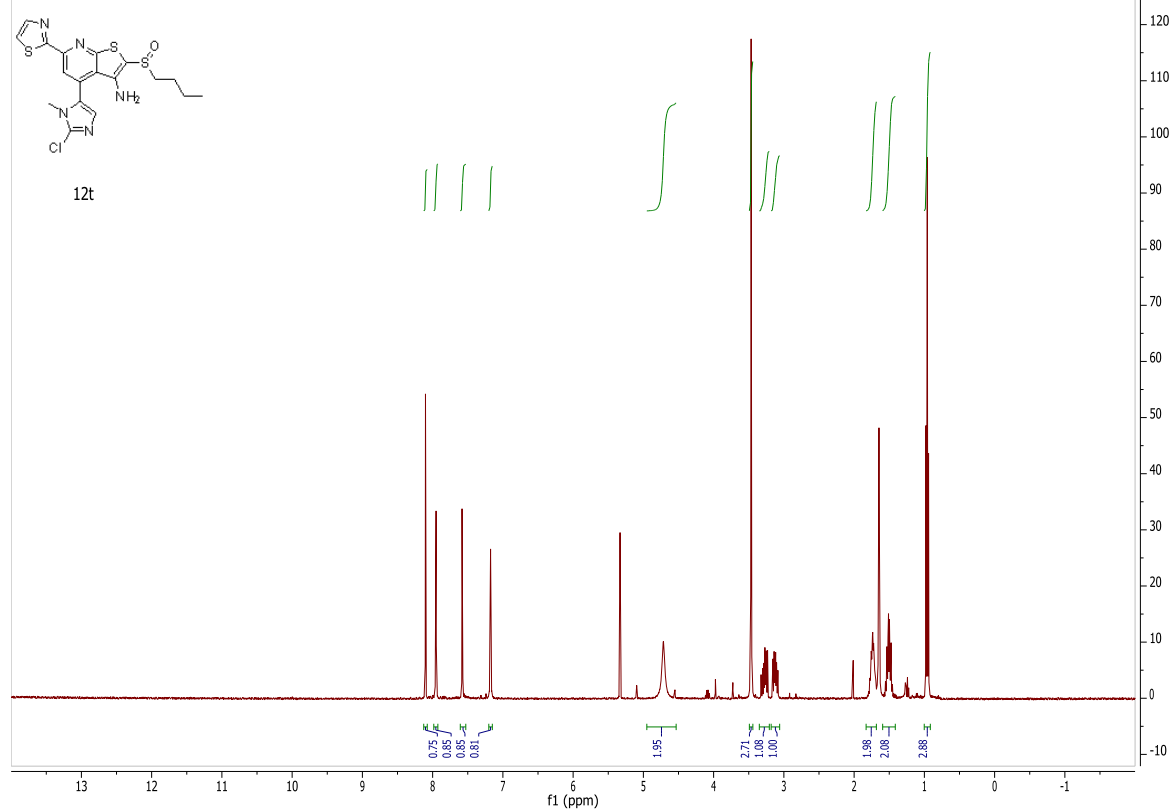


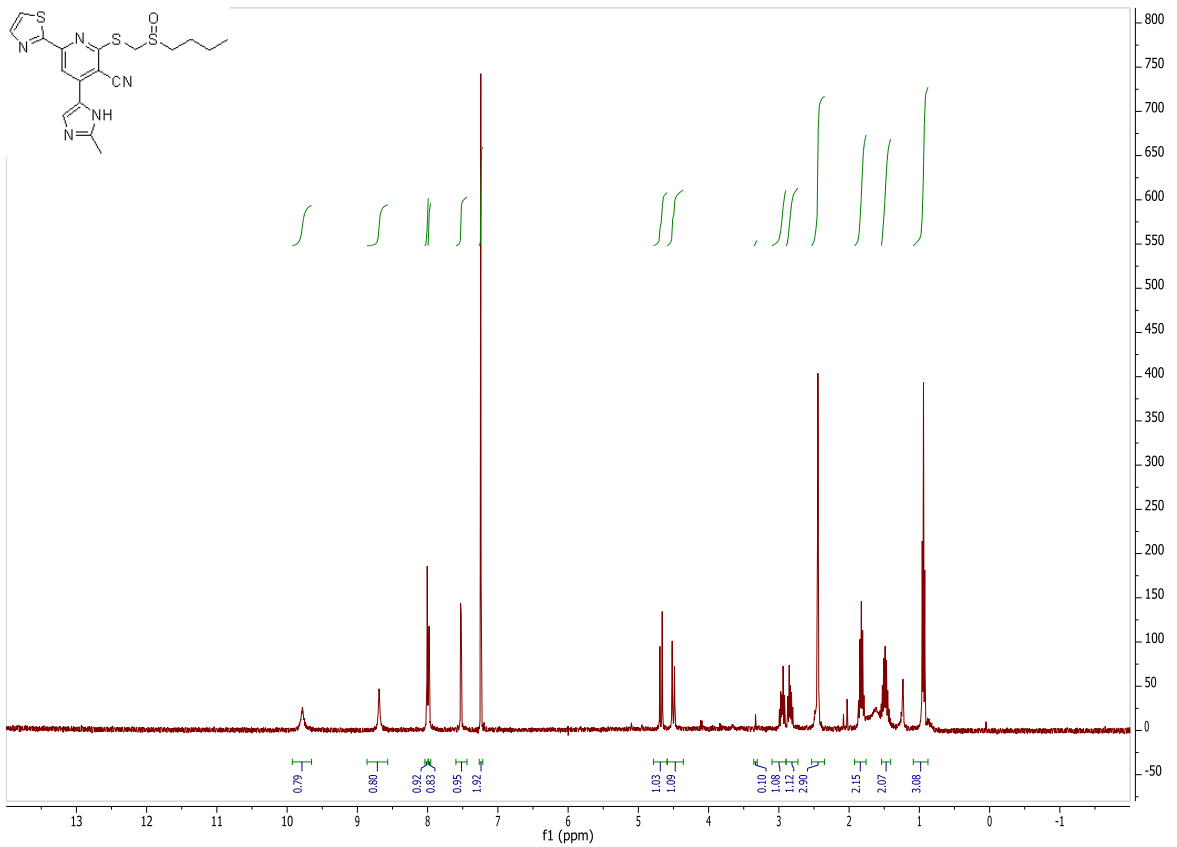
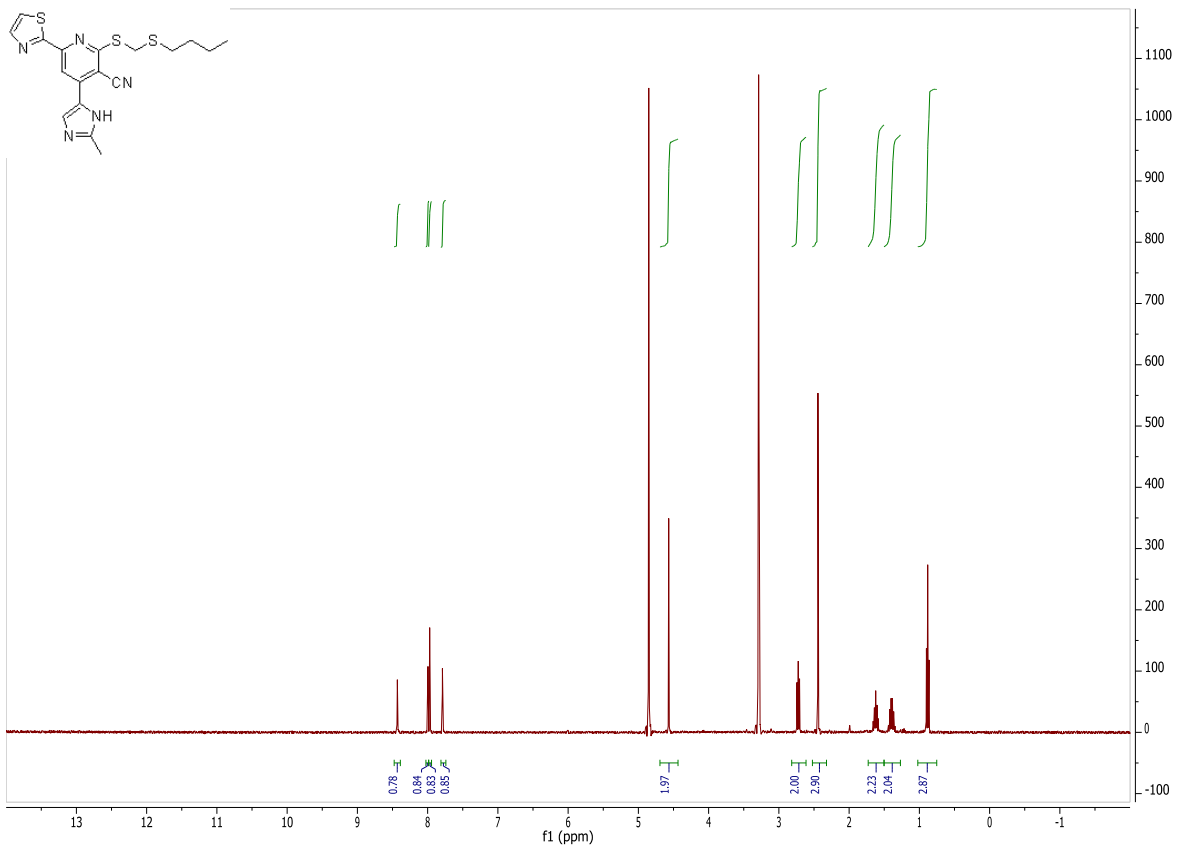


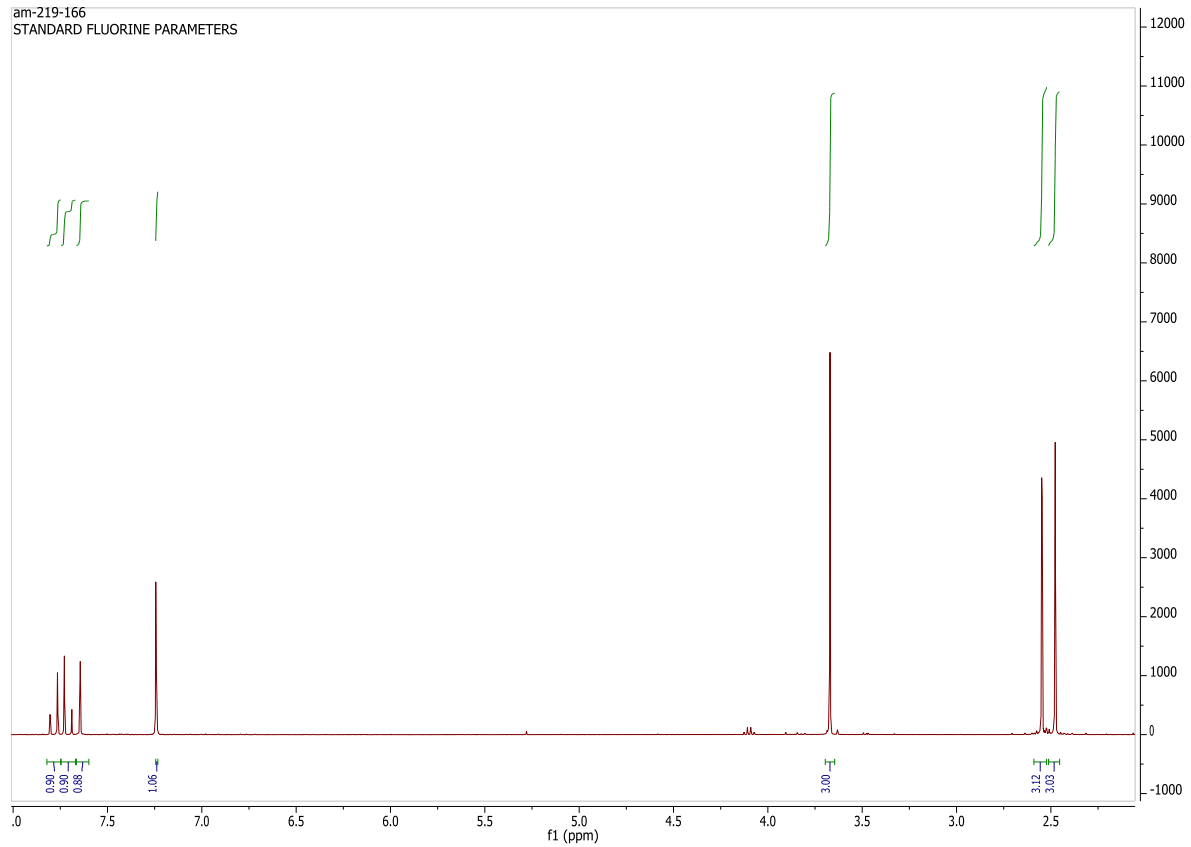
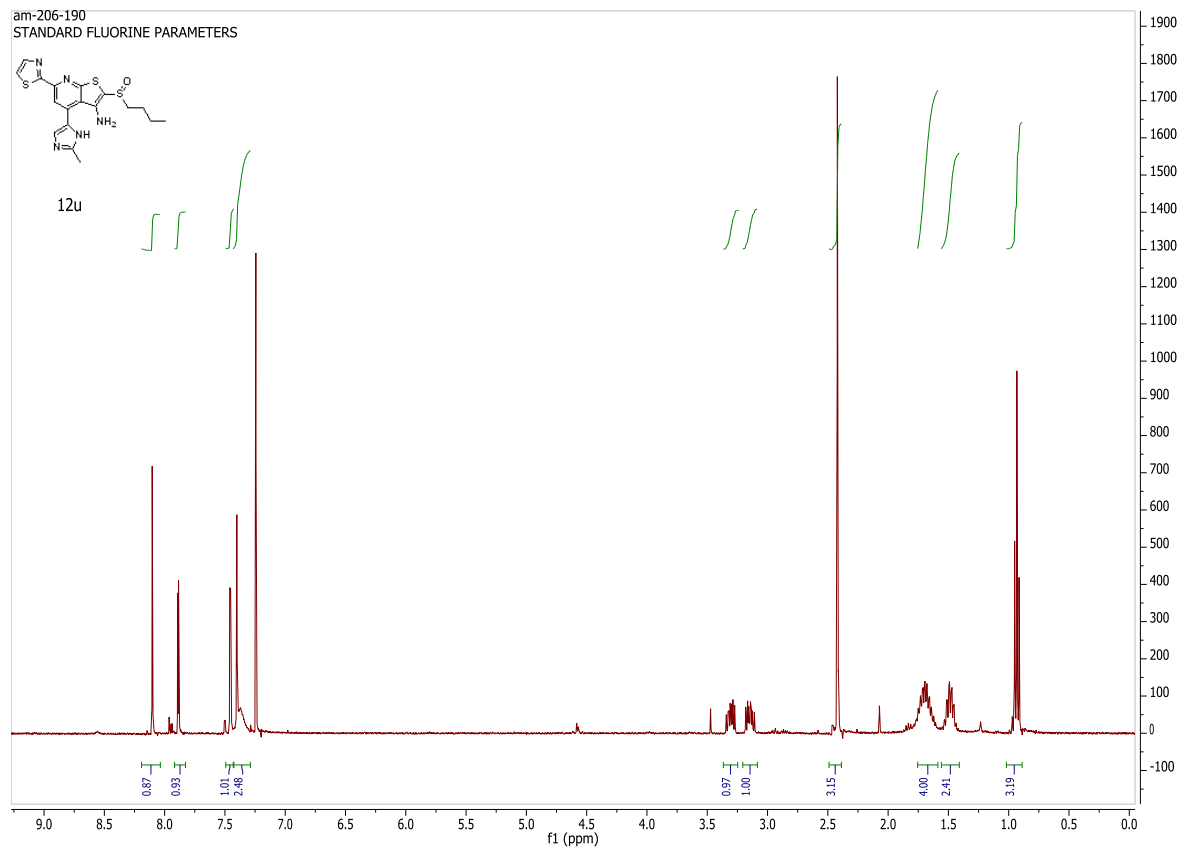


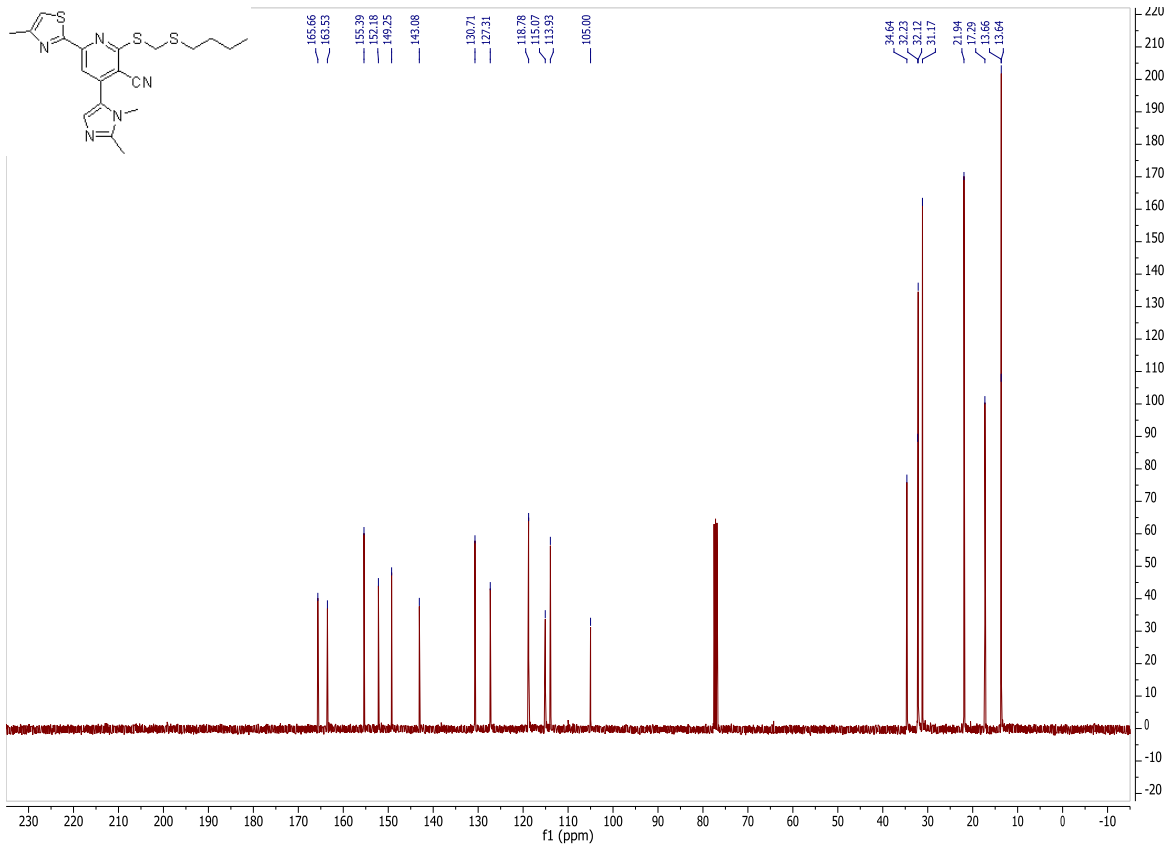
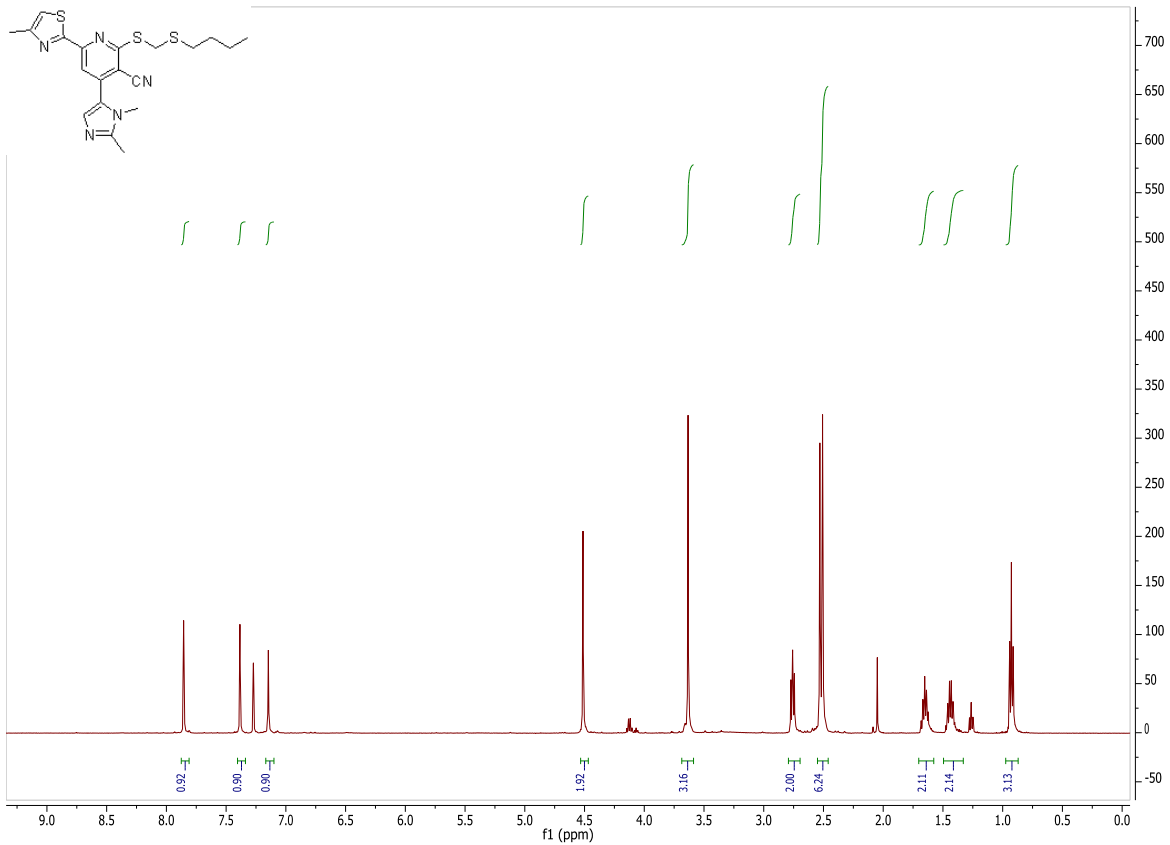


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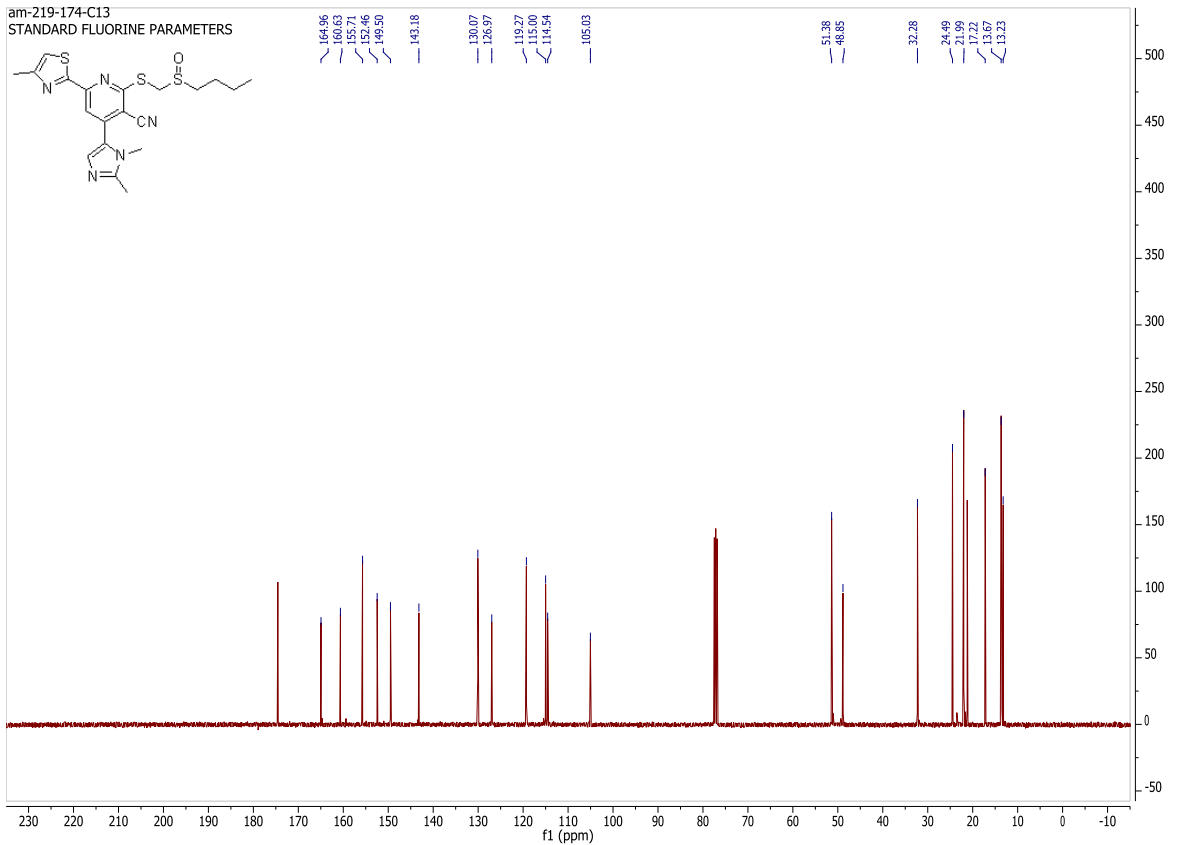
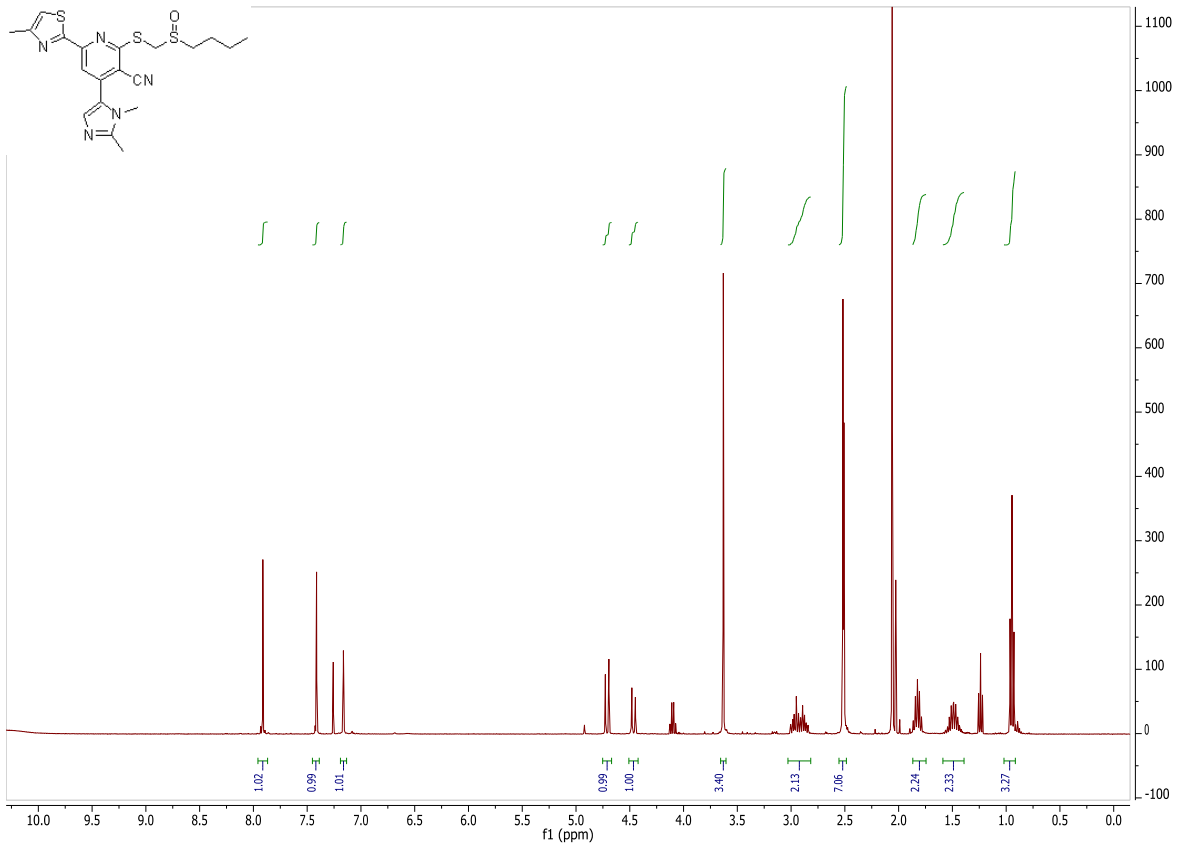


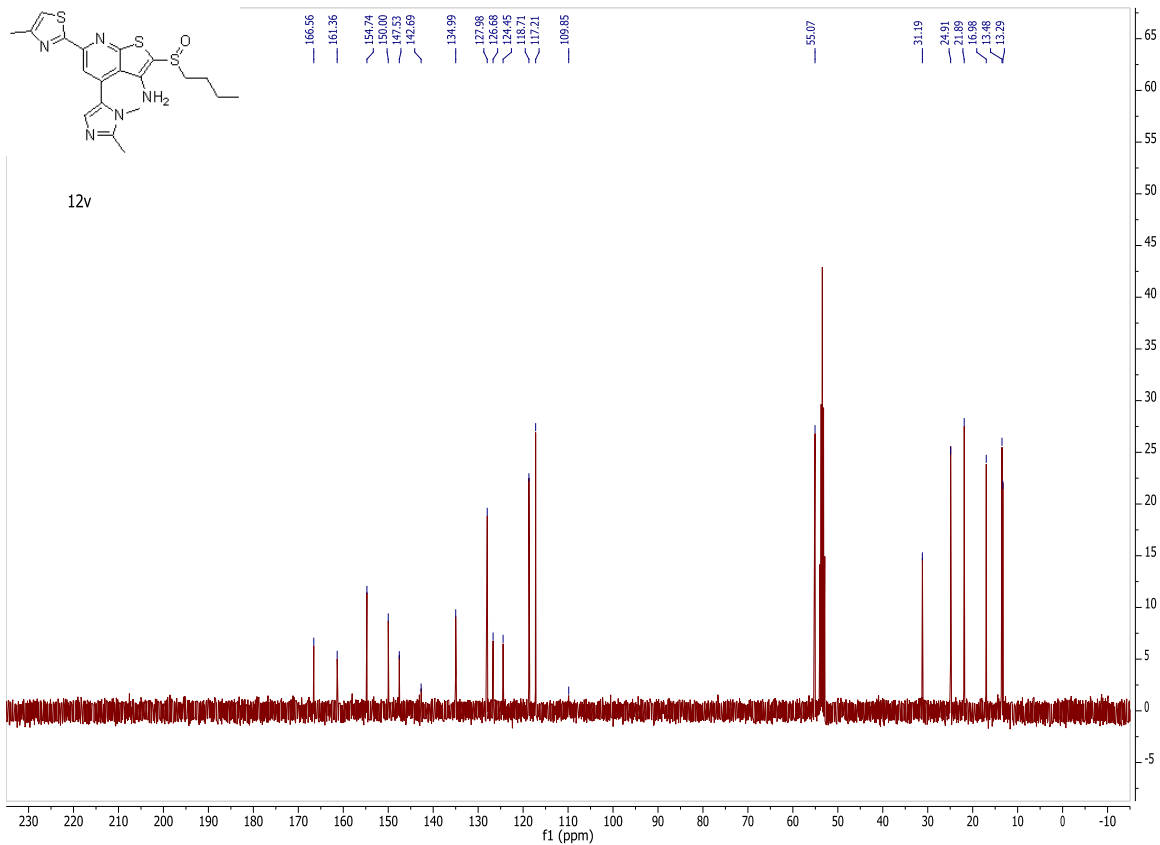
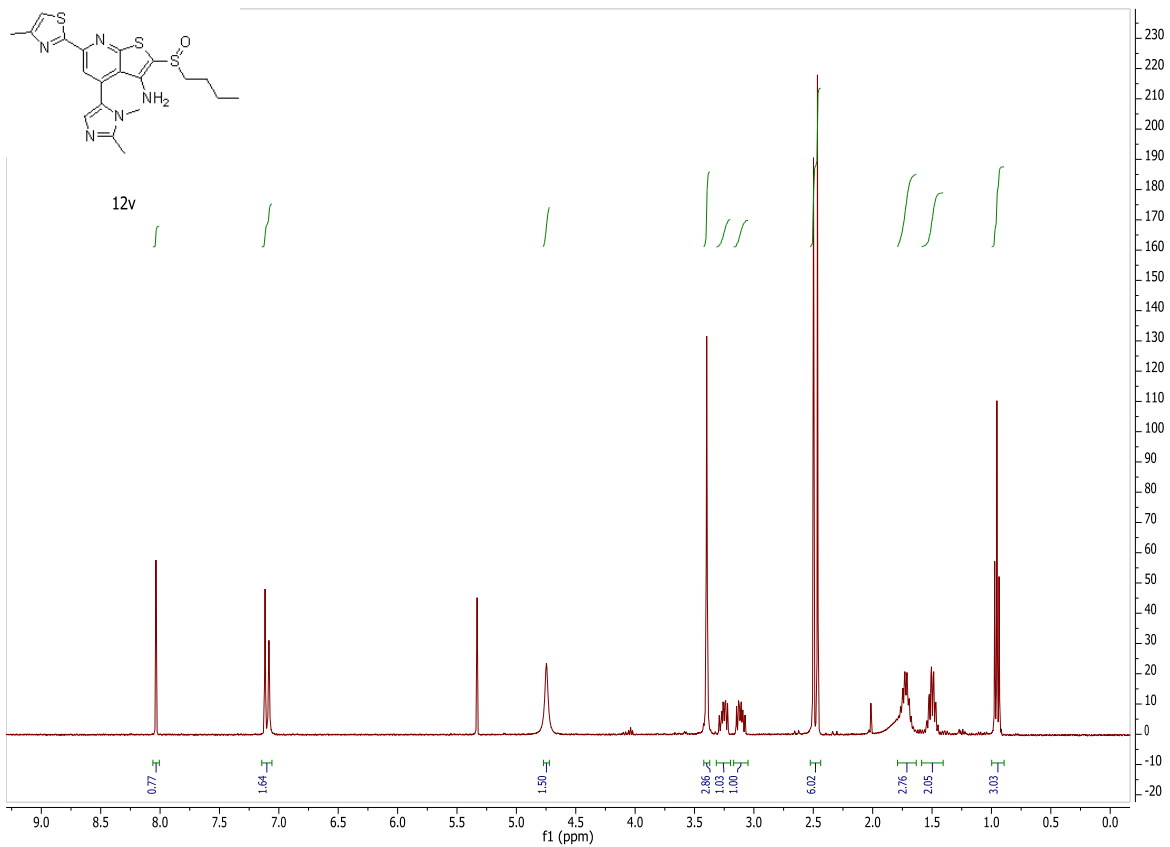


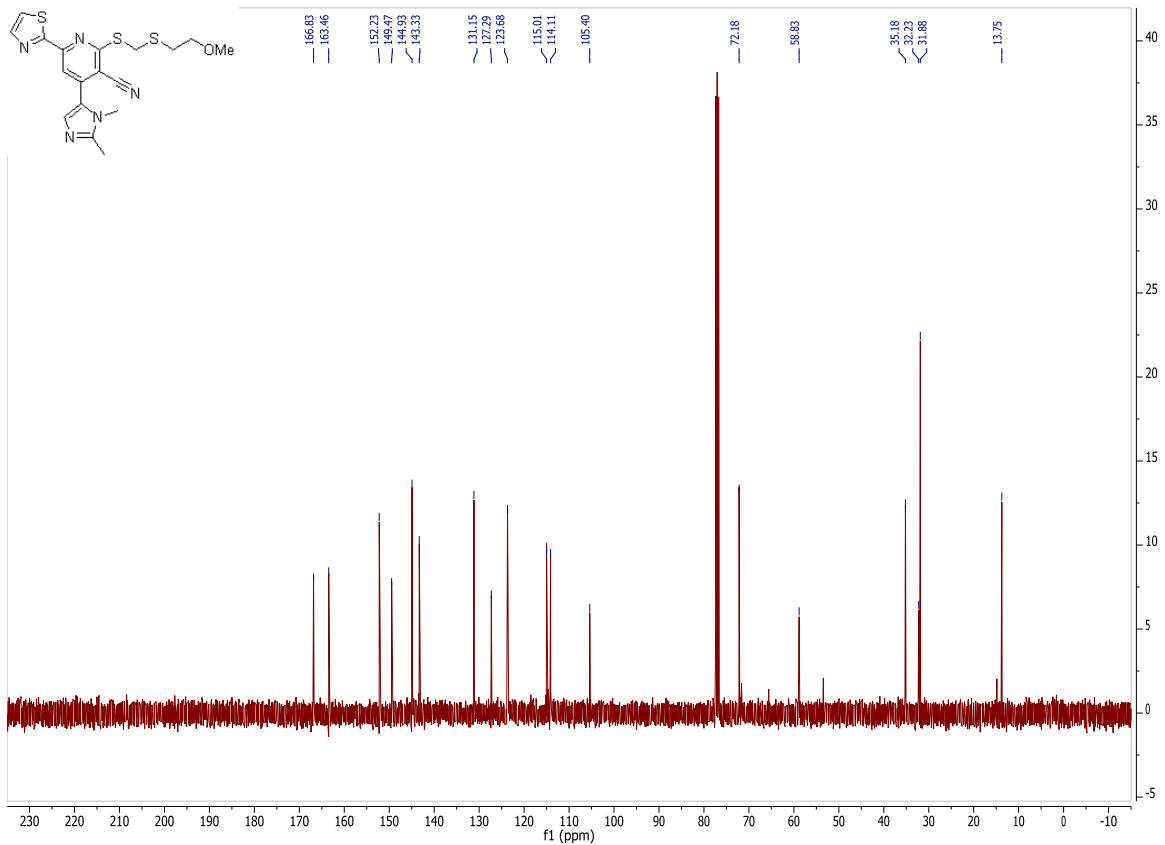
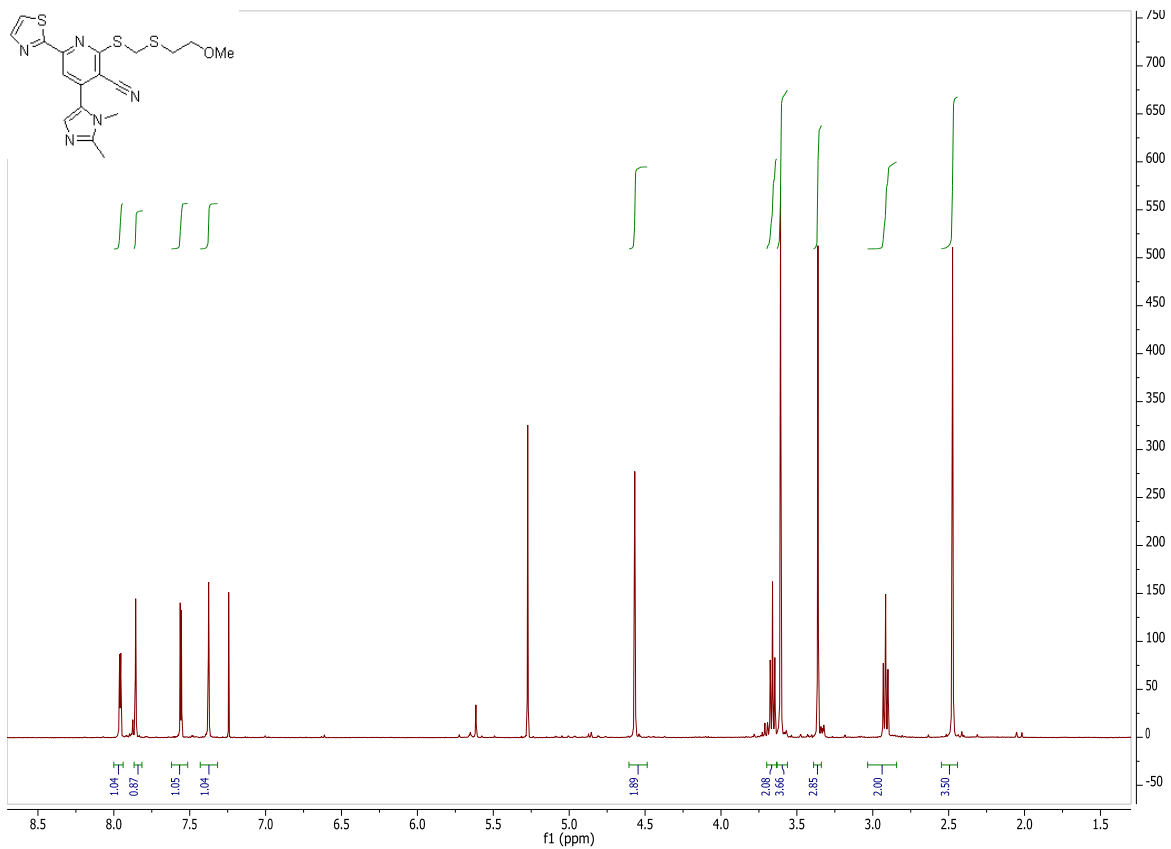


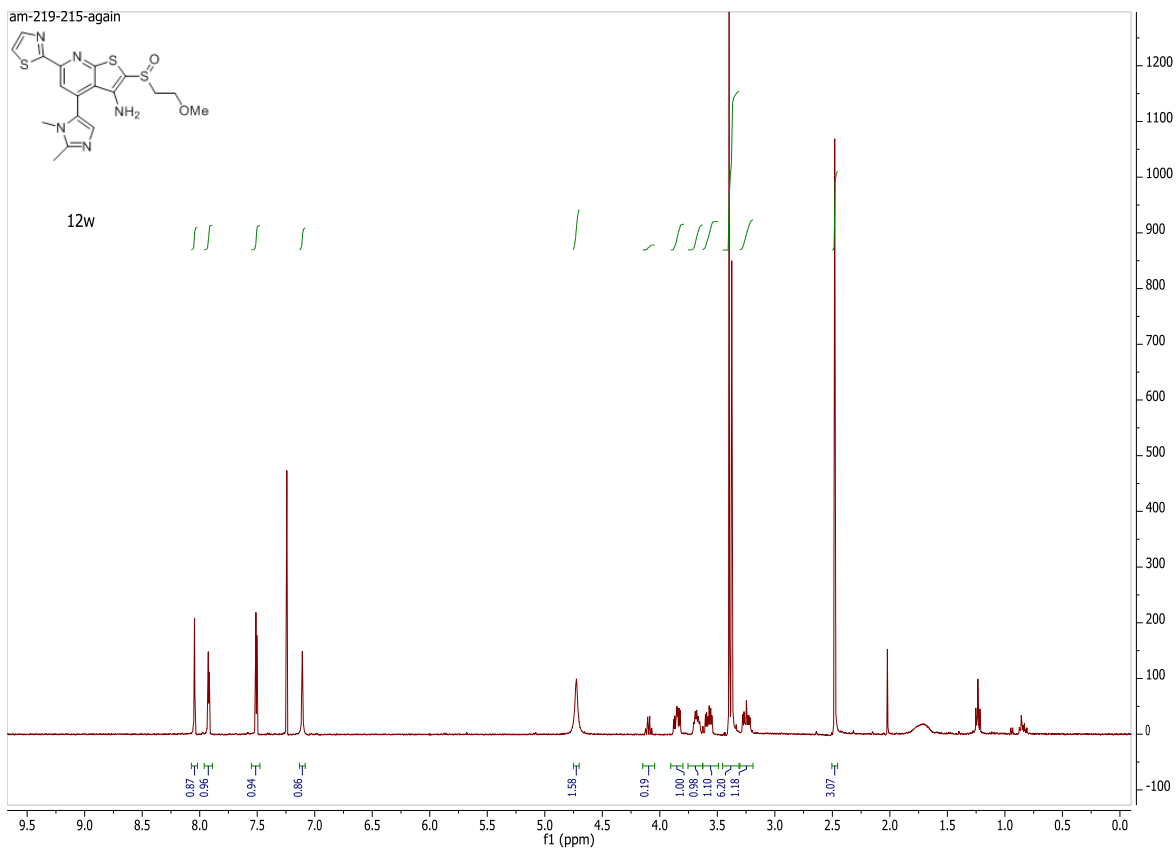
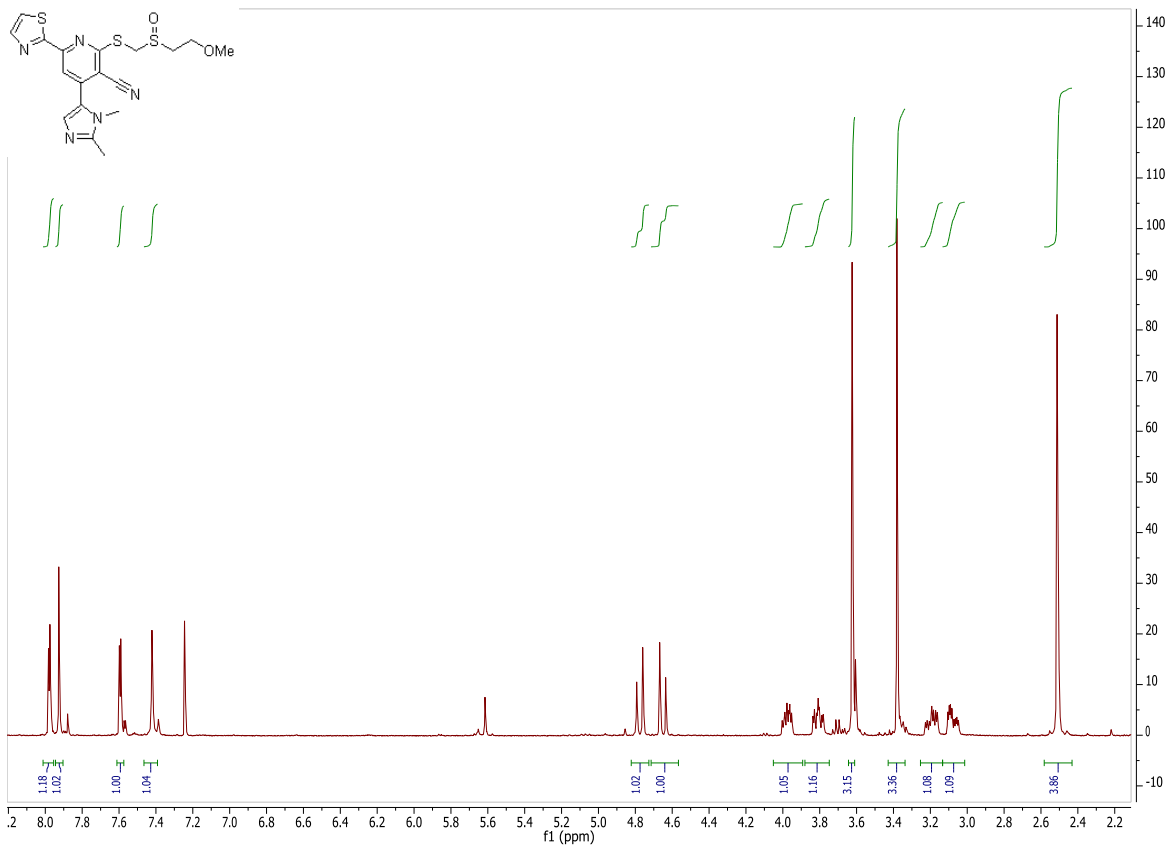


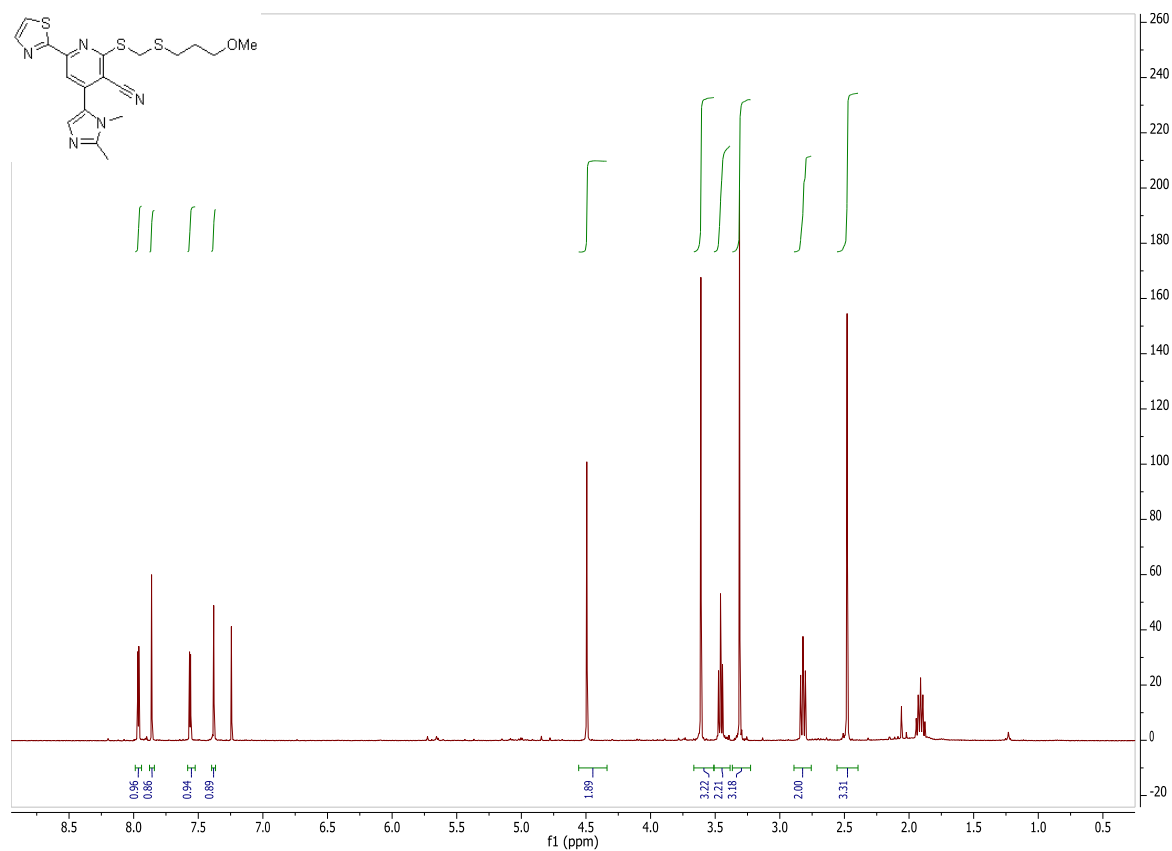
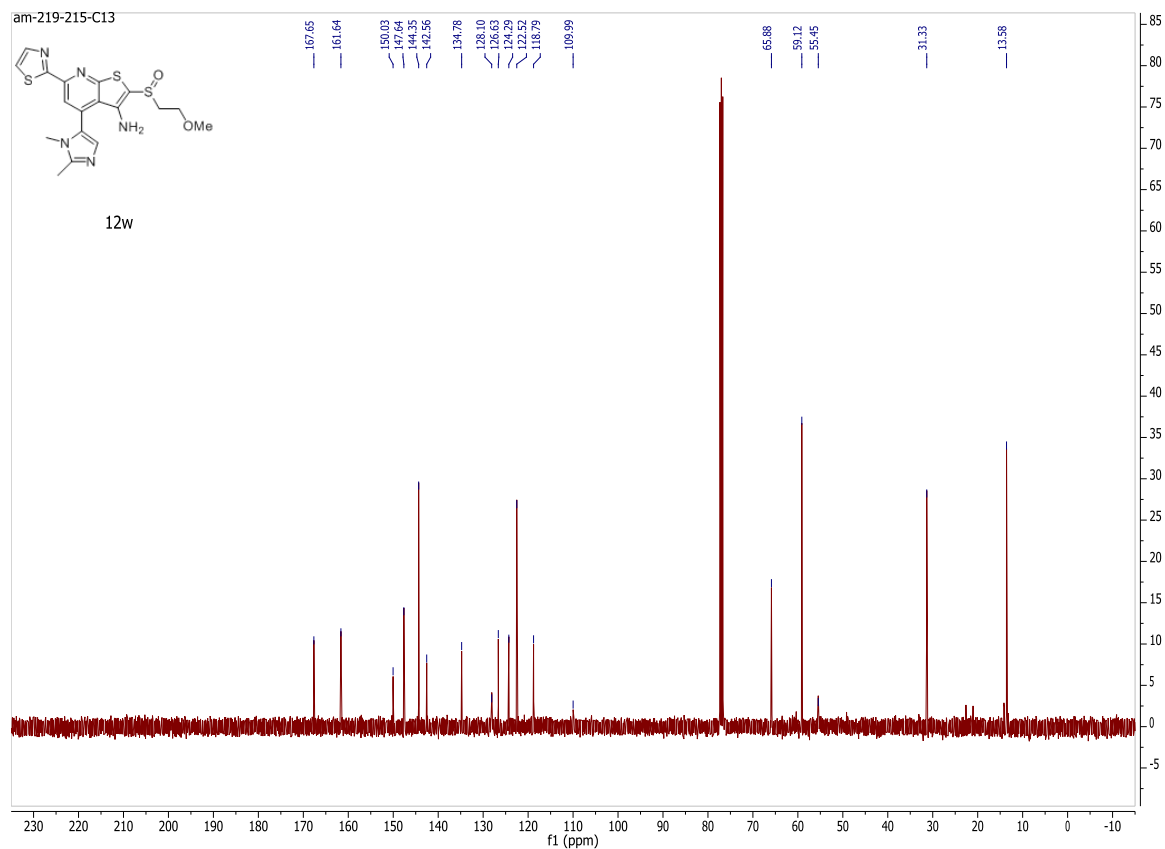


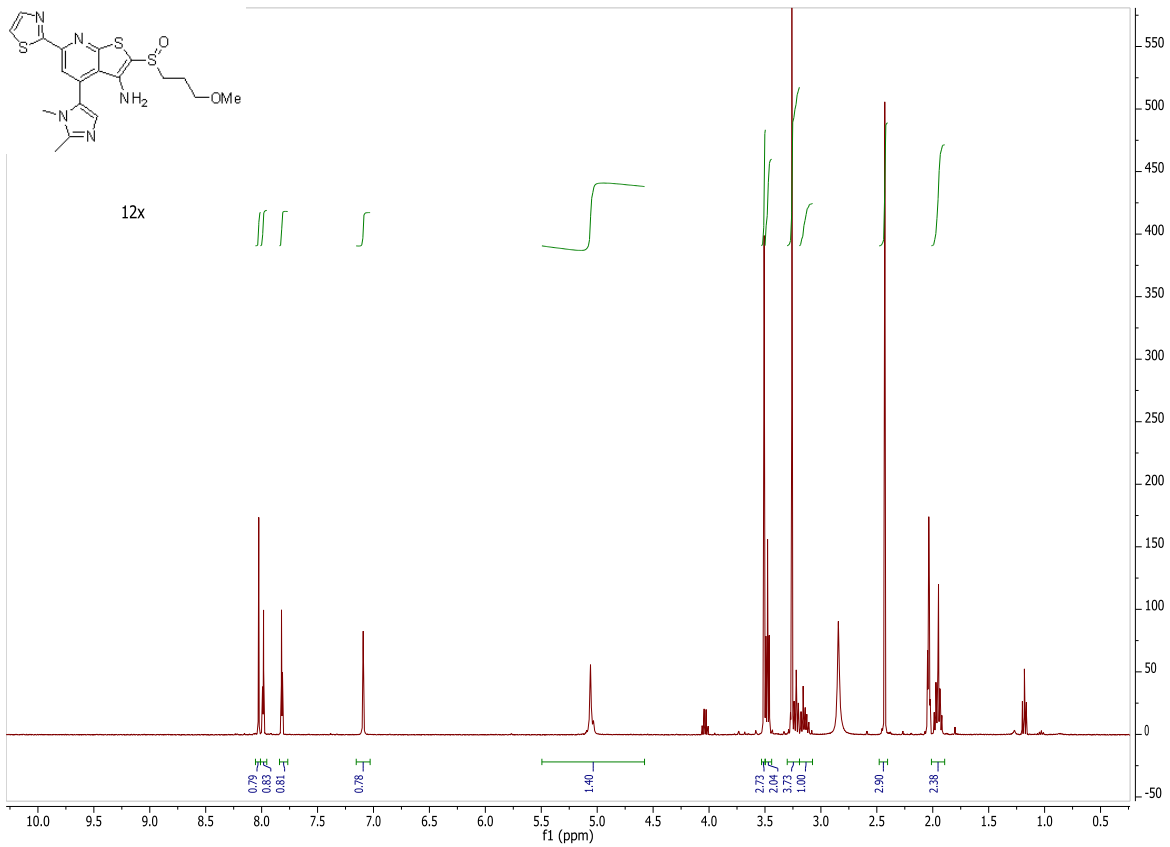
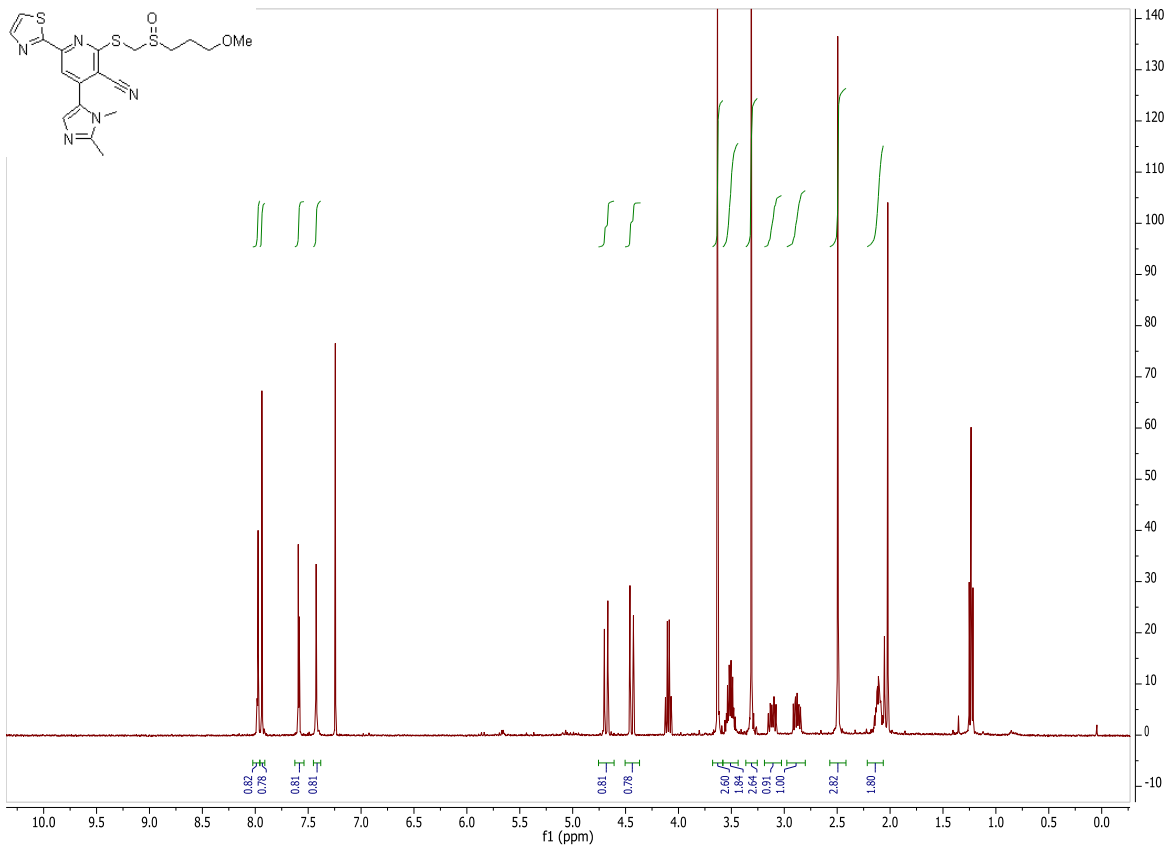


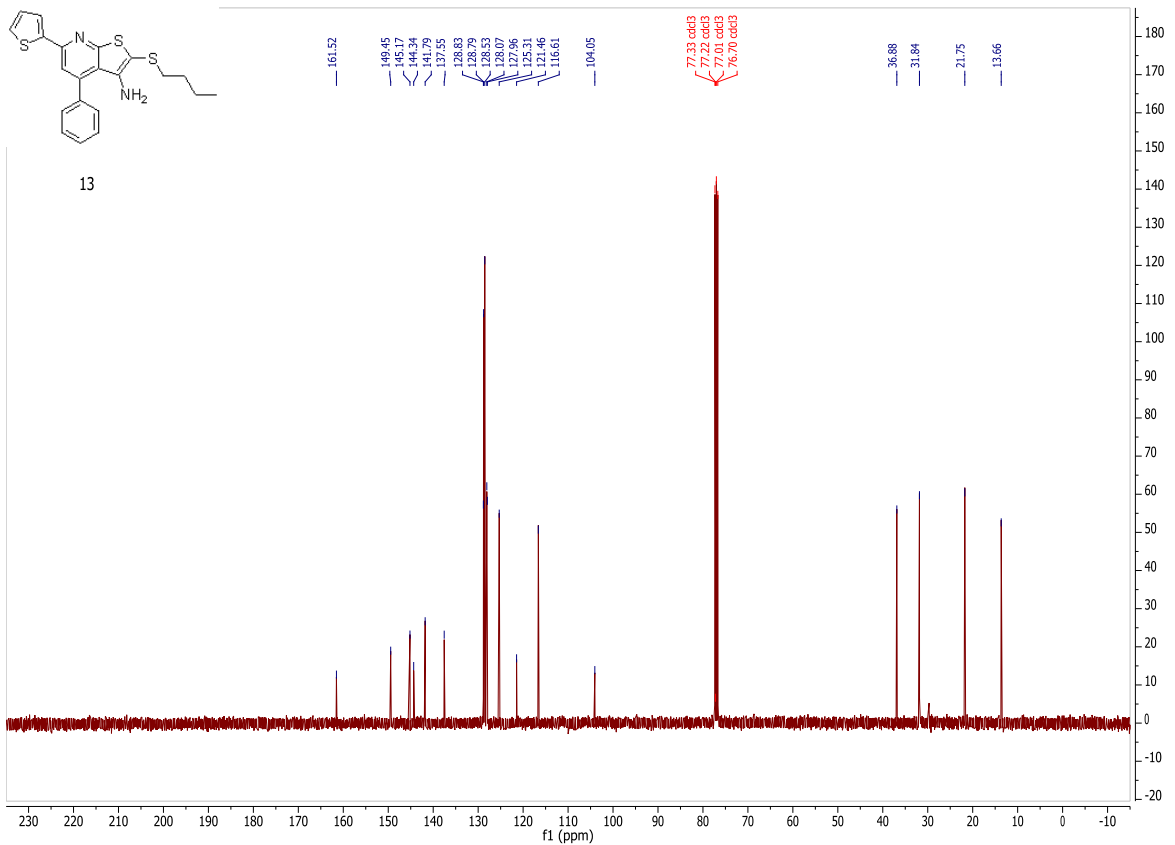
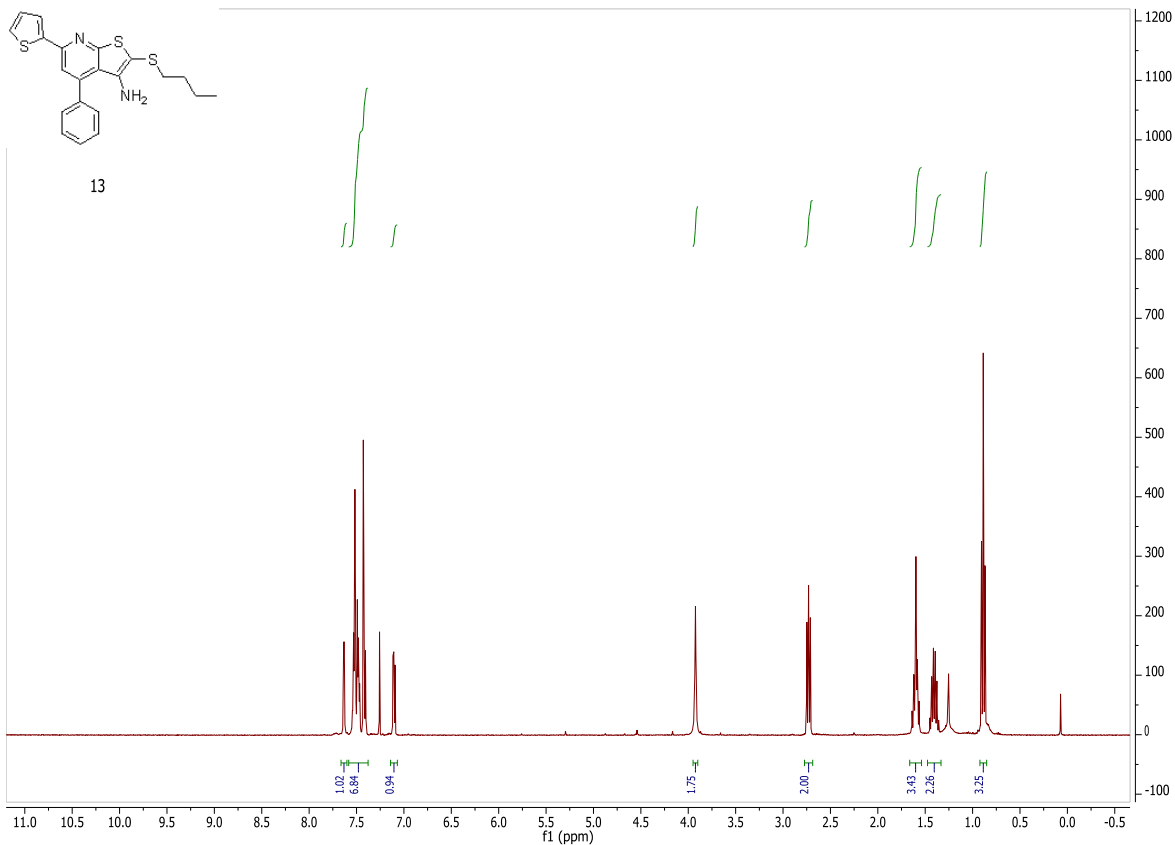


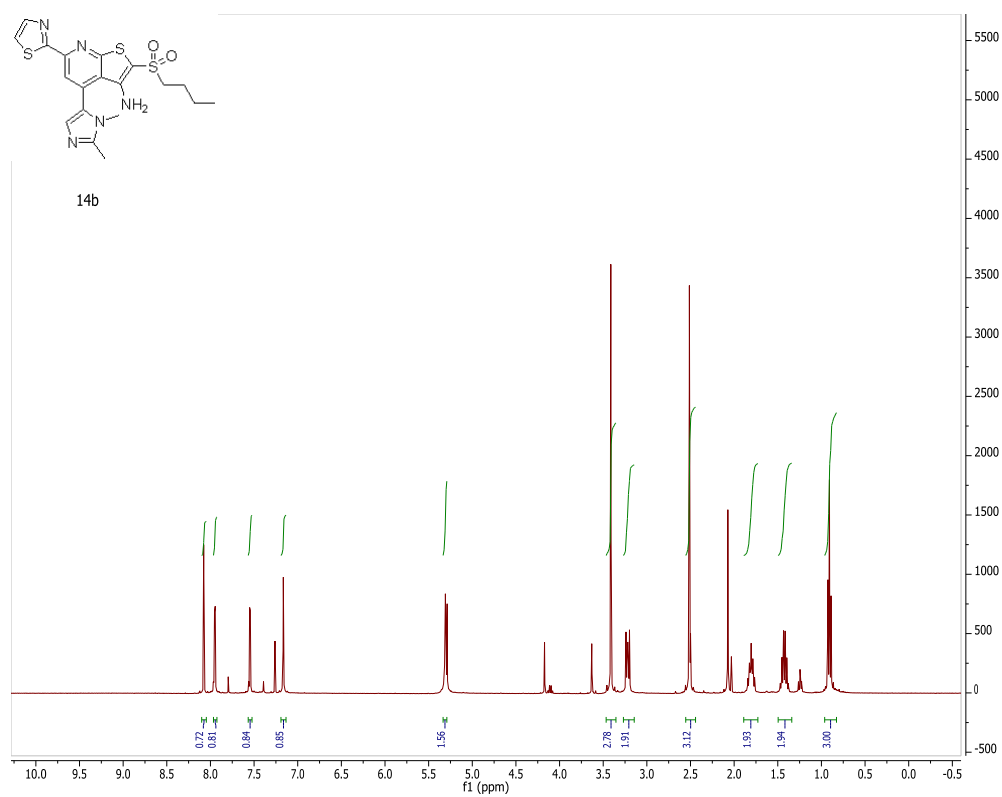
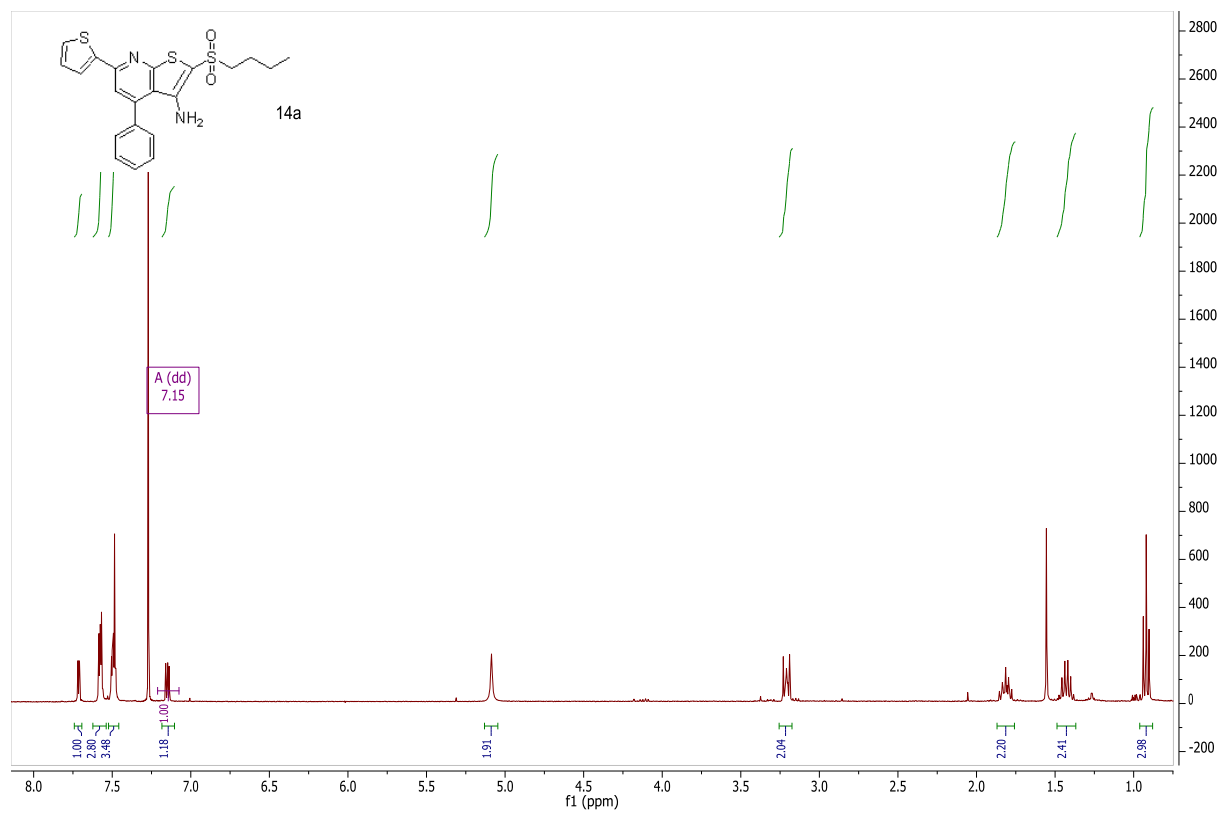




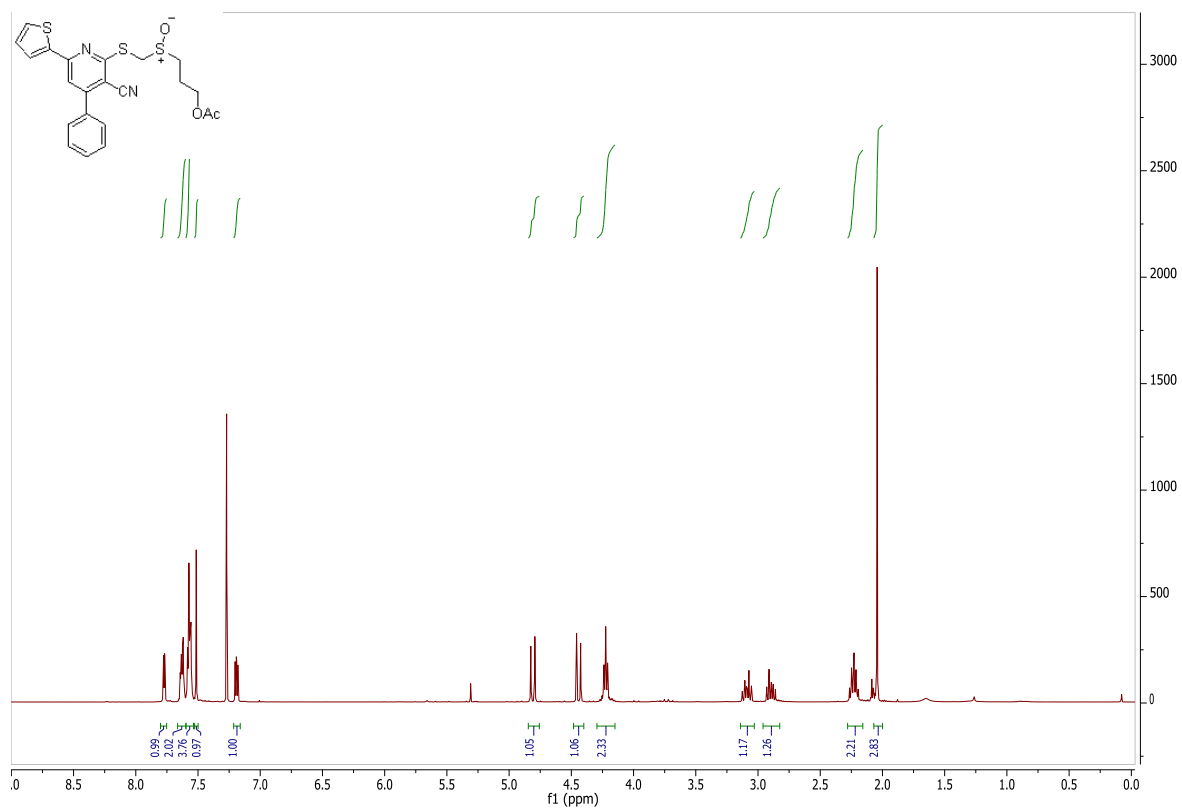
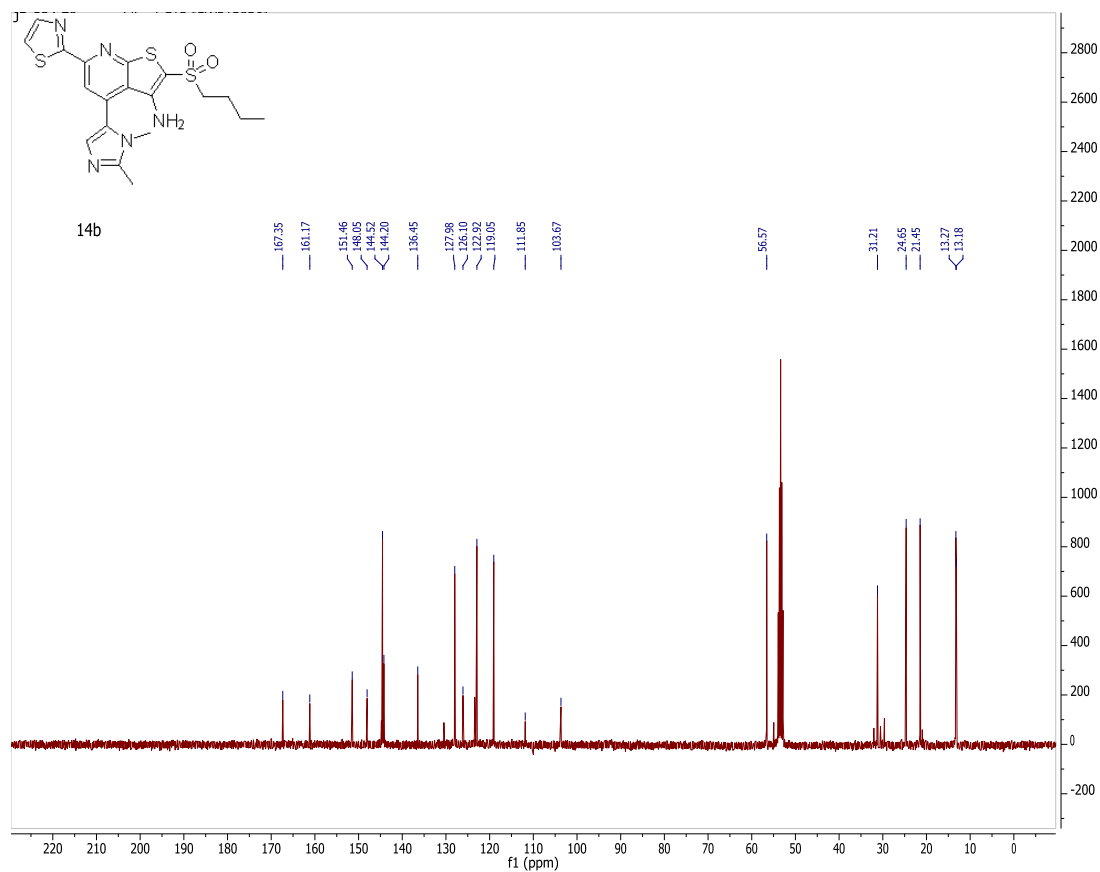


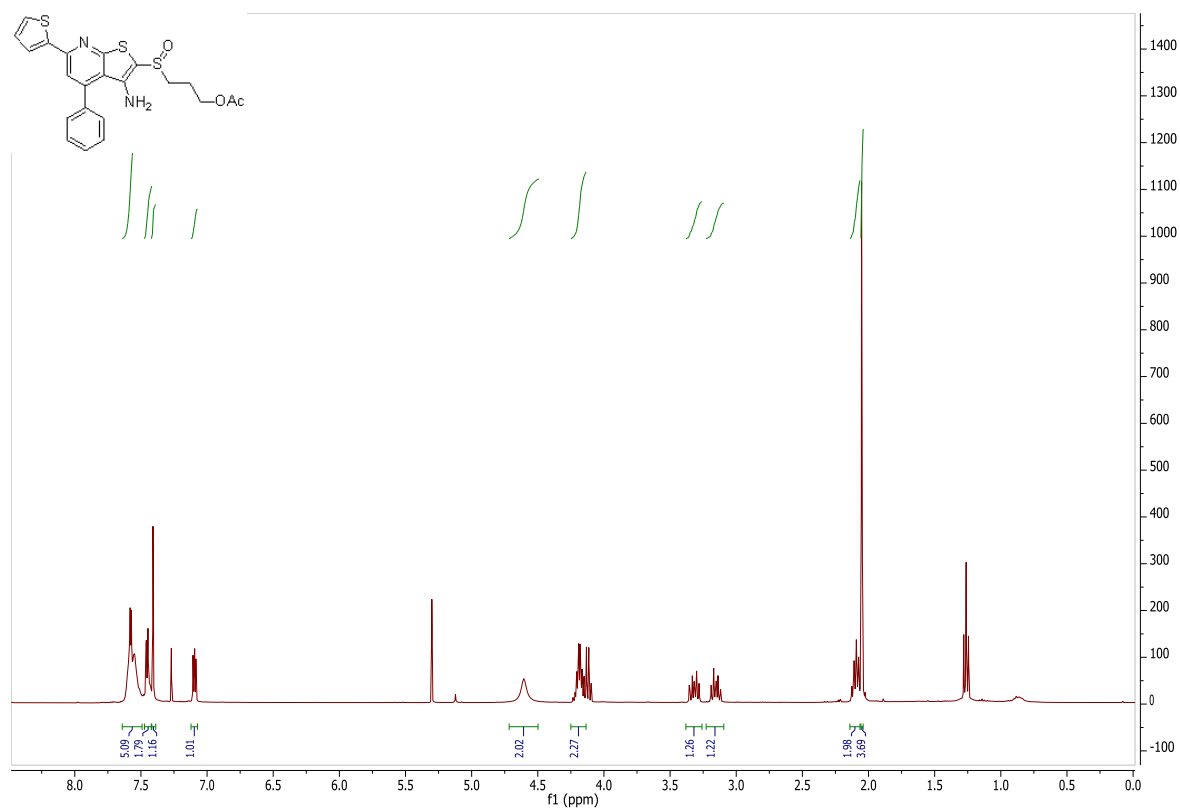
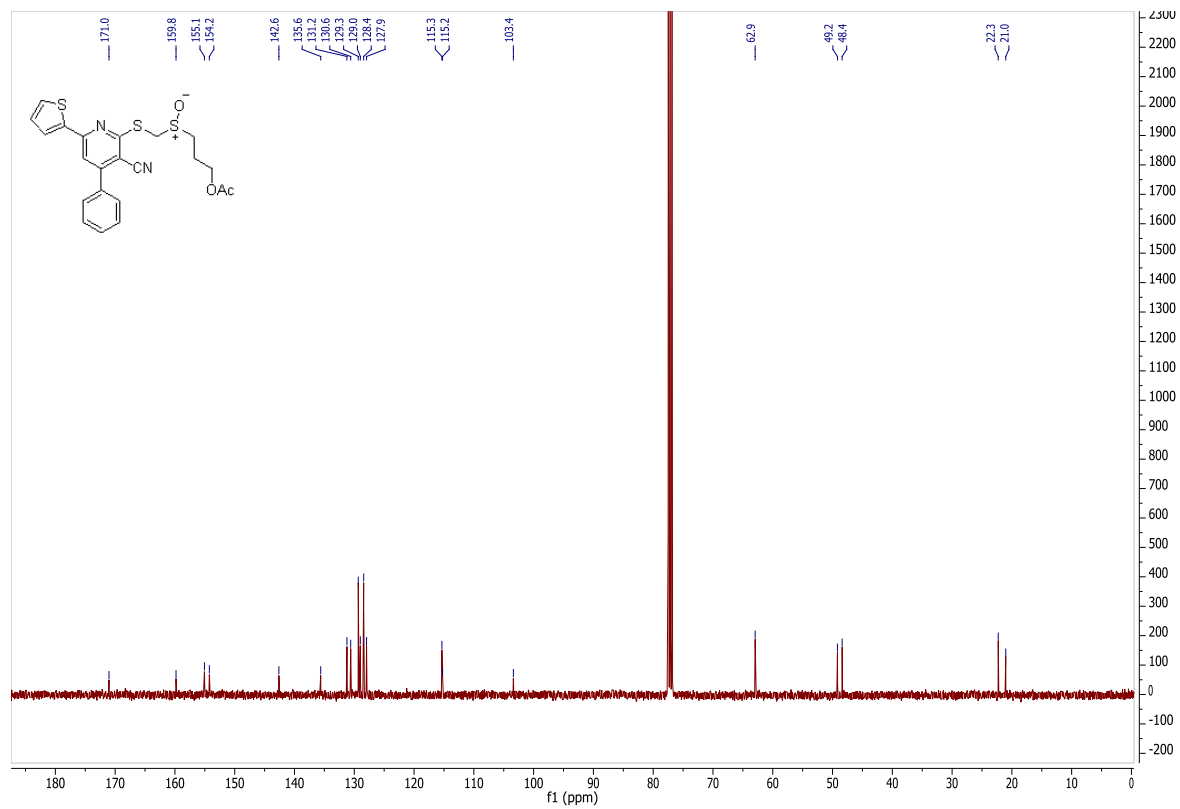


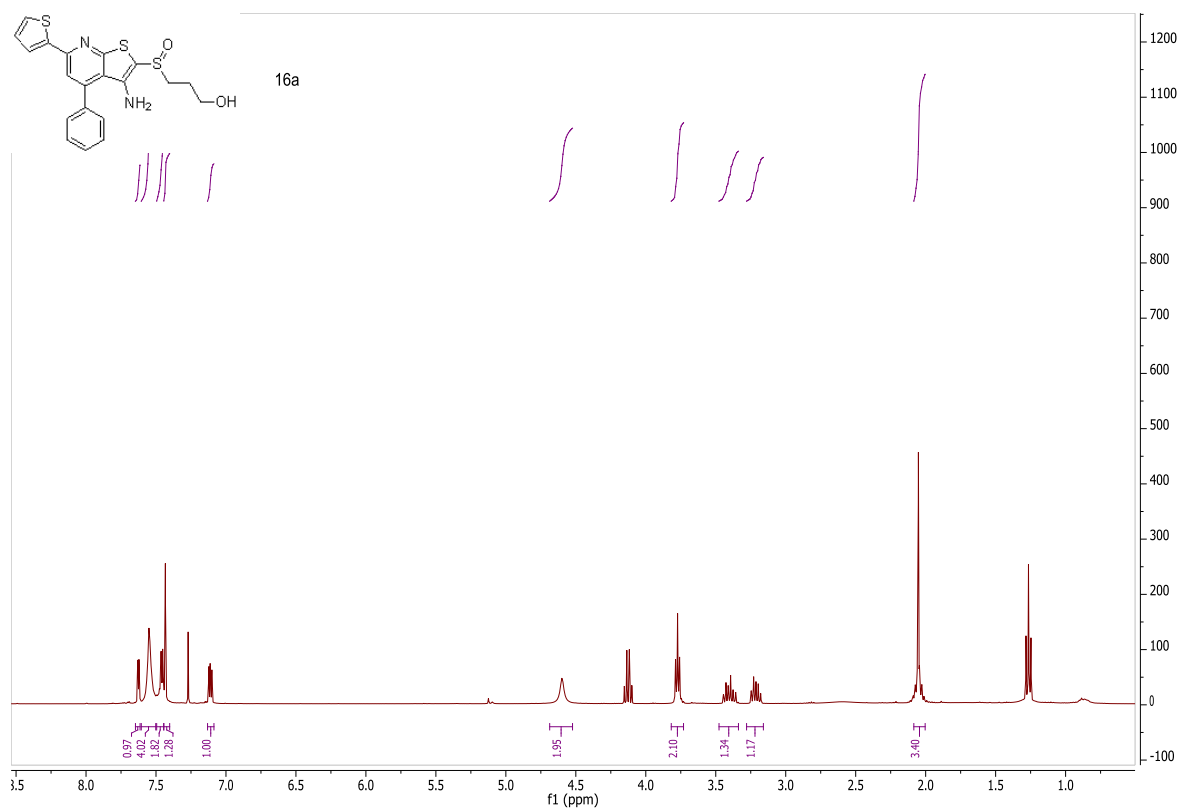
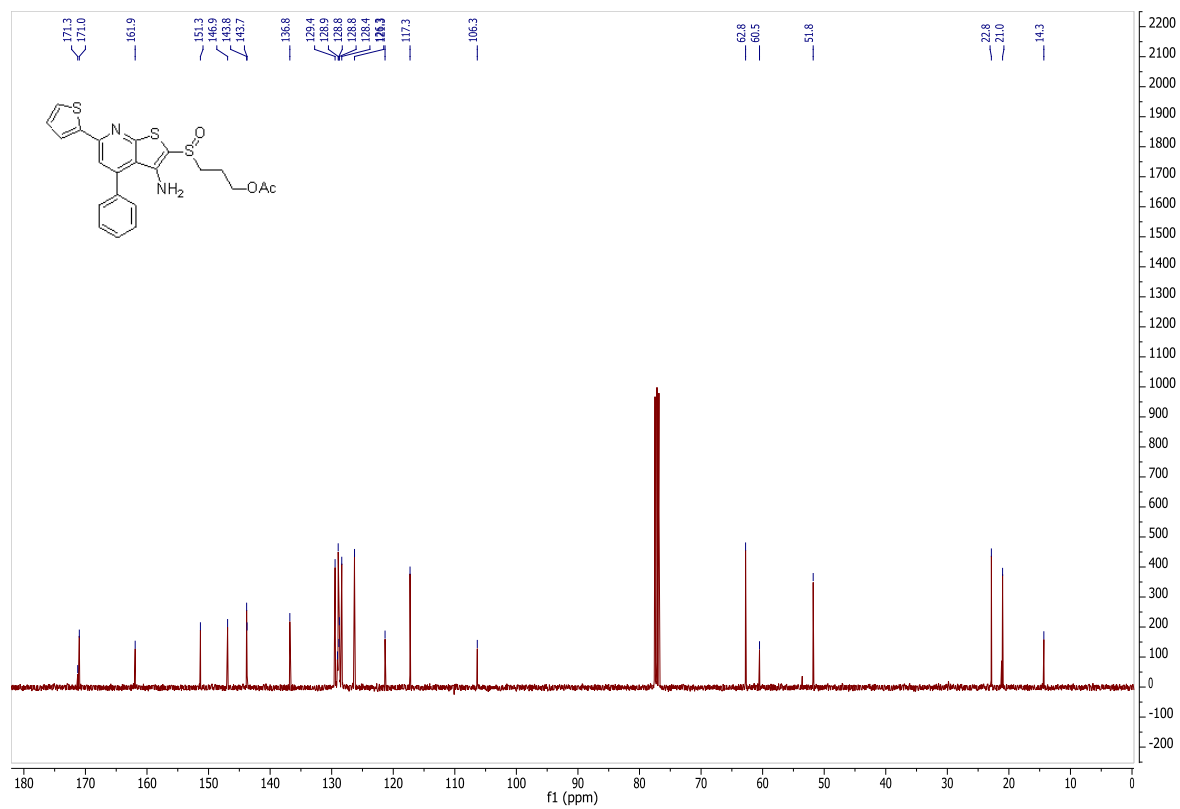


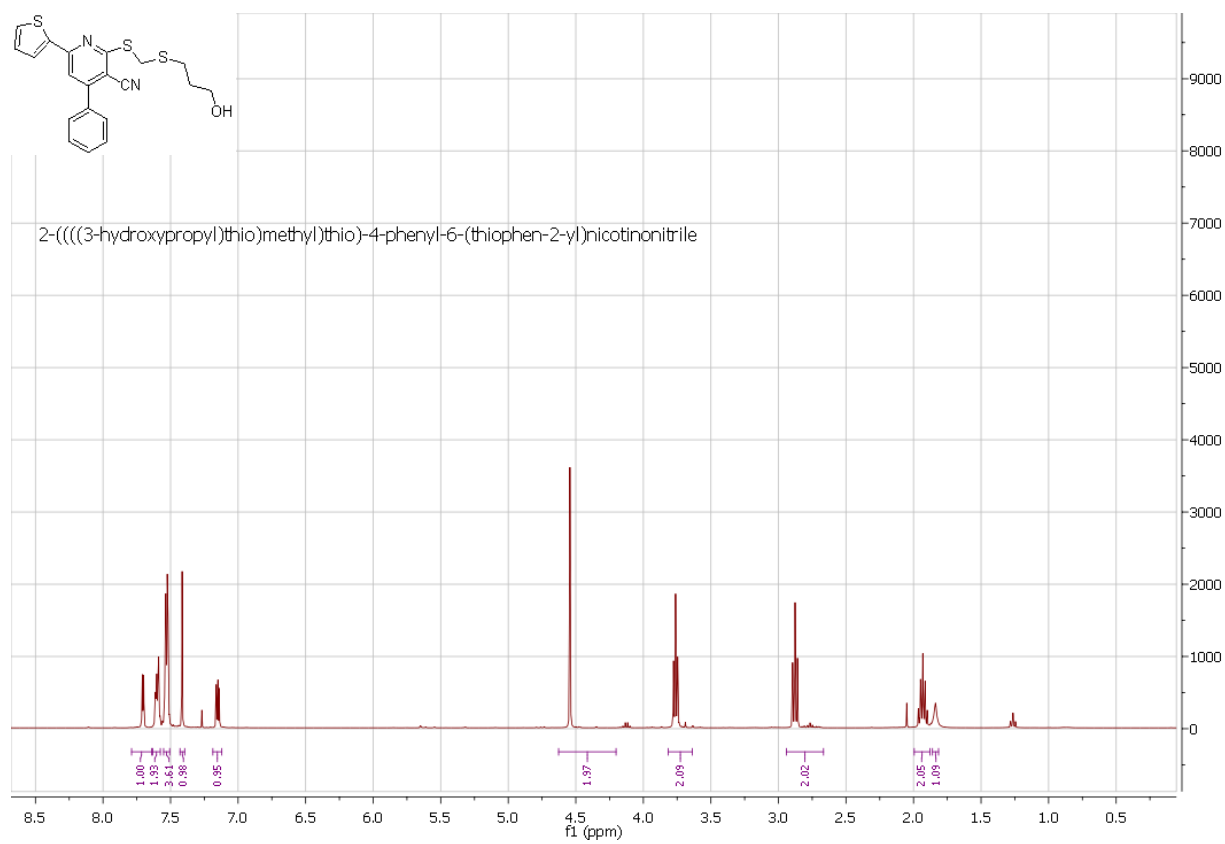
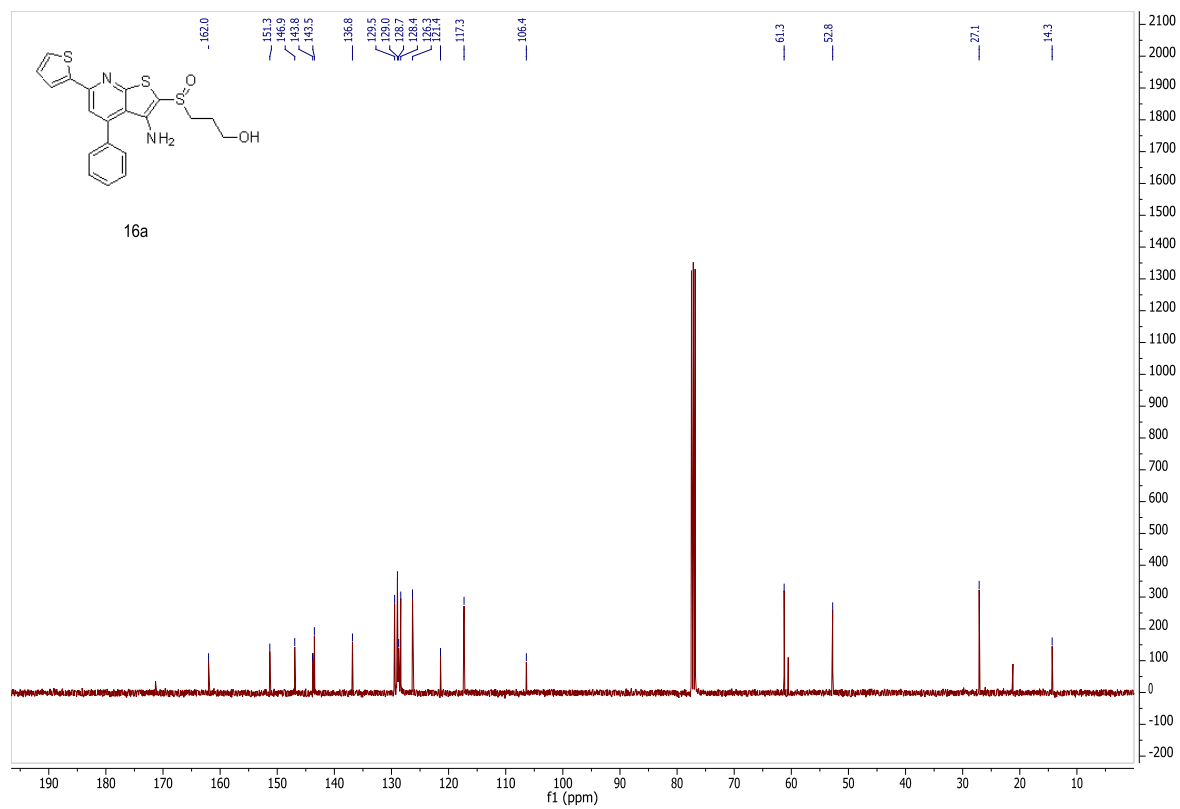


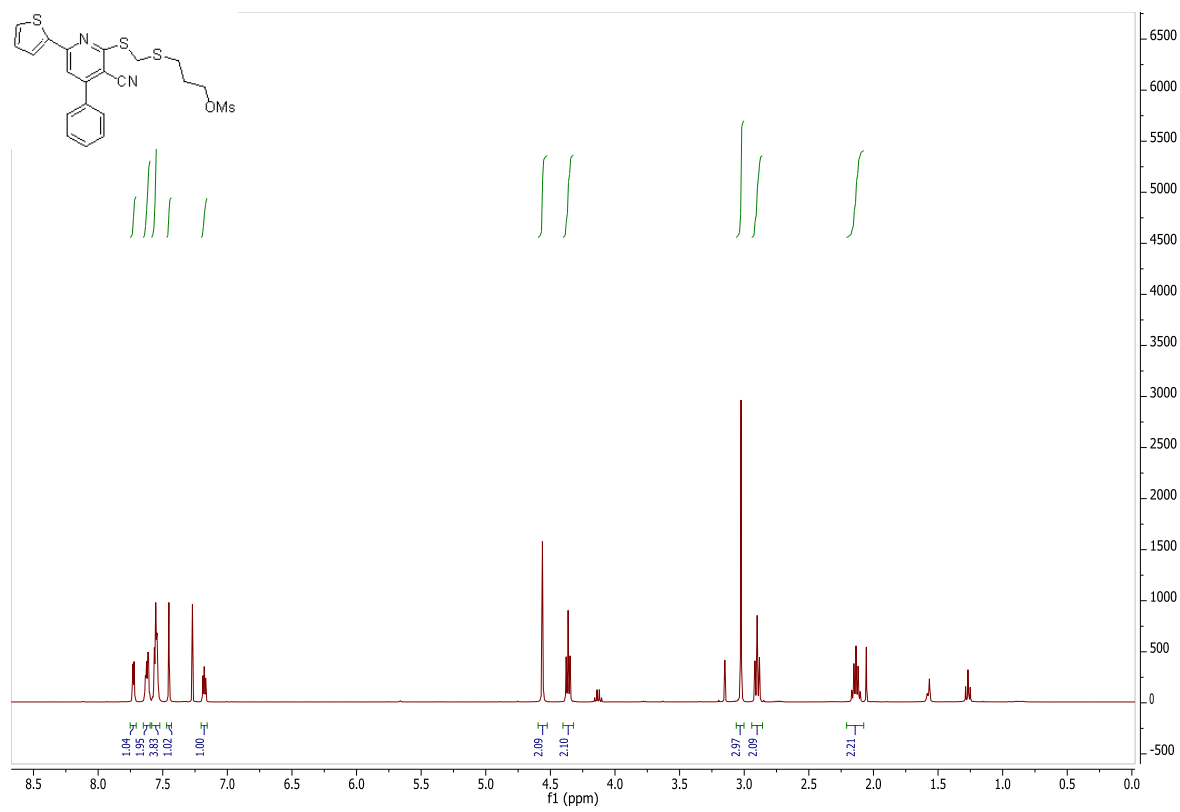
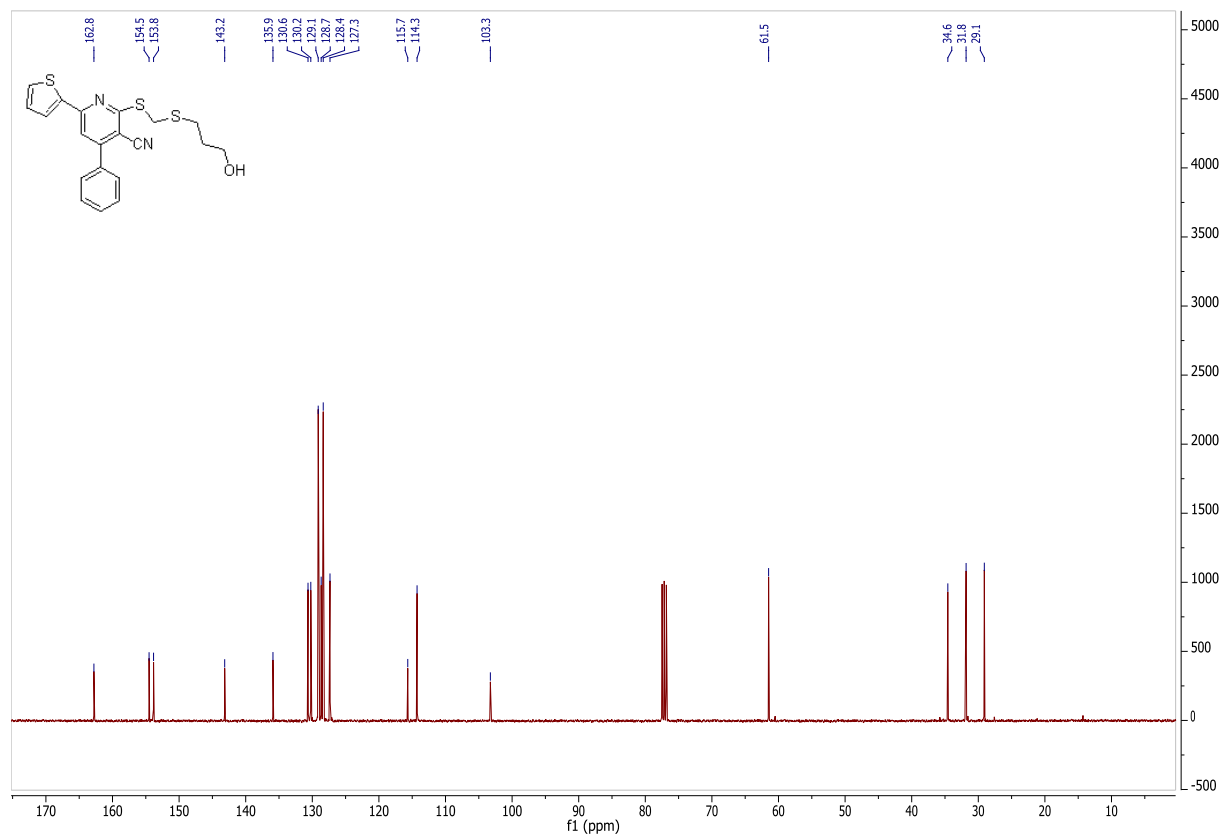


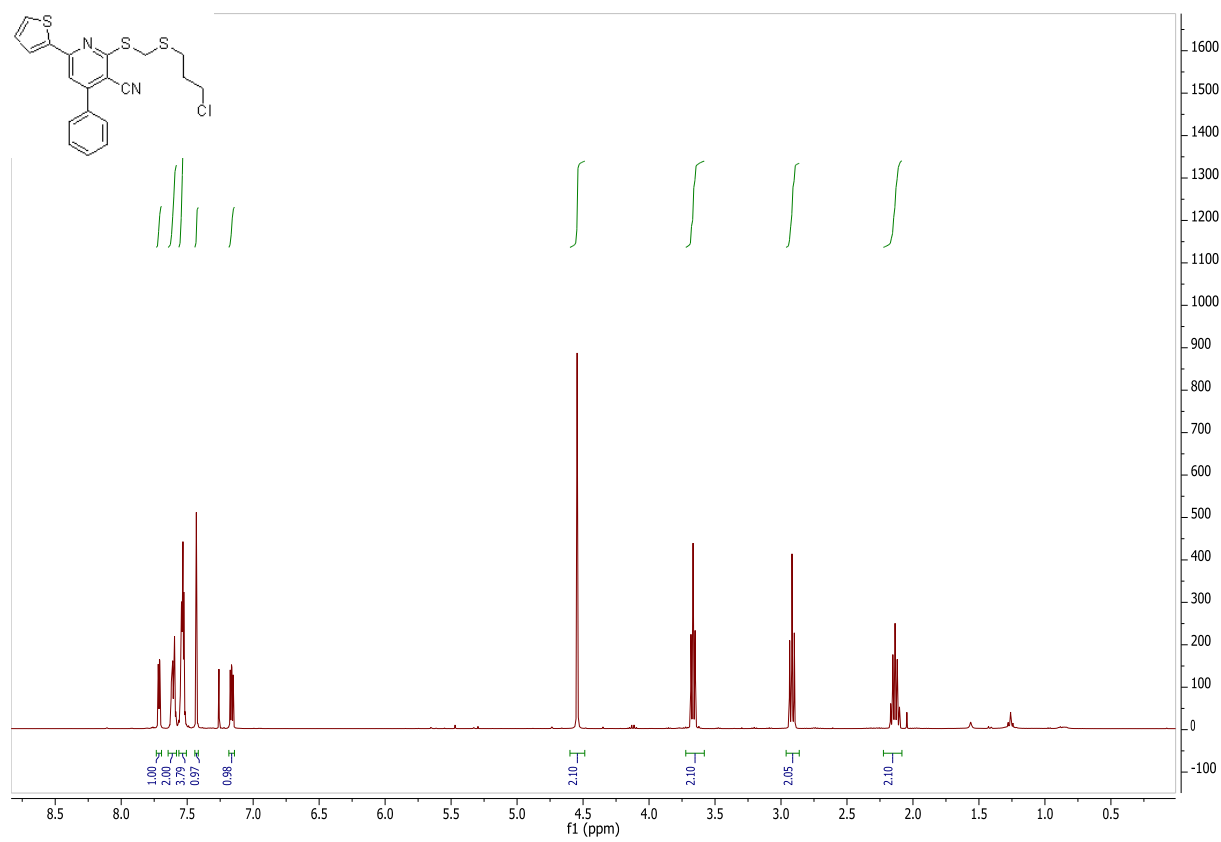
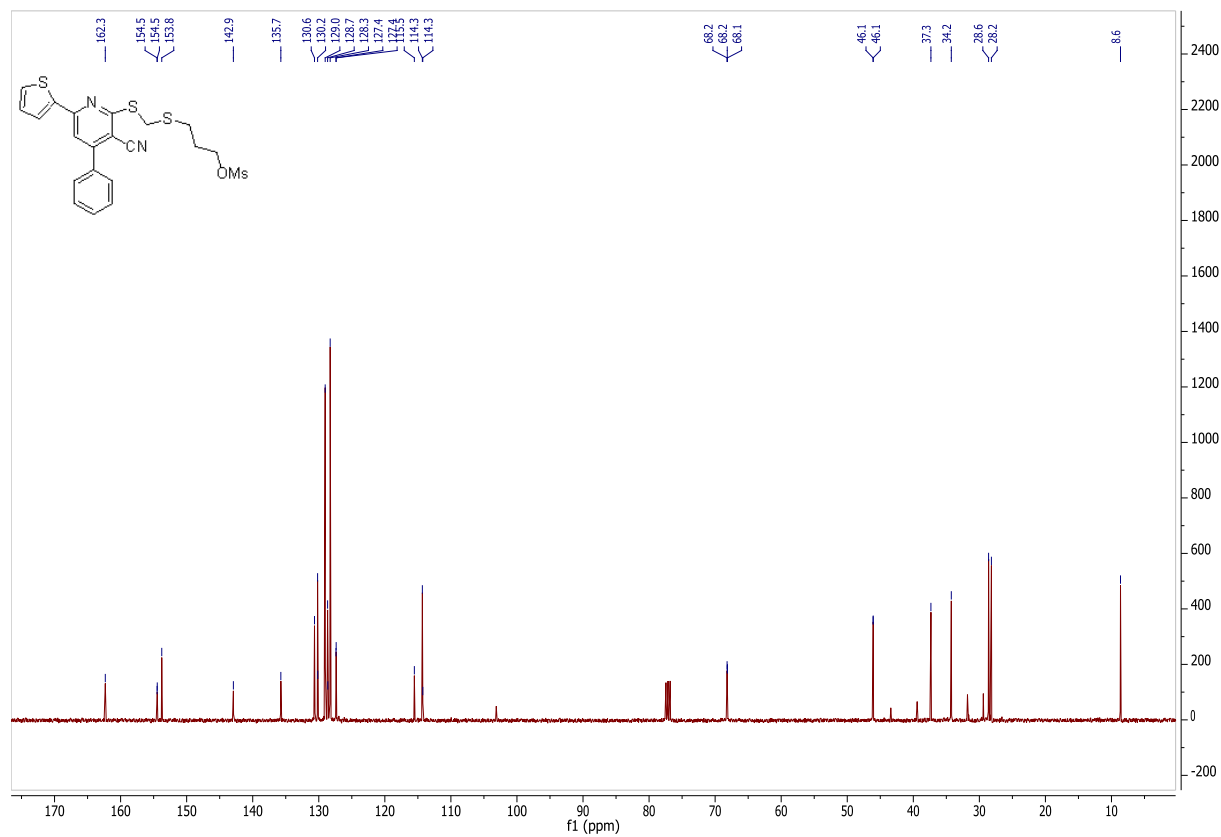


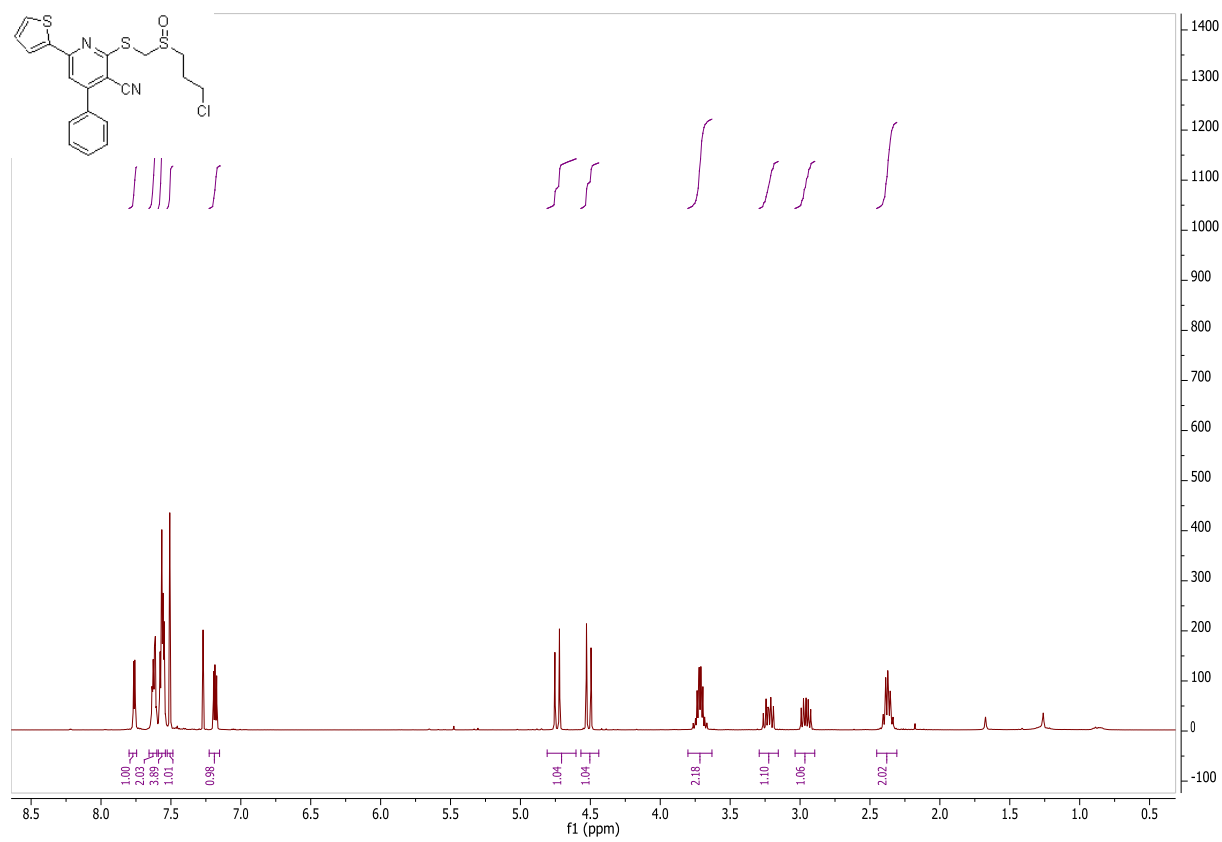
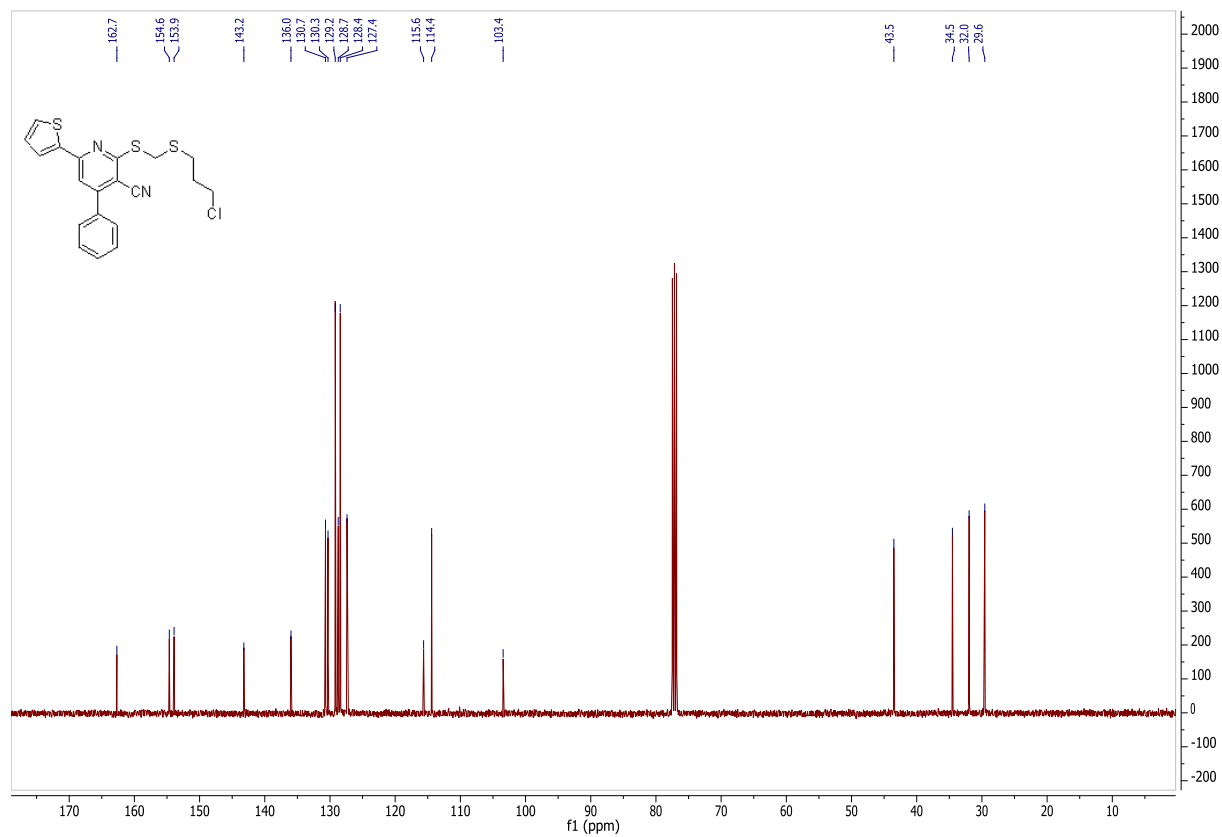


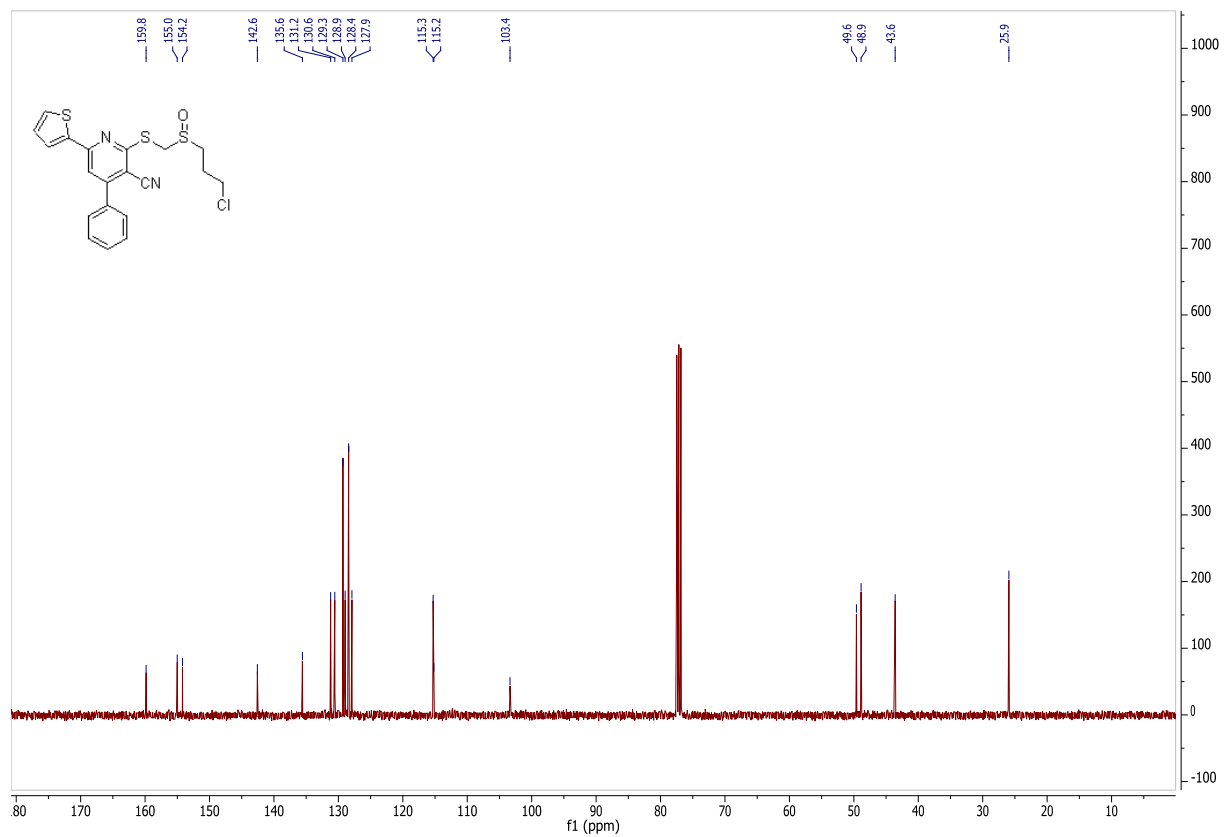




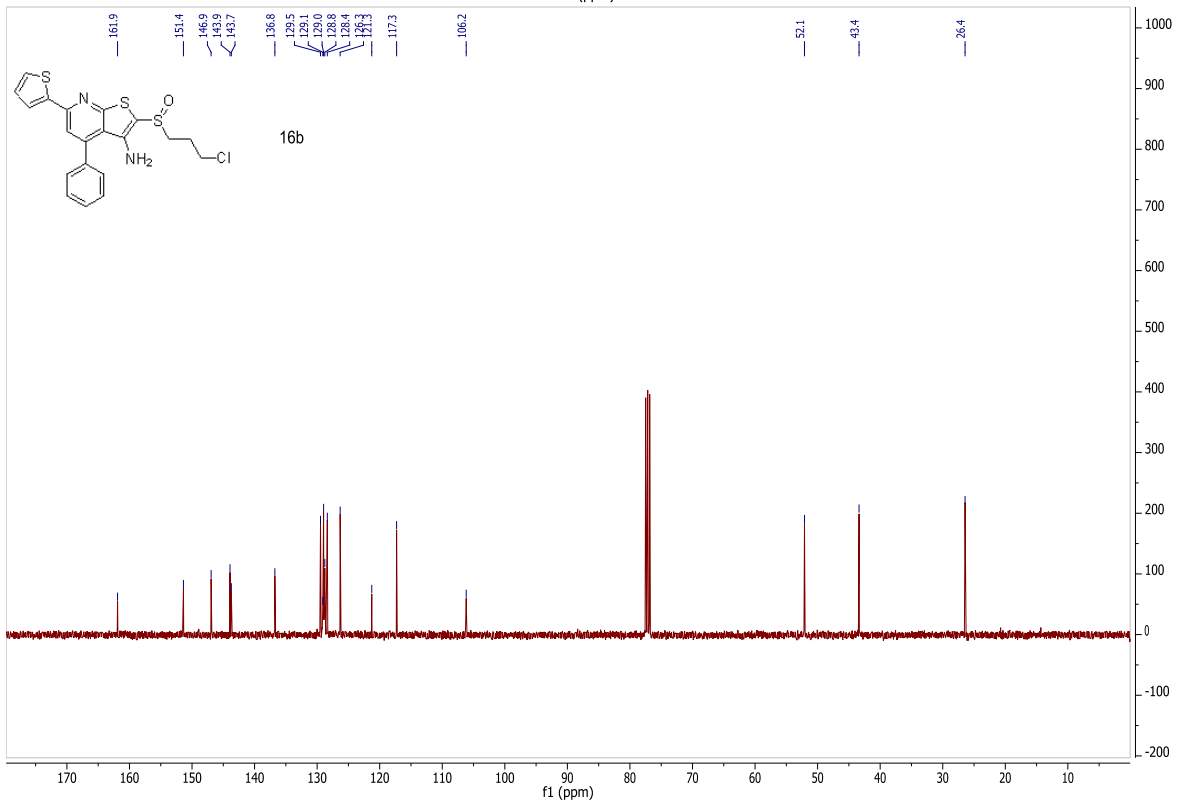
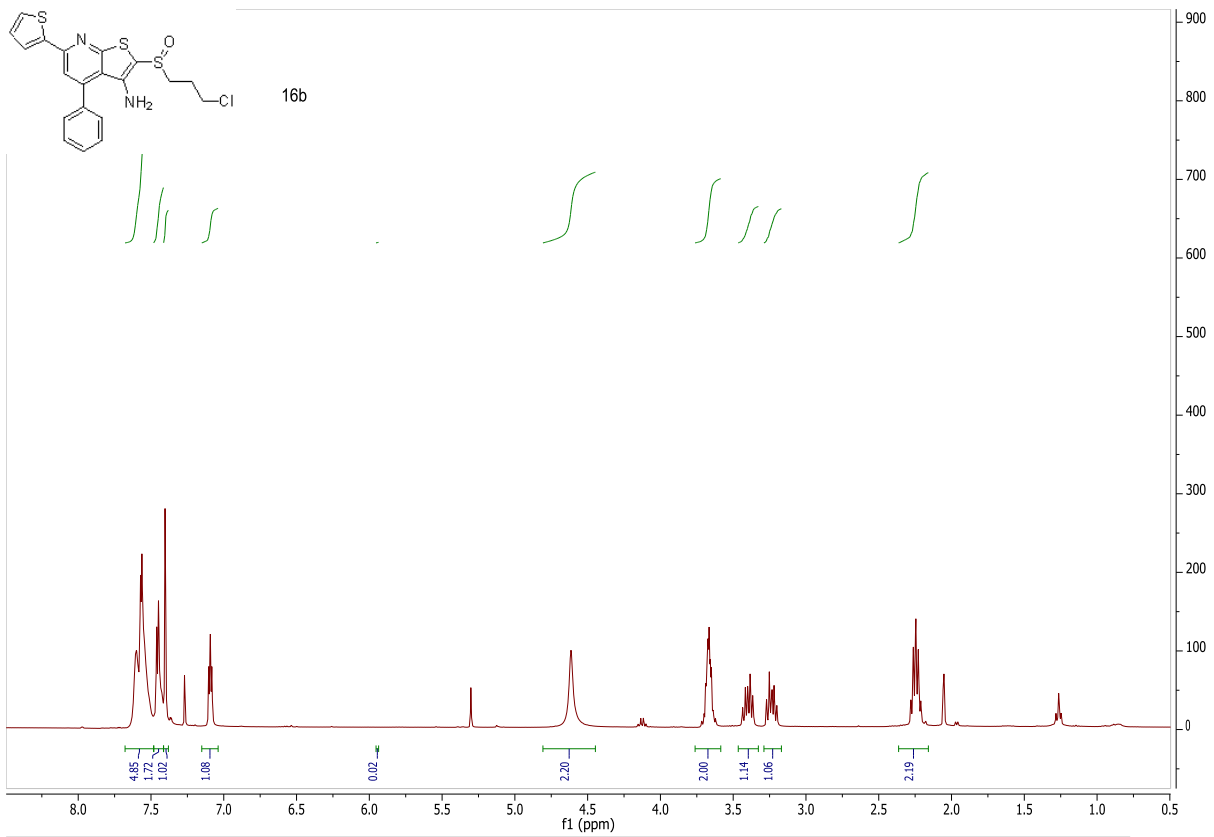


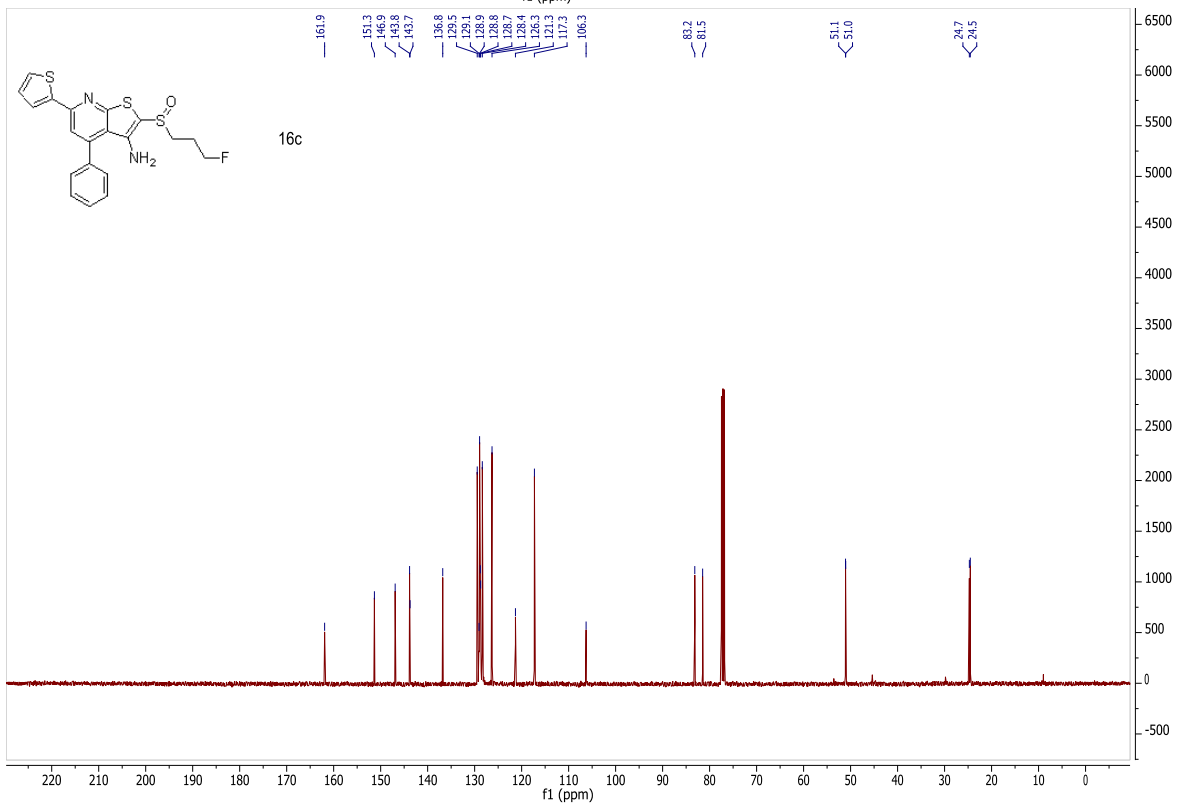
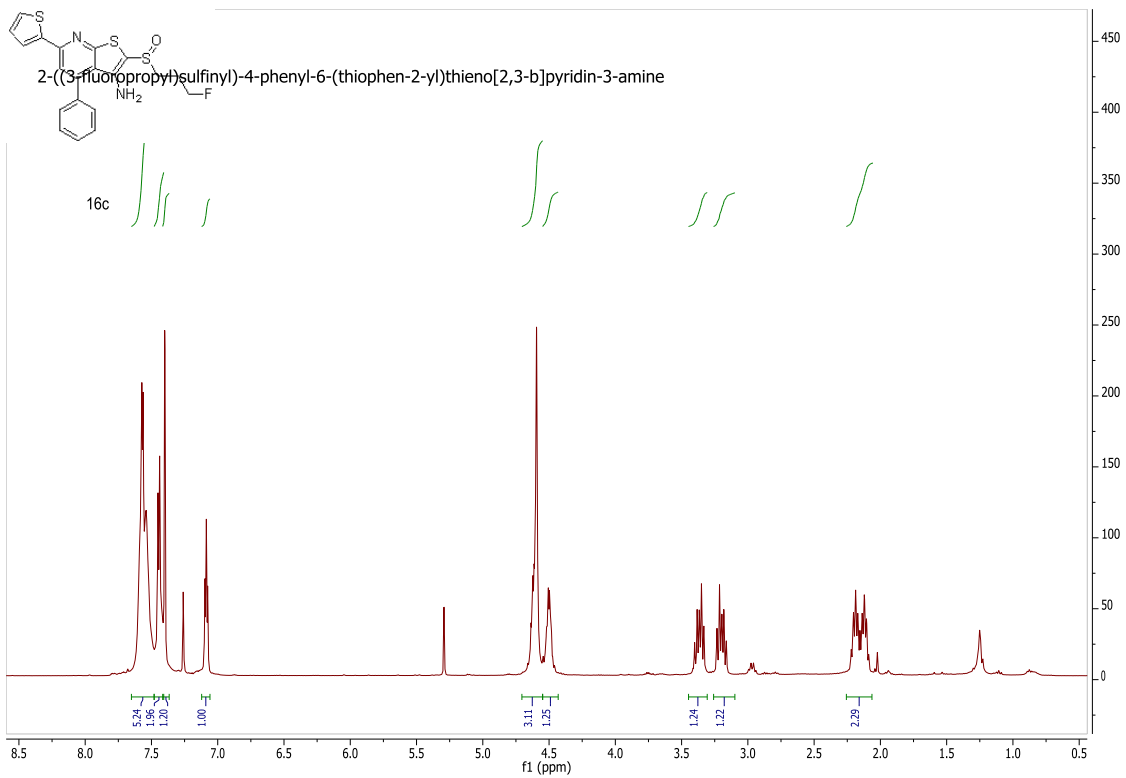


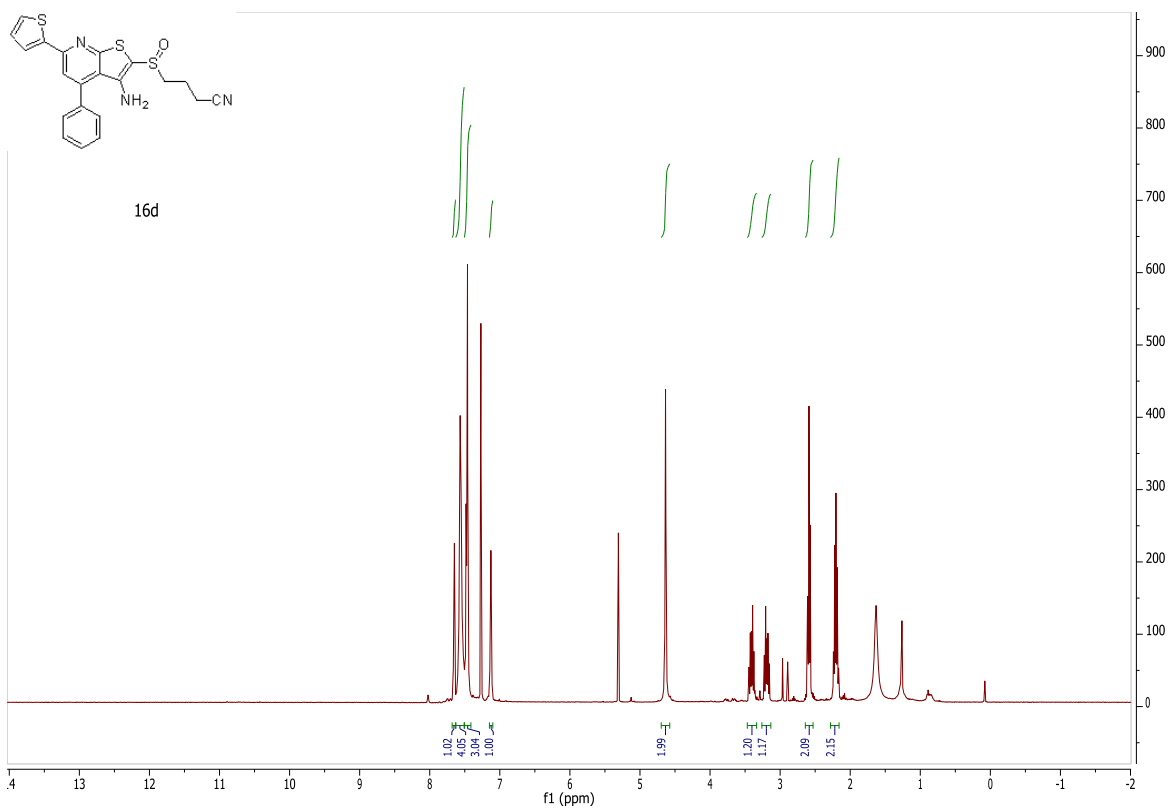
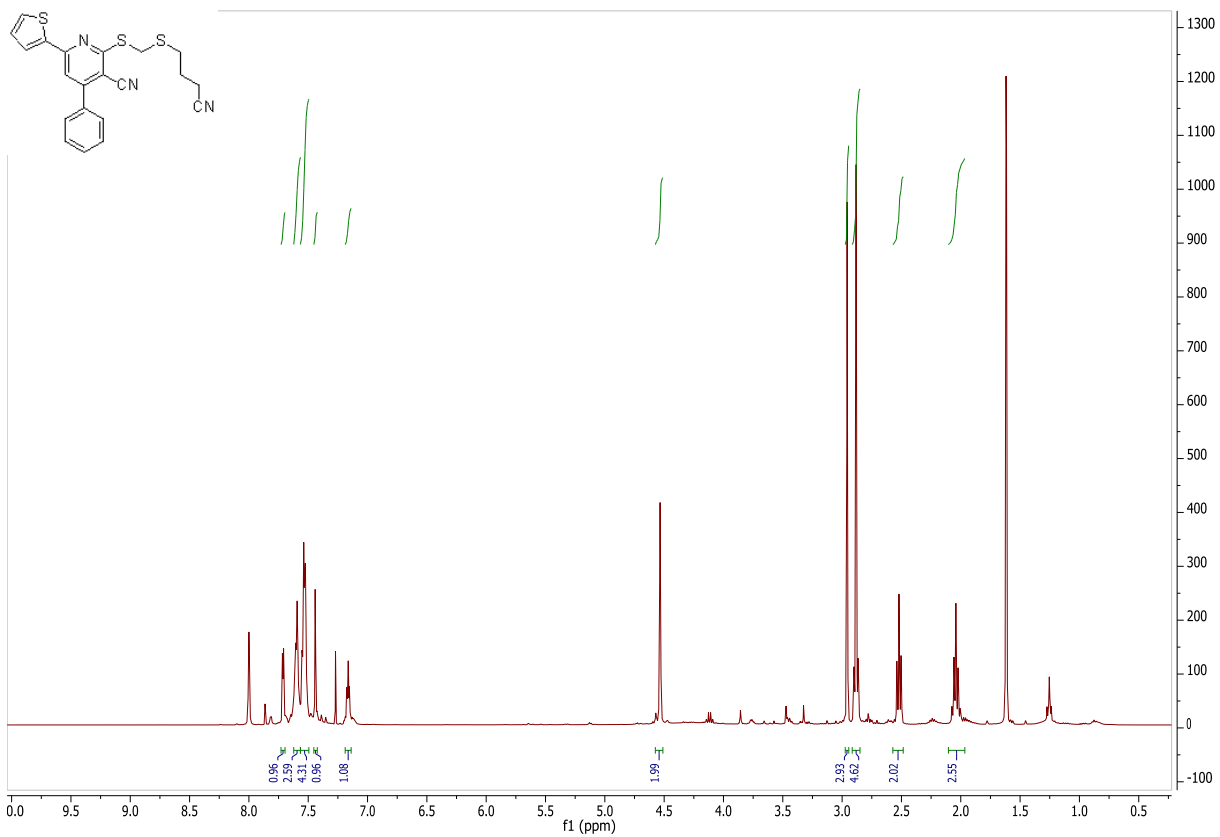


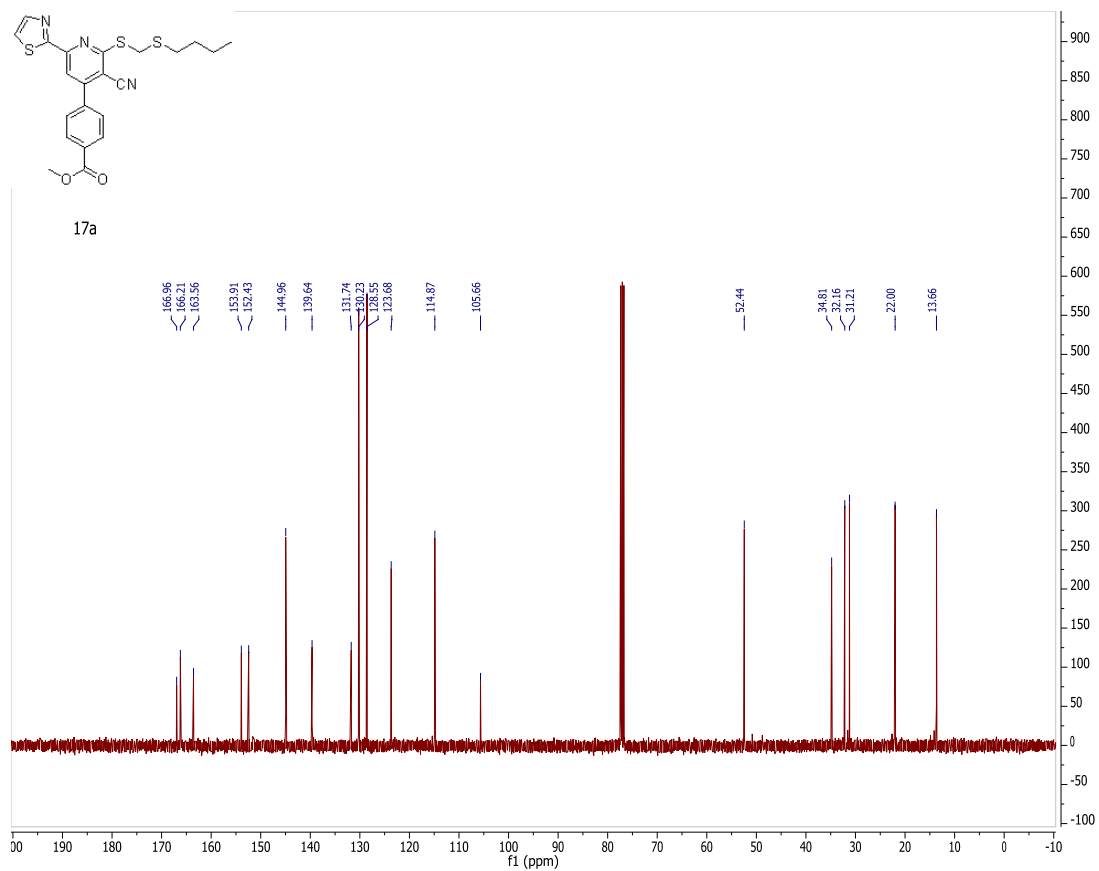
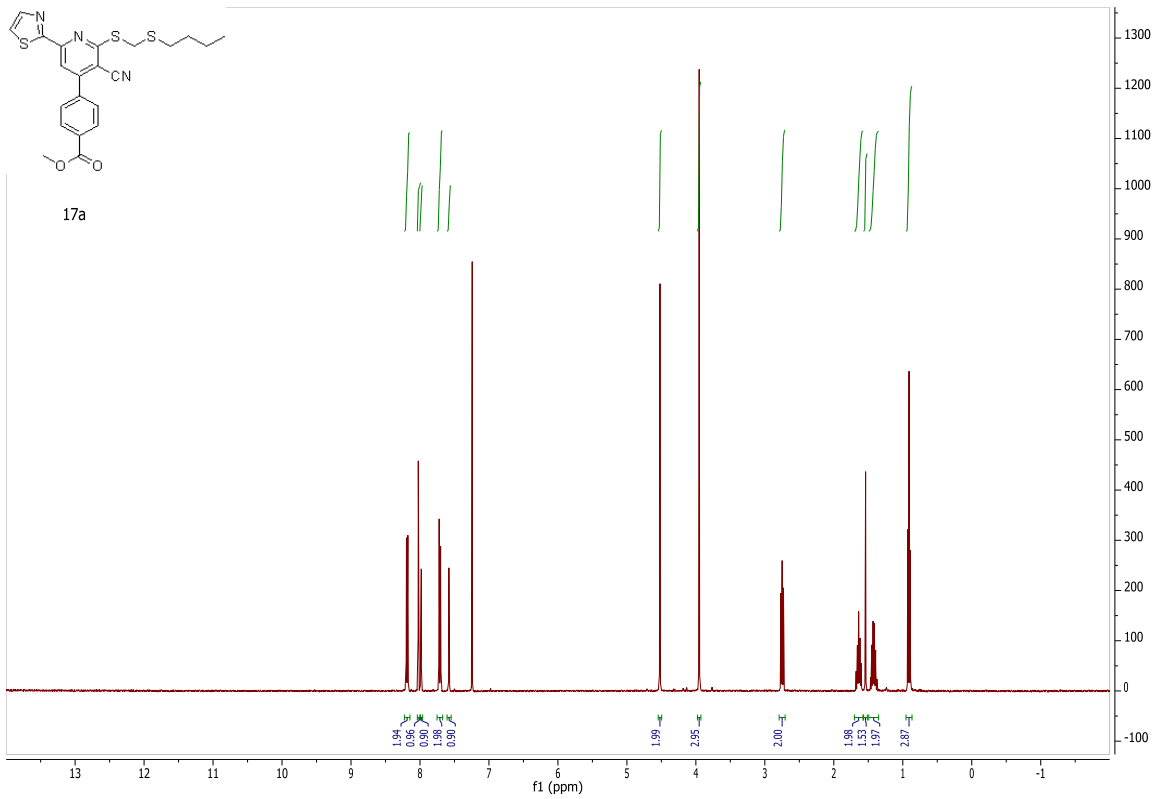


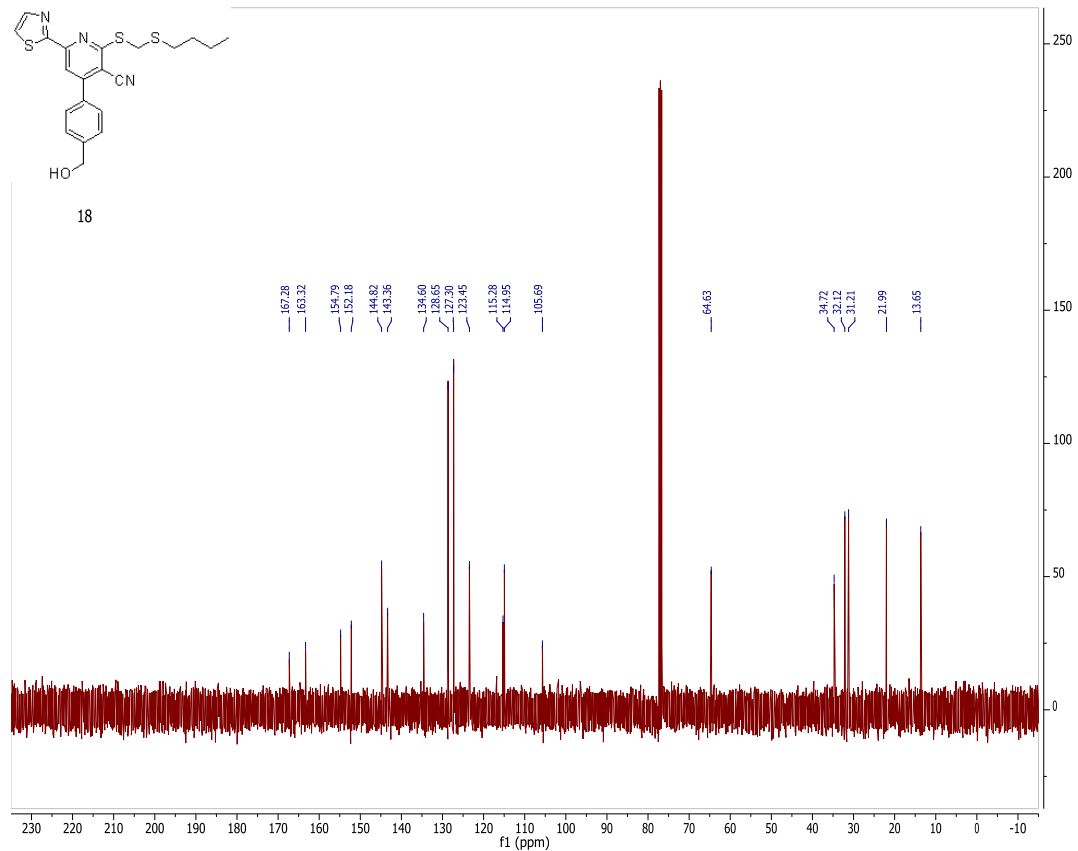
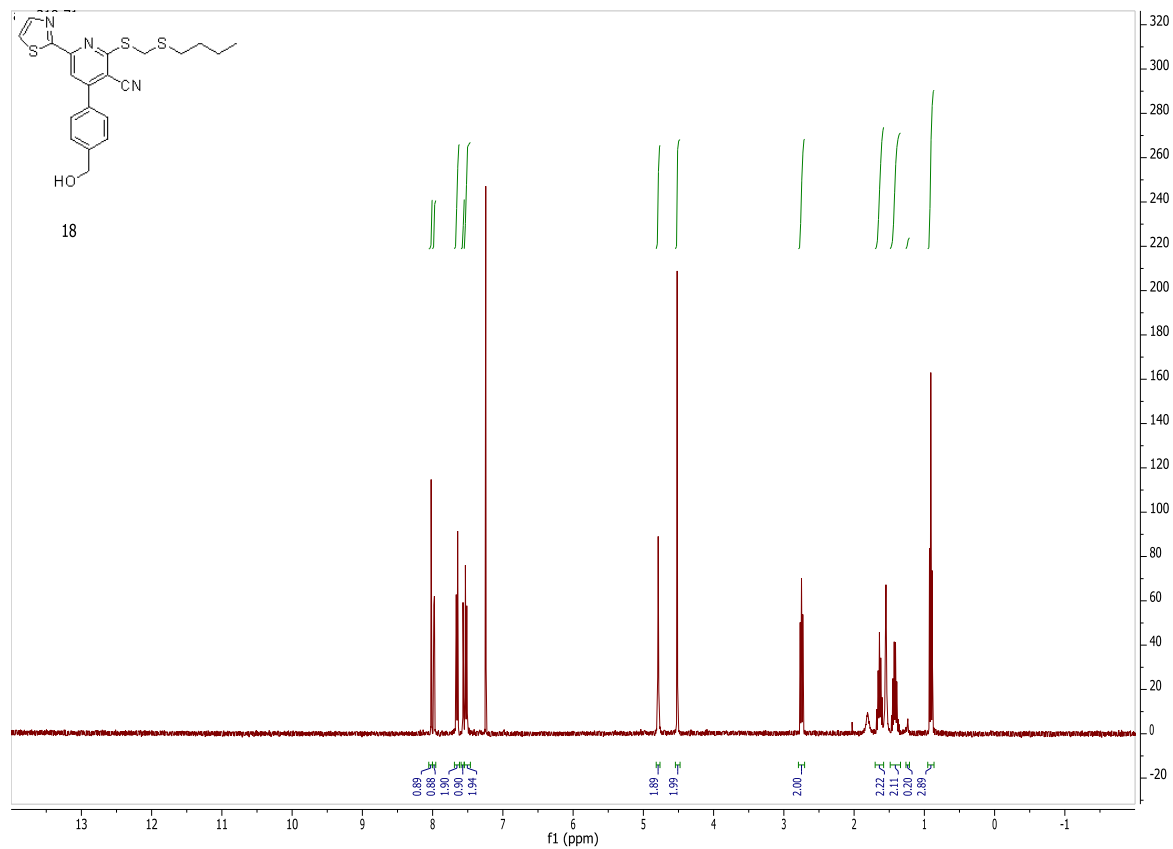


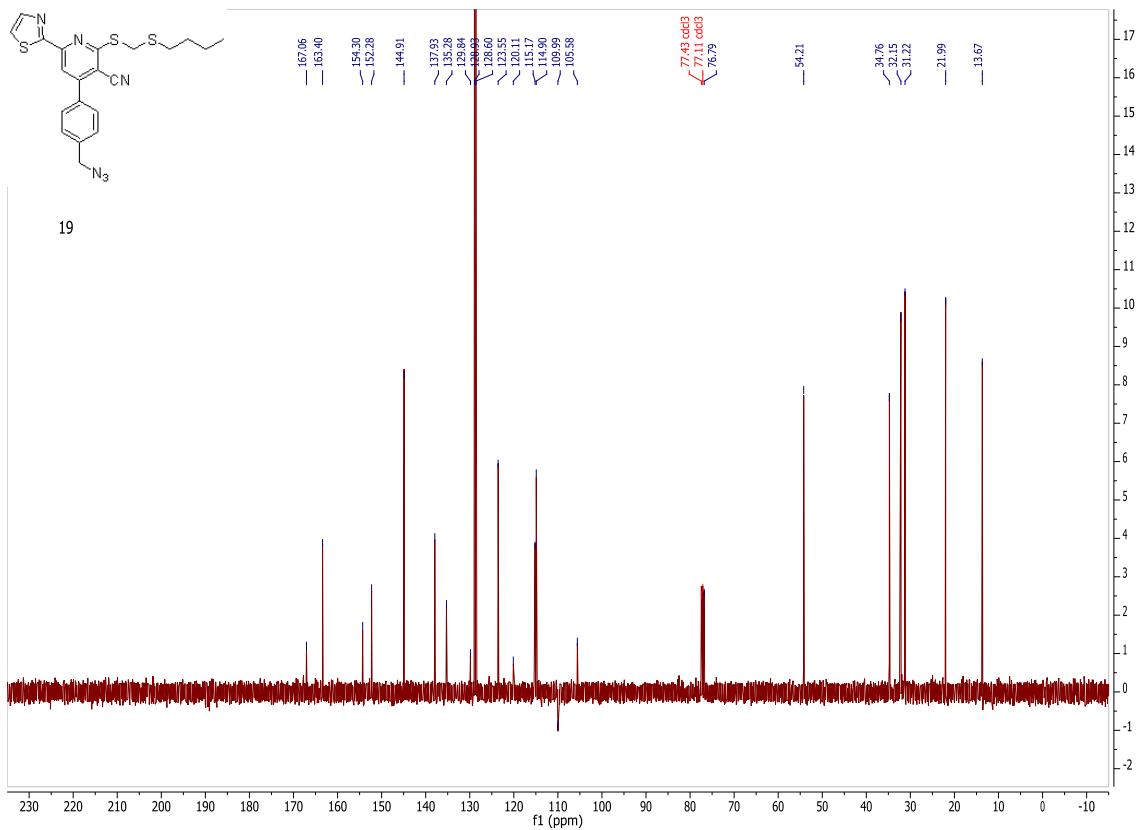
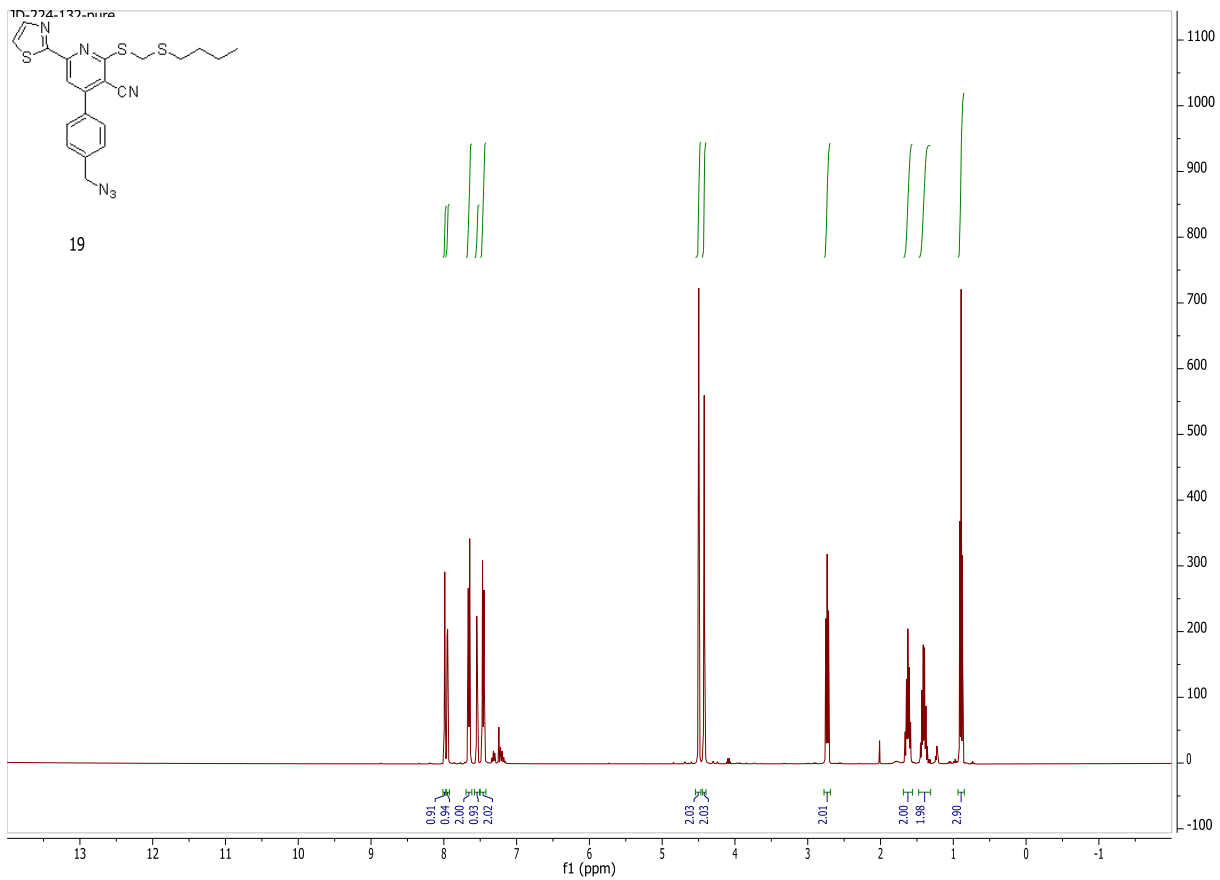


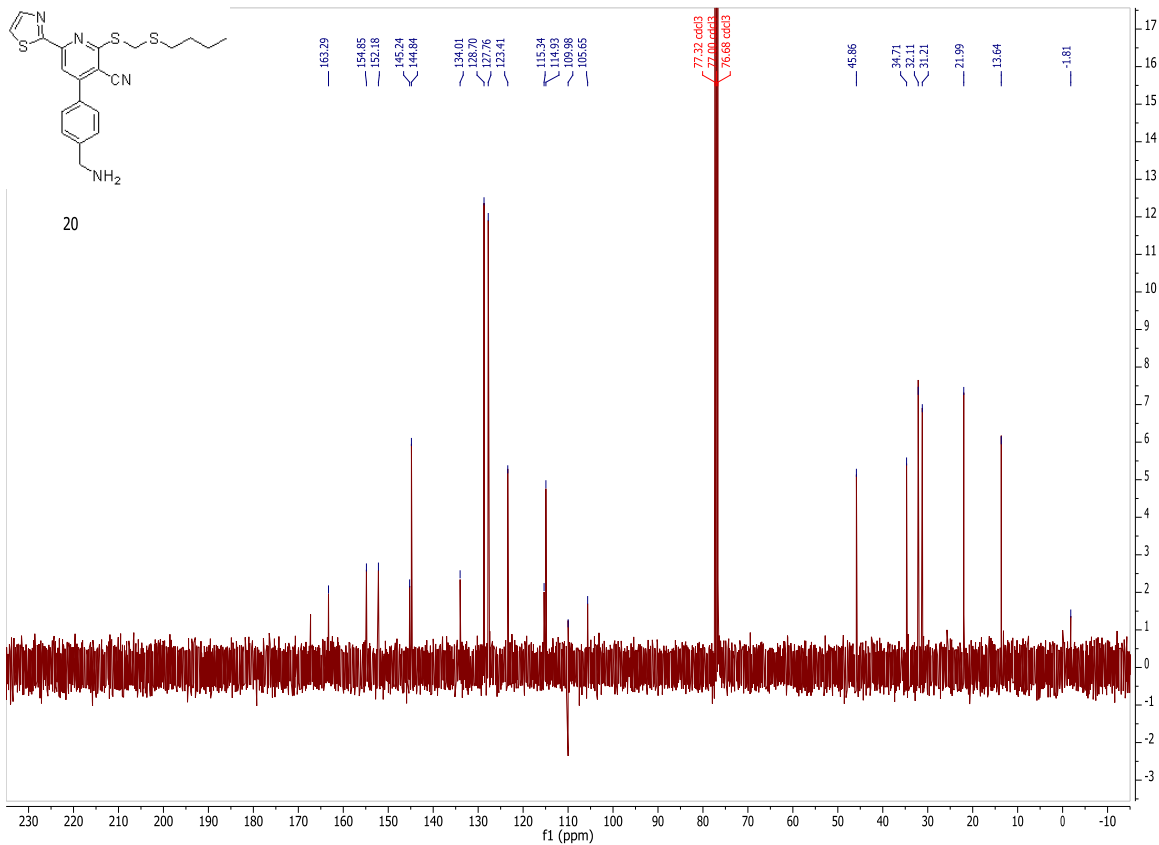
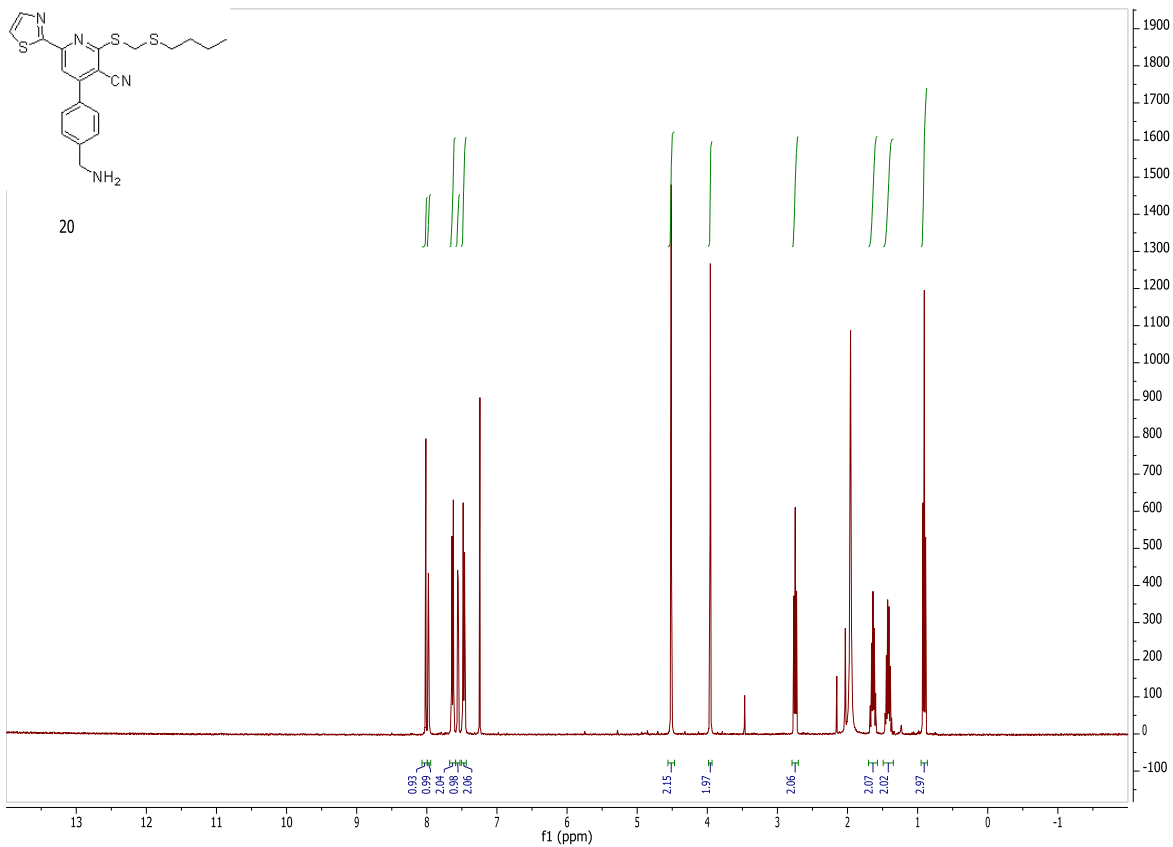


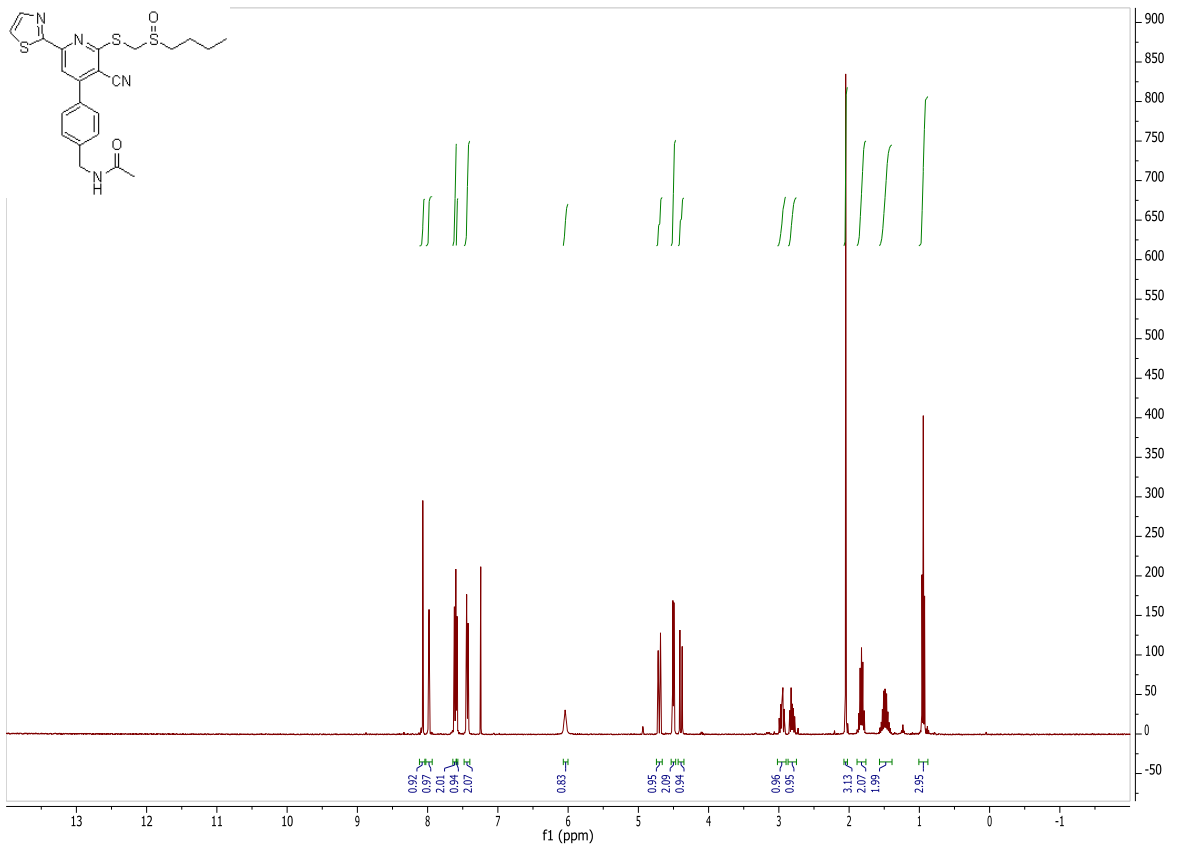
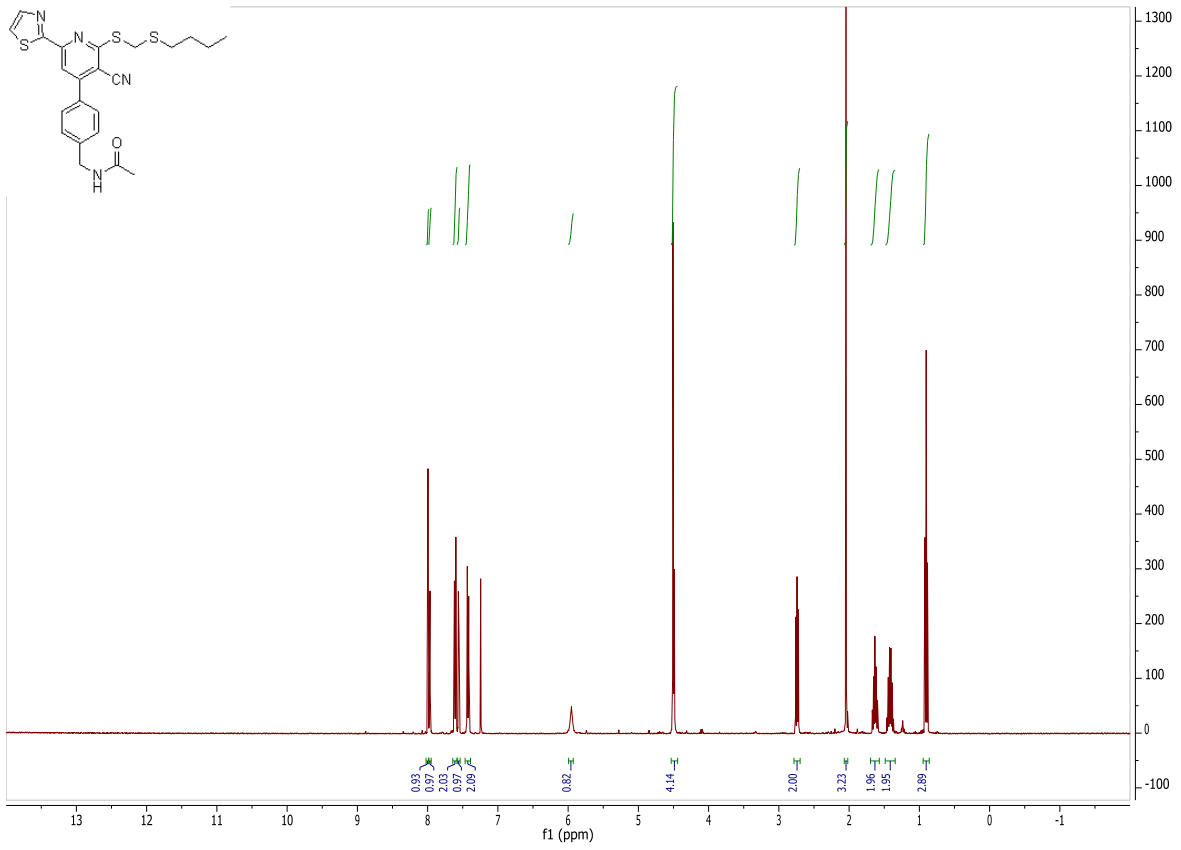




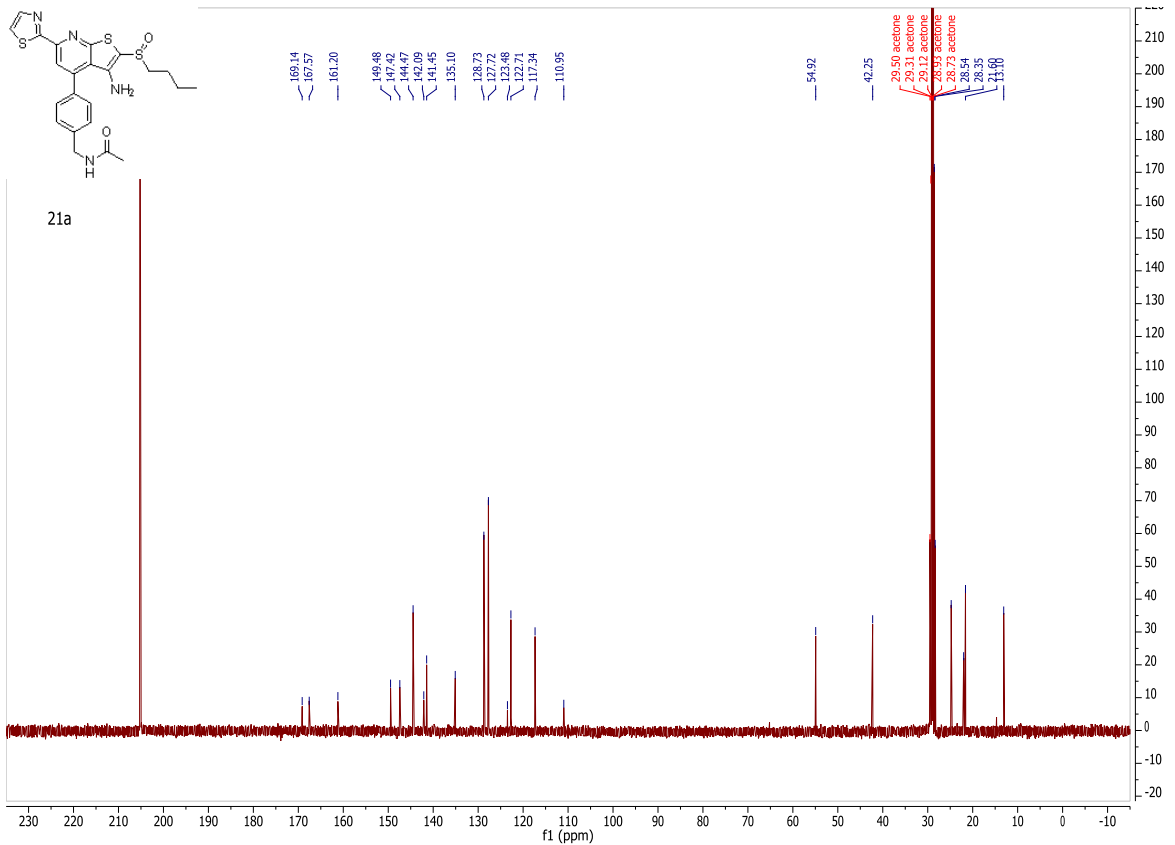
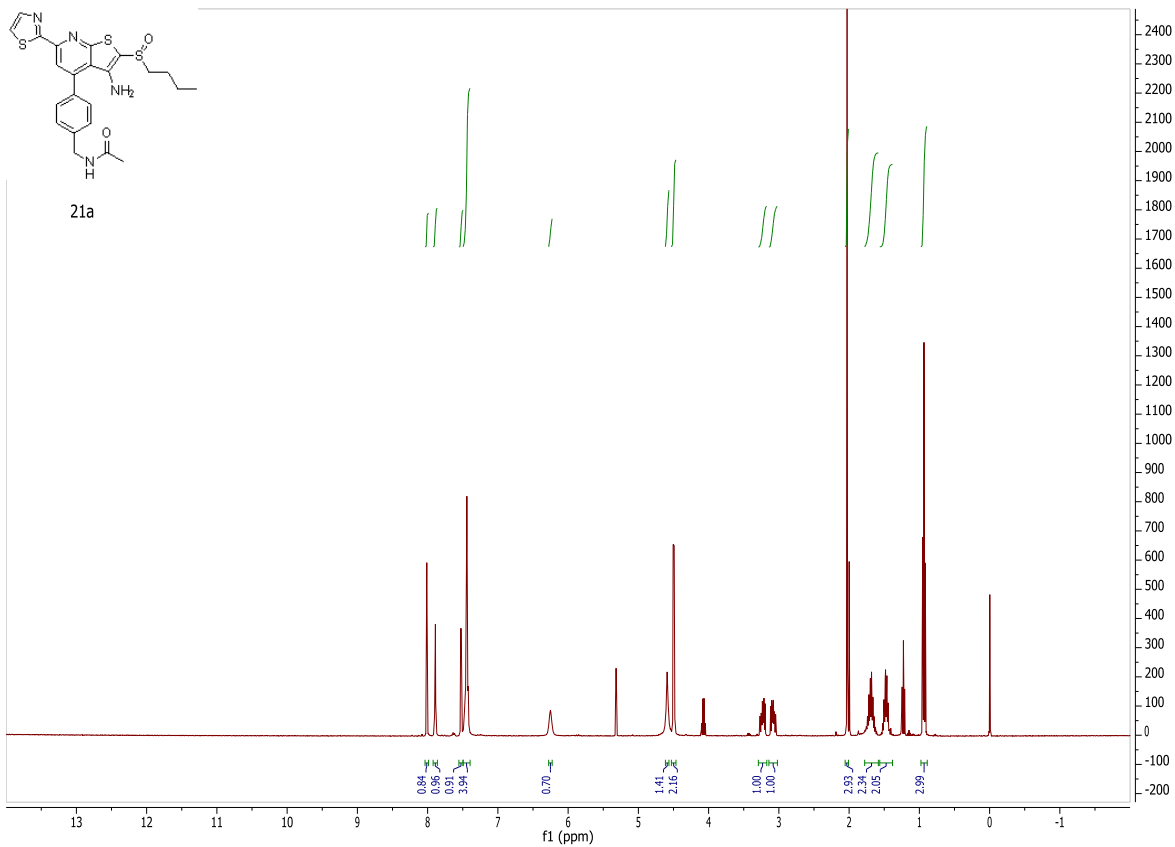


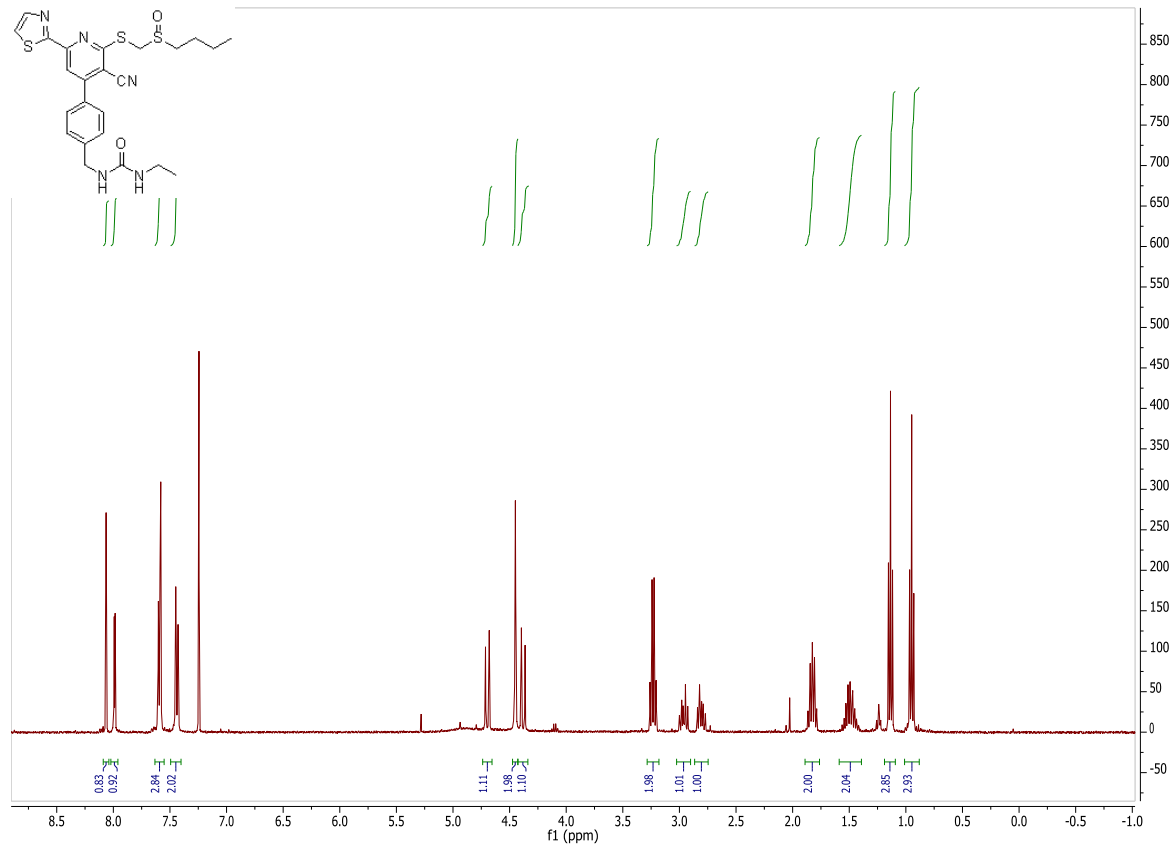
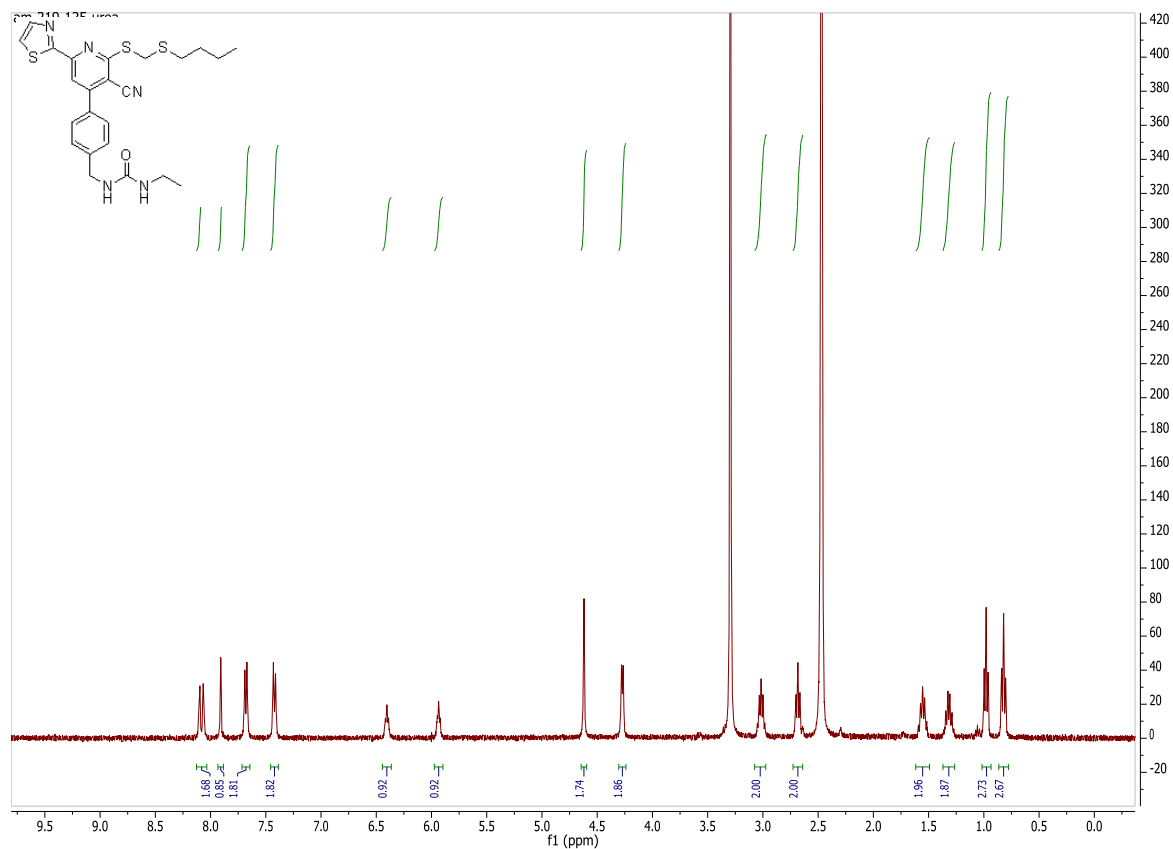


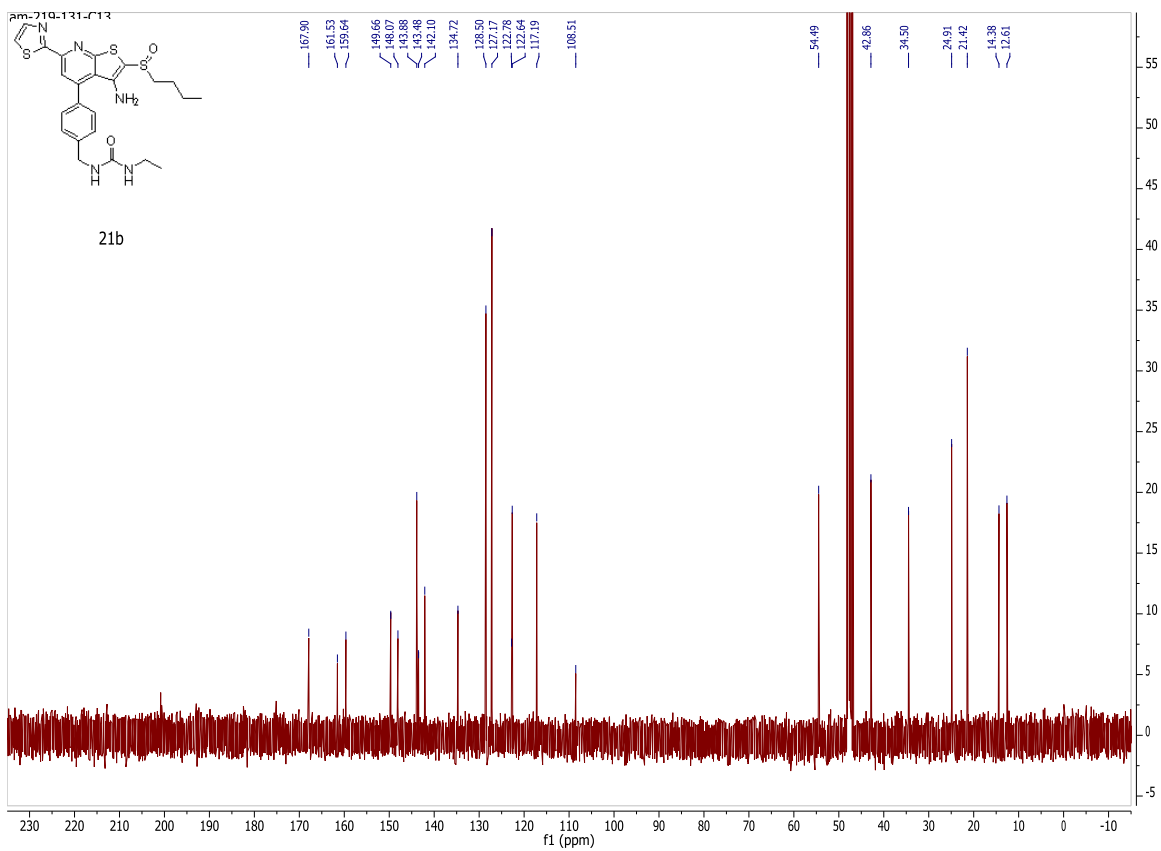
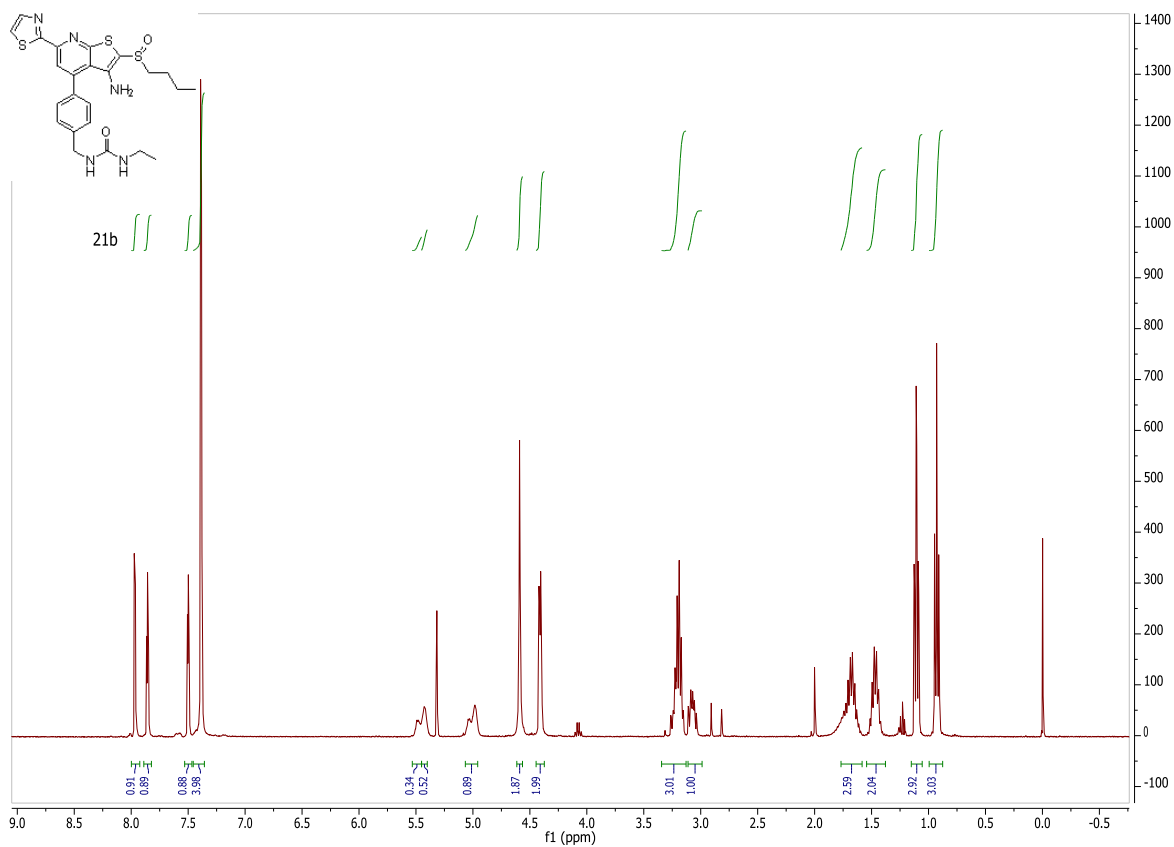












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STANDARD FLUORINE PARAMETERS

